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Leipzig Research Festival
for Life Sciences
2018

14th

Abstract Book

Prof. Dr. Thomas Arendt
Dr. Dr. John T. Heiker
Prof. Dr. Thomas Magin
Prof. Dr. Michael Schaefer
Prof. Dr. Michaela Schulz-Siegmund
Prof. Dr. Joachim Thiery
(Hrsg.)

UNIVERSITÄT LEIPZIG
Medizinische Fakultät

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Fakultät für
Lebenswissenschaften

UNIVERSITÄT(S)MEDIZIN
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IFB Adipositas
Erkrankungen

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KOGNITIONS- UND
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SFB 1052
Obesity Mechanisms

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Medizinische Fakultät der Universität Leipzig
Fakultät für Lebenswissenschaften der Universität Leipzig

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Für die Unterstützung der Veranstaltung danken wir:

Fakultät für Lebenswissenschaften, Universität Leipzig
Medizinische Fakultät, Universität Leipzig
Biotechnologisch-Biomedizinisches Zentrum (BBZ), Leipzig
Integriertes Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen
Innovation Center Computer Assisted Surgery (ICCAS)
Max-Planck-Institut für Kognitions- und Neurowissenschaften in Leipzig
Research Academy Leipzig
Sonderforschungsbereich 1052 "Mechanismen der Adipositas"

Vorwort

Liebe Kolleginnen und Kollegen, liebe Gäste,

wir begrüßen Sie sehr herzlich zu unserem **14. Leipziger Research Festival of Life Sciences** der Universität Leipzig. Nach einer mehrjährigen Pause freuen sich die Medizinische Fakultät und die Fakultät für Lebenswissenschaften, das traditionelle Festival wieder aufleben zu lassen.

Die 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 Neuauflage des Festivals hat eine hohe Zahl von Abstracteinsendungen erreicht und unterstreicht damit die Attraktivität dieses weit über die Fächergrenzen reichenden wissenschaftlichen Kommunikationsforums. Der vorliegende Abstractband 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 vergangenen Jahren freuen wir uns auch in diesem Jahr, dass wir durch die Forschungsverbünde in den Lebenswissenschaften – dazu gehören das Biotechnologisch-Biomedizinische Zentrum (BBZ), das Integrierte Forschungs- und Behandlungszentrum (IFB) AdipositasErkrankungen, das Innovation Center Computer Assisted Surgery (ICAAS), das Max-Planck-Instituts für Kognitions- und Neurowissenschaften in Leipzig, die Research Academy Leipzig und der Sonderforschungsbereich 1052 »Mechanismen der Adipositas« -eine großzügige Unterstützung erhalten haben.

Wir hoffen, dass unser Research Festival in seiner Neuauflage und im 14. Jahr seinen doppelten Zweck, die Präsentation eigener innovativer Forschungsergebnisse und als Kontaktforum mit jungen und älteren 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.

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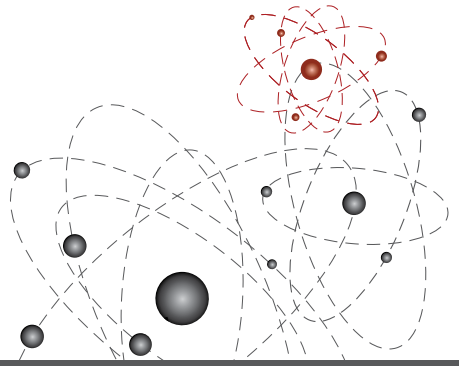
at Leipzig University
Life Science Transfer Office

EXPLOITATION OF RESEARCH RESULTS IN BIOTECHNOLOGY AND BIOMEDICINE



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Optimization and acceleration of technology transfer process in life science research

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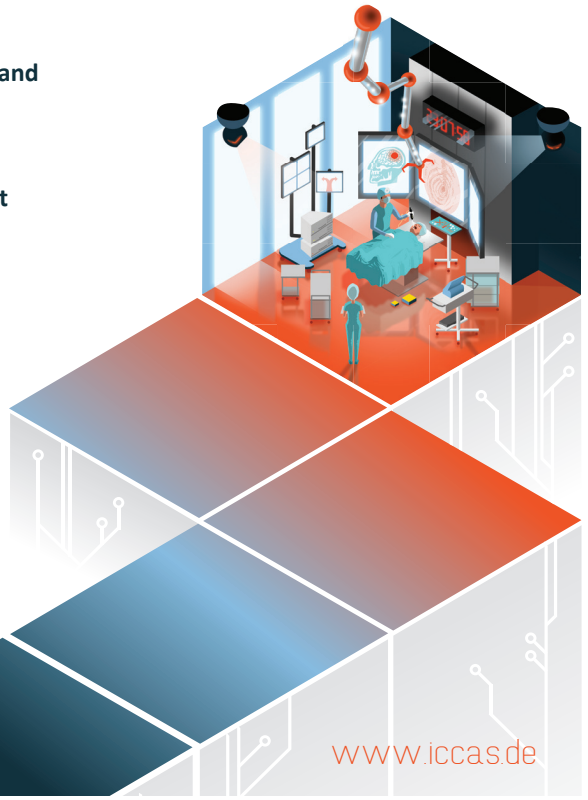

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IFB Adipositas Erkrankungen

Das IFB AdipositasErkrankungen ist eines von acht Integrierten Forschungs- und Behandlungszentren, die in Deutschland vom Bundesministerium für Bildung und Forschung gefördert werden. Es ist eine gemeinsame Einrichtung der Universität Leipzig und des Universitätsklinikums Leipzig AöR. Ziel der Bundesförderung ist es, Forschung und Behandlung krankhaften Übergewichts interdisziplinär so unter einem Dach zu vernetzen, dass Ergebnisse der Forschung weit schneller als bisher in die Behandlung adipöser Patienten integriert werden können (www.ifb-adipositas.de).

Das IFB AdipositasErkrankungen verfolgt im Konkreten folgende Ziele:

1. Ein Förderprogramm für den wissenschaftlichen Nachwuchs wird angebotent, um die besten Studierenden und den wissenschaftlichen Nachwuchs für das IFB gewinnen zu können.

2. Es wurden neue Behandlungspfade geschaffen, die kontinuierlich weiter ausgebaut, validiert und bewertet werden und mit Partnern in der Region und darüber hinaus in die klinische Versorgung überführt werden. Ein weiteres Ziel des IFB ist es, Adipositas-Präventionsprogramme mit verschiedenen lokalen und regionalen Akteuren zu entwickeln und durchzuführen, aber auch politische Akteure miteinzubeziehen.

3. Das Forschungsprogramm mit seinen klinischen und translationalen Aspekten der Adipositasforschung konzentriert sich auf sechs integrierte Forschungsbereiche: bariatrische und metabolische Chirurgie, Molekular- und Neuroimaging, Adipositas bei Kindern, Hormone, Genetik und psychosoziale Aspekte. Der Patient steht im Mittelpunkt. Schwerpunkte der Studien in diesen Bereichen sind Prädiktoren für Non-Responder bei chirurgischen Verfahren, die Rolle des Belohnungssystems bei übermäßiger Nahrungsaufnahme, Präventionsstrategien der Fettleibigkeit bei Kindern, die Rolle der Fettgewebsdysfunktion bei Adipositas, Mechanismen von Adipositas-Risiko-Genen und kognitive Maßnahmen zur Verbesserung des langfristigen Gewichtsverlusts.

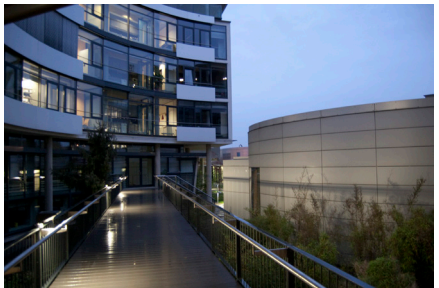
MAX PLANCK INSTITUT FÜR KOGNITIONS- UND NEUROWISSENSCHAFTEN LEIPZIG

Über das Institut

Das Ziel des Max-Planck-Instituts für Kognitions- und Neurowissenschaften in Leipzig ist die Erforschung von kognitiven Fähigkeiten und Gehirnprozessen beim Menschen.

Ein Hauptaugenmerk unserer Forschung gilt den neuronalen Grundlagen von höheren Hirnfunktionen wie Sprache, Emotionen und Sozialverhalten, Musik und Kommunikation. Dabei interessiert uns vor allem, wie diese wahrgenommen, verarbeitet, geplant und produziert werden, aber auch, wie sich Wahrnehmung und Produktion gegenseitig beeinflussen.

Weiterhin untersuchen wir das plastische Veränderungsvermögen des Gehirns und seinen Einfluss auf verschiedene kognitive Fähigkeiten sowie die neuronalen und hormonellen Grundlagen von Zivilisationskrankheiten wie Bluthochdruck und Übergewicht. Darüber hinaus ist die Weiterentwicklung von bildgebenden VerfaHren für die Neurowissenschaften ein zentraler Schwerpunkt unserer Forschung.



Derzeit hat das Institut vier Abteilungen:

Neurologie
Neuropsychologie
Soziale Neurowissenschaft
Neurophysik

Ein Markenzeichen des Instituts – und zugleich die Grundlage für seine forschungsstrategische Perspektive – ist die enge Verzahnung von inhaltlicher Forschung und technologischer Entwicklung. Das Institut entstand 2004 durch die Zusammenführung der Max-Planck-Institute für Neuropsychologische Forschung und für Psychologie. Mit der Gründung des Max-Planck-Instituts für Kognitions- und Neurowissenschaften hat die Max-Planck-Gesellschaft am Standort Leipzig einzig-artige Voraussetzungen für die interdisziplinäre Forschung auf dem Gebiet der verhaltensbasierten und neurobiologischen Grundlagen menschlicher Kognition geschaffen.

Leipzigs lange Tradition in der psychologischen Forschung verleiht der ultra-modernen technischen Ausstattung unseres neurowissenschaftlichen Instituts und unseren Arbeitsfeldern einen besonderen Rahmen. Moderne bildgebende Verfahren, die auch in traditionell verhaltenswissenschaftlichen Ansätzen einen immer größeren Stellenwert gewinnen, werden am Institut gepflegt und weiterentwickelt. Auch in methodischer Hinsicht steht an unserem Institut das gesamte Spektrum von Verfahrensweisen, die im Bereich der Kognitions- und Neurowissenschaften etabliert sind, an einem Ort zur Verfügung.

Max Planck Institute for Human Cognitive and Brain Sciences

About the Institute

Research at the Max Planck Institute for Human Cognitive and Brain Sciences revolves around human cognitive abilities and cerebral processes, with a focus on the neural basis of brain functions such as language, emotions and human social behaviour, music, and communication.

Our studies focus on the perception, planning, and generation of human cognitive abilities and cerebral processes, and analyse the interaction and common functional basis of their production and perception. We also investigate plastic changes in the human brain, the influence these have on various cognitive abilities, and on the neuronal and hormonal basis of modern diseases like high blood pressure and obesity. An additional focal point of research at the Institute is the further development of imaging methods for neurosciences.
The MPI for Human Cognitive and Brain Sciences provides an exciting framework for these topical and alluring theoretical domains, with the full gamut of cognitive and neuroscientific methodology available under one roof.

The Institute currently consists of four departments:

Neurology
Neuropsychology
Social Neuroscience
Neurophysics

A hallmark of the Institute and its research strategies is the dovetailing of research, development, and engineering. The centre draws on elaborate modern imaging techniques which are gaining ground as part of more conventional behavioural approaches.

Our institute at Stephanstrasse in Leipzig was established on 1 January 2004 by a merger between the former Leipzig Max Planck Institute of Cognitive NeuroScience and the Munich Max Planck Institute for Psychological Research. The new institute, joining two centres of expertise into one, reflects the development of psychological and neuroscientific research, which are being conducted increasingly closer together. The centre in Leipzig has established exceptional conditions for interdisciplinary behavioural and neurobiological research into human cognition.

RESEARCH ACADEMY LEIPZIG

Die Research Academy fördert als zentrale Service-Einrichtung den wissenschaftlichen Nachwuchs der Universität Leipzig.
Sie informiert, qualifiziert, fördert und vernetzt Promovierende und Postdocs der Universität Leipzig und unterstützt die Fakultäten und Hochschullehrenden bei der Förderung des wissenschaftlichen Nachwuchses.

Die Kompetenzschule bietet als Workshop-Programm der Research Academy allen Promovierenden und Postdocs die Möglichkeit, sich zielgruppenorientiert weiter zu qualifizieren und sich untereinander stärker zu vernetzen.

Darüber hinaus stehen Promovierenden aus den strukturierten Programmen sowie den registrierten Postdocs weitere Fördermöglichkeiten zur Verfügung: Die drei Graduiertenzentren Mathematik/Informatik und Naturwissenschaften, Lebenswissenschaften sowie Geistes- und Sozialwissenschaften gewähren ihren Mitgliedern finanzielle Unterstützung für aktive Konferenzreisen und zeichnen jährlich hervorragende Dissertationen mit Promotionspreisen aus. Auch für die Postdocs werden Maßnahmen konzipiert, die sich an das Personalentwicklungskonzept der Universität Leipzig ausrichten. Für beide Zielgruppen stehen die Angebote im Leibniz-Programm MOBILE zur Verfügung.

Die Research Academy Leipzig setzt sich ein für

- wissenschaftliche Personalentwicklung der Nachwuchswissenschaftlerinnen und -wissenschaftler,
- Qualitätssicherung in der Promotion,
- Förderung der Chancengleichheit und Gleichstellung von Wissenschaftlerinnen und Wissenschaftlern sowie
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Informieren Sie sich auf unserer Website www.ral.uni-leipzig.de!

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UNIVERSITÄT LEIPZIG

Sonderforschungsbereich 1052
„Mechanismen der Adipositas“

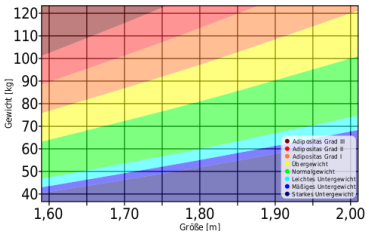
DURCH DICK UND DÜNN – EIN BLICK HINTER DIE KULISSEN DER ADIPOSITASFORSCHUNG

Was ist Adipositas?

Adipositas (von lateinisch „adeps“ = Fett) ist eine Ernährungs- und Stoffwechselkrankheit. Kennzeichen ist ein starkes Übergewicht mit einer starken Vermehrung des Körperfetts und krankhaften Auswirkungen. Nach Definition der Weltgesundheitsorganisation liegt ab einem Körpermasseindex von 30 kg/m² Adipositas vor. Ergänzend werden der Bauchumfang und das Taille-Hüft-Verhältnis zur Beurteilung herangezogen.

Die Adipositas wird unterschieden in drei Schweregrade: Grad I (BMI 30 – 34,9), Grad II (BMI 35 – 39,9) und Grad III (ab BMI 40).

In Deutschland ist fast ein Viertel der Bevölkerung von Übergewicht betroffen. Mit Adipositas werden verschiedene Begleiterkrankungen assoziiert, wie etwa Diabetes Typ 2, Bluthochdruck, Fettleber, koronare Herzerkrankungen.



Was erforscht der Sonderforschungsbereich (SFB)?

Krankhaftes Übergewicht ist eine multifaktorielle Störung, die durch eine Kombination von Genetik, Verhalten, Lebensstil und Umweltfaktoren beeinflusst wird. Unser Anliegen ist es, neue Ziele und Mechanismen für therapeutische pharmakologische Herangehensweisen in der Behandlung von Adipositas und ihren Begleiterkrankungen zu identifizieren.

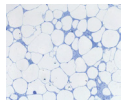
Der Sonderforschungsbereich konzentriert sich dabei auf drei Schwerpunkte: **Überernährung, Fetteinlagerung und Entzündung sowie Adipokine** (Hormone im Fettgewebe).

Überernährung

Aus evolutionärer Perspektive war es für unsere Vorfahren wichtig, dass in nahrungsreichen Zeiten überschüssige Kalorien in den Fettzellen gespeichert werden konnte. In Mangelzeiten konnte der Körper darauf zurückgreifen. Heute kann diese Speicherfunktion zu Adipositas führen, weil der Körper diese Reserve nicht in Anspruch nehmen muss. Wir wollen die evolutionäre Vergangenheit dieser genetischen Veränderungen verstehen. Und welche Unterschiede es zwischen Populationen gibt und in welchem Umfang diese Unterschiede für die Anfälligkeit für Krankheiten des Energiestoffwechsels vorhersagbar sind.

Fetteinlagerung und Entzündung

Es gibt verschiedene Arten von Fettgewebe: weißes, braunes und beiges Fettgewebe.
Die Speicherung von Fett in Fettzellen geschieht vorrangig über **weißes Fettgewebe**, das nur schwer abgebaut werden kann.

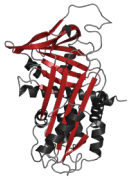

Weißes Fettgewebe.

Vor allem die viszerale Fetteinlagerung (in der Bauchhöhle) wird mit der Neigung zu Komplikationen assoziiert. Uns interessiert, welche genetischen Faktoren die Anzahl der Adipozyten (Fettzellen), Unterschiede in der Fettverteilung (visceral oder subkutan) und ihre Assoziation mit Stoffwechselstörungen bestimmen. Mit Hilfe der Fettgewebebank in Leipzig sollen Gene identifiziert werden, die darin involviert sind.

In den Fokus der Forschung gerät derzeit das **braune Fettgewebe**. Es ist an der Thermogenese beteiligt, bei der weißes Fettgewebe in braunes umgewandelt wird. Wenn der Mensch leichter Kälte ausgesetzt wird, kann so die Körpertemperatur erhalten werden. Es kann auch durch Sport aufgebaut werden. Braunes Fettgewebe wird in der Forschung mit Gewichtsverlust und der Unterdrückung von Stoffwechselerkrankungen (z. B. Diabetes) in Verbindung gebracht.

Adipokine (Fettgewebshormone)

Das Fettgewebe sondert zahlreiche Hormone ab. In den letzten Jahren wurden zahlreiche Adipokine identifiziert. Unser Anliegen ist es, für ausgewählte Adipokine ihre Funktion, ihre molekularen Ziele und ihre potentielle klinische Relevanz als Biomarker oder in der Behandlung von Adipositas und deren Begleiterkrankungen zu definieren.


Struktur des Adipokins SerpinA12 (Vaspin) pdb:4FI8

Was ist der SFB?

Der Sonderforschungsbereich 1052 vereint Wissenschaftlerinnen und Wissenschaftler aus den Bereichen Anatomie, Biochemie, Biophysik, Chemie, Dermatologie, Endokrinologie, Genetik, Kardiologie, Labormedizin, Neurologie, Pädiatrie, Physiologie.

Beteiligte Einrichtungen sind die Universität Leipzig (Medizinische Fakultät; Fakultät für Biowissenschaften, Pharmazie und Psychologie; Fakultät für Chemie und Mineralogie), das Universitätsklinikum Leipzig, das Max-Planck-Institut für Evolutionäre Anthropologie, das Max-Planck-Institut für Kognitions- und Neurowissenschaften und die Ben-Gurion-Universität in Beer-Sheva, Israel.

Gefördert von der Deutschen Forschungsgemeinschaft DFG

Technology transfer in biotechnology and biomedicine

Ebitsch, S.; Dornberger, U.; Wilken, D.; Eichler, S.

The transfer and subsequent application of academic research results has demonstrable benefits for health care, researchers, universities, companies and local economies. Main focus of technology transfer is the dissemination of scientific knowledge between researchers and research organizations and those who can make practical use of the information, e.g. health care providers and companies.

Located at the Life Science Transfer Office at Leipzig University, the technology transfer representative strives to transform scientific know how, expertise and results into novel products and technologies. We help to identify transferable results and offer information on how to protect your invention and potential markets. Moreover we support and initiate the implementation of transfer projects between research institutes of Leipzig University and Companies. Optionally we provide assistance in the funding process to propel the innovation toward application maturity. Our partners in industry and science benefit from our close cooperation with the nearby centers of biotechnology and medical research as well as the faculties of natural sciences, medicine and veterinary medicine. We work alongside the start-up initiative SMILE and the Technology Transfer Department of Leipzig University.

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Poster 1

COBL, MYOC and MKX are potential regulators of brown adipose tissue *in vitro*

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There are two types of adipose tissue: White adipose tissue (WAT), which stores energy in the form of lipids; and brown adipose tissue (BAT), which generates body heat by non-shivering-thermogenesis. Using microarray analysis, our research group identified Cordon-bleu WH2 repeat protein (COBL), Mohawk homebox (MKX) and Myocilin (MYOC) as candidate genes potentially involved in BAT development in children. The aim of this study is to characterize their role during processes of BAT formation.

To investigate the differentiation of brown (pre)adipocytes and the white-to-brite transdifferentiation of white (pre)adipocytes and the role of our candidate genes we used murine HIB1B and 3T3L1 cells and measured the expression of PPARγ, UCP1, COBL, MYOC and MKX. We used siRNA-mediated knockdown to investigate the function of our candidate genes.

We analyzed the expression level of the candidate genes in children's AT samples and showed that COBL and MKX were up- and MYOC was down-regulated in UCP1-positive compared to UCP1-negative biopsies. During differentiation of HIB1B cells COBL and MYOC expression increased, whereas MKX expression decreased. Knockdown of COBL and MKX resulted in increased, knockdown of MYOC led to decreased UCP1 expression in HIB1B cells. As for the 3T3L1 cells we established a protocol to transdifferentiate the white (pre)-adipocytes into brown adipocytes and are currently investigating the role of our candidate genes on this process.

Our results from analyses of brown adipocyte differentiation indicate that the respective genes might be involved in the classical pathway of brown adipocyte formation.

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Poster 3

T-cell depletion does not alter adipose tissue macrophage proliferation

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Obesity is frequently associated with a chronic low grade inflammation in the adipose tissue, a rise in various immune cells and ultimately insulin resistance. Adipose tissue macrophages (ATMs) have been shown to accumulate in the adipose tissue either by means of recruitment from the blood or local proliferation. ATM proliferation seems to be partially influenced by TH2 cytokines, such as IL-4 and IL-13, suggesting a link between T cells and ATM proliferation. In this study, we sought to examine a direct impact of CD4 and CD3 positive T cells on ATM activation and ATM proliferation.

For that purpose, mice were fed a high-fat diet for 20 weeks to induce obesity and insulin resistance. Subsequently, mice were injected with either CD3 or CD4 depleting antibodies or an appropriate isotype control for 3 consecutive days. Using flow cytometry and immunofluorescence, we then compared control and T-cell depleted mice with respect to ATM proliferation as detected by BrdU incorporation, Ki67 and PCNA expression respectively.

CD3 or CD4 specific antibodies efficiently depleted CD4 positive T cells by ~85% or ~99%, respectively. However, flow cytometry and immunofluorescence revealed no significant changes in fat cell diameter, crown-like structure density, ATM polarisation or proliferation following short-term CD3 or CD4 depletion.

Our data suggest that CD4 positive T cells exert no direct effect on local ATM proliferation or activation. Of note, this study does not rule out an indirect long-term effect of CD4 positive lymphocytes on ATM proliferation by changing the inflammatory microenvironment.

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Poster 4

Gesundheitsverhalten und affektive Zustände während der Schwangerschaft unter Berücksichtigung des mütterlichen Gewichtsstatus

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Einleitung:
Obwohl bekannt ist, dass ein mütterliches Gewicht außerhalb des Normbereichs zu Komplikationen in der perinatalen Periode führen kann, ist bislang wenig über den Einfluss des Gewichts zu Schwangerschaftsbeginn auf Gesundheitsverhaltensweisen sowie negative affektive Zustände während der Schwangerschaft bekannt. Ziel der Studie war es daher, die Unterschiede zwischen schwangeren Frauen mit und ohne Übergewicht bezüglich sechs verschiedener Gesundheitsverhaltensweisen sowie depressiver Symptome und Stress zu analysieren.

Methode:
466 schwangere Frauen (2. Trimester, 29.8 ± 4.2 Jahre) einer querschnittlichen Studie aus einer Bevölkerungsstichprobe füllten Selbstberichtfragebögen zur Erfassung des Gewichts vor Schwangerschaftsbeginn, Substanzkonsum, Verzehr von Süßigkeiten und Snacks, sportlicher Aktivität, Schlafqualität sowie Stress und depressiver Symptome aus.

Ergebnisse:
In beiden Gewichtsgruppen zeigten sich individuelle Zusammenhänge zwischen Gesundheitsverhaltensweisen und affektiven Zuständen. Verglichen mit schwangeren Frauen ohne (n=348) berichteten jene mit Übergewicht (n=118) weniger sportliche Aktivität, eine geringere Schlafqualität und höhere Werte in den Skalen zur Erfassung von depressiven Symptomen und Stress (kleine bis mittlere Effektstärken).

Diskussion:
Auch in der Schwangerschaft beeinflusst der mütterliche Gewichtsstatus Gesundheitsverhaltensweisen und affektive Zustände. Längsschnittstudien sind nötig, um die Effekte zu sichern sowie Prädiktoren von Gesundheitsverhaltensweisen und deren Folgen in der perinatalen Periode zu analysieren.

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Poster 5

Characterization of subcutaneous stromal vascular fraction cells from a patient with Beckwith-Wiedemann Syndrome

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Objective:
Besides the SGBS cell line derived from stromal vascular fraction (SVF) cells from a patient with Simpson Golabi Behmel Syndrome (SGBS), there is no established cell model for human adipogenesis. The Beckwith-Wiedemann Syndrome (BWS) is another overgrowth syndrome of which a SVF cell line does not exist so far. We aimed to characterize primary BWS SVF cells and compare them to primary and immortalized control cells and SGBS cells. We hypothesized, that BWS SVF cells maintain their capacity to proliferate and differentiate similar to SGBS cells.

Methods:
SVF cells were isolated from subcutaneous adipose tissue of an obese BWS patient and of three obese control children and were selected for preadipocytes via plastic adherence. Immortalization was achieved by retroviral transduction with the human telomerase reverse transcriptase (hTERT). The cells were functionally characterized for proliferation, differentiation and mitochondrial function.

Results and conclusion:
The first cells were successfully immortalized and expressed hTERT. Among all cells SGBS cells proliferated and differentiated best in early and later generations. Surprisingly, there was no significant difference in proliferation between BWS and control cells. However, while in the control cells the potential to differentiate declined over the generations, it was retained in the BWS cells. Although the immortalized cells didn't differentiate to the same degree, the pattern was still maintained. To draw reliable conclusions additional control cell lines are established, further characteristics assessed and experiments validated by repetitions.

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Poster 6

PTEN hamartoma tumor syndrome – Role of PTEN in the proliferation and differentiation of preadipocytes

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Germline mutations in the tumor suppressor gene PTEN predispose for the development of malignant and benign tumors (PTEN hamartoma tumor syndrome, PHTS) and frequently lead to the development of lipomas. PTEN antagonizes the PI3K/AKT/mTOR pathway, which promotes cell survival and proliferation. In this study we investigate the mechanisms leading to hyperproliferation of adipose tissue in patients with PHTS and examine potential treatment options using cell models.

Primary cells from human fat biopsies (stromal vascular fraction, SVF) were used to study the influence of PTEN on adipocyte differentiation. A cell strain (LipPD1) isolated from lipoma tissue of a PHTS patient with a heterozygous PTEN deletion served as a model to test potential inducers of growth arrest or apoptosis. The NAMPT inhibitor FK866, which induces apoptosis in cancer cell lines, was tested together with the mTOR inhibitor rapamycin.

Treatment of LipPD1 cells with FK866 resulted in a severely reduced cell viability measured via WST-1 assay (70 % viability reduction after 72 h). However, FK866 did not induce apoptosis alone or in combination with rapamycin or significantly decreased cell number after 72h. PTEN was transiently down regulated in SVF cells via siRNA (85 % knock-down), but a phenotype of enhanced adipocyte differentiation as shown by lipid accumulation was not observed.

Since PTEN haploinsufficient preadipocytes from patients retain their differentiation capacity over a prolonged period, a stable PTEN knockdown model will be established to investigate long-term effects of PTEN on differentiation and proliferation of SVF cells.

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Poster 7

Adipokines: A Targeted Quantitative Analysis using Tandem Mass Spectrometry

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Obesity is characterized by an excessive accumulation of white adipose tissue that presents a risk to health. Adipose tissue acts as an endocrine organ, secreting several different adipokines, which play a central role in the body homeostasis by influencing a variety of biological and physiological processes. In previous studies adipokines were measured by ELISA. Since ELISA is a very time consuming and expensive method, especially if the serum levels of several adipokines need to be determined, we aim to develop a LC-MS-based assay for the simultaneous analysis of >16 adipokines in serum samples in one MS run. Establishing such an assay involves the development of an efficient digestion protocol, ensuring a reproducible generation of proteolytic peptides, plus optimizing the MS method itself. Adipokines are a group of very low abundant proteins in human serum, thus injecting untreated serum into a MS instrument will lead to no identifications. This problem can be overcome by depleting human serum from very high abundant proteins using antibodies. Furthermore, isotopic-labelled peptides for each adipokine are needed for quantification by generating an external calibration curve. In a preliminary study, we show that even with a small sample set (3 lean vs. 3 obese sera), we can detect significantly altered adipokine levels between lean and obese individuals. In conclusion, we successfully established a multiplex LC-MS-based assay for the detection and quantification of serum adipokines. This method offers a valuable tool for the identification and characterization of biomarkers associated to obesity and -related diseases.

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Poster 8

Functional characterization of macrophage-specific Tribbles homolog-1 (Trib1) knockout mice

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Previous studies have associated Trib1 with inflammatory processes and proposed a role in adipose tissue (AT) inflammation in obesity. Own data and published data (Satoh et al., 2013) suggest, that Trib1-deficiency in macrophages may lead to alterations in macrophage polarization and activation patterns.

Macrophage-specific Trib1 (MΦ-Trib1) knockout mice on a C57BL/6 genetic background were used to investigate the impact of a Trib1-deficiency on inflammaion and lipolysis in adipose tissue during obesity. Further, an *in vitro* coculture system was established to explore the MΦ-Trib1-dependent interaction between macrophages and adipocytes regarding inflammation, lipolysis, insulin-sensitivity and adipokine secretion.

The macrophage-specific Trib1 knockout did not significantly alter pro-inflammatory gene expression in WAT. MΦ-Trib1 knockout mice showed a trend to lower anti-inflammatory gene expression in WAT and elevated *in vitro* lipolysis of WAT explants. The MΦ-Trib1 knockout did not elicit major differences in circulating adipokine levels compared to wild type.

In both the coculture and in conditioned media experiments, the deletion of Trib1 in macrophages did not significantly influence the response of adipocyes in terms of inflammatory gene expression, lipolysis, insulin sensitivity and adipokine secretion.

Overall, Trib1-deficiency in macrophages appeared to have only minor effects on AT inflammation and lipolysis in obesity. In the future, the impact of Trib1 in other tissues and cell types remains to be examined.

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Poster 9

Bariatrische Subtypen und ihr prädiktiver Wert für den Langzeiterfolg der Adipositaschirurgie

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Hintergrund: Trotz belegter Effektivität der Adipositaschirurgie zeigen 20-30% der Patienten einen unzureichenden postoperativen Gewichtsverlust. Es gibt Hinweise, dass dieser mit erhöhter Impulsivität, Emotionsdysregulation und enthemmtem Essverhalten assoziiert ist. In der jetzigen Arbeit wurden Patienten anhand dieser Aspekte vor und zwei Jahre nach Adipositaschirurgie subtypisiert und der prädiktive Wert der identifizierten prä- und postbariatrischen Subtypen für gesundheitsbezogene Variablen drei Jahre nach Operation (OP) bestimmt. Methode: Bei N=229 Patienten aus dem Psychosozialen Register der Adipositaschirurgie (PRAC) wurden zur Subtypisierung Temperament, Emotionsregulation und enthemmtes Essverhalten vor und nach OP via Selbstbericht erhoben. Zur Validierung der Subtypen wurden drei Jahre nach OP die Psychopathologie via Interviews und Selbstbericht sowie der Gewichtsverlust objektiv erfasst. Prä- und postbariatrische Subtypen wurden mittels latenter Profilanalysen identifiziert und ihr prädiktiver Wert mittels linearer Regressionen bestimmt. Ergebnisse: Post- vs. präbariatrische Subtypen klärten mehr Varianz an Psychopathologie drei Jahre nach OP auf. Der postoperative Gewichtsverlust konnte jedoch weder von prä- noch von postbariatrischen Subtypen vorhergesagt werden. Diskussion: Insbesondere die postbariatrischen Subtypen scheinen das langfristige psychologische Outcome nach OP vorherzusagen. Daher wird eine psychologische Diagnostik auch nach OP empfohlen, um frühzeitig postoperativ bestehende Defizite in Selbstkontrolle und Emotionsregulation sowie enthemmtes Essverhalten festzustellen und zu behandeln.

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Poster 10

Cholinergic network modulation in disinhibited eating behaviour

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Obesity refers partly to deficits in the control of eating behavior, which is region- and modalityspecific. The neurotransmitter acetylcholine (ACh) plays an important role in the regulation of hedonic aspects of feeding via (mainly) α4β2* nicotinic acetylcholine receptors (nAChR) in the forebrain, the thalamus, and parts of the mesolimbic system such as the nucleus accumbens and the ventral tegmental area. Thus, changes in α4β2* nAChR availability might influence prefrontal control of inhibitory processes but also might have an effect on the mesoaccumbens reward system. These associations have not been demonstrated in human obesity so far. Therefore, the aim of our study is to investigate whether there is altered α4β2*-nAChR availability in individuals with obesity, that is associated with high-disinhibited eating, together with changes in cortical-sub-cortical networks that subserve appetitive control.

To this aim, the project includes a prospective comparison of α4(α6) β2*-nAChR availability in individuals with high and low disinhibited eating behavior by using simultaneous PET-MR imaging under rest and task-related conditions and to connect the PET-MR outcome measures with data of neuropsychological evaluations.

Taken together, the results of the project will a) help to further identify key mechanisms of disinhibited eating behavior for a better understanding of the neurobiology of obesity, b) gain knowledge about the effect of nicotine on appetite and describe α4β2*-nAChR as a molecular treatment target, and hence c) offer potential translation to therapies for individuals with obesity.

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Poster 11

Psychometric properties of the Patient Assessment of Chronic Illness Care measure (PACIC-5A) among obese patients

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Background:
The Patient Assessment of Chronic Illness Care (PACIC-5A) was developed to assess the satisfaction with patient-provider interaction based on the Chronic Care Model. The aim of the study was to assess the psychometric properties of the German adaptation of the PACIC-5A questionnaire in a sample of obese general practitioners (GP) patients.

Methods:
Analyses were based on baseline data from the study „A 5A based guidance for obesity management in primary care: A cluster-randomized controlled study (INTERACT)". Data were collected via standardized questionnaires containing the 26-item version of the PACIC-5A questionnaire. A total of 117 patients were included in the analyses. Statistical procedures comprised descriptive analyses, the calculation of Cronbach´s alpha and a factor analysis in order to assess the psychometric properties including reliability and validity of the PACIC-5A.

Results:
The patient´s mean age was 43.3 years and the sample was mostly female (69%). Middle educational level was found for the majority (78%) and the mean Body Mass Index was 38.9kg/m². Descriptive analyses revealed a mean PACIC score of 2.33 and 5A sum score of 2.29. Floor and ceiling effects were found. PACIC-5A showed high internal consistency (Cronbach's alphas >0.9). Further results are expected.

Conclusion:
The results of this study will provide evidence regarding the psychometric properties of the German version of the PACIC-5A used in a sample of obese GP patients and make an important contribution to the reliable and valid assessment of the patient-GP interaction with regard to obesity counseling in primary care.

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Poster 12

Experimentelle und selbstberichtete Impulsivität bei 8- bis 13-jährigen Kindern in Abhängigkeit ihres Gewichtsstatus

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Einleitung:
Erste Befunde zeigen, dass Kinder mit Adipositas eine allgemeine und nahrungsbezogene Impulsivität sowie Inhibitionsdefizite aufweisen. Das Ziel dieser Studie war es, kindliche Impulsivität multimodal und in Abhängigkeit des Gewichtsstatus zu erfassen und klinische Korrelate zu bestimmen.

Methode:
Innerhalb der Kinder-EEG-Studie wurden n=12 Kinder mit Adipositas (EG; 10.9±1.9 Jahre) und n=22 Kinder mit Normalgewicht (KG; 10.1±1.6 Jahre) untersucht. Zur experimentellen Erfassung der allgemeinen Risikobereitschaft wurde der Balloon Analogue Risk Task-Youth (BARTY) eingesetzt. Etablierte Fragebögen dienten der Erfassung von Impulsivität, Essverhalten und allgemeiner Psychopathologie aus Mutter- und Kindsicht.

Ergebnisse:
Die EG zeigte im BARTY tendenziell weniger Risikobereitschaft als die KG, berichtete jedoch eine größere allgemeine und Essstörungspsychopathologie als die KG. Eine größere Risikobereitschaft innerhalb der EG war mit einer Reihe von klinischen Merkmalen assoziiert, darunter einer größeren selbstberichteten Impulsivität, während sich für die KG keine derartigen Zusammenhänge zeigten.

Diskussion:
Die Ergebnisse der Pilotstudie zeigen, dass Impulsivitätsmaße bei Kindern mit Adipositas versus Normalgewicht differentiell mit klinischen Merkmalen assoziiert sind. Aktuell wird untersucht, ob die Impulsivitätsdaten im Zusammenhang mit dem neurophysiologischen Profil der Kinder stehen. Perspektivisch gilt es, den relativen, prädiktiven Wert experimenteller versus selbstberichteter genereller und nahrungsspezifischer Impulsivität für den Gewichtsverlauf in größeren Stichproben zu identifizieren.

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Poster 13

Central noradrenergic neurotransmission and weight loss following gastric bypass surgery in obese individuals

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Roux-en-Y gastric bypass (RYGB) surgery is currently the most effective treatment strategy for obesity. Weight loss following RYGB is thought to result in part from changes in the regulation of appetite and food intake mediated by brain catecholamines. Although this has already been shown for dopamine, no studies on noradrenaline (NA) in humans undergoing RYGB exist. The aim of this study was therefore to investigate whether weight loss after RYGB is associated with alteration in central NA transmission.

We studied severely obese individuals (BMI 47±5 kg/m2) using NA-specivic [11C]MRB and PET to estimate NA transporter (NAT) availability twice shortly before surgery and after 6 months follow up. Kinetic modeling of regional time activity curves was performed using multilinear reference tissue model 2 to estimate distribution volume ratios (DVR).

Thus far, all patients responded to RYGB, comprising a change in BMI from pre-surgery (pre) to 6-months follow-up visit (post) of -11±3 kg/m2 (23±6%, $p<0.001$), a reduction in body weight (-31±11 kg, $p<0.001$) but no change in DVR (e.g. in the insula and the locus coeruleus LC). There was no significant association between changes in body mass index (BMI) or body- weight (BW) and changes in DVR. Preoperative DVR showed no significant correlation with changes in BMI or changes in BW.

Together, the data suggest that NA transmission has a role in modulating BW. However, whether preoperative NAT values predict long-term changes in BW need further consideration within this ongoing study together with neuropsychological and functional MRI data accompanying treatment.

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Poster 14

Mechanisms behind calcium-dependent activation of macrophages in adipose tissue

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In many patients obesity leads to a chronic inflammation. On cellular basis this is conducted by immune cell migration most prominently mediated through macrophage activation. Extracellular calcium ions ($exCa^{2+}$) were shown to amplify these processes by activating the NLRP3-inflammasome. The role of $exCa^{2+}$ and the higher reactivity in visceral adipose tissue however is not fully understood.

To determine the basic principles of obesity-induced inflammation, adipose tissue samples and monocyte derived macrophages (MDM) of obese patients are examined. By differentiating MDM with autologous serum a patient-specific in-vitro model is achieved to analyze individual macrophage reactivity under inflammatory conditions. It becomes apparent that IL-1β release in response to a proinflammatory stimulus depends on dosing, individual variance and tissue. For visceral adipose tissue far higher amounts of cytokines were detected compared to subcutaneous samples. Moreover inhibiting the G protein-coupled calcium sensing receptor (CaSR) results in lower expression of IL-1β.

To verify these findings in clinical context, a prospective clinical-experimental study is conducted, comparing cytokine release upon stimulation $exCa^{2+}$, subpopulations and protein expression in MDM as well as clinical parameters between obese and lean subjects.

These experiments can lead to a deeper understanding of obesity-induced inflammation, giving the opportunity to detect new target points and prognostic markers to reduce morbidity in obese patients.

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Poster 15

Perinatal exposure to Butylparaben increases body weight in female offspring

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Introduction:
Parabens are widely used preservatives in consumer products such as food and cosmetics. The risk of low-dose exposure for human health has been discussed in recent years. Previous data suggest that parabens like n-Butylparaben (BuP) may act as endocrine disruptors and affect the adipocyte differentiation. The aim of the study was to investigate the effect of maternal exposure to BuP on weight development in the offspring.

Methods:
Balb/c mice were subcutaneous exposed to 140 µg BuP/kg/week during pregnancy and breastfeeding. To investigate the effect of maternal BuP exposure to the offspring weight development, body composition, food intake and several parameters were monitored.

Results:
Perinatel exposure to BuP led to an increased body weight only in female offspring. The elevated body weight was linked to a higher fat mass and glucose levels. Besides we detect a higher food intake and leptin levels in obese female mice. In contrast to higher leptin levels we were able to show a lower expression of pro-opiomelanocortin (POMC) of hypothalamic neurons, which are important for the central regulation of satiety.

Conclusion:
Our data demonstrate that perinatel BuP exposure leads to an increased body weight only in female offspring which is coupled with a higher fat mass and food intake. These effects are probably mediated by paraben-induced disturbance of neural regulation of satiety in the hypothalamus.

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Poster 16

Pubertätsbeginn als Ursache für Wachstumsunterschiede zwischen schlanken und adipösen Kindern

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Die Körpergröße ist einer der wichtigsten Parameter der kindlichen Entwicklung. Sie wird durch Interaktion von Genetik und Umwelt (Patel 2005) und somit auch von der Ernährung (Gat-Yablonski 2011) beeinflusst. Mit 6849 Probanden aus der LIFE-CHILD-Kohorte konnten Wachstumsunterschiede zwischen schlanken, übergewichtigen und adipösen Kindern festgestellt werden: Einerseits unterscheidet sich die Height-SDS zwischen den nach BMI-SDS in Gruppen aufgeteilten Kindern. Adipöse und übergewichtige Kinder haben, insbesondere präpubertär, eine signifikant höhere Height-SDS. Anderseits gibt es eine positive Korrelation zwischen der Height-SDS und BMI-SDS, besonders stark ausgeprägt unter präpubertären Kindern. Diese vor allem präpubertären Größenunterschiede (bis zu 6,9 cm bei Mädchen; bis zu 7,5 cm bei Jungen) nivellieren sich weitestgehend mit dem Auswachsen der Kinder. Als mögliche Ursachen für die Wachstumsunterschiede konnten höhere Elterngrößen, früherer Wachstumsbeginn und höhere Wachstumsgeschwindigkeit der Adipösen ausgeschlossen werden. Stattdessen ist der Pubertätsbeginn eine mögliche Ursache: Adipöse Mädchen treten deutlich früher (>0,5 Jahre) als schlanke Mädchen in die Pubertät ein. Adipöse Jungen hingegen treten etwas später als schlanke Jungen in die Pubertät ein. Da ein späterer Pubertätsbeginn die Wachstumsunterschiede bei Jungen nicht erklärt, ist davon auszugehen, dass auch noch andere Faktoren wie das Geburtsgewicht einen Einfluss auf das Wachstumsverhalten von Kindern haben. Diese Faktoren gilt es weiter zu untersuchen.

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Poster 17

Functional characterization of two genetic variants identified in the leptin receptor (LEPR) gene in a patient with morbid obesity

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Objective:
At the University Children's Hospital a six-year-old girl presented with severe obesity and hyperphagia. Exome sequencing revealed a compound heterozygous deletion and substitution in the LEPR coding sequence. Since leptin and its receptor are important regulators of satiety in the hypothalamus, we want to investigate the effects of these genetic variants on LEPR signaling to answer the question if the variants are causal for the phenotype of the patient.

Material and methods:
We inserted the variants into a wildtype pcDNA3 myc-LEPR plasmid using site-directed mutagenesis. We transfected HEK293 cells with the control vector, myc-tagged wildtype or mutant receptors, each individually, and analyzed LEPR expression and signaling by qRT-PCR and immunoblot analyses using antibodies direct against myc-Tag, totalSTAT3, pSTAT3, totalJak2 and pJak2.

Results:
We controlled the mutagenesis by nucleotide sequencing and used those plasmids for transfection. After incubation and serum starving of the transfected cells we stimulated the cells with leptin or let them unstimulated as controls. None of the mutated receptors showed the ability to phosphorylate STAT3 after stimulation with leptin when we analyzed the protein lysates by western blot. We verified the higher expression of LEPR in the cells transfected with myc-LEPR than in none transfected cells using qRT-PCR.

Conclusions:
So far the mutant LEPR both seem to show an impaired signaling pathway in response to leptin. If also the combination of the variants is pathogenic, potentially a therapy with MC4R agonists might be possible in this young patient.

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Poster 18

Mimicking Paracrine Cell Communication in Fibrillar 3D Scaffolds *in vitro*

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Paracrine communication is one possibility for cells to interact with each other. As it is based on release of soluble mediators, so-called cytokines, into the cells' environment, the range of action is locally confined. Cytokine dilution by diffusion establishes concentration gradients around the source cell enabling distance-dependent cell reactions. We aim to establish *in vitro* 3D systems mimicking such paracrine cell communication to address related biomedical questions with in-depth analytical methods.

Cytokine releasing cells were mimicked by glycosaminoglycan-modified microparticles, enabling slow release of a specific cytokine. Release kinetics and gradient formation in the surroundings of the microparticles were quantified for SDF1 and TGF-b1. The impact of the paracrine signals on cells in 3D fibrillar matrices based on collagen I was shown by the induction of chemotaxis of hematopoietic stem cells towards an SDF1 gradient and by the differentiation of fibroblasts into myofibroblasts by TGF-b1. The SDF1-dependent chemotactic response was fast & directed migration towards the gradient was observed by single cell tracking. TGF-b1-dependent fibroblast differentiation was slow & gradient-independent. However, the sustained delivery of TGF-b1 caused cell response at a concentration level two orders of magnitude lower compared to standard cell culture approaches.

This work established 3D systems to mimic paracrine cell communication in cell culture setups. The successful implementation was demonstrated by two important biomedical examples, i.e., hematopoietic stem cell homing & fibroblast differentiation in wound healing.

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Poster 19

The influence of intrinsic and extrinsic factors on *in vitro* microglia differentiation

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Over the last decade cell-based therapy gained in interest as promising tool for incurable diseases. Microglia might have interesting clinical properties for treatment of neurological diseases by providing neuroprotective and regenerative effects. As the resident and innate immune cells of the brain, they play a pivotal role in neuro-inflammation and exist in a heterogeneous population with a high morphological and functional plasticity. Their phenotypes are not permanently polarized into two categories; they exist along a continuum where they acquire different profiles based on their local environment. The defined polarization status of the cells is activated by diverse stimuli, such as cytokines or chemokines. Simplified it is distinguished between 2 polarization states.

Our aim is to study polarization of the *in vitro* derived (IVD) microglia and whether GFP has an impact on the differentiation process. We use hematopoietic stem cells from C57Bl6- and transgenic eGFP-mice to differentiate into monocytes/microglia like cells. The balance between stem cell self-renewal and differentiation is controlled by concerted actions of extrinsic signals (cultivation procedure) and intrinsic factors (genetic influence of GFP). We compared the cell production of those two different mouse strains by using various differentiation protocols. The results of this study can contribute to improve differentiation of stem cells for cell based therapies in neurodegenerative diseases like Alzheimer's.

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Poster 20

Charakterisierung des Versagensverhaltens humaner Fascia thoracolumbalis im Zugversuch nach partieller Plastination der Proben

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Hintergrund:
Die strukturellen und funktionellen Parameter von Faszien sind bisher nur unzureichend erforscht, ungeachtet der hohen biomechanischen Relevanz dieser Gewebe. Das Verformungsverhalten von Faszien ist in Abhängigkeit von der Grundorientierung des scherengitterartigen Kollagennetzwerks stark anisotrop. Jedoch sind zur Testung von Bändern und Faszien Standard-Zugprüfverfahren im Einsatz, ungeachtet der Problematik, dass diese aufgrund der anisotropen Gewebestruktur eher ungeeignet sind.

Material & Methoden:
Untersucht wurde humane Fascia thoracolumbalis, welche in frischem Zustand freipräpariert, eingefroren und plastiniert wurde. Dabei wurde ein Verfahren zur Plastination verwendet, welches u.a. von Steinke et al. schon mehrfach erfolgreich angewandt wurde. Die Zugprüfung der Proben erfolgte bis zum Versagen entlang der Hauptfaserrichtung zum Musculus latissimus dorsi. Die zweite Hauptfaserrichtung verlief dabei in einem 30°-Winkel zur Prüfrichtung.

Ergebnisse:
Bei allen geprüften Faszienproben lag die Versagenszone im nichtplastinierten Prüfbereich und verlief in den Proben entlang der zweiten Hauptfaserrichtung, welche um 30° versetzt zur Prüfrichtung verliefen, in Folge einer Delamination der Fibrillen untereinander.

Schlussfolgerungen:
Die partielle Plastinationstechnik ermöglicht eine Adaption bestehender Zugprüfverfahren zur Testung von humaner Fascia thoracolumbalis. Die Testreihe bestätigt die Theorie, dass ein wesentlicher Faktor in der Lastübertragung in humanen Faszien die Anisotropie der kollagenen Hauptfaserrichtungen ist. Entlang dieser Hauptrichtungen sind die Gewebe wenig dehnbar und sehr fest.

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Poster 21

Entwicklung eines Messaufbaus zur *in vitro* Analyse differenter Implantatsysteme in humanen unfixierten Kieferpräparaten

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Entscheidend für eine erfolgreiche Einheilung von Dental-Implantaten ist die Primärstabilität in den ersten Wochen nach der Implantation. Zur biomechanischen Untersuchung der Primärstabilität differenter Implantatsysteme wurde ein Messaufbau entwickelt, der durch eine zyklische Belastung die Mahlbewegung unter Okklusion der Zähne möglichst physiologisch nachbildet und die resultierenden Mikrobewegungen über 10 000 Zyklen erfasst.

Die Dental-Implantate werden nach zahnärztlichen OP-Standards in den Kieferknochen eingebracht, der in einem geeigneten Einbettmaterial fixiert wird. Über die Zahnkrone wird durch einen axial gelagerten Prüfkopf eine konstante Prüfkraft eingeleitet, die die Beißkraft des stomatognaten Gegenspielers der prothetischen Implantatversorgung darstellt. Angetrieben durch einen Elektromotor wird der Kieferknochen senkrecht zur eingeleiteten Prüfkraft zyklisch in bukkal-lingualer Richtung bewegt. Auf diese Weise wird die Zahnkrone wechselnd außermittig belastet. Die resultierenden Mikrobewegungen zwischen der Zahnkrone und dem knöchernen Umfeld werden mithilfe eines optischen Bildkorrelationssystems erfasst. Anschließend erfolgt eine deskriptive und statistische Auswertung der Auslockerung in Abhängigkeit von der Zyklenzahl.

In Vorversuchen am Kunstknochen konnte die Funktionsfähigkeit des Messaufbaus nachgewiesen werden.

Mit steigender Zyklenzahl zeigte sich eine zunehmende Auslockerung der betrachteten Dental-Implantate, was sich mit Angaben aus der Literatur deckt. In weiterführenden Versuchen werden differente Implantatsysteme im humanen Kieferknochen paarweise gegeneinander verglichen.

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Poster 22

Cell type specific expression analysis of the extracellular matrix composition of the liver sinusoid

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Matrix remodeling linked to dedifferentiation plays a major role in liver fibrosis for successive loss of function. The maintenance of the innate liver cell differentiation is defined by interactions with the sinusoidal extracellular matrix (ECM), which is provided by its residential cell types: Hepatocytes, Kupffer, stellate and endothelial cells. So far, very limited data exist about the composition and contribution of each cell type to this attenuated network of ECM. The aim of the present study is a systematic analysis of the ECM protein contributions of the hepatic cell types in health and disease.

Human liver tissue, normal and fibrotic, was obtained from partial resections and classified by preclinical, macroscopic and pathological reports. Liver cells were isolated using a two-step EDTA/collagenase perfusion technique, purified by gradient centrifugation and separated by specific adherence and magnetic activated cell sorting. Extracted RNA was used for RT-PCR of selected target genes of liver specific ECM components.

Preliminary results revealed that only 19 out of 28 target genes were detectable in the sinusoid. Interestingly, the expression of some known liver ECM proteins (collagen 4, 6 and Tenascin subtypes) has not been observed yet. In addition, hepatocytes seem to contribute to the production of a limited number of 4 ECM proteins.

In conclusion, the non-parenchymal cell fraction is likely key to the production of a set of 19 particular ECM components in the sinusoid. This analytic approach could lead to a profound understanding of cell type specific ECM expression in healthy and fibrotic liver.

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Poster 23

Collagen cross-linking inhibits Collagenase I degradation of rabbit scleral tissue

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Idiopathic melting diseases or inflammatory degrading processes of scleral tissue lead to severe deformation of the eyeball and subsequent damage of the retina. Cross-linking of the sclera is a new promising approach to strengthen the scleral rigidity and stabilize the eye shape. Therefore, scleral patches of rabbit eyes were cross-linked using paraformaldehyde, glutaraldehyde, riboflavin combined with UV-A or with blue light to increase the rabbit scleral resistance to enzymatic degradation. Afterwards, the scleral patches were incubated with collagenase I (MMP1) for up to 24 h. Digested protein components in the supernatant were detected using Fluoraldehyde o-Phthaldialdehyde (OPA).

All cross-linking methods reduced the enzymatic degradation by MMP1 of rabbit scleral tissue. Glutaraldehyde (1 %) and paraformaldehyde (4 %) reduced the enzymatic degradation to 7 % ± 2.8 in dependence of the cross-linking incubation time. Cross-linking with riboflavin/UV-A-light reduced significantly the degradation by MMP1 to 62 % ± 12.7 after 24 h. Cross-linking with riboflavin/blue light also reduced significantly the degradation by MMP1 to 77 % ± 13.5 after 24 h. The tested light intensities, light exposure times and riboflavin concentrations did not change the generally observe cross-linking results, significantly.

Collagen cross-linking method by riboflavin and UV-A- or blue light might be a highly promising therapeutic approach to treat melting diseases of scleral tissue.

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Poster 24

Calcium und Phosphate as network modulators in bioactive hybrid glass scaffolds for bone tissue engineering

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Materials for the substitution of bone defects should provide 1) mechanical strength, 2) biodegradability, 3) a porous structure for bone forming cells to invade and attach as well as 4) bioactivity to support bone regeneration. Our group recently published a hybrid material from a sol-gel derived glass and 3- or 4-armed macromers functionalized with 3-(Triethoxysilyl)propyl isocyanate. These hybrid materials were processed to remarkably strong macroporous scaffolds by indirect 3D-printing [1]. In a second step, addition of 30% Ca^{2+} and 5% phosphate generated bioactive hybrid glass scaffold [2], but after incubation in aqueous media, mechanical strength of the materials rapidly decreased. In order to improve mechanical strength and keep bioactivity, we systematically reduced Ca^{2+} and varied phosphate content as well as macromeric crosslinker type and amount. A composition with 10% Ca^{2+} and 10% phosphate with 30% of functionalized 4-armed Pentaerythritol ethoxylate (Mn ~797) is currently considered to be most promising. This scaffold material shows high bioactivity and good compressive strength values in a dry state as well as acceptable mechanical stability after in-vitro incubation. Ca^{2+} and phosphate distribution as well as release kinetics from the scaffolds are currently under investigation.

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Poster 25

Tissue Engineering of the Liver sinusoid

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The liver performs its excretory function by its unique tissue architecture. A reconstruction of the latter requires differentiated cells and *in vivo* like extracellular matrix (ECM) combined in a cell culture system allowing compartmentalization. The use of Transwells enables the definition of a basolateral and an apical compartment, corresponding to liver sinusoid and bile canalicular network *in vivo*. Aim of this project is the reconstruction of the liver sinusoid using primary human liver cells that form an organized structure and display *in vivo* like transport processes.

Starting point for our approach are primary human hepatocytes (PHH) isolated from human liver tissue samples. Preliminary experiments on matrix selection showed a striking influence of the ECM composition on morphology and cellular arrangement of PHH. Therefore, an analysis of the sinusoidal matrix is work in progress using Proteomics. Additionally, results from the cultivation of PHH between matrices, mimicking sinusoidal and basal membrane matrix, led to a tight cellular arrangement combined with an increased expression of tight junctions. However, measurement of the transepithelial resistance showed an incomplete compartmentalization of this architecture.

In conclusion, the engineered liver model showed that the right combination of primary human liver cells and ECM led to a layer of tightly linked cells. However, the reconstruction of a functional liver tissue in terms of directed transport processes requires a closed cell layer. Therefore, further research is needed to optimize cell density, arrangement and ECM to achieve a full compartmentalization.

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Poster 26

Release of siRNA from crosslinked gelatin microparticles for bone tissue engineering applications

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RNA interference (RNAi) is a promising technique to down-regulate disease related proteins on a pre-protein level. We and others postulate that the release of nanoparticle-complexed small interfering RNA (siRNA) from implanted biomaterials could provide structural support for tissue repair, combined with local siRNA transfection of invading cells. Therapeutic application of bone inducing BMP-2 is known to stimulate antagonistic proteins, such as noggin and chordin as well as sclerostin and reduce the therapeutic efficiency of BMP-2. Hence, these antagonists are interesting targets for gene silencing in order to improve local bone regeneration[1,2]. The aim of this study was to investigate release of siRNA from oligomer-crosslinked gelatin microparticles (cGMP)[3] to support osteogenic differentiation. In a first step, we investigated stability of complexed siRNA in media as well as silencing efficiencies in dependence of the transfection system. Newly developed polyethylenimine (PEI) derivatives, P5Y and P10Y[4] were compared to Lipofectamine® RNAiMAX. In a second step, we investigated release of siRNA from cGMP. Uptake of released siRNA by SaOS-2 cells and silencing efficiency were determined via cell death siRNA.

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Poster 27

Injectable oligomer cross-linked gelatin hydrogels

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Gelatin-based chemically cross-linked hydrogels are mechanically resilient and mimic extracellular matrix (ECM) due to their inherent effects of adherent cells, degradability, immuno- and biocompatibility. In this study, we strive to synthesize hydrophilic anhydride-containing oligomers and fabricate injectable oligomer/gelatin formulations using amine-anhydride conjugation.

Oligomers were synthesized by free radical polymerization of pentaerythritol diacrylate monostearate (P), maleic anhydride (MA) and hydrophilic comonomers: acryloylmorpholine (Mo), N-vinylpyrrolidone (Vp) and hydroxypropyl acrylate (Hp) in defined ratios and were characterized physico-chemically. Injectable formulations of these oligomers were evaluated rheologically. Human adipose tissue derived stem cells (hASC) were encapsulated in hydrogels and assessed for cytocompatibility and mineralization capacity.

Three sets of hydrophilic oligomers (oPHpMoMA, oPVpMoMA and oPHpVpMA) were synthesized. Results confirmed high reactivity (MA intactness > 80%), successful integration of all participating comonomers and controlled molecular weights (M_n= 2-3 kDa). These oligomers dissolved in water faster than established derivatives. Gelatin-based hydrogels of such oligomers were fabricated using a multi-step programmable pipette. Gel stiffness depended on presence of comonomer P and hydrophilic comonomer type. Cross-linked hydrogels contained viable hASC that proliferated effectively over 7 days and showed good mineralization capacity when incubated with osteogenic medium. These gels hold promise for regenerative and biomedical applications.

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Poster 28

Physiological and structural lung maturation is positively affected by mesenchymal stem cell conditioned medium

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Impaired alveolar fluid clearance (AFC) and structural lung immaturity can lead to respiratory failure in preterm neonates. AFC is driven by vectorial Na^+ transport accomplished by the epithelial Na^+ channel (ENaC) and the Na,K-ATPase. Mesenchymal stem cells (MSCs) are suggested to harbor therapeutic potential for respiratory diseases, although effects on lung maturation have not been addressed. Beneficial effects of MSCs are attributed to paracrine signaling, i.e. growth factors involved in fetal lung development. We thus addressed whether MSC conditioned medium (MSC-CM) is able to stimulate lung branching morphogenesis and Na^+ transport in primary rat fetal distal lung epithelial (FDLE) cells and if inhibition of growth factor signaling attenuates the effect of MSC-CM. MSCs were isolated from full- and preterm umbilical cord. Effects of MSC-CM on Na^+ channel activity and expression were determined with Ussing chambers and RT-qPCR. Lung maturation and branching morphogenesis were analyzed in fetal rat lung explants. MSC-CM significantly ameliorated ENaC and Na,K-ATPase activity and gene expression. Furthermore, fetal lung explants cultivated in MSC-CM displayed an enhanced structural maturation. Inhibition of hepatocyte growth factor (HGF) signaling downregulated the effect of MSC-CM on ENaC activity. The results demonstrate that MSC-CM increases Na^+ transport in FDLE cells, possibly attributable to HGF signaling, and improves branching morphogenesis. Therefore, MSC-CM can stimulate lung structural and functional maturation *in vitro* and might represent a future therapeutic option for preterm infants.

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Poster 29

Niedrigviskose vs. hochviskose Bulk-fill Komposite – Bewertung des Zahn-Komposit-Verbundes

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Ziel:
Vergleich des Zahn-Komposit-Verbundes nach Anwendung von hochviskosen und niedrigviskosen Bulk-fill Kompositen.

Materialien und Methoden:
192 kariesfreie humane Molaren wurden mit Kl.II Restaurationen versorgt. Die Füllungslegung (je n=16) erfolgte mit den Kompositen SonicFill (SF), Tetric EvoCeram Bulk Fill (TEC), x-tra fil (XF), SDR/ Premise (SDR) und x-tra base/Premise (XB). Die Referenzgruppe wurde mit Premise (P) inkrementell restauriert. Als Adhäsive wurden Optibond FL (OFL) bzw. Xeno V+ (X) verwendet. Bei der Hälfte der Proben wurde eine Probenalterung durchgeführt. Nach Probenpräparation gemäß Laborstandard wurde an rasterelektronenmikroskopischen Abbildungen von Zahnschliffen die Länge (%) der interfazialen adhäsiven Defekte am Schmelz bzw. Dentin bestimmt und die Ausdehnung mit Score 1-4 bewertet: 0-25 %/>25-50 %/ > 50-75 %/ > 75-100 %. Die Daten wurde mittels Kruskal-Wallis- und Mann-Whitney-U-Test statistisch ausgewertet.

Ergebnisse:
1) In Kombination mit X ergaben sich für alle Komposite am Schmelz und Dentin ausgedehntere adhäsive Defekte als mit OFL. 2) Schmelz: Weniger Defekte erschienen in der Gruppe SF/X gegenüber XB/X und nach Alterung mit SDR/X gegenüber TEC/X und XF/X. 3) Dentin: Keine signifikanten Unterschiede zeigten sich zwischen den Gruppen mit OFL. Mit SDR/X erschienen ohne Alterung weniger adhäsive Defekte als mit TEC/X und XF/X.

Schlussfolgerung:
Der interne Verbund der Bulk-Fill-Komposite ist vergleichbar mit dem des konventionellen Komposites. Das Adhäsiv ist für den Zahn-Komposit-Verbund entscheidender als der Kompositтyp.

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Poster 30

Investigation of snake venom components as potential chemotherapeutic amplifiers in the treatment of liver cancer

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Besides the surgical liver resection the only available therapy to treat Hepatocellular carcinoma (HCC) is the growth factor receptor (GFR) inhibitor Sorafenib. HCC often develops in a proliferative environment consisting of atypical extracellular matrix (ECM), growth factor release and dedifferentiated hepatocytes. Both ECM and growth factors contribute to cell cycle progression via integrins and GFR. Snake venoms contain disintegrins, allowing to target the cell cycle related signaling. Aim of the presented study is the investigation of effects from snake venom components and GFR-inhibitors on signaling in HCC.

For display of HCC and healthy liver the hepatoma cell lines HepG2 as well as Huh7 and primary human hepatocytes were used. Dose response relationships of venoms from Vipera palaestinae, Calloselasma rhodostoma and Echis sochureki on these cells were used to determine non-toxic concentrations (XTT, LDH release). The evaluation of integrin interaction of these concentrations is work in progress. Preliminary experiments showed that snake venoms are capable to prevent hepatoma cells from adherence on cell culture dishes and to sensitize them towards the chemotherapeutic 5-fluorouracil.

In conclusion, snake venoms show an influence on the cell adherence suggesting integrin interaction. However, further research is needed using fractionized venoms to identify potential components. Further, co-incubations of snake venoms with Sorafenib are planned to determine effects on signaling. The identification of disintegrins as potential amplifiers of Sorafenib could allow to improve the therapeutic outcome of this tumor therapy.

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Poster 31

Healing from hair follicle – stem cells from the outer root sheath to treat chronic wounds

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Our research focuses on the generation of an autologous Advanced Therapy Medicinal Product (ATMP) designed for wound healing and repigmentation. We use hair follicles as starting biological material to isolate stem cells from the Outer Root Sheath (ORS) of human hair. The ORS presents an excellent non-invasively available source of material for regenerative therapies. It is obtained by harmless plucking of hair and harbours a collection of developmentally highly potent adult stem cells and precursors. Those cells are further differentiated into skin-relevant cells (keratinocytes, melanocytes, fibroblasts and mesenchymal stem cells) with the goal of generating a pre-clinically tested epidermal and dermoepidermal skin graft. We have generated melanocytes, keratinocytes, fibroblasts and mesenchymal stem cells (MSCs) from hair follicle ORS by the means of an optimized explant method by Savkovic et al. All cultures were analyzed on the basis of their morphology, gene- and protein-marker expression. In order to create epidermal equivalents, melanocytes were co-cultivated with keratinocytes. Integration of fibroblasts generated the dermal compartment, producing a dermoepidermal equivalent. Manufactured epidermal and dermoepidermal equivalents were anatomically and functionally comparable to human skin. Our autologous and non-invasively gained skin grafts offer an immense potential for personalized treatment of chronic wounds, accompanied by their use as toxicological tests in the industry and innovative cellbanking opportunities. Further use of the MSCs' exosomal content will improve the engraftment of the skin transplants.

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Poster 32

Chondrogenic differentiation of heart valve interstitial cells in Zebrafish: A chance to study the pathophysiology of valvular heart disease

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We studied the histo-architecture and ultrastructure of atrioventricular and bulboventricular valves in whole Zebrafish and dissected heart sections. The microarchitectures of both heart valves differed dramatically from the typical three extracellular matrix layer architecture in human heart valves. The tissue underneath the endocardium consisted of a thin, hypocellular and collagen rich layer at the inflow side and of an adjacent, broad, cellular and proteoglycan rich layer extending to the outflow side. The hypocellular layer contained collagen fibers without obvious periodicity. The cellular layer was packed with polygonal cells, reminiscent of chondroblasts. In 35dpf valves the cells showed a size increase from the inflow to the outflow side, whereas in 1ypf valves, most cells were large with abundant cytoplasm. The fibrous character of the small layer was documented by deep blue Azan Trichrome collagen staining. The chondrogenic character of the broad layer was substantiated by turquoise green Movat Pentachrome proteoglycan staining and by immunostaining of typical chondrocytic proteins (Sox-9, aggrecan, and type II collagen). Presence of cytokeratin and adherens junctions indicated ongoing epithelial to mesenchymal transition and remodeling. Our study outlines differences between Zebrafish and mammalian heart valve anatomy, indicates that in Zebrafish the relationship between heart valve and cartilage development continues beyond the embryonic period and suggests adult Zebrafish heart valves to be a potential model for the study of cartilage occurrence in heart valves, which, in human, is a pathologic change.

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Poster 33

Gelatin microparticles as hydrophilic organic drug carriers in a printable inorganic cement paste for bone grafting

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Bone tissue is a complex combination of inorganic calcium phosphates (hydroxyapatite), organic collagen, proteins, water and different cell populations. 3D printing of a novel self-setting, oily and water free calcium phosphate cement (CPC) paste enabled the fabrication of individually shaped implant material with interconnecting porosity. Through the incorporation of oligomer cross-linked gelatin microparticles (cGMP) as a hydrophilic organic component, we aim at mimicking natural bone composition, but also provide leachable porogens to support the ingrowth of cells and support regeneration. Further, we aimed to release the antibiotic gentamicin sulphate from the microparticles. Printing attempts of the cement paste with dry cGMP were successful. However, the scaffolds structure broke after immersion in water due to swelling of the cGMP. In order to solve this problem, pre-swelling of cGMP in glycerol was identified and cGMP was optimized for particle size. Mechanical testing of scaffolds with cGMP showed a loss of stability, but was still in the range of cancellous bone. Gentamicin sulphate incorporation had no effect on the stability. The release of the antibiotic from cGMP and CPC-cGMP-scaffolds was analysed. The drug-loaded CPC-cGMP-scaffold showed a different release profile compared to direct incorporation of gentamicin sulphate without cGMP.

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Poster 34

Mimicking Cell-Cell Interactions during Wound Healing in a 3D *in vitro* Model

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Wound healing is a highly dynamic process and requires a tightly balanced regulation of different cell types and a myriad of cytokines as well as their interactions with the extracellular matrix (ECM). Dysfunction in cell-cell or cell-matrix interactions can result in impaired tissue repair and pathological scarring. Our model system is based on fibrillar 3D matrices reconstituted from collagen I. We investigate primary human dermal fibroblasts (FB) as well as human monocyte-derived macrophages in their response to these matrices in co-culture experiments.

We demonstrated FB to differentiate into contractile myofibroblasts under global TGF-β1 stimulation. To mimic the influence of immunomodulatory macrophages, myofibroblasts were additionally exposed to IL-10. While removal of TGF-β1 from myofibroblasts led to increased cell death, subsequent IL-10 treatments without TGF-β1 presence led to dedifferentiation back to FB with almost no cell death. Co-culture experiments in this 3D biomaterial scaffold of FB and regulatory M2-macrophages under systemic TGF-β1 delivery revealed a dose-dependent regulation of FB differentiation in dependence on macrophage amount. While proliferation of FB increased with the number of co-cultivated macrophages, less differentiation into myofibroblasts was observed.

In conclusion, co-culture experiments with regulatory macrophages nicely recapitulates the control of FB proliferation and differentiation in an *in vivo* wound resolution phase. Ongoing studies cover the regulation of paracrine IL-10 and TGF-β1 signals between both cell types by interaction with 3D GAG-modified fibrillar matrices.

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Poster 35

Untersuchung des Krafteintrags bei der Herstellungder konischen Klemmung zwischen HTEP-Schaft und -Kopf unter realitätsnahen Bedingungen

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Nahezu alle heutigen Hüftendototalprothesen (HTEP) besitzen ein modulares Hüftstielsystem, bei dem der künstliche Gelenkkopf erst während der Operation mit dem femoralen Schaft der Prothese verbunden wird. Die Verbindung der beiden Komponenten wird über den Reibschluss einer konischen Klemmung realisiert. Entscheidend für die Verbindungsfestigkeit der Klemmung ist die in Richtung der Achse des Konus aufgebrachte Maximalkraft, die sowohl von dem eingeleiteten Impuls als auch von der Dämpfung des menschlichen Körpers abhängt. Die Herstellung der Klemmung erfolgt über einen Hammerschlag des Operateurs.

Um die Fügekräfte verschiedener Operateure und den Einfluss der dämpfenden Weichteilsituation zu untersuchen, wurde eigens dafür eine Messprothese entwickelt. Für die Messung der Fügekraft wird zum Einen ein piezoelektrischer Kraftaufnehmer zwischen Konus und Stiel des Schaftes einer dafür bearbeiteten Messprothese (CBC, Mathys AG) und zum anderen ein Impulshammer verwendet, welcher ebenfalls über einen piezoelektrischen Sensor verfügt.

Mit dieser Messanordnung wurde eine Studie mit 31 Operateuren durchgeführt. Die Messprothese war dabei in einem Block aus Ballistikgelatine eingebettet. Das Mischverhältnis der Gelatine wurde so gewählt, dass das Dämpfungsverhalten des Blocks dem in situ entspricht. Dazu wurden vor der Studie Versuche am Körperspender durchgeführt. Die Operateure fügten die Köpfe mit Kräften zwischen 822,5 N und 3835,2 N. Bei dieser erheblichen Differenz sollte man die Impaktion des künstlichen Gelenkkopfes mit Hilfe eines dafür vorgesehenen Instruments standardisieren.

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Poster 36

Using Next Gernation Sequencing and Antibody Array's to analyze Carnosine's primary Targets

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Previous studies demonstrated that carnosine (car) affects signaling molecules of different pathways in a number of experimental models. However, the primary targets of car are still unknown and its effect on complex signal transduction has not been revealed. This is especially the case for pathways that could be responsible for the anti-neoplastic effect of the dipeptide. Therefore, we performed a phosphoprotein antibody array and RNA-sequencing with U87 glioblastoma cells treated with 50 mM car for 24h, in order to obtain a precise and coherent picture of car's influence on signal transduction in single tumor cells. Sequencing detected 1998 genes significantly differentially expressed under the influence of the dipeptide and the array detected 42 phosphorylation sites to be influenced. A pathway analysis with array data revealed that carnosine may influence PI3K/AKT and MAPK signaling and cell cycle control. Combined analysis of RNA- and phosphoprotein data, revealed that carnosine should inhibit cell migration, cell cycle progression and synthesis of DNA. Finally, the results were validated by reporter genes for transcription factors down-stream of PI3K/AKT and MAPK signaling. Here, we observed a significant reduction of HIF, SRF and myc/max related reporter gene activity in U87 cells by car. In addition, we also observed a significant inhibition of SRF activity in LN405 and T98G glioblastoma cells. In conclusion, our data demonstrate that the dipeptide inhibits the transcriptional activity of SRF via PI3K/AKT and MAPK signaling.

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Poster 37

Metabolomic profiling in human spermatozoa and seminal plasma of smoking and non-smoking healthy male subjects

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The prediction of the male reproductive potential currently relies on semen analyses. Technologies like genomics, proteomics and metabolomics have spurred the search for novel male infertility biomarkers.

Up to now, there are very few data on the metabolome of human seminal plasma available. In human sperm, metabolomic profiles have not been described, yet. Therefore we established reliable protocols to identify and investigate the metabolome of sperm and seminal plasma from 10 smoking and 10 non-smoking healthy human donors. Concentrations of 186 metabolites, such as acylcarnitines (40), amino acids (21), the sum of hexoses, biogenic amines (19), phosphatidylcholines (76), lyso-phosphatidylcholines (14) and spingomyelins (15) were determined in sperm lysates and seminal plasma using a targeted metabolomic approach. Whereas biogenic amines and amino acids were analyzed by liquid chromatography tandem mass spectrometry, concentrations of the other metabolites were determined by flow injection analysis-MS/MS measurements and flow cytometry. Results of the analytical analyses were compared with standard spermiogram parameters.

Our data reveal significant differences between smokers and non-smokers in the concentration of glutamine ($P < 0.05$), glycine ($P < 0.05$), asymmetric dimethylarginine ($P < 0.05$), as well as in the activity of caspase 3 ($P < 0.01$) and the DNA fragmentation index ($P < 0.01$) in sperm lysates. The concentrations of some acyl carnitines are significantly different in the seminal plasma of smokers and non-smokers. Significant positive and negative correlations with smoking but also with classical spermiogram parameters were found for different metabolites. Additionally we found some significant correlations between sperm and seminal metabolites.

The detection of genes, proteins, or metabolites unique to the infertile male will lead to a much better understanding of male sub- and infertility. It would allow determining an accurate set of biomarkers to diagnose such patients.

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Poster 38

TiO2 Nanotube Arrays as Platform for Environmental Scanning Electron Microscopy Studies — from Imaging to Mechanical Response

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TiO_2 nanotube arrays are biocompatible and self-organized scaffolds composed of parallel aligned nanotubes with a highly tunable surface geometry in terms of tube diameter and surface roughness [1] which are suited for adult organotypic tissue cultures. In previous studies we could show, that good adhesion from tissue to substrate maintains the structure and integrity of the tissue of at least two weeks [2]. After culture, we are able to reuse these arrays for culture by cleaning them from organic residues using UV-light irradiation. While the biophysical origins of this adhesion behavior are the focus of current research, we also did structural investigations of retinal tissue using an environmental scanning electron microscope (ESEM). Since we have shown that TiO_2 nanotubes arrays can be employed for long-term culture of retinal tissue we want to combine this biotechnological concept with the ESEM and to measure mechanical properties of the retina by performing tensile tests within the ESEM chamber. Thus, we will be able to find correlations between structural components of retina and their variation in tissue mechanics. This will pave the way for *in vitro* studies on tissue regeneration and surgery techniques in combination with drug testing.

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Poster 39

Effects of rat tail and bovine dermal collagen I mixture on structural and elastic properties of 3D biomimetic ECM Models and their influence on cell migration

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Three-dimensional (3D) cell migration is studied mostly in biomimetic collagen I extracellular matrix (ECM) models. These *in vitro* collagen scaffolds are assumed to be mostly homogenous, unlike physiological *in vivo* ECM. How local variations of the ECM structure affect cell migration is mostly unknown. Thus, we investigated the effect of structure inhomogeneities on cell migration. We hypothesize that 3D pore size and elastic modulus of the surrounding matrix are the driving factors of 3D cell migration and invasion. Our findings implicate that these two parameters indeed seem to control both malignant and benign cancer cell invasion into these 3D collagen matrices. By using mixes of rat tail and bovine dermal collagen I, we are able to mimic scaffold inhomogeneity. Collagen from rat tail self-assembles to elongated fibrils, whereas bovine collagen tends to build node-shaped scaffolds. Influence of collagen monomer concentration as well as single component matrices made from solely rat or bovine collagen on 3D pore-size and elastic modulus have been studied using confocal laser scanning microscopy (CLSM) and atomic force microscopy (AFM), respectively. We found that a collagen concentration of 3 g/l with a median pore-size of around 2 µm and elastic modulus of around 200 Pa drastically promote migration and invasion of cancer cells. Our results show that by mixing elongated fibril matrices from rat tail and node-shaped scaffolds from bovine dermal collagen, we can adapt local inhomogeneities and matrix properties without introducing other migration affecting parameters of our biomimetic *in vitro* ECM models.

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Poster 40

Entwicklung eines Messsystems für Mikrobewegungen von Implantaten

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Allein in Deutschland finden jährlich etwa Hüftrevisionsoperationen statt. Durch geeignete operative Versorgung des vorliegenden acetabulären Defektes soll eine möglichst hohe Primärstabilität erreicht werden. Um diese fallabhängig zu untersuchen, haben wir ein Messsystem entwickelt, mit welchem sich die Mikrobewegungen zwischen Implantat und Knochen in deren Interface in allen sechs Freiheitsgraden am Prüfstand auf wenige Mikrometer genau bestimmen lassen.

Jenes Messsystem basiert auf einem Pin-Hülse-Sensor. In der verwendeten künstlichen Hemipelvis befinden sich wenige Millimeter breite Bohrungen, in welchen eine Metallhülse eingebracht ist. Axial durch diese verläuft ein dünner Metall-Pin, welcher fest mit der nach OP-Anleitung implantierten Hüftrevisionpfanne verbunden ist. Die Relativbewegung zwischen Implantat und Knochen wird folglich auf das applizierte Pin-Hülse-System übertragen und somit außerhalb des nicht einsehbaren Knochen-Implantat-Interfaces sichtbar. Pin- und Hülsenposition werden mit Hilfe eines optischen 3D-Bildkorrelationssystems während der Belastung mikrometergenau registriert. Die Kraftapplikation während der Messung entspricht in Betrag und Richtung dem Maximalkraftvektor beim aufrechten Gang.

Da die Messstellen über das gesamte Knochen-Implantat-Interface verteilt sind und die Mikrobewegung in jener Grenzschicht in allen Freiheitsgraden erfasst wird, stellt unser Messsystem einen großen Fortschritt im Bereich der Mikrobewegungsanalyse dar. Somit sind wir in der Lage verschiedene Verankerungsstrategien sowie die Implantatwahl selbst hinsichtlich resultierender Primärstabilität zu bewerten.

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Poster 41

Investigating retina mechanics with a self-designed tissue stretcher

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The biomechanical properties of the retina play a key role in many eye disorders. Up to now, little is known about acting forces inside the retina during mechanical malformation while a better understanding of the mechanical properties during deterioration processes could result in novel approaches to explain many eye diseases. To quantify forces and stresses during tissue deformation, a home-built tissue stretcher coupled with a self-designed force sensor gadget were developed. As we have shown previously, amorphous TiO_2 nanotube arrays support strong adhesion of adult tissue explants to the nanotube surface important for retina stretching. Thus, our stretcher device bases on two nanotube sheets placed closed to each other with the retina on top at the interface of the two sheets. One sheet is attached to a stepping motor which moves one nanotube sheet apart and stretches the retina on top. The other sheet is stationary and connected to a self-designed force sensor gadget which determines the acting forces for different strain rates during retina stretching. A chemically crosslinked gelatin hydrogels were employed as a testbed to verify the principle of the invented force sensor gadget and compared to rheology measurements. Both experimental data are in good agreement showing the working principle of our device. Thus, after proof-of-principle we are currently investigating the mechanical properties of retina explants from adult pigs collected from slaughter houses with the aim to pave new ways to study tissue mechanics and its relation to diseases together with the possibility to reduce animal experiments.

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Poster 42

Detailerkennbarkeit von Graustufenbildern

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Es wurde untersucht, wie sich unterschiedliche Kontrast- und Lichtverhältnisse auf die Erkennbarkeit von Details auswirken. Dazu wurden Landoldringe, Normsehzeichen für Sehtests nach DIN EN ISO 8596 verwendet und in den Kriterien 1 – 4 variiert und jeweils unter optimaler Ausleuchtung und Abdunklung des Raumes den Probanden gezeigt: 1) Schwarzer Ring + weißer Hintergrund 2) Weißer Ring + schwarzer Hintergrund 3) Grauer Ring + schwarzer Hintergrund 4) Grauer Ring + weißer Hintergrund.
Die Probanden wurden aufgefordert die Lage der Öffnung des Kreises zu benennen in einer für sie noch erkennbaren Skalierung. Jeder Fehler pro Zeile wurde so gewertet, dass nur die letzte fehlerfreie Zeile gewertet wurde, um ein „erraten“ auszuschließen. Es wurden Sehschärfen von 0,4 – 1,25 erreicht (also zwischen 40% und 125% Sehleistung).

Beste Ergebnisse wurden erzielt bei schwarzer Ring + weißer Hintergrund mit perfektem Raumlicht. Die schlechtesten Werte wurden bei abgedunkeltem Raum mit weißem Ring und schwarzem Hintergrund erreicht. Es wird vermutet, dass die Betrachtungssituation von Röntgenbildern am TV/PC Bildschirm mit abgedunkeltem Raumlicht sich negativ auf den Betrachter hinsichtlich der Detailerkennbarkeit und Ermüdung auswirkt. Ferner wird vermutet, dass sich keine qualitativen Änderungen im Ausdruck ergeben, sollten Graustufenbilder vorher invertiert werden (Röntgenpositiv wird ausgedruckt). Dies führt zu einem verminderten Tonerverbrauch sowie zu einem besseren Raumklima (weniger Toner-Luftverschmutzung in geschlossenen Büroräumen) und wirkt sich nur auf kurzlebige Dokumente mit einer Lebenszeit von weniger als 8 Wochen aus.

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Poster 43

Actin stress fiber patterns in laterally confined cells

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Cell shape and function are inseparably linked to each other. For example, coordinated shape change of neighboring cells is crucial for a successful completion of morphogenesis. Cell shape can be regulated intracellularly by structural proteins or extracellularly by adaptation to the surroundings. In this way, extracellular geometry can be used to manipulate cell shape and function.
We use glass substrates and soft polyacrylamide hydrogels that are micro-structured with stripe-like patterns of the adhesion protein fibronectin to study the adaptation of cells to spatial confinement. Isolated human vein endothelial cells are studied for several hours in order to correlate cell shape changes, actin cytoskeleton reorganization, and cell force dynamics.

Previously, we found that cells differentially form exterior and interior actin stress fibers under lateral constraint, leading to a bimodal distribution of actin stress fiber patterns. Current work focusses on live-cell imaging to reveal stress fiber dynamics. We found that aligned stress fibers in polarized cells exhibit centripetal motion, perpendicular to their orientation, with position-dependent speed. Furthermore, the overall magnitude of traction forces correlates with total cell size. On the other hand, the orientation of cell forces is strongly correlated to actin cytoskeleton morphology and the degree of confinement.

Overall, our setup allows us to analyze both the cells’ morphological and mechanical adaptation to spatial confinement in a time-resolved manner, highlighting the fundamental importance of the extracellular environment for shaping cell form and function.

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Poster 44

Analyzing Carnosine's Influence on Tumor Cell Metabolism by Gas Chromatography – Mass Spectrometry

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Previous studies indicated that carnosine (car) inhibits the metabolism of glucose in cancer cells. However, neither the precise metabolic step nor the mode of action of how the dipeptide affects cell metabolism is fully understood. Therefore, we used GC-MS based metabolomics in order to analyze car's influence on cell metabolism. As the presence of fetal bovine serum could conceal the primary effects of the dipeptide, we established serum-free condition. U87 glioblastoma cells were cultivated in the presence or absence of 50 mM Car and medium was collected after 3, 6, 12, 24 and 33 hours in order to determine extracellular metabolites. We also analyzed intracellular metabolites by GC-MS in U87 cells treated for 6 hours with 50 mM car under metabolic steady-state conditions. Although, the flux of glucose and lactate was unaffected in presence of the dipeptide, we observed significantly reduced intracellular abundances of glycolytic intermediates and intra- and extracellular pyruvate. Furthermore, car treatment strongly increased the intra- and extracellular abundances of arginine and ornithine. Moreover, our data suggests the induction of lysine degradation under the influence of the dipeptide. In conclusion, we could experimentally confirm that car inhibits glycolysis in glioblastoma cells. In addition, we demonstrated that the dipeptide strongly affects arginine and lysine metabolism. Furthermore, our data provides for the first time a comprehensive insight into car's influence on tumor cell metabolism, which will highly contribute to our understanding of the mode of action of the dipeptide.

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Poster 45

Light transmission through the guinea-pig retina is modulated by osmotic changes and the resulting morphological alterations of retinal cells

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Neuronal activity and pathological conditions are associated with osmotic imbalances in the retina and might influence the optic properties of retinal tissue. Therefore, we determined optical transparency of freshly isolated guinea-pig retinas modulated by different extracellular osmolarity and observed related cell morphological alterations. The retinal light transmission was measured with a photometer and the size of profiles of photoreceptor segments and of neuronal somata as well as Mueller cell endfeet in the ganglion cell layer was determined. Extracellular hyperosmolarity induced a decrease of the retinal transparency which was associated with shrinkage of photoreceptor segments, ganglion cell layer neurons, and Müller cell endfeet. Neurons and Müller cells are capable to reverse the shrinkage within minutes of hyperosmotic stimulation.

Moderate extracellular hypoosmolarity had no significant effects on the retinal transparency and the size of Müller cell endfeet while the size of photoreceptor segments and ganglion cell layer neurons was moderately reduced. High extracellular hypoosmolarity induced an increase of the retinal transparency which was associated with a cytotoxic swelling of photoreceptor segments.

The shrinkage of photoreceptor segments and Müller cells may explain the decrease of the retinal transparency under hyperosmotic conditions. The relatively maintained optical transparency under moderate hypoosmotic conditions may be an adaptation during physiologic neuronal activity in the retina. Detectable changes of the retinal transparency may indicate pathological changes.

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Poster 46

Biomimetic biosensors – biophysical protein interaction measurements by soft colloidal probes

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Artificial biomimetic systems for quantitative measurements are often inevitable to investigate protein-material as well as cell receptor interactions with their natural or engineered ligands in a hydrated environment.

Hence it is necessary to find a method that facilitates the measurement of biomolecular interactions with high sensitivity and enables the analysis of molecular binding at hydrated and mechanically flexible interfaces and the impact of external forces.

Therefore we came up with modifiable hydrogel particles which are also known as soft colloidal probes (SCP) as the basis of our sensor element. By functionalization of SCP we are in the position to quantify unspecific as well as specific interactions between SCP and the interacting surface. The readout of our method is based on the elastic SCP deformation caused by the adhesion energy at the SCP-substrate interface, which is optically evaluated by reflection interference contrast microscopy. Furthermore we used SCP in force spectroscopy measurements.

Applying this technique, we could gain closer insights into protein adsorption phenomena at different polymer surfaces, as shown in fibronectin experiments, as well as in specific cell adhesion effects like the interaction of the glycosaminoglycan hyaluronan and its primary cell surface receptor CD44.

In the end, we advanced our technique to a degree, where it can be used for industrial applications e.g. as a sensor for pollution of aqueous samples.

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Poster 47

Electron Irradiation Assisted Crosslinking of Collagen: Reagent-Free Modification towards Tailored Matrices

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Biological collagen hydrogels show a high potential in biology and medicine due to their strong biocompatibility and biodegradability. They are highly attractive materials for biomedical applications such as extracellular matrix components, coatings or implants. Thereby, precise adaption of structure and mechanics as well as stimuli-response is an interesting aspect of the modification of these materials. Reagent-free modification of hydrogels can be achieved by utilizing high energy electron irradiation inducing crosslinking. Without any additional reagents, electron irradiation represents an advantageous non-toxic crosslinking technique. We will demonstrate how crosslinking with high-energetic electrons allows fine-tuning of materials properties such as structure and mechanics towards precisely tailored extracellular matrices.

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Poster 48

Cell Uptake Enhancement of LbL-microcarriers by VSV-surface functionalization

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Due to an increasing interest in new therapeutical approaches, the necessity for an efficient application by novel drug delivery systems (DDS) is highly emphasized. With the development of DDS several important aspects have to be considered, e.g. biodegradability, protective packaging as well as targeted and controlled release. In the work presented a promising approach to improve some of those key aspects is highlighted with regard to Layer-by-Layer- (LbL-) based microcarriers, that is the application of a specific surface functionalization with inactivated vesicular stomatitis virus (VSV). Viruses have evolved a perfect machinery to infiltrate their host-cell and deliver their genetic material into the cell. By introducing VSV as an LbL-microcarrier functionalization, we made use of the capacity of the viral glycoprotein VSV-G to undergo reversible conformational changes and thus serving as a fusion moiety with the DDS surface as well as a cellular receptor for DDS uptake. The data show that VSV can be successfully applied to the microcarrier surface and the cellular interaction rate of the LbL-microcarrier can be significantly enhanced.

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Poster 49

A biomechanical analysis of arthroscopic acromioclavicular joint dislocation repair using two different techniques of coraco- and acromioclavicular reconstruction.

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Background: Acromioclavicular (AC) joint dislocations are a common sports injury. The best operative treatment for high-grade injuries is still controversial. The aim of this study was to evaluate the horizontal biomechanical performance of two techniques for coracoclavicular ligament reconstruction and the influence of the acromioclavicular ligament repair for the stability of the AC joint.

Material and methods: 10 AC joints of human cadaveric shoulders were included in the study and underwent cyclic anterior and posterior translational. The shoulders were assigned to two groups: group 1 (n=5): Double-Button-Fixation (single coracoid technique (SCT)) with horizontal augmented AC cerclage and group 2 (n=5): Double coracoid technique (DCT).

Results: Group 1 showed a mean anterior translation of 9.8mm (±4.3mm) after 10 cycles of precondition, a mean anterior translation of 13.4mm (±4.6mm) after 5000 cycles, and a mean posterior translation of 8.4mm (±4.4mm) and 11.3mm (±5.7mm) after 10 and 5000 cycles, respectively. Group 2 showed a mean anterior translation of 2.6mm (±1.8mm) after 10 cycles of precondition, a mean anterior translation of 3.4mm (±0.7mm) after 5000 cycles, and a mean posterior translation of 5.6mm (±3.7mm) and 7.4mm (±4.3mm) after 10 and 5000 cycles, respectively.

Conclusion: Isolated reconstruction of the CC ligaments with two suture devices in a specific position seems to be more sufficient for the stability in the horizontal plane of the AC joint than reconstruction of the CC ligaments with SCT-technique and additional horizontal augmented AC FiberTape® cerclage.

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Poster 50

Organization of Fibronectin and NIH/3T3 Fibroblasts on Bulk Microgrooved TiO2

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The choice of suitable nano- and microstructures of biomaterials is crucial for successful implant integration within the body. In particular, surface characteristics affect the adsorption of various extra cellular matrix proteins. This work illustrates the interaction of protein adsorption and early cell adhesion on bulk microstructured titanium surfaces with parallel grooves of 27 to 35 µm widths and 15 to 19 µm depths, respectively. In contact with low concentrations of fibronectin solutions, distinct adsorption patterns are observed on the edges of the ridges. Moreover, NIH/3T3 fibroblasts cultured in serum-free medium for 1 h, 3 h and 1 d show enhanced early cell adhesion on fibronectin coated samples compared to uncoated ones. In fact, early adhesion and cell contacts occur mainly on the groove edges where fibronectin adsorption was preferentially detected. Such adsorption pattern also supports cellular contact guidance on short time scales which is hardly seen for uncoated samples. Thus, surface structures can promote directed adsorption of low concentrated fibronectin which, furthermore, facilitates early cell adhesion. These results may give rise to new developments in surface engineering of biomedical implants for improved osseointegration.

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Poster 51

A tissue model with tunable properties by electron irradiation of elastin-collagen hydrogels

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Collagen matrices are common tissue models in the field of cancer research which constantly advance the understanding of processes such as (cancer) cell migration and nonlinear mechanics of tissue. However, some types of connective tissue exhibit a distinct proportion of the protein elastin of up to 50 weight-%. Thus, the creation of a tissue model with a tunable ratio of elastin to collagen and tunable rheological and topological properties can open new ways of precisely mimicking physiological environments.

This work aims to create an elastin/collagen tissue model by means of electron irradiation as well as to improve the understanding of the mechanisms of this crosslinking process and will thereby benefit progresses in regenerative medicine and tissue engineering.

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Poster 52

High-throughput method for screening of enzymes for plastic recycling

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Synthetic plastics can be degraded by microbial enzymes providing a green route alternative for plastic waste recycling. The enzymatic hydrolysis of polyethylene terephthalate (PET) by polyester hydrolases has shown to be improved in the presence of carboxylesterases capable of hydrolysing PET intermediate products formed during the degradation process. Here we report a novel screening method which enabled the fast detection of enzymatic activities against PET hydrolysis products. The enzymatic activity was determined by measuring the hydrolysis of bis(2-hydroxy-ethylterephthalate) nanoparticles entrapped in a polyacrylamide gel. The assay showed a high accuracy and reproducibility. We conclude that this method will be useful for the development of biocatalytic plastic recycling processes.

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Poster 53

RNAi-mediated Therapeutic Knockdown of the Neuropilin Axis and GIPC1 in Pancreatic Carcinoma

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The pancreatic ductal adenocarcinoma (PDAC) is a more common tumor in Germany with a 5-year survival rate of less than 4%. Due to the sometimes poor success rate of chemotherapy, targeted therapies affecting tumor relevant pathways and important cellular hallmarks of cancer have become prominent in the last years.

Neuropilins (NRP1, NRP2) are transmembrane glycoproteins that play important roles in angiogenesis and tumorigenesis. An aggressive phenotype and therapy resistance in PDAC is correlated with overexpression of the NRPs. The essential adaptor protein GAIP interacting protein C-terminus (GIPC1) is important for neuropilin signaling. Thus, in this project we focus on the three different targets, by exploring their single and combined inhibition.

RNA interference (RNAi) is an efficient strategy for the specific knockdown of any target gene, mediated by small interfering RNAs (siRNAs). Here, we analyze in detail the effects of RNAi-based transient GIPC1, NRP1 and NRP2 knockdown on the molecular and cellular level. In various cell lines, siRNA mediated knockdown led to a specific downregulation on mRNA and protein levels. As a result, reduced cell viability, activation of apoptosis and reduced proliferation occurs. Spheroid assays show altered shapes and densities after knockdown and decreased colony numbers are observed in colony-forming assays. Most importantly, treatment with nanoparticle-formulated siRNAs against these targets led to tumor growth inhibition in a xenograft mouse model, especially in the case of the NRP2.

Our data suggest that GIPC1, NRP1 and NRP2 are new promising targets in pancreatic cancer therapy.

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Poster 54

Non Coding RNAs in Extracellular Vesicles – Cancer Diagnostics by Liquid Biopsy

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Extracellular vesicles (EVs) are formed and secreted via the endosomal pathway or by budding of the cell membrane and thus carry proteins, DNA and RNA also present in their cells of origin. According to current scientific knowledge it is not clear if packaging of EVs is a specific process or if their content reflects an average of all molecules present in the cytoplasm of their originating cells. Since EVs are present in all body fluids they can be isolated from blood or urine samples and used as liquid biopsies for the diagnosis of various diseases without risks and disadvantages of regular biopsies. Their immense diagnostic value in discriminating between healthy and cancer patients was already shown in several studies but to date could not be successfully applied for clinical settings. The limiting factor is the low abundance of EVs in liquid biopsy samples relevant for diagnosis compared to vesicles secreted by divergent other cells throughout the whole body. That impedes the detection of significant biomarker patterns in patient samples.

Firstly, we analysed RNA profiles of vesicles derived from different cancer cell lines by Next-Generation sequencing to elucidate the composition of RNAs packed into vesicles. This data set gives rise to what extent amount and identity of RNA species differ between cancer types. Secondly, EVs of the same cancer cell lines will be investigated using mass spectrometry to identify surface protein markers specific for their cells or tissue of origin. This will enable us to isolate and enrich cell-specific EVs and to identify RNA tumor markers present in tumor-derived vesicles.

Subsequently, our findings will be used to establish a test system for the identification of highly specific diagnostic and prognostic biomarkers in blood or urine of prostate carcinoma (PCa) patients. If this approach is successful, the established protocols can be transferred and adapted to various tumor types as well as other complex diseases.

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Poster 55

Synthetic Riboswitches for the Regulation of tRNA Processing

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RNA molecules exhibit a number of biological functions such as the catalysis of chemical reactions or the ligand-dependent regulation of gene expression (riboswitches). Natural riboswitches are often located in the 5‘UTR of bacterial mRNAs. They enable an efficient control of gene expression mostly on the transcriptional or translational level. The regulation is accomplished by two domains: the aptamer domain and the expression platform. The aptamer domain is responsible for the high specificity by selectively binding small molecules. This interaction triggers a conformational change in the expression platform affecting the gene expression. New combinations of the two domains allow the development of synthetic riboswitches for an efficient control of gene expression. The aim of our project is the design of an artificial riboswitch, whose mechanism is based on a new regulatory system: the native processing of tRNA by RNase P, an essential enzyme in all organisms. For this purpose, we fused the well-characterized theophylline-aptamer to *in silico* predicted sequences, whose three-dimensional structure would sterically hinder the processing of tRNA by RNase P in the absence of theophylline. Initial experiments were performed in *Escherichia coli* using a suppressor-tRNA and the reporter gene *lacZ* (coding for β-galactosidase) with an integrated stop codon. First analysis of the riboswitch-candidates *in vivo* showed promising, theophylline-dependent activities. In the future, addressing this regulatory level may allow the development of a universal synthetic riboswitch acting in prokaryotes as well as in eukaryotes.

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Poster 56

Interlocking Layer-by-Layer microcarriers and DNA origami nanostructures: First steps towards a smart drug delivery system

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Structured drug delivery systems (DDS) with specific addressability and protectivity bear an opportunity in enhancing the transport of active agents. The modular design of Layer-by-Layer (LbL) microcarriers provides a firm base for any kind of modification. In particular, the stepwise assembly of a huge variety of biopolymers forming a multilayer on different core materials is highly beneficial. This provides several options to assemble any kind of molecules and nanoparticles either within the multilayer, the core or on the surface which makes the system very versatile. In contrast to the network-like appearance of the LbL multilayer, compactly designed DNA origami cage structures allow the encapsulation of a defined number of agent molecules. Controlled release can then be specifically induced by the tunable opening of an attached lid activated by different trigger reagents.

In our study, we successfully demonstrate the functional integration of LbL microcarriers and a controlled number of adsorbed DNA origami cage structures on the microcarrier surface. When the 22 nm x 22 nm x 40 nm origami cages are imbedded as an internal multilayer component they became highly resistant against variation of the pH value and enzymatic degradation. This further prevents the degradation of the structures inside living cells and shows the high potential of this system for drug delivery by improving the insufficient stability of DNA origami in physiological environments. Finally, we present first results for the encapsulation of bovine serum albumin (BSA) as a model agent inside the origami cages as the next step towards a functional DDS.

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Poster 57

Amino-Functionalization of copolymerized films from three-armed biodegradable macromers – cell adhesive materials ready for bioconjugation

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For guided tissue regeneration, surface properties of bone substitution materials are of high relevance. We aim to generate surface modifications on biodegradable scaffolds from 3-armed methacrylated oligolactid-containing macromers. Films made of the same material composition provide ideal geometries for analysis[2].

Established films cross-copolymerized from hydrophobic macromers with hydrophilic PEG required solvent mixtures and showed phase separation in AFM images[2]. In a new attempt, we intended to incorporate a small molecule as an anchor into the films, which then binds a suitable spacer. The small anchor glycidylmethacryle provided flexibility in the choice of the polymerization solvent. A further incubation with polyetheramines (e.g. Jeffamine® 900) resulted in amino-functionalized films available for further functionalization. As a model molecule for later immobilization of bioactive molecules, an amino-reactive fluorescent dye (5-(6)SFX) was employed. SFX allowed for a quantitative analysis of surface modification with a fluorescence scanner.

Different solvent systems were tested for their effect on SFX immobilization. Single solvents showed higher SFX-immobilization than solvent mixtures, probably preventing phase separation. Ethyl acetate and dioxane provided smooth films combined with high SFX-immobilization.

For Jeffamine incubation a short high temperature treatment in combination with a catalyst showed best binding capacities.

In a next step, functional surface modification and cell adhesion will be investigated.

1 Loth R et al, Acta Biomater. 2015;26:82-96.
2 Müller BM et al, Acta Biomater. 2017, 51:148-160.

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Poster 58

Computational pipeline for the design of transcription regulating theophylline riboswitches

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In synthetic biology and metabolic engineering, there is a strong demand for orthogonal or externally controlled regulation of gene expression. RNA-based regulatory devices like riboswitches represent a promising alternative to proteins. These natural regulatory elements, primarily found in bacteria, are mostly embedded in the 5'-untranslated region of the mRNA. They allow a fast and direct control of gene expression, as no synthesis of regulatory proteins is required. Riboswitches show a modular composition of an aptamer domain as sensor and an expression platform as response element. This allows a free combination of different modules in a plug-and-play-like mode for synthetic devices designed analogously to natural examples. The aptamer specifically interacts with a ligand, modulating the secondary structure of the adjacent response domain that controls the expression of the genes located downstream, in most cases at the level of transcription or translation. Here, we present an in silico pipeline for the rational design of transcription regulating theophylline riboswitches. For the design we use a theophylline binding aptamer, which induces a structural rearrangement of the expression platform in presence of theophylline that disrupts a terminator structure. In addition, we show that these computed riboswitches can control gene expression *in vivo* and that the intermediate secondary structure predicted computationally concurs with the *in vitro* data. Our work illustrates how synthetic riboswitches are especially suited for their application as genetic control element in cells.

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Poster 59

Structural basis of the inhibition of kallikrein7 by small molecule inhibitors

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Vaspin (Visceral adipose tissue-derived serine protease inhibitor) is a member of the serine protease inhibitor family. It is associated with insulin resistance and acts as a mediator in inflammatory processes, for example in the adipose tissue of obese individuals. The best characterized target protein of vaspin is the serine protease kallikrein7, a member of the human tissue kallikreins. Its dysregulation leads to pathophysiological inflammation processes in the skin, which causes diseases such as psoriasis. Furthermore, human kallikrein7 (hK7) can cleave insulin indicating a relationship between Vaspin and hK7 and making both proteins very interesting objects of research. It has been proposed that inhibition of hK7 by vaspin could increase the half-life of insulin, what probably could counteract adipose-induced insulin resistance. Currently, small molecule inhibitors for hK7 are developed for the treatment of kallikrein7 associated diseases. Coumaric acid derivatives inhibit hK7 in a µM range. We aim to understand the mode of inhibition of these compounds by X-ray crystallography. Based on this information, the potency of these inhibitors may be increased substantially by structure-based inhibitor development yielding specific and potent hK7 inhibitors for the development of drugs against obesity-related and other diseases.

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Poster 60

The Carnivorous plant: A potential heterologous protein-expression-system

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Carnivorous plants bear the special ability to produce and secrete well-defined digestive fluids consisting of pharmacological active secondary metabolites and digestive enzymes. Our aim is to produce pharmaceutical relevant substances in carnivorous plants by modifying plant-derived secondary metabolites or the expression of heterologous proteins. Furthermore, by interfering in plant secondary metabolite or signal transduction pathways we can gather information about biosynthetic and regulatory cascades of the plant.

Here we present the transformation of several genera of carnivorous plants with the marker protein GFP (green fluorescent protein) using the method of Hirsikorpi et al. (2002).

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Poster 61

Structural studies on the substrate and cofactor binding mode of FAD-dependent monooxygenases

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Styrene monooxygenases (SMOs) catalyse the enantioselective epoxidation of styrene and structurally related compounds. They are of interest for the development of new biocatalytical production processes for pharmaceuticals and fine chemicals. Our aim is to improve the substrate specificity and enantioselectivity of SMOs for such applications. An important step to reach this goal is the use of crystallography to get detailed insight into the binding mode of the substrates and cofactor FADH2. Substrate epoxidation requires FADH2, provided by an NADH – flavin oxidoreductase component. We used FAD and different substrates for co-crystallization. Crystal structures of the SMO StyA1 in the absence and presence of FAD revealed conformational changes involved in cofactor binding. We will report on challenges in the analysis of the substrate binding mode and our approaches to overcome these problems.

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Poster 62

Three-armed macromer platform with adjustable degradation properties

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In tissue engineering, the development of biodegradable materials with adjustable biochemical and -physical properties that can also be covalently modified is desired. Previously, we developed a platform of three-armed biodegradable macromers consisting of trivalent alcohols modified with biodegradable lactide (LA) or caprolactone oligoesters. Terminating the arms with methacrylic acid yields macromers that allow for cross-polymerization into solid or macroporous structures.

This macromer platform is expanded by copolymerization of glycolide (GA) and by varying the degree of macromer methacrylation. The hydrolytic *in vitro* degradation of macroporous scaffolds was assessed by monitoring mass and mechanical stability.

Onset of degradation occurred after 4 months of incubation for scaffolds made from established Tri134(LA6)3.75. Modification of the degree of methacrylation resulted in a reduction of the degradation onset to 3-3.5 months, but did not significantly affect initial elastic modulus of the scaffolds (25-30 MPa). Synthesis of macromers with increasing comonomer feed of GA was possible up to a LA:GA ratio of 2:4. Properties of the scaffolds changed with GA content. Increasing GA/arm reduced initial elastic modulus and accelerated hydrolytic degradation. For Tri134(LA2GA4)3.75, elastic modulus was reduced to 9.2±2.9 MPa, and degradation of scaffolds was detectable immediately from the start of the experiment.

These results illustrate that the composition of our three-armed macromers can be flexibly adapted and used to control mechanical and degradative properties of macroporous scaffolds fabricated thereof.

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Poster 63

Oligomer-cross-linked protein nanoparticles — potential intracellular drug delivery vehicles?

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Nanoparticles are versatile diagnostic and drug delivery vehicles for proteins, small molecules and DNA or RNA therapeutics. Natural polymers are preferable materials for nanoparticle fabrication due to their biocompatibility and biodegradability. Anhydride group-bearing oligomers developed in our group have been successfully used for the formation of hydrogels with different gelatin fractions. In this project, we aim at formulating nanoparticles from gelatin or albumin and reactive oligomers and integrate fluorescent probes and pharmacologically active molecules for intracellular delivery. Initial experiments focus on macrophage uptake.

OPNMA {oligo(PEDAS-co-NiPAAm-co-MA)} and oPDMA {oligo(PEDAS-co-DAAM-co-MA)} of different compositions have been synthesized according to an established protocol by free radical copolymerization of the comonomers. ANPs have been fabricated by desolvation and subsequently cross-linked by oPNMA and oPDMA. Macrophages were differentiated from human blood-derived monocytes and used for uptake experiments with FL-ANPs that were quantified by flow cytometry.

ANPs size distribution assessed by dynamic light scattering and found predictable and reproducible size (180-300nm). ANPs structural analysis by SEM revealed round shape, smooth surface and uniform size. Cellular uptake of FL-ANPs was efficient and concentration dependent and induced no undesired macrophage activation.

Stable and homogenous oligomer-cross-linked ANPs can be synthesized by optimized desolvation within reproducible size range. Macrophage uptake of ANPs hold promise for potential drug delivery strategies targeting these cells.

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Poster 64

Ficus natalensis – a medicinal plant from Benin. Antioxidant activity, phenolic profile analysis and phylogenetic characterisation.

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Medicinal plants used by traditional healers play an important role in the treatment of various diseases in Benin. *Ficus natalensis subsp. natalensis*, the coastal strangler fig, is used for the therapy of inflammatory conditions and wound healing. However, *Ficus natalensis susbsp. natalensis* is often confused with other Ficus species like Ficus thonningii and *Ficus craterstoma* due to similiar morphological features and phylogenetic studies propose an interbreeding process. A further analysis of the phylogenetic and phytochemical profile of *Ficus natalensis subsp. natalenis* from Benin is therefore fundamental. The presented research focuses on the analysis of the phenolic profile, phylogenetic characterization and the antioxidant effects of a methanolic leaf extract of *Ficus natalensis subsp. natalensis* from Benin. A combined approach of chromatographic profiling and antioxidant screening identified rutin, chlorogenic acid, neochlorogenic acid and kryptochlorogenic acid as the main constituents with antioxidant activities. The methanolic leaf extract showed a phenolic content of 1.43 ± 0.07 %. A phylogenetic analysis based on internal transcribed spacer sequences of the collected plant material confirmed the collected Ficus species as *Ficus natalensis subsp. natalensis*. The compounds chlorogenic acid, neochlorogenic acid and kryptochlorogenic acid could be reported for *Ficus natalensis subsp. natalensis* for the first time. Our study suggests that presence of the antioxidant compounds rutin, chlorogenic acid and its isomers, supports the application of this plant for anti-inflammatory and wound healing purposes.

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Poster 65

Surface modification of untreated and coated cell culture plastic by laser engraving for *in vitro* characterization of motility and adherence in cancer cells

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Malignant tumors are characterized by infiltrating growth and the capability to form metastases. A better understanding of these biological processes could provide the basis for novel treatment options complementing classic cytoreductive approaches. To study infiltrating growth and spreading of cancer cells, a number of elaborate *in vivo* models have been developed. However, there is an additional need for easy-to-use *in vitro* assays for screening tests or experiments focusing on specific issues requiring well-defined conditions. Thus, we made use of a laser engraver to modify normal cell culture plastic as well as various surface coatings. This technique enables the creation of defined gaps or cavities in the surface of cell culture vessels with altered adhesion characteristics. By this means, we performed analyses of cellular motility, cell-cell contacts and substrate adherence in a number of cancer cell types. We found marked differences between the investigated tumor cells regarding their migratory behavior or their adherence even in the absence of additional pharmacological interventions. Moreover, we delineated the impact of specific inhibitors of motility-regulating signaling pathways. Finally, we made use of this system to investigate two dimensional *in vitro* wound healing in comparison to conventional scratch assays. To summarize, we present proof-of-concept data regarding the applicability of laser engraving for fast and simple *in vitro* analyses of cell motility and adherence and show initial results addressing the role of distinct signalling pathways in the regulation of the migratory capacity of cancer cells.

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Poster 66

Extracting Microglia from human glioma

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Objective:
The role of microglia in brain cancer is increasingly recognized and there is urgent need to isolate highly pure microglia with high yield from human brain tumor samples to further analyse their contribution to tumor development and perturbation. Here, we demonstrate that this can be achieved by a method previously described for embryonic rodents and adult rats.

Methods:
Brain tumor samples (n=3) were obtained from patients during surgery which exhibited the typical morphological appearance of glioma in MRI-Scans. The tissues were mechanically dissected. After filtration and removal of debris cells were allowed to adhere to Aclar® plastic films placed in six-well-plates. After incubation an anti-F4-80 antibody and an Iba-1 antibody were employed to detect microglial markers. In addition, an anti-GFAP-antibody was used as control for astrocytic and glioma cells.

Results:
~80% of cells exhibited the typical needle-shape morphology of microglia in Aclar® covered wells. Although a small amount of GFAP-positive debris was detectable, no viable cells positive for GFAP were detected. ~60-80% of the cells stained positive for both F4/80 and Iba-1. Most importantly, we obtained ~5 times more cells using Aclar® covered wells in contrast to plain wells.

Discussion:
Here we demonstrate that Iba-1 and F4/80-positive microglia can be isolated in high yield and purity from human glioma using Aclar® film. The method presented is less time consuming and avoids mechanical stress. As Aclar® film is microscopy-compatible, cells can directly be monitored, treated and can also be removed by mild trypsinisation for further experiments.

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Poster 67

Enhanced real-time monitoring of NPY-receptor activation by combining microfluidics and microelectronics

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Microfluidic chip devices present a promising platform for compound testing due to short process times and low reagent consumption. However, combining multiple steps such as compound synthesis, separation and testing of biological activity within one device remains a challenge due to the diversity of conditions required.

To close this gap, we aim to develop a microfluidic chip for synthesis of small molecular compounds, their continuous separation as well as cell-based real time monitoring using non-destructive microelectrode array-based (MEA) impedance spectroscopy.

First, we successfully established human cell culturing conditions suitable for a miniaturized platform. Secondly, using finite element method (FEM) simulations, we optimized the MEA and microfluidic layout and found an optimal flow rate for the microfluidic structures leading to comparable impedance results for HEK293A cells cultured under static and microfluidic conditions. Detailed investigations of cell morphology and motility led to the conclusion that cultivation under microfluidic conditions potentially leads to an extended and stabilized cell–electrode interface. To demonstrate the capabilities of impedimetric monitoring of cellular alterations in a microfluidic chip setup, we successfully used HEK293A cells expressing Y1 receptors which exhibited a 2.8 fold increased signal compared to static conditions.

Thus, our chip system holds great potential to efficiently synthesize and test libraries of lead compounds in a physiologically relevant context at small scales which represents a significant advancement in the area of lab-on-a chip systems

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Poster 68

Scorpius – Robot assisted needle guidance and US monitoring

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In spite of using imaging techniques, inaccuracies or complex coordination efforts of the surgeon can still lead to errors in surgery. It is not unusual, that the insertion trajectory, e.g. of a biopsy needle needs to be corrected to reach a desired target. This leads to repetitive insertion of the instrument and therefore to stress for patient and surgeon respectively. A robotic guidance system with ultrasound monitoring may overcome these downsides.

Materials and methods:
A wireless ultrasound probe was attached to a robotic arm. A retainer for the probe was constructed in 3D printing and supplemented with a needle guide. The system was tested on a neck phantom with an ultrasound visible defect. To precisely position the robot on the target a tracking system is used, allowing for treatment planning by an augmented reality based tablet application. Utilizing a reconstructed 3D model from CT-Images, a target trajectory to the defect structure can be defined and the robot be steered. A second application allows for visualization of ultrasound images while advancing the needle.

Investigating the position accuracy of the needle tip showed a mean deviation of 2.93 mm. In an evaluation of the usefulness and acceptance, participants rated the functions of the system to be useful, but were unsatisfied with the usability at its current implementation.

Discussion and conclusion:
Robot assisted needle placement in combination with ultrasound monitoring can improve needle targeting. The system shall be enhanced with more sophisticated interaction possibilities to increase user-friendly handling and reduce treatment time.

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Poster 69

Towards Computational Navigation Intelligence In Computer-Assisted Minimally-Invasive ENT Surgery

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The work in this paper is based on the research project BIOPASS, that aims to develop a novel localization approach for markerless surgical navigation in minimally-invasive endoscopic ENT surgery. The system in development uses multimodal information (sensors, image, process, user) to learn surgical situations from endoscopic images and surgical procedures. Intraoperatively, the system classifies the current situation it is in and identifies the endoscope position automatically. The intended hardware reduction calls for increased computational capabilities and intelligent navigation behaviour. However, the value and efficiency of such a navigation system are highly dependent on the surgeon to be assisted. Based on a survey of 7 ENT surgeons and a mock-up study with ideal navigation functionality we identified critical navigation paradigms an intelligent navigation system needs to comply with. Subsequently, study results were used to develop navigation guidelines for intelligent assistance systems In the operating room. Furthermore, a concept for an information presentation model was designed to include surgical task, information presentation and the user's cognition process into the navigation process. Further work steps will focus on the translation of the defined navigation paradigms into intraoperative assistance functions and the development of an intelligent and comprehensive human-machine-navigation.

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Poster 70

Image based connector for the automatic configuration of 3D ultrasound data acquisition

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The use of intraoperative ultrasound (iUS) imaging supports the neurosurgeon in the identification of tumor tissue during brain tumor operations. Especially 3D data provides a complete overview of the surgical field. The commercial SonoNavigator product (Localite GmbH) includes a navigation system connected to an ultrasound device and performs the reconstruction of 3D iUS data based on 2D iUS images. The reconstruction step requires the manual selection of the corresponding calibration files which depend on US parameters. The goal of this project is the automatic identification of the parameter values in the US image data for the automatic selection of the calibration data file. An image based connector was implemented with MeVisLab on a laptop connected through a grabber to the US device. The tool performs a matching between the life iUS image and a data base of image templates including the different US parameters that have to be automatically recognized. The template with the highest correlation score is returned to the user configuration of US parameters. Finally, the known parameters are sent to the navigation system for the future selection of the corresponding calibration data. The image base connector identifies the following US parameters. US device model, transducer name, image depth and focus, modality, current used frequency, image shape and orientation. The tool was tested on 49 US images with different configurations acquired during 43 brain tumor operations of patients. The difference recognition scores were obtained: US device model, transducer, frequency and modality 100%; depth 71.42%, focus 67.34%.

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Poster 71

Realization of context-aware technical assistance in integrated operating rooms

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Although more and more medical devices provide standardized communication interfaces, they yet show only very limited cooperative behavior. The lack of contextual information during surgery hinders autonomous intelligent systems' adaptation. We implemented a context-aware assistance to establish a surgical working environment that actively cooperates with the surgical team.The ICCAS Demonstrator provides a fully integrated operating room, which implements the IEEE 11073 SDC standards family. Based on the open device interoperability, a pipeline for context-awareness was implemented.

First, the recognition data is consolidated and mapped to low-level work steps. This triggers a network-based classification to derive hierarchically structured contextual information. Finally, medical devices evaluate the contextual information to adapt themselves and realize intelligent systems' behavior.

Various assistance functionalities were implemented for Functional Endoscopic Sinus Surgery, which included the automated switching of the primary display and the parameterization of various medical devices. A technical validation study was conducted with twenty-four procedures on phantoms. The achieved accuracies of over ninety-four percent for the various assistance functionalities under noisy recognition input indicate a reasonable robustness of the implemented processing pipeline and context-aware assistance.

The assistance is designed to optimally support the OR team during surgery and in documentation. Additionally, the established demonstration setup serves as a basis for a pre-clinical evaluation and further implementations.

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Poster 72

Developement and Evaluation of an Instrument-Recognition-System for intraoperative activity-tracking through a mulit-sensor armband

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The observation and documentation of a surgeon's actions have become a steadily growing field of interest in the context of cost reduction and process optimization in the operating room. Different methods have been introduced to identify the surgical workflow and key actions during a procedure. One consistent data source for this identification task is the used surgical instrument. Many published works focused on the analysis of endoscopic images, identifying instruments through markers or integrated RFID chips. This work proposes another approach by using biometrical data provided by sensors applied directly to the surgeon. In this way, instrument activity is distinguishable by differentiating hand gestures. Using a multi-sensor armband, superficial electromyograms (sEMG) were acquired as a representation of performed actions. We used the Myo Armband by Thalmic Labs, which allows the recording and transmission of eight sEMG-Signals around the forearm. With datasets acquired through a multitude of experiments with different instruments in a laboratory environment the acquired data was preprocessed for the subsequent feature extraction and classification steps. In a proof-of-concept study artificial neural networks, decision trees as well as support vector machines were compared for a preliminary classification (highest classification rate: 95.4 %).

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Poster 73

Modular Infrastructure for the Integration of Decision Models into Hospital Information Systems

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Computerized decision models based on Bayesian Networks promise to be a valuable addition to personalized medicine. Clinical decision support systems (CDSS) using these models can evaluate complex diseases, like cancer, and propose different suitable treatments. Their calculations must be based on routinely recorded patient data. Working with these systems must be associated with little to no additional efforts by the physicians. To be fully integrated into the physicians' workflow, CDSS must also interlink smoothly with hospital information systems. We built a modular decision support system using web services to connect the different modules with the underlying information system. The four modules are: 1) a central processing unit containing methods from artificial intelligence to process the patient's status, 2) a model repository for storage and revision control of the patient specific decision models, 3) a data access unit connecting to several clinical data bases and 4) a connector to different user interfaces to provide the results in a suitable form. We prototypically implemented our infrastructure with a decision model for laryngeal cancer. Patient data is provided by a relational data base and processed in the central processing unit. Results, e.g. TNM-staging and personalized treatment options, are presented via a web application. This modular infrastructure allows exchanging individual modules. For instance, the same processing unit could be connected to a different clinical data base or calculated results could be presented in another user interface, e.g., on a mobile device.

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Poster 74

Virtuelle Bewertung der Versorgungsvarianten bei Beckenfehlverheilungen in der rekonstruktiven Chirurgie

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Hintergrund: Die Korrektur von Fehlverheilungen im Becken stellt sich als technisch äußerst anspruchsvoll dar. Detaillierte präoperative Planung zur Wahl der geeigneten Korrektur ist daher unabdingbar. Die Abschätzung der Stabilität gewählter Implantate bei komplexen Korrekturoperationen stellt sich als besonders schwierig dar, kann jedoch durch Methoden der Ingenieurwissenschaften deutlich erleichtert werden.

Methodik: Anhand der CT-Daten einer 38-jährigen Patientin, mit Beckenfehlverheilung vom Typ IV nach Mears (Mears et al. 2003) und damit assoziierter fortschreitender Immobilisierung, wurde ein patientenspezifisches Computer-Modell erstellt. Aufbauend folgten virtuelle Osteotomie, Reposition, sowie Erstellung und Prüfung verschiedener Osteosynthesevarianten. Die erfolgversprechendste Variante wurde mit der Methode der Finiten Elemente bewertet. Nach erfolgreicher Simulation wurden landmarkenbasiert Korrekturmaße und Winkel für die Operation abgeleitet. Die Korrektur erfolgte mittels transiliakaler Osteotomie und Symphysiotomie und wurde mit den geplanten Plattenosteosynthesen versorgt.

Ergebnisse/Schlussfolgerungen: Postoperativ keine Komplikationen, verbleibende Beinlängendiskrepanz ≤ 2 cm. Patientin schmerzfrei und fähig ohne orthopädische Hilfen zu gehen. Verglichen mit radiographischen Untersuchungen zeigte sich das Potential der virtuellen 3D-OP-Planung in der präzisen Bestimmung der Korrekturparameter und verkürzter Operationsdauer. Die transiliakale Osteotomie mit zusätzlicher Symphysiotomie offenbart eine operative Prozedur zur Korrektur der pelvinen Fehlverheilung unter Anpassung der Beinlängendiskrepanz.

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Poster 75

Auditory feedback system for intraoperative navigation during craniotomy in neurosurgery

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Digital intraoperative navigation systems are crucial devices to support neurosurgical interventions nowadays, especially for the intraoperative planning of the craniotomy. Besides the technical improvements in radiological imaging, there is also space for developing new assisted guidance systems. The use of auditory display as a complementary feedback system beneath the traditional only-visual monitor of the navigation system would create opportunities to improve ergonomic, concentration and self-assured working of the surgeon. Due to required parameters that are not provided through the traditional navigation system, a new tool is implemented using MeVisLab from the Fraunhofer MEVIS to fulfill the specified requirements. Beneath the measurement of the distance of the surgical instruments to the given target structure, it provides the functionality to project the contour of segmented intracranial structures to an outer surface like the cranium or skin depending on the current position of the pointer. The projected contour is intended to be used as a section line and therefor as reference for the audio feedback system. The goal is to indicate to the surgeon using an audio signal the distance of the pointer to the reference projected contour. A prepared head phantom is used to evaluate the system during the intraoperative planning and the navigation towards the target tissue. The development of the auditory display is based on the sparse field of previous research done regarding sonification in the medical context. So it could serve for another steps towards multiple perceptualization in intraoperative navigation.

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Poster 76

Hyperspektrale Untersuchungen von koagulierten tierischen Gewebeproben

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Die Hyperspektrale Bildgebungstechnologie ist eine innovative Bildgebungstechnologie um Tumorgewebe zu klassifizieren. Beispielsweise bei chirurgischen Eingriffen zur Entfernung von malignen Gewebe, wird bei der Entfernung des malignen Gewebes koaguliert. Dadurch werden z.B. Blutungen unterbunden.

Der Einfluss der Wärmeeinwirkung durch Hochfrequenzchirurgiegeräte (hier: bipolare Pinzette) auf das Gewebe wurde im Rahmen dieser Arbeit untersucht. Dazu wurde tierisches Fleisch koaguliert. Die hyperspektralen Auswirkungen auf das Gewebe wurden mittels Absorptionsspektren von 500 bis 1000 nm dokumentiert und ausgewertet.

Es konnte festgestellt werden, dass das koagulierte Gewebe nekrotische Stellen im Spektrum aufweist. Insbesondere der Bereich zwischen 650 und 680 nm zeigt einen anderen Verlauf als bei nicht koagulierten Gewebe. Zudem ist insgesamt die Absorption geringer bei koagulierten als bei nicht koagulierten Gewebe.

Die Hyperspektraltechnologie bietet dem medizinischen Personal neue Möglichkeiten zur besseren Behandlung des zu operierenden Patienten. Diese hier gewonnenen Erkenntnisse können genutzt werden, um Falschinterpretationen z. B. bei der Tumorklassifikation während chirurgischer Eingriffe im Situs zu vermeiden.

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Poster 77

Extending BPMN 2.0 Modeling Language for Surgical Interventions

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Surgical workflow management in modern integrated operating rooms (OR) enables the implementation of novel computer-aided surgical assistance systems and new applications in surgical process automation, situation-awareness, and decision support. The context-aware configuration and orchestration of interoperable, networked medical devices is a prerequisite for an effective reduction of the surgeons' workload. For this purpose, the information about the surgical situation can be described as Surgical Process Model (SPM) and must be distributed to the surgical assistance systems, medical devices and IT systems in the OR.

SPMs can be modeled with common business process modeling languages, such as BPMN 2.0. However, BPMN is a general-purpose language and lacks in representation of domain-specific concepts for surgical interventions. Therefore, a BPMN 2.0 extension for surgical process modeling was developed, which is called BPMN Surgical Intervention Extension ($BPMN^{SIX}$). Besides a suitable representation of surgical actions, new concepts for anatomical structures and different medical resources (e.g. surgical instruments, materials, clinical IT systems and medical devices), were developed. The resulting BPMN models are executable and could be implemented for surgical workflow management and context-aware surgical assistance in integrated ORs.

The generation of SPM with $BPMN^{SIX}$ was validated for a cataract surgery use case. The resulting model provides an efficient representation of the surgical workflow with different granularity levels and a visual representation of the used surgical resources.

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Poster 78

Development of a patient-specific dashboard application for decision-making in oncology

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The decision-making process in oncology involves an interdisciplinary review of each patient case by different domain experts. In practice, this procedure is realized in a collaborative tumor board meeting. Although the participants share the overall goal of finding the best possible therapy for each individual patient, their viewpoints on the case can be substantially different. Since the best therapeutic option involves the effective treatment of the tumor as well as a preferably high posterior quality of life, the foundation of the decision-making process needs to include a comprehensive overview about the case for all participants. This can be achieved by an integrated, consolidated view showing all patient- and disease-related aspects.

Our specialized dashboard application includes multiple views that provide a patient-specific overview on each case as well as detailed information in additional frontend components. The basic interface is separated into five parts. Each one is presenting one of the the following information clusters: patient anamnesis and therapy preference, information quality metrics (ICM), procedure timeline with corresponding results, TNM-staging based on anamnestic and/or histopathological results and therapy decision-support due to the instantiation of a decision-support system based on bayesian networks.

By integrating the patient-specific dashboard into the tumor board meeting, we are able to provide a complete and intuitive representation of all information that is relevant for the specific case. In this way, a holistic information foundation for all participants can be ensured.

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Poster 79

Qualitative Evaluation of an integrated operating room based on the IEEE11073-SDC

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Introduction:
The international OR.NET initiative focuses on interoperability of medical devices and IT systems. In the initial project, numerous partners, among them manufacturers of medical devices and IT systems, research institutes and clinical partners. They aim to create a technical base for an open, dynamic networking in the OR.

Material and Methods:
The ICCAS OR.NET demonstrator deals with clinical use cases of head and neck surgery. Additionally, we explored the use of workflow management technologies to actively assist the intraoperative process. All integrated systems share their data and control via the IEEE 11073 SDC standards family. In the work presented here, we evaluated the demonstrator with clinicians as well as with hospital operators. The OR and its unique features were introduced to the participants, followed by a questionnaire survey.

Results:
In our study, we qualitatively evaluate a subset of the developed concepts and systems based on an open OR integration technology. Hospital operators argued that they need support from medical device manufacturers, especially for subsequent implementation in hospitals. The clinicians requested a flexible integration, an intuitive human-machine interface and assistance functions in their daily work.

Discussion and Conclusion:
The implementation of openly integrated ORs will positively affect clinicians as well as the technical personnel and the hospital operators. The evaluation demonstrated the need for OR integration technologies and identified the missing tools to support risk management and approval as the main barriers for future installments.

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Poster 80

Prioritized Presentation of Surgical information to counteract information overload in the operating room

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Operating rooms (ORs) are evolving rapidly. Each new assistance funtionality has the potential to increase the amount of information that needs to be displayed and thus also increases the risk of information overload. To counteract this, available information has to be prioritized considering the current surgical situation (e.g. intervention type, phase, current work step etc.) Also similiar information entities should be grouped together and be displayed always at the same position in the surgeon's field of view.

To meet these challenges, a three component architecture was designed that is interposed between a variable set of OR displays and the OR network. The architecture, consisting of a Prioritizer, Layouter and Display Handler, is able to prioritize, orchestrate and toggle available information depending on its importance for the current OR situation. For this purpose, a predefined rule catalogue and a layout template are utilized.

The effect on information overload was examined in an explorative study at the use case of functional endoscopic sinus surgeries. Available information entities that would have required three displays in total were prioritized and orchestrated on two displays without noteworthy loss of information.

Thus, the proposed architecture seems well suited to minimize intraoperative information overload. It may contribute significantly to an efficient and safe surgical workfow.

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Poster 81

Bestimmung des Polyethylenabriebs basierend auf der röntgenbasierten Messung der Kopfdezentrierung bei verschieden großen Hüftendoprothesenköpfe

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Fragestellung: Es wurde eine neue Methode eingesetzt um den PE-Abrieb anhand routinemäßig erstellter Kontroll-Röntgenbilder bei Patienten mit primären Hüfttotalendprothesen (HTEP) abzuschätzen. Der geringeren Luxationsneigung von HTEP mit größerem Kopfdurchmesser steht die Befürchtung eines höheren Polyethylenabriebs und demzufolge kürzeren Standzeiten gegenüber. Im Rahmen einer Studie wurden Patienten nach primärer HTEP mit verschiedenen Köpfen untersucht.

Methodik: Diese retrospektive Studie schloss Patienten ein, welche in der Zeit von 01/2009 bis 09/2009 wegen primärer Koxarthrose mit einem zementfreien HTEP-System und Köpfen mit 28, 32, 36 und 40 mm Durchmesser versorgt wurden. Es wurden klinische und röntgenologische Untersuchungen durchgeführt sowie WOMAC- und des Harris-Hip-Scores (HHS) erhoben. Röntgenaufnahmen des betroffenen Hüftgelenkes in 2 Ebenen wurden mit der erweiterten Röntgenschattenrissanalyse analysiert.

Ergebnisse: Für N=41 Patienten (mit. Follow-Up: 83±3 Monate, mit. Alter 65±10a) betrug die Kopfdezentrierung für 5 Patienten mit 28mm-Kopf 2,14±1,44mm, für 10 Patienten mit 32mm-Kopf 2,18±1,04 mm, für 17 Patienten mit 36mm-Kopf 1,74±0,62 mm und für 9 Patienten mit 40mm-Kopf 1,88±0,43 mm.

Schlussfolgerung: Die Methode der erweiterten Schattenrissanalyse ist geeignet zur Abschätzung des lin. PE-Abriebs. Außerdem gab es keine Hinweise auf einen klinisch relevanten höheren Polyethylenabrieb bei Einsatz größerer Kopfdurchmesser in der primären Hüftendoprothetik. Die Argumentation gegen deren Einsatz sollte deshalb evidenzbasiert überprüft werden, da größere Köpfe das HTEP-Luxationsrisiko erheblich vermindern.

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Poster 82

Integration of a MR-compatible robotic arm into the clinical infrastructure

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Introduction: Focussed ultrasound (FUS) as a non-invasive therapy for treating tumor diseases is becoming more and more relevant. Although, only the ablation of benign and locally restricted tumors is approved, a combined therapy of FUS and radiation therapy (RT) is promising to improve the outcome while lowering the radiation dosage. Due to the integration in the patient table, currently available HIFU systems only allow the treatment in very specific regions. Hence, a robotic arm positioning the FUS system according to the treatment planning is more versatile. For further studies on combined FUS-RT treatment, the robotic arm system needs to be integrated into the existing clinical infrastructure. Materials and methods: A MR-compatible robotic arm system (InnoMotion by InnoMedic GmbH) was modified to fit onto the Biograph mMR MR-PET system (Siemens Healthineers) in the Department of Nuclear Medicine of the University Medical Center Leipzig.

Results: The robotic arm system was successfully modified to fit the Biograph mMR MR-PET system in the Department of Nuclear Medicine of the University Medical Center Leipzig. The robotic arm system was integrated into the clinical IT infrastructure

Discussion and Conclusion: Using MR-PET imaging technique improves the evaluation of the effectiveness of combined FUS-RT treatment. Due to the early stage of these combined therapies, MR-capable robotic systems are hardly available. Therefore, these systems lack standard for clinical integration. Further evaluation and validation studies will be conducted to investigate effects of the robotic arm on the MR-PET image quality.

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Poster 83

Beurteilung von Hüftgelenkspacern aus Knochenzement mithilfe der Finite-Element-Methode (FEM)

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Spacer aus Knochenzement sind ein bewährtes Mittel, um die schädlichen Folgen von infizierten Gelenkendoprothesen zu minimieren und dabei die Mobilität des Patienten zu erhalten. Häufig werden jedoch Brüche der Spacer in Folge von alltäglichen Bewegungen beobachtet. Ziel sollte es somit sein, die Haltbarkeit dieser Implantate zu erhöhen. Dafür können Designveränderungen oder die Augmentation z. B. mit Steinmann-Nägeln vorgenommen werden. Doch zuvor muss der Implantatausfall besser verstanden werden. So ist zu klären, bei welchen Lasten sie versagen und wo genau Brüche auftreten.

Für die Beurteilung eignet sich die Anwendung der Finite-Element-Methode (FEM). Ein Hüftgelenkspacer wurde simuliert der unter einer physiologischen Belastung eines Laufzyklus steht. Mithilfe des Principle of Independent Action (PIA) kann die Ausfallwahrscheinlichkeit des Spacers bestimmt sowie durch die Risk of Rupture Intensity (RRI) die kritischen Bereiche sichtbar gemacht werden. Die notwendigen Materialparameter entstammen der Literatur, wobei die Weibull Parameter für die PIA des Knochenzements Palacos® R aufgrund fehlender Literaturangaben zunächst nur angenommen werden können.

Die vorgestellte Methodik erlaubt es die Ausfallwahrscheinlichkeit eines Spacers und den Ort mit der höchsten Versagenswahrscheinlichkeit zu bestimmen. Damit ist es möglich, das Design der Spacer anzupassen, um sie langlebiger zu gestalten. Auch ist es möglich, den Einsatz von Armierungen durch z. B. Steinmann-Nägeln hinsichtlich der Steigerung der Festigkeit zu untersuchen.

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Poster 84

Enterovirus epidemiology and clinical presentations – a retrospective study from 2013 to 2017

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Background:
Enteroviruses (EV) cause a variety of diseases with neurological, respiratory and gastrointestinal manifestations. In 2014, US hospitals reported an increase of severe respiratory illness and cases of acute flaccid paralysis due to EV D68. Thereafter, outbreaks occurred in Canada, Europe and Asia.

Objectives:
We aimed to investigate the epidemiology and clinical presentation of EV infections in patients from the Leipzig University Hospital.

Methods:
Retrospective analysis included EV positive respiratory samples, received between January 2013 and March 2017. VP1-capsid sequences were determined for genotyping, and when necessary, additionally 5'UTR-VP2-VP4 and 3D region were sequenced. Clinical data were obtained from the charts.

Results:
Of 226 samples, 51 were typed as EV D68. While in 2013 to 2015 only 14 D68 cases were detected, the number increased to 36 in 2016. Almost all cases occurred in infants. The most common EV were Coxsackie virus A6 (17,3 %) and EV D68 (16,8 %). The most frequent diagnoses were respiratory infections. Hypoxia was present in 41 patients, half of them due to EV D68 infections. Six percent were noted to have a prior history of asthma, 10 % were premature infants, and 4 % were found in immune-compromised patients. In 16 cases, bacterial co-infection was detected. No cases of acute flaccid paralysis were detected.

Conclusion:
In 2016, EV D68 was the most commonly detected EV in our hospital. Those infected had more severe respiratory infections, requiring oxygen during their prolonged hospitalization. EV D68 might play an increasing role in respiratory illness, especially in children.

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Poster 85

Dextran sodium sulfate (DSS) induces necrotizing enterocolitis-like lesions in neonatal mice

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Background:
Necrotizing enterocolitis (NEC) is the most common life-threatening gastrointestinal disease in premature infants with yet unresolved etiology. Classic neonatal mouse models for NEC use enteral feeding and oral application of lipopolysaccharides (LPS) combined with hypoxia/hypothermia. In adult mice, administration of dextran sodium sulfate (DSS) results in ulcerative colitis (UC). Here we investigated the effect of DSS on the neonatal murine intestine compared with the established NEC model.

Methods:
3-day-old C57BL/6J mice were treated with DSS only or LPS plus hypoxia/hypothermia. After 72 h, mice were euthanized, the intestines harvested and analyzed by histology, qRT-PCR and flow cytometry. For comparison, adult C57BL/6J mice were fed with DSS for 8 days and examined likewise. Untreated, age matched animals served as controls.

Results:
Adult mice treated with DSS exhibited colonic inflammation with significantly increased Cxcl2 mRNA expression. In contrast, tissue inflammation was observed in colon and small intestine of neonatal mice treated with DSS or LPS plus additional stress. Additionally, a significantly increased lesion size and intestinal Cxcl2 mRNA expression after DSS exposure was demonstrated. Whereas LPS administration mainly induced local neutrophil recruitment, DSS treated animals displayed increased monocytes/macrophages infiltration.

Conclusions:
Our study demonstrates the potential of DSS to induce NEC-like lesions accompanied by a significant immune response in the small and

large intestine of neonatal mice. The new model therefore represents an alternative to classic NEC models.

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Poster 86

T helper cell (Th)1- and Th2-associated antigens in the fungal infection cryptococcosis

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Cryptococcosis, a life-threatening systemic fungal infection caused by Cryptococcus neoformans, has been demonstrated to be controlled by immune responses initiated by T helper (Th)1 cells, while Th2-mediated immune responses are associated with fungal growth and dissemination. Although cryptococcal immunoreactive protein antigens were previously identified, their association with Th1 or Th2 immune responses was not provided. In mice, Th1-dependent IFN-ɣ induces the production of IgG2a, whereas the Th2 cytokine IL-4 stimulates the expression of IgG1, rendering each isotype an indicator of the underlying Th cell response. Therefore, we performed an immunoproteomic study that distinguishes Th1- and Th2-associated antigens by their reactivity with Th1-dependent IgG2a or Th2-dependent IgG1 antibodies in sera from C. neoformans-infected wild-type mice. We additionally analysed sera from Th2-prone IL-12-deficient and Th1-prone IL-4Rα-deficient mice, extending the results found in wild-type mice. Interestingly, we were able to identify antigens specifically associated with IgG1 or IgG2a antibodies, as well as a limited number of antigens reactive with both isotypes. Th2-associated antigens represent promising candidates for development of immunotherapy regimens, whereas Th1-associated antigens may serve as candidates for vaccine development. In conclusion, this study points to intrinsic immunomodulatory effects of fungal antigens on the process of Th cell differentiation based on the identification of cryptococcal protein antigens specifically associated with Th1 or Th2 responses throughout mice of different genotypes.

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Poster 87

In vitro analysis of the *Streptococcus suis*-induced cytokine milieu in porcine peripheral blood mononuclear and tonsil cells

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S. suis is a problem in pig breeding causing death in up to 10 % of the weaning piglets in pig farms. Although the tonsils of healthy pigs are commonly colonized by *S. suis*, disease is only observed if the pathogen is invading peripheral locations such as brain or heart. While humoral immunity in piglets has been frequently investigated, the role of the T helper cells (Th) during *S. suis* colonization or invasion is unclear. We hypothesized that *S. suis* is able to influence secretion of the pro-inflammatory cytokine interleukin (IL)-6 or of the anti-inflammatory IL-10.
Here we show that *S. suis* is able to modulate the cytokine milieu in isolated peripheral blood mononuclear cells (PBMCs) and tonsils to a different extent and might thereby influence the polarization of Th subsets differently. In PBMC culture *S. suis* induced IL-6, but it decreased with higher doses of *S. suis*. Conversely, higher doses of *S. suis* induced IL-10. This suggests IL-6 is inhibited by IL-10. However, even after incubation with a neutralizing anti-IL-10 antibody, IL-6 decreased with higher doses of *S. suis*. Based on these results, we propose a *S. suis*-induced regulatory pathway where IL-6 secretion is inhibited by IL-10 and other unknown modulators, ultimately directing the T cell response towards a regulatory phenotype.

In comparison, in *S. suis*-stimulated tonsil leukocytes IL-6 levels were not detectable. Moreover, in combination with a polyclonal T-cell stimulus, *S. suis* was able to increase T cell-dependent IL-10 production in tonsil leukocytes.

In summary, we could show *S. suis*-induced immunosuppression in isolated porcine PBMCs and tonsils.

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Poster 88

Cytotoxicity of human pathogenic virus infection in human induced pluripotent stem cells — a hint for adverse pregnancy outcome?

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Human induced pluripotent stem cells (hiPSCs) offer various applications ranging from regenerative and personalized medicine to drug screening. Furthermore, hiPSCs as a cell culture model for the very early steps of embryogenesis enable examination of human pathogenic virus infections, as they could be used to represent the vulnerable period from blastocyst stage to gastrulation-like events. Beside teratogenic virus infections causing congenital malformations and disorders another risk during pregnancy are virus infections associated with spontaneous abortions. In this study the highly efficient teratogen rubella virus (RV) was contrasted to coxsackievirus B3 (CVB3) and measles virus (MV), both associated with miscarriage events. Accordingly, CVB3 as well as MV infection of hiPSCs caused cell dissociation and cell death at a different extent on the two tested hiPSC lines. In contrast, RV infection had no effect on colony morphology and viability. Moreover, RV-infected hiPSC lines could be passaged while maintaining pluripotency. Hence, the cytotoxicity of CVB3 and MV infection on hiPSCs could be correlated with their ability to cause spontaneous abortions while the non-cytotoxic activity of RV on hiPSCs enables its persistence. These findings provide insights in disturbances caused by pathogenic viruses during the very early phase of human embryonic development. Thus, hiPSCs are now established as a powerful *in vitro* cell culture model to examine virus infections relevant to human pregnancy.

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Poster 89

Gene expression patterns in blood predict the time course of community acquired pneumonia

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Community acquired pneumonia (CAP) is still a big challenge due to its severe manifestations and related costs. Gene-expressions in blood are promising biomarkers to predict disease course and support clinical decision making. Moreover, it provides insights into pathomechanisms of CAP.

Within the PROGRESS study, we followed the disease courses of 394 patients hospitalized with CAP for 28 days including daily assessments of clinical parameters within the first five days. Patient's disease courses differed in severity measured by the Sepsis-related Organ Failure Assessment (SOFA) score. Death and requirement of intensive care were considered as severe endpoints. Time series of genome-wide gene-expression measurements of whole blood samples were used to predict time courses and endpoints. We investigated pathway activation and compared expression patterns of sepsis studies.

Our results identified (after multiple-testing-correction) more than 5000 genes related with current disease severity and more than 250 genes associated with current severe endpoints. About 50 genes were associated with future severe endpoints. With increasing severity, pathway analysis showed increased inactivation of many immune-related pathways, especially those of T-cells. Previously proposed expression signatures correlate well with current severity but predict future severity less well.

In summary, we found genes and pathways related with present and future CAP-severity that inspire our modelling efforts and can be readily validated in additional cohorts. Our results may help to improve diagnosis, therapy, and outcome for patients with CAP.

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Poster 91

Determination of epitope profile before and after Hepatitis B and Influenza vaccinations direct from patient sera

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The humoral response to Hepatitis B and influenza vaccinations is mainly validated through antibody titer against their major antigens. Our ability to monitor changes in the antibody profile resulting from vaccination, e.g. epitope spreading or walking, is however limited. A new peptide phage display-based approach for mapping epitopes direct from patient sera has been established. With this technology, we determined epitope profiles before and after vaccination. Pre- and post-immunization serum was collected from a single patient and used for only two rounds of peptide phage display experiments. Phagemid DNA from the obtained clones was sequenced (illumina MiSeq®). The epitope profile was determined in silico by comparing the antigens' 4-mer motifs statistics between the selected phagemid pools and the naïve 17-mer library ENTE1. Potential immunogenic motifs of Hepatitis B surface antigen [HBsAg] and hemagglutinin [HA] were thus identified. Remarkably, most of these motifs are located within sites that have been reported as epitopes. Epitopes with 5 to 8 conserved amino acid residues could be identified. We observed significant enrichment of peptide sequences containing motifs of HBsAg after boost with Hepatitis B vaccination. HA epitopes were identified indistinctively before and after immunization. In summary, our technology allowed us to identify the epitope profile of the antibody repertoire with resolution at amino acid level. Further studies involving a larger number of patients may contribute to the current understanding of the immune response to vaccination and other immunotherapies.

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Poster 92

Development of test systems based on monoclonal antibodies for the detection of allergenic food ingredients produced from legume family proteins

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Innovative plant products made of legume crops like lupin seeds are more and more important in western nutrition, not only in the vegetarian cuisine. Besides a lot of health benefits lupin possesses an allergenic potential as well and therefore needs to be declared as one of 14 allergenic ingredients.

Four proteins have been shown to be the main lupin allergens, especially Lup an 1 (conglutin β). Allergic responses mediated by immunoglobulin E antibodies include itching, dermatitis, gastrointestinal pain and breathing difficulties. In some cases, sensibilised people will suffer from life-threatening anaphylactic responses. Hitherto, the only secure method for allergic subjects is to avoid food containing such allergens. However, lupin is classified as a “hidden allergen” especially as flour admixture in bakery products.

Hence, the goal is to develop an assay based on monoclonal antibodies (MABs) for detecting different allergenic legume proteins in processed food.

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Poster 93

Identification of antigens for a specific serological detection of dengue and Zika virus infections

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The high cross-reactivity of antibodies derived from flavivirus infections is a challenging fact in serodiagnosis of important human pathogens such as dengue, Zika, yellow fever, West Nile, Japanese encephalitis, and tick-borne encephalitis viruses (DENV, ZIKV, YFV, WNV, JEV, and TBEV, respectively). The massive co-circulation of DENV and ZIKV with similar clinical symptoms raises the need of a reliable serological differentiation of these infections. The envelope (E) protein is a major target of the humoral immune response and its highly conserved fusion loop (FL) domain binds the majority of cross-reacting antibodies. Therefore, we inserted mutations in the FL domains of DENV and ZIKV E proteins.

Recombinant quadruple E protein mutants (Equad) of DENV and ZIKV were stably expressed in Drosophila S2 cells and purified from culture supernatants with affinity and size exclusion chromatography. Antibody responses were measured in IgM- and IgG- based ELISAs with DENV, ZIKV, WNV, JEV, TBEV infected, YFV vaccinated and flavivirus negative human serum samples.

IgM antibodies against both viruses were detected with high specificity and sensitivity. Moreover, titration of IgM positive DENV sera enabled the differentiation of the infecting serotype. IgG measurements showed substantial cross-reactivity of DENV- and ZIKV positive sera. This was overcome by pre-incubation of the sera with the heterologous antigen in a competition ELISA setup.

Our results suggest that E-proteins bearing mutations in the FL-domain have a high potential for the development of serological DENV and ZIKV tests with high specificity.

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Poster 94

Longitudinal analysis of cytokine profiles in community-acquired pneumonia

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Factors influencing the clinical course of community-acquired pneumonia (CAP) are still incompletely known. Some patients recover quickly, whereas others develop severe sepsis requiring intensive care and high risk of mortality. Inflammatory response of the host is one of the factors linked to the severity of CAP.

In the PROGRESS project, 1,800 CAP patients were collected and studied for four days after admission to the hospital. The assessments include, among others, clinical parameters of organ function summarized by the SOFA score (sequential organ failure assessment), clinical outcomes and levels of 10 cytokines measured by ELISA (available for N=400 patients).

We performed time series analysis of these data asking what are the associations among the cytokines and between the cytokines and the clinical outcome parameters of the patients at the same day and over time. An answer to this question is relevant for systems-biological modeling of the immune response in CAP. The challenges in the analysis included: 1) short time series (T=4), 2) patient-specific levels of the cytokines, 3) patient-specific slopes of the trajectories over time, 4) within-patient contemporaneous correlation between the errors.

We present first results of the analysis and describe a way in which we attempted to solve the difficulties of estimating lagged associations in our time series data. The methods that we used included methods known from econometrics (dynamic panel models) and psychology (cross-lagged panel models) which, to our knowledge, have not been widely used for analyzing biomedical data.

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Poster 95

Relevance of immune checkpoint signals in NK cells

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The treatment of cancer has made impressive progress, even though it is still a challenge. The adaptive and innate immune system make use of different strategies to counteract tumor cells. Adaptive immune cells, like T cells convey antigen-specific responses and memory. The tumor counteracts immune response by employing immune escape mechanisms. Immune checkpoint control signals are either co-stimulatory or inhibiting signals that influence the scale of immune activation. It is known, that tumors upregulate especially T cell inhibitory signals to escape recognition. Checkpoint inhibitors, involved in tumor mediated immune downregulation, have proved to be efficient cancer therapeutics for a number of indications.

Especially NK cell lines are a promising new tool in the fight against cancer as they can function as a tumor-specific off-the-shelf cellular immunotherapeutic exhibiting considerable tumor killing capacities while showing less severe adverse effect compared to engineered T cells.

Here, we quantified the amount of selected checkpoint signals in clinical relevant NK cell lines on transcription and protein level by applying qPCR and flow cytometry. Furthermore, possible functional consequences of checkpoint signaling will be revealed by apply oligonucleotide-mediated knockdown of relevant signals in a tumor-effector co-culture model *in vitro*. Our approach might thus not only increase the basic knowledge on the role of checkpoint signaling in innate immunity, but might also provide a chance to develop an innovative new class of drugs for adjuvant cancer immunotherapy.

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Poster 96

Regulation of Macrophage Polarization by Fibroblasts – Impact for the Wound Healing Response

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A crucial checkpoint in the wound healing process is the resolution of inflammation which is regulated by M1/M2 macrophage (Ma) activity. Several soluble factors, which influence this polarization, have been described. Despite that, the mechanisms that control this M1/M2 switch are not completely understood. In previous experiments we could show that dermal fibroblasts (dFb) secrete under the influence of an inflammatory environment TSG-6 and cox-2 products. Underlining these facts we could furthermore show that the injection of dFb into mice with thioglycollate-induced peritonitis promotes the activation of alternative Ma and we could also show that the administration of dFb in wound margins improves defective tissue repair in db/db mice. Based on these results we currently investigate whether dFb perform crucial immunoregulatory functions during dermal wound healing and further characterize the mechanisms how dFb induce the Ma polarization.

To identify whether dFb are the source of immunomodulatory factors during the course of wound healing we used full-thickness wound healing model in mice. We observed in the early phase of healing process increased expression levels of TSG-6 in dFb fractions compared to other cell types. Since we could identify dFb as an important source of anti-inflammatory mediators, we will furthermore characterize phenotype change of dFb during the healing process and the corresponding intracellular signaling pathways, which are involved in mediator release.

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Poster 97

Keratin mutations trigger the itch-inducing cytokine TSLP in keratinocytes via EGFR signaling

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The epidermal barrier protects the body against dehydration, physical and chemical insults and pathogens. Barrier disruption which causes many inflammatory skin diseases including atopic dermatitis (AD) triggers the expression of proinflammatory cytokines such as TSLP (thymic stromal lymphopoietin) in keratinocytes. TSLP is strongly increased in skin lesions of AD patients and is involved in itch and inflammation by inducing TH2 cytokines. Current hypotheses claim TSLP upregulation upon barrier breach, however, the exact mechanisms need to be unraveled. Patients suffering from the skin blistering disease EBS (epidermolysis bullosa simplex), caused by keratin 5 or 14 mutations, frequently suffer from itch accompanied with inflammation. This raises the question whether keratins play a role in TSLP increase. We therefore hypothesized a link between keratin and TSLP expression.

We identified strongly elevated TSLP level in the serum and epidermis of mice lacking the entire keratin cytoskeleton. Corresponding keratin-free keratinocytes showed increased TSLP levels which were reduced upon re-expression of wt keratins but not by EBS-type mutant keratins, suggesting a keratinocyte-intrinsic, keratin-dependent mechanism of TSLP upregulation that acts independent from epidermal barrier defects. Pathway analysis revealed an EGFR-ERK1/2 signaling axis controlled by keratins which contributes to elevated TSLP expression in keratinocytes. These data underscore a major contribution of keratins in controlling skin-dependent immune responses and propose ERK1/2 kinases as potential targets for itch treatment in EB disease.

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Poster 98

High seroprevalence of DENV indicates that dengue virus infections are frequent in Central and Eastern Sudan

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Background:
Sudan is an endemic area of dengue virus. Repeated outbreaks suggest that seroprevalence is higher than previously reported. The aim of the study was to determine the seroprevalence of dengue virus in Sudan.

Methods:
Blood samples were drawn from patients who visited outpatient clinics in Red Sea State, Kassala and North Kordofan. The sera were tested for IgG and IgM antibodies by ELISA and in a neutralization test. To minimize the influence of an acute infection leading to a high rate of false positive results in immunoassays, sera with dengue IgM antibodies were excluded from further analyses.

Results:
The data show that dengue seroprevalence is substantially higher than previously reported. Furthermore, a large fraction of the samples neutralized all four dengue virus serotypes indicating that multiple infections had occurred.

Conclusion:
Our results indicate that the introduction of an anti-dengue vaccination policy would be beneficial towards public health in the regions examined.

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Poster 99

Proteomic profiling of peripheral human CD56neg NK cells

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Natural killer (NK) cells as part of innate immunity play a critical role in limiting viral infections. The definition of functionally distinct NK cell subsets is of growing importance to understand these control mechanisms. CD56neg NK cells expand notably in chronically HIV- or HCV-infected patients. However, CD56neg NK cells also exist in healthy individuals, albeit in significantly lower numbers. Although previous results suggested these cells to be functionally impaired, their specific role remains elusive.

An extensive proteomic characterization of peripheral blood CD56neg NK cells of healthy humans in comparison to their CD56dim and CD56bright counterparts based on accurate Orbitrap mass spectrometry was performed. The phenotype of CD56neg NK cells appeared surprisingly similar to cytotoxic CD56dim NK cells but also displayed distinct features. The study revealed a complete cytolytic inventory with high levels of perforin and granzyme H and M. Twelve proteins discriminated CD56neg from CD56dim NK cells. CD56neg NK cells showed *in vitro* modest cytotoxicity, degranulation, and IFN-ɣ secretion as compared to CD56dim NK cells. In conclusion, CD56neg NK cells constitute functionally competent cells sharing many features of bona fide CD56dim NK cells, but with some distinct characteristics. Furthermore, a systemic strategy to assess cell type-specific functions based on relative quantitative mass spectrometry data was developed and will be presented.

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Poster 100

Plant compounds of chamomile and coffee charcoal (apigenine, chlorogenic acid, trigonelline), present in a traditional herbal medicinal product, show inhibitory effects on the pro-inflammatory cytokine release of human macrophages

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Background:
Myrrhinil-Intest® is a traditional herbal medicinal product containing myrrh, coffee charcoal and chamomile flower extract. It is used i.a. in the treatment of Inflammatory Bowel Diseases. However, its mechanisms of action and active components have not yet been fully elucidated.

Aim:
The present study aimed to evaluate anti-inflammatory properties of apigenine, chlorogenic acid and trigonelline, which are known plant compounds of chamomile and coffee charcoal.

Methods:
PMA-differentiated THP-1-macrophages were used to assess the effect of the substances in various concentrations (0.001 µM – 100 µM) on LPS-induced pro-inflammatory cytokine release, with budesonide (1 nM) as a positive control. The supernatant was collected after 4 h and 24 h incubation for analysis of TNFα and IL-6 release using ELISA. Concomitant cytotoxicity testing was conducted with the MTT assay.

Results:
Apigenine, chlorogenic acid and trigonelline were able to reduce the TNFα secretion down to and beneath the level of budesonide (40 % inhibition) in a concentration-dependant manner. The release of IL-6 was also decreased concentration-dependently and comparable to budesonide (60 % inhibition) by all three substances. In comparison, apigenine (> chlorogenic acid-trigonelline) showed the highest inhibitory activity.

Conclusion:
The study gives important suggestions on active components of Myrrhinil-Intest®, which could be contributing to its positive effects in the treatment of gastrointestinal disorders. Further mechanistic research is needed to confirm the results and fully unravel the mode of action.

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Poster 101

Vergleich zur Verbundfestigkeit von Komposit-Matrix-Keramikkronen auf einteiligen ZrO2- und Ti-Implantaten – eine Pilotstudie

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Ziel der Studie war es, die Wirksamkeit der Vorbehandlung von Implantatoberflächen bezüglich des adhäsiven Verbundes mit Komposit-Matrix-Keramik-Kronen zu untersuchen.

Material und Methoden: 40 einteilige Versuchsimplantate (VI) (ZrO_2 n=20/Ti n=20) wurden randomisiert in 8 Gruppen aufgeteilt. Je 10 VI beider Materialgruppen wurden sandgestrahlt (sb) (CoJet™, ≤50µm, 2bar) und je 5 mit einer Krone aus Lava Ultimate (LU,3M Espe) und aus VITA Enamic (VE,VITA Zahnfabrik) versorgt. Alle Kronen wurden mittels CAD/CAM-Verfahren identisch hergestellt und adhäsiv mit RelyX Ultimate (3M Espe) befestigt. Nach den Abzugsversuchen (Z010, Zwick GmbH & Co.KG) wurden bei 0,65facher Vergrößerung lichtmikroskopische Abbildungen zur Verteilung des adhäsiven Befestigungsmaterials auf den Kroneninnenflächen und der Implantatoberflächen angefertigt. Die statistische Auswertung erfolgte deskriptiv.

Ergebnisse: Die Haftfestigkeit an sb Implantatoberflächen war höher als an nicht-sb. Bei Ti (sb) war der Mittelwert 509,1±126,6N. Bei ZrO_2 (sb) war M=604,1±66,9N. Die nicht sandgestrahlten Implantatoberflächen zeigten für Ti M=121,2±24,6N und für ZrO_2 M=51,1±14,5N. Die Kronen aus LU wiesen insgesamt eine erhöhte Verbundfestigkeit zum Ti (M=373,5±62,1N) als die VE-Kronen auf. Bei VE-Kronen war die Verbundfestigkeit (M=341,8±33,55N) zur Keramik erhöht. Das Befestigungsmaterial befand sich nach dem Abziehen fast ausschließlich in den Kroneninnenflächen.

Schlussfolgerung: Die Vorbehandlung der Implantatoberflächen von einteiligen Implantaten führt zu einer höheren Haftkraft der Restaurationen und sollte im klinischen Einsatz berücksichtigt werden.

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Poster 102

MAMMALIPO – Pilotstudie zur molekularen und metabolischen Charakterisierung der Assoziation von Mammakarzinom und Adipositas

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Brustkrebs ist weltweit eine der häufigsten Tumorerkrankungen bei Frauen. Große Kohortenstudien konnten zeigen, dass Übergewicht ein wesentlicher Risikofaktor für eine Brustkrebserkrankung darstellt und signifikant mit einer schlechteren Prognose, größerem Tumorvolumen und einer höheren Inzidenz von Lymphknotenmetastasen assoziiert ist. Der Zusammenhang von Brustkrebsrisiko, Prognose und Übergewicht ist epidemiologisch etabliert. Allerdings sind die molekularen Mechanismen dieser Assoziation noch nicht im Detail erforscht. Mit Hilfe von umfassenden, massenspektrometrischen Metabolomanalysen in Blut- und Tumorgewebeproben von normalgewichtigen (Body-Mass-Index >19 bis <25) und übergewichtigen (Body-Mass-Index >25) Patientinnen mit Mammakarzinom sollen erstmals ihm Rahmen der MAMMALIPO Pilotstudie zur Hypothesenfindung spezifische tumor- und übergewichtsassoziierte Metabolitenmuster identifiziert und verglichen werden. Ziel ist es neuartige, spezifische stoffwechsel-assoziierte Biomarker zu finden, welche zukünftig für eine nicht-invasive Diagnose- und Prognosestellung für Patientinnen mit Mammakarzinom, insbesondere im Zusammenhang mit Übergewicht, herangezogen werden könnten.

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Poster 103

Evaluation der Wirksamkeit von SCP-Neurofeedback auf die Reduktion von Essanfällen und Heißhunger bei Erwachsenen mit Binge-Eating-Störung

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Für die Binge-Eating-Störung (BES) werden allgemeine und nahrungsspezifische Impulskontrollschwierigkeiten als störungsaufrechterhaltende Faktoren angenommen. Zur Verbesserung der Impulskontrolle bei anderen, durch Impulsivität gekennzeichneten psychischen Störungen, wie Aufmerksamkeitsdefizit-/Hyperaktivitätsstörung, gilt Elektroenzephalographie (EEG)-Neurofeedback, vor allem ein Training der langsamen kortikalen Potentiale (slow cortical potentials; SCP), als wirksame Behandlung. Das Ziel dieser Interventionsstudie war es, die Wirksamkeit eines SCP-Trainings auf die Anzahl objektiver Essanfälle und das Heißhungergefühl bei Erwachsenen mit BES zu untersuchen. Erwachsene mit BES und Übergewicht (N=16) erhielten dazu nach einer 6-wöchigen Wartezeit 6 Wochen SCP-Training in 10 Sitzungen. Die primären Endpunkte (Anzahl der Essanfälle, Heißhunger) wurden vor Beginn der Wartezeit, vor Beginn und nach Ende des SCP-Trainings sowie drei Monate nach Behandlungsende im Selbstbericht mittels etablierter Fragebögen erfasst.

Vorläufige Auswertungen zeigen, dass das SCP-Training zu einer signifikanten Reduktion in der Anzahl der objektiven Essanfälle und des subjektiven Heißhungergefühls führte, die auch zum 3-Monats-Follow-up bestehen blieben. Während der Wartezeit wurden hingegen keine bedeutsamen Reduktionen der Essanfälle oder des subjektiven Heißhungergefühls verzeichnet.

Diese Studie liefert erste Ergebnisse zur Effektivität von EEG-Neurofeedback zur Reduktion objektiver Essanfälle und Heißhunger bei Erwachsenen mit BES. Ausblickend gilt es, die spezifischen Wirkmechanismen von EEG-Neurofeedback zu determinieren.

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Poster 104

Comparison of two shade taking lamps for visual tooth color matching

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Due to a recommendation of the DGZMK, the visual determination of tooth color is supposed to be taken at an illumination level of approximately 2000 lx and an illumination, which refers to diffuse Northern light at noon. Two such products are compared.

One of the lamps used was “Dialite Color” (Eickhorst, Hamburg), which had proven quality for years. It is equipped with two fluorescent lamps. The second lamp was the Swiss “Smile Lite”. The light sources here were six LEDs. Since these LEDs generate strong distracting reflections at the tooth surfaces, the lamp was equipped with a polarization filter. 23 students of preclinical semesters in dentistry participated in the trial. They determined the shades of 10 randomly chosen teeth of the VITA-3D-Master color range, applying VITA-linear-guide working under both shade taking lamps. To ensure a double-blinded setting the tooth shades were encrypted by barcode

For each tooth color determination (n=440), the difference of the chosen shade in relation to the right tooth ΔE in the L*a*b*- color scale was determined. The Eickhorst lamp revealed an average ΔE of 3.18 with a standard deviation of 1.05. For Smile Lite, the corresponding values were at 3.08 ± 0.75. Hence the Shapiro-Wilk-Test showed no normal distribution, the Mann-Whitney-Rank Sum Test was chosen, which resulted in a value of $p = 0.877$.There was no significant difference in the results of tooth color determination between the two shade taking lamps.

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Poster 105

Therapierung der autochthonen Rückenmuskulatur mittels eines computergestützten Trainingssystems

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Einleitung:
85 % aller chronischen Rückenschmerzpatienten leiden unter unspezifischen Beschwerden, welche nicht direkt auf Verletzungen oder andere klar zu benennende Pathologien zurückzuführen sind. Ursächlich hierfür sind vielmehr arthromuskuläre Defizite bzw. Dysbalancen im Bereich der autochthonen Rückenmuskulatur, welche nicht willentlich ansteuerbar ist und rein reflektorisch reagiert. Eine spezielle Therapierung ist somit unabdingbar. Die Anwendung von dosierten und kontrollierten physischen Beanspruchungen (Auslenkung aus Gleichgewichtslage) mittels des computergestützten Test- und Trainingsgerätes Centaur (BfMC GmbH) soll dabei Abhilfe verschaffen.

Methodik:
Ein neunwöchiges individuell angepasstes Trainingsprogramm mit zwei Trainingseinheiten pro Woche dient dem Aufbau der Rumpfmuskulatur. Messungen (Kippmomenttests) vor, während und nach Beendigung der Therapie fungieren als Verlaufskontrolle. Zusätzlich statistisch ausgewertet werden gerätespezifische Parameter, wie Momente (Nm), Haltungsabweichungen (%), Neigungswinkel (°) und Haltezeiten (s) sowie standardisierte Fragebögen.

Ergebnisse:
Die Ergebnisse zeigen, dass Trainingseinheiten im speziell konstruierten Gerät eine Kräftigung der rumpfstabilisierenden bzw. autochthonen Muskulatur bewirken können.

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Poster 106

Development of 1,8-substituted, fluorine-containing imidazo-quinoxaline derivatives as reference compounds for potential PET ligands for phosphodiesterase 10A

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Phosphodiesterases (PDE) are hydrolysis enzymes of secondary messengers and therefore important regulators of signal transduction. PDE10A, a cAMP- and cGMP-sensitive hydrolase is primarily expressed within the striatum and identified as a potential target for therapy and diagnosis of various disorders of the central nervous system (CNS) such as schizophrenia or Huntington's disease. Recently, it has been reported that 1-Arylimidazo[1,5-a]quinoxalines are potent and selective inhibitors of PDE10A and are suitable for imaging the enzyme in physiological and pathophysiological environments. The development and synthesis of new inhibitors should serve as reference compounds in view of their potential use for positron emission tomography.

After the successful adaptation of a 6-step synthesis, 6-chloro-imidazo[1,5-a]quinoxaline was prepared as basic structure and derivatized by Suzuki coupling. The obtained mono- and disubstituted pyridinyl derivatives and their precursors were elucidated by high-performance liquid chromatography (HPLC), nuclear magnetic resonance spectroscopy (NMR) and mass spectrometry (MS). The pharmacological characterization of 12 obtained target compounds was done by determining the inhibitory effect against human PDE10A at 10nM, against PDE2A at 1µM. Based on this data, 6-chloro-1,8-bis-(2-fluoropyridin-3-yl)-3,4-dimethylimidazo[1,5-a]quinoxaline was selected for the determination of the IC_{50}-values for PDE10A and PDE2A.

A docking study visualized possible binding modes of the inhibitors in the proteinogenic environment of PDE10A.

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Poster 107

Temporäre Hemiepiphysiodese zur Wachstumslenkung am Ellenbogen

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Die Umstellungsosteotomie hatte bisher einen hohen Stellenwert in der Therapie des posttraumatischen Cubitus varus. Im Gegensatz hierzu wurde die Wachstumslenkung der distalen Humerusepiphyse weniger häufig angewendet. Ziel der vorliegenden Studie war die Evaluation einer temporären radialseitigen Hemiepiphysiodese zur Korrektur des Cubitus varus nach Frakturen am distalen Humerus. Methode: Retrospektive Analyse von Kindern mit posttraumatischem Cubitus varus, die von 2008 – 2014 in unserem Zentrum operiert wurden. Ausgeschlossen wurden Patienten >12 Jahre. Die radialseitige Hemiepiphysiodese erfolgte mittels eight-plate (Orthofix, Verona, Italy). Die statistische Auswertung erfolgte mittels T-Test. Ergebnis: 20 Patienten mit posttraumatischem Cubitus varus wurden eingeschlossen (mittleres Alter: 8,2±2,0 Jahre (range: 1 - 12)). Der mittlere Varus betrug 12,5±6,5° (range 4 - 30°). Die Metallentfernung erfolgte bisher bei 9 Patienten (45%). In dieser Gruppe wurde die Hemiepiphysiodese im Mittel für 5,7±1,9 Jahre (range: 4 – 9,5) in situ belassen. Bei einem follow-up von bis zu 86 Monaten zeigte sich bei diesen 9 Kindern nach initialem Varus von 14,44±6,7 ° (range: 06° - 30°) eine signifikante mittlere Reduktion um 10,5° auf einen Varus von 3,9±5,9 ° ($p<0,01$; range: Valgus 3° bis Varus 14°). Schlussfolgerung: Zur Therapie des posttraumatischen Cubitus varus im Wachstumsalter stellt die temporäre Hemiepiphysiodese mittels eight-plate® eine alternative schonende Therapieoption dar. Bei allen untersuchten Patienten führte das korrigierende Restwachstum der distalen Humerusepiphyse zu einer Verbesserung der Armachse.

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Poster 108

Prospektive randomisierte Studie zur Biokompatibilität von Prothesenbasis-materialien unter Nutzung der konventionellen Zytologie

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Zielstellung:
Ziel der Studie war es, die Gewebeverträglichkeit eines methacrylatfreien (Valplast) mit einem methacrylathaltigen Kunststoff (PalaXPress) intraoral im Split-Mouth-Design zu vergleichen. Dazu wurde die Bürstenbiopsie mit konventioneller Aufbereitung der zytologischen Präparate genutzt.

Material & Methoden:
Die Studie folgte dem randomisierten Ablauf nach den Consort-Richtlinien. Mit einer individualisierten Molarenbandapparatur wurden bei n=10 Probanden 2 Prothesenkunststoffe intraoral befestigt. Die zytologische Untersuchung erfolgte anhand von 3 Abstrichentnahmen (vor und nach dem Tragen des Prüfkörpers, sowie eine Woche danach) der palatinalen Mukosa mit einem PapCone® Zellkollektor und dem konventionellen Ausstrich auf dem Objektträger. Die zytologischen Präparate wurden in der konventionellen Giemsa-Färbung hergestellt und lichtmikroskopisch (n=60) ausgewertet.

Ergebnisse:
Es wurden keine zytologischen Veränderungen zwischen Valplast und PalaXPress festgestellt. Jedoch zeigten sich in dieser Pilotstudie Unterschiede der Präparate zu den verschiedenen Zeitpunkten der Abstrichentnahme. Vor dem Tragen der Prüfkörper überwogen keratinisierte Zellen (Zellkern fehlend oder sehr klein) und die Präparate waren eher hell. Nach der vierwöchigen Tragedauer gab es mehr Zellen mit deutlichem Zellkern sowie häufiger Zellzusammenlagerung und die Präparate erschienen bläulicher. Zur Nachkontrolle war das Erscheinungsbild der Präparate durchmischt.

Schlussfolgerung:
Die Kunststoffe Valplast und PalaXPress zeigten in dieser Studie eine gleich gute Gewebeverträglichkeit unter einer vierwöchigen Tragdauer.

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Poster 109

Studie zur Häufigkeit und Lage von akzessorischen Foramina im interforaminären Bereich des Unterkiefers

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Ziel dieser Studie war es, bukkale und linguale akzessorische Foramina (AF) im interforaminären Bereich der Mandibula zu detektieren und diese in Bezug auf Größe, Lage und Vorkommen zu untersuchen.

Material und Methoden:
In die Untersuchung konnten n=108/1120 dentale Volumentomographiebilder (männlich n=60, weiblich n=48) von einem Patientenkollektiv der Universität Leipzig stammend aufgenommen werden. Bukkal und lingual liegende AF wurden dargestellt und vermessen. Zu den Parametern zählten Lage, Größe, Geschlechterverteilung und Häufigkeit. Die statistische Auswertung erfolgte deskriptiv. Statistische Signifikanzen wurden mit dem t-Test ermittelt.

Ergebnisse:
Es konnten insgesamt 62 akzessorische bukkale Foramina (ABF) mit einem durchschnittlichen Querschnitt von M=0,687mm und 166 akzessorische linguale Foramina (ALF) mit einem Mittelwert für den Durchmesser von M=0,894mm, in den 3D Röntgenaufnahmen, identifiziert werden. Es konnte keine statistische Signifikanz zwischen dem Geschlecht und dem Auftreten AF nachgewiesen werden. Auch bestand kein Zusammenhang zwischen dem Auftreten ABF und ALF.

Schlussfolgerung:
Es kann festgestellt werden, dass AF wichtige Strukturen in der menschlichen Mandibula darstellen. Die dentale Volumentomographie bietet derzeit das bestmöglichste radiologische Verfahren zur Darstellung auch kleinster anatomischer Strukturen im Unterkiefer.

Für eine ausreichende Diagnostik und Therapie durch oralchirurgische Maßnahmen, sollte daher eine ausführliche Anamnese, Aufklärung des Patienten, extra- und intraorale Untersuchung sowie 3D Bildgebung, stattfinden.

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Poster 110

Die unterschiedlichen Arten der Darstellung der Arteria thoracica interna (ITA) und ihrer Abgänge

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Tiefe sternale Wundheilungsstörungen sind seltene, aber verheerende Komplikationen nach medianer Sternotomie. Die verminderte Durchblutung von Knochen- und Weichgewebe nach Verwendung der Arteria thoracica interna (ITA) in der kardiochirurgischen Bypass-Chirurgie, begünstigt die Entwicklung von Wundheilungsstörungen. Das Ziel dieser Studie war die makroskopische und radiologische Darstellung des sternalen Gefäßsystems im Hinblick auf mögliche Kollateralkreisläufe. Das methodische Vorgehen gliederte sich in die makroskopischen Präparation, die Segmentierung mittels Mimics® und deren semi-quantitativer Vergleich. Bei der makroskopischen Präparation wurden vier Thorax-Schilde (vordere Brustwand), zwei Alkohol- und zwei Thiel-fixierte, entnommen und die ITA und deren Abgänge präpariert. Da nach Thiel-Fixierung Gewebe realitätsnahe Eigenschaften behalten, blieben die weichen Gefäße durchgängig und eigneten sich besonders zur Injektion des Microfil®-Gemischs oder der Arterienmasse Thiel's (1992), wobei die Injektionsweite im Fokus stand. Ein weiterer Vorteil der Massen war die Röntgenopazität, wodurch radiologische Untersuchungen am Präparat erfolgten. Da die segmentierungsbasierte Rekonstruktion zunehmend Einzug in die Diagnostik hält, wurden zur Diskussion, ob Kollateralkreisläufe des Sternums dargestellt werden können, zwei Thorax-CTs erstellt und mittels Mimics® segmentiert.

Die im Rahmen dieser Studie angewandten Methoden konnten das makroanatomische Gefäßsystem des Sternums darstellen, wobei die Injektion der Arterienmasse am Thiel fixierten Humanpräparat mit anschließender Segmentierung besonders geeignet war.

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Poster 111

Testicular descent revisited by micro-computed tomography (µCT)

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Aims and objectives:
Several authors claim that a normal testicular descent is controlled by the gubernaculum. Embryology and pathogenesis of retractile testis remains unclear. To date, studies on testicular descent are based on serial histological sections and scanning electron microscopy(SEM). These techniques require meticulous dissection, large specimen numbers and cause artificial changes to the original anatomy. Aim of this study was to use the µCT technique to describe pre- and postnatal development of the gubernaculum and testicular descent.

Material and Methods:
Fetal male rats from embryonic-day 17(ED17) to ED22 and newborns N0(n=2 per group) were fixed and dried. SkyScan 1172 micro-CT system(Bruker, Belgium) reaching a spatial resolution of 5?m with approximately 1 x 10-7mm3 voxel size was used and scans were analyzed using CTAn® and DataViewer®-software.

Results:
Fetal imaging by µCT technique clearly showed that the testis and the gubernaculum develop intraabdominally and not retroperitoneally throughout prenatal development. Post partum the gubernaculum evaginated and showed an extraabdominal position in newborns(N0), thus forming the processus vaginalis peritonei. Mean testicular volume was 0,300mm³(SD 0,015) on ED17 and continuously increased to 0,715mm³(SD 0,029) on N0.

Conclusion:
Our data clearly showed an intraabdominal position of the descending testis throughout fetal rat development. For the first time, µCT-technique precisely displays the course of the gubernaculum in fetal and neonatal rats from an intraabdominal to an extraabdominal, everted position forming the processus vaginalis peritonei.

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Poster 113

Improved MultiPArametric monitoring of blunt Chest Trauma, IMPACT — a project presentation

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In this project we develop a mobile system for lung function diagnostics in emergency situations. Based on electrical impedance tomography (EIT), changes of electrical properties in the lung are measured using an easily applicable electrode belt. This allows for a three-dimensional imaging and functional analysis to assess ventilation status. Emergency physicians can use this system to determine the need for mechanical ventilation, monitor regional changes of lung function, and detect potentially life-threatening complications like pneumothoraces. As clinically established procedures such as X-ray imaging and computer tomography are not available outside of the hospital, and existing EIT systems are designed exclusively for stationary use, this project opens up new perspectives for the mobile emergency use. Urgent decisions regarding mechanical ventilation and possible need for invasive interventions such as thorax drainage can be made quickly and reliably with the emergency EIT system. Hardware development is conducted in close cooperation with Fritz Stephan GmbH and HTWK Leipzig. Development of an innovative textile electrode belt is performed by Gesellschaft für Intelligente Textile Produkte (ITP GmbH). The Life Support Systems Group (LSS) at ICCAS institute focuses on the signal processing in EIT, such as the development of novel methods for three-dimensional image reconstruction and algorithms for the detection of pneumothoraces and other disfunctions in the lung.

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Poster 114

Langfristige kognitive Beeinträchtigung nach intensivmedizinischer Therapie — eine prospektive Kohortenstudie (CogICU)

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Fragestellung:
Patienten weisen nach Abschluss der intensivmedinischen Therapie kognitive Defizite auf. In welchen neuropsychologischen Teilbereichen bestehen diese, und sind sie auch im Langzeitverlauf nachweisbar?

Methoden:
Bei Patienten, die für unterschiedliche Zeiträume auf einer internistischen oder chirurgischen Intensivstation behandelt wurden, erfolgte direkt nach Beendigung der Intensivtherapie und 9 Monate später eine neuropsychologische Testung. Es wurden zudem Daten zu u.a. soziodemographischen Angaben, kognitivem Vorniveau und dem stationären Aufenthalt erhoben. Parallel dazu wurde eine Kontrollgruppe aus der Allgemeinbevölkerung etabliert.

Ergebnisse:
Es wurden insgesamt 109 Patienten in die Studiengruppe (SG) und bislang 39 Patienten in die Kontrollgruppe (KG) eingeschlossen. Von den 109 Patienten konnten 83 (76%) nachuntersucht werden. Die Patienten erzielten im Durchschnitt in allen getesteten Domänen (Gedächtnis, Aufmerksamkeit, Exekutivfunktion) signifikant schlechtere Ergebnisse als die Kontrollgruppe: z.B. Trailmaking Test B (65,29 vs. 37,54 Sekunden, $p<0,001$). Nach 9 Monaten zeigte sich eine Besserung der kognitiven Leistung, in bestimmten Tests, so z.B. dem Trailmaking Test B schnitt die SG jedoch weiterhin signifikant schlechter ab als die KG.

Schlussfolgerungen:
Patienten weisen nach Abschluss der intensivmedizinischen Therapie Defizite in den Teilbereichen Gedächtnis, Aufmerksamkeit und Exekutivfunktion auf. Im Langzeitverlauf kommt es zu einer Besserung, bestimmte Einschränkungen scheinen jedoch fortzubestehen. (Gefördert durch das Kurt-Goldstein-Institut, Bewilligung vom 10.06.2015.)

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Poster 115

Requirements and Visualization Methods for Visual Verification of Bayesian Networks

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Therapy Decision Models in form of Bayesian networks can assist physicians in diagnostic and prognostic reasoning, treatment selection, and discovering functional interactions among components of a system. Due to the increase in medical data collection, Bayesian networks can be learnt from data using machine learning algorithms. However, the quality of the learnt model is highly dependent on the data quality. Therefore, a domain expert is indispensable for validation of the learnt structure, parameters of the model, and probabilistic relationships. In the validation, the domain expert investigates: 1) how the model operates and 2) what the model produces. In this course, different information need to be highlighted. Therefore, we firstly defined the requirements for graphical network presentation supporting a visual verification. Secondly, we compared multiple common network presentations with respect to these requirements. We conclude that the causality flow visualization method for presenting the whole network and for visualizing the causal flow of the underlying system is the preferred layout method. Furthermore, the visualization of nodes in form of glyphs is optimal and an additional linked colormap view or table view for presenting the probability tables are preferable.

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Poster 116

Klinische prospektive randomisierte Studie zur mikrobiellen Besiedlung von Prothesenbasiskunststoffen

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Ziel der vorliegenden Studie war es, den individuellen bakteriellen Biofilm zweier Prothesenbasiskunststoffe im Split-Mouth-Design zu untersuchen.

Material und Methoden:
Es wurden Prüfkörper aus Polyamid (n=10; Valplast, Johannes Weithas KG) und Polymethylmethacrylat (n=10; PMMA, PalaXPress, Heraeus-Kulzer GmbH) über eine modifizierte Molarenbandapparatur bei n=10 Probanden intraoral befestigt. Nach vier Wochen in situ wurde die Plaqueakkumulation anhand eines modifizierten Plaque-Score-Index bestimmt. Die Prüfkörper wurden auf nichtselektiven und selektiven Nährmedien kultiviert und für 2 und 7 Tage lang bei 37°C aerob und anaerob inkubiert. Unter Verwendung von VITEK-MS (BioMerieux, Lyon, Frankreich) erfolgte die Identifizierung. Die Ergebnisse wurden anonymisiert und mit SPSS (SPSS GmbH Software 15.0) deskriptiv analysiert.

Ergebnisse:
Ein Plaquebelag wurde auf beiden Materialien beobachtet. Die Mehrheit der Proben hatte eine “kleine” bis “moderate” Plaque. Der Mittelwert (M) war in den PMMA-Proben bei M=1±0,67 am niedrigsten und in den Polyamidproben bei M=1,8±0,63 am höchsten. 110 verschiedene Bakterienarten wurden isoliert, einschließlich vermutlicher Parodontitis und Endokarditis-assoziierter Pathogene. Im Durchschnitt wuchsen 17,8 verschiedene Bakterienspezies auf den PMMA-Proben und 17,3 auf den Polyamid-Proben. Die höchste Anzahl verschiedener Bakterienspezies war n=24, gefunden auf einer PMMA-Probe.

Schlussfolgerungen:
Diese Studie zeigt, dass die Zusammensetzung des bakteriellen Biofilms nicht durch die stoffliche Zusammensetzung des Kunststoffes selbst beeinflusst wurde.

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Poster 117

Axonal degeneration of the vagus nerve in Parkinson's disease – a high-resolution ultrasound study

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Background:
Recent histopathological studies revealed degeneration of the dorsal motor nucleus early in the course of Parkinson's disease (PD). Degeneration of the vagus nerve (VN) axons following neurodegeneration of brainstem vagal nuclei should be detectable by high-resolution ultrasound (HRUS) as a thinning of the VN.

Methods:
We measured both VNs cross-sectional area (VN-CSA) of 35 patients with PD and 35 age- and sex-matched healthy controls at the level of the thyroid gland using HRUS. VN-CSA was correlated with motor and non-motor symptoms and the cognitive status.

Results:
On both sides, the VN-CSA was significantly smaller in PD patients than in controls (right: 2.1±0.4 vs. 2.3±0.5 mm², left 1.5±0.4 vs. 1.8±0.4 mm²; both $p < 0.05$). There was no correlation between either the VN-CSA and the Hoehn & Yahr stage, disease duration, the motor part of the Unified Parkinson's Disease Rating Scale (UPDRS-III) score or the Montreal Cognitive Assessment (MoCA) score.

Conclusions:
These findings provide evidence that structural pathology of the VNs in PD patients can be detected in-vivo by HRUS.

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Poster 118

Biomarkers for Mortality Risk Prediction in Cardiogenic Shock Complicating Acute Myocardial Infarction The CULPRIT-SHOCK Biomarker Substudy

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Objectives:
The aim of this study was to assess several novel and established biomarkers for potential mortality prediction in patients with cardiogenic shock (CS) complicating acute myocardial infarction (AMI). Biomarkers in early assessment of prognosis might be a powerful aid for decision-making regarding treatment escalation (e.g. use of mechanical circulatory support devices) after initial revascularization.

Material and Methods:
In the CULPRIT-SHOCK-trial two revascularization strategies in 706 Patients with CS complicating AMI were compared. Blood samples were collected (in the catheterization laboratory [baseline] and at days 1 to 3). The suitability of many established and novel biomarkers for deeper assessment in the whole CULPRIT-SHOCK cohort in terms of mortality prediction was tested in a small group of patients from the trial (n=20: 10 30 day-survivors vs. 10 30 day-non-survivors).

Results:
Among others HDL (median: 1.24 [IQR: 0.48] vs 0.93 [0.53] mmol/l; Mann-Whitney-U-test: p≤0.01), Angiopoietin-2 (2.61 [0.70] vs 6.11 [7.50] ng/ml; p≤0.01) and PCT (0.07 [0.05] vs 0.37 [1.05] ng/ml; p≤0.01) were distinctive at baseline, as well as myoglobin (e.g. day 2: 138.30 [223.80] vs 1513.50 [3532.00] µg/l; p≤0.01) and Copeptin (e.g. day 1: 13.77 [14,27] vs 114.70 [91.78]; p≤0.001) differed in the two groups at days 1 to 3.

Conclusion:
The biomarkers showing significant group-discrimination in the pilot cohort will be analyzed thoroughly in the whole CULPRIT-SHOCK cohort in terms of mortality prediction through methods such as pu²-test, ROC-analysis and multiple stepwise logistic regression.

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Poster 119

Untersuchung zur Farbbeständigkeit von Polymer-infiltrierten- und Resin-Nano-Keramik-Kronen nach dynamischer Kausimulation

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Ziel dieser in-vitro Studie war es, die Farbbeständigkeit von Polymer-infiltrierten- und Resin-Nano-Keramik-Kronen Kronen vor und nach dynamischer Kausimulation (KS) mit Thermocycling (TC) zu untersuchen.

Material & Methoden:
Es wurden 80 Kronen mittels CAD/CAM-Verfahren hergestellt (n=40 Vita Enamic (E; Vita Zahnfabrik) / n=40 Lava Ultimate (LU; 3M Espe)). Mit je n=20 der Kronen wurde eine klinische Tragedauer von ca. 5 Jahren simuliert (1,2 Mio. Zyklen mit TC). Die 4 Subgruppen (1. VE/KS, 2. VE, 3. LU/KS, 4. LU) der Materialien wurden jeweils in 4 Gruppen (n=5) aufgeteilt. Es folgte die Ausgangsfarbmessung jeder Krone mit dem VITA EasyShade (Vita Zahnfabrik). Diese Gruppen wurden in die Getränke Kaffee, Cola, Rotwein und in destilliertes Wasser für 14 d unter Standardbedingungen gelegt. Danach erfolgte erneut eine Farbmessung. Die Berechnung der Farbdifferenz erfolgte mit $\Delta E=(\Delta L^2+\Delta a^2+\Delta b^2)^{1/2}$. Die statistische Analyse wurde mittels one-way ANOVA ($p\leq0,05$) durchgeführt.

Ergebnisse:
Die größten ΔE-Mittelwerte wurden bei VE/KS (2,1±1,1) und bei VE (2,1±0,9) durch Rotwein und bei LU/KS (3,6±0,8) und LU (2,0±0,8) durch Kaffee verursacht. Der Summenscore (SSC) der ΔE-Mittelwerte der Subgruppen der 4 Flüssigkeiten zeigte bei LU/KS (SSC=8,0) die stärksten Farbdifferenzen. Bei VE mit und ohne KS zeigten sich zwischen den Färbelösungen keine signifikanten Farbdifferenzen. Die Summe der SSC der Subgruppen ergaben für VE 20,0 und LU 24,0.

Schlussfolgerungen:
Die Farbbeständigkeit der untersuchten Materialien wird nur geringfügig durch eine dynamische KS mit TC beeinflusst. Kein Material weist klinisch relevante Farbdifferenzen auf.

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Poster 120

Sicherheit der intraperitonealen Aerosol-Chemotherapie (PIPAC) für Patienten und medizinisches Personal sowie deren Wirksamkeit in Kombination mit einer simultanen systemischen Chemotherapie

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Bei der druckinduzierten intraperitonealen Aerosol-Chemotherapie (PIPAC) wird das Chemotherapeutikum (Cisplatin/Doxorubicin) mittels Druckpumpe als Aerosol in das Abdomen appliziert (NCT03100708). Es handelt es sich um eine innovative Methode für ausgewählten Patienten mit Peritonealkarzinose, deren Ziel eine palliativ intendierte Behandlung zur Reduktion von Aszites und die Regression der Peritonealkarzinose ist.

Es wurde eine prospektive Datenanalyse der im Behandlungsraum 11/15-10/17 vorgenommenen PIPACs zur Erfassung der Patientensicherheit mittels Platinnachweis durch ICP-MS (Inductively coupled plasma mass spectrometry), der Erhebung der postoperativen Komplikationsrate nach Clavien-Dindo und der Aszitesmenge bestimmt.

Bei der PIPAC handelt es sich technisch um ein sicheres Verfahren, bei dem die Platinkontaminationen auf OP-Boden, Instrumenten und Kleidung des Personals im tolerablen Bereich von unter 0,001ng/cm² lagen. Es wurden bei 55 Patienten (25 w/30 m) mit einem medianen Alter von 59 Jahren 111 Behandlungen durchgeführt. Es zeigte sich eine geringe Komplikationsrate und eine 90-Tage Letalität bei 1 Patienten.

Die ersten Daten zeigen, dass die PIPAC für das behandelnde Personal ungefährlich ist, von den Patienten gut vertragen wird und zusammen mit einer systemischen Chemotherapie sicher durchführbar ist. Die symptomatische Behandlung des Aszites durch PIPAC ist möglich und eine lokale Regression der Peritonealkarzinose kann erzielt werden. Weitere Studien sind nötig, um den Stellenwert PIPAC im Rahmen palliativer Therapiekonzepte zu evaluieren.

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Poster 121

Optical Coherence Tomography as a Diagnostic Tool in Avian and Reptilian Ophthalmology

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Optical coherence tomography (OCT) is a well-established and clinically applied procedure to detect and monitor anterior or posterior pathologies of human eyes. It has already been adapted to small animal models. However, OCT examinations of avian eyes were rarely performed and OCT was not yet applied to reptiles. Hence, little is known about the *in vivo* diagnostic of healthy or pathologically altered eyes and retinal structures. Therefore, we tested the applicability of a high-resolution spectral domain optical coherence tomography (SD-OCT) for diagnosis of various avian species and several reptiles. Eyes of a common buzzard (Buteo buteo) were additionally used for histologic and immunohistochemical examinations. We investigated 54 individual wild and domestic birds/reptiles from 27 different bird species and 5 different reptile species. OCT examination was possible in all species and allowed a detailed assessment of species-specific variations of retinal layers and specific retinal structures such as fovea centralis, fovea temporalis and other specific areas. Some individuals had diverse pathological indications due to body or head trauma. In these cases, OCT offered an objective assessment of retinal changes, e.g. retinal and choroidal degeneration, retinal detachment or chorio-retinal schisis. Histologic and immunohistochemical analysis of retinal tissue confirmed the findings of the OCT examination. OCT is applicable in a wide variety of species and, therefore, is a useful diagnostic tool in the veterinary clinical practice as it improves the diagnostic capabilities.

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Poster 122

Genetically encoded photo-crosslinkers to map GPCR-arrestin interfaces

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Arrestins play a major role in the signal transduction of G protein coupled receptors (GPCRs) by binding the active phosphorylated GPCR and terminating the G protein-dependent signalling (endocytic pathway). Furthermore, arrestins can work as scaffold for protein kinases or initiate other signalling cascades (non-canonical arrestin signalling). Along with hundreds of GCPRs in the human genome, there are only two non-visual arrestins (arrestin-2 and -3). Intriguingly, there are no conserved motifs in the intracellular part of GPCRs. Whether arrestins dock in the same way to different receptors, and how the alternative signaling pathways are determined is a matter of debate. Arrestin-GPCR complexes are challenging targets for crystallography and so far only the arrestin-1-rhodopsin complex has been characterized at high resolution. Therefore, alternative approaches are needed to investigate the arrestin-GPCR interaction.
The novel expanded genetic code technology allows us to incorporate the photocrosslinker p-benzoyl-Phenylalanine (Bpa) in a site specific manner throughout entire domains of arrestin and analyze the interaction with different GPCRs of the classes A and B. We show that the GPCR-arrestin complex can be captured using the genetically incorporated crosslinker. So far we have focused on mapping GPCR interactions with the finger loop and the following b-strand VI of arrestin-2. We obtained similar yet distinct crosslinking footprints of different receptors on arrestin. Importantly, our method addresses intact GPCR-arrestin complexes in the native context of the living cell.

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Poster 123

Studies of the Interaction between Orexin B and the Orexin Receptor-2

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The Orexin system is composed of two class A G-protein coupled receptors (GPCRs), the Orexin Receptor-1 and 2 (OX1R and OX2R), and two mid-length (~20 amino acids) neuropeptide ligands produced in the hypothalamus, Orexin A and Orexin B. the two Orexins bind to the two receptors with different affinity. Activation of Orexin receptors classically induces cellular calcium transients through Gq-dependent and Gq independent pathways. The Orexin system plays a crucial role in many behavioral functions of mammals, such as circadian sleep, energy homeostasis and reward system. This has generated growing interest, recognizing it as a potential target for sleep and wake disorders.

Although several structure-activity relationship studies on the Orexin system are found in the literature, only a crystal structure for the OX2R bound to the small molecule suvorexant has been solved (Yin et al, 2015, Nature 519, 247) and the binding mode of natural Orexins to their receptors remains largely unknown. Goal of this study is to build an accurate molecular model for the associate complex of Orexin B and OX2R based on experimental crosslinking constraints.

We present here our progress toward the establishment of a reliable system to express the OX2R in mammalian cells and detect it from analysis of whole cell lysates in Western Blot, including characterization of differently tagged receptors and ligand analogs.

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Poster 124

Fishing tRNAs with a Nucleotide Rod

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CCA-adding enzymes are unique nucleotidyltransferases that add and maintain the 3'-CCA triplet of tRNAs, which is essential for aminoacylation. As a tRNA without or with wrong 3'-CCA end cannot participate in protein biosynthesis, CCA-adding enzymes are indispensable for those organisms that do not encode CCA ends in their tRNA genes. Until now it was known that most organisms contain one single gene for the CCA-adding enzyme, except for some bacteria where the CCA-adding activity is split in CC- and A-adding enzymes. Recently, a detailed genetic analysis confirmed that some Eukaryotes like Choanoflagellates and Amoebozoa possess more than one gene for CCA-adding enzymes (1). The functional basis for this redundancy is not clear yet, but it is an intriguing possibility that such enzymes with identical activities have different substrate specificities, so that each enzyme acts only on an individual subset of the cellular tRNA pool. To test this hypothesis, we developed an *in vitro* procedure to identify tRNA substrates processed by the individual recombinant CCA-adding enzyme types. Using T4 DNA ligase and a hairpin oligonucleotide with a 3'-TGG overhang, it is possible to selectively isolate and amplify tRNAs with added 3'-CCA end. The isolated tRNAs are ligated to a second adapter and analyzed by high throughput sequencing. This procedure allows a specific identification of substrate transcripts selected by the recombinant enzymes, and the comparative analysis will show whether this surprising enzymatic redundancy is the result of specific substrate ranges of the individual CCA-adding enzymes.

[1] Betat H. et al, NAR (2015)

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Poster: 125

Structural Rearrangement of the Calcium-Sensing Receptor

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The calcium-sensing receptor is a G protein coupled receptor (GPCR) playing a major role in the maintenance of serum calcium homeostasis by regulating the circulating level of parathyroid hormone [1]. Recent studies have shown that also other extracellular stimuli, including amino acids, antibiotics, polyamines and glutathione analogues, can activate the calcium-sensing receptor [2]. It is not fully understood, how these ligands bias the signaling of the receptor towards specific intracellular responses. We analyzed crystal structures of the homodimeric calcium-sensing receptor extracellular domain. Each protomer is bipartite, consisting of a venus flytrap domain and a cysteine-rich region, an architecture known from other class C GPCRs. Orthosteric and allosteric ligands induce the domain closure of the ectodomain by a rotation of 29 ° to initiate the activation of the receptor. Furthermore, we determined specific binding affinities for several ligands and found that these ligands exhibit cooperative binding behavior. Our crystallographic and binding studies reveal insights into the complex signaling processes of the calcium-sensing receptor.

[1] Brown EM, Pollak M, Riccardi D, Hebert SC, 1994, Nephrol Dial Transplant 9: 1703–1706
[2] Saidak Z, Brazier M, Kamel S, Mentaverri R, 2009, Molecular Pharmacology 6: 1131–1144

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Poster 126

On the impact of relatedness on SNP association analysis

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Background:
When testing for SNP (single nucleotide polymorphism) associations in related individuals, observations are not independent and simple linear regression analysis results in an increased type I error and the power of the test is also affected in a more complicate manner. In the present work, we investigate how heritability and strength of relatedness contribute to variance inflation of the effect estimate of the linear model. Further, we study the consequences of variance inflation on hypothesis testing.

Results:
We derive explicit approximation formulae to estimate the impact of relatedness on the variance of the effect estimate of the linear regression model. Variance inflation increases with increasing heritability. Relatedness structure also impacts the degree of variance inflation as shown for example family structures. Type I error increases rapidly with increasing inflation. However, for smaller significance levels power increases with increasing inflation while the opposite holds for larger significance levels.

Conclusions:
Stronger relatedness as well as higher heritability result in increased variance of the effect estimate of simple linear regression. While type I error rates are generally inflated, the behaviour of power is more complex since power can be increased or reduced in dependence on relatedness and heritability of the phenotype. We provide a simple formula for estimating variance inflation given the relatedness structure and the heritability of a trait of interest. Variance inflation below 1.05 does not require correction and simple linear regression analysis is still appropriate.

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Poster 127

Identification of Glycoseaminoglycan binding Proteins by AP-MS

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Glycosaminoglycans (GAGs) are essential components of the extracellular matrix (ECM). They modulate multiple cellular functions including cell migration and adhesion as well as proliferation and differentiation. Due to this versatile and central function, GAGs, e.g. per-sulfated hyaluronic acid (psHA), are promising candidates for administration as a component of artificial ECMs to improve wound healing. Most of the GAG mediated effects are transmitted by protein interaction, e.g. binding to specific cellular receptors or binding to and sequestration of cytokines. Next to these extracellular functions, the internalization of GAGs has been described; however knowledge on intracellular effects and interactions is scarce.

Hence, we aim to identify novel and particularly intracellular GAG-binding proteins by affinity-purification mass spectrometry-based (AP-MS). Interacting proteins are enriched utilizing GAGs immobilized to paramagnetic particles from total cell lysates, including ECM localized and intracellular proteins. Interactors are then identified by means of quantitative mass spectrometry.

Using this approach we identified more than twenty intracellular psHA-interacting proteins. Nucleic acid-binding and cytoskeleton-modulating proteins were significantly enriched among these interactors. Particularly for the interaction with nucleic acid binding proteins, the high negative charge of psHA might be of importance. In ongoing experiments GAGs with different biophysical properties are included. Finally the importance of identified GAG-protein interactions in wound healing processes has to be characterized.

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Poster 128

Unusual substrates, unusual enzymes — coevolution of tRNAs and CCA-adding enzymes

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Canonical transfer RNAs (tRNAs) usually possess a cloverleaf-like secondary structure consisting of the acceptor-stem, D- and T-arm, a variable loop and the anticodon-stem. Additionally, every mature tRNA carries the nucleotide sequence 5'-CCA-3' at the 3'-end of the acceptor-stem, which is essential for the attachment of the corresponding amino acid and thus for the translation process. In most organisms, this CCA-triplet is not encoded in the tRNA genes and must be added post-transcriptionally by CCA-adding enzymes.

These enzymes predominantly recognize tRNAs by their secondary and tertiary structure. Interestingly, some mitochondrial tRNAs (mt-tRNAs) were discovered that differ from the canonical cloverleaf structure by lacking the D- or the T-arm or even both (armless tRNAs). Although forming a very different secondary structure, these mt-tRNAs are still a substrate for CCA-addition *in vivo*.

In this study, we investigate how the CCA-adding enzyme could be adapted to these minimalized substrates by analyzing two examples of armless mt-tRNAs and the corresponding enzyme from the nematode Romanomermis culicivorax. While CCA-adding enzymes from Escherichia coli or Homo sapiens do not recognize these armless tRNAs as a proper substrate, we show that the enzyme from Romanomermis culicivorax is able to process the complete CCA-triplet. With our results we hope to get a closer insight into the coevolution of tRNAs and their processing enzymes and thus aim to find out which features are essential for recognition and processing of one of the central molecules in all living cells.

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Poster 129

Characterization of Cleavage and polyadenylation factor I subunit 1 in mouse brain

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Synapse loss is a major contributor to the onset and progression of Alzheimer's disease and may also contribute to cognitive decline during normal aging. Similarly, alterations in the biological structure of synapses and ineffective neurotransmission are associated with cognitive disorders. However, these alterations may also be observed during the aging process. The neuronal plasticity is age-dependent and linked to RNA metabolism. The impairment of the tRNA splicing machinery contributes to the pathology of neurodegeneration. An essential part of the tRNA splicing machinery is the cleavage and polyadenylation factor I subunit 1 (Clp1). This RNA kinase co-controls the re-ligation of tRNA halves during their maturation process by catalyzing phosphorylation of the 5'ends. Deficits of the kinase are associated with the death of neuronal progenitors indicating a substantial role of Clp1 in mouse brain development. Though the involvement of Clp1 in neurodegeneration is currently discussed, no data on Clp1 during aging, the most relevant factor for neurodegeneration of the AD type, are available. Addressing this question, we observed an age-dependent alteration of the Clp1 expression in mouse brains. While total Clp1 protein levels in aged cortex and hippocampus clearly decreased, a significant increase of the kinase in synaptosomes of aged mice was detected. Furthermore, two new additional splice variants of the mouse's Clp1 mRNA were identified. As defects caused by splicing deficits are associated with Alzheimer's diseases and other diseases (e.g. cancer), the role of each splice variant is currently under investigation.

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Poster 130

Impact of amyloid-beta on aggregation of alpha-synuclein

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The deposition of the amyloidogenic proteins alpha-synuclein and amyloid-beta are the hallmarks of the two most common neurodegenerative diseases, Parkinson's and Alzheimer's, respectively. Recent studies revealed that both proteins share common mechanisms of aggregation, leading to the hypothesis of their mutual interaction.

Here, we studied the influence of Aβ1-42 and pGlu-Aβ3-42 on the aggregation of alpha-synuclein *in vitro*. Human alpha-synuclein was recombinantly expressed in *Escherichia coli* and purified using a combination of different chromatographic techniques: affinity, hydrophobic interaction and ion exchange chromatography. Aβ1-42 and pGlu-Aβ3-42 were synthesized by solid phase synthesis. The aggregation of alpha-synuclein was monitored by Thioflavin-T fluorescence, visualization of fibrils was established by transmission electron microscopy (TEM) and atomic force microscopy (AFM).

We observed a significantly increased aggregation velocity of alpha-synuclein in presence of Aβ1-42 and pGlu-Aβ3-42. Co-incubation of these proteins enhances the fibril formation in comparison to alpha-synuclein self-assembly, whereas the fibril structure was not altered upon seeding by amyloid-beta peptides.

Our results indicate an interaction between alpha-synuclein and amyloid-beta *in vitro*, leading to an accelerated fibril formation. We suggest this could be caused by an enhanced nucleus formation.

The results of this study may provide the basis to develop new specific antibodies to label heterogeneous deposits of amyloid peptides, leading the way to novel diagnostic and therapeutic approaches.

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Poster 131

Weighted Gene Correlation Network Analysis as Grouping Strategy for Nanomaterial Risk Assessment

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The public is increasingly exposed to various engineered nanomaterials (NMs) due to their wide application in e.g. medicine, cosmetics, building materials or packaging, and the continuous development of novel NMs. Since the respiratory tract is considered as the primary target organ for airborne NMs, the toxicological effect of NMs on alveolar epithelial cells (RLE-6TN) was investigated using shotgun proteomics with the aim to develop grouping strategies to facilitate NM risk assessment.

Obtained protein abundance ratios were analyzed using weighted gene correlation network analysis (WGCNA), where protein abundances are correlated to construct a gene co-expression network followed by hierarchical clustering to identify modules of proteins that are related to NM treatments. For this analysis, physicochemical properties of the NMs, e.g. size or coating, were integrated to get more powerful and reliable prediction models.

The results show just a few modules comprising proteins that show significant correlation with the treatments themselves. Most importantly however, several modules containing proteins correlated significantly with one or more of the physicochemical properties. For example one module containing proteins related to oxidative stress shows correlation with the size and coating of the NMs suggesting that these properties induce an oxidative stress response in alveolar epithelial cells.

In conclusion, these results indicate that WGCNA is a valuable tool to develop NM grouping strategies based on toxicological effects on protein level.

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Poster 132

Functional characterization of long non-coding RNAs in Alzheimer's disease

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Evidence is emerging that long noncoding RNAs (lncRNAs) modulate crucial molecular events underlying the aging process and expression of particular lncRNAs correlates closely with neurodegenerative diseases. Therefore, the aim was to establish the specific pathogenetic role of lncRNAs in Alzheimer´s disease (AD). Previously, the genome-wide pattern of lncRNA expression differences between AD and control brain was established applying a combination of tiling array and custom array platform. Enrichment analyses and adjustment with datasets on cell-cycle dependent expression of lncRNAs revealed 20 lncRNAs related to chromatin-association and cell cycle regulation. One meaningful cell-cycle relevant candidate upregulated in AD was selected to identify its binding partners relevant to AD. To this end, an approach based on Chromatin Isolation by RNA Purification (ChIRP) (Chu et al., 2011) was applied. A modified ChIRP method adapted for using human brain tissue was established and the specific RNA retrieval in human control brain, as well as in AD patient samples, was confirmed. Using Illumina sequencing, a series of loci and genes interacting with the chosen lncRNA in the AD brain were identified and over 60 % of the examined target loci were confirmed applying PCR. On chromosome 8 a set of sequences representing different isoforms of a RNA targeting protein was selected to investigate the complex interaction of lncRNA, DNA and protein applying EMSA binding studies.

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Poster 133

Analysis of tRNA modification patterns via high throughput sequencing

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Transfer-RNAs (tRNAs) are central players in protein biosynthesis and found across all domains of life. They show a highly conserved structure and the highest density of post-transcriptional modifications among all RNAs. These base and ribose alterations affect tRNA identity, decoding properties, translational fidelity and maintain the tRNA's structure by large structural rearrangements or local fine-tuning effects. Moreover, modification patterns depend on various cell historic and environmental factors.

Here, we will focus on modified bases in tRNAs of microorganisms as an adaptation to the environmental temperature. It is known that pseudouridinylation often leads to a higher rigidity of the molecule and stabilizes helical structures, resulting in an increased melting temperature. Dihydrouridine, on the other hand, can cause higher flexibility in tRNAs due to its non-aromatic chemistry, making this modification important for cold adaptation in organisms thriving at low temperatures.

To investigate such tRNA modifications linked to temperature adaptation, we isolate and analyze tRNAs from several psychrophilic, mesophilic and thermophilic Bacillales. These organisms are cultivated at temperatures ranging from 10 to 70°C (depending on the species). Specific chemical treatments combined with high throughput sequencing allow conclusions concerning the identity and position of post-transcriptional modifications in the individual tRNA preparations. Growing evidence demonstrates the importance of RNA modifications as an additional regulatory level in many cellular processes.

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Poster 134

The effect of N-terminal truncations and pyroglutamate formation on aggregation of alpha-synuclein

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Abnormally folded and deposited alpha-synuclein represents a hallmark of Parkinson's disease. N-terminal truncation as well as post-translational modifications has been shown to enhance the aggregation propensity of many amyloid peptides. Here, we studied the effect of truncation and pyroglutamate formation at the N-terminus of alpha-synuclein on the kinetics of fibril formation and the morphology of fibrils.

N-terminally truncated alpha-synuclein was expressed in Escherichia coli. Pyroglutamate was introduced by glutaminyl cyclase after purification. The kinetics of the aggregation was monitored using Thioflavin-T fluorescence. To visualize the amyloid fibrils, transmission electron microscopy was performed.

Our findings suggest that truncation up to a certain length enhances the aggregation but does not alter fibril morphology. Truncation, partially including the hydrophobic non-amyloid component (NAC-region), showed no aggregation.

Our results suggest that the elevated hydrophobicity due to truncation as well as pyroglutamate formation enhance the aggregation. Loss of the NAC-region results in a smaller hydrophobic interaction surface, which leads to fewer oligomer and fibril formation. Since we showed that pyroglutamate accelerates the fibril formation, it is our future goal to produce antibodies against this target for diagnosis and treatment of Parkinson's disease.

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Poster 135

Analysis of the relevance of the oncogene SATB1 in HNSCC

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SATB1 has been established as a candidate oncogene, by acting as a genome organizer and transcription factor in several types of cancer. Based on the multiple putative roles of SATB1 in dysplasia, we expected to target several pathways by SATB1 inhibition, eventually leading to tumor inhibitory effects in Head and Neck Squamous Cell Carcinoma (HNSCC). An approach of RNAi-mediated knockdown using siRNA was employed in 18 primary HNSCC and 3 established HNSCC cell lines. From these, 7 primary HNSCC and one cell line were selected for deeper analysis, initially considering the anti-proliferative effects upon SATB1 knockdown. Tumor cell inhibition was observed, dependent on the cell line and the type of assay (cells in monolayer on plastic, colony forming ability on plastic and spheroid forming ability). No strict correlation was found between initial levels of SATB1 expression and anti-proliferative effects upon knockdown. Furthermore, activation of Caspase 3/7 as a marker for apoptosis and decrease in cell cycle rates were observed, again dependent on the cell line. Systemic treatment of s.c. tumor xenograft-bearing mice with polymeric nanoparticles containing SATB1-specific siRNAs led to tumor growth inhibition. Transcription of several oncogenes was quantified, with no drastic difference upon SATB1 knockdown except for a slight reduction in HER3 mRNA levels. While our data indicate the possible relevance of SATB1 in HNSCC, therapeutic effects of SATB1 inhibition may depend on the cellular context or the individual tumor, thus requiring further studies.

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Poster 136

The HD domain of Escherichia coli tRNA-nucleotidyltransferase accepts non-canonical tRNAs

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tRNAs play an important role as adapter molecules by converting the genetic information into an amino acid sequence. All mature tRNAs carry the conserved triplet C-C-A at their 3' ends which is an important prerequisite for being charged with the cognate amino acid. In E. coli, this sequence is genetically encoded. A posttranscriptional addition by the tRNA-nucleotidyltransferase (CCA-adding enzyme) is not required. Therefore, it was suggested that the CCA-adding enzyme of E. coli (EcCCA) primarily fulfills its function in tRNA repair. Unlike eukaryotic CCA-adding enzymes, the CCA-adding enzymes of E. coli and other bacteria carries besides the N-terminal nucleotidyltransferase domain (NT domain) an additional HD domain in their C-terminus. In general, HD domain containing proteins are metallo-dependent phosphohydrolases and EcCCA was shown to be able to open and cleave 2'3'-cyclophosphates at the 3'-end of the tRNA – a feature that might be linked to its function in tRNA repair. For further characterisation of the HD domain in CCA-adding enzymes, the C-terminus of EcCCA was independently expressed, purified and found to be active. Surprisingly, NT and HD domain of EcCCA have different requirements for their substrates: Whereas the HD domain accepted small, armless as well as canonical tRNAs for dephosphorylation, the NT domain only uses canonical tRNA structures as substrate for CCA-addition. Further studies in vitro and *in vivo* will help to elucidate the role of this HD domain in the tRNA metabolism.

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Poster 137

Characterization of NirN in heme d1 biosynthesis

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Pseudomonas aeruginosa is a ubiquitous and important denitrifying bacterium and plays an important role in the nitrogen cycle. It can use nitrate as an electron acceptor for generating energy under anaerobic conditions, converting nitrate via nitrite, nitric oxide and nitrous oxide to molecular nitrogen. One key enzyme in this process is the homodimeric cytochrome cd_1 nitrite reductase NirS, which contains two different cofactors. A covalently bound heme c and the unique noncovalently bound heme d_1 in each subunit. Heme d_1 is the active center and catalyzes the one electron reduction from nitrite to nitric oxide (Zumft 1997). NirS and other proteins for heme d_1 biosynthesis and NirS function are encoded in the nir operon (nirSMCFDLGHJEN) (Kawasaki et al. 1997). It could be shown that NirN, despite all assumptions, is performing the last step in the biosynthesis of heme d_1, reducing a propionate side chain in the precursor dihydro-heme d_1 to an acrylate side chain via an electron bifurcating mechanism yielding heme d_1 (Adamczack et al. 2014). Recently the crystal structure of NirN could be solved (unpublished data) and further characterization of NirN could be made, including functional studies on catalytic amino acids within the protein. It could also be shown that NirS, NirN and NirF are interacting with each other *in vivo* (Nicke et al. 2013). Therefore, another important aspect of the study is the interaction with NirS and the transfer of heme d_1 from NirN. Also the role of NirF, which was thought to catalyze the last step in heme d_1 biosynthesis, and the purpose of the interaction with NirN remains elusive.

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Poster 138

Characterization of the heme d1 biosynthesis enzymes NirDLGH

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During denitrifcation nitrate is reduced to nitrogen via the intermediates nitrite, nitric oxide and nitrous oxide (Zumft 1997). In some denitrifying bacteria, the second step of denitrification is catalysed by the cytochrome cd1 nitrite reductase NirS. This homodimeric enzyme carries two tetrapyrrole cofactors, the covalently bound heme c and the noncovalently bound heme d1. The enzymes which are required for the biosynthesis of heme d1 are encoded in the nir operon (nirSMCFDLGHJEN) (Kawasaki et al. 1997).

During heme d1biosynthesis the intermediate siroheme (SH) is converted to 12,18-didecarboxy-siroheme (DDSH) by the enzyme siroheme decarboxylase. In denitrifying Pseudomonas species such as P. aeruginosa the siroheme decarboxylase is encoded by nirD, nirL, nirG and nirH forming the two heterodimeric complexes NirDL (1st decarboxylation) and NirGH (2nd decarboxylation). In other denitrifying bacteria such as Dinoroseobacter shibae the genes nirD and nirL are fused resulting in the fusion protein NirDL. Additionally they possess the heterodimeric complex NirGH, which is required for a complete conversion of SH to DDSH. Interestingly, there are other denitrifying bacteria such as Hydrogenobacter thermophilus, which contain only the fusionprotein NirDL. Here, the fusion protein catalyses both decarboxylation steps (Haufschildt et al. 2014). In order to understand the differences between the diverse forms of SH decarboxylases the crystal structure of NirDL from D. shibae should be solved. In addition, different enzyme variants are chracterized to get a better insight into substrate binding and enzyme catalysis.

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Poster 139

Proteomic analysis of the effects of sulfated hyaluronic acid and dexamethasone on the differentiation of human bone marrow stromal cells.

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The development of novel bone implants is of highest interest to face the socio-economical demands of an aging population in most western countries. Although being in the focus of research, autografts, allografts and xenografts are still the method of choice in the clinical application. Artificial bone implants that mimic the mechanical properties and composition of the natural tissue and actively support the osteoinductive and osteoconductive properties without triggering a persistent immune response are the ultimate goal of bone graft development.

The use of glycosaminoglycans (GAGs) as implant coatings is a novel approach in graft design. The potential of GAGs to modulate regenerative processes in skin and bones and their immune modulatory capabilities are widely accepted. In comparison Dexamethasone (Dex) is an established model to induce osteoblasts, the bone forming cells, in vitro and was successfully used in initial *in vivo* trails. In this study we provide the first proteomic characterization of the Dex effects on the human bone marrow stromal cell differentiation to osteoblasts and compared those to the effects driven by sulfated hyaluronan as an alternative osteogenic agent.

Although both agents induces the osteoblastic differentiation likewise we found distinct molecular effects for both used treatments on selected ECM proteins, coexpressed protein groups and affected metabolic and signaling pathways. While SH induces the ECM assembly and stabilizes its structures, Dex induces cellular processes involved in the cell adhesion. A further use of SH and/or Dex need to be tested in future studies.

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Poster 140

Designer tRNA variants for efficient incorporation of pyrrolysine derivatives into proteins in mammalian cells

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The expansion of the genetic code enables installing non-canonical amino acids (ncAAs) site-specifically into proteins by the host cells own biosynthetic machinery and thereby allows to investigate biological questions about protein structure and function directly in live cells. The pyrrolysyl-tRNA synthetase/$tRNA^{Pyl}$ pair is the most versatile and widespread system for the incorporation of non-canonical amino acids (ncAAs) into proteins in mammalian cells. However, low yields of ncAA incorporation severely limit its applicability to relevant biological targets. The $tRNA^{Pyl}$ shows a unique secondary structure. It folds to a near-canonical three-dimensional structure but features a tight core. We reasoned that such peculiar tRNA may be poorly compatible with the eukaryotic translational context and aimed at developing more efficient tRNAs. Here, we present two rationally designed $tRNA^{Pyl}$ variants that significantly boost the performance of the pyrrolysine system. These engineered tRNAs are structurally more stable, feature higher intracellular concentrations and bear partially distinct post-transcriptional modifications. We show that the new tRNAs enable efficient ncAA incorporation into a G-protein coupled receptor (GPCR) and simultaneous incorporation of two ncAAs at two different sites within the GPCR. Moreover, by incorporating last-generation ncAAs for bioorthogonal chemistry, we achieve GPCR labeling with small organic fluorophores on the live cell and visualize stimulus-induced GPCR internalization.

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Poster 141

Functional screening for novel self-cleaving ribozymes

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Ribonucleic acids (RNAs) can fold into complex secondary and tertiary structures, which allow them to perform a number of biological functions. Those RNAs able to catalyze chemical reactions are called ribozymes. A subset of all known ribozyme classes, so-called self-cleaving ribozymes, share that they cut their own phosphate backbone at a specific position to enable their biological function. However, despite thousands of self-cleaving ribozyme examples, only a few selected representatives in a few organisms have so far been linked to a biological role.

Here, we introduce a method with which we want to screen for novel self-cleaving ribozyme classes and which will enable us to study the *in vivo* activity of known self-cleaving ribozymes on a genomic scale. We hope that the discovery of additional self-cleaving ribozyme classes as well as further insight on self-cleaving ribozyme activity will allow us to decipher more biological functions of self-cleaving ribozymes in the future. At the same time, our research will help to expand the understanding of RNA versatility and open up entirely new research areas.

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Poster 142

Identification of a second vaspin (SERPINA12) protease target

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Vaspin is a member of the serine protease inhibitor family (SERPINA12). It was hown that vaspin does not inhibit common serine proteases. Kallikrein 7 (KLK7) was identified as the first target protease which has chymotrypsin-like specificity.
Here we report that KLK14 of the kallikrein family is a second target protease of vaspin and interesting similarities and differences between the two target proteases KLK7 and KLK14 were observed. Both proteases cleave the same unfavorable scissile bond in the RCL sequence (P1-P1' M^{378}-E^{379}) of vaspin but are unable to cleave the RCL-derived peptide (AA 365-388) indicating that exosite interactions are required for serpin activity.

Vaspin variants were analyzed in order to investigate relevant exosite residues for KLK14 inhibition. The exosite R^{302} in vaspin is crucial for KLK7 recognition. In contrast, R^{302} seemed to disrupt KLK14 recognition since the loss of this residue had a positive effect on complex formation. In addition, a further vaspin variant (D305A) showed significantly accelerated complex formation with KLK7 suggesting a repulsive effect on KLK7. In contrast, loss of residue D^{305} had no effect on vaspin-KLK14 complex formation. For KLK14, alanine mutations of R^{302} or D^{305} positively affected the stability of the serpin-protease complex.

Although previous data showed that heparin accelerates the vaspin-KLK7 reaction, heparin prevented vaspin-KLK14 complex formation.

Our results demonstrate that vaspin has target-dependent inhibitory activity and imply that different exosites seem to be important for the differential targeting of the two proteases identified.

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Poster 143

Broadening the DREAM: Identification of new DREAM-associated proteins using APEX2 biotinylation

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The DREAM complex is a major transcriptional regulator of genes differentially expressed during the cell cycle. The products of these genes are required for cell cycle progression and cell division. Nonetheless, repression of cell cycle genes in non-proliferating cells is essential to avoid uncontrolled cell division and cancerogenesis.

DREAM binds and represses cell cycle genes in G_0 and G_1. It comprises of five MuvB proteins as well as of E2F4/5, DP1/2 and the pocket proteins p130/p107. None of these proteins exhibit enzymatic activity and the mechanisms by which DREAM represses cell cycle genes are unknown. It is most likely that DREAM recruits additional proteins that may change chromatin structure or interact with the basal transcription machinery to prevent gene expression. However, despite extensive research, such interaction partners could not be identified by in vitro assays like immunoprecipitations or affinity purifications.

To overcome these limitations, we apply a novel *in vivo* proximity-based protein biotinylation assay using the engineered peroxidase APEX2. APEX2 provides biotin-phenol radicals in living cells that bind to proteins in close proximity. Thus, proteins are labeled in the physiological context of the cell. Biotin-carrying proteins are then isolated and identified by mass spectrometry.

We have constructed fusion proteins of DREAM components with APEX2. We show that these hybrid proteins integrate into DREAM, are functional, and biotinylate cellular proteins. Identification of these proteins will help us to understand how DREAM connects with the transcriptional machinery to repress cell cycle genes.

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Poster 144

Experimental cerebral ischaemia causes diminished perineuronal nets and damaged GABAergic neurons in the nucleus reticularis thalami of wildtype- and 3xTg-mice

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Clinically relevant experimental stroke models should consider the complex neurovascular unit, addressing neurons, vessels, glial cells and extracellular matrix (ECM). Perineuronal nets (PNs) of the ECM as highly anionic, chondroitin sulphate-rich coatings of certain neurons influence neuronal integrity and plasticity – which has not yet been considered for stroke therapy. This study focused on ischaemia-induced alterations of PNs and GABAergic neurons of the nucleus reticularis thalami (NRT).
One day after applying a filament model of focal cerebral ischaemia, clinically relevant lesions were caused in 3- and 12-month-old wildtype mice and co-morbid triple-transgenic (3xTg) mice with Alzheimer-like alterations. Forebrain sections including the NRT were applied to double labelling of biotinylated Wisteria floribunda agglutinin (WFA) as established marker for PNs and parvalbumin in fast-firing GABAergic neurons. Semiquantitative analyses revealed a drastic decline of WFA-staining in the ischaemia-affected NRT, but parvalbumin-immunoreactivity was diminished to a much lesser degree.

Ischaemia-induced loss of PNs in the NRT was also shown by immunostaining of aggrecan and neurocan. Multiple fluorescence labelling of ischaemia-affected NRT visualized damaged GABAergic neurons with persistent immunoreactivities for their marker enzyme GAD, parvalbumin, calbindin and the potassium channel subunit Kv3.1b.

In conclusion, PNs were shown as highly vulnerable constituents of the ECM under ischaemic conditions. Therefore, components of the ECM are promising targets of future neuroprotective strategies in acute ischaemic stroke.

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Poster 145

Social experience determines inter-individual behavioural differences in an insect model system

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Recent studies reveal that many invertebrates exhibit inter-individual behavioural differences. However, the cause of such behavioural syndromes, or animal personality is unclear. As in many animals, winning or losing an aggressive encounter leads to subsequently enhanced, respectively depressed aggressiveness. Winners and losers also differ in their general motility and exploratory behaviour. Winners tend to turn towards a mechanical stimulus directed at one antenna, whereas losers turn away. Interestingly, these differences are also evident before fighting in crickets, which were socially isolated for 48 h (short term isolated, STI). This is surprising since all known behavioural effects of social experience in crickets last only about 3 h. We therefore tested long term isolated crickets (LTI, > 14 d), separated from the breeding colony as larvae. This revealed that adult LTI crickets all tend to turn away from the stimulus before fighting, but again that winners of a single fight turn towards the stimulus, losers still turn away. This difference was no longer evident after 24 h. We then tested the effects of multiple (6 x) wins and defeats. Again, multiple winners turned towards the stimulus, whereas losers turned away. Now the effect lasted longer than 24 h. Together our data suggest that early social experience in crickets produces long term changes in behaviour, and is thus a major determinant of inter-individual behavioural differences. Since both aggression and neurones controlling turning responses are influenced by biogenic amines, we are currently investigating the role of amines in behavioural syndromes.

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Poster 146

Cortical encoding of auditory space in a multimodal reference frame

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Since the location of a sound is not represented on the level of the primary sensor, the cochlea, this information must be inferred based on the analysis of auditory localization cues. For the vertical plane, these cues are generated by the direction dependent filtering of sound through the outer ears or pinnae. In order to evaluate these cues the brain must be able to deconvolve the sounds spectrum and the contribution of the pinnae filters. While electrophysiological research has provided insight into the physical encoding of auditory localization cues in the auditory brainstem on a cellular level, very little is known about the encoding space in the primary auditory cortex and higher cortical areas.

Furthermore, auditory localization cues represent objects in a head-centered reference frame, since they are dependent on the relative position of the listener to the sound. However, in our daily life we have to localize auditory objects while constantly changing head and body position. This indicates that the brain is able to compensate for changes in head and body position by integrating information from other modalities like the somatosensory or proprioceptive system.

In a preliminary experiment, we measured the neuronal correlates of auditory localization using magnetoencephalography. Since MEG prohibits the use of actual loudspeakers we used headphone stimuli that were recorded through the subjects' ears and thus contain the filter function of the pinnae.

We changed the position of the subject in the scanner to investigate the influence of body position on the activity in the auditory cortex.

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Poster 147

Histochemical alterations of NF-L, NF-M, NF-H and INA after stroke in various animal models

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New approaches for neuroprotective strategies in stroke are currently focused on an improved understanding of mechanisms causing the ischaemia-induced tissue damage. In this context, the role of the cell-stabilising neuronal cytoskeleton, composed of light, medium and heavy neurofilament chains (NF-L, NF-M, NF-H) and α-internexin (INA), is of special interest. Therefore, the present study was aimed to characterise histochemical alterations of NF-L, NF-M, NF-H and INA in various animal models of stroke.
Middle cerebral artery occlusion was induced in mice and rats with 24 hours of ischaemia, and in sheep with a 2-week observation period. Fluorescence labelling and quantification of NF-L, NF-M, NF-H and INA was applied to ischaemic brain areas and control regions considering the neocortex and striatum.

As consistent observation throughout the analysed 3 stroke models, immunoreactivities for all addressed neurofilaments appeared substantially altered. Thereby, a strong up-regulation of NF-L immunofluorescence intensity was detected in ischaemic areas. In contrast, immunoreactivities for INA and NF-M were found to be diminished due to ischaemia, which was confirmed by quantitative analyses. Furthermore, immunolabelling for NF-L revealed an ischemia-related structural loss of fibres and cellular processes like disintegrated axons and cell bodies with inhomogeneous redistributions at the protein level.

Supported by the consistent finding of inversely altered immunoreactivities for neurofilaments and INA throughout the applied stroke models, cytoskeletal elements appear as promising targets for future neuroprotective strategies.

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Poster 148

If and Where: EEG methods for the study of predictive coding and sound localisation in rodents

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The ability to localise sounds sources, and make and verify predictions about one's auditory environment, is essential to adapt and survive.

A great deal of auditory neuroscience studies have been performed in humans, revealing for example the acoustic cues that mediate sound localization, and effects triggered by auditory stimulus predictability such as sensory attenuation and reduced stimulus perception.

However, due to the methodological limitations of the human model, the cortical correlates of cue representation and predictive coding are still unresolved.

The rodent model allows us to study underlying neural mechanisms inaccessible in humans by using invasive techniques (such as optical imaging and multiunit recordings).

By employing similar behavioral tasks and performing EEG we intend to enable comparability between human and rodent data, which will then allow us to employ higher resolution imaging methods.

In a preliminary effort, by implementing adaptation paradigms and stimulus omissions in isochronous sequences, we identified human like ERP components and omission responses in rodent EEG.

Our results also provided further evidence for the population rate code model of horizontal localisation, with hemispherically segregated neural populations encoding for sounds presented in the contralateral hemifield, and for the existence of a different mechanism for localisation processing on the vertical plane.

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Poster 149

The GPR17 is involved in neuronal fiber outgrowth

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The G-Protein coupled receptor 17 (GPR17) has recently been proposed as an interesting pharmacological target, e.g. in neurodegenerative processes.

We used the well-established rat ex vivo model of organotypic slice co-cultures of the mesocortical dopaminergic system, culturing slices of prefrontal cortex (PFC) and the substantia nigra/ventral tegmental area (SN/VTA) complex to investigate the influence of GPR17 ligands on neurite outgrowth (NOG) from SN/VTA to the PFC.

We characterized the growth promoting effects of the GPR17 antagonist Montelukast (MTL), the glial cell line-derived neurotrophic factor (GDNF) and two new GPR17 agonists ("PZB", "PSB").

The treatment with MTL (10 μM) resulted in a significant increase in mean neurite density, comparable with the effect of GDNF in comparison to untreated controls. The application of the GPR17 agonists alone did not have a significant effect on NOG. In addition, the combination of MTL and the agonist "PZB" significantly inhibited NOG.

Multiple immunofluorescence labelling in combination with laser scanning microscopy showed the expression of GPR17 on NG2-positive glia and NeuN-positive neurons. Western blot-experiments indicated a region-specific expression of GPR17 in the co-cultures and a MTL-induced increase in the SN/VTA. qPCR studies showed that MTL induced a significant increase in mRNA of GPR17, GAP43, Neurofilament light chain and TH in the SN/VTA as well as of TH in the PFC.

In conclusion, we identified MTL as potent stimulator of NOG, mediating its effects through GPR17, highlighting GPR17 as an interesting therapeutic target in neuronal regeneration.

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Poster 150

Hypertension related cognitive decline in spontaneous hypertensive mice could be influenced by an altered immunophenotype

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A shift in cerebral immune cell distribution is associated with lower cognitive performance in spatial memory- and working memory-related tasks. Especially lymphocytes were shown to be essential for a healthy cognitive function, with the Choroid Plexus (CP) as the central structure to orchestrate the lymphocyte traffic into the CNS. The lymphocyte migration into the CNS is mediated through several constitutively expressed adhesion molecules at the CP. This study aimed to investigate, if an alteration of the immune homeostasis evoked by changes in the adhesion molecule machinery of the CP could explain the cognitive decline accompanying hypertension. To address this question, spontaneous hypertensive mice (BPH) and their controls (BPN) underwent behavioral tests to investigate the eligibility of BPH mice as a model for hypertensive cognitive decline. Furthermore possible changes in the adhesion molecule expression pattern at the CP and the immunophenotype of BPH and BPN mice were analyzed. Anti-hypertensive treatment was conducted to determine if a pharmacological blood pressure reduction can reverse immunological and cognitive alterations. BPH mice showed a significantly impaired working- and spatial-memory. These cognitive differences were accompanied by higher mRNA expression of the adhesion molecules ICAM-1 and VCAM-1 at the CP and an altered immune cell phenotype. These findings could indicate, that hypertension related cognitive decline is not exclusively related to cerebral small vessel damages but also to deteriorated cerebral immune cell interaction. Anti-hypertensive treatment showed no influences.

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Poster 151

Amyloid-β-heme complexes: Does peroxidase activity contribute to Alzheimer's pathology?

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The increased deposition of amyloid-β (Aβ) and excessive oxidative processes are coinciding pathological processes at Alzheimer's disease (AD). These observations may be explained by the interaction of free heme with the named peptide, resulting in Aβ-heme complexes which exhibit a peroxidase activity in the presence of H_2O_2. Thereby the amino acids responsible for the formation and peroxidase activity of the named complexes are found in human but not e.g. in murine Aβ, which may explain the absence of AD-like neuropathology in mice despite plaque formation. Moreover, human-specific Y10 was shown as an endogenous peroxidase substrate of Aβ-heme complexes, contributing to fibril formation. In this study we verified the human-specific amino acids R5, Y10 and H13 as essential amino acids for the formation and enzymatic activity of Aβ-heme complexes. While increasing peptide-heme ratios led to constantly elevating peroxidase activities, an optimal dityrosine formation from Y10 was observed at an about 40-fold peptide excess. In line with the literature Thioflavin T-based measurements showed a delayed Aβ fibrillation in the presence of free heme. Thereby, however, different fibril morphologies were observed in the presence of H_2O_2 as verified by electron microscopy. Studies on a mouse model of AD confirmed the Aβ-derived destruction of micro-vessels in the brain. Thus we suggest hemolysis and Aβ-heme complex-formation as pathological key features of AD.

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Poster 152

Human APP transgene expression by hippocampal interneurons

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Amyloid precursor protein (APP) transgenic animal models that mimic the amyloid pathology of Alzheimer's disease have become versatile tools for basic and translational research. However, it is indispensable to ultimately demonstrate which neurons express the transgene and, therefore, contribute to pathological mechanisms in each animal model.

Here, we focus on the hippocampal formation of Tg2576 mice, which is severely affected by amyloid pathology in cellular and system function. Employing a novel, human APP-specific antibody in double immunofluorescent labellings we report a differential transgene expression by hippocampal interneurons immunoreactive for the calcium binding proteins parvalbumin, calbindin, calretinin and for the peptide hormone somatostatin in defined hippocampal layers. Overall, there was no GABAergic interneuron subpopulation that did not express the transgene. On the other hand, in no case all neurons of such a subpopulation expressed hAPP. In stratum oriens, human APP-expressing neurons frequently co-express these interneuron markers to different proportions, whereas in the dentate gyrus molecular layer and in stratum lacunosum moleculare less than 10% of human APP-positive interneurons co-express any of these markers. In the hilus of dentate gyrus and in stratum radiatum, 40% to 50% of human APP expressing neurons co-expressed parvalbumin, calbindin, calretinin or somatostatin, respectively.

We conclude that these neurons may contribute to deficits in long-term potentiation, neuronal network activity and learning/memory reported for young Tg2576 mice before the onset of Abeta plaque pathology.

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Poster 153

Pilocarpine-induced status epilepticus increases the sensitivity of P2X7 receptors to nucleotides at neural progenitor cells of the juvenile rodent hippocampus

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Adult neural progenitor cells (NPCs) have been identified in the subgranular zone of the hippocampal dentate gyrus (DG). Pilocarpine-induced status epilepticus of rodents increased the number of NPCs, fostered their migration and ectopic settlement/maturation in the hilus hippocampi and thereby caused recurrent spontaneous seizures. In hippocampal slices of transgenic Tg(nestin/EGFP) mice, we identified NPCs under fluorescence microscopic observation. Dibenzoyl-ATP (BzATP), a prototypic P2X7 receptor agonist initiated inward current in NPCs and the selective antagonist A-438079 reversed this effect. When hippocampal slices were taken from mice subjected to pilocarpine treatment, the current responses to BzATP markedly increased. Hippocampal slices were incubated with 4-AP for 1 h to increase the firing rate of DG neurons. The 4-AP effect could be antagonized by TTX and standard antiepileptic drugs. Incubation with ATP also caused a sensitivity increase of NPCs to BzATP. In conclusion, 4-AP appeared to facilitate the firing rate of DG neurons, causing larger ATP and glutamate release onto NPCs located in the underlying SGZ. Both transmitters/signaling molecules increased the Bz-ATP currents of NPCs. It is suggested that the activation of BzATP-sensitive P2X7 receptors at the NPCs might cause apoptosis/necrosis, thereby decreasing the chances of migration of these NPCs to ectopic locations in the hilus hippocampi. As mentioned above, ectopic granule neurons generated from NPCs were found to be responsible for the establishment of temporal lobe epilepsy after a one-time status epilepticus.

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Poster 154

Ischaemia-induced loss of perineuronal nets and histological characterization of vessels and other NVU components after stroke

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Perineuronal nets (PNs) are polyanionic, chondroitin sulphate proteoglycan (CSPG)?rich, web?like coatings of certain neurons, which are considered as important parts of the neurovascular unit (NVU). PNs are known to be affected in several neurological disorders such as schizophrenia and epilepsy, but their role in acute ischaemic stroke and during the related tissue damage is still poorly understood.

By applying three different models of focal cerebral ischaemia this study compares histological alterations of NVU components 24h after filament-based middle cerebral artery occlusion (MCAO) in mice, 24h after thomboembolic MCAO in rats and 14 days after electrosurgically induced MCAO in sheep. Qualitative data of NVU-components were obtained by multiple fluorescence labelling of Wisteria floribunda agglutinin (WFA)-binding sites and CSPG-immunoreactivity in PNs, several different CSPG-positive PNs, as well as astrocytes, microglia, neurons and vessel-associated collagen IV in histological sections. Furthermore, semi-quantitative data of WFA and collagen IV-labelled cortices of mice were conducted by measuring their staining intensity at the border of the infarct and within the ischaemic neocortex.

Thereby, severely degraded PNs in combination with an increased immunoreactivity of collagen IV within the ischaemic tissue were confirmed by qualitative and quantitative data. Furthermore, loss and structural alteration of different CSPGs and diminished markers for fast-firing GABAergic neurons were demonstrated. Therefore PNs appear as ischaemia-sensitive structures which might play a critical role in stroke-related tissue damage.

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Poster 155

Igsf9-eGFP mice allow targeted-stimulation of climbing fibers

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Climbing fibers (CFs) are neuronal projections of the inferior olivary nuclei (ION) innervating the cerebellum where they form synapses with Purkinje cells (PC), deep cerebellar nuclei (DCN) neurons and other neuronal cell types. Typically, CF responses in PCs are identified by their all-or-none behavior, a step-wise response curve (SRC) and paired-pulse depression (PPD). Immature PCs are innervated by multiple CFs resulting in varying levels of PPD and graded SRCs complicating the stimulation of single CFs. Synapses between CFs and other neurons remain basically uncharted, mostly due to the difficulty of unequivocally identifying CF responses in electrophysiological experiments. In Igsf9-eGFP mice a subset of CFs is labelled by GFP allowing their visual identification and hence, targeted stimulation of GFP positive (GFP^+) fibers. We aimed to characterize the origin of GFP^+ CFs in the ION, to study their innervation pattern in the cerebellum in the course of postnatal development and to test targeted stimulation of visually-identified GFP^+ CFs in Igsf9-eGFP mice. We show that all ION subdivisions give rise to GFP^+ efferents. GFP^+ CFs innervate the cerebellar lobules in a caudal-to-rostral gradient and all DCN. Postnatal development is undisturbed in this mouse line. Targeted stimulation of visually-identified CFs is possible in immature and mature cerebellum. GFP^+ CFs evoke normal electrophysiological responses in PCs, PPD and SRC respectively, which were also recorded in DCN neurons. Thus, Igsf9-eGFP mice are an ideal tool for studying CFs responses in multiple-innervated PCs as well as in other neuronal targets of CFs.

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Poster 157

Altered expression pattern and aggregation of huntingtin in a transgenic mouse model of Alzheimer's disease

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The objective of this study was to investigate whether Alzheimer's disease (AD) related Aß pathology in brains of the APP-transgenic Tg2576 mouse model has an impact on the endogenous expression and localization of the aggregation-prone protein huntingtin (Htt). Since little is known about the physiological brain- and cell type-specific expression pattern of Htt, wild type mice were investigated in comparison at different postnatal ages. Localization of Htt was revealed with immunohistochemical methods on coronal brain sections. The cell type-specific Htt expression was also analyzed by RT-qPCR of primary neuronal and glial cell cultures.

First, the physiological Htt expression in brains of wild type mice was characterized. Ubiquitous neuronal Htt expression was identified in a large number of brain regions including striatum, hippocampus, Edinger-Westphal nucleus and Locus coeruleus which are known to be affected in AD. In Tg2576 mice, no influence on physiological Htt expression patterns was detected. However, a distinct association of Htt with Aß-containing plaques and aggregate-like structures was revealed in the near periphery of larger plaques by immunohistochemical staining. Additionally, the localization of Htt in reactive astrocytes was demonstrated for the first time in Tg2576 mouse brain. Age-dependent processes seemed to further influence Htt recruitment to plaques and localization in astrocytes. An astrocytic Htt expression was also demonstrated in primary cultures by RT-qPCR.

Thus, we demonstrate an Aß-related influence on endogenous Htt expression and aggregation in the Tg2576 mouse model.

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Poster 158

Development of perineuronal nets in the medial nucleus of the trapezoid body of neurocan-deficient mice

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In the central nervous system, specific neurons are ensheathed by a unique composition of extracellular matrix (ECM) molecules, termed perineuronal nets (PNs). PNs are suggested to be involved in the modulation of synaptic activity and plasticity as well as neuroprotective mechanisms. They are composed of hyaluronan, chondroitin sulfate proteoglycans (such as aggrecan, brevican and neurocan (NCAN)), link proteins and tenascin-R. PNs typically appear late in development forming lattice-like structures which enwrap the soma, proximal dendrites and axon initial segment of neurons. At younger ages, PN subcomponents are either diffusely dispersed in the neuropil or are still accumulated in the neurons secreting these molecules. One exception is, the proteoglycan NCAN which exhibits defined net-like patterns already at early postnatal stages, suggesting a role of this proteoglycan in the early formation of PNs. In the present study we performed immunohistochemistry and protein biochemistry to investigate the structural development of PNs in the medial nucleus of the trapezoid body (MNTB), a PN-rich nucleus within the auditory brainstem. The MNTB was investigated in transgenic mice which were deficient for the proteoglycan NCAN. The results indicate that the absence of the proteoglycan NCAN leads to alterations in the developmental profile of PNs. This was accompanied by changes in the expression and distribution of other main PN constituents leading to prominent modifications in the molecular fine structure of PNs. These findings indicate that the PN component NCAN contributes to the early formation of PNs during development.

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Poster 159

Sound pattern recognition by an auditory feature detection circuit in the cricket brain

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From human language to chirps of insects, acoustic communication is based on amplitude and frequency modulation of sound signals. Frequency-processing starts at the ears, but temporal features like rhythms or pulse rates require central processing. Besides theoretical concepts, brain circuits detecting temporal sound patterns are poorly understood. We show how a neural circuit of just five neurons in the brain of female crickets forms an auditory feature-detector circuit for the species-specific sound pulse pattern of the male calling song. The pulse pattern recognition is based on delay-line and coincidence-detection mechanism. The network receives its direct auditory input from a single ascending interneuron. An internal delay that matches the pulse period of the calling song is established by a non-spiking brain neuron. In response to a sound pulse it receives transient inhibition that triggers a delayed rebound depolarization. The direct input and the delayed responses converge in a coincidence detector neuron, which responds best to the pulse pattern of the species-specific calling song as the rebound activation of the non-spiking neuron coincides with the response of the ascending interneuron to the subsequent sound pulse. The output of the coincidence detector neuron is further processed by a feature detector neuron to suppress unselective responses. The sparse but highly selective spike response of the feature detector neuron closely matches the pulse period tuning of the phonotactic behavior. The circuit reveals principal mechanisms of sensory processing underlying the perception of temporal auditory patterns.

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Poster 160

Establishment and evaluation of methods for the isolation and analysis of exosomes from blood serum as potential biomarker for neurodegeneration

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Exosomes are extracellular vesicles with a diameter of approximately 30 - 150nm present in all body fluids. Exosomes are involved in several physiological processes such as cell to cell communication. However, they also hold promise to represent a biomarker for a variety of pathological processes, including neurodegeneration. Designing techniques that will help to isolate and identify pure exosomes is crucial for further analysis. To investigate exosomes as potential peripheral biomarker we established and evaluated different techniques for the isolation and analysis from serum samples, particularly the enrichment and purification of exosomes using ultracentrifugation and different methods of immunomagnetic purification. Subsequent verification and analyses were performed by western blot and flow cytometry. Exosomes were identified indirectly by a variety of marker proteins e.g. CD9, CD63, CD81, ALIX, TSG101, Rab5, HSP70. Two main strategies were successfully established. Highly pure exosomes for functional studies were obtained by a combination of sedimentation and iodixanol density gradient ultracentrifugation techniques. The multiparameter analysis of distinct exosome subsets, however, was performed by immunomagnetic isolation and subsequent flow cytometry.

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Poster 161

Brevican-based, extracellular matrix complexes surround synapses of cochlear hair cells

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Perineuronal nets (PNs) are specialized aggregations of extracellular matrix (ECM) molecules surrounding specific types of neurons in the central nervous system (CNS). PNs are assumed to control neuronal activity and plasticity as well as synaptic transmission. They are mainly associated with neurons firing at high rates, including fast-spiking interneurons in the cortex and principal neurons of the nuclei within auditory brainstem. The origin of the high-frequency activity of auditory brainstem neurons is the high rate of sound-driven transmitter release of inner hair cells (IHCs) in the cochlea. Here, we show that IHCs are ensheathed by basket-like ECM complexes which are formed by the same molecules that constitute PNs of neurons in the CNS (brevican, aggrecan, neurocan, linkprotein 1 and 4) and which are likewise strongly associated with synapses contacting the IHCs at its basal pole. In contrast to the aggrecan-based PNs of neurons, ECM baskets at IHCs were found to be mainly composed of brevican. Brevican-deficiency resulted in a massive degradation of ECM baskets at IHCs going along with a significant impairment of the spatial coupling of pre- and postsynaptic elements. In conclusion, the presently described brevican-based ECM baskets at IHCs demonstrate the presence of specialized, pericellular ECM at highly active sensory cells in the peripheral nervous system. By controlling the spatial alignment of pre- and postsynaptic structures, these ECM baskets potentially contribute to the control of synaptic transmission at IHCs and might be functionally related to PNs of neurons in the CNS.

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Poster 162

The expression of transgenic human APP in Tg2576 mice is not neuron-specific

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The amyloid precursor protein (APP) that gives rise to Aß peptides which accumulate in brains of Alzheimer's disease (AD) patients is expressed by both, neurons and glial cells in human brain. In transgenic mouse models of AD, human APP expression is frequently targeted to neurons. For the widely used Tg2576 mouse model, human APP expression was reported to be restricted to neurons and absent from glial cells. However, a novel antibody that discriminates between endogenous mouse and transgenic human APP indicated transgene expression by non-neuronal cells.

Here, we used this antibody in double immunofluorescent labellings with neuronal and glial markers to reveal the cell type-specific transgene expression in Tg2576 mouse brain sections. Additionally, human APP transgene was analyzed in primary neurons and glial cells derived from transgenic Tg2576 mice by immunocytochemistry and by RT-qPCR.

We observed a predominant neuronal human APP expression in Tg2576 mouse brain, but an additional human APP immunoreactivity in oligodendroglia and in some – but not all – Aß plaque-associated microglial cells and astrocytes. Since glial immunoreactivity for human APP might result from uptake of APP produced by and secreted from neurons, primary neuronal and glial cells cultures of wild type and Tg2576 mice were analyzed for human APP expression. Both, human APP mRNA and protein were detected in all cell types of transgenic, but not of wild type mice.

We conclude that human APP expression in Tg2576 mouse brain is not strictly neuronal and that glial transgenic APP expression may contribute to aspects of Aß pathology present in these mice.

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Poster 163

Neuroanatomical characterization of perineuronal net components in the human cochlear nucleus and superior olivary complex

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The human auditory brainstem, especially the cochlear nucleus (CN) and the superior olivary complex (SOC) are characterized by an extremely high density of neurons associated with perineuronal nets (PNs). PNs are a specific form of extracellular matrix surrounding the neuronal somata, proximal dendrites and axon initial segments. They are assumed to influence synaptic plasticity and to control the availability of ions which is required for high-frequency synaptic activity, a prominent characteristic of the auditory system. The distribution of PNs within the auditory brainstem has been investigated in numerous studies on mammals. However, much less is known regarding the human CN and SOC.

This study aimed at the immunohistochemical identification of PNs in the CN and SOC of three human brainstems, thereby considering the complex nature and potential molecular variabilities of the PNs in CN and SOC by using specific antibodies against the main PN components (aggrecan, brevican, neurocan and hyaluronan link protein 1). Virtually all subnuclei within the ventral CN and SOC were found to be associated with PNs. Further, comparative analyses in the gerbil and human auditory brainstem demonstrated similar fine structure of PN molecules and confirmed the typical tight interdigitation of PNs with synaptic terminals in both species.

In conclusion, the present study shows that the composition, distribution and fine structural details of PNs in the human auditory brainstem are similar to what has been found in laboratory animals, suggesting that PNs serve similar functions in the human brain.

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Poster 164

"She is my best happiness" Preliminary Data on the Complex Dyadic Relationship between Refugee Mothers and their Children Born of Sexual Violence.

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The relationship between mothers and children conceived through sexual violence is highly complex (Johnson et al., 2010, Verelest et al., 2014) and the repercussions of a mother's own traumatic experiences can often be felt by the child (van Ee et al ., 2012; Theidon, 2015). Treating these mothers and children is understandably challenging, with little existing guidance on best practice. If migration and asylum factors are compounding the experience of such a dyad, another layer of complexity is added to pathway recovery (Laban et al., 2008). The purpose of this paper is to present a review of the current knowledge on interventions for children of victimized mothers and a Delphi process gathering expertise. Preliminary data of a case-control study, with mixed methods on child functioning, reflective functioning, resilience, stigma and emotional availability of mothers and children, therefore wants to be highlighted. The results of the combined studies strongly indicate the need for wider social care practices that address the specific needs of these mothers and children.

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Poster 165

Modulation of early visual processing by content extraction of emotional scenes: Evidence from EEG frequency-tagging approach

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The content extraction of emotionally significant cues from the visual environment is crucial for adaptive behavior. Here we utilized the frequency-tagging technique to record the steady-state visual evoked potential (SSVEP), to examine whether heightened activity in early visual cortex during viewing of affective images requires emotional content extraction of each individual picture in rapid serial visual presentation (RSVP) streams of unpleasant or neutral content. Images were displayed at 15 Hz (~67 ms per image), or at more slower frequencies of 6 Hz and 4 Hz (~167 and 250 ms per image), thus either permitting or not allowing sufficient time for emotional content extraction. The results revealed enhanced SSVEP amplitudes for negative compared to neutral images only at a presentation speed of 4 Hz, with no reliable differences at 15 Hz. Interestingly, SSVEP amplitudes decreased for unpleasant relative to neutral scenes when presented at 6 Hz. Moreover, the differential pattern of SSVEP modulations for 4 and 6 Hz was also demonstrated when unpleasant and neutral images were shown as task-irrelevant RSVP streams during a concurrent visual task in a subsequent study.

Overall, these findings suggest that not only the presentation duration of individual images is critical in driving SSVEP affective modulations with visual scenes, but also imply that linear superposition of event-related potentials evoked by each individual image may lead to superposition patterns that increase or decrease the power at the driving frequency, which in turn might produce the reversed emotional modulations as observed with SSVEP at 6 vs. 4 Hz.

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Poster 166

Going Above and Beyond (Stereotypical) Expectations: Interactive Effects Of Age, Gender, and Motives on Evaluations of Proactivity

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Due to the diversifying nature of the workforce in the 21st century, the perception of proactivity is likely to be shaped by personal characteristics, as well as the social context at work (Grant, Parker, & Collins, 2009). Our study examines how age (i.e., young and old adults), gender (i.e., female and male), and motives (i.e., achievement and benevolence) influence effectiveness evaluations of proactivity (i.e., "a set of self-starting, action-oriented behaviors aimed at modifying the situation or oneself to achieve greater personal or organizational effectiveness"; Unsworth & Parker, 2003, p. 177). In line with our hypotheses, proactivity was evaluated as most effectively if the performer's motive exceeded social role expectations regarding age and gender. More specifically, participants rated achievement motivations as more effective for older compared to young men, while rating young women motivated by achievement as more effective than older women. Furthermore, proactive behavior with a benevolence motive was rated as most effective for young men compared to older men, while there was no difference for women.

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Poster 167

Attentional facilitation of object constituent features underlies competitive interactions and is not spread automatically

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The integrated object account implies the mandatory spread of attention across all features bounded into one object. We scrutinize the fate of task-irrelevant features. A novel stimulation technique enables simultaneous measurements of the allocation of attention to two distinct features within one object, by driving two distinct steady state visual evoked potentials (SSVEPs). Results show that facilitation across features within one object underlies competitive interactions and is not mandatory.

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Poster 168

The Repercussions of Caregiver Burden on Mental Health after a Loss due to Cancer

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Background:
Caregiver burden was shown to influence mental health during caregiving. Yet, few studies examined the long-term repercussions of caregiver burden on caregivers of cancer patients. Theoretical perspectives conflict, suggesting either an improvement of psychological wellbeing after bereavement (due to the cessation of the stressful caregiver task) or a lasting detrimental effect of caregiver burden on mental health (due to accumulation of stress).

Methods:
A systematic review was conducted to provide a summary of (1) operationalizations of caregiver burden used in this field and (2) the effect of caregiver burden on post-bereavement mental health of adult caregivers of cancer patients. A systematic search of the electronic databases PubMed, Web of Science and PsycINFO was carried out across empirical studies published in a peer reviewed journal up until November 2016.

Results / Discussion:
Results of the 17 included papers indicate that caregiver burden has an adverse effect on post-bereavement mental health. This evidence suggests that intervention and prevention targeted at caregiver burden may improve mental health beyond bereavement. Future studies should examine further which aspects of caregiver burden may prove an appropriate target for prevention and intervention, applying a uniformly used, precise and multidimensional operational definition of the concept.

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Poster 169

Der Einfluss einer einfachen willkürlichen Fingerbewegung auf neuronale visuelle Verarbeitungsprozesse

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Wahrnehmung spielt eine zentrale Rolle für adaptives Verhalten. Wahrgenommene Umweltinformationen bilden die Grundlage motivierten Verhaltens und fungieren gleichzeitig als feedback Signal zur Bewertung und Anpassung motorischer Prozesse während der Interaktion mit der Umwelt.

Wie genau Wahrnehmung und Motorik jedoch interagieren ist noch nicht geklärt und Gegenstand aktueller Forschung.

In einer früheren Arbeit (Makeig et al., 1996) konnte gezeigt werden, dass willentliche, einfache Fingerbewegungen mit der Modulation nicht aufgabenrelevanter auditorischer Informationen, gemessen im EEG, einhergingen. In der aktuellen Studie haben wir untersucht, ob es bei willkürlichen Fingerbewegungen auch zu einer Modulation der neuronalen Repräsentation visueller Stimuli kommt.

Wir fanden, dass einfache willkürliche Bewegungen des rechten Zeigefingers bereits ab 1,5 s vor und bis mindestens 3,5 s nach der eigentlichen Bewegung zu einer Amplitudenmodulation motorischer, neuronaler Oszillationen im alpha- und beta-Band führten. Gleichzeitig war die neuronale Repräsentation visueller Stimuli in frühen visuellen Kortizes nicht moduliert. Allerdings fand sich für visuelle alpha-Oszillationen, als weiteres Maß visueller Verarbeitungsprozesse, eine Amplitudenmodulation dieser in einem Zeitraum von 1 s vor der Fingerbewegung.

Unsere Daten sprechen gegen eine Modulation der frühen neuronalen Stimulusrepräsentation durch willkürliche einfache Bewegungen. Gleichzeitig scheint es jedoch zu einer Modulation endogener visueller Aktivität zu kommen, deren mögliche funktionale Konsequenzen in weiteren Studien untersucht werden müssen.

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Poster 170

Investigating the dynamics of suicidal ideation. Findings from psychiatric inpatients with depression using ecological momentary assessment

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Background:
The fluctuating nature of suicidal ideation (SI) has been described previously, but longitudinal studies investigating the dynamics of SI are scarce.

Aim:
To investigate the fluctuation of SI in an inpatient sample using a smartphone-based fine grained real-time assessment.

Method:
74 inpatients with unipolar depression and current and/or lifetime SI rated their momentary SI 10 times per day over a 6-day-period. Intra-class correlation (ICC) and mean squared successive difference (MSSD) were used to quantify variability. Correlations of MSSD with severity of depression, number of previous depressive episodes and history of suicidal behavior were computed to examine associations of SI fluctuation with psychopathological parameters.

Results:
MSSD values ranged from 0.0 to 23.2 (M=4.8, SD=5.6), ICC was 0.73. When controlling for overall amount of SI across all measurement points, no significant correlations of MSSD with parameters of depression and suicidality could be found. Individual trajectories of SI are presented exemplarily to illustrate the diversity in fluctuation.

Discussion:
We found a considerable diversity in the trajectories of SI in depressive inpatients. A relevant proportion of participants showed a high degree of variability in SI over the short period of 6 days, implying the need of assessing SI repeatedly in short time frames to avoid missing important fluctuations. As there is no direct association between MSSD with psychopathological parameters, it remains unclear which variables are associated with the fluctuation of SI or predict changes in SI.

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Poster 171

Internettherapie für Hinterbliebene von Menschen mit hämatologischer Krebserkrankung

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Krebs gehört weltweit zu den häufigsten Ursachen für Morbidität und Mortalität. Der Verlust einer nahestehenden Person infolge einer Krebserkrankung ist mit Auswirkungen auf die psychische Gesundheit der Betroffenen verbunden, z.B. einem erhöhten Risiko zur Entwicklung einer Anhaltenden Trauerstörung. Dennoch werden die Unterstützungsbedürfnisse der Angehörigen von Krebspatienten wenig beachtet. Die Internettherapie ist eine leicht verfügbare und zugängliche Möglichkeit der therapeutischen Unterstützung. Ziel der Studie ist die Adaptation und Evaluation einer internetbasierten Schreibtherapie für Trauernde, die eine nahestehende Person durch eine hämatologische Krebserkrankung verloren haben.

Die kognitiv-verhaltenstherapeutisch fundierte Internettherapie erstreckt sich über 5 Wochen und besteht aus drei Abschnitten: (1) Selbstkonfrontation, (2) Kognitive Umstrukturierung und (3) Social Sharing. Die Wirksamkeit der Internettherapie wird in einer randomisiert-kontrollierten Studie mit einer Wartekontrollgruppe überprüft. Angestrebt werden insgesamt 42 Teilnehmende mit einer komplizierten Trauerreaktion. Primäres Outcome ist die Reduktion der Trauerreaktion. Sekundäre Outcomes umfassen Maße der generellen Psychopathologie sowie der Lebens- und Schlafqualität.

Die Intervention sowie erste Ergebnisse werden vorgestellt.

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Poster 172

Psycho-oncological intervention for closest relatives: a pilot study with partners of patients suffering from hemato-oncological diseases

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Background: Suffering from cancer confronts also the patient's partner with a variety of psychosocial challenges. To date, psycho-oncological interventions specifically for partners of hemato-oncological patients are scarce.

Aims: The study aims to develop a psycho-oncological group-intervention for partners of patients with hemato-oncological diseases at two oncological centers. Aim of the intervention is (1) a significant reduction of mental strain in the partners and patients and (2) an enhancement in dyadic coping. A pilot testing will be carried out to test applicability of the intervention.

Methods: The psycho-educative group intervention for partners is modularly structured. It will consist of five thematic sessions and will be conducted by psychotherapists. Participants and patients will undergo a written survey before and after the intervention. In addition, every single session will be evaluated by the participants. The variables of interest will be assessed with the PHQ and the Dyadic Coping Inventory.

Conclusion: This is one of the first studies that develop and evaluate a psycho-oncological intervention specifically for partners of patients with hemato-oncological diseases. The project has started in May 2017. The intervention will start in January 2018.

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Poster 173

Extensive picture-word interference repetition: tracing lexical-coactivation of naming alternatives in cyclic naming.

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Recent studies have shown that during object naming alternative object names, which are not produced by a speaker, become nevertheless phonologically co-activated during speech planning (e.g., the name bird when the produced name is duck and vice versa). The present study investigated whether the co-activation of such naming alternatives can be attenuated, when speakers consistently only use one particular name for a picture in a number of naming episodes. In two picture-word interference experiments we measured the phonological co-activation of basic-level naming alternatives when pictures were named at the subordinate-level (Experiment 1) and of subordinate-level naming alternatives when pictures were named at the basic-level (Experiment 2). We implemented 25 repetition cycles and measured the phonological co-activation of naming alternatives at 4 different points in time. If the pattern of lexical activation is shaped by previous naming episodes, then the phonological co-activation of the non-target naming alternatives should decrease over repetitions. Contrary to this prediction, phonological co-activation effects remained stable across the whole experiment. This suggests that, at least for fully adequate alternative object names, lexical activation patterns are largely unaffected by recent naming episodes.

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Poster 174

Anhaltende Trauerstörung: Ein systematisches Review der Messinstrumente

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Hintergrund:
Bei etwa 10% der Hinterbliebenen kommt es nach dem Verlust einer nahestehenden Person zu einem pathologischen Trauerverlauf. Pathologische Trauer wurde nun ins DSM-V als Anhaltende komplexe Trauerreaktion (AkT) aufgenommen und wird voraussichtlich als Anhaltende Trauerstörung (AT) in die ICD-11 eingehen. Zur Diagnosestellung sind daher valide und reliable Messinstrumente erforderlich. Ziel des systematischen Reviews ist es, bereits existierende Messinstrumente zur Erfassung von AT/AkT zu identifizieren und deren psychometrische Daten zu evaluieren.

Methodik:
In den Datenbanken Web of Science, PubMed and PsycINFO wurde eine systematische Literatursuche durchgeführt. Eingeschlossen wurden Artikel, die die Entwicklung und/oder Validierung eines Messinstrumentes zur Erfassung von AT/AkT beschreiben.

Ergebnisse:
Es wurden 9 Messinstrumente identifiziert, die in 16 Studien beschrieben wurden. Alle Messinstrumente weisen gute psychometrische Eigenschaften (z.B. ausreichende Inhaltsvalidität und Konstruktvalidität) auf. Das „The Traumatic Grief Inventory Self-Report Version (TGI-SR)" (Boelen und Smid, 2017) erfasst sowohl die diagnostischen Kriterien der AT nach ICD-11 als auch die der AkT nach DSM-V und kann als Selbstbeurteilungsfragebogen im klinischen Setting angewandt werden.

Diskussion:
Die Ergebnisse zeigen, dass reliable und valide Messinstrumente zur Erfassung von AT /AkT existieren. Besonders die neu entwickelten Messinstrumente erscheinen geeignet. Künftige Studien sollten die Reliabilität und Validität der neu entwickelten, aber viel versprechenden Messinstrumente, weiter untersuchen.

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Poster 175

Hearing “birch” hampers naming a “duck” – behavioral and electrophysiological evidence for the phonological co-activation of alternative names in speech production

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When speakers name pictures (e.g., “duck”), distractor words phonologically related to alternative names (e.g., “birch” related to “bird”) slow down naming responses compared to unrelated distractor words. This interference effect is assumed to reflect the phonological co-activation of close semantic competitors and is critical for modeling word production. In the present study, we traced the electrophysiological correlate of this behavioral effect. We implemented two task versions: Participants either responded directly after picture onset (immediate naming) or after the appearance of a go-signal (delayed naming). Auditory distractor words were presented simultaneously with picture onset. The behavioral data revealed longer naming latencies with related compared to unrelated distractors in immediate naming, replicating the phonological interference effect. Cluster-based permutation tests applied to the ERP data revealed a significant difference between the two distractor conditions which was independent of task version. We observed two clusters, one at 305-436 ms located at left fronto-central sites and one at 537-713 ms located at central sites with enhanced negativity in the related distractor condition. The time window of the earlier effect corroborates the emergence of the behavioral interference effect at a phonological processing level, while the functional significance of the later effect is as yet not clear. The finding of a robust ERP-correlate of the behavioral effect facilitates further research on fine-grained lexical processes during speech production.

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Poster 176

Adolescents’ electronic media consumption is associated with a decline in psychological health

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Objectives:
Associations between media consumption or physical activity and adolescents’ psychological health have been suggested by several cross-sectional studies. However, longitudinal studies in this field are sparse. The present work investigated independent associations of media consumption and physical activity with adolescents’ later psychological health.

Methods:
Electronic media consumption (TV/video, computer/internet, mobile phone) and physical activity (in and outside sports clubs) of 10- to 17-year-old adolescents were related to their psychological symptoms and quality of life at follow-up, one year later (N=697). Additionally, associations of media consumption and physical activity with age, gender, socio-economic status, and year of assessment were investigated.

Results:
A high baseline consumption of electronic media, especially a high (> 3 hours) consumption of computer/internet, predicted increased psychological symptoms and declined quality of life at follow-up. In contrast, physical activity at baseline showed no association with psychological health at follow-up. Both electronic media consumption and physical activity showed significant associations with age, gender, and socio-economic status. Furthermore, the results revealed an increase in the consumption of TV/video and mobile phones between 2011 and 2016.

Conclusions:
A high consumption of electronic media, especially of computer/internet, is associated with a decline in adolescents’ psychological health.

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Poster 177

Die therapeutische Adhärenz und Allianz im Rahmen von individueller kognitiver Verhaltenstherapie für Jugendliche mit Binge-Eating-Störung

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Hintergrund: Angaben zum Ausmaß von therapeutischer Adhärenz und Allianz stellen wichtige Voraussetzungen für Wirksamkeitsbelege psychotherapeutischer Interventionen dar. Belege für das Ausmaß dieser Prozessfaktoren und für deren Varianzaufklärung durch Therapie-, Therapeuten sowie Patientenmerkmale in der kognitiven Verhaltenstherapie (KVT) zur Behandlung von Jugendlichen mit Binge-Eating-Störung (BES) sind bisher nicht vorhanden. Methode: In einer randomisierten Behandlungsstudie zur Wirksamkeit von KVT für die Behandlung von Jugendlichen mit BES (N=64, Alter=12–19 Jahre) wurden Adhärenz und Allianz durch objektive Bewertung von Audiomitschnitten von 247 Sitzungen mittels standardisierter Instrumente erfasst. Die durch Therapie-, Therapeuten sowie Patientenmerkmale erklärte Varianz von Adhärenz und Allianz wurde mittels Mehrebenenmodellierung berechnet. Ergebnisse: Während das Ausmaß von Adhärenz und Allianz hoch und unabhängig von Therapiemodul und Therapeuten ausfiel, ergab sich eine signifikante Varianzaufklärung durch Patientenmerkmale für beide Prozessfaktoren. Eine verringerte Adhärenz war mit höheren Therapieerwartungen des Patienten, eine verringerte Allianz mit höherer Symptomschwere des Patienten assoziiert. Schlussfolgerung: Exzellente Ausprägungen der Adhärenz unterstützen die interne Validität sowie die Interpretierbarkeit der Ergebnisse der KVT der BES bei Jugendlichen. Zusammenhänge von Prozessfaktoren mit Patientenmerkmalen unterstreichen die Notwendigkeit für Schulung und Supervision der Therapeuten. Zusammenhänge von Prozessfaktoren und dem Therapieerfolg verbleiben als Gegenstand zukünftiger Forschung.

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Poster 178

Projekt Help@App: App-basierte Selbsthilfe für traumatisierte Geflüchtete aus Syrien

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Hintergrund:
Seit dem Jahr 2014 bilden syrische Menschen die größte Gruppe von nach Deutschland Geflohenen. Viele Geflohene tragen Kriegs- und Gewalterlebnisse bis hin zu Folter in sich. Zusätzlich können sequentielle Traumatisierungen auf der Flucht und im Ankunftsland hinzukommen. Diese traumatischen Erfahrungen hinterlassen tiefe Spuren und erhöhen das Risiko, psychisch zu erkranken. Die Prävalenzrate von PTBS bei syrischen Geflüchteten wird in neueren Studien auf etwa 34% geschätzt.

Methodik:
Im Projekt HELP@APP wird eine arabischsprachige interaktive Selbsthilfe-App für traumatisierte syrische Geflüchtete in Deutschland entwickelt, die psychische Belastung im Zusammenhang mit Traumatisierung reduzieren soll. Das Projekt ist in zwei Arbeitspakete (AP) unterteilt. AP 1 entwickelt die verhaltenstherapeutisch orientierte, modular aufgebaute App, die interaktive Elemente zur Psychoedukation sowie zum Umgang mit psychischer Belastung durch Flucht und Traumatisierung enthält. Ziel des zweiten Arbeitspakets ist die Prüfung der Wirksamkeit und Kosteneffektivität im Rahmen einer prospektiven randomisiert-kontrollierten Studie mit drei Messzeitpunkten.

Ergebnisse:
Die Evaluationsergebnisse werden voraussichtlich im März 2020 vorliegen. Der vorliegende Beitrag wird sich ausführlich mit der Konzeption und Umsetzung der App-Entwicklung beschäftigen, der Ablauf der Evaluationsstudie wird skizziert.

Diskussion:
Die Ergebnisse der Studie liefern Evidenz, ob die psychische Belastung von syrischen Geflüchteten durch einen App-basierten Ansatz verringert werden kann.

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Poster 179

Could high mental demands at work offset the adverse association between social isolation and cognitive functioning? Results of the population-based LIFE-Adult-Study

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Objectives:
The study investigated whether high mental demands at work, which have shown to promote a good cognitive functioning in old age, could offset the adverse association between social isolation and cognitive functioning.

Methods:
Based on data from the population-based LIFE-Adult-Study, the association between cognitive functioning (Verbal Fluency Test, Trail Making Test B) and social isolation (Lubben Social Network Scale) as well as mental demands at work (O*NET database) was analyzed via linear regression analyses adjusted for age, gender, education, and sampling weights.

Results:
Cognitive functioning was significantly lower in socially isolated individuals and in individuals working in low mental demands jobs – even in old age after retirement and even after taking into account the educational level. An interaction effect suggested stronger effects of mental demands at work in socially isolated than nonisolated individuals.

Conclusion:
The findings suggest that working in high mental demands jobs could offset the adverse association between social isolation and cognitive functioning. Further research should evaluate how interventions, that target social isolation and enhance mentally demanding activities, promote a good cognitive functioning in old age.

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Poster 180

Adult-attachment representations of German

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Background:
Estimates on war rape committed against German women by the Red Army vary from 900 000 up to 1.9 million. Also, thousands rapes were perpetrated by the Western allies. This topic was a societal taboo in Germany for decades. Thus, German occupation children (GOC) grew up under difficult circumstances such as poverty, adverse childhood experiences and discrimination. Particularly vulnerable subgroup of GOC is children born of war rape (CBOWR) being at higher risk for mental distress. Sometimes they serve as a living reminder of the rape which is challenging mother-child attachment and parenting behavior.

Methods:
Adult attachment was examined in GOC (N=146) and compared with a representative birth-cohort-matched sample (BCMS) from the German general population (N=786) using the Adult Attachment Scale (AAS; Schmidt et al., 2004). To expand the knowledge on attachment 10 narrative biographical interviews with CBOWR were conducted and qualitative content analysis was applied.

Results:
GOC report on different attachment representations compared to BCMS (e.g., less open to closeness and intimacy, lowered ability to depend on others in close relationships etc.). The majority of GOC (66%) report on secure adult attachment but with significant higher chances for fearful and dismissive adult attachment compared to BCMS. Attachment experiences in CBOWR in childhood and their impact on adult attachment will be described via a qualitative approach.

Conlusion:
CBOWR are a particularly vulnerable group of CBOW with rather adverse experiences of attachment and parenting.

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Poster 181

Wie beeinflussen Missbrauchserfahrungen in der Kindheit suizidales Erleben und Verhalten im Erwachsenenalter?

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Es ist inzwischen gut belegt, dass es Zusammenhänge zwischen Missbrauchserfahrungen in der Kindheit und Suizidalität über die Lebensspanne gibt. Die Befunde zu den dahinterliegenden Mechanismen sind jedoch noch sehr lückenhaft. Aus diesem Grund soll dieser Zusammenhang vor dem Hintergrund der Interpersonellen Theorie suizidalen Verhaltens (ITSV) untersucht werden. Es soll geprüft werden, ob körperlicher (KM), emotionaler (EM) und sexueller Missbrauch (SM) mit Suizidgedanken (SG) bzw. suizidalem Verhalten (SV) zusammenhängen und ob diese Zusammenhänge durch die Variablen der ITSV (Perceived Burdensomeness (PB), Thwarted Belongingness (TB) und Acquired Capability (AC)) mediiert werden.

Es wurden 84 stationäre Patienten (70 % Frauen, 18 – 85 Jahre) mit unipolarer Depression, bei denen aktuell oder in der Vorgeschichte SG vorlagen, untersucht. Zur Beantwortung der Fragestellung wurden Mediationsanalysen gerechnet, in denen für Depressivität kontrolliert wurde.

70% (n= 58) der Teilnehmer berichteten Missbrauchserfahrungen in der Kindheit. Es fanden sich keine direkten Zusammenhänge zwischen den verschiedenen Missbrauchsarten und SB bzw. SV. Jedoch hängen KM & SM indirekt über die AC mit SV zusammen und EM beeinflusst indirekt (über TB und PB) SG.

Missbrauchserfahrungen in der Kindheit haben einen indirekten Einfluss auf SG (EM) und SV (KM & SM) und stellen damit, unabhängig von der Schwere der depressiven Symptomatik, einen Risikofaktor für die Entwicklung von Suizidalität dar. Die ITSV bildet einen geeigneten theoretischen Rahmen um die Mechanismen dieser Zusammenhänge genauer zu verstehen.

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Endokrine und subjektive Stressantwort bei Kindern mit depressiven, Angst- und Verhaltensstörungen

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Ein ungünstiger Umgang mit Stressoren wird als ätiologisch bedeutsam im Zusammenhang mit der Entwicklung psychischer Störungen diskutiert. Bisher gibt es jedoch nur wenige Studien, die sowohl die endokrine als auch die subjektive Stressantwort auf diesen Stressor im Kindesalter untersuchten. Ziel der Studie war es, die endokrine und subjektive Stressantwort auf den Trier Social Stress Test for Children (TSST-C) bei Kindern mit depressiven, Angst- und Verhaltensstörungen und gesunden Kontrollen zu untersuchen. Die Stichprobe umfasste N=170 8-bis 14-Jährige. Zur Erfassung der psychischen Störungen der Kinder wurde ein diagnostisches Elterninterview durchgeführt. Während und nach dem TSST-C erfassten wir Speichelcortisol und subjektive Aufregung der Kinder. Die Kinder schätzten unmittelbar nach dem TSST-C ihre Leistung sowie eine Stunde später ihre stressorbezogenen Kognitionen ein. Die Cortisolausschüttung während und nach dem TSST-C war bei Kindern mit psychischen Störungen generell signifikant niedriger als bei Gesunden. Für die Parameter der subjektiven Stressreaktion fanden wir dagegen störungsspezifische Zusammenhänge. So schätzten Kinder mit depressiven Störungen ihre Leistung unmittelbar nach dem Stresstest signifikant schlechter ein als Gesunde und zeigten eine höhere Ausprägung der negativen Kognitionen eine Stunde später. Kinder mit Angststörungen zeigten signifikant mehr subjektive Aufregung vor und nach dem Stresstest. Im Regressionsmodell, unter Kontrolle von Alter/Geschlecht, waren sowohl endokrine wie auch subjektive Stressreaktionsparameter prädiktiv für die Zugehörigkeit zu den diagnostischen Gruppen.

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PROGRID – Psychotherapeutische Behandlung der anhaltenden Trauerstörung

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Der Verlust einer nahestehenden Person ist meist mit Gefühlen von Trauer und Schmerz verbunden, wobei mit zunehmender Verarbeitung des Verlustes die Intensität der Gefühle bei der Mehrheit der Betroffenen mit der Zeit nachlässt. Etwa 10% der Hinterbliebenen entwickeln jedoch eine anhaltende Trauerstörung (ATS), die mit deutlichen Beeinträchtigungen im Alltag verbunden ist. Die ATS ist mittlerweile als eigenständige psychische Störung anerkannt. Obwohl bekannt ist, dass diese Störung negative gesundheitliche Folgen hat und Leid verursacht, gibt es bisher nur wenig Forschung zur Behandlung der ATS.

Im Rahmen der multizentrischen Studie PROGRID (gefördert durch die DFG, PI Rita Rosner) soll in Leipzig, Marburg, Frankfurt und Ingolstadt die Wirksamkeit zweier Therapieprogramme für Menschen mit ATS in einer randomisiert kontrollierten Studie miteinander verglichen werden. Dabei handelt es sich zum einen um eine trauerspezifische integrative kognitive Verhaltenstherapie (Fokus auf der Trauer selbst, Interventionsgruppe) und zum anderen um eine gegenwartsakzentuierte Therapie (Fokus auf durch die Trauer verursachte Schwierigkeiten im Alltag, aktive Kontrollgruppe). Neben der Überprüfung der Effekte beider Therapieansätze auf die Trauersymptomatik (PG-13) als primäres Outcome, werden in der multizentrischen Studie zudem sekundäre Outcomes, wie beispielsweise der Schweregrad der Somatisierung, der allgemeinen psychischen Belastung und der depressiven Symptomatik untersucht. Die Evaluation und Adaptation von Behandlungsmöglichkeiten für Betroffene soll langfristig die Bereitstellung einer wirksamen Behandlung für ATS gewährleisten.

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Poster 184

Recognition memory associated with hippocampal pattern completion in young and older adults

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During pattern completion, original memory traces are restored (completed) via repeated reactivation.This process is thought to occur in hippocampal region CA3 given its extensive excitatory recurrent connections. With age, the number of projections from the entorhinal cortex to region CA3 decreases, while its interconnectivity remains unchanged. Consequently, the aged brain should show a bias toward pattern completion concurrent with CA3-hyperactivity.

Here, we have investigated pattern completion and concurrent changes in aging over the course of four experiments. First, we have developed a recognition memory paradigm specifically targeting pattern completion by manipulating stimulus completeness. Simultaneously, age-related recognition memory deficits were identified suggesting a bias towards- but also a deficit in pattern completion. Subsequently, we have eliminated perceptual contributions to memory performance with eye-tracking. From collaborative investigations in a patient with selective bilateral dentate gyrus lesions, first inferences could be derived over the differential contributions of hippocampal subfields to memory performance in the task. Finally, in a 7T-fMRI study, we could show that the hippocampus was involved in more general retrieval and the superior temporal sulcus was identified as a region of cortical reinstatement after successful pattern completion. Crucially, age comparisons revealed reduced activity in parahippocampal cortex and hyperactivity in CA3. The latter finding supports existing theories about cognitive aging, and is the first to specifically identify age-related CA3-hyperactivity.

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Poster 185

Präokkupation als Symptom der Anpassungsstörung – Revision der Skala zur Messung von Präokkupation von Sakamoto (1998)

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Das Ziel der vorliegenden Arbeit war es, die Eignung von Präokkupation als Klassifikationsmerkmal von Anpassungsstörungen gemäß den Forschungen von Sakamoto (1998) für den deutschsprachigen Raum zu bestätigen.

Außerdem sollte getestet werden, ob die Skala von Sakamoto (1998) geeignet ist, Präokkupation zu erfassen und zwischen einer klinischen und einer Referenzstichprobe zu unterscheiden.

Dazu wurde die englischsprachige Originalskala ins Deutsche übersetzt und anschließend an einer klinischen und einer Referenzstichprobe getestet. Die klinische Gruppe bestand aus 31 Probanden, die Referenzstichprobe aus 54 Probanden.

Zum großen Teil bestätigten die gewonnenen Ergebnisse die von Sakamoto gefundene Verbindung zwischen Anpassungsstörungen (erfasst durch die konstruktverwandte Depression) und Präokkupation.

Sie zeigten aber auch eine hohe Notwendigkeit gegenüber der Überarbeitung des von ihm entwickelten Fragebogens, sowohl hinsichtlich des Aufbaus als auch hinsichtlich der Gütekriterien.

Präokkupation messbar zu machen ist von großer Bedeutung für die Klassifikation und das Verständnis von Anpassungsstörungen.

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Poster 186

Response congruency effects in picture and sound categorization tasks – Does distractor word modality matter?

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Verbally categorizing a picture (e.g., picture: duck, response: bird) is facilitated by congruent compared to incongruent distractor words (e.g., distractor: duck vs. hammer). This facilitation effect has been attributed to response congruency of target and distractor processing. Previous studies suggest that response congruency effects are larger with visual than with auditory distractor words in picture categorization. From this observation one can derive the more general hypothesis that response congruency effects increase when distractor words and targets are presented in the same modality (Hantsch, Jescheniak, & Schriefers, 2009). In the present study we tested this hypothesis by manipulating both target and distractor modality. Participants verbally categorized either pictures or natural sounds (e.g., picture: duck or sound: quaking, response: bird). Targets were presented with visual or auditory distractor words, which were either congruent (e.g., distractor word: duck) or incongruent to the response (e.g., distractor word: hammer). Responses were generally faster with congruent distractor words. Importantly, this facilitation was larger with visual distractor words than with auditory distractor words, regardless of target modality. These results suggest that response congruency effects in categorization tasks are not increased when distractor and target are presented in the same modality. Instead response congruency effects appear to be generally larger with visual distractor words.

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Poster 187

Adipose Tissue Affects Lipid Homeostasis and Migration of Human Triple-negative Breast Cancer Cells

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Obesity and excess accumulation of adipose tissue are known risk factors of breast cancer. With the incidence of obesity constantly rising worldwide, understanding the molecular details of the interaction between adipose tissue and breast tumors becomes an urgent task. Recent studies indicate that adipose tissue promotes cancer progression, but the detailed molecular mechanisms remain elusive. In our work, we investigate the effect of adipose tissue on human triple-negative MDA-MB-231 breast cancer cells by using a two-dimensional co-culture system with adipose tissue from high-fat diet induced obese C57BL/6 mice. In genome-wide microarrays, we demonstrate that the co-culture activated genes in MDA-MB-231 cells which are known targets of PPAR nuclear receptors, established master regulators of cellular lipid homeostasis. Interestingly, we obtained similar results by culturing breast cancer cells with BSA-oleate or with adipocyte-conditioned media (ACM) obtained from human female overweight or obese patients by using qPCR analysis. PPARα inhibitor GW6471 reversed these effects. Furthermore, cell treatment with ACM or BSA-oleate resulted in an excessive formation of lipid droplets in MDA-MB-231 cells, as detected by AdipoRed and Oil Red O staining. In addition, treatment with ACM obtained from obese individuals significantly increased the wound healing capabilities of MDA-MB-231. Together, our data show that factors secreted from adipose tissue leads to changes in PPAR regulated gene expression and lipid homeostasis in MDA-MB-231 cells and induces a more aggressive breast cancer cell phenotype.

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Poster 188

MicroRNA-375 and -141 as potential new targets in prostate cancer

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Introduction:
Prostate cancer (PCa) is the second most frequent malignant tumor in men worldwide. MicroRNAs (miRs) are small non-coding RNAs (~22 bp) that negatively regulate gene expression post-transcriptionally, and their pathological up- or downregulation can be involved in tumorigenesis. MiR-375 and miR-141 have been identified to be significantly upregulated in PCa. The purpose of the present project is to neutralize those potentially oncogenic miRs by using synthetic miR inhibitors, “antimiRs”, thus preventing the selective binding of the given miR to its target mRNAs.

Methods:
Different PCa cell lines (PC3, DU145 and LNCaP) were transfected with anti-miR, a negative control or a Survivin siRNA as a positive control. For determining the inhibition of anchorage-dependent and -independent growth, numbers of viable cells were analyzed in WST-1 assays and soft agar assays. Caspase-Glo 3/7 assays for apoptosis were performed as well. Effects on cell cycle were investigated by flow cytometry.

Results:
DU145 and LNCaP cells showed significantly reduced viabilities in WST-1 assays upon antimiR transfection. In soft agar, cell inhibitory effects were observed only in DU145 cells. In contrast, apoptosis was increased in DU145 and PC3 cells after 72 hours, and in LNCaP cells after 96 hours. Cell cycle was slightly decelerated.

Conclusions:
The present findings demonstrate cell-inhibitory and pro-apoptotic roles for antimiR-375 and -141, and will be further explored preclinically with regard to novel treatment options in PCa.

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Poster 189

TNF-alpha induziert IL-8 im Barrett-Ösophagus zeit-, konzentrations- und stadienabhängig

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Gastroösophagealer Reflux kann zu einer chronischen Entzündung der Speiseröhre führen. Die Aktivierung proinflammatorischer Signalwege begünstigt hierbei die Entstehung einer Barrett-Metaplasie und letztendlich eines ösophagealen Adenokarzinoms (EAC), dessen Prognose weiterhin schlecht ist.

In einem Zellkulturmodell wurde an Zellen des gesunden mehrschichtigen Plattenepithels (EPC-1, EPC-2), der Metaplasie (CP-A), Dysplasie (CP-B) bis zum EAC (OE33, OE19) der Einfluss von TNF-alpha auf die Induktion von IL-8 entlang der Barrett-Sequenz untersucht.

Während der Barrett-Progression kommt es zu einer Zunahme der IL-6- und IL-8-Expression mit der höchsten Expression beider Interleukine in der dysplastischen Zelllinie CP-B. Im Vergleich zu EPC-1 und EPC-2 Zellen wiesen die Karzinomzelllinien OE33 und OE19 eine etwa 4,4-fach bzw. 8-fach gesteigerte basale IL-8-Expression auf. Unter Einfluss von TNF-alpha konnte eine zeit-, konzentrations- und stadienabhängige Zunahme der IL-8-Expression in allen sechs Zelllinien gezeigt werden. Die EAC-Zelllinie OE33 reagierte zudem mit einem veränderten EMT-Marker-Profil im Sinne einer Abnahme des epithelialen Markers E-Cadherin und Zunahme des mesenchymalen Markers Vimentin.

Die Zunahme der basalen IL-8-Expression im Verlauf der Barrett-Sequenz spricht für eine Aktivierung von NFkB und deren Beitrag in der Entstehung des ösophagealen Adenokarzinoms. Der Einsatz antiinflammatorischer Substanzen könnte daher möglicherweise die Chemosensitivität des ösophagealen Adenokarzinoms erhöhen.

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Poster 190

Carnosine inhibits the infiltrative growth of glioblastoma cells

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Carnosine (?-alanine-L-histidine) reduces growth of glioblastoma cells. Here, we investigated its anti-metastatic potential in a co-culture model of fibroblasts and tumor cells derived from patients.

Fibroblasts (FB) and primary glioblastoma (GBM) cells were exposed for 48h to carnosine and viability was determined. Co-cultures were created using cloning rings, placing GBM cells inside and patient derived FBs outside the ring and cultures were incubated in the absence or presence of carnosine for 3 weeks. Colony formation and area occupancies of FB and GBM cells were analyzed by microscopy and quantified using ImageJ.

FB and GBM cells respond to increased concentrations of carnosine with a reduced production of ATP although the effect was less pronounced in FB (50 mM: FB: 95.3±5.4%; GBM: 88.3±8.2%; 75 mM: FB: 85.1±5.8%; GBM: 71.3±6.8%). A comparable observation was made by measuring dehydrogenase activities. Co-culture experiments revealed that carnosine strongly inhibited the formation of tumor cell colonies within the fibroblast layer: 80.8±46.8 in the absence of carnosine compared to 46.6±24.4 (10 mM), 28.8±24.0 (25 mM) and 1.5±0.8 (50 mM). Furthermore, the area covered by tumor cells was reduced from 13.5±3.5% (control) to 7.7±2.5% (10 mM), 6.0±3% (25 mM) and 3.1±3.2% (50 mM).

The dipeptide significantly inhibited colony formation and migration in a fibroblast co-culture model leading to a reduced number of tumor cell colonies even at a concentration of 10 mM carnosine. Therefore, we assume carnosine may strongly inhibit the occurrence of recurrent tumors preventing the outspread of tumor cells into adjacent tissue.

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Poster 191

Histone modification ChIP analysis in cell cycle gene promoters of CRISPR/Cas generated cell lines

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One hallmark of the cell cycle is the oscillating gene expression. Cell cycle genes can be classified in two large groups with either expression maxima in S phase (early cell cycle genes) or in G_2 or M phases (late cell cycle genes). The timing of S phase gene expression is regulated through E2F sites, whereas CHR elements control late cell cycle genes. E2F and CHR sites are bound and repressed by the DREAM complex. E2F sites also bind E2F/RB complexes. It was already shown that RB recruits several histone modifiers, which might change histone modifications and chromatin accessibility of S phase genes. Based on structural similarities between E2F/RB and DREAM complexes, we asked whether there is a comparable mechanism for DREAM-regulated promoters. To test this hypothesis, we generated deletions of CHR and E2F elements by applying the CRISPR/Cas nickase system. Previous experiments showed that mutation of these promoter elements prevents binding of the complexes and leads to deregulation of gene expression. In the generated cell lines, we analyze cell cycle-dependent changes of histone modifications in wild-type and mutant promoters by chromatin immunoprecipitation (ChIP). To avoid cell line-dependent biases, we use heterozygous cell lines allowing a comparison of wild-type and mutant alleles in one cell line by allele-specific qPCR. We focus on activating (e.g. H3K4me3) and repressing (e.g. H3K27me3) histone modifications. Our experiments will provide a better insight into the mechanisms controlling cell cycle-dependent transcription of RB/E2F and DREAM target genes.

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Poster 192

The divergent calcium activity profiles of glioma initiating cells and their differentiated counterparts

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As a namesake “Glioblastoma multiforme” is recognized as a highly heterogeneous tumor with a plethora of different cellular subsets. Among these the so called glioma initiating cells (GICs) are thought to be a minor cell population that has the ability to maintain an undifferentiated condition and has the potential to give rise to tumors and initiate recurrences. The amount and shape of spontaneous intracellular calcium oscillations can be regarded both as a sign of maturation as well as an instructive cue to developmental processes in the central nervous system. In this study we aimed to assess whether undifferentiated and differentiated tumors cells could be distinguished by their calcium activity profiles. To address this question we compared the spontaneous calcium activity between three serum-free cultured primary GIC cell lines to their differentiated counterparts (DCs), grown for 1 week in medium supplemented with 10% FBS. DCs of all cell lines displayed a significantly enhanced spontaneous activity, with a higher percentage of cells showing one or more significant (F/F_0>30%) cytosolic calcium-peaks within the imaging interval of 10 minutes. While the clear difference in spontaneous calcium activity between undifferentiated and differentiated glioma cells warrants further investigation it is tempting to speculate that manipulation of calcium homeostasis, for example via the modulation of ionotropic glutamate receptors or via electrical stimulation might open new therapeutic avenues.

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Poster 193

Untersuchung zur Wirksamkeit von Chemotherapeutika an patientenspezifischen 3D-Gewebeschnittkulturen bei Patienten mit fortgeschrittener Peritonealkarzinose

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Die Behandlung einer Peritonealkarzinose (PC) in Folge gastrointestinaler Tumoren ist bis heute eine interdisziplinäre Herausforderung. Durch den schnellen Progress und das aggressiv- infiltrative Wachstum ist die Prognose oft schlecht. Eine Applikation der Zytostatika als Aerosol im Rahmen der Pessurized Intraperitoneal Aerosol Chemotherapy (PIPAC) kann zum histologischen Regress und zur Symptomlinderung führen.

Von Patienten mit fortgeschrittener PC in Folge eines Primärtumors im Magen, Pankreas oder des kolorektalen Bereichs wurden vor der PIPAC-Applikation Biopsien der peritonealen Metastasen entnommen, Gewebeschnittkulturen angfertigt und auf die Kavitäten einer 6-well-Platte verteilt. Nach 24h erfolgte in 5 Kavitäten die Applikation einer 10µM-Zytostatikalösung, die 6. Kavität diente als Kontrolle. Nach 96h wurde die Reaktion abgestoppt und immunohistochemisch Zytokeratin und Ki-67 angefärbt.

In PC-Biopsien ist die Expression des Ki-67-Proteins und des Intermediärfilaments Zytokeratin signifikant erhöht, sodass die Veränderung dieser Parameter zur Evaluierung der Zytostatikawirksamkeit verwendet werden kann. Die Chemotherapeutika führen zu einer verminderten Expression beider Marker, wobei der Regress unterschiedlich stark ausfällt. Eine Behandlung mit Zytostatika, vor allem von Platinverbindungen, zeigte ein patientenspezifisches Reaktionsmuster.

Tissue-Slice-Kulturen könnten ein gutes Modell für die individuelle Austestung von Zytostatika an patientenspezifischen Gewebsbiopsien im Vorfeld einer PIPAC-Behandlung sein.

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Poster 194

Charakterisierung von Wnt-Molekülen und –Rezeptoren in einem *in vitro* Barrett-Ösophagus Modell

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In den letzten Jahrzehnten stieg die Zahl der Neuerkrankungen des ösophagealen Adenokarzinoms (EAC) stark an. Der Wnt/?-Catenin Signalweg spielt bei der Karzinogenese verschiedener Tumorentitäten eine wichtige Rolle. Seine Bedeutung für EAC-Entstehung konnte bisher nicht hinreichend geklärt werden.

Verschiedene am Wnt-/?-Catenin Signalweg beteiligte Moleküle und Rezeptoren wurden mittels RT-/qRT-PCR und WesternBlot untersucht. Die Probengewinnung erfolgte aus 6 verschiedenen, die Barrett-Sequenz abbildenden Zelllinien (epitheliale (EPC-1, EPC-2), metaplastische (CP-A), dysplastische (CP-B) und Karzinomzelllinien (OE33, OE19)).

Die extrazellulären Liganden Wnt3a und Wnt5a werden vor allem in den epithelialen Zelllinien exprimiert, jedoch kaum in den Karzinomzelllinien. Die einzelnen membranständigen Rezeptoren Fzd1-10 zeigen ein stark variierendes Expressionsmuster. Des Weiteren konnte eine enorme Zunahme der Expressionsstärke der Co-Rezeptoren LRP5 und LRP6 entlang der Barrett-Sequenz detektiert werden. Die Expression des Wnt-Zielgens Axin2 nimmt innerhalb der Barrett-Sequenz stark zu, mit stärkster Expression in OE19. In den Karzinomzelllinien führte eine Wnt3a-Stimulation (200ng) zu einer Zunahme der Axin2-Expression in OE33, wohingegen OE19 keine Expressionsunterschiede aufzeigte. Es konnten keine Unterschiede in der Aktivierung von pGSK3? oder pAkt nach Wnt3a-Stimulation nachgewiesen werden.

Erstmals konnte eine Tiefenanalyse der Moleküle des Wnt/?-Catenin Signalweg entlang der Barrett-Sequenz durchgeführt werden. Diese Ergebnisse weisen einen starken Zusammenhang zwischen Wnt-Signalweg und der EAC-Karzinogenese auf.

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Poster 195

Hu-NSG3 – an innovative model for the development of new therapeutic strategies for ovarian cancer

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The ovarian carcinoma is a highly aggressive cancer with a mortality rate of 70%. Due to the unspecific and late occurring symptoms, an early detection is often difficult. The currently existing therapy is based on a radical chirurgical removal of the tumor followed by a combined chemotherapy using paclitaxel and carboplatin. However, 20% of the carcinomas have a primary platin resistance, so that a recurrence of the disease can be observed after 16 - 22 months. By the event of disease relapse, an immediate change of the therapy as well as alternative treatment strategies are decisive for the survival of the patients.

One of the greatest challenges in the treatment of malignant diseases are the variances in the the molecular and functional heterogeneity of tumor cells from primary tumor and tumor cells, which are already spread in distant organs. Despite this problem, almost exclusively information from the primary tumor is used for diagnostics and therefore also for the therapy decision. Therefore, differences in response to therapy or already existing resistance mechanisms can hardly be addressed.

In this project, we will establish a patient-derived ovarian carcinoma mouse model in order to develop new therapeutic strategies and personalized diagnostics. After tumor cell transplantation, the mice are analyzed by different imaging techniques e.g. CT or MRT. This allows the detection of the tumor as well as the assessment of the spread and growth in the organism. The injection of human hematopoetic stem cells into NSG-mice, to generate a human immune system, is already established in our group (Scholbach et al., 2010[1]).

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Poster 196

Organotypic glioblastoma tissue slices can be analyzed by RNA sequencing, whole slice histology and immunoblotting

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The individual treatment of tumor patients requires experimental models that can be used to propose the outcome of a certain therapy. For the development of test systems, cell culture or mouse models are often used but poorly reflect the tumor's biology. Therefore, we developed organotypic slice cultures which serve as model for the analysis of tumor response to treatment.

Here, we demonstrate that whole transcriptome sequencing of RNA from tissue slices can be applied. Glioblastoma (GBM) and normal brain slices are treated by radio-chemotherapy or left untreated as control. Ki67 expression within the tissue is determined by immunostaining of whole slices using a newly developed automated scanning technology. Protein and RNA are isolated for immunoblot analysis and whole transcriptome sequencing, respectively. Hereby it is possible to correlate mRNA and protein expression within one sample. We find that the treatment has an impact on the proliferation capacity of the GBM tissue. Quality control showed high quality RNA, libraries could be established and the RNA was sequenced with a depth of 200 x 10^6 reads per sample. Principal component analysis of annotated genes revealed significant differences between normal and tumor tissue and between treated and untreated samples. 4315 differentially expressed genes were found between untreated tumor and normal brain tissue.

Our model offers the opportunity to analyze the response of individual patient-derived GBM tissue to treatment and correlate it with the real clinical outcome of the equivalent patient, which we believe is an important step towards individualized therapy of GBM.

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Poster 197

Can biopsy samples be used for susceptibility testing ex vivo?

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Introduction: Oesophagus and gastric cancers are aggressive tumors with a poor prognosis. Response to standard therapy, including cytotoxic treatment, is unsatisfactory in many patients. Predictive tests are not available; therefore, we investigated whether response to cytotoxic treatment can be predicted ex vivo.

Method: Endoscopic samples were cut by a tissue chopper into 350µm thin slices. Slices were cultivated for 72 hours and treated with either 10µM cisplatin or 1µM irinotecan. The slices were processed for routine histopathology, immunohistochemistry and for qPCR analysis of ki67. Pancytokeratin (AE1/3) staining was done for determining tumor cellularity, ki-67 for proliferation, and cleaved PARP staining for apoptosis.

Results: Endoscopic biopsy samples can be cultured as tissue slices and preserved the morphological tissue characteristics in vitro. Routine histopathology and immunohistochemistry illustrated that tumor-size and the amount of double positive pancytokeratin and ki67 cells responded to drug treatment ex vivo. QPCR analysis showed a decline of the expression of ki67 whose extent was relative to treatment or non-treatment and comparable to ki67 staining. However, as biopsy samples are small and only one site of the tumor is represented, at least two or three samples are needed to obtain a reliable outcome. In addition, the histological sample is needed as it allows for the delineation of the tumor containing area with the specimen.

Conclusion: Endoscopic biopsy samples can be used for tissue slice culture and drug response could be analyzed immunhistochemically ex vivo.

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Poster 198

A tool for guided therapy adaptation to control for haematotoxic side-effects of multicycle chemotherapy

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Thrombocytopenia is a major side-effect of cytotoxic cancer therapies. The development of individual therapy adaptations is a non-trivial task since thrombocytopenic risk depends on many therapy-associated and individual factors. To solve this task, we developed an individualized bio-mathematical model of human thrombopoiesis under chemotherapy and implemented it in a software-tool usable for therapy management.

Methods & Results: We performed bio-mechanistic modelling of the dynamics of bone marrow thrombopoiesis and platelets by ordinary differential equations. Amplifications, death rates and transition times of the system are regulated by three types of biologically motivated feedback loops. Effects of cytotoxic drugs are modelled by a transient depletion of proliferating cells and a long-term depletion of osteoblasts reducing the supporting capacity of the bone marrow.

To parametrize the model, we used population data from the literature and close-meshed individual data of 138 non-Hodgkin's lymphoma patients treated with CHOP-like chemotherapies. The over-fitting issue of individual parameter estimates was successfully dealt with a virtual participation of each patient in 3 population-based experiments measuring 12 biological features.

We transferred the model into a user-friendly software tool allowing individual prediction of platelet-dynamics for CHOP-like chemotherapies and the effect of therapy adaptations with superior accuracy compared to statistical or semi-mechanistic competitors. The model can be used to make clinically relevant predictions regarding individual therapy adaptations.

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Poster 199

Innovative electron beam irradiation for NK cell therapy of cancer

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NK cell lines are an attractive tool in cellular immunotherapy. Their advantageous cytotoxic potential against multiple tumor types has been demonstrated extensively in vitro and *in vivo*. But NK cell lines themselves derive from tumorous tissues. For clinical usage, these cancerous cells must be irradiated to guarantee complete inhibition of proliferation in a patient's body after infusion. Unfortunately, the mainly used ionizing gamma or X-ray radiation does not only damage cellular DNA, thus preventing further proliferation, but also effector proteins, thus severely reducing anti-tumor efficacy of cell therapeutics. In contrast, electron beam irradiation can be used as an adjustable on-off technology and provides a much more exact dosing option than gamma radiation. Therefore, shorter exposure time is needed and potential degradation of proteins is reduced. This in turn might reduce potential of ROS formation and damaged surface proteins in irradiated cells. In the end, nuclear DNA will be sufficiently damaged by electron beam irradiation, thus incapacitating cellular proliferation sufficiently, while maintaining optimal viability and cytotoxic anti-tumor activity.

Results indicate significantly increased viability and cytotoxicity of electron beam irradiated NK cell lines compared to cell lines inactivated by X rays. Direct comparison of DNA and protein integrity derived from irradiated cells also yielded favourable results for electron beam irradiation.

In conclusion, innovative electron beam irradiation might be a suitable alternative to conventional X-ray irradiation of NK cells for cancer immunotherapy in the future.

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Poster 200

Nrf2: Ein potenzielles Target für die Therapie des ösophagealen Adenokarzinoms

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In den letzten Jahrzehnten nahm die Inzidenz des ösophagealen Adenokarzinoms in den industriellen westlichen Ländern um 600% zu und noch immer ist die Überlebensrate sehr begrenzt. Das Signalprotein Nrf2, welches mitverantwortlich ist für die zelluläre Stressantwort, induziert Enzyme wie HO-1. Hier wurde untersucht, in wie weit dieser Signalweg an einer Chemoresistenz gegenüber 5-FU in einem EAC Zellkulturmodell ist.

Untersucht wurden Zelllinien des physiologischen Plattenepithels (EPC1, EPC2), einer Metaplasie (CP-A), einer Dysplasie (CP-B) und des Adenokarzinoms (OE19, OE33), welche die Barrett-Sequenz vom Epithel zum EAC widerspiegeln. Nrf2, HO-1 und GLO-1 wurden mittels qPCRs, sowie die Reaktion der EAC Zellen auf 5-FU eruriert.

Die Enzyme GLO-1, HO-1 und Nrf2 sind in der Barrett-Sequenz vom Epithel zum Adenokarzinom verstärkt exprimiert. Die EAC-Zelllinie OE33 ist höchst vulnerabel für 5-FU und hat einen IC50 von 0,58µM, wohingegen in OE19 Zellen kein Effekt nachweisbar war. Werden diese jedoch mit 0,1µM bzw. 1µM Trigonellin, einem Inhibitor von Nrf2, behandelt, ergibt sich ein IC50 von 5,7µM. 5-FU induzierte eine leicht vermehrte Expression von GLO-1 und Nrf2 in beiden Karzinomzelllinien nach 48h. In primären Biopsien konnte histologisch eine verstärke Expression von Nrf2 in EACs im Vergleich zu entsprechenden Metaplasien nachgewiesen werden.

Die Expression von GLO-1, HO-1 und Nrf 2 ist in den EAC-Zellen erhöht. Eine Inhibition von Nrf2 führte zur Sensitivierung gegenüber 5-FU. Nrf2 könnte daher ein potenzieller Targets in der Therapiestrategie zur Behandlung chemoresistenter Tumoren sein.

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Poster 201

The 5T4 oncofetal glycoprotein does not act as a general organizer of the CXCL12-system in cancer cells

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The chemokine CXCL12 promotes cancer growth and metastasis by using either CXCR4 and/or CXCR7. This tumor-specific organization of the CXCL12 system obscures current therapeutic approaches, aiming at the selective inactivation of CXCL12 receptors. The oncofetal glycoprotein 5T4 is sparsely expressed in most normal adult tissues except foetal trophoblast cells but present in most tumors, enhancing their movement through epithelial-mesenchymal-transition (EMT). Since it has been previously suggested that the cellular use of CXCR4 or CXCR7 is dictated by the 5T4 oncofetal glycoprotein (McGinn et. al., 2012), we have now tested whether 5T4 would represent a general and reliable marker for the organization of the CXCL12 system in cancer cells. The CXCR4 antagonist, AMD3100, as well as the CXCR7 antagonist, CCX771, demonstrated that the cancer cell lines A549, C33A, DLD-1, MDA-231, and PC-3 use either CXCR7 and/or CXCR4 for mediating CXCL12-induced chemotaxis and cell proliferation. The use of CXCL12 receptors as well as their subcellular localization remained unchanged in most cell lines following siRNA-mediated depletion of 5T4. In distinct cell lines, inhibition of 5T4 expression, however, modulated tumor cell migration and proliferation per se, an effect not involving cadherins. Collectively, our analyses fail to demonstrate general organizational influences of 5T4 on the CXCL12 system in different cancer cell lines, and, hence, dismiss its use as a diagnostic marker.

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Poster 202

Adeno-associated virus vectors (AAV) transduce human primary neurospheres and slice cultures of glioblastoma multiforme

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Introduction:
Glioblastoma multiforme (GBM) is the most malign cancer. Remaining tumor stem cells after dissection lead to a rapid development of resistance to radiochemotherapy. Adeno-associated virus vectors (AAV) are a promising tool for gene therapy. Here we used primary GBM tissue to investigate the transduction efficacy of a novel AAV capsid variant based on serotype 2 (AAV_v) in comparison with AAVserotype 2 (AAV_2) both in GBM neurospheres and tissue slice cultures

Method:
GBM tissue is cut by a tissue chopper into 350µm slices. Slices are standardized and cultured on a membrane at an air-liquid interface. For preparation of neurospheres the tissue is dissociated by accutase and seeded in a 24 well-plate. After 10-15 days spheres are formed. Three spheres per well are transferred to a 96-well plate and transduced with $1x10^6$ genomic particles of respective AAV vectors, with GFP as a transgene. Slice cultures are treated equally.

Results:
After 24 hours cells express GFP, after five days the experiments are analysed. The transduced cells are spread throughout the neurospheres. Preliminary results indicate that the transduction rate is dependent on the patient sample and also differs between AAV_2 and AAV_v. GFP positive cells are also detected after five days in slice cultures throughout the entire tissue.

Conclusion:
AAV vectors can transduce GBM cells in neurospheres and cells with GFP expression are also found in slice cultures. In perspective, these models hold promise to be developed for various genetic approaches to manipulate GBM cells and potentially the microenvironment in slice cultures.

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Poster 203

Roadmap to Local Tumor Growth

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Cancer of the breast, prostate, colorectum, lung and cervix uteri are among the most commonly diagnosed cancers. All of these cancers are solid tumors and surgical or radio-oncological treatment are currently the only available options for curative treatment. 90% of cancer deaths, however, are due to metastatic disease. Therefore, the goal of surgery and radio-oncology must be to minimize loco-regional recurrence rates without increasing operative morbidity unnecessarily. Clinical data displays big differences in tumor infiltration rates dependent on tissue compartments. Tumor growth is non-isotropic. Here, we introduce plausible physical/mechanical anisotropies and elucidate whether these are sufficient to explain the clinical found tumor-spreading pattern. Furthermore, we provide a roadmap to local tumor growth based on clinical data. We show, that cervixal cancer follows a deterministic path in its invasive behaviour and show how to exploid the roadmap to optimise surgical outcomes in cancer survival rates.

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Poster 204

Carnosine's effect on tumor cells is independent from its degradation and the release of L-histidine

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Carnosine (ß-alanyl-L-histidine), a naturally occurring dipeptide, inhibits the growth of glioblastoma cells. As L-histidine mimics the anti-neoplastic effect, we investigated whether the release of L-histidine from carnosine is required.

Glioblastoma cell lines and primary cultures were exposed to carnosine or L-histidine in the presence of the carnosinase inhibitor bestatin. Cell viability was analyzed by cell based assays and carnosinase expression was determined by immunoblotting and qRT-PCR. Intracellular amounts of carnosine and L-histidine were determined by Liquid Chromatography coupled to Mass Spectrometry.

48 hour exposure to carnosine (50mM) significantly reduced viability in all tumor cells to an average of 73.6±20.5%, whereas L-histidine revealed a more pronounced effect (49.8±18.6%). We observed a significantly enhanced ($p<0.05$) abundance of L-histidine in 9 of 10 cell lines and in 4 of 5 primary cell cultures exposed to carnosine. However, no correlation between the release of L-histidine or the expression of carnosinases and the anti-neoplastic effect was observed. Furthermore, the aminopeptidase inhibitor bestatin did neither attenuate nor enhance the effect of carnosine.

These observations indicate that the release of L-histidine from carnosine is not required for its anti-neoplastic effect although L-histidine has a more pronounced effect on viability than carnosine. As L-histidine and most likely its imidazole ring appear to be responsible for growth-inhibition, this observation can be considered for the design of potential drugs that are able to deliver therapeutic amounts of imidazole groups to tumors.

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Poster 205

Viability of tumor cells and fibroblasts under the influence of imidazole containing compounds

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The dipeptide carnosine (β-alanyl-L-histidine) attenuates tumor growth. As it was previously shown that L-histidine mimics its effect, we investigated the influence of imidazole-containing compounds on viability of glioblastoma cells and fibroblasts.

Cells were treated with carnosine (Car), L-alanyl-L-histidine (LALH), β-alanyl-L-alanine (βALA), L-histidine (LH), Histamine (Hista), Imidazole (IM) and also with β-alanine (βA) and L-alanine (LA) (all 50 mM). After 48 hours, cell viability was assessed measuring ATP in cell lysates and dehydrogenase activity in living cells. In addition, the amount of intracellular metabolites of cells treated with carnosine or L-alanyl-L-histidine were determined by LC-MS.

In the presence of Hista and IM all cells exhibited a comparable loss of viability (<60%) whereas loss of viability in the presence of Car and LaLH was pronounced in tumor cells (<80%) and absent or weak in fibroblasts (90%-110%). The response to βALA was between 80 and 100% and almost absent in LA and β A. In the presence of LALH but not in the presence of carnosine a significant rise of intracellular amounts of LH was detected in all cells. Interestingly, a rise of intracellular glutamine was only observed in tumor cells and in the presence of carnosine.

In conclusion, although the imidazole moiety of carnosine appears to be responsible for its growth inhibitory effect, the combination of LH with βA or LA is responsible for tumor-specificity. Different responses of intracellular metabolites to Car and LALH indicate that they may not be interchangeable.

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Poster 206

The DREAM complex through its subunit Lin37 cooperates with Rb to initiate quiescence

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Rb/E2F and MuvB-based complexes play an essential role in coordinating expression of cell cycle genes. However, mammalian cells carrying Rb deletions can still arrest under growth-limiting conditions. The Rb-related proteins p107 and p130, which are components of the repressive MuvB-based complex DREAM, were thought to be responsible for a continued ability to arrest. DREAM is present in quiescent cells and consists of the MuvB core (Lin54, Lin52, Lin37, Lin9, Rbbp4) and the E2f4/5-Dp1-p130/p107 module which has been suggested to transmit repressor function of DREAM. The precise functions of MuvB core proteins are poorly understood. At this, Lin37 is the only MuvB core component without a defined role in transcription and cell cycle regulation. We applied a CRISPR/Cas9 nickase system to create Lin37-deficient cells. In contrast to cells lacking other MuvB core proteins, Lin37 knockout cells proliferate normally and arrest in response to serum deprivation. However, DREAM completely loses its ability to repress genes in G_0/G_1 even though all remaining subunits still assemble and bind to target gene promoters. To test if Rb/E2F complexes mediate G_1 arrest in the absence of Lin37 and DREAM function, we created $Rb^{-/-}$ and $Lin37^{-/-}/Rb^{-/-}$ cells. Cells lacking both Rb and Lin37 are incapable of exiting the cell cycle demonstrating that p130/p107 are not sufficient for mediating cell cycle arrest in the absence of Rb and DREAM function, respectively. Our results show that Lin37 is necessary for DREAM-dependent repression of cell cycle genes and cooperates as a part of DREAM with Rb in initiating quiescence.

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Poster 207

Charakterisierung von Histondeacetylasen in ösophagealen Adenokarzinomzelllinien

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Das Adenokarzinom des Ösophagus, das über eine Metaplasie-Dysplasie-Karzinom Sequenz entsteht, zeigt in den letzten Jahren eine steigende Inzidenz. Aufgrund der oft späten Diagnosestellung und der schwierigen Therapie, hat es stadienabhängig eine schlechte Prognose. Histondeacetylasen (HDACs), die epigenetisch direkt über die Deacetylierung von Histonen in die Genexpression von Zellen eingreifen, sind in dieser Karzinomentität noch wenig erforscht.

Zur Charakterisierung der Zn^{2+}-abhängigen HDACs wurde die Expression in verschiedenen Zelllinien ösophagealen Ursprungs untersucht Fibroblasten- (FEF-3), Plattenepithel- (EPC-1, EPC-2), Metaplasie- (CP-A), Dysplasie- (CP-B), sowie Adenokarzinom-Zelllinien (OE-33, OE-19, CP-B, Flo-1, SKGT-4).

Des Weiteren wurden mittels Proliferationsassay die Zelllinien OE-19 und OE-33 und deren Ansprechen auf den HDAC-Inhibitor Vorinostat vergleichend getestet.

In den analysierten Zelllinien konnte eine unterschiedlich starke Expression der verschiedenen HDACs gezeigt werden.

Eine Behandlung von OE-33 und OE-19 Zellen mit Vorinostat zeigte eine Hemmung der Proliferation (OE-33 IC_{50} von 1,1µM, OE-19 IC_{50} von 1,8µM).

Die Diversität der HDAC Expression in den verschiedenen Zelllinien lässt auf eine Veränderung der Expression in den unterschiedlichen Stadien der Karzinogenese schließen. Es sind weitere Arbeiten nötig, um den Stellenwert der HDACs in der Tumorentstehung und Progression des Barrett-Karzinoms besser zu verstehen.

Es ist zu klären, ob die hemmende Wirkung der Proliferation von Vorinostat die Chemosensitivität gegenüber Zytostatika wie 5-FU oder Platinverbindungen erhöht.

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Poster 208

Aktivierung der GSK3ß und die Auswirkung ihrer Inhibition auf die Proliferation in Zellen des ösophagealen Adenokarzinoms

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Das ösophageale Adenokarzinom ist eine Tumorerkrankung mit einer in den letzten Jahren ansteigenden Inzidenz und einem durch die späte Diagnosestellung bedingten geringen 5-Jahresüberleben. Verschiedene Studien konnten eine Rolle des Wnt-Signalwegs bei der Entstehung maligner Erkrankungen zeigen, seine Rolle bei der Entstehung des ösophagealen Adenokarzinoms ist noch nicht vollständig verstanden.

Methoden:
Es wurde der Einfluss eines GSK3ß Hemmers auf die Proliferation von zwei epithelialen (EPC1, EPC2), einer metaplastischen (CP-A), einer dysplastischen (CP-B) und vier Adenokarzinomzelllinien (OE33, OE19, SK-GT-4; Flo-1) ösophagealen Ursprungs mittels Proliferationsassays untersucht. Des Weiteren wurde die Zielgenexpression nach Inhibitorbehandlung mittels qPCR untersucht.

Ergebnisse:
Die epithelialen Zelllinien zeigten einen Anstieg der Proliferation mit ansteigender Konzentration des GSK3ß-Hemmers (GSK3ß Inhibitor IX, MerckMillipore). Bei den anderen untersuchten Zelllinien konnte keine Auswirkung auf die Proliferation der Zellen festgestellt werden. Auch bei der Expression der Zielgene CyclinD1 und Axin-2 konnten keine Unterschiede in den mit GSK3ß-Hemmer behandelten und unbehandelten Zellen festgestellt werden.

Schlußfolgerung:
Der Anstieg der Proliferationsrate in den epithelialen Zelllinien weist auf eine proliferationsfördernde Wirkung des GSK3ß-Hemmers hin. Grund hierfür könnte eine Aktivierung des Wnt-Signalwegs mit resultierendem erhöhten Entartungsrisiko sein. Um den ambivalenten Einfluss des GSK3ß-Hemmers auf die anderen Zelllinien zu erklären sind noch weitere Forschungsarbeiten erforderlich.

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Poster 209

Curcumin führt in vitro zum apoptose-vermittelten Zelltod von ösophagealen Adenokarzinomzellen

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Hintergrund:
Das ösophageale Adenokarzinom ist eine Tumorerkrankung mit einer ansteigenden Inzidenz in der westlichen Welt. Eine Diagnose erfolgt meist erst im fortgeschrittenen Stadium bei schon stattgefundener Metastasierung, somit ist die Prognose als ungünstig zu betrachten.

Verschiedene Studien zeigen eine pro-apoptotische Wirkung von Curcumin auf verschiedene Tumorentitäten, bezogen auf das ösophageale Adenokarzinom sind Untersuchungen bis jetzt jedoch weitestgehend vernachlässigt worden.

Methoden:
Zwei epitheliale (EPC-1, EPC-2), eine metaplastische (CP-A), eine dysplastische (CP-B) und zwei ösophageale Adenokarzinomzelllinien (SK-GT-4, Flo-1) wurden mit verschiedenen Curcuminkonzentrationen stimuliert. Anschließend wurde die apoptotische Wirkung von Curcumin anhand verschiedener Genexpressionen mittels qPCR (Ki67) und Proteinkonzentrationen mittels Westernblot (cleaved PARP und phospho-Akt) untersucht.

Ergebnisse:
Nach der Durchführung erster Versuche zeigen sich Tendenzen, dass Curcumin in allen untersuchten Zelllinien das Wachstum konzentrationsabhängig hemmt. Die Expression des Proliferationsmarkers Ki67 und die Phosphorylierung der Akt-Kinase werden ab einer Konzentration von 10µM Curcumin gehemmt. Eine Reduktion von PARP ist bei einer Konzentration von 25µM Curcumin zu sehen.

Schlussfolgerung:
Curcumin führt zelllinienspezifisch und konzentrationsabhängig zur Induktion der Apoptose in Zelllinien des Barrett-Ösophagus. Die Eignung von Curcumin als Agens zur Erhöhung der Chemosensitivität bei Zellen des ösophagealen Adenokarzinoms ist Gegenstand weiterer Untersuchungen.

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Poster 210

Molecular weight specific effect of stromal hyaluronan on malignant melanoma progression

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The glycosaminoglycan hyalouronan (HA) is increasingly deposited into the tumor-micro-environment (TME) of several aggressive tumor sub-types. Interaction between TME and tumor play a pivotal role for tumor progression and metastasis formation. Our work focuses on the progression of malignant melanoma (MM) in skin and the role of increased deposition of stromal HA.

Cultivated MM cells on fibroblast-derived extracellular matrix (ECM) decreased their expression of HA-metabolic enzymes depending on HA they found in their TME. In gene expression arrays, MM-cells showed an decrease of gene sets involved in proliferation, angiogenesis, and migration/invasion. In artificially generated ECM comprised of collagen with different low and high molecular weight (LMW/HMW) HA, ECMs with HMW HA showed a repression of MM-cell proliferation, whereas LMW had the oposite effect of increasing proliferation.

To simulate these findings *in vivo*, we developed a inducible HAS2-knockout (KO) mouse, which had a decreased HA skin deposition of ~70%. The HA reduction was specific to HMW HA. Tumors grown in HAS2-KO mice showed minor changes in tumor weigth and a significant decrease of endothelial marker expression. These findings support the dependency of MM proliferation on LMW HA, which was not targeted by the KO, and angiogenic potential on HMW HA, which was decreased on HMW HA depletion. Thus, the in vitro and *in vivo* models indicate a molecular-weight-specific HA effect on proliferation and angiogenesis in tumor cells.

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Poster 211

Molecular mechanisms underlying the tumorigenic influences of the chemokine CXCL11

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The chemokine, CXCL11, has been previously implied to control tumor growth and metastasis by either binding to CXCR7 or CXCR3. CXCR3 exists in the three splice variants, CXCR3A, CXCR3B, and the truncated splice form, CXCR3alt. While CXCR3A is associated with pro-tumorigenic effects CXCR3B rather exerts anti-tumorigenic influences. In the present studies, we sought to define the role of CXCR3 and CXCR7 in the migratory responses of tumor cell lines from different organs to CXCL11. We demonstrate that depending on the tumor cell line, CXCL11-induced cell migration either involves CXCR3, CXCR7 or both. This biased use of chemokine receptors is not reflected by their expression levels or subcellular localization in the various cell lines. We further observed that in distinct cancer cell lines, application of CXCR3 antagonists even potentiates the CXCL11-induced migratory responses, probably by preventing anti-tumorigenic influences associated with CXCR3B signaling. The observed cell type-specific signaling of CXCL11 puts clear limitations to the use of CXCR3 antagonists in cancer therapy.

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Poster 212

Tumor-associated macrophages (TAM) in human tumor slice cultures of gastric cancer

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Purpose:
High expression of Lipocalin-2 (Lcn-2), a siderophore binding protein, and TAM go along with a poor prognosis of patients with gastric cancer. Tissue macrophages are the main regulators of Lcn-2 in the extracellular matrix and have essential impact on tumor development and survival. Here we investigate whether iron deprivation influences the macrophage phenotype and chemotherapy resistance in tumor slice cultures (TSC) of gastric cancer.

Methods:
Tissue of gastric cancer is cut in 350µm thick slices and cultivated under standard conditions on a filter membrane, at an air-liquid interface. After 24h ex vivo, TSC are treated with Irinotecan (100nM) or Cisplatin (10µM) and Deferoxamin (10µM, 100?M) for 72h. After four days in vitro (DIV) the TSC are formalin-fixed, paraffin embedded and immunohistochemicallly analysed for tumor proliferation (KI67), CD68/ CD163 (macrophage marker) and Lcn-2 expression.

Results:
The proportion of Lcn-2 positive tumor cells and CD68 positive TAM remained stable after four DIV in TSC that did not respond to chemotherapy treatment. Deferoxamin alone significantly reduced tumor cell proliferation in TSC.

Conclusions:
TAM are well preserved and can be studied in TSC of gastric cancer. Iron deprivation reduced tumor proliferation significantly.

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Poster 213

Tumor slice cultures – a model for anti-angiogenic drugs?

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Angiogenesis plays an important role in tumor survival and progression. Many novel therapies target the vascular system; however in clinics most anti-angiogenic drugs, e.g. bevacizumab, yield limited benefit for the patients. In vitro models mimicing the complex tumor architecture are still scarce although they could serve as an enhanced model for preclinical drug testing. It has been shown that blood vessels persist in rodent organotypic hippocampal slice cultures even if there is no blood flow. The tight junctions formed by endothelial cells and the perivascular niche as well as the ability for vasoconstriction are preserved. Here we investigate the vascular system in tumor slice cultures of gastric and colon cancers.

Tumor resection specimen are cut by a tissue chopper into slices of 350 µm. The samples are cultivated on 6-well plates under standardized conditions for four days. Subsequently, slices are histomorphologically analyzed by staining the endothelial marker CD34.

For the analysis of the vascular system we reconstructed the vascular branches by CD34 staining. After four days in vitro a good preservation of the vasculature can be observed. First results indicate that the amount of small capillaries decrease at the site of the membrane, whereas the capillaries are still frequent at the tissue facing the air interface.

Blood vessels persist in tumor slice cultures from gastric and colon cancer without blood flow over four days of cultivation. As the tumor vasculature is an important part of the tumor micromilieu, this information is important when investigating drug effects on tumor stroma in tissue slice cultures.

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Poster 214

Evaluation von zellfreier DNA (cfDNA) aus Blut von Tumorpatienten

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Die Bedeutung zellfreier DNA und von Tumorexosomen aus Patientenblut als prognostischer und therapeutischer Marker wird gegenwärtig für eine Reihe von Tumorentitäten intensiv erforscht. Für Patienten mit Peritonealkarzinose fehlen allerdings aktuelle Daten zu diesem Thema. Des Weiteren ist die derzeitige Klassifikation der Peritonealkarzinose durch den Peritonealkarzionoseindex (PCI) durch eine eingeschränkte Interrater-Reliabilität gekennzeichnet. Die Berücksichtigung weiterer objektiver Parameter könnte zu einer Verbesserung der Klassifikation führen.

Es erfolgte eine Bestimmung der Konzentration an zellfreier DNA mittels direkter qPCR zur Amplifikation von LINE 1 Sequenzen.

Bei Magenkarzinompatienten und Patienten mit Peritonealkarzinose konnten wir mittels direkter qPCR den Gehalt an cfDNA im Plasma nachweisen. Der Vorteil dieser Methodik liegt daran, dass hier nicht erst aufwendige DNA-Aufreinigungsschritte notwendig sind. Der cfDNA Gehalt bei den von uns untersuchten Magenkarzinompatienten ist heterogen und patientenspezifisch, liegen aber im Mittel deutlich über dem von gesunden Vergleichsprobanden (1,65fach).

Die Nachverfolgung der cfDNA-Konzentrationen nach Chemotherapie und Operation soll Gegenstand weiterer Untersuchungen sein und Aufschluss über deren Anwendung als prognostischer oder diagnostischer Marker in der Behandlung von Tumorpatienten geben.

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Poster 215

Wie steht es um die Gesundheitskompetenz junger Tumorpatienten und was beeinflusst diese?

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Hintergrund:
Gesundheitskompetenz (GK) meint die Fähigkeit einer Person, Gesundheitsinformationen zu finden, zu verstehen, zu beurteilen und zu nutzen, um sich im Gesundheitssystem zurechtzufinden und informierte Entscheidungen treffen zu können. Eine gute GK führt wiederum zu einer Erhöhung der Lebensqualität. Bislang ist die Datenlage zur GK junger Tumorpatienten unzureichend.

Methodik:
234 Tumorpatienten zwischen 16 und 39 Jahren mit verschiedenen Tumorentitäten konnten in die Studie eingeschlossen werden. Die GK wurde mit der Kurzform des *European health literacy survey questionnaire (HLS-EU-Q16)* und die Lebensqualität mit der Kurzform des *Short Form Health Survey (SF-12v2)* erfasst. Um Prädiktoren von GK zu ermitteln, wurde eine multiple lineare Regression durchgeführt.

Ergebnisse:
Von allen eingeschlossenen Patienten hatten 28% eine ausreichende GK, verglichen zu 72% mit einer problematischen bzw. inadäquaten GK. In der Regression mit mehreren soziodemografischen und klinischen Variablen wurden folgende signifikante Prädiktoren für eine höhere GK ermittelt: höheres Einkommen, höhere Berufsausbildung, längere Zeit seit Diagnosestellung und Patienten, die nicht operiert wurden (R^2=0.10). Es besteht ein signifikanter Zusammenhang zwischen der GK und der psychischen Komponente von Lebensqualität (r=0.4).

Diskussion:
Die Ergebnisse verdeutlichen den Zusammenhang zwischen der GK und soziodemografischen bzw. klinischen Parametern. Auch kann eine Erhöhung der Lebensqualität durch eine Verbesserung der GK erzielt werden. Zukünftige Studien sollten anhand größerer Stichproben junger Tumorpatienten weitere Einflussfaktoren auf die GK untersuchen.

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Poster 216

Mimicking tumor microenvironments to study molecular weight specific impacts of hyaluronan and TGF-beta 1 presence on melanoma cells

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A higher expression of hyaluronan (HA) and transforming growth factor beta 1 (TGF-b1) in solid tumors is correlated with aggressive malignancy of melanoma both in preclinical models and in patients. However, the specific impacts of HA molecular weight (MW) and its presentation form (soluble vs immobilized) in combination with TGF-b1 levels are currently not understood in the regulation of tumor progression.

To address those questions, we set up biomimetic in vitro models to independently control the relevant parameters of the tumor microenvironment. We mimicked HA-rich microenvironments in the collagen I based 3D matrices by functionalization with HA of MW of 30–50 kDa (low MW; LMW-HA) and 500–750 kDa (high MW; HMW-HA). In there, we used covalent HA immobilization and presentation in soluble form. BRO melanoma cell lines with and without CD44 receptor expression were used to elucidate MW specific impacts and presentation forms of HA in the 3D matrices. We demonstrated that only soluble LMW-HA promoted cell proliferation in a CD44 dependent manner, while HMW-HA and immobilized LMW-HA did not. Furthermore, an enhanced cell invasion was found only for immobilized LMW-HA. In the presentence of TGF-b1 a further increase of cell invasion was observed only if immobilized HA of both molecular weights was presented. The above described MW specific impacts of HA correlated with a very strong and specific adhesive interaction of LMW-HA with CD44 expressing cells quantified by single cell adhesion measurements using soft colloidal force spectroscopy.

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Poster 217

Studying Glioma invasiveness using an ex vivo brain tissue slice co-culture model

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Glioblastoma multiforme (GBM) is the most common and invasive type of glial tumors, named so after their diverse radiological, histological and genetical footprint. Current treatment options are severely limited by the resistance of the tumors to radiation and available cytostatic drugs. Curative surgery is practically impossible because of the diffuse invasion of neoplastic cells into the brain tissue, leading to tumor remission. This makes the invasive aspect of the tumors a prime target for future therapies. Common approaches to study tumor cell invasiveness are performed in vitro, ignoring the importance of interactions between neoplastic and healthy brain tissues. *In vivo* animal models are difficult, costly and time consuming to perform. We developed an alternative system platform that combines the convenience of cell culture models and validity of *in vivo* studies by co-cultivating GBM spheroids ex vivo with organotypic murine brain tissue slices. Using tumor xenografts *in vivo*, we also prepared slices and co-cultured the xenografts with the brain tissue slices for the first time in the same fashion. Tumor proliferation and invasiveness was studied with common histological and immunohistochemical analysis methods. The slices were treated with temozolomide, Stattic and SGI-1776. The histological studies showed for the first time invasiveness of xenograft tumor cells into the healthy mouse brain tissue in an ex vivo model. We also modified the invasive behavior of tumor spheroids using small molecular inhibitors with this model, proving it as a modern and suitable screening platform for modern therapeutic compounds.

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Poster 218

Adipose tissue-secreted factors alter cellular lipid handling and induce a more aggressive phenotype in ER+ breast cancer cells

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Objective:
Recent studies demonstrate that obesity and excess accumulation of adipose tissue are independent negative prognostic factors for breast cancer. Our preliminary data, as well as published studies, indicate that factors secreted by adipocytes contribute to breast tumor progression by promoting migration and invasion capabilities of breast cancer cells. Our work focuses on the molecular mechanisms triggering epithelial-to-mesenchymal-transition (EMT) and tumor progression of human estrogen receptor-positive (ER+) breast cancer cells cultivated with adipocyte-conditioned medium (ACM), using a cell culture model.

Methods:
To analyze the impact of paracrine factors secreted from human adipocytes on breast cancer cells, we cultivated the ER+ cell line T47D with ACM. In addition, we performed quantitative real-time PCR, Oil Red O staining and immunofluorescence imaging of T47D cells to determine morphologic and molecular changes

Results:
Here we show that ER+ T47D breast cancer cells displayed morphological changes, enhanced lipid droplet accumulation, and mRNA up-regulation of EMT-associated genes, following cultivation with ACM. In addition, our analyses revealed changes in cell-cell contact formation and actin cytoskeleton reorganization.

Conclusion and Future Steps:
Our data indicate that factors secreted from adipocytes induce a more aggressive phenotype in ER+ breast tumor cells in vitro. Further we plan to investigate the molecular factors secreted by adipocytes which might be involved in breast tumor progression.

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Poster 219

Ösophageale Adenokarzinomzellen besitzen eine gesteigerte Säuretoleranz gegenüber gesunden Plattenepithelzellen

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Das Adenokarzinom des Ösophagus hat in den letzten Jahrzehnten in der westlichen Welt deutlich an Häufigkeit zugenommen, während der Entstehungsmechanismus weiterhin ungeklärt bleibt. 60% der ösophagealen Adenokarzinome entwickeln sich aus einem Barrett-Ösophagus heraus, einer durch Reflux von Magensäure verursachten Präkanzerose.

Die Zielsetzung dieser Arbeit war die Untersuchung der Säuretoleranz verschiedener Zelllinien, die unterschiedlichen Stadien des Barrett-Ösophagus‘ entsprechen. Dabei wurden die Zelllinien EPC-1 und EPC-2 (gesundes ösophageales Plattenepithel), CP-A (Barrett-Metaplasie), CP-B (high-grade Dysplasie), OE-33, OE-19, Flo-1 und SK-GT-4 (Adenokarzinom) mit einem angesäuerten Medium (pH 4, pH 3,5 und pH 3) in einem Proliferationsassay 15 oder 30 min stimuliert und mit einer Kontrolle verglichen.

Es zeigte sich, dass die Karzinomzelllinien und die Dysplasie-Zelllinie säureresistenter sind als die gesunden Plattenepithelzelllinien. Die EPC-1 und EPC-2 zeigten nach 15 min schon bei ph 4 lediglich eine Viabilität von 20% wohingegen die Karzinomzellen noch eine Viabilität zwischen 80 und 100% zeigten. Am resistentesten zeigten sich OE-33 und Flo-1 Zellen, die nach einer Behandlung bei pH 3 für 30 min noch eine Viabilität von 40% zeigten.

Daraus kann geschlussfolgert werden, dass gesundes ösophageales Plattenepithel durch gastrointestinalen Reflux *in vivo* vermutlich stark geschädigt wird und absterben kann. Dysplasien und Adenokarzinome des Ösophagus besitzen scheinbar säureprotektive Eigenschaften, die zu einer Resistenz gegenüber Reflux führen und Gegenstand weiterer Untersuchungen sein werden.

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Poster 220

Targeting the autophagic lysosomal pathway in glioblastoma with carnosine

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We investigated, whether inhibitors or inducers of autophagy (AP) enhance the anti-neoplastic effect of carnosine on glioblastoma (GBM) cells.

Cells from 2 GBM lines were exposed (48 h) to bafilomycin (Baf; inhibitor of AP; 100 nM) and rapamycin (Rap; inducer of AP; 100 nM), in combination with carnosine (Car; 50 mM). Cell viability was determined by measuring ATP in cell lysates. Expression of LC3B II and p62 as markers for AP was quantified by western blotting.

Both lines responded to Car with a loss of viability. Viability was also reduced in Baf. Combining Baf with Car revealed no synergistic effect. Rap reduced viability less pronounced than Car or Baf, but an additive effect was observed when Car was present. Immunoblotting revealed reduced expression of LC3B II in the presence of Car in U87 and enhanced expression in T98G. Baf induced LC3B II expression in both lines. In combination with Car, expression was further increased in T98G but not in U87. Incubation in Rap attenuated expression of LC3B II in U87 and augmented it in T98G. Combining Rap with Car decreased LCB II protein relative to treatment with Rap alone. The relative amount of p62 was not altered in the presence of Car, but was enhanced in the presence of Baf. Combining Car with Baf, p62 expression was further increased. Rap attenuated p62 expression in both lines with no additional effect of Car.

With regard to LC3B II expression Car mimics the effect of Rap whereas this is not the case with regard to p62. The AP inhibitor as well as the inducer reduced viability, but there appears to be no synergistic effects of Car in combination with the compounds.

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Poster 221

Loss of MARCKS increases chemoresistance

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The development of resistance against chemotherapy is a major cause of tumor relapse. Emerging evidence implicates the PIP_2 binding protein MARCKS in a critical role for the progession of chemoresistance. Especially in colorectal cancers (CRC), MARCKS is frequently genetically deleted or functionally uncoupled through enhanced phosphorylation. We found that either reintroduction of MARCKS or overcoming its hyperphosphorylation via the receptor tyrosine kinase inhibitor bosutinib resensitized different CRC models to chemotherapeutic interventions e. g. 5-fluorouracil (5-FU).
The activity increase of the ABCB1 transporter is a well-known mechanism how CRC protects itself against chemotherapy. We could show that mechanistically, upon bosutinib treatment, MARCKS translocates from the cytosol to the plasma membrane. Simultaneously, ABCB1 is expelled from the membrane to intracellular compartments. Measuring different pools of phosphatidylinositols with fluorescent biosensor proteins showed that reconstitution of MARCKS function reduces the amount of available PIP_2 via sequestration.

Subsequent time lapse microscopy revealed actin polymerization as well as clathrin and dynamin translocation typical for endocytic processes. Endocytosis is largely dependent on the precise spatial control of different PIP_2 species. Here the beneficial effect of bosutinib on ABCB1 activity could be significantly reduced via the inhibition of endocytosis. Taken together these findings show an important role for MARCKS in the progression of CRC malignancy as well as offering a pharmacological intervention to potentially reverse this undesirable state.

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Poster 222

Effects of the interaction of opioid- and CXCL12 receptors on tumor progression

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The CXC chemokine, CXCL12, promotes growth and metastasis of tumors from many organs. Depending on the tumor cell type these effects seem to be either mediated by the CXCL12 receptors, CXCR4 and/or CXCR7. Many tumors further express endogenous opioid peptides, which by acting via the opioid receptor subtypes MOR, DOR or KOR additionally control tumor progression; similar effects are further attributed to exogenously applied opioids. This is especially intriguing since CXCR4 and opioid receptor subtypes are known to interact at different levels, eventually allowing for silencing of CXCR4 signaling, receptor desensitization or changes of CXCR4 expression levels. Whether a similar interplay exists between opioid receptors and CXCR7 is presently unknown. It is further unknown of how such interactions interfere with the effects of the CXCL12 and opioid system on tumor progression. To address these issues, we have now tested how opioids affect CXCL12-dependent chemotaxis and cell invasion of various tumor cell lines which either use CXCR4 (A549, DLD-1, A772), CXCR7 (A767) or both (MDA231) for mediating CXCL12 signaling. We found that agonist-dependent activation of DOR (metenkephalin), KOR (U69593) or MOR (DAMGO) in the various cancer cell lines either potentiated or attenuated CXCL12-dependent chemotaxis and cell invasion. Moreover, these modulatory influences likewise occurred in cell lines using CXCR4, CXCR7 or both for mediating CXCL12-signaling. Our findings favor the assumption that opioids modulate CXCL12-dependent tumor progression in a complex manner, depending on both the opioid receptor subtype and cell type.

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Poster 223

An in vitro study of ultrasound-induced HT combined with radiation therapy for glioblastoma cells

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Ultrasound (US) is a precise way to generate hyperthermia (HT, 40-45°C) in tissue. Synergistic effects of US-HT and radiation therapy (RT) are expected. Up to now, few data are available regarding US impact on cancer cells. Glioblastoma is an invasive and common brain tumor with high recurrence rate. Therefore, new therapy options are necessary. Goal of this study was to combine US-HT and RT in a cell culture experiment to treat glioblastoma cells.

Glioblastoma cell line T98G was cultured and treated in 96 well plates. A 150kV X-ray device (DARPAC 150-MC) was used for RT at doses of 0-20 Gy. New developed US cell applicator with 96 elements sonicated cells with max. intensity of 1.5W/cm^2 at a frequency of 1 MHz for HT (40-45°C, 20 min). Temperature was monitored in real-time with a thermal camera (PI450). For combination, RT at 10 Gy was conducted 15 or 60 min post water bath-HT (43°C, 20 min). Cell viability (NAD(P)H); WST-1 assay), membrane damage (LDH release) and proliferation (DNA synthesis; BrDu assay) were evaluated 72h after treatment.

The RT dose curves demonstrated a dose-dependent loss on cellular NAD(P)H levels. Released LDH increased from 25% (0 Gy) to 55% (20 Gy). DNA synthesis nearly stopped at dose above 5 Gy. Cells treated by US-HT showed lower cell viability of 75% compared to water bath-HT (80%). Short time interval between HT and RT exhibited highest efficiency.

Compared to water bath-HT, the higher efficiency of US-HT indicates additional biomechanical effects on cells. In the future, mechanisms and effects of the combined treatment need to be investigated.

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Poster 224

STAiR18 – a novel long noncoding RNA and its role in glioblastoma cell invasion

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With an average survival of about a year, Glioblastoma is the most common and aggressive human cancer that arises within the brain. It is characterized by an uncontrolled proliferation and infiltration of glioblastoma cells into the adjacent healthy tissue, forming a tumor without clear margins. Given that the indefinable borders impede a complete surgical removal and the microenvironmental heterogeneity causes resistance to radio- and chemotherapy, glioblastoma remains essentially untreatable. Thus, analyzing the molecular mechanism of glioblastoma cell invasion is crucial in order to optimize therapeutic approaches.

In a genome-wide transcriptome analysis performed in different human cell lines, we previously identified several yet unknown long non coding RNAs differentially regulated in oncologically and cell cycle relevant processes. Amongst these transcripts, STAiR18 – an ubiquitously expressed lincRNA – maps to two actively transcribed genomic loci originating from a recent duplication event specific for the human lineage. Therefore, an impact of STAiR18 on cognitive processes is considered. To address this, we performed an RNAi-mediated STAiR18 knockdown in A172 glioblastoma cells, which led to an increased cell adhesion resulting in an elevated migration and invasion of A172 cells. Further, STAiR18 knockdown and subsequent genome-wide transcriptional analysis uncovered a pattern of differentially expressed genes involved in cytoskeleton regulation. Moreover STAiR18 seems to interact with the transcription factor FoxM1, which is overexpressed in malignant glioma and inversely correlated with patient survival.

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Poster 225

Trib1 deficiency modulates function and polarization of bone marrow derived macrophages

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Trib1, a member of the mammalian Tribbles homolog pseudokinase family, has been implicated in regulation of cell differentiation, proliferation and metabolism. Here, we investigated the functional consequences of Trib1 deficiency on macrophage phagocytosis, migration and M1/M2 polarization. Bone marrow derived macrophages (BMDMs) from Trib1 deficient (Trib1 $^{-/-}$) mice showed elevated phagocytotic capacity correlating with an upregulation of several scavenger receptors. Trib1 $^{-/-}$ macrophages also exhibited diminished migration in the presence of the chemokine MCP-1, associated with reduced expression of the MCP-1 receptor Ccr2. Furthermore, Trib1 deficiency attenuated the response of BMDMs to both M1 and M2 stimuli: We observed a reduced induction of M1-marker genes Il6, Il1b and Nos2 upon LPS/IFN? stimulation, as well as a reduced induction of M2-marker genes Cd206, Fizz1 and Arg1 upon IL-4 stimulation. Functionally, Trib1 deficiency led to lower secretion of proinflammatory cytokines (IL 6, TNF?, IL 1? and CXCL1) and lower NO production in M1 polarized macrophages. Moreover, Trib1 deficiency negatively influenced LPS/IFN? mediated JAK1/STAT1 signaling activation, resulting in reduced STAT1 and JAK1 phosphorylation. M2 polarized Trib1 -/- BMDMs showed decreased phosphorylation of STAT3, STAT6, JAK1 and JAK3 molecules. In conclusion, our findings suggest that Trib1 plays an important role in controlling macrophage M1 and M2 polarization via the JAK/STAT signaling pathway.

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Poster 226

Adamantanes as building blocks for novel TRPC5 channel modulators

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The transient receptor potential (TRP) channels are a family of non-selective cation channels, comprising 28 members in mammals. They are involved in a plethora of physiological and pathophysiological processes.

Among these, the canonical TRP channel 5 (TRPC5) is almost exclusively found in neuronal tissues. TRPC5 is involved in neuronal plasticity and axonal pathfinding in hippocampal neurons and has been shown to influence the formation of memory. Furthermore, TRPC5 may interfere with the reproductive axis in rodents. TRPC5-deficient transgenic animals show impaired motor coordination and reduced fear behavior.

In the past years, intensive research aimed at identifying novel small molecules to enable precise pharmacological modulation of TRPC5 channels. The screening of a compound library containing almost 17,000 different chemical structures revealed several compounds with adamantane substituents. These acted either as channel activators or channel inhibitors. Adamantanes without prominent side chains were selective, but poorly potent inhibitors of TRPC5 and TRPC4 channels (IC_{50} of 1-10 µM).

Adamantane derivatives like memantine and amantadine are used in the treatment of neurodegenerative diseases such as Parkinson's disease and dementia. As far as we know, potential effects on TRPC5 channels have not yet been considered. For the next generation of TRPC5 channel modulators adamantanes – as building blocks – might have the potential to promote the development of ready-to-use small molecules to treat TRPC5-associated disorders.

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Poster 227

Automated Classification of the Pap Smear Grade with an Artificial Neuronal Network

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The purpose of this work is the development of algorithms to assist biomedical scientists in the diagnosis of cancer in a microscope slide. An autonomous system detects pre-cancerous changes of cell nuclei in two-dimensional microscopy images of a Pap smear. Abnormal cells are classified in grades of dysplasia to predict the progression to cancer. Our approach utilises a method of machine learning based on supervised learning algorithms. We used annotated images of cell nuclei to train and test the system. Neural networks are a presently spreading technique which can be used for image recognition in a different way from traditional computing methods. Both medical care and research provide extensive image data, therefore machine learning is a reasonable software solution to analyse biomedical data sets.

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Poster 228

Erythrocytes prevent degradation of carnosine by serum carnosinase

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Oral administration of carnosine (β-alanyl-L-histidine) has successfully been applied for the treatment of different human diseases despite the fact that the dipeptide is rapidly degraded by serum carnosinase. Here we investigated whether red blood cells can protect the dipeptide from cleavage.

Human erythrocytes were incubated in the presence of carnosine and cell viability was determined by measuring the amount of ATP in cell lysates. Liquid Chromatography coupled to Mass Spectrometry was used to measure the intracellular concentrations of carnosine under different conditions.

After 48 hour incubation in the presence of carnosine (50 mM) viability was enhanced in red blood cells of 7 volunteers and unchanged in erythrocytes from 3. Measuring intracellular abundances of carnosine in erythrocytes after 4 hour exposure, we monitored a concentration dependent uptake of the dipeptide without visible saturation (0.1 mM to 100 mM) resembling a biphasic kinetic (85± 23.24 µM in erythrocytes exposed to 50 mM). After 4 hour incubation of erythrocytes in the presence of human serum, extracellular carnosine (initial concentration: 6 mM) was completely degraded. Nerveless, we could still detect 1.75± 0.21 µM of carnosine in the erythrocytes.

Here, we demonstrate that despite carnosine's inhibitory effect on glycolysis in tumor cells no impairment of ATP production can be observed in erythrocytes exposed to carnosine. Although, we do not know how the dipeptide enters red blood cells it is obviously taken up which may explain how it can be protected from degradation by serum carnosinase.

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Poster 229

Cultivation of human norovirus in B cells and colon adenocarcinoma cells.

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Question:
Human noroviruses are among the most common pathogens that cause acute gastroenterits. Currently there is no immunization or drug therapy available, because little is known about the molecular mechanisms of human noroviruses due to the lack of a sufficient cell culture system. The objective of the project is to verify a published cell culture model (Jones et al., Nature Protocols, 2015) and to improve its efficiency.

Methods:
B cells (BJAB cells) and colon adenocarcinoma cells (HT-29 cells) were incubated with norovirus positive stool. Most of the samples tested were GII.4 strains while some were GII.2 strains. They were investigated in a co-culture system and by direct infection of B cells. In the co-culture system BJAB cells and HT-29 cells were cultivated in the same well using a transwell insert (Sarstedt AG Co., Nümbrecht, Germany). BJAB cells were cultivated in the basal compartment and HT-29 cells on top of the transwell's membrane. Additional attempts were made to establish a direct infection of the HT-29 cells. Validation of infection was done by quantitative RT-PCR.

Results and conclusion:
Some samples showed a reproducible increase of virus after 3 to 5 days. An up to 7-fold change in the co-culture was observed while there was no increase of virus in the direct infection of the BJAB cells. However there was an increase of norovirus in HT-29 cells cultivated separately. This suggests that some noroviruses replicate in the colon adenocarcinoma cells without passage through B cells. Considering that a high number of samples did not replicate in this system, there is need for further optimization.

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Poster 230

FLICA method revealed unspecific binding

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Caspase-1 plays a pivotal role in inflammation and inflammasome research. It cleaves, in a multiprotein-complex with NLRP3 and ASC, the proinflammatory cytokines IL-1ß and IL-18 into their mature forms. Currently, three methods to demonstrate activation of caspase-1 exist: Western blot analysis detecting the cleaved p20 subunit, microscopy staining of ASC speck formation and flow cytometry using FLICA (Fluorescent Labeled Inhibitors of CAspases).

The FLICA method uses a designed ligand which covalently binds the active center of caspase-1 due to the fluoromethyl ketone (FMK) reactive entity. This leads to an irreversible inactivation of the enzyme. The specificity is based on an amino acid sequence and the fluorescent tag allows the detection of the protein, its interaction partners and its localization.

Our studies of inflammasome activation in primary monocytes revealed controversial results using FLICA staining. Flow cytometry analysis of monocytes stimulated with LPS and ATP revealed that FLICA preferentially marked dead cells. Only 1-2% FLICA-positive cells were detectable in the vital population. To further analyze the FLICA binding, the monocytic cell line THP1-defCASP1, deficient for caspase-1, was used. The differentiated THP-1 were mechanically disrupted to promote cell death. 92% of the disrupted THP1 control cells were FLICA-positive and 84% of the disrupted THP1-defCASP1 cells. Western blot analysis of THP1-defCASP1 cells confirmed the absence of caspase-1.

Our results show that FLICA does not only bind to active Caspase-1 but also to other cellular components, especially in dead cells.

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Poster 231

A modular multidirectional light sheet microscope for three-dimensional long-term analysis of living specimens

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Using three-dimensional long-term analysis of living specimens allows completely new insights into biological processes. But the standard commercial bioimaging systems are both closed and specialised for a single scientific application. To cover a large number of research problems we developed a highly modular multidirectional selective plane illumination microscopy (mSPIM) platform. One major advantage of this technology is the minimal phototoxicity and consequently the low impact on sample health and biological process. However, another formidable challenge is to handle several specimen-sizes. Thus, we designed a fully modular sample chamber that can adapted to fit the needs of a certain research problem, e.g. magnification, specimen size & environmental conditions. Additionally, we developed an all-in-one control software with a high degree of automation that offers advantages such as real-time processing, a high reproducibility by using measurement presets and logging all system parameters and also the upgradeability of sensors or new measurement methods.

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Poster 232

Ca2+-dependent macropinocytosis of non-crystalline calcium-phosphate nanoparticles triggers IL-1β release in human monocytes

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Calcium is responsible for mineralization of bone and tissue and therefore has to be strictly regulated to prevent uncontrolled ectopic and vascular calcification. Under pathological conditions or at sites of inflammation the extracellular calcium concentration increases, which could result in the spontaneous formation of calcium-phosphate-particles. Thanks to the presence of crystallization inhibitors in serum such as fetuin-A, these nanoparticles are stabilized in a non-crystalline state and could be cleared by phagocytes. Our investigations show that the uptake of spontaneously formed calcium-phosphate-nanoparticles under cell culture conditions leads to the activation of the NLRP3 inflammasome in human monocytes resulting in the release of high concentrations of the pro-inflammatory cytokine IL-1β. The results from our study reveal high extracellular calcium concentrations and the consequential formation of nanoparticles as danger signals for human monocytes. How the exact intracellular activation mechanism of these nanometer-sized particles looks like is still a conundrum which needs to be solved.

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Poster 233

Keratins regulate mitochondrial distribution and metabolic activity in human keratinocytes

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The epidermis undergoes a continuous cycle of proliferation, differentiation and regenerates upon wounding. In these settings, differential expression of cytoskeletal keratins supports adaptation of keratinocytes to mechanical stress. Additionally, keratins regulate protein biosynthesis, an energy-consuming process. Missense mutations in epidermal keratins K5 and K14 cause the blistering skin disorder epidermolysis bullosa simplex (EBS). The impairment of tissue regeneration and wound healing defects in EBS and additional keratin disorders suggests that keratin mutations may be involved in cell-specific and context-dependent regulation of mitochondrial activity. We have recently found an altered distribution of mitochondria in the skin of mice lacking all type I keratins. Corresponding keratinocytes showed an altered composition of the electron transport chain and of mitochondrial lipids, accompanied by a change in oxygen consumption.

Here we investigate the relationship of keratins and mitochondria in human keratinocytes derived from EBS patients, carrying a severe K14 mutation. In those keratinocytes, keratin filaments are collapsed into cytoplasmic aggregates. We show that this is accompanied by an altered mitochondrial distribution. Additionally, mitochondrial respiration is impaired in EBS cells, with differences in respiratory chain composition in comparison to control keratinocytes. These results indicate that keratin aggregation triggers mitochondrial dysfunction. Future work will aim for the mechanism how epidermal keratins directly or indirectly regulate mitochondrial function.

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Poster 234

Defined fibrillar collagen matrices and interfaces reveal regulating cues of cancer cell behavior

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Studying cells in 3D collagen matrices is far more representative of physiological and pathological conditions than a traditional 2D cell culture platform. Deciphering biophysical and biochemical parameters of such matrices to affect cell response would support a better understanding of native tissues.

Currently, many reports suggest that the local mechanical properties of single fibrillar components, rather than the bulk matrix stiffness, dominantly regulates cancer cell behavior. Here, we engineered collagen matrices with different fibril diameter (660 and 850 nm) and similar pore size (11 μm). Additionally, a zero-length crosslinking agent was used to stepwise increase fibril stiffness without affecting pore size and fibril diameter. We found that fibril bending stiffness as the local mechanical cue in the regulation of cell spreading and cluster formation of two distinct breast cancer cells, MDA-MB-231 and MCF-7 cells.

In another study we challenged breast cancer cells (MDA-MB-231) with sharp interfaces of defined collagen matrices, mimicking the impact of structural heterogeneous native tissues. Cell migration was found to change from a random to a persistent directed migration while crossing the matrix interface from dense to open network porosity (similar to breast cancer tissue). Importantly, this phenotypical switch was not observed in the opposite conditions and with independent increase of matrix stiffness by crosslinking. Ongoing studies show, phenotypically switched cells to exhibit a distinct cluster of relevance metastatic genes.

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Poster 235

Single cell genomics in AD pathology and healthy controls

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The human brain has been suggested to contain a certain number of aneuploid cells. Most of them die via programmed cell death during development, but a small but constant fraction apparently escapes those apoptotic processes. This variation in DNA content (DCV) was found to appear in around 10% of the neurons, but is certainly not evenly distributed throughout different brain regions and is also changing with age. However, this genomic alteration might cause chromosomal instability which is proposed to make neurons more vulnerable to disease related pathology like accumulation of Aβ-peptide or tau-protein in Alzheimer's disease (AD). Here, we used single cell genomics to analyse somatic genome variations in the temporal lobe of normal elderly subjects and AD patients. Cases with a high ratio of DCV were preselected through immunohistochemical DNA content quantification. Using laser capture microdissection and subsequent sequencing of single cells, we obtained first data on genome variations and chromosomic instability by bioinformatic analysis. The results might allow a deeper understanding how DCV in general and sequence variation in particular, are related to AD pathology.

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Poster 236

A biomathematical model of human erythropoiesis and iron metabolism

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A frequent complication of renal disease is anemia and iron deficiency. Anemia therapy of these patients requires both, EPO and iron medication. However, excessive iron medication can cause iron overload. It is a challenge of anemia treatment under chronic kidney disease to control hemoglobin levels of these patients in a desired range.

We combined our previously established model of human erythropoiesis including comprehensive pharmacokinetic models of EPO application with a newly developed model of iron metabolism including iron supplementation. Equations were derived by translating known biological mechanisms into ordinary differential equations. The model can explain time courses of erythrocytes, reticulocytes, hemoglobin, hematocrit, red blood cells, EPO, serum iron, ferritin, transferrin saturation, and transferrin under a variety of scenarios including EPO and iron application into healthy volunteers. Unknown model parameters were determined by fitting the predictions of the model to time series data from literature.

Following our ultimate goal of establishing a model of anemia treatment in chronic kidney disease, we aim at translating our model to this pathologic condition in the near future.

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Poster 237

Characterization of transcription factor variants in the brain of an Alzheimer's disease mouse model

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The neuropathological processes of Alzheimer's disease (AD), leading to neuronal death, are accompanied by dysfunctions of cell cycle related proteins and differentiation control of neurons. Especially neurons with a high competence of plasticity like hippocampal neurons are prone for these disturbances. Smad signaling, the canonical part of the TGF-β superpathway, governs neuronal differentiation during ontogenesis and contributes to neuronal activities in the adult brain. Recent reports suggest a substancial impact of Smad proteins on synaptic function and neuronal plasticity. In AD Smads reveal an altered subcellular location leading to compromised functionality.
A mechanism to regulate expression level and regional distribution of neuronal proteins is the use of varying lenghts of 3' untranslated regions (3'UTR) in mRNA. Brain-wise expressed transcripts often show longer UTRs to enable more specific expression in the nervous system. We aimed to identify different Smad mRNA isoforms in AD-related brains of transgenic APP mice which model a central neuropathological feature of AD.

Control and transgenic individuals aged 22-24 months were used to isolate tissue material from hippocampal areas by laser-based microdissection. After RNA isolation, transcript isoforms were identified using Illumina sequencing. Quantitative and qualitative analyses allowed the assessment of differences in expression between brain regions and individuals. Initial results suggest the presence of diverse polyadenylation sites leading to transcripts of varying length.

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Poster 238

The Neurokinin-1-Receptor as a possible site of action in lycorine induced emesis (LIE)

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Lycorine (Lyc) as the main alkaloid of the Amaryllidaceae plant family and induces severe nausea and emesis after oral or intravenous administration in humans and animals. Therefore lycorine induced emesis (LIE) serves as a model system for further investigation of molecular processes involved in common emesis.

Former studies concerning LIE have shown complete abolishing of symptoms through treatment with the Neurokinin-1-receptor (NK1-R)-antagonist maropitant, suggesting Lyc acts as an agonist on the NK1-R.

Whereas binding of the endogenous ligand substance P (SP) to the NK1-R leads to intracellular calcium mobilization and receptor internalization, own previous studies revealed Lyc is not able to induce calcium mobilization in HEK293 NK1-R overexpressing cells.

Further experiments were performed with confocal fluorescence laser scanning microscopy, where the effects of Lyc and SP on HEK293 cells stably overexpressing a NK1-cyan-fluorescent-protein (CFP) fusion-protein and cells expressing the NK1-R endogenously (Capan1) were examined.

Results show massive membrane blebbing induced by SP in both cell lines. In contrast to that Lyc was only able to induce blebbing inconsistently. Unexpectedly for neither SP nor Lyc receptor internalization could be shown.

To exclude the possibility of CFP interfering with the internalization process, fluorometric calcium assays with an internalization inhibitor are pending.

In case the mode of action of Lyc is not due to NK1-R signaling, to reveal yet unknown molecular mechanisms of LIE by interactions on other receptors may have potential therapeutic implications.

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Poster 239

Toward identification of keratin-associated proteins using BioID

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Keratin cytoskeletal proteins protect epithelia against various mechanical and other stresses by interaction with desmosomes and hemidesmosomes. Moreover, we have recently found that keratins affect mitochondrial distribution and activity, raising the question if keratins directly interact with mitochondria. The highly insoluble nature of keratins under physiological buffer conditions requires novel approaches to identify candidate proteins that mediate keratin-dependent mitochondrial distribution, composition and activity.
To identify novel keratin-interacting proteins in cultured mouse keratinocytes, we are exploiting the proximity-dependent biotinylation assay (BioID) to identify potential keratin K5 interaction partners involved in mitochondrial regulation. BioID includes a mutant biotin ligase from E-coli fused to a protein of interest which subsequently will biotinylate all proteins in a range of approximately 10nm. Expression of a K5-biotin ligase fusion protein in keratinocytes enabled formation of a normal cytoskeleton, highly similar to control transfectants. Pilot studies established optimal conditions for enrichment of biotinylated proteins which will be identified by mass spectrometry and bioinformatics tools. Candidate proteins will then be investigated by gain and loss of function studies, aiming to phenocopy the defects seen by altered keratin expression. Next, the mechanisms by which keratins affect mitochondrial protein and lipid composition will be addressed. This study utilizes a promising new method to elucidate the role of keratins on mitochondrial function and positioning in the epidermis.

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Poster 240

Characterization of the vitality status of vascularized and non-vascularized retinae of different post mortem ages

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Successful cultivation of organotypic retinal cultures depends on a complex variety of internal (e.g. vascularization, species differences) and external (e.g. culture conditions, post mortem time) factors. External conditions ca be standardized and monitored, whereas internal factors of the retinal tissue can differ considerably and therefore influence the vitality and the outcome of the cultivation. As part of the main-project we want to establish a long-term retina culture from pig eyes taken from a slaughter-house to reduce the use of laboratory animal (“3R principle”). Main problem is the critical post mortem time after enucleation due to transportation time. Therefore, we characterized cell vitality and oxidative stress level of Mueller glial cells and neuronal ganglion cells and compared vascularized (pig) and non-vascularized (guinea pig) retinae of different post mortem times (0-6 hours). Laser scanning microscopy combined with fluorescent *in vivo* dyes such as cell tracker green, mitotracker orange and FM143 were used to visualize the glutathione metabolism of retinal cells. Additionally, immunohistochemical stainings of microglia cells, astrocytes, Müller glia cells and photoreceptor segments were performed. We observed a post mortem time related change of increased oxidative stress in both retina types. However, our results indicated that a post mortem time (transportation time) of less than 6 hours might be tolerable to maintain the general vitality of retinal tissue and these retinas might be usable for further cultivation procedures.

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Poster 241

Quantification and cellular localization of iron in brain of patients with Parkinson's disease and age-matched controls

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Aims:
Iron is fundamental for neurons e.g. by playing key roles in transmitter synthesis or myelination. In contrast, high concentrations of free iron raise oxidative stress levels and it is well known that iron increases in the substantia nigra (SN) in Parkinson's disease (PD). However, there is only little knowledge on quantitative iron concentration and distribution in the human SN.

Methods:
This project aims at examining the localization and concentration of iron in different cell types in nigrosom 1, SN. Therefore, human brain stem was stained for cellular markers (anti-GFAP, IBA-1, Olig2, HuC/D). Ultrapure nickel was used to mark respecting cell types for quantitative analysis via ion beam microscopy using particle induced X-ray emission. The combination of PIXE and histology offers a huge variety to ascertain the localization and concentration of iron.

Results:
For the first time, quantitative analysis of iron was performed in selectively stained cells of the human PD SN. High iron concentrations are found in neurons bound to neuromelanin. In PD, oligodendroglia and microglia show higher iron deposits than neurons. The assumed depletion of ferritin storage combined with increased cellular iron implies ultimately an enlarged LIP in PD. This hypothesis is underpinned by an increased intensity of Perls stain.

Quantitative trace element analysis is essential to characterize the role of iron in oxidative processes in PD. Therefore, our approach gains new insights into iron levels of different cell types in neurodegeneration. Nevertheless, mechanisms leading to an increase in iron remain subject of further investigation.

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Poster 242

Small area variation in demographic aging: Informal and formal nursing care ratios and care preferences of senior citizens inform health care planners

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Objective:
Demographic aging affects the number of older individuals potentially in need of care and age groups of younger individuals potentially providing formal and informal care. This study examines the current and future demographic aging and care preferences on a county level in Saxony.
Methods:
To analyze demographic aging, formal (FISR) and informal intergenerational support ratios (IISR) based on population data from the Federal Institute for Research on Building, Urban Affairs and Spatial Development (BBSR) were used. Ratios were calculated for every county in Saxony from 2012 to 2035. Care preferences of senior German citizens were determined by a telephone survey (n=101). Individuals were asked to report the care preferences for care settings.

Results:
FISR and IISR tend to progress in similar ways and are reduced by 50% by 2035. Regarding nursing care preferences, the majority preferred being cared for at home.

Implications:
Upcoming care ratios may inform community health care planners and decision makers on critical constellations in advance. Strategies addressing informal and formal caregiving to ensure the future elderly care need to be developed and implemented.

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Poster 243

The LIFE-Biobank – High Quality Biospecimen for Reproducible Research

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The quality requirements for biological samples in biomarker research have grown over the last years. This is due to new high resolution Omics-technologies and developments in precision medicine. However, samples with high and comparable quality are hard to find. This could lead to non-reproducible data or false associations.

Biobanks are important research infrastructures and can support research and developments in precision medicine. The Leipzig Research Center for Civilization Diseases (LIFE) is searching for molecular and lifestyle associated causes of civilization diseases. As one of the central institutions of the LIFE-project the LIFE-Biobank is supporting this aim by assuring high quality and standardized handling of all samples collected from participants of the population based cohorts and patients from selected disease cohorts.

Due to the high diversity of collected samples different handling steps and types of storage are required. The samples are processed in a standardized way using standard operating procedures assisted by automation and documentation of processing times and all kinds of deviations from the protocols. The whole process can be tracked by CryoLab an inhouse laboratory information management system. The quality of the processed samples is assessed by using time stamps, HIL-indices and ratios of absorbance for nucleic acids. With this setting approximately 1 100 00 aliquots from 39 000 visits (25 000 participants) have been collected. Samples and data are available for researchers and more than 350 projects could be realized using data (45 projects also using biomaterial).

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Poster 244

Development of a LC-MS/MS-method for the quantification of resolvins and related lipids

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Objectives:
Many chronic diseases such as atherosclerosis or Alzheimer‘s disease share one unifying component, which is excessive inflammation. The acute inflammatory response can be divided into the initiation and resolution phase. While eicosanoids of the ?-6 PUFA arachidonic acid are the main players in the initiation phase, the resolution phase is orchestrated by metabolites of ?-3 PUFAs, such as resolvins. Their endogenous concentrations are very low.

Material and Methods:
Plasma samples were processed by protein precipitation and on-line solid phase extraction. Fast chromatographic separation coupled to MS analysis was performed in negative electrospray ionization mode. 36 scheduled multiple reaction monitoring transitions for the quantification of resolvins and related lipids are included in the presented method.

Results:
The chromatographic separation was performed within 7 min and a total run time of 10.5 min. Linearity was approved for a concentration up to 10,000pg/mL. The LODs were 4pg/mLto 13pg/mL for resolvins and 3pg/mL to 152pg/mL for related lipids. In native plasma 17,18-DiHETE, 19,20-DiHDPA, 8-, 15-, 18-HEPE and 7-, 10-, 13-, 16-, 17-, 20-HDoHE could be detected. These results may differ studying samples from patients with acute inflammatory state.

Conclusion:
A fast LC-MS/MS-method was developed and validated for the simultaneous quantification of 36 resolvins and related lipids. The method can be applied in disease cohorts or animal models together with the established LC-MS/MS-method for the quantification of eicosanoids. This allows us to investigate the agonist-antagonist-network in inflammation.

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Poster 245

Associations of apolipoproteins and coronary artery disease in the Leipzig LIFE Heart Study

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Objectives:
Dyslipoproteinemia is considered as one of the major risk factors of coronary artery disease (CAD). Lipoprotein-associated apolipoproteins (apos), which are key regulators of lipoprotein metabolism, are discussed as promising predictors of CAD. In the present study, we investigated associations of apo plasma levels with CAD to explore their value for diagnosis and risk assessment.
Methods:
In 911 subjects of the observational Leipzig LIFE Heart Study undergoing first coronary angiography for suspected CAD, associations of 8 apos with obstructive CAD (stenosis ?50%) were assessed using binary logistic regression analysis. Plasma apos were quantified via tandem mass spectrometry.

Results:
Basic plasma concentrations of apos A-I, A-II, A-IV, B-100 and C-I differed significantly between CAD cases and controls. Besides great influence of lipid?lowering therapy on apoB-100 and associated apos, highest impact of confounding variables on apo concentrations has been seen for fasting, decreasing apoA-IV levels by 20%. Upon adjustment for these factors, apos A-I, A-IV and B-100 were significantly associated with CAD in univariate analysis. After additional adjustment for related lipids, only association of apoB-100 remained significant (odds ratio, OR=1.39). However, significance was lost in consideration of traditional risk factors. In patients suffering from three-vessel disease, significant association of apoA-IV and CAD (OR=0.60) was independent from known risk factors.

Conclusion: Atherogenic apoB-100 and atheroprotective apoA-IV were confirmed as potential markers for CAD risk assessment in the general population.

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Poster 246

Bioactive Lipids, Inflammation, and Coronary Artery Disease

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Objectives:
The aim of this study is to investigate the relationship between the eicosanoid metabolism and atherosclerosis. Eicosanoids are bioactive lipids, which regulate the initiation, progression, and resolution of inflammation

Material and Methods:
Plasma of patients of the LIFE Leipzig heart study without coronary stenosis, patients with a stenosis (?50% in all three coronary vessels), as well as patients with acute myocardial infarction (n=1000 each) will be investigated. Detailed phenotyping and genotyping data as well as data of established markers of coronary artery disease are available. We developed a method applying liquid chromatography coupled to tandem mass spectrometry to quantify 94 eicosanoids as well as 7 polyunsaturated fatty acids mainly of the proinflammatoric arachidonic acid (AA) metabolism. This method is currently being extended by the proresolute metabolites of omega-3 fatty acids such as resolvins.

Results:
In a subcohort of 500 patients of the LIFE Leipzig heart study we already found 6 PUFAs and 20 eicosanoids, which derived mainly from AA with a high interindividual variation (from 16 % for 5,6-DHET (5,6-dihydroxyeicosatrienoic acid)) to 77 % for 13-HODE (13-hydroxyoctadecadienoic acid). We found a significant positive association of arachidonic acid (p=0.019) and a negative association of 5,6-DHET (p=0.036) and 13-HODE (p=0.023) with atherosclerosis.

Conclusion:
For the first time it is possible to determine the pro- and anti-inflammatory as well as proresolute lipids, which act as agonists and antagonists in the inflammatory process, from a well characterized collective of patients.

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Poster 247

Verlusterfahrungen im Alter – Auswirkungen auf das soziale Netzwerk und die psychische Gesundheit

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Hintergrund:
Verlusterlebnisse und Trauer im Alter sind häufig und das soziale Netzwerk der Betroffenen kann sich verändern. Die vorliegende Arbeit hat zum Ziel, die Auswirkungen von Verlusterfahrungen im Alter auf das soziale Netzwerk und die psychische Gesundheit (Depressionen) zu untersuchen.

Methoden:
Datengrundlage bildet die Leipziger Langzeitstudie in der Altenbevölkerung (LEILA 75+), eine bevölkerungsrepräsentative Längsschnittstudie, bei der strukturierte Interviews im häuslichen Setting durchgeführt wurden. In einer Stichprobe von 783 Personen (75+ Jahre) wurde mittels einer deskriptiven Analyse die Veränderung des sozialen Netzwerks (PANT) im Alter analysiert. Zudem wurden mithilfe einer logistischen Random-Effects Regression die Auswirkungen von Verlusterfahrungen und des Netzwerktyps auf Depressionen (ADS-L) untersucht

Ergebnisse:
59,96 % der Hochaltrigen lebte kontinuierlich in einem restriktiven Netz-werk. Bei knapp einem Drittel der Befragten änderte sich das soziale Netzwerk im Laufe der Zeit, jedoch konnte hierbei kein Zusammenhang mit Verlusterfahrungen festgestellt werden. Verlusterfahrungen und ein restriktives soziales Netzwerk stellten sich als einflussreichste Prädiktoren zur Entwicklung einer Depression heraus.

Diskussion:
Unsere Ergebnisse zeigen, dass ältere Menschen, die einen sozialen Verlust erfahren haben und Personen die in einem restriktiven sozialen Netzwerk leben, eher Depressionen entwickeln als Personen ohne Verlusterfahrungen und Personen in einem integrierten sozialen Netzwerk. Soziale Integration älterer Menschen ist ein dringendes Problem um Depressionen im Alter entgegenzuwirken.

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Poster 248

SFA-containing high fat diet amplifies psoriasiform inflammation independent of obesity

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The epidemic of obesity in the Western world comprises a major health threat. Moreover, obesity is linked to the risk and severity of various inflammatory disorders such as psoriasis. But, it is poorly understood how obesity-associated alterations and abnormal composition of adipokines and metabolites mechanistically augment inflammation in such diseases.

To investigate these mechanisms psoriasiform skin inflammation was induced by topical application of imiquimod in high fat diet (HFD)-induced obese mice. Already during disease onset obesity resulted in a marked exacerbation of inflammation which strongly correlated with free fatty acid (FFA) serum levels. Interestingly, this occurred independently of adipose tissue-derived cytokines, blood glucose and insulin levels, as well as leptin.

Mechanistically, in vitro saturated FAs (SFAs), which were dramatically increased in HFD-fed mice, revealed sensitizing effects on myeloid cells — key players in psoriasis. Upon additional stimuli these cells showed an amplified immune response which in turn activated a pro-inflammatory response in epidermal keratinocytes displaying the *in vivo* situation of HFD-fed mice.

Importantly, dietary reduction of pro-inflammatory SFAs, independent of polyunsaturated FA (PUFAs) supplementation, attenuated early psoriasiform inflammation even in obese mice.

In summary, we identified nutritional SFAs as a major risk factor for the severity of early psoriatic inflammation even before an obese phenotype has developed. These findings open translational perspectives for adjuvant dietary measures supporting anti-psoriatic therapies in human patients.

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Poster 249

Laser-based 3D Anthropometry: Reliability, Comparison with Classical Anthropometry, and GWAS for more than 150 Body Phenotypes

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Anthropometric quantities are widely used in epidemiologic research as possible confounders, risk factors, or outcomes. 3D laser-based body scans allow calculation of dozens of quantities such as body height, body weight, length of extremities, distances between body points, and body circumferences in short time with minimal physical contact between observers and probands. The importance of anthropometric quantities results from observed associations with health risks, morbidity, and mortality. For example, body mass index was identified as a risk factor for cardiovascular diseases, diabetes, and different neoplastic diseases. Abdominal fat, often operationalized as waist-to-hip ratio, appears to be associated with coronary heart disease independently of total body fat percentage. Body surface area is also a physiological quantity relevant for many medical applications. It can be used as a measure of standardization, e.g., for echocardiographic assessment or dosage of cytotoxic and cytostatic drugs in cancer therapy. For the latter, it is believed that body surface area correlates with size and function of drug-metabolizing organs. Another important area is the assessment of the severity of skin lesions, e.g., in case of burnings. 3D body scanning can be an alternative to classical anthropometry and might serve as a goldstandard method for determination of such quantities. Based on this, genome-wide association studies for dozens of quantities can be performed at once speeding up investigations in molecular genetics.

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Poster 250

Ocular history and symptoms stratified by age, gender and socio-economical status in a population-based study in Germany

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Purpose:
To investigate the status of self-reported ocular health in a large adult sample in Germany.

Methods:
The Leipzig Research Centre for Civilization Diseases (LIFE) is a population-based, prospective, observational, single-center study that investigates civilization diseases with regards to lifestyle (e.g. alcohol consumption), physiological risk factors (e.g. systolic/diastolic blood pressure), and measured subject characteristics from all medical subspecialties in adults aged 18-79 years. A detailed questionnaire investigated the following: patient ocular history (e.g. diagnosed eye diseases (with 45 subcategories), eye operations (with 26 subcategories), dry eye symptomatology, binocular vision status, orbital injury), family ocular history (including parents, grandparents, siblings, and children), subjective assessment of near, intermediate, and distance vision, and conditions affecting the binocular visual balance (e.g. amblyopia).

Results:
Subject characteristics were investigated stratified by age, gender, and socio-economical status. Following analyses on self-reported questionnaire data were performed: 1. incidence of above categories 2. correlation with lifestyle and physiological risk factors 3. stratification by systemic diseases to establish the frequency of ophthalmic associations 4. agreement of anamnestic data with objective ophthalmological findings (e.g. high-resolution ophthalmic imaging of the retina).

Conclusions:
Morphological and anamnestic criteria from this large dataset enable associations of ocular health with civilization diseases underlining the potential of early subclinical diagnosis.

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Poster 251

Versorgungsbedarfe im hohen Alter: Häufigkeit, alters- und geschlechtsspezifische Verteilung sowie deren Zusammenhang mit Depressionen — Ergebnisse einer bevölkerungsrepräsentativen Studie

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Hintergrund: Vor dem Hintergrund des demografischen Wandels nimmt der Behandlungs- und Versorgungsbedarf älterer Menschen stetig zu. Neben funktionellen Einschränkungen sind psychische Erkrankungen wie Depressionen im Alter mit spezifischen ungedeckten Bedarfen assoziiert. Im deutschsprachigen Raum ist bisher wenig über die Häufigkeiten und Verteilungen ungedeckter Bedarfen oder deren Zusammenhang mit depressiven Erkrankungen im hohen Alter bekannt.

Methoden: Basierend auf einer am ISAP laufenden DFG-Studie zur Messung des Versorgungsbedarfs bei Hochbetagten wurden die Daten einer bevölkerungsrepräsentativen Stichprobe von n=845 Personen im Alter von 75+ Jahren analysiert. In der telefonischen Befragung wurden Bedarfe mit dem Camberwell Assessment of Need for the Elderly (CANE) sowie die depressive Symptomatik mit der Geriatrischen Depressionsskala (GDS) erfasst. Neben deskriptiven Analysen wurde eine binär-logistische Regression durchgeführt.

Ergebnisse: Hochaltrige Menschen berichteten ungedeckte Bedarfe vor allem in den Bereichen Gedächtnis, körperliche Erkrankungen und Mobilität. Zudem wurden signifikante Alters- und Geschlechtsunterschiede im Hinblick auf berichtete ungedeckte Bedarfe identifiziert. Weiterhin waren ungedeckte Bedarfe signifikant mit einer depressiven Symptomatik assoziiert.

Diskussion: Die vorliegende Arbeit liefert erstmals für Deutschland umfassende bevölkerungsrepräsentative Ergebnisse zur Versorgungssituation hochaltriger Menschen (75+ Jahre) und leistet somit einen essentiellen Beitrag zur Gesundheitsversorgung, Versorgungsplanung und Generierung zielgerichteter Interventionen im hohen Alter.

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Poster 252

Impact of cardiac biomarkers in patients with stablecoronary heart disease on the severity of coronary obstruction and survival (LIFE Leipzig Heart Study)

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Introduction/Hypothesis: Cardiac biomarkers are well established diagnostic tools in patients with acute coronary syndrome and myocardial infarction. However there is only limited knowledge about the clinical and prognostic value of cardiac biomarkers in patients with stable coronary artery disease (CAD) with mild and obstructive stenosis. The aim of our study was to investigate the association of cardiac and inflammatory plasma biomarkers with the severity of CAD and 10 years survival.

Methods: We used plasma samples of 3417 patients from the LIFE Leipzig Heart study (total 6995 patients) undergoing first coronary angiography (72% males and 28% females). Patients with acute myocardial infarction were excluded from analysis. The following biomarkers were analyzed: copeptin, troponinT, CRP, IL-6, NT-proBNP. The severity of stable CAD was defined as no lumen stenosis, mild coronary stenosis (<50% stenosis) and obstructive stenosis affecting 1-, 2-, and 3- vessels. Cumulative survival of patients was followed up to approximately 10 years after first coronary angiography.

Results: We observed a significant and differently pronounced increase of the studied biomarkers with the severity of obstructive lesions in stable CHD also after adjusting for cardiovascular risk factors. The first and fourth quartiles of copeptin levels were associated with a cumulative 10 years survival of 96% and 22%, respectively (10g HR 0,52, p< 8,2 E-13). In addition to copeptin, the other biomarkers showed also a significant impact on long term survival.

Conclusion: We show in a large cohort of angiographically assessed patients with stable CAD a strong relationship of cardiac biomarkers with the severity of obstructive CAD. Our results demonstrate the potential clinical value of newer cardiac biomarkers to estimate the severity of CAD and the impact of long term survival in stable CHD patients.

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Poster 253

Association of olfactory dysfunction with diabetes and renal function: Results from the LIFE-Adult-Study

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Previous studies have suggested an association between diabetes mellitus (DM) and impaired olfactory function.It has been hypothesized that both macrovascular and microvascular sequelae of DM are the underlying causal mechanisms.In the present study we aimed to determine the association of olfactory dysfunction with the presence of known DM, parameters of glucose metabolism, and estimated glomerular filtration rate (eGFR). The study was undertaken as part of the 'LIFE-Adult-Study', a cohort study which has finished a baseline examination of 10,000 inhabitants (aged 18-79 years) of the City of Leipzig. Uni- and multivariable logistic regression analysis was employed to quantify associations of diabetes and renal function parameters with normosmia versus hyp-/anosmia. A total of 6,827 probands (48% male) was analyzed. The raw prevalence of known DM in the sample was 11% (of these, 57% male). The presence of known diabetes was associated with decreased olfactory function compared to individuals with a pre-diabetic status according to HbA1c and FPG levels. Likewise, pre-diabetic status was associated with a lower frequency of normosima compared to individuals with normal HbA1c and FPG levels. However, these associations could not be shown after adjustment for age, gender and socio-economic status (SES). Decreased eGFR was associated with worse olfactory function. Also, this association was no longer present after adjustment for age, gender, and SES.Diabetes and reduced eGFR are associated with impaired olfactory function, but not after adjustment for age, gender and SES.

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Poster 254

LC-MS/MS analysis for Oxystetrols and Bile Acids – Cholesterol Metabolism in the Brain

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Introduction:
In humans, the brain contains about 20% of the body's free cholesterol (CH), mostly synthesized de novo. CH itself cannot cross the blood-brain barrier (BBB). Bile acids (BA) as primary products of the CH catabolism and the oxidized CH metabolites collectively known as oxysterols are able to pass the BBB. Through their signaling function and activation of diverse signaling pathways, BAs and oxysterols can regulate lipid, energy and CH homeostasis. Little is known about the pathophysiological role of bile acids and oxysterols in neurodegenerative disease.

Methods:
MS/MS detection was performed on a QTRAP 5500 hybrid triple quadrupole linear ion trap mass spectrometer with positive electrospray ionization. Protonated precursor and fragment ions of oxysterols and BA were studied by MRM. Sample preparation of 45 µL human plasma was carried out by simple protein precipitation and centrifugation. Chromatographic seperation was performed after on-line solid phase extraction on a core shell C18 reversed phase column within 23 minutes. An external calibration and deuterated internal standards had been used for quantification.

Results:
35 Analytes of the CH metabolism, including 12 oxysterols (e.g. 24S-, 25-, 26-OHC and diOHC), 17 free and conjugated BAs (e.g. the most abundant CA, CDCA, DCA, LCA and UDCA). Inter-day CVs (n=10) were 3-26 % and LLOQs at 0.2-10 ng/mL, depending on the analyte. Applied in a LIFE study subcohort, significant results were observed for oxysterols and BAs in relation to their cognitive perfomance. Further method development for the analysis of tissue is currently under investigation.

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Poster 255

Is dementia incidence declining in high-income countries? A systematic review and meta-analysis

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Objective:
To perform a systematic review and quantitative synthesis of recent trends in dementia incidence in high-income countries (HIC), considering study quality.

Methods:
PubMed and Web of Science were searched for eligible studies, i.e. population-based/community-based prospective cohort studies investigating dementia incidence with similar methods over time, published after 1990. Study selection, data extraction, and quality assessment were performed in duplicate. Random-effect meta-analysis and meta-regression were used to estimate incidence change and to explore associations with study attributes.

Results:
The systematic review included 7 studies (42,485 individuals), the meta-analysis 5 studies of sufficient quality. Estimates yielded a non-significant decline across HIC (IC = 0.82; 95%CI 0.51–1.33), with high heterogeneity (I^2 = 94.9%, $p < .001$) and without publication bias (Egger's t = -1.77; p = .18). Excluding the Japanese Hisayama study, the only study suggesting an increase, indicated borderline evidence for a decline in Western HIC (IC = 0.69; 95%CI 0.47–1.00; I^2 = 88.1%, $p < .001$; Egger's t = -0.34, p= .77), again with high heterogeneity. Meta-regression did not associate incidence rate with calendar year, neither with study attributes; however, analyses were low-powered.

Conclusion:
There is evidence of favorable trends in dementia incidence in Western HIC (stabilizing/decreasing). Reverse trends may occur in HIC of other regions, as exemplified by Japan. However, study number was small and heterogeneity was high. Further cohort studies using consistent methods are needed to draw definite conclusions.

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Poster 256

Olfactory dysfunction in the general population – prevalence and association with lifestyle factors: Results from the LIFE-Adult-Study

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Loss of olfaction can severely impact quality of daily life. In the present study we aimed to determine the prevalence of olfactory dysfunction in the general population, depending on age, gender, and lifestyle factors. Olfactory function was assessed using the Sniffin' Sticks-Screening 12 Test. Smoking habits and alcohol consumption were determined using structured interviews or self-administered questionnaires. Gamma glutamyl transferase (GGT) was used as a sensitive biomarker for ethanol-induced liver damage. Uni- and multivariable logistic regression analysis was employed to quantify associations of lifestyle factors and GGT with normosmia versus hyp-/anosmia.The sample comprised 6,212 probands (48% male). The overall proportion of correct answers differed largely between the 12 odors. Lemon and cinnamon were recognized by only 60% and 64% of the participants, respectively, whereas peppermint was identified correctly in 95%. The prevalence of anosmia among subjects aged 20-79 years was 3.9% for men and 2.5% for women. Higher age, male gender, and lower SES were independent predictors for hyp-/anosmia.There was no significant association for alcohol consumption. However, higher GGT values were significantly associated with higher frequencies of hyp-/anosmia (OR 0.88 per ukat/l; 95%CI 0.80-0.95). While data strongly indicate the negative effect of current smoking on olfaction in a pack-year related manner, the influence of alcohol consumption needs further investigations. Revealing one more facet of the noxiousness of smoking, smoking cessation seems to be recommendable, especially in case of chemosensory loss.

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Poster 257

Zahngesundheit einer Kohorte Jugendlicher in Mitteldeutschland

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Ziel:
Untersuchung der Zahngesundheit einer mitteldeutschen Kohorte Jugendlicher im Rahmen der LIFE-Child-Studie unter Berücksichtigung des sozioökonomischen Status (SÖS) und der Schulform (SF).

Material und Methode:
1116 Jugendliche der LIFE-Child-Kohorte im Alter von 10 bis 18 Jahren wurden in die Auswertung eingeschlossen. Die Flächen von 6 Indexzähnen wurden entsprechend ICDAS II beurteilt, versiegelte und gefüllte Flächen erfasst. Es erfolgte zusätzlich eine schultypbezogene Differenzierung sowie die Erhebung von Informationen zum SÖS. Der familiäre SÖS wurde in hoch, mittel und niedrig (Winkler-Index) kategorisiert.

Ergebnisse:
Im Mittel zeigten die diagnostizierten Flächen mit ICDAS 5-6 und Füllung (D_{5+6}F-S) sowie ICDAS 1-6 und Füllung (D_{1-6}F-S) einen altersabhängigen Anstieg: Bei den 10-bis-12-Jährigen (n=555) waren 0,33 bzw. 3,56 Zahnflächen betroffen, bei den 13-bis-15-Jährigen (n=379) 0,64 bzw. 4,67 Flächen und 1,00 bzw. 5,65 Flächen in der Altersgruppe der 16-bis 18-Jährigen (n=182) ($p<0,001$). In der Kohorte der 13-bis-15-Jährigen zeigten sich bei hohem SÖS und Gymnasialbesuch im Vergleich zu mittlerem/niedrigem SÖS und Besuch anderer Schulformen, signifikant geringere Karieserfahrung (D_{5+6}F-S: $p_{SÖS}<0,006$; $p_{SF}<0,001$; D1-6F-S: $p_{SÖS}=0,025$; $p_{SF}=0,026$). Bei Besuch des Gymnasiums konnte ein signifikant höherer Mittelwert versiegelter Flächen im Vergleich zu anderen Schulformen ($p=0,002$) festgestellt werden.

Zusammenfassung:
Mit zunehmendem Alter konnte in der untersuchten Kohorte ein signifikanter Anstieg der Karieserfahrung festgestellt werden. Dabei zeigte sich ein Einfluss des SÖS sowie der Schulform.

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Poster 258

Prevalence of refractive errors examined by wavefront-based autorefraction in a large German cohort of children and adolescents

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Purpose: To investigate the prevalence of refractive errors in German children and adolescents.

Methods: The Leipzig Research Centre for Civilization Diseases (LIFE) is a population-based, prospective, observational single-center study that investigates the development of children and adolescents in Germany. Non-cycloplegic refractive error (3mm pupil diameter, right eye) was established as part of an optometric examination by wavefront-based autorefraction (ZEISS i.Profiler plus, Carl Zeiss Vision GmbH, Aalen, Germany) with the following definitions: myopia SE<=-0.75 diopters (D), hyperopia SE>=+1D, astigmatism >=1D.

Results: Over all children and adolscents, n=1396, aged 3-17 years (mean: 9.85 ± 4.0 years), the prevalence of emmetropia was highest (83%; mean: 0.02D ± 0.37D; hyperopia: 12.3%, mean: +2.19D ± 1.27D; myopia: 4.7%, mean: -2.14D ± 1.45D). Astigmatic refractive error was prevalent in 5.6% of the subjects (mean: 1.78D ± 0.87D). When subjects were separated into preschool children (n=416, mean age: 5.1 ± 1.2 years, range 3-6 years), school children and adolescents (n=980, mean age: 11.9 ± 2.8 years, range 7-17 years), prevalence of emmetropia was still highest (preschool: 93%; school children and adolescents: 79%), while the prevalence of myopia was higher in the group of school children and adolescents (17%) compared to preschool children (2.1%).

Conclusions: The prevalence of myopia is modest in urban children and adolescents living in Germany. When separated into two age bands, the prevalence of myopia was increased in the older group. The global trend towards an increased prevalence of myopia was not observed.

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Poster 259

Assessment of homogenous assays for HDL3-Cholesterol, LDL-Triglyceride and Remnant Cholesterol as biomarkers for coronary artery disease

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Objective:
Coronary artery disease (CAD) is a major health problem and main cause of death in the developed countries around the world. Altered plasma lipids are well established risk factors for CAD and can have an either protective or aggravating effect on CAD. In the present study, we assessed test performance of fully automated homogenous assays for HDL3-Cholesterol (HDL3-C), LDL-Triglyceride (LDL-TG) and Remnant Cholesterol (TRL-C) as new biomarkers for CAD.

Methods:
We analyzed 3506 plasma samples of patients from the LIFE-Heart study, admitted for suspected stable CAD and undergoing first coronary angiography. Plasma total cholesterol, LDL-C, HDL-C and triglyceride levels were available for all patients. Fully automated assays from Denka Seiken for HDL3-C, LDL-TG and TRL-C were applied on Cobas clinical chemistry analyzers. HDL2-C was calculated by subtracting HDL3-C from the total HDL-C-concentration. Sample stability over 48h at room temperature and after multiple freeze-thaw-cycles, as well as intra- and interassay-variability of these assays were evaluated using pooled plasma specimens.

Results:
We observed excellent intraassay-precision for HDL3-C (CV 1,56%), LDL-TG (CV 2,33%) and TRL-C (CV 1,66%), as well as convincing interassay-precision over 7 days for HDL3-C (CV 3,71%), LDL-TG (CV 4,34%) and TRL-C (CV 1,74%). Stability of analytes was adequate over 48 hours at room temperature for HDL3-C (CV 2,72%), LDL-TG (CV 5,89%), TRL-C (CV 2,13%) and for up to 4 freeze-thaw-cycles for HDL3-C (CV 0,71%), LDL-TG (CV 4,95%), TRL-C (CV 4,21%). HDL3-C and TRL-C levels differed significantly between males (HDL3-C: M=0,68±0,15mmol/L; TRL-C: M=1,46±0,82m-

mol/L) and females (HDL3-C: M=0,77±0,15mmol/L; TRL-C: M=1,28±0,66mmol/L), whereas LDL-TG levels were comparable (males: M=0,27±0,095mmol/L; females: M=0,27±0,14mmol/L). Measured TRL-C levels (mean 1,39±0,78mmol/L) differed significantly from calculated TRL-C (mean 0,77±0,49mmol/L).

Conclusion:
The assessed fully-automated assays showed excellent test performance and allow fast and easy quantification of HDL3-C, LDL-TG and TRL-C in large numbers of samples. The diagnostic and predictive value of these parameters is under investigation.

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Association between cognitive and olfactoryperformance: results from the population-based LIFE-Adult-Study

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Background: Dementia affects over 47 million people worldwide and is declared a public health priority by WHO. Studies in older or cognitively impaired adults have shown associations between cognition and olfaction. Population-based studies are largely lacking. We therefore cross-sectionally analysed this association using data from the population-based LIFE-Adult-Study.

Methods: 7,032 participant (age 18-79) datasets were analysed. Olfactory performance was assessed with "Sniffin' Sticks-Screening 12 Test", where identifying fewer than 11 of the 12 odours was considered olfactory dysfunction. Cognitive tests comprised 6 CERAD (Consortium to Establish a Registry for Alzheimer's Disease) tests (VF:verbal fluency, WLL/WLR:word list learning and recall, MMSE:Mini-Mental-Status-Examination) and the Trail Making Tests (TMT) A and B. MMSE was for subjects aged 60+ only. Binary logistic regression adjusted for sex, age, education, smoking and depression was used.

Results: Worse performance in 5 of the 6 cognitive tests was significantly associated with higher risk of olfactory dysfunction: VF: OR=0.98 per score point (psp), 95%CI 0.97-0.99, p<0.001; WLL: OR=0.95 psp, 95%CI 0.93-0.99, p=0.003; WLR: OR=0.94 psp, 95%CI 0.89-1.01, p=0.075; TMT-A: OR=1.01 psp, 95%CI 1.003-1.011, p=0.002; TMT-B/A: OR=1.07 psp, 95%CI 1.01-1.13, p=0.020; MMSE: OR=0.89 psp, 95%CI 0.83-0.96, p=0.003.

Conclusion: This cross-sectional study suggests lower cognitive function is associated with olfactory dysfunction. The value of olfactory testing in early screening for cognitive impairment needs to be investigated in prospective studies.

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Poster 261

The association between unemployment and depression – Results from the population-based LIFE-Adult-Study

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Background: Unemployment is a rik factor for impaired mental health. Based on a large population-based sample, in this study we therefore sought to provide detailed information on the association between unemployment and depression, including information on differences between men and women, different types of unemployment, and on the impact of material and social resources on the association.

Methods: We studied 4,842 participants (18-65 years) of the population-based LIFE-Adult-Study. Depression was assessed using the Center for Epidemiological Studies Depression Scale. Employment status was divided into three groups: being employed or unemployed, receiving either entitlement-based or means-tested benefits. Unadjusted and adjusted multivariate logistic regression models were applied to assess the association between employment status and depression.

Results: Increased depression risk was solely found in unemployed persons receiving means-tested benefits. Adjusting for sociodemographics, net personal income and risk of social isolation, comparable associations of being unemployed and receiving means-tested benefits with elevated depression risk were found for men (Odds Ratio/OR: 2.17, 95%-CI: 1.03-4.55) and women (OR: 1.98, 95%-CI: 1.22-3.20).

Conclusion: Unemployed persons receiving means-tested benefits in Germany constitute a risk group for depression that needs specific attention in the health care and social security system. The negative impact of unemployment on depression risk cannot be explained solely by differences in material and social resources. Contrasting earlier results, women are equally affected as men.

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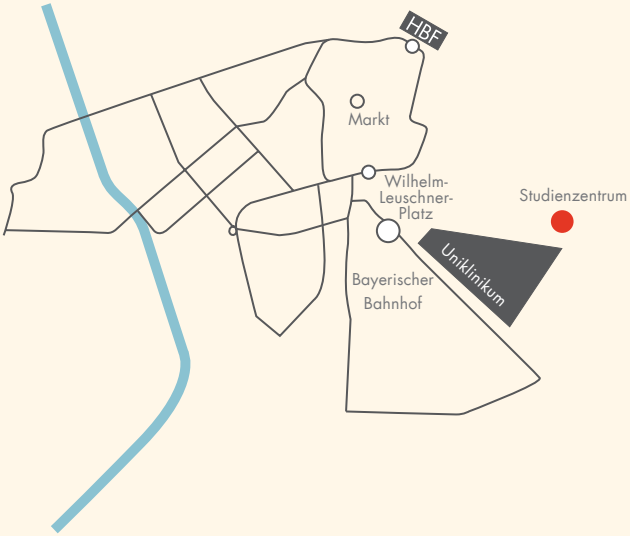
Leipzig Research Festival for Life Sciences

2018

Das 14. Research Festival Leipzig 2018, das von der Medizinischen Fakultät und der Fakultät für Biowissenschaften, Pharmazie und Psychologie gemeinsam veranstaltet wird, soll allen „Life Science"-Wissenschaftlern und Studenten aus Leipzig und dem Umland die Möglichkeit eröffnen, ihre Forschungsergebnisse in Form von Postern zu präsentieren und mit anderen Arbeitsgruppen zu diskutieren.



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