Leipzig Research Festival for Life Sciences 2014

13th

UNIVERSITÄT LEIPZIG
Medizinische Fakultät

UNIVERSITÄT LEIPZIG
Fakultät für Biowissenschaften, Pharmazie und Psychologie

iccas

IFB Adipositas Erkrankungen

LIFE Leipziger Forschungszentrum für Zivilisationserkrankungen

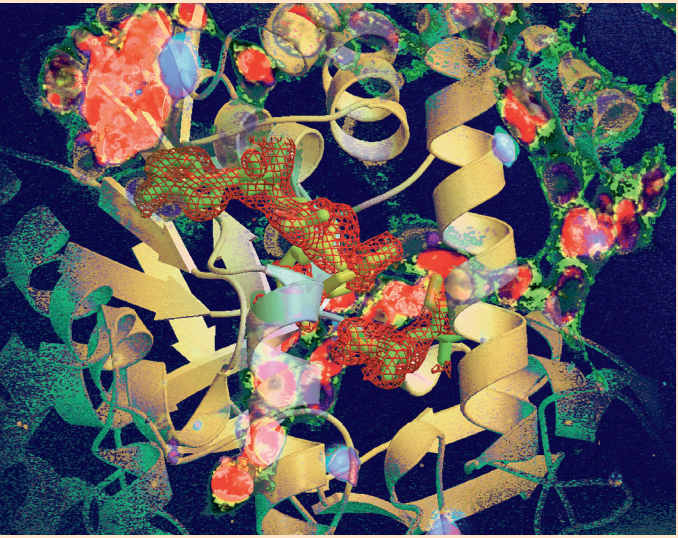
Europa fördert Sachsen. EFRE Europäischer Fonds für regionale Entwicklung

Gefördert aus Mitteln der Europäischen Union

SACHSEN

TRM Leipzig

UNIVERSITÄT LEIPZIG



ABSTRACT BOOK

18. Dezember 2014

Ort: Max-Bürger-Forschungszentrum

BIO CITY LEIPZIG
Biotechnologisch-Biomedizinisches Zentrum

SFB 1052
Obesity Mechanisms

RESEARCH ACADEMY LEIPZIG

J. Thiery, A. G. Beck-Sickinger, T. Arendt (Hrsg.)

J. Thiery, A. G. Beck-Sickinger, T. Arendt (Hrsg.)

13th Leipzig Research Festival for Life Sciences

18. Dezember 2014

Veranstalter:

Medizinische Fakultät der Universität Leipzig

Fakultät für Biowissenschaften, Pharmazie und Psychologie der Universität Leipzig

Impressum:

Konzeption / Organisation:	Prof. Dr. J. Thiery Prof. Dr. A. G. Beck-Sickinger Prof. Dr. T. Arendt
Lektorat:	I. Malerba, Dr. U. Wittig
Layout / Satz:	K. Plath
Titelbild:	N. Sträter und A. G. Beck-Sickinger
Auflage:	400 Exemplare
ISBN:	978-3-9817033-0-6

Inhaltsverzeichnis

Ort der Veranstaltung: Foyer Max-Bürger-Forschungszentrum
Johannisallee 30 · 04103 Leipzig

Organisation:

Prof. Dr. J. Thiery, I. Malerba
Institut für Laboratoriumsmedizin,
Klinische Chemie und Molekulare Diagnostik
Universitätsklinikum Leipzig AöR
Liebigstraße 27 · 04103 Leipzig
Telefon: (03 41) 97 224 93
Fax: (03 41) 97 223 79
E-Mail: thiery@medizin.uni-leipzig.de

Prof. Dr. A.G. Beck-Sickinger
Institut für Biochemie
Fakultät für Biowissenschaften, Pharmazie und Psychologie
Universität Leipzig
Talstraße 33 · 04103 Leipzig
Telefon: (03 41) 97 369 00
Fax: (03 41) 97 369 98
E-Mail: beck-sickinger@uni-leipzig.de

Prof. Dr. T. Arendt
Paul-Flechsig-Institut für Hirnfoschung
Universität Leipzig
Jahnallee 59 · 04109 Leipzig
Telefon: (03 41) 97 257 20
Fax: (03 41) 97 257 29
E-Mail: aret@medizin.uni-leipzig.de

Für die Unterstützung der Veranstaltung danken wir:

Fakultät für Biowissenschaften, Pharmazie und Psychologie der Universität Leipzig

Research Academy Leipzig

Medizinische Fakultät der Universität Leipzig

Translational Centre for Regenerative Medicine (TRM)

IFB Adiposity Diseases Leipzig

LIFE – Leipziger Forschungszentrum für Zivilisationserkrankungen*

ICCAS – Innovation Center Computer Assisted Surgery

BBZ – Biotechnologisch-Biomedizinisches Zentrum

SFB 1052 – Mechanismen der Adipositas

* LIFE wird finanziert aus Mitteln der Europäischen Union durch den Europäischen Fonds für regionale Entwicklung (EFRE) und aus Mitteln des Freistaates Sachsen im Rahmen der Landesexzellenzinitiative.

Vorwort

Liebe Kolleginnen und Kollegen, liebe Gäste,
wir begrüßen Sie sehr herzlich zu unserem *13. Leipziger Research Festival for Life Sciences* der Universität Leipzig. Die jährliche wissenschaftliche Leistungsschau gibt allen jungen »Life Science« Wissenschaftlern und Ärzten aus der Universitätsregion die Möglichkeit, ihre neuesten Forschungsergebnisse in einer öffentlichen »Wissenschaftswerkstatt« zu präsentieren. Die hohe Zahl von Abstrakteinsendungen unterstreicht die Attraktivität dieses weit über die Fächergrenzen reichenden wissenschaftlichen Kommunikationsforums. Der vorliegende Abstract-Band soll auch der interessierten Öffentlichkeit, der Politik und Industrieunternehmen dienen, die facettenreiche Aktivität und die Erfolge der Leipziger Wissenschaftslandschaft gerade im Bereich »Life Science« und der gesamten Medizin kennen zu lernen. Der Band ist mit Stichpunkten zur Forschungskompetenz und email-Verweisen zugleich ein wissenschaftliches »who is who«, um schnelle Problemlösungen durch Zusammenarbeit »next door« zu erleichtern.
Mit besonderer Wertschätzung des wissenschaftlichen Nachwuchses werden auch in diesem Jahr die besten Posterpräsentationen mit den renommierten Forschungspreisen des *Research Festivals Leipzig* ausgezeichnet.
Nach den Erfolgen und dem großen Interesse in den letzten Jahren werden wir auch in diesem Jahr den kompetitiv eingeworbenen Forschungsverbünden in den Lebenswissenschaften an der Universität Leipzig einen besonderen Raum geben, um Vorhaben und Ergebnisse im Rahmen der Landesexzellenzinitiative und Leipziger Forschungszentrums für Zivilisationserkrankungen (LIFE), des Integrierten Forschungs- und Behandlungszentrums (IFB AdipositasErkrankungen), des Translationszentrums für Regenerative Medizin (TRM) und des Kompetenzzentrums für computerassistierte Chirurgie (ICCAS) zu präsentieren und zur Diskussion zu stellen.
Wir hoffen, dass unser *Research Festival* auch in seinem 13. Jahr seinen doppelten Zweck, die Präsentation eigener innovativer Forschungsergebnisse und Kontaktforum mit jungen und erfahrenen Wissenschaftlern und Ärzten über Fach- und Hierarchiegrenzen hinaus, erfüllen wird. Das Research Festival begleitet und stärkt somit die zukunftsweisende Entwicklung des biomedizinischen und biotechnologischen Standorts der Universität Leipzig.
Für die engagierte Mitarbeit, ohne die dieses Festival nicht zustande gekommen wäre, danken wir allen Unterstützern sehr.

Prof. Dr. Annette G. Beck-Sickinger
Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie,

Prof. Dr. Joachim Thiery
Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik,

Prof. Dr. Thomas Arendt
Paul-Flechsig-Institut für Hirnforschung,

Prof. Dr. Andrea Robitzki
Direktorin des Biotechnologisch-biomedizinischen Zentrums (BBZ), Universität Leipzig

Prof. Dr. Erich Schröger
Dekan der Fakultät für Biowissenschaften, Pharmazie und Psychologie

Prof. Dr. Markus Löffler,
Prof. Dr. Joachim Thiery
Sprecher des Leipziger Forschungszentrums für Zivilisationserkrankungen (LIFE)

Prof. Dr. Frank Emmrich
Sprecher des Translationszentrums für Regenerative Medizin (TRM)

Prof. Dr. Michael Stumvoll
Dekan der Medizinischen Fakultät, Sprecher des Integrierten Forschungs- und Behandlungszentrums (IFB) AdipositasErkrankungen,

Prof. Dr. Jürgen Meixensberger
Sprecher des Kompetenzzentrums für computerassistierte Chirurgie (ICCAS)

Prof. Dr. Matthias Blüher
Sprecher des SFB 1052

POSTER 1

Nutrition-dependent changes of adipose tissue compositions monitored by NMR, MS and chromatographic methods

Biophysics and Bioanalytics

Popkova Y[1], Meusel A[1], Breitfeld J[2], Schleinitz D[2], Hirrlinger J[3,4], Dannenberger D[5], Kovacs P[2], Schiller J[1]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig
2 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
3 Carl-Ludwig-Institut für Physiologie, Universität Leipzig
4 Department of Neurogenetics, Max-Planck-Institut for Experimental Medicine, Göttingen
5 Leibniz Institute for Farm Animal Biology, Dummerstorf

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Many diseases are assumed to be caused by changes at the gene-level and, thus, many knockout mouse models were established. Consequently, effects of the life style such as the nutrition are often neglected. We will show that the nutrition has a tremendous impact on the lipid composition of different mouse fatty tissues. Mice were subjected to different (high fat (HF) and standard diet (SD)) diets and fatty tissues (brown, visceral and subcutaneous fat) were isolated. Subsequent to lipid extraction, the organic extracts were analyzed by mass spectrometry (MALDI and ESI), high-resolution 1D and 2D NMR spectroscopy as well as high-performance TLC.

Significant nutrition-dependent changes could be monitored when the total extracts were analyzed: HF led to (a) a decreased double bond content and (b) a decreased fatty acyl chain length of the triacylglycerols (TAG) which are the main constituents of the fatty tissues. Surprisingly, there was (c) also a more pronounced content of lipid oxidation products (by cleavage of the double bonds) when HF diet was supplied. Despite the low contribution of phospholipids, similar changes were also seen regarding the phosphatidylcholine (PC) fraction. However these changes were less pronounced in comparison to changes of the TAG composition.

➜ **Popkova, Yulia**
email: yulia.popkova@medizin.uni-leipzig.de

POSTER 2

Versagensverhalten humaner Muskelproben im Rahmen tumorendoprothetischer Versorgung des proximalen Femurs

Biophysics and Bioanalytics

Schleifenbaum S[1], Möbius R[2], Schmidt M[1], Hammer N[2], Wolfskämpf T[2], Grunert R[1], Prietzel T[1]

1 Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Universität Leipzig
2 Institut für Anatomie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Einleitung: Bei tumororthopädischen Eingriffen müssen oftmals umfangreiche Knochen- und Gelenkanteile reseziert und durch Tumorendoprothesen ersetzt werden. Um postoperativ eine adäquate Gelenkfunktion zu gewährleisten, ist die Fixierung des zuvor abgelösten Weichteilgewebes an das Implantat von großer Bedeutung. Im Rahmen proximaler Femurversorgungen kommen feinmaschige Anbindungssysteme (z. B. Trevira®) zum Einsatz.
Ziel: Ziel ist es erstmalig das mechanische Versagensverhalten einer künstlichen Weichteilanbindung zu untersuchen.
Methode: Es wurden 4 Femura (post mortem) mit frei präparierten Muskelanteilen des Quadriceps verwendet. Die Proben dienten für folgende Versuchsreihen:
V1: Muskel (parallel) vs. Muskel (senkrecht)
V2: Muskel-Knochen vs. Muskel-Anbindungsschlauch
Zur Ermittlung des Versagensverhaltens wurden uniaxialen Zugversuche unter Zuhilfenahme eines 3D-Bildkorrelationssystem durchgeführt.
Ergebnis: Innerhalb der Versuchsreihe V1 konnten die parallel zum Faserverlauf belasteten Proben eine signifikant höhere Reisskraft ($p < 0{,}001$) von 47,6N±11,5N gegenüber den senkrecht orientierten Proben 14,8N±4,1N aufnehmen. Bei V2 ergab sich eine Ausrisskraft von 26,7N±8,8N für die native Anbindung und 18,1N±9,9N für die künstliche Anbindungsvariante ($p = 0{,}026$). Ein Versagen unter Last wurde ausschließlich innerhalb der Muskelfasern beobachtet.
Schlussfolgerung: Die Ergebnisse deuten darauf hin, dass mit der Entfernung der natürlichen Anbindungsstellen auch die Verbindungsfestigkeit sinkt. Da das Versagen unter Last innerhalb der Muskelfasern lag, besteht die Vermutung, dass die Naht die Anbindung lokal verfestigt.

➜ **Schleifenbaum, Stefan**
email: stefan.schleifenbaum@medizin.uni-leipzig.de

POSTER 3

Matrix effects by substance overload in GC-MS analysis of biologically relevant compounds

Biophysics and Bioanalytics

Marcillo A[1], Davis C[1], Deshmukh S[1], Hutschenreuther A[1], Birkemeyer C[1]

1 Institut für Analytische Chemie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Recent trends in analyses of multi-component mixtures of biological origin anticipate analyzing the sample keeping its preparation to a minimum. However, when using these "omic" techniques the analytical chemist often faces the problem that the present compounds considerably vary with chemical nature and concentrations ranging from overload of the analytical method till presence only in traces. In GC-MS, overloading of individual compounds generated so-called matrix effects; those are defined by the presence of matrix compounds in the sample modifying the response factor of the target compound, i. e. the analyte.

Accurate quantitation of substances is difficult in the presence of matrix effects. Thus, highly abundant phosphate caused signal suppression of sugars and organic acids when analyzed by GC-MS. We show that similar retention was not responsible for this effect. Therefore, the contribution of the chemical nature of the compound to the type of matrix effect that will be exerted by overloading this compound has been explored. For this, sets of substances with similar chemical functionalities, namely phosphate, organic acids, amino acids and sugars, were also investigated in this project whether to be subject to signal suppression or causing matrix effects themselves. Though a clear conclusion relating the appearance of signal suppression effects to the chemical nature of the compound was not supported by the obtained results, we discuss the observed effects and extract trends for the behaviour upon GC-MS analysis within these groups.

→ **Birkemeyer, Claudia**
email: birkemeyer@chemie.uni-leipzig.de

POSTER 4

ELECTROSPRAY IONIZATION MASS SPECTROMETRIC STUDIES OF IRON AND ZINC COMPLEXES WITH p-BENZOQUINONES/HYDROQUINONES

Biophysics and Bioanalytics

Mitreska N[1], Oehme R[2], Birkemeyer C[2]

1 Institute of Chemistry, Faculty of Natural Sciences and Mathematics
2 Institute of Analytical Chemistry, Faculty of Chemistry and Mineralogy, Leipzig University

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Quinones and their reduced form, hydroquinones, are ubiquitous in nature. Quinones are widely distributed in nature and their basic structure is featuring important classes of compounds like Vitamin K1, various cofactors and coenzymes Q, flavonoids, etc. Next to their irreplaceable role in electron/proton transfer, many of the quinones function as effective radical scavengers and antioxidants, to protect the living cells from oxidative damages.

Electrospray mass spectrometry has been used to study the interaction of Fe(III), Fe(II) and Zn(II) ion in solution with a set of *p*-benzoquinones/hydroquinones: 1,4-dihydroxy-2,6-dimethoxybenzene (DHDMB), 2,6-dimethoxy-1,4-benzoquinone (DMBQ) and 2,3-dimethoxy-5-methyl-*p*-benzoquinone (CoQ_0). The ESI-MS analysis revealed the formation of different complexes between the biologically important metal ions and benzoquinones and hydroquinones, respectively. The mass spectra exhibited five main complexes, which proposed structures have been confirmed by isotopic patterns and accurate MS.

It was established that the metal binding sites of quinone structures are preferentially at 1-hydroxyl (DHDMB) and carbonyl oxygen (DMBQ and CoQ_0). Moreover, redox reactions were observed not only through the change of the oxidation state of the iron, but also the reduction of the quinone/ oxidation of the hydroquinone by loss/addition of hydrogen. Potential oxidation and reduction processes were discussed within the context of a time series and by comparison between Fe(II) to the behavior of Zn(II).

Keywords: Benzoquinones, hydroquinones, CoQ0, Metal chelation, ESI-MS.

➜ **Mitreska, Nikolina**
email: nin.mitreska@gmail.com

POSTER 5

Local Interactions Leave the General Morphology of Amyloid β Peptides Unchanged but Affect Local Structure and Dynamics

Biophysics and Bioanalytics

Adler J[1], Scheidt H[1], Krüger M[2], Huster D[1]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig
2 Institut für Anatomie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

A series of peptide mutants was studied to understand the influence of local physical interactions on the fibril formation mechanism of amyloid β (Aβ)(1-40). The well-known hydrophobic contact between residues phenylalanine 19 and leucine 34 was modified in six single site mutations at position F19 and two double mutations at F19 and L34. It was examined how flexibility, charges, the replacement of the hydrophobic contact by a salt bridge and the effect of an electrostatic repulsion affect amyloid formation. The influence of these mutations on the fibrillation kinetics, morphology, and the local structure and dynamics was probed using fluorescence, transmission electron microscopy, X-ray diffraction, and solid-state NMR spectroscopy. The overall morphology and cross-β structure of the fibrils remained very robust against all the probed interactions, while the fibrillation kinetics and the local structure and dynamics of the peptide variants were influenced by the introduction of these local fields. Overall, 7 out of the 8 mutated peptides formed fibrils of very similar morphology compared to the wildtype. However, characteristic local structural and dynamical changes indicate that amyloid fibrils show an astonishing ability to respond to local perturbations but overall show a very homogenous mesoscopic organization.

→ **Adler, Juliane**
email: juliane.adler@medizin.uni-leipzig.de

POSTER 6

Measurement of biomolecular interactions between hyaluronic acid and melanoma cells via Soft Colloidal Probes

Biophysics and Bioanalytics

Martin S[1], Rathke T[1], Schmidt S[1], Pompe T[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Cell surface protein receptors dynamically interact with their ligands in order to influence a myriad of biological functions at the molecular level, like recognition events, adhesion, inflammation and enzyme activity. To quantitatively analyze the interactions between surface anchored receptors and biomolecular ligands we adapted a novel screening method to study the receptor CD44 and its native ligand hyaluronic acid. The extracellular matrix component hyaluronic acid is known to influence various cell processes including cancer progression and metastasis.

We aim to reveal molecular interactions with regard to adhesion processes and therein the effects of CD44 presence, external forces, ligand density and multivalency. We applied soft colloidal probes using an atomic force microscope to quantify contact forces of the highly hydrated and flexible probes which were functionalized with hyaluronic acid. Human melanoma cells with presence or absence of CD44 receptor were tested to investigate the molecular binding of hyaluronic acid and CD44 receptors at mechanically flexible interfaces. First results show the feasibility of the concept of quantitatively measuring hyaluronic acid / CD44 interactions.

→ **Martin, Steve**
email: steve.martin@uni-leipzig.de

POSTER 7

Experimenteller Vergleich der Biegesteifigkeit eines menschlichen Hüftbeins (os coxae) mit einem biomechanischen Testknochen der Fa. Sawbones

Biophysics and Bioanalytics

Voigt C[1], Redmann M[2], Jakob P[2], Rieger B[2], Klöhn C[2]

1 Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Universität Leipzig
2 Fakultät Maschinenbau und Energietechnik, HTWK Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Ziel der Studie war es, die Biegesteifigkeit eines biomechanischen Testknochens der Firma Sawbones zu messen und mit einem etwa gleich großen anatomischen Präparat eines menschlichen Hüftbeins (PEG fixiert) zu vergleichen, um zu untersuchen, inwiefern der Testknochen dem realen menschlichen Knochen entspricht.
In Anlehnung an die Literatur wurde ein Versuchsaufbau mit einer speziellen Lagerung des Knochens entwickelt, die eine Belastung analog einem Drei-Punkt-Biegeversuch ermöglicht. Aus der Literatur ist bekannt, dass beim Stolpern Maximalbelastungen vom bis zu 12-fachen des Körpergewichtes auftreten können. Als Maximalbelastung wurde eine Prüflast von 5kN angestrebt und an einer Materialprüfmaschine Zwick Z050 mittels einer Durchbiegung von 2mm als linear rampenförmige Weg-gesteuerte Druckbelastung realisiert. Die Belastungsrate betrug 5mm/min.
Gemessen wurde die Durchbiegung in Abhängigkeit von der Prüfkraft und die horizontale Auslenkung des Knochens auf der Seite des Loslagers. Im zweiten Belastungsdurchlauf trat am anatomischen Knochenpräparat unter Volllast ein Bruch auf.
Der Vergleich ergab eine sehr gute Übereinstimmung der Biegesteifigkeit des biomechanischen Testknochens mit dem anatomischen Präparat. In einer anschließenden Computersimulation konnte die Lokalität des Bruches am anatomischen Knochenpräparat als Stelle der höchsten Zugbeanspruchung bestätigt werden. Die sehr gute Übereinstimmung zwischen biomechanischen Testknochen und PEG-Präparat zeigt, dass der Testknochen der Firma Sawbones das strukturelastische Verhalten des menschlichen Beckenknochens sehr gut abbildet.

→ **Voigt, Christian**
email: christian.voigt@medizin.uni-leipzig.de

POSTER 8

Quantification of eight apoproteins in murine plasma by LC-MS/MS

Biophysics and Bioanalytics

Wagner R[1], Dittrich J[1], Thiery J[1], Burkhardt R[1], Ceglarek U[1]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Plasma concentrations of ApoB100 and ApoA-I are used for risk assessment of cardiovascular disease (CVD). The utility of other apoproteins as clinical biomarkers is under investigation. Our laboratory has previously described a LC-MS/MS method to measure seven apoproteins in human plasma. The aim of the present study was to establish a method for the simultaneous quantification of eight apoproteins in murine plasma via proteotypic peptides.

Methods and Results: We identified unique peptide sequences for Apo A-I, A-II, A-IV, B48, B100, C-I, E and J using the NCBI Basic Local Alignment Search Tool (BLAST) and database. For sample preparation, mouse plasma (3 µL) was denatured, reduced, alkylated and tryptically digested. Trypsin incubation times ranged from 30 min (A-I, A-II, A-IV, B100, J) to 16 h (E, B48) to obtain a complete digestion. Method linearity was found between 0.07 and 240 µmol/L. Within- and between-day precisions (n=10) ranged from 2.06% to 15.9% and 3.75% to 19.3%, respectively, with the exception of ApoB48. A recovery rate of 107% was found for Apo A-I in spiked plasma. In a first analysis of apoprotein distributions in C57-Bl6 wild type mice and hyperlipidemic Apo E knockout mice, apoprotein plasma concentrations ranged from 0.29 µmol/L (Apo B100) to 60.6 µmol/L (Apo A-II).

Conclusion: We developed a novel LC-MS/MS method for the simultaneous measurement of eight apoproteins from 3 µL of murine plasma. This allows us a comprehensive characterization of murine apoprotein levels using normo- and hyperlipidemic strains under different nutritional conditions.

→ **Wagner, Richard**
email: richard.wagner@medizin.uni-leipzig.de

POSTER 9

Cell response to lateral constraints

Biophysics and Bioanalytics

Müller A[1], Pompe T[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Living cells rely on a multitude of exogenous signals for decision-making. These signals include, but are not limited to, mechanical and (bio-) chemical cues. One trigger for cellular fate decisions that is frequently overlooked is geometry which obviously plays a role in the organization of compartmentalized, multicellular, 2D and 3D organisms.

Soft hydrogel matrices micropatterned with adhesion ligands along with biochemical inhibition of acto-myosin machinery are used to test cellular behavior and its modulation in response to geometrical confinement. Specifically, immunofluorescence studies and cell traction force measurements are used to characterize changes in cell morphology and cell behavior. A bimodal organization of the actin cytoskeleton depending on the degree of lateral confinement can be observed, namely a change in the average spacing between actin stress fibers. This behavior is persistent for human umbilical vein endothelial cells on substrates with different stiffness and under the influence of biochemical inhibitors targeting mechanotransduction. Furthermore, the same behavior can be found in human dermal fibroblasts, implying that geometry can act as a universal regulator for cell behavior.

→ **Müller, Andreas**
email: andreas.mueller@uni-leipzig.de

POSTER 10

Early cell adhesion on hydrogels with graded stiffness and ligand affinity

Biophysics and Bioanalytics

Müller C[1], Pompe T[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Cell signaling in response to mechanical cues – mechanotransduction – is known as one control mechanism for several basic cell functions, like proliferation, differentiation and cell death. For a better understanding of mechanotransduction, we investigated early cell adhesion on hydrogels with an independent variation of substrate stiffness and the affinity of adhesion ligands to the hydrogel surface.

Thin film coatings of maleic acid copolymers on top of polyacrylamide hydrogel layers were fabricated to tune the affinity of fibronectin to the hydrogel surface via a variation of the fraction of polar groups on the surface. The stiffness of the hydrogel was modulated between 2.5 kPa and 9 kPa. Human umbilical vein endothelial cells were monitored during the first two hours of cell adhesion by time-resolved cell traction force microscopy to determine the cell traction stress.

Three different regimes of traction force generation were found. In the first regime (R0) cells spread fast, but traction forces were negligibly small. In the second regime (R1) spreading slows down and traction forces increased until they saturated in the last regime (R2). The force curve characteristics were substrate-dependent.

Averaged force values in R2 and the slope in R1 increased in between 2.5 kPa and 5 kPa. For the stiffer substrate (9 kPa) the increase in the saturation force is small. For the two hydrogel coatings an offset in the averaged forces on top of the stiffness dependence could be observed. The results can be interpreted as a superposition of conservative and dissipative forces.

➜ **Müller, Christina**
email: christina.mueller@uni-leipzig.de

POSTER 11

Investigating the binding of glycosaminoglycans to interleukin-10 by NMR spectroscopy

Biophysics and Bioanalytics

Künze G[1], Gehrcke J[2], Pisabarro M[2], Köhling S[3], Rademann J[3], Huster D[1]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig
2 BIOTEC, TU Dresden
3 Institut für Pharmazie, FU Berlin

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The immune response against microbial infections bears the intrinsic risk of an immune-mediated inflammatory damage to the host tissue. The cytokine interleukin (IL)-10 is a key regulator of the immune system, which prevents an overwhelming immune reaction and tissue damage. Glycosaminoglycans (GAGs) are a class of highly sulfated carbohydrates within the extracellular matrix that play a decisive role for the biology of many cytokines e.g. for receptor binding or protection from proteolytic degradation. GAGs can also inhibit IL-10 signalling by a so far unknown mechanism. Here, we studied the interaction between IL-10 and GAGs using NMR spectroscopy.

Saturation transfer difference NMR was used to identify the binding region and affinity of GAGs with different pattern of sulfation and glycosidic linkage geometry. We observed the highest binding affinity with fully sulfated heparin, whereas hyaluronan did not exhibit binding. Structural information about the bound GAG was obtained with transferred NOESY experiments, scalar couplings and molecular dynamics simulations.

The GAG binding site of IL-10 was identified with the help of chemical shift perturbation experiments and paramagnetic NMR. By means of a protein- and ligand-immobilized paramagnetic spin label pseudo contact shifts and paramagnetic relaxation enhancements were measured to reveal intermolecular distance information about the IL-10-GAG-complex. Our data suggest binding of the GAG ligand to a cluster of positively charged amino acid residues near the interface of the IL-10 dimer and provide a hypothesis by which mechanism GAGs could inhibit IL-10 signalling.

➜ **Künze, Georg**
email: georg.kuenze@medizin.uni-leipzig.de

POSTER 12

Structural elucidation of TSHR-ECD by chemical Crosslinking

Biophysics and Bioanalytics

Nagel M[1,2], Schaarschmidt J[2], Paschke R[2], Kalkhof S[1]

1 Department of Proteomics, Helmholtz Centre for Environmental Research – UFZ, Leipzig
2 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The Thyroid-Stimulating Hormone Receptor (TSHR) is one of three Glycoprotein Hormone Receptors (GPHRs). The peculiarity of this subgroup of the G-Protein Coupled Receptor (GPCR) is the large Extracellular Domain (ECD) and its extensive glycosylation. The TSHR plays a central role in the regulation of the thyroid gland and can be activated by the Thyroid-Stimulating Hormone (TSH), constitutively activating mutations and stimulating antibodies. The latter can lead to pathologic activation of the TSHR and cause Graves' disease or thyroid autonomy. For all GPHRs the protein structure is only partially solved or predicted by homology modelling. Furthermore, the hormone binding sites, the functional role of the hinge region which connects the transmembrane domain to the leucine-rich repeat domain, as well as the signal transduction via the transmembrane domain is not yet fully understood. Because of the size, the flexibility and the relatively low amounts of GPHR that could be expressed and purified, the application of classical methods like X-ray crystallography and Nuclear Magnetic Resonance spectroscopy (NMR) is limited. For these reasons we used chemical crosslinking combined with mass spectrometry to probe distances within the TSHR/TSH complex. All in all 27 crosslinks could be identified which enabled us to adjust and validate previous predicted structures.

→ **Nagel, Marcus M. B.**
email: marcus.nagel@ufz.de

POSTER 13

Structural Analysis of GPCR-Ligand Interaction by NMR: Neuropeptide Y bound to the Neuropeptide Receptor Type 1

Biophysics and Bioanalytics

Bosse M[1], Schmidt P[1], Kaiser A[2], Thomas L[1], Müller P[1], Beck-Sickinger AG[2], Huster D[1]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig
2 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

G protein-coupled receptors (GPCRs) allow cells to detect external signals, such as light or molecules, or to communicate with each other through hormones or neurotransmitters. With these tasks, GPCRs have become of high interest for the research community as well as for the pharmaceutical industry. Structural studies are crucial to understand the molecular details of these processes. Unfortunately, molecular characterisation of these large transmembrane proteins is difficult. Solution nuclear magnetic resonance (NMR) spectroscopy offers the opportunity to study structural and dynamical aspects in the interaction of ligand and receptor. Using different NMR experiments we try to understand how the neuropeptide Y (NPY) bound to one of its GPCR, the neuropeptide Y receptor type 1 (Y1R). Therefore, several differently $^{15}N/^{13}C$-labelled NPY variants were synthesized by solid phase peptide synthesis and studied bound to the receptor by NMR. The Y1R was produced recombinantly in *Escherichia coli* as inclusion bodies, solubilised in SDS, refolded and incorporated in DMPC/DHPC bicelles in a high micromolar concentration. We determined several changes in the NPY backbone bound to the receptor in comparison to the not bound state via recording different $^{1}H/^{15}N$ HSQC spectra by solution NMR in the presence and in the absence of the receptor. Finally, our $^{13}C/^{13}C$ correlation spectra recorded by solid state NMR indicate a change in the secondary structure of NPY bound to the receptor. Taken together, the binding of NPY to the Y1R is combined with a considerable altering in the structure of the ligand.

➜ **Bosse, Mathias**
email: matthias.bosse@medizin.uni-leipzig.de

POSTER 14

Development of an ITC based enzyme assay for nucleoside triphosphate diphosphohydrolases

Biophysics and Bioanalytics

Krauss M[1], Zebisch M[2], Sträter N[1]

1 Institut für Bioanalytische Chemie, Biotechnologisch-Biomedizinisches Zentrum, Universität Leipzig
2 Division of Structural Biology, Wellcome Trust Centre of Human Genetics, University of Oxford

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Nucleoside triphosphate diphosphohydrolases (NTPDases) are a physiologically important class of membrane-bound ectonucleotidases responsible for the regulation of extracellular levels of nucleosides. CD39 also named NTPDase1 is the dominant NTPDase of the vasculature and is an interesting drug target but also can be used as a protein therapeutic. Based on the hydrolysis of pro-inflammatory ATP and platelet-activating ADP to AMP the platelet-aggregation is blocked and blood flow is supported. Thus, the understanding of the structure and dynamics of the CD39 are vitally important. To routinely analyse the effect of enzyme modification on substrate binding, turnover and to support drug design, we intent to establish a more efficient kinetic assay for NTPDases which is based on calorimetric detection of phosphate hydrolysis via an isothermal titration calorimeter. This newly established assay allows a quick determination of the kinetic parameters kcat and Km of nucleoside triphosphatase and diphosphatase activities.

→ **Krauß, Michel**
email: michel.krauss@uni-leipzig.de

POSTER 15

The composition of matrix vesicles isolated from hBMSC-derived osteoblasts varies in the presence of sulfated GAG derivatives

Schmidt J[1], Kliemt S[1], Preissler C[1], Möller S[1], von Bergen M[1], Hempel U[1], Kalkhof S[1]

1 Department Proteomik, Helmholtz-Zentrum für Umweltforschung – UFZ

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Skeletogenesis is a highly complex process that involves differentiation and proliferation, but the most important step is the need for mineralization to enable bone to physically support bodily functions. During bone development osteoblasts regulate the production of extracellular matrix proteins and initiate the mineralization of bone matrix by releasing matrix vesicles (MV). MVs are released from apical microvilli of hypertrophic chondrocytes or osteoblasts into the ECM by pinching off or budding. They accumulate Ca^{2+} ions and Pi which promotes the formation of hydroxyapatite in their lumen. In the second phase of mineralization MVs release hydroxyapatite crystals which propagate further mineral formation in the ECM.

Recent investigations showed the capability of glycosaminoglycans (GAG) like sulfated hyaluronic acid (sHA1) to stimulate anabolic activity of human bone marrow stromal cell-derived osteoblasts that make GAG-coatings to a novel approach for bone graft design. Until now, the question to what extend this stimulation is attributed to an altered MV composition is still not answered.

High-throughput quantitative proteomics revealed 390 proteins from MVs collected from hBMSC-derived osteoblasts over a range of 22 days . Significantly up-regulated proteins after sHA1-exposition correspond mainly to functional clusters crucial for i) cell adhesion, ii) ECM organization and mineralization and iii) growth factor bioavailability and activation. These findings were validated by an increased TNAP-activity and a decreased MMP-activity in cell media after sHA1 treatment.

➜ **Schmidt, Johannes**
email: johannes.schmidt@ufz.de

POSTER 16

Integration of conventional quantitative and phosphoproteomics for analysis of Jurkat T-cell receptor pathway

Biophysics and Bioanalytics

Jouy F[1], Mueller S[1], Wagner J[1], Otto W[1], von Bergen M[1], Tomm J[1]

1 Helmholtz-Zentrum für Umweltforschung Leipzig – UFZ

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Recent years have seen a constant development of tools for the global assessment of phosphoproteins. Here, we outline a concept for integrating approaches for quantitative proteomics and phosphoproteomics by LC-MS. The strategy was applied to the analysis of changes in signalling and protein synthesis occurring after activation of the T-cell receptor (TCR) pathway in a Jurkat cell line.

For this purpose, proteins were obtained from four biological replicates of activated and control Jurkat T-cells, digested using Trypsin and the resulting peptides went through a TiO_2-based chromatographic step in order to enrich them in phosphorylated peptides. Both phosphopeptide-enriched and flow-through fractions were analysed by LC-MS.

We observed 1314 phosphopeptides in the enriched fraction whereas 19 were detected in the flow-through, enabling the quantification of 414 and 8 phosphoproteins in the respective fractions. Pathway analysis revealed the differential regulation of many metabolic pathways. Among the quantified proteins, 11 kinases with known TCR-related function were detected. A kinase-substrate database search for the phosphosites identified also confirmed the activity of a further ten kinases. In total, these two approaches provided evidence of 19 unique TCR-related kinases.

The combination of phosphoproteomics and conventional quantitative shotgun analysis led to a more comprehensive assessment of the signalling networks needed for the maintenance of the activated status of Jurkat T-cells.

→ **Jouy, Florent**
email: florent.jouy@ufz.de

POSTER 17

Structural Studies on Ectophosphodiesterase

Biophysics and Bioanalytics

Döhler C[1], Zebisch M[1], Sträter N[1]

1 Institut für Bioanalytik, Biotechnologisch-Biomedizinisches Zentrum (BBZ), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Nucleotide pyrophosphatses/phosphodiesterases (NPPs) are a family of ectophosphodiesterases compromising 7 members in vertebrates. NPPs are glycoproteins and able to hydrolyze a wide range of signal molecules involved in different signaling pathways (e.g., purinergic signaling). Whereas NPP1 and 3 are specific for Nucleotides and Dinucleotides, the natural substrates of NPP2, NPP5 and NPP7 are phospholipids. NPP1–3 include besides the catalytic domain a nuclease-like domain, which has no catalytic activity. Furthermore at the N-terminus of NPP1–3 harbor two consecutive cysteinerich somatomedin B (SMB)like domains, which are involved in substrate binding (NPP2) and membrane anchoring (NPP1 and 3). NPP4–7 are only build up by the catalytic domain. Apart from NPP2 all NPP family members are membrane associated. Concerning their involvement in a lot of physiological functions and diseases NPPs are regarded as attractive drug targets. Crystal structures of these proteins should give a new understanding in substrate specificity and functionality. Structures of NPP1 and NPP2 from vertebrates revealed first insights in domain arrangement and ligand binding. Nevertheless for further investigations of the functionality of NPP enzymes further high resolution structures are an achievable goal. Here, we present a new crystal structure of NPP3 from rattus norvegicus expressed in HEK293S cells in combination with AMP.

➜ **Döhler, Christoph**
email: christoph.doehler@bbz.uni-leipzig.de

POSTER 18

Probing experimental parameters to improve electrospray ionization efficiency for detection of aromatic amino compounds by mass spectrometry

Biophysics and Bioanalytics

Kiontke A[1], Oliveira A[1], Oswald C[1], Birkemeyer C[1]

1 Institut für Analytische Chemie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Aromatic amino compounds exhibit an enormous importance for the chemical and life sciences. The aromatic ring decreases the alkalinity of the amine, depending on its substituents; in return, the presence of the amino group strongly increases the reactivity of the aromatic ring due to the electron-donating mesomeric effect. Therefore, aromatic amines are used frequently as building blocks in chemical synthesis. Apart from production of convenient goods such as rubber, dyes, pharmaceuticals, photo-chemicals and pesticides, one of the most common applications in analytical chemistry is the reaction with ketones and aldehydes. An exposition to aromatic amines may occur during production, use, and disposal of the above goods, by tobacco smoke and in foods. Many aromatic amines are carcinogenic and mutagenic causing DNA damage; their biological monitoring is an important topic in occupational health.

The chemical analysis of amines is, however, often troublesome. Among other critical factors such as their stability, the high polarity of the amines which do not easily dissolve in classical organic solvents restricts the choice of analytical methods. On the other hand, their basicity makes them a promising target for analysis using electrospray ionization mass spectrometry (ESI-MS) for detection. Thus, we tested parameter that would allow a sensitive analysis of aromatic amines with ESI-MS. Among those, type and position of the substituents, pKb, solvent pH and electrolyte concentration were the most important ones; parameters influencing the ESI-MS response beyond the extent of protonation are also discussed.

→ **Kiontke, Andreas**
email: andreas.kiontke@uni-leipzig.de

POSTER 19

Ion-Beam-Microscopy and Confocal-Raman-Spectroscopy, an outstanding combination to determine the distribution of nanomaterials in cells

Meyer T[1]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The interaction of manufactured nanomaterials with living cells is a highly interesting field. Due to their large surface compared to their volume they exhibit extraordinary physical properties. This led to expansive scientific and industrial interest. Although there is little known about their long term influence on cell mechanisms they are widely used in e. g. food and packing industries.
So it is of major importance to get information about the interaction, localization, internalization and toxicity of nanoparticles in cells.
The Ion-Beam-Microscopy – which is provided by the LIPSION particle accelerator at the University of Leipzig – is a very powerful and unique tool to examine these properties. With its high spatial resolution we are able to get detailed information about the colocalization and internalization of label-free nanomaterials in cells.
Confocal-Raman-Spectroscopy – which will be established within the next months in our laboratory – is a second extraordinary tool to get information about distribution of label-free nanomaterials in cells.
In addition to toxicity tests like MTT assay this is a unique combination of methods which will lead us to a deeper understanding of the physics of nanomaterials in their interaction with cells.

→ **Meyer, Thomas**
email: thomasmeyer85@gmx.net

POSTER 20

Analysis of tissue lipids by quantitative constant time INEPT 13C NMR spectroscopy

Biophysics and Bioanalytics

Meusel A[1], Kovacs P[2], Dannenberger D[3], Huster D[1]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig
2 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
3 Leibniz Institute for Farm Animal Biology, Institute of Muscle Biology and Growth, Dummerstorf

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

^{1}H-NMR is a suitable method for investigating lipid compositions of tissues in a quantitative manner. However, due to the relatively small signal range in ^{1}H-NMR spectra severe signal overlap occurs in complex mixtures. To avoid signal overlapping ^{13}C NMR can be applied instead, leading to spectra with a much higher dispersion. Unfortunately quantitative ^{13}C measurements suffer from low signal to noise ratios and thus increase the amount of time for experiments tremendously compared to ^{1}H NMR. To increase the sensitivity in ^{13}C NMR experiments, polarization of ^{1}H can be transferred to ^{13}C by the widely used INEPT pulse sequence. This transfer depends only the heteronuclear coupling constant J_{CH}. A major drawback of INEPT is the loss of quantitative information due to different J_{CH} values within molecules. Depending on the molecular structure J_{CH} range from 115 Hz up to 170 Hz. As a consequence the polarization transfer for different functional groups in a molecule is heterogenous. Here we present a recently published improved quantitative INEPT (Q-INEPT) pulse sequence circumventing disadvantages of regular INEPT experiments. Spectra recorded with Q-INEPT show results comparable to quantitative ^{13}C measurements, thus making it a promising tool in analyzing molecular compositions in tissues. As an example for lipid analysis the comparison of visceral, subcutaneous and brown adipose tissue of mice under two different diets is shown. The results of the Q-INEPT measurements are compared with data obtained by gas chromatography, the current gold standard in lipid analysis.

Funding: ifb

→ **Meusel, Andrej**
email: andrej.meusel@medizin.uni-leipzig.de

POSTER 21

Characterization of highly sulfated Glycosaminoglycan-Oligosaccharides – a MS Study between Sulfation Loss and Salt Concentration Artefacts

Biophysics and Bioanalytics

Lemmnitzer K[1], Blaszkiewicz J[2], Schiller J[1], Rademann J[2]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig
2 Institut für Pharmazie, Freie Universität Berlin

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Glycosaminoglycans (GAGs) are natural polysaccharides which occur in many biological tissues i. a. as main components of the extracellular matrix (ECM).
Certain growth factors and cytokines are known binding to GAGs and therefore initiating and mediating wound healing processes. But details of the binding processes as well as the role of the sulfation pattern of GAGs remain unclear. Thus, well characterized and defined-sulfated GAGs are needed first towards the elucidation of these effects. For this purpose we are working on the regiospecific or the complete sulfation of defined oligosaccharides.
To make a proper assessment of the effects of sulfation in further *in vitro* and *in vivo* studies a detailed structure validation of these newly synthesized materials is required. One standard method to verify a new structure and to monitor the outcome of a chemical synthesis is – beside NMR – mass spectrometry (MS).
Electrospray (ESI) and matrix assisted laser desorption ionization (MALDI) MS was used for characterization. Both methods showed advantages regarding sulfated carbohydrates. However, also method-specific drawbacks like sulfation loss and high sensitivity to the remaining salt in the specimen were obvious.
Commercially available compounds were used as standards for the refinement of the methods and to observe limitations. Eventually, the comparison of results from both ionization methods yielded in the first characterization of the persulfated Hyaluronan-Tetrasaccharide.

➜ **Lemmnitzer, Katharina**
email: katharina.lemmnitzer@medizin.uni-leipzig.de

POSTER 22

Methylglyoxal recovery from the deproteinized biological material

Biophysics and Bioanalytics

Tarakhovskaya E[1], Billig S[2], Frolov A[3], Birkemeyer C[2]

1 Department of Plant Physiology and Biochemistry, St. Petersburg State University
2 Institut für Analytische Chemie, Universität Leipzig
3 Institut für Bioanalytik, Biotechnologisch-Biomedizinisches Zentrum (BBZ), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Methylglyoxal (MGO) is a one of main representatives of reactive carbonyl compounds (RCC), occurring both in plant and animal cells. MGO reacts readily with amino- or thiol groups of proteins, and the increased production of this carbonyl under stress conditions causes the formation of the advanced glycation end products leading to the irreversible protein damage. Effective determination of MGO is of high interest for medicine as it may contribute to understanding the role of the RCC in diabetes-related complications and other diseases.

As in biological material a high percentage of MGO is constantly bound to the proteome and thus inaccessible for the determination, the samples need to be deproteinized. We tested several common deproteinization protocols (salt precipitation, methanol, perchloric acid etc.) on the model system containing the powder of dried yeast cells as a biological matrix and MGO spiked into the matrix just prior the analysis to assess its relative recovery. MGO was determined after derivatization with *O*-(2,3,4,5,6-pentafluorophenyl)-methylhydroxylamine hydrochloride using GC-MS. MGO recovery from the non-deproteinized samples was generally very low and did not exceed 0.25% of the MGO reference standard. Of all agents tested 70% methanol produced the highest level of MGO recovery (up to 10%) and most of the other methods showed the results not significantly exceeding the blank control. The information about the poor RCC recovery needs to be considered for accurate quantitative analysis of biological samples.

➜ **Kiontke, Andreas**
email: andreas.kiontke@uni-leipzig.de

POSTER 23

Cytochrome P450 BM3 coupled carbon nanotube-electrode for the development of an in vitro hydroxylation system

Biophysics and Bioanalytics

Klenner M[1], Frank R[1], Azendorf R[1], Jahnke H[1], Robitzki A[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hydroxylation reactions of non-activated carbon chains are commonly used in the industrial production of fine chemicals. Thereby, cytochrome P450 enzymes are often used due to their ability to perform these reactions with a high regio- and stereoselectivity.
Cytochrome P450 BM3 (CYP102A1) is a self-sufficient enzyme in which the reductase domain required for transfer of electrons from NADPH is fused to the hemoprotein. CYP102A1 is not yet commercially used due to its need for the expensive co-factor NADPH. To overcome this problem we aim to develop an electrochemical enzyme regeneration system in which the enzyme is reduced directly at the electrode.
One of the major challenges to achieve our aim is to engineer a high conductivity but also biocompatible electrode surface on that the enzyme can be immobilized. Therefore, unmodified as well as amine-functionalized carbon nanotubes (CNT) were immobilized on a thiol-modified gold electrode surface. All modification steps were proved by cyclic voltammetry and electrochemical impedance spectroscopy. We could show that the CNTs are able to provide a conductive surface for enzyme immobilization. Native expressed CYP102A1 enzyme was adsorbed to the modified electrodes, subsequently. Turnover numbers determined via a fluorometric assay indicate higher substrate turnover for the CNT-CYP-electrodes than for the electrodes with CYP adsorbed directly to the gold surface which shows the better biocompatibility provided by the CNT coating.
Within this work we could demonstrate a method for the immobilization of CYP102A1 on a highly conductive surface while maintaining the enzyme activity.

➜ **Klenner, Marcus**
email: marcus.klenner@uni-leipzig.de

POSTER 24

Electricity driven biobased production of platform chemicals: Electrochemically steered fermentation

Biotechnology / Biomedicine

Gimkiewicz C[1], Hunger S[1], Aurich A[1], Harms H[1], Harnisch F[1]

1 Department für Umweltmikrobiologie, Helmholtz-Zentrum für Umweltforschung – UFZ

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In future alternative technologies are needed to produce platform chemicals from renewable resources in order to become independent of petrochemistry. Biobased approaches are a key strategy, but currently face several potential limitations with one major bottleneck being the need to maintain a redox-balance. Thus, yields and titers are decreased due to bacterial growth, storage and side reactions needed for redox balancing. Here the external "feeding" of electrons – allowing to maintain the microbial redox-balance – are an upcoming and promising concept being also summarized as "Electrochemically steered fermentation".

In this work we use the fermentation process of *Gluconobacter* as a model system to investigate the potential of electrochemically steered fermentations and the tools needed therefore. Subsequently, we provide the proof-of-principle on this model organism of white biotechnology.

➜ **Gimkiewicz, Carla**
email: carla.gimkiewicz@ufz.de

POSTER 25

Revisiting polarography for assessing bioavailability of trace metals and heavy metals

Biotechnology / Biomedicine

Stang C[1], Gimkiewicz C[1], Harnisch F[1]

1 Department für Umweltmikrobiologie, Helmholtz-Zentrum für Umweltforschung – UFZ

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Apart from carbon, hydrogen, oxygen and nitrogen, also numerous trace metals are essential for microbial cell development. These trace metals include for example copper, cobalt, iron, or zinc. In substrates with high organic contents, as they are commonly found in biogas plants, the metals are often bound, i. e. chelated, by organic matter rather than dissolved in solution. Thus, their bioavailability is decreased, if existent at all.

In order to assure that trace element availability does not hamper biogas production, it is therefore common to add vast amounts of trace elements in dependency of the dry content of the substrate in the biogas plant (Oechsner et al., 2008).

The aim of the proposed study is to determine the capacity of different potential substrates to bind trace metals as well as heavy metal ions via voltammetric titration using polarography (details see e. g. Kahlert & Schröder, 2002). Additionally, polarographic measurements should reveal whether conventional addition of trace elements to substrate suspensions results in freely dissociated and then potentially bioavailable metal ions or immediate coordination in a complex.

Kahlert, H., & Schröder, U. (2002). *Praktikum der Elektroanalytik mit dem 757 VA Computrace*. Metrohm-Monographie.

Oechsner, H., Lemmer, A., Ramhold, D., Mathies, E., Mayrhuber, E., & Preissler, D. (2008). Verfahren zur Herstellung von Biogas bei kontrollierter Konzentration von Spurenelementen. Google Patents. Retrieved from http://www.google.com/patents/WO2008145362A1?cl=de

➜ **Stang, Carolin**
email: carolin.stang@ufz.de

POSTER 26

In vitro expression and purification of P450 enzymes for immobilization on chip surfaces

Biotechnology / Biomedicine

Zernia S[1], Beck-Sickinger AG[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Cytochrome P450 proteins form a large class of enzymes. They share a NAD(P)H dependent reductase domain that transports electrons to a heme dependent monooxygenase for catalyzing the activation of molecular oxygen. The subsequent regioselective and stereoselective oxidation on various substrates is exceedingly important for many applications in chemical industry and biotechnology. However this reaction is not used in industry because most of the attractive enzymes are membrane associated and hence difficult to handle in a cell-free environment. P450BM3 (*Bacillus megaterium*) forms an exception in the P450 family classification as it is a self-sufficient single polypeptide bacterial cytochrome. It acts as a model for newly designed recombinant cytochromes with bacterial and eukaryotic properties. We recombinantly expressed P450BM3 to optimize the enzyme structure, the electron flow and the substrate recognition. After purification by the IMPACT system the protein thioester was successfully ligated to a peptide for immobilization on chip surfaces. Besides the characteristic red color, CO spectrum and NADPH assay confirm the activity of the enzyme.

➜ **Zernia, Sarah**
email: sarah.zernia@uni-leipzig.de

POSTER 27

Calorimetric Process Control for Microbial Product Formation Using Toxic Feedstocks

Biotechnology / Biomedicine

Weichler M[1], Paufler S[1], Rohwerder T[1], Harms H[1], Maskow T[1]

1 Department für Umweltmikrobiologie, Helmholtz-Zentrum für Umweltforschung – UFZ

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In future, petrochemical industry may be replaced by biotechnological processes producing building block chemicals from renewable carbon and employing genetically engineered microorganisms. However, besides searching for suitable microbial production platforms, a major hurdle for a large-scale implementation of bioprocess-based technologies is the availability of economic and sustainable carbon sources.

Currently, by using traditional feedstocks such as simple sugars and fatty acids, already established biotechnology directly competes with food production for agricultural resources. In search for alternative substrates, methanol is discussed due to high synthesis capacities and its potentially sustainable production from natural gas, agricultural waste materials and biogas. However, in contrast to other carbon sources, this C1 compound is highly volatile and acts toxic at high concentrations. Its application as a substrate within fermentation processes therefore calls for an innovative real-time control strategy.

In this study, we decided on biocalorimetry as a basis for optimizing C1 substrate feed regimes in fermentations with the methylotrophic bacterium *Methylobacterium extorquens*. By applying this method, we achieved better growth rates of *M. extorquens* on methanol as well as a higher final content of the product polyhydroxybutyrate. Additionally, we could show that our control strategy can be extended to other, even more toxic substrates such as formic acid. In conclusion, biocalorimetry has been proved as a very efficient tool for process control and can be applied to optimize any microbial product formation process.

→ **Weichler, Maria-Teresa**
email: maria-teresa.weichler@ufz.de

POSTER 28

Engineering Biomimetic Microenvironments for Studying Cancer Behavior in vitro

Biotechnology / Biomedicine

Sapudom J[1], Rubner S[1], Martin S[1], Pompe T[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Cells are surrounded in the tissue context by extracellular matrices (ECM). Changes in biophysical and biochemical properties of ECM lead to loss of cell function and fate decision. It has been reported that tumor microenvironments exhibit distinct changes in biophysical parameters such as pore size, fibril diameter and tissue elasticity. Moreover, interfacial boundaries of the heterogeneous extracellular microenvironments can act as a physical barrier for migration, invasion and phenotype changes of cancer cells.
In this work we reconstructed topologically and mechanically defined three-dimensional (3D) individual and step-gradient collagen matrices. Pore size and fibril size can be controlled by adjusting collagen concentration and pH during fibrillogenesis. Topological parameters were imaged using confocal laser scanning microscopy (cLSM) and were characterized using in-house developed image analysis tools. Matrix elasticity was measured by colloidal probe technique using atomic force microscopy (AFM). We demonstrated that topological parameters alone can influenced invasive cell phenotypes of both MDA-MB-231 and MCF-7 breast cancer cell lines independent of overall matrix elasticity. Invasiveness increased and clustering decreased with increasing fibril diameter for both cell lines. Furthermore, directional migration towards matrix gradient of increasing pore size and decreasing elasticity could be observed combined by phenotypical changes of migration pattern at the matrix boundary.
The step-gradient platform is suggested as a novel system for studying metastatic behavior of tumor cells at tissue boundaries.

➜ **Sapudom, Jiranuwat**
email: jiranuwat.sapudom@uni-leipzig.de

POSTER 29 **The Microbiota of the Long Living Naked Mole-Rat**

Biotechnology / Biomedicine

Aklilu TD[1,2,3], König B[2], Holtze[4], Hildebrandt T[4], Rodewald S[5], Huse[6], Shubo M[7], Yirga F[7], Wyohannes D[7], Thieme R[1], Kolb M[1], Trettner S[1], Birkenmeier G[1]

1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig
2 Institut für Medizinische Mikrobiologie und Infektionsepidemiologie, Universität Leipzig
3 College of Medicine and Health Sciences, Bahir Dar University, Ethiopia
4 Leibniz Institute for Zoo and Wildlife Research, Berlin
5 Institut für Pharmazie, Universität Leipzig
6 Leibniz Institute for Age Research-Fritz Lipmann Institute, Jena.
7 College of Natural Sciences, Addis Ababa University, Ethiopia

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The naked mole-rat (NMR) (Heterocephalus glaber) is a mammal with an eusocial behavioral pattern. This mouse-size subterranean rodent lives more than 30 years in captivity. It is known to miss many age-related changes, displays resistance to oxidative stress and is remarkably resistant to both spontaneous cancer and experimentally induced tumorigenesis. Microbiota, which colonize different parts of the body of the human, has been shown to have a pivotal role in host health and disease. In this line, the present study was aimed at analyzing the gut microbiota of the NMR and diet consumption pattern in wildlife for the first time. Appropriate culture media under aerobic and anaerobic conditions, and further identification of isolates by Matrix Laser Desorption Ionization Time-of-Flight (MALDI-TOF) mass spectrometry were conducted. Diet consumption pattern of NMR in wildlife was also assessed. Bacteroides spp were found in both captive and wildlife NMRs. Bacteria such as Bacillus, and Clostridium *spp* were identified in NMR living in the wild. In contrast, Staphylococcus *spp* were found in NMR kept in the captivity. The primary food of NMRs in the wild were natural polyphenol and related compound-rich plants, with anti-inflammatory, anticancer, antioxidant and antimicrobial activities. Overall, the gut of the NMRs is composed of diverse microbiota, and their diet comprises natural plant species, mainly rich in polyphenols and related compounds. However, a detailed characterization of the microbiota by e. g. 16s RNA gene-based approach and a multi-parametric investigation of further factors involved are ongoing.

➜ **Aklilu, Tewodros Debebe**
email: tewodrosdebebe.aklilu@medizin.uni-leipzig.de

POSTER 30

Studying Stem Cell Migration in vitro – Limits of Global Protein Stimulation

Biotechnology / Biomedicine

Ansorge M[1], Wang W[2], Krinner A[3], Zandstra P[2], Roeder I[3], Pompe T[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 Donnelly Center for Cellular and Biomolecular Research, University of Toronto
3 Institute for Medical Informatics and Biometry, TU Dresden

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hematopoietic stem cells (HSC) are responsible for creation of all blood cells. Its regulation is orchestrated by the local environment of the bone marrow, called HSC niche. Among other regulating cues cytokines secreted by various cells form different microenvironments. Migration is suggested to enable HSC to choose particular microenvironments for specific fate decisions. Based on a systems biology approach, we hypothesized that specific cytokines can act as direct triggers of migratory behavior.

We used human HSC ($Lin^- CD34^+ CD38^- CD45RA^- CD49f^+$) derived from umbilical cord blood. The HSC were seeded into fibronectin coated silicone microwells with constant cytokine background (SCF/TPO/FLT3L). HSC were imaged every 2 min for 24 h to ensure high-resolution single cell tracking. After adding a potential mobilization factor (SDF1, GCSF …) tracking was continued for another 24 h.

After analyzing a first dataset of 1000 cell tracks for all 10 cytokines we found, that – independent of the added factor – the mean & standard deviation of cell velocity increased during the experiment, while the coefficient of variation remains constant. Simultaneously other migration properties did not change. Correlated modeling approaches indicate increasing mean & heterogeneity of cell's diffusion coefficient to explain the observed behavior. In conclusion the chosen setting of global cytokine stimulation does not allow for evaluation of different influences on HSC migration. It is suggested that delivery of cytokines in a gradient fashion will better mimic the *in vivo* situation and allow for physiological relevant conclusions.

➜ **Ansorge, Michael**
email: michael.ansorge@uni-leipzig.de

POSTER 31

Modification potential of oligomer cross-linked gelatin gels containing ketone groups

Biotechnology / Biomedicine

Kascholke C[1], Krusch S[1], Kohn C[1], Schulz-Siegmund M[1], Hacker M[1]

1 Pharmazeutische Technologie, Institut für Pharmazie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction: Hydrogels of cross-linked natural extracellular matrix-derived polymers such as gelatin are promising cell carriers and delivery systems. In this study, we synthesized a novel type of oligomer comprising two types of functional groups that allow for gelatin cross-linking and subsequent chemical functionalization, e. g. with glycosaminoglycans.
Materials/Methods: The oligomeric cross-linkers were synthesized by free radical polymerization of pentaerythritol diacrylate monostearate (PEDAS), maleic anhydride (MA) and diacetone acrylamide (DAAm) and were analyzed physico-chemically. In the resulting macromers (oPDMA), anhydride groups provide high reactivity for chemical cross-linking of gelatin. In addition, DAAm units enable further chemical modification of the oligomers due to their carbonyl groups. Hydrogels were formed by cross-linking of gelatin (Collagel® B, Gelita). Post-fabrication modification was analyzed using 2,4-dinitrophenylhydrazine (DNPH).
Results/Discussion: Oligomer composition (M_n = 2400–7400 Da) was controlled by feed ratio of co-monomers during synthesis. MA content was varied between 7 and 20% (m/m) and 70% of copolymerized anhydrides remained chemically intact. The potential of hydrazine immobilization was quantified by coupling DNPH to the hydrogels. The conversion was analyzed by UV/VIS spectroscopy. A pH-dependent shift of the absorption maximum from 340 to 367 nm was found which indicates a covalent coupling of DNPH to the hydrogels. Upon hydrolysis of derivatized gels the amount of reactive ketones per gel disk was quantified. DNPH immobilization increased with decreasing pH.

➜ **Kascholke, Christian**
email: kascholke@uni-leipzig.de

POSTER 32

Quantitative monitoring of TRPV1 channel activity by impedance spectroscopy

Biotechnology / Biomedicine

Weyer M[1], Jahnke H[1], Robitzki A[1]
1 Biotechnologisch-Biomedizinisches Zentrum (BBZ), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Transient receptor potential (TRP) channels are involved in diverse physiological functions like the perception of sensory stimuli such as pain, temperature, mechanical forces, and taste. Most of the TRP channels are non-selectively permeable to cations including Na^+, Ca^{2+} and Mg^{2+}.

Up to now cell-based impedance spectroscopy was generally applied to monitor morphological changes of the cell layers caused by processes like proliferation, migration and apoptosis. We present a cell-based impedance assay to monitor the activity of TRPV1 recombinantly expressed in HEK293 cells.

Confluent cell layers of high density grown on microelectrode arrays (MEA) were impedimetrically analysed. The cellular contribution was calculated using impedance spectra of cell-covered and non-covered electrodes. This revealed a maximum cell-specific signal at a frequency of approximately 100 kHz for monitoring TRPV1 activity. The induced channel opening causes a decrease of the impedance signal, which can be quantified in a concentration and time dependent manner. In the case of the TrpV1 channel, we demonstrated the capability of the impedimetric monitoring by determination of the EC_{50} value (0,8 μM). Transfected cells pre-treated with 10 μM ruthenium red as an inhibitor of the TRPV1 channel, as well as control cells lacking TRPV1, showed no impedance changes upon capsaicin stimuli.

In summary, we developed a quantitative impedimetric monitoring system for the analysis of ion channel activity in living cells. This measurement system has the capabilities for a high content screening system to identify novel ion channel activators and inhibitors.

➜ **Weyer, Maxi**
email: maxi.weyer@bbz.uni-leipzig.de

POSTER 33

Die Rolle von Noradrenalin bei Hypoxieexposition – Kardiopulmonale Untersuchungen an Ratten

Biotechnology / Biomedicine

Gabriel P[1], Appelt P[1], Bölter C[1], Fiedler N[1], Schierle K[2], Raßler B[1]

1 Carl-Ludwig-Institut für Physiologie, Universität Leipzig
2 Institut für Pathologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hypoxie triggert neben einem Druckanstieg im Lungenkreislauf pulmonale Ödeme und eine Sympathikusaktivierung. Letztere führt zu einer gesteigerten Kreislaufleistung, die die Sauerstoffversorgung der Gewebe verbessern kann. Ein verstärkter Sympathikotonus kann allerdings auch pulmonale Ödeme induzieren und damit zur Entwicklung eines hypoxischen Lungenödems beitragen. In der vorliegenden tierexperimentellen Studie soll die Rolle des sympathischen Transmitters Noradrenalin (NE) bei der kardiopulmonalen Reaktion auf kurzdauernde Hypoxie näher untersucht werden.

Dazu erhielten Sprague-Dawley-Ratten über 6 Stunden entweder NaCl- oder NE-Infusionen in Norm- bzw. Hypoxie. Anschließend wurde die kardiale Funktion mittels links- (LV) und rechtsventrikulärer (RV) Herzkatheterisierung überprüft. Pulmonale Veränderungen wurden histologisch beurteilt.

Unter Hypoxieeinwirkung sanken der LV Spitzendruck (LVSP) um 25%, der diastolische Aortendruck (Pd Ao) und die LV Kontraktilität (LV dP/dt max) sogar um über 35%. Der rechtsventrikuläre Spitzendruck (RVSP) änderte sich nicht signifikant. Histologisch zeigte sich ein mäßig ausgeprägtes interstitielles Lungenödem. Zusätzliche NE-Infusion führte LVSP und Pd Ao auf Werte normoxischer Kontrollen zurück, LV dP/dt max wurde darüber hinaus noch weiter gesteigert. Auf den RVSP und die Schwere der Lungenödeme unter Hypoxie hatte die NE-Infusion keinen Einfluss.

Die Ergebnisse zeigen, dass NE die durch kurzdauernde Hypoxie induzierte Beeinträchtigung der linksventrikulären Funktion ausgleichen kann ohne die pulmonale Situation zu verschlechtern.

→ **Appelt, Peter**
email: peter.appelt@medizin.uni-leipzig.de

POSTER 34

Weniger ist mehr – Volumenzufuhr bei hypoxieexponierten Ratten

Biotechnology / Biomedicine

Appelt P[1], Gabriel P[1], Bölter C[1], Fiedler N[1], Schierle K[2], Raßler B[1]

1 Carl-Ludwig-Institut für Physiologie, Universität Leipzig
2 Institut für Pathologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Die vorliegende Untersuchung ist Teil einer größeren tierexperimentellen Studie zur Rolle adrenerger Agonisten und Blocker im Kontext kardialer und pulmonaler Veränderungen unter akuter Hypoxie. Die betreffenden Substanzen sollen intravenös verabreicht werden. Bisher ist nicht bekannt, wie sich eine applikationsbedingte Volumenzufuhr auf die kardiale Funktion und die Entwicklung hypoxischer Lungenödeme auswirkt.

Wir behandelten Ratten in Norm- bzw. Hypoxie über einen Zeitraum von 1,5 und 6 h mit NaCl-Lösung, die entweder kontinuierlich infundiert (1ml/h) oder einmalig injiziert (0,5 ml) wurde. Die kardiovaskuläre Funktion wurde mittels Herzkatheterisierung überprüft. Die Beurteilung von Lungenödemen erfolgte histologisch.

Bei 1,5 h Hypoxieexposition hatte die Applikationsform keinen Einfluss auf die kardiovaskuläre Funktion. Histologisch stellten sich blande Lungen dar. Hypoxie über 6 h führte zu einem signifikanten Abfall des totalen peripheren Widerstandes. Im Vergleich zu injizierten und normoxischen Tieren wiesen die infundierten Tiere zusätzlich eine erniedrigte Inotropie auf. Linksventrikulärer Spitzendruck und Kontraktilität waren vermindert. Die Tiere zeigten ein deutliches Lungenödem. Der systolische Druck im rechten Ventrikel blieb bei beiden Applikationen auf normoxischem Niveau.

Die Ergebnisse zeigen, dass Volumenzufuhr unter Hypoxie die kardiopulmonale Funktion beeinträchtigt. Während die Tiere bei Exposition über 1,5 h dies noch ausgleichen können, versagt die Kompensation bei 6 h Hypoxiedauer. Für die weitere Versuchsplanung sollte daher die Injektion der Infusion vorgezogen werden.

→ **Appelt, Peter**
email: peter.appelt@medizin.uni-leipzig.de

POSTER 35 **Chondrocyte culture as a model for canine osteoarthritis**

Biotechnology / Biomedicine

Adler N[1], Fuhrmann H[1]
1 Veterinär-Physiologisch-Chemisches Institut, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Osteoarthrtitis (OA) is a chronic, progressive disease characterized by an over-production of proinflammatory mediators such as IL-1β, which leads to the breakdown of the cartilage. More than 20 % of middle-aged dogs were estimated to suffer from OA. Affected dogs show joint pain, joint stiffness and therefore, often have a decreased quality of life. The aim of this study was to develop a cell culture model of canine OA for investigation of this degenerative joint disease.

Cartilage slices are harvested aseptically from apparently normal knee joints from canine cadavers and digested in a mix of enzymes. The isolated chondrocytes are cultured until confluence and cryoconservated at –80 °C. After thawing, the cells are cultured for 4 days and then stimulated with IL-1β for 48 h. Glucosaminoglycane production is measured using the dimethylmethyleneblue assay. Nitric oxide is determined by Griess assay.

We established a technique of collecting chondrocytes from canine cadavers, cultivated them successfully and cryoconservated them for further examinations. As proven by an active production of glycosaminoglycane, the cells maintain their cartilage phenotype. IL-1β stimulated chondrocytes produced high levels of nitric oxide, which provides evidence for the abiltity of the cells to trigger an inflammation cascade comparable to the pathogenesis of OA.

All in all, we present a simple method to simulate canine OA *in vitro*, which can be used to test new concepts for the treatment of this degenerative joint disease thereby avoiding animal experiments in the first instance.

This study is granted by Boehringer Ingelheim.

→ **Adler, Nadja**
email: nadja.adler@vmf.uni-leipzig.de

POSTER 36

Improving multielectrode array designs for in vivo and in vitro applications

Biotechnology / Biomedicine

Schmidt S[1], Jahnke H[1], Azendorf R[1], Robitzki A[1]

1 Molecular biological-biomedical Processing Technology, Center for Biotechnology and Biomedizine (BBZ), Leipzig University

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Multielectrode array (MEA) technology is a widely use method for bioelectronic monitoring of cellular alterations. Our *in vitro* MEAs are fabricated to take measurements of single cells, monolayers and 3D cultures. For sensitive and feasible bioelectronic detection of cellular alterations like cell damage, proliferation, subcellular cytoskeletal rearrangements or even signal cascade activation MEAs need to be individually optimized in electrode size, geometry, electrode material and passivation layer material. For optimization procedures, we use our small scale prototype platform. If for a certain application and target the optimum parameters are identified the transfer to specific array types like an up scaling to full 96- or 384-well format for high throughput measurements are possible. For the bioelectronic *in vivo* monitoring we established MEAs based on flexible substrates with a high number of microelectrodes with short inter-electrode distances. In combination with our self-developed bioelectronic measurement platform including mobile setups for flexible in-vitro/*in vivo* monitoring experiments as well as our high-content screening stations, we are able to cover a broad range of applications with regard to label-free non-invasive monitoring of alterations in cells and tissues.

➜ **Schmidt, Sabine**
email: sabine.schmidt@bbz.uni-leipzig.de

POSTER 37

A Hybrid Impedance/Field Potential Platform for Neurophysiology and Toxicity Assessment on Biochip

Biotechnology / Biomedicine

Seidel D[1], Jahnke H[1], Laustriat D[2], Girard M[2], Semkova V[3], Haupt S[3], Brüstle O[3], Robitzki A[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 I-STEM, Genopole Campus 1, France
3 Institute for Reconstructive Neurobiology, Universitätsklinikum Bonn

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

When developing active pharmaceutical ingredients in health care or cosmetic, a major aim is the identification of toxic substances early on. Therefore, a meaningful cell model combined to a high-content (HC)/high-throughput (HT) read-out technology is essential. In today's neuropathology assessment, human induced pluripotent stem cell (hiPS)-derived neuronal networks are the only *in vitro* cell model combining standardized HT generation with a primary human phenotype. A biosensor for the identification of neuronal differentiation/maturation characteristics as well as the monitoring of drug-induced de- and regenerative processes completes the real-time, non-invasive *in vitro* screening system.

We established a bioelectronics impedance/field potential platform, which allows the HC monitoring of complex cellular properties that accompany neuronal differentiation of hiPS-derived neurons. The observed distinct relative impedance progression, spectrum shape and frequency shift could be specifically associated with the quality and state of neuronal differentiation.

Electrophysiologically active neuronal networks fulfilling the above mentioned criteria were further used in acrylamide neurotoxicity tests. We were able to detect molecular and structural changes causing neurotoxicity much faster and with increased sensitivity using our biosensor compared to molecular-based methods.

Connecting a mature human neuronal cell model with a highly efficient hybrid impedance/electrophysiology read-out, we established a HC/HT platform for label-free neuronal differentiation and toxicity monitoring in short- as well as long-term applications.

➜ **Seidel, Diana**
email: diana.seidel@bbz.uni-leipzig.de

POSTER 38

Isolation and characterization of CD271+ and CD90+ subpopulation of human dermal cells

Biotechnology / Biomedicine

Jahroomishirazi R[1], Zscharnack M[1], Bader A[1]

1 Institut für Bioanalytische Chemie, Biotechnologisch-Biomedizinisches Zentrum (BBZ), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Mesenchymal stem cells (MSCs) exist in variety of human tissues such as dermis. Despite the importance of human dermal MSCs to wound healing, characterization of these cells has rarely been reported. This study aimed to isolate human dermal stem cells based on MSC markers or plastic adherence to compare their growth rate as well as their mesenchymal differentiation potential.

Materials & Methods: Immunohistochemical (IHC) staining was used to detect the abundant of MSC markers within the skin. $CD271^+$ and $CD90^+$ of primary isolated dermal cells were sorted by flow cytometry. CD271 and CD90 dermal MSCs (CD90-dMSCs, CD271-dMSCs) as well as unsorted cells isolated by plastic adherence, were cultured in monolayer. Colony formation efficiency, population doubling time (PDT), and the cellular growth rate of these cells were assessed. Multipotency of all cell groups was compared.

Results: IHC staining of skin cryosections showed the higher expression of CD90 compared to CD271. Isolated dermal cells which were sorted by flow cytometry expressed 15.26 ± 2.06% CD90 and 1.7 ± 0.40% CD271. Colony formation efficiency of CD271-dMSCs was lower compared to others. CD271-dMSCs showed lowest proliferation rate, and PDT in comparison with CD90-dMSCs and unsorted cells. Unsorted cells relieved the highest amount of adipocytes and osteocytes among others. All cell groups indicated no difference in qualitive and quantitive chondrogenesis analysis.

Conclusion: The findings indicate that specific dermal MSCs possess variable multipotency as well as different growth rate that might play a pivotal role in regenerative medicine.

➜ **Jahroomishirazi, Roomina**
email: roomina.jshirazi@bbz.uni-leipzig.de

POSTER 39

Creating a cytochrome P450 test system to cross the bioelectrocatalytic barrier

Biotechnology / Biomedicine

Frank R[1], Klenner M[1], Azendorf R[1], Schmidt S[1], Jahnke H[1], Robitzki A[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

There is ongoing pharmaceutical and chemical interest in easy regio- and enantioselective functionalization of inert C-H-bonds. Although cytochrome P450 enzymes are promising in this regard, their drawbacks lay in the costly cofactor NADH/NADPH and product purification. We take this challenge within the margin of Biotechnology 2020+ by elucidating the direct electric cofactor regeneration of immobilized self-sufficient CYP102A1.

Our ready-to-embark system includes a multi-sided enzyme and electrode engineering. We restructured the substrate binding pocket of CYP102A1 to accept fluorescent aromatic compounds for monitoring of enzyme activity. Besides, we designed C-terminal tandem-tags of histidine and cysteine residues, which were incorporated into CYP102A1 to generate an electron-rich amino acid backbone and to enable the site-directed immobilization by sulfhydryl crosslinker. Furthermore, we truncated CYP102A1 based on crystallographic data to expose redox relay center, facilitating electrode-enzyme electron transfer. In parallel we produced unprecedented multi-electrode arrays from 9- to 96-well size, capable to integrate of up to four different electrode materials simultaneously. Focusing on indium tin oxide as electrode material due to high surface-to-area ratio, transparency and still high conductivity, we achieved grain boundary control by RF/DC sputtering techniques. Thereby, we are able to vary arbitrarily the topography and conductivity.

Summing up, we developed a cytochrome P450 test system, that is designed to fathom and eventually to break the barrier in joining electrode and enzyme to one catalytic entity.

→ **Frank, Ronny**
email: ronny.frank@bbz.uni-leipzig.de

POSTER 40

Eine Ontologie für die Unterstützung der Lehre und des Informationsmanagements im Gesundheitswesen

Biotechnology / Biomedicine

Tahar K[1], Jahn F[1], Schaaf M[1], Kücherer C[2], Paech B[2], Winter A[1]

1 Institut für Medizinische Informatik, Statistik und Epidemiologie (IMISE), Universität Leipzig
2 Institut für Informatik, Lehrstuhl Software Engineering, Universität Heidelberg

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Einleitung: Heutzutage wird die schnell wachsende Masse an komplexen Daten und Prozessen im Krankenhaus immer größer. Um die Komplexität des Informationsmanagement (IM) in der Lehre und Praxis zu erleichtern, wird ein Semantisches Netz des IM im Krankenhaus (SNIK) entwickelt.
Methodik: Der Entwicklungsprozess unterteilt sich in drei Phasen. Zuerst wird SNIK durch das Lesen relevanter Literatur erhebt und in einer Excel-Tabelle erfasst. Um die gewonnenen Konzepten und Relationen brauchbar zu machen, wurde ein Programm Exel2OWL entwickelt. Damit kann man automatisch die RDF-Tripel aus der Tabelle extrahieren und in einer redundanzfreien OWL-Ontologie exportieren. Am Ende dieser Semantikanalysephase soll die SNIK-Ontologie mittel SPARQL-Anfragen getestet werden, um semantische Fehler oder Inkonsistenzen zu beheben. Zum Schluss soll SNIK im Rahmen der Wissensvermittlungsphase durch eine übersichtliche verständliche Darstellungsweise veranschaulicht.
Ergebnisse: Auf Basis dieses Verfahren wird zurzeit ein E-Learning-Modul entwickelt und iterativ weiteroptimiert. Dabei wurde eine redundanzfreie Ontologie für zwei Kapitel über IM [1] erstellt und in Form eines semantischen Graphs in Protegé [2] fehlerfrei visualisiert. Die Visualisierungsergebnisse haben die semantischen Zusammenhänge der extrahierten Begriffe zwar sichtbar dargestellt, allerdings sollen sie noch evaluiert und an die E-Learning-Modul-Anforderungen angepasst werden. Bei höherem Reifegrad der Entwicklung wird ein neue prototypische Software CIO-Navigator (CION) entwickelt, die dem CIO und der Krankenhausleitung die Navigation durch das vernetzte IM ermöglicht.

➜ **Tahar, Kais**
email: kais.tahar@imise.uni-leipzig.de

POSTER 41

Steroidogenese in der Leber – jetzt doch?!

Cell Biology

Rennert C[1], Böttger J[1], Matz-Soja M[1], Gebhardt R[1]
1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In den letzten Jahren hat sich die Idee der personalisierten und „gender" Medizin etabliert, was ein gesteigertes Interesse an geschlechtsspezifischen Forschungsergebnissen erzeugt. Unser Interesse bezieht sich auf die Untersuchung des Geschlechtsdimorphismus der Genregulation in der Leber. Neueste Untersuchungen zeigen, dass die morphogenen Signalwege Hedgehog (Hh) und Wnt/β-Catenin (Wnt) in adulten Hepatozyten aktiv sind und die Zonierung der Leber maßgeblich beeinflussen (Gebhardt & Matz-Soja, WJG, 2014). Aktuell untersuchen wir die Verbindung der Signalwege zur geschlechtsspezifischen Regulation der Genexpression anhand zweier Mausmodelle. Überraschender Weise zeigten sich hier Veränderungen in der Expression von steroidogeneseassoziierten Genen. Ein Fokus liegt dabei auf der Expressionsregulation von Cyp17a1, einem zentralen Enzym der Steroidogenese. Generell ist die Expression von Cyp17a1 in Weibchen wesentlich höher als in Männchen und wird durch Estradiol aktiviert. Im Mausmodel mit über-aktiviertem Wnt Signalweg zeigt sich eine deutlich verringerte Expression, wohingegen ein deaktivierter Hh Signalweg zu einer Hochregulation führt. Außerdem wurde die Expression vom Estrogen Rezeptor Esr1, entscheidend für die Signalvermittlung der Steroidhormone, untersucht und es zeigt sich eine deutliche Korrelation zwischen Esr1 und Cyp17a1 Expression.
Die Ergebnisse zeigen, dass die Cyp17a1 Expression in der Leber vom Estradiolspiegel abhängt und durch die veränderten Signalwege Hh und Wnt reguliert wird. Möglicherweise nimmt die Leber unter pathologischen Zuständen eine neue Funktion in der Homöostase der Steroidhormone ein.

➜ **Rennert, Christiane**
email: christiane.rennert2@medizin.uni-leipzig.de

POSTER 42 **A fly model of Epidermolysis Bullosa Simplex**

Cell Biology

Bohnekamp J[1], Cryderman D[2], Paululat A[3], Wallrath L[2], Magin T[1]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
2 Department of Biochemistry, 3136 MERF, University of Iowa, USA
3 Department of Biology, Zoology/Developmental Biology, University of Osnabrück

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The human blistering skin disorder Epidermolysis bullosa simplex (EBS) is caused by dominant mutations in keratin genes K5 or K14, products of which form the intermediate filament network in basal keratinocytes of the epidermis. Mutations in K5 and K14 can cause collapse of the epidermal cytoskeleton, cytolysis, tissue fragility and subsequent tissue repair and in some cases results in lethality. The molecular mechanisms by which mutations in keratin genes cause EBS are still not well understood.

Drosophila lacks keratins or other cytoplasmic intermediate filaments, providing a 'null' *in vivo* system to understand mechanism of keratin network formation and how mutant keratins cause molecular defects. We generated the first *Drosophila* model for EBS by transgenic expression of human wild type (wt) K5 in combination with either human wt K14 or the $K14^{R125C}$ mutant. Simultaneous expression of wt K5 and K14 permitted the formation of intermediate filament-like assemblies. This demonstrated for the first time, that *Drosophila* provides a permissive environment for the formation of a cytoskeletal network formed by human keratins. In contrast, expression of the dominant disease allele $K14^{R125C}$ together with K5 caused the formation of EBS-like cytoplasmic keratin aggregates. When ubiquitously expressed, $K14^{R125C}$/K5 flies show a semi-lethality, flightlessness and surviving adults can develop an EBS-like wing blister phenotype.

Thus, our novel *Drosophila* model will be of great value for identifying the biological pathways altered by mutant keratins and for the development of EBS therapy approaches.

➜ **Bohnekamp, Jens**
email: jens.bohnekamp@trm.uni-leipzig.de

POSTER 43

Thy-1 (CD 90) – a crucial surface marker controlling the balance between fibroblast proliferation and differentiation

Cell Biology

Schmidt M[1], Gutknecht D[1], Simon J[1], Anderegg U[1], Saalbach A[1]

1 Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Thy-1 (CD90) has been described as a cell-cell adhesion molecule mediating interaction of myeloid cells and melanoma cells to activated endothelial cells (ECs) but in contrast to ECs, Thy-1 is constitutively expressed on fibroblasts. In this study, we investigated the effect of Thy-1 expression on fibroblast proliferation and differentiation using skin fibroblasts from Thy-1 deficient and wild type mice. We demonstrate that a lack of Thy-1 resulted in a significantly higher proliferation rate and less apoptosis compared to wt fibroblasts. In contrast, wt fibroblasts displayed a more differentiated phenotype reflected by an enhanced ability to contract free-floating collagen lattices as well as an increased synthesis of the myofibroblast-specific marker alpha smooth muscle actin (αSMA) and ED-A fibronectin as well as collagen I + III. The increased proliferation of Thy-1$^{-/-}$ fibroblasts was completely abolished by seeding Thy-1$^{-/-}$ fibroblasts on immobilized recombinant Thy-1 protein. Moreover, this Thy-1 interaction with Thy-1$^{-/-}$ fibroblasts promotes the production of myofibroblast marker. Additionally, transfection of the human Thy-1$^{-/-}$ fibrosarcoma cells HT1080 with Thy-1 down-regulated proliferation and up-regulated apoptosis. During wound healing proliferation of dermal fibroblasts is a central key step. In full thickness wounds Thy-1 deficient mice revealed more proliferating cells compared to wt mice. We demonstrate here that these Thy-1 mediated effects on cell growth requires interaction with β3 integrins and are not restriced to fibroblasts but also to β3^{+} tumour cells by generating multicellular tumour spheroids.

➜ **Schmidt, Manuela**
email: manuela.schmidt@medizin.uni-leipzig.de

POSTER 44

Thermal instability of cell nuclei

Cell Biology

Warmt E[1]

1 Institut für Experimentelle Physik I, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

DNA is known to be a mechanically and thermally stable structure. In its doublestranded form it is densely packed within the cell nucleus and is thermo-resistantup to 70 °C. In contrast, we found a sudden loss of cell nuclei integrity atrelatively moderate temperatures ranging from 45 to 55 °C. In our study, suspended-cells held in an optical double beam trap were heated under controlledconditions while monitoring the nuclear shape. At specific critical temperatures,an irreversible sudden shape transition of the nuclei was observed. These temperatureinduced transitions differ in abundance and intensity for various normaland cancerous epithelial breast cells, which clearly characterizes different celltypes. Our results show that temperatures slightly higher than physiologicalconditions are able to induce instabilities of nuclear structures, eventuallyleading to cell death. This is a surprising finding since recent thermorheologicalcell studies have shown that cells have a lower viscosity and are thus moredeformable upon temperature increase. Since the nucleus is tightly coupled tothe outer cell shape via the cytoskeleton, the force propagation of nuclearreshaping to the cell membrane was investigated in combination with theapplication of cytoskeletal drugs.

→ **Warmt, Enrico**
email: enrico.warmt@uni-leipzig.de

POSTER 45

Euphrasia officinalis L.: Isolation of iridoids, their quantification by CE and effects on choroidal endothelial cells

Cell Biology

Liebold S[1], Hennig L[2], Rauwald H[1], Eichler W[3]

1 Institut für Pharmazie, Universität Leipzig
2 Institut für Organische Chemie, Universität Leipzig
3 Klinik und Poliklinik für Augenheilkunde, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The hemiparasite *Euphrasia officinalis* (Orobanchaceae) grows unattached or attached to various host plants in grasslands of Eurasia. Traditionally but not evidence based used for eye sufferings it is also known as eyebright. Typical active constituents beside phenolics (phenylethanoids, lignans, phenolic acids and flavonoids) are iridoids (aucubin, catalpol, euphroside, melampyroside, boschnaloside and others). Interestingly, the transfer of iridoids from the host plant to *Euphrasia* species was described, too [1]. Recently, we described the first isolation of the iridoid glucosides 8-epiloganin, gardoside methyl ester, ipolamiide, shanziside methyl ester and 5-deoxypulchelloside I from Euphrasiae herba using a practicable droplet counter-current chromatography (DCCC) [2, 3]. A modern MECC-method for quantification showed higher contens of the iridoid melampyroside in the drug and polar extracts. To explore the traditional usage of *E. officinalis* for vascular diseases of the eye MTT and BrdU assays with choroidal endothelial cells (bCEC) were performed.

References
1. Rasmussen, L. S. et al. (2006) Biochem. Syst. Ecol. 34: 763–765.
2. Strahler (Liebold), S. et al. (2010) Planta Medica 76: 1243.
3. Liebold, S. et al. (2011) Terpnet 2011: P84.

➜ **Liebold, Sabine**
email: sabine_liebold@gmx.de

POSTER 46

Growth inhibiting effect of the lignan prinsepiol isolated from Dipsacus sylvestris Huds against Borrelia burgdorferi s.s. in vitro

Cell Biology

Liebold T[1], Hennig L[2], Rauwald H[1], Lehmann J[3]

1 Institut für Pharmazie, Universität Leipzig
2 Institut für Organische Chemie, Universität Leipzig
3 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Borrelia burgdorferi sensu stricto is known for causing lyme borreliosis. To find alternative ways for curing this infection beside chemical antibiotics, extracts from plants are studied, too. As a first step an *in vitro* model can be used for antibacterial activity of the substances to be tested. For extracts and isolated compounds from *Dipsacus sylvestris* Huds. (Dipsacaceae) this technique was used. Only a few compounds of *D. sylv.* are known: iridoids like sweroside, loganin, cantleyoside and several sylvestrosides, phenolic acids, saponarin, fatty acids, mono- and disaccharides. Since antiquity *D. sylv.* has a variety of traditional usages such as a remedy against diseases of the skin, disorders of the digestive tract and of the joints. Nowadays the application of extracts from the root of *D. sylv.* against borreliosis in folk medicine was reported. Formerly, we investigated the effect of different extracts against the bacteria *B. burgd. in vitro*. To find the active compounds, several isolated substances from the most active fractions were tested, among them prinsepiol.

The lignan prinsepiol was gained from the dichloromethan fraction of a methanolic extract from the roots of *D. sylv.* The serial combination of two normal phase column chromatographies with different gradients lead to a crude sample, that had to be purified by thin layer chromatography. Its structure was established by spectroscopic evidence. Prinsepiol showed a strong growth inhibiting effect on *B. burgd. in vitro*, although it was not found to be cause for the full activity of the apolar extracts. Other compounds might be involved in this effect.

➜ **Liebold, Tobias**
email: tliebold@gmx.de

POSTER 47

Enhancing mesenchymal stem cell trafficking towards lesion sites

Cell Biology

Nitzsche F[1], Bosse I[2], Deten A[2]

1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Mesenchymal stem cells show great potential for the development of cell based therapies for neurodegenerative diseases. In clinical settings, systemic delivery of MSCs has several advantages and circumvents serious problems compared to site-directed transplantation. However, MSC homing and migration towards injured tissues is not yet satisfying after intravasal administration and need to be improved to enhance functional recovery. Thus, this study aimed to improve adhesion and migration of MSCs by engineering their surface receptor expression. Various vectors were designed for expression of integrin alpha 4 ([ITGA4] part of very late antigen 4 [VLA4]) and C-C-Motif Chemokine Receptor 2 (CCR2). Lentiviral constructs were driven by either CMV-, EF-1alpha or UbC promoter. Additional vectors contained a T7 promoter for RNA polymerase dependent *in vitro* synthesis of mRNA. Capping (ARCA, Cap-0, Cap-1) and poly-A tailing of the *in vitro* transcribed mRNA were performed for stabilization and effective translation after transfection. GFP-containing vectors served as controls. All control vectors showed efficient expression of GFP. Of note, however, only MSCs infected with UbC driven surface receptor constructs expressed the intended transgene. After mRNA transfection, on the other hand, detectable expression was achieved only from physiologically capped constructs, but not ARCA. Even more interesting, this difference was much less pronounced for GFP. Taken together, these data indicate that transgenic surface receptor expression depends on promoter activity in the target cell, but also correct mRNA and nascent protein processing.

→ **Nitzsche, Franziska**
email: franziska.nitzsche@izi.fraunhofer.de

POSTER 48

Liver Regeneration is Modulated by Microparticles Acting as Novel Carriers of Immunomodulatory MicroRNA

Cell Biology

Kuhn S[1], Splith K[1], Hegewald C[1], Robson S[2], Schmelzle M[1,3]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
2 The Transplant Institute and Division of Gastroenterology, Beth Israel Deaconess Medical Centre, Harvard University, Boston, MA, USA
3 Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

To understand and mimic stem cell reaction in liver regeneration is relevant to find alternative therapies in acute liver failure. Hematopoietic stem cell (HSC) associated liver regeneration is mainly defined by HSC derived microparticles (MP). These are small submicron vesicles ($\leq 1\mu m$) serving as distinct cell-specific carriers of e.g. microRNAs (miR). In liver failure, MP shedding and packaging is dependent on the purinergic signaling. Extracellular pro-inflammatory ATP is hydrolyzed to anti-inflammatory adenosine via the main ecto-enzymes CD39 and CD73. After liver injury, murine plasma MP are enriched in the immunomodulatory miR-142-3p when compared to mice lacking Cd39 or Cd73 ($p< 0.01$; $p< 0.001$). These mice are not able to completely degrade extracellular ATP to adenosine. *In vitro* studies using murine bone marrow derived mononuclear cells (MNC) show that stimulation with ATP leads to a significant lower miR-142-3p level in MP compared to untreated cells ($p< 0.01$). This effect is mediated by the P2X7 receptor. In contrast, stimulation with adenosine increases the miR-142-3p level. Human peripheral blood MNC (PBMNC) derived MP enriched in miR-142-3p are able to dock human HUVEC *in vitro*, preferentially fuse and transfer their miR. Experiments show a significant increase in the miR-142-3p level in HUVEC after coculture with MP derived from stimulated PBMNC ($p< 0.05$; $p< 0.001$). Subsequent transfection studies in HUVEC reveal a role for miR-142-3p in modulating the mRNA expression level of pro-inflammatory TNFα. Therefore, MP enriched in miR-142-3p seem to modulate vascular inflammation and promote liver regeneration.

➜ **Kuhn, Stephanie**
email: stephanie.kuhn@trm.uni-leipzig.de

POSTER 49

Mutation in NADH dehydrogenase subunit 2 leads to delayed fibroblast ageing

Cell Biology

Schauer M[1], Kottek T[1], Ibrahim S[2], Kunz M[1]

1 Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Universität Leipzig
2 Klinik für Dermatologie, Allergologie und Venerologie, Universität zu Lübeck

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Mitochondrial dysfunction of parts of the mitochondrial respiratory chain is suggested to contribute to organismal ageing. To analyze the influence of mutations in mitochondrial genes of the respiratory chain in the context of skin ageing we analyzed isolated skin fibroblasts of the mouse strain C57BL/6J-mt$^{ALR/LTJ}$ with a single nucleotide polymorphism (nt4738A) in the NADH dehydrogenase subunit 2 gene (Nd2-mutant) in complex I.

Skin fibroblasts of Nd2-mutant mice showed decreased ROS production, enhanced ATP levels and an enhanced proliferation rate compared with the control strain C57BL/6J-mt$^{AKR/J}$. Furthermore, the mutation in Nd2-mutant fibroblasts led to a higher complex I activity and reduced β-galactosidase activity (as an important senescence marker). Immunoblots showed a transient activation of the age-related marker p38α in Nd2-mutant mouse fibroblasts as compared with control fibroblasts. Pathway analysis revealed that the MAPK pathway is strongly involved in the mediation of reduced senescence effects of Nd2- mutant fibroblasts.

These results demonstrate an obvious reduction in senescence features in fibroblasts of mutant mice as compared with control mice. The investigation of life span is still ongoing. However, in humans it has been shown, that a single nucleotide polymorphism (C5178A) in the NADH dehydrogenase subunit 2 gene is associated with longevity in a Japanese population. Taken together, in the present report we identified a mitochondrial gene polymorphism that could be age-protective in mice and humans.

➜ **Schauer, Marianne**
email: marianne.schauer@medizin.uni-leipzig.de

POSTER 50

Regulation of energy metabolism in hepatocytes with induced steatosis.

Cell Biology

Schönefeld K[1], Matz-Soja M[1], Böttger J[1], Seibel P[2], Gebhardt R[1]

1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig
2 Molekulare Zelltherapie, Biotechnologisch-Biomedizinisches Zentrum (BBZ), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Mitochondria are cellular organelles involved in variety of metabolic pathways and important for ATP production. Based on our new findings the Hedgehog (Hh) signaling pathway is an active pathway in healthy mature hepatocytes with relevant impact on endocrine liver function and is involved in lipid metabolism [1,2]. In this study we explored the effects of nutritive induced steatosis in combination with hepatocyte-specific deletion of Hh signaling transcription factor Gli3 on the regulation of energy metabolism in mitochondria. For this analysis we used a transgenic mouse model with deletion of Gli3 (KO) and fed mice for four and ten weeks with control (CD) and high fat diet (HFD). To explore the endogenous respiration a Clark type oxygen electrode was used and the oxygen consumption was monitored. The ATP-level was determined by the CellTiter-Glo® Luminescent Cell Viability Assay. Furthermore, the activity of mitochondrial enzymes of respiratory chain complexes was assessed by photometric assays. The mRNA expression levels of selected complex subunits and genes encoded mitochondrial proteins were analysed by qrt-PCR. In general we could observe that hepatocytes from control mice fed with HFD show higher oxygen consumption than control mice fed with CD after ten weeks. Compared with wild type mice, hepatocytes from Gli3-KO mice fed with CD showed increased oxygen consumption after four and ten weeks, which is also true for Gli3-KO mice fed with HFD. Considering the ATP-level the results show that hepatocytes from control mice fed with HFD have decreased amount compared to control mice fed with CD. Referring Gli3-KO mice fed with CD we measured reduced ATP-amount compared to wild type mice after four and ten weeks. The same was true for Gli3-KO mice fed with HFD for four weeks. Interestingly, ATP-level in Gli3-KO mice fed with HFD for ten weeks was slightly increased compared to control mice. We could show that mice fed with HFD have altered mitochondrial functions characterized by higher oxygen consumption and lower ATP-level.

➜ **Schönefeld, Kristin**
email: kristin.schoenefeld@medizin.uni-leipzig.de

POSTER 51

Keratin isotypes control desmosome stability and hyperadhesion through PKCα

Cell Biology

Loschke F[1], Homberg M[1], Magin T[1]
1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The epidermis is a stratified epithelium in which the differentiation-specific expression and stable interaction of desmosomal components and the keratin cytoskeleton is necessary to protect against mechanical and other forms of stress. It is assumed that the composition of the keratin cytoskeleton and of desmosomes (Dsm) plays a major role in regulating adhesive strength in a context-dependent manner. In support, wounding, a setting characterized by decreased cell adhesion, is accompanied by expression of keratins K6/16/17 at the expense of K5/14 and K1/10. This allows cell migration required for wound closure. The significance of altered keratin expression for desmosomal adhesion is not well understood. We have shown that keratins regulate the maintenance of Dsm`s through restricting PKCα-mediated desmoplakin (DP) phosphorylation. Here, we addressed keratin isotype-specific functions by stable expression of K5/14 or K6/17 in keratinocytes lacking all keratins. This revealed that expression of K5/14 leads to stable Dsm's, whereas keratinocytes expressing K6/17 show elevated PKCα-mediated Dsm disassembly and destabilization of epithelial sheets. This suggests that expression of "wound healing" keratins weakens intercellular adhesion. To investigate how keratin isotypes regulate DP, we currently test the hypothesis that K5/14 sequester PKCα on filaments through the scaffold protein Rack1, whereas K6/17 or lack of all keratins allow PKCα-translocation to the membrane and induction of Dsm disassembly. Our data suggest that certain keratin isotypes promote wound healing and invasion by modulating intercellular adhesion.

➜ **Loschke, Fanny**
email: fanny.loschke@trm.uni-leipzig.de

POSTER 52

Extracellular matrix compositions and mechanics affects melanoma cell behavior in dependence on CD44 receptor presence

Cell Biology

Ullm F[1], Sapudom J[1], Martin S[1], Anderegg U[2], Pompe T[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The extracellular matrix (ECM) surrounding cancer cells is of dynamic composition and actively promotes tumor progression by providing biophysical and biochemical cues via direct binding of adhesion receptors. As one of these receptors the hyaluronan receptor CD44 is known to be involved in controlling tumor cell behavior.

To investigate the impact of different cues of the cellular microenvironments in correlation with proliferation and invasion of melanoma cells, RPM-MC cells with low-expressed (CD44-) and overexpressed (CD44+) CD44 receptors were cultivated on collagen matrices of defined mechanics, topology and composition for 4 days. Collagen matrices of different pore sizes were additionally crosslinked with EDC to enhance stiffness and were functionalized with fibronectin and GAGs. Cell proliferation was investigated by WST-1 assay. Cell invasion depth and nucleus size of migrating cells were determined by count of DAPI-stained cell using an automated quantitative image analysis tool. Furthermore, cell morphology and cell-matrix interactions were assessed after immunocytochemical staining using confocal laser scanning microscopy.

Our results suggest that collagen network topology and the presence of fibronectin and hyaluronan ligands influence viability and invasion of melanoma cells. RPM-MC CD44+ showed a lower viability and higher invasive distance compared to CD44- cells in stiffer collagen networks. In conclusion, we demonstrated the impact of ECM topology, mechanics and composition in dependence on CD44 receptor presence in regulating the behavior of melanoma cells.

➜ **Sapudom, Jiranuwat**
email: jiranuwat.sapudom@uni-leipzig.de

POSTER 53

Keratin-dependent regulation of the antioxidant transcription factor Nrf2

Cell Biology

Bouameur J[1,2], Kumar V[1,2], Bär J[1,2], Roop D[3], Honig-Do H[4], Roth W[5], Heller S[6], Thiering S[1,2], Schwartz N[7], Leube R[7], Wiesner R[4], Seibel P[6], Magin T[1,2]

1 Institut für Biologie, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
3 Department of Dermatology and Charles C. Gates Center for Regenerative Medicine and Stem Cell Biology, University of Colorado
4 Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), Medical Faculty, University of Cologne
5 German Center for Neurodegenerative Diseases, Bonn
6 Biotechnoligisch-Biomedizinisches Zentrum, Universität Leipzig
7 Institute of Molecular and Cellular Anatomy (MOCA), Aachen University

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The cytoskeleton of epidermal keratinocytes is formed from heterodimers of type I and type II keratins (KtyI and KtyII). They provide resilience against various stresses by interacting with cell junctions and by participating in epidermal barrier formation. To address the respective function of KtyI and KtyII during epidermal differentiation, barrier formation and stress responses, the entire gene clusters comprising 28 and 26 keratin genes, were deleted in two strains of mice.

Without keratins, the epidermis is very fragile and suffers from prenatal barrier defects in KtyII$^{-/-}$ and KtyI$^{-/-}$ embryos. Transcriptome profiling, in combination with proteomic analysis of isolated cornified envelopes (CEs), revealed keratin-dependent composition changes and dysfunction of CEs. The latter caused an upregulation of the antioxidant transcription factor Nrf2 and several of its target genes in the epidermis of keratin-deficient mice. Thus, keratins are essential for epidermal barrier function. Addressing the mechanism underlying Nrf2 upregulation, we established keratin-deficient keratinocytes. In these, we found elevated mitochondrial oxygen consumption, causing increased ROS levels, coinciding with misdistribution of mitochondria in the absence of keratins. Re-expression of keratins in keratin-deficient cells normalized this phenotype. Thus, a novel, cell-autonomous and keratin-dependent mechanism is involved in Nrf2 upregulation. We propose a model in which keratins control Nrf2 via mitochondria-derived oxidative stress, implying keratins control chronic inflammation in keratinocytes.

➜ **Bouameur, Jamal-Eddine**
email: jamal-eddine.bouameur@trm.uni-leipzig.de

POSTER 54

Characterisation of the role of the adhesion-GPCR latrophilin in fertility

Cell Biology

Fiedler F[1], Tretzschock J[1], Binder C[1], Schöneberg T[1], Prömel S[1]

1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Adhesion-G protein-coupled receptors (aGPCR) form the second largest group of GPCRs. However, little is known about their function and signalling pathways. They play essential roles in diverse biological processes and mutations in human aGPCRs are associated with diseases such as Usher Syndrome or Polymicrogyria rendering them interesting drug targets. Among the most conserved family members of aGPCRs are latrophilins. The *C. elegans* latrophilin homolog LAT-1 has implications in embryonic development and fertility. While the function of LAT-1 in embryogenesis is well understood its involvement in fertility of the self-fertilising hermaphrodite *C. elegans* is still unclear. Previous studies suggest that in *lat-1* null mutants sperm function is impaired hypothesised that LAT-1 plays a crucial role in sperm fertilisation or development.
To elucidate these possibilities we first studied *lat-1* expression in reproductive tissues using a transcriptional fluorescent *lat-1* reporter. Interestingly, we found no LAT-1 in mature sperm. However, strong *lat-1* expression in other tissues essential for fertility was detected implicating that LAT-1 mediates its effect on sperm via a different organ. First functional analyses using imaging as well as biochemical techniques show that *lat-1* null mutants have less sperm than wild type individuals. These results correspond to the observation that the total number of produced oocytes is similar in *lat-1*-deficient and wild type nematodes. These data are a first step towards an understanding of LAT-1 function in fertility suggesting that the receptor is required for proper sperm production.

→ **Fiedler, Franziska**
email: franziska.fiedler@medizin.uni-leipzig.de

POSTER 55

A novel signaling mechanism of the adhesion-GPCR latrophilin to mediate embryonic development in C. elegans

Cell Biology

Müller A[1], Tretzschock J[1], Fiedler F[1], Binder C[1], Hennig C[2], Schnabel R[2], Schöneberg T[1], Prömel S[1]

1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig
2 Institut für Genetik, Universität Braunschweig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Although adhesion-G protein-coupled receptors (aGPCR) are the second largest class of GPCRs and are involved in various essential biological processes, their functions and signaling mechanisms, especially in distinct biological contexts, are still poorly understood. We have previously shown that the highly conserved aGPCR latrophilin (LAT-1) in *C. elegans* is required for correct positioning of cell planes in the early embryo. However, the underlying molecular mechanisms of receptor function in this context remain elusive. We have used *in vitro* and *in vivo* approaches to clarify LAT-1 signaling in *C. elegans* embryogenesis. *In vitro* studies show that LAT-1 pathway is based on a classical G_s protein-mediated cascade via cAMP. The physiological relevance of this signal was shown *in vivo* by artificially complementing the signal in the absence of the receptor in a *C. elegans lat-1* null mutant implicating that the function of LAT-1 on a cellular level is mediated by cAMP potentially via a G_s protein/adenylyl cyclase/cAMP pathway. We found that to mediate this cascade, LAT-1 is activated by an internal peptide sequence. Upon activation by this tethered agonist LAT-1 triggers the cAMP-dependent signal mediating correct embryonic cell division plane orientations. In summary, we have identified a signaling pathway of the aGPCR LAT-1, linking its biological function in cell division plane orientation in the early *C. elegans* embryo to a signal on a cellular level.

Funding: formel1

→ **Müller, Antje**
email: antje.mueller2@medizin.uni-leipzig.de

POSTER 56

Establishment and preliminary characterisation of a bovine SV40 large T-antigen-transduced hepatocyte-derived cell line

Cell Biology

Gleich A[1], Schöniger A[1], Fuhrmann H[1]
1 Veterinär-Physiologisch-Chemisches Institut, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Due to distinct differences in cytochrome P450 systems between ruminants and other species and lack of reliable *in vitro* models for bovine liver metabolism, there is great demand for a bovine hepatocyte-like cell line.Transduction of bovine foetal hepatocytes with SV40 large T-antigen (SV40LTAg) was performed by using the vector pRetro-E2 SV40. For evaluation of morphology, phase contrast microscopy was carried out routinely. Immunofluorescent staining (IF) was conducted to attest expression of keratins, tight junction proteins zona occludens-1 (ZO-1) and claudin-1 (CLDN1) and transporters glucose transporter-2 (GLUT2) and P-glycoprotein (Pgp). Urea and triglyceride production was quantified by UV-Vis spectroscopy. Histochemical staining of glycogen by Periodic-acid-Schiff (PAS/D) stain and of lipids with Oil red O were performed after 24h incubation with 20 mM glucose and 100 μM palmitic acid, respectively.We obtained a SV40LTAg-transduced extended passage cell line, referred to as BFH12. This cell line possesses a hepatocyte-like phenotype: polygonal growth; keratins, tight junction proteins ZO-1 and CLDN1 and transporters GLUT2 and Pgp were attested by IF. Urea production calculated as cell-specific rate was 14.2±2.0 fmol/h (early passage) and 17.6±3.7 fmol/h (late passage). Cell-specific triglyceride rate was 1.6±0.5 fmol/h (early passage) and 2.1±0.3 fmol/h (late passage). Additionally, cells were positive for glycogen and lipid content.Summarising, since BFH12 shows a hepatocyte-like phenotype and metabolic performance, it might be usable as *in vitro* model of bovine liver metabolism.

➜ **Gleich, Alexander**
email: alexander.gleich@vetmed.uni-leipzig.de

POSTER 57

Sex specific differences in alveolar sodium absorption – role of male and female sex steroids

Cell Biology

Haase M[1], Laube M[1], Thome U[1]

1 Abteilung für Neonatologie, Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

One of the most frequent complications in preterms, the respiratory distress syndrome (RDS), exhibits a sex-related difference in its incidence and morbidity. In addition to the contribution of surfactant, fluid clearance across the alveolar epithelia is crucial for prevention of RDS and is facilitated by the epithelial Na^+ channel (ENaC) and the Na,K-ATPases. To determine sex specific differences, we used rat fetal distal lung epithelial (FDLE) cells, separated by sex. Previous studies demonstrated that female-derived FDLE cells exhibit an increased basal, amiloride- and ouabain-sensitive short-circuit current in Ussing camber analysis, confirming an increased ENaC and Na,K-ATPases activity in females. In addition, the level of female sex steroid receptor transcripts was higher in female cells. To elucidate responsible mechanisms, the effect of sex steroids was studied. FDLE cells cultured in serum-free (SF) media showed an increased Na^+ transport and also lacked the sex-specific difference observed in serum-supplemented media. Androgens added to SF medium caused a decreased Na^+ transport in male-derived FDLE cells, whereas female cells were not affected. In contrast, SF medium with estradiol and progesterone resulted in an increased Na^+ transport in female FDLE cells. Male FDLE cells were not stimulated by female sex steroids. In conclusion, a decreased alveolar Na^+ transport in males, attributable to an inhibiting influence of male hormones, and an increased Na^+ transport in female FDLE cells, due to a stimulating effect of female sex steroids, might explain the sex-related differences in RDS occurrence and outcome.

→ **Haase, Melanie**
email: melanie.haase@medizin.uni-leipzig.de

POSTER 58

Serine protease inhibitor vaspin activates insulin signalling pathways in stably transfected 3T3-L1 cells

Cell Biology

Zieger K[1], Krause K[2], Kovacs P[3], Stumvoll M[2,3], Blüher M[2,3], Heiker J[1,2]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
3 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Vaspin (serpinA12) is an adipokine with glucose-lowering and anorexic effects acting in the periphery. Published data on cellular effects of vaspin is rather limited and focused on diabetes associated cardio-vascular disease. In adipose tissue, vaspin was reported to potentially exert anti-inflammatory effects due to inhibition of pro-inflammatory adipocytokine expression, e.g. resistin and TNF-α, and vice versa TNF-α induces reduction of vaspin expression in 3T3-L1 adipocytes during differentiation (reviewed in Heiker JT, 2014, J Pept Sci). Nevertheless, distinct direct effects and underlying molecular mechanisms of vaspin on adipocytes, e.g. adipogenesis, adipocyte differentiation and adipose tissue function remain unknown.

In our stably vaspin-transfected 3T3-L1 cells, vaspin mRNA and protein expression is significantly higher in comparison to control native cells and expression of differentiation markers (*Ppar γ*, *aP2*, *adiponectin*) and lipid accumulation during differentiation is slightly increased. Furthermore we found first evidence, that vaspin overexpressing 3T3-L1 cells exhibit significantly higher expression levels for different brown or beige adipose tissue specific genes. We found altered phosphorylation states of several intracellular proteins involved in the intracellular AKT signaling cascade comparing native 3T3-L1 and vaspin overexpressing 3T3-L1 cells.

We have established an adipocyte cell line to study vaspin function *in vitro* which shows a modified activation status of different proteins which are involved in the insulin signaling pathway.

➜ **Zieger, Konstanze**
email: konstanze.zieger@uni-leipzig.de

POSTER 59

Extracellular matrix assembly at the apical cell surface controls cuticle maturation.

Cell Biology

Pesch Y[1], Behr M[1]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Epidermal cells secrete proteins and enzymes that assemble at the apical cell surface to provide epithelial integrity and stability during developmental growth and upon tissue damage. In all arthropods organization of apical extracellular-matrix aECM is crucial for survival, but underlying molecular mechanisms remain poorly understood. We analyzed molecular mechanisms of aECM assembly and identified the conserved chitin-binding protein Obstructor (Obst)-A as an essential regulator. Obst-A is enriched specifically at the apical cell surface within the apical assembly zone where matrix components start to form a first extracellular barrier. In contrast, *obst-A* null mutant larvae lack the assembly zone resulting in severe disturbance of normal matrix-scaffold organization and impaired aECM integrity. Furthermore, enzymes that support aECM maturation and stability are mislocalized in *obst-A* mutants. As a biological consequence, cuticle architecture, integrity and barrier function are disturbed in *obst-A* mutants resulting in dehydration and lethality upon wounding. Our studies identify a new core-organizing center, the assembly zone that controls aECM assembly at the apical cell surface. We propose a genetically conserved molecular mechanism by which Obst-A forms a matrix-scaffold to coordinate trafficking and localization of proteins and enzymes in the newly deposited aECM. This mechanism is essential to mature and stabilize the aECM in a growing and remodeling epithelial tissue as an outermost barrier.

➜ **Pesch, Yanina-Yasmin**
email: yanina.pesch@gmail.com

POSTER 60

Pigment Epithelium-Derived Factor of Glial Origin enhances Survival of Retinal Ganglion Cells through Activation of NFκB and STAT3 Pathways

Cell Biology

Savkovic-Cvijic H[1], Eichler W[1], Unterlauft J[1]
1 Klinik und Poliklinik für Augenheilkunde, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Purpose: Retinal neurodegeneration secondary to diabetic and hypertensive retinopathy and glaucoma leads to irreversible loss of vision and is among the leading causes of blindness worldwide. Our purpose was to show that pigment epithelium-derived factor (PEDF), secreted by Müller glial cells (MGC) exerts neuroprotective and neurotrophic actions towards retinal ganglion cells (RGC) and which pathways are therefore activated.
Methods: Homotypic and co-culture experiments using immunoisolated primary RGC and cultured Müller glial cells were conducted for 24h under normoxic (95% air; 5% CO_2) and hypoxic conditions (0% O_2; 5% CO_2; 95% N_2). PEDF was either substituted to homotypic RGC cultures or depleted from RGC/MGC co-cultures. NF-κB and STAT3-pathways were inhibited using antibodies in homotypic RGC and RGC/MGC co-cultures.
Results: After 24h of normoxic treatment RGC survival was 54.04±0.03% in homotypic and 68.52±0.03% in co-cultures. Corresponding hypoxic survival was 32.84±0.02% in homotypic and 44.83±0.02% in co-cultures. Supplementing PEDF in homotypic RGC cultures led to a significant increase, depletion of PEDF in RGC/MGC co-cultures led to a significant decrease of RGC survival under normoxic and hypoxic conditions. Inhibition of NF-κB and STAT3-pathways led to a significant decrease of survival of RGC in co-cultures which was comparable to results found in homotypic RGC cultures.
Conclusion: Glia-derived PEDF exerts neuroprotective/neurotrophic actions towards RGC in cell culture. Further experiments are needed to reveal the underlying mode of action and to prove the effectiveness of PEDF in a mammalian model.

Funding: formel1

→ **Unterlauft, Jan**
email: jandarius.unterlauft@medizin.uni-leipzig.de

POSTER 61

Comparison of two dominant keratin disease mutations reveals distinct effects on cell-cell adhesion and keratinocyte stiffness

Cell Biology

Homberg M[1,2], Kumar V[1], Ramms L[1], Hoffmann B[1], Magin T[1,2]

1 Institut für Biologie, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Keratins (K) form the major epidermal cytoskeleton from heterodimers of type I and type II keratin subunits. Missense mutations in K5 or K14, highly expressed in the basal epidermis, cause the severe skin blistering disease Epidermolysis bullosa simplex (EBS) by rendering the keratin cytoskeleton sensitive to mechanical stress. The mechanisms by which individual mutations cause cell fragility and squamous cell carcinoma in rare cases are incompletely understood.

To analyze two keratin mutations giving rise to severe but distinctly different entities of EBS, corresponding cDNAs were stably expressed in separate keratin-free keratinocyte cell lines by lentiviral transduction. The mutant proteins had distinct effects on keratin cytoskeletal organization, in agreement with *in vivo* observations, thus validating the cell system. Further, the K14R131P mutation led to highly impaired desmosome formation and weakened epithelial sheet integrity upon shear stress, while the K5E471D mutation did not impact these respective functions. Moreover, atomic force microscopy (AFM) showed impaired mechanical properties of K14R131P cells compared to control cells without keratins. Thus, expression of mutant keratins compromises cell stiffness and integrity to a greater extent than the lack of keratins. Coexpression of wildtype K14 in K14R131P cells failed to improve the above phenotypes, underscoring the dominant negative nature of this mutation. Taken together, these results imply that unlike previously thought, EBS partially results from a gain of toxic function. Our findings have implications for EBS therapy approaches.

→ **Homberg, Melanie**
email: melanie.homberg@trm.uni-leipzig.de

POSTER 62

Different selective Antagonists are Recognized by Transmembrane Helix 2 and 7 of the Human Y2 Receptor

Cell Biology

Burkert K[1], Mittapalli G[1,2], Roberts E[1,2], Beck-Sickinger AG[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 Department of Chemistry, The Scripps Research Institute, USA

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The human Y_2-receptor (hY_2R) is one out of four human neuropeptide Y (NPY) receptor subtypes named hY_1R, hY_2R, hY_4R, hY_5R. This receptor family belongs to the G protein coupled receptors (GPCR) and activates G_i or G_0 proteins. The hY_2R consists of 381 amino acids and binds three different ligands with different affinities: neuropeptide Y, peptide YY (PYY) and pancreatic polypeptide (PP). It is involved in angiogenesis, appetite regulation, bone formation, and the regulation of the circadian rhythm. In various tumor tissues the hY_2R is overexpressed and promotes tumor growth and vascularization. Therefore, the hY_2R has great therapeutic potential and antagonists could represent promising drugs for the treatment of neuroblastoma or glioblastoma.

In this study the interaction of BIIE0246, compound 40 and compound 46 at the hY_2R are characterized in more detail. Therefore receptor mutants were generated and the proteins were tested for signal transduction by inositol phosphate accumulation assay in presence of pNPY and pNPY/antagonist. All receptor variants were localized in the cell membrane comparable to the wild type hY_2R as demonstrated by fluorescence microscopy. Preliminary results showed that the replacement of residues in transmembrane helix 2 and 7 reduces the activity of pNPY and all antagonists. Variation of $Q^{6.55}$ however, reduced antagonistic activity for BIIE0246, compound 40 and compound 46. Our data suggest specific binding modes for hY_2R agonists and antagonists, which opens up the possibility for the development of selective drugs.

➜ **Burkert, Kerstin**
email: kerstin.burkert@uni-leipzig.de

POSTER 63

Neue Aspekte der Regulation des Lipidmetabolismus während der Entstehung von NAFDL

Cell Biology

Marbach E[1], Thiel C[1], Böttger J[1], Matz-Soja M[1], Arnold K[1], Sales S[2], Shevchenko A[2], Gebhardt R[1]

1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig
2 Max-Planck-Institut für molekulare Zellbiologie und Genetik, Dresden

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In der westlichen Überflussgesellschaft tritt die nicht alkoholinduzierte Fettlebererkrankung immer häufiger als Diagnose auf. Als Ursache für die Entstehung der NAFLD wird die Dysbalance zwischen Kalorienzufuhr und -verbrauch genannt, wobei die konkreten Mechanismen nicht bekannt sind und der Einfluss nutritiver Faktoren und deren Auswirkung auf Lebermetabolismus weiterer Charakterisierung bedürfen. Mit diesem Ziel vor Augen wurde eine Studie gestartet, die am murinen Model durch fettreiche Diät die Entstehung einer reversiblen Lebersteatose auf der Ebene der Lipidoms charakterisieren soll. Besonders ist, dass die Untersuchungen unter dem Aspekt der circadianen Regulation, vergleichend für beide Geschlechter, durchgeführt wurden. Hierzu wurde den C57BL/6-N Mäusen über einen Zeitraum von 4 bzw. 10 Wochen eine Hochfett-Diät mit einem Rohfettanteil von ca. 42% verabreicht. Nach Beendigung der entsprechenden Diät-Periode wurden die Hepatozyten zu zwei Tageszeitpunkten isoliert und den Analysen unterzogen. Als Folge der HFD wurden geschlechter-speifische Unterschiede der circadianen Regulation des Lipidmetabolismus festgestellt. Zunahme der Triglyceride und Cholesterinester zeigten eine ausgeprägte Tagesrhythmik, die bei Männchen invers zu der bei Weibchen verlief. Nach 10 Wochen HFD erfolgte bei Männchen eine Angleichung des Rhythmus an den der Weibchen. Durch weitere Analysen wird derzeit untersucht, ob dieses Phänomen als Folge einer fortscheitenden „Femininisierung" der Männchen unter dem Einfluss der HFD gedeutet werden kann. Die erlangten Erkenntnisse befähigen zu neuen Denkanstößen bezüglich der Entstehung von NAFLD.

→ **Marbach , Eugenia**
email: eugenia.marbach@medizin.uni-leipzig.de

POSTER 64

Keratin-depedent actin organization and MRTF-A nuclear translocation

Cell Biology

Czogalla R[1,2], Loschke F[1,2], Magin T[1,2]

1 Institut für Biologie, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The coordinated interaction of keratins, actin and microbules is crucial for many cellular processes including control of signal transduction and transcription. Actin regulates the intracellular distribution of the mechano-sensitive transcription of myocardin related transcription factor – A (MRTF-A) which is sequestered in the cytosol by G-actin binding. Increased actin polymerization releases MRTF-A, enabling nuclear translocation in order to activate transcription of a large number of target genes involved in control of actin and mediating stress responses. To which extent keratins, which form the major cytoskeleton of all epithelial cells and tissue, affect actin organization and possible actin functions, remains unknown. We have recently shown that adhesive, migratory and invasive properties of keratinocytes are strongly influenced by the keratin composition of keratinocytes. This has led to the hypothesis that keratins affect cell properties partially through modulating actin, either indirectly through upstream actin regulators including Rac/Rho as well as through affecting the G-F actin ratio. Therefore, we investigated the G-F actin ratio in keratinocyte cell lines lacking all keratins compared to WT controls. This revealed a decrease in G-actin in the absence of keratins. To investigate functional consequences, we asked whether actin-organization and MRFT-A nuclear translocation were altered by analyzing the kinetics of nuclear MRTF-A translocation. This showed an increased nuclear MRTF-A translocation in keratin-deficient cells. Our data indicate that keratins partially act through actin reorganization.

➜ **Czogalla, Rebekka**
email: rebekka.czogalla@trm.uni-leipzig.de

POSTER 65

The influence of Polyunsaturated fatty acids on phospholipids in lipid rafts

Cell Biology

Hellwing C[1], Fuhrmann H[2], Schumann J[1]

1 Universitätsklinik für Anästhesiologie und operative Intensivmedizin, Universität Halle-Wittenberg
2 Veterinär-Physiologisch-Chemisches Institut, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Polyunsaturated fatty acids (PUFA) have a beneficial impact on health-related processes, e.g. inflammation and immune response. Previous results of our group have demonstrated that supplementation of macrophages with PUFA leads to reduced levels of pro-inflammatory cytokines and attenuates NF-κB activity as well as macrophage respiratory burst. Further studies of our working group revealed that lipidrafts can be enriched in unsaturated fatty acids by supplementation of cells with PUFA.

There is some evidence that the phospholipid composition plays a crucial role in modulating inflammatoryprocesses. Therefore the aim of this study is to elucidate the effects of PUFA on phospholipid patterns in lipid rafts of murine macrophages.

RAW264.7 cells were cultured for 72 h in medium containing 15 μM alpha-linolenic acid (LNA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), linoleic acid (LA) or arachidonic acid (AA), while unsupplemented cells served as control. Cells were harvested and lysed by syringe passage in ice-cold lysis buffer. Lipid raft and non-raft domains were isolated by a detergent-free density gradient method. The fractions were collected and analysed for total protein content by bradford assay. Cholesterol levels were determined by COD-PAP method. The phospholipid composition was analysed using mass spectometry by our collaboration partner in Helsinki.

We expect this study to reveal a PUFA-mediated shift in the phospholipid pattern of lipid rafts. This for the first time will give new insights into how PUFA affect membrane properties thereby contributing to anti-inflammatory processes.

➜ **Hellwing, Christine**
email: christine.hellwing@uni-leipzig.de

POSTER 66

Cell cycle-dependent transcription of the H2A.X histone gene

Cell Biology

Binder L[1], Engeland K[1], Müller G[1]
1 Molekulare Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Packaging of DNA in the eukaryotic nucleus is important for the regulation of many cellular mechanisms like gene expression. Histones are central to these mechanisms and constitute the most evolutionary conserved proteins in eukaryotes. Some histones like H2A.X are found to be mutated in different types of cancer. In contrast to other histones, H2A.X plays a central role in DNA repair and is expressed independently of replication. Furthermore, gene and mRNA structures are different from replication-dependent histones. Here, we provide novel insights in the transcriptional regulation of this unique histone gene. We observed that *H2A.X* mRNA is expressed in a cell cycle-dependent manner with a maximum in G2 and M phases. This expression pattern stands in contrast to former observations that *H2A.X* is expressed independently of the cell cycle and underlines its unique role under the histones which are usually expressed in S phase. We also discovered two CHR (cell cycle genes homology region) elements necessary for cell cycle-dependent activation of the *H2A.X* promoter and the proteins binding to these elements. In G_0 and G_1 phases the multiprotein complex DREAM binds to the CHR elements of *H2A.X*. We hypothesize that there is an evolutionary conserved safety system, which allows *H2A.X* to be activated in the late phases of the cell cycle, even if one of the CHRs is mutated. In this model, the remaining CHR could compensate for the mutated element, which would represent a novel mechanism in the regulation of cell cycle genes through CHRs.

→ **Binder, Lars**
email: lars.binder@medizin.uni-leipzig.de

POSTER 67

MicroRNA-21 increases M-CSF-Receptor expression during PMA induced myeloid differentiation of U937 cells

Cell Biology

Gerloff D[1], Wurm A[1], Niederwieser D[1], Behre G[1]

1 Abteilung für Hämatologie und Internistische Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction: MicroRNAs (miRs) are important mediators of myeloid differentiation and leukemia development. MiR-21 was shown to be oncogenic in serveral solid tumors. Contrary, it was identified to be up-regulated during Phorbol 12-myristate 13-acetate (PMA) stimulated monocytic differentiation of HL60 cells. In this study, we could confirm these findings in PMA mediated monocytic differentiation of U937 cells. Furthermore, we could show that miR-21 expression affects induction of monocytic marker M-CSF-R (Macrophage Colony Stimulating Factor Receptor).

Results: In microarray analysis, we found several differentially expressed miRNAs after PMA treatment of U937 cells. We confirmed our data by qRT-PCR and identified miR-21 as an up-regulated miRNA during PMA induced myeloid differentiation. In *in silico* analysis, we identified *SKI* as a putative target of miR-21. We could show that miR-21 and SKI expression correlate inversely during myeloid differentiation. SKI is a well known inhibitor of M-CSF-R transcriptional activation. In further analysis, we could show that miR-21 overexpression enhances the M-CSF-R expression of PMA stimulated U937 cells. In contrast to this, LNA mediated knockdown of miR-21 reduces the expression of M-CSF-R. Finally, we found that overexpression of myeloid transcription factor PU.1 induces miR-21 expression.

Conclusion: In our study, we reveal that miR-21 expression is enhanced during PMA induced myeloid differentiation. We hypothesize that miR-21 is essential for PU.1 to induce M-CSF-R expression by targeting SKI. Thus, miR-21 is an important member of the myeloid differentiation machinery.

➜ **Wurm, Alexander**
email: alexander.wurm@medizin.uni-leipzig.de

POSTER 68 Activated apoptotic cascades in spermatozoa – mechanisms and consequences

Cell Biology

Springsguth C[1], Fitzl G[1,2], Paasch U[1], Grunewald S[1]

1 Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Universität Leipzig
2 Institut für Anatomie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

There is a fundamental body of evidence that induced apoptotic signalling in ejaculated human sperm influences the fertilisation potential negatively. However, it is still controversially discussed whether this apoptosis signalling is a relict of an abortive apoptotic process related to spermatogenesis or it should be regarded as a functional pathway in matured sperm leading to stereotypical morphological changes reflecting nuclear disassemble. To address this question apoptosis has been induced by calcium ionophore, thapsigargin and betulinic acid in mature ejaculated human sperm enriched by density gradient centrifugation and execution of apoptosis has been followed up by observation of ultra morphological changes using electron microscopy. The signalling pathway was monitored by measuring acrosome reaction (CD46), mitochondrial membrane potential disruption (JC1), caspase 9 and 3 activation, and fragmentation of DNA (TUNEL). As a result the simultaneous presence of typical ultra-morphological changes and molecular signalling of apoptosis as triggered by its inducers has been demonstrated. Electron microscopy revealed typical fragmentation of sperm nuclei, bleb formation and mitochondrial damage. Interestingly acrosomes were in the majority of investigated cells absent indicating a fully developed acrosome reaction in response to apoptotic stimuli. In relation to apoptosis induction acrosome reaction, disruption of JC1, caspase activation and TUNEL positivity could be visualized. Taken together the results of our study confirm the functional competence of the apoptotic signalling pathway in mature ejaculated human sperm.

➜ **Springsguth, Christopher**
email: christopher.springsguth@medizin.uni-leipzig.de

POSTER 69

Gegenseitige Beeinflussung des Hedgehog Signalweg und lipogener Transkriptionsfaktoren in der adulten Leber

Cell Biology

Arnold K[1], Matz-Soja M[1], Aleithe S[1], Gebhardt R[1]
1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Morphogene Signalwege, wie z. B. der Hedgehog (Hh) Signalweg, spielen eine entscheidende Rolle während der Embryo- und Organogenese. Seit einiger Zeit ist bekannt, dass diese auch in adulten Organen vorkommen, auch wenn sie dort eine geringere Aktivität aufweisen. Kürzlich haben wir die Hypothese erstellt, dass der Hh ein Hauptregulator des Lipidstoffwechsels der Leber ist (Matz-Soja *et al.* 2013). Die Regulation der Lipidhomöostase wird weiterhin im Wesentlichen durch die Expression von lipogenen Transkriptionsfaktoren (TFs) gesteuert, wobei Peroxisomen Proliferations-aktivierten Rezeptoren (PPARs) eine zentrale Rolle einnehmen. Diese Ausgangssituation veranlasste uns die gegenseitige Beeinflussung des Hh- und Ppar-Signaling in der murinen adulten Leber zu untersuchen.
Erste Hinweise erhielten wir durch unser konditionelles transgenes Mausmodel, in dem die Hh Signalkaskade durch einen Smoothened (Smo)-KO unterbrochen ist (Matz-Soja *et al.* 2014). Anschließende RNAi Experimente wurden durchgeführt um Komponenten beider Signalwege zu inhibieren. RNA der Zellen wurde nach 24–72 h Inkubation isoliert und für qRT-PCR-Analysen verwendet. Die erhaltenen Ergebnisse lassen vermuten, dass eine gegenseitige Regulation der beiden Signalwege besteht. In derzeitigen Experimenten versuchen wir herauszufinden, ob es sich um eine direkte oder indirekte Beziehung handelt.

➜ **Arnold, Katrin**
email: katrin.arnold@medizin.uni-leipzig.de

POSTER 70

Chemosensitization of leukemia cells through inhibition of NAMPT

Cell Biology

Gorski T[1], Petzold-Quinque S[1], Richter S[1], Schuster S[1], Penke M[1], Kiess W[1], Garten A[1]

1 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

NAMPT (Nicotinamide phosphoribosyltransferase) catalyzes the rate-limiting step in the NAD-biosynthesis from nicotinamide and regulates the activity of NAD-dependent enzymes. Cancer cells are highly dependent on NAD for energy and DNA repair processes and are expected to be more susceptible to the inhibition of NAD synthesis than non-transformed cells. Can inhibition of NAMPT by FK866 sensitise leukemia cells for chemotherapeutic agents?
NAMPT expression and enzymatic activity was significantly higher in leukemia cell lines compared to normal PBMCs. Incubation with FK866 [10nM] for 24h reduced NAMPT activity by 91.1±3.6% in Jurkat cells and by 97.8±1.2% in Molt-4 cells. NAD levels were reduced by FK866 by 83.9±1.0% (Jurkat) or 79.2±2.8% (Molt-4). The combination of etoposide and FK866 caused increased cell death compared to each substance alone. Apoptosis induction as measured by caspase-3 and -7 activation was not further increased by the addition of FK866 to etoposide. Interestingly, etoposide decreased the expression of the NAD-dependent deacetylases Sirtuin1 and Sirtuin2. The acetylation of the Sirtuin1 target p53 was enhanced after combining etoposide with FK866, which was confirmed by an increased expression of p21. In contrast, acetylation of the Sirtuin2 target α-tubulin was decreased.
The combination of etoposide and FK866 caused increased cell death which was not caspase-mediated, but induced acetylation and transcriptional activity of p53. Combining FK866 and etoposide could therefore be a novel therapeutic strategy to enhance the efficacy of etoposide against leukemia cells.

➜ **Gorski, Theresa**
email: theresa.gorski@medizin.uni-leipzig.de

POSTER 71

FK866-induced NAD Depletion Leads to AMPK Activation and Inhibition of mTOR Signalling in human hepatoma cells

Cell Biology

Schuster S[1], Penke M[1], Gorski T[1], Richter S[1], deGiorgis T[1], Kiess W[1], Garten A[1]

1 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

NAMPT (Nicotinamide phosphoribosyltransferase) is the key enzyme in the NAD-biosynthesis starting from nicotinamide. Tumor cells have a high energy demand due to their high proliferation rate and have a high rate of NAD turnover making them more susceptible to NAMPT inhibition than normal cells. Here, we investigated the effects of NAMPT inhibition by its inhibitor FK866 on human hepatoma cells to elucidate its effects on the nutrient sensing metabolic regulator AMPK and mTOR signalling.

NAMPT activity was significantly decreased in all tested hepatoma cell lines after 24h treatment with FK866 [10nM] which caused a sharp decline of intracellular NAD levels. Already after 24h, a decreased cell proliferation was noted (HepG2 cells -29%, Huh7 cells -49%, Hep3B cells -21%). A significantly increased phosphorylation of AMPKα (Thr172) (+3-fold) was found in cells treated with FK866 for 48h. This was associated with a decrease of phosphorylation of mTOR (Ser2448) by -51% and its down-stream target p70S6 kinase (by -95%). The administration of NMN [500μM] was able to completely reverse the FK866-induced effects on AMPK activation and mTOR signalling. We also found that FK866 treated cells showed a significantly increased mRNA expression of PGC1α, a major integrator of transcriptional responses to nutrient stress.

NAMPT inhibition by FK866 induces energy stress in human hepatoma cells by depleting intracellular NAD levels which leads to growth inhibition and activation of the metabolic sensor AMPK. Taken together, these novel findings reveal an important role for NAMPT inhibitors in finding more effective liver cancer therapies.

➜ **Schuster, Susanne**
email: susanne.schuster@medizin.uni-leipzig.de

POSTER 72

Keratin-dependent regulation of the proinflammatory cytokine TSLP in keratinocytes

Cell Biology

Scheffschick A[1], Behr M[1], Kumar V[1], Homberg M[1], Magin T[1]
1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Atopic diseases such as atopic dermatitis and asthma result from barrier defects leading to modified immune responses in combination with exogenous and endogenous factors. The cytokine thymic stromal lymphopoietin (TSLP), mainly produced in keratinocytes, is implicated in the pathogenesis of atopic diseases and leads to activation of dentritic cells and T helper type 2 cell responses. The mechanisms regulating TSLP expression in patients suffering from atopic dermatitis are poorly known.
Here we identify elevated TSLP levels in the prenatal epidermis and in the serum of keratin knockout mouse mutants. Furthermore, we uncover a novel, cell-autonomous mechanism responsible for highly increased TSLP levels in primary mouse keratinocytes lacking all keratins or expressing a dominant keratin mutant causing epidermolysis bullosa simplex in humans. Re-expression of keratins decreased TSLP in keratinocytes. Additional data suggest a molecular scenario in which keratins control phospholipase C and calcium signaling leading to NFkB and AP-1 transcriptional regulation of TSLP. We therefore hypothesize that TSLP induction results from keratin-dependent mechanisms. Of note, we detected significantly increased TSLP protein levels in the skin of epidermolysis bullosa simplex patients, a genetic skin disease resulting from keratin missense mutations. The elucidation of keratin-mediated TSLP expression mechanisms will offer new opportunities for genetic and drug target studies in clinically relevant atopic diseases. Our data provide the first genetic link between cytoskeletal keratins and TSLP gene activity in epidermal cells.

➜ **Scheffschick, Andrea**
email: andrea.scheffschick@trm.uni-leipzig.de

POSTER 73

Overexpression of DPP10a in rat ventricular cardiomyocytes affects properties of the transient outward current Ito

Cell Biology

Metzner K[1], Schaefer M[1], Kämmerer S[1]

1 Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The transient outward potassium current (I_{to}) underlies the early repolarization phase of cardiac action potentials. In patients with heart failure, I_{to} is dramatically reduced due to the down-regulation of the channel subunits Kv4.3 and KChIP2, contributing to ventricular arrhythmias. In contrast, the transmembrane β-subunit dipeptidylpeptidase-like protein 10a (DPP10a) is up-regulated in heart failure. The DPP10a interaction with Kv4.3/KChIP2 channels is well characterized in CHO cells, resulting in higher current amplitudes, accelerated activation and inactivation and shifted voltage dependence. Here, we have studied whether DPP10a overexpression in rat ventricular myocytes exerts similar effects on native I_{to}. To this end, cardiomyocytes were obtained from adult rats. Isolated cells were infected with adenovirally encoded DPP10a and cultured for 24-72h. DPP10a expression was increased at all time points investigated, as determined by immunoblotting. In electrophysiological experiments, significant increases in peak and late K^+ current densities compared to control-infected cells were detectable 48 hours after the infection, indicating an impact of DPP10a on newly formed but not pre-existing Kv4.3-bearing channel complexes. Like in CHO cells, DPP10a expression in rat cardiomyocytes also shifted potentials of steady-state inactivation to more negative values. Thus, DPP10 modulates native cardiac I_{to} with respect to channel availability, current amplitudes and kinetic properties. Ongoing work focuses on the role of increased DPP10a expression on I_{to} in animal models of heart failure.

➜ **Metzner, Katharina**
email: katharina.metzner@medizin.uni-leipzig.de

POSTER 74

The transcriptional regulation of Cyclin F is mediated through two conserved CHR sites

Cell Biology

Castillo Schwennicke P[1], Engeland K[1], Müller G[1]

1 Molekulare Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Cyclins and cyclin-dependent kinases (CDKs) are known as key regulators of the cell cycle. Interestingly, Cyclin F has a unique role in the cyclin family as it is not a regulatory subunit of a cyclin-dependent kinase. Instead, Cyclin F as the founding member of the F-box family plays an important role in cell cycle control following DNA damage by serving as an SCF-ubiquitin ligase. These observations make Cyclin F an interesting target for cancer research. Here we show how the gene expression of *Cyclin F* is controlled during the cell cycle.

Gene expression of late cell cycle genes with maximal expression and function in G_2- or M-phases are regulated mainly through cell cycle genes homology regions (CHR). Comparison of *Cyclin F* genes from different species revealed the existence of two conserved CHR sites in the promoter of *Cyclin F*. Our studies demonstrate that the cell cycle-dependent transcriptional regulation of *Cyclin F* is mainly mediated through these two conserved CHR sites and that the DREAM and MMB complexes bind to both identified sites. Generally, binding of DREAM to CHR promoter elements mediates repression in G_0 and MMB activation in G_2/M. Interestingly, reporter assays revealed that no de-repression in G_0 can be observed after mutating the CHRs in the *Cyclin F* promoter. Similar results have been found for the *Ki-67* promoter. Taken together we show that CHR sites exist and that the mechanism of transcriptional regulation deviates from the classical model of DREAM/MMB-regulated genes.

➜ **Castillo, Paola**
email: castillo@medizin.uni-leipzig.de

POSTER 75

Long-term stability of prenatally induced differentially methylated genomic regions due to maternal smoking

Cell Biology

Thürmann L[1], Bauer T[2], Trump S[1], Bieg M[2], Weichenhan D[2], Mücke O[2], Röder S[1], Herberth G[1], Ishaque N[2], Herrmann C[2], Eils R[2], Lehmann I[1]

1 Helmholtz-Zentrum für Umweltforschung Leipzig
2 German Cancer Research Center – DKFZ

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The prenatal period represents a developmental window that is remarkably susceptible to environmental stressors. Many lines of evidence indicate that this period of increased susceptibility plays a pivotal role for disease development across the entire span of human life. As a likely interface between environmental factors and their functional impact on disease development epigenetic mechanisms have been recognized. However, little is known about the global long-term stability of environmentally induced epigenetic changes.

To fill this gap we studied the long-term stability of changes in methylation pattern caused by tobacco smoke exposure during pregnancy. Blood samples of children from the prospective mother-child cohort LINA were analyzed by whole-genome-bisulfite sequencing. Differentially methylated regions (DMRs) were determined at time of birth and compared to the methylation pattern of four year old children.

We show that the vast majority of the environmentally induced DMRs detected at birth are surprisingly stable over time. Even when considering the impact of the genetic background (i.e. CpG-destroying SNPs). Our data clearly show that environmental exposure during the prenatal period determines a stable epigenetic landscape, which can link the prenatal period to disease susceptibility later in life.

➜ **Thürmann, Loreen**
email: loreen.thuermann@ufz.de

POSTER 76

The impact of surface modification on cytotoxicity and uptake of CuO nanoparticles in A549

Cell Biology

Merker C[1], Donath E[1], Estrela-Lopis I[1]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Increasing applications of nanoparticles (NPs) in the industry and private consumption demand the thoroughly identification of hazards and potential adverse effects on human and environment. Many metal oxide NPs, especially CuO, offer a wide range of physicochemical properties and increased reactivity because of their large surface. These characteristics are used versatile in different application areas (e.g. gas sensors, solar cells and lithium batteries).

In this study the impact of surface modifications (PEGylation, Carboxylation and attaching of amide) of CuO NPs were analyzed in the human lung adenocarcinoma epithelial cells A549.

With ion beam microscopy it was possible to investigate the uptake and intracellular distribution of the unmodified (CuO Core) and modified (CuO-PEG, -COOH, $-NH_3^+$) NPs label-free. The two methods, proton-induced X-ray emission (PIXE) and Rutherford backscattering spectroscopy (RBS) were applied simultaneously to study cellular element concentration (P, S, K, Ca, Fe, Zn) as well as NP content in individual cells. Furthermore the cell viability after CuO NP exposure was analyzed by means of flow cytometry. Ratio between living, apoptotic and necrotic cells was investigated using annexin V/ propidium iodide cell staining. A further flowcytometric assay was done to study the intracellular generation of reactive oxygen species (ROS), which indicate oxidative cell stress.

In conformity with animal experiments A549 cells exposed to unmodified CuO NPs revealed decreased cell viability. PEGylation and Carboxylation of the surface however reduced the cytotoxicity of copper.

➜ **Merker, Carolin**
email: carolin.merker@medizin.uni-leipzig.de

POSTER 77

Childhood asthma and coronary risk factor genes modulate airway clearance and tube sizes in Drosophila

Cell Biology

Pesch Y[1], Jacob A[1], Behr M[1,2]

1 Institut für Biologie, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Airways and cardio-vascular-tubes control oxygen delivery. Yet, little is known about molecular pathways affecting tube efficiency in widespread lung and heart diseases. In a meta-study we identified 56 human genes as potential coronary- and asthma-risk-factors, however their molecular roles in tube formation are poorly understood. In the *Drosophila* tracheal system and mammalian lung key molecular mechanisms of patterning and branching morphogenesis are mediated by conserved growth factors and signaling cascades. Furthermore, both systems convert during late embryogenesis from liquid- to air-filling. We therefore studied the role of risk factors in *Drosophila* tracheal tube formation. Genome wide blast searches for orthologs of the risk factors identified *Drosophila ORMDL, LRRK2 and LDLR-like Lpr1, Lpr2, Lrp1* and *Megalin* genes. In tracheal specific RNAi-mediated knock down mutants respiratory tube-length is increased and airway lumen clearance abolished. The increased tubes are caused by apical cell membrane enlargement due to cell-shape changes and apical extracellular matrix deformation. We further found that LDLR-like proteins are essential for clathrin-mediated endocytosis, which is required for size determination and lumen clearance of the airways. ORMDL and Lrrk2 modulate cellular sphingolipid levels affecting secretory pathway and lysosome function in tracheal cells. Thus, uptake and further trafficking of luminal proteins and lipids could be essential in clinical relevant syndromes caused by failure of tube clearance and size control.

➜ **Behr, Matthias**
email: matthias.behr@trm.uni-leipzig.de

POSTER 78

Gene editing of the ncRNA STAiR18- a keyplayer in the survival of multiple myeloma cells

Cell Biology

Zipfel I[1], Horn F[1]

1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The transcription factor STAT3 is constitutively activated in many cancer types such as multiple myeloma and mediates the expression of anti-apoptotic and proliferation promoting proteins. To identify STAT3-dependent transcripts and to investigate the oncogenic potential of STAT3 a genome-wide transcriptom analysis in multiple myeloma cells INA-6 was conducted. In addition to predicted protein-coding target genes of STAT3 the study exposes several yet unknown noncoding transcripts, which are called STAT3-induced RNAs (STAiRs). One of those noncoding transcripts, STAiR18, seems to play a major role in the survival of multiple myeloma cells. Knockdown of STAiR18 leads to distinct apoptosis of INA-6 as well as U266 cells and reduces the STAT3-RNA and -protein level in multiple myeloma cells, suggesting an interplay between STAT3 and its target ncRNA STAiR18.

The STAiR18 transcript is located at two almost identical loci at the second chromosome. Both STAiR18 loci are expressed in multiple myeloma cells in nearly equal shares. To examine whether the vitality of INA-6 cells is regulated by both loci, they were manipulated with the aid of the new TALEN (transcription activator-like effector nucleases) technology. Due to precise binding at their target nucleotides TALENs induce locus-specific DNA double-strand breaks, in which exogenous loxP oligos can be inserted. Mediated by a Cre recombinase STAiR18 could be extracted locus-specific and stable subsequently.

→ **Zipfel, Ivonne**
email: ivonne.zipfel@medizin.uni-leipzig.de

POSTER 79

Bisphosphonate – Stolpersteine in der zahnärztlichen Implantologie

Clinical Studies

Meier F[1], Birkemeyer C[2], Berger F[3], Hofmann F[4], Löffler S[1]

1 Institut für Anatomie, Universität Leipzig
2 Institut für Analytische Chemie, Universität Leipzig
3 Saxonia-Klinik GmbH Leipzig
4 Hofmann & Ilgner Praxis für Oralchirurgie

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In der Humanmedizin werden häufig Bisphosphonate in der Therapie von Tumoren und Osteoporose eingesetzt. Dies kann zu schwerwiegenden Komplikationen in der Zahnmedizin führen, z. B. zur Osteonekrose des Kieferknochens und daraus resultierender fehlender Osseointegration von Implantaten. Es stellt sich die Frage, ob Bisphosphonate generell im Kieferknochen nachweisbar sind und wie eine Implantation bei Bisphosphonat therapierten Patienten gelingen kann. Zwei Bisphosphonate, Alendronat und Risedronat (TCI Deutschland GmbH, Eschborn, Deutschland), wurden mittels Massenspektrometrie in reiner Form und in Verbindung mit humanem Knochenmaterial chemisch analysiert. Weiterhin erfolgte eine histologische Untersuchung der gingival-periostalen Verbindung nach Entkalkung eines Unterkiefers und Färbung mit Hämatoxylin-Erosin und van-Gieson mittels Lichtmikroskopie. Anhand des Falles einer erfolgreichen Implantation bei einer 82-jährigen Patientin unter langjähriger Bisphosphonateinnahme wird die Technik und Vorgehensweise dieses oralchirurgischen Eingriffes beschrieben. Wichtigste Ziele dieser Arbeit waren es, Empfehlungen bezüglich der Behandlung von Patienten unter Bisphosphonattherapie zu geben sowie Möglichkeiten für eine erfolgreiche Implantation trotz Einnahme dieser Medikamente aufzuzeigen. Es wird ein Informationsblatt für Humanmediziner erstellt, welches auf die gravierenden Nebenwirkungen von Bisphosphonaten in der Zahnmedizin aufmerksam macht. Perspektivisch soll die Methode zum Nachweis von Bisphosphonaten in Zusammenarbeit mit dem Institut für analytische Chemie der Universität Leipzig weiter entwickelt werden.

➜ **Meier, Friederike**
email: f.meier90@gmx.de

POSTER 80

Clinical validation of response and resistance factor candidates to targeted therapy in gastric cancer

Clinical Studies

Haffner I[1], Lordick F[1]
1 Universitäres Krebszentrum (UCCL), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Gastric cancer is the second leading cause of cancer mortality worldwide. In 10–20% of patient derived gastric cancer tumor tissue HER2 is found to be overexpressed. Trastuzumab is a therapeutic monoclonal antibody directed against HER2. Used in addition to conventional chemotherapy it improves outcomes in patients suffering from advanced HER2 positive gastric cancer. Unfortunately, some of the tumors have a primary resistance to trastuzumab and others develop resistance over the course of treatment. Therefore, we want to examine tissue samples of patients on biomarkers that can predict a response or resistance to this targeted therapy. We aim to establish promising biomarkers in laboratory experiments done within the SYS-Stomach consortium. This shall be subsequently validated in patient samples. Tissue samples and treatment data of HER2 positive patients treated with trastuzumab, the only currently approved targeted therapy in gastric cancer, are required to verify the HER2 biomarker candidates and obtain reliable and statistically meaningful results.
This is done by a non-interventional multicenter study called "VARIANZ" that has already been approved by the leading Ethic Committee at the Medical Faculty of the University of Leipzig. All over Germany investigators conduct this study and enroll patients. Investigators provide us with information about the disease, treatment course and outcome. Patients donate tissue to our consortium. These tissues and treatment data are necessary to evaluate biomarkers for the prediction of response or resistance of target therapy used in the treatment of gastric cancer.

➜ **Haffner, Ivonne**
email: ivonne.haffner@medizin.uni-leipzig.de

POSTER 81

Risikofaktoren für schwere Hypoglykämien bei Typ-1-Diabetes

Clinical Studies

Wohland T[1], Tiemann T[2], Patzer O[3], Holstein J[4], Kovacs P[1], Holstein A[3]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Diabetologische Schwerpunktpraxis, Rinteln
3 Medizinische Klinik I, Klinikum Lippe-Detmold, Detmold
4 Medizinische Klinik mit Schwerpunkt Nephrologie und Internistische Intensivmedizin, Charite Universitätsmedizin Berlin

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Fragestellung: Die Fallkontrollstudie untersuchte Risikofaktoren für schwere Hypoglykämien (SH) bei Typ-1-Diabetikern.
Methoden: Im Zeitraum 2007–2013 wurden prospektiv für eine ostwestfälische Region mit ca. 200.000 Einwohnern die Charakteristika von SH registriert. SH waren durch eine neuroglukopenische Symptomatik, eine initiale Blutglukose von < 50 mg/dl und die Notwendigkeit der i.v. Glukose- bzw. Glukagon-Gabe definiert. Merkmale von Patienten mit SH wurden mit denen einer unselektionierten regionalen Kontrollgruppe von 165 Typ-1-Diabetikern ohne SH verglichen.
Ergebnisse: Im Untersuchungszeitraum wurden bei 189 Typ-1-Diabetikern insgesamt 356 Ereignisse von SH registriert. 50,6% (180/356) aller Episoden traten bei nur 29 Patienten auf, die ≥3 SH erlitten. Bei ähnlichem Lebensalter, HbA1c und vergleichbarer Diabetesdauer waren hypoglykämische Typ-1-Diabetiker gegenüber der Kontrollgruppe durch vermehrte Störungen der Hypoglykämie-Wahrnehmung (20,1% vs. 15,2%; p=0,024), seltenere Blutglukoseselbstkontrollen (31,8±11,3 vs. 35,9±13,8 Messungen/Woche; p=0,026), häufigere Demenz (6,9% vs. 1,2%; p=0,002) sowie höhere Pflegebedürftigkeit (Heimversorgung bzw. amb. Pflegedienst 9% vs. 1,8%; p=0,0004) gekennzeichnet. Hypoglykämische Typ-1-Diabetiker verwandten seltener Kurzzeit-Insulinanaloga (52,4% vs. 83,6%; p< 0,001).
Schlussfolgerungen: Typ-1-Diabetiker mit SH grenzen sich gegenüber der Gruppe ohne SH klar ab. Der Komplex multipler additiver Risikofaktoren für SH dürfte teilweise therapeutisch beeinflußbar sein. Insbesondere auch die große Gruppe von Typ-1-Diabetikern mit rekurrenten SH erfordert besondere Betreuungskonzepte.

➜ **Wohland, Tobias**
email: tobias.wohland@medizin.uni-leipzig.de

POSTER 82

Studie zur Erlernbarkeit der visuellen und digitalen Zahnfarbdifferenzierung

Clinical Studies

Olms C[1], Jakstat H[1]

1 Poliklinik für Zahnärztliche Prothetik und Werkstoffkunde, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Das an der Universität Leipzig entwickelte Curriculum klinische Zahnfarbdifferenzierung (ZD) ermöglicht es dem Zahnmedizinstudenten durch eine Lernspirale die erlangten Fähigkeiten im Bereich des Farbsehens auf die klinische Situation zu übertragen.
Das Ziel der vorliegenden prospektiven randomisierten Studie war es zu untersuchen, ob mit einem elaborierten Feedback anhand standardisierter Checklisten eine qualitative Verbesserung der Farbergebnisse bei der visuellen und digitalen ZD erreicht werden kann.
Material/Methodik: An der Studie nahmen insgesamt 60 Studierende teil. Das mittlere Durchschnittsalter lag bei 23 Jahren (20–40J.), davon waren 37 weiblichen (61,7%) und 23 männlichen (38,3%) Geschlechts. Die Einteilung der Studenten in eine Studien (SG)- und Kontrollgruppe (KG) erfolgte randomisiert. Die SG (N=30) erhielt nach dem Eingangstest ein elaboriertes informatives Feedback vom Dozenten. Dieses wurde anhand einer Checkliste erhoben. Im Eingangstest (T_1)- und Ausgangstest (T_2) wurden die Farbergebnisse der SG und KG dokumentiert. Daraus wurde dE berechnet.
Ergebnisse/Diskussion: Der Mittelwert E_{T2} =0,9 in der SG zeigte eine hochsignifikante Verbesserung gegenüber dE_{T1} =2,7 (p=0,0092) in der visuellen Farbnahme. In der KG (N=30) konnte keine Verbesserung der dE-Werte im Ausgangstest nachgewiesen werden.
Für die digitalen dE-Werte gab es keine Veränderungen auf Signifikanzniveau. Die dE- Werte zu T_1 lagen auf einem niedrigen Niveau von 1,3 (dE_{Min} =0, dE_{Max} =4,6). Zum Zeitpunkt T_2 war dE_{Gesamt} =0,9 (dE_{Min} =0, dE_{Max} =5,0).
DE-Werte von < 1 sprechen für einen optimalen Lernerfolg in der SG für die visuelle Farbnahme.

➜ **Olms, Constanze**
email: constanze.olms@medizin.uni-leipzig.de

POSTER 83

Häufigkeiten von Allergien auf zahnärztliche Materialien – eine Metaanalyse

Clinical Studies

Sieber A[1], Olms C[1,2]

1 Poliklinik für Zahnärztliche Prothetik und Werkstoffkunde, Universität Leipzig
2 Klinik und Poliklinik für Zahnärztliche Prothetik und Werkstoffkunde, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Einleitung: Übermäßige Hygiene, eine ansteigende Umweltverschmutzung und das Auftreten immer neuer Stoffe können Auslöser von Sensibilisierungen und allergischen Reaktionen sein.
In der zahnärztlichen Praxis werden jedes Jahr eine Vielzahl neuer Materialien eingesetzt.
Empfindungsstörungen nach zahnärztlichen Behandlungen werden häufig mit den verwendeten Materialien assoziiert und geht man daher oft von allergischen Reaktionen aus.
Zielstellung: Ziel der vorliegenden Metaanalyse war es, die Häufigkeit von Allergien auf zahnärztliche Materialien zu untersuchen.
Material und Methode
Es erfolgte eine gezielten schlagwortbasierte Literatursuche in PubMed, Medline und Google Scholar sowie durch Recherche einschlägiger Kataloge der deutschen Universitätsbibliotheken. Studien, Reviews und Fallberichte wurden erfasst. Die gewonnenen Daten wurden statistisch bewertet.
Ergebnisse: Bis Oktober 2014 wurden 35 derartige Studien erfasst. Der Großteil dieser war retrospektiv. Der Zeitraum der Publikationen erstreckt sich von den Jahren 1978 bis 2014 mit Patientenzahlen zwischen 4 und 60.000 Patienten pro Studie. Die bevorzugte Allergietestmethode war der Epikutantest. Am häufigsten waren Frauen betroffen. Das häufigste Allergen ist Nickel gefolgt von Palladium.
Schlussfolgerung: In der Literatur sind gegenwärtig nur wenige aktuelle Studien über Materialunverträglichkeiten auf zahnärztliche Werkstoffe zu finden. Vor allem zu den heutzutage viel verwendeten Kompositen gibt es aktuell keine ausreichenden Informationen bezüglich der Häufigkeit von Allergien.

→ **Olms, Constanze**
email: constanze.olms@medizin.uni-leipzig.de

POSTER 84

Verbesserung der Diagnostik des Triangulären Fibrokartilaginären Komplexes durch Segmentierung

Clinical Studies

Hirschfeld U[1], Hammer N[1], Strunz H[1,2], Wolfskämpf T[1], Löffler S[1]

1 Institut für Anatomie, Universität Leipzig
2 Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Verletzungen des Triangulären Fibrokartilaginären Komplexes (TFCC) sind häufig Ursache ellenseitiger Schmerzen des Handgelenks. Unsere Untersuchungen beschäftigten sich mit der Frage, ob sich die Segmentierung, eine Erstellung eines dreidimensionalen Objekts aus Bildreihenfolgen der verwendeten MRT- und CT-Datensätze mittels Mimics® (Software/Materialise HQ, Technologielaan 15, 3000 Leuven, Belgium), ein ergänzendes diagnostisches Hilfsmittel bei unklaren klinischen und röntgenologischen Befunde eignet. Hierfür wurden MRT und microCT Aufnahmen von präparierten Handgelenken zweier alkoholfixierter und zweier unfixierter Körperspender des Instituts für Anatomie gemacht und mittels Mimics® segmentiert. Die präparierten Handgelenke wurden plastiniert, ein Verfahren bei welchem Wasser durch farblosen Kunststoff ersetzt wird. Durch Färbung der Schnittbilder (1mm Schichtdicke) wurden die gewünschten Strukturen besser sichtbar gemacht. MRT, microCT, Segmentierung und Plastination der Proben wurden visuell auf ihre morphologische Korrelation geprüft. Unklare MRT- und CT-Aufnahmen von 3 Patienten mit Verdacht auf Läsion des TFCC sind segmentiert und mit deren arthroskopischen Befunden verglichen worden. Der TFCC der Proben korreliert in Segmentierung und Plastination. MicroCT-Datensätze zeigen eine hohe Detailschärfe der Segmentierung für Knochen, nicht jedoch für den TFCC. Eine von drei Segmentierungen von präoperativen MRT-Datensätzen von Patienten korreliert mit deren arthroskopischen Befunden. Die dreidimensionale Darstellung des TFCC kann ein ergänzendes diagnostisches Hilfsmittel meist bereits vorhandener Daten sein.

➜ **Hirschfeld, Ulrich**
email: ulihir@gmx.de

POSTER 85

Klinische Charakterisierung einer Patientengruppe mit ADHS im Erwachsenenalter

Clinical Studies

Paucke M[1], Stark T[2], Yue Q[2], Exner C[2], Hegerl U[1], Strauß M[1]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 Institut für Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Die ADHS ist eine häufige psychiatrische Erkrankung mit Beginn im Vorschulalter. Die im Erwachsenalter persistierenden ADHS-Symptome verändern sich in der Regel klinisch im Vergleich zum Kindesalter und erschweren damit die diagnostische Einschätzung. Auch die häufig zusätzlich vorhandenen psychiatrischen Komorbiditäten wie z. B. affektive Störungen führen im Erwachsenenalter nicht selten zu diagnostischen Fehleinschätzungen.

Ziel dieser Studie ist es, die klinische Diagnose ADHS in Abgrenzung zu anderen psychiatrischen Erkrankungen bei erwachsenen Patienten mittels ADHS spezifischer Selbstbeurteilungsbögen mit Hilfe eines Regressionsmodells vorherzusagen.

Von Januar 2013 bis April 2014 wurden in der Spezialsprechstunde für ADHS im Erwachsenenalter der Klinik und Poliklinik für Psychiatrie und Psychotherapie der Universitätsklinik Leipzig konsekutiv 80 Patienten untersucht. Die diagnostische Einschätzung (ADHS vs. kein ADHS) erfolgte durch einen erfahrenen Psychiater gemäß der DSM-IV-Kriterien. Folgende ADHS-spezifische Instrumente kamen zum Einsatz: Selbstbeurteilung zu soziodemografischen Daten, zu aktuellen (ADHS-SB, ASRS) und zu retrospektiven (WURS) Beschwerden sowie Angaben zur Anamnese/Psychopathologie (z. B. SKID I, BDI-II).

Zwei ADHS-spezifische Instrumente (WURS, ADHS-SB Aufmerksamkeit) waren ausreichend, um die Diagnose (ADHS vs. kein ADHS) bei 71–81 % der untersuchten Patienten korrekt vorherzusagen.

Perspektivisch könnte eine weitere Unterteilung der Patientengruppe ohne ADHS in diagnostische Subgruppen, die Abgrenzbarkeit von ADHS im Erwachsenenalter zu anderen psychiatrischen Diagnosen präzisieren.

➜ **Paucke, Madlen**
email: madlen.paucke@medizin.uni-leipzig.de

POSTER 86

Prognostic impact of CD34+/CD38- cell burden at diagnosis of acute myeloid leukemia (AML) in patients (pts) undergoing allogeneic stem cell transplantation after reduced-intensity conditioning (RIC-HCT)

Clinical Studies

Jentzsch M[1], Bill M[1], Leiblein S[1], Weidner H[1], Schmalbrock L[1], Wildenberger K[1], Cross M[1], Pleß M[1], Bergmann U[1], Schubert K[1], Pönisch W[1], Franke G[1], Vucinic V[1], Behre G[1], Niederwieser D[1], Schwind S[1]

1 Abteilung für Hämatologie und Internistische Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In AML, leukemia stem cells (LSC) exist within the CD34+/CD38- cell compartment, are thought to be less chemotherapy sensitive, enriched as minimal residual disease and responsible for relapse. The therapeutic approach of RIC-HCT is based on an immunological graft-versus-leukemia (GvL) effect. The prognostic impact of CD34+/CD38-cells at diagnosis for pts undergoing RIC-HCT remains unknown.

We analyzed 120 AML pts (median age 65 years[y]) receiving RIC-HCT. At HCT all pts were in complete remission (CR). Donors were human leucocyte antigene (HLA)-matched related (14%) or HLA-matched (58%) or mismatched (28%) unrelated. Median follow-up was 3.8y.

Medical research council (MRC) genetic classification was fav. 3.4%, interm. 71%, adv. 25%. At diagnosis pts were characterized for NPM1, FLT3-ITD & CEBPA mutations & %of bone marrow (BM) CD34+/CD38- cells was assessed using flow cytometry.

A cutpoint at 5% defined low & high burden of BM CD34+/CD38- cells. Pts with a high one were more likely to have secondary AML (P=.055) & CEBPA wild-type (P=.11) by trend. High diagnostic CD34+/CD38- burden associated with higher cumulative incidence of relapse (CIR, P<.001) & shorter overall survival (OS, P=.018). In multivariate analysis, the prognostic impact of CD34+/CD38- cells for OS was confirmed.

AML pts with high CD34+/CD38-cell burden at diagnosis had higher CIR & shorter OS after RIC-HCT. This may be mediated by LICs, escaping the GvL effect after RIC-HCT. Thus the assessment of CD34+/CD38-cell burden at diagnosis may help to identify pts at high risk of relapse.

➜ **Jentzsch, Madlen**
email: madlen.jentzsch@medizin.uni-leipzig.de

POSTER 87

Clinical role of microparticles in the setting of a two different low energy diet in obese patient's prior bariatric surgery

Clinical Studies

Wiltberger G[1], Splith K[1,2], Krenzien F[1], Atanasov G[1], Hau H[1], Blüher M[1], Schütz T[1], Peter V[1], Busse H[1,3], Dietrich A[1], Schmelzle M[1,2]

1 Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
3 Klinik und Poliklinik für Diagnostische und Interventionelle Radiologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Obesity is one of the most serious public health problems worldwide and its prevalence has dramatically increased in the last few decades. Recent studies noted high levels of plasma microparticles (MP) in obese patients with chronic liver disease, however, profound conclusions, especially with regard to complex mechanisms involved in inflammation and immune responses, are limited.
Material Methods: A randomized controlled prospective study with patients who were scheduled for bariatric surgery, receiving two different preoperative low energy diets for two weeks prior surgery was conducted. Blood samples. Isolation of plasma microparticles, clinical radiological and laboratory analysis were performed. Histopathological grading of liver biopsy was obtained after surgery.
Results: After two weeks of the low energy diet a decrease of total count of circulating MP was observed in all patients.($p < 0.001$) Also the BMI, γ-GT values, AP values, CRP values, serum lipid levels (total cholesterol, HDL, LDL, TG), and blood sugar values (glucose, HbA_{1c}) decreased significantly, whereas ALAT, ASAT and bilirubin values increased. Furthermore, also the total count of CD4, CD25, CD39, CD31, CD73, CD56, CD68, CD4CD25CD39, CD68CD39, and CD56CD39 MP decreased significantly after two weeks of diet.
Conclusion: MP are significantly increased in obese patients compared to lean volunteers, reflecting their important role in the setting of chronic inflammation. MP might therefore serve as potential biomarkers predicting efficiency of low energy diets in patients scheduled for bariatric surgery.

Funding: ifb

→ **Wiltberger, Georg**
email: georg.wiltberger@medizin.uni-leipzig.de

POSTER 88

High CD11b expression is associated with poor prognosis in patients (pts) with acute myeloid leukemia (AML) undergoing allogeneic stem cell transplantation (SCT)

Clinical Studies

Schuhmann L[1], Jentzsch M[1], Bill M[1], Leiblein S[1], Schubert K[1], Wildenberger K[1], Bergmann U[1], Pleß M[1], Weidner H[1], Schmalbrock L[1], Cross M[1], Pönisch W[1], Franke G[1], Vucinic V[1], Behre G[1], Niederwieser D[1]

1 Abteilung für Hämatologie und Internistische Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In AML clinical and genetic factors contribute to prognosis. CD11b is commonly expressed on monocytic AML blasts and known to associate with poor outcome after chemotherapy. SCT is another possible consolidation therapy for AML pts with donors available. The prognostic impact of CD11b expression at diagnosis for pts receiving SCT has not been reported yet which to evaluate was our objective.

We analyzed 164 AML pts (median age 62 years (y)) who received SCT from human leukozyte antigen (HLA) matched related (25%) or HLA-matched (47%) or mismatched (28%) unrelated donors. Median follow up was 3.4y. Cytogenetic risk according to the medical research council (MRC) was 7.5% favorable, 65.5% intermediate & 27% adverse. NPM1 & CEBPA mutations and the presence of FLT3-ITD were assessed. Using flow cytometry we measured the expression of CD11b on bone marrow (BM) cells at diagnosis & over 10% expression was defined as CD11b positive (+, n=114).

CD11b+ associated with lower blast count in peripheral blood (P<.001) and BM (P=.001), CEBPA wild type (wt, P=.007) and more monosomal karyotype (P=.03). We also saw a trend towards more complex karyotype (P=.11) and NPM1 wt (P=.1). CD11b+ pts had shorter event free survival (EFS, 66% vs. 49% after 5y, P=.04) and overall survival (OS, 72% vs. 58% after 5y, P=.12) by trend. This effect was particularly seen in adverse MRC pts (EFS P=.07 and OS P=.01).

To our knowledge, we are the first to show prognostic influence of CD11b in AML pts after SCT. This may contribute to better risk stratification for newly diagnosed AML pts and may help to develop new therapies in the future.

➜ **Jentzsch, Madlen**
email: madlen.jentzsch@medizin.uni-leipzig.de

POSTER 89

Response-Adapted Sequential Azacitidine and Induction Chemotherapy in Patients > 60 Years Old with Newly Diagnosed AML Eligible for Chemotherapy (RAS-AZIC): Results of the Phase I of the DRKS00004519 Study

Clinical Studies

Jäkel N[1]

1 Abteilung für Hämatologie und Internistische Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Survival in elderly patients (pts) with AML is poor. Azacitidine (AZA) prolongs OS in elderly patients (pts) even with >30% marrow (BM) blasts.

Patients and methods: RAS-AZIC is a prospective, multicentric, phase I/II trial evaluating the efficacy of priming with AZA followed by a sequential, response-adapted therapy on day (d)17, d56, and d90 with AZA or induction chemotherapy (IC) in eligible pts. In the monocentric phase I the safety and dose level (DL) of priming with AZA for 5 (DL 1) or 7 days (DL 2) followed by IC on d17 was established through a 3+3 design. The level at which not more than 1/6 pts had a dose limiting toxicity (DLT) would be used in phase II.

Results: The first 3 pts were enrolled in DL 1 with no DLT. In both cohorts of DL 2 no DLT (0/6 pts) occurred. The phase I was completed after enrolling 9 pts. Median age was 71 years. Secondary/therapy-related AML, and unfavourable cytogenetics were 56%, and 33%. AZA priming was well-tolerated and given as out-patient therapy in 67%. IC could be started as per protocol in 8 pts. Median WBC regeneration > 1 x109/L following IC occurred after 24 (range 7-35) days. No early death on d90 ensued. CR/CRi on d56 in phase I was 78%. After a median follow-up of 13 (range 6-19.5) months, median survival time was 12 months with a survival rate of 78%. Dose level 2 was considered feasible and safe.

Conclusions: Results of the phase I are very encouraging in terms of safety and efficacy. Priming with AZA followed by IC is feasible in elderly pts with AML. Integrating epigenetic therapy with AZA and IC in well-designed trials might further optimize outcome in elderly pts.

➜ **Jäkel, Nadja**
email: nadja.jaekel@medizin.uni-leipzig.de

POSTER 90

Prospektive Erfassung des Schub-Outcome bei Multipler Sklerose

Clinical Studies

Krizek L[1]

1 Klinik und Poliklinik für Neurologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Einleitung: Die quantitativen Daten zum Outcome nach einem Schub der Multiplen Sklerose (MS) stammen überwiegend aus randomisierten Studien zur Steroidtherapie aus Zeiten, in denen die heute etablierten Dauertherapien selten oder nicht angewandt wurden. Zudem hat sich die Schubtherapie selbst gewandelt. Klinische Schwellenwerte zur Indikationsstellung für eine Eskalation, Zeitpunkt und ggf. Abfolge der Verfahren sind bisher nicht standardisiert. Um klinische Studien hierzu sinnvoll zu planen, sind Verlaufsdaten unter den aktuellen Bedingungen erforderlich.
Methoden: Prospektive Erhebung aller Schübe bei MS und klinisch isoliertem Syndrom (CIS), die am UKL behandelt werden mit Dokumentation von Frequenz, klinischer Schwere, Therapie und Therapieerfolg. Nachuntersuchung der Patienten ca. 14 Tage nach Schubbehandlung und Prüfung der Indikation einer Eskalation.
Ergebnisse: 2013 wurden 119 MS/CIS-Schübe in der Klinik für Neurologie behandelt.114 (=96%) erhielten eine Schubtherapie mit Methylprednisolon über 3–5 Tage. Davon wurde 27mal (=23%) die Indikation zur Therapieeskalation gestellt und erfolgte mittels erneuter Methylprednisolongabe (n=18, 67%), Plasmapherese (n=2, 7%) oder Immunadsorption (n=4, 15%). Bei 3 Schüben (=11%) erfolgte keine Therapie aufgrund bestehender Schwangerschaft (n=2) bzw. auf Wunsch des Patienten (n=1).
Schlussfolgerungen: Bei standardisierter Nachuntersuchung wurde in 23% der Fälle die Indikation zu einer Eskalation gestellt. Wir empfehlen die Integration der Nachuntersuchung ca. 14 Tage nach Schubtherapie. Die erhobenen Daten erleichtern die Planung prospektiver Studien zur Schubtherapie.

➜ **Krizek, Luise**
email: luise_krizek@t-online.de

POSTER 91

BOLD-Correlates of EEG Alpha Phase Synchronization: Toward a Biomarker for Major Depression

Clinical Studies

Surova G[1], Gawlitza M[1], Hegerl U[1], Hoffmann K[1], Lobsien D[1], Schönknecht P[1], Olbrich S[1]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Major depressive disorder (MDD) belongs to the leading causes of disability worldwide. Identifying biomarkers facilitating precise diagnosis and predicting response to specific medical treatment is, thus, of critical importance. At the functional level, several potential electrophysiological biomarkers of MDD including increased synchronisation at EEG alpha and theta frequencies have been reported. In parallel, functional magnetic resonance imaging (fMRI) studies suggest altered blood oxygen-level dependent (BOLD) signals in e.g. frontal and prefrontal brain areas. However, the association between electrophysiological alterations and differences of fMRI activity in MDD remains vague. The goal of this study is to shed more light on the linkage between neurophysiological activity and hemodynamic changes as assessed by simultaneous EEG-fMRI recordings.

Therefore, EEG-fMRI resting state measurements of 22 unmedicated MDD-patients and 15 healthy controls were conducted. The first results show that there are significant hemodynamic correlates of the EEG alpha synchronisation. This allows searching for brain structures that are involved in the pathomechanism of altered EEG alpha synchronization in MDD in contrast to healthy controls.

The comparison of EEG-phase informed fMRI datasets from patients and controls will be presented. It is further intended to evaluate the predictive power of these altered EEG-fMRI patterns in MDD patients in the course of treatment.

➜ **Surova, Galina**
email: galina.surova@medizin.uni-leipzig.de

POSTER 92

Prognostic Significance of Pri-miR-320a Expression in Acute Myeloid Leukemia (AML) Patients (Pts) Undergoing Hematopoietic Stem Cell Transplantation (HCT) after Reduced Intensity Conditioning (RIC)

Clinical Studies

Gaber T[1], Bill M[1], Jentzsch M[1], Schubert K[1], Weidner H[1], Kloss L[1], Schmalbrock L[1], Bonifacio L[1], Wildenberger K[1], Pönisch W[1], Vucinic V[1], Franke G[1], Lange T[1], Cross M[1], Behre G[1], Niederwieser D[1]

1 Abteilung für Hämatologie und Internistische Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Most AML pts have a poor prognosis. Better risk stratifications are needed to improve pts outcomes. The expression of microRNAs (miRs) has been shown to be altered in AML. MiR-320a, maps to chromosome 8 & is known to play a role in several tumors. Here we investigated whether a differential expression of pri-miR-320a associates with outcome in AML pts receiving RIC-HCT. The pre-treatment expression levels of pri-miR-320a, a precursor of miR-320a was assessed by quantitative reverse transcription PCR & the 75th percentile was chosen to define high & low expressers. The pts were also characterized for CEBPA & NPM1 mutations, as well as FLT3-ITD status. We analyzed 129 AML pts who received RIC-HCT. High pri-miR-320a expressers less frequently had NPM1 (P=.038) or CEBPA (P=.025) mutations. Pri-miR-320a expression was significantly lower in trisomy 8 pts (P=.018) especially in the European LeukemiaNet (ELN) intermediate II group. High pri-miR-320a expressers had a longer overall survival (OS;P=.086) by trend & a significantly longer event-free survival (EFS;P=.032). The strongest impact was found in the ELN intermediate II group, where high pri-miR-320a expression was associated by trend with longer OS (P=.059) & a significantly longer EFS (P=.034). In AML pts with trisomy 8 pri-miR-320a has a significantly lower expression, indicating a possible leukemogenic link to trisomy 8 associated AML. High pri-miR-320a expression associates with improved outcomes, which suggests that it could be used as a marker to refine current AML risk stratification. Thus, miR elevation by e.g. miR-replacement therapies, might improve pts outcomes.

➜ **Gaber, Taqiuddine**
email: med08ivg@studserv.uni-leipzig.de

POSTER 93

Are plasma amino acid concentrations predictors of mortality in patients with liver cirrhosis?

Clinical Studies

Kinny-Köster B[1], Becker S[1,2], Bartels M[3], Ceglarek U[1,2], Thiery J[1], Kaiser T[1]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
3 Klinik und Poliklinik für Viszeral-, Transplantation-, Thorax- und Gefäßchirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objectives: In patients affected by liver cirrhosis mortality is predicted by MELD score that is used for organ allocation. Complications such as ascites, hepatic encephalopathy and cachexia are often observed in end-stage liver disease but don't have direct influence on MELD score. It is known that concentrations of several amino acids change during progression and complications of cirrhosis. Aim of this study was the evaluation of the prognostic value of amino acid concentrations and identification of amino acid constellations that predict mortality.

Methods: Amino acid levels in citrated-plasma from 168 patients were measured by LC-MS/MS. For all samples, corresponding MELD scores consisting of the parameters bilirubin, creatinine and INR were available.

Results: Plasma concentrations of branched chain amino acids (BCAA) especially valine decreased with increasing MELD score (Spearman-ρ=-0.425; $p < 0.001$***). In contrast, levels of aromatic amino acids (AAA) such as phenylalanine (ρ=0.332***) and sulfur-containing methionine (ρ=0.347***) increased. Ratio of val/(phe+met) decreased significantly with increasing MELD score (ρ=-0.577***).

Conclusion: BCAA plasma level decrease might be explained by changes in skeletal muscle metabolism whereas AAA increase may promote hepatic encephalopathy. AAA and methionine increase may occur through shunt effects. Ratio of valine/(phenylalanine+methionine) could be an innovative biomarker in prediction of mortality in end-stage liver disease. Further studies for identification of underlying pathophysiological mechanisms and potential treatment strategies i. e. BCAA supplementation are necessary.

➜ **Kinny-Köster, Benedict**
email: benedict.kinny-koester@medizin.uni-leipzig.de

POSTER 94

Exon 23 DNMT3A mutations in patients (pts) with Acute Myeloid Leukemia (AML) receiving Hematopoietic Stem Cell Transplantation (HSCT) after Reduced Intensity Conditioning (RIC)

Clinical Studies

Bonifacio L[1], Schmalbrock L[1], Bill M[1], Jentzsch M[1], Schubert K[1], Wildenberger K[1], Kloss L[1], Weidner H[8], Gaber T[1], Pönisch W[1], Vucinic V[1], Franke G[1], Lange T[1], Cross M[1], Behre G[1], Niederwieser D[1]

1 Abteilung für Hämatologie und Internistische Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Epigenetic dysregulation contributes to AML pathogenesis. Mutations affecting the gene encoding the DNA methyltranfserase 3A (DNMT3A), that regulates DNA methylation, are commonly observed in AML. Most *DNMT3A* mutations (mut) affect exon 23, are known to occur in pre-leukemic cells & have been suggested as a minimal residual disease (MRD) marker. Today most studies showed a negative impact of *DNMT3A* mut on outcome in specific AML subgroups (e.g. pts with molecular high risk). The prognostic impact of exon 23 *DNMT3A* mut in RIC-HSCT treated pts is unknown.

Genomic DNA from pre-treatment samples of 104 AML pts (median age 64 years (y), range 47–75 y), of which 67 had *de novo* disease, were analyzed for *DNMT3A* mut in exon 23 by Sanger sequencing. EuropeanLeukemiaNet (ELN) risk categories were favorable 18.4%, intermediate (int) I 32.0%, int II 24.2% & adverse 25.2%. All pts underwent RIC-HSCT (Fludarabine 30mg/m2 day -4 to -2 followed by total body irradiation 2 Gray at day 0). Outcome & associations with clinical & molecular aberrations (i.e *NPM1, CEBPA, IDH1* & *IDH2* mut & presence of *FLT3*-ITD) were evaluated.

DNMT3A mut in exon 23 were common (16.3%) & occured at codon R882 (n=16) & P904 (n=1), associated with higher age (p=.037) & *NPM1* (p=.005) & *IDH1* mut (p=.025). There was no significant impact of exon 23 *DNMT3* mut status on overall survival (OS; p=.757) or event-free survival (EFS; p=.814), even when considering specific AML subgroups or adjusting for older age, molecular high risk, or cytogenetic subtypes. Thus it is tempting to speculate that RIC-HSCT may abrogate the negative impact of *DNMT3A* mut.

➜ **Schwind, Sebastian**
email: sebastian.schwind@medizin.uni-leipzig.de

POSTER 95

Reduced Intensity Conditioning Allogeneic Haematopoietic Stem Cell Transplantation – a Treatment Option in Elderly or Comorbid Patients with Acute Lymphatic Leukemia

Clinical Studies

Tumewu T[1], Vucinic V[1], Franke G[1], Schwind S[1], Jäkel N[1], Heyn S[1], Pönisch W[1], Al-Ali H[1], Leiblein S[1], Krahl R[1], Behre G[1], Niederwieser D[1]

1 Abteilung für Hämatologie und Internistische Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Allogeneic hematopoetic stem cell transplantation (HCT) with myeloablative conditioning was the only curative treatment option for eligible pts with acute lymphoblastic leukemia (ALL). In this retrospective survey we analyzed the outcomes of ALL pts not eligible for conventional myeloablative HCT who were treated with reduced intensity conditioning (RIC)-HCT.

28 pts, who underwent RIC-HCT from sibling (MRD) or unrelated donors (MUD) between 2003 and 2013 were analyzed. The median age at transplantation was 58 (range 23 to 71) years. The conditioning regimen consisted of Fludarabine 30 mg/m2 from days -4 to -2 and a 200 cGy total body irradiation on days -1 or 0 before HCT. Reasons for RIC HCT was age over 50 years for MUD, and age over 55 years for MRD HCT or severe comorbidities in younger patients. Median follow up was 2.4 years.

6 HCTs were performed from sibling donors, 17 from human leukocyte antigen (HLA) matched unrelated donors and 8 from HLA mismatched (> 1 allele) donors. 8 patients (28.5%) were Philadelphia chromosome (Ph) positive.

After 2 years the overall survival (OS) was 49±10% and event-free survival (EFS) was 40.5±9.4% with a non-relapse mortality incidence of 34±9.6%. The cumulative incidence of relapse (CIR) was 37±9.6% at 2 years. Patients in CR1 had higher 2 years OS 63.1+12.1 compared to patients in CR2 or worse 42.4+14.8 without reaching statistical significance. Noteworthy, 6 of 8 Ph+patients are still alive.

RIC-HCT can be used in pts with ALL and is a curative option for pts with higher age (up to 71 years) or severe comorbidities. In the high-risk Ph+ cohort we observed remission rates of 62.5%.

➜ **Vucinic, Vladan**
email: vladan.vucinic@medizin.uni-leipzig.de

POSTER 96

NPM1 mutations as minimal residual disease (MRD) marker in Acute Myeloid Leukemia (AML) patients (pts) after reduced-intensity conditioning (RIC) hematopoietic cell transplantation (HCT)

Clinical Studies

Kloss L[1], Bill M[1], Schubert K[1], Jentzsch M[1], Wildenberger K[1], Weidner H[1], Schmalbrock L[1], Gaber T[1], Bonifacio L[1], Pönisch W[1], Franke G[1], Vucinic V[1], Lange T[1], Behre G[1], Cross M[1], Niederwieser D[1]

1 Abteilung für Hämatologie und Internistische Onkologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The outcome of most AML pts remains dismal. RIC-HCT is a frequently used consolidation therapy for older or comorbid AML pts. Preventing hematologic relapse by MRD monitoring & early treatment intervention is considered crucial for mortality reduction. *NPM1* mutations (muts) are frequent aberrations (up to 30%) in AML, with mut types A, B, and D being most frequent (95% of all *NPM1* muts). Some studies demonstrated *NPM1* muts as useful MRD markers after achievement of complete remission (CR). We analyzed the usefulness of *NPM1* muts as MRD marker for AML pts after RIC-HCT.

We identified 14 pts with *NPM1* muts (25%; type A n=11; type D n=3) in 56 screened pts. *NPM1* mut burden was determined by real-time polymerase chain reaction using a plasmid standard curve for calibration, at diagnosis & 3 follow-up dates (day [d] 28, 54 & 84 after HCT or at relapse). Expression was normalized to the *ABL* transcripts number. Exemplarily 2 representative courses are described. Pt A was diagnosed at 69 years (y) with *NPM1* mut positive (pos), therapy-related, normal karyotype (CN) AML. The pt was *CEBPA* & *FLT3* wild type (wt). After achievement of CR & RIC-HCT the pt was *NPM1* mut negative (neg). Samples became *NPM1* mut pos at d56 with an increase of *NPM1* mut burden to 160%. Hematological relapse occurred at d83 after RIC-HCT. Pat B was diagnosed with *de novo*, *NPM1* & *CEBPA* mut pos CN-AML at 65y. The pt was *FLT3* wt. At the time of RIC-HCT & all follow-up time points *NPM1* mut levels were neg & the pt remained relapse-free.

The presented preliminary results encourage further prospective studies for the usefulness of *NPM1* muts after RIC-HCT in AML pts.

➜ **Kloss, Laura**
email: laura.kloss@medizin.uni-leipzig.de

POSTER 97

Langzeitatmungsausdauertraining bei Patienten mit Myasthenia gravis

Clinical Studies

Freitag S[1], Hallebach S[1], Baumann I[2], Kalischewski P[2], Raßler B[1]

1 Carl-Ludwig-Institut für Physiologie, Universität Leipzig
2 Neurologische Praxis, Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Myasthenia gravis (MG) ist durch verminderte Muskelausdauer gekennzeichnet und führt oft zu respiratorischen Komplikationen. Eine Verbesserung der Atmungsfunktion ist daher ein wichtiges Behandlungsziel in der Therapie der MG. Eine frühere Studie zeigte, dass ein vierwöchiges Atmungsausdauertraining (AAT) die Ausdauer der Atmungsmuskeln von Patienten mit MG gegenüber dem Ausgangswert nahezu verdoppeln konnte. Das Ziel der aktuellen Studie war, ein Langzeittraining zu entwickeln und dessen Effekte über einen Zeitraum von 7 Monaten zu beobachten. Zehn Patienten mit milder oder mäßiger MG nahmen als Trainingsgruppe (TG) teil. Während des ersten Monats absolvierten sie fünf Trainingseinheiten pro Woche. In den folgenden 6 Monaten wurde die Häufigkeit des Trainings auf fünf Einheiten in zwei Wochen reduziert. Nach dem ersten, vierten und siebenten Monat wurden jeweils der Myastheniescore, die Lungenfunktion und die Atmungsausdauer bestimmt. Fünf Patienten dienten als Kontrollgruppe (KG). Sie absolvierten kein AAT, wurden jedoch in gleicher Weise getestet wie die Patienten der TG. Das AAT verbesserte Myastheniesymptome, die maximale inspiratorische Muskelkraft (PImax) sowie die Atmungsausdauerzeit (AAZ) signifikant. Der Myastheniescore verbesserte sich von 0,63 ± 0,1 auf 0,44 ± 0,1 ($p < 0,001$), der PImax stieg von 7,3 ± 0,4 auf 8,4 ± 1,0 kPa ($p = 0,002$) und die AAZ erhöhte sich von 8,8 ± 1,4 auf 24,2 ± 3,4 min ($p < 0,001$). In der KG konnte keine signifikante Verbesserung beobachtet werden. Die Ergebnisse zeigen, dass ein Langzeit-AAT realisierbar ist und Patienten mit MG einen therapeutischen Nutzen bringen kann.

→ **Freitag, Sophie**
email: freitag.sophie@googlemail.com

POSTER 98 Anatomische und klinische Aspekte der Arteria profunda femoris bei peripherer arterieller Verschlusskrankheit

Clinical Studies

Wattenbach K[1], Bürkigt T[1], Kohlhaw K[1], Löffler S[2]

1 Klinik für Allgemein-,Visceral-,MIC- und Gefäßchirurgie, Kliniken Leipziger Land Borna
2 Institut für Anatomie, Universität Leipzig

Aufgrund des demographischen Wandels mit zunehmender Erhöhung der Lebenserwartung wird die Inzidenz der pAVK künftig drastisch ansteigen.

Nach Studienlage sind ca. 20% der über 65 Jahre alten Patienten betroffen und durch ihre Begleiterkrankungen, vorwiegend kardiovaskulärer Genese, global gefäßgeschädigt.

Viele der Patienten haben eine deutlich eingeschränkte Lebensqualität, insbesondere durch eine schmerzbedingte Gehstreckenminderung, und sind durch bestehende Wunden von einer Amputation bedroht.

Die derzeitigen Therapiemöglichkeiten sind vielfältig, große operative Eingriffe haben aufgrund der assoziierten Komorbidität jedoch eine oft negative Prognose.

Die isolierte Thrombendarteriektomie-Ausschälplastik der A. profunda femoris ist dabei in Vergessenheit geraten und erscheint nicht mehr zeitgemäß.

Dieses Widerstandsgefäß ist mit oft nur im Abgangsbereich bestehender funktioneller Stenose geeignet, um die häufig verschlossene Oberschenkeletage zum Unterschenkel zu überbrücken, da sie sich stark erweitern und Kollateralen zu den peripheren Gefäßen bilden kann.

Ziel der Studie ist es, durch die detaillierte Präparation der A. femoralis profunda an 22 Alkohol-fixierten Humanpräparaten fundierte anatomische Kenntnisse bezüglich der Gefäßvariationen zu erlangen, um somit durch eine mögliche Modifizierung des aktuellen operativen Vorgehens ein verbessertes Outcome zum Extremitätenerhalt und folglich dem Erhalt der Mobilität zu erzielen.

Durch das gewonnene anatomische Wissen soll die klinische Versorgung verbessert werden, da das Verfahren durch ein geringes Operationsrisiko einem breitem Patientengut zugänglich ist.

➜ **Wattenbach, Kathrin**
email: kathrin.wattenbach@web.de

POSTER 99

Einsatz einer intraoralen Testmethode zur Biokompatibilitätsprüfung von zahnärztlichen Materialien – eine Pilotstudie

Clinical Studies

Groß G[1], Olms C[1]

1 Poliklinik für Zahnärztliche Prothetik und Werkstoffkunde, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Einleitung: Eine Vielzahl der zahnärztlichen Werkstoffe kann Unverträglichkeitsreaktionen innerhalb des Munds auslösen. Für Medizinprodukte, die auf unbestimmte Zeit im Mund verbleiben, fehlen geeignete, standardisierte intraorale Testsysteme. In der vorliegenden Pilotuntersuchung wurde eine neu entwickelte Testapparatur im intraoralen Milieu von Probanden über einen Zeitraum von vier Wochen untersucht. Die Apparatur ermöglicht es, Werkstoffproben im direkten mukosalen Kontakt zu testen.
Material und Methode: An der Pilotstudie nahmen gesunde 10 Probanden (6 weibliche, 4 männliche) mit guter Mundhygiene und Compliance teil. Das Durchschnittsalter betrug 25,7 Jahre (24–28 Jahre). Die Apparatur wurde mit einem Testplättchen am oberen ersten Molar befestigt. Klinischen Nachkontrollen wurden wöchentlich durchgeführt. Nach 4 Wochen erfolgte die Ausgliederung. Die Evaluation der Probanden zur subjektiven Bewertung der Studie erfolgte mit einem aus 14 Fragen und Freitextantworten konzipierten Fragebogen. Die mundgesundheitsbezogene Lebensqualität wurde mit dem validierten standardisierten Oral Health Impact Profile (OHIP) vor und nach der Studie dokumentiert.
Ergebnisse: Es gab keinen Drop-Out und es traten keine biologischen und materialtechnischen Komplikationen in der klinischen Untersuchung auf. Eine tägliche Mundhygiene war aus Probandensicht möglich und kein Proband gab Einschränkungen im Alltag an. Die Auswertung des OHIP zeigte keine wesentlichen Veränderungen im Antwortverhalten der Probanden zu den beiden Erhebungszeitpunkten an.
Die vorgestellte Testmethode kann für eine klinische Biokompatibilitätsprüfung genutzt werden.

➜ **Olms, Constanze**
email: constanze.olms@medizin.uni-leipzig.de

POSTER 100

BICpoly: A new biodegradable and biocompatible polymer based on D-glucuronic acid and L-cysteine for biomedical applications

Drug Development and Delivery

Ewe A[1], Jansen de Salazar A[2], Geyer A[2], Aigner A[1]

1 Selbstständige Abteilung für Klinische Pharmakologie, Rudolf-Boehm-Institute für Pharmakologie und Toxikologie
2 Organische Chemie, Fachbereich Chemie, Philipps-Universität Marburg

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Biodegradable polymers have received much attention in the last years for biomedical applications especially as drug delivery devices and in tissue engineering. Well-known materials are natural (collagen, starch) and synthetic polymers (polycaprolacton, poly lactic-glycolic acid, polyamino acids).

We synthesized a new biodegradable polymer made from the natural occurring, non-toxic compounds D-glucuronic acid and the amino acid L-cysteine and extensively analyzed its physicochemical properties and its utility for drug delivery. The monomer unit is synthesized by a condensation reaction of the two compounds and forms a 7, 5-bicyclic thiazolidinlactam (BIC). It can be polymerized in two steps by a ring opening reaction (ROP).

The polymer (BICpoly), only soluble in DMSO or DMF, can be precipitated in water or organic solvents. Dependent on the conditions, negatively-charged nano- or microparticles, or polymer films can be produced. First degradation studies of the nanoparticles revealed an interesting pH-depended process. BICpoly is almost stable in acidic conditions, starts slowly to degrade at pH 7.4 and is rapidly degraded at pH 8. Cytotoxicity experiments of BICpoly and the monomer indicated high biocompatibility. Furthermore, the potential as drug delivery carrier was demonstrated with the chemotherapeutic agent doxorubicin.

The highly selective and multi-gram scale synthesis of the polymer made from naturally occurring educts, the pH-dependent degradation profile as well as the promising results from the first application experiments make BICpoly an interesting candidate for biomedical research.

➜ **Ewe, Alexander**
email: alexander.ewe@medizin.uni-leipzig.de

POSTER 101

Release of liposome–polyethylenimine complexes from Poly (vinyl alcohol) hydrogel micro particles – a feasibility study

Drug Development and Delivery

Schulze J[1]

1 Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The nucleic acid based treatment of diseases offers great opportunities, even in the case of targets considered as otherwise undruggable. Due to its potential applications the interest in gene therapy, and consequently in gene delivery, has grown continuously over the past years. Considering their function and chemical structure, nucleic acids are susceptible to degradation, predominantly by nucleases, and suffer from low permeation rates through cell membranes. To overcome these drawbacks, a large number of lipid or polymeric carrier systems have been explored. Among those, polyethylenimine (PEI) is a prominent candidate due to its high transfection efficacy. The combination of PEI and Liposomes resulted in transfecting agents (lipopolyplexes) combining the beneficial properties of a lipid system (low cytotoxicity, high stability) and the advantages of PEI. The next step is to establish a system for their controlled delivery and controlled release. The purpose of this study was to evaluate if the combination of nanoscale lipopolyplexes with a hydrogel carrier will yield an appropriate dosage form. To this end we incorporated diphosphatidyl-polyethylenimine-DNA (DPPC-PEI) complexes into poly (vinyl alcohol) hydrogel micro particles (PVA-HMP). This feasibility study aimed at investigating whether high transfection efficacy, particle stability, zeta-potential and particle size of the lipopolyplexes remain unchanged during the manufacturing process, storage and upon release.We demonstrate that both biological activities and physicochemical properties are preserved.

➜ **Schulze, Jan**
email: jan.schulze@medizin.uni-leipzig.de

POSTER 102

Targeting a kidney disease-causing overactive cation channel with new inhibitors

Drug Development and Delivery

Neuser S[1], Urban N[1], Schaefer M[1]

1 Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

TRPC6 is a calcium-permeable cation channel, which is expressed in kidney podocytes and critical for glomerular filtration. Mutations in the TRPC6 gene have been identified in patients with autosomal dominant forms of focal segmental glomerulosclerosis (FSGS) which is one of the leading causes of steroid-resistant terminal kidney failure in youth and adults. Most mutations lead to increased basal or stimulated channel activity.

Functional characterisation of six individual FSGS-related TRPC6 mutations by Ca2+ imaging and whole cell voltage clamp analyses confirmed the overactive phenotype in transiently transfected HEK293 cells. Förster resonance energy transfer assays showed that mutated TRPC6 subunits freely assemble with wild-type TRPC6 into heteromeric channel complexes, which is consistent with the dominant inheritance of the disease.

We next examined the pharmacological modulation of mutant TRPC6 by two newly identified TRPC6 inhibitors: larixyl-monoacetate and larixyl-carbamate. Single-cell Ca2+ influx analysis and electrophysiological patch-clamp experiments revealed that TRPC6 inhibitors are biologically active towards mutated forms of TRPC6 upon channel activation. One mutation features a high basal activity, which is also strongly suppressed by larixyl derivatives. Applying TRPC6 inhibitors at various concentrations in a fluorescence imaging plate reader-based Ca2+ assay demonstrated that the potency of TRPC6 inhibitors is not impeded in FSGS-related TRPC6 mutations.

The results provide promising hints to develop a pharmacotherapy for FSGS patients, which may prevent kidney failure and organ transplantation.

➜ **Neuser, Sonja**
email: sonja-neuser@gmx.de

POSTER 103

High energy electron irradiation of gelatin towards tailored hydrogels

Drug Development and Delivery

Engert F[1], Wisotzki E[1,2], Hennes M[1], Schuldt C[2], Knolle W[1], Decker U[1], Käs J[2], Zink M[2], Mayr S[1,2,3]

1 Leibniz-Institut für Oberflächenmodifizierung e. V., Leipzig
2 Fakultät für Physik und Geowissenschaften, Universität Leipzig
3 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

As a derivative of the naturally prevalent substance collagen, gelatin is a highly interesting biomaterial for application in areas of regenerative medicine to bioengineering. Reagent-free treatment methods to tune the properties of hydrogels such as gelatin are highly desirable in order to preserve existing biocompatibility and biodegradability of the material, while tuning other material properties as required for specific applications. Electron irradiation can be used to crosslink gelatin without the addition of other potentially toxic chemicals.

Gelatin hydrogels were synthesized and irradiated by a 10 MeV linear accelerator in order to induce the formation of new chemical crosslinks. Electron irradiation was shown to control important material properties including the rheology, swelling and sol-gel transition temperature, without altering biocompatibility or biodegradability.

Quantification of the degree of crosslinking was carried out by rheological measurements and investigation of swelling behaviour to observe hydrogel strengthening and elasticity. From this data, rubber elasticity theory and the Flory-Rehner equation for isotropically swollen elastomers were used to estimate the crosslinking densities and polymer mesh size. Fourier transform infrared spectroscopy and scanning electron microscopy were used to analyze changes of the gelatin structure with respect to the irradiation dose.

➜ **Engert, Florian**
email: florian_engert@web.de

POSTER 104

The role of the proventricle in reproduction of Syllinae (Syllidae, Annelida)

Evolution and Molecular Diversity

Weidhase M[1], Bleidorn C[1], Aguado M[2]

1 Institut für Biologie, Universität Leipzig
2 Department of Biology, Faculty of Sciences, Universidad Autónoma de Madrid

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

With about 700 valid species, the Syllidae are one of the largest annelid families. Although usually being very small, syllids are easy to recognize by their modified foregut, the so called proventricle. This structure, proposed to be a synapomorphy of this family, is described to act as a sucking pump and also as a gland involved in reproduction. However, both assumptions are questionable in the light of morphology. Additionally, Syllidae exhibit some of the most outstanding reproductive modes: epigamy and schizogamy. Epigamy is quite common in annelids, meaning that the whole specimen is transformed into an epitoke, gamete producing and swarming individual, which often dies after mating. In specimens reproducing by schizogamy, just the posterior part is transformed into an epitoke. This new individual, called stolon, detaches and mates, whereas the residual specimen regenerate its posterior end. Schizogamy is exclusively found in the two subfamilies Autolytinae and Syllinae. Herein we invesigate *Typosyllis antoni* Aguado et al. 2014, a member of Syllinae, concerning effects on stolonization after proventricle removement by dissection. Our results reveal several effects including a change to exclusively production of males, the production of aberrant stolons, and a repeated stolonization without complete regeneration of the lost segments. Our findings clearly support the controlling function of the proventricle and will be the basis for further studies to reconstruct the evolution of this special reproductive mode and its relation with regenerative processes.

➜ **Weidhase, Michael**
email: michael.weidhase@uni-leipzig.de

POSTER 105

Vascular structure tracking in intraoperative ultrasound data of brain tumors

ICCAS – Computer Assisted Surgery

Ilunga Mbuyamba E[1], Lindner D[2], Arlt F[2], Müns A[2], Chalopin C[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig
2 Klinik und Poliklinik für Neurochirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Intraoperative ultrasound imaging is a common tool used in brain tumor surgery to detect the residuals of tumor. In B-mode ultrasound, tumor remnants are difficult to distinguish from other hyperechogenic structures. The use of an ultrasound contrast agent enables to highlight them, but also the vascular structures which have to be identified in the images.

Because of image noise the automatic segmentation of vascular structures in ultrasound data is complex. An alternative method consists in tracking a vascular segment in the image data involved in brain tumor operations: preoperative MR data and 3D intraoperative contrast enhanced ultrasound (3D-iCEUS) data acquired before and after tumor resection. A user selects in the preoperative MR data a blood vessel close to the tumor. Using rigid registration method this pattern is searched in the 3D-iCEUS data before and after resection within a limited region of interest taking into account the brain shift.

Our method was tested on data of three patients overcoming a brain tumor operation. Its validation was performed by computing an overlap index of the vascular segments before and after tracking and by comparing it with manual registration. Three different similarity measures were tested: the Normalized Cross Correlation (NCC), the Mutual Information (MI) and the Normalized Gradient Field (NGF).

Despite of the small size of the blood vessels and the image noise, it was possible to successfully identify a vascular segment in the 3D-iCEUS data acquired after tumor resection. The MI similarity measure provided the best performance in comparison to the manual registration.

➜ **Chalopin, Claire**
email: claire.chalopin@iccas.de

POSTER 106 **Approach for a web-based anesthesia documentation**

ICCAS – Computer Assisted Surgery

Rockstroh M[1], Lippert S[1], Glaser B[1], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The anaesthesiology as a central discipline in modern hospitals as well as in private clinics is under increasing personnel and time pressure. In order to offer a better and faster response to a situation in the OR and assess the situation from a distance, a mobile solution for visualizing the anesthesia data form several ORs would be an option.

To implement a mobile application to support the anesthesia in the OR, a Web-based solution has been developed. Based on the Vaadin Framework and an interface for Dräger anesthesia systems an application is under development which enables the anesthesiologist to observe the actual vital signs of the patient from every location. In addition, the demographic data of the patient and his medical history can be documented. During a procedure the medication can also be documented using the presented system. To assist the permanent medical documentation, a solution for the data storage in a PDF document based on a currently used anesthesia protocol was developed. In a next step, the documentation of the medication doses should be simplified and algorithms for the detection of measurement errors will be developed and evaluated.

The project is a further step for the digital representation of the OR. Along with the completed project for the detection of device data and the device usage based on the video signals of the medical devices and other ICCAS projects, the data transmitted and received by the presented project can be stored at a central location, the surgical recorder. This will support research projects in the area of workflow recognition, workflow support and documentation.

➜ **Rockstroh, Max**
email: max.rockstroh@medizin.uni-leipzig.de

POSTER 107

Usefulness of Information Extraction Methods in Medicine for Clinical Decision Support

ICCAS – Computer Assisted Surgery

Gaebel J[1], Denecke D[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In patient treatment a physician has to process a lot of information. This information is usually stored in unstructured format in electronic health records (EHR). Finding the releveant facts is a time-consuming process. We developed a natural language processing system that identifies relevant information in the clinical documentation or other electronic sources. Using the example of critical events, our system detects text passages that mention the occurence of unwanted, critical happenings. In a first step, the texts are semantically structured. Medical concepts are mapped onto a medical semantic network. Second, concepts representing critical events are identified. If they appear in the appropriate context, they are marked as relevant. These marked passages are then extracted and saved in a structured format. They can be used for multiple purposes. One major use case is the use of the information as an input for clinical decision support systems.We conducted a user study with neuro surgeons. They all agreed on the correctness and the good applicability for clinical decision support. Our research shows that the extraction of complex clinical correlations from narrative texts is possible and useful.

Funding: BMBF

➜ **Gaebel, Jan**
email: jan.gaebel@medizin.uni-leipzig.de

POSTER 108

CephaLens – Towards a 3D Augmented Reality Visualization in Neurosurgery

ICCAS – Computer Assisted Surgery

Bieck R[1], Franke S[1], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The visualization of crucial anatomical structures in minimal invasive surgery is a constantly challenging issue. Taking the 3D nature of the real patient condition and realistic surgery circumstances into account, the principle of augmented reality was introduced to surgical visualization. Based on this a first prototype system adopted the "Magic Lens" concept for minimal invasive cardiac surgery, where a mobile device, e.g. tablet, displayed additional patient-specific information (context) depending on its position and the position of the user (focus) in reference to the patient. The intra-operative system combined optical tracking and time-of-flight (TOF) recording to track lens and surgeon positions simultaneously. Patient-specific internal anatomical structures were pre-operatively reconstructed and then displayed corresponding to the surgeon's angle of view, while offering an easy-to-use interaction concept to switch between visualization presets. A preliminary user study indicated the strong potential of the proposed concept and provided important information for further working steps. As a result, the system will be introduced to the field of neurosurgery, primarily for navigated interventions. Here, detailed information on the internal cerebral tissue and vascular structure shall support the surgeon with treatment-dependent visualization presets, primarily for deep-tissue interventions such as ventricular puncture and hydrocephalus.

Funding: MAI/BMBF

➜ **Bieck, Richard**
email: richard.bieck@medizin.uni-rostock.de

POSTER 109

Expert-Based development of CDSS by using MEBN with an example for laryngeal cancer.

ICCAS – Computer Assisted Surgery

Cypko M[1], Stöhr M[2], Denecke K[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig
2 Klinik und Poliklinik für Hals-, Nasen-, Ohrenheilkunde, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The increasing understanding of the complexity of oncological diseases and the dramatic growth of available patient information allow, in principle, for a highly individualized treatment of patients. At the same time, optimal treatment decision-making has become more difficult. Clinical decision support system (CDSS) with artificial intelligence based on Multi-Entity Bayesian Network (MEBN) can help to model and simulate complex decision-making. An MEBN is based on a graphical model with nodes and directed edges between these nodes representing information entities and their relation to each other, and a probabilistic model with conditional probability tables in each of these nodes representing how strong they are dependent from their direct causes. The focus of our project is an expert-based modelling of a CDSS by a close collaboration between computer scientists and clinicians. In a one year term at ICCAS, we worked on a first example, the modelling of treatment decisions of laryngeal cancer therapy. The experience confirmed that handcrafted modelling is complex in the beginning and, as a whole, very time consuming. A main reason for the time effort is the unusual way of characterizing diseases in a MEBN model structure and the setting of probabilities. Therefore, special tools will be developed in the future that enable guiding an expert-based modelling through intuitive and practical questions formulated in natural language.

Funding: BMBF

→ **Cypko, Mario**
email: mario.cypko@medizin.uni-leipzig.de

POSTER 110 **Analysis of surgical workflows in the frequency domain**

ICCAS – Computer Assisted Surgery

Maktabi M[1], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Optimal clinical workflow automation is all the more crucial. One essential deed towards automation is being able to assess surgical processes effectively and efficiently. Signal analysis, for instance speech recognition, could conduce to an accurate evaluation of surgical processes. Therefore, in this work we apply spectral analysis known from speech recognition and biosignal analysis to predict future steps in surgical processes.

We assume that the surgeons activities were timed. Afterwards, we generated activity time signals from recorded workflows corresponding to anatomical structure, action, surgical instruments, and the hand used.

The Power density spectra of the activity time series can be obtained by means of nonparametric methods such as short time Fourier transformation (STFT) or Welchs power spectral density estimation. Moreover, we assume the volatility of activities in surgeries by applying a linear time-invariant system (LTI). Thus, we can predict future surgical process activities.

The accuracy of our prediction results was estimated in a study. The method was applied to lumbar discectomy. We simulated an ongoing surgery to test the method. Based on the evaluation study, the activity prediction of devices in specific time windows was calculated and showed excellent outcomes.

In future work, the activity signals analysis can be tested on further surgical intervention types.

Funding: BMBF

→ **Maktabi, Marianne**
email: marianne.maktabi@medizin.uni-leipzig.de

POSTER 111

Towards a structured suitability determination of identification approaches for surgical instruments

ICCAS – Computer Assisted Surgery

Glaser B[1], Schellenberg T[1], Franke S[1], Dänzer S[1], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Various approaches have been presented in recent years for the purpose of automatic identification of surgical instruments. Studies covering the topic of intra-operative surgical instrument identification often focus on a limited set of surgical instruments in a specific domain and are rarely transferable to the overall situation in the operating room (OR). Hence, there is currently no methodology available to quantify surgical instrument sets regarding their suitability for a certain identification approach. The project aims for the concept of a surgical instrument similarity metric, which can be used to classify sets of surgical instruments in relation to their suitability for a certain identification method. It is planned to use it for the generalization of the results of a previous study for intra-operative surgical instrument identification, which are limited to the domain of ENT (ear, nose and throat) surgery. The upcoming results will not only provide a deeper insight into the methodology of the preceding project, but also deliver valuable information for video and weight based surgical instrument detection approaches as a whole by including a broad range of surgical domains.

Funding: BMBF

➜ **Glaser, Bernhard**
email: bernhard.glaser@medizin.uni-leipzig.de

POSTER 112 **Concept for a clinic-wide Operating Room Control Center**

ICCAS – Computer Assisted Surgery

Maktabi M[1], Öser A[1], Rockstroh M[1], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

For several years integration and modular networking of medical devices in the OR are a underlined issue. Many commercial integrated solutions are based on proprietary interfaces and protocols. Thus, several initiatives and projects now develope systems of OR integration based on open standards. However, financial and security specific aspects in hospitals require a more advanced approach – like the presented concept of process control in the OR with centralized supervisory control.

To design a control room, the control center is divided in a three-unit structure consisting of a representation level, a transmission level, and a processing level. Thus, essential requirements were identified.

The first, more closely considered user group is the medical technology domain in the hospital. After extensive user surveys an primary user interface prototype and the corresponding database scheme were developed. The SPARC indicates wide approval of the users. However,aspects of data traffic and data security have to be considered closely.

In future works, the implementation of a control center used by medical engineers at ICCAS in cooperation with Leipzig University Hospital should be done. Moreover, the medical engineers can check out SPARC.

Funding: BMBF

→ **Maktabi, Marianne**
email: marianne.maktabi@medizin.uni-leipzig.de

POSTER 113

Towards IHE Surgery Profile for Implant Template Distribution and Implant Plan Distribution

ICCAS – Computer Assisted Surgery

Maktabi M[1], Liebmann P[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Nowadays, rigid implants are widely used in such endoprosthetic or dental surgeries. The surgeon's daily practice can be enhanced by using standards. The Digital Imaging and Communications in Medicine (DICOM) supplement 131 represent a standardized way of storing, accessing and sharing rigid implant templates. Actors like manufacturers, software planning vendors and PACS System Integrators have to interact. The implementation of standards can be accomplished efficiently by IHE (Integrating the Healthcare Enterprise). The IHE Surgery Profile for Implant Template Distribution and Implant Plan Distribution (ITD/IPD) can bring together several clinics as well as manufacturers and customers.

Surveys with international clinical endoprosthetic experts from several hospitals are performed by us. The surgeons formulated points of criticism such as the demand for enhancement of the selection workflow process of a rigid implant.

Thus, the process from planning implants through to backtrace the implant is elucidated in the ITD and IPD Profile. In this way, implant manufacturers will have new ways to provide digital data about their products; Patient care will be fundamentally improved by proper and widespread using of rigid implant templates from acquisition through planning software to intraoperative medical devices.

Funding: EFRE

➜ **Maktabi, Marianne**
email: marianne.maktabi@medizin.uni-leipzig.de

POSTER 114

Application of the openEHR approach to support an innovative defect classification for patients with cervical spinal canal stenosis

ICCAS – Computer Assisted Surgery

von Sachsen S[1], Groll M[2], Meixensberger J[2], Leimert M[3]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig
2 Klinik und Poliklinik für Neurochirurgie, Universität Leipzig
3 Klinik für Neurochirurgie, Universitätsklinikum Carl Gustav Carus Dresden

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Purpose: Development of an electronic patient record (EPR) which supports defect specific treatment of cervical spinal canal stenosis. The usage of defect encoding in diagnostics requires a storage of defect-specific data in the EPR using a standardized format. This is also a precondition to provide a study data base for supporting evidence-based medicine.
Methods: To represent defect classification in a clinical data set the usage of the specification *open*EHR was analyzed. The existing *open*EHR library was checked for archetypes which can be used to describe defect-specific data. As simple evaluation schemes for diseases found are not sufficient for defect description new archetypes were developed. To integrate defect-specific data into an EPR new archetypes were embedded in a composition with other archetypes which describe further intervention related data.
Results: The new archetype *Defect encoding (morphological)* contains defect characteristics. This includes stenosis dimension, defect position, grade of concomitant pathology, information to vertebrae disorder, diseased segments and cause for stenosis. The developed archetype *Defect classification Spinal Canal Stenosis* contains defect codes to indicate severity both for morphological state and clinicalsymptoms.
Conclusion: The introduced archetypes show the ability of *open*EHR to model new classification schemes. The integration of clinical knowledge in the EPR is supported by free software tools (archetype editor, template designer) which automatically generate XML-based source code for further data processing in clinical systems.

Funding: SMWK, EFRE

➜ **von Sachsen, Sandra**
email: sandra.vonsachsen@medizin.uni-leipzig.de

POSTER 115

Clinical workflow assistance in head and neck tumor therapy

ICCAS – Computer Assisted Surgery

Meier J[1], Bohn S[1], Krauß O[1], Boehm A[2], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig
2 Klinik und Poliklinik für Hals-, Nasen-, Ohrenheilkunde, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Information management in tumor therapy is a challenging process for physicians and surgeons because the documentation of clinical results is primarily driven by economic rather than clinical considerations. Numerous assistance and decision support systems are used in daily clinical routine to relieve physicians and surgeons from repetitive, time-consuming tasks and to provide support for complex therapy planning scenarios. However, these systems do not integrate smoothly into the clinical workflow and are poorly integrated into the clinical IT landscape. This leads to inefficient, time-consuming clinical workflows, error-prone copy and paste procedures, and internal department databases for clinical studies or quality management even though all the information is already available in digital form.

We developed a sophisticated, web-based clinical information system known as *oncoflow* which is intended to support the physician and clinical staff throughout the entire therapy process. Relevant patient-specific information is automatically imported from leading clinical information systems such as the Hospital Information System (HIS) and the Tumor Therapy Manager (TTM) into a central database, restructured according to clinical needs, and presented within a structured web interface. The oncoflow system supports the entire oncological treatment process from the initial consultation until follow-up documentation. Additional information is gathered within each process step to efficiently support clinical studies, quality management and cancer center certification processes.

➜ **Meier, Jens**
email: j.meier@medizin.uni-leipzig.de

POSTER 116 **Cross-Enterprise Model Sharing**

ICCAS – Computer Assisted Surgery

Schreiber E[1], Sommer G[1], Liebmann P[1], Meier J[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Sharing data across healthcare enterprises is crucial for the efficiency and success of both treatment and research. For one thing, healthcare enterprises need to share their experience and specialist services. Furthermore, redundant data input by hand and media faults that could cause misentries are minimized when institutions pool their treatment-related documents.

The IHE Integration Profile Cross-Enterprise Document Sharing (XDS) provides a standards-based specification for sharing all kinds of clinical documents between healthcare enterprises. Documents are uploaded into federated document repositories. Additionally, metadata and the repository of each document are stored in a registry to enable quick access without having to waste time searching in all the repositories.

Unfortunately, XDS only supports documents related to a specific patient. However, there are plenty of non-patient-dependent documents (e.g. generalized workflows, treatment guidelines or study data), which could usefully be shared such as surgical procedure models, treatment guidelines or study data.

To resolve this discrepancy, ICCAS aims to develop a generalized data model within a new Integration Profile named Cross-Enterprise Model Sharing (XMS), to embrace all kinds of clinical documents, regardless of whether they relate to a specific patient. XMS systems are hence capable of sharing any type of clinical documents among healthcare enterprises as well as communicating patient-specific data with XDS-compliant systems.

Funding: EFRE

➜ **Schreiber, Erik**
email: erik.schreiber@medizin.uni-leipzig.de

POSTER 117

Generic estimation of predictors and their impact on surgical processes

ICCAS – Computer Assisted Surgery

Schreiber E[1], Franke S[1], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Interaction between patients, medical personnel and technical resources means that workflows in medicine are subject to multiple influencing factors. As a result, surgical procedures are very costly and their outcome is highly variable. In fact the operating room is one of the most expensive units in a hospital because many resources are tied up there for a very short time frame on a very small space.

Although some clinical studies have tried to identify and evaluate the factors affecting treatment workflow and predict specific workflow progressions, they mainly focus on very specific treatments and address only a handful of possible factors.

The SWAP module for oncoflow currently being developed at ICCAS provides a method to compute the impact of various factors on a surgical workflow. They include for instance the patient's age, their body mass index, the surgeons, or even the method chosen to reach a target structure during surgery. The preoperative parameters (the factors to be considered during computation) can be chosen by the user. SWAP then identifies the impact of these preoperative parameters on a given surgery type.

Furthermore, recorded surgical workflows can now be weighted by the SWAP module in terms of their similarity to the workflow of an upcoming surgery, enabling a personalized general process model adapted to each patient. This will make intraoperative forecasts of the further progress of a surgical procedure more precise. Moreover, this method is a first step towards a generic analysis tool allowing the effect of preoperative parameters on any type of surgical procedure to be assessed.

Funding: BMBF

→ **Schreiber, Erik**
email: erik.schreiber@medizin.uni-leipzig.de

POSTER 118

Adaptive Surgical Process Models for workflow-driven assistance in the digital operating room

ICCAS – Computer Assisted Surgery

Franke S[1], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Methodologies of formal workflow modeling have proven their usefulness to document, quantify and analyze surgical procedures. Although the OR is one of the most complex and expensive working environments in a hospital, technically supported process management has not yet been established there. Process management in the OR needs to be as flexible as possible and yet still be able to accurately assess upcoming situations to be beneficial for the establishment of an intelligent and cooperative working environment for the surgeon and the OR staff.

In this project, we focused on dynamic adaptation of process models used for intraoperative workflow-driven assistance. The proposed Adaptive Surgical Process Model is generated on the fly as a union of formerly recorded process instances. The instances are continuously weighted according to their similarity to the ongoing process instance. The transition probabilities as well as time and frequency information included in the model are hence continuously adapted.

We studied the model in terms of its suitability for intraoperative application. The analyzed probabilities of the assumed next transitions are an indicator for the quality of representation of the course of the intervention within the given model as well as the ability to anticipate the forthcoming surgical work steps. The results demonstrate the significantly improved ability to anticipate the next work step for Adaptive Surgical Process Models.

The implementation of the workflow-driven adaptation of medical systems will contribute to a cooperative OR environment that increases patient safety and reduces costs.

➜ **Franke, Stefan**
email: stefan.franke@medizin.uni-leipzig.de

POSTER 119

EVENTOR – A framework for event-driven operating room infrastructure

ICCAS – Computer Assisted Surgery

Franke S[1], Maktabi M[1], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The project aims to enable the workflow-driven interconnection of medical devices which do not share a common interface. A centralized unit known as the CommBox is to be developed which implements various communication protocols by integrating process logic and communication frameworks. The interfacing of medical devices is to be controlled by process logic based on surgical process models. As a result, the CommBox will be able to automatically set up communication pathways between components of the overall OR system depending on the surgical situation. Surgical process models represent specific types of surgery by breaking them down into work steps. A workflow engine, the core component of the CommBox, processes these models to follow the surgical process. Each medical device can be attached to the process logic using connector modules. The process logic's open interface enables application-specific connector modules to be developed for medical devices of any kind. Each connector module provides two main functions: protocol transformation and situation adaptation. Workflow-driven adaptation for each medical device type is implemented by processing a rule set.

The actual data transport medium depends on the specific circumstances. Videos for instance are handled by a dedicated video bus with a control unit connected to the CommBox via a connector module.The integration of process logic and communication frameworks facilitates assistance functions such as the situation-aware configuration of devices, the import of data from external systems, and integrated information visualization.

Funding: BMWi

➜ **Franke, Stefan**
email: stefan.franke@medizin.uni-leipzig.de

POSTER 120

Messsystem zur Ermittlung der hüftzentrierten Beinlänge für Hüft-Implantat-Operationen

ICCAS – Computer Assisted Surgery

Grunert R[1,2], Schmidt M[1], Maschke R[3], Hammer N[4], Rotsch C[2], Prietzel T[1]

1 Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Universität Leipzig
2 Fraunhofer-Institut für Werkzeugmaschinen und Umformtechnik IWU
3 Institut für Angewandte Naturwissenschaften, Fakultät Physikalische Technik/Informatik Leupold, Westsächsische Hochschule Zwickau
4 Institut für Anatomie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Einleitung: Die exakte Beinlänge und Lage des Hüftrotationszentrums sind wichtige Qualitätskriterien zur Wiederherstellung der ursprünglichen Biomechanik. Operationsbedingte Beinlängendifferenzen führen zu funktionellen Einschränkungen und können Revisionsoperationen hervorrufen. Die Beinlänge kann bislang nur mittels CT-basierten Messungen ermittelt werden. Das Messsystem soll die Beinlänge vor der Operation und nach der Implantat-Probeeinrenkung objektiv bestimmen.
Methoden: Das entwickelte Messsystem, bestehend aus einem Marker mit zwei LEDs und einer inertialen Messeinheit sowie einer Kamera, wird auf dem Schienbein des Patienten befestigt. Das Hüftrotationszentrum wird Marker basiert bei Bewegung des überstrecken Beins erfasst. Software basiert wird dann eine Kreisbahn bestimmt, die Rückschluss auf den Abstand Hüftrotationszentrum – Sensorsystem zulässt. Die technische Genauigkeit wurde in einer Messreihe (n=30) mittels eines definierten Bewegungsmodells evaluiert.
Ergebnisse: Die ermittelte technische Genauigkeit des Systems beträgt (393,6 ± 2,0) mm mit einem Maximum von 396,9 mm und einem Minimum von 389,9 mm. Der Sollwert für die Beinlänge des Bewegungsmodells beträgt 395,0 mm.
Diskussion: Die technische Genauigkeit des Messsystems erlaubt präzise Messungen und kann somit für die Hüftendoprothetik eine sinnvolle Ergänzung und ein objektives Instrument zur Qualitätssicherung darstellen. Die Bewertung der Genauigkeit im klinischen Einsatz soll nachfolgend bewertet werden.

→ **Grunert, Ronny**
email: ronny.grunert@medizin.uni-leipzig.de

POSTER 121

Automatic Cervical Spine Defect Classification based on Clinical Narratives

ICCAS – Computer Assisted Surgery

Deng Y[1], Denecke K[1]

1 Innovation Center Computer Assisted Surgery (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Classifying the defects occurring in the cervical spine provides the basis for treatment planning. This process requires evidence from clinical narratives and the degree of defect needs be encoded in a standardized form to facilitate data exchange and multimodal interoperability. Hitherto, surgeons have based their decisions mainly on radiological images. Nevertheless, the defect situation and patient status described in the radiological report, anamnesis and admission note are also crucial for classification and follow-up therapy planning.

To improve existing defect classification, an approach based on information extraction from the clinical narratives is proposed. We are addressing this problem with the following components: 1) Establishment of defect ontology based on defect-related terminologies. 2) Configuration of an extraction pipeline. Defect-related concepts are extracted through concept mapper, regular expression and other components. 3) Definition of classification rules to map the extracted feature and defect categories (defect type, position and additional pathology). 4) Clinical data interface is to be established to gather the documents from the hospital information system (HIS), while employing the corresponding authentication and authorization process to protect patient privacy. 5) User interface: A web-based user interface will be employed to offer the high accessibility. The final system will provide suggestions for defect classes and show the relevant information extracted from the patient record, including the radiological image to enable cross-checking by the physician.

Funding: BMBF

→ **Deng, Yihan**
email: yihan.deng@medizin.uni-leipzig.de

POSTER 122

Histological investigations of cervical anterior and posterior longitudinal ligaments and their neuronal structures

ICCAS – Computer Assisted Surgery

Stegmann T[1], Kollan J[1], Pieroh P[1], Wolfskämpf T[1], Leimert M[1], Groll M[1], Dheghani F[1], Steinke H[1]
1 Institut für Anatomie, Universität Leipzig

List of topics
Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction: Postoperative pain following cervical spine surgery (Failed Back Syndrome, "FBS") presents a common, not entirely understood problem. A possible explanation might be the sprouting of sensory and nociceptive elements after surgical resection of the anterior longitudinal ligament "ALL" and the posterior longitudinal ligament "PLL". The knowledge of their innervation is still scarce. Thus, this study is focused on pain related nerve fibers, free nerve endings and proprioceptive elements in ALL/PLL.
Materials and Methods: ALL and PLL of 20 body donors without macroscopic degeneration were dissected at the level of C3–C7. After paraffin embedding the slides were stained with Hematoxylin- Eosin. Based on Hematoxylin-Eosin "HE" morphological findings, immunohistochemistry "IHC" with antibodies against Protein Gene Product "PGP 9.5" and Calcitonin Gene Related Peptide "CGRP" was performed in a standardized setup. Proprioceptive elements were searched in HE stained slices, immunostained nerve fibers evaluated qualitatively in IHC.
Results: IHC determined free nerve endings and assumed nociceptive nerve fibers in both ALL and PLL.The immunoreactivity for PGP 9.5 was stronger in C3–C5 compared to C6/7. No morphological evidence was found for the presence of proprioceptive elements in or near the ALL and PLL.
Discussion: The dense innervation of the segments C3–C5 underlines the importance for elasticity and movement in the cervical region. The intraoperative resection of ALL also removes nerve tissue which might have an influence on FBS. However, proprioceptive elements seem to play a minor role in the function of ALL and PLL.

➜ **Stegmann, Tina**
email: tina.stegmann@medizin.uni-leipzig.de

POSTER 123 **Röntgenschattenrissanalyse RSRA**

ICCAS – Computer Assisted Surgery

Sommer G[1], Prietzel T[1], Schleifenbaum S[1], Schmidt M[1], Möbius R[2], Treichel T[1], Seiwerts M[4], Grunert R[5], Hammer N[2]

1 Klinik und Poliklinik für Orthopädie, Universität Leipzig
2 Institut für Anatomie, Universität Leipzig
3 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig
4 Klinik und Poliklinik für Diagnostische und Interventionelle Radiologie, Universität Leipzig
5 Fraunhofer-IWU, Dresden

Eine korrekte Inklination und Anteversion von Hüftendoprothesenpfannen innerhalb der „safe zone" nach Lewinnek sichert eine adäquate Gelenkbeweglichkeit und minimiert das Risiko von Impingement, Luxation, Implantatschäden sowie Verschleiß. Die Kenntnis der real erzielten Winkel ist wichtig für den Operateur, weshalb eine Messung nach jeder HTEP-Implantation anzustreben ist. Die CT-basierte Messung gilt als präzise, ist jedoch wegen der Strahlenbelastung und aus ökonomischen Gründen nicht routinemäßig durchführbar.

Das Ziel bestand darin, eine neue Methode zur Messung von Inklination und Anteversion zementfreier Pfannen basierend auf vorhandenen Röntgenaufnahmen zu entwickeln. Die Genauigkeit der Methode sollte im Rahmen eines Modellversuches und im Vergleich zur CT-basierten Messung evaluiert werden.

Die mittels RSRA gemessenen Inklinations- und Anteversionswinkel (1,78° ± 0,74° und 1,56° ± 0,98°) zementfreier Pfannen ergaben im Vergleich zur CT-basierten Messung (1,58° ± 0,79° und 1,74° ± 0,99°) nur geringe Abweichungen. Der Lagerungsfehler war mit 2,65 ° vernachlässigbar gering. Zum Ausschluss einer Retroversion muss gegenwärtig bei Verdacht eine zweite Röntgenuntersuchung in einer um 5° abweichenden Ebene erfolgen. Mit der RSRA steht somit eine zuverlässige Methode zur Routinemessung von Inklination und Anteversion zementfreier, röntgenintransparenter Pfannen zur Verfügung. Deren Einsatz lässt eine Optimierung der Pfannenausrichtung durch Selbstkorrektur der Operateure sowie eine bessere Vergleichbarkeit von Studien zur HTEP-Luxation erwarten.

➜ **Sommer, Gerald**
email: gerald.sommer@medizin.uni-leipzig.de

POSTER 124

Collagen polymorphism of the cervical longitudinal ligaments

ICCAS – Computer Assisted Surgery

Stegmann T[1], Hobusch C[1], Pieroh P[1], Wolfskämpf T[1], Leimert M[1], Werner M[1], Groll M[1,2], Steinke H[1]

1 Institut für Anatomie, Universität Leipzig
2 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction: "Collagen polymorphism", "Collagen remodeling" as a matrix change of collagens is age-dependent and associated todiseases. However, data are not entirely reported for collagen distribution in spine ligaments.In operation, the thin anterior longitudinal ligament "ALL" is often removed assuming to be "connective" of less function. The presented study investigated collagen distribution in ALL and in the posterior longitudinal ligament "PLL" taken from body donors and to reveal possible changes, from patients underwent surgery.
Material and Methods: Western Blot I: 11 body donors, probes from ALL and PLLof segments C3–C7, each for collagen types I, II, III and forelastin, standardization to GAPDH (semi quantitative data). Western Blot II: 24 probes of ALL and PLL from operated patients with the same setup.
Result:In both ALL and PLL, collagen distribution of all types of collagen and of elastin yielded dependencies in relationto the segments. The ratio of collagen types resulted in typical curves for ALL and PLL. For type I, we determined a significant difference of patients' tissue samples compared to those of body donors.
Discussion: In body donors, cranial-caudal dependencies of collagen distribution were found as a feature of segmental anatomical structures. Thus, ALL is functional and not a "connective". Patient probes of high values in collagen I may be related to calcification, of collagen II to beginning ossification, where collagen II is expressed. An explanation for the high elastin and the low collagen III values in the patients' probes is missing. However, those findings may be explained by any illness also.

➜ **Stegmann, Tina**
email: tina.stegmann@medizin.uni-leipzig.de

POSTER 125

Modeling and development of Electronic Health Records using the openEHR standard

ICCAS – Computer Assisted Surgery

Kropf S[1], Chalopin C[1], Denecke K[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Electronic Health Records (EHRs) are main information source of clinicians, and researchers. An integrated disease-specific view can often not be gained from EHRs given their distributed nature. A Digital Patient Model (DPM) addresses this problem by a mapping of distributed digital information in one overarching model. The objective of this work was to evaluate the applicability of the information modeling standard *openEHR* for generating a DPM and EHRs.

A prototype information system for supporting the treatment of patients with pituitary adenoma was developed using *openEHR*/EN 13606 for information modeling.

OpenEHR enables the opportunity to decouple the application modeling from the domain modeling; free available modeling tools are provided by *openEHR* to integrate the domain experts in the modeling process. They can model their information structures themselves better than computer scientists. Archetypes which are queried in the online repository are narrowed down and composed for specific use cases. The resulting composite of information is used as a template for the application development. The application development delivers basically XML based EHRs and dedicated entry forms, on which clinical data can be submitted. The EHRs are finally persisted in an XML database.

The development of a prototype system for the treatment of pituitary adenoma shows that the openEHR approach is more than feasible to provide the underlying information structure for the patient model. It is a recommendable approach for the development of standardized, interoperable EHRs.

Funding: BMBF

➜ **Kropf, Stefan**
email: stefan.kropf@medizin.uni-leipzig.de

POSTER 126

Recognition of clinical workflow steps from patient-specific information

ICCAS – Computer Assisted Surgery

Meier J[1], Neumuth T[1]

1 Innovationszentrum für Computerassistierte Chirurgie (ICCAS), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Knowledge about the clinical context is crucial for the development of sophisticated clinical workflow assistance and decision support systems. This clinical context may include information about the patient, disease patterns, attending physicians, and the current working step in the overall treatment process. Unfortunately, this information is hardly available in an appropriate manner in well-established clinical information systems.

This research project focusses on recognizing the patient's progress in the overall treatment process based on the information entities available in clinical information systems. Therefore, we used anonymized Electronic Patient Records (EPRs) from the *onco-flow* information system and created stochastic models based on Hidden Markov Models (HMMs). These models represent average clinical workflows for the treatment of tumor patients in head and neck surgery consisting of first consultation, panendoscopy, tumor board, surgical interventions, radiochemotherapy and follow-up meetings. In each of these workflow steps, information entities such as ICD10 or ICPM codes, radiological reports, OR reports or follow-up documentation was created and served as observations during model creation and evaluation. These patient-specific information entities were then manually tagged with the correct workflow step and afterwards used for model training. Subsequently, these models were used for the classification of untagged patient-specific information within a controlled leave-one-out cross validation study. Forty EPRs were included in the study with promising recognition results up to 90%.

➜ **Meier, Jens**
email: j.meier@medizin.uni-leipzig.de

POSTER 127

Adaption und Evaluation eines Leitfadens zum Gewichtsmanagement in der Praxis

IFB – Adiposity Diseases

Sikorski C[1,2], Jung F[2], Luppa M[2], Riedel-Heller S[2]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Ziele: Ziel der vorliegenden Studie ist es, eine für den breiten Einsatz geeignete deutsche Version des kanadischen Best-Weight-Leitfadens zur adäquaten Behandlung von Adipositas zu etablieren. Der auf den Five As (Ask, Assess, Advise, Agree und Assist) basierende Leitfaden der Behandlung muss unter Umständen noch für das deutsche Versorgungssystem angepasst werden.
Methoden: Im Rahmen einer Mixed-Method-Studie kommen hier qualitative Methoden zum Einsatz. Der Adaptionsbedarf des Leitfadens wurde in n = 3 Fokusgruppen eruiert. Die moderierte Diskussion mehrerer Teilnehmer orientiert sich an einem Leitfaden, der im Vorfeld entwickelt wurde. Insgesamt wurden Fokusgruppen (6–8 Teilnehmer) mit drei Akteursgruppen durchgeführt: Hausärzte, Internisten sowie Diätassistenten. Alle Fokusgruppen wurden mittels Tonband aufgezeichnet, transkribiert und mit Unterstützung des Programms Maxqda inhaltsanalytisch nach Mayring ausgewertet.
Ergebnisse: Der Ansatz der Five As wurde von allen Teilnehmern positiv bewertet. Das vorgegebene Material (ein Würfel, der die Five As veranschaulicht und Tipps und Hinweise beinhaltet) wurde kritisch diskutiert und von den Behandlern als unpraktisch bewertet. Die Behandler wünschen sich im Gegenzug klare Leitfäden, Abbildungen sowie Checklisten. Besonders Material für die Patienten wird gefordert.
Diskussion: Die Fokusgruppenanalyse bestätigt die Notwendigkeit des Leitfadens: Er kann das Ansprechen des Themas „Gewicht" erleichtern und dient als Hilfestellung für die Behandler. Es besteht großer Bedarf nach Materialien für den Beratungsablauf sowie Patienteninformation seitens der Behandler.

Funding: formel1

→ **Sikorski, Claudia**
email: claudia.sikorski@medizin.uni-leipzig.de

POSTER 128

Modulation der Adipozytenvitalität nach autologer Fettgewebstransplantation

IFB – Adiposity Diseases

Sauber J[1,2], Meyer S[1,2]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Abteilung für Plastische-, Ästhetische- und spezielle Handchirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Einleitung: Autologe Fettgewebstransplantationen werden in der Plastischen Chirurgie zur Füllung von Gewebeverlusten eingesetzt. Die Vorteile liegen in der hohen Verfügbarkeit sowie in der fehlenden Fremdkörperreaktion. Diese Technik geht jedoch mit einer Resorptionsrate des Fettgewebes von bis zu 50% einher. Eine suffiziente Gewebedurchblutung verringert die Rückresorptionsrate. Durch Behandlung des Fettgewebstransplantates mit dem Hormon Leptin soll eine Steigerung der Angiogenese und somit der Adipozytenvitalität erzielt werden.
Material und Methoden: In einem C57Bl/6-Mausmodell wird inguinales Fettgewebe in eine Rückenhautkammer autolog transplantiert. Dem Transplantat wird Leptin in den Konzentrationen 1μg/ml und 3μg/ml zugefügt (je n=16) und dieses danach in die Rückenhautkammer transplantiert. Dem Fettgewebe der Kontrollgruppe wird NaCl zugefügt. Im Verlauf werden an den p. o. Tagen 1,3,7,10,15 und 21 intravitalmikroskopisch die funktionelle Kapillardichte und die Adipozytenmorphologie beurteilt. Ergänzt wird die Studie durch histologische und immunhistochemische Untersuchungen mit den Markern CD31, Perilipin und Ki67.
Ergebnisse und Diskussion: Das Rückenhautkammermodell ermöglicht die kontinuierliche *in vivo* Visualisierung der Angiogenese. Es zeigt sich eine Steigerung der Angiogenese im Fettgewebstransplantat in der Leptin 3μg/ml-Gruppe, welche am Tag 3–7 einsetzt. Im Verlauf tritt in allen Gruppen eine morphologische Veränderung der Adipozyten von polygonalen zu runden Adipozyten auf. Die histologischen und immunhistochemischen Untersuchungen zur Beurteilung der Adipozytenvitalität werden aktuell durchgeführt.

Funding: ifb

➜ **Sauber, Jeannine**
email: jeannine.sauber@medizin.uni-leipzig.de

POSTER 129

Der Einfluss von gewichtsbezogener Diskriminierung und nicht-normativem Essverhalten auf den Gewichtserhalt nach erfolgreicher Gewichtsreduktion

IFB – Adiposity Diseases

Hübner C[1], Baldofski S[1], de Zwaan M[2], Hilbert A[1]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Klinik für Psychosomatik und Psychotherapie, Medizinische Hochschule Hannover

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hintergrund: Gewichtsbezogene Diskriminierung (GBD) in Kindheit/Jugend ist mit nicht-normativem Essverhalten (EV) assoziiert, welches einen negativen Zusammenhang mit dem Gewichtserhalt aufweist. Der Einfluss der GBD auf den Gewichtserhalt ist jedoch noch unklar. In der vorliegenden Arbeit soll daher der Einfluss der GBD in Kindheit/Jugend auf den Gewichtserhalt und die Rolle des EV als möglicher Mediator untersucht werden.
Methode: Im Rahmen des Deutschen Gewichtskontrollregisters wurden bei $N = 381$ Probanden nach vergangenem Gewichtsverlust (≥10% des Maximalgewichts, mind. 1 Jahr gehalten) die GBD in Kindheit/Jugend, das aktuelle EV sowie die Veränderung des Body-Mass-Index (BMI) prospektiv über 2 Jahre erfasst. Strukturgleichungsmodelle wurden genutzt, um Mediationsbeziehungen zu testen.
Ergebnisse: Nach Kontrolle von Alter und Geschlecht prädizierte eine stärkere Belastung durch GBD ein höheres aktuelles Ausmaß restriktiven, externalen und emotionalen EV. Letzteres sagte wiederum eine größere BMI-Zunahme oder eine kleinere BMI-Abnahme vorher und mediierte den Zusammenhang zwischen erlebter Belastung und BMI-Veränderung vollständig.
Schlussfolgerung: Der Gewichtserhalt ist bei einer stärker erlebten Belastung durch GBD während Kindheit/Jugend ungünstiger, v. a. bei einem stärkeren emotionalen EV. Die Resultate verdeutlichen, dass die erlebte Belastung durch GBD zwar mit nicht-normativem EV einhergeht, sie jedoch über das emotionale EV hinaus keinen Beitrag zur Vorhersage des Gewichtserhalts nach 2 Jahren leistet. Die Ergebnisse unterstreichen somit die Relevanz von Interventionen zur Reduktion von GBD und emotionalem EV.

➜ **Hübner, Claudia**
email: claudia.huebner@medizin.uni-leipzig.de

POSTER 130

DNA 5-Hydroxymethylation in human adipose tissue differs between subcutaneous and visceral fat depots

IFB – Adiposity Diseases

Rohde K[1], Keller M[1], Stumvoll M[1,2], Dietrich A[1,3], Blüher M[2], Böttcher Y[1]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Sektion Nephroplogie, Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
3 Sektion Bariatrische Chirurgie, Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Epigenetic mechanisms such as DNA methylation at the 5-carbon of cytosine (5-mC) were shown to have tissue specific patterns and play a role in post-transcriptional regulation of gene expression. While 5-mC is well studied, the discovery of a stable intermediate during DNA demethylation (5-hydroxymethylcytosin (5-hmC)) raises questions about its function and distribution. The aim of this study was to test whether 5-hmC exists in human subcutaneous (SAT) and visceral adipose tissue (VAT). Further, we analyzed for a potential relationship with anthropometric and metabolic parameters.
Material and Methods: We used a sample set of 81 subjects (42 women and 39 men) to measure the % 5-hmC in both SAT and VAT by using ELISA technology. To test for associations with anthropometric and metabolic parameters we used paired students *t*-tests, bivariate correlation analyses and linear regression models.
Results: We observed an average 5-hmC content of 0.47 % in SAT and 0.51 % in VAT while VAT is significantly higher hydroxymethylated ($P = 0.005$). In the total cohort we found that % 5-hmC in VAT is positively associated with age ($P = 0.034$). Furthermore we identified a significantly negative relationship between % 5-hmC in VAT and LDL cholesterol levels which withstands adjustment for covariates and remains significant after correction for multiple testing ($P = 0.008$).
Conclusion: Our data suggest adipose tissue depot specific 5-hydroxymethylation levels with significantly higher levels in VAT.

Funding: ifb

→ **Rohde, Kerstin**
email: kerstin.rohde@medizin.uni-leipzig.de

POSTER 131

Indications for potential parent of origin effects within the FTO gene using long range phasing algorithms

IFB – Adiposity Diseases

Liu X[1,2], Scholz M[3,4], Tönjes A[5], Stumvoll M[1,5], Stadler P[2], Böttcher Y[1]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Bioinformatics Group, Department of Computer Science, Universität Leipzig
3 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
4 Institute for Medical Informatics, Statistics and Epidemiology, Universität Leipzig
5 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background and aim: Genome-Wide Association Studies (GWAS) were successfully applied to discover associations with obesity. However, the GWAS design is usually based on unrelated individuals and inheritance information on the parental origin of the alleles is missing. Taking into account parent of origin may provide further insights into the genetic mechanisms contributing to obesity. We hypothesized there may be variants within the robustly replicated fat mass and obesity associated (*FTO*) gene that may confer different risk for obesity depending on the transmission from father or mother.
Material and methods: Genome-wide genotypes and pedigree information from the Sorbs population (N=525) were used. Phasing was done by applying long-range phasing and haplotype library imputation algorithm. Phased genotypes among 525 individuals were generated by AlphaImpute. Subsequently, 22 SNPs within *FTO* introns 1 to 3 were selected and parent of origin specific association analyses were performed using PLINK: (i) standard association test, (ii) considering paternal and (iii) maternal alleles.
Results: We identified several SNPs conferring different P values depending on parental origin. Among them, rs1861868, rs1121980 and rs9939973 (all intron 1) show significantly different effect estimates beta (Student´s t-Test; $P< 0.05$). Of note, rs1121980 tags rs8050136 (r^2=0.98) which was well replicated to be strongly associated with BMI. Conclusion: Our results suggest that the obesity risk transmitted by several *FTO* variants may depend on the parental origin of the allele. Larger family-based studies are warranted to replicate our findings.

Funding: ifb

➜ **Liu, Xuanshi**
email: xuanshi.liu@medizin.uni-leipzig.de

POSTER 132

Genome wide DNA promoter methylation: Differences in human subcutaneous vs. omental visceral adipose tissue

IFB – Adiposity Diseases

Keller M[1], Hopp L[2], Liu X[1], Rohde K[1], Klös M[1], Dietrich A[3], Schön M[4], Gärtner D[4], Lohmann T[5], Dreßler M[5], Stumvoll M[1,6], Kovacs P[1], Binder H[2], Blüher M[6], Böttcher Y[1]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Interdisziplinäres Zentrum für Bioinformatik (IZBI), Universität Leipzig
3 Sektion Bariatrische Chirurgie, Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Universität Leipzig
4 Klinik für Viszeral Chirurgie, Städtisches Klinikum Karlsruhe
5 Städtisches Klinikum Dresden-Neustadt, Dresden
6 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Differences in DNA methylation pattern between subcutaneous adipose tissue (SAT) and omental visceral adipose tissue (OVAT) may contribute, to the distinctivemetabolic activity. In the present study we examined genome wide DNA promoter methylation and mRNA expression pattern in 80 paired human SAT and OVAT samples including lean and obese subjects.
Methods: DNA methylation analysis was performed using methylated DNA immunoprecipitation (MeDIP) and subsequent hybridising on Affymetrix Human Promoter 1.0R tilling arrays. All genes with at least 30% methylation difference between SAT and OVAT or lean and obese subjects in the same fat depot were taken forward to corresponding mRNA expression analyses. The expression profiles were generated using Illunima human HT-12 chips. Finally, epigenome wide association analysis (EWAS) between methylation levels and the individual Body Mass Index (BMI in kg/m^2) were conducted.
Results: We identified 35 genes in the lean and 38 in the obese subgroup conferring negative correlation between DNA methylation and mRNA expression comparing SAT and OVAT. 37 genes were found in the SAT and 76 in the OVAT subgroup comparing lean and obese individuals. The top hits included known candidate genes such as *PPARG* but also unexpected genes, e. g. *BHMT*. EWAS identified *GPS2* as the top gene being strongly associated with BMI (p-value = 4.3x10^{-7}).
Conclusion: To the best of our knowledge, we show the first genome wide epigenetic data set comparing SAT and OVAT in a considerably large cohort. Our data significantly contribute to identifying novel genes related to human obesity.

Funding: ifb

➜ **Keller, Maria**
email: maria.keller@medizin.uni-leipzig.de

POSTER 133

Adipositas und exzessive Gewichtszunahme in der Schwangerschaft: Prävalenz und Zusammenhänge zu Missbrauch und Vernachlässigung in der Kindheit

IFB – Adiposity Diseases

Nagl M[1,2], Lehnig F[1,2], Stepan H[3], Wagner B[4], Kersting A[1,2]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Psychosomatische Medizin und Psychotherapie, Universität Leipzig
3 Abteilung für Geburtsmedizin, Universität Leipzig
4 MSB Medical School Berlin

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hintergrund: Adipositas und eine exzessive Gewichtszunahme in der Schwangerschaft sind mit besonderen Risiken (z. B. Geburtskomplikationen) für Mutter und Kind assoziiert. Ziel der Studie war die Bestimmung der Prävalenz von Adipositas und exzessiver Gewichtszunahme in der Schwangerschaft sowie die Untersuchung von Zusammenhängen zu Misshandlungserfahrungen in der Kindheit.
Methode: Bisher liegen Daten von *N*=497 Frauen im Alter von 19–44 Jahren vor. Innerhalb der ersten vier Monate nach Entbindung wurden Kindesmissbrauch und Vernachlässigung retrospektiv mit dem Childhood Trauma Questionnaire erfasst. Der Body Mass Index vor der Schwangerschaft wurde aus selbstberichtetem Gewicht und der Körpergröße berechnet, die Gewichtszunahme anhand der Angaben aus dem Mutterpass.
Ergebnisse: Die Prävalenzrate für Adipositas lag bei 7%, für exzessive Gewichtszunahme bei 48%. Ein erhöhtes Risiko für Adipositas zeigte sich für Frauen mit schwerem emotionalem Missbrauch (*OR*=3,44, 95%CI=1,1–11,0) sowie schwerer körperlicher (*OR*=5,8, 95%CI=1,7–19,4) und emotionaler Vernachlässigung (*OR*=5,8, 95%CI=2,1–16,4). Frauen mit leichtem körperlichem Missbrauch wiesen ein erhöhtes Risiko für exzessive Gewichtszunahme auf (*OR*=6,6, 95%CI=1,5–29,6).
Diskussion: Die Ergebnisse liefern Hinweise darauf, dass emotionaler Missbrauch sowie Vernachlässigung in der Kindheit mit Adipositas in der Schwangerschaft im Sinne einer Dosis-Wirkungsbeziehung assoziiert sind. Frauen mit körperlichen Missbrauchserfahrungen weisen ein erhöhtes Risiko für exzessive Gewichtszunahme auf. Mögliche Mechanismen des Zusammenhangs und Implikationen für die Praxis werden diskutiert.

Funding: ifb

→ **Nagl, Michaela**
email: michaela.nagl@medizin.uni-leipzig.de

POSTER 134

The adipokine preadipocyte factor-1 is downregulated in preeclampsia and expressed in human placenta

IFB – Adiposity Diseases

Schrey S[1], Wurst U[2,3], Ebert T[2,3], Kralisch S[2,3], Drewlo S[4], Stepan H[1], Lößner U[2,3], Platz M[2,3], Kratzsch J[5], Stumvoll M[3], Faßhauer M[2,3]

1 Abteilung für Geburtsmedizin, Universität Leipzig
2 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
3 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
4 Centre for Trophoblast Research, Medical School, Wayne State University, Detroit, MI, USA
5 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Various adipocyte-secreted factors – so-called adipokines – contribute to the development of preeclampsia (PE), a severe systemic complication in pregnancy which increases the future risk for cardiovascular and metabolic disease in both mother and newborn. Pre-adipocyte factor-1 (Pref-1) was recently introduced as a novel antiangiogenic and antiadipogenic adipokine.
Methods: Pref-1 was quantified in patients with PE (n=51) and healthy pregnant controls (n=51) during pregnancy, as well as 6 months after delivery (study population 1). Furthermore, Pref-1 was investigated in the immediate peripartal period in 40 healthy pregnant women undergoing elective cesarean section (study population 2). Moreover, placental expression of Pref-1 was assessed.
Results: In study population 1, median Pref-1 serum concentrations during pregnancy were significantly lower in women with PE (0.49 μg/l) as compared to healthy pregnant controls (0.68 μg/l) ($p < 0.001$). Furthermore, Pref-1 serum concentrations were independently predicted by PE, leptin levels, and gestational age in study population 1. In both study populations, Pref-1 serum levels significantly decreased after delivery as compared to antepartum levels. Moreover, significant expression of Pref-1 was detected in placental tissue.
Conclusion: Maternal serum concentrations of antiangiogenic and antiadipogenic Pref-1 are significantly decreased in PE. Furthermore, the placenta significantly contributes to circulating Pref-1 in pregnancy. The pathophysiological significance of Pref-1 downregulation in PE needs to be studied in more detail in future experiments.

Funding: ifb

➜ **Wurst, Ulrike**
email: ulrike.wurst@medizin.uni-leipzig.de

POSTER 135

Nutzung neuer Medien in der Adipositas-Nachsorge für Jugendliche: Case Management via Telefon, Web Forum und SMS-Nachrichten (TeAM-Programm)

IFB – Adiposity Diseases

Markert J[1], Herget S[1], Blüher S[1]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Fragestellung: 1.) Wie viel Prozent der angesprochenen Jugendlichen nehmen am Programm teil und durchlaufen alle Beratungssitzungen? 2.) In welcher Form findet das Programm den größeren Zuspruch (Telefonberatung & SMS ODER Telefonberatung, SMS & Web Forum)?

Methodik: TeAM (Telefonberatung als Adipositas-Management) ist ein Nachsorgeprogramm für Jugendliche (14–18 Jahre) nach stationärer Adipositas-Rehabilitation. Die telefonische Beratung basiert auf dem Systemischen Ansatz nach Steve DeShazer. Zwei verschiedene 4-monatige Interventionsformen wurden in der Pilotstudie geprüft: Gruppe A (Telefonberatung & SMS), Gruppe B (Telefonberatung, SMS & passwortgeschütztes Web Forum zum Austausch mit anderen Programmteilnehmern.

Ergebnisse: 80 Jugendliche erklärten in den Reha-Kliniken ihre Teilnahmebereitschaft. 71 schickten gemeinsam mit ihren Eltern die ausgefüllten Teilnahmebögen. 38 füllten das Baseline-Material aus und wurden randomisiert. 14 Jungen und 24 Mädchen mit einem mittleren Alter von 15.82 Jahren und einem mittleren BMI-SDS 2.48 ± 0.59 nahmen an der Pilotstudie teil. Damit lag die Teilnahmerate bei 47.5%. Die Dropout-Rate lag in Gruppe A bei 16.7%, in Gruppe B bei 30.8% (OR 2.2, 95% CI 0.2–29, p=0.6). Die aktive Teilnahme am Web-Forum betrug < 10.0%.

Schlussfolgerungen: Systemische Telefonberatung als Adipositas-Nachsorge-Maßnahme für Jugendliche wird von der Zielgruppe angenommen. Derzeit untersucht eine Effektivitätsstudie die Wirkung des Nachsorge-Programms TeAM (Telefonberatung & SMS-Nachrichten) auf die Stabilisierung des BMI-SDS und das Gesundheitsverhalten der jugendlichen Teilnehmer.

Funding: ifb

➜ **Markert, Jana**
email: FF_Markert@web.de

POSTER 136

Epidemiologie des Loss of Control Eating bei Jugendlichen

IFB – Adiposity Diseases

Schlüter N[1], Schmidt R[1], Tetzlaff A[1], Hilbert A[1]

1 Abteilung für Medizinische Psychologie und Medizinische Soziologie, Universität Leipzig

Hintergrund: Essstörungssymptome sowie klinisch relevante Essstörungen zeigen eine Erstmanifestation insbesondere im Jugendalter. Zur Epidemiologie des Loss of Control (LOC) Eating, einem Risikofaktor für die Binge Eating-Störung, liegen bisher nur wenige Daten von deutschen Jugendlichen vor.
Methodik: Im Rahmen von Schulbesuchen wurden Jugendliche (12–20 Jahre) zum Essverhalten befragt. Erfasst wurden die essstörungsspezifische Psychopathologie (Eating Disorder Examination-Questionnaire-8) sowie die psychosoziale Beeinträchtigung durch die Essstörungssymptome (Clinical Impairment Assessment). Mit dem Eating Disorder Examination wurden die Kernsymptome des LOC Eating erfasst. Die Berechnung des Body Mass Index-Standard Deviation Score (BMI-SDS) erfolgte durch Selbstbericht.
Ergebnisse: Insgesamt wurden Daten von 1643 Jugendlichen (Alter: M = 15.0 ± 2.8 Jahre; Geschlecht: 1025 weiblich, 62.4%; BMI-SDS: M = -0.1 ± 0.9) erhoben. Von diesen waren 122 (7.7%) übergewichtig und 41 (2.6%) adipös. Bezogen auf die letzten 28 Tage gaben 226 (13.8%) mindestens eine LOC-Episode an (subklinisches LOC), weitere 156 (9.5%) zeigten eine klinisch relevante Häufigkeit von LOC-Episoden (≥ 4 Episoden). Jugendliche mit klinisch relevantem LOC Eating waren häufiger weiblich, übergewichtig oder adipös und berichteten häufiger essstörungsspezifische Psychopathologie sowie eine stärkere Beeinträchtigung infolge der Essstörungssymptome als Jugendliche ohne bzw. mit subklinischem LOC Eating.
Schlussfolgerung: Symptome des LOC Eating sind bereits im Jugendalter stark prävalent und mit Übergewicht und Adipositas assoziiert.

Funding: ifb

➜ **Schlüter, Nora**
email: NoraEllen@web.de

POSTER 137 **Obesity and Discrimination – A Systematic Review**

IFB – Adiposity Diseases

Spahlholz J[1,2], Baer N[2], Riedel-Heller S[2], Sikorski C[1,2]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hintergrund: Personen mit Adipositas sind häufig mit einer Vielzahl an Vorurteilen innerhalb der Gesellschaft konfrontiert. Ob und inwiefern sich eine ablehnende Haltung tatsächlich in diskriminierendem Verhalten niederschlägt, ist jedoch unklar. Bislang gibt es keine Arbeit, die den aktuellen Forschungsstand zu den Erscheinungsformen und der Häufigkeit von Diskriminierung gegenüber Personen mit Adipositas zusammenfassend diskutiert, um aufbauend Möglichkeiten der Einflussnahme und Maßnahmen zur Gegensteuerung abzuleiten.
Methoden: Systematische Literaturübersicht in den folgenden 3 Datenbanken ohne Zeitbegrenzung: Medline, ISI Web of Knowledge und The Cochrane Library. Ergebnisse aus den einzelnen Studien wurden aggregiert und Kernaussagen abgeleitet.
Ergebnisse: Es konnten 19 Studien extrahiert werden, die belegen, dass sich Diskriminierung gegenüber Personen mit Adipositas in nahezu allen Lebensbereichen zeigt. In experimentellen und nicht-experimentellen Studien konnte gezeigt werden, dass Diskriminierung nicht nur subjektiv, sondern auch objektiv auf der Verhaltensebene erkennbar ist. Die Prävalenzangaben in bevölkerungsrepräsentativen Studien schwanken zwischen 6.1 % und 60.7 % in den USA. Die Befunde zeigen, dass ein weibliches Geschlecht und ein steigendes Körpergewicht mit einer höheren Diskriminierung einhergehen. Häufigkeitsangaben für den deutschen Sprachraum liegen bislang nicht vor.
Schlussfolgerung: Die berücksichtigen Studien liefern Hinweise dafür, dass Diskriminierung bei Adipositas und die damit einhergehenden negativen Konsequenzen von gesellschaftlicher und versorgungspolitischer Relevanz sind.

Funding: ifb

➜ **Spahlholz, Jenny**
email: jenny.spahlholz@medizin.uni-leipzig.de

POSTER 138

Parental weight-teasing in overweight adolescents with and without binge-eating disorder

IFB – Adiposity Diseases

Tetzlaff A[1], Rudolph A[1], Schmidt R[1], Hilbert A[1]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction:Relatively little is known about parental critical comments about weight and shape and the role for the self in overweight adolescents with and without binge-eating disorder (BED). Therefore, the current study sought to better understand adolescents' perceptions of parental weight-teasing and their weight bias internalization. Methods: Overall, $N = 90$ adolescents aged 12 to 20 years participated in the present study. Overweight adolescents with BED (BED; $n = 40$), overweight adolescents without BED (OW; $n = 25$), and normal-weight adolescents without any eating disorder symptoms (NW; $n = 25$) were stratified according to age, sex, BMI percentile, and socio-economic status. All adolescents filled out modified parent-oriented versions of the *Perception of Teasing Scale (POTS)* and the *Weight Bias Internalization Scale (WBIS)*. Results: The BED group reported higher frequency ($p = >.001$) of parental weight-teasing compared to both the OW and NW group, whereas the latter two did not differ significantly ($p > .05$). In addition, the BED group reported significantly higher internalized weight-bias than the OW, and the OW revealed higher scores than the NW (WBIS; $p < .001$). Conclusion: This is the first study examining parental weight-teasing and internalization in overweight adolescents with and without BED. Results confirmed previous findings in adults and further emphasized the important role of weight-teasing by parents in adolescents. Further investigations should focus on the relation between perceived weight-teasing and parental stigmatizing attitudes.

Funding: ifb

➜ **Tetzlaff, Anne**
email: anne.tetzlaff@medizin.uni-leipzig.de

POSTER 139 **Cytokines in general and central obesity**

IFB – Adiposity Diseases

Weschenfelder J[1], Schmidt F[1], Sander C[1], Minkwitz J[1,2], Thormann J[2,3], Chittka T[2,3], Mergl R[3], Faßhauer M[2], Stumvoll M[2], Holdt L[4], Teupser D[4], Hegerl U[1], Himmerich H[1,2]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
3 Klinik für Psychiatrie, Psychotherapie und Psychosomatik des Kindes/ Jugendalters, Universität Leipzig
4 Institut für Laboratoriumsmedizin, Klinikum der Universität München

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objective: To characterize the profile of a broad range of pro- and anti-inflammatory cytokines and the impact of physical activity and energy expenditure in individuals with general obesity, central obesity, and non-obese subjects.
Design, Setting, and Participants: A cross-sectional study comprising 117 obese patients (body mass index (BMI) ≥ 30) and 83 non-obese community-based volunteers.
Main Outcomes Measures: Serum levels of interleukin (IL)-2, IL-4, IL-5, IL-10, IL-12, IL-13, granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon (IFN)-γ and tumor necrosis factor (TNF)-α were measured. Physical activity and energy expenditure (MET) were assessed with actigraphy. Adipometrics comprised BMI, weight, abdominal-, waist- and hip-circumference, waist to hip ratio (WHR), and waist-to-height-ratio (WHtR).
Results: General obesity was associated with significantly elevated levels of IL-5, IL-12, IL-13, IFN-γ and reduced IL-10, central obesity with significantly elevated IL-5, IL-10, IL-12 and IL-13. All 9 cytokines were significantly elevated in general obesity participants with low versus high physical activity. Subjects with low METs had higher levels of IL-5 and IL-13 and lower levels of IL-10, independent from diagnosis. Cytokines significantly correlated with adipometrics, particularly in obese participants.
Conclusions: Results confirm up-regulation of certain pro- and anti-inflammatory cytokines in obesity. In obese subjects, physical activity may lower levels and thus reduce pro-inflammatory effects of cytokines that may link obesity, insulin resistance and diabetes.

Funding: ifb

→ **Weschenfelder, Julia**
email: julia.weschenfelder@medizin.uni-leipzig.de

POSTER 140

Subjektiver Gesundheitszustand und Lebenszufriedenheit – erste Ergebnisse adipöser Patienten vor und nach einem bariatrischen Eingriff

IFB – Adiposity Diseases

Peterhänsel C[1,2], Nagl M[2], Wagner B[3], Dietrich A[1,4], Blüher M[1,5], Kersting A[1,2]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Psychosomatische Medizin und Psychotherapie, Universität Leipzig
3 MSB Medical School Berlin
4 Sektion Bariatrische Chirurgie, Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Universität Leipzig
5 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In Deutschland gibt es weiterhin einen Anstieg bariatrischer Verfahren, da diese als effektivste Methoden einer langfristigen Gewichtsreduktion und der Verbesserung komorbider Erkrankungen gelten. Mithilfe der vorliegenden Längsschnittstudie wird untersucht, ob zeitlich relevante Unterschiede in der Lebensqualität und dem Gesundheitszustand zwischen adipösen Personen mit einem chirurgischen Eingriff und einer stark übergewichtigen Vergleichsgruppe vorliegen. Als Messinstrumente wurden der Short Form Health Survey–12 und Fragen zur Lebenszufriedenheit eingesetzt. Die statistische Analyse bezog Testergebnisse vor der Operation sowie 6 und 12 Monate nach OP ein. Es wurden Varianzanalysen mit Messwiederholung und post-hoc-Tests berechnet. Unterschiede zu den einzelnen Messzeitpunkten wurden mit Mittelwertvergleichen überprüft. In der bariatrischen Gruppe standen n=107 Personen, in der adipösen Kontrollgruppe n=92 Personen zur Verfügung. Präoperativ wiesen bariatrische Patienten im SF-12 signifikant niedrigere Werte auf der Skala zur körperlichen und höhere Werte auf der Skala zur psychischen Gesundheit auf als Personen der Kontrollgruppe. Im FLZ gab es keine Unterschiede in der allgemeinen und gesundheitlichen Lebensqualität. Nach einem Jahr unterscheiden sich die Gruppen auf allen vier Skalen, wobei die Werte der operierten Gruppe signifikant über denen der Kontrollpersonen liegen. Trotz der deutlichen postoperativen Besserung der Gesundheit und Lebenszufriedenheit ist eine langfristige psychologische Betreuung indiziert, um die Stabilisierung dieser Parameter auch nach der Phase der Gewichtsreduktion zu ermöglichen.

Funding: ifb

→ **Peterhänsel, Carolin**
email: carolin.peterhaensel@medizin.uni-leipzig.de

POSTER 141

Verarbeitung von Nahrungsreizen bei Erwachsenen mit Binge-Eating Störung und Night Eating Syndrom: Eine Eyetracking Studie

IFB – Adiposity Diseases

Baldofski S[1], Sperling I[1], Lüthold P[2], Krummenacher J[2], Hilbert A[1]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Departement für Psychologie, Universität Fribourg

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Fragestellung: Bisher wurden Unterschiede in der kognitiven Verarbeitung von Nahrungsreizen für Personen mit Anorexia Nervosa und Bulimia Nervosa im Vergleich zu Kontrollprobanden belegt. Zugrunde liegende Aufmerksamkeitsprozesse der Verarbeitung von Nahrungsreizen bei Personen mit Binge-Eating Störung (BES) oder Night Eating Syndrom (NES) wurden bisher jedoch kaum untersucht. Da überlappende Mechanismen beider Störungsbilder angenommen werden, war es das Ziel, Unterschiede in der visuellen Aufmerksamkeit zwischen Personen mit BES und NES zu untersuchen.

Methodik: In zwei Gruppen mit BES (n = 23) und NES (n = 23) wurde die Aufmerksamkeitsverteilung bei der freien Betrachtung gematchter Bildpaare von Nahrungs- und neutralen Bildern mittels Eyetracking untersucht. Die Position der initialen Fixation sowie die Blickdauer auf jede Reizkategorie wurden erfasst.

Ergebnisse: Gruppenübergreifend war die initiale Fixation tendenziell häufiger auf Nahrungsreize als auf neutrale Reize gerichtet. Für die Blickdauer ergaben sich keine signifikanten Unterschiede zwischen Nahrungs- und neutralen Reizen. Personen mit BES und NES unterschieden sich nicht hinsichtlich der Position der initialen Fixation sowie der Blickdauer.

Schlussfolgerung: Es ergaben sich keine differentiellen Effekte in attentionalen Aspekten der kognitiven Verarbeitung von Nahrungsreizen zwischen Personen mit BES und NES. Jedoch zeigte sich über beide Gruppen hinweg die Tendenz einer frühen Aufmerksamkeitszuweisung auf Nahrungsreize im Vergleich zu neutralen Reizen.

Funding: ifb

➜ **Baldofski, Sabrina**
email: sabrina.baldofski@medizin.uni-leipzig.de

POSTER 142

MR-Spektroskopie und T1-Relaxationszeiten im viszeralen Fettgewebe von adipösen Patienten

IFB – Adiposity Diseases

Garnov N[1,2], Linder N[1,2], Schaudinn A[1,2], Blüher M[1,3], Kahn T[1,2], Busse H[1,2]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Diagnostische und Interventionelle Radiologie, Universität Leipzig
3 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Zielsetzung: Die veränderte Funktion des Fettgewebes spielt eine entscheidende Rolle bei Begleiterkrankungen der Adipositas. Die T1-Relaxationszeiten im viszeralen Fettgewebe (VAT) von adipösen Patienten unterscheiden sich von denen der schlanken Probanden, was auf Veränderungen des Fettgewebes im Verlauf der Adipositas deuten kann. Diese Studie vergleicht an adipösen Patienten die T1-Zeiten im VAT mit MR-spektroskopisch (MRS) ermittelten Konzentrationen relevanter Lipidanteile.
Material und Methodik: Die MRT-Analyse (1,5 T) umfasste 52 adipöse Patienten (BMI 37±5 kg/m²), bei denen T1 und MRS-Messungen durchgeführt, sowie das gesamte abdominelle VAT-Gewicht bestimmt wurde. Die ROIs lagen im retroperitonealen VAT (infrarenal).
Ergebnisse: Das mittlere VAT-Gewicht betrug 3,8±2,2 L, T1 lag im Mittel bei 318±27 ms. Das Fettspektrum zeigte gut definierbare Triglyzerid-Peaks bei 0,9 ppm (Methyl); 1,3 ppm (Methylen); 2,1 ppm (a-Methylen, Allylgruppe); 2.8 ppm (Diallylgruppe); 5,3 ppm (Vinyl) sowie bei 4,8 ppm (Wasser). Die T1-Zeiten korrelierten signifikant ($p < 0,05$) mit dem VAT-Gewicht ($r=-0,39$), mit dem Wassergehalt ($r=0,44$), sowie den relativen Methyl- ($r=-0,46$), Methylen- ($r=-0,43$) und Vinyl-Konzentrationen ($r=-0,38$).
Schlussfolgerungen: Wie bereits früher vermutet, bestätigt diese Studie, dass die T1-Zeiten im VAT adipöser Patienten mit dem gesamten abdominellen VAT-Volumen korrelieren. Grund für diese Unterschiede könnten Zusammenhänge zwischen den T1-Zeiten und dem mittels MRS gemessenen Wassergehalt, sowie einigen Fettmetaboliten des viszeralen Fettes sein, welche durch die Adipositas verändert sein können.

➜ **Garnov, Nikita**
email: nikita.garnov@medizin.uni-leipzig.de

POSTER 143

Reflective Functioning in attachment related scenes of an online computer game

IFB – Adiposity Diseases

Weinberger NA[1,2], Wendt V[1,2], Keitel-Korndörfer A[2]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Klinik für Psychiatrie, Psychotherapie und Psychosomatik des Kindes/ Jugendalters, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The current study investigated participants' Reflective Functioning (RF) in the context of adult romantic attachment by using an implicit assessment tool. We aimed to explore weight-group differences and the influence of RF on attachment related game indices. The sample consisted of 30 obese and 30 normal weight women. Participants played an online computer game which contained attachment related key scenes (Schönbrodt & Asendorpf, 2012). Three game indices were analysed: emotion ascription to the game protagonist, mean physical distance between protagonist and virtual spouse and initiated actions during the game. RF was measured by coding Adult Attachment Interview transcripts (AAI; George et al., 1985) using the RF Scale (Fonagy et al., 1998). We found that overall (1) obese mothers initiated more positive actions in general and more positive interactions with the spouse in particular (2), RF did neither predict emotion ascription ratings nor mean distance and (3) RF predicted positivity and spouse-directedness of actions during the game. Implications of these findings are discussed.

→ **Weinberger, Natascha-Alexandra**
email: natascha-alexandra.weinberger@medizin.uni-leipzig.de

POSTER 144

Chronische Stressbelastung bei adipösen Patienten mit und ohne Binge Eating-Störung

IFB – Adiposity Diseases

Schumacher B[1], Rudolph A[2], Schwalm S[2], Hilbert A[2]

1 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
2 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Adipositas (Body Mass Index [BMI] ≥ 30 kg/m²) bezeichnet eine überproportionale Vermehrung des Körperfetts, die mit einer Reihe von physischen und psychischen Komorbiditäten einhergeht. Bisherige Studien zeigten einen positiven Zusammenhang zwischen Adipositas und psychischen Störungen in der Allgemeinbevölkerung. Insbesondere adipöse Patienten mit Binge Eating-Störung (BES), die durch regelmäßige Essanfälle mit Kontrollverlust ohne gewichtskompensatorische Maßnahmen gekennzeichnet ist, zeigen eine deutlich erhöhte Psychopathologie.
Ziel unserer Studie ist es, Zusammenhänge zwischen Adipositas, BES und chronischer Stressbelastung in einer konsekutiven Stichprobe von Patienten des Gewichtsreduktionsprogramms in der IFB Adipositas Ambulanz zu untersuchen. Berichtet werden Daten der Eingangsuntersuchung, in der valide und normierte Fragebögen zum Screening für Essstörungspsychopathologie (EDE-Q) und zur chronischen Stressbelastung (LKCS) eingesetzt wurden.
Bisher wurden N = 138 Patienten mit Adipositas (71,7% weiblich) eingeschlossen. Bei 18,0% der Patienten ergab sich ein Verdacht auf BES. Adipöse Patienten mit BES zeigten eine signifikant erhöhte chronische Stressbelastung im Vergleich zu adipösen Patienten ohne BES, die wiederum vergleichbare Werte zur Allgemeinbevölkerung aufwiesen.
Zu Beginn des Gewichtsreduktionsprogramms zeigen adipöse Patienten mit BES eine deutlich erhöhte chronische Stressbelastung. Dieses Ergebnis legt nahe, dass nicht per se ein Zusammenhang zwischen Adipositas und chronischer Stressbelastung besteht, sondern nur dann, wenn adipöse Patienten zusätzlich unter einer BES leiden.

Funding: ifb

➜ **Schumacher, Bettina**
email: bettinaschumacher@yahoo.de

POSTER 145 **Tamoxifen: how it influences adipocyte biology in vivo**

IFB – Adiposity Diseases

Hesselbarth N[1], Pettinelli C[1], Kunath A[1], Böge E[1,2], Kern D[1], Kern M[1], Klöting N[1,2]

1 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
2 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Tamoxifen is a selective oestrogen receptor modulator (SERM): it can activate the oestrogen receptor (ER) in some tissues acting as an oestrogen agonist, while inhibits it in others, behaving as an antagonist. This drug is commonly used in two important fields: in chemotherapy as endocrine treatment of choice for metastatic ER-positive tumours in women and in genetic engineering as a widespread activation system of inducible Cre-mediated recombination technology.
However, effects of Tamoxifen treatment on adipose tissue are not well characterized in literature. Therefore, this study had the aim to investigate how Tamoxifen influences adipocyte biology *in vivo*.
To analyse the role of the drug on adipose tissue biology *in vivo*, inbred male mice (C57Bl/6NTac) were treated with Tamoxifen and analysed in terms of adipocyte biology, energy homeostasis, insulin sensitivity and lipid profile.
In this study we obtained that Tamoxifen treatment leads to: (I) different body composition (II) increased insulin sensitivity (III) higher Triglyceride level in serum (IV) browning effects in subcutaneous adipose tissue and (V) an increased *Ki67* mRNA expression.
In conclusion, Tamoxifen has significant effects on adipose tissue biology, body composition and glucose metabolism, which need to be considered when using Tamoxifen as a tool to generate inducible knockout mouse models. Our data further suggest that Tamoxifen treated control mice should always be characterized in addition to the transgenic models to avoid misinterpretation of data related to Tamoxifen effects.

Supported by GV-SOLAS

➜ **Hesselbarth, Nico**
email: nico.hesselbarth@medizin.uni-leipzig.de

POSTER 146 **Combining PETMR data to analyse structural and functional alterations of the central norepinephrenic network in obesity**

Imaging

Melasch JT[1,2], Rullmann M[1,2], Luthardt J[2], Becker G[2], Arelin K[3], Müller K[3], Lobsien D[4], Ding Y[5], Sabri O[1,2], Pleger B[3,6], Hesse S[1,2]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Nuklearmedizin, Universität Leipzig
3 Max-Planck Institut für Evolutionäre Anthropologie Leipzig
4 Abteilung für Neuroradiologie, Universität Leipzig
5 Depts. of Radiology, Psychiatry and Chemistry, New York University School of Medicine, New York, USA
6 Tagesklinik für kognitive Neurologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Aim: Single PET and MR imaging provided evidence for distinct changes in central nervous norepinephrenic (NE) system in obesity. As a new approach our aim was to assess the relation between NE PET data and structural/functional MR data to identify brain regions and their connectivity related to changes in NE signaling in obesity.
Method: Structural/functional connectivity (resting-state, rs-)MR scans and C-11-methylreboxetine PET scan of 9 OB (BMI 42±4kg/m²; age 34±9 yrs; 4♀) and 10 HC (24±3kg/m²; 33±10yrs; 4♀) were acquired. We regressed T1-weighted MR data voxel-wise with PET data and correlated significant cluster with BMI. A seed-based correlation analysis of rs-MR data was performed to assess the functional connectivity of the detected area. Regions with altered connectivity were correlated with neuropsychological scores.
Results: Regression analysis showed a cluster (T=14.9, p=.000015 FWE-corr) in left middle temporal lobe (Brodmann Area BA 21) with reduced grey matter density (GMD) in relation to NE activity across whole brain. GMD within BA 21 neg correlated with BMI (r= -.57). Three functionally linked prefrontal regions and both hippocampi showed a BMI-related weakened connectivity to BA 21, and their neural activity neg correlated with scores for dysthymia.
Conclusion: Results suggest that NE transporter density is predicted by BMI-related reduced GMD in BA 21, may pointing to an local cortical atrophy in obesity. BA 21 is also linked to a lower BMI-related NE network activation which in turn is linked to mood alterations. It all may point to a NE-related brain network pathology linking obesity with dysthymia.

Funding: ifb

➜ **Melasch, Juliana Teresa**
email: juliana.melasch@yahoo.de

POSTER 147

Quantification of internal carotid artery stenosis – Comparison of 3D-ultrasound with common colour-coded duplexsonography

Imaging

Pelz J[1], Weinreich A[1], Fritzsch D[1], Saur D[1]
1 Klinik und Poliklinik für Neurologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Currently, colour-coded duplexsonography (CDS) can be regarded as clinical gold standard for detection and grading of internal carotid artery stenosis (ICAS) due to its good sensitivity and specificity. However, a second imaging modality is often desirable before undergoing intervention. Here, we want to compare 3D-ultrasound (3D-US) with CDS for quantifying ICAS.
Methods: 25 ICAS were examined by 2 neurologists and graded by CDS applying the multi-parametric "DEGUM ultrasound criteria" and by 3D-US using Curefab CS (Curefab Technologies GmbH, Munich, Germany) and calculating the distal cross section area reduction percentage (NASCET). Briefly, a magnetic field tracking system allows concatenation of common 2D B-mode images with spatial and temporal information, enabling their exact positioning in a virtual 3D-stack. Subsequently, carotid vessels and stenosis will be reconstructed semi-automatically.
Results: Reconstruction of ICAS was successful in 21 of 25 respectively in 19 of 23 cases. Using intraclass correlation, the intermethod agreement between 3D-US and CDS for grading ICAS was 0.8 for the first and 0.72 for the second sonographer. The Bland and Altman analysis revealed a moderate agreement between both methods. Concerning 3D-US, 15 of 18 ICAS showed a difference in stenotic value of ± 10% between both examiners while the remaining 3 ICAS showed a difference of 20%.
Conclusions: Quantification of ICAS by 3D-US is feasible and a promising complementary method to the well-established flow-based classification. However, accuracy should be further improved, probably by contrast enhanced ultrasound.

➜ **Pelz, Johann**
email: johann.pelz@medizin.uni-leipzig.de

POSTER 148

Modulation of Resting State Functional Connectivity by Continuous Theta Burst Stimulation within the Semantic Network

Imaging

Wawrzyniak M[1], Hoffstaedter F[2,3], Stockert A[1], Wrede K[1], Klingbeil J[1], Hartwigsen G[1], Eickhoff S[2,3], Saur D[1]

1 Klinik und Poliklinik für Neurologie, Universität Leipzig
2 Institute of Clinical Neuroscience and Medical Psychology, Heinrich Heine University Düsseldorf, Germany
3 Institute of Neuroscience and Medicine 1, Jülich Research Center, Germany

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Anterior inferior frontal gyrus (aIFG) and left posterior middle temporal gyrus (pMTG) are associated with semantic integration processes on sentence level. We combined continuous theta burst stimulation (cTBS) and resting state functional magnetic resonance imaging (rfMRI) to investigate how a focal perturbation over these areas changes resting state functional connectivity (rsFC) within the semantic network.

Twenty healthy right-handed subjects underwent three sessions of neuronavigated cTBS (over aIFG, over pMTG and a placebo stimulation) followed by 6 minutes of rfMRI. Variance explained by motion parameters and mean global signal per time point was removed and data were band pass filtered (0.01 – 0.08 Hz). The first Eigenvariate of voxel time courses within spheres (r=8 mm) around the stimulation sites was calculated. Connectivity was expressed as Fisher z-transformed Pearson correlation coefficients between this time courses and time courses of all brain voxels. Resulting rsFC maps were fed into a second level analysis in SPM8.

Left aIFG and pMTG show overlapping rsFC with a left lateralized fronto-temporal network including left IFG, MTG, supramarginal gyrus, precentral gyrus, supplementary motor area and right aIFG and MTG. This pattern is in accordance with meta-analytic data on the semantic network. CTBS did not show a significant influence on this pattern, although there were some statistical trends. Considering the literature it is likely that pre- and post-cTBS rfMRI sessions, a longer interval between cTBS and rfMRI and cTBS at higher intensities would increase the experiment's sensitivity for cTBS effects.

➜ **Wawrzyniak, Max**
email: max.wawrzyniak@medizin.uni-leipzig.de

POSTER 149

Semantische Integration beim auditiven Sprachverständnis

Imaging

Wendt C[1], Henseler I[2], Hartwigsen G[1], Saur D[1]
1 Klinik und Poliklinik für Neurologie, Universität Leipzig
2 Max-Planck Institut für Kognitive Neurowissenschaften Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Bisherige Bildgebungsstudien haben gezeigt, dass die Integration semantischer Information in den Satzkontext mit einer Aktivierung links-hemisphärischer frontotemporaler Hirnregionen assoziiert ist [1]. Die Aktivierungsmuster werden dabei in Abhängigkeit von der Schwierigkeit der semantischen Integration moduliert, wobei der Grad der Prädizierbarkeit des finalen Nomens eine große Rolle spielt. Um diesen zu variieren, wurden Sätze mit erwarteten, unerwarteten, semantisch inkorrekten und Pseudowort-Endungen experimentell im Rahmen einer lexikalischen Entscheidungsaufgabe verglichen. Im Gegensatz zu bisherigen Bildgebunsgsstudien wurden in dieser Studie das Paradigma auditiv präsentiert. Die vorliegenden Ergebnisse deuten darauf hin, dass sowohl der Gyrus frontalis inferior als auch der Gyrus temporalis medialis Kernreale für die semantische Integration beim auditiven Sprachverständnis darstellen. Die Konnektivitätsanalysen liefern zudem Hinweise darauf, dass diese Hirnregionen Teil eines fronto-temporalen Netzwerkes sind, das auf eine erhöhte Schwierigkeit beim Abruf und der Integration semantischer Information reagiert. Insgesamt zeigt sich ein Effekt der Integrationsschwierigkeit sowohl in den Verhaltenseffekten, als auch in den Hirnaktivierungen und der überregionalen Konnektivität. Das verwendetet Paradigma ist damit ein valides Instrument für die Untersuchung der semantischen Integration beim auditiven Sprachverständnis.

Referenzen:
1. Baumgaertner, A., C. Weiller, and C. Buchel, Event-related fMRI reveals cortical sites involved in contextual sentence integration. Neuroimage, 2002. 16(3), p. 736–45.

➜ **Wendt, Christin**
email: christinwendt@web.de

POSTER 150

Estrogen mediates fractional anisotropy changes in the hippocampus during the menstrual cycle – A pilot DTI study

Imaging

Barth C[1], Steele C[1], Arelin K[1,2,3], Müller K[1], Burmann I[1], Kratzsch J[4], Villringer A[2,3,5], Sacher J[1,2]

1 Max-Planck-Institut für Kognitions- und Neurowissenschaften
2 Tagesklinik für kognitive Neurologie, Universität Leipzig
3 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
4 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
5 Max-Planck Institut für Evolutionäre Anthropologie Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Several lines of evidence suggest sex hormones to be important modulators of neuroplasticity. The menstrual cycle offers a unique natural setup to study whether physiological sex hormone fluctuation can influence brain morphology. Here, we utilize diffusion weighted imaging (DWI) to investigate the impact of fluctuating hormone levels during the menstrual cycle on fractional anisotropy (FA). DW-images were acquired during 30 scanning sessions across four menstrual cycles with a 3-Tesla Magnetom Verio scanner (Siemens, Erlangen, Germany). Diffusion imaging data were processed with the FMRIB's software library (www.FMRIb.ox.ac.uk/fsl). Based on previous work that links the menstrual cycle to gray matter changes and to changes in functional connectivity in the hippocampus, we chose this structure as our Region-of-Interest (ROI). Hand drawn ROIs were derived from the thresholded (FA > 0.2) mean FA image. Mean FA values of mask regions were extracted, correlated with hormone levels and fed into partial correlation analysis (scan acquisition time) using SPSS Statistics 22 ($p < 0.05$). In the ROI analyses, the extracted mean FA values of the left hippocampus showed a positive correlation with estrogen ($r = 0.504$, $p = 0.005$). Our findings suggest that estrogen-fluctuations across the menstrual cycle modulate FA in the hippocampus, which is in line with established evidence froms rodents and humans demonstrating hippocampal plasticity to be mediated by sex steroids. To our knowledge, this exploratory single-subject study is the first to link the subtle hormonal fluctuations that occur during the menstrual cycle to changes in FA.

➜ **Barth, Claudia**
email: cbarth@cbs.mpg.de

POSTER 151

Influence of thyroid hormones on the activation of brown adipose tissue

Imaging

Steinhoff K[1], Krause K[2], Tönjes A[2], Stumvoll M[2,3], Sabri O[1,3], Hesse S[1,3]

1 Klinik und Poliklinik für Nuklearmedizin, Universität Leipzig
2 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
3 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Brown adipose tissue (BAT) is crucial in the thermal regulation and energy balance. Its activation via β3-adrenergic receptors leads to increased intracellular conversion of thyroid hormones (TH) T4 to T3 and hereby stimulates mitochondrial heat production by increased UCP-1 transcription. To date, only few studies have been conducted targeting TH-mediated BAT activation, providing contradictory data. Our aim was therefore to investigate the effects of peripheral TH on BAT activity. From own preclinical data we assumed that hyperthyroidism is associated with higher BAT activity.

Methods: Six manifest hyperthyroid subjects were investigated by F-18-FDG PET/CT and successively PET/MRI to assess metabolic activity. CT-based VOI analysis was applied to calculate the glucose uptake in BAT (supraclavicular) and in the skeletal muscle as ratios between BAT and muscle, respectively, normalized to liver and blood pool activity (SUVmean).

Results: In the hyperthyroid subjects, F-18-FDG uptake was increased in skeletal muscle and BAT depending on TH levels. Semiquantitatively, TH levels showed a positive correlation with the BAT/liver and BAT/blood pool ratio (R=0.87 und 0.86; p=0.009) as well as with the muscle/liver and muscle/blood pool ratio (R=0.9 und 0.89; p=0.009).

Conclusion: In line with the assumption derived from the preclinical studies, our results suggest that BAT activity strongly depends on TH levels also in humans. This emphasizes that TH might lead directly to BAT activation. Further studies including an intraindividual comparison of PET/CT and PET/MR data after reaching an euthyroid metabolic state are planned.

➜ **Steinhoff, Karen**
email: karengeva.steinhoff@medizin.uni-leipzig.de

POSTER 152

The visualization of nanoparticle uptake by Laser Ablation – Inductively Coupled Plasma Mass Spectrometry (LA-ICP-MS)

Imaging

Böhme S[1]

1 Helmholtz-Zentrum für Umweltforschung, Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

During the last decade, much attention has been paid to potential adverse effects of engineered nanomaterials (ENM) towards environmental organisms. But beside the observation of the biological/toxicological effects of nanoparticles *in vivo* and *in vitro*, there is a need of adequate analytical detection methods covering the individual properties of ENM. In order to quantify the uptake of metal containing nanoparticles by environmental organisms or cells, often Inductively Coupled Plasma Mass Spectrometry (ICP-MS) as a robust element detection method is applied. However, imaging methods to visualize the localisation of incoperated nanoparticles require further development, especially with regard to a suitable calibration strategy.

In this study, a quantitative visualization method was developed by using a Laser Ablation ICP-MS (LA-ICP-MS) to quantify and visualize the nanoparticle uptake in environmental organisms (e.g. *Danio rerio*, *Daphnia magna*) in parallel. The technique combines information about the uptake amount and the distribution of nanoparticles inside the organism. In our experiments, we already proved the applicability of the method to detect nanoparticles (AuNP, Al_2O_3-NP and AgNP) in a ppb concentration range. The accordance to earlier quantification experiments of whole organisms confirmed the developed calibration strategy. The applied quantitative LA-ICPMS method allows a better comprehension of the processes of the internalization, the bioaccumulation, and the occurrence of toxic effects by nanomaterials. For instance, the chorion of *Danio rerio* was identified as a biological particle barrier.

➜ **Böhme, Steffi**
email: steffi.boehme@ufz.de

POSTER 153

Morphological basics of the human subthalamic nucleus: An attempt to improve DBS in Parkinson's Disease

Imaging

Zwirner J[1], Möbius D[1], Hammer N[1], Morawski M[2], Jäger C[2], Bechmann I[1], Lobsien D[3], Winkler D[4]

1 Institut für Anatomie, Universität Leipzig
2 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig
3 Abteilung für Neuroradiologie, Universität Leipzig
4 Klinik und Poliklinik für Neurochirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Clinical Background and Aims: Deep brain stimulation (DBS) of the subthalamic nuclei (STN) is a routinely performed treatment in advanced Idiopathic Parkinson's disease (IPD). Despite of the improving symptoms in IPD by means of STN-DBS, the onset of side effects such as depression, mania and speech abnormalities are poorly understood. In this respect some studies suggest a subdivision of the STN into sensomotorical, associative or limbic parts. The aim of our combined histological and radiological study is to estimate the number of cells and volume of the human STN and the relative position of the DBS electrodes in a surgery-like scenario.Based on this investigation we will analyze if there are site or shape-dependent alterations in the neurons of the STN. This could be a criterion for subdivisions within the STN and impact the stimulation site in STN-DBS.

Material and Methods: Ten brains of human body donors donated to science are investigated by means of 3Tesla magnetic resonance imaging (MRI) before paraffin sections are obtained throughout the entire midbrain. The slices are stained using an anti-human neuronal protein HuC/HuD antibody before being investigated stereoscopically. On basis of the MRI datasets, a virtual planning of the DBS electrodes is performed.

Outlook: The cell count and their concentration as well as the shape and volume of the STN will be evaluated radiologically and stereoscopically regarding if potential subdivisions can be indentified.Combining the radiological findings with histology will help determining the potential stimulation site and the morphological basis of STN-DBS.

➜ **Zwirner, Johann**
email: medijo@gmx.de

POSTER 154

Classifying Prostate Malignancy by Geometric Measurements

Imaging

Greim T[1], Braumann U[1,2], Muders M[3], Löffler M[4]

1 Interdisziplinäres Zentrum für Bioinformatik (IZBI), Universität Leipzig
2 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig
3 Institut für Pathologie, Unversitätklinikum Dresden
4 Institut für Medizinische Informatik, Statistik und Epidemiologie (IMISE), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Grading of prostate Cancer can be done by using the Gleason scheme, which depends on morphological and architectural aspects of prostate glands. Intra- and inter-observer reproducibility remains even after two revisions (Epstein et al. 2005; Epstein 2010) the main problem of this powerful classifier. To further improve and standardize malignancy analyses, computer-assisted approaches should be done in future.

Overall 112 specimens of prostate needle biopsies were available containing both malignant and benign structures. Because of treating complete specimens, we had to detect malignant glandular structures at first. For classifying malignancy two measures addressing the morphology of glands (i) inverse compactness and (ii) inverse solidity were applied. Combining both measures accuracy has reached 85% for full biopsies with only one tumor pattern.

Additionally to our former works with a reached accuracy of 95% these findings suggest that computer-assisted grading by using architectural and structural measurements is promising. Unlike in our previous work (Loeffler et al. 2012; Braumann et al. 2014) using ROIs with one Gleason grade and lots of glands exhibiting all the same tumor pattern, even full images of needle biopsies only cover a few glands, and in particular only few tumor glands. We always have a mixture of tumorous and non-tumorous glands. Against this background an accuracy of 85% still is amazing. We believe during this ongoing work certain modifications with regard to the detection of tumorous glands will improve accuracy toward a similar level as in previous work under restricted conditions.

➜ **Greim, Timo**
email: greim@izbi.uni-leipzig.de

POSTER 155

Labelling of GPCR based on a new peptide-templated acyl transfer reaction

Imaging

Lotze J[1], Reinhardt U[1], Seitz O[1], Beck-Sickinger AG[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Live cell imaging plays an important role in understanding and characterization of G protein coupled receptors (GPCR) in their native environment. To achieve this fluorescent moieties have to be attached to the protein of interest. Widely used strategies such as fusion proteins e. g. fusion of GFP or specific labelling tags such as SNAP-tag or Halo-tag have their advantages. But they also have certain drawbacks, for example the size, the labelling time and in case of the fusion protein its permanent fluorescence after folding. To overcome these disadvantages a new covalent labelling approach based on a coiled-coil interaction is presented. The *de novo* designed E_3/K_3 coiled-coil is characterized by a small size with 5–6 kDa and a high binding affinity with a K_D of 60–70 nM. The GPCR of interest is genetically fused to the Cys-E_3 peptide (acceptor) at its N-terminus which is capable to interact with the thioester-armed K_3 peptide (donor). After interaction of the donor and acceptor peptide an acyl transfer reaction takes place, which transfers only the reporter group from the K_3 peptide to the Cys-E_3 tagged GPCR. The advantages of this labelling strategy are high target specificity, fast reaction time and the free choice of the reporter group. Moreover the mass increase during the acyl transfer of the reporter group is minimal. This new chemical method for labelling GPCR in living cells is suitable for e. g. pulse-chase experiments. First experiments showed a successful labelling for several class A GPCR in HEK293 cells. Signal transduction assays demonstrate that the Cys-E_3 tagged GPCR are still fully functional.

➜ **Lotze, Jonathan**
email: jonathan.lotze@uni-leipzig.de

POSTER 156

Intensity standardisation of 7T MR images for intensity-based segmentation of subcortical brain structures

Imaging

Schindler S[1], Bazin P[2], Schreiber J[2]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 Max Planck Institut für Kognitions- und Neurowissenschaften

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In search of biomarkers of mental disorders, 7T MRI enables us to identify subtle volume changes in brain structures but intensity-based volumetry is undermined by artificial differences in the brightness between MR images. We compared five different techniques for intensity standardisation of T1-weighted images with T1 maps – quantitative measurements of the tissue's T1 parameters. 17 target images, acquired with a 7T whole-body MR scanner and a MP2RAGE sequence, were skull-stripped and intensity standardised to a template image. Within the diencephalon as region of interest we calculated the absolute errors between the normalised cumulative distributions of the targets and the template. In addition, the images were colour-coded and the contrast in the region of the hypothalamus was rated on a numerical scale.

Compared with the native T1-weighted images, the T1 maps had significantly ($p<.01$) reduced average absolute errors but similar ($p>.05$) maximum absolute errors. Colour-coding revealed differences between T1 maps similar to those of the native T1-weighted images suggesting a comparable impact of imaging artifacts on both MP2RAGE contrasts.

All five standardisation techniques significantly reduced both error measures of the T1-weighted images. Significantly improved ratings for the colour-coding were obtained after matching of the cumulative histograms, normalisation based on a region of interest (limbic system and brainstem), and standardisation of tissue clusters, whereas piece-wise linear and nonlinear matching of histogram peaks missed significance.

➜ **Schindler, Stephanie**
email: stephanie.schindler@medizin.uni-leipzig.de

POSTER 157

Fully Automated Calculation of Image-Derived Input Function in Simultaneous PET/MRI

Imaging

Zeisig V[1], Jochimsen T[1], Werner P[1], Barthel H[1], Dreyer A[2], Boltze J[2], Sattler B[1], Sabri O[1]

1 Klinik und Poliklinik für Nuklearmedizin, Universität Leipzig
2 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Aim: Obtaining the arterial input function from image data in dynamic PET examinations can serve as a non-invasive alternative to arterial blood sampling.
The present study describes a fully automated method to acquire the image-derived input function (IDIF) in simultaneous PET/MRI. Results are compared to those obtained by arterial blood sampling.
Materials and Methods: Major neck arteries were segmented, using a high-resolution time-of-flight MR angiography. Together with the measured point spread function (PSF) of the PET subsystem, the arterial mask was used for geometrical deconvolution, yielding the mean time-resolved activity concentration. The method was compared to manual arterial blood sampling at the hind leg of 20 sheep (animal stroke model) during measurement of blood flow with $[^{15}O]H_2O$. Absolute quantification of activity concentration was compared after bolus passage during steady state, i.e. between 2.5 and 5 min post injection.
Results: Activity in blood samples during steady state was 2.5% higher than in the IDIFs (averaged over individuals). In all examinations, the IDIF provided an earlier and sharper bolus peak than in the time course of activity concentration obtained by arterial blood sampling.
Conclusion: The small deviation between blood sampling and IDIF during steady state indicates that the influnece of PVE and PSF is well corrected for with the method presented. The different sampling locations can explain the diversities in bolus dynamics. The IDIF method using simultaneous PET/MRT will be further tested in humans with the perspective of replacing invasive blood sampling.

➜ **Zeisig, Vilia**
email: vilia.zeisig@medizin.uni-leipzig.de

POSTER 158

Depletion of CD4+FoxP3+ regulatory T cells promotes fatal T helper (Th)2 cell development in pulmonary fungal infection

Immunology and Infectiology

Schulze B[1], Piehler D[1], Eschke M[1], von Buttlar H[1], Köhler G[2], Sparwasser T[3], Alber G[1]

1 Institut für Immunologie, Veterinärmedizinische Fakultät, Universität Leipzig
2 Insitut für Pathologie, Klinikum Fulda
3 Institut für Infektionsimmunologie, TWINCORE, Hannover

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Regulatory T (Treg) cells play an important role in controlling immune responses and homeostasis. However, their functional role during fungal infection is largely unknown. The opportunistic fungal pathogen *Cryptococcus neoformans* causes fatal meningitis and lung inflammation in immunocompromised patients. In this study, we investigated the role of Treg cells during experimental murine pulmonary *Cryptococcus neoformans* infection. We show that the frequency of *Cryptococccus*-induced Treg cells in the lung is doubled early after intransal infection of BALB/c mice. We next removed Treg cells during the early phase of infection using DEREG mice (DEpletion of REGulatory T cells). In Treg cell-depleted mice, stronger pulmonary allergic inflammation with enhanced mucus production and pronounced eosinophilia, and increased IgE production were found. This was accompanied by higher frequencies of GATA-3$^+$ Th2 cells with elevated capacity to produce interleukin (IL)-4, IL-5 and IL-13. In contrast, no significant effect on Th1 or Th17 response development was observed. Enhanced Th2 responses upon Treg depletion resulted in loss of pulmonary control of cryptococci and higher fungal lung burden. In conclusion, the data demonstrate that during cryptococcal infection pulmonary Treg cells are induced and preferentially suppress Th2 cells thereby mediating enhanced fungal control.

→ **Schulze, Bianca**
email: bianca.schulze@vetmed.uni-leipzig.de

POSTER 159

Time course of a refined and translational relevant model of chronic DSS-induced colitis in BALB/c mice

Immunology and Infectiology

Hoffmann M[1], Seydel A[1], Schwertassek U[1], Lehmann J[1]
1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction: The clinical forms of inflammatory bowel disease (IBD), ulcerative colitis (UC) and Crohn's disease (CD), are chronic-relapsing inflammatory disorders of the gastrointestinal tract. The model of dextran sulfate sodium (DSS)-induced acute colitis is one of the most widely used models in IBD research. Although it reflects clinical symptoms of UC and CD, a caveat is the lack of chronicity and a chronic inflammatory response. We aimed to develop a refined and more translational relevant chronic DSS model that reflects signs of chronic inflammation and clinical symptoms of IBD without weight loss and death of mice.
Methods: To monitor the induction and persistence of colitis, body weight loss, stool consistency, and colonic hemorrhage were assessed daily. To evaluate morphological changes and the extent of local inflammatory response in the colon, we determined a histological score based on tissue sections as well as the colon length as a marker for the severity of inflammation. Chronification of inflammatory processes was evaluated by analyzing pro-inflammatory cytokines and acute phase proteins in colon homogenates.
Results & Conclusion: We propose a model of DSS-induced chronic colitis in BALB/c mice that reflects important features of IBD without excessive weight loss. Pathology is mainly determined by diarrhea and blood in stool – important features of IBD in humans. We also show that an established therapeutic for treatment of IBD in man significantly reduces clinical symptoms recommending this refined model for evaluating the efficacy of new therapeutics for IBD as well as identifying their mode of action.

→ **Hoffmann, Maximilian**
email: maximilian.hoffmann@izi.fraunhofer.de

POSTER 160

A novel VLP-based method to deliver DNA-vaccines

Immunology and Infectiology

Wierich L[1]

1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

DNA-vaccines are gaining popularity due to their inexpensive production and good stability even at room temperature.While it was possible to overcome the originally unsatisfyingly low antigen-specific antibody response in larger animals and humans by use of electroporation, which greatly increases the cellular uptake of the DNA, this method is however comparatively laborious and painful for the vaccinee. Novel delivery methods are thus necessary. Our approach seeks to combine the advantageous properties of DNA-vaccines with a mucosal delivery system. The latter bears the advantages of inducing an immune response at the site where many pathogens enter the body – the mucosa – and being delivered pain-free in form of a nasal spray or inhalator.

Being the DNA-delivery specialists that viruses are, packaging the vaccine-plasmid in virus-like-particles (VLP) could fulfill all the requirements: delivery of the vaccine via the mucosa, and efficient shuttling of the vaccine-DNA into the cells.

The production of VLPs occurs by co-transfecting cells with expression plasmids coding for virus-shell proteins and a plasmid containing the genetic information for the vaccine. Based on a self-assembly system, virus capsid proteins assemble into virus-shaped shells, packaging the DNA-vaccine.

➜ **Wierich, Lea**
email: lea.wierich@izi.fraunhofer.de

POSTER 161

Interaction of Cryptococcus neoformans and lung epithelium in an experimental mouse model

Immunology and Infectiology

Heyen L[1], Piehler D[1], Eschke M[1], Schulze B[1], Alber G[1]

1 Institut für Immunologie, Veterinärmedizinische Fakultät, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The opportunistic fungal pathogen *Cryptococcus neoformans* causes an asymptomatic respiratory infection in immunocompetent individuals; whereas immunosuppression, e.g. by HIV, promotes fungal growth and may result in a life-threatening meningitis.
This hematogenous dissemination of *Cryptococcus* is favoured by an immune response dominated by Th2 helper cells and their key cytokines Interleukin-4, -5 and -13. They lead to an alternative activation of macrophages, thereby inhibiting their pathogen killing capacity and further result in development of allergic airway inflammation (AAI). Yet, the precise mechanism of Th2 cytokine induction is not known in pulmonary cryptococcosis.
As the lung epithelium is the first contact site for the lower respiratory tract infection our study will focus on the interaction of *Cryptococcus* and epithelial cells and in particular on the cytokine Interleukin-33 (IL-33), which can be an early inducer of Th2 immunity. Therefore, we perform a kinetic analysis of intranasally infected IL-33 reporter mice with several time points of analysis up to 70 days post infection (dpi).
We aim to identify the specific cell types in the lung, due to their surface marker expression, which produce and release IL-33 during the cryptococcal infection using FACS (=fluorescence-activated cell sorting) and immunofluorescence.
The results could contribute to a detailed understanding of the Th2 immune response during an infection with *Cryptococcus* and, moreover, could provide new opportunities for early, effective future therapy not only for pulmonary cryptococcosis but AAI in general.

➜ **Heyen, Laura**
email: laura.heyen@uni-leipzig.de

POSTER 162

Induction of chronic gut inflammation by infection with Salmonella enterica

Immunology and Infectiology

Seydel A[1], Hoffmann M[1], Schwertassek U[1], Lehmann J[1]
1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic-relapsing disorder of the gastro-intestinal tract. Clinical symptoms have been broadly described, but the pathophysiological mechanisms of the disease are still poorly understood. Next to genetic predisposition and environmental factors, an inappropriate immune response to the commensal flora is discussed as a major cause. Chemically-induced models reflect certain aspects of established IBD very well, but their potential to study the etiology and pathophysiology of the disease is limited.

Our aim was to establish bacteria-induced gut inflammation to investigate the role of commensal versus pathogenic bacteria in the development of IBD.

C57BL/6 mice were infected with *Salmonella enterica* after treatment with Streptomycin or application of bacteria was followed by treatment with a subtherapeutical dose of antibiotic, resulting in a persistent infection and chronic inflammation in the gut. A clinical score was assessed daily and bacterial load in fecal pellets was evaluated systematically. Histological changes in colon tissue were assessed and bacterial load was determined in several organs. Expression of inflammatory markers was analyzed in colon tissue homogenates.

We observed a chronic infection in mice represented by a significantly elevated clinical score and persistent bacterial load in fecal pellets. Signs of chronic inflammation were also evident in sections of the colon tissue.

In summary, we propose a potential model of IBD that better reflects the natural etiology and the clinical features of the disease.

➜ **Seydel, Aleksandra**
email: aleksandra.seydel@izi.fraunhofer.de

POSTER 163

Hepatitis C virus (HCV)-specific IgG+ memory B cells directed against the HCV glycoprotein E2 show strong clonal expansion after spontaneous resolution of an HCV infection in a single-source outbreak

Immunology and Infectiology

Olbrich A[1], Wardemann H[2], Berg T[1], Benckert J[1]

1 Klinik und Poliklinik für Gastroenterologie und Rheumatologie, Universität Leipzig
2 Max-Planck-Institut für Infektionsbiologie, Berlin

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Spontaneous resolution of a HCV infection occurs only in a small percentage of acutely infected individuals. For the successful control of the viral replication in the early phase of infection the adaptive immune system is crucial. Several studies have shown that protective antibodies are able to prevent an infection with HCV. We therefore aimed to characterize differences in antibody response to HCV in patients with spontaneous resolution and with chronic infection that were infected in a single-source outbreak.
The B cell receptor on the cell surface was used to isolate single HCV-specific IgG+ memory B cells directed against HCV-E2 by FACS from the blood of 3 patients with chronic hepatitis C and 3 patients with spontaneous resolution. A RT-PCR based approach was applied to monoclonally express antibodies from these single cells *in vitro*. In the process of affinity maturation of B cells somatic hypermutations occur stepwise in the course of cell proliferation and contribute to antibody selection and diversity. In 298 analysed antibodies of the spontaneous resolvers, we could confirm 9+-5 somatic hypermutations/100bp, implying affinity maturation of these cells for up to 9*10E3 generations. In addition, we identified 7 % of clonally expanded sequences with at least a pair of antibodies showing the identical V(D)J rearrangement in heavy and light chain and shared somatic hypermutations underlining the strong clonal expansion and preferential selection of these clones of E2-specific B cells. Expression and reactivity testing of these clonally expanded antibodies will offer new therapeutic options as infection prophylaxis.

➜ **Olbrich, Anne**
email: anne.olbrich@medizin.uni-leipzig.de

POSTER 164

Activation of aryl hydrocarbon receptor alters differentiation of bone marrow-derived macrophages and affects immune response after antigen stimulation

Immunology and Infectiology

Riemschneider S[1], Kohlschmidt J[1], Füldner C[1], Lehmann J[1]
1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The aryl hydrocarbon receptor (AhR) is a ligand activated transcription factor which is involved in regulation of development, immunity and xenobiotic-metabolizing enzymes. One well-known AhR-Ligand is the polycyclic aromatic hydrocarbon Benzo[a]pyrene (BaP). High BaP concentrations can cause mutations and cancer, but in addition to the mutagenic effects, there is evidence for immunomodulatory functions of BaP by AhR-activation. In this study we investigated the effects of BaP on the function of the early innate immune response, using an *in vitro* model with bone marrow-derived macrophages (BMDMs). Since BaP exerts its effects mainly via activation of the AhR, we compared the effects of subtoxic BaP concentrations on the differentiation of BMDMs from *Ahr*$^{+/+}$ or *Ahr*$^{-/-}$ mice.
We show that a permanent exposure to a subtoxic concentration of BaP reduces the number of differentiated adherent CD11b^{+}/F4/80^{+} macrophages, but leads in contrast to an increased expression of specific macrophage markers. After activation with a bacterial stimulus BaP reduces secretion of pro-inflammatory cytokines and enhances secretion of the anti-inflammatory cytokine IL-10. These results suggest that subtoxic concentrations of BaP cause immunomodulatory effects in activated macrophages.

➜ **Riemschneider, Sina**
email: sina.riemschneider@izi.fraunhofer.de

POSTER 165

CD11c-positive cells from brain, spleen, lung, and liver exhibit site-specific immune phenotypes and plastically adapt to new environments

Immunology and Infectiology

Immig K[1], Gericke M[1], Menzel F[1], Merz F[1], Schiefenhövel F[1], Jäger K[2], Lösche A[2], Hanisch U[3], Biber K[4], Bechmann I[1]

1 Institut für Anatomie, Universität Leipzig
2 FACS-Core Unit, Universität Leipzig
3 Institut für Neuropathology, Universität Göttingen
4 Institut für Psychiatrie und Psychotherapie, Universität Freiburg

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The brain's immune privilege has been attributed to the lack of dendritic cells (DCs) within its parenchyma and the adjacent meninges, which implies the maintenance of antigens than their presentation in lymphoid organs. Using transgenic mice expressing CD11c-Green Fluorescent Protein, a DC marker, we identified a juxtavascular population in the brain expressing CD11c. We phenotypically compared this population with $CD11c^+/CD45^+$-cells from lung, liver and spleen in healthy mice using flow cytometry. We identified unique, site-specific expression patterns of DCs reflecting the common markers F4/80, CD80, CD86, CX3CR1, CCR2, FLT3, CD103 and MHC-II. Further, we observed the two known $CD45^+$-populations ($CD45^{high}$ and $CD45^{int}$) in the brain, whereas liver, lung and spleen exhibited a homogeneous $CD45^{high}$ population. Compared to spleen, lung and liver, $CD45^{int}/CD11c^+$-cells from the brain almost lack MHC-II-expression. In order to test whether phenotypical differences are fixed by origin or develop due to environmental factors, we transplanted brain and spleen mononuclear cells on organotypic slice cultures from brain and spleen. We demonstrate that ramification of $MHC\text{-}II^+$- splenocytes is paralleled by down-regulation of MHC-II while brain-derived mononuclear cells neither ramified nor up-regulated MHC-II in spleen slices. Thus, brain-derived mononuclear cells maintain their $MHC\text{-}II^-$-phenotype within the environment of an immune organ and intraparenchymal $CD11c^+$-cells share established immunophenotypical characteristics of DCs derived from other organs but are unique for their low MHC-II expression.

Funding: DFG FOR 1336

➜ **Immig, Kerstin**
email: kerstin.immig@medizin.uni-leipzig.de

POSTER 166

Characterization of the influenza virus-specific plasma and memory B-cells in immunized Balb/c mice

Immunology and Infectiology

Nestler C[1], Reiche S[2], Jassoy C[1]

1 Institut für Virologie, Universität Leipzig
2 Friedrich-Loeffler-Institut, Greifswald – Insel Riems

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The scope of the study is the characterization and comparison of the antigen-specific B-cell receptor repertoires against one specific antigen in genetically identical individuals.
Balb/c mice were immunized three times over 8 weeks with recombinant influenza virus nucleoprotein (NP). Four to seven days after the last immunization, spleen cells were harvested and CD138+ and CD19+ B-cells were isolated. The isolated B-cell fractions were analysed directly or stimulated for 5 days to induce further differentiation of memory B-cells to antibody-secreting plasma cells (ASC). The frequency of ASC and NP-specific plasma cells was determined by ELISpot. The IgG heavy (VH) and light (VL) chain variable regions were amplified from single B-cells by RT-PCR, cloned into an expression plasmid and sequenced. Antibodies were produced in HEK293T cells transfected with the plasmids. Reactivity of the antibodies with NP was analyzed by ELISA.
Freshly prepared CD138+ B-cells contained 0.8–2.0% IgG-secreting plasma cells in the ELISpot. 30% of the ASC secreted influenza NP-specific antibodies. Activation of the CD138+ and CD19+ B-cell fractions over five days with three different activation mixtures did not result in a significantly increased differentiation into ASC. RNA of single CD138+ cells were used to clone antibody gene sequences. By screening 13 heavy and light chain antibody pairs one influenza NP-specific monoclonal antibody could be obtained.
The data show a protocol to clone and characterize the VH and VL chain of influenza virus NP-specific monoclonal antibodies directly from single B-cells of immunized mice.

→ **Nestler, Claudia**
email: claudia.nestler@medizin.uni-leipzig.de

POSTER 167

PCR-based methods for the detection of fungal DNA and its clinical relevance in patients with chronic liver diseases

Immunology and Infectiology

Krohn S[1], Engelmann C[1,2], Zeller K[1], Böhm S[1,2], Hoffmeister A[1,2], Herber A[1,2], Tuennemann J[1,2], Berg T[1,2]

1 Klinik und Poliklinik für Gastroenterologie und Rheumatologie, Universität Leipzig
2 Sektion Hepatologie, Klinik und Poliklinik Gastroenterologie und Rheumatologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Patients with end-stage liver disease are at high risk for fungal infections most frequently caused by candida species. We applied a culture-independent PCR assay targeting the 18S rRNA gene for the detection of fungal DNA in sterile and colonised material. 319 samples (150 blood, 93 ascites, 64 duodenal fluids, 12 bile fluids) from 150 patients predominantly with liver cirrhosis were collected. All samples were analysed by standard microbiological culture and screened for presence and quantity of fungal DNA by real-time PCR. Duodenal fluid results were correlated with clinical data. Detection rates of fungal pathogens were low in sterile specimens (blood 0.7%, ascites 1.0%) and comparable with PCR-results (blood 1.3%) showing low copy numbers (median $3.6x10^1$ copies ml^{-1}). Colonised material revealed significantly higher pathogen detection rates (duodenal fluid 69%, bile 33%) and fungal DNA-positive samples (83%, 50%) with higher DNA quantities (duodenal fluid $1.24x10^5$ copies ml^{-1}, bile $5.04x10^8$ copies ml^{-1} (both median)) comprising several *Candida* spp. and *S. cerevisiae*. The risk for fungal DNA detection in the small intestine was significantly decreased if patients were not on antibiotic treatment (OR=0.830; CI: 0.701–0.982; p=0.039). Patients with fungal DNA-negative intestinal fluid samples had an increased 60-day survival (fungal DNA-negative 100% vs. positive 87.5%). In this study the diagnostic value was comparable between culture methods and PCR analysis. The influence of antibiotic treatment on growth of fungal species in the duodenum might have a clinical relevance if intestinal derived infections are suspected.

➜ **Krohn, Sandra**
email: sandra.krohn@medizin.uni-leipzig.de

POSTER 168

Associations of genetic variants of regulators of the innate immunity with hepatitis C virus infection

Immunology and Infectiology

Fischer J[1], Böhm S[1], Wiese M[1], Gardiner C[1], Sarrazin C[1], Berg T[1,2]

1 Sektion Hepatologie, Klinik und Poliklinik Gastroenterologie und Rheumatologie, Universität Leipzig
2 Klinik und Poliklinik für Gastroenterologie und Rheumatologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Host genetic factors essentially influence the natural and therapy-induced course of hepatitis C virus (HCV) infection. The innate immunity forms the first line of host defence determining HCV susceptibility and the likelihood of treatment response.
In our study we investigated the effects of several single nucleotide polymorphisms (SNP) in genes of regulatory proteins of the innate immune system on the prediction of spontaneous viral clearance and sustained virologic response (SVR).We analyzed 18 distinct SNPs with a frequency of> 5% or leading to an amino acid change in 16 candidate genes (IRF7, MAVS, MyD88, TLR3 and TLR9). The evaluation cohort included 333 well characterized patients infected with chronic HCV type 1 from the INDIV-1 study and 161 (33%) patients who spontaneously cleared the infection. Three independent cohorts were analyzed to confirm the results: German anti-D cohort (n=305), Irish anti-D cohort (n=198) and a part of the INDIV-2 cohort (n=386). All chronic patients were treated with interferon-based therapy. Genotyping of the SNPs in the candidate genes was performed via realtime PCR and melting curve analysis. Significant associations with the likelihood of spontaneous viral clearance were observed for the IRF7 SNP rs1061502 (p=0.016) and for the TLR9 SNP rs187084 (p=0.001) in women. Treatment response was associated with SNPs in the genes MAVS (rs454370969, p=0.034) and TLR3 (rs3775291, p=0.009).
Genetic variants in immune-regulatory proteins affect the natural and treatment-induced eradication of HCV infection. Further investigations in larger cohorts and functional analyses are recommended.

➜ **Fischer, Janett**
email: janett.fischer@medizin.uni-leipzig.de

POSTER 169

Non-structural 2A Protein as Candidate for Differential and Specific Diagnosis of Dengue Virus Infection

Immunology and Infectiology

Adam A[1,2], Mathew A[3], Emmerich P[4], Schmidt-Chanasit J[4], Reiche S[5], Jassoy C[1]

1 Institut für Virologie, Universität Leipzig
2 Department of Microbiology, Faculty of Sciences, International University of Africa, Khartoum, Sudan
3 Division of Infectious Diseases and Immunology, University of Massachusetts, Medical School, Worcester MA, USA
4 Bernhard Nocht Institute for Tropical Medicine, WHO Collaborating Centre for Arbovirus and Haemorrhagic Fever Reference and WHO Collaborating Research Centre Hamburg, Germany
5 Friedrich-Loeffler-Institut, Greifswald – Insel Riems, Germany

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Serological diagnosis of dengue virus (DENV) infection is complicated due to cross-reactivity of antibodies against other flaviviruses in existing antibody tests. This may be due to the use of viral lysates in the traditional DENV antibody Enzyme Linked Immunosorbent Assay (ELISAs). The aim of this study was to establish an antibody ELISA based on recombinant protein for specific diagnosis of DENV infection and for differentiation between dengue virus serotypes.
Amino acid sequences of DENV proteins were aligned with sequences of the corresponding proteins from other flavivirus. DENV NS2A protein was expressed in E. coli as fusion proteins. Protein antigenicity was tested by ELISA and Western blot. Antibody ELISA was developed based on recombinant protein. A panel of sera was examined initially in the DENV-2 lysate ELISA and then in the DENV-NS2A ELISA. For evaluation of cross-reactivity, sera positive for flaviviruses were examined.
Among seven DENV proteins, the NS2A protein showed the lowest sequence homology with other flaviviruses (18.3–21.8%). Sera that were positive in the DENV lysate ELISA showed strong reactivity with the NS2A protein. Sera positive for flaviviruses showed less cross-reactivity in NS2A ELISA compared with DENV-2 lysate ELISA.
Infection with DENV induces a vigorous antibody response against the NS2A protein suggesting that the protein can replace viral lysate as antigen in serological diagnosis. As the protein has low sequence homology with NS2A proteins from other flaviviruses, antibody testing based on the NS2A protein could increase the specificity of serological testing for DENV infection.

→ **Adam, Awadalkareem**
email: awadalkareemali.mohammed@medizin.uni-leipzig.de

POSTER 170

Analysis of CXCL12 signal transduction in astrocytes and microglia during experimental autoimmune encephalomyelitis

Immunology and Infectiology

Puchert M[1], Pelkner F[1], Lipfert J[1], Ödemis V[1], Flügel A[2], Engele J[1]

1 Institut für Anatomie, Universität Leipzig
2 Abteilung Neuroimmunologie, Universitätsmedizin Göttingen

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The chemokine CXCL12/SDF-1 induces and modulates major steps of ontogenesis, regeneration, tumorigenesis and inflammation. In the CNS, CXCL12 and its alleged primary receptor, CXCR4, are indispensable for proper brain development, and are upregulated following injury to promote regenerative processes. However, information about the function of the recently identified second CXCL12 receptor, CXCR7, in neural tissue is still sparse.
To elucidate the roles of CXCR7 and CXCR4 in glial cells, we have initially analyzed the effects of CXCL12 on cultured primary rodent astrocytes and microglia. It turned out that CXCL12-induced ERK phosphorylation and proliferation of astrocytes is solely evoked by the CXCL12-CXCR7 axis, whereas microglia need both receptors for signal transduction. Since proliferation/activation of these glial cell types is a typical feature of central nervous (auto)immune disorders such as multiple sclerosis, we have now investigated the protein expression patterns of CXCR4 and CXCR7 in the spinal cord of rats with experimental autoimmune encephalomyelitis (EAE). In wild-type animals CXCR4-immunostaining was detectable in a small subset of microglia and an even smaller subset of astrocytes. Induction of EAE remained without obvious effects on receptor expression in both glial cell types, however, resulted in the appearance of an additional population of CXCR4-immunoreactive cells, which showed double-labelling for the microglial/monocyte marker, Iba-1, and exhibited a round monocyte-like morphology. In control spinal cords, CXCR7 was marginally expressed by astrocytes, but virtually absent from microglia. Unlike CXCR4, CXCR7 was clearly upregulated in both cell types after induction of EAE, but remained undetectable in monocyte-like cells.
Our findings imply that CXCL12 signalling in glial cells is initiated or elevated by the increased expression of CXCR7, but not CXCR4 under pathological conditions, whereas CXCR4 represents the sole CXCL12 receptor in immigrated monocytes.

➜ **Puchert, Malte**
email: malte.puchert@medizin.uni-leipzig.de

POSTER 171

Discovery of new feline Paramyxoviruses in domestic cats

Immunology and Infectiology

Sieg M[1], Heenemann K[1], Burgener I[2], Oechtering G[3], Vahlenkamp T[1]

1 Institut für Virologie, Veterinärmedizinische Fakultät, Universität Leipzig
2 University Clinic for Companion Animals, Utrecht University, The Neverlands
3 Universitätsklinik für Kleintiere, Veterinärmedizinische Fakultät, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Paramyxoviruses are enveloped, single-stranded RNA viruses which are associated with emerging infectious diseases in humans and animals. In the last years many new paramyxoviruses from wild living and domestic animals were discovered and presumably most of them have originated from paramyxoviruses of bats and/or rodents showing their high potential to cross species barriers.
Here we describe the discovery of two novel feline paramyxoviruses showing highest homology to known rodent and/or bat paramyxoviral sequences based on conserved regions of the polymerase gene. In addition we prove for the first time the existence of previously described feline morbilliviruses (FmoPV) outside of Hong Kong and Japan. From 107 urine samples investigated about six percent (four out of 65) from cats with chronic kidney disease were positive for paramyxoviruses. In contrast, none out of 42 urine samples from cats without any kidney diseases gave positive results for paramyxoviral RNA within the urine.
Our results highlight that there is a clear association between Infection with feline paramyxoviruses and chronic kidney disease (CKD) in domestic cats. Whether they are the cause or only an auxiliary finding of CKD in cats cannot be stated at this moment due to limited data regarding their molecular pathogenesis. Further investigations are needed to elucidate the exact role of different feline paramyxoviruses in development of chronic kidney diseases.

➜ **Sieg, Michael**
email: michael.sieg@vetmed.uni-leipzig.de

POSTER 172

Differences in quantitative composition of large, middle and small Hepatitis B virus (HBV) surface antigen (HBsAg) in acute and chronic HBV infection

Immunology and Infectiology

Großmann M[1], Böhm S[1], Glebe D[1], Berg T[1], van Bömmel F[1]

1 Sektion Hepatologie, Klinik und Poliklinik Gastroenterologie und Rheumatologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction: HBsAg is an important marker to predict seroconversion and viral clearance in acute and chronic HBV infection. It consists of three components as large (L-), middle (M-) and small (S-) HBsAg, which differ in amino-terminal sequences and glycosylation status. In different distributions, all HBsAg components are part of infectious virions and non-infectious subviral particles. Quantitative analysis of HBsAg composition in serum can be a potential marker to assess the relative proportion of infectious virions and to characterize the natural course of HBV infection or the response to antiviral therapy.

Aims: To establish a sensitive ELISA for quantitative detection of the different HBsAg components and to determine the HBsAg composition in acute and chronic infection.

Methods: Microtiter plates were coated with specific antibodies, blocked and sealed with different reagents to optimize and preserve the test. L-, M- and S-HBsAg were quantified in serum samples of 12 acutely infected patients and 15 chronic inactive HBsAg-Carriers with different quantities of total HBsAg (1,68–124000 IU/ml).

Results: Detection of lowest quantities (2–40 ng/ml) of all HBsAg components was possible. The mean proportions of L-, M- and S-HBsAg were 25%, 8% and 66% during acute infection compared to 18%, 5% and 77% for inactive HBsAg-Carriers, respectively.

Conclusion: With the new ELISA differences in HBsAg composition can be detected during different phases of HBV infection. This may give a possibility to follow up acutely and chronically infected patients in order to better characterize the individual course of hepatitis B.

➜ **Großmann, Maria**
email: maria.grossmann@medizin.uni-leipzig.de

POSTER 173

Nicotinamide – a vitamin with immune-modulating properties

Immunology and Infectiology

Weiß R[1,2,3], Kölling V[1,2], Schilling E[2,3], Grahnert A[2,3], Sack U[2,3], Hauschildt S[1]

1 Institut für Biologie, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
3 Institut für Klinische Immunologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Nicotinamide (NAM) a component of vitamin B3 is produced by several enzymes (sirtuins, ARTs, PARPs, CD38) that are involved in fundamental cellular processes such as DNA-repair, signalling, apoptosis, metabolism and differentiation. Because NAM regulates the activity of these enzymes its intracellular concentration has a high impact on these metabolic events. Here we asked whether NAM affects differentiation of human monocytes to M1 and M2 macrophages and whether NAM treated cells display different functional activities.

After differentiation of monocytes into macrophages in the presence of 800 μM NAM, the cells were stimulated with LPS and following parameters were determined: morphology, apoptosis/necrosis, cytokine production, antigen presentation and phagocytosis.

We found that differentiation of monocytes to macrophages with 800 μM NAM has no influence on apoptosis/necrosis. The pretreatment with NAM results in a significant increase in elongated cells within M1 macrophages whereas the morphology of M2 macrophages was not affected. We identified nicotinamide as a compound capable of inhibiting LPS induced TNF-α production of M1 but not M2 macrophages. In contrast nicotinamide decreased the LPS induction of IL10 in M2 but not M1 macrophages. The phagocytic activity and antigen presentation hardly changed in response to NAM.

Taken together NAM applied during differentiation has the potential to interfere with important immunological properties of M1 and M2 macrophages.

➜ **Weiß, Ronald**
email: ronald.weiss@trm.uni-leipzig.de

POSTER 174

Environmental chemicals and their effects on regulatory T-cells

Immunology and Infectiology

Winter M[1]

1 Helmholtz-Zentrum für Umweltforschung Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Impaired regulatory T-cell (T_{reg}) function contributes to the development of atopic diseases, since these cells are pivotal to maintain self-tolerance and immune homeostasis. To further evaluate how environmental chemicals might impair suppressive immune function, this study elucidates the impact of electrophilic environmental chemicals on T_{reg} cells using isolated and expanded human T_{reg} ($CD4^+CD25^{hi}CD45RA^+$) as an *in vitro* model.

Starting with human buffy coats, PBMCs were isolated via density centrifugation. T_{reg} were selected by magnetic depletion of $CD25^-$ cells and subsequent purification via FACS sorting. Two weeks of expansion yielded bulk T_{reg} populations.

Expanded T_{reg} were exposed to the DNA- and protein-reactive electrophilic benzene metabolite 1,4-benzochinon and assessed in a time-resolved manner for suppressive function, interleukin production, and protein expression by FACS. mRNA expression and DNA-methylation of the TSDR region were monitored.

Exposure to 1,4-benzoquinone induced a concentration-dependent decrease in Foxp3 expression, which was accompanied by a decrease in suppressive function of T_{reg}, concomitant with a change in interleukin expression.

These preliminary data suggest that electrophilic metabolites of benzene perturb the suppressive activity of T_{reg} with a potential impact on atopic disease development.

➜ **Winter, Marcus**
email: marcus.winter@ufz.de

POSTER 175

The effect of acetylcholinesterase inhibition on T-cells in rheumatoid arthritis

Immunology and Infectiology

Gowayed M[1]

1 Klinik und Poliklinik Gastroenterologie und Rheumatologie, Sektion Rheumatologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Regulatory T cells (Treg) are known to accumulate in the synovium of patients with active rheumatoid arthritis (RA) and play a vital role in preventing autoimmune disorders and controlling autoimmune responses. Pro-inflammatory cytokines (including TNF-α) inhibit the Treg cells suppressive effect causing their inability to control ongoing inflammation in RA, while anti-TNF therapies, like methotrexate and infliximab, interestingly proved to augment their suppressive function.

The "cholinergic anti-inflammatory pathway" is a new concept referring to the stimulation of the vagus nerve via the interaction of ACh with the α7 subunit of the nicotinic acetylcholine receptor (α7nAChR), present in neurons, as well as inflammatory cells. This stimulation of α7nAChR by ACh or other specific agonists was reported to suppress cytokine production, such as TNF-α, and macrophage activation.

The fact that lymphocytes express the α7nAChR and the new evolution of the "cholinergic anti-inflammatory pathway", opened up the prospective in this study of targeting the Treg cells by the anticholinesterase and cholinergic drug, galantamine, and compare its effect to the chimeric anti-TNF-α monoclonal antibody, infliximab and the TNF-α blocker, etanercept, from blood of RA patients.

➜ **Gowayed, Mennatallah**
email: mennatallah.gowayed@medizin.uni-leipzig.de

POSTER 176

Identifizierung potentiell allergener Sojaprotein Epitope mittels Peptid Phage Display

Immunology and Infectiology

Kern K[1], Delaroque N[1], Lehmann J[1], Ueberham E[1], Szardenings M[1]

1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Food allergies have become of significant medical and legal concern worldwide. Soybean is one of the "big 8" of the most allergenic foods. Many soybean proteins are known to trigger allergy. A detailed characterization of the peptide sequences on the amino acid level using patient material has not been possible so far. Classical method, e.g. 2D-PAGE in combination with western blot and mass spectroscopy, cannot identify epitopes of antibodies in patient sera at amino acid resolution. Peptide arrays of full or partial proteomes are costly and still cannot identify all epitopes. The aim of this ongoing project is the identification of the allergy relevant epitopes of soybean protein. An improved peptide phage display technology has been developed in our laboratory to allow the study of the immunome of patients. Peptide phage display in combination with next generation sequencing is a powerful method to identify allergy-related epitopes. Sera from several persons (so far 20) with soy allergy were challenged with peptide phage display. 10^6 sequences have been obtained per serum and analysed after Next Generation Sequencing (NGS). These were searched for epitopes by comparison with the known proteins of soy beans. So far we have identified the essential binding amino acids of several epitopes, which were described in the literature as peptides of 10 and more amino acids and many new potential epitopes. Antibodies could be captured from serum with the synthesized peptide epitopes. The method has the potential to analyze complete sera for other epitopes or to identify peptides binding to other serum proteins.

➜ **Kern, Karolin**
email: karolin.kern@izi.fraunhofer.de

POSTER 177

Eating behaviour in the general population: An analysis of the factor structure of the German version of the Three-factor-Eating-Questionnaire (TFEQ) and its association with the body mass index

LIFE – Civilisation Diseases and Genetics

Löffler A[1,2], Luck T[1,2], Then F[1,2], Sikorski C[1,3], Kovacs P[3], Böttcher Y[3], Breitfeld J[3], Tönjes A[4], Horstmann A[3,5], Löffler M[6], Engel C[6], Thiery J[7], Villringer A[5,8], Stumvoll M[3], Riedel-Heller S[1]

1 Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP), Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
3 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
4 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
5 Max-Planck-Institut für Kognitions- und Neurowissenschaften
6 Institut für Medizinische Informatik, Statistik und Epidemiologie (IMISE), Universität Leipzig
7 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
8 Tagesklinik für kognitive Neurologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The Three-factor-Eating-Questionnaire (TFEQ) is an established instrument to assess eating behaviour. Analysis of the TFEQ-factor structure was based on selected, convenient and clinical samples so far. Aims of this study were (I) to analyse the factor structure of the German version of the TFEQ and (II) – based on the refined factor structure – to examine the association between eating behaviour and the body mass index (BMI) in a general population sample of 3,144 middle-aged and older participants (40–79 years) of the ongoing population based cohort study of the Leipzig Research Center for Civilization Diseases (LIFE Health Study). The factor structure was examined with principal axis factor analysis. Associations between TFEQ-scores and BMI values were tested with variance analyses adjusted for age, gender, and education. We found a three factor solution for the TFEQ with a 'disinhibition', a 'cognitive restraint' and an 'emotional eating' domain including 34 of the original 51 TFEQ-items. Higher scores in 'disinhibition' ($F=3.075$, $p< 0.001$) and 'emotional eating' ($F=5.529$, $p=0.001$) were significantly associated with higher BMI values. Subjects with scores above the median in both 'disinhibitional eating' and 'emotional eating' showed the highest BMI values (mean=29.58 kg/m^2), subjects with scores below the median in all three domains showed the lowest BMI values (mean=25.8 kg/m^2; $F=48.35$, $p< 0.05$).

Our findings suggest that the TFEQ is suitable to identify subjects with specific patterns of eating behaviour that are associated with higher BMI values. Such information may help health care professionals to develop and implement more tailored interventions for overweight and obese individuals.

Funding: life

➜ **Löffler, Antje**
email: antje.loeffler@medizin.uni-leipzig.de

POSTER 178

Preanalytical investigation on PUFA and eicosanoid analysis in human plasma by LC-MS/MS

LIFE – Civilisation Diseases and Genetics

Dorow J[1,2], Becker S[1,2], Kortz L[1,2], Thiery J[1,2], Ceglarek U[1,2]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

Background: The Quantification of polyunsaturated fatty acids (PUFAs) and eicosanoids in human blood is challenging due to low endogenous concentrations (pg/mL) and *in vitro* autoxidation. Thus, standardization of preanalytical conditions is required to minimize data variability.
Methods: 6 PUFAs and 94 related metabolites were analyzed by on-line solid phase extraction coupled to ultra high performance liquid chromatography combined with tandem mass spectrometry on a 5500 QTrap instrument. Analyte stability was tested in whole blood, serum, and plasma stabilized with different anticoagulants. Influence of short-term storage until sample pretreatment, long-term storage up to 6 months (-20 °C,-80 °C, and -150 °C), and freeze-thaw-cycles (n=5) were compared.
Results: Serum is not suited for eicosanoid analysis due to the activation of cyclooxygenase and lipoxygenase pathways, which was also seen for citrated and lithium-heparinized plasma (> 250% increase of eicosanoid concentration) compared to EDTA-plasma. PUFA metabolites were stable in EDTA-stabilized whole blood after blood taking for 120 min, while EDTA plasma showed no changes for 30 min when stored at 4 °C. Protein depletion by addition of MeOH (60% v/v) could further increase plasma stability at 4 °C up to 7 days. Long-term storage at -80 °C/-150 °C revealed changes in eicosanoid composition after 180 days and storage at -150 °C showed no advantage over -80 °C. Repeated freeze-thaw-cycles (n> 1) resulted in eicosanoid formation up to 63%.
Conclusion: We developed a standardized pre-analytical protocol for PUFA and eicosanoid analysis in human blood.

Funding: life

➜ **Dorow, Juliane**
email: juliane.dorow@medizin.uni-leipzig.de

POSTER 179

Standardized Targeted Proteomics Approach for the Simultaneous Determination of Eight Apolipoproteins in the Leipzig Heart Study

LIFE – Civilisation Diseases and Genetics

Dittrich J[1,2], Becker S[1,2], Hecht M[1], Thiery J[1,2], Ceglarek U[1,2]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Recently, targeted proteomics emerged as an alternative to cost-intensive, individual immunoassays. Sample pretreatment strategies for the reliable, absolute protein quantification of 8 apolipoproteins in human plasma and serum using proteotypic peptides and corresponding stable isotope labeled peptides as internal standards were investigated.

The single steps of the sample preparation procedure were optimized and micro-liquid chromatography coupled to a quadrupole-linear ion trap mass spectrometer was used for quantification and simultaneous peptide confirmation. A method comparison with routinely used immunoassays was performed for Apo A-I and Apo B using 500 human plasma samples of the Leipzig Heart study.

Applying the standardized protocol, only 3 μL of human plasma or serum were required for sample preparation. Between 5 min (Apo A-I, E, A-IV) and 16 h (Apo A-II) were needed for a complete tryptic digestion.The chromatographic separation was performed in 5 min with a total run time of 7.6 min.

Linearity was approved for a concentration range between 0.1 nmol/L and 100 mmol/L. The lower limits of quantification were $\leq$0.4 μmol/L for Apo A-I, A-IV, B-100, C-I, C-III, E and J and $<$ 1.4 μmol/L for Apo A-II. Mean intra and inter assay coefficients of variation of $<$ 10% and $<$ 13% were determined, respectively. The method comparison with commercial immunoassays showed good agreements for Apo A-I and Apo B.

Conclusively, the validated LC-MS/MS method was firstly applied in an observational angiographic study, the Leipzig Heart study, to reliably investigate the distribution of 8 apolipoproteins in cardiovascular disease.

Funding: life

➜ **Dittrich, Julia**
email: julia.dittrich@medizin.uni-leipzig.de

POSTER 180

Evaluation of pediatric satisfaction in context of a cohort study

LIFE – Civilisation Diseases and Genetics

Winkler T[1], Vogel M[1], Kiess W[1]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The LIFE Child study is a large prospective population-based cohort study of children in Leipzig, Germany. Its aim is to understand which mechanisms and aspects influence the health and development of children in modern societies. Cohort studies depend on participants and their will to support the study as a follow-up for many years. This poster want to show the correlation between participants' satisfaction and the overall commitment to the study. The participant's satisfaction was determined by an evaluation questionnaire. Therefore, participants reviewed their examinations, giving each a grade from "very good" to "not good at all". It turned out that general factors like breakfast, staff friedlyness and the overall study day were predominantly rated "very good" and "good". The most critizised point was waiting time in between examinations. The best graded examinations, mostly ranging from "very good" to "good" were pysical examination, measuring of blood pressure, anthopometric measures and motoric test. Taking a blood, urine or hair sample is liked less with participants. However, grades ranging from "very good" to "indifferent" were quite common here, too. It was not possible to detect a relationship between the evaluation of the blood withdrawal and their impact on follow-up appointments. Overall, it can be noted that the participants satisfaction in LIFE Child is high. Surprisingly, the blood withdrawal got better evaluations than expected – there is no significant relationship between the evaluation of blood withdrawal and follow-up appointments. Our results rather point out that waiting time should be minimized.

Funding: life

→ **Winkler, Theodor**
email: twinkler@life.uni-leipzig.de

POSTER 181

Pre-analytical standardization for blood withdrawal, biobanking and sample preparation based on Analysis of Reactive Oxygen Species-induced Oxysterols in Human Plasma

LIFE – Civilisation Diseases and Genetics

Schröter J[1], Helmschrodt C[1,2], Becker S[1,2], Thiery J[1,2], Ceglarek U[1,2]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objectives: Reactive oxygen species (ROS)-derived oxysterols (7-keto-, 7-α/β-hydroxy-, 5α,6α-epoxy-, 5β,6β-epoxycholesterol and cholestane-3ß,5α,6ß-triol) are sensitive for autoxidation processes. Therefore, ROS-derived oxysterols are potential markers for the pre-analytical standardization of blood withdrawal, biobanking and sample preparation.
Methods: Oxysterol concentrations were compared after the following attempts: investigation of different sample matrices, storage time and temperature of EDTA-whole blood until plasma separation, freeze-thaw cycles, addition of butylated hydroxytoluene (BHT) and long-term storage up to one year at different temperatures using different storage containers. Sample preparation prior to liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis was reduced to a simple protein precipitation step.
Results: After blood withdrawal, the storage of EDTA-whole blood for 30 min at room temperature resulted in concentration changes of < 25% within an acceptable change limit (ACL). In freshly prepared EDTA-plasma, free oxysterols were stable for 90 min at 4 °C with concentration changes < 23.5%. Even nine freeze-thaw cycles did not affect the analyte concentrations. Whereas 7-ketocholesterol was stable for two years in plasma stored at < -80 °C, the remaining oxysterols were only stable for two to four weeks without exceeding the ACL. The BHT addition did not improve analyte stability at temperatures < -80 °C.
Conclusion: Prior to the analysis of ROS-derived oxysterols in human plasma by LC-MS/MS, the suggested conditions of pre-analytical standardizations should be strictly adhered.

Funding: life

➜ **Schröter, Jenny**
email: jenny.schroeter@medizin.uni-leipzig.de

POSTER 182

Impact of chronic smoking on P3 components in a three-stimulus oddball paradigm

LIFE – Civilisation Diseases and Genetics

Mauche N[1,2], Sander C[1,2], Jawinski P[1,2], Enzenbach C[2], Olbrich S[1,2], Schönknecht P[1,2], Hegerl U[1,2], Hensch T[1,2]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The P3 is related to central information processing associated with attention and memory functions. A reduction of the P3 amplitude in chronic smokers has been reported in some studies. This reduction has also been reported in former smokers indicating either a preexisting trait and/or long-lasting effects of smoking. Moreover, it was found that P3 amplitude is negatively correlated with smoking level, which may reflect substance dose-effects and/or a preexisting liability to higher cigarette consumption.
Only few studies have examined chronic effects of smoking on P3 using an *auditory* oddball paradigm. Furthermore, to the best of our knowledge, only one study examined the P3a subcomponent using, however, a two-tone oddball paradigm, which is suboptimal to elicit a P3a.
The current study tries to replicate previous smoking associations applying a three-stimulus oddball paradigm in a well-diagnosed population-based sample of healthy elderly subjects.
From the Leipzig Health Care Study current, former and never smokers without mental or neurological disorders were carefully matched by age, sex and qualification. Subjects were presented with a 15-minute auditory novelty oddball paradigm.
P3 components and behavioral measures in current, former and never smokers will be compared, and a dose-response relationship will be analyzed by correlating amount and duration of smoking with P3 parameters. It will be discussed whether smoking status is a relevant confounder in P3 research if smoking is kept ad libitum in a naturalistic protocol.

Funding: life

→ **Mauche, Nicole**
email: nicole.mauche@medizin.uni-leipzig.de

POSTER 183

Einflüsse traumatischer Kindheitserfahrungen auf die Verarbeitung emotionaler Information bei Patienten mit Depression

LIFE – Civilisation Diseases and Genetics

Guenther V[1,2], Kersting A[1,2], Suslow T[1,2]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Psychosomatische Medizin und Psychotherapie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Experimentalpsychologische Studien im Bereich der Depressionsforschung haben gezeigt, dass bei depressiv Erkrankten eine veränderte kognitive Verarbeitung emotionaler Informationen vorliegt. Stimmungskongruente Verzerrungsmuster („Biases") konnten in verschiedenen kognitiven Funktionsbereichen nachgewiesen werden, wie der Aufmerksamkeitskontrolle und bei der Interpretation affektiver Informationen. Kognitive Modelle der Depression postulieren, dass diesen Wahrnehmungsverzerrungen bei der Entstehung von depressiven Störungen eine bedeutsame Rolle zugeschrieben werden kann. Erlebte Traumata in der Kindheit gelten als Risikofaktoren für die Entstehung einer depressiven Episode. Es ist weitestgehend ungeklärt, über welche Mechanismen dieser Vulnerabilitätsfaktor das Erkrankungsrisiko erhöht. In der vorliegenden Studie wurden Zusammenhänge zwischen frühen Misshandlungserfahrungen und verzerrten Evaluations- und Aufmerksamkeitsprozessen bei depressiven Patienten untersucht. Wir fanden Zusammenhänge zwischen stimmungskongruenten Aufmerksamkeitstendenzen und traumatischen Kindheitserfahrungen. Patienten mit Missbrauchserfahrungen orientierten ihre Aufmerksamkeit präferiert auf traurige Gesichter. Weiterhin schrieben Patienten mit erlebten Traumata schematischen Gesichtern weniger positive Emotionen zu. Die gefundenen Zusammenhänge blieben auch nach Kontrolle der aktuellen Depressivität und Ängstlichkeit signifikant. Unsere Ergebnisse stehen im Einklang mit der Annahme, dass frühe, traumatische Erfahrungen mit langfristigen, negativen Veränderungen in der kognitiven Verarbeitung emotionaler Information einhergehen.

Funding: life

→ **Guenther, Vivien**
email: vivien.guenther@medizin.uni-leipzig.de

POSTER 184

Psychometrische Güte des Child Feeding Questionnaire in der deutschen Allgemeinbevölkerung

LIFE – Civilisation Diseases and Genetics

Richter R[1,2], Brauhardt A[1], Hiemisch A[2], Kiess W[2,3], Hilbert A[1]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
3 Klinik und Poliklinik für Kinder- und Jugendmedizin, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hintergrund: Der Child Feeding Questionnaire (CFQ; Birch et al., 2001) ist ein Selbstbeurteilungsfragebogen, der auf sieben Skalen elterliche Einstellungen zum und Steuerungsstrategien des kindlichen Essverhaltens (Pressure to Eat, Restriction, Monitoring) erfasst. Bisherige psychometrische Evaluationsstudien wurden überwiegend im nicht-europäischen Raum anhand mittelgroßer Stichproben ($N < 500$) mit begrenztem Altersrange der Kinder durchgeführt. Diese Studie strebt an, den CFQ in einer großen deutschen Bevölkerungsstichprobe teststatistisch zu untersuchen, sowie die faktorielle Struktur und Normwerte zu ermitteln.
Methoden: Im Rahmen der „Leipzig Research Centre for Civilization Diseases (LIFE) Child Study" wurden $N = 1497$ Mütter und Väter mithilfe des CFQ befragt. Es wurden psychometrische Kennwerte wie interne Konsistenz, faktorielle Struktur mittels konfirmatorischer Faktorenanalyse und geschlechtsspezifische Normen ermittelt.
Ergebnisse: Item-Analysen zeigten variierende Trennschärfen ($.34 \leq r_{it} \leq .84$), in meist mittlerer bis starker Ausprägung. Die interne Konsistenz der Skalen lässt sich überwiegend als gut bis sehr gut einzuschätzen ($.61 \leq$ Cronbach's $\alpha \leq .91$). Die siebenfaktorielle Struktur des CFQs konnte bestätigt werden. Alters- und geschlechtsspezifische Normwerte wurden ermittelt.
Schlussfolgerung: Die Analysen zeigten gute psychometrische Eigenschaften des CFQ. Die Verfügbarkeit von Normen ermöglicht es, Studienergebnisse zuverlässig zu interpretieren. Weitere Forschung wird benötigt, um beispielsweise Veränderungssensitivität und prognostische Validität zu bestimmen.

Funding: life

→ **Richter, Robert**
email: robert.richter@medizin.uni-leipzig.de

POSTER 185

Salivary diagnostic for the assessment of the HPA-axis in children and adolescents with psychiatric disorders

LIFE – Civilisation Diseases and Genetics

Bae Y[1], Gaudl A[1], Jaeger S[2], Stadelmann S[2,3], Döhnert M[3], von Klitzing K[3], Hiemisch A[4], Kiess W[4], Schaab M[1], Thiery J[1], Ceglarek U[1], Kratzsch J[1]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
3 Klinik für Psychiatrie, Psychotherapie und Psychosomatik des Kindes/ Jugendalters, Universität Leipzig
4 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Salivary cortisol (F) is routinely measured with immunoassay (IA). However, the interference of IA often hampers the specificity of IA. LC-MSMS (MS) enabled the measurement of cortisol with high specificity. Our objectives were 1) to compare salivary F IA and F MS values, 2) to test the interference from cortisone (E) and alpha-amylase (AA) in salivary cortisol IA, and 3) to assess the impact of E and AA on F IA in relation to F MS in clinical samples. Methods: 1510 saliva samples were collected during the Trier Social Stress Test for Children (TSST-C) in three groups with different psychiatric disorders (55 internalizing patients, 33 externalizing patients, and 81 healthy children). Biochemical analyses were performed with IA (F), MS (F and E) and enzyme kinetic assay (AA). Results: F IA values were about 2.56 times higher than F MS values, which is mainly due to the standardization of IA (IBL Lot. RE62011). Cross-reactivity with E and interference of AA at IA was pronounced in low F concentration. During the TSST-C, multiple regression analyses showed that high F IA values are highly correlated with F MS (β =.878, T=24.2, $p<.001$ in healthy children). At the same concentration range, the degree of influence of F MS, E and AA in predicting F IA varied across different diagnostic groups. Conclusion: Since cortisone and AA vary depending on the physiological status, e.g. 11β-HSD2 activity and sympathetic stimulation, the use of F IA across diverse disease status should be considered cautiously.

Funding: life

→ **Bae, Yoon Ju**
email: yoonju.bae@medizin.uni-leipzig.de

POSTER 186

Monitoring Motor Skills of Children and Adolescents in LIFE-Child

LIFE – Civilisation Diseases and Genetics

Lang J[1], Warnatsch C[1], Vogel M[1], Kirsten T[1], Kiess W[1]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Life Child is an epidemiological study running at the LIFE Research Center for Civilization Diseases (University of Leipzig) since 2011. It aims at monitoring the development in children and adolescents by examining thousands of children in and around Leipzig. Of particular interest in this study are motor skills and physical activities of children between 6 and 18 years. There are multiple examinations including interviews, self-completed questionnaires and physical examinations (e. g., sport tests) to generate data describing the determined child as well her lifestyle and environment. The goal is to find causes for low to non physical activity and unincisive motor skills and capabilities since they are commonly attended with diseases, such as obesity and diabetes.

As a first step in this direction, we analyzed data of specific sport tests, such as pushups, side steps and long jumps, according to the body mass index (BMI) of participants. We found that participants with high BMI achieve a similar number of pushups in early years like the normal BMI group, while in later years the pushup number of participants with normal BMI exceeds the pushup number of high BMI group. Surprisingly, the number of side steps is indifferent over age categories (6–18, yearly) between both groups. Conversely, the normal BMI group achieve higher distances throughout all age categories than the high BMI group. In future, we will associate these results with socio-economic and lifestyle indicators, e. g., interest in sport and physical activities of child and parents.

Funding: life

→ **Lang, Jenny**
email: jennylang93@gmx.de

POSTER 187

Data Quality Control and Data Analysis of Body-Scanner Measurement Values in Children and Adolescents

LIFE – Civilisation Diseases and Genetics

Fischer AL[1], Vogel M[1], Bucher C[2], Kiess W[1,2], Kirsten T[1,3]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig
3 Interdisziplinäres Zentrum für Bioinformatik (IZBI), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction: LIFE child as a part of the 'Leipzig Research Centre for Civilization Diseases' is a longitudinal cohort study aiming, inter alia, at monitoring normal development in children and adolescents from fetal life to adulthood. As an important part of the study, anthropometric dimensions are measured via classic methods, e. g. stadiometer or tape measure (ca. 15 items), but also via 3D body scanner technology (ca. 150 items). Because of missing standards data quality control and analysis of the latter one is a particular challenge.
Methods: We address the problem of absent reference values by using the data itself as a reference sample.
Applying the LMS-method using the VGAM/GAMLSS packages on a reference sample which is large enough results in age and gender corrected standard deviation scores (SDS) respectively percentile curves. A combination of variable clustering and clustering of values using these SDS is applied to the detect groups of dependend variables and peculiar cases respectively.
Results: In LIFE child the current reference sample consists of around 4000 scans of 1700 children. The age dependend λ, μ, and σ values are generated for each item by dedicated R-routines and stored in a relational database system. The transformation algorithm by Cole is implemented as database function and dynamically applied on all associated raw data. Conspiciuous values can be detected using the SDS itself or the SDS in comparison with the belonging variable cluster and/or taking into account the follow-up data of the respective participant. These values can be reported and visualized using automated routines.

Funding: life

➜ **Fischer, Anna-Lena**
email: anna-lena-fischer@gmx.de

POSTER 188

Ycasd – a tool for capturing and scaling data from graphical representations

LIFE – Civilisation Diseases and Genetics

Groß A[1], Schirm S[1], Scholz M[1]

1 Institut für Medizinische Informatik, Statistik und Epidemiologie (IMISE), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Mathematical modelling of biological processes often requires a large variety of different data sets for parameter estimation and validation. It is common practice that clinical data are not available in raw formats but are provided as graphical representations. Hence, in order to include these data into environments used for model simulations and statistical analyses, it is necessary to extract them from their presentations in the literature. For this purpose, we developed the freely available software ycasd. After establishing a coordinate system by simple axes definitions, it supports convenient retrieval of data points from arbitrary figures.
Results: On the basis of a working example, we demonstrate how to use ycasd. A major advantage of our tool is that it does not require a certain input file format to open and process figures. All options are accessible through a single window which eases handling and speeds up data extraction. Finally, for subsequent processing of extracted data points, results can be formatted as a Matlab or an R matrix.
Conclusions: We conclude that our tool is suitable for convenient and accurate data retrievals from graphical representations such as papers. It offers a good compromise between easy and quick capturing of scientific data from publications and complexity. Our tool is routinely applied in the context of biological modelling, where numerous time series data are required to develop models. The software can also be useful for other kinds of analyses for which published data are required but are not available in raw formats such as systematic reviews and meta-analyses.

→ **Groß, Arnd**
email: arnd.gross@imise.uni-leipzig.de

POSTER 189 **Test-Retest Reliability of Epworth Sleepiness Scale**

LIFE – Civilisation Diseases and Genetics

Schermaul P[1], Huang J[1], Hegerl U[1,2], Sander C[1,2], Hensch T[1,2]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Daytime sleepiness is a bothersome complaint and symptom of several sleep disorders; and sleepiness was suggested to play a pathogenetic role in affective disorders and ADHD (Hegerl & Hensch, 2014). The Epworth Sleepiness Scale (ESS, Johns, 1991) is a self-rating scale to assess daytime sleepiness and has been translated into many languages including German. However no studies on test-retest reliability of the German version of the ESS are available until today. Therefore, the current study examines temporal stability of daytime sleepiness as assessed with the ESS in healthy subjects.

In 3 samples the ESS was filled in twice with an interval of 7.2 (49 young subjects, age = 23.6), 9.8 (27 older subjects, age = 71.0) and 267.6 days (162 older subjects, age = 70.1).

The test-retest reliability coefficients for the young and older group with the short interval and for the older group with the long interval were rho = .581, .588 and .685 (all $p < .001$), respectively.

Sleepiness as assessed with ESS showed moderate test-retest-reliability in healthy subjects without pathological sleepiness. Higher stability is expected in case of disease-associated sleepiness. Pathology-associated variance sources might have contributed to higher stability in the 19 elderly subjects who had been excluded due neurological or psychiatric disorders (rho = .847, $p < .001$).

Funding: life

➜ **Huang, Jue**
email: jue.huang@medizin.uni-leipzig.de

POSTER 190

Rektales Diazepam als Notfallmedikation in der Neuropädiatrie: Entwicklung eines Simulationsmodells zur Ermittlung von Anwendungsfehlern mit dem Ziel einer optimierten Arzneimittelsicherheit

LIFE – Civilisation Diseases and Genetics

Kaune A[1,2], Schumacher P[1,2], Hoppe S[1,2], Höde E[1,2,3], Frontini R[2,3], Kiess W[4,5], Bertsche A[4,5], Neininger M[1,2], Bertsche T[1,2]

1 Institut für Pharmazie, Universität Leipzig
2 ZAMS – Zentrum für Arzneimittelsicherheit, Universität Leipzig
3 Apotheke des Universitätsklinikums Leipzig AöR
4 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig
5 Zentrum für pädiatrische Forschung, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Dauert ein epileptischer Anfall länger als 2–3 Minuten, sollte für eine Beendigung des Krampfgeschehens unmittelbar eine antikonvulsive Notfallmedikation verabreicht werden. Häufig wird Diazepam hier als rektal anzuwendende Arzneiform verordnet. Welche Anwendungsfehler treten auf, wenn ein Diazepamklistier im Notfall durch medizinische Laien, z. B. Eltern oder Betreuer von epilepsiekranken Kindern, angewendet wird? Da die Notfallsituation eines Krampfanfalls aus organisatorischen und ethischen Gründen einem Monitoring nur schwer zugänglich ist, fehlen Methoden, mit denen Fehler bei der rektalen Anwendung antikonvulsiver Notfallmedikation ermittelt werden können. Daher haben wir ein standardisiertes Simulationsmodell zur Ermittlung und Intervention von Anwendungsfehlern bei der rektalen Klistieranwendung entwickelt. Um mögliche Fehler bei der rektalen Anwendung von Diazepam zu identifizieren, wurde ein interdisziplinäres Expertenpanel aus Ärzten und Klinischen Pharmazeuten etabliert. Weiterhin wurde auf Basis einer Literaturanalyse ein Standard zur Dokumentation (Prozessalgorithmus) entwickelt, der durch das Expertenpanel anhand erster Testläufe auf seine praktische Anwendbarkeit hin überprüft und optimiert wurde. Für die Simulation der Applikation diente hierbei eine präparierte Babypuppe. Das vorgestellte Modell soll es ermöglichen, Fehler in der Notfallanwendung von Diazepamklistieren zu identifizieren. Weiterhin kann präventiv durch Interventionsschulungen von medizinischen Laien am entwickelten Simulationsmodell die Arzneimittelsicherheit in einer mitunter lebensbedrohlichen Anfallssituation erhöht werden.

➜ **Kaune, Almuth**
email: almuth.kaune@uni-leipzig.de

POSTER 191

Bukkales Midazolam als Notfallmedikation in der Neuropädiatrie: Entwicklung eines Simulationsmodells zur Optimierung der Arzneimittelsicherheit bei medizinischen Laien

LIFE – Civilisation Diseases and Genetics

Schumacher P[1,2], Kaune A[1,2], Hoppe S[1,2], Höde E[1,2,3], Frontini R[2,3], Kiess W[4,5], Bertsche A[4,5], Neininger M[1,2], Bertsche T[1,2]

1 Institut für Pharmazie, Universität Leipzig
2 ZAMS – Zentrum für Arzneimittelsicherheit, Universität Leipzig
3 Apotheke des Universitätsklinikums Leipzig AöR
4 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig
5 Zentrum für pädiatrische Forschung, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Epileptische Anfälle in der Neuropädiatrie sind schnell zu behandeln. Dauert ein Anfall länger als 2–3 Minuten sollte zügig eine Notfallmedikation, z. B. Midazolam als orale Dosierspritze, angewendet werden, um eine gute Wirksamkeit zu erreichen. Im Alltag müssen daher medizinische Laien, wie z. B. Eltern epilepsiekranker Kinder, die zeitnahe Applikation durchführen. Ist diese Anwendung fehlerhaft, kann dies den Therapierfolg in Frage stellen. Wir haben ein Simulationsmodell entwickelt, das zur Untersuchung der bukkalen Notfallanwendung von Midazolam durch medizinische Laien dienen soll. Zur fachlichen Begleitung des Projektes wurde ein interdisziplinäres Expertenpanel aus Medizinern und Pharmazeuten gegründet. Es wurde ein standardisierter Prozessalgorithmus entwickelt. Dieser dient der Erfassung von Anwendungsschritten bei der Applikation und basiert auf Angaben zur Anwendung von bukkalem Midazolam aus der Literatur (Primär-/Sekundärliteratur, Fachinformation, Firmenangaben). Dabei wurden möglicherweise auftretende Handhabungsprobleme für spätere Anwendungen des Modells definiert. Anhand erster Testläufe wurde dieser Prozessalgorithmus durch das Expertenpanel auf seine Anwendbarkeit hin überprüft und optimiert. Das Simulationsmodell soll zur Untersuchung der Anwendung von bukkalem Midazolam durch Eltern oder Betreuer angewendet werden. Weiterhin kann das Modell zur Schulung medizinischer Laien im Krankenhaus, in der Arztpraxis, in betreuenden Einrichtungen oder in Apotheken dienen. Auf diese Weise sollen der Behandlungserfolg in der Notfallsituation gesichert und die Arzneimittelsicherheit erhöht werden.

➜ **Schumacher, Pia**
email: pia.schumacher@uni-leipzig.de

POSTER 192

Hepatic NAD salvage pathway is enhanced in mice on a high-fat diet

LIFE – Civilisation Diseases and Genetics

Penke M[1,2], Larsen P[3], Schuster S[2], Gorski T[2], Meusel A[4], Richter S[2], Vienberg S[5], Treebak J[5], Kiess W[2], Garten A[2]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig
3 The Novo Nordisk Foundation,Center for Basic Metabolic Research, Section of Integrative Physiology, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
4 Institut für Medizinische Physik und Biophysik, Universität Leipzig
5 The Novo Nordisk Foundation, Center for Basic Metabolic Research, Section of Integrative Physiology, Faculty of Health and Medical Sciences, University of Copenhagen

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objective: Nicotinamide phosphoribosyltransferase (NAMPT) is the rate-limiting enzyme for NAD salvage and the abundance of Nampt has been shown to be altered in non-alcoholic fatty liver disease. It is, however, unknown how hepatic Nampt is regulated in response to accumulation of lipids in the liver of mice fed a high-fat diet (HFD).

Design and Methods: C57BL/6 mice were fed a control diet (n=12) or a HFD containing 60% of total energy from fat (n=12) for 11 weeks. Glucose and insulin tolerance tests were performed. Hepatic lipids were measured by ^{1}H-NMR spectroscopy. Apart from Nampt mRNA and protein levels, we also assessed NAD concentrations and Nampt activity.

Results: HFD mice gained more weight, stored more hepatic lipids and had an impaired glucose tolerance compared with control mice. NAD levels as well as Nampt mRNA expression, protein abundance and activity were significantly increased. Enhanced NAD levels were associated with increased activation of Sirt1 and deacetylation of p53 and Nfκb.

Conclusion: Despite impaired glucose tolerance and increased hepatic lipid levels in mice fed a HFD, NAD metabolism was significantly enhanced. Thus, improved NAD metabolism may be a compensatory mechanism to counteract the negative impact of hepatic lipid accumulation.

Funding: life

→ **Penke, Melanie**
email: melanie.penke@medizin.uni-leipzig.de

POSTER 193 **Objective and subjective sleep in Hypomanic Personality**

LIFE – Civilisation Diseases and Genetics

Wozniak D[1], Sander C[1,2,3], Spada J[1,3], Jawinski P[1,2], Hegerl U[1,2,3], Hensch T[1,2]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
3 Forschungszentrum Depression, Stiftung Deutsche Depressionshilfe, Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hypomanic personality (HYP) has been suggested as a risk factor for affective disorders, especially for bipolar disorder (BD). Sleep quality and duration may be causally linked to affective disorders (Hegerl & Hensch, 2014).
Therefore, the current study analyzes the association of HYP with objectively and subjectively assessed sleep in healthy subjects.
Subjects were selected from the population-based Leipzig Health Care Study (LIFE) if they completed objective and subjective sleep assessments (actigraphy and Pittsburgh Sleep Quality Index (PSQI), respectively) and a medical questionnaire. All subjects had to be free of any current psychiatric or neurological disorder or any medication that might have a significant impact on sleep. 611 subjects (male: 323; age 65–79, mean: 70.7) were suitable for analysis. Sleep parameters were associated with the HYP score and compared between HYP-extreme groups (upper and lower decile of the HYP scale).
Actigraphy showed decreased sleep duration, longer sleep onset latency, decreased sleep efficiency and higher number and duration of awakenings in HYP high-scorers. Additionally, subjective sleep quality was reduced in HYP high scorers. For the whole group, results of correlational analyses between HYP and the sleep variables were similar.
The shorter sleep and decreased sleep quality found in HYP high-scorers are in line with theories of lack of sleep contributing to manic symptoms.

Funding: life

➜ **Wozniak, David**
email: Davidwozniak@gmx.de

POSTER 194

Effects of the serotonin transporter gene-linked polymorphic region (5-HTTLPR) on actigraphic sleep measures and self-reported chronotype.

LIFE – Civilisation Diseases and Genetics

Spada J[1,2], Sander C[1,2,3], Jawinski P[1,3], Huang J[1], Reif A[4], Hegerl U[1,2,3], Hensch T[1,3]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 Stiftung Deutsche Depressionshilfe, Leipzig
3 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
4 Klinik und Poliklinik für Psychiatrie, Psychosomatik und Psychotherapie, Universität Würzburg

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Serotonin plays a major role in sleep-related brain systems. However, its specific influence on circadian behaviour is not well understood. The current study aimed to investigate this influence by associating 5-HTTLPR with actigraphic and self-reported circadian parameters. The study was performed in a sample of elderly subjects (64–79yrs), who were genotyped for 5-HTTLPR. The subjects completed the Morningness-Eveningness-Questionnaire (D-MEQ) and/or participated in an actigraphic assessment. Another two samples of elderly (64–79yrs) and middle-aged subjects (40–63yrs) who were genotyped for a two-SNP proxy of 5-HTTLPR served as replication samples. Utilizing a heterozygous genetic model, the circadian preference as assessed with the D-MEQ score was significantly associated with 5-HTTLPR or its two-SNP proxy in all three independent samples ($p < 0.05$). Actigraphic analysis revealed an earlier sleep onset and prolonged sleep duration in heterozygous individuals of the screening sample and an earlier sleep offset in subjects of the elderly replication sample. No genetic association could be identified in the middle-aged actigraphic sample. The current study shows for the first time that in elderly adults 5-HTTLPR is associated with both self-reported and objectively measured circadian parameters. Further studies are necessary to investigate the underlying molecular and functional mechanisms.

Funding: life

→ **Spada, Janek**
email: janek.spada@medizin.uni-leipzig.de

POSTER 195

Prader Willi – Syndrome and non-syndromal obesity: a pilot study about analogies in behavioral problems and eating behaviour

LIFE – Civilisation Diseases and Genetics

Sonnengrün L[1,2]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Prader-Willi syndrome (PWS) is the most common syndromal cause of obesity. Individuals show a distinctive preoccupation with food, an insatiable appetite, linked with neurological, cognitive, endocrine and behavioral/psychiatric disturbances. Behavioral problems in a milder occurrence have also been observed in non-syndromal overweight children. Psychosocial factors of eating behavior, contributing to childhood obesity, are recent object of research. The current study aims to disclose potential analogies of PWS and non-syndromal childhood obesity with respect to behavioral problems and a range of factors concerning eating behavior.
Methods: We compare children and adolescents with PWS, age-matched obese subjects and normal weight controls via standardized questionnaires in body esteem, degree of eating disorder, parental feeding behavior and behavioral problems.
Results: Mean score values of the PWS and obese group differed significantly from values of lean subjects regarding: more concern about eating, weight and shape, more restraint in eating behavior, parent's concern about child weight and a more restrictive parental feeding behavior. Besides, the scores of problem behavior were significantly higher in both groups, whereby the difference between scores of PWS and obese group was also significant.
Conclusion: There are similarities between PWS and non-syndromal obesity in behavior and psychosocial, eating related factors. More structured studies with greater sample sizes are necessary to distinguish which characteristics of PWS might be attributable to the psychopathology of non-syndromal obesity.

Funding: life

→ **Sonnengrün, Lilli**
email: lilli.sonnengruen@medizin.uni-leipzig.de

POSTER 196

A trip to mars in epidemiological studies – Analysis of traditional anthropometry values for children and adolescents using a three-dimensional whole body scanner

LIFE – Civilisation Diseases and Genetics

Naumann S[1], Hiemisch A[1,2], Koch C[1], Bucher C[1], Woller A[1], Warnatsch C[1], Grafe N[1], Geserick M[1], Ahnert P[3], Scholz M[3], Bogatsch H[4], Vogel M[1], Kirsten T[1], Kiess W[1,2]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig
3 Institut für Medizinische Informatik, Statistik und Epidemiologie (IMISE), Universität Leipzig
4 Zentrum für Klinische Studien, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Accurate data are fundamental in gaining insights into growth and its corresponding processes. The possibility to generate virtual body models from a cloud of points or pixels with the help of different scanning systems break a new ground for measuring accurately and precisely. Various studies confirm the validity and reproducibility for different body scanner methods in adults. For use in children, there are no comprehensive studies. We aimed to evaluate the reliability and validity of the VITUS Smart XXL body scanner for children and adolescents in comparison with traditional anthropometry. The study population consists of participants from the LIFE Child Study cohort. 244 boys and 216 girls aged 6 – 17 years with a maximum range in BMI-SDS (-3 – 4.5) were tested. All subjects were measured three times using traditional anthropometry and three-dimensional whole body scanner and compared in 8 measurements. The visual data analysis was carried out using Bland-Altman plots. The statistical analysis was supplemented by calculating the intraclass-correlation-coefficient (icc) and intraindividual concordance-correlation-coefficient (ccc). The research project will make a contribution to the insufficient data regarding the three-dimensional whole body scanner technology for children and adolescents. Depending on the results, the body scanner can represent a simple and well applicable method to collect a wider range of measurements than traditional anthropometry. In conjunction with additional data, the measured values can be used to understand more complex issues in relation to children's development and health.

Funding: life

➜ **Naumann, Stephanie**
email: snaumann@life.uni-leipzig.de

POSTER 197

Tracking of BMI from infancy to adolescence and predictive value for the development of obesity

LIFE – Civilisation Diseases and Genetics

Geserick M[1], Vogel M[1], Gausche R[1], Wallborn T[1,2], Pfäffle R[1,2], Kiess W[1,2], Körner A[1,2]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

We aimed to assess the predictive value of BMI at earlier ages for the risk of developing obesity in adolescence and to identify vulnerable age periods that may be crucial for subsequent overweight/obesity.

We retrieved anthropometric data of 33.537 subjects from the CrescNet® data base and included those with measurements at two or more time points.

Overweight and obesity were present in 10% and 9% of the adolescents (15–18 years), respectively. Changes from normal weight to overweight/obesity in childhood were considered and probability of being overweight/obese in adolescence given a certain BMI-SDS in childhood was calculated.

Retrospectively seen, 53% of the children, who were obese in adolescence were normal weight until the age of 4 years. By the age of 5 years, however, half of them were overweight/obese. Prospectively, 60% of children who are overweight already at the age of 4 years remained overweight/obese in adolescence. The probability of being overweight/obese in adolescence in those who are already obese at the age of 4 was 79%. In a subgroup of 26.344 children we considered the influence of BMI acceleration in different age periods. Dynamically, children in the age of 2 to 6 years, who had a rise in BMI-SDS by 0.2–2 during one year had a higher risk of being overweight/obese in adolescence than older children with the same BMI acceleration.

In conclusion, overweight/obesity in adolescence is already determined in early childhood. Periods of increased BMI acceleration in early childhood should be recognised for an optimized strategy in obesity prevention.

Funding: life

→ **Geserick, Mandy**
email: mgeserick@life.uni-leipzig.de

POSTER 198

Soziodemographische Merkmale und soziökonomischer Status der Teilnehmer in der LIFE Child Kohorte im nationalen Vergleich

LIFE – Civilisation Diseases and Genetics

Meißner L[1], Bucher C[1], Vogel M[1], Kirsten T[1,2], Igel U[3], Kiess W[1,4], Hiemisch A[1,4]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
2 Institut für Medizinische Informatik, Statistik und Epidemiologie (IMISE), Universität Leipzig
3 Hochschule für Technik, Wirtschaft und Kultur – HTWK, Leipzig
4 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Soziodemographische und sozioökonomische Merkmale gelten in den Humanwissenschaften als bedeutende, globale Einflussfaktoren in fast allen Gebieten der Forschung. Sie geben Einblick in die Sozialstruktur einer Untersuchungspopulation und bilden damit das Basiselement von Kohortenstudien. In vielen Bereichen wurde darüber hinaus bereits ein direkter Zusammenhang zwischen soziodemographischen/-ökonomischen Faktoren und körperlicher wie auch psychischer Gesundheit nachgewiesen. Insbesondere im Kindes- und Jugendalter hat der sozioökonomische Status einer Familie entscheidenden Einfluss auf die physische aber auch mentale Entwicklung. Bisherige Studien konnten unter anderem bereits negative Einflüsse sozialer Deprivation auf subjektive Gesundheit, Gewicht, Ernährungsverhalten und -praktiken, körperliche Aktivität oder auch Zahngesundheit belegen. Andererseits werden Krankheitsbilder wie Anorexia nervosa, atopisches Ekzem und Asthma bronchiale hingegen häufiger bei Kindern und Jugendlichen aus Familien mit höherem sozialem Status diagnostiziert. Diese und eine ganze Reihe weiterer Forschungsfragen stehen auch im Blickpunkt der Projektes LIFE Child. Dabei handelt es sich um eine longitudinale Single-Center-Studie mit regionalem Bevölkerungsbezug zur Stadt Leipzig. In diesem Zusammenhang ist es für die Beantwortung von wissenschaftlichen Fragestellungen wichtig, wie sich die LIFE Child Teilnehmerstruktur soziodemographisch und sozioökonomisch im nationalen Vergleich einordnen lässt? Darüber hinaus zeigt der Sozialatlas der Stadt Leipzig schon innerhalb des Stadtgebietes eine große Heterogenität.

Funding: life

➜ **Hiemisch, Andreas**
email: ahiemisch@life.uni-leipzig.de

POSTER 199

Heterozygous Trib1-deficiency increases atherosclerotic lesions in ApoE-knockout mice

LIFE – Civilisation Diseases and Genetics

Arndt L[1], Dokas J[1], Jeromin F[1], Thiery J[1], Burkhardt R[1]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objective: We have previously identified Trib1 as a novel regulator of plasma cholesterol and triglyceride levels in mice. In the present study, we used heterozygous Trib1-deficient mice on the atherosclerosis prone apolipoprotein E knockout background (Trib1+/-ApoE-/-) to study the functional role of Trib1 in atherosclerosis development.

Methods: Male Trib1+/-ApoE-/- and Trib1+/+ApoE-/- control mice, generated by crossing heterozygous Trib1 with homozygous ApoE deficient mice, were fed a semisynthetic AIN76 diet (0.02% cholesterol) for 14 weeks. Triglyceride and cholesterol concentrations were determined in plasma and isolated lipoproteins. Atherosclerosis was analyzed at the aortic root and the brachiocephalic artery (BCA) In addition, gene expression studies in liver and aorta were carried out to characterize functional consequences of Trib1 deficiency.

Results & Conclusion: Trib1+/-ApoE-/- mice showed significantly elevated plasma total cholesterol and non-HDL cholesterol levels, but no differences in triglycerides. These mice also exhibited a significant elevation of key genes associated with hepatic lipid metabolism. Furthermore, atherosclerotic lesion size in the aortic root was significantly increased by 40% in Trib1+/-ApoE-/- mice, In addition, gene expression analysis in the thoracic aorta suggests an increase of inflammatory processes in the vessel wall of Trib1+/-ApoE-/- mice. In conclusion, we demonstrate that Trib1 deficiency leads to increased atherosclerotic lesion formation in mice. Future studies will address the precise molecular mechanisms by which Trib1 mediates its effect on atherosclerosis.

→ **Arndt, Lilli**
email: lilli.arndt@medizin.uni-leipzig.de

POSTER 200

Can the blues make it harder to breathe?

LIFE – Civilisation Diseases and Genetics

Schitke J[1]

1 Abteilung für Pädiatrische Onkologie, Hämatologie und Hämostaseologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Asthma ist eine der häufigsten chronischen Erkrankungen im Kindesalter. Laut Ergebnissen der KIGGS-Studie haben 6,3 % der Kinder und Jugendlichen in Deutschland Asthma. Während es bereits gut etablierte Therapiemethoden gibt, sind die Empfehlungen zur Primärprevention nach wie vor sehr begrenzt.
Um die Entstehung von Asthma zu erklären, wird derzeit von einem Zusammenspiel aus genetischer Prädisposition (z. B. Mutation auf Chromosom 17), immunologischen Faktoren (u. a. mit Fokus auf die immunologische Wirksamkeit von Epithelien der Haut, des Respirations- und Darmtraktes) und Umwelteinflüssen (z. B. Medienkonsum, Bewegung) ausgegangen. Auch psychische Faktoren (z. B. Depression) scheinen die Entstehung von Asthma zu beeinflussen.
Ziel dieser Studie ist es näher zu untersuchen, inwiefern Verhaltensauffälligkeiten und -stärken von Kindern und Jugendlichen mit dem Auftreten von Asthma korrelieren. Datengrundlage hierfür sind die von Eltern und Kinder ausgefüllten SDQ-Fragebögen sowie die ärztlich erhobenen Anamnesen im Rahmen der LIFE-Child Studie.

→ **Schitke, Julia**
email: motschekiepchen@posteo.de

POSTER 201

CACNA1C and Chr1p31.1 gene variations are linked to EEG-vigilance regulation

LIFE – Civilisation Diseases and Genetics

Jawinski P[1,2], Sander C[1,2], Mauche N[1,2], Spada J[1,2], Häntzsch M[2,3], Burkhardt R[2,3], Hegerl U[1,2], Hensch T[1,2]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
3 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objectives: According to the vigilance regulation model, manic and depressive episodes may partly be induced by profound alterations in vigilance (i. e., neurophysiological arousal). Aside from that, Bipolar Disorder ("manic-depressive illness", BD) has been shown highly heritable and genome-wide association studies established several risk alleles. The present study assessed whether carriers of the most reliable BD risk alleles differ in vigilance regulation compared to non-risk carriers when faced with a twenty-minute eyes-closed resting EEG paradigm.
Methods: We selected healthy participants of the large scale Leipzig Health Care Study (LIFE), who completed a comprehensive medical examination. During the EEG paradigm, participants were allowed to follow their natural decline of vigilance. EEGs were analyzed applying the Vigilance Algorithm Leipzig (VIGALL). Participants were genotyped for ten of the most replicable BD risk variants. The final sample comprised 540 participants (M=71.1 yrs, SD=3.6 yrs, 307 male).
Results: Vigilance regulation was most significantly linked to a variation within CACNA1C (rs1006737, $p<.001$, $\eta^2=.016$) with risk-allele carriers showing faster vigilance declines. Aside from that, carriers of two Chr1p31.1 risk alleles (rs472913) showed generally lower vigilance levels for the duration of the resting EEG paradigm ($p=.003$, $\eta^2=.028$).
Conclusion: The reported associations are in line with the vigilance regulation model and, regarding rs1006737, results are consistent with the notable role of ion-channels in BD, since CACNA1C encodes an alpha-1 subunit of the L-type calcium channel.

Funding: life

→ **Jawinski, Philippe**
email: philippe.jawinski@medizin.uni-leipzig.de

POSTER 202

Simultaneous Identification and Quantification of Triacyglycerol Species in Human Plasma by Flow Injection Electrospray Ionization Tandem Mass Spectrometry

LIFE – Civilisation Diseases and Genetics

Sander M[1], Becker S[1,2], Thiery J[1,2], Ceglarek U[1,2]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
2 LIFE – Leipziger Forschungszentrum für Ziilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Civilization diseases like atherosclerosis and type II diabetes are associated with elevated triacylglycerol (TG) levels. Fatty acyl (FA) residue 16:0 had shown to have atherogen potential. TGs containing FA residue 20:4 were associated with a decreased risk in the development of diabetes mellitus. With increasing knowledge of the effects of FA distribution in TGs, it is necessary to study the TG molecular species. Using conventional enzymatic methods, the TG molecular species cannot be differentiated.

In this study a tandem mass spectrometric method was developed on an AB Sciex API 4000 triple quadrupole mass spectrometer with positive electrospray ionization to analyze 19 TG species by combination of 9 neutral loss (NL) experiments.

The method was validated including linearity, coffiecient of variation, lowest detectable concentration, lower limit of quantification and recovery. The predominant TG species in human plasma are 52:2 and 52:3. The most abundant FA residues in plasma TGs have been found to be 16:0, 18:1, 18:2 and 20:4. Inter-individual differences in composition of TG molecular species could be identified. Good correlation for total TG concentration between the conventional photometric and MS/MS method had been obtained. Significant differences between fasting and non-fasting subjects were obtained.

The developed MS/MS method can be applied to get knowledge of the normal physiological distribution of TG molecular species in human plasmain patients with coronary heart disease and diabetes.

➜ **Sander, Madlen**
email: madlen.sander@medizin.uni-leipzig.de

POSTER 203

Interactions between 3T3-L1 adipocytes and different breast cancer cell lines

LIFE – Civilisation Diseases and Genetics

Nickel A[1,2], Schaab M[1], Jeromin F[1], Schwagarus N[1,2], Spindler N[3], Thiery J[1,2], Kratzsch J[1], Burkhardt R[1,2], Stadler SC[1,2]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen , Universität Leipzig
3 Abteilung für Plastische-, Ästhetische- und spezielle Handchirurgie, Universität Leipzig

Objective: Obesity and its associated morbidities pose a great challenge on global health. Recent studies demonstrate that obesity and excess accumulation of adipose tissue are independent negative prognostic factors for breast cancer. However, the molecular mechanisms by which breast cancer cells and surrounding adipocytes affect each other, remain elusive. Here, we investigate molecular interactions between human breast tumor cells and adipocytes, leading to a more progressive phenotype of breast tumor cells.
Methods: To analyze the interactions between human breast tumor cells and adipocytes we established a two-dimensional cell culture system which separates the breast tumor cells and adipocytes physically but allows communication via soluble paracrine factors. Furthermore, we performed migration and invasion assays, microarray analysis and quantitative real time PCR assays on human breast tumor cells to determine morphologic and molecular changes upon co-culture with mature adipocytes *in vitro*.
Results: We demonstrate that human breast tumor cells show enhanced migration and invasion capabilities upon co-culture with mature adipocytes. Additionally, microarray analysis and ELISA assays of co-cultured breast tumor cells revealed an increased expression level of proinflammatory cytokines in triple-negative breast cancer cells.
Conclusion: Our data indicate that mature adipocytes promote the progression of human breast tumor cells *in vitro*. Further investigations will focus on analyzing the molecular mechanisms by which adipocytes influence the characteristics and invasive behavior of malignant human breast tumor cells.

Funding: life

→ **Nickel, Annina**
email: annina.nickel@medizin.uni-leipzig.de

POSTER 204

Spatial Analysis of Anthopometric and Lifestyle Data for Children and Adolescents

LIFE – Civilisation Diseases and Genetics

Vogel M[1], Gausche R[2], Kiess W[1,2], Grande G[3], Molis D[4], Igel U[3], Kiel A[1], Rühle M[1], Kirsten T[1]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig
3 HTWK Leipzig
4 AOK PLUS

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

LIFE Child is an epidemiological cohort study at the Leipzig Research Center for Civilization Diseases (Leipzig University). A main goal of LIFE Child is to study the influence of environment and lifestyle factors to the development of children and adolescent in and near Leipzig. In particular, we search for predominant aspects in the development of children with obesity.
Typically, data is analyzed by different statistical methods and approaches to find (perhaps multivariate) pre-dominant markers. Additionally, we map selected data to geographical maps to study their spatial distribution over urban districts of Leipzig, on the one hand. This allows to comparatively analyze anthropometric measurements, such as age- and gender-corrected height, weight, and body mass index, together with further participant-related data including social indicators, e.g., income, education, socio economic indexes and lifestyle data, to distinguish city districts with a high correlation to those with low or no correlation. On the other hand, we associate anthropometric measurements with publicly available data, such as official statistics including district-specific unemployment rates and inhabitant densities by taking the participant's place of living into account.
Scientific results will be translated into public health practice within an innovative multilevel evaluation model for community-based health promotion in cooperation with HTWK Leipzig, City Leipzig and the AOK PLUS.

Funding: life

→ **Vogel, Mandy**
email: mandy.vogel@medizin.uni-leipzig.de

POSTER 205

Identification of agonists on GPR171

Molecular Biology/Protein Biochemistry

Schulze A[1], Schulz A[1], Schöneberg T[1], Brüser A[1]
1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

GPR171 is an orphan G protein-coupled receptor (GPCR) and belongs to the P2Y12-like receptor group within the family of rhodopsin-like receptors. Phylogenetically, this group includes the ADP receptors P2Y12 and P2Y13, the UDP-glucose receptor P2Y14 and the orphan receptors GPR34, GPR87, GPR82, and GPR171. Very little is known about the physiological function of these members, besides P2Y12 with its central role in platelet aggregation and being the therapeutic target of clopidogrel. GPR171 was identified in different vertebrates and has been conserved over the past 450 million years. It appears to be a highly relevant receptor for vertebrate physiology, because by comparison of 60 orthologs no GPR171-deficient vertebrate has been identified yet. The human and mouse GPR171 are located on chromosome 3 clustering with P2Y12, P2Y13, P2Y14, and GPR87 (3q24-25). However, it is not clear whether nucleotides are agonists of GPR171. Quantitative PCR analyses in mice showed GPR171 expression in all tissues specifically in peripheral and nervous central immune cells. Treatment of microglia and astrocytes with lipopolysaccharide resulted in a down-regulation of GPR171 in these cells. *In vitro* studies revealed Gαi-protein coupling and adenylyl cyclase inhibition. Screenings of compound libraries for GPR171 ligands were performed and revealed nine nucleotide derivatives acting as agonist on GPR171 .

Funding: formel1

→ **Brüser, Antje**
email: antje.brueser@medizin.uni-leipzig.de

POSTER 206

Psychrophilic tRNA nucleotidyltransferases: insight into flexibility and fidelity

Molecular Biology/Protein Biochemistry

Ernst F[1], Erber L[1], Sammler J[1], Betat H[1], Mörl M[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

During evolution, organisms showed remarkable capabilities to adapt to cold habitats including oceans, polar and permafrost regions, representing the majority of the earth surface. In such psychrophilic organisms, cold adaptation of enzymatic activities is achieved by reducing optimal reaction temperatures via an increased structural flexibility of the corresponding proteins. One enzyme with certain flexible elements even in meso- or thermophilic organisms is tRNA nucleotidyltransferase, which is responsible for addition and maintenance of the CCA-terminus of tRNAs. Here, we investigate the molecular adaptation of this type of enzyme and the corresponding consequences in fidelity in several psychrophilic bacteria.

Sequence alignments indicate that even in the psychrophilic enzymes, the active site motifs A to E show a very high level of conservation. Hence, as the recombinant CCA-adding enzymes from two psychrophilic bacteria show a lowered optimal reaction temperature compared to mesophilic and thermophilic counterparts, cold adaptation obviously involved less conserved protein regions. Furthermore, the unfolding properties of these enzymes matched their activity temperature profiles. An initial analysis of the polymerization fidelity indicates that for one of the psychrophilic tRNA nucleotidyltransferases, the cold adaptation comes at the price of additionally incorporated nucleotides, leading to a considerable amount of heterogeneous tRNA 3'-ends. Whether an increased flexibility of the catalytic core or the tRNA binding region of this enzyme is responsible for this reduced fidelity is currently not known.

➜ **Ernst, Felix**
email: felix.ernst@uni-leipzig.de

POSTER 207

Expression of the G protein-coupled receptor GPR34 is regulated through MAPKs and NFκB

Jäger E[1], Lede V[1], Schulz A[1], Schöneberg T[1], Le Duc D[1]
1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig

Molecular Biology/Protein Biochemistry

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

GPR34 is an orphan $G_{i/o}$ coupled receptor of the $P2Y_{12}$-like receptor group. GPR34 deficiency leads to an impaired immune response in mice and overexpression was reported in the spread of several solid tumors. However, its expression regulation is unknown. Here we integrate GPR34 transcription in the signaling network of Toll-like receptors (TLRs). Murine bone-marrow derived dendritic cells (DCs) were stimulated with different TLR-agonists and GPR34 expression was analyzed via quantitative PCR and RNA sequencing.
Our results point toward a highly regulated expression of this receptor during immunological responses. Down-regulation occurs after ERK and NFκB activation and up-regulation seems to be triggered by stimulation of p38 and JNK- MAPKs. Involvement of p38- and JNK-MAPKs in expression regulation hints to a function of this receptor in apoptosis. Treatment of GPR34 deficient and wild type DCs with staurosporine led to a significantly increased caspase 3/7 activity in GPR34 knock out DCs, indicating a further function of GPR34 in regulating apoptosis.
Our study identifies pathways which allow the GPR34 switch on and off. Given the reported involvement in many physiological and pathological processes future studies will have to inquire the relevance of the GPR34 regulation pathways as putative therapeutic targets.

→ **Jäger, Elisabeth**
email: elli.jaeger@online.de

POSTER 208

Expression and Purification of kallikrein 7, a target of the visceral fat tissue derived serpin vaspin (serpinA12)

Molecular Biology/Protein Biochemistry

Pippel J[1], Heiker J[2], Ulbricht D[2], Küttner B[1], Beck-Sickinger AG[2], Sträter N[1]

1 Institut für Bioanalytik, Biotechnologisch-Biomedizinisches Zentrum (BBZ), Universität Leipzig
2 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Kallikrein 7, a serine protease belonging to the tissue kallikreins, was identified as target for vaspin, a visceral fat tissue derived serpin. The crystal structure of vaspin was previously determined by our group. Since kallikrein 7 is able to cleave human insulin it has been proposed that the inhibition by vaspin could be a compensating mechanism to increase insulin half-life and to counteract adipose-induced diminished insulin sensitivity. This hypothesis has been underpinned by further studies indicating that the kallikrein 7-vaspin-interaction is a potential target for anti-diabetic treatment.
Methods: Kallikrein 7 was expressed in inclusion bodies in E.coli, refolded via fast dilution and purified with a combination of ion exchange, affinity and size exclusion chromatography. Enzyme activity and crystallization properties were assayed.
Results: Via a novel expression strategy utilizing SUMO or Strep-tag with subsequent refolding we were able to obtain native kallikrein 7 in mg amounts and high purity. Enzyme activity was comparable to commercially available protein. In addition, the purified enzyme could be crystallized in an condition that was published by Fernández et al. in 2008. The crystals belong to space group H32 and diffract to 3 Å resolution at home source.
Conclusion: Large amounts of pure recombinant proteins are a requirement for structural studies of the vaspin-kallikrein 7 interaction. Our procedure resulted in sufficient amounts of active and crystallizable kallikrein 7, demonstrating the suitability of this effective protein preparation strategy for further crystallographic studies.

➜ **Pippel, Jan**
email: Jan.Pippel@bbz.uni-leipzig.de

POSTER 209

Selection of aptamers binding to heparin-binding hemagglutinin

Molecular Biology/Protein Biochemistry

Etzel M[1], Peter F[2], Haltenhof T[2], Mayer G[3], Mörl M[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 Universität Leipzig
3 Universität Bonn

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

One third of the world population is infected with the pathogen *Mycobacterium tuberculosis*, which causes tuberculosis. On the cell surface of this bacterium, heparin-binding protein (HBHA) is expressed, mediating the adherence of the bacterium to the host cell. Pethe *et al.* could show that lysine-rich repeats, located in the C-terminal domain of HBHA, are essential for the adhesion to sulfated glycoconjugates on epithelia cells. For this reason, HBHA is an important protein in the pathogenesis of tuberculosis (Menozzi, 1996).

There is evidence that an increasing number of current tuberculosis strains is resistant to various common antibiotics. Therefore, new anti-tuberculosis drugs are needed. DNA- or RNA-aptamers represent potential molecules that became popular in the last 20 years as promising alternatives to antibodies. They are generally used as diagnostic tools or as therapeutic agents.

In this project, the *in vitro* selection method SELEX (*Systematic Evolution of Ligands by Exponential enrichment*) is performed to identify RNA aptamers binding to HBHA with high affinity and specificity. In the selection procedure, recombinant HBHA overexpressed in *E. coli* is used as target. After ten selection rounds, RNA sequences were isolated and sequenced. Furthermore the binding parameters of selected RNA sequences were determined by using SPR and filter binding assays. Our results indicate that some sequences are able to bind specific to recombinant HBHA. Such RNA aptamers could serve as a potential drug against *Mycobacterium tuberculosis* Infections.

➜ **Etzel, Maja**
email: maja.etzel@uni-leipzig.de

POSTER 210

Resveratrol potentiates growth inhibitory effects of rapamycin in LipPD1 cells by suppressing p70S6K activity

Molecular Biology/Protein Biochemistry

Leipert J[1], Kässner F[1], Richter S[1], Kiess W[1], Garten A[1]

1 Klinik und Poliklinik für Kinder und Jugendmedizin, Universität Leipzig

Background: Rapamycin (rapa) was shown to reduce the growth of PTEN-deficient lipoma cells (LipPD1), but concomitantly induced an upregulation of AKT activity, possibly leading to drug resistance. We asked whether or not co-treatment with resveratrol (resv) could suppress the rapa induced phosphorylation of AKT.

Methods: Preadipocytes were stimulated with resv or a combination of resv with rapa. Cell viability, apoptosis and cell cycle arrest were measured. PTEN expression, AKT and p70S6K phosphorylation were analyzed by western blot. Normal primary preadipocytes were used as controls.

Results: Treatment of LipPD1 cells with resv resulted in a significant dose-dependent inhibition of cell viability, induction of apoptosis and a G1-cell cycle arrest. AKT phosphorylation was not significantly changed, whereas the phosphorylation level of p70S6K was decreased significantly in cells treated with resv compared to controls. Co-incubation with rapa and resv further decreased viability at low concentrations compared to resv alone and significantly decreased p70S6K phosphorylation compared to both resv and rapa alone. Viability and p70S6K phosphorylation of normal preadipocytes were less affected compared to LipPD1 cells by equimolar concentrations of resv or the combination with rapa.

Conclusion: Resv potentiates the growth inhibitory effects of rapamycin potentially by reducing p70S6K activation in LipPD1 cells. These results support the concept of combining chemopreventive, natural compounds with PI3K/AKT/mTOR inhibitors in cancer therapy to increase the effectivity of chemotherapeutic drugs.

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

➜ **Leipert, Jenny**
email: jenny.leipert@medizin.uni-leipzig.de

POSTER 211

Artificial Metallocatalysts based on RNase S

Molecular Biology/Protein Biochemistry

Reiser P[1], Genz M[1], Singer D[1], Hassert R[1], Holldorf J[2], Surgenor B[2], Hey-Hawkins E[2], Hoffmann R[1], Sträter N[1]

1 Institut für Bioanalytische Chemie, Biotechnologisch-Biomedizinisches Zentrum (BBZ), Universität Leipzig
2 Institut für Anorganische Chemie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

About 1/3 of all proteins contain a bound metal ion, which may have a structural or catalytic function. Natural metalloenzymes utilize only a small subset of the metal ions of the periodic system, mainly the first transition row metals in addition to Ca^{2+} and Mg^{2+}. However, in particular the 4d and 5d transition metals exhibit excellent and unique chemical reactivities which are not utilized bynature due to the limited bioavailability or toxicity of these metals. A prominent example is Rh^{+}, which is commonly used in organo-metal synthesis. It is of great biotechnological interest to develop methods to include such metal centers into enzymes, thereby com-bining the unique chemical reactivity of the metal center with theselectivity (stereoselectivity, substrate specificity or regioselectivity) that can be provided by the protein environment. Many organometal centers require special coordinating ligandspheres for activity, for instance phosphines for Rh^{+} activitation. We aim to develop new designed metallocatalysts based on the RNase S scaffold. The S-protein derived from bovine RNaseA hasthe feature of binding an peptide (termed S-peptide) consisting of 15 to 20 amino acid with remarkable high affinity, thereby formingthe RNase S complex. We introduce novel metal-coordinating sidechains into RNase S by chemical synthesis of the S-peptide. Firstmodel systems consist of cysteine and homocysteine coordinatingheavy metal ions such as mercury. The resulting artificial metallo-proteins are characterized by X-ray crystallography.

➜ **Reiser, Peter**
email: peter.reiser@bbz.uni-leipzig.de

POSTER 212

The fate of tRNAs and their precursors – processing or degradation?

Molecular Biology/Protein Biochemistry

Wellner K[1], Betat H[1], Mörl M[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

In protein translation, tRNAs play a crucial adaptor role converting genetic information into an amino acid sequence. An important prerequisite is the CCA triplett at the 3'-end of tRNAs which is usually added posttranscriptionally by the CCA-adding enzyme. Prior to CCA-addition, a series of RNases must act on nascent tRNA precursors to process them into mature tRNAs in both pro- and eukaryotes.

It has been shown that the quality of tRNA precursors is tightly controlled. Upon polyadenylation, defective tRNA precursors are tagged and marked for subsequent degradation. This process is fundamental to avoid fatal effects of misfolded tRNAs within a cellular environment. Recently, also CCACCA has been described as a tRNA 3'-tag. Incorporation of the additional CCA triplett can be achieved by the CCA-adding enzyme if the RNA structure is unstable and therefore nonfunctional. So far, little is known about the regulatory potential of the CCACCA tag. However, a tag like this closely resembles the 3'-trailer of a tRNA precursor which is recognized by the 3'-end processing machinery. In this project, we want to investigate how *E. coli* exonucleases acting on tRNA discriminate between a tRNA precursor (3'-trailer) and a tRNA targeted for degradation (CCACCA).

Our first results confirm that the degrading enzyme RNase R breaks down tRNA-CCACCA and not tRNA-CCA. More interestingly, tRNA-CCACCA is also a substrate for the processing enzyme RNase T, which produces tRNA-CCACC and tRNA-CC. In future studies we plan to perform enzyme kinetics that will give insight into preferences of individual RNases for substrate specificity and affinity.

➜ **Wellner, Karolin**
email: karolin.wellner@uni-leipzig.de

POSTER 213 **Evaluation of biofunctionalized biomaterials in vitro**

Molecular Biology/Protein Biochemistry

Thönes S[1], Kascholke C[2], Hacker M[2], Anderegg U[1]

1 Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Universität Leipzig
2 Institut für Pharmazie, Universität Leipzig

Dermal fibroblasts (dFb) play a crucial role in the healing of chronic and acute wounds of the dermis. As main producers of extracellular matrix they are essential for the synthesis of granulation tissue and the replacement of tissue defects. For this purpose dFb are regulated by cell-matrix interactions, physical properties of tissues, other cells and paracrine mediators. Earlier findings suggest the ability of two dimensional coatings of artificial extracellular matrices (aECM) to alter proliferation and differentiation of human dFb *in vitro*. For the cure of wound defects, the development of three dimensional (3D) aECM, which are physiologically more similar to the *in vivo situation*, is needed. These aECM should show a target-oriented interaction with dFb through their physical properties and the incorporation of growth factors. As a possible main substance for the construction of a 3D aECM, the binding of rhTGFβ1 to the carrier substance Tri450La6 and the effect on dFb are examined. It could be shown that the binding of bioactive substances to the scaffold is possible. Furthermore modified Tri450La6 shows a good bioactivity on dFb and a good colonization *in vitro* and thus could work as a scaffold for tailormade 3D artificial extracellular matrices.

→ **Thönes, Stephan**
email: stephan.thoenes@medizin.uni-leipzig.de

POSTER 214

Construction and analysis of synthetic streptomycin and tetracycline riboswitches

Molecular Biology/Protein Biochemistry

Domin G[1], Wachsmuth M[1], Heidenreich S[1], Findeiß S[2], Stadler P[3], Mörl M[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 Research Group Bioinformatics and Computational Biology, Institute for Theoretical Chemistry, University of Vienna
3 Bioinformatics Leipzig, Institute of Computer Science, Faculty of Mathematics and Computer Science, University Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Riboswitches represent a specific type of regulatory RNA that gained strong attention in the field of synthetic biology. Usually located in the 5′ UTR of mRNAs, these elements regulate gene expression at the level of transcription or translation without the need for a protein factor. Consisting of a ligand-specific aptamer domain fused to a regulatory platform (ribosomal binding site or transcriptional terminator), riboswitches show a modular organization that can be used to generate new custom-made regulatory elements. For such synthetic riboswitches responding to a certain effector molecule, an *in vitro* selected aptamer specific for a ligand of interest can be fused to an RNA sequence that forms either an intrinsic terminator (for regulation of transcription) or sequesters the ribosomal binding site (regulation of translation).
We could recently show that *in silico* designed transcriptional terminator elements fused to an upstream located theophylline aptamer function as highly specific ON switches regulating transcription in *Escherichia coli* (Wachsmuth, Findeiß *et al*. 2013).
Here, we demonstrate that our strategy is generally suited to create transcriptional riboswitches responding to different ligand molecules, such as streptomycin and tetracycline.

➜ **Domin, Gesine**
email: gdomin@uni-leipzig.de

POSTER 215 **Heparin Binding and Vaspin/SerpinA12 Activity**

Molecular Biology/Protein Biochemistry

Ulbricht D[1], Schultz S[1], Meier R[1], Heiker JT[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Vaspin (serpinA12) was discovered in a rat type II diabetes model andimproves glucose tolerance as well as reduces food intake in mouse models [1,2]. Inprevious work, we have crystallized vaspin and identified kallikrein 7 (KLK7) as the first target protease of vaspin [3]. The association rate constant of native vaspin and KLK7 is moderate compared to association rate constants of other serpin-protease complexes. Several serpins, e. g. antithrombin III (ATIII), are activated by glycosaminoglycans as demonstrated by X-ray structures of native and heparinbound ATIII [4]. In the vaspin X-ray structure the P1 residue is pointing towards the protein comparable to the P1 orientation in free ATIII prior to heparin binding [3,4]. As we observed heparin binding for vaspin, we hypothesized free vaspin is present in a pre-activated state. In a first approach we aimed to fixate the vaspin reactive center loop (RCL) in a conformation with an exposed P1 side chain by introduction of an artificial disulfide bond to mimick the activated state. The association rate constant for KLK7 of this mutant was increased ~9 fold compared to the native serpin. Furthermore, in KLK7 inhibition assays we observed activation of vaspin by heparin. We have identified different potential heparin binding sites of vaspin via selective labeling and addressed their relevance in binding by site directed mutagenesis and heparin affinitychromatography.

[1] Hida et al. 2005, PNAS
[2] Klöting et al. 2011, Diabetologia
[3] Heiker et al. 2013, Cell Mol Life Sci
[4] Johnson et al. 2006, EMBOJ

Research Support: Funded by the European Union and the Free State of Saxony.

➜ **Ulbricht, David**
email: david.ulbricht@uni-leipzig.de

POSTER 216

Genotyping bacterial and fungal pathogens using sequence variation in CCA-adding enzymes

Molecular Biology/Protein Biochemistry

Franz P[1], Betat H[1], Mörl M[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

An increasing prevalence of antibiotic resistances in human pathogens is driving the establishment of a fast and precise identification approach. In a world undergoing persistent climate changes some genera of microorganisms like *Vibrio* or *Aspergillus* take advantage of warmer living conditions, which raise their infection incidence every year. Consequently, sequence-comparing methods like the 16S rRNA analysis have become standard tools for pathogen verification. However, the distinction of closely related organisms still remains challenging. To overcome such limitations we choose to work with another special target, which fulfills the crucial requirements of a ubiquitous and conserved single gene sequence making a whole genome predictable: The flexible loop sequence from CCA-adding enzymes. Compared to the 16S rRNA analysis sequencing studies revealed a seven to 30-fold higher distinction potential between three *Vibrio* and *Aspergillus* species. Taking benefit from this capability, we performed a multiplex PCR using color-labeled primers annealing to loop sections carrying characteristic and identifying point mutations. After separation applying agarose gel electrophoresis PCR products were detected in a Typhoon imager adjusting suitable laser-filter combinations. The data exhibit the absolute genome specificity of the designed primers even in PCRs with a 1000-fold excess of human genomic DNA. With these results, we are looking forward to test our new genotyping approach in different areas of application like clinical routine diagnostics or water/food hygiene controls extending our primer sets to further relevant pathogens.

➜ **Franz, Paul**
email: pfranz@uni-leipzig.de

POSTER 217

Genetic Incorporation of Photocrosslinking Amino Acids: Agonist and Antagonist Binding Patterns on a Class B GPCR

Molecular Biology/Protein Biochemistry

Seidel L[1], Coin I[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The site-specific incorporation of unnatural amino acids by expanding the genetic code is a powerful method to modify proteins directly in the live cell, with a broad field of applications in biochemical research. Orthogonal tRNA-synthetase pairs for more than 40 unnatural amino acids have been developed so far, which enable introducing chemical moieties with a variety of properties into proteins. Aim of this study is to compare the binding path of agonist and antagonist peptide ligands of the class B GPCR corticotropin-releasing factor receptor type 1 (CRF1R), in order to identify which ligand-receptor interactions lead to receptor activation. Amino acids throughout the juxtamembrane domain of CRF1R were systematically replaced with the photoactivatable amino acid p-azidophenylalanine. Upon UV irradiation, the generated reactive nitrene moiety forms a covalent bond with neighboring molecules, which reveals positions of the receptor coming into proximity of the bound ligand. CRF1R was screened for interactions with its natural 41mer agonist CRF and the N-terminally truncated derivative antagonist CRF(9–41). The data, which so far refer to the screening of about the half of the binding pocket, show that the binding path of CRF is consistent with existing conformational models for agonist binding to CRF1R. CRF(9–41) yields many crosslinking hits overlapping with those of the agonist, but also additional interaction sites, which suggest for the antagonist a deeper binding path into the CRF1R transmembrane domain.

→ **Seidel, Lisa**
email: lisa.seidel@uni-leipzig.de

POSTER 218

Capturing protein-protein interactions of NF-kB precursors via site specific photo-crosslinking

Molecular Biology/Protein Biochemistry

Serfling R[1], Coin I[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The site specific incorporation of photo-crosslinking unnatural amino acids (Uaas) into protein baits is emerging as a novel powerful tool to investigate protein-protein interactions directly in the live cell. Amino acids bearing photo-activatable moieties are incorporated into proteins at desired sites in response to an amber stop codon, by using orthogonal acyl-tRNA synthetase/tRNA pairs previously evolved to selectively recognize the crosslinking Uaa.
The NF-kB (nuclear factor-kB) transcription factor family is involved in fundamental cellular signaling pathways, including cell survival, proliferation, adhesion/invasion and immune response pathways, which are often dysregulated in carcinogenesis and tumor progression. It has been recently demonstrated that the NF-kB precursors p100 and p105 form a heteromeric complex. However, the topology and the stoichiometry of such complex are unknown, and also it cannot be excluded that third parties are involved in the complex. Aim of this project is to characterize the p100-p105 complex and explore possible interactions of NF-kB precursors with other proteins using site-specific photo-crosslinking. By incorporating crosslinking amino acids into one of the precursors intriguing crosslinking products were formed, which now have to be characterized. The poster describes preliminary crosslinking results and the methodological work aimed at achieving optimal expression of the protein bait containing the unnatural amino acid. This is a necessary step to produce and isolate the crosslinked product in sufficient amounts for mass spec analysis.

➜ **Serfling, Robert**
email: r.serfling@uni-leipzig.de

POSTER 219

Potential of hydroxylated (poly)-phenols to promote the hypothiocyanate production by lactoperoxidase

Molecular Biology/Protein Biochemistry

Gau J[1], Flemmig J[1,2], Arnhold J[1]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The immunological relevant heme peroxidase lactoperoxidase (LPO) contributes to the humoral immune defence against pathogens. LPO is primarily secreted into body fluids such as saliva or tear fluid. In the presence of hydrogen peroxide (H_2O_2) the enzyme is able to form hypothiocyanous acid (HOSCN) which acts bactericidal. The formation of HOSCN takes place in the halogenation cycle. In the peroxidase cycle compound II is formed, an enzymatic intermediate unable to oxidize thiocyanate. Substances like H_2O_2 or nitric oxide formed during inflammation processes are known to cause compound II accumulation. Dysregulations of the LPO activity are associated with the development of inflammatory diseases especially of the buccal cavity. Therefore we investigated the potential of several substances to reactivate the enzymatic activity after hydrogen peroxide induced compound II accumulation. Based on preliminary investigations with extracts and single components from *Olea europea* or *Leonorus cardiaca* we systematized the structural and chemical properties of (poly)-phenolic substances to find out potent enzyme regenerators. Hydroxylation in meta and para position is structurally essential for a potent regeneration of the $^{\cdot}$OSCN formation. Furthermore we could show a positive correlation between substrate hydrophobicity and affinity to LPO probably due to the hydrophobicity of the LPO binding pocket. Our results give some first structure–activity relationships important to further investigate enzyme regenerators in anti-inflammatory acting phytopharmaceuticals and provide new insights in the mode of action of herbal medicine.

➜ **Gau, Jana**
email: jana.gau@medizin.uni-leipzig.de

POSTER 220

Eukaryotic transient expression of recombinant in vitro transcribed rotavirus mRNA

Molecular Biology/Protein Biochemistry

Rückner A[1], Sieg M[1], Vahlenkamp T[1], Fabian C[2,3]

1 Institut für Virologie, Veterinärmedizinische Fakultät, Universität Leipzig
2 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig
3 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

To date, no helper virus-free reverse genetics system for rotaviruses, which are one of the major causes of gastroenteritis in infants, could be established. Such a system is urgently required for the analysis of the segmented double-stranded RNA genome. In many cases plasmid-based systems fail due to poor transfection efficiencies. mRNA-based systems are unsuccessful because of the low stability and complicated production of the capped but non-polyadenylated RNAs.Here we present a system for the expression of a recombinant rotavirus non-structural protein 5 intended for the analysis of transfection efficiency, mRNA stability and cellular protein localization. To this end, the red fluorescent protein gene was cloned within a variable region of the rotavirus gene and the mRNA was produced using *in vitro* transcription. Following lipofection the resulting fusion protein was already detectable ten hours post transfection using either flow cytometry or immunofluorescence assay. Depending on the presence of additional rotaviral proteins the recombinant protein has displayed varying cellular distributions: During rotavirus infection the recombinant protein tends to form the typical viroplasm-like structures, whereas a solitary transfection leads to the diffuse contribution within the cytoplasm.Furthermore, we established an siRNA-based system, which is suitable for the knockdown of the wild type gene (resulting in silencing efficiency up to 90 %), but is not interfering with the recombinant gene segment. Using this siRNA, the recombinant rotavirus mRNA is a powerful tool for the establishment of a reverse genetics system.

➜ **Rückner, Antje**
email: antje.rueckner@vetmed.uni-leipzig.de

POSTER 221

A single amino acid in natural occurring isoforms of the adhesion G protein-coupled receptor GPR114 confers constitutive activity

Molecular Biology/Protein Biochemistry

Wilde C[1], Schöneberg T[1], Liebscher I[1]
1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Adhesion G protein-coupled receptors (aGPCR) display the second largest class of G protein-coupled receptors. The physiological functions of various aGPCRs are already known, while the signal transduction and corresponding agonists remain to be elucidated. The aGPCR GPR114 is yet another orphan representative. There are two isoforms of the murine GPR114 which are solely distinguished through the amino acid glutamine downstream of the cleavage site in the GPCR proteolytic site (GPS) of the N terminus. These isoforms are due to alternative splicing since the glutamine occurs at the splice site in the beginning of exon 8 and is further encoded by the codon CAG representing an additional splice acceptor site. Here, we report the murine GPR114 is constitutively active in Gs protein/adenylylcyclase pathway. Both isoforms showed clear tissue specific expression leading to the assumption of tissue specific splicing and regulation of receptor activity. Further, the receptor can be activated through a tethered agonist previously described as *Stachel* sequence. However, both isoforms displayed different G protein-mediated cAMP levels. Interestingly, isoform 1 exhibit high constitutive activity due to the presence of the glutamine within the *Stachel* sequence, while isoform 2 shows significantly reduced basal activity. Mutational analysis at this position within the GPS in mice revealed a structural insight in activation of GPR114.

→ **Wilde, Caroline**
email: caroline.wilde@medizin.uni-leipzig.de

POSTER 222

Impact on the product profile of human 5-lipoxygenase after interaction with myeloperoxidase-derived oxidants

Molecular Biology/Protein Biochemistry

Zschaler J[1,2], Dorow J[3], Röthig L[2], Ceglarek U[3], Arnhold J[1,2]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
2 Institut für Medizinische Physik und Biophysik, Universität Leipzig
3 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In neutrophils the 5-lipoxygenase (5-LOX) oxidizes arachidonic acid to 5S-hydroperoxyeicosatetraenoic acid (5-HpETE) and leukotriene (LT)A4 which is further converted to the potent chemoattractant LTB4. These cells contain also the heme enzyme myeloperoxidase producing several potent oxidants such as hypochlorous acid (HOCl) and monochloramine (NH_2Cl) involved in pathogen defense. Here we addressed the following question: Do myeloperoxidase-derived oxidants affect the activity or product profile of 5-LOX?

For this task recombinant human 5-LOX was incubated with increasing amounts of HOCl or NH_2Cl. Afterwards arachidonic acid metabolites of 5-LOX were analyzed by C18-HPLC. The incubation of 5-LOX with HOCl or NH_2Cl resulted in a significant decrease of 5S-hydroxyeicosatetraenoic acid (5-HETE) and 6-trans-LTB4, the non-enzymatic hydrolysis product of LTA4. The 5-HpETE concentration was only slightly affected. Interestingly, new oxidation products were detected at the C12 and C15 position of arachidonic acid. Thus, the impact of metabolites synthesized by 5-LOX drastically changed after incubation with HOCl or NH_2Cl. These results were confirmed by LC-MS/MS measurements. Furthermore, the myeloperoxidase-hydrogen peroxide-chloride system caused a comparable modification of the product profile of 5-LOX.

In summary, myeloperoxidase-derived oxidants changed the product profile of 5-LOX. Apparently, this was due to a modification of critical amino acid residues of 5-LOX. Further work is necessary to assess the position of oxidation in 5-LOX and to specify whether this interaction takes also place in stimulated neutrophils.

➜ **Zschaler, Josefin**
email: josefin.zschaler@medizin.uni-leipzig.de

POSTER 223

Gaining insight into thiocyanate oxidation by myeloperoxidase

Molecular Biology/Protein Biochemistry

Schlorke D[1,2], Flemmig J[1,2], Furtmüller P[3], Obinger C[3], Arnold J[2]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
2 Institut für Medizinische Physik und Biophysik, Universität Leipzig
3 Department of Chemistry, Division of Biochemistry, University of Natural resources and Life Sciences, Vienna, Austria

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The mammalian immune system relies, inter alia, on the activity of haem peroxidases such as myeloperoxidase (MPO). Under physiological conditions. MPO utilizes Cl^- as well as SCN^- to form immunological potent oxidants (e.g. HOCl and HOSCN). While it is generally accepted that MPO is oxidised by H_2O_2 to compound I followed by regeneration of the ferric form during two-electron Cl^- oxidation, the reaction mechanism of SCN^- oxidation is still under discussion. Here, we carefully reinvestigate this mechanism of SCN^- oxidation by MPO.

Several publications state that SCN^- is oxidised one-electronically via a MPO compound I-to-compound II-conversion. However, by using stopped-flow spectroscopy, we were able to show an intermediate formation of ferric enzyme correlating with a two-electron oxidation mechanism. Thereby, the equilibrium between compound I and native enzyme was shifted towards the latter one with increasing SCN^- concentration. At low SCN^- concentrations, a transition to compound II followed while higher SCN^- concentrations led to a cyanide-like binding complex due to HOSCN decomposition products. Since SCN^- competes effectively with H_2O_2 for compound I, the observed compound II formation could neither be attributed to H_2O_2 nor to HOSCN or derived decay products.

Hence, it is discussed whether at low pseudohalide concentrations another, stronger SCN^- oxidation product might be formed by MPO that is able to convert native enzyme into compound II and that is inactivated by an excess of SCN^-. A second MPO-derived SCN^- oxidation product besides HOSCN may give new insights into the immunological role of this haem peroxidase.

➜ **Schlorke, Denise**
email: denise.schlorke@medizin.uni-leipzig.de

POSTER 224

Regulation of glucose homeostasis by G protein-coupled receptors in pancreatic α-cells

Röthe J[1], Schöneberg T[1], Thor D[1]
1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig

Molecular Biology/Protein Biochemistry

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

G protein-coupled receptors (GPCRs) are the largest group of cell surface receptors and are expressed in various tissues. GPCRs play a pivotal role in the regulation of glucose homeostasis. While the role of GPCRs in regulating pancreatic β-cell-function has been intensively investigated, their function in pancreatic α-cells is only poorly understood. However, besides their insulin deficiency type 2 diabetes mellitus (T2D) patients additionally have unphysiological high glucagon concentration in the blood. GPCRs might represent an interesting target to reduce glucagon secretion in T2D patients. Therefore, it is very important to characterize GPCRs involved in α-cell functions, such that therapeutic agents which normalize the glucagon concentration could be identified.
αTC1-9 cells which produce glucagon but no insulin were used as an *in vitro* model for pancreatic α-cells. To investigate the G protein signaling pathways and their impact in glucagon secretion, I took advantage of the RASSL (receptors solely activated by synthetic ligands) system.
The characterization of the RASSLs revealed that they are functionally expressed in αTC1-9 cells. So αTC1-9 cells are a suitable model to investigate pancreatic α-cell functions. Next, a set-up will be established which will allow for glucagon measurement using the AlphaLISA system. Thereto, different glucose concentrations will be used to trigger glucagon secretion. Finally, glucagon secretion will be monitored after stimulating the different G protein signaling pathways.

➜ **Röthe, Juliane**
email: juliane.roethe@medizin.uni-leipzig.de

POSTER 225

Characterization of armless mitochondrial tRNAs in Romanomermis culicivorax

Molecular Biology/Protein Biochemistry

Müller T[1,2], Betat H[1], Pütz J[2], Florentz C[2], Mörl M[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 Architecture et Réactivité de l'ARN, Université de Strasbourg, CNRS, IBMC, Strasbourg France

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Transfer RNAs (tRNAs) are important adapter molecules linking the genetic information of the messenger RNA (mRNA) into the primary amino acid sequence of a protein. In all kingdoms of life, these transcripts have a typical cloverleaf-like secondary structure in common, consisting of acceptor stem, D-arm, anticodon arm, variable loop and T-arm. The 3' terminus ends with the CCA sequence, which is post-transcriptionally added by a CCA-adding enzyme. The CCA-tail is an important prerequisite for the attachment of the correct amino acid by the aminoacyl synthetase. Mitochondrial tRNAs show a high derivation of this canonical tRNA structure with reduced D- or T-arms or even completely lack one of these elements. An extreme case of structural truncations is found in the mitochondria of Enoplea, resulting in transcripts of half the size of their cytosolic counterparts, representing the smallest tRNAs identified so far. It could already be shown that several of these miniaturized armless tRNAs are indeed functional in the nematode worm *Romanomermis culicivorax*. This situation raises several questions concerning the molecular mechanisms of co-evolution of tRNA and their partner proteins, ensuring the maintenance of a functional protein synthesis.
This study aims the biofunctional characterization of such "bizarre" tRNAs in defining their structural properties and studying different aspects of their functionality, especially their interaction with CCA-adding enzymes from different organisms. These data will indicate the minimum size as well as the structural properties required for a tRNA to be substrate for their interacting proteins.

➜ **Müller, Tina**
email: tina.mueller@uni-leipzig.de

POSTER 226

GPR133 – Single nucleotide polymorphisms change receptor function

Molecular Biology/Protein Biochemistry

Fischer L[1], Schöneberg T[1], Liebscher I[1]
1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

As a member of the adhesion GPCR, the GPR133 displays all characteristic hallmarks of this family including a large N-terminus with annotated functional domains being a pentraxin domain and the GPCR Autoproteolysis INducing domain/GPCR proteolytic site. Here, adhesion GPCR are autoproteolytically cleaved into two parts: an N-terminal (NTF) and a C-terminal fragment (CTF). Studies identified single nucleotide polymorphisms (SNP) within the non-coding region of the GPR133 locus. Genome wide associations are reported for human height, with very low density lipoproteins and influences RR duration increasing heart rate. Analysis in the 1000Genomes and exome sequencing projects revealed over 4,800 SNP in the human GPR133 gene. Out of those, only 4.7% SNP are located in coding regions leading to 112 amino acid changes on 104 positions. 52.7% of those are located in functional domains. Taking advantage of the previously found basal activity in cAMP-dependent pathway, we functionally analyzed all amino acid changing SNP in human GPR133. Indeed, we could show that there are natural occurring variants changing receptor function. 12.5% of them display constitutive activity in cAMP responsive element while 11.6% strongly reduce signaling function. One SNP leads to a premature stop after the first transmembrane region which underlines the idea of an autonomous function of the NTF. Surprisingly, a functional spectrum from natural occurring missense SNP from 50% to 200% of GPR133 activity seems to be accepted in nature, while GPR133 itself is highly conserved. That points towards a non-lethal phenotype in knock-out organisms.

Funding: ifb

→ **Fischer, Liane**
email: liane.fischer@medizin.uni-leipzig.de

POSTER 227

Functional Characterization of SDF-1α GAG Binding Variants

Molecular Biology/Protein Biochemistry

Panitz N[1], Baumann L[1,2], Theisgen S[3], Huster D[3], Beck-Sickinger AG[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 Department of Chemistry, University of British Columbia, Canada
3 Institut für Medizinische Physik und Biophysik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The stromal cell-derived factor 1α (SDF-1) belongs to the CXC chemokines and interacts with its CXC-receptor 4 and 7. It plays an important role in recruitment of tissue specific stem cells. Therefore the SDF-1 is an interesting target for the regeneration of damaged tissue. The aim of this study is to generate a stable, long-term chemotactic gradient by using immobilized SDF-1, which leads to the recruitment of stem cells and therefore to the regeneration of the affected tissue. The present work focusses on the characterization of SDF-1 variants with different GAG binding properties to recruit different cell types that express the CXCR4.

^{1}H-^{15}N-HSQC NMR with ^{15}N-labeled SDF-1 was used to provide an overview on the interaction of SDF-1 with different types of GAGs. This led to the hypothesis, that the sulfation of the GAG may play an important role for the interaction with the protein.

Based on the NMR-measurements single amino acids were exchanged by mutations. The migration assay demonstrated that the single mutation does not influence the ability of the SDF-1 to recruit specific cells.

To identify the influence in signaling pathways, IP_3 assays were performed. For all receptor variants a similar effect in signaling strength could be detected compared to SDF-1.

Additional knowledge on the specific interaction of SDF-1 with different GAGs could be achieved and the influence of the GAG binding site of the interaction of the SDF-1 with its CXCR4 could be determined in more detail. Future experiments will give further information, which can be used to generate SDF-1 variants to form a long-term chemotactic gradient.

➜ **Panitz, Nydia**
email: nydia.panitz@uni-leipzig.de

POSTER 228

NMR investigations of the Y2 receptor: Providing selectively labelled receptor using cell-free expression

Molecular Biology/Protein Biochemistry

Vogel K[1], Müller P[1], Bernhard F[2], Schmidt P[1]

1 Institut für Medizinische Physik und Biophysik, Universität Leipzig
2 Institut für Biophysikalische Chemie, Universität Frankfurt a.M.

The Y receptors, a family of class A G protein-coupled receptors (GPCRs), are well known to be involved in numerous physiological processes (e.g. memory retention, food intake, energy homeostasis). In spite of their clinical relevance little is known about the structural basis of their highly divers functions. Here, we report the establishment of a cell-free expression system for human neuropeptide Y receptor type 2 (Y2R), which can provide specifically labelled receptor in low milligram quantities for NMR experiments. So far, up to 600 μg/mL non-labelled Y2R have been expressed, purified and reconstituted in DHPC/DMPC bicelles (q = 0.25). Expression yields were increased by an N-terminal Ser-tag (MKSSSSSG). It was shown by ligand binding assays as well as in G protein activation experiments that the reconstituted Y2R is functional. Furthermore, up to 470 mg/mL [^{15}N-Trp]-Y2R have been expressed and will be used in NMR studies for further characterization in terms of its structure and even dynamics. Because the cell free expression allows for selective incorporation of isotope labelled amino acids the resulting NMR spectra are less complex in comparison to the fingerprints of uniformly labelled receptor samples. It is therefore possible to investigate specific receptor sites.

➜ **Vogel, Kristina**
email: kristina.witte@medizin.uni-leipzig.de

POSTER 229

Long non-coding RNAs in multiple myeloma

Molecular Biology/Protein Biochemistry

Riedel D[1], Horn F[2]

1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig
2 Institut für Klinische Immunologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Since the beginning of genetic research, two paradoxes in molecular biology have become more and more evident. Concerning the complexity of eukaryotic organisms neither their DNA-content, nor the number of their protein-coding genes correlate to the increase in cognition and intricacy. In recent years, the focus of research changed from protein-coding to non-coding RNAs, as transcriptome studies revealed almost the whole genome is transcribed. In the past referred to as junk, these non-coding RNAs have since become a possible answer to the D- and G-paradoxes. Though many transcripts have been functionally analyzed, the role of the majority of these ncRNAs remains still elusive. Based on a genome-wide tiling array study, we found several long ncRNAs to be differentially expressed upon cytokine stimulation in multiple myeloma cells. As STAT3 is essential for the survival of these cells, the found RNAs are called STAIRs (STAT3 induced ncRNAs). ChIRP- and Capture-Seq approaches give information about characteristics of the lncRNA itself as well as interacting transcripts. Here we show the results of these ChIRP and Capture approaches of some STAiRs with distinct functions.

➜ **Riedel, Diana**
email: diana.riedel@medizin.uni-leipzig.de

POSTER 230

The role of the tRNA acceptor stem in binding the CCA-adding enzyme

Götze O[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig

Molecular Biology/Protein Biochemistry

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In the fundamental biological process of protein translation, tRNA plays a crucial role as translator of genetic code into amino acid sequence. Each tRNA is specifically charged with its corresponding amino acid. The position of aminoacylation is the CCA triplet found at the 3'-end of every tRNA. In most organisms, this triplet is not genetically encoded and has to be added by a highly specific nucleotidyl transferase, the CCA-adding enzyme. In general, this CCA-adding enzyme recognizes the tRNA in its cloverleaf-like structure, but addition of CCA to other RNA substrates has also been shown. Moderate structural constraints for the RNA substrate could be expected, since CCA-adding enzymes have to recognize mitochondrial tRNAs as well, which frequently show structural deviations and may lack one or even both arms of the cloverleaf structure. We want to understand the precise structural requirements for an RNA to be accepted as a substrate for CCA-addition. Using a randomized RNA pool of 36 nucleotides in length, combined with high-throughput sequencing, we found that many of these simple RNA-oligonucleotides are indeed substrates for the CCA-adding enzyme. On many of these candidates, even poly-CCA addition was detected. Since it has been shown *in vivo* that the addition of such CCACCA repeats to tRNA can function as a tag for subsequent decay of the transcript, we want to investigate the substrate features that lead to poly-CCA-addition.Subtypes of CCA-adding enzymes are using different mechanisms for CCA-addition, which makes it interesting to investigate the different structural substrate requirements for these enzymes.

→ **Götze, Oskar**
email: oskar.goetze@web.de

POSTER 231

Melanin-concentrating hormone (MCH) in major depressive disorder during antidepressant therapy

Neurobiology

Nowak C[1], Schmidt F[1], Kratzsch J[2], Sander C[1], Hegerl U[1], Schönknecht P[1]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: In preclinical studies, the hypothalamic polypeptide melanin-concentrating hormone (MCH) has been shown to be involved in depression-like behavior and modulations of MCH and MCH-receptors were proposed as potential new antidepressant drug targets.
Methods: For the first time, MCH serum levels were explored in 30 patients with major depressive disorder (MDD) prior to (T1) and after 2 (T2) and 4 weeks (T3) of antidepressant treatment and in 30 age- and sex-matched healthy controls by applying a fluorescence immunoassay.
Results: Levels of MCH did not differ significantly between unmedicated patients (444.11 ± 174.63 pg/mL SD) and controls (450.68 ± 210.03 pg/mL SD). In MDD patients, MCH levels significantly decreased from T1 to T3 ($F = 4.663$; $p = 0.013$). Post-hoc analyses showed that these changes were limited to patients treated with mirtazapine but not escitalopram and female but not male patients. MCH-levels showed high correlations from T1 to T3 ($r \geq 0.964$, $p < 0.000001$) and were found to correlate significantly with parameters of sleep within the controls.
Limitations: Small sample size. No follow-up measures were performed within the control group.
Conclusions: Our findings suggest peripheral MCH-levels not to be altered in depression but possibly reflecting depression-related state properties that can be modulated by sleep, medication and sex.

➜ **Nowak, Claudia**
email: claudia.nowak@medizin.uni-leipzig.de

POSTER 232

The extracellular matrix restricts spreading and internalization of aggregated Tau-protein

Neurobiology

Suttkus A[1]

1 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Each type of pathology in the central nervous system follows a specific spatio-temporal pattern. In Alzheimer´s disease (AD) the progression of amyloid deposits, made of A?-(amyloid) peptide and aggregated Tau-protein, causing neurofibrillary degeneration even provides the basis of a scoring system, now widely accepted for neuropathological staging. Previously, we could demonstrate that in AD cortical and subcortical neurons are less frequently affected by neurofibrillary degeneration if they are enwrapped by a specialized form of the hyaluronan-based extracellular matrix (ECM), the so called 'perineuronal net' (PN). PNs are composed of large aggregating chondroitin sulphate proteoglycans connected to a hyaluronan backbone, stabilized by link proteins and cross-linked via tenascin-R. Under experimental conditions in mice, PN-associated neurons are better protected against iron-induced neurodegeneration compared to neurons without PN, indicating a neuroprotective function. Here, we want to investigate a role of PN in spreading and uptake of exogenous tau-protein by using organotypic slice cultures of wt mice as well as mice lacking the ECM-components aggrecan, HAPLN1 or tenascin-R. After applying tau-protein, a restrictive role of PN regarding distribution and internalization was observed. In Wt mice, tau spreading was limited by PN-rich layers. Furthermore, PN-ensheathed neurons were less frequently affected by Tau-uptake, than neurons without PN. The analogue experimental approach using culture tissue from mice deficient for different ECM-components revealed a contribution of these constituents to this action of the PN.

➜ **Suttkus, Anne**
email: anne.suttkus@medizin.uni-leipzig.de

POSTER 233

NMDA receptors enable processing of high-frequency inputs at mature cerebellar granule cells

Neurobiology

Baade C[1], Byczkowicz N[1], Hallermann S[1]
1 Carl-Ludwig-Institut für Physiologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The capability to integrate and transmit signals at high frequencies is a distinct feature of many neurons and is import for rapid information processing. It has been shown *in vivo* and *in vitro* that cerebellar mossy fiber axons (MFs) can fire action potentials (APs) at frequencies of more than one kilohertz. However, it is unclear whether and how the postsynaptic cerebellar granule cell (GC) is able to process these high-frequency inputs. Here, we address these questions by combining whole-cell patch clamp recordings of GCs and single MF high-frequency stimulation. Measuring AP firing in the current-clamp mode during high-frequency MF stimulation revealed that CGs could integrate MF inputs in a non-linear fashion. In order to investigate the contribution of N-methyl-D-aspartate receptors (NMDARs) on GC firing, we applied D-2-Amino-5-phosphonopentanoic acid (APV), a potent inhibitor of NMDARs. APV significantly impaired integration of high-frequency trains but had no effect on GC excitability. In voltage-clamp, APV did not affect time course and amplitude of single evoked excitatory postsynaptic currents (EPSCs), but reduced summation of EPSCs after high-frequency stimulation. Thus, our results show that currents mediated by NMDARs play an essential role in GC processing by amplifying high-frequency MF inputs.

→ **Byczkowicz, Niklas**
email: niklas.byczkowicz@medizin.uni-leipzig.de

POSTER 234

LEGASCREEN – Progress in the development of early dyslexia diagnostics

Neurobiology

Wilcke A[1]

1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Dyslexia, a severe disorder in the acquisition of reading and writing, is one of the most common developmental disorders, affecting 4–5% of all school children. Effective therapies/trainings exist in form of special classes for dyslexic children. However, the possibility to identify affected children at an early stage of speech development, when specialised training is the most promising, is still lacking. In the case of an appropriate therapy at an early stage, the child's brain could unfold its self-healing potential, leading to diminished problems at school or to no problems at all. The project´s final aim is the development of an early screening test for dyslexia, based on genetics and EEG.

Dyslexia has a strong genetic background. 50–70% of this disorder can be explained by genetics. Furthermore it is known that dyslexics show characteristically changed EEG-signatures. These signatures represent a certain EEG response named mismatch negativity (MMN).

Within the LEGASCREEN projects, these two approaches should be combined to enable an early and reliable diagnostic: genetics and EEG.

A third component of the project, not being part of the final test, will be MRI measurement to study white matter differences between dyslexics and normal reading children. MRI measurement will serve as a link between genetics and EEG.

First genetic results indicate a role of specific markers on chromosome 18, while markers on chromosome 12 are correlated with structural integrity of the Fasciculus arcuatus, a fiber tract important in language. Further preliminary EEG-results show different patterns between dyslexics and controls using MMN.

➜ **Wilcke, Arndt**
email: arndt.wilcke@izi.fraunhofer.de

POSTER 235

Elevated levels of cerebrospinal fluid neuron-specific enolase (NSE), but not S100B, in major depressive disorder.

Neurobiology

Schmidt F[1], Mergl R[1], Stach B[2], Jahn I[1], Schönknecht P[1]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objectives: Alterations in neuronal and glial integrity are considered to be of pathogenic impact on major depressive disorder (MDD). For MDD, data on cerebrospinal fluid (CSF) levels of neuron-specific enolase (NSE) are lacking and scarce for glial protein S100B.
Methods: We measured CSF-levels of NSE and S100B in 31 patients with MDD and 32 mentally healthy controls using electrochemiluminescence immunoassays (*ECLIA*).
Results: Adjusted means of NSE were significantly elevated in the MDD patients (11.73 ng/mL (9.95 – 13.52 95% CI) compared to the controls (6.17 ng/mL (4.55 – 7.78), F = 9.037, p = 0.004. Effect size for adjusted mean group difference of 5.57 ng/mL was found invariably high (Cohens d: 1.23). Differentiating MDD from controls, a NSE cut-off of 7.94 ng/mL showed sensitivity of 81% (95% CI 63.7 – 90.8) and specificity of 75% (95% CI 57.9 – 86.7). Adjusted levels of S100B did not differ significantly between the two groups (1.12 ng/mL (0.77 – 1.48) in MDD, 0.97 ng/mL (0.64 – 1.30) in controls).
Conclusions: Our results of elevated CSF-NSE-levels support neuronal pathology in MDD and the potential use of CSF-NSE as marker in clinical diagnostics. Missing group differences in S100B do not promote a specific glial pathology in depressive disorders.

Schmidt FM, Mergl R, Stach B, Jahn I, Schönknecht P. Elevated levels of cerebrospinal fluid neuron-specific enolase (NSE), but not S100B in major depressive disorder. World J Biol Psychiatry. 2014 Sep 29:1–8. [Epub ahead of print]

➜ **Schmidt, Frank**
email: frank.schmidt2@medizin.uni-leipzig.de

POSTER 236 **Variations in cervical vagus nerve anatomy – pitfalls in vagus nerve stimulation?**

Neurobiology

Planitzer U[1,2], Hammer N[2], Glaetzner J[1], Meixensberger J[1], Bechmann I[2], Winkler D[1]

1 Klinik und Poliklinik für Neurochirurgie, Universität Leipzig
2 Institut für Anatomie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Vagus nerve stimulation (VNS) is increasingly applied to treat epilepsy, psychiatric conditions and chronic heart failure. After implanting electrodes to the cervical vagus nerve (CVN), side effects or missing therapeutic effects are observed at different frequencies. CVN branching might partly be responsible for these effects. However, vagus nerve anatomy and CVN branching have not yet been described in the context of VNS.
Materials and Methods: In 35 body donors the CVN anatomy was investigated macroscopically with focus on the location in the carotid sheath and on nerve branching. After X-ray imaging for determining the vertebral levels of occurring CVN branching, samples were removed to histologically prove the nerve and to calculate CVN diameters and cross-sections.
Results: For the position of the CVN in the carotid sheath 18 different combinations were observed. CVN branching was detected in 29 % and proven histologically. Right- sided branching was more common than left-sided branching and occurred on the level of the fourth and fifth vertebra on the left and on the level of the second to fifth vertebra on the right side. CVN without branching were significantly larger than CVN with branches, concerning their diameters (4.79 mm vs. 3.78 mm) and cross-sections (7.24 mm2 vs. 5.28 mm2).
Conclusion: This study gives new insights into CVN anatomy, proving that anatomical variations and branching are more common than described previously. This knowledge should be taken into account when identifying main trunk of the CVN for implanting VNS to minimize potential side effects or lacking therapeutic benefits.

➜ **Planitzer, Uwe**
email: uwe.planitzer@medizin.uni-leipzig.de

POSTER 237

Microglia as radio-resistant macrophages independent from their local environment

Neurobiology

Menzel F[1], Immig K[1], Merz F[1], Bechmann I[1]
1 Institut für Anatomie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Microglia are regarded as the brain's immune cells, but they differ from other mononuclear populations by their origin from the yolk sac, their long-term survival, and capability of self-renewal by local proliferation. An additional fundamental difference is their high radio-resistance which provides the basis for work with bone-marrow chimeras dissecting functions of microglia and de novo recruited blood-derived monocytes. We wanted to test whether microglia are radio-resistant even as single cells without the brain microenvironment which would imply intrinsic anti-apoptotic or repair-related mechanisms independent on the local environment. Therefore we isolated brain monocytes and monocytes from spleen as an example for a lymphoid organ. These acutely isolated monocytes from spleen and brain were irradiated with 30 Gy and sorted for the leukocyte marker CD45 by FACS. To detect apoptosis, PI (as cell death marker) and Annexin V (as an early apoptotic marker) were used. We found that splenocytes (CD45high) and brain macrophages (CD45high) die within 4h after irradiation whereas microglia (CD45int) are radio-resistant. Furthermore, we investigated the expression pattern of 7 DNA-repair related and of 84 apoptosis-relevant genes 4h after irradiation to identify prominent apoptosis genes which seem to be most important for the radioresistance of microglia. In addition to DNA-repair related genes we also found several pro- and anti-apoptotic genes which are not only significantly but also contrarily regulated in microglia and splenocytes 4h after x-irradiation.

Funded by DFG FOR 1336.

→ **Menzel, Franziska**
email: franziska.menzel@medizin.uni-leipzig.de

POSTER 238

Investigations on the relationship between nervous system immune imbalances and age and hypertension-related cognitive decline.

Neurobiology

Didwischus N[1,2], Wagner DC[2,3]

1 Institut für Biologie, Universität Leipzig
2 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig
3 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Current data indicate a strong immunological impact during hypertension. There are evidences, that a non-functional adaptive immune system prevents hypertension in RAG -/- mice. Likewise, the impact of the immune system on cognitive function can be seen in *scid* mice, which show a worse performance in spatial learning and memory tasks compared to wild type mice. The cognitive performance of these *scid* mice was improved by transplantation of CD4+ T Cells. In this study we want to investigate if the CNS immune homeostasis is altered during hypertension and if these changes can lead to cognitive decline. First results of RT-qPCR of SHR and WKY show a preliminary trend in down regulation of the learning and memory associated factors BDNF and Arc-1 in the hippocampus of SHR. Furthermore there is an observable trend in up regulation of adhesion molecules such as ICAM-1 and VCAM-1 in the choroidal tissue of SHR, which could support immune cell invasion from the periphery into the CNS through the choroid plexus, which serves as the gate for immune cells into the CNS. In previous studies our group showed a decrease of anti-inflammatory IL-10 in the cerebrospinal fluid of SHR compared to normotensive WKY. We also observed significantly decreased absolute T cell counts in SHRs. In further studies the immune cell distribution in the periphery and the CNS of spontaneously hypertensive mice (BPH/2) and their controls will be flow cytometrically analyzed.
Hypertension might have an immunological effect on cognitive function. We want to investigate the underlying mechanisms for a better understanding and possibly better treatment.

➜ **Didwischus, Nadine**
email: nadine.didwischus@izi.fraunhofer.de

POSTER 239

Lentiviral-mediated gene transfer to slow down progressive neurodegeneration

Neurobiology

Glöckner P[1], Uney J[1], Ueberham U[1], Arendt T[1]
1 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

In Alzheimer's disease (AD) as well as in other neurodegenerative disorders neurons show an enhanced expression of cell cycle proteins (cyclin dependent kinases cdks, cyclins and cdk inhibitors cdkis), that leads to the hypothesis that differentiated neurons re-enter the cell cycle. Previously, neuronal cell cycle activation driven by oligomers of amyloid ß, has been identified as one of the events critically involved in initiating neuronal cell death. Accordingly, under experimental conditions the activation of the cyclin cdk4/6-complex, the critical guard of the G0-G1 transition, is known to induce apoptosis. Here we examine gene therapeutic tools in transgenic mice models of neurodegeneration to specifically target activity of cdk4 and cdk6. Down regulation of cdk activity will be achieved through ectopic expression of p16INK4a and related cdk inhibitors. Lentiviral vectors are the tools of choice for gene delivery into the central nervous system. Our new therapeutic strategy uses non-integrating lentiviral vectors, which can regulably express physiological cell cycle inhibitors.We generated a pool of lentiviral vectors containing cdki cDNAs under control of different promoters and established reliable methods for production and purification of these viral particles. We infected primary neurons (mouse), derived neuronal and non neuronal cells (human, mouse) with the virus. Subsequently, we started *in vivo* experiments with different mouse lines. We injected the virus by stereotactical surgery in different brain regions and analysed viral expression patterns and biodistributation by immunofluorescent staining.

→ **Glöckner, Pia**
email: pia.gloeckner@medizin.uni-leipzig.de

POSTER 240

EEG-Neurofeedback bei Idiopathischem Parkinson-Syndrom

Neurobiology

Röthing S[1]

1 Klinik für Neurologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

EEG-Neurofeedback ist eine Form der operanten Konditionierung, bei der mithilfe eines Feedbacks (z. B. optische oder akustische Signale) gezielt biologische Parameter – in diesem Fall bestimmte EEG-Frequenzbänder – trainiert werden können. Es ist bereits bei einigen Krankheitsbildern wie Epilepsie, AD(H)S und Migräne in der Praxis etabliert und soll im Rahmen unserer Studie nun erstmals bei Patienten mit Idiopathischem Parkinson-Syndrom (IPS) verwendet werden mit dem Versuch, gezielt ihre kognitive Leistungsfähigkeit (wieder) zu verbessern. Bei vergleichsweise wenigen Trainingssitzungen konnten wir bereits feststellen, dass es eine z. T. erhebliche Verbesserung von Konzentration und Aufmerksamkeit, resultierend in besseren Testergebnissen, bei den Patienten gab, wohingegen gesunde Probanden gleichen Alters nicht ganz so starke Verbesserungstendenzen zeigten. Dies zeigt zum einen, dass unser Feedback-Training bei IPS-Patienten durchaus erfolgsversprechend ist, zum anderen legt es die Vermutung nahe, dass bereits eingebüßte kognitive Fähigkeiten der Patienten noch nicht unwiederbringlich verloren sein müssen.

➜ **Röthing, Sophia**
email: sophia.roething@gmail.com

POSTER 241

Effects of brevican deficiency onto molecules mediating neuronal plasticity

Neurobiology

Weigel S[1], Meißner J[1], Arendt T[1], Roßner S[1], Morawski M[1]

1 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Chondroitin sulfate proteoglycans (CSPG) are main components of the extracellular matrix (ECM) of the nervous system consisting of a core protein and a specific number of glycosaminoglycan side chains. The latter causes the polyanionic character of the ECM which exerts influence on processes like axonal guidance and regeneration. Accessorily CSPG are involved in neuronal plasticity, cell adhesion, receptor binding and are therefore considered to play a role in neural development and several neurological and psychiatric disorders. One member of the CSPG family is brevican which was already shown to be very closely located to the active zone of synapses. In addition, brevican deficiency was reported to cause lateral receptor diffusion, reduced LTP and recruitment of local plasticity. In this study we therefore focused on the impact of brevican onto the neuronal cell adhesion molecule NCAM and PSA-NCAM involved in neural plasticity and memory formation, as well as the prolylendopeptidase PREP, the matrix metallo proteinase 9 (MMP) and tissue inhibitors of MMPs (TIMP). Immunohistochemical and western blot analyses of hippocampus tissue of brevican knockout mice and wild type littermates revealed no changes of MMP9, PREP, NCAM nor PSA-NCAM, but a significant reduction of TIMP1 and 3 in brevican deficient mice. Consequently, effects of brevican deficiency onto LTP in hippocampus and local plasticity may not be mediated by a modulation of NCAM and PSA-NCAM, but may be caused by alterations of the activity of matrix cleaving enzymes.

→ **Weigel, Solveig**
email: solveig.weigel@medizin.uni-leipzig.de

POSTER 242

Partial reversal of radiation-induced decline of neural progenitor cells by resveratol

Neurobiology

Prager I[1], Kaatzsch P[1], Himmelbach K[1], Patties I[1], Oppermann H[2], Merz F[3], Kortmann R[1], Glasow A[1]

1 Klinik und Poliklinik für Strahlentherapie, Universität Leipzig
2 Klinik und Poliklinik für Neurochirurgie, Universität Leipzig
3 Institut für Anatomie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Radiation therapy plays an essential role in the treatment of primary or metastatic CNS malignancies, but radiation-induced adverse effects remain a significant risk. Radiation-induced damage of the neural stem cell pool in the hippocampus is thought to be one of the major reasons for the long-term decline in neurocognitive performance, especially in pediatric patients. Here, we investigate the short- and long-term dose-response relationship of neurogenesis, covering a dose range relevant for whole and partial brain irradiation. Furthermore, we evaluate the radioprotective potential of resveratrol, a plant polyphenol, which is newly recognized for its bifunctional tumor-preventive and anti-cancer effects.

A dose-dependent decline of nestin-positive neural stem cells together with a decrease of proliferation could be detected already at low doses of 0.2 Gy two days after IR. A partial recovery of the stem cell pool was found at late time points (14 and 42 days after IR). PI staining showed a dose-dependent increase of dead cells, reaching significance at 12 Gy. Resveratrol was able to enhance the cell viability significantly in irradiated slices 3 and 9 days after irradiation (4.5 and 8 Gy). Il6, KC and MCP1 release increased 4 and 24 h after IR at 1.5 Gy (Il6) and 3 Gy (KC, MCP1).

Relatively low IR doses lead to a decrease of nestin-positive stem cells. Our data indicate that this is a result of increased cell death and decreased proliferation but might also be triggered by an increase of inflammation. The neuroprotective action of resveratrol on irradiated hippocampal tissue warrants further investigation.

➜ **Glasow, Annegret**
email: annegret.glasow@medizin.uni-leipzig.de

POSTER 243 **Genetic modulators of dyslexia related MMR**

Neurobiology

Müller B[1], Wilcke A[1,2], Schaadt G[3], Boltze J[1,2], Kirsten H[1,2,4]

1 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
3 HU Berlin
4 Institut für Medizinische Informatik, Statistik und Epidemiologie (IMISE), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Dyslexia is a learning disorder which affects the ability to read and write with a prevalence of ~5% and a strong genetic component with a heritability of 50–70%. The impairment may result from a deficit in the phonological component of language processing. Auditory discrimination is an important prerequisite for phonological language processing and, thus, important for the ability of learning to read. This capability can be measured by electroencephalography (EEG) and quantified as mismatch reaction (MMR). It is well known that dyslexics show an altered MMR in response to auditory input.
In this project, we analyzed the association of dyslexia-specific MMR with dyslexia-realted genetic variants.
Methods: The MMR of 53 controls and 14 dyslexics with a mean age of 9.6 years was measured with a passive oddball paradigm and were genotyped for 133 SNPs which are known to associate with dyslexia-related phenotypes. We compared the prediction power of each MMR among different electrodes. Subsequently, we used the most predictive MMRs for a genetic association analysis in a multifactorial regression model.
Results & Discussion: We identified the MMRs of the frontal electrodes as the most predictive ones. With these MMRs, we identified 13 dyslexia-related SNPs with potential relevance for MMR. This approach investigates the triangular relationship between dyslexia status, genetics and MMR. It emphasizes the potential of MMR as an endophenotype in the investigation of how specific genetic variants are related to dyslexia thereby contributing to the understanding of the pathomechanisms underlying this disorder.

➜ **Müller, Bent**
email: bent.mueller@izi.fraunhofer.de

POSTER 244 **Frequency dispersion in the cerebellar cortex**

Neurobiology

Straub I[1], Hoidis M[1], Delvendahl I[1], Bechmann I[2], Krüger M[2], Hallermann S[1]

1 Carl-Ludwig-Institut für Physiologie, Universität Leipzig
2 Institut für Anatomie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

To control timing of motor function, the cerebellar cortex receives broad-bandwidth neuronal signals with up to kilohertz frequencies from mossy fibers. However, it is unclear if the postsynaptic granule cells (GCs) are tuned to specific frequencies and whether such frequency dispersion is topographically organized. Here, we combined structural and functional analyses to investigate frequency tuning of GCs. We found that GCs near white matter (inner-zone GCs) are functionally different from GCs near Purkinje cells (outer-zone GCs). Inner-zone GCs fired action potentials with higher current-threshold, shorter half-duration, and higher frequency during current injection. Consistent with these functional differences, we recorded larger voltage-depended potassium currents from inner-zone GCs. Structurally, inner-zone GCs tend to give rise to parallel fibers located close to Purkinje cell somata (inner-zone parallel fibers). The diameter of these inner-zone parallel fibers was larger compared with outer-zone parallel fibers. These data suggest that the broad-bandwidth input signal from a single mossy fiber is distributed to hundreds of postsynaptic GCs in a frequency dependent manner. Furthermore, the diameter and location of GC axons are tuned to optimally convey a preferred frequency to Purkinje cells. Thus, we demonstrate frequency dispersion within the cerebellar cortex, which provides a new concept for cerebellar information processing.

➜ **Byczkowicz, Niklas**
email: niklas.byczkowicz@medizin.uni-leipzig.de

POSTER 245

The Glutaminylcyclases are differentially expressed in brain regions affected in Alzheimer´s disease

Neurobiology

Höfling C[1], Waniek A[1], Morawski M[1], Cynis H[2], Schilling S[2], Demuth H[2], Roßner S[1], Hartlage-Rübsamen M[1]

1 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig
2 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Glutaminyl cyclases (QCs) catalyze the physiological formation of pyroglutamate (pGlu) from glutamine precursors at the N-terminus of a number of peptide hormones, neuropeptides and chemokines. However, QCs are also implicated in the pGlu modification and stabilization of pathogenic Abeta variants and of pro-inflammatory CCL2. For the generation of respective animal models and for pharmacological treatment studies the characterization of the mouse strain and brain region-specific expression of QC and isoQC is indispensible.

We used enzymatic activity assays and specific antibodies to detect both QC and isoQC variants by immunohistochemistry in nine different mouse strains.

The highest enzymatic QC/isoQC activity was detected in ventral brain, followed by cortex and hippocampus. Immunohistochemical stainings revealed that QC/isoQC activity in cortex mostly arises from isoQC expression. For most brain regions, the highest QC/isoQC activity was detected in C3H and FVB mice, whereas low QC/isoQC activity was present in CD1, SJL and C57 mice. Quantification of QC- and isoQC-immunoreactive cells by unbiased stereology revealed a higher abundance of isoQC- than of QC-immunoreactive neurons in Edinger-Westphal nucleus and in substantia nigra. In the locus coeruleus, however, there were comparable densities of QC- and of isoQC-immunoreactive neurons.

These observations are of considerable importance with regard to the selection of appropriate mouse strains for the study of QC/isoQC relevance in mouse models of neurodegeneration and neuroinflammation and for the testing of therapeutical interventions in these models.

➜ **Höfling, Corinna**
email: hoefling@medizin.uni-leipzig.de

POSTER 246

Identification of thyrotropin-releasing hormone as hippocampal glutaminyl cyclase substrate in neurons and reactive astrocytes

Neurobiology

Waniek A[1], Hartlage-Rübsamen M[1], Höfling C[1], Kehlen A[2], Schilling S[3], Demuth H[3], Roßner S[1]

1 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig
2 Institute for Medical Microbiology, Martin-Luther-University Halle-Wittenberg, Germany
3 Fraunhofer Institute of Cell Therapy and Immunology IZI Leipzig, Department of Drug Design and Target Validation MWT Halle, Germany

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objectives: Aβ variants with an N-terminal truncation and pyroglutamate modification were shown to be highly neurotoxic and prone to aggregation. This modification of Aβ is catalyzed by glutaminyl cyclase (QC) and inhibition of QC diminishes Aβ deposition and gliosis in transgenic mouse models of Alzheimer's disease (AD). QC expression was initially described in hypothalamus, where thyrotropin-releasing hormone (TRH) is a physiological substrate. Recently, a function of TRH following excitotoxicity and Aβ-mediated neurotoxicity has been reported in the hippocampus. Functionally matching this finding, we recently demonstrated QC expression by interneurons of mouse hippocampus.
Methods: We used brain tissue of Tg2576 mice and primary astrocytes for qPCR and immunohistochemistry to reveal brain region and cell type-specific expression of QC and TRH.
Results: We detected neuronal co-expression of QC and TRH in the hippocampus of adult wild type mice. In neocortex of aged but not of young mice transgenic for amyloid precursor protein an increase of QC mRNA levels was found compared to wild type littermates. This was not observed in hippocampus, which is later affected by Aβ pathology. However, in hippocampus of transgenic mice a correlation between QC and TRH mRNA levels was revealed. Interestingly, the enzyme QC and its substrate TRH were detected in reactive astrocytes in proximity of Aβ deposits.
Conclusions: Functionally, the expression of QC in astrocytes could play a role in neuroprotection by the activation and release of TRH, thereby reducing excitotoxicity and in neurodegeneration due to the formation of pGlu-Aβ.

→ **Waniek, Alexander**
email: alexander.waniek@medizin.uni-leipzig.de

POSTER 247

Impact of lithium alone and in combination with antidepressants

Neurobiology

Petersein C[1], Sack U[2], Mergl R[3], Schönherr J[1], Schmidt F[1], Lichtblau N[1], Bauer K[2], Himmerich H[1]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 Institut für Klinische Immunologie, Universität Leipzig
3 Klinik für Psychiatrie, Psychotherapie und Psychosomatik des Kindes/Jugendalters, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Lithium is an important psychopharmacological agent for the treatment of unipolar as well as bipolar affective disorders. Lithium has a number of side effects such as hypothyroidism and aggravation of psoriasis. On the other hand, Lithium has pro-inflammatory effects, which appear beneficial in some disorders associated with immunological deficits, such as human immunodeficiency virus (HIV) infection and systemic lupus erythematosus (SLE).
We measured the levels of the cytokines interleukin (IL)-1ß, IL-2, IL-4, IL-6, IL-22, IL-17 and tumour necrosis factor (TNF)-α in the stimulated blood of thirty healthy subjects supplemented with lithium alone, the antidepressants citalopram, escitalopram or mirtazapine alone, the combination of each antidepressant with lithium, and a no drug control. These drugs were tested under three blood stimulant conditions: murine anti-human CD3 monoclonal antibody OKT3 and the 5C3 monoclonal antibody (OKT3/5C3), phytohemagglutinin (PHA), and unstimulated blood.
Lithium, alone and in combination with any of the tested antidepressants, led to a consistent increase of IL-1ß, IL-6 and TNF-α levels in the unstimulated as well as the stimulated blood. In the OKT3/5C3- and PHA-stimulated blood, IL-17 production was significantly enhanced by lithium. Lithium additionally increased IL-2 concentrations significantly in PHA-stimulated blood.
The data support the view that lithium has pro-inflammatory properties. These immunological characteristics may contribute to side effects of Lithium, but may also explain its beneficial effects in patients suffering from HIV infection or SLE.

→ **Petersein, Charlotte**
email: charlotte.petersein@googlemail.com

POSTER 248

Developmental switch in the influx-release topography at the active zone of the parallel- fiber to Purkinje neuron synapse

Neurobiology

Baur D[1], Bornschein G[1], Eilers J[1], Schmidt H[1]
1 Carl-Ludwig-Institut für Physiologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The coupling distance between presynaptic Ca^{2+} channels and the sensor for vesicular release is a key determinant of speed and reliability of synaptic transmission (1). Recently, it was shown that mature parallel-fiber (PF) to Purkinje neuron (PN) synapses, conventional small cortical synapses, operate at tight nanodomain coupling (< 30 nm), unexpected for an excitatory synapse (2). Here, we addressed the question whether tight coupling is a specific of PF synapses or if it is a feature of postnatal synapse maturation as suggested for the giant Calyx of Held synapse in the brain stem (3). While presynaptic Ca^{2+} signals were not different between maturation stages, we observed differential effects of the slow and fast exogenous Ca^{2+} chelators EGTA and BAPTA (4), respectively, on release in young and mature synapses, indicating that coupling in young synapses is significantly less tight and less homogenous than in the adult. This was accompanied by reduced transmitter release probability and increased paired-pulse facilitation in young synapses (adult: PPR = 1.9 (1.8–20); young: PPR = 2.2 (1.9–2.6); at 50 ms interstimulus interval). These data suggest that a substantial functionally relevant rearrangement of the influx-release topography occurs during postnatal development of PF to PN synapses.

(1) Bucurenciu et al., Neuron, 2008
(2) Schmidt et al., Curr Biol, 2013
(3) Fedchyshyen and Wang, J Neurosci, 2005
(4) Adler et al., J Neurosci, 1991

➜ **Baur, David**
email: david.baur@medizin.uni-leipzig.de

POSTER 249

Amyloid precursor protein is regulated by ncRNAs: implications for Alzheimer´s Disease

Neurobiology

Riekena B[1], Ueberham U[1], Arendt T[1]
1 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Alzheimer´disease (AD) is the most common dementing disorder in the elderly. It is characterized by synapse loss associated with aggregates of amyloid-ß, derived from the amyloid precursor protein (APP) and hyperphosphorylated microtubule-associated protein tau. For both depositions of amyloid and taus, a critical role in neuronal dysfunction is discussed. Related to the upcoming focus on alterations in the transcriptome in association with pathology, non protein-coding RNA (ncRNA) molecules were considered to have important regulatory function. A fast growing pool of ncRNA data strengthens their role in controlling gene expression or protein function and implication in complex biochemical processes in AD. Based on preliminary results obtained by combining genome-wide expression analyses (tiling and custom arrays) and bioinformatic processing, a set of ncRNAs specifically altered in AD was identified. Validation of these results with quantitative PCR revealed four candidate transcripts suitable for further functional characterisation. Combining RNA interference (RNAi) in a human, neuron-like cell culture system (SH-SY5Y) with microarray analyses, we were able to identify two regulated target sequences with one of them coding for the amyloid precursor protein. This effect was confirmed by immunofluorescence subsequent to RNAi treatment of SH-SY5Y cells. Our results identify upstream regulators of the amyloid precursor protein which is critically involved in the AD pathomechanism. Ongoing studies will further characterize this regulatory pathway and establish potential strategies for experimental/therapeutic manipulation.

➜ **Riekena, Boris**
email: boris.riekena@medizin.uni-leipzig.de

POSTER 250

Equal patterns of blood-brain barrier damage after transient and permanent ischemic stroke

Neurobiology

Krueger M[1], Bechmann I[1], Immig K[1], Reichenbach A[2], Härtig W[2], Michalski D[3]

1 Institut für Anatomie, Universität Leipzig
2 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig
3 Klinik und Poliklinik für Neurologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Treatment of patients suffering from ischemic stroke primarily focuses on recanalization of occluded vessels. However, these strategies inherit the risk for hemorrhagic transformation and intracerebral bleeding, which are traditionally attributed to the term 'reperfusion injury'. Although ischemia is linked to blood-brain barrier (BBB) breakdown, the critical role of reperfusion on vascular damage has not yet been confirmed. Therefore, we investigated the mechanism of BBB dysfunction 24 hours after focal ischemia using multiple fluorescence labeling of classical BBB markers and electron microscopy in a rat model of embolic middle cerebral artery occlusion (eMCAO) as well as mouse models of permanent (pMCAO) and transient (tMCAO) ischemia. Areas of BBB breakdown were identified by intravenous application of FITC-albumin. Of note, tight junction (TJ) proteins consistently remained detectable in areas of tracer extravasation. However, fluorescence microscopy revealed structural alterations of the endothelium, which were confirmed by electron microscopy. Further, direct comparison of cerebral vessels from animals submitted to pMCAO and tMCAO revealed an equal pattern of vascular damage, which could be classified into four distinct stages, including loss of endothelial cells. Thus, our data suggest that ischemia-related BBB breakdown is primarily caused by endothelial degeneration, which is not limited or further aggravated by reperfusion of occluded vessels. Therefore, protection of endothelial cells in combination with established recanalizing strategies may turn out as a promising concept for future treatment strategies.

Funding: formel1

→ **Krueger, Martin**
email: martin.krueger@medizin.uni-leipzig.de

POSTER 251

The role of the extracellular matrix proteoglycan brevican at the calyx of Held in the auditory brainstem

Neurobiology

Blosa M[1], Sonntag M[1,2], Jäger C[1], Weigel S[1], Arendt T[1], Rübsamen R[2], Morawski M[1]

1 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig
2 Institut für Biologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Specific neurons of the central nervous system are surrounded by a specialized composition of extracellular matrix (ECM) molecules classified as perineuronal nets (PNs). PNs are suggested to be involved in the modulation of synaptic activity and plasticity, but to date, the specific function of PNs remain unclear. One of the major PN components, the proteoglycan brevican is characterized by a unique organization among the various ECM components. It forms a ring-like structure around presynaptic terminals potentially sealing the synaptic cleft, while other ECM components (e.g. aggrecan) surround the entire cell body. Because of this close association with synaptic terminals, brevican might control synaptic activity and synaptic transmission. The medial nucleus of the trapezoid body (MNTB) in the auditory brainstem is characterized by an extraordinarily high density of PN-associated principal neurons, which makes this nucleus a suitable model system to study the functions of PNs. MNTB principal neurons are further targeted by huge axosomatic terminals, the calyces of Held, enabling the acquisition of both the presynaptic and the postsynaptic discharge activity and thus, allowing unique insights into the mechanisms of synaptic transmission. In the present study we performed immunohistochemistry, electron microscopy and electrophysiology to study the structural and electrophysiological properties of the calyx of Held in transgenic mice which were deficient for the proteoglycan brevican. The results indicate that the complex structure of PNs was not disturbed in brevican-deficient mice. Still, we found a significant change in the dynamics of synaptic transmission at the calyx of Held in brevican-deficient mice compared to wildtype animals. These electrophysiological changes were accompanied by a reduction in the size of subsynaptic, extracellular spaces and by a reduction in the amount of vGlut1. These findings suggest that the ECM component brevican modulates synaptic activity, potentially by establishing spatially and functionally separated synaptic compartments at the calyx of Held.

➜ **Blosa, Maren**
email: blosa@medizin.uni-leipzig.de

POSTER 252 **How to speed up active zone calcium clearance**

Neurobiology

Delvendahl I[1], Jablonski L[1], Matveev V[2], Hallermann S[1]
1 Carl-Ludwig-Institut für Physiologie, Universität Leipzig
2 New Jersey Institute of Technology

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Calcium must be cleared from the presynaptic active zone to allow synchronous high-frequent synaptic transmission, but little is known about the mechanisms of active zone calcium clearance. Here, we use quantitative two-photon calcium imaging to analyze the calcium dynamics in cerebellar mossy fiber boutons, which exhibit exceptionally high firing rates. We show that the fixed endogenous calcium buffers have a very low Ca^{2+}-binding ratio of ~18 and fast binding kinetics. The mobile endogenous buffers at mossy fiber boutons have a binding ratio of ~300 and slow kinetics. Constrained multi-compartment modeling of calcium diffusion and buffering demonstrates that the low Ca^{2+}-binding ratio of the fixed buffers enables large active zone calcium signals with rapid clearance, and the mobile buffers counteract facilitation. Finally, we performed ultra high-resolution calcium imaging and measured calcium signals at different distances from the active zones during single action potentials consistent with our model predictions. Thus, our data explain the features of endogenous calcium buffers required to maintain high-frequency signaling at a central synapse.

➜ **Delvendahl, Igor**
email: igor.delvendahl@medizin.uni-leipzig.de

POSTER 253

In vitro model of multiple sclerosis

Neurobiology

Dafir M[1]

1 Klinik für Neurologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS). The cause of disease is not still known. It has been discussed that external factors such as nutrition and infections or internal factors such as genetic predisposition and autoimmune disorders could influence the pathogenesis of MS. One of the currently discussed hypotheses about MS is that it begins in the early disease stages as a neurodegenerative event in the CNS, which then leads to an involvement of the immune system. The proposed cause of such neurodegenerative events is the effect of intracellular or extracellular induced oxidative stress. Investigating this hypothesis requires a direct insight into the molecular occurrences in the CNS of MS patients. This is not possible without surgical intervention. A feasible alternative is generating neural tissue from patient-specific dermal fibroblasts.

We successfully reprogrammed dermal fibroblasts into pluripotent induced stem cells by viral transduction and differentiated them into neural progenitors. Currently we are trying to differentiate these neural progenitors into mature neural cells, which are the cells of interests for studying the MS-specific characteristics.

→ **Dafir, Mesar**
email: mesar.dafir@medizin.uni-leipzig.de

POSTER 254

Identification of a salt bridge that is crucial for human P2X3 receptor function

Neurobiology

Stephan G[1], Zens C[1], Kowalski M[1], Illes P[1]

1 Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The P2X3 receptor (R) belongs to the family of purinergic ligand-gated ion channels (P2XR). It is expressed by sensory neurons and particularly involved in pain sensation. P2X3R responds to extracellular ATP with conformational changes of its three subunits leading to the opening of the channel pore.

To gain more knowledge of P2X3R function and dynamics it is important to investigate the influence of hydrogen bonds and salt bridges on subunit movement. For this purpose we selected mutants based on the crystal structure of P2X3R by means of software that is recognizing those interactions. Several cysteine mutants have been generated and expressed in HEK293 cells. They were tested by whole cell patch clamp recordings of α,β-methylene ATP (α,β-meATP) – induced current amplitudes. The current responses were inhibited in the double mutant E112C/R198C. The reducing agent dithiothreitol reversed this inhibition in turn by breaking up the disulfide bridge that has been spontaneously developed. Moreover, the effect of α,β-meATP was depressed when E112 was replaced by lysine or R198 was replaced by aspartic acid. Swapping charges to E112K/R198D resulted in a recovery of the receptor sensitivity. Double mutant cycle analysis of this mutant further documented a stabilizing effect. Linking positive (MTSEA) or negative (MTSES) charge to E112C or R198C lead to a recovery of receptor function. This also confirmed the charge swap data.

In conclusion, we provide evidence that the predicted E112/R198 salt bridge is crucial for P2X3R function and channel opening by affecting conformational changes.

→ **Stephan, Gabriele**
email: gabriele.stephan@medizin.uni-leipzig.de

POSTER 255

TEST-RETEST RELIABILITY OF EEG VIGILANCE REGULATION

Neurobiology

Huang J[1], Hegerl U[1,2], Sander C[1,2], Hensch T[1,2]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Vigilance stages denote different states of global brain function. Vigilance regulation is the adaptation of vigilance to situational requirements, which is of crucial importance for human behavior. Several clinical studies suggested a pathogenetic role of vigilance regulation in affective disorders and attention deficit / hyperactivity disorder.

The Vigilance Algorithm Leipzig (VIGALL) 2.0 is an EEG- and EOG-based algorithm which allows objectively determining the levels of brain arousal by considering the frequency patterns as well as the cortical distribution of EEG activity. The VIGALL has been already applied in clinical studies. However, no study on test-retest reliability of VIGALL is so far available. Thus the present study aimed to close this gap.

Data from 27 healthy subjects (18 females, age = 22.93), who underwent two sessions of a 20-minute eyes-closed resting EEG paradigm, were accessed into final analysis. The test-retest reliability coefficients for vigilance temporal dynamic were between .61 and .70, and for single vigilance stages were between .59 and .96 (all $p<.01$). This study demonstrated temporal stability of vigilance stages, as assessed with VIGALL 2.0, and also of their temporal dynamic across 20 minutes. The trait aspect of vigilance regulation was confirmed and the obtained reliabilities are suited for applications on group level.

➜ **Huang, Jue**
email: jue.huang@medizin.uni-leipzig.de

POSTER 256

Munc13-3 is involved in mediating tight Ca2+ -influx release coupling during postnatal synapse development

Neurobiology

Kusch V[1], Baur D[1], Bornschein G[1], Schmidt H[1], Eilers J[1]
1 Carl-Ludwig-Institut für Physiologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The coupling distance between presynaptic Ca^{2+} channels and the sensor for vesicular transmitter release is a major determinant of synaptic fidelity. It has been shown that coupling is significantly tightened during postnatal synapse maturation. The underlying mechanisms, however, remain largely unclear. We present evidence that Munc13-3, a cytomatrix-protein at the active zone, is involved in narrowing the channel to sensor distance. The coupling distance was probed at immature and mature parallel-fiber (PF) to Purkinje neuron synapses in Munc13-3 mutant (Munc13-$3^{-/-}$) mice and their wild-type siblings (Munc13-$3^{+/+}$) making use of the differential effects of the slow exogenous Ca^{2+} buffer EGTA on release in tight vs. loose coupling regimes. If coupling is tight, the slow Ca^{2+} binding kinetics of EGTA do not permit substantial interference with release, while EGTA reduces release, if coupling is loose. We found that EGTA similarly reduced release from immature PF terminals in both genotypes, which is consistent with loose coupling in young mice. Release from mature terminals, however, was affected by EGTA only in Munc13-$3^{-/-}$ but not in Munc13-$3^{+/+}$, suggesting that the developmental shift from loose to tight coupling requires Munc13-3. Munc13-3 has been implicated in a superpriming process, which increases the Ca^{2+} responsiveness of already release-competent vesicles. It remained unclear, however, whether superpriming increased the Ca^{2+} sensitivity of the release machinery (molecular superpriming) or tightened coupling (positional superpriming). Our data indicate that Munc13-3 mediates positional superpriming.

➜ **Kusch, Valentin**
email: valentin.kusch@medizin.uni-leipzig.de

POSTER 257

Beitrag frontaler und parietaler Hirnregionen zu semantischen und phonologischen Entscheidungen im gesunden Gehirn: Eine Studie mit transkranieller Magnetstimulation

Neurobiology

Weigel A[1]

1 Klinik und Poliklinik für Neurologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Ziel dieser Studie war die Untersuchung von parieto-frontalen Hirnnetzwerken für phonologische und semantische Sprachaspekte. Hierzu wurde eine konditionierende kontinuierliche Thetaburststimulation (cTBS) vor der Aufgabe („offline“) mit einer anschließenden repetitiven transkraniellen Magnetstimulation (rTMS) während der Aufgabe („online“) kombiniert. Dabei wurden die Auswirkungen virtueller Läsionen über verschiedenen parietalen und frontalen Hirnarealen der linken Hemisphäre auf phonologische und semantische Kategorisierungsaufgaben untersucht. Im vorliegenden Experiment wurde je eine effektive Stimulation mit einer Placebo-Stimulation kombiniert. Die Ergebnisse bieten Evidenz für eine doppelte Dissoziation innerhalb parieto-frontaler Netzwerke für Phonologie und Semantik. Während der anteriore Teil des Gyrus frontalis inferior (aIFG) und der Gyrus angularis (ANG) zur semantischen Verarbeitung beitragen, können der posteriore Teil des Gyrus frontalis inferior (pIFG) und der Gyrus supramarginalis (SMG) mit der phonologischen Verarbeitung assoziiert werden. Dabei sind die beiden semantischen Areale in ihrer funktionellen Integrität voneinander abhängig, da eine virtuelle Läsion eines der beiden Areale durch die Funktion des anderen kompensiert werden kann. Die beiden phonologischen Areale hingegen weisen keine Kompensationsmöglichkeit für eine virtuelle Läsion des jeweils anderen Areals auf. Phonologische und semantische Verarbeitungsprozesse scheinen somit in verschiedenen Netzwerken organisiert zu sein, die sich bezüglich ihrer Kompensationsfähigkeit und der Robustheit gegenüber einer fokalen Störung unterscheiden.

➜ **Weigel, Anni**
email: anniweigel@rocketmail.com

POSTER 258 **Neuroanatomical correlates of pain-deficiency and pain-induced synesthesia**

Neurobiology

Landmann J[1], Oros-Peusquens A[2], Claßen J[3], Shah N[2], Penninger J[4], Bechmann I[1]

1 Institute of Anatomy, University of Leipzig
2 Institute of Neuroscience and Medicine (INM-4), Research Centre Jülich
3 Department of Neurology, University of Leipzig
4 Institute of Molecular Biotechnology of the Austrian Academy of Sciences

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Functional MRI studies with pain-deficient mice (CACNα2δ3KO) revealed sensory cross-activation (synesthesia) in different cortical areas traditionally considered unimodal, while pain-related areas were inhibited (Neely et al., Cell 2010). As synesthesia is still a barely understood phenomenon, α2δ3KO mice may provide a model to gain mechanistic insights. Quantifications of the expression pattern of Ca^{2+}channels revealed modification of the electrochemical properties of cortical neurons, suggesting an altered excitability in α2δ3KO animals. Moreover, histological and MRI analysis showed that the α2δ3 deficit can cause some severe anatomical alterations in white and grey matter structures. Although the gross connectivity between thalamus and cortex appeared similar between WT and α2δ3KO mice, the differentiation in afferents and efferents show a massive disparity in projection and commissural fibers. We found a reduction of thalamocortical fibers reaching somatosensory/motor cortical areas, which could lead to an insufficient transmission of the pain signal to cortical areas in the α2δ3KO mice. Moreover, observed aberrant fibers nearby visual cortical areas may contribute to the sensory cross-activation found in the mutant. We could also demonstrate alterations in the intra- and intercortical connectivity. These alterations are in line with the concept of hyperconnectivity for the development of synesthesia. Our data demonstrate various differences in neuroanatomical connectivity of α2δ3KO mice which from a hodological point of view go along with their observed synesthetic phenotype.

DFG Research Training School InterNeuro

➜ **Landmann, Julia**
email: julia.landmann@medizin.uni-leipzig.de

POSTER 259

The extracellular matrix molecule tenascin-R affects the neuronal expression of prolyl endopeptidase

Neurobiology

Meißner J[1], Weigel S[1], Roßner S[1], Morawski M[1]
1 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Extracellular matrix (ECM) molecules are expressed in specialized neurons and glial cells at the cell soma or axonal surfaces and play a pivotal role in cellular communication and during normal brain pattern formation, but also in the course of diverse neuropathologies and tissue repair. One of these ECM molecules is the glycoprotein tenascin-R (tn-R) which is exclusively expressed in the brain of vertebrates by neurons and oligodendrocytes. Tn-R has been implicated in a variety of functions, e.g. during myelination, cerebellar neurite fasciculation and hippocampal long-term potentiation (LTP). In the hippocampus, tn-R is located between fasciculating nonmyelinated axon bundles of mossy fibers and axons of the perforant path, between cell somata of pyramidal neurons and at gap junctions between astrocytic processes. In addition, decreased perisomatic inhibition, increased basal excitatory synaptic transmission and reduced LTP were observed in the hippocampus of tn-R knock-out mice. In this study, we focused on the affect of tn-R deficiency onto the prolyl endopeptidase (PREP) involved in cell division, signal transduction, learning and memory. Further, neuronal cell adhesion molecule (NCAM), matrix metalloprotease 9 (MMP9) and tissue inhibitors of MMPs (TIMPs) were investigated. Immunohistochemical and western blot analyses of hippocampus tissues revealed a significant reduction of PREP and an increase of MMP9 in tenascin-R knock-out mice compared to wild type mice. MMP9 can protolytically cleave tn-R to smaller fragments which in turn could be potential substrates for PREP.

→ **Meißner, Juliane**
email: juliane.meissner@medizin.uni-leipzig.de

POSTER 260

Differentielle Reorganisationsmuster des Sprachnetzwerks nach linksseitigen frontalen und temporalen Hirninfarkten

Neurobiology

Stockert A[1]

1 Klinik und Poliklinik für Neurologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Die Spracherholung nach einem Schlaganfall hängt von der Reorganisation des Sprachnetzwerk ab. Wie sich die Reorganisationsmuster bei frontalen und temporalen Läsionen unterscheiden ist unklar. In einer longitudinalen fMRT-Studie wurden bei je 14 Patienten mit frontalen (FC) oder temporoparietalen (TPC) Infarkten und bei 14 Kontrollen (CG) mehrfach (t1< 1Wo, t2< 2Wo, t3> 6Mon) mit einer auditiven Verständnisaufgabe BOLD-Signalantworten für Sprache (SP) und Rückwärtssprache (REV) erhoben. Die Analyse erfolgte mittels ANOVA mit den festen Effekten *Zeit* (t1-t3) und *Bedingung* (SP, REV), auf zweiter Ebene mit gemischtem Design (Within-Subject-Faktoren *Zeit, Bedingung*; Between-Subject-Faktor *Gruppe* (FC, TPC)). Ein Spracherholungswert (LRS) wurde longitudinal erhoben. CG zeigen das Sprachnetzwerk mit bilateraler, linkslateralisierter temporofrontaler Aktivierung (SP>REV). Aktivierung bei Patienten wird bilateral im inferioren frontalen (IFG), anterioren (ATG) und mittleren (MTG) temporalen Gyrus moduliert durch *Bedingung*, *Zeit* und *Gruppe*. Aktivierung bei TPC zeigt das bekannte Muster: t1 globale Abnahme, t2 bifrontale Zunahme, t3 Normalisierung rechts. Bei FC moduliert *Zeit* die rechtsseitige Aktivierung nicht, Aktivierung im MTG links normalisiert zu t3. Bei TPC ist stärkere Aktivierung rechts zu t2 mit Besserung im LRS assoziiert, bei FC hingegen nur erhaltene Sprachaktivierung im linken IFG zu t1 mit besserem LRS. Diese Muster zeigen die differentielle Einbindung von IFG/MTG in Spracherholung in Abhängigkeit vom Läsionsort und könnten die Basis sein für den Einsatz Plastizitätsinduzierender Techniken in der Sprachrehabilitation.

→ **Klingbeil, Julian**
email: julian.klingbeil@medizin.uni-leipzig.de

POSTER 261

The time course of semantic interference from context pictures

Psychology and Cognition

Matushanskaya A[1], Mädebach A[1], Forschack N[1,2], Jescheniak J[1], Müller M[1]

1 Institut für Psychologie, Universität Leipzig
2 Max-Planck-Institute for Human Cognitive and Brain Sciences

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

A number of studies have demonstrated semantic context effects from distractor words, but typically no semantic context effects from distractor pictures are found. We hypothesized that semantic effects become visible if sufficient attention is allocated to distractor picture. For this reason, we combined simple picture naming with a spatial cueing paradigm. Participants were asked to name a target object in the presence of a distractor object, which were either semantically related or unrelated. Attention was manipulated by means of arrow cues pointing to the target (valid), to the distractor (invalid), or to both pictures (neutral). We investigated the time course of semantic interference effect using event-related potentials. In the EEG studies of speech production lexical stage of speech production process is associated with the time window of 150–275 ms, while later time windows are assumed as post-lexical processing. In the naming latencies, semantic interference was observed in the neutral condition, where attention was directed to both objects. Related to that, ERP-analysis revealed an increased negativity around 155–185 ms (N1 range) for semantically related pictures compared to unrelated pictures in the neutral cueing condition.

Our findings emphasise the role of attention in the activation of context object names and are difficult to be reconciled with models assuming lexical selection to occur at the post-lexical stage of speech production process.

➜ **Matushanskaya, Asya**
email: asya.matushanskaya@uni-leipzig.de

POSTER 262

Erfassung kognitiver Leistungen bei ADHS im Erwachsenenalter – Vergleich verschiedener Ebenen und Settings

Psychology and Cognition

Kallweit C[1], Exner C[1]
1 Institut für Psychologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Erwachsene mit einer Aufmerksamkeitsdefizit-/Hyperaktivitätsstörung (ADHS) berichten häufig kognitive Funktionsdefizite im Alltag. Diese werden aber nur bedingt in neuropsychologischen Standardtests deutlich. Unterschiedliche Anforderungen zwischen Alltag und Labor könnten hierfür relevant sein. Daher wurde ein Aufgabenparadigma entwickelt, das unter kontrollierten Laborbedingungen stattfindet, aber Alltagsleistungen eher simulieren soll als standardisierte neuropsychologische Verfahren. Die Aufgaben wurden an bereits standardisierte Verfahren angelehnt, um Settings vergleichen zu können. Unter Hinzunahme von Selbstberichten kann eine erweiterte Leistungsbeurteilung bei ADHS im Erwachsenenalter erfolgen.

Zu den Bereichen Planungskompetenz, selektive Aufmerksamkeit, Inhibition, Flexibilität (Set Shifting) und Arbeitsgedächtnis wurden jeweils klassisch neuropsychologische und alltagsnahe Aufgaben durchgeführt. Allgemeine kognitive Leistungen wurden im Selbstbericht erfasst. Aus einer laufenden Studie werden Ergebnisse von 15 erwachsenen Patienten mit ADHS und 10 gemachten Kontrollprobanden berichtet.

Im Selbstbericht sind kognitive Defizite von Patienten im Vergleich zu den Kontrollprobanden am deutlichsten ausgeprägt. Bei den alltagsnahen und neuropsychologischen Aufgaben ergeben sich uneinheitliche Ergebnisse. In einzelnen Funktionsbereichen fanden sich Defizite bei den Patienten, die bei neuropsychologischen oder alltagsnahen Aufgaben auftraten.

Die Studie läuft aktuell noch. Tendenziell ergeben sich die eingangs beschriebenen diskrepanten Befunde, das alltagsnahe Setting scheint differentielle Informationen zu liefern.

➜ **Kallweit, Claudia**
email: claudia.kallweit@uni-leipzig.de

POSTER 263

Soziale Situation und soziale Unterstützung von Jungen Erwachsenen mit Krebs (AYA)

Psychology and Cognition

Leuteritz K[1], Friedrich M[1], Sender A[1], Nowe E[1], Stöbel-Richter Y[1], Geue K[1]

1 Abteilung für Medizinische Psychologie und Medizinische Soziologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hintergrund: Menschen, die zwischen 15 und 39 Jahren an Krebs erkranken (adolescent and young adult patients (AYA) stellen in Deutschland etwa 3% aller Personen die jährlich neu an Krebs erkranken dar. Die Unterstützung von Familienangehörigen oder Freunden ist eine wichtige Ressource für das Wohlbefinden von AYA. In dieser Studie werden AYA hinsichtlich ihrer Lebens- und Versorgungssituation untersucht. Zwischenergebnisse zur sozialen Unterstützung (SU) werden dargestellt.

Methoden: Krebspatienten im Alter von 18 bis 39 Jahren werden nach Abschluss der Akutbehandlung und ein Jahr später online bzw. postalisch befragt. Für die soziale Einbindung werden neben soziodem. Daten die soziale Unterstützung (SSUK-8) erhoben.

Ergebnisse: Die bisher in die Studie eingeschlossenen Patienten (N=106, 81 Frauen, 25 Männer) waren zum Diagnosezeitpunkt im Mittel 29,7 Jahre alt. Rund 71% der Befragten hat kurz nach Abschluss der Akutbehandlung einen festen Partner von denen ca. 85% auch zusammen leben. Rund 23% der Patienten leben allein, 13% noch bei seinen Eltern. Die Mehrheit (ca. 69%) der AYA ist kinderlos und fast jeder fünfte ist nicht erwerbstätig. Für 74% der AYA steht die Verwirklichung mind. einer dieser Entwicklungsschritte noch aus. Positive Aspekte SU waren bei AYA mit Partner höher ausgeprägt als bei AYA ohne feste Partnerschaft. Ebenso wurden bei AYA mit festem Partner aber auch belastende Interaktionen angegeben.

Schlussfolgerung: Das Vorhandensein einer festen Partnerschaft wirkt sich positiv auf die wahrgenommene SU der AYA aus. In einer Partnerschaft erleben AYA aber auch belastende Aspekte SU. Weitere Analysen folgen.

➜ **Leuteritz, Katja**
email: katja.leuteritz@medizin.uni-leipzig.de

POSTER 264

Stressbewältigung bei adipösen Personen mit Misshandlungserfahrungen in der Kindheit

Psychology and Cognition

Kuhn J[1], Klinitzke G[1], Kersting A[1,2]

1 Klinik und Poliklinik für Psychosomatische Medizin und Psychotherapie, Universität Leipzig
2 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hintergrund: Über Zusammenhänge von Misshandlungserfahrungen im Kindheitsalter (MiK), Stresserleben, Coping und Essstörungssymptomatik bei adipösen Personen ist derzeit wenig bekannt.
Methode: In einer online-basierten Studie wurden 355 Personen (u.a. 142 normalgewichtige und 134 adipöse TN) im Selbstrating zu allgemeiner Psychopathologie (PHQ-D), essstörungsbezogener Psychopathologie (EDE-Q, YFAS), Misshandlungserfahrungen im Kindesalter (CTQ), Psychotraumatologie (TEC; IES-R), Stresserleben (PSS) und Coping (Brief Cope, SCI) befragt.
Ergebnisse: Bei Vorliegen von MiK erhöht sich das Risiko für Adipositas um den Faktor 2,34 (OR = 2,343; 95% CI = 1,439-3,814). Die Häufigkeit der Binge-Eating-Störung ist in der Gruppe der Adipositasbetroffenen um ein fast 5faches erhöht (OR = 4,881; 95% CI = 2,57-9,26). Liegen neben Adipositas zudem schwere Misshandlungserlebnisse vor, steigt das Risiko für das Vorkommen einer pathologischen Essstörungssymptomatik um ein 3,3faches (OR = 3,302; 95% CI = 1,172-9,303). Adipöse TN zeigen eine höhere aktuelle Stressbelastung ($t(274) = -3,922$; $p<.001$; $d = 0,47$), stärkere körperliche und psychische Stresssymptome ($t(274) = -4,986$; $p<0,001$; $d = 0,60$) und weniger funktionales Coping ($t(274) = -4,986$; $p<0,001$; $d = -0,62$) im Vergleich zu Normalgewichtigen.
Diskussion: Misshandlungserlebnisse in der Kindheit gehen mit einem erhöhten Risiko für hohes Stresserleben, dysfunktionale Stressbewältigung, das Auftreten einer Essstörungspathologie und Adipositas einher. Mögliche Mechanismen des Zusammenhangs und Implikationen für die (therapeutische) Praxis werden diskutiert.

Funding: formel1

➜ **Kuhn, Juliane**
email: juliane.kuhn@medizin.uni-leipzig.de

POSTER 265

AUDITORY EVENT RELATED POTENTIALS DURING DIFFERENT VIGILANCE STAGES

Psychology and Cognition

Huang J[1], Spada J[1,2], Sander C[1,2], Hegerl U[1,2], Hensch T[1,2]

1 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The Vigilance Algorithm Leipzig (VIGALL) is an EEG- and EOG-based algorithm, which classifies 1-second-EEG segments into one of 7 vigilance stages from high alertness (stage 0) to relaxed wakefulness (stages A1, A2, A3) to drowsiness (stages B1, B2/3) up to sleep onset (stage C) (Hegerl & Hensch, 2014). VIGALL has been validated by studies using fMRI, PET, behavioral and autonomic parameters. However, a validation using vigilance-sensitive auditory event-related potentials (ERPs) is still lacking. Former studies showed that the *latencies* of the P1, N1, P2 and N3 increase with decline of vigilance. Concerning *amplitudes*, the N1 decreases with increasing drowsiness, whereas the P2 and N3 increase. However, in these former studies no fine-graded assessment of the different vigilance stages before sleep onset was available. Thus, the aim of this study was to investigate the ERPs during the different vigilance stages as assessed with VIGALL 2.0.

48 subjects (31 females, age = 23.8) took part in a two-hours, eyes-closed passive oddball-paradigm. A frequent (500 Hz) and a rare tone (1000Hz) were presented.

Latencies of standard P1, N1, P2 and N3 increased from stage A to C. Amplitudes of P1, P2 and N3 increased with decline of vigilance, whereas N1 decreased. Concerning the deviant tone, the same was found for amplitudes, but no consistent association between vigilance stages and latencies was found. Our findings are in line with previous studies and go beyond by assessing ERPs within the fine-graded vigilance stages as assessed by VIGALL 2.0, thereby further contributing to the validation of its vigilance classification.

➜ **Huang, Jue**
email: jue.huang@medizin.uni-leipzig.de

POSTER 266

Der Purdue Pegboard Test: Besonderheiten bei der Durchführung nur eines Subtests

Psychology and Cognition

Henger S[1]

1 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Der Purdue Pegboard Test ist ein etabliertes Verfahren, das die neuropsychologische Funktionsfähigkeit eines Menschen, speziell die Feinmotorik der Hände misst und heute im klinischen Kontext bei der Erforschung von Depression, Schizophrenie oder dem Tourette-Syndrom sowie in der Altersforschung Anwendung findet. Er besteht aus den folgenden 4 Subtests.

1. Stecken der Stifte mit der dominanten Hand (30 sec)
2. Stecken der Stifte mit der nichtdominanten Hand (30 sec)
3. Gleichzeitiges Stecken der Stifte mit beiden Händen (30 sec)
4. Montageaufgabe, Zusammenstecken von Stiften, Scheiben und Hülsen (30 sec)

Die Studie soll zeigen, ob bei Reduzierung der Testung auf den Subtest 3 aus ökonomischen Gründen (z. B. für große Kohortenstudien wie die Nationale Kohorte) dessen Ergebnisse mit denen anderer großer Studien vergleichbar ist, die alle 4 Subtests in definierter Reihenfolge durchgeführt haben.

Der Fragestellung, ob es Lerneffekte durch die vorhergehende Testung der dominanten und nichtdominanten Hand bei der beidhändigen Testung gibt, wurde durch eine randomisierte Zuordnung der Probanden zu 2 Testbedingungen Rechnung getragen. Testbedingung 1: klassische Reihenfolge, Subtest 1, 2 und dann 3. Testbedingung 2: beginnend mit Subtest 3, dann 1 und dann 2. Von den 500 LIFE-Probanden (Alter: 60 bis 80 Jahre, 256 männlich, 244 weiblich) führten 235 die Subtests 1 bis 3 in der Testbedingung 1 durch; 265 in der Testbedingung 2.

Ergebnis: Unter Testbedingung 1 ergibt sich ein signifikant höherer Mittelwert für den Subtest 3 (10,25 Stifte) im Vergleich zur Testbedingung 2 (9,84 Stifte).

Funding: life

➜ **Henger, Sylvia**
email: shenger@life.uni-leipzig.de

POSTER 267

Klk7 plays a role in body weight regulation, insulin sensitivity and glucose metabolism

SFB 1052 – Obesity mechanisms

Kunath A[1,2], Kern M[1], Stumvoll M[1], Blüher M[1], Klöting N[1]

1 Department of Internal Medicine, Neurology and Dermatology, Clinic for Endocrinology and Nephrology, University of Leipzig, Leipzig
2 Molecular Diabetology & DZD-Paul Langerhans Institute Dresden, TU Dresden, Dresden

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Previous studies showed that beneficial effects on glucose metabolism of vaspin are at least in part mediated through inhibition of the protease Kallikrein 7 (Klk7). Based on these findings, we investigated the physiological relevance of the Klk7-vaspin system in mice with a targeted whole-body disruption of Klk7 *in vivo*.
Methods: We generated a whole-body Klk7 knockout mouse ($Klk7^{-/-}$) and systematically characterized the consequences of Klk7 deficiency on body weight, fat mass, serum concentrations of leptin and parameters of glucose and lipid metabolism.
Results: Klk7 deficiency causes significant changes in body weight dynamics, body fat content as well as leptin serum concentrations. At an age of 20 weeks, male $Klk7^{-/-}$ mice have significantly lower body fat (4.9±1.1%) than the controls (9.2±2.0%) ($p < 0.05$). Moreover, male $Klk7^{-/-}$ mice have significantly lower leptin concentration in the serum (23.6±2.0ng/ml) in relation to the controls (43.2±2.6ng/ml). In female $Klk7^{-/-}$ mice, food intake (4.3±0.5g/day) was significantly lower compared to controls (4.7±0.3g/day,$p < 0.05$). Although glucose tolerance was indistinguishable between $Klk7^{-/-}$ and control mice of both genders, female $Klk7^{-/-}$ mice are characterized by impaired insulin sensitivity compared to littermate controls ($p < 0.05$).
Conclusion: Our data indicate that Klk7 plays a previously unrecognized role in body weight regulation, food intake, insulin sensitivity and glucose metabolism. The mechanisms, how Klk7 disruption affects these traits need to be explored in further studies.

Supported by: DZD e.V. funded by BMBF, SFB1052 (B1 to MB and B4 to NK)

➜ **Kunath, Anne**
email: anne.kunath@medizin.uni-leipzig.de

POSTER 268

Adipose tissue telomere lengths are fat depot specific and associated with age, HbA1c and adipocyte size

SFB 1052 – Obesity mechanisms

Lakowa N[1,2], Trieu N[1], Flehmig G[1,2], Lohmann T[1], Schön M[1], Dietrich A[1,3], Langer S[1], Stumvoll M[1,2], Blüher M[1,2], Klöting N[1]

1 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
2 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
3 Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Telomere length has been considered as biological marker for aging and cell proliferation, and obesity seem to be related to shorter telomeres. Since obesity itself and obesity related metabolic disturbances are related to adipose tissue (AT) mass, depot distribution and gender, we hypothesis that telomere length (TL) are different between fat depots in humans, we aimed to investigate whether the telomere length is associated with parameters of obesity and with metabolic traits.

Telomere length was analyzed by quantitative PCR in samples of total human genomic DNA from 97 paired subcutaneous and visceral adipose tissue samples of 47 non-obese and 50 obese subjects as well as in adipocytes vs. stromal vascular fraction (SVF), and small vs. large adipocytes.

We observed significantly shorter ($P < 0.001$) telomere length in subcutaneous AT than in visceral AT, which neither was independent from gender, BMI nor type 2 diabetes. In SC fat depot telomere length was shorter in adipocytes and SVF than in whole adipose tissue. TL analysis in small and large adipocytes indicated no differences. In whole SC fat depot, we detected a negative correlation between telomere length with age ($r=-0.205$, $P=0.045$) and HbA_{1c} levels (%) ($r=-0.240$, $P=0.03$). Our data indicate that telomere length differ between fat depots mainly due to different lengths in SVF. Telomere length is not associated with gender, BMI and T2D.

➜ **Lakowa, Nicole**
email: nicole.lakowa@medizin.uni-leipzig.de

POSTER 269

Keeping in touch: T-cadherin impedes dissociation of adiponectin receptor 1 dimers

SFB 1052 – Obesity mechanisms

Leimer T[1], Kosel D[1], Mörl K[1], Ranscht B[2], Beck-Sickinger AG[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
2 Sanford-Burnham Medical Research Institute, La Jolla, California, USA

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Adiponectin and its receptors possess a powerful potential for the treatment of the metabolic syndrome and other diseases (1). However, the complexity of the receptor-ligand-system limits our understanding of the molecular mechanism, which is important for pharmaceutical therapies. It is known that AdipoR1 and AdipoR2 are able to form homo- and heteromers which dissociate upon adiponectin stimulation and seem to have an impact on the signal transduction (1, 2). In addition T-cadherin emerges as a third adiponectin receptor, which is not only able to bind adiponectin but also able to alter cellular response of this adipokine (3).
Bimolecular fluorescence complementation and flow cytometry analysis were applied to investigate the effect of T-cadherin on AdipoR1 dimerization. AdipoR1 and T-cadherin were co-transfected in different ratios in HEK293 cells and incubated with adiponectin. The quantification of the mean fluorescence demonstrates that T-cadherin impedes the adiponectin-induced dissociation of the AdipoR1 dimers.
Consequently, the interaction of the three adiponectin receptors has to be considered in terms of cellular response and regulation of the adiponectin signaling.

1) Kosel et al. (2010). Dimerization of adiponectin receptor 1 is inhibited by adiponectin. J Cell Sci.;123(Pt 8):1320–8.
2) Almabouada et al. (2013). Adiponectin receptors form homomers and heteromers exhibiting distinct ligand binding and intracellular signaling properties. J Biol Chem.;288(5):3112–25.
3) Denzel et al. (2010). T-cadherin is critical for adiponectin-mediated cardioprotection in mice. J Clin Invest.;120(12):4342–52.

Funding: ifb

➜ **Leimer, Tobias**
email: tobias.leimer@uni-leipzig.de

POSTER 270

Examination of ex-vivo viability and proliferation of human connective and adipose tissue in Slice-Cultures

SFB 1052 – Obesity mechanisms

Schopow N[1,2], Kallendrusch S[1], Körfer J[1], Merz F[1], Langer S[2], Bechmann I[1]

1 Institut für Anatomie, Universität Leipzig
2 Abteilung für Plastische-, Ästhetische- und spezielle Handchirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: In basic research, the need for human test systems has increased over the last decade due to ethical and scientific reasons. Organotypic tissue cultures mimic the *in vivo* situation more closely than cell culture systems, and animal experiments can be reduced. We have, therefore, developed slice culture models of human tissues which maintain the organotypic environment known to provide important signaling for cell differentiation (Nitsch et al., Lancet 2000; Merz et al., Neuro-Oncology 2013; Gerlach et al., British J Cancer 2014).
Method: Tissue slices of 500μm can be produced of tissues obtained from surgery and cultivated on semipermeable membranes. Connective and adipose tissue survives at least 14 days *in vivo*. During the cultivation it is possible to monitor morphology of the tissue and to visualize vitality (Calcein-AM, JC-1) or cell death (Annexin V, Propidium Iodid) via live imaging, or to monitor native morphology of the tissue. Also we fixed slices on day 0, 1, 7, and 14 in PFA and performed histological analyses.
Results: Our tissue culture showed stable conditions for at least 14 days both with and without serum in the culture medium. The cultivating conditions were optimized and a live imaging setup as well as immunohistochemical stainings were established. Metabolism, proliferation, immune response, but also Caspase 3-activity and apoptotic fragmentation of cell nuclei could be observed. We now adapt our method for human soft-tissue sarcoma to develop a novel test system for local and systemic treatment techniques and to pave the way for a personalized therapy.

➜ **Schopow, Nikolas**
email: schopow@medizin.uni-leipzig.de

POSTER 271 **Role of Leptin in Vascular Function**

SFB 1052 – Obesity mechanisms

Hoffmann A[1], Kralisch S[1], Dühring S[1], Ebert T[1], Jeßnitzer B[1], Lößner U[1], Jeromin F[2], Klöting N[1], Blüher M[1], Burkhardt R[2], Faßhauer M[1]

1 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
2 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Obesity can lead to metabolic complications like insulin resistance, dyslipidemia, and cardiovascular disease. Leptin is a hormone produced by adipose tissue and circulates in proportion to adipose tissue mass. Intriguingly, both lack of leptin and high leptin levels are suspected to have a negative influence on the development of atherosclerotic plaques. The aim of this study is to elucidate the dose-dependent impact of leptin on glucose and lipid homeostases, whole body composition, and the development of atherosclerosis.
Leptin-deficient, atherosclerosis-prone mice (LDLR-/-;ob/ob) were placed on a semi-artificial 0.15% cholesterol diet from 4 weeks of age for 16 weeks. From 8 weeks of age, animals were treated with increasing concentrations of recombinant leptin ranging from sub- to supra-physiological levels, or saline for 12 weeks. The effect of leptin during the treatment regime was determined by daily body weight monitoring. A comprehensive characterisation of metabolic parameters and body composition was performed. Furthermore, atherosclerotic lesion area at the aortic root and brachiocephalic artery was quantified by immunohistology.
As expected, treatment with recombinant leptin significantly and dose-dependently reduced body weight in both male and female mice after only one week of treatment. Whole body fat mass was significantly and dose-dependently decreased after leptin treatment. Levels of HbA1c as a marker of glucose metabolism as well as lean mass were not affected by leptin treatment. The effect of leptin on atherosclerotic lesion area and composition are currently being elucidated in these animals.

➜ **Hoffmann, Annett**
email: annett.hoffmann@medizin.uni-leipzig.de

POSTER 272

Molecular Determinants of Arrestin Recruitment to the Human Y4 Receptor

SFB 1052 – Obesity mechanisms

Wanka L[1], Babilon S[1], Burkert K[1], Gurevich V[1], Beck-Sickinger AG[1]

1 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The neuropeptide Y receptor system plays a role in different physiological functions and diseases such as obesity and cancer. This multiligand/multireceptor system consists of four Y-receptor subtypes that have been cloned from human genome: hY_1, hY_2, hY_4 and hY_5.

The hY_4-receptor conveys anorexigenic effects and is an attractive target for the development of new drugs to treat obesity. [1] To this end, it is essential to understand the molecular mechanism of receptor signaling, including arrestin recruitment. For the investigation of distinct amino acids that are important for arrestin recruitment, different hY_4-receptor mutants were generated. The influence of a hypothetical internalization motif within the C-tail of the hY_4-receptor was studied first and distinct positions were varied. The mutants that either contain single amino acid replacements or partial truncation within this motif were investigated in an inositol triphosphate accumulation assay and by bioluminescence resonance energy transfer to investigate G protein activation and arrestin recruitment. It was shown that the deletion of the possible C-terminal internalization motif and the substitution of glutamic residues by alanine within this motif led to the inhibition of internalization and of arrestin recruitment. The replacement of serine or threonine residues by alanines within this motif resulted in a decrease of internalization as well as of arrestin recruitment. Thus, we identified for the first time individual residues that contribute to arrestin recruitment and subsequent internalization of the human Y4-receptor.

[1] Babilon et al. Biol Chem. 2013: 394

Funding: DFG

➜ **Wanka, Lizzy**
email: lizzy.wanka@uni-leipzig.de

POSTER 273

The role of vaspin in adipose tissue thermogenesis and energy homeostasis

SFB 1052 – Obesity mechanisms

Weiner J[1,2], Krause K[1], Zieger K[2], Klöting N[1,3], Kovacs P[1,3], Stumvoll M[1], Blüher M[1,3], Heiker J[1,2]

1 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig
2 Institut für Biochemie, Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig
3 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Obesity is characterized by excessive fat accumulation, initiating and facilitating the dysfunction of adipose tissue (AT). Human AT consists of white and brown AT depots (WAT and BAT). While energy-storing WAT constitutes the bulk of AT, the energy-burning thermogenic capacity of BAT represents an attractive therapeutic target for weight loss induction through energy expenditure. Besides cold exposure and β-adrenergic stimulation, several adipokines have been identified to promote a white-to-brown switch in AT (e.g. FGF-21, irsin) (Townsend KL et al. 2014).
In our preliminary work, we observed an up-regulation of BAT related genes (PGC-1α, Cidea, Cox7a1) in a 3T3-L1 cell line stably overexpressing human vaspin (serpinA12). We also found improved cold adaption of C57BL/6NTac mice upon vaspin treatment (unpublished data). Interestingly, vaspin was also shown to be amongst the top five up-regulated genes upon cold exposure in AT of mice (Rosell M. et al., 2014).
Based on these observations, the aims of our project are (1) to analyze nutritional and thermogenic influences on vaspin expression in AT and (2) to determine the role of vaspin in AT thermogenesis. C57BL/6NTac mice will be fed a high fat, high sugar or control diet to determine nutritional effects on vaspin expression and secretion. Furthermore, mice will be housed at 8°C to investigate cold induced changes of AT vaspin expression. Additionally, application of vaspin will ascertain its role in thermogenesis.

Funded by DFG (SFB1052-C07).

→ **Weiner, Juliane**
email: juliane.weiner@medizin.uni-leipzig.de

POSTER 274

A role for the adhesion-GPCR GPR110 in the liver

SFB 1052 – Obesity mechanisms

Tretzschock J[1], Schulz A[1], Binder C[1], Ricken A[2], Schöneberg T[1], Prömel S[1]

1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig
2 Institut für Anatomie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

GPR110 belongs to the class of adhesion-G protein-coupled receptors (aGPCRs). Despite the vital roles in many biological processes shown for several members of this second largest class of GPCRs has long been neglected. One prime example is GPR110, for which neither biological functions nor signalling pathways have been described. However, its high evolutionary conservation suggests essential physiological roles for this aGPCR.
To shed light on the biological functions of GPR110 we characterised transgenic mice knockout for *Gpr110*. *Gpr110* is specifically expressed in liver, kidney, and adrenal gland and first analyses showed that livers of *Gpr110* knockout mice are significantly heavier than the ones of respective wildtype litter mates. Further, adult knockout mice also retain a larger total body weight when fed a standard diet. Consistent with these data, metabolic analyses revealed an increased food intake in these mice on a standard diet which might be causative for the observed increased weight.
Our results point towards a role of GPR110 in processes in the liver related to food intake and metabolism. In further studies we aim to gain greater understanding of the function of this promising receptor.

→ **Tretzschock, Jana**
email: jana.tretzschock@medizin.uni-leipzig.de

POSTER 275 **Metabolic Characterization of Trib1-deficient mice**

SFB 1052 – Obesity mechanisms

Dokas J[1], Arndt L[1,2], Kern M[3,4], Klöting N[3,4], Blüher M[3,4], Thiery J[1,2], Burkhardt R[1,2]

1 Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
3 Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, Universität Leipzig
4 Klinik und Poliklinik für Endokrinologie und Nephrologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Genetic variants near *TRIB1* have been associated with plasma lipids and the risk of CHD. We recently demonstrated that Trib1 deficiency (Trib1-/-) in mice increases hepatic lipogenesis and VLDL production, leading to elevated plasma cholesterol and triglycerides. In the present study, we aimed to investigate whether Trib1 is also involved in regulating energy homeostasis and might therefore fulfill additional functions in metabolism.
Methods: Trib1-/- mice were fed a high fat diet and body weight was recorded weekly. Glucose tolerance was assessed with intraperitoneal glucose tolerance tests and insulin sensitivity with insulin tolerance tests. In addition, *TRIB1* mRNA expression was determined in human white adipose tissue samples and analyzed for correlations with clinical phenotypes and metabolic markers.
Results: Trib1-/- mice were significantly lighter than littermate controls and displayed an altered body composition: Trib1-/- mice remained leaner than wildtype or heterozygous littermates and were resistant to weight gain and adiposity. Furthermore, glucose tolerance as well as insulin sensitivity was significantly increased in Trib1-/- mice. Our findings in mice correlated well with data obtained in human adipose tissue, where higher *TRIB1* mRNA expression was associated with increased body weight and percentage of body fat, as well as increased plasma HbA1c.
Conclusion: Our data strongly indicate that Trib1 contributes to metabolic pathways involved in the regulation of whole body energy homeostasis in mice. Trib1 regulates, by yet unknown mechanisms, body weight as well as glucose and lipid metabolism.

➜ **Dokas, Janine**
email: janine.dokas@medizin.uni-leipzig.de

POSTER 276 **The relationship between obesity and Psoriasis**

SFB 1052 – Obesity mechanisms

Herbert D[1]

1 Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Obesity and Psoriasis (PSO) are common diseases in today´s population with an increasing prevalence. PSO is an inflammatory autoimmune skin disease characterized by epidermis thickening, parakeratosis and a mixed cellular infiltrate consisting mainly of dendritic cells (DC), T cells (TC) and macrophages in the dermis and neutrophils and some TC in the epidermis. There is a correlation between severity of PSO and body mass index (BMI), but at present it is unclear how obesity is involved mechanistically in the pathogenesis of this inflammation. It is known that white adipose tissue (WAT) is a rich source of pro-inflammatory adipokines that contribute to a 'low-grade inflammatory state' of obese subjects promoting autoimmune inflammatory diseases. Thus, the cytokine gene expression profiles of subcutaneous fat (SF) of lean (BMI $\leq$ 30 kg/m^2) and obese (BMI $>$ 30 kg/m^2) patients was analyzed by RT-PCR. However, SF of lean and obese patients did not differ significantly in the expression of pro-inflammatory, PSO-relevant cytokines like IL17, IL23, IL6, TNFa or IL1ß. Accordingly, analysis of fat supernatants by multiplex analysis underlined these results. Next, the effect of soluble mediators produced by SF of lean and obese patients on DC and macrophages was studied. Surprisingly, soluble mediators of fat tissue of lean and obese patients reduced the release of TNFa and IL12 by DC and macrophages. However, there were no differences between fat samples of lean and obese patients. Thus, quiescent subcutaneous AT in general seems to be harmless according to inflammation.

Funding: DFG

➜ **Herbert, Diana**
email: diana.herbert@medizin.uni-leipzig.de

POSTER 277

Dyadisches Coping und psychische Belastung bei Patienten mit hämatologischen Erkrankungen und deren Partnern im Verlauf – eine Kohortenanalyse

Social Medicine

Pankrath A[1], Ernst J[1], Niederwieser D[2], Döhner H[3], Hönig K[4,5], Gündel H[5], Vogelhuber M[6], Weißflog G[1]

1 Abteilung für Medizinische Psychologie und Medizinische Soziologie, Universität Leipzig
2 Abteilung für Hämatologie und Internistische Onkologie, Universität Leipzig
3 Klinik für Innere Medizin III, Universitätsklinikum Ulm
4 Comprehensive Cancer Center Ulm (CCCU), Integratives Tumorzentrum des Universitätsklinikums und der Medizinischen Fakultät
5 Universitätsklinik für Psychosomatische Medizin und Psychotherapie Ulm
6 Universitätsklinikum Regensburg, Klinik und Poliklinik für Innere Medizin III

Hintergrund: Eine hämatologische Krebserkrankung ist für die Patienten und deren Partner mit großen Belastungen verbunden. Mit Hilfe des Dyadischen Coping (DC) inkl. der Subformen positives und negatives DC kann analysiert werden, wie Paare im Krankheitsverlauf mit diesen Belastungen umgehen.
Methode: Im Rahmen einer trizentrischen Querschnittstudie wurden 326 Paare schriftlich befragt. Eingeschlossen wurden Patienten mit den ICD-10 Diagnosen C81-C96 bzw. D46 und deren Partner. Das DC wurde mit dem Dyadischen Coping Inventar (DCI), die psychische Belastung mit dem Patient Health Questionnaire (PHQ-4; Cut-Off ≥6) erfasst. Bezüglich des Diagnoseabstands wurden die Paare in drei Kohorten eingeteilt (K1: < 1 Jahr, K2: 1 bis 4 Jahre und K3: > 4 Jahre).
Ergebnisse: In der Varianzanalyse ergab sich lediglich für das positive DC des Patienten ein Unterschied zwischen den Kohorten (K1: 3,67 vs. K3: 3,42; p=0,03). Keine Unterschiede ergaben sich im negativen DC der Patienten sowie für beide Subformen des DC der Partner. Der Anteil psychisch belasteter Patienten und Partner war in Kohorten wie folgt verteilt: K1: 24,8/20,8%, K2: 11,3/8%, K3: 12,7/4,6% (p=0,01 bzw. p< 0,001). Die psychische Belastung der Patienten korrelierte signifikant mit dem eigenen negativen DC (r=0,25; p< 0,001), nicht jedoch mit dem des Partners (r=0,08; p=0,16).
Schlussfolgerungen: Es ergeben sich Hinweise auf eine zeitliche Variabilität des positiven DC der Patienten, nicht jedoch für deren negatives DC. Das positive und negative DC der Partner ist über die Zeit stabil. Insbesondere das negative DC ist mit psychischer Belastung assoziiert.

➜ **Pankrath, Anna-Luise**
email: analupa@gmx.de

POSTER 278

Depression, Somatization and Posttraumatic Stress isorder in German Children Born of Occupation after WW II in comparison with a birth- cohort-matched general population sample

Social Medicine

Kaiser M[1], Kuwert P[2], Brähler E[3], Glaesmer H[1]

1 Abteilung für Medizinische Psychologie und Medizinische Soziologie, Universität Leipzig
2 Klinik für Psychiatrie und Psychotherapie der Ernst-Moritz-Arndt Universität Greifswald am Helios- Klinikum Stralsund
3 University Medical Center of the Johannes Gutenberg University Mainz, Clinic for Psychosomatic Medicine and Psychotherapy, Mainz, Germany

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objectives: At the end of World War II and during the first decade after the end of the warnumerous children (children born of war) were fathered in intimate contacts between Germanwomen and foreign soldiers. So far, the experiences of these German "occupation children"were described in case reports and from historical perspective using oral history approachesor archival studies. Research on psychosocial consequences of growing up as a German"occupation child" was missing so far.
Methods: This study examines traumatic experiences, posttraumatic stress disorder (PTSD),somatization and depression in the German "occupation children" (N=155) using self-reportinstruments (Posttraumatic Diagnostic Scale (PDS); Patient Health Questionnaire(PHQ)).The findings will be compared with representative data from the general population.
Results: German "occupation children" showed significantly higher prevalence of traumaticexperiences, higher one-month prevalence rates of full and partial PTSD I, depression andsomatization.
Discussion: We know that "occupation children" often grew up under difficult conditions (e.g.poverty, single mothers, stigmatization). Even decades later, they show higher rates ofdepression, somatization and posttraumatic stress. These findings underline the complexand long-term impact of these difficult social, financial and familial conditions.
Key words: Children born of war, occupation children, aversive childhood experiences,psychosocial consequences, mental distress, posttraumatic stress

➜ **Kaiser, Marie**
email: marie.kaiser@medizin.uni-leipzig.de

POSTER 279

Sexual Reproductive Health Service Utilization of Young Disabled People in Ethiopia

Social Medicine

Kassa T[1], Luck T[1,2], Michel M[1], Luppa M[1], Birru S[3], Riedel-Heller S[1]

1 Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP), Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
3 School of Medical Laboratory Sciences, Faculty of Medicine, Addis Ababa University, Addis Ababa, Ethiopia

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: In Ethiopia, delivery of sexual reproductive health services (SRHS) to young people with disability (YWPD) is poorly understood, as such people are often marginalized and not recognized as being sexual. This study therefore aimed to assess the SRHS utilization and associated factors of YPWD in Ethiopia.
Methods: A cross-sectional survey was conducted in 2012. Data were collected by trained interviewers using a standardized questionnaire covering socio-demographic information as well as information on SRHS utilization.
Results: Only one-fourth of the YPWD (26.1%) had ever visited a SRHS. Main reasons for SRHS utilization stated by the respondents were to get contraceptives (48.1%), to get condoms (21.2%), and HIV counseling and testing (21.2%). 62.9% of the sexually active YPWD had ever used a modern contraceptive method, 54.3% had ever used a condom. 56.1% of the participants were ever tested for HIV. Regarding type of SRHS, most of the YPWD (68.5%) stated that they would prefer governmental facilities. Main reasons for not utilizing SRHS were inconvenience of the health institution (48.8%) followed by poor handling and scolding of the service provider (22.1%).
Conclusions: This study revealed that many young people with disability in Ethiopia experience barriers to access SRHS, particularly due to inconvenient health institutions and poor handling of service providers. This has a significant impact on the sexual and reproductive health of this group of the population and confirms the need to intervene on the available and upcoming SRHS and programs to make them youth and disability friendly.

➜ **Kassa, Tigist Alemu**
email: tigist.alemukassa@medizin.uni-leipzig.de

POSTER 280

Sexual and Reproductive Health of Young People with Disability in Ethiopia: A Study on Knowledge, Attitude and Practice

Social Medicine

Kassa T[1], Luck T[1,2], Bekele A[3], Riedel-Heller S[1]

1 Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP), Universität Leipzig
2 LIFE-Leipziger Forschungszentrum für Zivilisationserkrankungen, Universität Leipzig
3 Gondar College of Medicine and Health Sciences, School of Medicine, University of Gondar, Gondar, Ethiopia

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objective: As is common in developing countries, in Ethiopia young people with disabilities (YPWD) are more likely than the general population to be illiterate, unemployed and impoverished. They often lack equal access to information and education for reasons ranging from physical access to services to varied special learning needs. Very little is known about knowledge, attitude and practice (KAP) of YPWD regarding sexual and reproductive health (SRH) related issues. We, therefore, aimed to assess the KAP of 426 YPWD in Ethiopia.

Methods: A cross-sectional survey was conducted in 2012. Data were collected by trained interviewers using a structured questionnaire covering socio-demographic information, as well as information on KAP regarding SRH.

Results: Only 64.6% of YPWD were aware of SRH services. Radio and TV were mentioned as the main sources of information by 62.2% of the participants. 77.9% had never had a discussion about SRH topics with their parents. Even though 96.7% of the respondents had heard about HIV, 88% had poor knowledge about ways of preventing HIV. Perception of the risk of getting infected with HIV was found to be generally low in YPWD; only 21.6% believed that they were at risk of acquiring HIV.

Conclusions: Our study, in general, demonstrated that there is a lack of comprehensive knowledge, appropriate practice and favorable attitude of YPWD regarding different SRH-related issues. Our findings thus clearly indicate the need for strategies and programs to raise SRH-related awareness and to help YPWD to develop the appropriate skills and attitudes needed for a healthy reproductive life.

➜ **Kassa, Tigist Alemu**
email: tigist.alemukassa@medizin.uni-leipzig.de

POSTER 281

Determinanten der Lebensqualität von bandscheibenoperierten Patienten: eine Längsschnittstudie.

Social Medicine

Mücke M[1], Löbner M[1], Stein J[1], Konnopka A[2], Meisel H[3], Günther L[4], Meixensberger J[5], Stengler K[6], König H[2], Riedel-Heller S[1]

1 Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP), Universität Leipzig
2 Institut für Medizinische Soziologie, Sozialmedizin und Gesundheitsökonomie, Universitätsklinikum Hamburg-Eppendorf
3 Klinik für Neurochirurgie, BG-Kliniken Bergmannstrost, Halle (Saale)
4 Klinikum St. Georg gGmbH, Klinik für Neurochirurgie, Leipzig
5 Klinik und Poliklinik für Neurochirurgie, Universität Leipzig
6 Klinik und Poliklinik für Psychiatrie und Psychotherapie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Hintergrund: Bandscheibenvorfälle sind häufig Ursache für akute und chronische Rückenschmerzen. Ziel dieser Untersuchung war es, die Entwicklung der Lebensqualität (LQ) von Patienten nach einer Bandscheibenoperation im Zeitverlauf zu untersuchen und Determinanten zu identifizieren, die die LQ in diesem Zeitraum beeinflussen.
Methodik: Es wurden 534 infolge eines Bandscheibenvorfalls operierte Patienten wenige Tage nach der OP (T0) persönlich befragt und 3 Monate (T1), 9 Monate (T2) und 15 Monate (T3) nach der OP telefonisch interviewt. Erhoben wurden LQ (mit dem Fragebogen SF-36) sowie soziodemographische, arbeitsbezogene, psychologische und krankheitsbezogene Variablen. Statistische Verfahren waren T-Tests, Wilcoxon-Tests und multiple lineare Regressionen.
Ergebnisse: Die körperliche LQ verbesserte sich nach der OP signifikant. Der Referenzwert der Allgemeinbevölkerung wurde dabei nicht erreicht. Die psychische LQ war zu T1, T2 und T3 besser als die der Allgemeinbevölkerung. Assoziiert mit einer besseren körperlichen LQ ($p < 0{,}001$) waren: Erwerbstätigkeit (T1, T3), geringe Schmerzintensität (T1, T3) und keine vorherige Bandscheibenoperation (T3). Determinanten einer besseren psychischen LQ ($p < 0{,}001$) waren: geringe Angst (T1, T3), geringe Depressivität (T3) und berufliche Zufriedenheit (T1, T3).
Schlussfolgerungen: Den Ergebnissen zufolge verursachen Bandscheibenvorfälle mit Operationsindikation langfristige Einschränkungen der körperlichen LQ, haben aber geringeren Einfluss auf die psychische LQ. Durch frühzeitiges Screening könnten Patienten mit erhöhtem Risiko rechtzeitig identifiziert und gezielter behandelt werden.

➜ **Mücke, Manuel**
email: manuel.muecke@medizin.uni-leipzig.de

POSTER 282

GTG-banding, SKY, genome-wide high resolution SNP-array, gene expression of three gangliogliomas and review of the literature

TRM – Translational Regenerative Medicine

Xu L[1,2], Holland H[2], Kirsten H[3,4], Ahnert P[2,4], Krupp W[1], Bauer M[5], Schober R[5], Müller W[5], Fritzsch D[6], Meixensberger J[1], Koschny R[7]

1 Klinik und Poliklinik für Neurochirurgie, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
3 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig
4 Institut für Medizinische Informatik, Statistik und Epidemiologie (IMISE), Universität Leipzig
5 Abteilung Neuropathologie, Universität Leipzig
6 Abteilung für Neuroradiologie, Universität Leipzig
7 Abteilung Innere Medizin IV, Universität Heidelberg

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Gangliogliomas (WHO I or III) are classified as well differentiated and slowly growing neuroepithelial tumors, composed of neoplastic mature ganglion and glial cells. It is the most frequent tumor entity observed in patients with long-term epilepsy. Comprehensive cytogenetic and molecular cytogenetic data including high-resolution genomic profiling (SNP-array) of gangliogliomas are scarce but necessary for a better oncological understanding of this tumor entity. We analyzed genomic alterations of three gangliogliomas using GTG-banding and SKY in combination with SNP-array and gene expression array experiments. By GTG and SKY, we confirmed frequently detected chromosomal aberrations (losses within chromosomes 10, 13, and 22; gains within chromosomes 5, 7, 8, and 12), and identified so far unknown genetic aberrations like the unbalanced non-reciprocal translocation t(1;18)(q21;q21). Interestingly, we report on the second so far detected ganglioglioma with ring chromosome 1. Analyses of SNP-array data from two of the tumors and respective germline DNA (peripheral blood) identified few small gains and losses and a number of copy neutral regions with loss of heterozygosity (LOH) in germline and in tumor tissue. In comparison to germline DNA, tumor tissues did not show substantial regions with significant loss or gain or with newly developed LOH. Gene expression analyses of tumor-specific genes revealed similarities in the profile of the analyzed samples regarding different relevant pathways. Taken together, we described overlapping but also distinct and novel genetic aberrations of three gangliogliomas.

➜ **Xu, Li-Xin**
email: lixin.xv@gmail.com

POSTER 283

Modulatory effects of starPEG-heparin-based hydrogels on human M1 macrophage functions

TRM – Translational Regenerative Medicine

Lohmann N[1,2], Wagner F[1,2], Forstreuter I[1,2], Schirmer L[2,3], Freudenberg U[2,3], Werner C[2,3], Simon J[1,2], Franz S[1,2]

1 Department of Dermatology, Venerology and Allergology, Leipzig University, Leipzig, Germany
2 Collaborative Research Center (SFB-TRR67) Matrixengineering, Leipzig and Dresden, Germany
3 Leibnitz Institute of Polymer Research Dresden, Max Bergmann Center of Biomaterials Dresden, Center for Regenerative Therapies Dresden

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Impaired wound healing is a problem of immense clinical and economic relevance. Persistent inflammation in impaired wound healing is primarily driven by unresisted inflammatory M1 macrophage (*inf*M1) activation. Therefore, the principal objective of this project is the development of immunomodulating wound dressings capable to bring unopposed inflammation under control by repressing *inf*M1 activity and thus enabling inflammatory resolution. Here, we use biohybrid starPEG-heparin-based hydrogels. They can be used as carrier for growth factors and have been shown to encourage angiogenesis when loaded with VEGF and FGF-2. Since both reduction of uncontrolled inflammation and induction of vascularization are suggested to improve wound healing, we tested different 3D starPEG-heparin-based hydrogels with respect to their immunomodulating capacity on *inf*M1.

Our results show that starPEG-heparin-based hydrogels functionalized with RGD adhesion sites allow survival and adhesion of *inf*M1. They modulate the cytokine response of *inf*M1 via two manners: 1) downregulation of cytokine expression and release in *inf*M1 (e.g. IL-12p40, TNFa, IL-8, MCP-1) and 2) binding of cytokines released from *inf*M1 (e.g. IL-12p40, IL-8, MCP-1). Interestingly, modulation of the cytokine response is determined by the sulfation level of heparin.

From these results we conclude that starPEG-heparin-based hydrogels provide immunomodulating capacities on *inf*M1 which may be fine-tuned by usage of heparin derivatives with adjusted levels of sulfation. We suggest that the hydrogels may be capable to modulate unopposed *inf*M1 activity *in vivo*.

➜ **Lohmann, Nadine**
email: nadine.lohmann@medizin.uni-leipzig.de

POSTER 284

Tissue engineered ureteral grafts: Biocompatible crosslinked porcine ureteral scaffolds

TRM – Translational Regenerative Medicine

Koch H[1], Metzger R[2], Ossmann S[3], Emmrich F[1,4], Sack U[1,4], Boldt A[1,4]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
2 Salzburg County Hospital, Department of Pediatrics and Adolescent Medicine, Salzburg, Austria
3 Clinic for Cardiac Surgery, Heart Center, Universität Leipzig
4 Institut für Klinische Immunologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Question: The reconstruction of severe ureter defects is often associated with postoperative complications. Tissue engineered decellularized porcine ureters (PUS) could represent an alternative therapeutic option. This study aimed to investigate biocompatible PUS for tissue engineering a ureteral graft.
Methods: Ureters were obtained from pigs and decellularized. The success of decellularization, scaffold composition and morphology were characterized histologically/immunohistologically. *In vitro*: PUS were crosslinked with carbodiimide (CDI), genipin (GP) glutaraldehyde (GA) or left untreated. PUS in each group were seeded with cells lines (Caco2, LS48, 3T3) or native smooth muscle cells (SMC). *In vivo*: PUS were implanted subcutaneously into rats. Depending on scaffold pre-treatment (untreated, GP, GA, CDI), number and type of infiltrating cells were determined to quantify the host response after 1, 9 and 30 days.
Results: Acellular PUS show intact matrix morphology and composition. Furthermore, crosslinking with GP and CDI increased the number of ingrown 3T3 and SMC. *In vivo*, explants were infiltrated with a combination of fibroblasts and macrophages, whereas predominantly M2 anti-inflammatory macrophages were present after CDI crosslink at day 30. In contrast to MMP3, TIMP1 could not be detected.
Conclusions: In this study, we demonstrated the potential of PUS as tissue engineered ureteral grafts. Crosslinking with CDI may support a faster remodeling process indicated by M2-macrophages, MMP3 and the absence of TIMP1. Further investigations in mechanical characteristics will be necessary to manufacture a ureteral graft.

➜ **Koch, Holger**
email: holger.koch@trm.uni-leipzig.de

POSTER 285

Scleral crosslinking with riboflavin and blue light – a promising therapeutic approach to treat progressive myopia -

TRM – Translational Regenerative Medicine

Göhler C[1,2], Körber N[1,2], Koch C[2,3], Rattunde U[2], Reichenbach A[1], Wiedemann P[3], Francke M[1,2], Karl A[1]

1 Paul-Flechsig-Institut für Hirnforschung, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
3 Klinik und Poliklinik für Augenheilkunde, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Pathologic myopia is characterised by an excessive eye growth leading to severe short-sightedness, chorioretinal degenerations, retinal tears and blindness. Application of riboflavin and blue light, as a crosslinking method for scleral tissue (SXL), has been proved to increase scleral stiffness and to inhibit eye elongation. Hence, it might be a promising therapeutic approach to treat progressive myopia.

Our rheological measurements of isolated rabbit scleral patches revealed stiffening effects after SXL. Safety and efficacy parameters were determined using histological methods and ultrasonic A scans. Young animals treated with riboflavin and a minimal effective blue light energy dose of 10 mW/cm² displayed a significant reduction of the eye growth. Using higher light intensities (> 400 mW/cm²), we observed altered scleral collagen fibril profiles and activated scleral fibroblasts as signs of remodelling processes. Therefore, we characterised expression profiles of cellular markers and relevant enzymes involved in extracellular matrix (re)organisation by means of immunocytochemistry in cell cultures from human and rabbit scleral tissue.

Our results confirm the idea that SXL by riboflavin and blue light is an applicable method to increase biomechanical stiffness of scleral tissue and thus, SXL might be a treatment for progressive myopia. In the future we have to investigate the influence of relevant enzymes on remodelling processes after SXL to optimise the therapeutic approach. Furthermore, we develop a special substance application and irradiation system adapted to the patient's eyes for a future clinical SXL therapy.

Funding: formel1

➜ **Göhler, Claudia**
email: claudia.goehler@trm.uni-leipzig.de

POSTER 286

From Hair to Repair: Potentials of MSCORS in Chondrogenesis and Cartilage Regeneration

TRM – Translational Regenerative Medicine

Li H[1], Schneider M[1], Simon J[2], Savkovic V[1]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
2 Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Human hair follicle Outer Root Sheath (hf-ORS) is responsible for hair cycling and skin regeneration containing heterogeneous populations of stem cells and progenitors. Mesenchymal Stem Cells from the Outer Root Sheath (MSCORS) possess high differentiation competence and therapeutical potentials as an alternative stem cell source. We have developed a non-invasive autologous stem cell source using plucked hair follicles, and identified the chondrogenic potentials of MSCORS for Translational Regenerative Medicine. Obtaining the MSCORS with ORS technologies, we have isolated, cultivated, and characterized MSCORS, as well as differentiate towards chondrogenic lineage via 3D cells culture and tissue engineering. MSCORS exhibit MSC-like properties with various MSC markers in gene and protein level. Through immune staining, different cell populations and location were identified in ORS, which are highly viable with high multipotency and superior stemness. Using human adipose-derived MSC and 3D cell culture scaffolds, we have successfully established a standardized procedure for chondrogenic differentiation with promising chondrogenic gene expressions and cartilaginous ECM accumulation, confirming the functional chondrogenesis. Our future work will focus on rapid MSCORS scale-up with phenotype maintenance and full characterizations, as well as optimization of chondrogenesis via 3D cell culture and tissue engineering. With therapeutical potentials and efficiency of MSCORS, the functional Superficial Articular Cartilage are the ultimate gateways towards the clinical applications on Osteoarthritis treatments.

➜ **Li, Hanluo**
email: hanluo.li@trm.uni-leipzig.de

POSTER 287

Prevention of Graft versus Host Disease (GvHD) by Antisense mediated ex vivo Gene Therapy

TRM – Translational Regenerative Medicine

Przybylski S[1], Hilger N[2], Gasch M[1], Ebert M[1], Ewe A[3], Fricke S[2], Aigner A[3], Burkhardt J[1]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
2 Fraunhofer-Institut für Zelltherapie und Immunologie, IZI Leipzig
3 Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

GvHD is a common and fatal complication of allogenic hematopoietic stem cell transplantation. Donor T-cells react against host antigens and initiate a cytokine release, which induces tissue damage in the host.To prevent GvHD, we applied chemically modified antisense oligonucleotides (AON) in combination with modified polyethylenimine (PEI,AG Aigner) to the transplant *ex vivo* in a murine model of GvHD.

AONs were designed to target T-cell receptor genes cd4 or cd28 and tested *in vitro*.For this, murine spleen cells were transfected with AONs and stimulated with conA or cd3e/cd28 antibodies. Subsequently, AONs were then tested in a murine model of GvHD based on transplantation of *ex vivo* transfected donor spleen and bone marrow cells into irradiated host mice. Mice were scored daily, hemograms and blood flow cytometry (FC) were done bi-weekly. Upon sacrifice, tissues were preserved for RNA extraction and histological analysis.

AON transfected cells were able to reduce surface receptors up to 50%, as well as cytokine expression and proliferation. *Ex vivo* application of AON significantly increased survival. Engraftment of donor cells was detected by FC analyses and hemograms showed successful restoration of white blood cell count according to decrease after irradiation. Results of real-time PCR analysis revealed reduced cytokine expression in spleen and colon.

We conclude that transfection of a-cd4 and a-cd28 AON by PEI into a transplant *ex vivo* was able to prevent GvHD. In the future, AONs might also be applied to treat GvHD by *in vivo* application and results might be even transferred to other T-cell mediated immune disease.

→ **Przybylski, Susanne**
email: susanne.przybylski@trm.uni-leipzig.de

POSTER 288

Mid part of the Outer Root Sheath of hair follicle harbours a substantial regenerative potential

TRM – Translational Regenerative Medicine

Schneider M[1]

1 Translationszentrum für Regenerative Medizin (TRM) Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The Outer Root Sheath (ORS) of human hair follicle harbours a collection of developmentally potent adult stem cells and precursors. The highest developmental potential is ascribed to the upper part of the ORS, especially the bulge region of the hair follicle. Since the bulge region is anatomically attached to the piliary muscle, it is retained in the skin. Nonetheless, developmental potential of the mid and lower parts of ORS, available by plucking, is higher than initially thought. For the purposes of treating depigmentation disorders such as Vitiligo, our Group developed a method for melanocyte cultivation from the mid ORS part.

We investigated the developmental potential of lower, middle and upper part of hair follicles by analyzing gene expression (pluripotency, neural and melanocyte lineage) as well as the functionality of the ORS derived melanocytes. Furthermore, in order to identify candidates for biocompatible graft carriers, we are working on a palette of 3D niches.

Since melanocytes descend from neural-crest derived stem cells, we tested the relative expression of *NES* and *NGFR* as neural lineage markers across ORS. The expression of these two genes was the highest in the middle part of the follicle. Moreover, expression of *LGR6* in the middle ORS part indicates presence of cells with remarkably high variety of endpoints. This emphasizes our hypothesis, that not only the bulge region but also the middle part of the ORS sustains a very high developmental potential. Melanocytes can be differentiated and display melanotic features, which were increased in different 3D niches imitating the native epidermis.

➜ **Schneider, Marie**
email: marie.schneider@trm.uni-leipzig.de

POSTER 289

Tumorigenicity and cytogenetic analysis on chondrocyte cultures using GTG-banding, SKY, and locus-specific FISH

TRM – Translational Regenerative Medicine

Wallenborn M[1], Hantmann H[1], Rudolf D[1], Ahnert P[1,2], Holland H[1]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
2 Institut für Medizinische Informatik, Statistik und Epidemiologie (IMISE), Universität Leipzig[

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Objectives: The development of cell-based therapy raises the question whether the application of cell-based products to humans is safe. Therefore, it is useful to determine the genetic stability at several times during manufacturing process.
Material and Methods: In a preclinical study, we analyzed 372 chondrocyte samples (78 adherent cultures and 294 spheroids) from six donors using Trypsin-Giemsa staining (GTG-banding), spectral karyotyping (SKY) and locus-specific fluorescence in situ hybridization (FISH). Further analyses are in progress.
Results: For at least 3 passages, our genetic analyses revealed no significant chromosomal abnormalities applying these techniques [e.g. fra(4)(q31)- only single event in passage 3 of PM 4]. We were able to identify clonal occurrence of polyploid metaphases and endomitoses with increasing cultivation time (passage 4–10). Furthermore, we detected Y-chromosomal losses in the two male donors with increasing frequency during cultivation time. Interestingly, in one donor we identified trisomy of chromosomes 1,7,8,12, and translocation of chromosomes 7 and 9, which are characteristic chromosomal aberrations for extraskeletal myxoid chondrosarcoma.
Conclusion: Our results attest to the necessity of (molecular) cytogenetic analyses at certain cultivation times in preclinical studies. More investigations are needed to evaluate the potential tumorigenic risk for osteoarthritic patients to an extension of articular chondrocyte implantation.

➜ **Wallenborn, Marco**
email: marco.wallenborn@trm.uni-leipzig.de

POSTER 290

MONITORING OF PEI TRANSFECTION NANOPARTICLES

TRM – Translational Regenerative Medicine

Ebert M[1], Przybylski S[1], Ewe A[2], Köberle M[1], Polte T[3], Burkhardt J[1], Aigner A[2], Gasch M[1]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
2 Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Universität Leipzig
3 Helmholtz-Zentrum für Umweltforschung Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Successful transfer of genetic information is challenging and to optimize *in vivo* transfection it is essential to determine basic pharmacological parameters, such as toxicity and biodistribution.
Here, we applied different detection methods to analyze biodistribution of the polycationic transfection reagent polyethylenimine (PEI) in mice: iron-oxide PEI was injected in murine organs *ex vivo* to observe suitability of X-ray microtomography (μCT) monitoring and intratracheally applied iron-oxide PEI was analyzed post mortem in lung tissue by Prussian Blue stain. Suitability of fluorescent labeled PEI was established *in vitro* and transfection rate was monitored over time by flow cytometry. *In vivo* biodistribution of fluorescence labeled PEI was investigated following i. p. application by flow cytometry of separated tissue.
Iron-oxide PEI nanoparticles were detected by μCT in a 16 fold dilution series and in *ex vivo* injected murine organs. Following intratracheal application, magnetic PEI nanoparticles were detectable in murine lung tissue after Prussian blue stain. Murine T cells transfected with fluorescence labeled PEI were analyzed by flow cytometry showing a transfection rate of over 80% after 24 hours of transfection and analysis of PEI biodistribution showed that primarily lung tissue was targeted with approximately 90% transfected cells.
In this study we successfully demonstrated suitability of monitoring *in vivo* transfected PEI in murine tissues and cells with different detection methods such as X-ray microtomography, Prussian Blue stain, and flow cytometry.

➜ **Przybylski, Susanne**
email: susanne.przybylski@trm.uni-leipzig.de

POSTER 291

Neue nicht-klinische Sicherheitsprüfungen für ATMPs

TRM – Translational Regenerative Medicine

Schellenberg K[1], Kämmerer I[1], Sawitzky D[1]

1 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Der Fortschritt in der Translationalen Regenerativen Medizin eröffnet innovative Heilungsansätze basierend auf einer neuen Art von Arzneimitteln, den sogenannten „Arzneimittel für Neuartige Therapien" (ATMPs). Zu diesen „neuen Arzneimitteln" zählen gentherapeutische Produkte, somatische Zelltherapien oder biotechnologisch bearbeitete Gewebeprodukte. Per Gesetz sind ATMPs regulatorisch den klassischen Arzneimitteln gleichgestellt. Damit werden im Rahmen des Zulassungsverfahrens auch für ATMPs nicht-klinische Sicherheitsprüfungen entsprechend der Richtlinien der „Guten Laborpraxis" (GLP) notwendig.

Daraus ergibt sich die Forderung nach einer neuen Art von GLP-konformen Prüfungen, welche unter anderem Fragen zur Zellidentität, -reinheit, Zellmigration und In-vivo Stabilität bestimmen. So ist das Potenzial der Tumorbildung (Tumorigenität) ein zentrales Sicherheitsproblem bei zellbasierten Therapien, da primäre oder stabile Zellkulturen *in vivo* progressiv wachsende Tumore hervorrufen können.

Die am TRM ansässige Prüfeinrichtung für nicht-klinische Sicherheitsprüfungen hat neben anderen Prüfsystemen einen In-vitro Tumorigenitäts Assay entwickelt. Das hier vorgestellte Verfahren beruht auf dem Zusammenhang zwischen dem tumorbildendem Potential einer Zelle *in vivo* und dem verankerungsunabhängigen Wachstum einer Zelle in-vitro. Gleichzeitig werden Zellen in Kultur auf Kontaminationen mit Mykoplasmen getestet.

Der In-vitro Tumorigenitätstest ermöglicht somit in einer schnellen in-vitro Bestimmung die sensitive Detektion des tumorigenen Potentials von primären Zellen (ATMPs) im Vorfeld zu aufwendigen und kostenintensiven Tierstudien.

➜ **Schellenberg, Katja**
email: katja.schellenberg@trm.uni-leipzig.de

POSTER 292

Makrozirkulatorische Auswirkungen einer MSC-Therapie nach ausgedehnter Leberresektion im Schwein

TRM – Translational Regenerative Medicine

Tautenhahn HM[1,2], Brückner S[1], Brach J[1], Pankow F[1], Uder C[1], Gittel C[1,3], Hempel M[1], Berthold C[1,2], Lange U[1], Broschewitz J[1], Bartels M[1], Pietsch U[1,4], Christ B[1,2]

1 Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Sektion Bariatrische Chirurgie, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
3 Veterinär-Anatomisches Institut, Universität Leipzig
4 Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Aufgrund hämodynamischer Veränderungen während ausgedehnter Leberresektionen werden hohe Anforderungen an das anästhesiologische Management gestellt. Oft kommt es zu schweren Kreislaufbeeinträchtigungen oder dem SIRS. Mesenchymale Stammzellen (MSC) sind eine vielversprechende Therapieoption, um die Leberfunktion zu unterstützen. Zur Translation dieses Verfahrens in die Klinik sollte daher geprüft werden, ob die systemische oder portalvenöse Applikation der Zellen die hämodynamischen Verhältnisse beeinflusst. Zur Untersuchung dieser Veränderungen wurden die Versuchstiere in 3 Gruppen (n=4) unterteilt [Gruppe 1 zentralvenös (ZV), Gruppe 2 portalvenös (PV), Gruppe 3 PBS(ZV)]. Während des Versuchs wurden Vitalparameter, wie systolischer-, diastolischer- und mittlerer arterieller Blutdruck (MAD) gemessen. Das Herzzeitvolumen (HZV) und der mittlere Druck der *A. pulmonalis* (MPAP) wurden bestimmt. Durch die Applikation von Noradrenalin wurde der MAD bei 80 mmHg gehalten. In keiner der untersuchten Gruppen konnte ein signifikanter Anstieg des MPAP gemessen werden. Darüber hinaus konnte festgestellt werden, dass die zentralvenöse Applikation der MSC den Katecholaminbedarf signifikant verringert und zu einer Stabilisierung des HZV beiträgt. Somit können die MSC die hämodynamischen Verhältnisse stabilisieren. Die Gabe von MSC sowohl portalvenös als auch zentralvenös appliziert, hat keinen Einfluss auf die Drücke der pulmonalen Strombahn als starker Hinweis für das Ausbleiben von Embolien. Der geringere Katecholaminbedarf lässt auf einen parakrinen Wirkmechanismus der MSC in Bezug auf die Systemstrombahnveränderungen schließen.

Funding: formel1

➜ **Tautenhahn, Hans-Michael**
email: hans-michael.tautenhahn@medizin.uni-leipzig.de

POSTER 293

Mesenchymale Stammzelltherapie zur Unterstützung der Leberfunktion nach ausgedehnter Resektion im Schwein

TRM – Translational Regenerative Medicine

Tautenhahn HM[1,2], Brückner S[1], Pankow F[1], Uder C[1], Brach J[1], Gittel C[1,3], Hempel M[1], Berthold C[1,2], Lange U[1], Broschewitz J[1], Dietel C[1], Bartels M[1], Pietsch U[1,4], Christ B[1,2]

1 Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Universität Leipzig
2 Translationszentrum für Regenerative Medizin (TRM), Universität Leipzig
3 Veterinär-Anatomisches Institut, Universität Leipzig
4 Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Nach ausgedehnter Leberresektion muss das verbleibende Restlebergewebe alle metabolischen Funktionen der Leber übernehmen. Das Operationstrauma und die hohen regenerativen Ansprüche an das Restlebergewebe können zur Organdysfunktion und schließlich zum akuten Leberversagen (POLF) führen. Eine neue Therapieoption könnte die Transplantation von mesenchymalen Stammzellen (MSC) zur regenerativen Unterstützung des Restlebergewebes sein. In einem Großtiermodell wurde eine 2/3 Hepatektomie mit einer warmen Ischämiezeit (150 min) durchgeführt, wodurch ein akutes postoperatives Leberversagen (POLF) ausgelöst wurde. Die Wirkung systemisch oder portalvenös applizierter MSC auf die Leberfunktion sollte evaluiert werden. Dazu wurden Schweine der deutschen Landrasse in 3 Gruppen (n=4) unterteilt. Eine Gruppe bekam die Zellen zentralvenös (ZV), eine Gruppe portalvenös (PV) und eine Gruppe bekam PBS verabreicht. Die Leberfunktion wurde mittels Indocyaningrün (ICG) und dem Limon System (Fa Pulsion) über den Versuchszeitraum von 24 h gemessen. Es konnte für beide MSC Gruppen (ZV und PV) eine signifikant verbesserte Leberfunktion gegenüber der PBS Gruppe gezeigt werden. Darüber hinaus zeigte die Applikation von MSC auch eine signifikante Verbesserung der leberspezifischen Funktionsparameter wie INR, Ammoniak und Serumtransaminasen. Sowohl die portalvenöse als auch die zentralvenöse Applikation der MSC führte zur signifikanten Verbesserung der Leberfunktion und klinisch relevanter hepatobiliärer Parameter. Somit stellt die Stammzelltransplantation eine neue vielversprechende Therapieoption zur Vermeidung des postoperativen Leberversagens dar.

Funding: formel1

➜ **Tautenhahn, Hans-Michael**
email: hans-michael.tautenhahn@medizin.uni-leipzig.de

POSTER 294

Human gastric cancer slice cultures, a future bridge between preclinical research and clinical practice?

Tumor Targeting

Körfer J[1,2], Kallendrusch S[2], Merz F[2], Schopow N[2], Kubick C[3], Kassahun W[4], Schumacher G[5], Möbius C[5], Gaßler N[6], Eckmann C[7], Weimann A[8], Wiechmann V[9], Geister D[9], Aigner A[10], Lordick F[1], Bechmann I[2]

1 Universitäres Krebszentrum (UCCL), Universität Leipzig
2 Institut für Anatomie, Universität Leipzig
3 Institut für Pathologie, Universität Leipzig
4 Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Universität Leipzig
5 Klinik für Viszeralchirurgie, Städtisches Klinikum Braunschweig
6 Institut für Pathologie, Städtisches Klinikum Braunschweig
7 Klinik für Allgemein-, Viszeral- und Thoraxchirurgie, Klinikum Peine
8 Klinik für Allgemein- und Viszeralchirurgie, Klinikum St. Georg, Leipzig
9 Institut für Pathologie, Klinikum St. Georg, Leipzig
10 Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Gastric cancers (GC) are heterogeneous and aggressive tumors, having an unpredictable response to cytotoxic treatment. Therefore, new research methods allowing for the analysis of chemotherapy resistance and tumor heterogeneity are urgently needed. Here, we describe a novel technique by which GC specimens can be cultured *in vitro* and maintained in their own microenvironment.

Methods: Using a tissue chopper, fresh surgical tissue samples from GC were cut in 400 μm slices and cultivated in 6-well plates for up to 6 days. The slices were processed for routine histopathology and immunohistochemistry. Cytokeratin stains (CK8 and AE1/3) were applied for determining tumor cellularity, ki-67 for proliferation, and cleaved caspase 3 staining for apoptosis. The slices were analyzed under naïve condition and following *in vitro* exposure to 5-FU, cisplatin or docetaxel over a period of 2–4 days.

Results: GC slice cultures from resection specimens revealed a good preservation of tissue morphology and tumor cell integrity during the culture period in most cases. After chemotherapy, a significant loss of tumor cellularity and an increase of apoptotic cells were observed in cultured tissue, although a systematic and reproducible read-out still needs to be established.

Conclusion: Slice cultures of GC were successfully established. They can be used to examine mechanisms of drug-resistance and analyze tumor heterogeneity in patient samples. They may provide a unique and powerful *in vitro* platform for the determination of sensitivities of a given tumor to specific drugs.

➜ **Körfer, Justus**
email: justus.koerfer@medizin.uni-leipzig.de

POSTER 295

Endothelial EphB4 mediates vascular resistance to antiangiogenic therapy

Tumor Targeting

Markel M[1]

1 Klinik und Poliklinik für Kinderchirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction: Antitumor effects of antiangiogenic treatment are limited by vascular resistance mechanisms. The underlying molecular pathways are currently unknown. It was the aim to analyze the role of the Ephrin B2-EphB4 pathway in mediating vascular resistance to antiangiogenic treatment.
Material and Methods: An ecotropic retroviral vector (pLXSN) encoding full length EphB4 (EphB4 wt) was established and Phoenix E virus producing cells were coimplanted with SF126 glioma cells in dorsal skinfold chambers (N=5) and sc xenografts (N=5). Intravital microscopy was performed focusing on vessel density (TVD). Subcutaneous tumor growth was assessed when tumors reached 50mm^3. Sunitinib (SU) treatment (40mg/kg BW) was applied for 6 days. Immunohistochemistry included Pecam-Desmin staining.
Results: SU led to reduced TVD in control tumors (NaCl: 100± 8 cm/cm^2, SU: 40± 2 cm/cm^2). In EphB4wt tumors, TVD was not reduced by SU therapy (NaCl: 98± 34cm/cm^2, SU: 97± 19 cm/cm^2). Correspondingly, EphB4 wt tumors were resistant to SU therapy in sc xenografts (Control: 81± 24,6mm^3, EphB4wt: 136± 55,8mm^3. Tumor vessels in EPHB4 wt tumors were characterized by reduced P (Control: 0,86± 0,03, EphB4: 0,76± 0,07) and increased pericyte-endothelial cell interactions (Control: 0,41± 0,13, EphB4: 0,82± 0,02).
Conclusion: EphB4 mediates resistance to antiangiogenic treatment by stabilizing vessel density and by altering pericyte-endothelial cell interactions.

Data from Department of Neurosurgery, Universitätsmedizin Charite, Berlin, Germany

➜ **Markel, Moritz**
email: moritz.markel@medizin.uni-leipzig.de

POSTER 296

Msh2 conditional knockout mice show microsatellite instability (MSI) in intestinal stem cell organoids

Tumor Targeting

Keyßelt K[1], Kreutzmann T[1], Buske P[2], Kerner C[1], Sittig D[1], Krohn K[3], Galle J[2], Aust G[1]

1 Department of Surgery, Research Laboratories, University of Leipzig, Leipzig, Germany
2 Interdisciplinary Center for Bioinformatics (IZBI) University of Leipzig
3 Interdisciplinary Center for Clinical Research Leipzig (IZKF), Core-Unit DNA Technologies, University of Leipzig, Leipzig, Germany

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Aim: 60 percent of patients with hereditary nonpolyposis colorectal cancer (HNPCC) have a mutated Msh2 gene leading to MSI. Here, we examined MSI in self-organizing, intestinal stem cell-derived organoids of Msh2 conditional knockout mice and analyzed whether the growth pattern and rate of these organoids correlate to the MSI status and mouse genotype.Methods: The growth of organoids of Msh2-/-, Msh2+/- and control Msh2+/+ mice was followed up by time-lapse microscopy. After growth, single organoids were investigated for their MSI status by three nucleotide repeat markers. Organoids were judged as stable (0) or unstable (1) in each marker to generate a MSI score.

Results: Normal organoids of Msh2-/- mice showed MSI scores higher than 2 irrespective of the age of the mice. MSI scores of normal Msh2+/- organoids were lower but significantly higher than that of control organoids. The marker allele size in normal organoids of Msh2+/- and markedly of Msh2-/- mice decreased compared to that of control mice.

The branched growth pattern known from control normal organoids was found in all types of mice. However, organoids of Msh2+/+ and Msh2+/- mice grew with a broad spectrum of growth rates, whereas the growth rates of Msh2-/- organoids represented the lower and upper bound of the spectrum observed in controls. Tumor-derived Msh2-/- organoids showed a cystic growth pattern, the highest growth rate and always a MSI score of 3.

Conclusion: The distribution of growth rates but not the pattern of normal intestinal organoids depends on the respective genotype. MSI is partially present in organoids of Msh2 carrier mice.

➜ **Keyßelt, Kerstin**
email: kerstin.keysselt@medizin.uni-leipzig.de

POSTER 297 **Effects of stromal hyaluronan on melanoma cells**

Tumor Targeting

Brazel C[1], Schmidt S[2], Käs J[2], Anderegg U[1]

1 Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Universität Leipzig
2 Institut für Experimentelle Physik I, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The tumour microenvironment is composed of tumour cells, fibroblasts, endothelial and infiltrating cells, released soluble mediators and extracellular matrix (ECM) and is crucial for tumour development. In malignant melanoma (MM) the stroma is typically rich in hyaluronic acid (HA), and MM cells stimulate synthesis in fibroblasts *in vitro*. HA is a major ECM-component promoting tumour angiogenesis, migration, and proliferation. However, the mechanisms behind the tumour promoting effects of HA remain poorly understood.

Here we aim to define the role of HA on tumour cells, either as a component of fibroblast-derived ECM or as a soluble ligand of the cells. We analysed how MM cells respond to different artificial and *in vivo*-like ECM on the levels of cell adhesion, proliferation and cell elasticity. We found that most MM cell lines spread well on fibronectin and collagen I, whereas HA alone impaired cell spreading substantially. On the other hand, physical cell stretcher studies revealed that HA may enhance the relaxation capability of tumour cells depending on CD44 expression probably resulting in increased flexibility and mobility of HA-exposed MM cells.

Further, we used fibroblast-derived ECM (Fb-ECM) to create a more *in vivo*-like environment. Immunofluorescence staining revealed that Fb-ECM were composed of fibrillar collagen I, fibronectin and HA. MM cells readily attached to Fb-ECM and showed increased proliferation compared to growth on fibronectin. Taken together, HA substantially modifies MM-cell properties and stromal HA synthesis is a potential issue of anti-metastatic intervention.

➜ **Brazel, Christina**
email: christina.brazel@medizin.uni-leipzig.de

POSTER 298

Potential implications of Pim kinases in aggressiveness of glioblastoma cells

Tumor Targeting

Weirauch U[1], Aigner A[1]
1 Abteilung für Klinische Pharmakologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The Pim family of proteins comprises three members (Pim1 – 3) of constitutively active serine/threonine kinases. These proto-oncogenes are involved in the regulation cell survival by accelerating cell cycle progression, reducing apoptosis, influencing cell metabolism, as well as increasing cell motility and invasion. Pim family members are frequently upregulated in solid tumors and malignant hematopoietic diseases and are associated with poor prognosis and drug resistance.

Glioblastoma multiforme (GBM) is the most common and aggressive form of malignant astrocyte tumors (WHO grade IV). After diagnosis, the patients' mean overall survival is about one year. This is due to the invasion of tumor cells into the surrounding tissue and their resistance to radiation and temozolomide chemotherapy. Thus, new treatment strategies are needed to improve the patients' survival and life quality.

In GBM, very little is known about the role of Pim kinases in tumor initiation and progression. There is first evidence that Pim kinases are overexpressed in this tumor entity. Previously, we reported the functional relevance of Pim1 in GBM cells. Pim1 knockdown led overall to antitumor-effects. Since Pim family members exhibit overlapping activities, we then extended our studies towards Pim2 and Pim3. Using RNA interference (RNAi), we knocked down the three Pim family members in GBM cell lines as well as in primary cells. Here, we present data, revealing that, in addition to Pim1, also Pim2 and Pim3 might be relevant in glioblastoma and contribute the aggressive nature of GBM cells.

→ **Weirauch, Ulrike**
email: ulrike.weirauch@medizin.uni-leipzig.de

POSTER 299

Resveratrol radiosensitize human medulloblastoma cell lines

Tumor Targeting

Patties I[1], Kortmann R[1], Glasow A[1]
1 Klinik und Poliklinik für Strahlentherapie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: In recent years, the natural plant polyphenol resveratrol (RV) attracted an increasing attention in tumor therapy. Thereby, RV has to been shown to exhibit tumor preventive as well as anticancer effects. These are of particular interest for the therapy of pediatric medulloblastoma (MB), as low-risk patients require a therapy focused on the reduction of late adverse effects (i. e. neurological and endocrine disorders), whereas patients belonging to the high-risk group (5-yr survival 13 %) urgently need a more intensive therapy to improve survival. In the present study, we analyzed RV-mediated changes on the clonogenic survival and proliferation of irradiated medulloblastoma cells. Furthermore, we investigated if RV may induce double-strand breaks (DSB), and if combined RV/irradiation (IR) treatment affects the number of potential tumor stem cells (TSC).
Results: The RV treatment of irradiated MB cells significantly decreased their clonogenic survival. Both, IR and RV alone, induced DSB. Examining the number of potential TSC, we revealed an enrichment of CD15+ and CD133+ cells after RV or IR alone, which was slightly enhanced by combination of both. We found no differences in proliferation rates between TSC and non-TSC. Therefore, we assume that the enrichment of TSC is caused by a higher treatment resistance of potential TSC compared to non-TSC.
Conclusion: RV radiosensitize human MB cells for clonogenic cell death, possibly through an increased induction of additional DSB. Further studies in animal models are warranted to clarify if the observed *in vitro* effects translate into improved survival rates *in vivo*.

→ **Patties, Ina**
email: ina.patties@medizin.uni-leipzig.de

POSTER 300

The Special AT-rich Binding Protein 1 as a potential target for therapeutic intervention in glioblastoma

Tumor Targeting

Frömberg A[1], Rabe M[1], Aigner A[1]
1 Abteilung für Klinische Pharmakologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

The Special AT-rich Binding Protein 1 (SATB1) is a DNA-binding protein, which is critical for the structure of chromatin and coordinates the expression of a large number of genes in direct and indirect manners by its dual function as a chromatin organizer and a regulator of gene expression. Recent studies demonstrated the overexpression of SATB1 in several human cancers and connected it to carcinogenesis. Furthermore, the expression of SATB1 correlates with tumor progression and is associated with poor prognosis.

In this project, we analyze the function and therapeutic potential of SATB1 in glioblastoma multiforme (GBM).

To this end, an RNAi-mediated knockdown of SATB1 was achieved in G55T2- and U-87 MG cells by transient transfection with specific siRNAs, resulting in markedly reduced SATB1 mRNA and protein. SATB1 knockdown led to antiproliferation, a deceleration of cell cycle progression and pro-apoptotic effects. Further analyses regarding the underlying cellular mechanisms revealed effects of SATB1 on multiple signaling pathways.

The therapeutic potential of SATB1 inhibition was explored *in vivo* in mice bearing s.c. xenografts from U-87 MG cells. Mice were treated with polymeric nanoparticles containing siRNAs, i.e., polyethylenimine (PEI)/siRNA-complexes. Notably, a marked inhibition of tumor growth was observed in the specific siRNA treatment group, indicating profound therapeutic effects of SATB1 knockdown in GBM.

Taken together, these results indicate an important and complex role of SATB1 in GBM, and establish SATB1 inhibition or knockdown as a promising target for pharmacological intervention.

➜ **Frömberg, Anja**
email: anja.froemberg@medizin.uni-leipzig.de

POSTER 301

Generation of a miRNA transgenic mouse model for melanoma development

Tumor Targeting

Bhattacharya A[1], Schmitz U[2], Simon J[1], Naumann R[3], Kunz M[1]

1 Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Universität Leipzig
2 Department of Systems Biology and Bioinformatics, University of Rostock
3 Max-Planck-Institute of Molecular Cell Biology and Genetics, Transgenic Core Facility, Dresden

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Malignant tumors may depend on the activity of one oncogene termed as oncogene addiction. Recently, the concept of oncogene addiction has been applied to microRNAs (miRNAs), underscoring the role of individual miRNAs in tumor development and progression. We performed a miRNA expression profiling involving primary melanomas, lymph node metastases, and distant cutaneous metastases patient, and compared the expression profiles with those of primary melanocytes. The most significantly upregulated candidates miRNAs (miR-126, 142, 150, 214, 221, 345 and 93) were tested for their growth-promoting potential in an *in vitro* clonogenicity assay in six human and mouse melanoma cell lines. All miRNAs (except miR-214) increased the clonogenicity of human melanoma cells. Remarkably, miR-345, miR-150 and miR-93 significantly enhanced the clonogenic growth of both human and mouse melanoma cells. Overexpression of miR-93 also increased the migratory properties of melanoma cells *in vitro* and significantly improved the growth of melanoma cells under attachment-independent growth conditions. Furthermore, miR-345 and miR-142 overexpression significantly increased the resistance to BRAF(V600E) inhibition. These miRNAs were therefore cloned into a pROSA26-PA vector for generation of a conditional miRNA knock-in mouse under the control of a melanocyte specific tyrosinase promoter. The role of these miRNAs will be tested in a Braf mutant/PTEN-deficient melanoma mouse model. These experiments will most closely resemble the *in vivo* situation in humans and provide a unique opportunity to analyse miRNA-induced tumor development and progression.

Funding: formel1

➜ **Bhattacharya, Animesh**
email: animesh.bhattacharya@medizin.uni-leipzig.de

POSTER 302

Using human organotypic tissue slices in cancer research

Tumor Targeting

Merz F[1], Kallendrusch S[1], Gerlach M[1], Schopow N[1], Körfer J[1], Höbel S[2], Aigner A[2], Gaunitz F[3], Bechmann I[1]

1 Institut für Anatomie, Universität Leipzig
2 Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Universität Leipzig
3 Klinik und Poliklinik für Neurochirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Cancer is one of the major causes of death worldwide. Research to improve therapy is mostly done with xenograft models by injecting (human) tumor cell lines e. g. into the flanks of mice or rats. This means a great burden for the animals, especially when the endpoints of the experiments are represented by Kaplan-Meier-curves which depict the time point where half of the animals in the study died. It also involves problems like the lack of cellular heterogeneity or inter-species differences. Therefore, only few animal studies can be successfully translated into a clinical setting for humans.
We have previously established a human test system consisting of 3D-tissue slice cultures of tumor tissue from surgeries which can be kept in culture for several weeks and used for radio- and chemotherapeutic experiments. So far, this system is used for glioblastoma, squamous cell carcinoma and gastric cancer tissue from resections as well as fat from plastic surgery. In these settings, we can monitor response to known therapies, test new compounds, analyse cell proliferation or death, or track behavior of special cell types via live imaging over time. With our model system, animal testing could be reduced and species differences are eliminated.

Merz F, Gaunitz F, Dehghani F [...] Bechmann I (2013) Organotypic slice cultures of human glioblastoma reveal different susceptibilities to treatments. *Neuro Oncol* 15(6):670–81.
Gerlach MM, Merz F, [...] Bechmann I. Slice cultures from head and neck squamous cell carcinoma: a novel test system for drug susceptibility and mechanisms of resistance. *Br J Cancer.* 2014 Jan 21;110(2):479–88.

→ **Merz, Felicitas**
email: felicitas.merz@medizin.uni-leipzig.de

POSTER 303

Photodynamic therapy (PDT) with Tetrahydroporphyrin-Tetratosylate (THPTS): A new option for minimal-invasive treatment of bladder cancer?

Tumor Targeting

Schulze P[1], Berndt-Paetz M[1], Sieger N[1], Wang Q[1], Stenglein P[1], Schastak S[1], Horn L[1], Stolzenburg J[1], Neuhaus J[1]

1 Klinik und Poliklinik für Urologie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Background: Low therapeutic penetration depth due to short excitation wavelength of available photosensitizers hampers PDT of invasive bladder cancer. We used the near-infrared (760nm) excitable photosensitizer THPTS for PDT, allowing a tissue penetration of> 20 mm. We examined the effects of THPTS-PDT in rat AY-27 bladder cancer cells and established an orthotopic rat bladder cancer model.

Material and Methods: We examined cell viability, apoptosis and cytotoxicity using standard assays, and pharmacokinetics by flow cytometry and confocal laser scanning microscopy. THPTS-PDT was done in female F344 Fischer-rats (n=30) 10 days after transurethral tumor inoculation with AY-27 cells. Bladders were examined by sonography, macroscopy and histology.

Results: Dark toxicity of THPTS was low in AY-27 cells and rat detrusor myocytes (BSMC). PDT significantly reduced cell survival, induced apoptosis and concentration dependent cytotoxicity. Cellular uptake of THPTS started within 1 minute at 37°C and increased linearly up to 120 min. At 4°C the THPTS uptake was almost completely inhibited. Subcellular accumulation was mainly seen in endosomes and lysosomes. We found invasive tumors (≥ pT1; 4/10 ≥ pT2a) in 10/10 rats in the untreated group 10 days after tumor inoculation. THPTS-PDT resulted in significant reduction ($p < 0,05$) of macroscopic tumors.

Conclusions: THPTS uptake in AY-27 cells is mediated by a fast and temperature-dependent mechanism.

THPTS preferentially accumulates in endosomes and lysosomes.

THPTS-PDT in an orthotopic rat bladder cancer model shows good tumor control.

Funding: DFG NE425/6-1; SCHA791/3-1; MF Uni Lpz (PS).

➜ **Schulze, Philipp**
email: philipp.schulze@medizin.uni-leipzig.de

POSTER 304

Synergistic anti-tumor effects after combined inhibition of c-met and HER family receptors in gastric cancer cells

Tumor Targeting

Jenke R[1], Büch T[1], Lordick F[2], Aigner A[1]

1 Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Universität Leipzig
2 Universitäres Krebszentrum (UCCL), Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Conventional cytoreductive chemotherapy has limited efficacy in gastric cancer. Consequently, targeted therapeutics, which are directed against critical oncogenic signaling molecules (e.g. c-met or receptors of the HER family), have been proposed in the treatment of this tumor entity. However, the redundancy of tumor promoting signaling cascades and compensatory up-regulation of alternative oncogenic pathways often leads to resistance against single targeted therapeutics. The aim of the present study was to evaluate the combined inhibition of c-met and HER receptors with regard to potential synergistic anti-tumor effects. For this purpose, we have made use of a panel of established human gastric cancer cell lines and took advantage of specific RNAi-based knock-down strategies, small molecule inhibitors or monoclonal antibodies to inhibit c-met or HER-promoted signaling. Using quantitative RT-PCR analyses, we found a pronounced expression of c-met as well as HER1, HER2, and HER3 in all cell lines used in this study, whereas HER4 was not expressed. Single inhibition of HER3 resulted in a marked growth inhibition in all gastric cancer cells. In contrast, three cell lines were resistant against single inhibition of HER1 or HER2 and two of these cell lines were also resistant against c-met inhibition. Of note, combined inhibition of c-met and HER2 showed a very strong synergistic anti-tumor effect in gastric cancer cells, which was cell type specific, since this effect could not be observed in gynecological cancer cells. Thus, we propose that combined targeting of c-met and HER2 should be further evaluated in gastric cancer.

➜ **Jenke, Robert**
email: robert.jenke@medizin.uni-leipzig.de

POSTER 305

A Truncated Splice Variant of LRP1 – a New Diagnostic Biomarker for Cancer?

Tumor Targeting

Kolb M[1], Trettner S[1], Wichmann G[1,2], Birkenmeier G[1]

1 Institut für Biochemie, Medizinische Fakultät, Universität Leipzig
2 Klinik und Poliklinik für Hals-, Nasen-, Ohrenheilkunde, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Cancer is one of the most frequent causes of death per year. So far, early diagnosis and treatment are the best chance of a cure and accordingly, research focuses on identifying specific tumour markers. The scavenger receptor LRP1 is a member of the LDL receptor superfamily and involved in different signalling pathways and tumour promotion. To date, several studies indicate LRP1 as a biomarker in numerous cancer entities since its expression is associated with the clinical outcome. However, it is not established.
We confirmed expression of LRP1 mRNA in several healthy human tissues, blood cells and corresponding tumour cell lines. Beyond that, we recently detected a truncated mRNA splice variant of LRP1 (shLRP1). Interestingly, direct comparison of LRP1 and shLRP1 expression in healthy tissues and corresponding tumour cell lines showed similar trends: LRP1 mRNA expression was decreased whereas shLRP1 mRNA expression was increased in tumour cell lines. Next, we confirmed LRP1 and shLRP1 protein expression in tumour cell lines of different origin, whereas shLRP1 protein was detected in both tumour cell lysates and cell culture supernatants indicating that shLRP1 is secreted by tumour cells. Furthermore, first results from primary HNSCC samples show different LRP1 expression depending on HPV infection.
The results suggest that LRP1 and its truncated splice variant shLRP1 are ubiquitously expressed markers useful as new tumour diagnostic markers. Hence, further experiments have to be performed to corroborate shLRP1 in particular as a diagnostic tool for cancer.

➜ **Kolb, Marlen**
email: marlen.kolb@medizin.uni-leipzig.de

POSTER 306

Detection of miR 24 in Hepatocytes and Cholangiocytes using laser capture micro dissection and qPCR

Tumor Targeting

Beeskow A[1], Dietel C[1], Fügenschuh M[1], Felgendreff P[1], Faroch A[1], Kunze K[1], Klunk S[1], Leonhardt C[1], Reutzel-Selke A[1], Raschzok N[1], Morgül H[1], Bartels M[1]

1 Sektion Bariatrische Chirurgie, Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Universität Leipzig

List of topics

Biophysics and Bioanalytics
Biotechnology / Biomedicine
Cell Biology
Clinical Studies
Drug Development and Delivery
Evolution and Molecular Diversity
ICCAS – Computer Assisted Surgery
IFB – Adiposity Diseases
Imaging
Immunology and Infectiology
LIFE – Civilisation Diseases and Genetics
Molecular Biology / Protein Biochemistry
Neurobiology
Psychology and Cognition
SFB 1052 – Obesity mechanisms
Social Medicine
TRM – Translational Regenerative Medicine
Tumor Targeting

Introduction: The microRNAs (miRNAs) have been shown to be responsible for cell metabolism and differentiation. For examination of miRNA expressions in intrahepatic cholangiocarcinoma cells, it is essential of precise dissection of these cells by laser capture micro dissection (LCM). This method allows the comparison of different miRNAs of unique cell populations of heterogenic liver parenchyma

Methods: Tissue samples were harvested from explanted livers of patients underwent liver transplantation. Tissue sections were prepared on RNAse free slides and stained immunohistologicaly. Areas of hepatocytes and cholangiocytes are separately dissected on LCM. RNA is purificated using an isolation kit. The two-step RT-PCR is performed with hsa-miR-24.

Results:

The staining against CK-19 allowed clear distinguish of cholangiocytes from hepatocytes. Using q-PCR comparable amount of miR-24 could be detected both in hepatocytes and cholangiocytes (Ct 23–28).

Conclusion: miRNA-24 is a well-described miRNA for liver and HCC. In this study miRNA-24 detection is examined in cholangiocytes and hepatocytes. An equal detected amount of miRNA-24 in both cell types could alow using miR-24 as normalizer to find specific miRNA's for cholangiocytes by qPCR.

➜ **Beeskow, Anne**
email: anne.beeskow@medizin.uni-leipzig.de

Autorenindex

C

D

Index E–G

H

I

J

K

L

M

N

O

P

R

S

Index S

T

U

V

W

X

Y

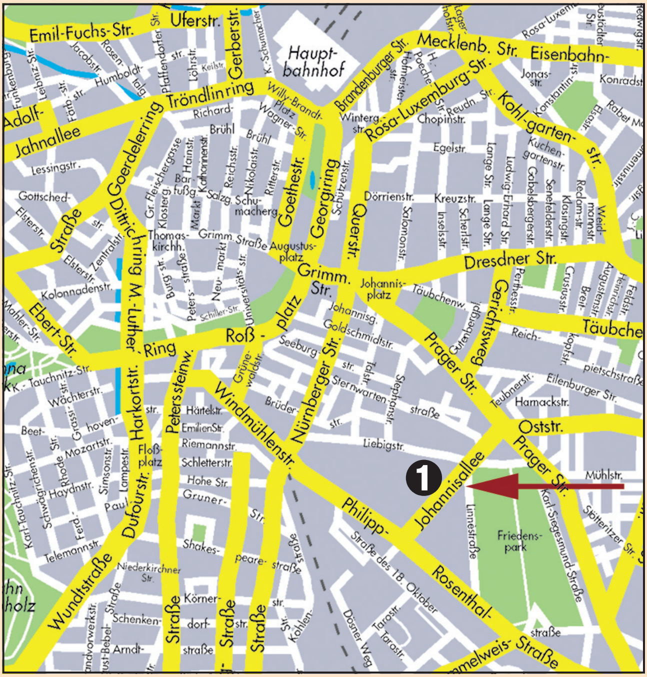
Z

Notizen:

Notizen:

Notizen:

Die Medizinische Fakultät, die Fakultät für Biowissenschaften, Pharmazie und Psychologie der Universität Leipzig und Forschungseinrichtungen der Region Leipzig präsentieren im Rahmen des Research Festival 2014 die biomedizinische und Life Science Forschung in ihrer beeindruckenden Vielfalt. Innovation und produktive Zusammenarbeit des Campus der Universität und der Forschungseinrichtungen werden in einer Vielzahl von Kurzbeiträgen der interessierten Öffentlichkeit vorgestellt.



1 Max-Bürger-Forschungszentrum
Johannisallee 30 · 04103 Leipzig

9 783981 703306