UNIVERSITÄT LEIPZIG

Medizinische Fakultät

18th Leipzig Research Festival for Life Sciences

30|01|2025

ABSTRACT BOOK

PD Dr. Dr. John T. Heiker
PD Dr. Felix Hussenöder
Prof. Dr. Tobias Piegeler
Prof. Dr. Steffi G. Riedel-Heller
Prof. Dr. Michaela Schulz-Siegmund
Prof. Dr. Ruth Stassart
Prof. Dr. Andreas Thum

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Organizer

Faculty of Medicine, Leipzig University
Faculty of Life Sciences, Leipzig University

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Peggy Darius
Head of Press and Public Relations
Universität Leipzig
Faculty of Medicine
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Venue

Leipzig University
Clinical Trial Center of the Faculty of Medicine
Liebigstraße 27
04103 Leipzig

Scientific Committee

PD Dr. Dr. John T. Heiker
Helmholtz Institute for Metabolic, Obesity and Vascular Research (HI-MAG)
Leipzig University

PD Dr. Felix Hussenöder
Institute of Social Medicine, Occupational Medicine and Public Health
Leipzig University, Faculty of Medicine

Prof. Dr. Tobias Piegeler
Clinic and Polyclinic for Anaesthesiology and Intensive Care
Leipzig University Medical Center

Prof. Dr. Steffi G. Riedel-Heller
Institute of Social Medicine, Occupational Medicine and Public Health
Leipzig University, Faculty of Medicine

Prof. Dr. Michaela Schulz-Siegmund
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Prof. Dr. Ruth Stassart
Paul Flechsig Institute of Neuropathology
Leipzig University Medical Center

Prof. Dr. Andreas Thum
Institute of Biology
Leipzig University, Faculty of Life Sciences

Preface

Dear young researchers, dear colleagues, dear guests,

We are delighted to welcome you to the 18th Research Festival for Life Sciences! Since its inception in 2002, this festival has become an important platform for young scientists in the life sciences and medicine in Leipzig. This year's event promises to provide exciting insights into innovative research and to facilitate valuable exchanges among participants.

A total of 190 abstracts have been submitted, covering a wide range of topics in medicine and the life sciences, including psychology, pharmacy, chemistry, biology, informatics, and applied clinical research. We are particularly pleased to see active participation not only from the Leipzig University but also from various regional and national research centres.

The Research Festival for Life Sciences offers an excellent platform to present research results to a broad audience, to network, and to gain valuable insights for your own scientific work. We encourage you to take advantage of this opportunity to discuss your innovative ideas and findings, to learn from fellow researchers, and to explore new avenues in science together.

The success of the Research Festival for Life Sciences would not be possible without the generous support of many key partners and institutions. We would like to express our sincere thanks to all those who contribute with their dedication and expertise.

We look forward to shaping the 18th Research Festival for Life Sciences with you and wish you an exciting and inspiring event!

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PD Dr. Felix Hussenöder
Prof. Dr. Tobias Piegeler
Prof. Dr. Steffi G. Riedel-Heller
Prof. Dr. Michaela Schulz-Siegmund
Prof. Dr. Ruth Stassart
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University of Leipzig Medical Center

Abstracts Research Festival 2025

Poster 1

Accelerated growth of preadipocyte cultures with TSC1 downregulation might be linked to lipoma development and can be reversed by rapamycin treatment

A. Kirstein[1], J. Friedrich[1], J. Hentschel[2], S. Richter[1], H. Kiep[3], M. Arelin[3], K. Platzer[2], T. Schulz[4], A. Merkenschlager[3], W. Kiess[1], S. Mayer[5], R. Abou Jamra[2], D. Le Duc[2], A. Garten[1]

[1]University Hospital for Children & Adolescents, Leipzig University, Center for Pediatric Research, Leipzig, Germany, [2]Faculty of Medicine, Leipzig University, Institute of Human Genetics, Leipzig, Germany, [3]University Hospital for Children and Adolescents, Leipzig, Germany, [4]Leipzig University Hospital, Department of Orthopedic, Trauma and Plastic Surgery, Leipzig, Germany, [5]University Hospital for Pediatric Surgery, Leipzig University, Center for Pediatric Research, Leipzig, Germany

Background:

Tuberous Sclerosis Complex Subunit 1 (*TSC1*) encodes for a growth inhibitory protein, which suppresses mTOR signaling. Patients with *TSC1* pathogenic variants are prone to developing benign tumors in different organs. We identified a likely pathogenic heterozygous germline *TSC1* splicing variant in a boy with developmental delay and a large lipoma within the gluteal muscle. We observed a *TSC1* loss of heterozygosity and loss of TSC1 protein in the lipoma.

Methods:

We downregulated *TSC1* via siRNA knockdown (KD) in human preadipocytes and compared proliferation (nuclei counting, proliferation marker Ki67), pathway activation (Western blot) and adipogenic differentiation (lipid staining) to control cells. *TSC1* KD cells were treated with inhibitors of mTOR (rapamycin and torin) and Phosphoinositide 3-kinase (PI3K) (alpelisib) and the effect on cell growth was quantified.

Results:

TSC1 KD cells showed a 1.7-fold higher cell count on day 7 and 7.4-fold increase in the proliferative fraction (Ki67) on day 3. Western blots demonstrated higher ribosomal protein S6 phosphorylation in *TSC1* KD cells. Adipogenic differentiation was not affected. mTOR and PI3K inhibitors all decreased proliferation of *TSC1* KD cells to similar extents (47-59% decreased cell count, 59-66% decreased Ki67) but inhibited different pathway components as shown via Western blots.

Conclusion:

Since *TSC1* KD led to higher proliferation of preadipocytes the variant is likely causative for the lipoma formation. mTOR and PI3K inhibitors decreased growth of *TSC1* KD cells and could be options for lipoma treatment.

Poster 2

Activation of preoptic PNOC neurons regulates energy expenditure

A. Ben-Kraiem[1], A. Ilango Micheal[2], H. Martin[3], H. U. Zeilhofer[4], J. Brüning[5], N. Klöting[6], M. Blüher[6], A. Jais[1]

[1]Helmholtz Institute for Metabolism, Obesity and Vascular Research, Diet Induced Metabolic Alterations Group, Leipzig, Germany, [2]Helmholtz Institute for Metabolsism, Obesity and Vascular Research, Diabetes Induced Metabolic Alterations Group, Leipzig, Germany, [3]Helmholtz Institute for Metabolism, Obesity and Vascular Research, Vascular Epigenetics, Leipzig, Germany, [4]ETH Zürich, Department of Chemistry and Applied Bioscience, Zürich, Switzerland, [5]Max Planck Institute for Metabolism Research, Cologne, Germany, [6]Helmholtz Institute for Metabolism, Obesity and Vascular Research, Clinical Obesity Research, Leipzig, Germany

The preoptic area (POA) of the hypothalamus has garnered attention due to its pivotal role in energy balance control and thermoregulation. Activation or inhibition of specific POA neurons has been shown to affect body temperature, locomotor activity and energy expenditure. To gain novel insights into this intricate regulatory mechanism, we have conducted a comprehensive analysis of a distinct cluster of neurons within the POA that express the neuropeptide prepronociceptin (PNOC).

Using chemogenetic techniques, we selectively activated PNOC(POA) neurons of mice and observed a significant reduction in brown adipose tissue (BAT) temperature and energy expenditure. Further examination of PNOC(POA) neuronal projections unveiled robust connectivity to various brain regions involved in autonomic control, including the dorsomedial hypothalamus (DMH), a key relay in BAT thermogenesis regulation. Interestingly, the activation of PNOC(POA) neurons initiated an acute inflammatory response in BAT, characterized by the upregulation of immediate early genes associated with inflammation and chemotaxis.

While extensive research has focused on investigating hypothalamic circuits, there has been limited exploration of the complex communication between hypothalamic neurons and innervated tissues, such as brown adipose tissue. By unraveling the regulatory mechanisms that are governed by PNOC(POA) neurons, we can significantly advance our understanding of the neural control of whole-body energy expenditure and adipose tissue function.

Poster 3

ADGRL1/LPHN1 in adipose tissue function

M. Strnadová[1], S. Prömel[2], T. Schöneberg[3], D. Thor[3]

[1]Leipzig University, Faculty of Medicine, RSI of Biochemistry, Leipzig, Germany, [2]Heinrich Heine University Düsseldorf, Germany, [3]Leipzig University, Germany

G protein-coupled receptors (GPCRs) are involved in several different cellular functions and, thereby, are important regulators of adipocyte function and adipocyte lipid content. However, the physiological role for many GPCRs expressed in adipose tissue (AT) is still unknown yielding a huge potential for new targets modulating adipocyte function. Among those highly expressed receptors is ADGRL1/LPHN1, which was mainly described for its involvement in neuronal and developmental processes.

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Recently, it was demonstrated that ADGRL1/LPHN1 dysfunction results in excessive fat storage and obesity in knock-out (KO) mice compared to wildtype (WT) littermates at an age of 30 weeks. Results are pointing towards ADGRL1/LPHN1 being necessary for different mechanisms involved in the regulation of energy homeostasis including changes in adipocyte physiology. Currently, I am characterizing metabolic parameters of KO and WT animals (12-16 weeks age) prior to the onset of overweight/obesity. To clarify the mechanisms, I take advantage of the cell line 3T3-L1 as an *in vitro* model, which can be differentiated into adipocytes. My latest findings indicate a direct influence of ADGRL1/LPHN1 onto adipocyte function.

Further work will focus on how ADGRL1/LPHN1 dysfunction modulates adipocyte function and influences overall energy homeostasis leading to obesity. These data will help to understand how functional variability of ADGRL1/LPHN1 receptor impacts energy homeostasis and weight gain. With different receptor variants found in humans, ADGRL1/LPHN1 might be a contributor to excessive weight gain.

Poster 4

Adipose tissue myoglobin is crucial for functional lipid metabolism and thermoregulation

C. Strehlau[1], H. Broghammer[1], R. Nuwayhid[2], S. Langer[2], J. Weiner[3], J. Heiker[1]

[1]Helmholtz Zentrum München, Helmholtz Institut für Metabolismus, Adipositas und Gefäßforschung, Leipzig, Germany, [2]University of Leipzig Medical Center, Department of Orthopaedic, Trauma and Plastic Surgery, Leipzig, Germany, [3]University of Leipzig Medical Center, Medical Department III – Endocrinology, Nephrology, Rheumatology, Leipzig, Germany

Activating brown adipose tissue (BAT) can boost energy expenditure through thermogenesis, offering a promising therapeutic approach to tackle obesity-related metabolic diseases. Thermogenesis in BAT requires an increased and efficient supply of energy substrates and oxygen. Myoglobin (MB) plays a key role in oxygen storage and shuttling during exercise. Our previous studies have demonstrated that MB is highly expressed in BAT and its expression levels significantly impact BAT function and metabolism. Specifically, the recently described lipid-binding property of MB is essential for enhancing substrate flux, brown adipocyte metabolism, and ultimately thermogenesis.

We now investigate the physiological impact of MB on lipid mobilization, thermoregulation, and energy expenditure using the first adipose tissue (AT)-specific MB knockout (KO) mouse. Our initial findings indicate that loss of MB only in AT increases susceptibility to diet induced obesity and impairs thermoregulation under cold exposure. Additionally, fatty acid oxidation and lipid mobilization seem to be impaired in these animals. Through the Seahorse Analyzer, we show that MB is vital for rapid uptake and oxidation of exogenous fatty acids.

Besides BAT, MB is also expressed in human brown/ beige adipocytes. Pilot experiments with our human mature adipocyte culture show that MB overexpressing human adipocytes have enhanced metabolic capacity, such as increased lipolysis rates. Hence, understanding the function and regulation of MB may contribute to metabolic health and enhanced energy expenditure in humans.

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HI-MAG

The Helmholtz Institute for Metabolic, Obesity, and Vascular Research in Leipzig investigates the causes of pathological weight gain and aims to develop new therapies for obesity and its comorbidities, including metabolic and vascular diseases. The institute excels in integrating preclinical research in the laboratory with clinical trials at its outpatient clinic, facilitating the rapid implementation of the most current research findings into clinical practice. It is one of 14 Helmholtz Institutes within the Helmholtz Association, resulting from a long-standing partnership between Helmholtz Munich and the Medical Faculty of Leipzig University including the University of Leipzig Medical Center.

Our research stands on four fundamental pillars: Obesity Research, Metabolic Research, Vascular Research – each of which consists of two work groups with different scientific goals - and Clinical Studies, where our findings are tested in clinical research.

More information:
https://www.helmholtz-munich.de/en/hi-mag

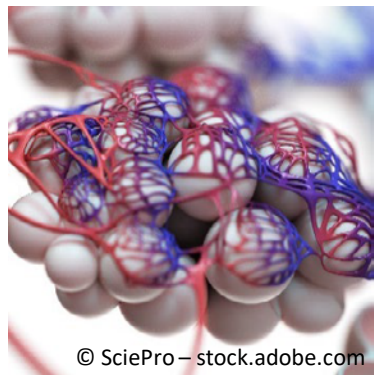
SCAN ME

Obesity Research

We are examining the mechanisms underlying adipose tissue dysfunction and their contribution to the development of obesity and related metabolic and vascular disorders. Our goal is to design novel therapeutic interventions aimed at preventing and treating obesity.

Metabolic Research

We study the interaction between peripheral organs and the central nervous system to gain a better understanding of metabolic processes, including the regulation of appetite and satiety, and to develop new drug therapies.



Vascular Research

We investigate arterial and veinous vascular diseases and create novel therapeutic alternatives to hinder disease progression and re-occlusion (restenosis) after vascular procedures.

Clinical Studies

Clinical studies at HI-MAG are a vital aspect of researching new treatments for obesity and other metabolic disorders. We collaborate with Leipzig University Medicine to perform these studies.

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Poster 5

B Cell-Derived Non-Classical Opioid Peptide Nociceptin Contributes to Metabolic Disease by Promoting Immune Cell Trafficking and Insulin Resistance in Diet-Induced Obesity

S. Puente-Ruiz[1], A. Hoffman[1], N. Klöting[1], F. T. Wunderlich[2], J. C. Brüning[2], M. Blüher[1], A. Jais[1]

[1]Helmholtz Institute for Metabolic, Obesity and Vascular Research (HI-MAG), Leipzig, Germany,
[2]Max Planck Institute for Metabolism Research, Cologne, Germany

Obesity-induced insulin resistance is associated with inflammation and changes in immune-cell population in metabolic .

Opioids are well known for their central analgesic effects but also play a role in modulating peripheral inflammation. During acute inflammation, immune cells release opioid peptides that bind to opioid receptors, mediating analgesia. Nociceptin/orphanin FQ (N/OFQ), a non-classical opioid peptide, is primarily expressed in B lymphocytes. Given the key role of B cells in inflammation during obesity, our study aimed to investigate how B cell-derived nociceptin affects immune function and glucose response under high-fat diet (HFD) conditions.

We generated a B cell-specific Pnoc knockout model (PnocΔCd19) by crossing Pnoc loxP-flanked mice with Cd19-Cre mice. These knockout mice underwent metabolic phenotyping following a 16-week HFD. Additionally, in vitro models were used to investigate how nociceptin affects immune cell trafficking.

PnocΔCd19 mice fed on a 16-week HFD showed significant improvements in metabolic profiles, including enhanced insulin sensitivity and glucose tolerance. Additionally, markers of inflammation and immune cell infiltration were reduced in both visceral adipose tissue and the liver of these mice. These results were consistent with our in vitro experiments, which demonstrated a strong effect of nociceptin on macrophage migration, mediated by the nociceptin receptor.

In conclusion, our study highlights a critical role for B-cell-specific PNOC expression in modulating immune-cell trafficking and metabolic health.

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Poster 6

Circulating cell-free DNA load is associated with parameters of fat distribution, inflammation and glucose homeostasis

A. Pollastri[1,2], L. Müller[2], S. Aurich[2,3], S. Bernhart[4,5,6], A. Hoffmann[1], T. Hagemann[1], A. Ghosh[7], F. Noé[7], C. Wolfrum[7], I. Schamarek[2], K. Rohde-Zimmermann[1,2], M. Blüher[1,2,8], P. Kovacs[2,8], M. Keller[1,2]

[1]Helmholtz Munich, Helmholtz Institute for Metabolic, Obesity and Vascular Research, Leipzig, Germany, [2]University of Leipzig Medical Center, Medical Department III - Endocrinology, Nephrology, Rheumatology, Leipzig, Germany, [3]Leipzig University, Department of Animal Physiology, Faculty of Life Sciences, Leipzig, Germany, [4]Leipzig University, Interdisciplinary Center for Bioinformatics, Leipzig, Germany, [5]Leipzig University, Bioinformatics Group, Department of Computer, Leipzig, Germany, [6]Leipzig University, Transcriptome Bioinformatics, LIFE Research Center for Civilization Diseases, Leipzig, Germany, [7]ETH Zurich, Institute of Food, Nutrition and Health, Schwerzenbach, Switzerland, [8]Deutsches Zentrum für Diabetesforschung e.V., Neuherberg, Germany

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Cell-free DNA (cfDNA) consists of small DNA fragments, released from apoptotic and necrotic cells, that retain epigenetic signatures of their tissue of origin. Thus, cfDNA could be used to investigate epigenetic tissue-specific changes associated with metabolic disorders. In the current study, EDTA-blood samples from the Leipzig Obesity BioBank (LOBB) and Obese Taste Bud (OTB) patient cohorts were used to extract and quantify cfDNA. Blood cfDNA load positively correlated with phenotypical traits associated with fat distribution (*e.g.*, BMI, and waist-to-hip ratio), inflammation (*e.g.*, IL-6 and C-reactive protein) and glucose homeostasis (*e.g.*, HOMA-IR and HbA1c). Consistently, significant differences were found in cfDNA load between groups classified according to their BMI, IL-6 or HOMA-IR. In addition, bulk RNA sequencing in omental visceral adipose tissue (OVAT) from LOBB patients and subsequent weighted gene co-expression network analysis (WGCNA) identified a proliferation-, differentiation- and apoptosis-related transcriptional gene cluster associated with circulating cfDNA levels. Finally, we established a pipeline using captured enzymatic-methylation sequencing and a human atlas for tissue-specific methylation pattern deconvolution of mixed LOBB cfDNA samples to determine the contribution of different tissues to the cfDNA pools. This enabled us to identify adipocytes as important contributors to blood cfDNA in obese patients, together with pancreas- and liver-derived cells. Overall, our data highlighted cfDNA potential as diagnostic biomarker in metabolic disorders.

Poster 7

Effects of fertility treatment on pregnancy and long-term consequences for parents and children

N. Kabbani[1], R. Baber[2], C. Meigen[3], E. Rossi[3], S. Grunewald[4], J. Bartley[1], M. Köhler[5], T. Kretschmer[6], A. Schumacher[6], C. Pelka[7], R. O. Grabowska[8], B. Aktas[1], . Kramuschke[9], S. Kohli[2]

[1]University of Leipzig Medical Center, Clinic and Polyclinic for Gynecology, Leipzig, Germany, [2]University of Leipzig Medical Center, Institute of Laboratory Medicine, Clinical Chemistry und Molecular Diagnostics, Leipzig, Germany, [3]Leipzig University, LIFE Child, Leipzig Research Center for Civilisation Diseases, Leipzig, Germany, [4]University of Leipzig Medical Center, Clinic and Polyclinic for Dermatology, Venerology, and Allergology, Leipzig, Germany, [5]Leipzig University, Institute for Laboratory Medicine, Clinical Chemistry und Molecular Diagnostic, Leipzig, Germany, [6]Helmholtz Centre for Environmental Research – UFZ, Department of Environmental Immunology, Leipzig, Germany, [7]University of Leipzig Medical Center, Clinic and Polyclinic for Gynecology, Department for Obstetrics, Leipzig, Germany, [8]
Helmholtz Centre for Environmental Research – UFZ, Institute for Laboratory Medicine, Clinical Chemistry und Molecular Diagnostic, Leipzig, Germany, [9]University of Leipzig Medical Center, Clinic and Polyclinic for Pychosomatic Medicine and Psychotherapy, Leipzig, Germany

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The project Leipzig Reproductive Health Research Center (LE-REP) is a cooperation between the Faculty of Medicine at Leipzig University, Leipzig University Hospital and the Helmholtz Centre for Environmental Research - UFZ, funded by the Federal Ministry of Education and Research. The project aims to investigate the effects of fertility treatment on pregnancy and its long-term consequences for parents and children.

Our study group consists of people with intact and non-intact pregnancy after fertility treatments (ART: assisted reproductive technology), as well as people who have been affected by involuntary childlessness for more than one year. In contrast, our control group consists of people with intact and non-intact pregnancy without fertility treatment as well as pregnant individuals with the desire to terminate the pregnancy. We have further established 5 different work packages (WP) within LE-REP, each with their own subprojects. WP1 aims to assess risk factors for pregnancy complications after ART. WP 2 aims to assess the effects of ART and obesity on child health. WP 3 will investigate the pathomechanisms of miscarriage and preeclampsia after ART. WP 4 will explore the effects of ART on long-term psychosocial health. WP 5 will investigate the effects of endocrine disrupting chemicals on pregnancy after ART.

Recruitment started in 2024 and will continue until 2029. Blood samples taken from participants at different time-points will be analyzed to identify biomarkers of pregnancy outcomes and fertility, and develop risk-models for predicting pregnancy complications.

Poster 8

Galanin neurons in the mediobasal hypothalamus regulate glucose homeostasis

J. Schuller[1], L. M. Dropmann[1], H. Backes[2], J. C. Brüning[2], M. Blüher[1], N. Klöting[1], A. Jais[1]

[1]Helmholtz Institute for Metabolic, Obesity and Vascular Research, Leipzig, Germany, [2]Max Planck Institute for Metabolism Research, Cologne, Germany

The central nervous system, and especially the hypothalamus, play a pivotal role in controlling glucose metabolism and energy homeostasis. However, the neurocircuitry that responds to specific dietary factors and regulates feeding and energy homeostasis upon caloric overload still needs to be elucidated.

To acquire further insights into the pathophysiology of obesity and diabetes, we employed an unbiased experimental approach to characterize molecular signatures, defining neuronal populations activated after the ingestion of a hypercaloric, palatable high-sucrose diet (HSD). Our experiments reveal that galanin-expressing neurons (GAL neurons) within the mediobasal hypothalamus (MBH) are activated upon acute HSD consumption. Importantly, the role of these GAL neurons in the regulation of feeding and energy homeostasis remains unclear and requires further investigation.

We used the designer receptor exclusively activated by designer drugs (DREADD) system to chemogenetically activate GAL neurons in the MBH of Gal-Cre mice. Activation of these neurons results in a reduction in food intake during normal chow diet feeding and, surprisingly, an increase in circulating insulin levels. Additionally, transcriptomic analysis of metabolic organs, such as adipose tissue, indicates a decrease in peripheral insulin sensitivity.

Collectively, these findings provide insights into the molecular nature and metabolic function of specific galanin-expressing neuronal populations that respond to consumption of hypercaloric palatable food and regulate whole-body energy homeostasis.

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Poster 9

Identification of maternal dietary patterns during pregnancy and their impact on the newborn

T. Zacher[1,2,3,4,5], M. Vogel[1,2,3,4,5], W. Kiess[1,2,3,4,5]

[1]Leipzig University, Germany, [2]Faculty of Medicine, Leipzig, Germany, [3]Hospital for Children and Adolescents, Leipzig, Germany, [4]Center of Pediatric Research, Leipzig, Germany, [5]LifeChild Study, Leipzig, Germany

The objective of this study was to identify distinct dietary patterns among pregnant women. In addition, the study aimed to investigate associations between these patterns and neonatal outcomes.

We included 1325 mother-child-pairs from the LIFE Child cohort who completed a Food Frequency Questionnaire during their pregnancy. Data was collected between 2011 and 2024. To identify food groups and dietary patterns, hierarchical clustering was applied. Linear and generalized linear models were used to examine how these dietary patterns are associated with (a) maternal parameters such as BMI and socioeconomic status (SES), as well as (b) infant birth outcomes, e.g., birth weight.

Clustering of foods yielded nine food categories: vegetables, fish, meat, dairy, carbohydrates, convenience foods, unhealthy items, healthy breakfast, and bread meal. Based on these, 6 clusters of distinct dietary behaviors were identified. Our analysis found significant differences in dietary habits and a corresponding difference in BMI. For example, women in one cluster (C3) consumed more unhealthy foods and convenience products, while those in another cluster (C4) had a higher intake of vegetables and avoided unhealthy foods. These behaviors were associated with the weight status of mothers and children: Women in C3 had significantly higher BMIs ($p < .001$), whereas those in C4 had lower BMIs ($p = .006$). Furthermore, newborns from mothers in C3 had a higher BMI at birth ($p = .04$) than the reference cluster, whereas infants from mothers in C4 were more likely to have a lower BMI at birth ($p = .007$).

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Poster 10

Intranasal Peptide Delivery for Modulation of Food Intake: Targeting NPY, MC4R, and GhrR Systems

B. Özbay[1], E.-M. Jülke[2], K. Immig[1], M. Nowicki[1], I. Bechmann[1], A. G. Beck-Sickinger[2]

[1]Leipzig University, Faculty of Medicine, Institute of Anatomy, Leipzig, Germany, [2]University of Leipzig, Faculty for Life Sciences, Institute of Biochemistry, Leipzig, Germany

This study explores the modulation of food intake through the targeted intranasal administration of peptides that influence key receptors involved in energy homeostasis, namely the neuropeptide Y system (Y1R and Y2R), the melanocortin 4 receptor (MC4R), and the ghrelin receptor (GhrR). Obesity and cachexia represent opposite but equally challenging health issues, both of which are influenced by imbalances in the regulation of energy intake. By selectively targeting these receptors, peptides have shown promise as therapeutic agents. However, effective delivery to the brain remains a major challenge due to the blood-brain barrier and low bioavailability. In this study, fluorescently labeled peptides were administered intranasally to mice. The mice were euthanized under anesthesia, and the brain tissues were analyzed using fluorescent imaging techniques to monitor their uptake and distribution in key brain regions, such as the olfactory bulb, hypothalamus, and cortex. Additionally, we investigated the impact of repeated daily administration over 14 days on food intake and body weight. The results demonstrated a tendency in daily food intake consistent with the expected effects: MC4R agonists reduced intake, while GhrR agonists increased it compared to the control group. These findings highlight the potential of intranasal peptide delivery as a non-invasive and effective approach for modulating food intake, with significant implications for the treatment of obesity and other metabolic disorders.

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Poster 11

Investigating adipocyte function and dysfunction in human mature and SVF-derived adipocytes

H. Broghammer[1], C. Gebhardt[1], R. Nuwayhid[2], S. Langer[2], M. Blüher[1], J. T. Heiker[1]

[1]Helmholtz Institute for Metabolic, Obesity and Vascular Research, Molecular Obesity Research, Leipzig, Germany, [2]Universitätsklinikum Leipzig, Klinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Germany

To date, much of the basic obesity research relies on immortalized or primary adipocyte cell lines derived from mice. However, the translation of these findings to human disease is limited. Thus, there is an urgent need for advanced human adipocyte cell culture models to bridge the gap between basic research and clinical applications.

To address this need, we have established two human adipocyte cell culture models: mature adipocyte aggregate cultures (MAAC) and SVF-derived adipocyte cultures. These models are derived from human patients and can be used in various metabolic assays or for genetic manipulation to investigate human adipocyte function. The cell culture models enable us to carry out gene expression analyses, metabolic investigations and treatments in order to map and investigate the complexity and heterogeneity of obesity. Furthermore, we are able to analyze the role of certain molecules or proteins on adipocyte function in both MAAC and SVF-derived adipocytes by gene editing using siRNA and plasmid transfections. In addition, we have succeeded in measuring the oxygen consumption rate of MAAC using the Seahorse XF Analyzer and thus gaining detailed insights into cell metabolism.

The use of these human adipocyte models is crucial for the confirmation and detection of pathological processes in human adipose tissue and may strengthen scientific knowledge that has the potential to be followed up or used for therapeutic approaches.

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Poster 12

Linking Salivary Extracellular Vesicle-Derived MicroRNAs to Taste Cell Transcriptomics

K. Röhrborn[1], D. Thor[2], A. Hoffmann[1], T. Hagemann[1], A. Lorenz[3], C. Nottmeier[4], M. Schmidt[5], A. Roesner[6], S. Hahnel[5], T. Koehne[4], P. Kovacs[7], M. Stumvoll[7], M. Blüher[1,7], I. Schamarek[7], K. Rohde-Zimmermann[1]

[1]Helmholtz Institute, HI-MAG, Leipzig, Germany, [2]Rudolf Schönheimer Institute for Biochemistry/ Leipzig University, Germany, [3]Department of Prosthodontics and Materials Science, Leipzig, Germany, [4]Department of Orthodontics, Leipzig University, Germany, [5]Clinic of Prosthodontics, University Clinic of Regensburg, Germany, [6]Department of Prosthetic Dentistry, University Hospital Freiburg, Center for Dental Medicine, Freiburg, Germany, [7]Leipzig University, Faculty of Medicine, Leipzig, Germany

Research question:

Extracellular vesicles (EVs) hold significant medical prospect as carriers of molecules like microRNAs for targeted therapeutic and diagnostic purposes on a cellular level. In the context of obesity research, EVs have gathered attention for their potential role in influencing eating behaviour.

Objectives:

This study examines the link between metabolic changes in obesity, taste perception, and EV composition. A total of 111 subjects from the Obese Taste Bud Study were analyzed for salivary EVs.

Methods:

EVs were isolated from 2 ml of saliva using the ÄKTA, a size- and molecular weight-based separation system. Nanosight technology and western blot were used for EV quantification and characterization. RNA extraction was performed with the miRNeasy Micro Kit, followed by sequencing on the NovaSeq6000 platform to assess the microRNA content of salivary EVs.

Results:

The findings show a link between EV size and nutritional markers (all $P<0.05$). Higher EV concentration is associated with lower body weight ($P=0.032$) and reduced arm ($P=0.011$) and calf circumference ($P=0.042$), indicating body composition affects salivary EVs more than obesity itself. Clean vesicles were isolated, confirmed by EV markers like HSC70, CD63, ALIX, and the intriguing presence of PPARg, hinting at a possible origin EVs from fat cells.

Conclusion:

These findings offer insights into the relationship between EVs, taste perception, and obesity, aiding the development of interventions. Ongoing analyses of salivary EV microRNA may further reveal their impact on taste buds.

Poster 13

Molecular characterisation of galanin neurons in the mediobasal hypothalamus

L. M. Dropmann[1], J. Schuller[1], H. Backes[2], J. C. Brüning[2], N. Klöting[1], M. Blüher[1], A. Jais[1]

[1]Helmholtz Institute for Metabolic, Obesity and Vascular Research, Leipzig, Germany, [2]Max Planck Institute for Metabolism Research, Cologne, Germany

The mediobasal hypothalamus (MBH) plays an important role in regulating energy balance by sensing and integrating peripheral metabolic signals. Dietary factors and circulating nutrients can aRect the central regulation of energy homeostasis and feeding behaviour via genetically, anatomically and functionally distinct neuronal populations. They thus represent important cues in the aetiology of obesity and diabetes.

One of the major contributors to energy intake in the Western diet is sugar. However, it is still unknown how high sugar intake aRects the neurocircuitries involved in regulating energy balance.

PhosphoTRAP screening reveals that acute high sucrose diet feeding leads to the activation of hypothalamic galanin (GAL)-expressing neurons, which are distinct from the already known classical feeding-regulating neurons.

Spatial transcriptome analysis of the mouse MBH indicates diRerential gene expression between adult and old mice. Interestingly, galanin expression increases with age. Moreover, a small subset of GALMBH neurons was found to express Glp1r that is known to be critically involved in the control of blood glucose levels.

Translatome profiling of these neurons allows us to delineate which neuropeptides, ion channels, G-protein coupled receptors and transporters are endogenously expressed and which neurotransmitters are released by these cells. These results may provide further means of targeting GALMBH neurons for pharmacological manipulation in the context of glucose metabolism and feeding regulation.

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Poster 14

Significant body fat reduction and its role as a predictor for liver steatosis in participants of the intensive weight loss program DocWeight 2.3®

L. Hohenstein[1], R. Schürfeld[1], J. Wiegand[2], M. Blüher[1,3], T. Karlas[4], H. Schlögl[1,3]

[1]Leipzig University Medical Center, Clinic for Endocrinology, Nephrology and Rheumatology, Leipzig, Germany, [2]Leipzig University Medical Center, Department of Medicine II, Division of Hepatology, Leipzig, Germany, [3]Helmholtz Institute for Metabolic, Obesity and Vascular Research (HI-MAG) [4]University of Leipzig Medical Center, Department of Medicine II, Division of Gastroenterology, Leipzig, Germany

In persons with obesity, behavioral weight loss (BWL) programs can lead to significant weight reductions and improvements of associated comorbidities like steatotic liver disease. DocWeight 2.3® is a one-year BWL program including intensive dietary counselling, cognitive behavioral therapy and sports. In the DocWeight 2.3® study, participants were randomized into three groups: the DocWeight 2.3® program with an initial eight-week formula diet phase (DW-F), the program without the formula phase (DW) or a control group (CG). This preliminary data from the six-month follow-up evaluates its effectiveness and impact on liver steatosis.

Liver steatosis was measured using ultrasound-derived fat fraction (UDFF), controlled attenuation parameter (CAP) and attenuation imaging (ATI). We developed a linear mixed model (LMM), adjusted for time, sex, and group, in order to identify the best predictors of CAP, UDFF and ATI.

Data were collected from 37 patients (62% female, median [1st; 3rd quartile] age 49 [37; 59] years, body mass index 38.9 [34.7; 43.2] kg/m²). The DW-F group had greatest reductions in body fat (BF, -33.6%, p=0.0005), followed by the DW group (-12.3%, p=0.002), while the CG group showed no significant decreases (-11.8%, p=0.4). Muscle mass did not change significantly in all groups. The LMM analysis indicated that BF reduction was the best predictor of CAP (p=0.003) and UDFF (p=0.01) decreases, but not of ATI (p=0.2).

We observed clinically meaningful reductions in BF in both DW groups. These decreases were identified as a key predictor of improved liver steatosis.

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Poster 15

Systematic comparison of cell culture models for metabolically activated macrophages

J. Ackermann, L. Bremkamp, C. Hobusch, F. Kirmse, M. Gericke

Leipzig University, Institute of Anatomy, Faculty of Medicine, Leipzig, Germany

Obesity triggers low-grade inflammation in adipose tissue, which correlates with the onset of metabolic disease. This inflammation is characterized by an increase of adipose tissue macrophages and a pro-inflammatory phenotypic switch. Recent evidence highlights the differences between LPS-induced *classically activated* macrophages and *metabolically activated* or *lipid-associated* macrophages, which occur during obesity.

Here, we systematically compare the reliability and validity of several published murine cell culture models used to induce *metabolic activation*. We compare three cell culture media, two bone marrow-derived macrophage protocols, three cell lines, and four protocols for *metabolic activation*. *Metabolic activation* was assessed by morphology, flow cytometry, and qPCR.

With the various protocols, we were able to induce multiple hallmarks of *metabolic activation* at gene and protein levels, which differ significantly from *classical activation*. The choice of cell culture medium resulted in minor differences in gene and protein expression. We show that *metabolic activation* induced by the widely used MMe protocol depends primarily on palmitate and less on glucose and insulin. The adipose tissue co-culture protocol reflects many hallmarks of *metabolically activated* or *lipid-associated* macrophages *in vivo*.

iBMDMs, MPI cells, and J774A.1 cells were compared in parallel to develop a model suitable for applications that require proliferating cells or higher cell numbers.

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Poster 16

The impact of fat-body-specific Neurexin-1 Knockdown in Drosophila and its role in metabolism and eating behaviour

L. Brunner[1], J. Giesche[1], S. Aurich[1], M. Saurbrey[1], B. Gutsmann[1], D. Pauls[2], P. Kovacs[1], A. Tönjes[1], J. Breitfeld[1]

[1]University of Leipzig Medical Center, Department of Medicine lll, Division of Endocrinology, Nephrology and Rheumatology, Leipzig, Germany, [2]Leipzig University, Department of Animal Physiology, Institute of Biology, Leipzig, Germany

Background:

Genetic variants in human *neurexin-3 (NRXN3)* have been linked to body fat distribution metrics, such as waist-to-hip-ratio [1]. *Neurexin1*-null flies present a significantly altered metabolic profile characterized by decreased lipid and carbohydrate stores [2]. In this study, we examined whether *Nrx-1* plays a role in regulating food intake and body weight in *Drosophila melanogaster.*

Methods:

Due to the high conservation of glucose and fat metabolism pathways between fruit flies and humans, *Drosophila melanogaster* serves as an excellent model to study physiological parallels. Using the GAL4-UAS system, we created an adipose tissue-specific knockdown (KD) of *Nrx-1* (the fly homologue of the human *NRXN3*) by crossing a *UAS-Nrx-1* line with a tissue-specific driver line. We then investigated its localized effect on adipocytes and its influence on whole-body metabolic processes. In addition, we assessed whether the KD of *Nrx-1* in the fat body alters the food intake of the flies.

Results and conclusion:

The downregulation of *Nrx-1* appears to affect the metabolic phenotypes, as we observed a significant reduction in body weight in both KD-flies and larvae, despite no detectable changes in food intake. Ongoing analyses aim to further explore metabolic processes, including triglycerides and glycogen storage, to gain more insights into the underlying mechanisms behind the observed body weight alterations.

References:

[1] Heard-Costa NL, Zillikens MC, Monda KL, et al., (2009), NRXN3 is a novel locus for waist circumference: a genome-wide association study from the CHARGE Consortium, PLoS Genet, e1000539, 5/6, doi:10.1371/journal.pgen

[2] Levy, Kyra A.; Weisz, Eliana D.; Jongens, Thomas A., (2022), Loss of neurexin-1 in Drosophila melanogaster results in altered energy metabolism and increased seizure susceptibility, Human molecular genetics, 3422–3438, 31/20, doi: 10.1093/hmg/ddac115.

Poster 17

The role of macrophages in adipocyte degradation – extracellular digestion via lysosomal exocytosis

R. Wehr, N. Raulien, M. Gericke

Leipzig University, Institute of Anatomy, Faculty of Medicine, Leipzig, Germany

Macrophages play a central role in tissue homeostasis, such as in adipose tissue (AT). They are essential for the clearance of dead cells and tissue regeneration. In general, death cells are degraded via phagocytosis. However, adipocytes can reach a size about five times the size of the macrophages, they cannot be easily phagocytosed and anti-inflammatory removal is a challenge.

One strategy of degradation is the activation of AT macrophages (ATMs) and their accumulation around dead adipocytes, forming crown-like structures (CLS). ATMs in CLS tend to exhibit an inflammatory polarization. So, instead of a classical, anti-inflammatory efferocytosis, extracellular digestion by ATMs via lysosomal exocytosis is proposed as a degradation pathway. During lysosomal exocytosis, the lysosomes fuse with the macrophage membrane and release their lysosomal enzymes into the extracellular space. Therefore, the area of the macrophage-adipocyte-interface becomes acidic, which enables the activity of lysosomal acid hydrolases.

We aim to find a pharmaceutical approach to encourage the anti-inflammatory clearance of dead adipocytes in macrophages. We wanted to influence lysosomal exocytosis with activators and inhibitors and examine the macrophages in this process.

We found that CLS formation and exocytosis markers increased over time in our ex-vivo model of AT inflammation, with an enhanced surface abundance of lysosomal proteins. In summary, lysosomal exocytosis can be modulated by different treatment strategies that directly or indirectly impact macrophage numbers and activation states.

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Poster 18

Biomarkers Troponin and Procalcitonin in Addition to CRB-65 Enhance Risk Stratification in Patients with CAP

I. Farhat[1], M. Rosolowski[1], K. Ahrens[2], J. Lienau[2], P. Ahnert[1], M. Pletz[3], G. Rohde[4], J. Rupp[5], G. CAPNETZ Study Group[6], M. Scholz[1], M. Witzenrath[2]

[1]Leipzig University, Institute for Medical Informatics, Statistics, and Epidemiology (IMISE), Leipzig, Germany, [2]Universitätsmedizin Berlin, Department of Infectious Diseases, Respiratory Medicine and Critical Care, Berlin, Germany, [3]Universitätsklinikum Jena, Germany, [4]Goethe University Frankfurt, University Hospital, Medical Clinic I, Department of Respiratory Medicine, Frankfurt/Main, Germany, [5]Universitätsklinikum Schleswig Holstein, Lübeck, Germany, [6]CAPNETZ Stiftung, Hannover, Germany

Background:

Community-acquired pneumonia (CAP) remains a leading cause of infectious disease mortality globally, necessitating ICU admission for approximately 10% of hospitalized patients. Accurate prediction of disease severity facilitates timely therapeutic interventions.

Methods:

Our study aimed to enhance the predictive capacity of the clinical CRB-65 score by evaluating eight candidate biomarkers: TnT-hs, PCT, NT-proBNP, Ang-2, copeptin, ET-1, lipocalin-2, and MR-proADM. We utilized a machine-learning approach on 800 samples from the German CAPNETZ network to refine risk prediction models combining these biomarkers with the CRB-65 score regarding our defined endpoint: death or ICU admission within 28 days after study inclusion.

Results:

Elevated levels of biomarkers were associated with the endpoint. TnT-hs exhibited the highest predictive performance among individual features (AUC = 0.74), followed closely by PCT (AUC = 0.73). Combining biomarkers with the CRB-65 score significantly improved prediction accuracy. The combined model of CRB-65, TnT-hs, and PCT demonstrated the best balance between high predictive value and parsimony, with an AUC of 0.77 [95% CI: 0.72-0.82] while CRB-65 alone achieved an AUC of 0.67 [95% CI: 0.64-0.73].

Conclusion:

Our findings suggest that augmenting the CRB-65 score with TnT-hs and PCT enhances the prediction of death or ICU admission in hospitalized CAP patients. Validation of this improved risk score in additional CAP cohorts and prospective clinical studies is warranted to assess its broad clinical utility.

Poster 19

Characterization of two Klebsiella pneumoniae phages for potential therapeutic applications

Z. Selpiev[1], M. Müsken[2], S. Leptihn[3,4], B. Loh[1]

[1]Fraunhofer Institute for Cell Therapy and Immunology, Department of Vaccines and Infection Models, Leipzig, Germany, [2]Helmholtz Centre for Infection Research, Central Facility for Microscopy, Braunschweig, Germany, [3]Health and Medical University Erfurt, Department of Biochemistry, Erfurt, Germany, [4]University of Southern Denmark, Department of Biochemistry and Molecular Biology, Odense, Denmark

Bacteriophages present a promising way to treat bacterial infections, especially in the cases where traditional antimicrobials yield little effect. When considering phages for therapeutic purposes, a process of characterization is required. The characterization includes assessment of key properties like infectivity, stability, as well as genomic identity; These would provide an insight into the phages' spectrum of activity, storage conditions, and presence of undesired virulence genes, respectively. In this study, two different bacteriophages targeting a clinical *Klebsiella pneumoniae* strain have been isolated and characterized.

Poster 20

Critical role for CD97/ADGRE5 in the induction of allergic airway inflammation

M. Quaas[1], A.-L. Hoh[1], C. Kerner[1], M. Wagner[2,3], M. Steinert[1], J. Hamann[4], T. Polte[2,3], G. Aust[1,5]

[1]Leipzig University and University of Leipzig Medical Center, Research Laboratories and Department of Visceral, Transplantation, Thoracic, and Vascular Surgery, Leipzig, Germany, [2]Helmholtz Centre for Environmental Research - UFZ, Department of Environmental Immunology, Leipzig, Germany, [3]Leipzig University Medical Center, Department of Dermatology, Venerology and Allergology, Leipzig, Germany, [4]Amsterdam Institute for Infection and Immunity, Department of Experimental Immunology, Amsterdam, Netherlands, [5]Leipzig University and University of Leipzig Medical Center, Research Laboratories and Department of Orthopaedics, Trauma and Plastic Surgery, Leipzig, Germany

Allergic asthma, a chronic inflammatory disease affecting more than 340 million people worldwide, is caused by an inappropriate type 2-biased immune response to inhaled allergens such as house dust mite (HDM). The adhesion GPCR CD97/*ADGRE5* is expressed on immune and lung epithelial cells in human and mouse. Here, we investigated its role in the development and maintenance of allergic asthma. Loss of CD97, induced either genetically in *Cd97-/-* mice or by targeting CD97 with a CD97 antibody (Ab), increased allergic asthma in ovalbumin- and HDM-induced acute and chronic mouse asthma models. Based on our data, CD97 plays a critical role in the induction of a specific type 2-biased allergic immune response.

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Poster 21

Deep learning-aided inter-species-comparison of immune response in drug development involving cynomolgus monkey

V. D. Friedrich[1,2], B. Fogal[3], Z. Loncova[4], K. Neier[3], M. Rade[5], M. Scholz[1,6], M. Shoaib[7], H. Kirsten[1], K. Reiche[2,5,8]

[1]Leipzig University, Institute for Medical Informatics, Statistics, and Epidemiology, Leipzig, Germany, [2]Center for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI), Leipzig, Germany, [3]Boehringer Ingelheim Pharmaceuticals, Inc., United States of America, [4]Biocenter, Institute of Bioinformatics, Medical University of Innsbruck, Austria, [5]Department of Diagnostics, Fraunhofer Institute for Cell Therapy and Immunology, Leipzig, Germany, [6]Leipzig University, Faculty of Mathematics and Computer Science, Leipzig, Germany, [7]Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Luxembourg, [8]Institute for Clinical Immunology, Leipzig University, Germany

Examining the efficacy and safety of therapeutic agents in the preclinical stage is integral to the early phase of drug development. Cynomolgus monkeys (Macaca fascicularis) are a commonly used animal model in preclinical studies investigating the immune system. Transferring findings from such studies to humans remains challenging. Single-cell transcriptomics (scRNA-seq) data presents a promising technique for in-depth analyses, offering a comprehensive snapshot of gene expression within an organism. Here, within the framework of the project imSAVAR (immune safety avatar: https://imsavar.eu/), we propose a cross-species analysis pipeline for scRNA-seq data from peripheral blood mononuclear cell subpopulations (PBMCs) in cynomolgus monkeys (Macaca fascicularis) and healthy humans following anti-CD3/anti-CD28 T Cell activation. By integrating biological domain knowledge into data-driven deep learning (DL) models, we try to exploit the power of DL while retaining interpretability. Our goal is to identify shared characteristics and divergences within T Cell-triggered immune response across cynomolgus monkey and humans, thus contributing to improved immunomodulating therapies in drug development strategies involving animal models. Our computational workflow can be applied to other species, stimuli, or disease, enabling data-driven cross-species analyses of the transcriptome.

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Poster 22

Development of a novel therapeutic approach for inflammatory bowel disease targeting IL-12/IL-23p40 through endogenously produced recombinant IL-12p80

S. S. Pethaperumal[1], S. Przybylski-Wartner[1], L. Kaysser[2], J. Lehmann[1]

[1]Fraunhofer Institute for Cell Therapy and Immunology(IZI), Preclinical Development and Validation, Leipzig, Germany, [2]Leipzig University, Institute of Drug Discovery, Leipzig, Germany

Inflammatory bowel disease (IBD) is an idiopathic, chronic inflammatory disease of the digestive tract with increasing incidence. Involved innate immune cells, i.e., neutrophils and macrophages, produce cytokines, proteolytic enzymes and free radicals that causes superficial mucosal ulceration along with other symptoms and hypoxia. So far, there is no curative therapy for IBD. Available conventional therapies can reduce symptoms, control complications and extent symptom-free intervals but may exert severe side effects. Therefore, there is an unmet medical need for a novel, curing therapeutic strategies in IBD. Considering the blooming genetics-based treatment for IBD, we developed a therapeutic concept pursues the aim of using a cytokines IL-12p40 and IL-12p80 (p40 homodimer) that can naturally regulate the excessive proinflammatory effects of IL-12p70 and IL-23 through gene therapy by a bacterial vector. The main objectives of the project is to confirm the efficacy and safety of IL12B-transduced live-attenuated Salmonella Enteritidis bacteria (S.E.) transferring the IL12B gene into murine macrophage cell lines in vitro and into macrophages and dendritic cells in a IBD mouse model in vivo and to examine the role of IL-12p40 and its homodimer IL-12p80 in the gut inflammation and its capacity to act as a natural antagonist for IL-12p70 and IL-23.

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Poster 23

Establishing human intestinal slice cultures as a pharmacological ex vivo model of inflammatory bowel diseases

J. Werner[1,2], L. Schiller[1,2], K. Hill[3], A. Hoffmeister[4], S. Kallendrusch[5], C. Vissiennon[1,2]

[1]Leipzig University, Faculty of Medicine, Institute of Medical Physics and Biophysics, Leipzig, Germany, [2]Repha GmbH Biologische Arzneimittel, Langenhagen, Germany, [3]Leipzig University, Faculty of Medicine, Rudolph-Boehm-Institute for Pharmacology and Toxicology, Leipzig, Germany, [4]University of Leipzig Medical Center, Clinic for Gastroenterology, Interdisciplinary Endoscopy, Leipzig, Germany, [5]Health and Medical University Potsdam, Medicinal Faculty, Potsdam, Germany

Current medications do not sufficiently treat all IBD patients, underscoring the need for new therapies. Preclinical models can elucidate drug mechanisms, supporting their use in IBD treatment. This project intends to establish precision cut intestinal slices (PCIS) from colon biopsies of IBD patients as a novel ex vivo model.

Influences of test substances (ref. compound: budesonide 1µM) on inflammatory processes were monitored by histological staining and examination of mediator release into the culture media. Initial results of HE-staining confirm a conserved intestinal morphology in PCIS ex vivo for 24 h (88,4% of samples) with no signs of tissue impairment after treatment with test substances. Preserved tissue viability during cultivation time was confirmed by immunofluorescence staining of apoptotic cells using cleaved-PARP as a marker. Compared to healthy tissue, IBD-typical morphological changes were observed. Immunohistochemistry reveals comparable percentages of $CD68^+$ macrophages but increased neutrophil elastase-positive granulocytes. After budesonide treatment immunofluorescence staining shows increased M2 subtype ($CD68^+/CD163^+$) macrophages compared to untreated tissue. The release of 24 mediators (like TNF, IL8, IL6) into the culture media was quantified using multiplex-ELISA. Budesonide significantly influenced this mediator pattern (e.g. decreased concentrations of proinflammatory cytokines).

By combining histology and mediator release results, this model allows investigating pharmacological active substances within the context of IBD's complex pathophysiology.

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Poster 24

How Effective Are Flurofamide And Pantoprazole Compared To Widely Used Antibiotics In Inhibiting Ureaplasma Growth?

J. Malle[1], K. Glaser[1,2], M. Laube[1]

[1]Leipzig University, Department of Pediatrics, Department of Neonatology, Leipzig, Germany, [2]University of Leipzig Medical Center, Center for Women's and Children's Medicine, Department of Neonatology, Germany

Background:

Ureaplasma colonization of the urogenital tract of pregnant women is associated with preterm birth and adverse neonatal pulmonary short- and long-term outcomes. *Ureaplasma* generate ATP by urea degradation through the enzyme urease, forming ammonia and altering the pH, both discussed as virulence factors. Effective eradication is needed to reduce chronic complications. Current treatments involve antibiotics such as macrolides and quinolones, but rising resistance has been reported.

Objective:

The present study aims to investigate flurofamide and pantoprazole as novel alternative treatment options in the eradication of *Ureaplasma* in comparison to commonly used antibiotics.

Methods:

Dilution series of *Ureaplasma urealyticum* serovar 8 were treated either with antibiotics, flurofamide or pantoprazole. Based on each minimum inhibitory concentration (MIC), we analyzed the pH shift, measured ATP concentrations, and determined the genome equivalents by qPCR, after a 10 hour incubation.

Results:

The MIC of flurofamide (5 µM) and pantoprazole (500 µM) were higher than antibiotics (1 µM). Notably, at this concentration, flurofamide effectively prevented pH changes, inhibited ATP release, and reduced genome equivalents similar to antibiotics, while pantoprazole had weaker effects. Variations in antibiotic efficacy were also noted.

Conclusion:

Our findings indicate that flurofamide inhibits *Ureaplasma* growth as effectively as standard antibiotics, while pantoprazole requires a concentration that is too high to be a feasable alternative. Future trials should focus on flurofamide.

Poster 25

Hypoplastic CDH lungs have abnormally increased alveolar macrophages that interfere with normal lung development

K. Sturm[1], J. Riedel[1], N. Peukert[1], R. Hiller[2], M. Boettcher[3], J. Martinovic[4], S. Mayer[1], M. Lacher[1], J.-H. Gosemann[1], A. Benachi[4], R. Wagner[1]

[1]University of Leipzig Medical Center, Department of Pediatric Surgery, Leipzig, Germany, [2]University of Leipzig Medical Center, Department of Diagnostics, Institute of Pathology, Leipzig, Germany, [3]University Hospital Mannheim, Clinic for Pediatric and Adolescent Surgery, Mannheim, Germany, [4]Hospital Antoine Beclere, Department of Gynaecology and Obstetrics, Clamart, France

Background:

Lung hypoplasia in patients with congenital diaphragmatic hernia (CDH) is a common developmental defect with significant neonatal mortality/morbidity and associated with abnormally enriched pro-inflammatory signaling. To better understand the molecular processes, we analyzed the involvement of alveolar macrophages in the pathobiology.

Material and Methods:

Lung hypoplasia was induced through the application of nitrofen in rat fetuses in vivo or in an ex vivo model. Fetal human and rat lungs CDH and controls were analyzed with untargeted proteomics, via Immunofluorescence, RT-qPCR, Multiplex assays and Western Blots. Tracheal aspirations from CDH control newborns were analysed via flow cytometry.

Results:

Untargeted proteomics revealed that pathways associated to macrophage activation were especially enriched in CDH. We observed an increase of CD68+ pulmonary macrophages in fetal human/rat CDH lungs. Macrophage-associated chemoattractants were significantly elevated in fetal rat CDH lungs during pseudoglandular lung development. Co-culture of hypoplastic rat lungs with fetal rat macrophages further impaired fetal lung growth/budding and induced the expression of pro-inflammatory markers in the co-cultured macrophages. Additionally, tracheal aspirations from CDH newborns showed a significant increase in alveolar macrophages.

Conclusion:

Our results indicate an abnormal presence of alveolar macrophages in CDH lungs in human and animal models. This suggests an immune cell mediated pro-inflammatory molecular program involved in the pathobiology of lung hypoplasia in CDH.

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Poster 26

Increased Aspergillus fumigatus-binding IgG1 and IgA in bronchoalveolar lavage fluid in equine asthma – Not simply allergic?

A. Keilhaue[1], M.-C. Jentsch[1], B. Wagner[2], C. Rhyner[3,4], S. Lübke[1], M. Karagulyan[1], C. Arnold[5], K. Lohmann[5], C. Schnabel[1]

[1]Institute of Immunology, Faculty of Veterinary Medicine, Leipzig, Germany, [2]Department of Population Medicine and Diagnostic Sciences, College of Veterinary Medicine, Cornell, Ithaca, NY, United States of America, [3]CK-CARE, Christine Kühne Center for Allergy, Research, and Education, Davos, Switzerland, [4]Swiss Institute of Allergy and Asthma Research (SIAF), Davos, Switzerland, [5]Department for Horses, Faculty of Veterinary Medicine, Leipzig, Germany

Introduction:

Horses exposed to hay dust often develop equine asthma (EA), a common equine airway disease. *Aspergillus* (*A.*) *fumigatus*, often found in moldy hay, is a confirmed EA stimulus; however, it is unclear if the underlying pathogenesis of EA is allergic. We aimed to analyze equine immunoglobulin (Ig) isotype binding to *A. fumigatus* antigens comprehensively, both locally in the lung (bronchoalveolar lavage fluid, BALF) and systemically (serum).

Methods:

In an ELISA approach, plates were coated with one of eight recombinant *A. fumigatus* antigens or *A. fumigatus* lysate. After incubation with either BALF or serum from healthy (n=18), mild to moderately asthmatic (MEA, n=20) or severely asthmatic (SEA, n=24) horses, *A. fumigatus*-binding equine isotypes (IgG1, IgG3/5, IgG4/7, IgG6, IgA, IgE) as well as overall binding Ig (Pan-Ig) were detected. Total Ig content of the samples was determined by bead-based assays.

Results:

Compared to healthy horses, *A. fumigatus*-binding Pan-Ig, IgG1 (in BALF and serum) and IgA (in BALF) were increased in asthmatic horses. Binding of other isotypes, including IgE, were similar in all groups. Horses with MEA and SEA showed overall similar Ig binding. Total serum IgG4/7 content was increased in MEA, and BALF IgG1 and IgG4/7 contents were elevated in SEA compared to healthy horses.

Discussion:

IgG1 and IgA, but not IgE, appear to be relevant isotypes in neutrophilic EA. This questions allergy/type I hypersensitivity as the only mechanism underlying EA. However, equine IgG1 can activate complement and could contribute to type III hypersensitivity.

Poster 27

Long-lasting changes in circulating dendritic cell and monocyte subsets, and altered expression of EMR2, CD97 and EMR3 on these cells in the posttraumatic course

L. Zheng[1], C. Fuchs[1], C. Kleber[1], G. Osterhoff[1], G. Aust[2]

[1]Leipzig University and University of Leipzig Medical Center, Research Laboratories and Department of Orthopaedics, Trauma and Plastic Surgery, Leipzig, Germany, [2]Leipzig University and University of Leipzig Medical Center, Research Laboratories and Department of Orthopaedics, Trauma and Plastic Surgery, Research Laboratories and Department of Visceral, Transplantation, Vascular and Thoracic Surgery, Leipzig, Germany

Traumatic injury leads to a sudden release of damage-associated pattern (DAMP). Dendritic cells (DCs) and monocytes play central roles in DAMP sensing, uptake, and presentation to naïve T-cells.

Here, we monitored the circulating DC and monocyte subsets in traumatized patients and uninjured volunteers using flow cytometry. Simultaneously, EMR2 and its closest relatives CD97 and EMR3 were quantified on these subsets to get insight in their (patho)physiological regulation and clinical relevance.

Posttraumatically, the percentage of conventional and partly plasmocytoid DCs among $CD45^+$ leukocytes decreased and correlated inversely to adverse clinical parameters 120-240 h after trauma. EMR2 increased transiently in cDCs, whereas CD97 decreased on pDCs in the posttraumatic course. Simultaneously, trauma caused injury-dependent phenotype changes in monocytes. The percentage and absolute number of classical monocytes was increased over a long period, whereas intermediate and non-classical monocytes partly decreased. After trauma EMR2 levels increased transiently independent of injury severity in all monocyte subsets. CD97 showed a similar, less pronounced time course, whereas EMR3 decreased and remained posttraumatically low.

The composition of circulating DC and monocyte subsets changed, frequently related to injury severity and further clinical parameters, in the posttraumatic course. EMR2, CD97 and EMR3, were partly differently regulated on these subsets, indicating different functions after injury.

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Poster 28

Metabolomics Pipeline for Comparative Analysis of Glycerophospholipid and Sphingolipid Metabolism between Healthy and Community Acquired Pneumonia Patients: Insights into Disease Pathogenesis

P. Jhawar, P. Ahnert, M. Rosolowski, H. Kirsten, M. Scholz, M. Löffler

Leipzig University, Institute of Medical Informatics, Statistics and Epidemiology, Leipzig, Germany

There is growing evidence that alterations in lipid metabolism, particularly in glycerophospholipids and sphingolipids, are associated with inflammatory conditions such as seen in community-acquired pneumonia (CAP). While these lipid classes are crucial for maintaining membrane integrity and cellular signaling, their involvement in the pathophysiology of CAP is not yet fully understood. Understanding how disruptions in these metabolic pathways contribute to the disease could help identify new, more effective biomarkers for CAP diagnosis and prognosis. This research aims to elucidate the molecular mechanisms behind pneumonia using a targeted metabolomics approach.

A total of 237 patient samples from 5 different studies were included in this study, including 79 CAP cases from the PROGRESS study and 79 healthy controls from the population-based LIFE-ADULT study. A liquid chromatography-mass spectrometry (LC-MS) pipeline was developed and applied for metabolic profiling. Significant metabolites with variable importance in projection (VIP) score ≥ 1 in PLS-DA and volcano plot analysis of fold-change > 2 and P values < 0.05 were integrated with existing literature to explore the underlying mechanisms of Pneumonia.

The study revealed that in CAP patients, reduced levels of sphingomyelins, LPCs and LPEs were accompanied by a marked increase in ceramides. The elevated ceramide levels are associated with increased inflammation and sepsis severity, while the reduced LPCs and LPEs, which typically have anti-inflammatory effect may worsen immune responses.

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Poster 29

Molecular Evolution of Mycobacterium avium subsp. paratuberculosis (MAP) in Africa

W. A. Elmagzoub[1,2], S. Idris[3], J. Ssekitoleko[4], P. Schweizer[1], A. Gameel[3], L. Ojok[4], J. B. Okuni[4], A. Amanzada[5], E. Eltayeb[6,7], K. Eltom[8], A. Abd El Wahed[1]

[1]Leipzig University, Institute of Animal Hygiene and Veterinary Public Health, Leipzig, Germany, [2]University of Bahri, Department of Biology and Biotechnology, College of Applied and Industrial Sciences, Khartoum North, Sudan, [3]University of Khartoum, Faculty of Veterinary Medicine, Department of Pathology, Khartoum, Sudan, [4]Makerere University, College of Veterinary Medicine, Animal Ressources and Biosecurity, Kampala, Uganda, [5]University Medical Centre Göttingen, Department of Gastroenterology and Gastrointestinal Oncology, Göttingen, Germany, [6]Ibn Sina Specialised Hospital, Khartoum, Sudan, [7]Al Neelain University, Khartoum, Sudan, [8]University of Khartoum, Unit of Animal Health and Safety of Animal Products, Institute for Studies and Promotion of Animal Exports, Khartoum North, Sudan

In Africa, research on *Mycobacterium avium* subsp. *paratuberculosis* (MAP) is limited. MAP causes Johne's disease in ruminants, leading to economic losses, and has been implicated in Crohn's disease. This DFG-funded project, conducted in the Sudan and Uganda with collaboration of two German universities. It investigated the prevalence of MAP infection in 1814 cattle samples in Uganda and in the Sudan in 1080, 810, 270 and 270 samples from cattle, small ruminants, camels, and wild animals, respectively. The susceptibility and resistance genes in local African breeds were explored. The virulence factors in four local isolates were analysed in murine cell lines. MAP was also tested in 116 human patients. A salient milestone was the first-time link between MAP infection and human gut microbiome, despite extensive zoonosis research. Parallel investigation on gut microbiome in infected cattle revealed potential effect of MAP and hormones on the microbiome. Moving forward, gut species correlated with MAP will be examined in human organoids to assess their role in infection establishment. Advancing identification of virulence factors in African isolates bovine macrophages and organoids will be utilized. The high MAP incidence in humans (40%) in the Sudan is likely due to close contact with animals, and highlight the need to address exposure via animal products and water. Given it is the same situation in Uganda, a similar study will be conducted there. Weather effects on MAP survival and infection endemicity, considering UV, temperature, dryness, and humidity, will also be explored.

Poster 30

Point-of-care solution for rapid monitoring of cytokine release syndrome by chemiluminescence cytokine detection on sensitive Single Photon Avalanche Diodes (SPAD) sensors

A. Lopes[1], P. Scholz[1], B. Saft[2], E. Schäfer[2], M. Wiener[2], N. Isserstedt-John[3], K. Naumann[4], S. Allelein[1], D. Kuhlmeier[1]

[1]Fraunhofer IZI, Leipzig, Germany, [2]IMMS, Erfurt, Germany, [3]Microfluidic ChipShop, Jena, Germany, [4]LUCAS instruments GmbH, Jena, Germany

Cytokine Release Syndrome (CRS) is a serious complication arising from both infectious and non-infectious origins. This exacerbated immune reaction leads to a rapid release of inflammatory cytokines into the blood stream, with potential to cause multi organ failure and death. Therapeutic preventive immunosuppression is not always the answer, as it can affect the capacity to control an infection or also reduce the efficacy of immunotherapies which rely on a pro-inflammatory environment. Consequently, early detection of CRS is essential to prevent such negative outcomes, especially by controlling the level of circulating cytokines including interleukin (IL)-6 and interferon gamma. A solution for a sensitive, fast and frequent cytokine monitoring tool would be of great interest, in order to support a more customizable, patient-specific treatment plan.

Unlike conventional photomultiplier tube or fluorescence-based readouts, which rely on excitation light sources, expensive filters and bulky setups, using a SPAD-based sensor for light detection can not only reduce costs, as none of those features are needed, but also enable higher sensitivities. Our aim is to fully integrate multiplex cytokine detection on a microfluidic cartridge in a table-top device, including blood plasma separation from a few microliters sample, incubation and chemiluminescence analysis. This device will provide patient-near and timely cytokine levels, supporting a physician on early decision making on handling CRS, thereby ensuring that patients receive prompt treatment and experience fewer complications.

Poster 31

Right sided Loefflers endocarditis leading to heart transplantation: a case report

P. Buske, J. Jozwiak-Nozdrzykowska, M. Sandri, H. Thiele

Herzzentrum Leipzig, Kardiologie, Leipzig, Germany

Loeffler endocarditis is a rare form of cardiomyopathy marked by myocardial infiltration with eosinophilic leukocytes, leading to progressive cardiac dysfunction. Due to its low incidence and varied clinical presentations, it is frequently underdiagnosed. Early identification is essential, as it can prevent the progression to an irreversible restrictive phenotype. Here, we report the case of a patient with Loeffler endocarditis and a large fibrotic structure in the right ventricle, who presented to the Leipzig Heart Center in 2021 with a confirmed diagnosis. We outline the patient's clinical presentation, laboratory findings, and comprehensive multimodal imaging upon admission. Despite receiving standard therapy, the patient's condition progressively worsened, ultimately necessitating high-priority listing for cardiac transplantation, which was successfully performed in 2022. This case underscores the importance of timely diagnosis and the challenges in managing advanced cases of Loeffler endocarditis.

Poster 32

The role of sCD206 as a biomarker for classification and early diagnosis of Juvenile Idiopathic Arthritis Subtypes

L. Fuhrmann[1], A. Grahnert[2], S. Hauschildt[3], M. Friedrich[2], N. Fischer[4], P. Haas[4], C. Klemann[1]

[1]Hospital for Childrens and Adolescents, Department of Pediatric Immunology, Rheumatology and Infectiology, Leipzig, Germany, [2]Institute of Clinical Immunology, Leipzig, Germany, [3]Faculty of Life Sciences, Institute of Biology, Leipzig, Germany, [4]German Centre for Pediatric and Adolescent Rheumatology, Garmisch-Partenkirchen, Germany

Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children, presenting with several clinical subtypes that vary in severity. Early diagnosis and appropriate treatment are crucial, but classification and treatment planning often become possible only as the disease advances. The soluble mannose receptor (sCD206) is known to be elevated in inflammatory processes and has demonstrated significant promise as a biomarker in several diseases. In this study, we analyzed the potential of sCD206 as a biomarker for early JIA subtype classification. Serum sCD206 levels were measured using enzyme-linked immunosorbent assay (ELISA) in 283 untreated patients aged 1-18 years with four different JIA subtypes. Mean rank comparisons were performed to assess differences in sCD206 levels across the JIA subtypes. Higher mean ranks corresponded to higher sCD206 levels. We could demonstrate significant ($p<0,0019$) differences in serum sCD206 levels among JIA subtypes, though the observed differences do not consistently reflect disease severity, contradicting initial expectations. Age and gender do not appear to have a significant influence on the overall results. While elevated sCD206 levels distinguish between certain subtypes, the utility of sCD206 as a biomarker for JIA subtype classification appears limited, warranting further investigation to elucidate its potential role in the management of this complex pediatric rheumatic condition.

Poster 33

Type-Specific Impacts of Protein Defects in Pathogenic NFKB2 Variants: Novel Clinical Findings from 138 Patients

J. Meissner[1], M. Fliegauf[2], B. Grimbacher[2,3,4,5,6], C. Klemann[1]

[1]Klinik und Poliklinik für Kinder- und Jugendmedizin, Leipzig, Germany, [2]Institute for Immunodeficiency, Center for Chronic Immunodeficiency (CCI), Medical Center, Faculty of Medicine, Albert-Ludwigs-University, Freiburg im Breisgau, Germany, [3]Clinic of Rheumatology and Clinical Immunology, Center for Chronic Immunodeficiency (CCI), Freiburg im Breisgau, Germany, [4]DZIF – German Center for Infection Research, Satellite Center, Freiburg im Breisgau, Germany, [5]CIBSS – Centre for Integrative Biological Signalling Studies, Freiburg im Breisgau, Germany, [6]RESIST – Cluster of Excellence 2155 to Hannover Medical School, Satellite Center, Freiburg im Breisgau, Germany

The non-canonical NF-κB2 pathway is crucial in regulating immune function, development, and homeostasis. NFKB2 encodes the precursor p100, which undergoes processing of its C-terminal half to generate p52. While C-terminal defects are known to cause PID, the impact of N-terminal truncations is less understood. We characterized clinical phenotypes linked to three protein defect types: (I) Early truncations, affecting the RHD and reducing p100 and p52 generation; (II) Central truncations, impacting the ARD, leading to immediate p52-like protein expression and a 50% reduction of p100; (III) C-terminal defects, preventing p100 processing and reducing p52 levels while retaining IκB-like activity. Literature reviews from PubMed, ClinVar, and HGMD provided data on defect-specific clinical impacts in NFKB2 patients. Early-onset PID and antibody deficiency were most prevalent in the C-terminal defect group, which also exhibited endocrine issues and T-cell autoimmunity often requiring immunosuppression. Immunological workups showed these patients had pan-hypogammaglobulinemia, reduced antibody responses, and impaired B cell differentiation but normal/elevated T cell counts. In contrast, N-terminal and central truncations showed milder, partially penetrant symptoms with reduced T-cell autoimmunity. This establishes a clear genotype-phenotype correlation in NFKB2 mutations.

References:

[1] Jan Meissner; Manfred Fliegauf, PhD; Bodo Grimbacher, MD; Christian Klemann, MD, (2024), Type-Specific Impacts of Protein Defects in Pathogenic NFKB2 Variants: Novel Clinical Findings from 138 Patients, Elsevier, JACI: In Practice, https://www.sciencedirect.com/science/article/pii/S2213219824010705?via%3Dihub

Poster 34

Understanding confined functions of neutrophils in the pathophysiology of diabetic wound healing

J. Kessler, A. Kakpenova, S. Franz

Leipzig University, Faculty of Medicine, Department of Dermatology, Venereology and Allergology, Leipzig, Germany

Neutrophils are among the first cells recruited to injury sites, where they respond through phagocytosis, degranulation, NET formation, and cytokine release to stimulate inflammation and tissue repair. Sustained activation of neutrophils is linked to chronic inflammation and impaired wound healing, such as in diabetic ulcers. However, altered functions of neutrophils in diabetic wound healing are not fully understood.

We assessed neutrophil organization in full-thickness wounds in wild-type and diabetic mice. Wild-type wounds show Ly6G+ neutrophils from 12 h to 5 days post-injury, with changes in subpopulations over time. Neutrophils infiltrate from the wound bed and accumulate in the eschar. In contrast, diabetic wounds show delayed and prolonged neutrophil infiltration with increased NET formation. Similarly, human diabetic wounds exhibit more neutrophils and NETs in the wound bed compared to acute wounds, where neutrophils are found in the eschar.

To understand altered neutrophil function in diabetic wounds, we assessed peripheral blood neutrophil subsets. Low density neutrophils (LDN), linked to chronic inflammation, were characterized alongside high-density neutrophils (HDN) from healthy and diabetic donors. Flow cytometry identified distinct subsets of LDN, including CD16-low, which had higher CD11b and lower CD66b expression compared to CD16-high subsets. Reduced CXCR2 expression was observed in CD16-low LDN, which is linked to impaired neutrophil tissue infiltration.

Future studies will further decipher subpopulations to determine their roles in diabetic wound healing.

Poster 35

Fabrication of 4D printed, deployable and magnetically guided gastric patches as a local therapy for gastric cancer

D. B. Mahmoud[1], M. Börner[2], C. Wölk[1], M. Schulz-Siegmund[1]

[1]Institute of Pharmacy, Pharmaceutical Technology, Leipzig, Germany, [2]Institut für Anorganische Chemie und Kristallographie, Leipzig, Germany

We propose 4D printed deployable and magnetically guided local patches for non- or minimally-invasive drug delivery to treat gastric cancer. The patches act as a platform to achieve high concentrations of the active pharmaceutical ingredient (API) in the immediate vicinity of the tumor site, thus improving therapeutic efficiency and minimizing side effects of anticancer drugs. Folded/deployable patches were fabricated from a composite hydrogel ink by extrusion 3D printing which permits flexible customization, quick prototyping and precise dose control. Hence, patches of different surface areas and shapes could be quickly developed. We fabricated a composite hydrogel with water-actuated shape transformation capabilities, magnetic guidance and mucoadhesion properties. An enteric backing layer was utilized to confer unidirectional drug release properties to the patch. We tested the physicochemical properties of the composite hydrogel and its printability, fabricated the patches and evaluated shape actuation, magnetization, and mucoadhesion. Further, Patches were loaded with a model drug and in vitro and ex vivo characterization were performed. Our 4D printed patches represent a tool for implementing the next generation of personalized medicines which allows “on-demand” production of dosage forms and have the potential to advance gastric cancer treatment.

Poster 36

CD86 is linked to apoptosis in canine histiocytic sarcoma

B. Diehl[1], A. Kirchhoff[2], F. Hansmann[1]

[1]*Institute of Veterinary Pathology, Faculty of Veterinary Medicine, Leipzig University, Germany,*
[2]*Practice of Veterinary Pathology, Gelsenkirchen, Germany*

Histiocytic sarcomas are malignant neoplasms that occur in dogs and humans. It often has a cautious prognosis and therapeutic options are limited. Binding of immune checkpoint molecules, like CD80 and CD86 to their receptor CTLA-4, inhibits T cell activation. In recent years immune checkpoint inhibitors have been used for treatment of cancer in humans and first clinical trials in dogs were initiated. The aim of this study was to identify immune checkpoint molecules in canine histiocytic sarcoma that play a pivotal role in regulating tumor growth and potentially serve as therapeutic targets.

Ten skin samples from dogs with histiocytic sarcoma were investigated using immunohistochemistry targeting CD80, CD86, cleaved Caspase-3 and Ki-67. Immunolabeled tissue specimens were digitized and whole slides images subjected to analysis using the QuPath software.

CD80 was expressed in 30.81 % of the tumor cells, while 3.19 % of the tumor cells were immunolabeled by CD86. The apoptosis marker cleaved Caspase-3 was expressed in 0.46 % of tumor cells while the proliferation marker Ki-67 was detected in 9.85 % of the tumor cells. CD86 correlated with cleaved Caspase-3 ($\rho = -0.83$, $p < 0.05$) indicating a potential inhibitory effect of CD86 on tumor growth.

The observed correlation aligns with mechanistic studies that have identified distinct functions of CD80 and CD86 when both molecules are co-expressed. Whether monoclonal antibodies targeting CTLA4 represent a promising target for cancer therapy in dogs will require further studies.

Poster 37

Characterizing multi-drug resistance and exploring novel treatment strategies in relapsed/refractory T-prolymphocytic leukemia

A. Klages[1], Y. Peng[1], Q. Jiang[1], L. Wahnschaffe[2], J. von Jan[2], D. Jungherz[1], J. Bischoff[1], U. Platzbecker[1], M. Hallek[2], T. Braun[2], M. Herling[1]

[1]University of Leipzig Medical Center, Department for Hematology, Cell Therapy, Hemostaseology, and Infectious Diseases, Leipzig, Germany, [2]University Hospital Cologne, Germany

T-prolymphocytic leukemia (T-PLL) is a rare, poor-prognostic, mature T cell malignancy associated with an aggressive clinical course (survival <2.5 years) and marked chemotherapy resistance. Currently, the CD52 antibody alemtuzumab is the only treatment option that can reach high remission rates in patients. However, without a consolidating allo-HSCT, over 90% of T-PLL patients eventually relapse within 1-2 years. Therefore, achieving long-term remissions is one of the major challenges in treating T-PLL. The phenomenon known as multi-drug resistance (MDR) occurs in T-PLL when resistance develops after first-line therapy, rendering subsequent treatments ineffective. To characterize MDR, we performed an in vitro drug screen with the most commonly used substances in treatment-naïve and relapsed/refractory (r/r) T-PLL samples. Interestingly, our established venetoclax-resistant cell lines also exhibited resistance to these substances. In seeking CD52+ cell lines for in vitro alemtuzumab evaluation, flow cytometric analysis revealed reduced CD52 levels in venetoclax-resistant cells, suggesting potential resistance to alemtuzumab. This CD52 downregulation can be reversed by cladribine treatment. Clinically, r/r T-PLL patients responded to alemtuzumab after cladribine and valproic acid treatment. Furthermore, single-cell RNA-seq confirmed the upregulation of CD52 following cladribine and valproic acid treatment. Overall, our data suggest that epigenetic pre-conditioning followed by alemtuzumab could be a therapeutic strategy for the treatment of r/r T-PLL.

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Universität Leipzig
Liebigstraße 27
04103 Leipzig
Tel.: 0341 97-15300
presse-mf@medizin.uni-leipzig.de
www.uni-leipzig.de

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Poster 38

Functional analysis and validation of candidate targets, relevant in adaptive oesophageal adenocarcinoma tumour response: from acquired resistance to acquired vulnerability and treatment optimisation

G. Costella

University Cancer Center Leipzig, Faculty of Medicine, Germany

Oesophageal adenocarcinoma is at >600,000 new cases per year worldwide (2020) and its incidence is expected to increase further, especially in the Western world. The long-term survival rate for this cancer is still poor due to its late diagnosis and high resistance to treatment. Current therapies, including radiotherapy, chemotherapy and surgery, offer limited efficacy and considerable side effects. Therefore, understanding the molecular biology of this cancer and developing targeted therapies are essential for improving the treatment outcome in patients suffering from EAC. This project investigates molecular changes associated with treatment resistance using various models, including resistant and wild-type cell lines as well as ex vivo tissue slices from patient-derived and cell-derived xenografts. The aim is to identify secondary therapeutic targets that can be used to employ targeted inhibitors, either alone or in combination, to overcome resistance. In particular, four EAC cell lines are treated for acquiring resistance to four widely used chemotherapeutics, in order to investigate mechanisms of resistance compared to wild-type conditions. They will also be used in CDX models, allowing for identifying most promising drug combinationsunder chemoresistance. Additionally, tissue slice cultures from PDX models are used to study resistance mechanisms and ex vivo targeted therapies. Among different viability and cytotoxicity assays tested, the WST (viability assay) was identified as the most promising readout method for chemotherapy efficacy in tissue slices.

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Poster 39

Genome-wide high resolution analyses on matched colorectal-based lung and brain metastases using SNP array

V.-P. Brandt[1],[2], C. Sander[1], L. Holland[2], R. Koschny[3], W. C. Müller[4], H. Bläker[5], U. Nestler[1], E. Güresir[1], H. Holland[2]

[1]Department of Neurosurgery, University of Leipzig Medical Center, Germany, [2]Saxonian Incubator for Clinical Translation (SIKT), Leipzig University, Germany, [3]Interdisciplinary Endoscopy Center (IEZ), Department of Gastroenterology and Hepatology, University Hospital Heidelberg, Germany, [4]Paul Flechsig Institute of Neuropathology, University Medicine Leipzig, Germany, [5]Institute of Pathology, University of Leipzig Medical Center, Germany

The formation of brain metastases is a rare and late event in colorectal cancer (CRC) patients and is associated with a poor survival. So far, the knowledge about copy number variations (CNV) in brain metastases is still limited compared to other metastatic sites. Therefore, we applied high resolution CytoScan HD array with a higher density of SNP markers for the analysis of chromosomal regions. These investigations were performed on matched colorectal-based lung and brain metastases of two patients. For brain metastases, we detected more CNVs (77 CNVs) compared to pulmonary metastases (24 CNVs). The following chromosomal aberrations were not previously described: gains of 1p36.33-p36.32, 4p16.3-p16.1, 6q27, 12q24.33, 16p13.3, as well as 16p12.1-p11.2 in lung metastases and gains of 1p36.33-p36.21, 5q11.1-q13.2, 21q22.2-q22.3, 22q11.21-q12.2, as well as 22q12.3-q13.33 in brain metastases. Interestingly, we found 20 copy-neutral losses of heterozygosity (cn-LOHs) exclusively in brain metastases, whereby 11 of these cn-LOH regions have not been previously described. Possibly, these cn-LOHs could be relevant for the CRC-based metastases formation. Further analyses are needed to define the causal role and time course of these CNV in lung and brain metastasis formation.

Poster 40

HER2 downregulation by histone deacetylase inhibitors (HDACi) in gastric cancer and impact of basal HER2 levels on susceptibility against HDACi

T. Zenz[1], H. Borchardt[1], R. Jenke[1,2,3], I. Gockel[4], R. Thieme[4], T. R. Büch[1,2], A. Aigner[1,2]

[1]Leipzig University, Clinical Pharmacology, RBI, Leipzig, Germany, [2]Comprehensive Cancer Center Central Germany (CCCG), Leipzig and Jena, Germany, [3]University of Leipzig Medical Center, University Cancer Center Leipzig (UCCL), Leipzig, Germany, [4]University of Leipzig Medical Center, Department of Visceral, Transplant, Thoracic and Vascular Surgery, Leipzig, Germany

Background:

Gastric carcinoma shows a still unsatisfactory response towards antineoplastic therapies. The best established targeted therapies in this entity to date are based on therapeutic antibodies against HER2, but even here resistance is a common problem. This project investigates the effect of histone deacetylase inhibitors (HDACi) on the expression of HER2 in gastric cancer and, vice versa, the susceptibility of HER2-high vs. low-expressing cells towards HDACi.

Methods:

The effects of HDACi on HER2 were analyzed in a panel of gastric carcinoma cell lines and in 3D tissue slice cultures of cell line- and patient-derived xenografts on the mRNA (RT-qPCR) and protein level (Western blot). The tumor-inhibiting effect of HDACi was tested using WST, colony forming, apoptosis and cell cycle assays.

Results:

The cell lines differed significantly in their basal HER2 expression on the mRNA and protein level. Treatment with different HDACi led to a marked downregulation of HER2 in all cell lines, irrespective of basal HER2 expression levels. This was also associated with a clear inhibition of the AKT signaling pathway in HER2-high expressing cells, while HER2-low expressing cells showed a more inhomogeneous response pattern. Notably, cells with a high basal HER2 level showed pronounced susceptibility towards HDACi in proliferation and apoptosis assays.

Conclusion:

HDACi exert particularly strong inhibitory effects in gastric cancer cells where HER2 is a major driver of proliferation, offering an interesting approach for a therapeutic stratification in this entity.

Poster 41

miRNA-454: A Promising Novel Therapeutic Target in Prostate Cancer

R. Kudchi, H. Borchardt, A. Aigner

Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Selbständige Abteilung Klinische Pharmakologie, Leipzig, Germany

Prostate cancer is one of the most common cancer types, causing high mortality rates in men. Since the existing medicines are associated with side effects and often do not show long-term efficacy, novel therapeutic approaches are required. One such strategy is miRNA therapy.

Our study aims to explore the role of miRNA-454 in prostate cancer. Two approaches were investigated: miR-454 replacement and miR-454 sponging using circ-RNAs. In particular miR-454 inhibition led to a significant induction of cell death and reduced proliferation in different 2D and 3D models. Moreover, colony formation assays (CFA) revealed substantial effects on the cells‘ ability to form colonies, indicating decreased tumorigenic potential. In some cases, miR-454 replacement exerted tumor cell-inhibitory effects as well.

These results demonstrate the functional relevance of miRNA-454 in prostate cancer and establish miR-454 as promising potential target in prostate cancer. The dual approach of either replacing or inhibiting miRNA-454 provides flexibility in treatment design and may offer personalized options based on individual patient profiles. Finally, the circ-RNA mediated miR-454 is identified as powerful strategy for miRNA inhibition.

Poster 42

NRF1 as a transcription factor controlling cell cycle gene expression

L. F. Schmidbauer, K. A. M. Azzahrani, R. Kohler, K. Engeland

Leipzig University, Faculty of Medicine, Molecular Oncology, Leipzig, Germany

The cell cycle and the regulation of the cell cycle are essential for life, as uncontrolled proliferation can lead to cancer, a life-changing diagnosis. The treatment for cancer patients often relies on basic research. Therefore, investigating the intricate mechanisms that control gene expression during the cell cycle can advance our understanding of tumor cells and help in the development of new cures. The transcription factor NRF1 was discovered to regulate mitochondrial gene expression. Several new studies have implicated NRF1 also in the control of cell cycle genes. However, the role of NRF1 regulating cell cycle-dependent expression has hardly been investigated.

Therefore, we examined the role NRF1 plays in the control of cell cycle genes. We found that NRF1 binds to the NRF1 consensus sites in promoters of several such genes. Reporter gene assays suggested that NRF1 functions as a transcriptional activator of these genes. Activation through the NRF1 site in promoters is cell cycle-dependent, with no activity observed in G_0 cells and increasing activation beginning in G_1 phase. Furthermore, we investigated NRF1 knockdown using siRNA and assessed NRF1 binding to promoters via chromatin immunoprecipitation (ChIP).

In summary, we develop a model suggesting that NRF1 binding to promoters of cell cycle genes drives their expression starting in G_1 phase.

Poster 43

Optimized nanocarriers for delivery of p53 mutant-wild-type switch oligonucleotides

T. Heinrich, T. Matthé, A. Ewe, A. Aigner

Rudolf-Boehm-Institut für Pharmakologie und Toxikologie, Selbstständige Abteilung für klinische Pharmakologie, Leipzig, Germany

The tumor suppressor gene p53 is one of the most frequently dysregulated genes across various cancer types, including glioblastoma (GBM). In GBM, around 84% of cases exhibit deregulation of the p53 pathway, contributing to the aggressive nature of this malignancy. Due to the tumor‘s infiltrative nature and high recurrence rates, current treatment modalities for GBM, including surgery and chemotherapy, largely fail. This underscores the urgent need for innovative therapeutic strategies.

Gene therapy approaches targeting p53 have shown some promise. More specifically, reactivation of wild-type p53 or degradation of mutant variants demonstrated their ability to restore normal cellular functions Nevertheless, studies have also shown that the gene transfer of p53 alone does not achieve sufficient anti-tumor effects in many GBMs, as the endogenous (mutated) protein can exert dominant negative effects over the wild-type p53.

Therefore, our project aims to develop a gene therapy system that delivers wild-type p53, while simultaneously abolishing endogenous mutant p53 levels via RNA interference (RNAi). For this purpose, we develop non-viral nanoparticles based on tyrosine modified PPIs and PEIs for the parallel delivery of two different nucleic acids to the cell. This includes the identification of optimal conditions for gaining high dual transfection efficacy while minimizing cytotoxicity. This dual-action approach represents a promising strategy for p53-based cancer therapies, potentially enhancing treatment efficacy and expanding the application of gene therapy in oncology.

Poster 44

Role of IRE1α in therapy-resistance of hypoxic cancers

E. Pogander[1], S. Zimmermann[1], U. Anderegg[2], S. Jiang[1], B. Isermann[1], M. Akash[1]

[1]Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik Leipzig, Germany,
[2]Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie, Leipzig, Germany

Glioblastoma and melanoma are two of the most aggressive cancers with insufficient treatment possibilities. Despite the severe hypoxia in the tumor-core, these cancer cells are still viable and often resistant to known cancer treatments. These changes are associated with endoplasmatic reticulum stress, characterized by activation of IRE1α. Mutations of IRE1α have been reported in some cancers. Upon cellular stress, IRE1α initiates an adaptive ER-stress response and facilitates cell survival. Yet, IRE1α is a "double edged sword", as IRE1α leads to apoptosis when the cellular stress persists.

To evaluate the role of IRE1α in therapy-resistance of hypoxic cancers.

IRE1α expression was abolished using CRISPR-Cas 9 in glioblastoma (LNC229 and U87) and melanoma (B16-F10) cell lines. After adding the anti-cancer drug Doxorubicin (4 µM) and 2-Deoxyglucose (20 mM) to knockout and control (sgRNA) cells, cells were subjected to hypoxic conditions for 24 hours. To quantify the impact on mitochondrial dysfunction and cell death we used western blot, genomic DNA fragmentation (laddering) assay and calcium imaging.

The analyses revealed increased cleaved caspase 3, mitochondrial Ca^{2+} concentration and DNA laddering in control cell lines compared to IRE1α-KO cells. This indicates a function of IRE1a in promoting cell death via Ca^{2+} influx into mitochondria.

We postulate that IRE1α promotes the transfer of Ca^{2+} stored in the endoplasmatic reticulum into mitochondria, which leads to apoptosis. Hence the loss of IRE1α, e.g. due ot mutations, may promote drug resistance in hypoxic cancer cells.

Poster 45

Structural changes in the extracellular matrix affect invasion and biophysical characteristics of liver cancer cells

A. Hayn, M. Matz-Soja, T. Berg, F. van Bömmel

Leipzig University Medical Center, Department of Medicine II, Division of Hepatology, Laboratory for Clinical and Experimental Hepatology, Leipzig, Germany

Fibrosis is the crucial factor for altering tissue structure by progressive accumulation of extracellular matrix (ECM). During disease progression liver tissue drastically changes in form of tissue heterogeneity and stiffening caused by fibrosis. In this study, we investigate the influence of altered ECM structures to cell-matrix interactions and invasion of hepatoma cells.

Collagen-based ECM-model-systems differing in stiffness and heterogeneity were established and biophysically characterized. The interactions of different hepatoma cell lines, representing a wide variety of liver cancers, such as hepatocellular carcinoma, hepatoblastoma and intrahepatic cholangiocarcinoma (ICC), were studied regarding cell elasticity, invasion and fiber displacements.

Structural changes directly influenced cell elasticity linked to higher aggressiveness in dependence of heterogeneity and stiffness of the ECM-model-systems. Cell invasion into ECM-model-systems mirrored this in terms of invasiveness and invasion depth. 3D fiber displacement analyses revealed the cell-matrix interaction in dependence of structural changes of the matrices. Additionally, differences with respect to the pathologically origin of the used cells were measured, which show a general increase in malignancy in highly heterogeneous ECM structures and the high aggressiveness of ICC.

We established a tunable platform to investigate cancer cell–matrix interaction with potential for a large set of applications. Structural influence to primary cancer cells and pharmacological influences will be addressed in further studies.

Poster 46 The use of CT-based Node-RADS for Esophageal Cancer

J. Leonhardi[1], T. Denecke[1], A.-K. Höhn[2], S. Tiepolt[3], D. Seehofer[4], H.-J. Meyer[1]

[1]Universitätsklinikum Leipzig AöR, Klinik und Poliklinik für Diagnostische und Interventionelle Radiologie, Leipzig, Germany, [2]Universitätsklinikum Leipzig AöR, Institut für Pathologie, Leipzig, Germany, [3]Universitätsklinikum Leipzig AöR, Klinik und Poliklinik für Nuklearmedizin, Leipzig, Germany, [4]Universitätsklinikum Leipzig AöR, Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie, Leipzig, Germany

In esophageal cancer, lymph node metastasis is a important prognostic factor.[1] Accuracy of computed tomography on this matter is reported with a low sensitivity of 54% and specificity of 77%.[2]

Node-RADS (Reporting and Data System) is a newly proposed classification system aimed at an improved categorization of lymph nodes.[3] The score is being determined by the categories size (normal, enlarged, bulk-like) and configuration. Configuration is further characterized by sub-categories shape, border and texture. The total score ranges from 1 to 5, higher values are reflecting higher likelihood of lymphnode metastasis.

To evaluate the usefulness of the score in esophageal cancer, we conducted a retrospective analysis of a cohort of 126 patients (mean age 62.1 years, 15 female [11.9%]) with histologically proven esophageal cancer. All patients underwent surgery in curative intention and had contrast-enhanced pre-treatment CT-imaging available. N = 54 patients were nodal positive (42.9%).

In total, 182 lymph nodes were scored. Malignancy rates were 0% for Node-RADS 1, 14% for Node-RADS 2, 43% for Node-RADS 3, 90% for Node-RADS 4 and 87% for Node-RADS 5. Node-RADS scores were significantly higher in node-positive cases ($p<0.001$). ROC analysis revealed an AUC of 0.69 for lymph node discrimination, which did not significantly differ from the AUC of 0.72 for discrimination based on short axis diameter. In conclusion, our study revealed only moderate diagnostic accuracy. Node-RADS should be evaluated further and revised to better reflect malignancy.

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Poster 47

Therapeutic potential of HDAC targeting in T-PLL

Y. Peng, Q. Jiang, M. Herling

University of Leipzig Medical Center, Department for Hematology, Cell Therapy and Hemostaseology, Leipzig, Germany

T-cell prolymphocytic leukemia (T-PLL) is a rare and aggressive T-cell neoplasm with limited treatment options and dismal outcome. Building on a previous ex vivo drug screen identifying HDAC inhibitors as effective single agents in T-PLL, we conducted a comprehensive evaluation of HDAC inhibitors, including novel compounds, across 38 T-cell leukemia/lymphoma cell lines. Selected HDAC inhibitors were further tested in primary T-PLL cells and in healthy compartments to assess efficacy and toxicity, and in co-culture systems with NKtert stromal cells to mimic the tumor microenvironment. Western blot analysis confirmed increased histone acetylation and enhanced PARP cleavage. RNA-seq analysis revealed that HDAC1/3/5/7 are highly expressed in T-PLL, with HDAC2/3 significantly upregulated compared to healthy T cells. Higher HDAC expression was correlated with increased HDAC activity. Fimepinostat, a selective HDAC1/2/3/10 inhibitor, showed the highest efficacy in reducing HDAC activity and inducing apoptosis. Combination screening with Bcl-2, MDM2, DNA methyltransferase inhibitors, and purine analogs identified Fimepinostat and Venetoclax as the most potent synergistic pair. Scheduling studies revealed that priming T-PLL cells with Fimepinostat followed by Venetoclax achieved better efficacy than simultaneous application. The combinations of Fimepinostat/Tucidinostat/Belinostat with Venetoclax were selected for in vivo studies due to their selective inhibition and favorable clinical profiles. Overall, these findings reveal the potential of co-targeting HDAC and Bcl-2 in T-PLL.

Poster 48

Transport Mechanisms and Metabolic Regulation: Understanding Metformin's Therapeutic Potential in Glioblastoma Treatment

K. Mamadaliev[1], F. Gaunitz[2], C. Bach[2], E. Güresir[2]

[1]Leipzig University, Germany, [2]Leipzig University, Neurosurgery, Germany

Metformin demonstrates antineoplastic effects in various cancers, including glioblastoma (GBM), a highly malignant brain tumor in adults. However, the mechanisms and molecular targets of these effects are unclear, and tumor sensitivity to the drug may vary. This study investigates pyruvate carboxylase (PC) and transporters involved in metformin metabolism as potential contributors to its anticancer efficacy.

RT-qPCR and Western blotting were used to quantify the expression of PC and the transporters MATE1, MATE2, OCT1, OCT2, and OCT3 in ten different GBM cell lines. The effect of metformin on cell viability was assessed through cell-based assays, and live-cell imaging was used to monitor growth under various nutrient conditions (glucose, pyruvate, and glutamine). siRNA knockout experiments targeting PC were performed to clarify its role in mediating metformin's effects.

Analysis of ten GBM cell lines revealed significant variability in nutrient preferences and impaired growth in the presence of metformin, irrespective of nutrient composition. Cell lines with robust mitochondrial function, like LN229 and 1321N1, preferred pyruvate/glutamine, while adaptable lines such as MZ18 and MZ54 thrived in diverse conditions. PC expression varied significantly, with T98G showing the highest (1.6×10^3 per 12.5 ng RNA) and U343 the lowest (0.2×10^3 per 12.5 ng RNA). Variations in the expression of efflux transporters MATE1 and OCT1 were also noted across the cell lines.

Understanding the variability in metformin's effects may enhance its potential for stratified tumor therapies.

Poster 49

TRPA1 Expression in Glioblastoma: A Novel Target for Enhancing Chemotherapy Efficacy

D. Marquar, T. Büch, A. Aigner, H. Kalwa

Rudolf-Boehm-Institut für Pharmakologie und Toxikologie - selbstständige Abteilung für klinische Pharmakologie, Leipzig, Germany

Glioblastoma multiforme (GBM) is an aggressive brain tumor with a poor prognosis due to its invasive nature and resistance to conventional therapies. Recent studies have identified the transient receptor potential ankyrin 1 (TRPA1) channel as a potential player in GBM pathophysiology. This study investigates the role of TRPA1 in GBM cell migration, adhesion, and chemoresistance, exploring its potential as a therapeutic target. We demonstrate that TRPA1 is expressed in GBM cell lines and patient-derived samples. Activation of TRPA1 by agonists such as allyl isothiocyanate (AITC) or noxious substances, including chemotherapeutic agents, significantly alters GBM cell behavior. Specifically, TRPA1 activation induces changes in the direction of cell migration and modulates cell adhesion properties. These cellular responses are hypothesized to serve as an evasion mechanism, potentially contributing to increased chemoresistance in GBM. To elucidate the functional significance of TRPA1 in GBM, we employed the selective TRPA1 inhibitor A96. Inhibition of TRPA1 with A96 mitigates the altered migration and adhesion patterns observed upon channel activation. Our findings suggest that TRPA1 activation in GBM cells may contribute to their ability to evade chemotherapy-induced cell death by modulating cellular migration and adhesion. The observed effects of TRPA1 inhibition on chemosensitivity highlight its potential as a novel therapeutic target in GBM treatment. Further in vivo studies are warranted to fully evaluate the therapeutic potential of TRPA1 inhibition in GBM management.

Poster 50

Addressing Antimicrobial Resistance Research Gaps in sub-Saharan Africa: A One Health Approach

R. M. Kobialka[1], J. B. Okuni[2], Y. Dieye[3], M. Frimpong[4], O. G. Ademowo[5], S. Makiala[6], Y. W. Mulate[7], K. Eltom[8], A. Käsbohrer[9], D. Nakanjako[10], U. Truyen[1], A. Abd El Wahed[1]

[1]Leipzig University, Institute of Animal Hygiene and Veterinary Public Health, Leipzig, Germany, [2]Makerere University, College of Veterinary Medicine, Animal Ressources and Biosecurity, Makerere, Uganda, [3]Institut Pasteur de Dakar, Senegal, [4]Kwame Nkrumah University of Science and Technology, Kumasi Centre for Collaborative Research in Tropical Medicine, Kumasi, Ghana, [5]University of Ibadan, Nigeria, [6]Institut National de Recherche Biomédicale, Kinshasa, the Democratic Republic of the Congo, [7]Centre for Innovative Drug Development & Therapeutic Trials for Africa, Addis Ababa, Ethiopia, [8]University of Khartoum, Sudan, [9]The German Federal Institute for Risk Assessment, Berlin, Germany, [10]Makerere University, College of Health Sciences, Makerere, Uganda

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Disease outbreaks and management are a huge challenge for public health systems worldwide. The excessive use of drugs in veterinary and human medicine leads to a reduction in effectiveness and even to the development of antimicrobial resistances (AMR). Monitoring AMR as well as the coinfection with neglected tropical diseases (NTDs) remains a significant challenge especially across sub-Saharan Africa.

The aim of this project is to strengthen the capacity across 7 Sub-Saharan countries for improved management of AMR and NTDs. The focus lies on identifying the linkages and transmission of AMR in a One Health context. In order to better control AMR, academic and research institutions from the eight participating countries have investigated and developed 6 Tasks to build the local capacity to identify the main transmission routes.

The Tasks include screening for AMR in humans and livestock; investigating relationships between helminthic infections and drug resistant bacteria; developing capacities for point of need diagnostics using mobile tests for field use; identifying any changes in antimicrobial use and AMR incidence during the COVID-19 pandemic; controlling communicable disease transmission and building capacity for sustainable leadership in antimicrobial stewardship (AMS).

With the established diverse consortium this project proposes unique solutions for AMR/AMS through the development of both knowledge and technological infrastructure.

Poster 51

Assessing Actionable and Non-Actionable Alarms in Intensive Care Units: Insights from Post-Alarm Medication Administration and Vital Sign Trends

M. Hayler[1], T. Kirsten[1], A. R. Flint[2]

[1]Leipzig University Medical Center, Dept. Medical Data Science, Leipzig, Germany, [2]Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Institute of Medical Informatics, Germany

Introduction:

Numerous approaches have been proposed to address alarm fatigue, with many focusing on IT-based solutions. A literature review highlights a key issue: many alarms lack clinical relevance. The INALO project[1] developed a dataset that automatically classifies alarms as actionable or non-actionable. Our study aimed to explore the most frequent post-alarm medications following specific alarm indications and their impact on vital signs.

Methods:

With IRB approval (EA1/127/18), we retrospectively analyzed 10,694 adult ICU patients (42% female, mean age 67.3) at a tertiary hospital from July 2019 to June 2021, each with at least 24 hours of annotated alarm data. We identified 937,796 actionable alarms, defined as those followed by a clinical action (e.g., medication) within 15 minutes. We focused on the top three most frequently administered post-alarm medications and grouped the top 25 by active ingredient for vital sign analysis. Average vital sign changes were calculated every 5 minutes from the alarm baseline.

Results & Conclusion:

No notable differences were observed between individual drugs and post-alarm vital signs. High blood pressure alarms frequently led to medication reduction or discontinuation, suggesting overtreatment and potentially contributing to alarm fatigue and increased patient risk. Optimizing medication management and refining alarm thresholds could reduce alarm frequency and improve patient safety. Our findings highlight the need to evaluate alarm triggers and responses.

[1] https://www.inalo.ai/

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Poster 52

Clonal Hematopoiesis Is Highly Prevalent in Patients with R/R Multiple Myeloma Receiving Anti BCMA CAR T-Cell Therapy, Does Not Associate with Increased Risk of Adverse Events or Inferior Outcomes, but Can Evolve into Post-CAR T Myeloid Neoplasia

B. G. Shibru[1], P. Born[1], D. Fandrei[1], A. Weigert[1], S. M. Krauß[1], T. Wiemers[1], H. Simone[1], W. Song-Yau[1], L. Fischer[1], R. Baber[2], C. D. Herling[1], M. Herling[1], M. Jentzsch[1], G.-N. Franke[1], U. Platzbecker[1], V. Vucinic[1], M. Merz[1], K. H. Metzeler[1]

[1]University of Leipzig Medical Center, Department of Hematology, Cellular Therapy, Hemostaseology and Infectious Diseases, Leipzig, Germany, [2]Leipzig University, Leipzig Medical Biobank, Germany

Anti-BCMA CAR T-cell therapy has revolutionized treatment for relapsed/refractory multiple myeloma (rrMM) but can cause adverse effects, including cytokine release syndrome (CRS), neurotoxicity & immune effector cell–associated hematotoxicity (ICAHT). Cases of treatment-related myeloid neoplasms (tMN) have been reported, yet a putative connection remains uncertain. Clonal hematopoiesis (CH) has been linked to systemic inflammation & tMN. Its relevance in anti-CD19 CAR T therapy has shown mixed results, but data on rrMM patients receiving anti-BCMA CAR T-cells is limited. We studied 71 rrMM patients intended for CAR T therapy using targeted Next-Generation Sequencing to evaluate CH. Pre-CAR CH prevalence was 62%, with 44% of mutations predating a prior autologous stem cell transplantation. CH status did not affect the incidence or severity of CRS, ICANS, or ICAHT, regardless of clone size, age, CAR T product, or CH subtype. Two patients developed tMN post-CAR T, with all tMN-associated mutations present pre-CAR, though 5/6 increased VAF post-CAR. CH did not impact best overall response rate (ORR), PFS, or OS (median follow-up 7.7 months [m]). However, larger clones (VAF≥5%) correlated with lower ORR (57% vs. 88%, p=0.017). During follow-up, 65% of CH clones expanded, with PPM1D showing the fastest (86% per 6m) & TET2 the slowest growth (28% per 6m). Our findings reveal that CH is prevalent in rrMM but does not influence toxicity, response, or outcomes after anti-BCMA CAR-T therapy. However, preexisting CH clones may expand post-therapy, potentially leading to overt tMN.

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Poster 53

Comparison of acquisition modes in High-Resolution Accurate Mass- Mass spectrometry- based Untargeted metabolomics

H. El Boudlali, L. Lehmicke, U. Ceglarek

Institute for Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, Research Group Clinical Mass Spectrometry, Leipzig, Germany

Untargeted metabolomics leverages high-resolution accurate mass- tandem mass spectrometry (HRAM-MS/MS) for comprehensive analysis. However, sensitivity and reproducibility of the method depend on how fragmentation spectra are acquired. This study compares the performance of Data-Dependent Acquisition (DDA), Data-Independent Acquisition (DIA), and AcquireX in terms of sensitivity and reproducibility.

Bovine liver Total Lipid Extract (TLE) spiked with 15 eicosanoid standards (10–0.01 ng/mL) was used to assess sensitivity, and reproducibility was tested over three independent measurements, one week apart. Chromatographic separation used a C18 Kinetex Core-Shell column, and data acquisition was performed on an Orbitrap Exploris 480. Data analysis was performed using Compound Discoverer.

DIA identified the highest number of features, averaging 1,036 across three measurements, followed by DDA and AcquireX, which identified 18% and 37% fewer features, respectively. DIA also showed the best reproducibility, with a 10% coefficient of variance, compared to 17% for DDA and 15% for AcquireX. DIA‘s consistent fragmentation patterns contributed to a 64% overlap in identified compounds across measurement days, compared to 41% for DDA and 50% for AcquireX. In terms of sensitivity, DIA detected one standard at 0.01 ng/mL as upregulated between spiked and unspiked TLE, while DDA and AcquireX did not detect any at this level.

DIA outperformed DDA and AcquireX in both sensitivity and reproducibility, making it a superior choice for untargeted metabolomics applications.

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Poster 54

Efficacy of Psychostimulants in Menstruating Individuals with Adult ADHD and PMS

D. R. Ammann, H. Findeis, C. Sander, N. Mauche, M. Strauß

University of Leipzig Medical Center, Department of Psychiatry and Psychotherapy, Germany

Attention Deficit Hyperactivity Disorder (ADHD) is a chronic, childhood-onset disorder characterized by inattention, impulsivity, and hyperactivity. Previous research has shown an association between adult ADHD and premenstrual syndrome (PMS), with evidence suggesting that individuals with ADHD who experience PMS perceive a decrease in stimulant efficacy during this phase. The primary objective of this pilot study is to examine the relationship between adult ADHD and PMS in menstruating individuals with ADHD, focusing on whether the efficacy of ADHD-specific stimulant medications decreases during PMS. Conducted as a prospective, monocentric, observational study, this research project will examine fluctuations in stimulant efficacy throughout the menstrual cycle, as well as general cycle-dependent symptom changes. Several validated assessment tools will be used: the Conners Adult ADHD Rating Scales (CAARS) for ADHD symptoms, the Beck Depression Inventory II (BDI-II) for depression severity, the Premenstrual Assessment Form (PAF20) for PMS symptoms, the Premenstrual Symptoms Screening Tool (PSST) for identifying premenstrual symptom severity, and a Visual Analog Scale for ADHD (VAS-ADHS) for subjective ratings of stimulant efficacy. By collecting data at specific points in the menstrual cycle, this study aims to provide a better understanding of symptom variability and medication response to support gender-sensitive, individualized treatment strategies for ADHD management in menstruating patients.

Poster 55

Exploring the Impact of Assisted Reproductive Technologies on Pregnancy Outcomes: Introduction to the Leipzig Reproductive Medicine Study (LEREP), Workpackage ILM

M. Köhler, K. Singh, R. Baber, B. Isermann, S. Kohli

Universitätsklinikum Leipzig, Institut für Laboratoriumsmedizin (ILM), Leipzig, Germany

Assisted reproductive treatments (ART), such as in-vitro fertilization (IVF), are common methods used to address involuntary childlessness. In Germany, approximately 120,000 ART cycles are conducted each year, with 2-3% of all births resulting from these treatments. While ART can offer hope for many, it also increases the risk of preeclampsia from about 5% in natural pregnancies to as high as 20% in pregnancies resulting from ART.

Currently, 70% of all reproductive treatments in Germany are performed in private clinics, which poses challenges for academic research. The Leipzig Reproductive Medicine Study (LEREP) aims to address this gap by building a cohort of couples undergoing ART and collecting biomaterials during and after pregnancy. The study is based at the University Clinic Leipzig, with participating departments including Gynecology and Obstetrics, Psychiatry, Andrology, the LIFE Child Study, Laboratory Medicine (ILM), and UFZ as an external partner.

In addition to building up an ART-related biobank for research purposes, the ILM team is analyzing soluble and cell-based markers for preeclampsia to better understand the differences between natural and ART pregnancies. Our measurements include FACS analysis for neutrophil and platelet activation, as well as ELISA for sVCAM, sTM, and sTF. Furthermore, we will conduct scRNA sequencing on placental samples and experiments with isolated human umbilical vein endothelial cells (HUVECs) from these pregnancies. This research will allow us to evaluate the effects of ART on vascular changes in both mothers and their offspring.

Poster 56

Image-derived input function (IDIF) for (-)-[^{18}F]Flubatine using a long axial field of view (LAFOV) digital PET system

L. M. Barth[1], G. A. Becker[1], M. Rullmann[1], S. Hesse[1], P. Meyer[1], A. Schildan[1], B. Sattler[1], F. R. Zientek[1], P. Schönknecht[2], M. Leitzke[1,3], O. Sabri[1]

[1]University of Leipzig Medical Center, Department of Nuclear Medicine, Leipzig, Germany, [2]University of Leipzig Medical Center, Department of Psychiatry and Psychotherapy, Leipzig, Germany, [3]Department of Anesthesiology, Helios Clinics, Leisnig, Germany

Aim:

Highly sensitive LA-FOV PET-CT systems enable dynamic data acquisition of all body regions covered by the axial FOV. The objective of this work is to ascertain the suitability of the IDIF for whole-body analysis with a new PET-CT scanner using (-)-[^{18}F]Flubatine in comparison to the gold standard of arterial blood sampling. This tracer - with a comparatively low metabolic degradation targeting α4β2* nicotinic acetylcholine receptors – simplifies the otherwise complex radiometabolite correction.

Methods:

Within 26 days two whole-body PET-CT scans were performed with continuous measurement for the first 90 minutes and a total imaging time of 360 minutes (0-90min, 195-225min, 330-360min p.i.). The scans were conducted following a bolus injection of approximately 300 MBq of (-)-[^{18}F]Flubatine. Metabolites, plasma to whole blood ratios, and tracer binding to plasma protein ratios were determined by taking arterial blood samples, which served as the gold standard. The IDIF was extracted from the aortic arch based on the segmentation of the thoracic aorta AC-CT data. Kinetic modeling of the body including the brain was performed based on arterial as well as IDIFs.

Results/Conclusion:

The IDIF shows minor discepancies to the arterial input function (0.43 ± 0.92 kBq/ml, 0.20 ± 1.29 kBq/ml, n=29). The ratio of the V_T based on non-metabolite corrected function as well as based on an IDIF to V_T based on metabolite corrected function is similar. (-)-[^{18}F]Flubatine is a tracer that seems suited for kinetic modeling using an IDIF. Further studies are warranted for validation.

Poster 57

Immobilizing effect of a semi-rigid cervical orthosis compared to a soft and a rigidcervical orthosis in healthy subjects

M. Schulz, D. Wiersbicki, C.-E. Heyde, G. Osthoff, M. Heilemann, S. Schleifenbaum, T. Wendler

Universitätsklinikum Leipzig, Klinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Germany

The aim of this study is to compare the immobilizing effects of a semi-rigid collar to a soft and a rigid cervical orthosis on C-spine mobility in healthy subjects, in relation to their free maximum range of motion (ROM). The movements of C-spine were examined in 20 healthy subjects, including maximum active flexion/extension, lateral flexion and rotation, without a orthosis and while wearing 3 orthoses: soft: Cervi-moll, Thuasne; semi-rigid: PDC, Thuasne; rigid: MiamiJSelect, Ossur. The ROM was measured through optical tracking of markers using a high-resolution 3D camera system. Differences between the orthoses were analyzed using a one-sided paired t-test. All 3 cervical orthoses restrict the ROM of the C-spine compared to the free ROM in all subjects. The rigid orthosis leads to a significantly (p<0.01) greater mobility restriction than the other two orthoses. The semi-rigid orthosis thus restricts flexion/extension significantly more than the soft orthosis (p<0.01), however, there is no significant difference in lateral flexion and rotation (p=0.10, p=0.14). Based on the literature, cervical orthoses can serve as proprioceptive aids, enabling patients to regulate their own neck movements. This study also indicates that soft and semi-rigid orthoses can sufficiently restrict the ROM of the C-spine, potentially reduce the need for rigid orthoses and the associated complications. The semi-rigid orthosis appears to restrict the ROM, particularly flexion/extension, more effectively than a soft orthosis, and therefore could represent the preferred therapeutic alternative.

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Leipzig Protocol for Exchange Fluid in Therapeutic Plasma Exchange

N. Kassir[1], J. Emonds[1], S. Petros[2], N. Thriemer[1], M. Bourgeois[1], R. Buhmann[1], R. Henschler[1]

[1] Leipzig University Faculty of Medicine, Institute of Transfusion Medicine, Leipzig, Germany, [2] Leipzig University, Faculty of Medicine, Interdiscipliary Intensive Care Unit, Leipzig, Germany

Background:

Therapeutic plasma exchange (TPE) provides evidence-based clinical benefit in a variety of disorders. Since clear rules are lacking, we initiated a protocol for standardized selection of exchange media in TPE.

Methods:

Patients are categorized into a total of five groups as to liver status, fibrinogen (Fg) levels before TPE and recent (24h) bleeding. Principally, 100% Albumin+crystalline solution is used if Fg is > 1.5 g/l with healthy liver. In cirrhosis, 50%/50% FFP/ Albumin or 100% Albumin plus 2g Fg post TPE i.v. are used if Fg is 1.5-2 g/l and no bleeding. If bleeding is recorded in the last 24h or if Fg is <1.5 g/l, 100% GFP is used.

Results:

We treated a cohort of 26 patients with indications for TPE acute autoimmune exacerbation (n=13), acute liver failure (n=7), suspected or confirmed TTP (n=3), imminent transplant rejection (n=2) and pretransplant conditioning (n=1) in total of 132 TPE procedures. The procedure was applicable and protocol adherence was nearly complete. Preliminary data show a significantly lower consumption of donor plasma compared to historical controls. No increased bleeding tendency or bleeding complications were observed in the patients.

Conclusion:

Our protocol proved feasable and represents a novel instrument to standardize the use of colloids vs FFP in patients undergoing TPE procedures. It is expected to reduce transfusion incidents and immune sensitizations without exposing patients to additional risks of bleeding complications. Further this preserves donor plasma and could be cost-efficient for hospitals.

Poster 59

Modeling Clinical Reasoning in Medication Review: A Graph-Based Approach

J. Kiesel[1], K. Karsten Dafonte[2], A. Wermund[3], D. Neumann[1]

[1]Leipzig University, Institute for Medical Informatics, Statistics and Epidemiology, Leipzig, Germany, [2]Universität Bonn, Abteilung für klinische Pharmazie, Bonn, Germany, [3]Universitätsklinik Bonn, Institut für klinische Chemie und klinische Pharmakologie, Bonn, Germany

Understanding clinical reasoning is critical to improving healthcare practices such as medication reviews. Effective clinical reasoning allows pharmacists to identify and address drug-related problems (DRPs) to ensure that prescribed therapies are safe, appropriate, and effective for each patient. One method to study this process is the Think-Aloud technique. However, analysis of this free-text data can be highly susceptible to rater bias and methodological variation, often leading to inconsistent results. This study proposes modeling a medication review as a graph to address these challenges. The method involved five clinical pharmacists from university hospitals performing clinical medication reviews (CMRs) using the think aloud technique. Their verbalizations were recorded, transcribed, and modeled as graphs based on a defined set of node and edge labels. The graphs were visualized and analyzed using Neo4j. This approach allowed the representation of pharmacists‘ reasoning processes and facilitated the comparison of different strategies for detecting DRPs. Challenges include the difficulty of standardizing the process and identifying and scoring similar reasoning patterns because pharmacists use different terminology. In conclusion, modeling medication reviews as graphs offers a promising way to structure clinical reasoning and improve the comparability of decision making. Future work should focus on improving graph construction methods to more effectively identify similar reasoning processes.

Poster 60

PRospective Evaluation of clinical parameters anD initial cerebral CT for the prediction of Malignant Media Infarction (PREDICT MMI)

A. Dabbagh, F. Welle, J. Mielke, M. Wawrzyniak, C. Scherlach, K.-T. Hoffmann, J. Pelz

Universitätsklinikum Leipzig AöR, Department of Neurology, Leipzig, Germany

Background:

Early identification of patients at high risk for space-occupying cerebral infarction (malignant middle cerebral artery infarction, MMI) allows for targeted therapies against infarct edema. Based on retrospective data, we developed a model to predict MMI, using CT-based parameters combined with clinical data with overall good sensitivity (78.57%) and specificity (79.45%, AUC 0.86). The aim of this study was to validate this model in a prospective cohort.

Methods:

From September 2023 to August 2024, 120 patients with proximal large-vessel occlusion (LVO) and symptom onset within 24 hours were included in this interim analysis. The model utilized CT-based parameters (CSF volume, net water uptake), occlusion site, severity of ischemic stroke (NIHSS), age, and dichotomized recanalization success. The primary endpoint was occurrence of MMI within one week, based on imaging criteria (midline shift >4 mm) or clinical factors (hemicraniectomy, consciousness impairment, anisocoria).

Results:

Thirteen patients were excluded, mainly due to missing outcome data. Among 107 patients (mean age 74, mean NIHSS 17), 18 patients (16.8%) developed MMI. At a prediction probability cut-off of ≥80%, 15 of 18 MMI cases and 83 of 89 non-MMI cases were correctly predicted (sensitivity 83.3%, specificity 93.2%, AUC 0.965).

Conclusion: This interim analysis confirms the accuracy of our model to predict MMI in patients with proximal LVO. Its app-based usability and analysis of data available upon admission offer practical advantages. Further validation in a multicenter cohort is planned.

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Poster 61

Predicting the deleteriousness of synonymous variants based on cumulative computational metrics (SyMetrics)

L. Bundalian, D. Le Duc

University of Leipzig Medical Center, Institute of Human Genetics, Leipzig, Germany

Synonymous single nucleotide variants (sSNVs) which have been established to be neutral – not causing any functional and/or biological consequence, are now having growing evidence for their potential to disrupt biological processes which includes but not limited to mRNA stability, splicing efficiency and translation kinetics. In this study, we introduced SyMetrics, a predictive model that integrates existing sSNVs effect measure to predict the variant's deleteriousness. The model is built using an ensemble machine learning framework and has a 96.3% accuracy, outperforming the classification done by individual sSNV effect measure. Using SyMetrics, we were able to estimate the possible deleterious unobserved sSNVs which is approximately 1.98% or roughly 1,181,435 unobserved sSNVs. The model was further validated in a private clinical cohort where we successfully identified pathogenic variants missed by standard analyses, underscoring the functional relevance of these sSNVs as well as the use case of the model in clinical setting. SyMetrics is available as a Python library and web application, providing access for researchers and clinicians.

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Poster 62

Predictors of outcomes for near-infrared spectroscopy and electroencephalography neurofeedback in binge-eating disorder: the role of rapid response and baseline neurophysiological data

B. Schreglmann[1], R. Schmidt[1], M. Lührs[2], A. Hilbert[1]

[1]Universität Leipzig, Verhaltensmedizin, Medizinische Fakultät, Leipzig, Germany, [2]Maastricht University, Faculty of Psychology and Neuroscience, Vision, Maastricht, Netherlands

Binge-eating disorder (BED) is characterized by recurrent binge eating without regular compensatory behaviors. Pioneer studies pointed to the efficacy of food-specific electroencephalography (EEG) and real-time (rt) functional near-infrared spectroscopy (fNIRS) neurofeedback (NF) trainings in the treatment of BED. However, supposed key predictors remain unexplored.

In this preregistered secondary analysis (https://osf.io/xsrj3), data from a randomized-controlled trial on 47 adults (47±13 years, 81% f) with interview-assessed BED were analyzed. Participants underwent 12 sessions of EEG- or rtfNIRS-NF over 8 weeks. Linear models assessed rapid response (RR), which reflects early reductions in objective binge-eating episodes (OBEs), and neurophysiological data as predictors for binge-eating abstinence, OBEs, and eating disorder psychopathology at posttreatment (t1) and 6-month follow-up (t2).

Results showed that RR predicted more abstinence at t1 and t2, fewer OBEs at t1, and lower eating disorder psychopathology at t2. EEG data indicated that higher food-specific fronto-central high beta predicted more abstinence and fewer OBEs at t1 and t2. For fNIRS data, increased food-specific prefrontal oxygenation predicted more abstinence at t1 and t2, as well as lower eating disorder psychopathology at t1.

Uniquely, this study showed that RR as well as neurophysiological data can help identify individuals with BED likely to respond to NF. EEG-NF was more efficacious for individuals with greater baseline dysregulation, while rtfNIRS-NF benefited those with greater baseline regulation.

Poster 63

Risk factors for mortality in periprosthetic femur fractures about the hip - a retrospective analysis

K. Müller[1], S. Zeynalova[2], J. K. M. Fakler[3], C. Kleber[1], A. Roth[1], G. Osterhoff[1]

[1]Universitätsklinikum Leipzig, Klinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Germany, [2]Universität Leipzig, Institut für Medizinische Informatik, Statistik und Epidemiologie, Leipzig, Germany, [3]Klnikum Passau, Klinik für Orthopädie und Unfallchirurgie, Passau, Germany

Fractures around the hip are known to be an indicator for fragility and are associated with high mortality and various complications. A special type of fractures around the hip are periprosthetic femur fractures (PPF) after Total Hip Arthroplasty (THA). The aim of this study was to investigate the mortality rate associated with PPF after THA and to identify risk factors that may increase it.

Consecutive patients ($N = 158$) who were treated for a PPF after THA in our university hospital between 2010 and 2020 were identified and mortality was assessed using the residential registry. Univariate (Kaplan-Meier-Estimator) and multivariate (Cox-Regression) statistical analysis was performed to identify risk factors influencing mortality.

One-year-mortality rate was 23.4% and 2-year mortality was 29.2%. Mortality was significantly influenced by age, gender, treatment, type of comorbidity and time of surgery ($p < 0.05$). Surgical treatment during regular working hours (8 to 18 h) reduced mortality by 53.2% compared to surgery on call (OR: 0.468, 95% CI 0.223, 0.986; $p = 0.046$). For every year of age, mortality risk increased by 12.9% (OR: 1,129, 95% CI 1.078, 1.182; $p < 0.001$). The type of fracture according to the Vancouver classification had no influence on mortality ($p = 0.179$).

Surgical treatment during regular working hours is associated with lower mortality compared to surgery outside these hours. In this retrospective cohort, time to surgery showed no significant impact on all-cause mortality.

Poster 64

Stress Markers in Premenstrual Dysphoric Disorder and Health across the Menstrual Cycle

K. Hoffmann[1,2,3,4], R. G. Zsido[4,5], A. Villringer[2,3], V. Engert[6], J. Sacher[2,3,4,7]

[1]Humboldt-Universität zu Berlin, Berlin School of Mind and Brain, Berlin, Germany, [2]Max Planck Institute for Human Cognitive and Brain Sciences, Department of Neurology, Leipzig, Germany, [3]University of Leipzig Medical Center, Cognitive Neurology, Leipzig, Germany, [4]University of Leipzig Medical Center, Center for Integrated Women's Health and Gender Medicine, Faculty of Medicine, Leipzig, Germany, [5]Massachusetts General Hospital, Harvard Medical School, Department of Psychiatry, Clinical Neuroscience Laboratory for Sex Differences in the Brain, Boston, United States of America, [6]Institute of Psychosocial Medicine, Psychotherapy and Psychooncology, Jena University Hospital, Friedrich-Schiller University, Jena, Germany, [7]University of Leipzig Medical Center, Medical Department III - Endocrinology, Nephrology, Rheumatology, Leipzig, Germany

With a prevalence rate of 3-8 percent, Premenstrual Dysphoric Disorder (PMDD) impacts millions of females each month. While no changes in ovarian hormones have been detected, irregularities in the hypothalamic-pituitary-adrenal (HPA) axis of patients with PMDD have been observed. We have applied a longitudinal design to investigate the cortisol awakening response (CAR), a key component of the HPA axis, in PMDD and health across the menstrual cycle.

We tested 30 PMDD patients and 29 healthy controls in the periovulatory and premenstrual phase. Participants self-collected 8 saliva samples (awakening, +30min, +60min, 9am, 12pm, 3pm, 6pm, 9pm) to assess the CAR and the diurnal cortisol slope.

We found a significant group*cycle phase interaction on cortisol peaks (estimate=0.78, p=0.05, d=0.62) and on increase from awakening to peak concentrations (estimate=0.92, p=0.03, d=0.77). Patients showed blunted +60min cortisol concentrations compared to controls during the periovulatory phase ($t[55]=-2.17$, $p=0.03$). Cortisol peaks correlated negatively with HAM-D scores ($r=-0.26$, $p<0.01$, $R^2=-0.07$).

Patients showed lower cortisol peaks and smaller increases from awakening to peak concentrations across the cycle compared to controls, who showed not only increased but also plastic changes in CAR indices across the cycle. Depressive symptoms correlated negatively with cortisol peak concentrations, paralleling patients increased depressive symptoms compared to controls. Findings elucidate potential alterations in cortisol response and their association with depressive symptoms in PMDD.

Poster 65

Technologies for a development and rapid prototyping of point-of-care diagnostic tests

K. Mattern, N. Sandetskaya, A. Kölsch, S. Rau, A. Menge, D. Heinrich

Fraunhofer Institute for Cell Therapy and Immunology IZI, Diagnostics; AG MicroDiagnostics, Leipzig, Germany

In the recent past years, in vitro diagnostics becomes more and more decentralized. Point-of-care testing (POCT) bases on laboratory-independent test devices: Nowadays, even sophisticated assays can be transferred to POCT-format by merging special technologies.

MicroDiagnostics Unit at Fraunhofer IZI provides expertise and infrastructure for the development and prototyping of such tests, which can be implemented at the point of need. Our portfolio includes the following technologies:

- Customized design of the lab-on-chip devices
- Rapid prototyping in polymers by combination of additive manufacturing (3D-Printing) and hot embossing
- Development and production of lateral flow assays
- Electricity-free chemical heating for a defined reaction temperature
- Precise spotting of reagents & microarrays down to picolitre volumes
- Freeze-drying for a stable storage of reagents on a test device
- Development & transfer of user-friendly detection assays and sample preparation.

The available technologies & expertise enable rapid iterative development of even complex POCT systems with high precision and speed up the way from an idea to a clinical evaluation of a diagnostic test.

Our exemplary projects are:

- DjinniChip - a novel molecular rapid diagnostic device for the detection of Chlamydia trachomatis
- CampyTube – a seamlessly integrated amplification and instrument-free detection of nucleic acids in a single tube
- Snifits4Health – Innovative platform technology for point-of-care analysis.

We look forward to creative and ambitious projects together with partners in Leipzig and beyond.

Poster 66

tDCS as Treatment for Attention Deficit Hyperactivity Disorder? Effects of Neurostimulation on Event-Related Potentials in ADHD-Patients

O. von Borries[1], N. Mauche[1], J. Huang[1], M. Strauß[2]

[1]Leipzig University, Faculty of Medicine, Department of Psychiatry and Psychotherapy, Leipzig, Germany,
[2]University of Leipzig, Medical Center, Department of Psychiatry and Psychotherapy, Leipzig, Germany

Event-related potentials (ERPs), such as the P300, are regarded as possible biomarkers for attention processes and are linked to Symptoms related to Attention Deficit Hyperactivity Disorder (ADHD), including deficits in executive functions.[2] Current research suggests the potential of reduced P300 waves in ADHD patients relative to healthy control samples.[5][3] Concurrently, alternative ADHD treatments, such as transcranial direct current stimulation (tDCS), are garnering heightened interest, as they target the neurophysiological correlates of ADHD. tDCS could enhance P300 Amplitudes and therefore affect ADHD-related Symptoms, however current research cannot fully confirm or refuse corresponding hypotheses.[1][4]

The objective of this study is to examine the effects of tDCS on ERPs, such as the P300, in patients diagnosed with ADHD. In this double-blind, randomised and sham-controlled study, ERPs were recorded in an auditory novelty oddball paradigm directly before, after and two weeks after five consecutive sessions of tDCS. The subjects were presented with three acoustic signals during the EEG measurements. It is anticipated that the P300 amplitudes will be higher directly after, as well as in the follow-up, than before tDCS. Due to the large sample size and high-quality methodology employed, significant insights into the neurophysiological effects of tDCS on ADHD patients, as well as its general application, can be gained.

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Poster 67

Is Virtual Reality Set to Transform Education in Orthopedic and Trauma Surgery? - An Evaluation of Initial Experiences with VR Glasses in the Orthopedic Trauma Surgery Curriculum

L. Schuschke[1], T. Schöbel[1], D. Rotzoll[2], C.-E. Heyde[1], G. Osterhoff[1], J. Theopold[1]

[1]University of Leipzig Medical Center, Department of Orthopedics, Trauma and Plastic Surgery, Leipzig, Germany, [2]Leipzig University, Skills and Simulation Centre LernKlinik Leipzig, Faculty of Medicine, Leipzig, Germany

Introduction:

Through immersive virtual reality students can engage in hands-on practice without the risks associated with real life scenarios. Therefore VR-modules are a well-known training tool in diverse medical specialties. The aim of this study was to assess the usability of VR glasses for students in the orthopedic trauma surgery curriculum.

Methods:

According to the curriculum fourth year students complete a one-week bedside teaching in orthopedic and trauma surgery. In addition to that one third of these students (n=56) were able to use VR glasses simultaneously with the bedside course. Using the PrecisionOS platform on Meta Quest 2 VR-headsets the students were able to train and experiment with thematically relevant surgical modules. To gain user feedback, two different questionnaires were administered before and after the course.

Results:

The mean usage time within one week was 3.3 hours. The students had high expectations but also indicated that the VR glasses were a valuable addition to the bedside course. A large portion (94,3%) indicated that their understanding of orthopedic procedures improved through the VR glasses. The confidence to assist in a real surgery after using the surgery platform decreased to some degree from 68.5% to 58.2%. Almost half of the students (49%) developed motion sickness. However, only 20% experienced severe symptoms.

Conclusion:

Integrating a virtual surgical course into the curriculum is highly feasible. Students appreciated the tool and wanted it to continue. VR is well-suited to enhance traditional teaching methods.

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Poster 68

A Tale of two Migrations: How REDCap took over LiSyM Cancer, but not LIFE Child

C. Meigen[1], M. Matz-Soja[2]

[1]Leipzig University, Faculty of Medicine, Leipzig, Germany, [2]Leipzig University, Hepatology, Leipzig, Germany

Data management in large, long running projects faces unique challenges, not the least of which is a changing IT landscape which requires adoption of new tools. The REDCap electronic data capture software has emerged as a new standard tool to manage large studies. We present two projects - the long-running LIFE Child study, and the multicenter LiSyM-Cancer collaboration - and compare the initial set-up with a variant that includes REDCap as a central data management platform. Migrating projects to new platforms highlights the close relationship between organisatorical structure and technical implementation and allows us to question our implicit assumptions about how data management should be done.

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Poster 69

Analyzing B-mode ultrasonography images using neural networks to predict fibrosis risk in patients with metabolic dysfunction-associated steatotic liver disease (MASLD)

J. Stansch[1], T. Karlas[1], J. Wiegand[2], T. Berg[2], V. Blank[3], K. Vu Trung[4], M. Herzog[5], J. Kather[5]

[1]University of Leipzig Medical Center, Gastroenterology, Department of Medicine 2, Leipzig, Germany, [2]University of Leipzig Medical Center, Hepatology, Department of Medicine 2, Leipzig, Germany, [3]University Hospital, Interdisciplinary Ultrasound Department, Halle, Germany, [4]University of Leipzig Medical Center, Gastroenterology, Leipzig, Germany, [5]University Hospital, EKFZ for Digital Health, Dresden, Germany

With a prevalence of over 20%, MASLD is the most common liver disease in industrialized countries. Identifying patients at high risk of progression is a clinical challenge. Currently, the guideline recommendations for patients at risk include an assessment of the extent of fibrosis using liver elastography. However, this technology is not yet widely available, meaning that further stratification methods are required to guide patient flows. The application of AI-based assessment to B-scan ultrasonography may prove an effective method of identifying patients at high risk of fibrosis, offering a convenient and cost-efficient approach.

205 patients with standardized documented B-mode ultrasonography images of the liver and available vibration controlled transient elastography examination have been identified from already established MASLD cohorts. A convolutional neural network (CNN) was trained and tested as a deep learning model. The fibrosis risk was initially classified into two categories: ‚non-increased fibrosis risk' (liver stiffness <8 kPa) and ‚increased fibrosis risk' (liver stiffness ≥8 kPa). The diagnostic significance of the model was evaluated using classification metrics of the scikit-learn software, AUROC and DeLong test.

According to preliminary analyses, the sensitivity and positive predictive value for the detection of an increased risk of fibrosis are 90.6% and 79.1% with an overall accuracy of 75 %.

Deep learning models could help to cost-effectively improve the identification of high risk disease progression. Further adjustments and validations are planned.

Poster 70

Architecture for a telemedicine application using nomadic radio networks

D. Lepach, M. Rosenau, S. Bohn, T. Neumuth

Leipzig University, Faculty of Medicine, ICCAS, Leipzig, Germany

Providing day-to-day medical care in remote and rural areas has recently been challenged with increasing difficulties, especially regarding the decreasing coverage by general practitioners and specialists in those regions. The project TeleNoma aims to mitigate this problem by providing patients and medical professionals in areas with unreliable Internet connection the necessary software to stream medical data to a tele-doctor and optionally providing bi-directional communication.

A nomadic 5G-Network provides both a network for modern medical equipment and an improved Internet connection. Modularity of features and offline capabilities are key to accommodate varying connection quality. A connection manager controls priority and detail of different data (e.g. biosignals, medical images) to facilitate optimal assessment by the tele-doctor, while a device manager provides the professional with full overview and control of the available remote devices for an adequate diagnostic process.

During a diagnostic measurement, the remote medical devices provide their functionality via the Service-Oriented Device Connectivity standard (IEEE 11073 SDC) within a secure VPN. Once finished, the collected data is stored in a local database (using HL7-FHIR) which automatically synchronizes with an online-server.

The presented architecture provides a framework for remote medical care in regions where a physician‘s physical presence cannot be guaranteed. The use cases targeted in this project are stroke aftercare by nurses, home visits by therapists and pregnancy care by delivery nurses.

Poster 71

Classification of leukodystrophy versus multiple sclerosis MRIs based on white matter changes with deep learning

M. Abedi[1,2,3], N. Shekarchizadeh[2,3,4], J. Lier[5], C.-C. Bergner[5], N. Scherf[6], P.-L. Bazin[7], W. Köhler[5], T. Kirsten[2,3,4]

[1]Mittweida University of Applied Sciences, Faculty Applied Computer and Bio Sciences, Mittweida, Germany, [2]Leipzig University, Institute for Medical Informatics, Statistics, and Epidemiology, Leipzig, Germany, [3]Leipzig University Medical Center, Department of Medical Data Science, Leipzig, Germany, [4]Leipzig University, Center for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI) Dresden/Leipzig, Germany, [5]University of Leipzig Medical Center, Department of Neurology, Leipzig, Germany, [6]Max Planck Institute for Human Cognitive and Brain Sciences, Neural Data Science and Statistical Computing, Leipzig, Germany, [7]Full Brain Picture Analytics, Leiden, Netherlands

Leukodystrophies (LD) are a group of rare genetic neurological disorders typically characterized by the progressive degeneration of white matter (WM) in the brain. LDs are usually diagnosed through a combination of symptomatic observations, MRI images, and genetic testing. In neurology clinics not specialized in LD, LDs may sometimes be misdiagnosed as multiple sclerosis (MS) or other differential diagnoses due to their clinical and radiological similarities, such as WM abnormalities and neurological decline. Utilizing machine learning approaches can assist clinicians in identifying potential LD patients and referring them to specialized centers for further investigation.

We utilize HeteroMRI [1] approach that uses a convolutional neural network to classify (FLAIR) MRIs. In HeteroMRI, the model is trained with a subset of the WM which includes significant signs of WM lesions. For differentiating LD from MS MRIs, the binary classifier relies solely on a label indicating the disease, without the need for manual annotation of WM lesions in the training data. The LD dataset (109 MRIs) includes a range of diseases, all of which present with WM lesions. Being a rare disease, the LD MRI data are collected from various centers with different scanners. This makes the classification task challenging for the model. The HeteroMRI approach addresses this issue by mitigating the effects of heterogeneity in MRI classification. Preliminary results show promising potential in distinguishing between LD and MS, with an accuracy interquartile range spanning from 75% to 100% in 400 data shuffles.

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Poster 72

Developing a data trustee for health data – the role of trust

P. Herrmann, M. Radic

Fraunhofer-Zentrum für Internationales Management und Wissensökonomie IMW, Digital Health, Leipzig, Germany

The poster addresses the research question (RQ) which dimensions of trust are relevant in the context of sharing health data for secondary utilization. It does so by validating the mHealth trust framework by van Haasteren et al. (2020) in the context of a data trustee for health data. The RQ is significant in the context of the efforts by the European Union to establish a European Health Data Space (European Commission, 2022). The current proposal risks eroding trust which has been shown to be key for stakeholder adoption.

To answer the RQ, we conducted 27 semi-structured interviews with patients, data providers and data users following a multi-source-multi-method approach. We find privacy, reputation, and transparency to be most relevant for trust across stakeholders and methods. Data providers and data users emphasize the importance of information accuracy while patients have a need for usability, understandability, and brand familiarity. Aspects of user control are less relevant across groups and methods. Finally, we find that the data users and data providers consider the design of the business model to be relevant for their trust which has not been considered yet in the framework.

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Poster 73

Development of a Pipeline for the Anonymization of Medical Image Data by Clinical Staff

N. Baumann[1], M. Rucińska-Simon[2], H. Köhler[1], A. Melzer[1,3], V. Schnabel[2], A. Pfahl[1]

[1]Leipzig University, Faculty of Medicine, Innovation Center Computer Assisted Surgery, Leipzig, Germany, [2]University of Leipzig Medical Center, Department of Dermatology, Venerology and Allergology, Leipzig, Germany, [3]University of Dundee, School of Medicine, Institute for Medical Science and Technology, Dundee, United Kingdom

Medical image data often contains information about the identity and health status of patients. With the increasing utilization and sharing of imaging data for research, telemedicine, and AI-based analysis, simply blackening the eye region is insufficient for privacy protection. To date, there are no unified legal standards governing the anonymization of medical images. While removing large image areas may protect privacy, it also limits usability. This work aims to develop a process for anonymizing medical images in line with data protection and usability.

A requirements analysis for the anonymization process was conducted based on an examination of the General Data Protection Regulation and the German Health Data Utilization Act, as well as an analysis of a hyperspectral image dataset of skin lesions. A user interface was implemented with Python 3.8.6, OpenCV, and dlib.

It enables users to select regions of interest (ROI) in which relevant information remains unchanged. Outside, personal characteristics are automatically or manually modified or removed so that the localization of the ROI is still possible. A face recognition algorithm, tools for masking image areas, thresholding methods, edge detectors and morphological image processing operators are available to make diagnostically irrelevant areas unrecognizable.

The clinical applicability of the developed pipeline, as well as potential limitations for AI-based analyses, particularly for classification algorithms, now require systematic investigation to evaluate their reliability and relevance in the clinical context.

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Poster 74

Early detection of heart failure through integration of clinical and ECG data

R. Kutzner[1,2], S. Sadeghi[1,2], T. Kirsten[1,2]

[1]Leipzig University Medical Center, Department for Medical Data Science, Leipzig, Germany,
[2]Leipzig University, Institute for Medical Informatics, Statistics and Epidemiology, Leipzig, Germany

Heart failure (HF) represents a major global health burden, with a high prevalence of morbidity and mortality among patients. It is often associated with significantly reduced quality of life and frequent hospitalizations. Early diagnosis and treatment of HF are therefore critical to improving patient outcomes and can enhance patient prognosis. However, the diagnostic process can be challenging due to the variety of potential structural and functional causes of HF [1].

The objective of this study is to facilitate early diagnosis by developing a conventional machine learning binary classifier to determine whether a patient is afflicted with HF, and to investigate the impact of various medical features on prediction accuracy. The data utilized in this study were obtained from the publicly available Medical Information Mart for Intensive Care III (MIMIC-III) dataset. The model incorporates clinical parameters collected during the first 24 hours after admission, including vital signs and laboratory measurements such as NT-proBNP, which are recommended by the European Society of Cardiology guidelines for HF diagnosis [2]. In addition, electrocardiogram (ECG) waveform data were integrated to assess the diagnostic impact of specific ECG features and their contribution to model performance improvement. The findings indicate that the incorporation of ECG-derived features improves HF prediction performance compared to models based solely on clinical parameters, and highlight the significance of measuring specific parameters in the diagnostic process.

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Poster 75

Enhancing Medical Machine Learning through High-Quality Synthetic Data

J. Gamisch[1,2], S. Sadeghi[1,2], T. Kirsten[1,2]

[1]*Leipzig University Medical Center, Department for Medical Data Science, Leipzig, Germany,*
[2]*Leipzig University, Institute for Medical Informatics, Statistics and Epidemiology, Leipzig, Germany*

A major challenge in advancing predictive models for medical applications is the limited availability of high-quality data, especially for rare diseases where well-documented cases are sparse. Furthermore, privacy concerns impose additional constraints on data accessibility, limiting scientific exchange and advancement of machine learning (ML) research in the medical domain. Generative models offer a potential solution by creating an unlimited number of synthetic data (SD) that preserve the statistical properties of the real data while maintaining patient privacy. This facilitates data sharing, supporting scientific collaboration and potentially improving ML performance.

The present study focuses on generating and evaluating high-quality SD derived from the small dataset of Pima Indians Diabetes. To this end, we developed and optimized two generative models, namely Copula-GAN and Conditional-Tabular-GAN, as well as a tabular variational autoencoder. The quality of the SD are evaluated through statistical measures, including Pairwise Correlation Distance (PCD). In addition, the SD are evaluated for a target application of diabetes classification through an evaluation framework that employ SD of a similar size to real dataset or larger, considering SD alone or combined with real data. The results demonstrate that classifiers with increased SD size exhibit enhanced ML performance, while preserving the statistical properties of the real data and protecting the privacy of patients. We propose that PCD is an adequate metric for ML optimization and a key indicator of SD quality.

Poster 76

Enhancing Trust in AI-Assisted Medical Decision-Making Through Reliable Uncertainty Estimation

A. Lindenmeyer[1,2], D. Schneider[1], T. Neumuth[1]

[1]Innovation Center Computer Assisted Surgery – ICCAS, Leipzig, Germany, [2]Center for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI) Dresden/Leipzig, Germany

Medical decision-making is an increasingly complex process, now pushing the boundaries of human comprehension. The growing adoption of Electronic Health Records (EHR) and Artificial Intelligence (AI) holds great potential for improving safety, quality of care, and efficiency. However, the critical nature of medical decisions means that reliability and trustworthiness often take precedence over raw performance, raising ethical and safety concerns that currently limit widespread AI adoption in medicine. One major concern is the overconfident behavior of Deep Learning architectures under data shifts, which can create a dangerous false sense of security when applied to cases beyond well-supported evidence.

Although this issue is recognized in simpler architectures, purpose-built advanced methods, such as uncertainty estimation Ensembles (ENN) and Spectral Normalized Gaussian Processes (SNGP), attempt to address it by estimating local uncertainty with each prediction. In our study, we examine the reliability and efficacy of ENN and SNGP methods through a series of targeted experiments and a mortality prediction use case utilizing Transformers and MIMIC3 data. Our findings indicate that overconfidence in ENN, due to posterior collapse, remains a significant issue, while SNGP shows promising improvements. Our study highlights the essential considerations for generating medically sound uncertainty predictions, a crucial step toward fostering trust and confidence in AI-supported medical decision-making.

Poster 77

Implementierung einer automatisierten Software-Lösung zur Umsetzung der Empfehlungen zum Ablauf strahlentherapeutischer Planbesprechungen in der Klinik für Strahlentherapie

S. Schäfer, N. Nicolay

Universitätsklinikum Leipzig AöR, Klinik für Strahlentherapie, Leipzig, Germany

Fragestellung:

Peer-Review-Prozesse und das 4-Augen-Prinzip sind entscheidend für die Fehlervermeidung und Qualitätssicherung in der klinischen Strahlentherapie. Aktuelle Leitlinien empfehlen Maßnahmen zur Steigerung der Patientensicherheit. Ziel dieses Projekts war die Entwicklung einer Software, die diese Empfehlungen zur physikalischen und ärztlichen Planabnahme umsetzt und den Workflow der Patientenvorstellung verbessert.

Methodik:

Aus der Literatur wurden Mindestanforderungen an die Software abgeleitet, darunter:

- 1-Click-Lösung zum Einpflegen vorzustellender Patienten
- Dokumentation aller Entscheidungen in der Frühbesprechung
- Klassifikation der Ablehnungsgründe für statistische Analysen
- Sinnvolle Vorstellungsreihenfolge nach Priorität

Die Software wurde in Python entwickelt. In Abstimmung mit den Beteiligten wurden relevante Workflow-Änderungen identifiziert und in die bestehenden Strukturen integriert.

Ergebnisse:

Seit 04/2024 ergänzt die Software den Frühbesprechungs- und Planabnahmeprozess. Mehr als 1500 Pläne wurden eingetragen, klassifiziert und für statistische Auswertungen aufbereitet. Kommentare, Ablehnungsgründe und Verbesserungsvorschläge sind dokumentiert. Zudem wurde von einer zufälligen zu einer prioritätsbasierten Vorstellungsreihenfolge gewechselt.

Schlussfolgerung:

Die Empfehlungen zur Planabnahme wurden erfolgreich durch die Software umgesetzt. Die Automatisierung verbesserte den Prozess erheblich, was zu einer signifikanten Zeitersparnis in mehreren Schritten führte und somit zur Einhaltung der hohen Qualitätsstandards in der Strahlentherapie beiträgt.

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Poster 78

Improving Preparedness in the Emergency Trauma Room: The Development and Impact of a Real-Time Data Transmission and Dashboard Visualization System

A. Schatz[1], G. Osterhoff[2], C. Georgi[1], F. Joeres[3], T. Neumuth[1], M. Rockstroh[1]

[1]Leipzig University, Faculty of Medicine, Innovation Center Computer Assisted Surgery, Leipzig, Germany, [2]Leipzig University Hospital, Department of Orthopaedics, Trauma and Plastic Surgery, Leipzig, Germany, [3]Otto-Von-Guericke-University Magdeburg, Department of Simulation and Graphics, Magdeburg, Germany

Purpose:

This study, conducted in collaboration with clinical end users, examines the potential of a visualization system for the real-time transmission of patient data from the ambulance to the emergency trauma room (ETR). The aim is to assess whether transfer of real-time data can facilitate more informed and timely interventions in the ETR, both before and after patient‘s arrival.

Methods:

In-depth qualitative interviews were conducted with 32 physicians from six hospitals in Germany and Switzerland. A prototype visualization system was developed to display patient data transfer in real-time and to provide a basis for evaluation by the participating physicians.

Results:

The prototype demonstrated the potential to improve ETR workflows by providing critical patient information in real-time. Physicians highlighted the importance of features such as the ABCDE scheme and vital signs as critical to patient care. In order to meet the specific needs of each clinic and to allow for the transmission of only essential information, the prototype would benefit from configurability and mobility.

Conclusion:

The findings highlight the need for flexible interfaces in medical communication tools that streamline processes without adding unnecessary workload for emergency services. The use of pre-notification systems to facilitate ambulance-clinic communication appears promising. Further research is recommended to evaluate the practical application and to re-evaluate the refined prototype in clinical practice.

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Poster 79

Improving record linkage quality on identification data in the Leipzig Obesity BioBank

M. Jugl[1,2], A. Hoffmann[3], M. Kern[3,4], M. Blüher[3,4], T. Ebert[4], T. Kirsten[1,2]

[1]University of Leipzig Medical Center, Medical Informatics Center, Dept. Medical Data Science, Leipzig, Germany, [2]Leipzig University, Institute of Medical Informatics, Statistics, and Epidemiology, Leipzig, Germany, [3]Leipzig University and University of Leipzig Medical Center, Helmholtz Institute for Metabolic, Obesity and Vascular Research (HI-MAG), Leipzig, Germany, [4]University of Leipzig Medical Center, Department of Endocrinology, Nephrology and Rheumatology, Leipzig, Germany

Within longitudinal medical studies, identification data (IDAT) is collected from participants which enables them to be reidentified across multiple sessions. Trusted third parties may then consolidate medical records obtained from the same person before handing them off to data scientists to conduct their research[1]. This process of merging records using stable or quasi-identifiers is referred to as „record linkage“[2]. Due to the nature of these studies, errors arise in the collected data due to changing data entry methods and staff over time[4][5]. Determining the required level of similarity to classify a record pair as a match therefore becomes a reoccurring challenge in the field of record linkage.

We present a method for estimating similarity thresholds for privacy-preserving record linkage (PPRL) using IDAT from two sub-studies of the Leipzig Obesity BioBank (LOBB). LOBB collects samples from over 8000 patients to conduct research on diseases related to obesity. We analyze the types and frequencies of typographical errors present in their IDAT. This information is used to infer a configuration for Gecko, which is a software library used to generate a set of realistic personal IDAT that closely replicates the errors found in the LOBB data[3]. We then evaluate the impact of each error class on match quality using these datasets. Our findings provide needed insights into the challenges of integrating real-world IDAT, which is necessary in PPRL where access to such data is often prohibited, and underline its significance in enhancing research validity and reliability.

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Poster 80

Predicting chemotherapy-induced thrombotoxicity by NARX neural networks and knowledge-driven transfer learning

M. Steinacker[1,2,3], Y. Kheifetz[2], M. Scholz[2,3]

[1]Center for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI) Dresden/Leipzig, Germany,
[2]Institute for Medical Informatics, Statistics and Epidemiology (IMISE), Leipzig University, Germany,
[3]Leipzig University, Faculty of Mathematics and Computer Science, Leipzig, Germany

Cytotoxic treatment in cancer therapy is frequently accompanied by dose-limiting hematotoxic side-effects. Predicting an individual's risk holds significant clinical relevance, but proves to be challenging due to high between-patient heterogeneity. To solve this task, several (semi-) mechanistic models of bone marrow hematopoiesis have been developed, but a subset of patients exhibiting irregular dynamics are particularly difficult to predict. We proposed a data-driven hypothesis-free machine learning approach to model individual time courses and provide here a comparative analysis on the basis of real-world patient data. We apply non-linear auto-regressive networks with exogenous inputs (NARX), based on feed-forward networks or gated recurrent units (GRU), to describe the highly non-linear dynamics of hematologic lineages under chemotherapy. We compare prediction performances of these approaches, biologically motivated semi-mechanistic models and combinations of it using transfer learning. Among the examined models, the NARX network based on a GRU architecture performed best if trained with transfer learning. For scenarios where the semi-mechanistic model fails to make good predictions, the improvement can be substantial. Prediction performances of our approach strongly depend on the amount of training data available per patient, in particular during the first therapy cycle. We recommend at least three well-spaced measurements which ideally cover the decline and recovery phase of blood count dynamics, as well as the nadir.

Poster 81

In vitro and in vivo effects of the new TRPV3 agonist AV3-1

C. Zosel, J. Janenz, K. Hill, M. Schaefer

Leipzig University, Rudolf-Boehm-Institut, Leipzig, Germany

The Ca^{2+} permeable transient receptor potential vanilloid 3 channel (TRPV3) is expressed in various epithelia, such as the colon mucosa and the skin. To investigate TRPV3's functions, selective, non-toxic agonists are required. Therefore, a $[Ca^{2+}]_i$-based screening of the Enamine library, containing 50,000 compounds, was performed and the new selective, low-toxic TRPV3 agonist, AV3-1, identified. Subsequently, mRNA and functional TRPV3 expression was investigated in various epithelial cell lines and could be found in several bladder carcinoma cell lines and as expected in primary mouse keratinocytes. In urothelial cancer cells, TRPV3 activation by AV3-1 caused an ATP-release, hinting to a potential role of TRPV3 in micturition.

Given that TRPV3 activation enhances proliferation and migration of primary mouse keratinocytes *in vitro*, an accelerating role of TRPV3 in dermal wound healing *in vivo* is discussed. To investigate this, two 5-mm dorsal biopsy punch wounds were excised on wild-type (WT) and TRPV3 knockout (TRPV3 KO) mice. The wounds received either AV3-1 or the corresponding vehicle and were histologically assessed. Surprisingly, no significant differences in wound areas or histological parameters of WT and TRPV3 KO mice were observed. Furthermore, AV3-1 could not increase the wound healing rate, neither in WT nor in TRPV3 KO mice. Therefore, the known *in vitro* effects of TRPV3 activation on keratinocytes proliferation and migration cannot be directly transferred into an *in vivo* context.

Poster 82

Deciphering Regulatory Biomarkers Associated with Cardiogenic Shock

R. Prajapati

Herzzentrum Leipzig - Helios, Universitätsklinik für Kardiologie, Leipzig, Germany

The endothelium, a pivotal component of vascular biology, plays a crucial role in orchestrating inflammation within blood vessels. Endothelial cells (ECs) actively express chemotactic molecules that attract immune cells and produce adhesion molecules that facilitate the attachment and infiltration of immune cells into cardiac tissues. Cardiogenic shock (CS), a severe condition marked by hypoxia, disrupts metabolic and cytokine environments. Studies using a biomarker panel, including cystatin C, lactate, interleukin-6, and N-terminal pro-B-type natriuretic peptide (CLIP score), demonstrate high sensitivity in predicting 30-day mortality in cardiovascular stroke patients. This biomarker approach offers comprehensive insight into the complex pathophysiology of CS.

Our investigation focuses on characterizing the endothelial inflammatory response to CS-related molecular patterns using in-vitro models. Literature indicates that CS patients exhibit elevated IL-6 levels, which correlate with cardiac dysfunction, though the direct impact of IL-6 on CS severity remains unclear.

Preliminary findings suggest an inverse relationship between IL-6 levels and endothelial cell proliferation. Additionally, we continue to analyze the effects of CLIP score components on EC functionality. This research aims to elucidate key mechanisms in CS and holds potential implications for targeted treatments.

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Differential effects of direct oral anticoagulants (DOACs) on experimental diabetic kidney disease

M. A. Farhan, S. Fatima, K. Shahzad, S. Pal, K. Singh, S. Ambreen, H. Khawaja, A. Mathew, R. Rana, S. Kohli, B. Isermann

Institute For Laboratory Medicine Clinical Chemistry and Molecular Diagnostics, University of Leipzig Medical Center, Leipzig, Germany

Diabetic kidney disease (DKD) is the main cause of end-stage renal disease worldwide. The underlying mechanism remain incompletely defined, but dysregulated coagulation activity has been closely linked to DKD. Direct oral anticoagulants (DOACs) inhibit specific coagulation factors and may hence differentially affect the hemostatic system. Here we studied the effects of DOACs targeting coagulation factor fXa or fIIa in experimental DKD. Kidney damage, as reflected by albuminuria, glomerular mesangial expansion, glomerular basement membrane thickness, renal fibrosis and premature senescence was strongly reduced in diabetic mice treated early with fXai. In contrast, diabetic mice treated with fIIai early showed only partial protection. Plasma levels of resolvin D2 (pro-resolving eicosanoid) was higher in fXai treated mice compared to fIIai. Inhibition of the resolvin D2 receptor GPR18 using O-1918 abolished the nephroptotective effect associated with fXai. At the later timepoint, the fXai and not fIIai treatment reduced indices of both glomerular and tubular damage.

Thus targeted interventions of specific coagulation proteases using DOACs differentially modulates experimental DKD. fXai provided superior protection against DKD by promoting resolvin D2 signaling and may be a potential therapeutic approach to treat DKD.

Keywords: Diabetic kidney disease, DOACs, resolvin D2, inflammation

Poster 84

Effects of prolonged normobaric hypoxia and norepinephrine on the cardiovascular system in rats

C. Bambor[1], S. Daunheimer[1], A. Hoschke[1], B. Raßler[1], A. Salameh[2]

[1]Leipzig University, Carl-Ludwig-Institute for Physiology, Leipzig, Germany, [2]University of Leipzig Medical Center, Department of Pediatric Cardiology, Heart Centre, Leipzig, Germany

Background:

Normobaric hypoxia for 24h reduces left ventricular inotropic function in rats. We speculated that prolonged hypoxia for 72h would induce acclimatization of left ventricular function. Since sympathetic blockade worsened left ventricular function, we examined the effects of norepinephrine (NE) on cardiovascular system during hypoxia. We also investigated the recovery extent after 72h of normoxia.

Methods:

Rats were exposed over 72h either to normal room air or to normobaric hypoxia in a chamber with 10% oxygen in nitrogen. The animals received infusion with NaCl (control groups) or norepinephrine. After 72h of hypoxia, a subgroup from each group was transferred to a normoxic environment with NaCl infusion for further 72h (recovery groups). At the end of the experiment, heart catheterization was performed in all animals for examination of hemodynamic function.

Results:

After 72h of hypoxia, left ventricular pressure and contractility were still significantly diminished. Interestingly, NE infusion reduced both parameters in normoxia and even more in hypoxia compared to the respective controls. After three days of recovery, both parameters returned to their initial values. The haematocrit was increased after hypoxia and remained elevated after 72h under normoxic conditions.

Conclusions:

After 72h of hypoxia, left ventricular depression is not fully restored. NE did not prevent hypoxic depression of left ventricular inotropic function. Left ventricular pressure and contractility completely recovered after three further days under normoxic control conditions.

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Effects of prolonged normobaric hypoxia and norepinephrine on the rat lung: Development of pulmonary edema and inflammation

S. Daunheimer[1], C. Bambor[1], I. Riha[1], J. Koedel[2], C. Raffort[3], A. Salameh[3], B. Raßler[1]

[1]Leipzig University, Carl-Ludwig-Institute for Physiology, Leipzig, Germany, [2]Leipzig University, Institute for Pathology, Leipzig, Germany, [3]Leipzig University, Department of Pediatric Cardiology, Heart Centre, Leipzig, Germany

Background:

Hypoxia can induce a hydrostatic pulmonary edema (PE). In addition, the sole activation of the sympathetic nervous system can provoke PE. We studied the influence of hypoxia and of sympathetic overactivation on the lungs of rats. We assessed PE and inflammation (by analysing TNFα) after 72h of hypoxia and after a normoxic recovery phase of another 72h.

Methods:

Rats were exposed over 72h either to normal room air (N) or to hypoxia in a chamber with 10% oxygen in nitrogen (H). The animals received infusion with 0.9% NaCl or norepinephrine (NE). After 72h of hypoxia, a subgroup from each the H-NaCl and H-NE groups was transferred to a normoxic environment with NaCl infusion for further 72h (recovery groups). At the end of the experiment, heart catheterization was performed in all animals for hemodynamic measurements. Finally, lung tissue was obtained for histological analysis.

Results:

PE developed during exposure to hypoxia and showed only partial resolution after 3d of recovery. NE infusion induced formation of PE even in normoxia but aggravated it only slightly under hypoxic conditions. The TNFα-levels increased especially under hypoxia exposure. NE infusion did not intensify the inflammation in the lung. After 72h of recovery, all groups showed a reduction in TNFα-levels to the normoxic level.

Conclusions:

The results show that inflammation is caused more by hypoxia than by NE infusion. While inflammation regresses quickly, PE needs a longer recovery period. PE and the inflammatory reaction develop in parallel, but are at least partly independent from each other.

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Psychology, Cognition and Public Health I

Psychology, Cognition and Public Health II

Molecular and Systemic Neurobiology

Biotechnology | Protein Biochemistry | Pharmaceutical Chemistry

Biomaterials | Translational Regenerative Medicine | Drug Delivery

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Poster 86

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

I. Siad, A. Kaiser

University of Leipzig Medical Center, Anesthesiology and Intensive Care, Leipzig, Germany

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, it is currently not possible 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 mRNA datasets under ischemic and control conditions in SH-SY5Y [GSE183546] as well as mouse [GSE270958] and rat models [GSE114609] and identified GPCRs with regulated expression, among them many orphan receptors. To investigate their functional contribution, we use the human neuroblastoma cell line SH-SY5Y as a model. Differentiation of SH-SY5Y into mature neurons was performed by a 3-step procedure[3] and verified by immunocytochemistry. We observed a 26.4 fold increased neurite outgrowth, as well as increased expression of the neuronal markers GAP-43, Tau and Tubulin. This system will be used to investigate the impact of different GPCRs on cell viability under oxygen-glucose deprivation conditions. Thus, we aim to identify new molecular targets with good accessibility and druggability to improve stroke therapy options in the future.

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[2] Wang, T. et al. Stroke 2020 (51): 3690.

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Poster 87

Extracellular Vesicles in Liquid Biopsy: Advancing early disease detection

S. Allelein, K. Aerchlimann, S. Arbaciauskaite, N. Mytzka, A. Kölsch, D. Kuhlmeier

Fraunhofer IZI, Leipzig/ Saxony, Germany

Liquid biopsy is a minimally invasive method that analyzes circulating biological material from body fluids for diagnosis. Unlike conventional solid tissue biopsies, it can be repeated frequently, offering real-time, continuous data. It analyzes entities like cell-free DNA, circulating tumor cells, and extracellular vesicles (EVs), aiding early diagnosis, patient stratification, and therapy monitoring. EVs have a high diagnostic potential. The cell-derived vehicles are found in all body fluids and carry biomarkers reflecting a cell‘s state. EVs are encased in a lipid bilayer, ensuring their stability as a source of information.

The MicroDiagnostics Unit at Fraunhofer IZI provides expertise and infrastructure for liquid biopsy sample profiling and assay development. Our technologies include:

- EV and lipoprotein isolation (ultracentrifugation, size exclusion chromatography density gradient centrifugation, immunoaffinity, large scale processing)
- EV and lipoprotein characterization (western blot, nanoparticle tracking analysis, electron microscopy)
- Spotting and analysis of molecules
- Antibody microarray analysis of surface molecules on EVs
- Assay integration in microfluidic devices

Our projects include:

- NanoCapture – Multiplex analysis of prostate cancer-derived EVs in urine and plasma
- BrainLab – Isolation of neural EVs for RNA NGS from Alzheimer’s patients
- PureEX – Proteomic profiling of lipoproteins and EVs in atherosclerosis
- CAR-EVs – Isolation and characterization of CAR-T-cell-derived EVs

We are looking for innovative projects and partnerships in Leipzig and beyond!

Poster 88

Identification and Analysis of Drug-Related Problems in Pediatric Patients with Inborn Errors of Metabolism

T. Harings[1,2], M. P. Neininger[1,2,3], S. Eisenhofer[1,2], A. G. Thiele[4], W. Kiess[4], A. Bertsche[3,4], S. Beblo[4], T. Bertsche[1,2]

[1]Clinical Pharmacy, Institute of Pharmacy, Faculty of Medicine, Leipzig University, Germany, [2]Drug Safety Center, Leipzig University and University Hospital, Leipzig, Germany, [3]Division of Neuropediatrics, University Hospital for Children and Adolescents, Greifswald, Germany, [4]Center for Pediatric Research, University Hospital for Children and Adolescents, Leipzig, Germany

Introduction:

Pediatric patients with inborn errors of metabolism (IEM) are potentially at increased risk of drug-related problems (DRPs) when treated with both IEM-related or non-IEM-related medication.

Methods:

We analysed the medication of pediatric patients with IEM for DRPs. These analyses included IEM-related medication and medication for other chronic or acute conditions, both prescribed and self-purchased. Parents were interviewed by phone to assess medication available at home for their children.

Results:

We analysed 884 preparations of 114 patients. DRPs were identified in 83/884 (9%) preparations which affected 50/114 (44%) patients. Clinically relevant DRPs that were avoidable due to safe alternatives were identified for 20 (2%) preparations of 24 (21%) patients. These DRPs did not relate to the patients' IEM. Clinically relevant DRPs that were unavoidable due to lack of safe alternatives affected 26 (3%) preparations of 15 (13%) patients, of which 12 (1%) preparations of 10 (9%) patients were used to treat IEM. In 37 (4%) preparations of 26 (23%) patients, DRPs were identified that were not clinically relevant in the context of these patients, though this may not apply to other patients.

Conclusion:

One in ten preparations used in pediatric patients was associated with DRPs. Most avoidable DRPs identified were unrelated to the patients' IEM indicating that the issues resulted primarily from the patient being a child rather than IEM-specific factors. This underscores the need for careful selection of medications especially in chronically ill pediatric patients.

Poster 89

Innovative Organ-on-Chip Model Systems with Applications in Cancer, Neurology, and Infectious Diseases

K. Hennig[1], A. Malheiro[2], K. Mattern[1], D. Heinrich[1], K. Aerchlimann[1], A. Friedrich-Stöckigt[3], E. R. Gomes[2], D. Kuhlmeier[1]

[1]IZI Fraunhofer, MicroDiagnostics, Leipzig, Germany, [2]Gulbenkian Institute of Molecular Medicine, Lisbon, Portugal, [3]IZI Fraunhofer, Vektorbasierte Immuntherapie, Leipzig, Germany

Organ-on-Chip (OoC) technologies enable the precise replication of human organs in microfluidic systems. In comparison to traditional preclinical model systems such as animal models and 2D cell cultures, which often fail to capture the complexity of human physiology, OoC models provide significant advantages. They allow for more accurate simulations of human organ functions, cellular interactions, and disease mechanisms.

At the Fraunhofer Institute for Cell Therapy and Immunology (IZI), we specialize in the development of several OoC systems and focus on their applications in areas such as immuno-oncology, infectious diseases, neurodegenerative diseases, and drug testing. The following cutting-edge technologies have been developed:

NeuroChip: A 3D cell culture platform to screen drugs for neurodegenerative diseases or cancer.

Muscle-Chip: An innervated and irrigated muscle model for drug screening in (neuro)muscular diseases.

Bone Marrow-Chip: A hydrogel-based 3D platform for research in hematological cancers and the optimization of cell therapies.

Lung-Chip: A membrane-based microfluidic chip to study infectious lung diseases and validate the efficacy of immunotherapies.

Our expertise includes the rapid design and prototyping of these systems, along with the development of quantitative assays based on molecular biology tests and microscopy. With our capabilities, we are actively seeking collaborations with research institutes and industry partners who are interested in exploring innovative solutions based on OoC technologies across various application fields.

Poster 90

Insect perception and mental well-being associated with eco-tourims and citizen science participation in the Peruvian Amazon rainforest (on goin master thesis)

A. G. Avellaneda Vergara[1], K. Rozario[1,2,3], M.-T. Meemken[2,3,4], R. Y. R. Oh[2,3], A. Bonn[1,2,3]

[1]Friedrich Schiller University Jena, Germany, [2]German Centre for Integrative Biodiversity Research (iDiv) Halle-Jena-Leipzig, Biodiversity and Health Hub, Leipzig, Germany, [3]Helmholtz-Center for Environmental Research, Leipzig, Germany, [4]Leipzig University, Germany

In face of global biodiversity and mental health crisis, interdisciplinary approaches are needed to reconcile biodiversity conservation and mental health promotion. Arthropods, 75% of earth's living organisms, only recieve 10% of all conservation actions, a mismatch that poses a significant threat to global biodiversity. Insects, despite their ecological significance, often lack the popular appeal associated to charismatic organisms. This perception can be attributed to factors such as urbanization, which disconnects people from nature and limits their understanding of insects. Extinction of experience not only affects people's attitude towards insects, it also impedes people from experiencing benefits associated with nature wich seem to be particularly pronounced for environments high in biodiversity. Citizen science emerges as a valuable avenue to engage people in biodiversity monitoring while exposing them to nature. Citizen science fosters interest in both, science and the environment, nurturing a continuous desire for learning that results in the acquisition of knowledge. Studies have further documented personal and community benefits resulting from participation in citizen science, also promoting mental health and wellbeing. Our study therefore aims to investigate the impact of ecotourism in high biodiversity environments in the Peruvian Amazon rainforest on insect perception, mental well-being and participation in citizen science projects. To achieve this, we conducted a questionnnaire-based study.

Poster 91

Nanopore sequencing driven mapping of the antimicrobial resistance genes in Escherichia coli from pigs and poultry layers in Nigeria

P. Ghosh[1], R. M. Kobialka[1], A. O. Ogunleyeo[2], A. G. Olusegun[3], A. A. E. Wahed[1], U. Truyen[4], C. Fall[5]

[1]Leipzig University, Institute of Animal Hygiene and Veterinary Public Health, Leipzig, Germany, [2]Department of Veterinary Microbiology, Faculty of Veterinary Medicine, University of Ibadan, Nigeria, [3]Leipzig University, Germany, [5]Pole de Microbiologie, Institut de Pasteur de Dakar, Senegal

Despite the huge burden of deaths associated or attributable to antimicrobial resistance, studies on antimicrobial resistance (AMR) monitoring in Africa are scarce, specifically in the animal sector. With a view to rapid AMR monitoring through maneuvering the advanced technologies, in the current study, nanopore sequencing was performed with 10 *E. coli* strains isolated from rectal swabs of pigs and poultry layers in Nigeria. Two sequence analysis methods including command line where bacterial genomes were assembled and subsequently antimicrobial resistance genes (ARGs) were detected through the online databases, and EPI2ME, an integrated cloud-based data-analysis platform with MinION were used to detect ARGs. A total of 94 ARGs were identified where most of the genes are known to be expressed in the chromosome. Interestingly, few genes including *qnrS1, qnrS15, qnrS10, kdpE, cmlA1, MIR-14, Sul3, dfrA12* were identified which were reported previously as transferred through MGEs. The antibiotic susceptibility assay explored that the E coli isolates were resistant to Penicillin (100%), Ciprofloxacin (70%), Tetracycline (50%) and Ampicillin (40%). The accuracies of the command line and EPI2ME have been found to be 57.14% and 32.14% respectively, in predicting the AMR. Moreover, the analysis methods showed 62.5% agreement in predicting AMR for the *E coli* isolates. Considering the multiple advantages of nanopore sequencing, application of this rapid and field-feasible sequencing technique has the promises for rapid AMR monitoring in LMICs including Nigeria.

Poster 92

Peptide-based activation and modulation of GPR68 as a novel approach for the treatment of acute myocardial infarctions

M. Wygas[1], P. Hartmann[2], H. Junker[3], C. Schoeder[3], K. Guan[2], M. Schubert[2,4], A. Kaiser[1,4]

[1]University of Leipzig Medical Center, Department of Anesthesiology and Intensive Care, Leipzig, Germany, [2]Dresden University of Technology, Institute of Pharmacology and Toxicology, Dresden, Germany, [3]University of Leipzig Medical Center, Institute for Drug Discovery, Leipzig, Germany

Myocardial infarctions remain a global health threat, and there are currently no pharmacological options to effectively increase cell viability and limit the infarct zone. G protein-coupled receptors (GPCRs) and especially currently understudied orphan GPCRs may represent new target structures to improve cell survival.

We re-analyzed mRNA-seq data (GSE110209, 132143) and found upregulated expression of several orphan GPCRs the infarct zone including the proton-activated receptor GPR68. In proof of concept experiments, application of the GPR68 small molecule positive allosteric modulator (PAM) ogerin [1] onto differentiated iPS cardiomyocytes increased cell survival. To investigate the underlying signaling pathways, we used heterologous HEK293 cells. GPR68 activated G_s, G_q, and $G_{12/13}$ pathways at acidic pH. Moreover, we showed recruitment of arrestin-3 to GPR68 for the first time. Ogerin acted as a PAM in all pathways, albeit to different degrees. In agreement with an earlier study [2], structural prediction of GPR68 suggested a potential for binding peptides which might be exploited to improve specificity over ogerin. Our current peptide lead structures are weak PAMs for arrestin-3 recruitment and G_s activation, demonstrating the potential of peptide modulators at GPR68.

GPR68 presents a promising molecular target to improve cell survival during myocardial infarctions. Further work is needed to increase the moderate activity of peptide modulators.

References:

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Poster 93

Physiology of molecular Adhesion GPCR dynamics

L.-S. Brodmerkel[1], A. Bormann[1], F. Seufert[2], P. Hildebrand[2,3], D. Ljaschenko[1], N. Scholz[1]

[1]Leipzig University, Rudolf Schönheimer Institute of Biochemistry, Division of General Biochemistry, Leipzig, Germany, [2]Leipzig University, Institute for Medical Physics and Biophysics, Leipzig, Germany, [3]Charite-Universitätsmedizin Berlin, Institute of Medical Physics and Biophysics, Berlin, Germany

The GPCR autoproteolysis-inducing (GAIN) domain is ancient and has thus far only been found in adhesion G-Protein-coupled receptors (aGPCR) and polycystins. Importantly, specific point mutations within this domain have been associated with devastating pathologies including polycystic kidney disease and bilateral frontoparietal polymicrogyria signified by malformation of the cortex. The GAIN domain harbors a tethered agonist (TA) able to trigger intracellular second messenger pathways.

Here, we exchanged specific amino acids within the GAIN domain that are according to molecular dynamics simulations key for domain flexibility and thus hypothetically aGPCR function. To test this hypothesis, we studied ADGRL/Latrophilin homologue Cirl in *Drosophila melanogaster* by combining biochemical, immunohistochemical, functional and behavioral readouts. Collectively, our data suggests that single modifications within the Cirl GAIN domain, even at supposedly critical positions, is compensated leaving the receptor intact.

Poster 94

Reconstruction and analysis of anterior descending neurons in a complete female connectome of Drosophila melanogaster

F. Klemm[1], P. Brooks[2], J. Phelps[3], M. Kim[3], W.-C. A. Lee[3], G. Jefferis[2,4], T. Stürner[2,4], A. Thum[1], K. Eichler[1,2]

[1]Leipzig University, Genetics, Leipzig, Germany, [2]University of Cambridge, Zoology, Cambridge, United Kingdom, [3]Boston Children's Hospital, Harvard Medical School, Boston, United States of America, [4]Neurobiology Division, MRC Laboratory of Molecular Biology, Cambridge, United Kingdom

In insects, the neck connective represents a signalling bottleneck between the brain and the ventral nerve cord (VNC, spinal cord analog), with most sensory processing taking place in the former and motor control in the latter. Systematic descriptions of the diverse populations of descending neurons (DNs) sending their axons through the neck connective in *Drosophila* have been incomplete surveys constrained to light microscopy (LM).

With the emergence of whole brain electron microscopy (EM) datasets a dense survey of the entire fly neck connective is now possible. Systematic comparison between EM-datasets and LM images made bridging the gap between the brain and the VNC connectomes possible. In a recent study we reported the identification of more than half of the DN population in a brain and two VNC connectomes.

However, a complete EM dataset containing the neck connective and thus covering both the brain and the VNC was not available to the *Drosophila* community until now. With BANC, a complete female dataset, a comprehensive analysis of all DNs, including the previously unmatched ones, is now possible.

In this project, a subpopulation of DNs with anterior soma, the DNa-population, is investigated. We report their morphology in the BANC dataset and matched them to the DNa neurons of the FAFB (female brain) EM-dataset (DNa - with previous LM data, DNae - without, newly described in EM).

In addition, a circuit-analysis of DNa08 in the male (MANC) and female (FANC) VNC dataset is carried out, as the morphology of the neuron provides indications of a possible sexual dimorphism.

Poster 95

Reimbursed inhalation consultations in German community pharmacies – a multi perspective evaluation

A.-C. Kroenert, L. Freyberg, T. Bertsche

Institute of Pharmacy, Department of Clinical Pharmacy, Leipzig, Germany

Background:

Benefits of inhalation consultations have been proven in various outcome studies. In June 2022 inhalation consultations became remunerable for German community pharmacies. The aim of our study was to investigate how this remunerated service is performed under routine conditions.

Methods:

We analysed inhalation consultations performed by community pharmacies in Saxony. To objectively assess the routine services an external trained monitor observed the inhalation consultations. We documented patients' handling problems during the inhalation demonstration and the content of the following consultation with predefined checklists. Additionally we interviewed patients and pharmaceutical staff after the consultation with a questionnaire about the preceded inhalation consultation.

Results:

We evaluated 48 inhalation consultations in 13 different community pharmacies. We could observe a median of 2 predefined problems (Q25: 1;Q75: 3) in a patients' inhalation technique. 54% (13 of 24 patients) of the patients using metered dose inhalers had problems holding the head appropriately during the inhalation process. This problem was addressed by the pharmaceutical staff in 69% (9 consultations) of the following consultations. CONCLUSION: In evaluating the inhalation consultations we figured out many problems with patients' inhalation technique that mostly have been resolved by the pharmaceutical staff during the following inhalation consultation. The contentment of the patients with the consultation was high to very high and usually higher than those of the pharmaceutical staff.

Poster 96

The granulation (t)issue in equine distal limbs -myofibroblast culture, characterization and scratch assay

J. K. Michler[1], W. De Spiegelaere[2]

[1]Leipzig University, Institute of Veterinary Anatomy, Histology and Embryology, Leipzig, Germany,
[2]Gent University, Department of Morphology, Faculty of Veterinary Medicine, Gent, Belgium

Wound healing disorders like exuberant granulation tissue (EGT) occur frequently in equine distal limbs as horses are flight animals. In up to 25% of cases, these 2nd intention wound healing disorders results in prolonged and costly treatments and may even lead to euthanasia. EGT is a fibroproliferative disorder characterized by massively proliferating (myo)fibroblasts, which outcompete the keratinocytes that are responsible for closing the wound. These wounds are stuck between the inflammatory and proliferative phase of the wound healing cascade. We isolated equine skin fibroblasts (n=10 horses) from the body wall and the distal limb as well as from surgically trimmed EGT tissue. Cells were compared regarding their growth characteristics (population doubling time (PDT) and scratch assays) as well as immunofluorescent expression of alpha smooth muscle actin (αsma), Vimentin and Collagen I. Although we subjectively monitored the body wall fibroblast growth as slightly faster in our 2D cultures, statistics in PDT and scratch assay found them to be equal. The majority of cells expressed αsma, Vimentin and Collagen I with a a semiquantitatively increased expression of αsma and Collagen I for the distal limb fibroblasts, whereas Vimentin was expressed in comparable levels.

With the upregulation of αsma and Collagen I, we draw the conclusion that the 2D activated cutaneous fibroblast features the characteristics of fully differentiated wound healing myofibroblasts. Therefore, the activated cutaneous fibroblast seems to be an applicable in-vitro model for future EGT research.

Poster 97

Transient contacts of neuropeptide receptors detected by crosslinking coupled with mass spectrometry in cells

K. D. Leitner[1], A. Baischew[2,3], A. Sinz[2,3], A. Kaiser[1]

[1]University of Leipzig Medical Center, Department of Anesthesiology and Intensive Care, Leipzig, Germany, [2]Martin Luther University Halle-Wittenberg, Department of Pharmaceutical Chemistry and Bioanalytics, Institute of Pharmacy, Halle, Germany, [3]Martin Luther University Halle-Wittenberg, Center for Structural Mass Spectrometry, Halle, Germany

G protein-coupled receptors (GPCRs) are valuable for pharmaceutical development, as almost 34% of all FDA approved drugs target GPCRs.[1] Despite current research, the dynamics of ligand-receptor interactions are poorly understood. We investigated transient interactions of the neuropeptide Y (NPY) to its Y_2 receptor (Y_2R).

We devised photoreactive diazirine-labeled NPY variants that cross-link with the receptor on µs timescale upon activation by UV-A irradiation. The peptides were cross-linked to stably transfected Y2R-FLAG in live HEK293 cells. After cell lysis and receptor solubilization, the sample was enriched by immunoprecipitation, enzymatically digested and proteolytic peptides were analyzed by LC-MS/MS.

Even with minimal GPCR isolation from eukaryotic cells, 44 Y_2R peptides and 21 peptide-receptor crosslinks were identified. The cross-links concentrated to the NT of the receptor, which matches a recent study[2] that used *in vitro* preparations of Y_2R. Despite their transient nature, contacts of NPY proved important for stabilizing the recruitment of arrestin-3 to the Y_2R, inducing receptor internalization.

Our results complement the high-resolution cryo-electron microscopy structure of the NPY-Y_2R [3] that did not resolve the NT due to its high flexibility. We suggest that transient peptide-receptor contacts shape receptor functionality.

References:

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Poster 98

Adherence as Crux of the Matter? Secondary Analysis of the AgeWell.de Lifestyle Intervention against Cognitive Decline

F. Wittmann[1], A. Pabst[1], A. Zülke[1], M. Luppa[1], D. Czock[2], B. Wiese[3], J. R. Thyrian[4,5], W. Hoffmann[4,5], J. Gensichen[6], H.-H. König[7], H. Kaduszkiewicz[8], T. Frese[9], S. G. Riedel-Heller[1]

[1]Institute of Social Medicine, Occupational Health and Public Health (ISAP), Leipzig University, Faculty of Medicine, Leipzig, Germany, [2]Heidelberg University Hospital, Department of Clinical Pharmacology and Pharmacoepidemiology, Heidelberg, Germany, [3]Hannover Medical School, Institute for General Practice, Hanover, Germany, [4]German Centre for Neurodegenerative Diseases (DZNE), Greifswald/Rostock, Germany, [5]University Medicine Greifswald (UMG), Institute for Community Medicine, Greifswald, Germany, [6]University Hospital LMU Munich, Institute of General Practice and Family Medicine, Munich, Germany, [7]University Medical Centre Hamburg-Eppendorf, Department of Health Economics and Health Service Research, Hamburg, Germany, [8]University of Kiel, Institute of General Practice, Kiel, Germany, [9]Martin-Luther-University Halle-Wittenberg, Institute of General Practice and Family Medicine, Halle, Germany

Aim:

To investigate the effect of adherence to AgeWell.de as multi-domain lifestyle intervention against dementia on health-related outcomes.

Methods:

We analyzed adherence of 366 participants of the intervention group aged 60-77 at increased risk of dementia (CAIDE score ≥9) to nutritional counseling, enhancement of physical and social activity and cognitive training as sum-score of seven time points, answered by study nurses regarding the achievement of individually set goals. Outcomes were function of everyday activities, depressiveness, social inclusion and quality of life.

Results:

Better adherence to nutritional counseling and physical and social activities was positively associated with health-related quality of life and depressiveness. Adherence to physical and social activity improved function in everyday activities. However, the impact of cognitive training remained marginal. No effect was found on social inclusion.

Conclusion:

While nutritonal counseling and social activity were already reported to be associated with better cognitive function, these results are an important addition. Quality of life and depressiveness are not only associated with cognition, they may also effect the effectiveness of an intervention through feelings of improvement and increased motivation. The results suggest that nutritional counseling and enhancement of physical and social activity, as implemented in AgeWell.de, were effective, yet they have not been able to improve all outcomes the same way. The results help to design future intervention studies in a more targeted and effecive way.

Poster 99

Anosognosia in Mild Alzheimer's Disease: Overconfidence in the Face of Uncertainty

T. Ritter[1], J. Klingbeil[1,2], E. Bahr[1], F. Welle[1], M. Wawrzyniak[1], D. Saur[1]

[1]*University of Leipzig Medical Center, Department of Neurology, Leipzig, Germany,*
[2]*University Hospital Halle, Department of Neurology, Halle (Saale), Germany*

Objective:

A lack of awareness of cognitive decline is common in early stages of Alzheimer's disease (AD), impacting treatment decisions and overall well-being of both patients and caregivers. This study aims to explore the cognitive dysfunctions underlying anosognosia for AD. We hypothesized that patients with anosognosia for mild AD or amnestic mild cognitive impairment (aMCI) would exhibit overconfidence in their prior beliefs despite conflicting information, independent of memory deficits and major personality traits.

Methods:

Employing a prospective approach, 59 patients with a clinical aMCI/AD diagnosis and 20 healthy age-matched controls underwent cognitive assessment, anosognosia evaluation, a personality test and a riddle-paradigm. The riddles create a situation of uncertainty that is resolved in five consecutive steps which progressively reveal the target solution. After each clue, participants must guess the solution and rate their confidence on a scale. The presence of anosognosia was evaluated by a psychologist during clinical examination and by the discrepancy between self- and caregiver-assessment.

Outlook:

Of the 47 aMCI/AD patients included in the final analysis, 24 were rated unaware of their limitations. Unaware patients were significantly more confident in their guesses when lacking necessary information. Analyses of cognitive subtests, personality traits and the control group are still ongoing. With a better understanding of overconfidence, this research may aid in developing therapeutic strategies for anosognosia in patients with aMCI/AD in the future.

Poster 100

Associations between sensation seeking and disordered eating, and moderating effects of weight status and behavioral difficulties in healthy adolescents

M. Bogner[1], R. Schmidt[2], W. Kiess[1,3], T. Poulain[1,3]

[1]LIFE Leipzig Research Center for Civilization Diseases, Leipzig University, Germany, [2]Behavioral Medicine Research Unit, Department of Psychosomatic Medicine and Psychotherapy, University of Leipzig Medical Center, Germany, [3]Department of Women and Child Health, Hospital for Children and Adolescents and Center for Paediatric Research (CPL), Leipzig, Germany

Previous findings suggest associations between the personality trait sensation seeking (SS) and disordered eating, focusing mainly on binge eating in young adults. Far less is known about this relationship in adolescents, particularly with respect to SS and eating disorder psychopathology. Therefore, the present study aimed to investigate the role of SS and disordered eating in a sample of healthy adolescents taking into account relevant sociodemographic variables and moderating effects of standardized Body Mass Index (BMI) and behavioral difficulties.

We analyzed data of 400 13- to 16-year-old participants from the LIFE Child study (Leipzig, Germany). They provided information on SS, disordered eating, behavioral difficulties, and sociodemographic data. Anthropometric measurements were objectively assessed. Multiple linear regression models were applied to assess associations.

Boys displayed higher levels of SS than girls, and novelty seeking was positively associated with socioeconomic status. Analysis revealed significantly positive associations between SS and eating disorder psychopathology (restraint and eating concerns), overeating, loss of control eating, and binge eating. A higher BMI, more hyperactivity and more emotional symptoms strengthened the association between SS and disordered eating.

Our results indicate that higher SS levels are associated with correlates of disordered eating in adolescence. Emotional symptoms and hyperactivity were shown to moderate this association and might display promising targets for prevention strategies and interventional measures.

Poster 101

Depressive and Anxiety Symptoms and the Association with Social Factors in Patients with Long COVID Symptomatology

S. K. Gerhards[1], M. Luppa[1], A. Zülke[1], C. Sander[2], G. Schomerus[2], K. Wirkner[3,4], M. Reusche[3,4], S. Zeynalova[3,4], V. Witte[5,6], A. Villringer[5,6], M. L. Schroeter[5,6], D. Saur[5], M. Löffler[3,4], C. Engel[3,4], S. G. Riedel-Heller[1]

[1]Leipzig University, Faculty of Medicine, Institute for Social Medicine, Occupational Health and Public Health, Leipzig, Germany, [2]University of Leipzig Medical Center, Department of Psychiatry and Psychotherapy, Leipzig, Germany, [3]Leipzig University, Leipzig Research Center for Civilization Diseases, Germany, [4]Leipzig University, Institute for Medical Informatics, Statistics and Epidemiology, Leipzig, Germany, [5]University of Leipzig Medical Center, Cognitive Neurology, Leipzig, Germany, [6]Max Planck Institute for Human Cognitive and Brain Sciences, Department of Neurology, Leipzig, Germany

Background:

Approximately one third of patients who were previously infected with the Sars-Cov-2 virus develop symptoms that are subordinated to the term Long COVID (LC). Of those even two years post infection 13.4% suffer from anxiety and 18.0% show depressive symptomatology (Fernandez-de-las-Peñas et al. 2024). Little is known about the influence of social characteristics on depressive and anxiety symptoms in patients with LC.

Methods:

Depressive Symptomatology was assessed with the Center for Epidemiological Studies Depression Scale (CES-D). Anxiety symptoms were measured with the General Anxiety Disorder Scale (GAD-7). Living situation was assessed with a single item question. Social Network was assessed with the Lubben Social Network Scale (LSNS). Multivariate regression analysis was conducted.

Results:

In *n*=410 participants with PCS (mean age= 47.12 years, SD=12.29, range= 19-82 years; 77.1% female) in Leipzig and close surroundings living with someone compared to living alone was associated with less depressive symptoms (*B*=-2.13, *p*=.017). A larger social network (*IRR*= .983, *p*=.002) was associated with less anxiety symptoms in patients with LC symptomatology.

Conclusion:

Social network may be targeted when addressing anxiety symptoms in patients with LC by facilitating access to social exchange groups such as LC specific self-help groups. Social contact within ones household may be important in terms of targeting depressive symptoms. More research with longitudinal data is needed for clarification.

Poster 102

Differences in EEG-based Brain Arousal Regulation between subgroups of Attention-Deficit Hyperactivity Disorder with and without Emotional Dysregulation

M. Sander, J. Huang, N. Mauche, M. Strauß

Leipzig University Medical Center, Department for Psychiatry and Psychotherapy, Leipzig, Germany

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental chronic condition marked by inattention, hyperactivity and impulsivity, affecting 2 to 7 % of the population. Up to 70% of ADHD patients experience emotional dysregulation (ED), characterized by challenges in modulating emotions and social consistent responses. ED is linked to a more severe symptomatology and more comorbidities, but is seldom addressed in clinical diagnostics. While the exact pathomechanism remains unclear, the Brain Arousal Regulation Model suggests that ADHD patients may display a lower level of wakefulness and an altered regulation itself requiring external stimulation to balance out that deficit. This study aimed to investigate the differences in brain arousal regulation between adult ADHD patients with and without ED (ED+ vs. ED-).

Methods:

Clinical and EEG data were collected from adult ADHD patients at our specialized outpatient clinic. Using latent class analysis (LCA) on the Wender-Reimherr interview (WRI), patients were classified into ED+ and ED- subgroups. EEG data were analyzed by an algorithm assessing the brain arousal regulation.

Results:

No significant differences in brain arousal regulation were found between ED+ and ED-.

Discussion:

Our findings suggest that ED may not be directly related to arousal regulation, but other neural mechanisms may be involved. Finding a consensus on the concept of ED and an operationalization based on more parameters could help defining subtypes and unmasking confounding variables.

Diseases of Civilisation | Obesity

Immunology | Infectiology | Inflammation

Clinical and Molecular Oncology

Clinical Research

Digital Health

Life Science Research

Psychology, Cognition and Public Health I

Psychology, Cognition and Public Health II

Molecular and Systemic Neurobiology

Biotechnology | Protein Biochemistry | Pharmaceutical Chemistry

Biomaterials | Translational Regenerative Medicine | Drug Delivery

Molecular Biology | Biomedicine

Poster 103

Dyadic coping of cancer patients with mental disorders six months and one year after cancer diagnosis

A.-K. Köditz[1], A. Mehnert-Theuerkauf[1], U. Görling[2], T. Zimmermann[3], B. Hornemann[4], J. Ernst[1]

[1]University of Leipzig Medical Center, Department of Medical Psychology and Medical Sociology, Leipzig, Germany, [2]Charité - Universitätsmedizin Berlin, Charité Comprehensive Cancer Center, Berlin, Germany, [3]MHH - Medizinische Hochschule, Department of Psychosomatic Medicine and Psychotherapy, Hanover, Germany, [4]NCT/UCC - National Center for Tumor Diseases Dresden, Psycho-Oncology, Dresden, Germany

Purpose:

Coping of couples with one partner facing cancer is considered as a dyadic process (dyadic coping, DC). Psychological comorbidities can lead to a challenging situation for cancer patients and potentially affect their coping. We want to investigate the DC of cancer patients with a mental disorder six months after their cancer diagnosis and at a six-month follow-up.

Methods:

Data were collected as a part of the prospective multi-center "LUPE"-study. Here we report the second and the third measurement time point (first time point within 8 weeks after diagnosis of a solid cancer, following at intervals of 6 months). Validated questionnaires (Dyadic Coping Inventory, dimensions of DC: supportive, negative, delegated, common) as well as a SCID-5-Interview (by telephone) were used.

Results:

The sample comprises the results of 70 patients (67% women; average age 53 years; 40% married). Most prevalent cancers were gynecological tumors (23%), prostate cancer (16%) and breast cancer (16%). The data are currently being processed. The DC of patients (total score and dimensions) with a mental disorder will be presented at the research festival.

Conclusion:

Psychological comorbidity is a particular burden during cancer. There has been little research on DC in this patient group. Findings may have implications for the improvement of psycho-oncology care for this particularly vulnerable patients. The results will be discussed at the research festival.

Poster 104

Empirical-ethical recommendations for teaching research ethics in public health

C. Diegmann[1,2]

[1]*University of Bremen, Faculty 11 Human and Health Sciences, Bremen, Germany,*
[2]*University of Leipzig Medical Center, Academy & Medical vocational college, Leipzig, Germany*

Introduction:

The appropriate (re-)use of research data is mandated and in line with current efforts towards digital sustainability and open science. However, standards for research data and research ethics vary and are sometimes contradictory. The different standards are the result of different teaching of research ethics. There is no evidence of comprehensive teaching and learning in research ethics in the public health infrastructure. However, as we are dealing with health-related personal data, responsible handling and teaching is essential. This PhD project aims to answer the question of how researchers can be empowered and supported in matters of research ethics in public health. The aim is to identify uncertainties and needs.

Methods:

Firstly, I analyse the existing curricula and module handbooks for German-language public health degree programmes with a focus on the subject research ethics.

Secondly, I develop and conduct interviews with module and program directors of this degree programmes.

Thirdly, once this stocktaking has been completed, it is planned to set up focus groups with public health students to gather their views and to identify their needs.

Expected results: Handouts:

Finally, practicable solutions and guidelines for public health researchers will be developed. In addition to the normative considerations, the result should contain documents in the form of very clear instructions and recommendations. With these documents, this PhD project aims to support and promote the qualification of researchers throughout Germany, especially in early career phases.

Poster 105

Engaging with the stigma of mental illness and economic pressure in modern life worlds: a maximal contrast analysis

C. Helmert[1], S. Speerforck[1], A. Leonhard[1], M. C. Angermeyer[2], B. Link[3], I. Matuschek[4], G. Schomerus[1]

[1]Leipzig University, Faculty of Medicine, Department of Psychiatry and Psychotherapy, Leipzig, Germany, [2]Center for Public Mental Health, Gösing am Wagram, Austria, [3]University of California Riverside, Riverside, United States of America, [4]Hochschule der Bundesagentur für Arbeit, Schwerin, Germany

The stigmatization process includes labeling, stereotyping, separation, status loss, and discrimination and reflects different social functions. Little is known about how modern life worlds shape understandings of mental illness and stigmatization toward people with mental illness. Purposive theoretical sampling selected 5 focus groups with 3 to 5 participants from different life worlds (operationalized through shared occupational and sociopolitical life goals). Using the method of maximum contrasts, we conducted a qualitative content analysis of 2 focus groups (group 1: n = 4, mean age: 37.7y, volunteer fire fighters; group 2: n = 4, mean age: 41.3y, self-employees working in the service and media sector). Different life worlds correspond with different manifestations of stigma and strategies in engaging with people with mental illness. Self-employees as workforce entrepreneurs rationalize their social behavior. Engaging with people with mental illness comprises a cost-benefit-analysis considering possible costs regarding performance and self-optimization. In contrast, volunteer fire fighters described trying to integrate people with mental illness in a familial way. We hypothesized that life worlds not only interrelate with stigmatizing attitudes but shape the stigma-process itself. These results can be used to design modern questionnaires to examine stigmatization and support targeted intervention and prevention strategies.

Poster 106

Feasibility of the virtual reality optokinetic stimulation training (VR-OKS) for chronic stroke patients with unilateral spatial neglect

L. P. Peters[1], J. Belger[1,2], A. Thöne-Otto[1,2]

[1]*University of Leipzig Medical Center, Day Clinic for cognitive Neurology, Leipzig, Germany,*
[2]*Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany*

Unilateral spatial neglect (USN) is a debilitating neuropsychological disorder that is common in right-hemisphere stroke patients[1][2][3][4]. Evidence-based treatments such as optokinetic stimulation therapy (OKS) and active visual exploration are recommended for USN rehabilitation as they redirect attention to the contralesional side[1][2][3][4]. However, traditional treatments for USN lack direct, objective feedback and therapists have limited insight into patients' head and eye movements. This makes it difficult to translate effects into functioning in daily life[1][2]. Virtual reality (VR) may improve these shortcomings by providing precise experimental control and immediate objective feedback, allowing patients to adapt their behaviour[1]. Here, we investigate the feasibility of our VR-OKS training[5], which adapts traditional rehabilitative measures for USN to immersive VR with integrated eye tracking. Our sample of $N = 12$ post-stroke USN patients (female $n = 5$, age $M = 56.92$, $SD \pm 10.87$) completed 10 VR-OKS training sessions of increasing difficulty. Patients were asked to visually transport objects from right to left using their gaze while keeping their head in a fixed straight position. Linear regression results revealed a significant positive effect of session on the number of objects transported on successful task completion ($\beta = 0.27$, $t(358) = 5.78$, $p < .001$). Patients rated the VR-OKS highly in terms of likeability and usability, with no significant increase in cybersickness. The results support the high feasibility and positive effects of the VR-OKS in the rehabilitation of USN.

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Poster 107

How Can We Improve the Quality of Life for Patients and relatives affected by Amyotrophic lateral sclerosis (ALS)? – Insights from the Participatory Multi-Method Study "potentiALS"

S. Heyne[1], A. Kuzmanova[1], P. Esser[2], A. Mehnert-Theuerkauf[1], M. Metelmann[3]

[1]University of Leipzig Medical Center, Department of Medical Psychology and Medical Sociology, Leipzig, Germany, [2]Family Counseling Center, Volkssolidarität Stadtverband Leipzig e.V., Betriebsstätte Wurzen, Germany, [3]University of Leipzig Medical Center, Clinic and Polyclinic for Neurology, Leipzig, Germany

Background and Purpose:

ALS is a progressive disease that impacts daily life and places psychological strain on patients and families. Despite high unmet need, targeted psychosocial interventions are lacking. The potentiALS project aims to develop tailored psychotherapeutic treatments by engaging ALS patients, relatives, and healthcare professionals through participatory research.

Methods:

In this observational, multi-method study, we evaluated variables related to anxiety, depression, and quality of life, in addition to psychosocial needs. Psychoherapeutic approaches such as Acceptance and Commitment Therapy, Meaning-centered Therapy, Cognitive Behavioral Therapy (CBT), and Psychodynamic Therapy (PT) were discussed in focus groups. Participants identified the most relevant elements for an ALS-specific treatment program.

Results:

13 patients, 17 caregivers, and 11 professionals completed the study. Anxiety scores were higher for both patients and caregivers compared to depression scores. A key finding was the need for immediate support following diagnosis, with further assistance required during the onset of new impairments. Patients and relatives voted as most helpful aspects open dialogue, emotional support and clear goals across all four types of therapy. Medical staff voted PT as most helpful for patients, while CBT most suitable for relatives.

Conclusions:

This study shows the feasibility of using a participatory research approach with ALS patients, caregivers, and healthcare professionals and demonstrates components for a tailored psychosocial counseling program.

Poster 108

Mammillary body and hypothalamic volumes in mood disorders: A high-resolution 7 Tesla MRI study

M. Nowak[1], S. Schindler[1], M. Storch[1], S. Geyer[2], P. Schönknecht[1,3,4]

[1]Universitätsklinikum Leipzig, Klinik für Psychiatrie und Psychotherapie, Leipzig, Germany, [2]Max-Planck-Institut für Kognitions- und Neurowissenschaften, Leipzig, Germany, [3]Sächsisches Krankenhaus Altscherbitz, Fachkrankenhaus für Psychiatrie und Neurologie, Leipzig, Germany, [4]Universitätsklinikum Leipzig, Selbstständige Ambulanz für sexualtherapeutische Prävention und forensisch-psychiatrische Forschung, Leipzig, Germany

We have previously reported an in vivo enlargement of the left hypothalamus in mood disorders using 7 Tesla MRI. The aim of this follow-up study was to find out whether the hypothalamic volume difference may be located in the mammillary bodies (MB) rather than being widespread across the hypothalamus.

We developed and evaluated a detailed segmentation algorithm that allowed a reliable segmentation of the MBs, and applied it to 20 unmedicated (MDDu) and 20 medicated patients with major depressive disorder, 21 medicated patients with bipolar disorder, and 23 controls. 20 out of 23 healthy controls were matched to the MDDu. We tested for group differences in MB and hypothalamus without MB (HTh) volumes using analyses of covariance. Associations between both volumes of interest were analysed using bivariate and partial correlations.

In contrast to postmortem findings, we found no statistically significant differences of the MB volumes between the study groups. Left HTh volumes differed significantly across the study groups after correction for intracranial volume (ICV) and for ICV and sex. Our result of an HTh enlargement in mood disorders was confirmed by a paired t-test between the matched pairs of MDDu and healthy controls.

Our results indicate that our previous in vivo finding of a hypothalamus enlargement does not extend to MBs, but is limited to the HTh. The enlargement is more likely related to the dysregulation of the HPA axis than to cognitive dysfunctions accompanying mood disorders.

Poster 109

Neural correlates of reward-enhanced food memory in a high-fibre diet interventional trial of overweight adults: A pre-registered analysis

D. E. Jensen[1,2], R. Thieleking[2], E. Medawar[2], M. Vartanian[2], A. Villringer[1,2], F. Beyer[2], V. Witte[1,2]

[1]*University of Leipzig Medical Center, Clinic of Cognitive Neurology, Leipzig, Germany,*
[2]*Max Planck Institute for Human Cognitive and Brain Sciences, Neurology, Leipzig, Germany*

With the worldwide rise of obesity prevalence, the need for effective prevention and treatment becomes increasingly important. Unhealthy food decisions and overconsumption are often considered as one of the factors leading to obesity. Memory processes have long been known to determine food choices but recognition memory of food and its cognitive, homeostatic, and neuroanatomical predictors are still largely understudied. Moreover, fiber-rich diets have been suggested to modulate brain-behaviour communication by altering homeostatic and hedonic control of food decision-making. We aim to test the effects of a dietary fiber intervention (30g inulin/day over 14 days) compared to equicaloric placebo, on food memory and its neuronal correlates in overweight adults in a double-blinded cross-over within-subject randomized clinical trial (NCT03829189, osf.io/fc2g4/). Food versus art memory encoding and retrieval was tested in n=59 healthy overweight adults (19 females, 28 years±6.2, BMI 27.3kg/m^2±1.4) during a 3T task functional magnetic resonance imaging. Inference tests are performed using a homeostatic and memory-related hypothalamus brain mask on 1st-level contrasts and 2nd-level factors time (baseline, follow-up), group (high-fibre/placebo), and time*group interactions using the Sandwich Estimator (SwE, implemented in SPM). Analyses for this pre-registration are ongoing. Overall, this study will shed light on food-related neuronal correlates of memory processes, which may offer new avenues for detecting treatment options for people with obesity.

Poster 110

Sex differences in the associations between visceral fat, brain aging, and cognition

C. Koch[1,2], L. Ruehr[1,3,4,5], F. Beyer[1,6], D. Jensen[1,5], L. Lammer[1], S. Riedel-Heller[7], R. Baber[8,9], S. Zeynalova[10,11], V. Witte[1,5], J. Sacher[1,3,4,5,12]

[1]Max Planck Institute for Human Cognitive and Brain Sciences, Neurology, Leipzig, Germany, [2]Biological Faculty, Leipzig University, Germany, [3]Center for Integrated Women's Health and Gender Medicine, Faculty of Medicine, Leipzig University, Germany, [4]Max Planck School of Cognition, Leipzig, Germany, [5]Clinic of Cognitive Neurology, University Medical Center, Leipzig, Germany, [6]Bordeaux Population Health Research Center, University of Bordeaux, France, [7]Institute of Social Medicine, Occupational Health and Public Health (ISAP), Faculty of Medicine, Leipzig University, Germany, [8]Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostic, University of Leipzig Medical Center, Leipzig, Germany, [9]Leipzig Medical Biobank, Leipzig University, Germany, [10]LIFE - Leipzig Research Centre for Civilization Diseases, Leipzig University, Germany, [11]Institute for Medical Informatics, Statistics and Epidemiology, Leipzig University, Germany, [12]Medical Department III - Endocrinology, Nephrology, Rheumatology, Leipzig University, Germany

Alzheimer's disease (AD) disproportionately affects females, who account for two-thirds of cases, highlighting the need to explore sex differences in how the human brain ages. Brain aging is characterized by reduced hippocampal volume (HCV), cortical thinning (CT), and cognitive decline as well as markers of cerebral small vessel disease (cSVD) such as white matter (WM) hyperintensities, perivascular space burden and free water in WM. Visceral adipose tissue (VAT) is a known risk factor for brain aging and vascular complications, and notably, accumulates differently by sex. Moreover, VAT accumulation and brain aging in females may be modulated by estradiol (E2), especially after menopause, when E2 levels drop sharply. Building on these associations, this study seeks to explore the impact of VAT accumulation on brain aging and how this effect is influenced by sex. We hypothesize that higher VAT volume is linked to accelerated HCV reduction, CT, cSVD markers, and cognitive decline, with these effects depending on sex, age and potentially females' E2 levels. We will use data from approximately 900 participants, aged 40-85 years, from the LIFE-Adult Baseline and Follow-Up study. Linear and linear mixed regression models will serve to investigate cross-sectional and longitudinal effects of VAT, age and sex, and their interactions on brain aging. With our findings, we strive to provide insights into how VAT influences brain health and cognition - potentially shedding light on the underlying causes of brain aging disparities between sexes.

Poster 111

Unveiling General Practitioners' Perspectives on Dementia Prevention – Analysis of AgeWell.de

J. Kappe[1], F. Wittmann[1], M. Luppa[1], B. Wiese[2], W. Hoffmann[3,4], T. Frese[5], J. Gensichen[6], H.-H. König[7], J. R. Thyrian[3,4,8], H. Kaduszkiewicz[9], S. Riedel-Heller[1]

[1]Institute of Social Medicine, Occupational Health and Public Health (ISAP), Leipzig University, Faculty of Medicine, Leipzig, Germany, [2]Institute for General Practice, Work Group Medical Statistics and IT Infrastructure, Hannover Medical School, Hanover, Germany, [3]Institute for Community Medicine, University Medicine Greifswald (UMG), Germany, [4]German Centre for Neurodegenerative Diseases (DZNE), Greifswald, Germany, [5]Institute of General Practice and Family Medicine, Martin-Luther-University Halle-Wittenberg, Germany, [6]Institute of General Practice and Family Medicine, University Hospital of LMU Munich, Germany, [7]Department of Health Economics and Health Service Research, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany, [8]Faculty V: School of Life Sciences, University of Siegen, Germany, [9]Institute of General Practice, University of Kiel, Germany

Background:

With dementia's growing prevalence, the priority is on a proactive management of modifiable dementia risk factors, particularly in primary care, for minimizing the risk. Therefore, this study examines (1) General practitioners'(GPs') views on lifestyle changes for cognitive preservation, (2) GPs' beliefs about modifiable health and lifestyle factors, and (3) if these differ by GP age. Methods:

As part of the AgeWell.de trial, 72 GPs (M = 53.2 years, 52.2% female) completed a process evaluation questionnaire assessing their perceptions of lifestyle changes for maintaining cognitive performance in the elderly. GPs rated the overall promise of lifestyle interventions and the effectiveness of specific modifiable risk factors on a 5-point Likert scale. Descriptive statistics, Spearman's correlations and ordinal logistic regressions were used. Results:

GPs rated the efficacy of lifestyle changes to preserve cognitive performance neutrally (Mdn = 3, IQR = 2). Physical and social activity received the highest ratings with the narrowest range (Mdn = 5, IQR = 1). GP age was not significantly associated with beliefs about most factors, except for a moderate positive correlation with nutritional optimization (ρ = .255, p = .041), suggesting that older GPs were more likely to rate the efficacy of this factor high. Conclusions:

This study reveals a nuanced perspective among GPs regarding dementia prevention strategies. While recognizing the potential of changing individual risk factors, GPs appear neutral about an overall lifestyle change for cognitive preservation.

Poster 112

Wirksamkeitsprüfung einer multidisziplinären Online-Intervention für symptomatische Frauen mit X-chromosomaler Adrenoleukodystrophie: Eine randomisiert-kontrollierte klinische Studie

L. Schäfer, A. Unterlauft, B. Froebrich-Andreß, C. Wollny, M. Rößler, R. Fischer, C. Bähr, J. Lier, D. Wasmus, C.-C. Bergner, W. Köhler

Universitätsklinikum Leipzig, Leukodystrophie-Ambulanz, Klinik und Poliklinik für Neurologie, Leipzig, Germany

Hintergrund:

Die X-chromosomale Adrenoleukodystrophie (X-ALD) führt durch Demyelinisierung des zentralen und peripheren Nervensystems bei 60-80% der betroffenen Frauen zu progredienten Gleichgewichts-, Gang-, Sensibilitäts- und Blasenfunktionsstörungen. Ziel der Studie war es, die Wirksamkeit einer krankheitsspezifischen, multidisziplinären Online-Intervention auf die Lebensqualität von symptomatischen Frauen mit X-ALD zu prüfen.

Methode:

Symptomatische Frauen wurden in eine Experimentalgruppe (EG, *n*=34) und eine Wartelisten-Kontrollgruppe (WL-KG, *n*=34) randomisiert. Die EG erhielt eine 12-monatige Online-Intervention (SMART-ALD), die neurologische, soziale, psychologische und Ernährungsberatung sowie individuelles Fitnesstraining umfasste. Die WL-KG erhielt SMART-ALD für 6 Monate nach einer 6-monatigen Wartezeit. Alle Interventionen fanden online statt und wurden auf die spezifischen Bedürfnisse der Teilnehmenden angepasst. Lebensqualität wurde zu Beginn (T0), nach 6 (T1) und nach 12 Monaten (T2) mittels Fragebögen bewertet. Fitnesstracker und klinische Scores erfassten objektive Veränderungen. Gruppen-, Zeit- und Interaktionseffekte wurden mittels ANOVAs mit Messwiederholungen getestet.

Ergebnisse:

Die EG vs. WL-KG berichtete eine deutlich verbesserte Lebensqualität zu T1, jedoch erreichten nur mittlere bis große Effekte (η^2=.07-.14) statistische Signifikanz.

Schlussfolgerung:

Eine leicht zugängliche, multidisziplinäre, krankheitsspezifische Lebensstil-Intervention hat das Potenzial, die Lebensqualität symptomatischer Frauen mit X-ALD bereits nach 6 Monaten zu verbessern.

Poster 113

Addressing Cultural Competence in Hospital Nutrition for Foreign mothers: A case of University of Leipzig Medical Center

I. Y. Barnes[1], S. Owusuah[2]

[1]Private/Consultant, Leipzig, Germany, [2]Leipzig University, Small Enterprise Promotion and Training Programme (SEPT), Leipzig, Germany

Parturition is an intensive exercise and a daunting task; demanding physical, psychological, emotional and social care prior to during and after delivery. One critical component under the physical needs is proper nutrition and supply of dietary needs. Proper nutrition is a source of energy needs for labour and assist in postpartum recovery and support breastfeeding. In this vein, cultural competent care, remains a cornerstone to achieve an inclusive, effective and equitable healthcare system. Regardless, many healthcare facilities dietary needs of foreign or culturally diverse patients are often overlooked contributing to dissatisfaction and potential health risks.

This paper explores the lived experiences of culturally diverse population, particularly from West Africa during postpartum care at University of Leipzig Medical Center. Both online survey and face-to-face interview were conducted. The paper used the snow ball sampling to identify the groups to interview and purposeful sampling to select individuals whose experience. The interviewee respondents were as follows: Ghana: 60%, Nigeria: 30%, Other West African countries: 10%. Out these respondents 30% of the interviewees had local family support while 70% did not. 65% and 35% of respondent underwent cesarean and vaginal delivery respectively. About 80% of respondents rated the staff's cultural understanding as poor or very poor, showing a need for cultural competence training to improve patient satisfaction.

The paper recommends cultural approporiate nutrition in healthcare setting as a means to acheive inclusive health care.

Poster 114

Changes and predictors of social support in adolescent and young adult (AYA) cancer survivors – Results of a 7-year longitudinal study

S. Merz[1], M. Friedrich[1], H. Brock[1], K. Leuteritz[1], K. Geue[2], D. Richter[1], A. Mehnert-Theuerkauf[1], A. Sender[1]

[1]University of Leipzig Medical Center, Comprehensive Cancer Center Central Germany (CCCG), Department of Medical Psychology and Medical Sociology, Leipzig, Germany, [2]Medical Faculty, Otto von Guericke University Magdeburg, Department of Psychosomatic Medicine and Psychotherapy, Magdeburg, Germany

Objective:

Given that social support has been shown to positively influence coping with cancer, our study aims to address the research gap regarding perceived social support among adolescent and young adult (AYA) cancer survivors.

Methods: AYAs assessed their perceived positive social support (PS) and detrimental interactions (DI) by completing the Illness-Specific Social Support Scale (ISSS-8) after finishing acute treatment (t1), one year (t2) and seven years (t6) later. Mean values and changes in social support over time were determined. Sociodemographic, psychological, and medical factors were investigated as predictors for PS and DI using mixed effects models.

Results:

Data from 319 cancer survivors were examined (74.9% women). At baseline, the average score for perceived positive social support (PS) was 13.73 (SD=2.52), while the score for detrimental interactions (DI) was 3.92 (SD=2.85). DI remained consistent, whereas perceived PS changed over time, although the effect was low. Males, AYAs who were single, and those experiencing clinically significant anxiety or depression reported lower levels of PS. Greater efforts to cope with the illness, along with elevated anxiety and depression levels, were associated with higher perceived DI.

Conclusions:

Regular assessments of existing social networks and perceived social support are essential for AYA cancer survivors. Additionally, addressing the mental health of AYAs should be a standard part of survivor consultations, as higher levels of depression and anxiety were associated with lower perceived PS and increased DI.[1]

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Poster 115

Differences between fathers and mothers in the assessment of their child's behavioral strengths and difficulties and physical complaints

M. Lorenz[1], M. Vogel[1,2], W. Kiess[1,2], S. Ibe[1], T. Poulain[1,2]

[1]Leipzig University, LIFE Child, Leipzig Research Center for Civilization Diseases, Leipzig, Germany, [2]Leipzig University, Department of Women and Child Health, University Hospital for Children and Adolescents and Center for Pediatric Research, Leipzig, Germany

Background:

Our study aimed to assess parental (dis)agreement on children's behavioral difficulties and physical complaints.

Methods:

We compared the answers of fathers and mothers to the Behavioral Strengths and Difficulties Questionnaire and the Giessen Complaints List for 493 respective 351 participants of the LIFE Child Study (1-18 years old).

Levels of agreement were evaluated, and the influence of a child's sex, age, and family SES on mother-father agreement was estimated.

Results:

Parental agreement was moderate to substantial regarding children's behavioral difficulties and physical complaints, but only slight to fair on prosocial behavior, depressive mood, irritability, nervousness, and dizziness.

Mothers reported higher levels of internalizing problems, stomachache, and better prosocial behavior in their children, while fathers reported higher levels of externalizing difficulties and physical complaints. Mother-father-agreement was higher for girls than for boys, except for back pain. Agreement on behavioral difficulties was likelier for children younger than 6 years old. For physical complaints, in contrast, agreement tended to be higher for older children. A higher SES was associated with a higher agreement on peer problems. Overall, agreement was significantly lower in children with high levels of difficulties or complaints.

Conclusion:

Parents' reports should not be considered interchangeable, as the parents' perspectives on their child's abilities and problems may differ. Moreover, levels of agreement may be affected by sex and age of the child, and/or SES of the family.

Poster 116 Ecstasis and Stigma – Images of Addiction

L.-J. Peter, C. Helmert, J. Kummetat, R. Büchner, S. Göbel, T. Fleischer, L. Christochowitz, S. Speerforck, G. Schomerus

Leipzig University, Faculty of Medicine, Leipzig, Germany

As we conduct research into the stigmatization of people with mental illness — working at the intersection of healthcare and the public — science communication is an important concern. This inspired us to create the film and discussion series "Rausch und Stigma – Bilder von Sucht" (English: "Ecstasy and Stigma – Images of Addiction"). For over two years, we have invited people to share their insights as experienced experts, their work within related associations, and their artistic perspectives, all aimed at sparking conversations around stigma research.

In this poster presentation, we share our experiences and outline our approach to using this film and discussion series as a tool to recognize and address barriers to seek help for people with mental illness.

Poster 117

Effect of Sex Differences on Brain Perfusion and Mild Cognitive Impairment in Patients with Vascular Risk

E. May[1,2,3,4], V. Witte[3,4], K. Schönrath[5], M. Endres[6], J. Weber[5,6], K. Villringer[6], A. Khalil[6], J. Sacher[1,2,3,4,7]

[1]Max Planck School of Cognition, Leipzig, Germany, [2]Centre for Integrative Women's Health and Gender Medicine, Faculty of Medicine & University of Leipzig Medical Center, Germany, [3]University of Leipzig Medical Center, Cognitive Neurology, Germany, [4]Max Planck Institute for Human Cognitive and Brain Sciences, Neurology, Leipzig, Germany, [5]Berlin Institute of Health (BIH) at Charité - Universitätsmedizin Berlin, Germany, [6]Center for Stroke Research Berlin, Charité - Universitätsmedizin Berlin, Germany, [7]University of Leipzig Medical Center, Department of Endocrinology, Nephrology, Rheumatology, Division of Endocrinology, Leipzig, Germany

While women with diabetes face an increased risk of vascular disease, they also encounter challenges related to underdiagnosis and undertreatment for cardiovascular disease, which significantly impact brain morphology and function. One biomarker linking change in vasculature and cognitive decline is brain perfusion. Although premenopausal females exhibit protective, higher perfusion than males, this declines after menopause. To understand how different cerebrovascular risk factors affect the brain and thus cognitive outcomes critically mediated by sex, we analyze brain perfusion using resting-state functional MRI derived BOLD delay in acute cardiovascular disease (n=138, $\bar{x}_{age}$= 63.1 yrs) and chronic diabetes (n=111, $\bar{x}_{age}$= 65.0 yrs) patients in the Berlin Long-term Observation of Vascular Events (BeLOVE) study, a complementary patient study to LIFE-Adult. We analyze the effect of sex and disease severity on region-of-interest (ROI)-based and whole-brain perfusion. We identify association between ROI-based BOLD delay and the Montreal Cognitive Assessment (MoCA) score, a measure of cognitive impairment. By establishing these connections and integrating a targetable brain biomarker into our predictive model, we aim to contribute valuable insights underlying sex differences in the cardiovascular-brain axis, with the ultimate goal of advancing personalized therapy and prevention of cognitive decline. Further, based on the widespread comparability of the perfusion measure, we seek to expand and compare our results across large dataset cohorts including LIFE and UKBiobank.

Poster 118

LOGOS: Meaning-Centered Psychotherapy in a hybrid design for adult cancer survivors in aftercare

A. Sender, L. Schiebeck, A. Lehmann-Laue, A. Mehnert-Theuerkauf

University of Leipzig Medical Center, Comprehensive Cancer Center Central Germany (CCCG), Department of Medical Psychology and Medical Sociology, Leipzig, Germany

Objectives:

Existential distress in coping with cancer still remains a major issue even after the end of treatment, along with physical short- and long-term effects. Meaning-Centered psychotherapy (MCP), initially shown high clinical efficacy in dealing with these issues, could support patients in improving their quality of life and coping with the disease after the acute illness. The aim of this pilot study is to adapt MCP for cancer survivors with a curative prognosis.

Methods:

Adult cancer survivors participate in 8 manualised MCP sessions over 16 weeks in face-to-face or online group or individual sessions. Feasibility, satisfaction and initial trends are assessed by standardized validated questionnaires and qualitative interviews (LAP-R; PTGI, GAD-7, PHQ9, EORTC QLQ-C30) at 3 time points.

Results:

To date, 42 survivors have been enrolled in the ongoing study, 13 of them have already completed the intervention. Qualitative and quantitative results regarding primary and secondary outcomes will be presented. Furthermore, adaptation processes for survivors in aftercare and empirical results on the implementation of the hybrid design will be discussed.

Conclusion and clinical implications:

MCP as a psycho-oncological tool in aftercare can improve quality of life, sense of meaning, and reduce anxiety and depressive symptoms of cancer survivors. With the completion of LOGOS, a proven brief, structured and manualised group and individual MCP programme will be available. The hybrid approach facilitates access to a larger group of cancer survivors.

Poster 119

Prevalence of Anxiety Symptoms across Different Employment Status Groups and Associated Factors - Results from the LIFE-Adult-Study

C. Görres[1], A. Pabst[1], A. E. Zülke[1], H. Glaesmer[2], A. Hinz[2], C. Engel[3,4], T. Kirsten[3,4,5], N. Reyes[3], M. Löffler[3,4], S. G. Riedel-Heller[1], M. Löbner[1]

[1] Leipzig University, Faculty of Medicine, Institute of Social Medicine, Occupational Health and Public Health (ISAP), Leipzig, Germany, [2]Faculty of Medicine, Leipzig University, Department of Medical Psychology and Medical Sociology, Leipzig, Germany, [3]Leipzig University, Institute of Medical Informatics, Statistics and Epidemiology, Leipzig, Germany, [4]Leipzig University, LIFE - Leipzig Research Centre for Civilization Diseases, Leipzig, Germany, [5]University of Leipzig Medical Center, Department for Medical Data Science, Leipzig, Germany

Background:

Previous research has shown an association between unemployment and poor mental health. However, the relationship between different forms of unemployment (in Germany “Arbeitslosengeld I”(ALG I) and “Arbeitslosengeld II” (ALG II)) and anxiety in Germany has not been investigated yet.

Methods:

The sample consisted of 4,885 participants aged 18 to 65 years from the baseline survey of the LIFE-Adult-Study. The objective was to examine sex-specific prevalence rates for existing anxiety symptoms across the employment status groups (full-time, part-time, ALG I, ALG II). Furthermore, negative binomial regressions were conducted to examine the potential correlation between anxiety, employment status, socio-demographic variables, depression, and social resources.

Results:

The group of unemployed individuals receiving ALG II exhibited a markedly elevated prevalence (17.6%) compared to all other groups ($p < .001$). As indicated by the initial regression model, there is a significant association between anxiety symptoms and the receipt of ALG II ($p < .001$) and part-time work ($p = .006$). Upon the introduction of additional variables into the analysis, the previously observed effect lost its significance. The results indicated a higher risk of anxiety symptoms among the female sex ($p < .001$) and higher values in relation to depressive symptoms ($p < .001$).

Conclusions:

Future psychosocial support services should consider the diverse unemployed population‘s risk of anxiety symptoms.

Poster 120

Prevalence of posttraumatic stress symptoms among physicians – a meta-analysis

J. Reinhardt, K. Linde, A. Kersting

Universität Leipzig, Department für Psychische Gesundheit, Klinik und Poliklinik für Psychosomatische Medizin und Psychotherapie, Leipzig, Germany

Background:

The medical profession is associated with high demands that have an impact on mental health. Stress factors include confrontation with serious illness and death, long working hours and pressure at work. These factors increase the risk of traumatization and the occurrence of PTSD. Our study aims to synthesize the results of previous studies on the prevalence of posttraumatic stress symptoms among doctors.

Methods:

Four Databases were systematically searched for peer-reviewed articles describing PTSD prevalence among physicians. Two independent raters assessed the included articles. Information on methodology, measurement instruments, region, specialty, time of survey (pre-/"post"- Covid) was extracted. A quantitative synthesis of the frequency measures and an analysis of the influence of potential moderators (e.g. pre/"post" Covid, specialty, and region) on the prevalence rate were carried out.

Results: The random-effects model was used for the analysis. The weighted mean prevalence of all studies (n=60) studies was 14.5% (95% CI 0.125 - 0.168). Studies in high-income countries estimated the occurrence of PTSD significantly lower than studies in middle-income countries. Further moderators were investigated.

Conclusion:

The results provide evidence that post-traumatic stress symptoms are higher among physicians compared to the general population, with an average prevalence of 14.5%. Creating appropriate working conditions in hospitals is important to protect the well-being of healthcare workers and minimize negative consequences of mental illnesses such as PTSD.

Poster 121

Prevalence of suicidal ideation and suicide attempts among survivors of intimate partner violence: a meta-analysis

J. Deller[1], J. Treml[2], A. Kersting[2]

[1]Universität Leipzig, Medizinische Fakultät, Klinik und Poliklinik für Psychosomatische Medizin und Psychotherapie, Leipzig, Germany, [2]Universitätsklinikum Leipzig, Klinik und Poliklinik für Psychosomatische Medizin und Psychotherapie, Leipzig, Germany

Introduction:

Intimate Partner Violence (IPV) has been widely acknowledged as a global health risk and violation of human rights. Some studies suggest an increased prevalence of suicidal ideation and suicide attempts among those affected by IPV. We set out to provide prevalence estimates in IPV-survivors of different genders and across diverse sampling frames, thereby significantly expanding the scope of previous syntheses.

Methods:

Four databases were systematically searched for relevant articles. Identified articles were screened and rated by two independent raters using predefined inclusion and exclusion criteria. The methodological quality of the studies was assessed and relevant study characteristics were coded. Multilevel meta-analyses were performed to synthesise proportions. In addition, the influence of possible moderators (e.g. gender, form of violence experienced) was analysed using meta-regressions.

Results:

Of 6582 abstracts identified in our first search in 2023, 80 studies were included. A weighted mean prevalence of 18.7% (95% CI: 13.0 - 25.3%, k = 30) was found for suicide attempts among those affected by IPV. The weighted mean prevalence of suicidal ideation among those affected by IPV was 29.8% (95% CI: 24.1 - 35.8%, k = 50). We updated our systematic searches in 2024, further studies are currently being included. Our updated results and moderator analyses will be presented.

Discussion:

Our results indicate suicidal outcomes are widely spread among survivors of IPV and emphasise the clinical relevance of assessing suicidality in this population.

Poster 122

Qualitative analysis of German general practitioners' attitudes towards eHealth applications for dementia risk reduction: implications for development and implementation

A. Schultz, M. Luppa, M. Bleckwenn, S. Riedel-Heller, A. Zülke

Universität Leipzig, Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP), Leipzig, Germany

eHealth interventions are a promising approach for dementia prevention by facilitating lifestyle change. This study explores the perspective of general practitioners (GPs) on using eHealth applications to support dementia prevention. We aim to understand potentials and barriers GPs perceive in primary care settings.

We conducted semi-structured expert interviews with n=9 GPs working in an outpatient setting in and near Leipzig, Germany. Data was fully transcribed and analyzed using qualitative content analysis according to Mayring.

GPs expressed favorable but balanced views towards eHealth for dementia prevention and emphasized specific conditions for successful implementation. eHealth applications need to be user-friendly, free and provide individualized information without overwhelming patients. GPs only address dementia once abnormalities are present and are concerned about inducing health anxiety in patients. Patient's wishes focus on diagnostics and care rather than preventive measures. GPs see a significant lack in patient knowledge on dementia and its risk factors.

GPs need to address dementia more routinely, assess risk factors, and aid patients in a preventive role. While GPs recognize that eHealth could help patient education and support self-management, GPs were concerned over limited patient interest or addressing patients already motivated for lifestyle changes. Effective implementation needs eHealth applications for dementia to complement routine care, provide evidence for usefulness, address patient concerns and target patients with high risk of dementia.

Diseases of Civilisation | Obesity

Immunology | Infectiology | Inflammation

Clinical and Molecular Oncology

Clinical Research

Digital Health

Life Science Research

Psychology, Cognition and Public Health I

Psychology, Cognition and Public Health II

Molecular and Systemic Neurobiology

Biotechnology | Protein Biochemistry | Pharmaceutical Chemistry

Biomaterials | Translational Regenerative Medicine | Drug Delivery

Molecular Biology | Biomedicine

Poster 123 Social functioning in individuals with Alzheimer's disease and the situation of caregivers

S. Kraake[1], M. Luppa[1], D. Saur[2], J. Dietzel[3], J.-P. Bach[4,5], S. G. Riedel-Heller[1], J. Stein[1]

[1]Leipzig University, Faculty of Medicine, Institute of Social Medicine, Occupational Health und Public Health, Leipzig, Germany, [2]Leipzig University, Faculty of Medicine, Department of Neurology, Neuroimaging Laboratory, Leipzig, Germany, [3]University of Leipzig Medical Center University, Department of Psychiatry and Psychotherapy, Leipzig, Germany, [4]Medical Practice for Neurology, Psychiatry, and Family Counseling, Gernsheim, Germany, [5]University Hospital of Gießen and Marburg (UKGM), Marburg site, Department of Neurology, Marburg, Germany

Introduction:

Currently, research on social functioning in Alzheimer's disease (AD) across the entire spectrum of the disease is lacking. Accordingly, this study aimed to describe the social functioning of individuals with AD at different stages of the disease and to explore how impaired social functioning affects caregiver burden.

Methods:

Cross-sectional data was collected from memory clinics across Germany as part of the pilot study "Social functioning in individuals with Alzheimer's disease and the situation of caregivers". In this study, a total of N = 87 relatives providing care for individuals with mild (n = 20), moderate (n = 40), and severe (n = 23) AD were included. The caregiver-rated German version of the Social Functioning in Dementia Scale (SF-DEM) was employed to measure social functioning of individuals with AD; caregiver burden was assessed via the Zarit Caregiver Burden Interview (ZBI-12). A linear regression analysis was conducted to examine the association between social functioning and caregiver burden.

Results:

The main study results indicated that social functioning significantly differs across the spectrum of AD severity. Furthermore, higher levels of social functioning but not AD severity were associated with less caregiver burden.

Conclusions:

The findings highlight the importance to incorporate social functioning assessments into clinical practice to enhance early detection, diagnosis and interventions for AD. Early interventions to enhance social functioning may diminish caregiver burden.

Poster 124

The Stigma Of Psychiatric Disorders In German Newspaper Articles: Using Word Embeddings To Capture Disease Representation Over 23 Years

J. Steglich

Arbeitsgruppe Psychiatrische Epidemiologie, Klinik und Poliklinik für Psychiatrie und Psychotherapie, Leipzig, Germany

Research on the stigma of mental illness mirrors persistent negative conceptions of these diseases by the public [1], [3]. So far, survey studies on stigma toward people with mental illness have often focused on individual reports. To think further, I examine news coverage of psychiatric diseases as a way to measure stigmatizing meanings that circulate and influence the opinions found in surveys [4]. I employ ALC Embeddings [2] on a corpus of 1.6 million German-speaking news snippets covering 23 years. As an indicator for stigmatization, a metric calculated on the embeddings measures how people with different psychiatric diseases are reported about in terms of negative character traits. Results show that psychotic disorders relate to the most stigmatizing news coverage over time, which means journalists often refer to them in the context of negative personality traits. Pairwise comparisons for estimated marginal means further indicate that articles mentioning psychotic disorders are more stigmatizing than those about mood disorders. Moreover, in the past 23 years, the stigma score for psychotic disorders has shown an increase, while the stigma of mood disorders remains approximately stable. The results resemble those of survey research and research using the same method on a dataset of US news articles [4]. Thus, it seems plausible that individual attitudes toward mental illness are influenced by cultural meanings present in news articles.

Diseases of Civilisation | Obesity

Immunology | Infectiology | Inflammation

Clinical and Molecular Oncology

Clinical Research

Digital Health

Life Science Research

Psychology, Cognition and Public Health I

Psychology, Cognition and Public Health II

Molecular and Systemic Neurobiology

Biotechnology | Protein Biochemistry | Pharmaceutical Chemistry

Biomaterials | Translational Regenerative Medicine | Drug Delivery

Molecular Biology | Biomedicine

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Poster 125 The protective effect of meaning in life on mental comorbidities in cancer patients (LUPE-Study)

L. Schiebeck[1], A. Sender[1], U. Goerling[2], T. Zimmermann[3], J. Ernst[1], A. Mehnert-Theuerkauf[1]

[1]University of Leipzig Medical Center; Comprehensive Cancer Center Central Germany (CCCG), Department of Medical Psychology and Medical Sociology, Leipzig, Germany,
[2]Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin Institute of Health, Charité Comprehensive Cancer Cente, Berlin, Germany,
[3]Hannover Medical School, Department of Psychosomatic Medicine and Psychotherapy, Hanover, Germany

Background:

Cancer remains one of the most prevalent causes of death worldwide. Through the diagnosis an unexpected reminder of one´s mortality surfaces. Various existential fears characterize life afterwards, among them the struggle to find meaning in life. Aim of this study is to investigate whether meaning in life can serve as a protective factor for mental comorbidities in cancer patients.

Methods:

Data was collected in a prospective multi-center observational cohort study. Meaning in life was assessed via the LAP-R. Mental comorbidities were rated using the SCID-5-CV. To test the present hypothesis, a multinomial logistic regression will be computed using meaning in life within 2 months after the diagnosis as predictor for mental disorder diagnoses 18 months later. Additional regression analysis will test for moderating factors.

Impact on practice

The identification of such a protective factor could deepen our understanding of mental processes following the incisive diagnosis of cancer but could also provide an outlook on future effective psycho-oncological care with meaning-centered psychotherapy at hand. Moderation analysis can help to individualize therapy offers.

Discussion:

The present study design covers the cancer population broadly, including various cancer entities and stages. The structured clinical interview enables to detect cancer-related psychological strain. Nevertheless, since recruitment starts at diagnosis, this study cannot establish a true baseline measurement of meaning in life before diagnosis, suggesting a need for future research.

Poster 127

What self-help online programs are available that reduce depressive symptoms for people who are overweight or obese? A systematic review

K. Schladitz, A. Seibel, S. G. Riedel-Heller, M. Löbner

Institut für Sozialmedizin, Arbeitsmedizin und Public Health (ISAP), Medizinische Fakultät, Leipzig, Germany

Introduction:

About one-fifth of the German adult population is affected by obesity, with increasing trend. Given the elevated risk of comorbid depressive symptoms, there is a need for low-threshold interventions to improve mental health in individuals with obesity. Internet- and mobile-based interventions (IMI) hold high potential as flexible, low-threshold and scalable add-on options in healthcare.

Objective:

This systematic review examines the current availability of IMI to improve mental health in people who are overweight or obese.

Methods:

A systematic literature search was conducted to identify randomized controlled trials (RCTs) examining IMI for adults with overweight or obesity and comorbid depressive symptoms that aim to improve mental health. Study quality was assessed using the RoB 2 tool.

Results:

From *N*=790 search results, *n*=3 RCTs evaluating two English-language interventions met all inclusion criteria. One intervention was a therapist-supported program for adults with obesity. The other intervention was an unguided self-management program for male adults with overweight/obesity. Both interventions aimed to reduce both weight and depressive symptoms. All three RCTs showed significantly greater reductions in depressive symptom severity compared to the control group.

Conclusion:

This systematic review provides initial evidence that IMI for people with overweight or obesity and comorbid depressive symptoms are effective in improving mental health. The study highlights the need for more high-quality study designs (RCTs) and for interventions in German language.

Poster 128 3D mapping of parvalbumin interneuron-derived cortico-striatal axonal projections

H. Hosseinnia[1], M. Lehning[1], A. O. Sasmita[2], C. Menschel[1], P. Spisse[1], R. Fledrich[3], K. Lippmann[4], M. Morawski[1], R. Stassart[1], M. Schwab[1]

[1]Paul Flechsig Institute for Neuropathology, Faculty of Medicine, Leipzig, Germany, [2]Max Planck Institute for Multidisciplinary Sciences, Göttingen, Germany, [3]Institute for Anatomy, Faculty of Medicine, Leipzig, Germany, [4]Carl-Ludwig Institute for Physiology, Faculty of Medicine, Leipzig, Germany

Fast-spiking parvalbumin-expressing interneurons (PV-IN) provide robust GABAergic inhibition in cortical networks,crucial for synchronized network activity tightly linked to learning and memory. PV-IN follow a protracted trajectory during brain development, including complex axonal outgrowth, and (partial) axonal myelination. Combined with a high energy demand due to their fast-spiking behavior, these features render PV-IN vulnerable to various cell-autonomous and external insults during neurological disease conditions. While the local axonal arborization and integration of PV-IN into cortical microcircuits is well documented, there is an emerging appreciation of a subpopulation of cortical PV-IN with long-range axonal projections to subcortical regions, including the striatum. However, a comprehensive map of PV-IN-derived cortico-striatal projections is not available.

This research aims to bridge this gap in the current state of knowledge by a detailed mapping of PV-IN-derived cortico-striatal axonal projections, their local arborization, and associated myelin in the striatum which would serve as a framework for studies into regulatory mechanisms of axonal connectivity in the cortico-striatal pathway using mouse mutants lacking the EGF-like signaling factor Neuregulin (NRG)-1.

Taken together, a more detailed insight into the cortico-striatal connectome and NRG1-mediated signaling functions into the development of PV-IN-derived axonal projections will be instrumental for better understanding of GABAergic network functions in the striatum during normal and disease conditions.

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, memory, music, and communication.

Our studies focus on the key coding principles of the brain enabling human thinking and 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 such as magnetic resonance imaging 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:

- Neuropsychology (Angela D. Friederici)
- Neurology (Arno Villringer)
- Neurophysics (Nikolaus Weiskopf)
- Psychology (Christian Doeller)

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 MPI 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 cutting-edge interdisciplinary behavioural and neurobiological research into human cognition.

Contact

Max Planck Institute
for Human Cognitive and Brain Sciences
Stephanstraße 1A | D-04103 Leipzig
Phone: +49 341 9940-00
www.cbs.mpg.de | info@cbs.mpg.de

Poster 129

A zinc transporter mediates encephalitogenic T cell function

D. Drmic, L. Wang, L. Noyer, S. Feske

New York University Grossman School of Medicine, Department of Pathology, New York, United States of America

Multiple sclerosis (MS) is a debilitating autoimmune disease marked by focal central nervous system (CNS) lesions associated with demyelination of nerve fibers and axonal damage, in which pathogenic Th17 (pTh17) cells play a pivotal role. While extensive efforts have been made to decipher MS pathophysiology, curative therapies for MS remain elusive. To uncover new regulators of pTh17 cell function in MS, we employed a forward genetic screen using the experimental autoimmune encephalomyelitis (EAE) model. This screen identified a member of the Zrt-/Irt-like protein (ZIP) family as potential regulator of EAE onset and severity. Mice injected with T cells in which the ZIP transporter was deleted showed significantly delayed disease onset and reduced severity, along with decreased leukocyte infiltration into the CNS. In vitro, knockdown of ZIP expression did not alter cytokine expression or proliferation of T cells but led to increased early apoptotic signatures, suggesting that ZIP may be involved in the regulation of cell viability. Because ZIP proteins regulate zinc levels of cells, we used genetically encoded zinc indicators and live-cell imaging to determine the effects of ZIP deletion on cellular Zn2+ concentrations. We observed reduced labile Zn2+ concentrations in the cytosol of ZIP-deficient cells, potentially altering intracellular signaling. Collectively, our findings identify a member of the ZIP protein family as a novel regulator of T cell function and EAE.

Poster 130

Assessing different mouse models for CSF1R related Leukoencephalopathy

A. Moein Alsadat, C. Bergner

University of Leipzig Medical Center, Neurology, Leipzig, Germany

The CSF1 receptor (CSF1R) is a transmembrane tyrosine kinase protein, which is involved in signaling pathways of survival, expansion, and cell division in myeloid cells. Heterozygous loss-of-function in the receptor are associated with a severe neurodegenerative disease, CSF1R-associated leukoencephalopathy (ALSP). Histopathologically, the disease includes pronounced tissue damage in the white matter, with outstanding severe axonal spheroids and significant loss of homeostatic microglia cells. Full CSF1R knockout exhibit a severe phenotype in mice with incomplete brain development and these mice rarely survive to adulthood. Heterozygous mice with deletion of the CSF1R gene show microgliosis and axonal pathology at an older age, which better mimics the pathology of ALSP characterized by a long asymptomatic phase and sudden onset of motor and/or cognitive impairment. However, unlike in human pathology, a reduction in microglia is never observed in these mice.

In this study, through utilizing the CX3CR1 promoter to highly target Microglia cells, we try to investigate, whether the severe phenotype of CSF1R full-knockout mice is caused by loss of myeloid cells only, or due to the deletion of CSF1R from neuronal or other cells. In addition, we investigate differences in the phenotype of mice of with heterozygous deletion in CSF1R at different time points in adulthood and during the early embryonic stages.

Taken together, a valid mouse model could give us a more detailed insight into the role of homeostatic Microglia cells and their function in the ALSP pathology.

Poster 131

Caliber-specific myelin composition secures the long-term integrity of small axons

N. Fleischer[1], T. Kungl[1], R. M. Stassart[1], R. Fledrich[2]

[1]Paul-Flechsig-Institut – Zentrum für Neuropathologie und Hirnforschung, Leipzig, Germany,
[2]Institut für Anatomie, Leipzig, Germany

The peripheral nervous system (PNS) enables movement and sensation through distinct motor and sensory fibers of varying axonal size and myelination status. For unknown reasons, peripheral neuropathies often affect only a subset of fiber types, indicating specific intrinsic vulnerabilities. By combining single-cell RNA sequencing with imaging approaches and myelin proteomics, we delineate a thus far unresolved diversity of PNS fibers. In detail, we discovered that individual Schwann cell transcriptomes do not seem to correlate strongly with motor or sensory nerve modalities, but instead depend strongly on cell size – a finding that is easily lost when analyzing whole nerves in bulk. We identified marker genes and myelin proteins, including 2'3'-cyclic nucleotide-3'-phosphodiesterase (CNP), that specifically define small myelinated fibers and demonstrate, in principle, that myelin composition is functionally relevant. Indeed, CNP is specifically required for the maintenance and integrity of small myelinated fibers, which convey tactile and pain sensations.

Our study sheds new light on the diversity of Schwann cells and underlines that myelin composition is intricately linked to specific Schwann cell types. These findings have important implications for the ongoing research into peripheral nerve disorders that are characterized by distinct symptomatology.

Poster 132 Criteria for identification and accurate quantification of spinal motor neurons in healthy and disease mouse models

L. Sowoidnich[1], A. L. Norman[1], F. Gerstner[1], J. K. Siemund[1], J. M. Buettner[1], J. G. Pagiazitis[2,3], K. Pilz[1], K. S. Apel[1], G. Z. Mentis[2,3], C. M. Simon[1]

[1]Leipzig University, Carl-Ludwig-Institute for Physiology, Leipzig, Germany, [2]Columbia University, Center for Motor Neuron Biology and Disease, New York, United States of America, [3]Columbia University, Department of Pathology and Cell Biology and Neurology, New York, United States of America

Motor neuron (MN) death is the hallmark of the MN diseases spinal muscular atrophy (SMA) and amyotrophic lateral sclerosis (ALS). Quantification of MN loss in mouse models is an important readout for disease progression and therapeutic assessment.

Here, we performed a meta-analysis from 77 papers, that revealed a lack of dissection specificity, usage of unspecific neuron markers, and a wide distribution of reported MN loss within the same mouse models, underlining the need for a consistent pipeline for MN quantification. Therefore, we established several criteria to ensure consistent MN quantification. First, we describe a spinal cord dissection, allowing segment specific MN isolation and counting. Utilizing ex vivo ventral-root back fills and immunohistochemistry, we conclude ChAT as a reliable marker for MN identification. In combination with tissue clearing, we showed that distinct spinal segments contain different numbers of MNs. Second, we showed that MN loss is restricted to select spinal segments of SMA mice. In contrast, MN loss was evident throughout the entire spinal cord in an ALS mouse model. Finally, MNs marked with HB9 and ChAT within select spinal segments of SMA and control mice were counted by an automated open-source software, Cellpose, to provide an unbiased quantification of MNs.

Our procedural account demonstrates that a select set of criteria is required for the valid identification of MNs and their accurate quantification in mice. Furthermore, our results can be used as a reference for future studies requiring accurate MN counts.

Poster 133 Deletion of Thy-1 induces a distinct partially activated astrocyte phenotype

J. Loui[1], U. Krügel[2], J. Hirrlinger[3], A. Saalbach[1]

[1]Leipzig University, Department of Dermatology, Venerology and Allergology, Leipzig, Germany, [2]Leipzig University, Institute of Pharmacology and Toxicology, Leipzig, Germany, [3]Leipzig University, Carl-Ludwig-Institute for Physiology, Leipzig, Germany

Thy-1 (CD90) is a highly conserved GPI-anchored cell surface protein. In the brain, Thy-1 is expressed exclusively on the surface of mature neurons. Although the Thy-1 promoter is widely used as a neuron-specific promoter for transgenic expression, the exact role of the endogenous Thy-1 protein remains largely unknown. Thy-1 receptors, ITGB1, ITGB5 and Syndecan 4, are expressed on astrocytes (ASC) suggesting an interaction of both cell types. Since the interplay of neurons and ASC plays a series of indispensable roles in maintaining normal CNS health and function, we investigated the role of Thy-1 in neuron-ASC communication.

To investigate the impact of Thy-1 loss on ASC function, two knockout mouse models were used: a complete and a neuron-specific Thy1-KO mouse model. In both models, ASC exhibited increased expression of a distinct set of activation-associated genes, such as Gfap, Vim, and Tnc, suggesting heightened reactivity. These changes were more prominent in aged mice, indicating a delayed onset of the ASC phenotype. Further, functional assays demonstrate that Thy-1 significantly restricts ASC growth and inhibits proliferation, while apoptosis remained unaffected. Whole genome expression analysis showed that Thy-1 regulates the expression of neurotransmitter receptors and potassium channels, highlighting its role in synaptic clearance.

Taken together, our data demonstrate that Thy-1 controls the activation of ASC, resulting in a special ASC phenotype characterized by reduced expression of a subset of activation-associated genes and reduced proliferation.

Poster 134 Dynamics of myelination and synaptic connectivity of parvalbumin-positive interneurons

M. Lehning[1], H. Hosseinnia[1], A. Przemeck[1], R. Fledrich[2], K. Lippmann[3], R. Stassart[1], M. Schwab[1]

[1]Paul-Flechsig-Institute, Centre of Neuropathology and Brain Research, Leipzig University, Germany, [2]Institute of Anatomy, Leipzig University, Germany, [3]Carl-Ludwig-Institute for Physiology, Leipzig University, Germany

Parvalbumin-expressing GABAergic interneurons (PV-IN) provide strong inhibition to excitatory and inhibitory neurons and thereby represent a powerful modulator of cortical network functions. Due to their extensive energy demands PV-IN are highly susceptible to external insults. Hence, PV-IN functions are disturbed in several neurological and psychiatric diseases. In contrast to other IN classes, PV-IN display 'patchy' myelination but the exact role of myelination in PV-IN network integration is not well defined. This immunohistochemical study aims at a detailed examination of the dynamics of PV-IN myelination and synaptic connectivity from postnatal into adult stages in wildtype and murine models of hypomyelination and disturbed PV-IN function.

We found that while overall myelination and synaptic connectivity of PV-IN are established at postnatal day 25, individual myelin sheaths seem to undergo dynamic changes into adult stages. Concomitantly, somatic coverage by glutamatergic and GABAergic synapses moderately decreases with ongoing PV-IN development. When compared to a mouse model with genetically induced hypomyelination, we observed a modest increase in GABAergic connectivity. Remarkably, a mouse model of hypoactive PV-IN displayed an increase in PV-IN internodal length followed by a subtle reduction in GABAergic PV-IN coverage. These findings point towards a link between PV-IN function, myelination and synaptic connectivity. A better understanding of how PV-IN myelination and network integration interact is crucial to decipher the role of PV-INs in health and disease.

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Poster 135

Familial hemiplegic migraine and epilepsy associated mutations in voltage-gated calcium channels affect life span, motor function and nocifensive behaviour in a Drosophila melanogaster model

M. Noß[1], M. B. Körner[1], J. Classen[2], T. Langenhan[1], N. Scholz[1], S. Dannhäuser[3], A. Mrestani[1,2]

[1]Rudolf Schönheimer Institute of Biochemistry, Division of General Biochemistry, Faculty of Medicine, Leipzig University, Germany, [2]Department of Neurology, University of Leipzig Medical Center, Germany, [3]Institute of Physiology, Department of Neurophysiology, University of Würzburg, Germany

Over 20 missense mutations in the human gene *CACNA1A*, which encodes the pore-forming subunit of P/Q-type voltage-gated calcium channels, are associated with the rare autosomal-dominant familial hemiplegic migraine type 1 (FHM1). Strikingly, subsets of the FHM1 mutations are linked to distinct additional clinical manifestations, i.e., cerebellar degeneration and ataxia (R583Q, T666M) or epileptic seizures and brain edema (S218L), while others cause pure hemiplegic migraine (R192Q, R195K). By contrast, several *CACNA1A* mutations contribute to epileptic encephalopathies without FHM1 features (A713T). Explanations for the diversity of these phenotypes at individual synapses are still missing.

In this study, we investigated these mutations using scarless CRISPR/Cas9 edited *Drosophila melanogaster*. Lifespan analyses indicated specific deleterious effects in epilepsy-linked mutations, while a subset of the mutations negatively impacted motor function and coordination. Notably, the S218L mutation caused a significant increase in nocifensive behavior when exposed to mechanical stimuli. We plan to evaluate various pharmacological agents to mitigate the effects of the mutations. Further, the collection of mutations will be subjected to an in-depth structure-function analysis of the neuromuscular junction using a combination of super-resolution microscopy and two-electrode voltage clamp electrophysiology.

Our research aims to clarify the molecular pathophysiology underlying *CACNA1A*-related neurological disorders, potentially identifying new molecular targets for therapeutic intervention.

Poster 136 Hyperleptinemia as a driver of obesity-induced neuropathy

E. Ernst-Sánchez[1], V. K. Sundaram[2], V. Schütza[2], N. Schröter[1], N. Schwaragus[2], R. Stassart[2], R. Fledrich[1]

[1]Institut für Anatomie, Universität Leipzig, Germany, [2]Paul-Flechsig-Institut für Neuropathologie, Universitätsklinikum Leipzig, Germany

Peripheral neuropathies are chronic conditions significantly affecting the peripheral nervous system, leading to motor and sensory impairments. Neuropathies can have various underlying causes, with metabolic disorders, particularly obesity, emerging as prominent contributors. However, the exact pathological mechanisms and the interactions between different cell types within the nerves, including peripheral axons and Schwann cells, in the context of peripheral neuropathy remain poorly understood. Obesity is closely linked to elevated levels of circulating leptin, a hormone produced by adipocytes. Previous research from our laboratory has shown that leptin receptor signaling in Schwann cells is beneficial in promoting nerve repair following acute trauma, by triggering a series of catabolic pro-regenerative processes. Paradoxically, in cases of obesity, a positive correlation between hyperleptinemia and the neuropathic symptoms has been reported, suggesting a potential adverse causal relationship. Therefore, we follow the hypothesis that chronic leptin stimulation may transition from a pro-regenerative signal to a detrimental driving force in obesity-induced neuropathy. To investigate this hypothesis, we use mouse mutants lacking the leptin receptor in Schwann cells. These mice are fed with a high-fat diet (HFD) to trigger obesity-induced neuropathy. In line with our hypothesis, preliminary data indicate that neuropathic symptoms, such as impaired gait parameters and altered electroneurographic properties, are improved in the leptin receptor mutant mice compared to the control.

Poster 137

IsoAsp7-Aβ – A major Aβ variant in Alzheimer's disease, dementia with Lewy bodies and vascular dementia

S. Schrempel[1], A. K. Kottwitz[2,3], A. Piechotta[2], K. Gnoth[2], L. Büschgens[4], M. Hartlage-Rübsamen[1], M. Morawski[1], M. Schenk[2], M. Kleinschmidt[2], G. E. Serrano[5], T. G. Beach[5], A. Rostagno[6], J. Ghiso[6], M. T. Heneka[7], J. Walter[8], O. Wirths[4], S. Schilling[2,3], S. Roßner[1]

[1]Paul Flechsig Institute – Centre of Neuropathology and Brain Research, Medical Faculty, Leipzig, Germany, [2]Fraunhofer Institute for Cell Therapy and Immunology, Department of Molecular Drug Design and Target Validation, Halle (Saale), Germany, [3]Anhalt University of Applied Sciences, Center for Natural Products-based Therapeutics, Köthen, Germany, [4]University Medical Center Göttingen, Georg-August-University, Department of Psychiatry and Psychotherapy, Göttingen, Germany, [5]Civin Laboratory for Neuropathology, Brain and Body Donation Program Banner Sun Health Research Institute, Sun City, United States of America, [6]New York University School of Medicine, Department of Pathology, New York, United States of America, [7]University of Luxembourg, Luxembourg Centre for Systems Biomedicine, Belval, Luxembourg, [8]University Hospital Bonn, Center of Neurology, Molecular Cell Biology, Bonn, Germany

The formation of amyloid beta (Aβ) aggregates in brain is a neuropathological hallmark of Alzheimer's disease (AD). However, there is mounting evidence that specific post-translational modifications (PTMs) of Aβ contribute to its pathogenic profile and that Aβ plays a pathogenic role in other types of dementia. This study examined the hypothesis that distinct types of dementia are characterized by specific patterns of post-translationally modified Aβ variants. We conducted a comparative analysis and quantified total Aβ as well as pGlu3-Aβ, Aβ(4-X), isoAsp7-Aβ, pSer8-Aβ and pGlu11-Aβ in *post mortem* human brain tissue from non-demented controls in comparison to tissue classified as pre-symptomatic-AD (Pre-AD), AD, dementia with Lewy bodies (DLB) and vascular dementia (VAD). Aβ modification-specific immunohistochemical labelings of brain sections were examined by machine learning-based segmentation protocols and immunoassay analyses in brain tissue were carried out. With both analytical methods, we identified the isoAsp7-Aβ variant as a highly abundant form in all clinical conditions, followed by Aβ(4-X) and pGlu3-Aβ. There was a strong positive correlation between isoAsp7-Aβ and Thal phase and a moderate negative correlation between isoAsp7-Aβ and MMSE assessment. In aggregation assays, the isoAsp7-Aβ, pGlu3-Aβ and pGlu11-Aβ variants showed instant fibril formation without lag phase. We conclude that targeting Aβ PTMs, and in particular the highly abundant isoAsp7-Aβ variant, might be considered for diagnostic and therapeutic approaches in different types of dementia.

Poster 138

Motor neuron pathology drive spinal circuit defects and phenotype of a mouse model for spinal muscular atrophy with respiratory distress type 1

F. Gerstner[1], K. S. Apel[1], M. Koehler-Sanchez[1], A. L. Norman[1], L. Sowoidnich[1], N. Otte[1], M. L. Stephan[1], S. Jablonka[2], C. M. Simon[1]

[1]Leipzig University, Carl-Ludwig Institute, Leipzig, Germany, [2]University Hospital Würzburg, Institute for Clinical Neurobiology, Würzburg, Germany

Spinal muscular atrophy with respiratory distress type 1 (SMARD1), caused by a deficiency of IGHBMP2, is a subtype of spinal muscular atrophy but the main pathology remains enigmatic. SMARD1 mouse model exhibits MN loss and NMJ denervation, however it is unknown whether spinal motor circuits are affected and which cell types drive the pathology. Confocal and super resolution microscopy together with whole-cell patch-clamp recordings allowed us to investigate motor circuits of SMARD1 mouse model to quantify MN death, muscle denervation spinal synaptic loss and MN function. MN death and NMJ denervation occurred within the first two weeks of life and degeneration of excitatory synapses selectively in distal motor circuits. Whole-cell patch-clamp of spinal SMARD1 MNs revealed reduced and delayed proprioceptive synaptic transmission. To identify the driver of motor circuit degeneration and dysfunction, we selectively restored IGHMBP2 in MNs or proprioceptive neurons, respectively. The MN specific restoration resulted in an almost complete rescue of the entire motor circuit pathology, demonstrating that MN defects drive SMARD1 pathology. In our study, we developed a novel cell type-specific IGHMBP2 expression and demonstrate that MNs alone drive SMARD1 pathology. These findings lay the ground for identifying novel disease markers and candidate therapeutic targets to ameliorate this incurable disease.

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Poster 139 Pathogenic mechanisms of LGI1 auto-antibodies induced encephalitis

F. Lehmann, J. Wang, T. Kirmann, S. Hallermann, J. Nerlich

Universitätsklinikum Leipzig, Carl-Ludwig-Institut für Physiologie, Leipzig, Germany

Antibody-mediated encephalitis (AE) compromises a group of rare diseases characterized by autoantibodies against antigens in the central nervous system. A common target is the Leucine Rich Glioma Inactivated protein 1 (LGI1), exhibiting a range of neurological and psychiatric manifestations. LGI1 autoantibodies are known to interfere with neuronal function by enhancing the probability of release and neuronal excitability. Currently, the treatments are based on an escalating immunotherapy, including plasma exchange, steroids, and B cell depletion. However, these therapies often have delayed efficacy and lack specificity, requiring more rapid and targeted alternatives. To address these problems, we are developing and testing fusion constructs called „Baitbodies", combing the Fc region of immunoglobulin G with the proposed antibody binding sites of the LGI1 protein.

First, we investigated the pathogenic effects of patient-derived LGI1 autoantibodies on synaptic function and neuronal excitability of cultured human stem cell-derived neurons (human iPSCs). As a second step, we will test the neutralization ability of the Baitbodies to prevent the pathogenic antibody-mediated effects. Consistent with the results in mouse cells, first experiments in human neurons showed that polyclonal LGI1 antibody induced a widening of the action potential compared to neurons treated with control IgG. The autoantibody-induced change of the action potential waveform represents a promising mechanism to validate the efficacy of the newly engineered Fc-constructs.

Poster 140

Rabies and canine distemper exhibit distinct patterns of axonal damage and apoptotic cell death in the central nervous system of dogs and foxes

S. Pfetzing[1], C. Freuling[2], C. Puff[3], D. Driemeier[4], J. P. Teifke[5], T. Müller[2], W. Baumgärtner[3], R. Ulrich[1]

[1]Institute of Veterinary Pathology, Faculty of Veterinary Medicine, Leipzig University, Germany, [2]Institute of Molecular Virology and Cell Biology, WHO Collaborating Centre for Rabies Surveillance and Research, Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, Greifswald–Insel Riems, Germany, [3]Department of Pathology, University of Veterinary Medicine Hanover, Germany, [4]Department of Veterinary Pathology, Faculty of Veterinary Medicine, Federal University of Rio Grande do Sul, Porto Alegre, Brazil, [5]Department of Experimental Animal Facilities and Biorisk Management, Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, Greifswald-Insel Riems, Germany

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Rabies is a fatal zoonosis caused by the rabies virus which enters the central nervous system from the entry site via a retrograde axonal pathway with few or no histopathological lesions. In comparison, canine distemper virus-infection of the central nervous system is characterized by early-onset axonal damage followed by demyelination and inflammation, depending on the stage of the disease.

This study aimed to compare the extent of axonal damage and the number of apoptotic cells in cases of rabies and canine distemper in dogs and foxes.

Immunohistochemistry for active caspase-3 (a marker for apoptosis), β-amyloid precursor protein (a marker for early axonal damage), canine distemper virus, and rabies virus was performed on archival formaldehyde-fixed, paraffin-embedded brain specimens from dogs and foxes infected with rabies or canine distemper virus, alongside non-infected control groups.

Dogs and foxes infected with rabies virus showed no change in the amount of active caspase-3-immunoreactive cells and β-amyloid precursor protein-immunoreactive axons, as compared to the control groups. In contrast, canine distemper virus-infection was characterized by an increase in active caspase-3-immunoreactive cells and β-amyloid precursor protein-immunoreactive axons in both species.

In summary, rabies is not associated with early-onset axonal damage or apoptotic cell death in the central nervous system. Conclusively, the rabies virus effectively evades recognition by intrinsic neuroaxonal antiviral mechanisms on its route to the central nervous system.

Poster 141

Smad signaling controls GABA receptor expression

J. Cornelißen, J. Bochmann, T. Arendt, R. Stassart, U. Ueberham

Paul Flechsig Institute - Centre of Neuropathology and Brain Research, Leipzig, Germany

In Alzheimer`s disease (AD) the dysregulation of γ-aminobutyric acid (GABA) signaling already very early contributes to circuit dysfunction. Several GABA receptors (GABARs) are severely and early affected. Reasons for these receptor dysfunctions are mainly still unknown. GABARs potentially represent downstream targets of Smad signaling in the TGFβ pathway network. Recent data show that Smad deficiency abolished long term potentiation (LTP) in dentate gyrus with unchanged GABA release, while GABAR inhibition restored LTP. In AD brain, we have previously observed a strong reduction of neuronal Smads. We also found alterations of Smad immunoreactivity associated with redistribution of GABARs in brain under conditions of reduced body temperature. Therefore, we hypothesize, that Smad deficiency in AD brain is strongly affecting GABAR expression and distribution. To prove this assumption we modified Smad availability and activation in cultured primary neurons and subsequently determined GABAR expression on RNA and protein level. We could identify a highly specific impact of Smad on selected GABARs. Moreover, using receptor biotinylation and western blotting analysis an impact of Smad on neuronal receptor distribution was also detectable. This data show Smad as an important regulator of GABAR function and suggest the underlying pathway as a possible therapeutic target to reconstitute GABAR disturbance in AD brain.

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Poster 142

Synaptic dysfunction and p53 activation cause cerebellar circuit pathology in spinal muscular atrophy

A. Vankova[1], F. Gerstner[1], S. Wittig[1], C. Menedo[1], S. Ruwald[1], L. Sowoidnich[1], G. Martin Lopez[1], C. Grzyb[1], L. Pellizzoni[2], C. J. Sumner[3], C. M. Simon[1]

[1]Carl-Ludiwg-Institut, Leipzig, Germany, [2]Columbia University, Center for Motor Neuron Biology and Disease, Department of Neurology, Department of Pathology and Cell Biology, New York, United States of America, [3]Johns Hopkins University School of Medicine, Departments of Neurology and Neuroscience, Baltimore, United States of America

Spinal muscular atrophy (SMA) is a motor neuron disease, primarily characterized by the degeneration of sensory motor circuits resulting in impaired voluntary movement and muscle atrophy. Impairments of proprioception and motor control – key features of SMA – are also primary functions of the cerebellum. A few studies reported alteration of Purkinje cells (PC) - the sole functional output of the cerebellar cortex - in SMA patients, implicating a cerebellar contribution to the disease pathology.

In this study, we performed immunohistochemistry and confocal analysis in a mouse model and postmortem tissue from patients to study the mechanisms of cerebellar pathology in SMA.

Our results show that both SMA mice and patients exhibited significant PC death. Subsequent analysis indicates smaller PC dendritic trees and a reduction of excitatory synaptic inputs onto PC in SMNΔ7 mutant mice. To gain insight into the pathomechanism of PC death, we investigated the p53 pathway which has been shown to induce motor neuron death in SMA. Importantly, vulnerable PC exhibited a robust p53 upregulation in mice and patients. Furthermore, p53-knockdown experiments restored PC number to almost wild-type level, suggesting p53-dependent neurodegeneration in the cerebellum.

In summary, these results reveal cerebellar pathology as a consistent hallmark in SMA mice and patients. Mechanistically, p53 drives PC death, akin to the situation in motor neurons. Our results indicate that cerebellar pathology could contribute to SMA phenotype and should be considered in future therapeutic approaches.

Poster 143 The role of PERP expression in motor neuron death of SMA mice

A. Alonso, L. Sowoidnich, C. Simon

Carl-Ludwig-Institute for Physiology, Leipzig, Germany

Motor neuron death is one of the major hallmarks of Spinal Muscular Atrophy (SMA) and is caused by a reduction of Survival of Motor Neuron (SMN) protein levels. Previous studies have shown that the occurring motor neuron degeneration is executed by the activation of the p53 pathway in SMA mice. However, due to the role of p53 as a tumor suppressor, its inhibition is not a viable SMA treatment. Therefore, cell-death associated p53 downstream targets that execute motor neuron death, need to be identified for future therapeutic approaches. One candidate is p53 apoptosis effector related to PMP-2 (PERP), which was recently shown to be upregulated in vulnerable motor neurons. Thus, the study aims to define the role of p53-dependent PERP expression in the context of motor neuron death in a severe SMA mouse model. Here, we applied fluorescence in situ hybridization (FISH) and immunofluorescence in combination with confocal microscopy to evaluate the role of PERP in motor neuron death of the SMNΔ7 mouse model. First, we provided evidence that a successful virus-mediated knockdown of PERP does not alter p53 nuclear accumulation of vulnerable SMA motor neurons, suggesting that PERP is a downstream transcriptional target of p53. Moreover, immunostaining of a vulnerable spinal segment revealed that the virally mediated knockdown of PERP does not prevent motor neuron death in SMA. Additionally, we were able to demonstrate that PERP knockdown tends to alleviate NMJ pathology in SMA mice. This study shows that PERP inhibition does not rescue p53-dependent motor neuron death in SMA.

Poster 144

CardioEpiX – a novel high-dense microelectrode array based multimodal bioelectronic monitoring system for cardiac arrythmia re-entry analysis

S. Schmidt, T. Haensch, M. Meier, H.-G. Jahnke

Leipzig University, Biochemical Cell Technology, Leipzig, Germany

Recent advances in heart disease treatment, particularly in personalized medicine, highlight limitations in current genetic testing approaches.Many patients lack detectable mutations, complicating risk stratification for sudden cardiac death. Current assessments rely heavily on clinical findings and invasive methods. Therefore, there is an urgent need for novel, label-free, non-invasive in vitro functional analysis systems to improve patient stratification, therapy planning, and safety pharmacology.

To address this problem, a novel multilayer high-density microelectrode array (HD-MEA) with an application-specific optimized configuration of 512 sensing electrodes and 4 pacing electrodes on a sensor area of 100 mm² together with a multimodal data acquisition system for combined electrophysiological recording and high temporal resolution impedance spectroscopy was developed for label-free detection of re-entry arrhythmia patterns. In proof of principle experiments, human induced pluripotent stem cell derived cardiomyocytes were cultured on HD-MEAs and used to demonstrate the sensitive quantification of contraction strength modulation by cardioactive drugs such as blebbistatin (IC50 = 4.2 µM), omecamtiv and levosimendan. More strikingly, disease-typical rotor patterns (re-entry) could be induced by specific electrical stimulation sequences and thus a patient-specific correlation could be successfully established on a functional level.

Thus, this innovative system paves the way for diagnostics and testing of patient-specific therapeutic approaches in the field of cardiac diseases.

Poster 145 Chimeric antigen receptors targeting adhesion GPCRs

P. Annadurai[1], T. Langenhan[1,2,3]

[1]Rudolf Schönheimer Institute of Biochemistry, Division of General Biochemistry, Faculty of Medicine, Leipzig University, Germany, [2]Comprehensive Cancer Center Central Germany, Leipzig University, Germany, [3]Institute of Biology, Faculty of Life Sciences, Leipzig University, Germany

Chimeric surface receptors such as CARs (Chimeric Antigen Receptors) have been revolutionising cancer immune therapies. These synthetic receptors recognise a specific antigen expressed on cancer cells and target and control T cells responses against them. While the structure of CARs is modular, only few novel CAR targets have been explored in the past.We suggest to develop CARs against a surface receptor family that is involved in many cancer types: adhesion G protein-coupled receptor (aGPCRs), which constitute a large family within the GPCR superfamily. ADGRE5/CD97 is an aGPCR known to promote hepatocellular carcinoma, glioblastoma, colorectal cancer, acute lymphocytic leukemia, and pancreatic cancer. Currently, no drugs target aGPCRs due to the limited understanding of their structure and signaling mechanisms. However, the immune profile of ADGRE5 and its ligands CD55 is well understood with several monoclonal immune sera targeting epitopes in their extracellular regions. Second, ADGRE5 and CD55 both are overexpressed on tumour cell surfaces making them attractive antigen targets for CARs.Our goal is to modify an established CAR design, the anti-CD19 CAR used in Tisagenlecleucel (Kymriah), such that it recognises CD55 on tumor surfaces by swapping the paratope region of the CAR for CD55's endogenous ligand recognition motif of the CD55 receptor ADGRE5. We will also engineer another novel CAR with the inverse logic, i.e. by fusing the CAR to CD55's extracellular protein region that interfaces with its receptor ADGRE5 to render it recognising the aGPCR on tumour cells.

Poster 146

Computational Investigation of Y-Receptor Dynamics

M. Pankonin[1], M. Voitel[2], P. W. Hildebrand[3]

[1]Institut für medizinische Physik und Biophysik, Universität Leipzig, Biophysik, Leipzig, Germany, [2]Institut für medizinische Physik und Biophysik, Membrane Physics, Leipzig, Germany, [3]Institut für medizinische Physik und Biophysik, Computational Biophysics, Leipzig, Germany

The Y-receptors are a subclass of GPCRs involved in appetite and energy regulation, characterized by their binding affinity to the shared ligand neuropeptide Y, yet they display significant genetic diversity. This diversity makes them an excellent case study for understanding ligand-dependent signal transduction in functionally similar but genetically distinct systems. This study combines molecular dynamics simulations and NMR spectroscopy to examine Y-receptor structural dynamics and ligand interactions. Conformational differences in the critical „toggle switch“ region between the Y1 and Y2 receptors provide potential insights into the mechanisms of modulation within these systems.

Poster 147 Development and characterisation of complex blood vessel structures on anorgan-on-chip platform

M. Butting

Universität Leipzig, BBZ Professur für Biochemische Zelltechnologie, Leipzig, Germany

The human vascular system is a complex and dynamic network responsible for maintaining homeostasis in all organs. The interplay between endothelial cells (ECs) and smooth muscle cells (SMCs) is crucial for regulating blood flow, nutrient delivery, and immune cell trafficking. Given their central role in vascular dysfunction, such as in atherosclerosis, a deeper understanding of the interactions between these cells and their environment is essential. However, there remains a lack of ethical and reliable models for studying these increasingly prevalent diseases.

To address this, we are developing a 3D-printed, human stem cell-based blood vessel-on-chip platform designed for the co-cultivation of ECs and SMCs within a hydrogel environment. This poster presents the engineering of the 3D-printed co-culture platform, detailing the design process, hydrogel modification, and cell type specifications. Platform characterization was performed through imaging analysis, barrier function assays, and immunostaining using high-resolution microscopy.

As a next step, the co-culture vessel-on-chip platform will be stimulated with oxidized low-density lipoprotein (oxLDL) to investigate early atherosclerosis mechanisms, such as reactive oxygen species (ROS) production and nitric oxide synthesis. Additionally, the platform has the potential for downstream applications, including MALDI imaging, to provide broader insights into the metabolome and spatial organization of the involved cell types.

Poster 148

Engineering high-sensitivity flavoproteins for hyperpolarized EPR spectroscopy

V. Apet[1], S. Krebs[2], M. Elgeti[3], J. Meiler[2], I. Coin[1]

[1]Leipzig University, Institute for Biochemistry, Leipzig, Germany, [2]Leipzig University, Institute for Drug Discovery, Leipzig, Germany, [3]Leipzig University, Institute for Drug Discovery, Institute for Medical Physics and Biophysics, Leipzig, Germany

Electron Paramagnetic Resonance (EPR) and Nuclear Magnetic Resonance (NMR) are essential techniques in structural biology, offering high spatial resolution and timescales ranging from picoseconds to milliseconds. However, these magnetic resonance methods face inherent challenges due to an unfavourable Boltzmann ratio, resulting in intrinsically low polarization and consequently limited sensitivity. To address this issue, we propose the development of a hypersensitive spin tag specifically designed for hyperpolarized EPR spectroscopy. Our initial approach involves the utilization of flavoprotein sensors, such as Light-Oxygen-Voltage (LOV) domains, Blue Light-Using Flavin (BLUF) domains, and cryptochromes. These proteins naturally contain a spin-correlated radical pair (SCPR), which forms upon illumination between a flavin molecule (as the electron donor) and an aromatic amino acid (as the electron acceptor). We aim to use this SCPR-containing proteins as a fused tag for G protein -coupled receptors (GPCRs) for further double electro-electron resonance (DEER) experiments. The final goal of this project is to design a de novo protein tag—termed “maquette”— that retains the desired functions while exhibiting simplified structural properties. In addition to structural experiments, this tag will enable investigations into electron transfer and hyperpolarization mechanisms across various protein structures, including α-helices and β-sheets. The hyperpolarized electron-spin system will serve as a valuable tool for in cell EPR experiments on samples with extremely low concentrations

Poster 149

Exploring Chemical Modifications in Peptide Helices to Control Chiral-Induced Spin Selectivity

A. Kazimir, C. Lamers

Leipzig University, Insitute for Drug Discovery, Leipzig, Germany

The chirality of molecular systems is closely linked to their electronic properties, as demonstrated by the chiral-induced spin selectivity (CISS) effect observed in these systems.[1] The CISS effect enables chiral molecules absorbed on the metal substrate to preferentially ‘’filter’’ electrons of specific spin orientations (spin *up* for right-handed or *down* for left-handed helices). This leads to hyperpolarization, characterized by a highly populated spin state. The hyperpolarization enhances the system‘s interaction with external magnetic fields, opening avenues for applications in molecular spintronic devices, quantum-based biosensors and enhanced NMR (MRI) signal detection.[2]

Studies[1] show that the CISS effect is more pronounced in helical molecular structures. Importantly, longer helices amplify the CISS effect, with the strength of this effect changing in response to the helicity type. Our research investigates how chemical modifications to alanine-rich, lysine-containing α-helical peptides[3] affect their structure-property relationships in the context of the CISS effect. The modifications include: (a) introducing alkyl linkers in the side chain to create spacers between the metal substrate and the helix; (b) incorporating photo-linkers to enable helicity changes through light activation; and (c) adding amino acids with different chiralities to disrupt helicity at the helix edges. Our findings on these modified structures aim to clarify the dependence of the CISS effect on specific molecular modifications, advancing the understanding of structure-dependent CISS behaviors.

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Poster 150 Exploring Interactions of Y5 Receptor

A. Alkara

Leipzig University, Germany

The Neuropeptide Y system is a multi-receptor and multi-ligand network, encompassing four G protein-coupled receptors in humans (Y1, Y2, Y4, Y5) and three native ligands (NPY, PYY, PP) that induce varying degrees of receptor activation. The internalization mechanisms of GPCRs have been the subject of extensive investigation in recent decades. A pivotal phase of this process involves the interaction of the receptor with β-arrestins, following phosphorylation of the receptor by GPCR kinases (GRKs).

The biological regulation of human Y receptors through internalization has been widely studied. However, the specific internalization mechanism of Y5 and the role of β-arrestins or GRKs in this process have not yet been identified. The Y5 receptor provides a model of a GPCR that lacks a C-terminal tail but features a long ICL3, which harbors many serine and threonine residues that could serve as potential phosphorylation sites for GRKs. This could be a factor in accelerating the internalization process and potentially interacting with β-arrestins.

This study aims to investigate the internalization mechanism of hY5 and determine the roles of β-arrestins and GRKs in its cellular internalization. Using cloning techniques, we generated deletion mutants within the ICL3 region of the Y5 receptor. We then studied the effects of these deletions on signaling pathways using BRET assay and fluorescence microscopy. Furthermore, chimeras between Y5R and M2R, which share similarities in the length of ICL3 region, provided additional insights into the internalization mechanism of Y5R.

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Poster 151

HyperMPNN – A general strategy to design thermostable proteins learned from hyperthermophilic organisms

P. Schlegel[1], M. Ertelt[1], M. Beining[1,2], L. Kaysser[1], J. Meiler[1,2,3,4], C. T. Schoeder[1,3]

[1]Institute for Drug Discovery, Leipzig, Germany, [2]School of Embedded Composite Artificial Intelligence (SECAI), Leipzig, Germany, [3]Center for Scalable Data Analytics and Artificial Intelligence ScaDS.AI, Leipzig, Germany, [4]Vanderbilt University, Center for Structural Biology, Nashville, United States of America

Stability is a key factor to enable the use of recombinant proteins in therapeutic or biotechnological applications. Deep learning protein design approaches like ProteinMPNN have shown strong performance both in creating novel proteins or stabilizing existing ones. However, it is unlikely that the stability of the designs will significantly exceed that of the natural proteins in the training set, which are biophysically only marginally stable. Notably, ProteinMPNN fails to recover their unique amino acid composition. Therefore we collected predicted protein structures from hyperthermophiles, which differ substantially in their amino acid composition from mesophiles. Here we show that a retrained network on predicted proteins from hyperthermophiles, termed HyperMPNN, not only recovers this unique amino acid composition but can also be applied to proteins from non-hyperthermophiles. Using this novel approach on a protein nanoparticle with a melting temperature of 65°C resulted in designs which remained stable at 95°C. In conclusion, we created a new way to design highly thermostable proteins through self-supervised learning on data from hyperthermophiles.

Poster 152

Interaction of the Y2R with arrestin

S. Fürst, I. Coin

Universität Leipzig, Institut für Biochemie, Leipzig, Germany

The neuropeptide Y receptor type 2 (Y2R) is a G protein-coupled receptor (GPCR) that plays a role in numerous physiological processes, including the regulation of food intake. As most GPCRs its internalization is regulated by β-arrestins. Previous results have demonstrated that the Y2R binds arrestin and subsequently internalizes. In comparison to other GPCRs (e.g. PTH1R), the Y2R binds arrestin only transiently and with a lower affinity so that arrestin does not co-internalize with the receptor. This project aims to identify the interaction points between arrestin and Y2R using crosslinking techniques.

Therefore, we expand the genetic code by incorporating non-canonical amino acids into arrestin, which can bind covalently to the receptor based on proximity. The arrestin-receptor complex can be analyzed using western blot and ELISA.

We have already been able to show first crosslinking between different regions of arrestin and the receptor. We now aim to identify additional points of interaction to eventually be able to build a model of the Y2R-arrestin complex.

Poster 153

Investigating M_2R-Arrestin Interactions in the Live Cell: Structural Insights via Genetically Encoded Crosslinkers

T. Müller, I. Coin

Universität Leipzig, Institut für Biochemie, Leipzig, Germany

Arrestins are key regulators of G protein-coupled receptors (GPCR). While most activated GPCRs bind arrestins through their phosphorylated C-tails, the muscarinic acetylcholine receptor M_2 (M_2R) lacks this feature. In contrast, M_2R relies on the phosphorylation of its third intracellular loop (ICL3). However, structural details of the M_2R-arrestin complex remain scarce, with only a few receptor residues resolved by cryo-EM.

To explore the interface of the M_2R-arrestin complex, we employed genetically encoded crosslinkers incorporated into arrestin, followed by analysis via western blot and ELISA.

Through unspecific photocrosslinking, we mapped the interaction surface of the M_2R on the N-domain and central crest of arrestin 3 (arr3), and compared it to that of arrestin 2 (arr2). Using pairwise crosslinking, we could identify proximity points between the ICL3 of M_2R and arr2 and map interactions not resolved in any structure. This crosslinking data suggest a semicircular arrangement of the M_2R ICL3 around the arrestin N-domain.

Despite detecting strong photocrosslinks in the central crest of arrestin, we could not connect them to any pairwise interaction. Nevertheless, we found the region of the M_2R that interacts with the central crest is the receptor core upstream of the ICL3. Additionally, we demonstrated the necessity of the arrestin finger loop for full recruitment to the receptor via a BRET-based assay.

We now aim to identify the interactions between the M_2R core and arrestin and to use the crosslinking data to build an accurate model of the M_2-receptor-arrestin 2-complex.

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Poster 154 Macrocyclic Peptides Targeting Complement Receptor 3 as Potential Therapeutic Candidates

B. Alo[1], T. Götze[1], S. A. Vogt[2], C. Sommer-Plüss[2], L. Ciullo[2], R. Mancuso[2], D. Ricklin[2], C. Lamers[1]

[1]Leipzig University, Institute of Drug Discovery, Leipzig, Germany, [2]University of Basel/Molecular Pharmacy, Department of Pharmaceutical Sciences, Basel, Switzerland

Complement-related integrin receptors CR3 and CR4 are of vital importance in the field of immunology, where they perform essential functions including those associated with complement-mediated phagocytosis, leukocyte activation, adhesion, and extravasation. It is postulated that the pathogenesis of various disorders, including autosomal leukocyte adhesion deficiency, systemic lupus erythematosus, dry eye disease, and other leukocyte-mediated dysfunctions such as atherosclerosis, is significantly influenced by CR3 [1]. Consequently, targeting of CR3 has emerged as a promising approach for drug discovery.

By employing chemically modified phage display techniques, we successfully identified macrocyclic peptides that bind to the main binding domain of CR3 (α_MI) with low µM affinity. To gain insights into the structure-activity relationship (SAR), an alanine scan was conducted combined with SPR analysis. The results of this scan enabled us to conduct further SPR-based SAR studies to identify peptide residues crucial for β_2-subtype specificity and binding affinity to α_MI.

Furthermore, to ascertain the potential therapeutic efficacy of the peptides, we established an LC-MS-based stability assay. This assay will identify residues that render the peptide susceptible to degradation in plasma, thereby facilitating the enhancement of plasma stability for the peptides. The developed peptides have demonstrated considerable promise as therapeutics, exhibiting high affinity. SAR studies revealed the possibility to obtain peptides with β_2-subtype specificity and increased binding affinity.

References:

[1] Lamers Christina, Plüss Carla Johanna, Ricklin Daniel, (2021), The Promiscuous Profile of Complement Receptor 3 in Ligand Binding, Immune Modulation, and Pathophysiology, Frontiers in Immunology, https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2021.662164

Poster 155

Mapping The Interaction Between The μ-Opioid Receptor And β-Arrestin

A. M. Röhlig, I. Coin

Institute for Biochemistry, Leipzig, Germany

G protein-coupled receptor kinases (GRKs) and β-arrestins are critical in regulating the desensitization and internalization of the μ-opioid receptor (MOR). Understanding how these transducers interact with MOR is crucial, as β-arrestin interactions can contribute to side effects in opioid-based pain therapies. Due to the lack of 3D structures for MOR signaling complexes, we employ genetic code expansion to map the β-arrestin-MOR interaction. By incorporating an electrophilic, genetically encoded unnatural amino acid into β-arrestin-1 and selectively replacing cysteines in the receptor, we induce a proximity-driven reaction, allowing us to probe the β-arrestin-1-MOR interface in live mammalian cells with single-residue resolution. A systematic scan of the intracellular surface of MOR reveals a complex network of interactions that link the receptor's intracellular loops and C-terminal tail to the N-terminal domain of β-arrestin-1. These data provide a comprehensive set of structural constraints that will be instrumental in developing an accurate model of the β-arrestin-1-MOR complex, for which no experimental structure is currently available.

Poster 156

Potential Degradation of Microplastics by Bacteria Detected in the Human Lung Microbiome

A.-L. Mory[1], M. R. Belisário-Ferrari[1], I. Ivanikov[2], G. Künze[2], L. Kaysser[1]

[1]Leipzig University, Faculty of Medicine, Institute for Drug Discovery, Pharmaceutical Biology, Leipzig, Germany, [2]Leipzig University, Faculty of Medicine, Institute for Drug Discovery, Computational Structural Biology, Leipzig, Germany

Micro- and nanoplastics (MNPLs) accumulation in the human lung poses potential health risks, and the body's ability to degrade these particles remains unclear. This study investigates the potential of bacteria from the human respiratory microbiome to enzymatically hydrolyze polyethylene terephthalate (PET), a common plastic pollutant. A comprehensive bioinformatics analysis, incorporating phylogenetic studies and comparative sequence alignments, was performed to identify potential PET–hydrolyzing enzymes (PETases) among proteins from lung microbiome bacteria. A putative PETase from *Microbulbifer hydrolyticus* was identified, showing significant homology to known PETases such as IsPETase. Structural analysis revealed the presence of conserved motifs and a catalytic triad essential for PETase activity. *M. hydrolyticus* was cultured in the presence of PET and other polyesters, and esterase activity assays demonstrated the bacterium's ability to degrade these substrates, particularly at physiological temperatures. A promising gene was codon–optimized, cloned into the pET28a(+) vector, and expressed in *Escherichia coli* BL21 (DE3). The findings suggest that *M. hydrolyticus* and its putative PETase have the potential to degrade PET in the human lung, which could influence our understanding of the health effects of MNPL exposure. Further research is needed to explore the biological and medical implications of possible PET degradation within the respiratory system.

Poster 157

RecT: A phage-derived recombinase for ATP-independent, in vitro, isothermal point-of-care diagnostics

R. G. Pais[1], S. Leptihn[2,3], D. Kuhlmeier[4], B. Loh[1]

[1]Fraunhofer Institute for Cell Therapy and Immunology, Department of Vaccines and Infection Models, Leipzig, Germany, [2]Health and Medical University Erfurt, Department of Biochemistry, Erfurt, Germany, [3]University of Southern Denmark, Department of Biochemistry and Molecular Biology, Odense, Denmark, [4]Fraunhofer Institute for Cell Therapy and Immunology, Department of Diagnostics, Leipzig, Germany

Recombinase polymerase amplification (RPA) is an *in vitro*, isothermal nucleic acid amplification technique which can amplify DNA and RNA targets from a variety of organisms and samples in a single-tube reaction format. The rationale behind the development of RPA technology is the sensitive, rapid and convenient diagnosis of infectious diseases for point-of-care testing and in resource-limited settings.

The operation of the RPA process involves three crucial enzymatic components - a homologous recombinase, a single-stranded DNA-binding protein (SSB) and a strand-displacing polymerase.

Currently, RPA kits on the market employ the homologous recombinase RecA which is bacterial-derived and ATP-dependent. These kits are capable of amplifying target nucleic acid sequences, provided a certain concentration of ATP is present in the reaction mix. The requirement of ATP for the functionality of these kits results in the need for stringent temperature storage parameters (-20°C to 4°C), so as to ensure the stability of ATP.

This project aims to develop RPA technology using RecT, a phage-derived, ATP-independent homologous recombinase and evaluate whether it can serve as a suitable substitute or improvement to RecA. With the usage of RecT in RPA technology, stringent temperature storage conditions are eliminated, thereby improving the shelf-life and reducing the overall costs of these products. Additionally, the project will investigate the ATP-independent mechanism of RecT which is not fully understood.

Poster 158

Screening for Tau Aggregation Inhibitors Using a NanoLuciferase Binary Technology

N. Ma[1], J. Stieler[1], M. Metelmann[2], J. Claßen[2], I. Hilbrich[1], M. Schaefer[3], M. Holzer[1]

[1]PFI-Paul Flechsig Institute of Brain Research, Leipzig University, Germany, [2]Department of Neurology, Leipzig University, Germany, [3]Rudolf-Boehm-Institute of Pharmacology, Leipzig University, Germany

Recent studies suggest that soluble tau oligomers formed before fibril assembly are more harmful to Alzheimer‘s disease. Pathogenic tau aggregation begins with monomer assembly into oligomers, then forms paired helical or straight tau filaments and ultimately develops into intracellular neurofibrillary tangles, with dimerization as the rate-limiting step. Hence, a crucial therapeutic strategy involves the disruption of tau oligomerization or control of the rate-limiting process of dimerization before the formation of tau aggregate. Our study aims to identify tau aggregation inhibitors from the Spectrum Collection and the protein kinase inhibitors library by targeting tau self-interaction in a cellular system using NanoLuciferase Binary Technology (NanoBit) as a read-out. Eventually, we created the NanoBit tau interaction assay, which can sensitively detect tau self-interaction in vitro and is a high-throughput screening tool for finding potential candidates that can stop tau aggregation. From the spectrum collection, we discovered that ritanserin, 3-methoxycatechol, and gambogic amide could effectively inhibit tau interaction in cells. In addition, we identified 2 protein kinase inhibitors and 1 GluR6 antagonist that also led to inhibition of tau interaction in cells. We established a cell-free seed amplification assay to study the kinetics of tau aggregation and found that two inhibitors directly interact with tau. We also developed a cellular tau dGAE aggregation biosensor to monitor tau aggregation induced by extracellular misfolded pathological tau seeds.

Poster 159 Studying the process of GTP-induced activation of G protein heterotrimer from Mu-opioid receptor

H. Geraili Daronkola, P. Hildebrand

Leipzig University, Faculty of Medicine, Institute of Medical Physics and Biophysics, Leipzig, Germany

G-protein-coupled receptors (GPCRs) initiate cellular signaling by promoting the exchange of guanine nucleotides in heterotrimeric G proteins. In this study, we investigate the activation mechanism of the Gi protein in complex with the Mu-opioid receptor (MOR).

Our focus is on the Gi protein coupled with guanosine triphosphate (GTP) within the Gα subunit‘s binding pocket, approaching dissociation from the receptor. Upon GTP binding, the alpha-helical (AH) domain of the Gα subunit undergoes a conformational closure, leading to the retraction of the α5 helix from MOR. This structural change leads to the dissociation of the Gα and βγ subunits. We employed cryogenic electron microscopy (cryo-EM) to resolve the membrane protein structures of the MOR-Gi complex in the presence of two distinct ligands: the partial agonist mitragynine pseudoindoxyl (MP) and the super agonist lofentanil (LFT).

Our analysis reveals two primary activation states along the signaling pathway:

1. State A (Loosely AH Domain Closed Ensemble): Characterized by a partially closed AH domain where the α5 helix remains somewhat engaged with the receptor.

2. State B (Tightly AH Domain Closed Ensemble): Defined by a fully closed AH domain, resulting in complete disengagement of the G protein from the receptor‘s canonical intracellular pocket.

To further elucidate the temporal progression of these structural states, we are conducting molecular dynamics simulations. These simulations are employed to highlight the dynamic separation of the Gα and βγ domains, providing insight into the pathways of Gi protein activation.

Poster 160 The Metabolic Potential of the Human Microbiome

F. Semmler, M. Regis Belisário-Ferrari, M. Kulosa, L. Kaysser

Leipzig University, Institute for Drug Discovery, Department of Pharmaceutical Biology, Leipzig, Germany

The human lung microbiome remains largely underexplored, despite its potential implications in the pharmacokinetics of inhaled drugs and its involvement in lung diseases. Interactions within these bacterial communities and with the host are complex processes which often involve microbial small molecules. In this study, we employed a computational approach to describe the metabolic potential of the human lung microbiome. By utilizing antiSMASH and BiG-SCAPE software, we identified 1831 biosynthetic gene clusters (BGCs) for the production of specialized metabolites in a carefully compiled genome database of lung-associated bacteria and fungi. It was shown that ribosomally synthesized and post-translationally modified peptides (RiPPs) represent the largest class of natural products within the bacteriome, while non-ribosomal peptides (NRP) constitute the largest class of natural products in the lung mycobiome. All predicted BGCs were further categorized into 767 gene cluster families, and a subsequent network analysis highlighted that these families are widely distributed and contain many uncharacterized members. Moreover, in-depth annotation allowed the assignment of certain gene clusters to putative lung-specific functions within the microbiome, such as osmoadaptation or surfactant synthesis. This study establishes the lung microbiome as a prolific source for secondary metabolites and lays the groundwork for detailed investigation of this unique environment.

Poster 161

A Platform for Testing the Biocompatibility of Implants: Silicone Induces a Proinflammatory Response in a 3D Skin Equivalent

R. Nuwayhid, O. Kurow

Universitätsklinikum Leipzig AöR, Klinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Germany

Biocompatibility testing of materials is carried out in 2D cell cultures or animal models despite serious limitations. 3D skin equivalents are advanced in vitro models for human skin. Silicone has been shown to be noncytotoxic but capable of eliciting an immune response. Our aim was to (1) establish a 3D skin equivalent to (2) assess the proinflammatory properties of silicone. We developed a coculture of keratinocytes and fibroblasts resulting in a 3D skin equivalent with an implant using samples from a breast implant. Samples with and without the silicone implant were studied histologically and immunohistochemically in comparison to native human skin samples. Cytotoxicity was assessed via LDH-assay, and cytokine response was assessed via ELISA. Histologically, our 3D skin equivalents had a four-layered epidermal and a dermal component. The presence of tight junctions was demonstrated in immunofluorescence. The only difference in 3D skin equivalents with implants was an epidermal thinning. Implanting the silicone samples did not cause more cell death, however, an inflammatory cytokine response was triggered. We were able to establish an organotypical 3D skin equivalent with an implant, which can be utilised for studies on biocompatibility of materials. This first integration of silicone into a 3D skin equivalent confirmed previous findings on silicone being non-cell-toxic but capable of exerting a proinflammatory effect.

Poster 162

Biomaterials Engineering Assisted by Low-energy Non-thermal Electron Beam Technology

N. Gürtler, U. König

Fraunhofer FEP, Biokompatible Materialien, Dresden, Germany

Enhanced control of the biological response of interfacing biomaterials can be achieved by surface modification technologies. Particularly, low-energy, non-thermal electron beam technology (e-beam) represents a multifunctional tool for surface and material engineering.

Exemplary, this technology can be applied to create anti-adhesive surface properties. Surface characterization methods like ATR-FTIR spectroscopy, AFM or wettability measurements were used to prove the successful thin layer immobilization and evaluate the hydrophilicity increase by a significant reduction of the water contact angle. The biological response was investigated via cytotoxicity and cell adhesion tests. The low-energy e-beam technology is also suitable for cross-linking bio-based materials. The solvent casting process was used to produce a nanocellulose film that was cross-linked with citric acid and coated with chitosan. The materials were characterised using ATR-FTIR spectroscopy and tensile tests. The cytocompatibility of the resulting material was analysed using human keratinocytes.

Furthermore, the low-energy e-beam technology can also be applied for the biological tissue preparation. A newly developed and patented process, called SULEEI, makes it possible to sterilize (S) and preserve decellularized tissue like pericardium by means of photo-initiated ultraviolet (U) crosslinking and subsequent low-energy electron irradiation (LEEI). The SULEEI process is a unique multi-stage approach increasing the biocompatibility and reducing the calcification of prepared biological tissues.

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Poster 163 Characterization of a durable biopolymer from Chlamydomonas reinhardtii zygospores

P. Ranganathapura Basavaraju[1], V. Rohr[2], C. Song[2], R. Nagel[1], J. Matysik[2], S. Sasso[1]

[1]Institute of Biology, Department of Plant Physiology, Leipzig University, [2]Institute for Analytical Chemistry, Leipzig University, Germany

Chlamydomonas reinhardtii is a single-celled model alga (Chlorophyta) that thrives in temperate soils. We know the indispensability of the *PKS1* gene during the formation of the zygotic cell wall, which facilitates the maturation of newly generated zygotes into zygospores (Heimerl et al. (2018), *The Plant Journal*, *95*, 268–281). Zygospores represent a quiescent phase of the alga, marked by their resilience against challenging environmental conditions. The objective of this project is the purification and structure elucidation of the resilient biopolymer present in the cell wall of *C. reinhardtii* zygospores. A series of organic solvent washes and refluxing with various acids and bases, 1.2 mg of a highly resistant biopolymer was obtained from 5 g of initial fresh weight cell material. Analytical techniques, including solid-state ^{13}C-nuclear magnetic resonance, and Fourier transform infrared spectroscopy were used to investigate the chemical structure of the purified polymer. Our preliminary analysis elucidated an aliphatic polymer consisting of hydroxylated fatty acids crosslinked via ester and ether bonds to form a resistant polymeric network. Our structure is similar to the polymer model proposed for zygospores of *Chlamydomonas monoica* (Blokker et al. (1999), *Planta, 207*, 539–543). To determine the length distribution and molecular weight of the polymer building blocks, we will degrade and analyze the polymer using pyrolysis-GC/MS. Detailed structure elucidation and examination of its mechanical properties will pave the way for beneficial applications in the future.

Poster 164

Computational Design of a Metagenomic Enzyme from Leipzig for Enhanced Plastic Degradation

P. Blazquez-Sanchez[1], J. Gunkel[1], A. Useini[2], A. Zlobin[3], A. Schöler[3], F. Engelberger[3], J. D. Zakary[3], C. Sonnendecker[4], G. Künze[3]

[1]Institute for Drug Discovery, Faculty of Medicine, Leipzig, Germany, [2]Institute of Bioanalytical Chemistry, Centre for Biotechnology and Biomedicine, Leipzig, Germany, [3]Institute for Drug Discovery, Leipzig, Germany, [4]Biotechnologisch-Biomedizinisches Zentrum, Leipzig, Germany

Polyester Hydrolase Leipzig 7 (PHL7), a newly identified enzyme from a compost metagenome, can break down amorphous PET from post-consumer plastic waste in under a day. Despite its rapid degradation capabilities, the enzyme‘s application in industrial processes has been constrained by its instability and short operational lifespan at low salt levels and elevated temperatures, which are essential for optimal PET hydrolysis.

To tackle these challenges, we employed a computer-aided design strategy to enhance the enzyme’s stability and activity. By performing Rosetta energy calculations, we pinpointed a series of stabilizing mutations, which, when combined, increased the enzyme thermal melting temperature to over 95°C. Subsequent rounds of mutagenesis targeting the PET binding site led to a PHL7 variant with significantly enhanced performance—over 110 times greater activity and a melting temperature improvement of 10.6°C in a low concentrated buffer.

Detailed insights into the mechanisms behind these improvements were obtained through X-ray crystallography and molecular dynamics simulations, which highlighted structural changes responsible for the enzyme’s increased stability and activity. These results mark a pivotal advancement in the development of PET hydrolases suitable for industrial use.

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Poster 165

Development of a 3D-Printed Artificial Hand with Functional Gripping Mechanisms Based on Soft Robotics

J. Focking[1], D. Riemer[2], A. M. Bloße[1]

[1]Innovation Center Computer Assisted Surgery (ICCAS), Leipzig, Germany, [2]University of Applied Sciences (HTWK Leipzig), Faculty of Engineering, Leipzig, Germany

Introduction:

The human hand is a dexterous and powerful tool. This work focuses on designing and producing a 3D-printed artificial hand using soft robotics, emphasizing flexible materials and pneumatic actuation to mimic human hand functions for enhanced dexterity in automation of complex scenarios.

Methods:

The artificial hand replicates human joints with five identical fingers, including metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints. It combines soft resin and rigid PLA components, all 3D-printed for complex design and uniform quality with minimal post-processing. The fingers were printed with a flexible UV-curable resin. Mechanical properties were tested for lifting a mobile ultrasound device. Fingers were mounted on a rigid PLA metacarpus. Pneumatic chambers are controlled by electric valves and operate below 1 bar. Bending angles and exerted forces were measured using a Bosche S40S load cell.

Results:

Each finger achieves flexion angles of 91°, 66°, and 50° at the respective joints. At 0.72 bar pressure, each finger generates approximately 1 N of force.

Conclusion:

The 3D-printed hand mimics human finger bending through pneumatic actuation, capable of lifting a mobile ultrasound device and similar objects, making it suitable as an assistance end-effector in medical applications. However, the force exerted by a single finger is significantly lower than that of a human finger. Future work should enhance the hand's force generation to improve grip strength, essential for effective object manipulation and expanding medical applications.

Poster 166

Establishing of a human ex vivo bone regeneration model to find a therapeutic approach for aseptic osteonecrosis

J. Kubat[1], F. Mitrach[1], B. Burghardt[2], J. Wach[3], D. Halama[4], A. König[5], M. Hacker[6], S. Kalkhof[2], E. Güresir[3], M. Schulz-Siegmund[1]

[1]Leipzig University, Faculty of Medicine, Institute of Pharmacy, Leipzig, Germany, [2]Fraunhofer IZI, AG Proteomics, Leipzig, Germany, [3]University of Leipzig Medical Center, Clinic and Polyclinic for Neurosurgery, Leipzig, Germany, [4]University of Leipzig Medical Center, Clinic and Polyclinic for Oral and Maxillofacial Surgery, Leipzig, Germany, [5]University of Leipzig Medical Center, Polyclinic for Dental Prosthetics and Materials Science, Leipzig, Germany, [6]HHU Düsseldorf, Institute for Pharmaceutical Technology and Biopharmacy, Düsseldorf, Germany

The necessity of creating bone defects in connection with neurosurgical procedures can subsequently lead to wound healing defects, which in rare cases can cause the reimplanted bone tissue to die. One of these complications is the aseptic osteonecrosis, which is a long-term side effect especially of hemicraniectomies but also of craniotomies. Craniotomies are a common neurosurgical procedure to treat diseases like aneurism or brain tumors.

The long-term aim of our project is to find a therapeutic approach to prevent and heal aseptic osteonecrosis employing tissue engineering strategies. To this end, we aim to investigate the use of osteogenic microtissues as osteogenic elements consisting of crosslinked gelatine microparticles and osteogenic cells. Gelatine microparticles serve as cell adhesive substrate that on the one hand reduce cell density in the spheroid cultures and on the other hand serve as a delivery system for siRNA to silence anti-osteogenic proteins and support bone regeneration. In order to investigate the therapeutic potential of these microtissues, we aim to develop a human ex vivo model for cranial bone defect regeneration. To this end, we use small bone pieces taken from neurosurgical operations that would be discarded otherwise. The microtissues are precultured in osteogenic medium and subsequently cocultured with such bone pieces to investigate the interactions between bone tissue and microtissues. We expect that this model will help us to explore the effects of different siRNAs on bone regeneration.

Poster 167

Inter- and intra-individual variability of the human seminal plasma metabolome

J. Blaurock[1], S. Grunewald[1], K. M. Engel[2]

[1]Leipzig Reproductive Health Research Center (LE-REP), Andrology Unit, Department of Dermatology, Allergology and Venereology, Leipzig University Medical Center, Leipzig, Germany, [2]Institute for Medical Physics and Biophysics, Faculty of Medicine, Leipzig University, Germany

Background:

Metabolomic studies provide insights into the molecular composition of seminal plasma far beyond the spermiogram. The inter- and intra-individual variability of individual parameters in conventional spermiograms is well known. The magnitude of such fluctuations in the seminal plasma metabolome is largely unknown and was therefore the subject of this study.

Materials and Methods:

A comparative analysis of the metabolome (Biocrates, AbsoluteIDQ p180 kit) was performed in ejaculates from 15 healthy donors at an average interval of 8 weeks. In addition to the intraclass correlation coefficient (ICC), the coefficients of variation within (CVW) and between persons (CVB) were calculated for each metabolite.

Results:

The majority of seminal plasma metabolites (75%) measured by targeted LC-MS/FIA-MS were within the measurable range. Significant intra-individual variations were observed for 18 metabolites. The variability was higher when the sperm concentration differed by more than 25%. Biogenic amines were the least reliable analytes over time, while e.g. sphingomyelins were stable over time in seminal plasma. Inter-individual differences were mainly found for ether-bound glycerophosphatidylcholines and were lowest for amino acids.

Conclusion:

For the majority of metabolites the measurement of a single sample is sufficient. However, highly variable metabolites should be interpreted with caution. We recommend a stratified analysis by sperm concentration to avoid a possible influence of different sperm concentrations on metabolite levels.

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Poster 168

Investigation of the impact of polymerization conditions on the properties of cross-linked gelatin methacrylate hydrogels

J. Krieghoff, M. Geng, J. Ebrahim, M. Schulz-Siegmund

Institut für Pharmazie, Pharmazeutische Technologie, Medizinische Fakultät, Leipzig, Germany

Introduction:

Gelatin methacrylate (GelMA) is a widely researched material that is produced by modification of gelatin, a degradation product of naturally occurring collagen, with methacryloyl groups. Through polymerization of the methacryloyl functionalities, GelMA can be cross-linked to form hydrogels that do not show melting at physiological temperatures. Hydrogels from GelMA have been investigated for a variety of biomedical purposes, from tissue engineering scaffolds to microparticles for drug delivery.

Objective:

The properties of a cross-linked GelMA (cGelMA) hydrogel depend on the polymerization process. We investigated the effect of different photoinitiators, varied degrees of methacrylation (DoM) of GelMA as well as introduction of co-polymerized moieties on the properties of the resulting gels.

Materials and methods:

GelMA was synthesized from gelatin through adaptation of a published approach. DoM was quantified by NMR and colorimetric assay. Properties of the UV-cross-linked gels were quantified by oscillation rheology for both prefabricated gels as well as *in-situ* gelation.

Results and conclusion:

Gelation kinetics accelerated and mechanical properties increased for gels made from GelMA with increasing DoMs from 40%-95%. Of three investigated photoinitiators, LAP (lithium phenyl-2,4,6-trimethylbenzoylphosphinat) yielded the most stable hydrogels. Co-polymerization of methacrylic acid slowed gelation rate, whereas co-polymerization of *N*-vinyl pyrrolidone increased it. Co-polymerization of acryloyl morpholine resulted in softer gels at physiological temperatures.

Poster 169

Method development for the in-depth analysis of the human cranial proteome – Towards the correlation of the human cranial proteome to bone regeneration following neurosurgical procedures

B. M. Burghardt[1], J. Kubat[2], J. R. Schmidt[1,3], J. Wach[4], J. Lehmann[1,3], E. Güresir[4], M. Schulz-Siegmund[2], S. Kalkhof[1,3,5]

[1]Fraunhofer Institute for Cell Therapy and Immunology IZI, Department of Preclinical Development and Validation, Leipzig, Germany, [2]Leipzig University, Faculty of Medicine, Pharmaceutical Technology, Institute of Pharmacy, Leipzig, Germany, [3]Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIM, Frankfurt/Main, Hanover, Leipzig, Germany, [4]University of Leipzig Medical Center, Department of Neurosurgery, Leipzig, Germany, [5]University of Applied Science Coburg, Institute for Bioanalysis, Coburg, Germany

Cranial neurosurgery is performed for medical indications like brain tumors, vascular disorders or traumatic brain injuries, necessitating the temporary removal of a section of the cranial bone. Removal and reimplantation of bone tissue can lead to post-operative complications related to bone regeneration, like aseptic osteonecrosis. We aim to identify causes and predictors for aseptic osteonecrosis following neurosurgical procedures using mass spectrometry-based proteome analysis of non-reimplantable human bone fragments. Therefore, a sample preparation method for the in-depth analysis of human cranial proteome must first be developed.

Proteins were extracted from whole bone fragments or pulverized bone tissue using a two-step extraction protocol and either directly digested to peptides or pretreated with a collagenase to deplete high abundant collagen. Finally, samples were analyzed using protein mass spectrometry (timsTOF Pro 2; Bruker, Bremen, Germany).

Extraction of proteins from pulverized bone tissue in combination with depletion of collagen (collagenase/protein ratio 1:20) enables the quantification of more than 2500 proteins, which can be annotated to cellular compartments, biological processes and signaling pathways that are potentially relevant in downstream analysis.

Proteome profiles of over 100 patients will be analyzed and retrospectively correlated with clinical data to identify predictors and causes of aseptic osteonecrosis following cranial neurosurgery. This may enable preventive measures to be initiated at an early stage, and thus minimize the incidence.

Poster 170

Multi-omics profiling of bone regeneration in diabetes links healing impairment with increased mast cell activity

V. Wiltzsch[1], D. B. Dias[2], J. R. Schmidt[1], W. L. Chan[2], J. Lehmann[1,3], J. A. Kirwan[4,5], P. S. Poh[2], S. Kalkhof[1,3,6]

[1]Department Preclinical Development and Validation, Fraunhofer Institute for Cell Therapy and Immunology, Leipzig, Germany, [2]Julius Wolff Institute, Berlin Institute of Health at Charité - Universitätsmedizin Berlin, Germany, [3]Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD, Frankfurt/Main, Hanover, Leipzig, Germany, [4]BIH Metabolomics, Berlin Institute of Health at Charité Universitätsedzin, Berlin, Germany, [5]Max-Delbrück-Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany, [6]Institute for Bioanalysis, University of Applied Science Coburg, Germany

Type 2 diabetes mellitus impairs bone healing and complicates the treatment of critical-sized bone defects. Understanding the molecular mechanisms is crucial for optimizing biomaterial-guided bone regeneration.

This study examines bone healing over 42 days post-surgery in a diabetic rat femur defect model. We developed the first sequential multi-omics extraction protocol for bone tissue, enabling mass spectrometry-based metabolome and proteome analyses of explants at 21 and 42 days post-surgery. Results from differential abundance and functional analyses were integrated with µCT imaging and histology to correlate molecular findings with clinical outcomes.

The protocol allowed quantification of approximately 4,000 proteins and over 500 metabolites, providing an in-depth perspective on bone healing under diabetic conditions. Integration with histological data revealed decreased levels of structural proteins essential for soft callus formation and prolonged inflammation in diabetic animals. Further, an imbalanced population of mast cells (MCs), characterized by clusters of MC proteases, elevated levels of the MC mediator histamine, and an increased MC presence, was identified in regenerating tissue, suggesting MCs are potential targets in compromised diabetic bone healing.

This study demonstrates the effectiveness of our new multi-omics extraction protocol, offering critical insights into molecular disruptions in diabetic bone regeneration. Our ongoing preclinical study assesses interventions targeting dysregulated mast cell activity to enhance bone regeneration in diabetes.

Diseases of Civilisation | Obesity

Immunology | Infectiology | Inflammation

Clinical and Molecular Oncology

Clinical Research

Digital Health

Life Science Research

Psychology, Cognition and Public Health I

Psychology, Cognition and Public Health II

Molecular and Systemic Neurobiology

Biotechnology | Protein Biochemistry | Pharmaceutical Chemistry

Biomaterials | Translational Regenerative Medicine | Drug Delivery

Molecular Biology | Biomedicine

Poster 171

Performance of CAD/CAM manufactured partial crowns: the three-dimensional material layering and adhesive bonding as a µCT imaging approach in human dentistry

O. Giesa[1], D. Ziebolz[1], T. Meißner[1], N. Oberück[1], P. D. Lösel[2], S. Handschuh[3], R. Haak[1], E. Schulz-Kornas[4]

[1]Universität Leipzig, Poliklinik für Zahnerhaltung und Parodontologie, Leipzig, Germany,
[2]The Australian National University, Department of Materials Physics, Canberra, Australia,
[3]Veterinärmedizinische Universität Wien, VetCore Facility for Research/Imaging, Vienna, Austria,
[4]Universität Leipzig, Germany

Objective:

Development of a semi-automated 3D method for in vitro evaluation of adhesive luting of CAD/CAM partial crowns (PC) made of lithium disilicate ceramic (LS2) or nanohybrid composite (RBC) by micro-computed tomography (µCT).

Materials and methods:

16 lower molars were restored with CAD/CAM PC made of LS2 (IPS e.max® CAD; n=8) or RBC (Tetric® CAD; n=8). After adhesive luting (Variolink® Esthetic D; LC), samples were stored in water for 90 days (t1) and subjected to thermomechanical loading (TCML) (5x600 5°C/55°C, 1.2x106x50N, 60mm/s, 1.6Hz; t3). PC were analysed using a new approach (software: Avizo, Biomedisa). The parameters LC volume (VLC), LC thickness (TLC), PC contact surface relative to tooth structure (CPT) were analysed using ANOVA and Tukey HSD test.

Results:

The new approach reduced the processing time of by app. 75%. LS2 and RBC did not differ in VLC and TLC (VLC LS2/RBC t1: 21.1±5.3/19.2±4.0; t3: 20.9±5.4/19.0±3.9 mm³; TLC LS2/RBC t1: 213.44±80.4/204.4±83.2; t3: 212.9±81.3/205.7±84.0 µm). VLC and TLC remained constant over time in both materials. CPT was smaller at t1 for LS2 (2.2±1.2%) than for RBC (4.5±1.3%) and stable over time for both materials.

Summary:

Using a the new approach, LC including voids and PC contact surfaces of CAD/CAM-manufactured and adhesively luted LS2/RBC PC are visualised before/after TCML. RBC PC have larger PC contact surfaces to the tooth structure, which presumably occurred in the marginal area during cementation.

Poster 172 siRNA Delivery via Cross-Linked Gelatine Microparticles for Bone Tissue Engineering

F. Mitrach[1], A. Liebezeit[1], A. H. Springwald[1], M. Schmid[2], S. Hinkelmann[1], C. Wölk[1], M. C. Hacker[2], M. Schulz-Siegmund[1]

[1]*Pharmaceutical Technology, Institute of Pharmacy, Faculty of Medicine, Leipzig University, Germany,*
[2]*Institute of Pharmaceutics and Biopharmaceutics, Heinrich-Heine-University Düsseldorf, Germany*

Introduction:

BMP-2 is known to be an important growth factor to support regeneration of vascularized bone tissue. However, administration of BMP-2 leads to upregulation of antagonists that partially neutralize effects. siRNAs could be a promising approach to enhance BMP-2 effects by decreasing antagonist expression. To study effects, we developed a microtissue-based approach where we aggregated cells with cross-linked gelatine microparticles (cGM) that can serve as siRNA delivery system.

Methods:

cGM were loaded with siRNA against the BMP-2 antagonist Chordin via oligomer-stabilized CaP nanoparticles [1]. After loading, we aggregated cGM with hMSCs to form microtissues and stimulated differentiation with osteogenic supplements as BMP-2. To study effects of Chordin silencing on angiogenic processes, vascular microtissues were established and combined with osteogenic microtissues in a fibrin hydrogel.

Results:

The loading of cGM with siRNA-carrying CaP-NP resulted in an increased, successful silencing of Chordin. We found that Chordin silencing improved BMP-2 effects on osteogenic differentiation, which led to a remarkably increased mineralization and upregulated secretion of the important pro-angiogenic factor VEGF.

Conclusion:

Here, we provide an interesting microtissue-based approach to study effects of siRNA on bone tissue engineering. In a first study, we observed that siRNA-mediated silencing of the BMP-2 antagonist Chordin increases synergistic interaction between osteogenic and angiogenic processes.

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Poster 173

The influence of 3D fibrillar collagen and fibrin scaffolds on macrophage immune response

L. M. Rhein, T. Pompe, K. Pietsch

Leipzig University, Institute of Biochemistry, Biophysical Chemistry, Leipzig, Germany

During wound healing the extracellular matrix (ECM) undergoes significant remodeling that might trigger polarization of macrophages (MPh) into inflammatory or anti-inflammatory phenotypes. While fibrin is enriched in early wound tissue, this wound closure is replaced mainly by collagen during wound healing. As it is not fully understood whether and how the ECM influences the phenotype of MPh detailed MPh phenotype studies are required focusing on the direct interaction of MPh with fibrin and collagen.

For this purpose we derived MPh from THP-1 cells with the use of the phorbol ester PMA and polarized these MPh into an inflammatory (M1) or anti-inflammatory (M2) phenotype by using either a combination of LPS and interferone γ (IFNγ) or interleukin 4 (IL4) alone. During those experiments the cells resided in either collagen scaffolds of varying topological properties or a fibrin scaffold. MPh secreted cytokines as well as localization of M1/M2 marker proteins were investigated by ELISA and fluorescence microscopy to assess the MPh phenotype.

Our results show that THP-1 cells were successfully polarized into M1 MPh using this approach within 3D scaffolds. However, current protocols fail to induce M2 MPh polarization. Our results further show that 3D fibrin scaffolds promote the M1 MPh polarization. M2 MPh polarization was shown to be supported in 3D fibrin scaffolds, too. In 3D collagen networks M2 MPh polarization was found to be dependent on network topology, with only networks of thin, flexible fibrils supporting M2 polarization after differentiation with 50 ng/ml PMA.

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Talstraße 33
04103 Leipzig
Tel.: 0341 97 36700
dekanat.lw@uni-leipzig.de
www.lw.uni-leipzig.de/

Poster 174

Towards analysis of exogenous siRNA loading homogeneity of bovine milk extracellular vesicles

M. Kieckhöfer[1], C. Schmidt[2], F. Mitrach[1], B. Demir[3], C. Wölk[1], M. Schulz-Siegmund[1], M. C. Hacker[3]

[1]Institut für Pharmazie, Pharmazeutische Technologie, Leipzig, Germany, [2]Division of Rheumatology, Department of Endocrinology, Nephrology, Rheumatology, Leipzig, Germany, [3]Institut für pharmazeutische Technologie und Biopharmazie, Düsseldorf, Germany

Introduction:

Bovine milk extracellular vesicles (mEV) provide interesting options as oral drug delivery system due to their abundance, accessibility, and stability in the gastrointestinal tract. In prior studies we established an mEV loading strategy yielding an average of 150 siRNA copies per mEV. However, we assume the siRNA distribution is uneven. To analyze the siRNA distribution in mEV, we investigated nanoparticle tracking analysis (NTA), imaging flow cytometry (iFCM) and nano flow cytometry (nFCM) to distinguish loaded and non-loaded mEV.

Results:

NTA detected distinctly less particles when changed from scatter (SSC) to fluorescence mode and needed an 100x increase in sample concentration. Colocalization to determine siRNA within mEV was not possible. 10% of the mEV showed fluorescence.

With iFCM no particles were visible in SSC. With MG488 labeling, mEV detection and colocalization were enabled but no particle size is provided. iFCM detected 18% loaded mEV.

With nFCM colocalization of fluorescence and SSC is possible, providing information on siRNA loading, size and particle concentration. nFCM showed loading for larger particles. Overall loading efficiency was determined at 50% for mEV.

Conclusion:

We confirmed uneven loading of mEV. Our findings show that direct measurement of siRNA loading of single mEVs is possible but may be limited by fluorescence yield per vesicles, depending on the instrument. For loading assessment, we found colocalization crucial. With iFCM and nFCM colocalization is possible but fluorescence detection might be less sensitive compared to NTA.

Poster 175

Use of 2D cell culture and air-liquid interface (ALI) culture for comparing various polyethylenimine (PEI)- and polypropylenimine (PPI)-based polyplexes for their potential in pulmonary delivery

S. Noske, A. Ewe, A. Aigner

Leipzig University, Rudolf-Boehm-Institute for Pharmacology and Toxicology, Clinical Pharmacology, Leipzig, Germany

According to the WHO, lung tumors are the leading cause of cancer related deaths worldwide. To address this issue, the development of new therapeutic strategies is required. In this context, the exploration of RNA interference (RNAi) via direct delivery of siRNAs has gained increasing interest.

However, naked siRNAs exhibit some unfavorable properties, including their proneness to degradation and the resulting poor biodistribution and cellular uptake. The formulation into suitable (nano-)carriers can be used to address this bottleneck. In this context, polymeric nanoparticles, such as polyethylenimine (PEI)- and polypropylenimine (PPI)-based complexes, have been described previously to be very efficient for siRNA delivery.

In this study, a variety of PEIs, including different structure classes and chemical modifications, as well as a tyrosine-grafted fourth-generation PPI were compared for their transfection efficacy in A549-eGFP/Luc and 16HBE-eGFP/Luc cells. The initial testing in 2D cell culture revealed differences between the nanocarriers, with some polymers also showing profoundly different knockdown efficacies dependent on the complexation buffer. Furthermore, the more complex ALI system was used to monitor the reporter gene knockdown as well as the siRNA uptake over time.

In conclusion, we identified nanoparticles mediating high knockdown efficacies not only in 2D cell culture, but also in a more complex air-liquid interface system. The data presented here will provide the basis for further exploration of polymeric nanoparticles in pulmonary siRNA delivery.

Poster 176

GUK1, IRF8, and CD74 are novel regulators of adipocyte differentiation associated with childhood obesity

C. Zeitler[1], O. Karges[1], A. Berthold[1], J. Felix[2],
C. Vales-Villamarin Fernandez[1], A. Körner[1,3], K. Landgraf[1,3]

[1]Leipzig University, Faculty of Medicine, University Hospital for Children and Adolescents, Center for Pediatric Research, Leipzig, Germany, [2]University Medical Center Rotterdam, Department of Pediatrics, Erasmus MC, Rotterdam, Netherlands, [3]Helmholtz Institute for Metabolic, Obesity and Vascular Research (HI-MAG) of the Helmholtz Zentrum München at the Leipzig University and University of Leipzig Medical Center, Germany

Early childhood is a critical phase for the development of sustained obesity. The increase in body fat is accompanied by alterations in adipose tissue (AT) biology, leading to adipocyte hypertrophy and inflammation, which contribute to comorbidities such as metabolic and cardiovascular diseases. The aim of this project is to discover novel regulators affecting the development of childhood obesity and AT dysfunction. We selected 10 candidate genes for investigation based on OMICs association studies in children. These genes demonstrated an association between BMI-SDS and expression in blood cells and AT cells. We focused on genes that showed a significant association with adipocyte hypertrophy in AT samples of children and/or regulation during adipocyte differentiation *in vitro*. Nine genes were significantly regulated during adipocyte differentiation as shown by qPCR. To assess their potential role in adipocyte formation, we used siRNA-mediated gene knockdown. All genes were successfully downregulated throughout the entire adipocyte differentiation process. Nile Red/Hoechst cell counting—where Nile Red fluorescence marks neutral fat—showed that *GUK1, IRF8, SOX5, PTGES3*, and *CD74* had a significantly lower number of lipid-containing adipocytes. This observation was confirmed for *GUK1, IRF8,* and *CD74* using Oil Red O staining and absorbance measurement as an indicator of the amount of accumulated fat. In conclusion, our results suggest that *GUK1, IRF8*, and *CD74* are novel regulators of adipocyte differentiation associated with childhood obesity.

Poster 177

Antiplatelet and anticoagulant compound (APAC) restricts thromboinflammation to ameliorates myocardial ischemia reperfusion injury

A. Arif[1], S. Fatima[1], H. Khawaja[1], C. Mäder[2], S. Gaul[2], J.-N. Boeckel[2], R. Lassila[3], B. Isermann[1], K. Shahzad[1]

[1]Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, Universitätsklinikum Leipzig University, Germany, [2]Klinik und Poliklinik für Kardiologie, Universitäts-klinikum Leipzig University, Germany, [3]Research Program Unit in Systems Oncology, Faculty of Medicine, University of Helsinki and Helsinki University Hospital, Comprehensive Cancer Center, Department of Hematology, Helsinki, Finland

Myocardial injury (IRI) is hallmarked by thromboinflammation, both thrombotic and inflammatory effects contribute to organ damage. Therapies which not only target coagulation but simultaneously convey cytoprotective effects by dampening inflammatory mechanisms are expected to provide benefits. We speculate that a novel compound conveying both antiplatelet and anticoagulant (APAC) functions may ameliorate thromboinflammation triggered by myocardial IRI. Wild type mice were either pretreated or post-treated with APAC (0.5mg/kg, intravenously) or PBS (control). Myocardial IRI was induced via LAD ligation (30 min ischemia followed by 24 h of reperfusion). APAC pretreatment efficiently reduced infarct size, inhibited coagulation and platelet activation. Mechanistic studies revealed that APAC restricts NLRP3 inflammasome activation, which is known to convey a pathogenic in myocardial. Congruently APAC prevented inflammatory cell infiltration into injured heart tissue and restricted the expression of cytokines IL-1β, IL-6, and TNFα. Importantly APAC treatment post myocardial IRI likewise provide cardioprotection. The constitutively active Nlrp3A350V mutation abolished the effect of APAC, indicating that NLRP3 suppression is important for APAC-mediated cardioprotection. APAC also alleviated myocardial fibrosis and improved the LV ejection fraction, output, and stroke volume at 28 days after IRI, indicating beneficial cardiac effects beyond the effects on acute tissue injury.

Poster 178

BRET-based detection of succinate

F. Flemming[1], G. Kleinau[2], A.-D. Liebing[1], P. Scheerer[2], C. Stäubert[1]

[1]Leipzig University / Rudolf Schönheimer Institute of Biochemistry, AG Stäubert, Leipzig, Germany, [2]Charité - Universitätsmedizin Berlin, Germany

Succinate is a key intermediate of the tricarboxylic acid cycle, a fundamental pathway governing aerobic energy metabolism. Novel physiological roles for succinate have emerged including its involvement in muscle fiber remodeling and immunity. Accumulation of succinate has been observed in various pathological states including chronic inflammation, ischemia and cancer. Despite succinate‘s increasing significance, current methodologies for its detection *in vivo* or in live cells remain inadequate. This project aims to fill this gap with a succinate-specific BRET-Sensor that allows label-free detection and dynamic measurements of succinate concentrations under different metabolic conditions.

Diseases of Civilisation | Obesity

Immunology | Infectiology | Inflammation

Clinical and Molecular Oncology

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Psychology, Cognition and Public Health I

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Biotechnology | Protein Biochemistry | Pharmaceutical Chemistry

Biomaterials | Translational Regenerative Medicine | Drug Delivery

Molecular Biology | Biomedicine

Poster 179

Characterization of Stress Induced Stem Cell-Derived Ductal Organoids by Mutated KRAS Expression

M. Schrottenholzer, M. Schricker, A. Sailer, M. Meier

Institute of Biochemistry, BBZ, Leipzig University, Germany

Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies, with limited understanding of its early-stage progression. Consequently, effective methods for early diagnosis are lacking. A prevalent genetic alteration in PDAC is the KRAS-G12D mutation, which is present in the majority of patients and serves as a key driver mutation. KRAS-G12D is implicated in the transition of normal pancreatic tissue to the earliest stage of pancreatic intraepithelial neoplasia (PanIN-1), a precursor lesion to PDAC.

In this study, we generated human induced pluripotent stem cells (hiPSCs) transfected with an inducible KRAS-G12D construct and differentiated them into pancreatic duct-like organoids (PDLOs). The newly established KRAS-G12D-hiPSC cell line retained pluripotency. To characterize the new cell line immunofluorescence, western blotting, PCR and genome-sequencing were performed. The differentiation efficiency was confirmed by flow cytometry. Upon induction of KRAS-G12D expression, the PDLOs underwent neoplastic transformation, providing insight into the genetic and histological changes associated with the early development of PDAC. This model offers a valuable platform for studying the initial molecular events that drive PDAC progression and opens the possibility of researching early-PDAC-stage diagnosis and medication.

Poster 180 Exploring G protein-coupled Signaling of vasodilatory Kynurenine Metabolites

F. Gilch[1], S. Stehr[1], S. Laudi[1], M. T. Völker[1,2], A. Kaiser[1,2]

[1]Leipzig University / Rudolf Schönheimer Institute of Biochemistry, AG Stäubert, Leipzig, Germany, [2]Charité - Universitätsmedizin Berlin, Germany

Introduction:

Tryptophan metabolites (TrpM) such as kynurenine (Kyn) are synthesized in the inflamed lung and possess vasodilatory properties.[1] They contribute to the impairment of hypoxic pulmonary vasoconstriction as seen in acute respiratory distress syndrome.[2] Molecular targets of TrpM, however, remain poorly characterized. Our aim is to investigate whether TrpM signal via G protein-coupled receptors (GPCR).

Methods:

Primary human pulmonary artery smooth muscle cells (HPASMC) and human pulmonary artery endothelial cells (HPAEC) were stimulated with TrpM under basal and interferon-γ-induced inflammatory conditions. G_i/G_s and G_q activation were measured using competitive immunoassays, $G_{12/13}$ activity by using luminescent biosensors.[3]

Results:

In HPASMC, the G_i pathway was activated by Kyn, Kyn-acid, 5-hydroxyindoleacetic acid (5-HIAA) and tryptophan, while Kyn-acid and 5-HIAA also activated G_q. In HPAEC, G_i was activated by Kyn, 5-HIAA and tryptophan, but not Kyn-acid. Activation of G_s or $G_{12/13}$ pathways was not detected in either cell line. GPCR activation was similar in basal and inflammation conditions suggesting that the corresponding receptors are constitutively expressed.

Conclusion and Outlook:

We show that different TrpM stimulate endogenous GPCR in primary pulmonary artery cells and activate G_i and partially G_q pathways. Candidate target GPCR are now being identified using mRNA sequencing.

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Poster 181

Exploring substrate specificity of α-arrestins in cellular models of pathological states

I. Paetzolt, S. Stehr, A. Kaiser

University of Leipzig Medical Center, Department of Anesthesiology and Intensive Care, Leipzig, Germany

α-Arrestins are the phylogenetically oldest members of the arrestin family.[1] First studied in yeast, α-arrestins are involved in the ubiquitinylation and degradation of membrane proteins, including amino acid and glucose transporters and are hence closely related to cellular metabolism. The functions and specificity of the six conserved proteins in humans (ARRDC1-5, TXNIP) are not well understood. Some of the α-arrestins are associated with glucose metabolism regulation in human cells and knockout of ARRDC4 in mouse is reported to improve cardiac function and overall survival after myocardial infarction through elevated glucose uptake.[2] Yet the substrate specificity and mode of interaction is currently unknown. We hypothesize an association of α-arrestins with other transport proteins that regulate cellular metabolism in healthy and diseased states.

We first aimed to investigate the expression profile of the six human α-arrestins in different cellular models. Initial RT-PCR experiments in HEK293 showed mRNA expression of ARRDC1-4 and TXNIP but not ARRDC5, which seems to be specific for testis.[3] The corresponding cDNA was then used to create expression plasmids. Next, we plan to investigate how different α-arrestins affect uptake of glucose and essential amino acids. With this, we aim to better elucidate α-arrestin function and substrate specificity in humans. We expect that a targeted modulation of α-arrestin function can be useful in diverse pathologies.

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Poster 182 Generation of novel Drosophila models for the study of NEDCAM disorder

P. Goldine[1], L. Pellizzoni[2], B. Blanco-Redondo[1]

[1]Rudolf Schönheimer Institute for Biochemistry, Leipzig, Germany, [2]Columbia University Medical Center, New York, United States of America

The RNA-binding protein GEMIN5 is a key component of the survival motor neuron (SMN) complex, which functions in RNP assembly and RNA regulation.

SMN gene mutations lead to the autosomal, recessive inherited neurodegenerative disease spinal muscular atrophy (SMA). In contrast, disruptions of the GEMIN5 gene cause a recently identified neurodevelopmental disorder with cerebellar atrophy and motor dysfunction (NEDCAM).

This project aims to elucidate the effects of disease-causing GEMIN5 mutations and the pathophysiology of NEDCAM. To adress the current lack of animal models for NEDCAM, we plan to generate a complete knock-out of GEMIN5 (also known as *rigor mortis*) in Drosophila melanogaster (DM*)* using the CRISPR/Cas9 system. In parallel, we will introduce an attP cassette to aid the generation of multiple knock-in lines expressing WT or pathogenic GEMIN5 variants for further characterization. This approach enables us to study the disease through physiological levels of gene expression, avoiding potential confounding effects that might arise from gene overexpression.

Furthermore, recent studies suggest an eminent reciprocity between SMN and GEMIN5, arguing that overexpression of SMN could rescue the lethal phenotype observed in GEMIN5-depleted DM. By replicating a series of crosses from previous studies we want to investigate this interaction and wheter or not SMN overexpression can rescue the phenotype.

Our goal is to determine whether SMA and NEDCAM share a common pathogenic pathway and if SMN inducing therapies approved for SMA could be a viable strategy for treating NEDCAM.

Poster 183 Genotypic and Phenotypic Characterization of Families with Proximal Renal Tubular Acidosis Caused by SLC4A4 Variants

S. Stopp, F. Baalmann, J. de Fallois, F. Petzold

Uniklinik Leipzig, MK III Nephrology, Leipzig, Germany

Ultra-rare proximal renal tubular acidosis (pRTA, MIM #604278) is characterized by defective reabsorption of HCO3- with subsequent metabolic acidosis and hypokalemia. PRTA is caused by pathogenic variants in *SLC4A4* (Igarashi 1999) encoding the Na+/HCO3- co-transporter NBC1. To date, 27 pathogenic variants have been reported leading to chronic kidney disease, intellectual disability, skeletal, ocular and dental anomalies (Kurtz 2013; Igarashi 2002). No specific therapy for pRTA is available and patients rely on lifelong substitution. Recently, a prolonged-release combination of potassium citrate and hydrogen carbonate (Sibnayal) has been approved for the treatment of distal RTA (Bertholet-Thomas 2021).

We describe a pRTA family with three affected females of consanguineous healthy parents who presented with intellectual disability, short stature, impaired vision and genua valga. Laboratory analysis revealed severe metabolic acidosis, hypokalemia and hypercalciuria. Genetic analysis revealed a novel homozygous likely pathogenic *SLC4A4* variant (c.1170G>C, NM_001098484) located in the N-terminal region of NBC1. IF studies on patient derived urinary renal epithelial cells (URECs) suggest preserved *SLC4A4* expression with pH dependent pattern. Preliminary data indicates that substitution with Sibnayal might at least be non-inferior to the standard of care with lower pill count and fewer side effects. Further quantitative analyses are required to evaluate the functional impact of the mutated *SLC4A4*. Investigation of Sibnayal substitution will continue to assess long-term effects.

Poster 184

HBV genotype E expression model exhibits lower HBV RNA and viral protein levels compared to other genotypes in vitro

R. Kamga Wouambo[1], M. Pfefferkorn[1], F. Lehmann[2], M. Piehler[1], M. Matz-Soja[1], T. Berg[1], D. Glebe[3], F. van Bömmel[1]

[1]Division of Hepatology, Department of Medicine II, University of Leipzig Medical Center, Germany, [2]Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Institute of Virology, Berlin, Germany, [3]Institute for Medical Virology, National Reference Centre for Hepatitis B viruses and Hepatitis D viruses, Justus Liebig University Giessen, Germany

Background:

Hepatitis B virus genotype E (HBV-E) predominates in sub-Saharan Africa, a region with high incidence of HBV-associated hepatocellular carcinoma. However, little is known about its replication capacity and pathogenesis. This project aims to compare a developed expression model of HBV-E with other HBV genotypes.

Method:

1.5mer overlength plasmids of HBV-E and other HBV wildtype genotypes (A2, B2, C1, D1) were generated (source:WHO reference panel). Plasmids were separately transfected into Hepatoma cells for 48h and followed-up to 7 days post transfection(dpt). HBcAg-immunostaining and biomarkers measurement(HBV DNA, HBV RNA, total HBsAg, MHBs, HBeAg) were done.

Results:

Expression of HBV pregenomic RNA was assessed by HBcAg-staining after 7days, with lower HBcAg-expression in HBV-E transfected cells. Interestingly, similar mean HBVDNA(logcp/mL) were found in all genotypes(7.8-9.6 log cp/mL). In constrast, mean HBVRNA(logcp/mL) and HBsAg(log ng/mL) were lower in HBV-E ([6.6 in HBV-E vs. 8.1-8.4 logcp/mL in others] and [1.7 in HBV-E vs. 2.8-3.4 logng/mL in others]) after 7dpt, respectively. Moreover, MHBs (logng/mL) was undetectable in HBV-E after 2(0.0 for HBV-E vs. 1.3-1.7 logng/mL for others) and 7dpt(0.0 for HBV-E vs. 2.1-2.7 logng/mL for others). In addition to lower biomarker, a high nucleus localisation of HBcAg was more found in HBV-E.

Conclusion:

The newly established HBV-E expression model shows similar extracellular HBVDNA levels but lower HBVRNA and protein expression in vitro compared to other HBV genotypes. Further characterisation is needed and ongoing.

Poster 185

Iron overload and Wnt Signaling dysregulation drive Lipodermatosclerosis progression

M. Torregrossa[1], A. Grigoryan[2], M. Tamazyan[2], M. Schmidt[3], H. Löffler-Wirth[3], H. Binder[2,3], S. Franz[1]

[1]Leipzig University, Department of Dermatology, Leipzig, Germany, [2]Armenian Bioinformatics Institute, Yerevan, Armenia, [3]Interdisciplinary Centre for Bioinformatics (IZBI), Leipzig, Germany

Chronic venous insufficiency often leads to iron overload in the skin, resulting in lipodermatosclerosis (LDS), a condition associated with a high risk of leg ulcers. This study investigates the pathological mechanisms underlying LDS, highlighting iron overload as a key driver. We developed a novel mouse model of local skin iron overload, which mirrors human LDS. In parallel, we conducted in vitro experiments on human cells to understand underlying mechanisms and validate results found in the animal model. Using a combination of immunofluorescence staining, gene expression and protein analyses, besides in vitro approaches we demonstrate that iron-induced dermal adipose tissue lipolysis and the release of chemokines contribute to monocyte-driven inflammation. Iron overload also repressed Wnt signaling resulting in decreased expression of pro-adipogenic genes and adipose stem cell loss as shown by flow cytometry. Additionally, functional studies confirm that iron overload induces oxidative stress while impairing adipogenesis. scRNA Sequencing and flow cytometry analyses reveal changes in the dermal fibroblast populations from iron mice versus control. Dysregulation of Wnt activation in the dermal compartment was associated with disrupted ECM homeostasis and defective hair follicle growth. Collectively, our findings identify iron overload and Wnt signalling dysregulation as critical factors driving dermal fat loss and extracellular matrix dysfunction in lipodermatosclerosis, suggesting potential therapeutic strategies to prevent venous ulcers and reverse tissue fibrosis.

Poster 186

Next generation sequencing out of the mobile suitcase lab as an early warning system for emerging infectious diseases

A. Ceruti[1], A. Michaelakis[2], M. Bisia[2], G. Balatsos[2], R. M. Kobialka[1], J. R. Palmer[3], M. S. Alam[4], U. Truyen[1], A. Abd El Wahed[1]

[1]Leipzig University, Institute of Animal Hygiene and Veterinary Public Health, Leipzig, Germany, [2]Benaki Phytopathological Institute, Laboratory of Insects & Parasites of Medical Importance, Athens, Greece, [3]Universitat Pompeu Fabra, Barcelona, Spain, [4]International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh

Mosquito-borne diseases are responsible for spillover to around 700 million people each year, including many neglected tropical diseases such as Dengue fever. Case reports are rising over the last decades, as mosquito species flare-up as a result of climate change and globalization. Next generation sequencing technologies offer great advantages for disease outbreak investigation. The aim of this study was to develop a field deployable sequencing platform to identify potential mosquito pathogens, species and host from blood meals.

A rapid extraction reverse purification method was developed using mosquito specimens collected in the field in Greece (Athens) and Dhaka (Bangladesh), including *Culex pipiens*, *Aedes albopictus*, *and -aegypti.* Nucleic acids were isolated using a rapid extraction protocol based on lysis buffer, glass beads, magnetic beads, heating, and vortexing. Oxford Nanopore Technologies rapid barcoding sequencing. A reverse transcription step was performed for RNA targets. All steps were carried out in the fully equipped suitcase lab. A specific offline BLAST database was created to identify mosquito species, host in blood meal, and pathogens.

The species was correctly identified in all samples. Both animal and human DNA could be detected in the mosquito blood meal. Mosquito-associated viruses were detected.

The protocol performed in the suitcase lab allows fast mosquito “footprint” analysis directly in the field, allowing an early warning for mosquito-borne diseases and on-site outbreak investigation.

Poster 187

Plant sterols alter membrane microdomain composition and cellular inflammatory response in microglia

C. Wassermann, M. Reinicke, A. Didio, U. Ceglarek

Universität Leipzig, Institut für Laboratoriumsmedizin, Klinische Chemie und Molekulare Diagnostik, Sektion Klinische Massenspektrometrie, Leipzig, Germany

Plant sterols (PS), structurally similar to cholesterol, are exclusively derived from plants and have demonstrated anti-inflammatory properties in brain (Reinicke *et al*., 2021). Membrane microdomains are rich in cholesterol; facilitate specific cellular signalling, and trafficking by organising free sterols, phospholipids and proteins. This work investigates the impact of PS on inflammatory responses in microglial cells.

SIM-A9 cells were cultured with PS-enriched medium containing varying concentrations of campesterol and sitosterol. The eicosanoid, long-chain fatty acid (LCFA) and sterol composition of membrane microdomains from LPS-activated SIM-A9 cells was analysed by LC-MS/MS following detergent-free extraction (Begcevic Brkovic *et al*., 2023). Additionally, untargeted proteomics and RNA sequencing was conducted. The oxidative stress response was assessed by NO assays.

Microglia cultured with PS, displayed a dose-dependent effect of elevated PS content in membrane microdomains ($p \leq 0.01$) resulting in an increase of LCFAs. Untargeted proteomics revealed a downregulation of HMGCS1, involved in the *de novo* synthesis of cholesterol, and an upregulation of ABCG1, involved in the cholesterol efflux. The NO release of microglia cultured with PS is reduced by 10% ($p \leq 0.05$) after LPS activation, indicating anti-inflammatory effects. RNA sequencing data demonstrated that cells treated prior to LPS activation with PS exhibited a downregulation of inflammatory genes compared to the control.

PS exhibit anti-inflammatory effects as demonstrated by reduced NO release in microglia.

Poster 188

Refinement of FDCP-Mix cell cultivation and promoter optimisation for hematopoietic stem cell research

A. Pak[1], H. Schaller[2], M. Cross[2], S. Uxa[2]

[1]Karolinska Institute, Stockholm, Sweden, [2]University of Leipzig Medical Center, Hematology, Cell Therapy, and Hemostaseology, Leipzig, Germany

FDCP-Mix cells are murine non-leukemic, multipotent hematopoietic progenitor cells that respond to self-renewal and differentiation signals. They share many features of normal stem/progenitor cells. The ability to generate large numbers of cells at defined stages of differentiation has made them particularly useful for studying connections between metabolism and signalling pathways. Our present goal is to characterise the role of the "Non-metastatic 2" (Nme2) nucleoside diphosphate kinase in mediating the cellular response to low energy niche conditions through direct interaction with signalling proteins. On the one hand, we are refining FDCP-Mix culture conditions to better model stem cell metabolism. On the other hand, we are developing viral vectors with which to modulate the expression of wild type and tagged Nme2. To this end, we have focussed on Serpin 2A, a stem cell specific gene. We extrapolated its minimal promoter sequence using the mouse mm39 genome annotation. We cloned this fragment into a lentiviral backbone, replacing the original CMV promoter and driving the expression of an EGFP transgene. We transduced undifferentiated FDCP-Mix cells with this construct and with a range of established viral vectors for comparison. The new promoter directs a level of expression 3-4-fold higher than the CMV promoter does. We are currently assessing the activity in differentiating cells, in which we expect reduced expression, enabling us to direct stem cell specific expression of Nme2 and investigate protein/protein interactions specific to low-energy conditions.

Poster 189 The influence of FPLD2-associated LMNA mutations on endothelial identity and senescence

E. S. Schandert[1], K. Kokot[1], K. Miehle[2], U. Laufs[1], J.-N. Boeckel[1]

[1]*Universitätsklinikum Leipzig, Klinik und Poliklinik für Kardiologie, Leipzig, Germany,*
[2]*Universitätsklinikum Leipzig, Klinik und Poliklinik für Endokrinologie, Nephrologie, Rheumatologie, Leipzig, Germany*

Laminopathies such as Familial partial lipodystrophy type 2 (FPLD2) can be caused by mutations in the LMNA gene, coding for Lamin A/C. As part of the nuclear lamina, Lamin A/C plays an important role in nuclear integrity and chromatin organization. Besides the effects on adipose tissue, early clinical cardiovascular symptoms are observed in FPLD2 patients with LMNA mutations. Senescence or loss of endothelial cells (EC) identity, such as through endothelial-to-mesenchymal transition (EndMT), can lead to cardiovascular diseases.

12 LMNA mutations found in FPLD2 patients were analyzed on their effects on EC identity and integrity to identify potential pathological variants.

LMNA was introduced into a plasmid, mutated and then used to synthesize modified mRNAs for each variant. The transfer of LMNA mRNA in EC resulted in a significant elevation of LMNA expression, whereas some mutations reduced Lamin A/C protein level (c.1445G>A, c.1699-2A>G and c.1930C>T). Overexpression of the LMNA variant c.1444C>T induced EndMT and EC senescence. IF revealed increased nuclear abnormalities after overexpression of LMNA variants c.1304G>A, c.1444C>T and c.1445G>A. This was further enhanced when EC were stressed by additional induction of EndMT resulting in increased nuclear abnormalities for LMNA mutations c.1304G>A, c.1411C>G, c.1445G>A and c.1445G>C.

The results indicate that LMNA mutations affect endothelial identity and survival via a reduction in nuclear integrity.

Poster 190

The role of sex-specific mitochondrial changes in the pathogenesis of fatty liver disease.

C. Bergmann[1], F. Ott[1], C. Körner[1], S. Burbano De Lara Carrillo[2], U. Klingmüller[2], T. Berg[1], M. Matz-Soja[1]

[1]Leipzig University, Division of Hepatology, Clinic and Polyclinic for Oncology, Gastroenterology, Hepatology, Infectious Diseases and Pneumology, Leipzig, Germany, [2]German Cancer Research Center (DKFZ), Systems Biology of Signal Transduction, Heidelberg, Germany

Mitochondria are more than merely the primary source of cellular energy. Their physiological functionality exerts a pivotal influence on energy metabolism, which in turn affects the overall function of the cell. Mitochondrial dysfunction has been identified as a significant contributing factor in the progression of fatty liver disease. However, there is a lack of knowledge regarding the differences between males and females.

To investigate sex-specific changes in mitochondrial functions, an animal study was performed, whereby a western diet (WD) was administered for several time points (13, 26 and 32 weeks) to induce fatty liver disease. A control group of mice was given a standard diet (SD). Liver samples from the mice were processed for proteomic analysis and also underwent measurement of mitochondrial respiration via Seahorse analysis. Proteomics was utilized for a comprehensive core network analysis using Ingenuity Pathway Analysis (IPA) software.

The data of the IPA analysis indicate an inverse effect between the sexes in the WD groups, characterized by up-regulation of essential mitochondrial pathways in females. Unexpectedly, no notable differences are observed between the WD and SD groups over time when considering only mice of the same sex. However, in this context, there is a greater degree of mitochondrial down-regulation in male WD mice.

The results suggest a notable discrepancy between males and females in the progression of fatty liver disease related to mitochondrial functionality, a subject that requires further investigation.

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