UNIVERSITÄT LEIPZIG
Medizinische Fakultät

Universitätsklinikum Leipzig
Medizin ist unsere Berufung.

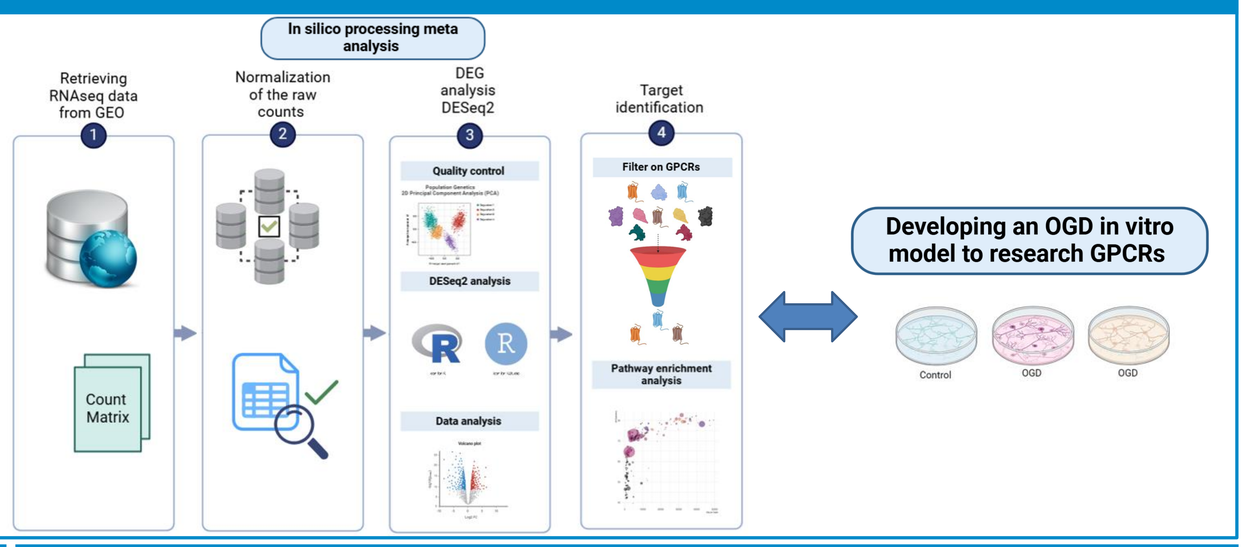
Exploring new molecular targets to improve neuronal survival during stroke in a SH-SY5Y model

Ibtisam Siad[1] and Anette Kaiser[1]
[1]Department of Anesthesiology and Intensive Care, University of Leipzig Medical Center

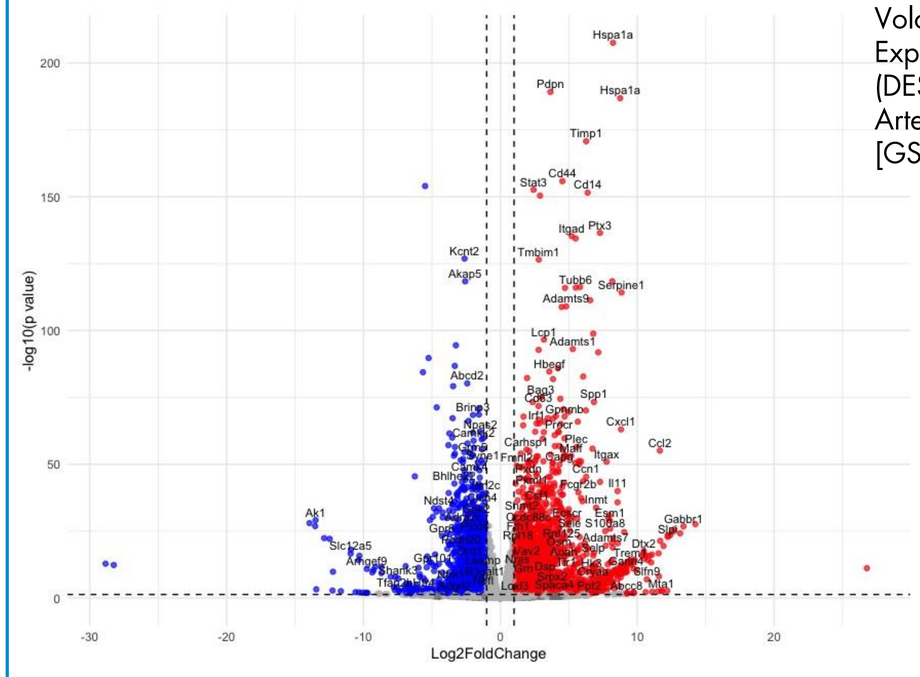
INTRODUCTION

Stroke is a neurological disorder affecting millions a year[1], often caused by a thrombus blocking arteries (ischemic stroke). Currently, the only available treatments are reperfusion and infusion of thrombolytic agents, but it is currently not feasible to directly address neuronal survival during the ischemic event. Pioneering studies suggest that G protein-coupled receptors (GPCRs) can be physiologically upregulated in ischemic areas and might improve cellular survival.[2] We re-analyzed 13 mRNA datasets under ischemic and control conditions from in vitro and in vivo studies conducted in Rattus norvegicus and Mus musculus. We also re-analyzed mRNA human in vitro studies. Here, we identified GPCRs with regulated expression which include many orphan receptors. We plan to investigate their functional contribution using the human neuroblastoma cell line SH-SY5Y as a model.

METHODS



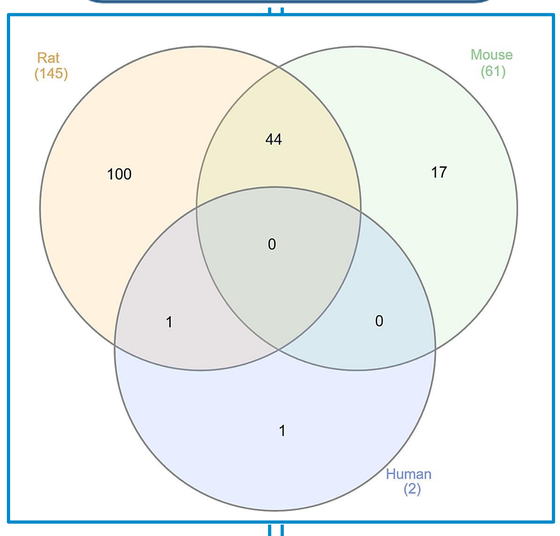
DIFFERENTLY EXPRESSED GENE ANALYSIS



Volcano plot of Differently Expressed Gene Analysis (DESeq2 in R) Middle Cerebral Artery Occlusion of adult rats [GSE268634].

In red the significant upregulated genes (log2FoldChange >=1, padjusted <=0.05 (Benjamini Hochberg procedure)) and in blue the significant downregulated genes (log2FoldChange >=1, padjusted <= 0.05 (Benjamini Hochberg procedure)) are seen.

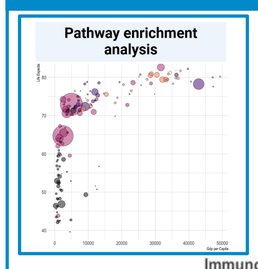
Venn Diagram of 208 upregulated GPCRs

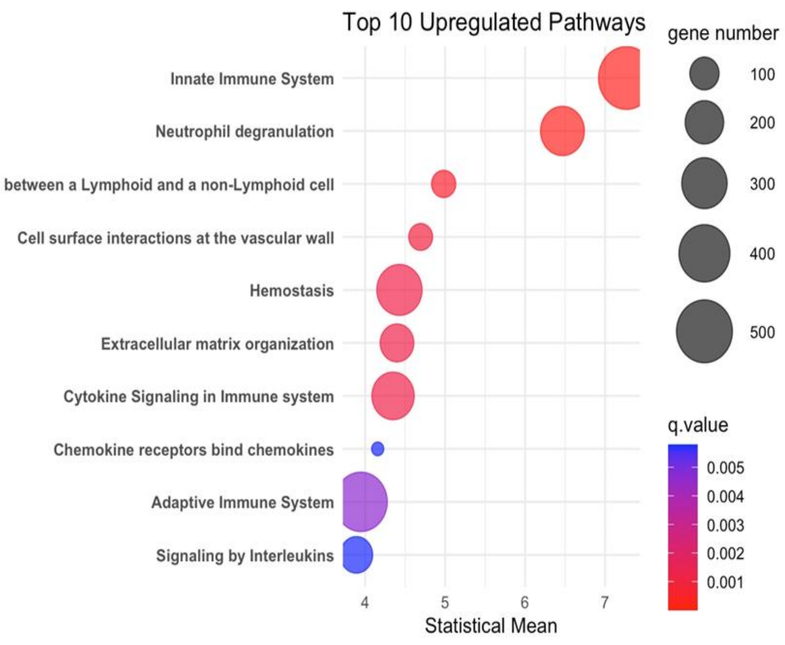


Filter on GPCRs

After implementing a GPCR filter, 333 GPCRs found to be significantly upregulated and 336 GPCRs are significantly downregulated [GSE268634].

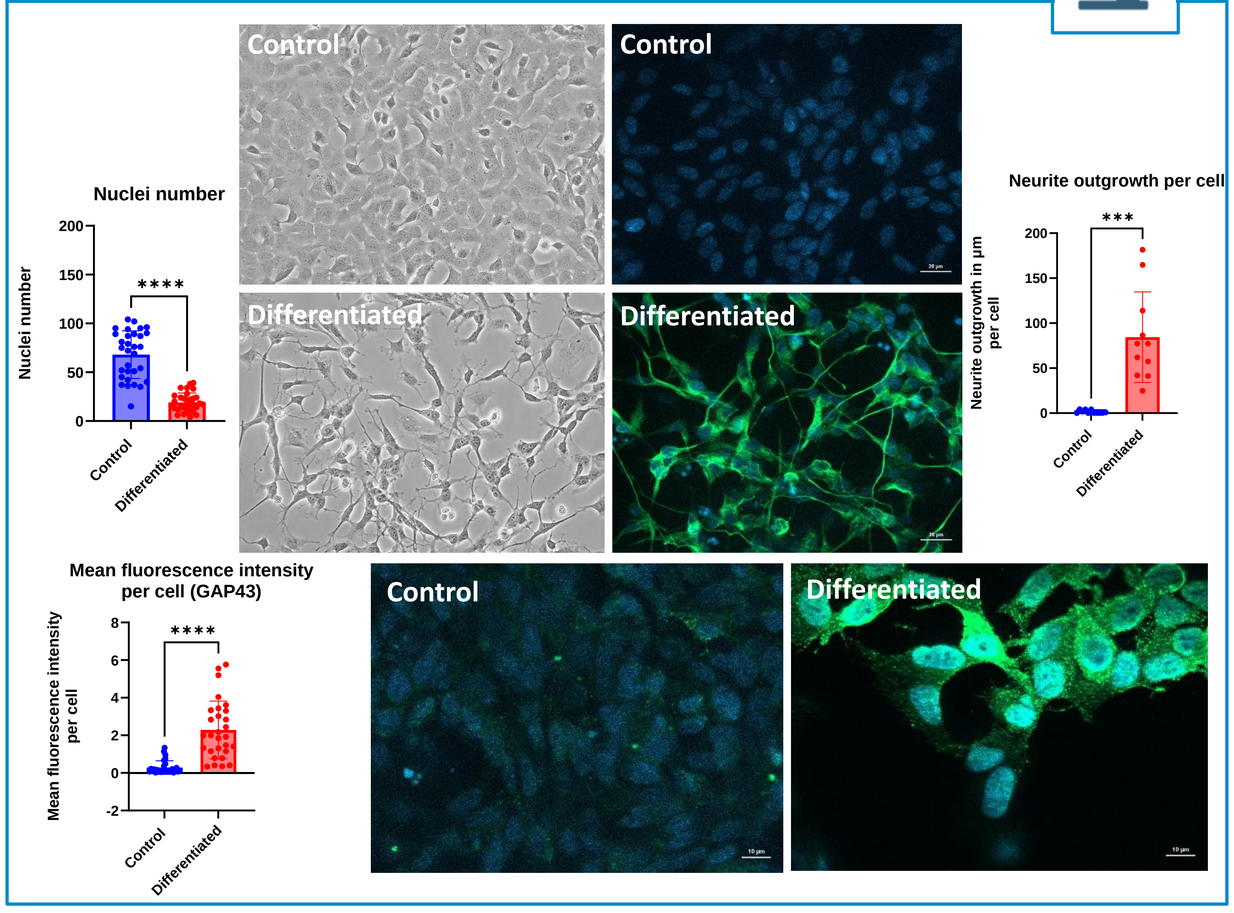
PATHWAY ENRICHED ANALYSIS





Bubble plot of an Enrichment Pathway Analysis (Generally Applicable Gene Set Enrichment (GAGE) with Reactome database in R). A False Discovery Rate (q-value) of <= 0.05 is significant (Benjamini-Hochberg procedure) [GSE268634].

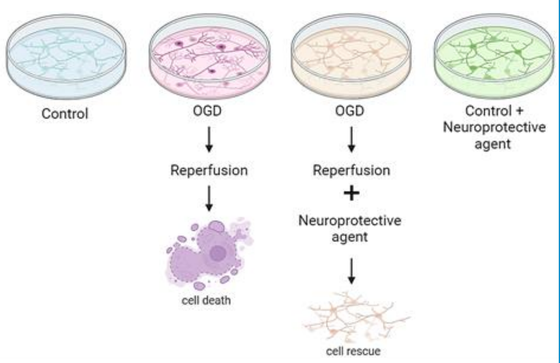
DIFFERENTIATION OF SH-SY5Y



CONCLUSION & OUTLOOK

We found promising targets by re-analyzing 13 RNAseq studies. However, we want to increase the statistical strength by doing a meta-analysis of more ischemic RNAseq studies. We also want to extend our strategy by adding more filters to gain more information about the GPCRs involved in ischemic injury. The SH-SY5Y cells were, therefore, differentiated into a neuronal network. The next step is to create an in vitro stroke model to investigate the functional role of the selected GPCRs.

Developing an OGD in vitro model to research GPCRs



References:
1 Kuriakose D, Xiao Z. Int J Mol Sci 2020 (21): 7609.
2 Wang, T. et al. Stroke 2020 (51): 3690.
3 Dravid, A. et al. Sci. Rep. 2021 (11).

Illustrative figures created in BioRender.com

SFB1423

UNIVERSITÄT LEIPZIG
Graduate Academy Leipzig