MMS SCIENCECON 2026

KEYNOTE

Dr. PHILIPP BAASKE

Vice President LMU

The Munich Medical Student Science Conference : for students of all medicine related fields from around the world

Saturday, 13th of June

9 – 17 Uhr

Biomedical Centre, LMU

@forschungsmodul_medizin

mms

MMS SCIENCECON

CONTENTS

Dear Students, Participants, Jury Members, and Guests,

Welcome to the 10th MMS ScienceCon.

Over the years, the conference has grown into a space where students can present their work, exchange ideas, and experience research as an open and collaborative process. This year, we are especially happy to welcome participants not only from LMU and universities across Germany, but also from our international partner institutions within the GAME network and beyond.

We are deeply grateful to **all students who submitted abstracts** and contributed to this year's scientific program. Whether through talks or posters, presenting research requires commitment, curiosity, and the willingness to engage in discussion. Thank you for bringing such a wide range of perspectives and projects to this year's conference.

Our sincere thanks go to **all supervisors and faculty members** who support student research throughout the year. Many of the projects presented today would not have been possible without your mentorship, trust, and encouragement.

We are especially grateful to **our jury members** for contributing their time and expertise to evaluating this year's presentations and posters. Our thanks go to Prof. Michael Bernhagen, Dr. Adrian Hoffmann, Prof. Shibo Lahiri, Prof. Itzel Bustos, as well as our student jury members Magdalena Sophia Schwarz, Lamija Ibrahimpasic, and Taehee Kim.

We would also like to sincerely thank **Prof. Alexander Gerbes** for his continued support of LMU's international partnerships and for helping strengthen the global perspective of this year's conference.

A special thank you goes to our keynote speaker, **Prof. Philipp Baaske**, for joining us today and sharing his perspective on entrepreneurship, innovation, and the translation of scientific ideas into real-world impact.

We are deeply grateful to **Prof. Michael Meyer**, whose vision and long-standing commitment helped shape the Forschungsmodul and establish the MMS ScienceCon as a platform for student research at LMU. As he retires this year, we would like to express our sincere gratitude for his many years of support and his dedication to creating opportunities for young researchers.

We would also like to warmly thank **Wencke Vonderhagen** and the International Board of LMU Medicine. Their commitment and generous support made it possible to welcome students from our GAME partner universities and strengthen the international character of this year's conference. Through travel grants, conference support, and the Best Talk Awards, they helped create opportunities for meaningful scientific exchange across borders.

We are grateful to **RNhale** for sponsoring this year's Best Poster Awards and for supporting scientific excellence and innovation among the next generation of researchers.

A special thank you goes to **Julia Karpf**, our student coordinator. We greatly appreciated her reliability, initiative, and fresh perspective throughout the preparation of this year's conference and all the practical support she contributed behind the scenes.

Finally, thank you to everyone whose work often remains invisible but is essential to making a conference possible. Events like the MMS ScienceCon are always a collective effort, and we are grateful to be part of a community that values student research and creates space for ideas to grow.

We hope you enjoy the conference and wish you an inspiring day full of interesting discussions, new ideas, and meaningful connections.

With appreciation,

Johanna Canady Romana Ruiß

Dr. Johanna Canady and Dr. Romana Ruiß

Conference coordinators and coordinators of the undergraduate research module
LMU Medical Faculty

Prof. Frederik Klauschen

Dean of Research

LMU Medicine, Munich

Dear students,

Medicine is advancing at a remarkable pace, yet it is also facing increasing complexity ranging from demographic change and workforce shortages to the growing burden of chronic disease and rapid technological transformation. In such times, the role of scientific thinking in clinical practice becomes even more essential.

It is precisely here that students from medicine and biomedical sciences play a crucial role. Engagement in research during training should not be considered optional, but a fundamental contribution to maintaining and strengthening high scientific standards in medicine. By actively participating in research projects, you help ensure that clinical decisions remain grounded in evidence, and that innovation in healthcare is guided by medical need and domain expertise.

At the same time, your involvement in research shapes the healthcare system of tomorrow. The questions you choose to ask, the methods you apply, and the curiosity you bring forward all contribute to how medicine will address future challenges. Whether in basic science, translational projects, clinical studies, or digital health, your work helps bridge the gap between today's knowledge and tomorrow's solutions.

This year's ScienceCon once again highlights the importance of scientific exchange within the medical community. It provides a platform for presenting research across the full spectrum of biomedical science and for fostering dialogue between students from different backgrounds and institutions. Such exchange is vital for developing new ideas and strengthening a commitment to evidence-based medicine.

LMU Medicine remains committed to supporting this early engagement in research through structured programs and funding opportunities. We encourage you to take advantage of these opportunities and to see research not as separate but as an integral part of clinical medicine.

I would like to thank all organizers, mentors, and participants who make this conference possible!

With best wishes for an inspiring and productive conference.

Prof. Frederik Klauschen

Dean of Research

From Learning to Contributing: How international networks and interdisciplinary work can shape the future of medicine

The 10th edition of MMS ScienceCon is a great success for all those who have been doing their best for years to actively shape the research module and the future of medicine.

Our conference shows not only the hard work of the participants and presenters, but also of the team behind the scenes. As a highlight of our working year, we not only strive to create a successful day full of science, networking and amazement, no, we also want to motivate and inspire.

The future of the world, and especially of science, is changing so fast that it's hard to keep up. But despite the uncertainties, we can connect with our international networks and make a contribution to a better future together across borders and disciplines in Health.

Listening to the next generation and seeing the contribution they are already making today inspires me every year anew and I am happy to be a part of this great project.

I would like to use a quote from Arthur Penrhyn Stanley (English clergyman, 19th century) to sum up exactly what we are talking about today:

„The true calling is not to do extraordinary things, but to do ordinary things in an extraordinary way.“

That's what science is all about. What we can listen to today and what we can learn from each other. The ups and downs the trial and error. The happiness in our accomplishments and sometimes the hard truth of reality.

I am grateful for all those who contribute to the research module and the MMS ScienceCon and wish us all a wonderful day and a special thanks to Romana & Johanna without which neither the research module nor the ScienceCon would be possible – congratulations to you and thank you for your work – here's to the next 10 years!

Julia Kristina Karpf, MBA

Medical Student and Student Coordinator of the ScienceCon 2026

Dr. Philipp Baaske

Vice President for Entrepreneurship

Ludwig-Maximilians-Universität München (LMU Munich)

Executive Chairman, NanoTemper Technologies GmbH

From Research to Impact: How Entrepreneurship Turns Science into Innovation

Scientific excellence creates value through knowledge, education, and application. In this keynote, Philipp Baaske explores how entrepreneurship can help translate research into impact in medicine, technology, and society. Rather than separating universities from application, the talk highlights them as places where ideas, talent, and responsibility come together to shape the future.

Drawing on his experience as founder of NanoTemper Technologies and as Vice President for Entrepreneurship at LMU Munich, he reflects on the role of speed, execution, and responsible leadership in building innovation ecosystems. The keynote addresses how outstanding research can lead to tangible change for patients, clinical practice, and society while remaining grounded in scientific rigor and academic values.

At its core, the talk asks how universities can create conditions in which discoveries do not lose momentum, researchers are empowered to act entrepreneurially, and innovation becomes a responsible extension of scientific excellence.

Dr. Philipp Baaske is Vice President for Entrepreneurship at LMU Munich and founder of NanoTemper Technologies, a Munich-based life-science company active globally. At LMU, he is committed to strengthening entrepreneurship, technology transfer, and spin-off creation as key pathways for translating academic excellence into practical application. His work is guided by the belief that innovation should combine scientific rigor, speed of execution, long-term responsibility, and meaningful value for society.

Program ScienceCon

time		Work Group / Univ.
08:30	Participant registration at the reception desk	
09:00	Welcome by the conference coordinators	

Advanced and International Students Session

09:15	**Developing an Animal Model to Investigate Acute Peripartum Twin-to-Twin Transfusion Syndrome** *Elizabeth Hoye*	Monash
09:30	**Timing of Cardiopulmonary Bypass and Risk of Mortality or Neurological Injury in Premature Infants with Congenital Heart Disease** *Julia Hoffmann*	LMU Munich
09:45	**Environmental and Economic Impact of Single use vs. Reusable Laparoscopic Instruments: A Systematic Review** *Malik Tariq*	Nottingham
10:00	**The role of AI in analyzing the inflammatory microenvironment in lung tumors** *Caterina Dies*	Bologna
10:15	Short Coffee Break	
10:30	**Comparison of Radiosensitization in HPV-Positive HNSCC Cells via Xevinapant, Olaparib and Tuvusertib** *Amir Babak Vahedi*	Hamburg
10:45	**Real-world medical long-term treatment strategy in children with Kawasaki disease** *Erik Wollenweber*	LMU Munich
11:00	**Evaluation of Generative AI Models for Lung Tumour Detection and Characterisation on Chest CT** *Ka Hei Man (Ricky)*	Hong Kong

11:15	**Poster Session 1**	
12:00	🍽 Lunch Break	

Research Module Students – Cellular Mechanisms in Health and Disease

12:45	**Visualization of activity-dependent dendritic translation in hippocampal neurons** *Johanna Rauhmeier*	Kiebler
13:00	**Neuronal Reprogramming as a Therapeutic Strategy: Neurogenin-2 Targets Patient-Derived Glioblastoma Cells** *Diana Auer*	Ninkovic
13:15	**Plaque-Associated Perineuronal Net Alterations in a Mouse Amyloidosis Model** *Dagna Dąbrowska*	Neher
13:30	**Apremilast-Mediated Stabilization of Intercalated Disc Integrity in Arrhythmogenic Cardiomyopathy** *Ezgi Akarsu*	Yeruva / Waschke
13:45	**Poster Session 2**	
14:30	Group Picture and Afternoon Break	

Research Module Students – Mechanisms, Models and Translation in Disease

15:00	**Elucidating the impact of dietary fibre on temporal progression in Alzheimer's disease** *Anna Wolf*	Lahiri
15:15	**Atherosclerotic Chemokine MIF is inhibited through allosteric transinhibition between CXCR4-CXCR3 Receptors** *Nikolaos Chavakis*	Bernhagen
15:30	**Structure–function relationships in polysarcosine-based lipid nanoparticles for mRNA delivery** *Justine Aogastin*	Merkel

15:45	**Preterm neutrophils lack full maturation at birth** *Yui Arjuna Fuchs*	Kim-Hellmuth

Greeting Message

16:00	**Greetings by** *Prof. Alexander Gerbes, LMU Medicine International Board, Spokes Person International Networks & Strategic Partnerships*

Keynote

16:15	**From Research to Impact: How Entrepreneurship Turns Science into Innovation** *Prof. Philipp Baaske, LMU Vice President for Entrepreneurship*

17:00 🏆 Best Talk and Poster Awards — Closing Ceremony

Talk Abstracts

in the order of presentation

1_Developing an Animal Model to Investigate Acute Peripartum Twin-to-Twin Transfusion Syndrome

Lizzie Hoye[1,2], Indya M. Davies[1,2], Femmie Bloem[1,3], Pierre-Yves Rabattu[1,4], Alison Thiel[1,2], Sharmony Kelly[1,2], Hui Lu[1,2], Emily J.J. Horn-Oudshoorn[5], Paige J. Riddington[1,2], Ebony R. Cannata[1,2], Enrico Lopriore[3], Arjan B. te Pas[3], Kelly J. Crossley[1,2], Stuart B. Hooper[1,2]

[1] The Ritchie Centre, Hudson Institute of Medical Research, Clayton, Victoria, Australia [2] Department of Obstetrics and Gynaecology, Monash University, Clayton, Victoria, Australia [3] Department of Pediatrics, Leiden University Medical Centre, Leiden, The Netherlands [4] Department of Pediatric Surgery, Children's Hospital, University Hospital of Grenoble, France [5] Division of Neonatology, Erasmus MC University Medical Centre, Rotterdam, The Netherlands

Purpose: Most (96%) monochorionic twins (twins that share a placenta) have placental vascular anastomoses that connect their circulations and allow intertwin blood transfer. While most monochorionic twins' circulations remain 'balanced' in utero, at birth the circulations can become unbalanced and large blood transfusions from one twin ('donor') to the other ('recipient') can occur. This complication is termed acute peripartum twin-to-twin transfusion syndrome (TTTS). We have developed the first animal model to investigate the physiological factors regulating acute peripartum TTTS at birth.

Methods: Twin-pregnant sheep were anaesthetised and underwent caesarean section at 132±2 days of gestation (n=7). Both fetuses were instrumented with carotid artery catheters to measure blood pressure and heart rate, and were then returned to the uterus. An umbilical artery-to-artery anastomosis was created between one artery of each twin using a silastic catheter (~30 cm), with intertwin blood flow measured by an ultrasonic flow probe. The anastomosis catheter was opened to determine net flow direction and assign 'donor' and 'recipient' twins. The 'donor' twin was then delivered and mechanically ventilated with an intact umbilical cord for 10 minutes before cord clamping, while the 'recipient' twin remained in utero. Intertwin blood flow was recorded throughout.

Results: The arterial blood pressure gradient between twins determined anastomosis flow ($p < 0.05$), with flow from high to low pressure. Greater heart rate differences between twins were associated with the twins' heartbeats coming into and out of phase more frequently, with one in systole and the other in diastole ($p < 0.001$). Clamping the donor twin's umbilical cord caused rapid blood loss from the recipient twin into the placenta ($p < 0.0001$).

Conclusion: This novel animal model demonstrated that the intertwin blood pressure difference directly controls blood flow through an artery-to-artery anastomosis. Second-born twins may be at higher risk of blood loss into the placenta following the birth of the first twin.

2_Timing of Cardiopulmonary Bypass and Risk of Mortality or Neurological Injury in Premature Infants with Congenital Heart Disease

Giulia P Lima[1*], Allison Davila[23*], **Julia K. Hoffmann**[14*], Jenna Katz[15], Samantha Butler[67], Anjali Sadhwani[67], Mariana Chavez[2], Sarah Morton[15], Philip Levy[15], Christopher Baird[28**]

*[1] Division of Newborn Medicine, Boston Children's Hospital, Boston, MA [2] Department of Cardiac Surgery, Boston Children's Hospital, Boston, MA [3] Department of Cardiac Surgery, Northwestern [4] Department of Pediatric Cardiology and Pediatric Intensive Care, LMU Munich, Germany [5] Department of Pediatrics, Harvard Medical School, Boston, MA [6] Departments of Psychiatry and Behavioral Sciences, Boston Children's Hospital, Boston, MA [7] Department of Psychiatry, Harvard Medical School, Boston, MA [8] Department of Surgery, Harvard Medical School, Boston, MA * shared co-first authorship ** shared co-senior authorship*

Purpose: Premature infants with congenital heart disease (CHD) face high perioperative mortality and neurological risk. The impact of cardiopulmonary bypass (CPB) timing on survival and neurodevelopment is unclear.

Methods: We conducted a 16-year (2008–2023) single-center retrospective cohort study of premature infants (<37 weeks' gestational age) who underwent CPB for cardiac surgery before two months of age. The primary outcome was in-hospital mortality. Secondary outcomes were postoperative neurologic injury, defined as new or progressive intraventricular/parenchymal hemorrhage, or electroencephalography-confirmed seizures, and neurodevelopmental performance assessed using the Bayley Scales of Infant and Toddler Development. Multivariable logistic regression was used to evaluate the association between age at CPB and outcomes.

Results: Mortality was 23.5% among 285 premature infants (median gestation of 35 weeks) who underwent CPB before two months of age. Surgery within 48 hours of life was independently associated with increased mortality (odds ratio 7.61, 95% confidence interval 2.30–29.86), whereas age beyond 48 hours was not. Cardiac lesion severity and operative weight were robust mortality predictors. Postoperative neurological injury occurred in 24% of infants but was not associated with CPB timing (odds ratio 0.97, 95% CI 0.94–1.00). CPB timing was not associated with neurodevelopmental delay.

Conclusion: In premature infants with CHD, CPB within the first 48 hours carries high mortality risk, but timing beyond this window does not independently affect survival, acute neurological injury, or long-term neurodevelopment. Lesion complexity and operative weight are more informative than chronological age for perioperative risk stratification, supporting individualized timing of surgery after physiologic stabilization.

3_Environmental and Economic Impact of Single use vs. Reusable Laparoscopic Instruments: A Systematic Review

Malik Tariq

Nottingham University

Purpose: Surgical departments are contributors to hospital waste and carbon emissions. This review synthesises quantitative data from life-cycle assessments (LCAs) to evaluate the environmental and financial benefits of transitioning from single-use to hybrid and reusable laparoscopic systems.

Methods: A systematic review was conducted focusing on LCAs of laparoscopic equipment. Quantitative data were extracted from UK and Swedish cohorts to compare carbon footprints (CO_2e), resource depletion, and costs across single-use, hybrid, and reusable systems.

Results: UK-based data on laparoscopic cholecystectomy using hybrid instruments demonstrated a mean reduction of 60% across 17 environmental midpoint impacts compared to single-use equivalents. The carbon footprint of a hybrid instrument set was 75% lower than single-use versions (1756 g vs 7194 g CO_2e per operation). Carbon contributions for hybrid clip appliers, scissors, and ports were only 17%, 33%, and 27% of their single-use counterparts. Hybrid models also reduced disability-adjusted life years (DALYs) by 74%. Total financial costs for hybrid instruments were less than half of single-use equivalents (£131 vs £282). Analysis of a Swedish trocar system study revealed that single-use models had a 379% higher impact on climate change (difference: 446 kg CO_2e) and a 182% higher impact on resources than reusable systems. Human health impacts were 240% higher for single-use trocars. Reusable and mixed trocar systems were approximately 50% cheaper (€17,360 vs €37,600). Sensitivity analyses confirmed that the environmental superiority of reusable and hybrid systems remained robust under scenarios of low instrument reuse, fossil-fuel-intensive sterilisation, or high-intensity transportation.

Conclusion: Reusable and hybrid laparoscopic instruments significantly outperform single-use alternatives in both environmental sustainability and financial cost-effectiveness across different European healthcare settings. Adopting these systems can reduce surgical carbon footprints by up to 75% and halve procedural costs. These data support a policy shift toward circular procurement in surgical practice to align with global healthcare sustainability targets.

4_The role of AI in analyzing the inflammatory microenvironment in lung tumors

Caterina Dies

Bologna University

Purpose: The tumor microenvironment (TME) is a key determinant of tumor behavior, affecting anti-tumor immune response and clinical outcomes, yet the spatial immune composition of TME and its relationship with clinicopathological features in lung squamous cell carcinoma (LSCC) remain incompletely characterized. This study aimed to quantitatively characterize the spatial immune profile of LSCC using brightfield multiplex immunohistochemistry (BF-mIHC) and artificial intelligence (AI)-based whole-slide image (WSI) analysis; to calculate an Immunoscore-like model and define three immune phenotypes; and to evaluate associations between immune profiling, clinicopathological features, including PD-L1 expression and worst pattern of invasion (WPOI), and clinical outcomes.

Methods: Forty-seven surgically resected primary LSCC cases were retrospectively analyzed. CD4+, CD8+, CD20+, and CD68+ cells were quantified across distinct TME compartments using BF-mIHC and the AI-based TIME software. The Immunoscore-like model was calculated from CD4+, CD8+, and CD20+ cell densities, classifying cases into cold, excluded, and hot immune phenotypes. Associations between immune profiling, PD-L1 expression, WPOI and other clinicopathological variables were assessed using MANOVA, Chi-squared, and Kruskal-Wallis tests. Survival analysis was performed using Kaplan-Meier curves with log-rank tests.

Results: PD-L1 expression revealed a statistically significant multivariate effect with the immune cell composition across the whole TME ($p = 0.010$) and at the invasive tumor front (ITF) ($p = 0.009$). The combined variable PD-L1/WPOI also showed a significant multivariate effect with immune cell composition at the ITF ($p = 0.022$). WPOI was associated with AJCC Stage ($p = 0.0005$), nodal stage ($p = 0.0002$), advanced stage ($p = 0.002$), lymphovascular invasion ($p = 0.033$), and perineural invasion ($p = 0.020$). Immunoscore-like model was associated with tumor differentiation ($p = 0.005$). Kaplan-Meier analysis revealed significant differences in relapse-free survival according to AJCC Stage/IS ($p < 0.001$) and PD-L1/WPOI ($p = 0.007$).

Conclusion: AI-based BF-mIHC analysis enables reproducible compartment-specific immune quantification and Immunoscore-like model calculation in LSCC. The application of WPOI to LSCC showed associations with clinicopathological features of aggressiveness, supporting its potential utility as histopathological marker in LSCC. Overall, the integration of immune profiling with morphological features contributes to a better understanding of tumor behavior and offers additional prognostic value beyond conventional staging.

5_Comparison of Radiosensitization in HPV-Positive HNSCC Cells via Xevinapant, Olaparib and Tuvusertib

Amir Babak Vahedi[12], Adriana Perugachi-Heinsohn[12], Julius Röhrle[1], Fruzsina Gatzemeier[12], Sabrina Christiansen[12], Nanik Wahrhausen[12], Cordula Petersen[2], Christian Betz[1], Kai Rothkamm[2], Thorsten Rieckmann[12] §

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Introduction: Recently, the pro-apoptotic SMAC mimetic xevinapant was shown to confer inferiority when added to chemoradiation in a phase 3 trial (TrilynX) for HPV-negative HNSCC, despite a previous successful randomized phase 2 trial. HPV-positive HNSCC harbor wtp53 and may thus show residual p53 activity under therapy despite HPV E6 mediated p53 degradation. Such cells may be more prone to apoptosis inducing agents but data are sparse. Therefore, we tested the radiosensitizing effect of xevinapant in comparison to olaparib and the ATR inhibitor tuvusertib and their combinations in HPV-positive HNSCC cell lines.

Materials and Methods: Assessment of inhibitor impact through proliferation and colony formation assays. Assessment of radiosensitization through analysis of colony formation after inhibitor treatment in combination with X-irradiation. Analysis of apoptosis induction through annexinV/DAPI staining.

Results: A single HPV+ HNSCC cell line demonstrated explicit sensitivity towards xevinapant but without induction of apoptosis or lytic cell death. Regarding radiosensitization, xevinapant alone resulted in no to minimal, olaparib in moderate and tuvusertib in the most profound radiosensitization. Combining xevinapant and tuvusertib did not enhance radiosensitization, while combining xevinapant and olaparib partly did. The by far most effective approach was the combination of PARP and ATR inhibition through olaparib and tuvusertib.

Conclusion: Based on these cellular results, a clinical benefit from xevinapant in HPV-positive HNSCC is unlikely. As single intervention ATR inhibition induced profound radiosensitization, which was further augmented when combined with PARP inhibition, which we thus suggest as the most promising approaches for further investigation.

6_Real-world medical long-term treatment strategy in children with Kawasaki disease: Data from the Kawasaki Disease – Coronary Assessment Registry (KD-CAR)

Erik Wollenweber[1], Delphina Gomes[1], Marcel Müller[2], Samar Shamas[2], Wolfgang Wällisch[3], Daniel Quandt[4], Bernd Opgen-Rhein[5], Florentine Gräfe[6], Frank-Thomas Riede[6], Raoul Arnold[7], Daniel Tanase[8], Ulrike Herberg[9][19], Jörg Michel[10], Heike Schneider[11], Mali Tietje[12], Gleb Tarusinov[12], Christoph Happel[13], Marianna Fabi[14], Enrico Perre[14], Jochen Grohmann[15], Johanna Hummel[15], Álvaro Lafuente Romero[16], Gunter Kerst[17], Guido Mandilaras[17], André Rudolph[18], Ruth Heying[20], Nikolaus A. Haas[1], André Jakob[1]

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Purpose: Evidence-based recommendations for long-term medical management in Kawasaki disease, particularly in patients with persistent coronary artery aneurysms, remain limited. We analyzed real-world data from the KD-CAR (Kawasaki Disease - Coronary Assessment Registry), which comprises patients who underwent coronary imaging via conventional angiography, computed tomography, or magnetic resonance imaging, to assess how coronary pathology and/or patient-specific factors influence pharmacological selection.

Methods: Data from the KD-CAR, including detailed information on coronary artery pathology and prescribed medications, were used for this analysis. Anticoagulation strategies and other cardiovascular therapies were evaluated in relation to patient age and sex, as well as coronary pathology-specific factors, including aneurysm size, aneurysm burden, and the presence of coronary artery stenosis or thrombosis.

Results: Among 179 registry patients, 119 (78 male, age range 0-312 months) received anticoagulant or cardiac medication guided by cross-sectional imaging. Acetylsalicylic acid (ASA) was prescribed in 97% of treated patients, most commonly in combination with vitamin K antagonists (VKA; 49%). Patients receiving VKA were significantly older than those treated with ASA and low-molecular-weight heparin (LMWH; 12%). Clopidogrel was administered in 16% of patients, either as dual antiplatelet therapy or in combination with anticoagulation. VKA monotherapy was given in 3% of the patients, all with large coronary artery aneurysms. Anticoagulant selection was significantly associated with aneurysm quantity, size, and location, but

not with the presence of coronary stenosis. β-blockers and statins were infrequently used and predominantly in patients with multiple aneurysms.

Conclusion: Long-term medical management was highly heterogeneous and primarily guided by coronary aneurysm characteristics rather than the presence of coronary stenosis. Adjunctive therapies, such as statins, were used only infrequently. These findings emphasize the pivotal role of aneurysm morphology in therapeutic decision-making and highlight the need for stronger evidence to support standardized long-term treatment strategies in Kawasaki disease.

7_Evaluation of Generative AI Models for Lung Tumour Detection and Characterisation on Chest CT

Ka Hei MAN[1], Shing Yau TAM[2]

[1] Faculty of Medicine, The Chinese University of Hong Kong [2] School of Medical and Health Sciences, Tung Wah College

Purpose: This study evaluates the diagnostic performance of generative artificial intelligence (GenAI) models for lung tumour detection and characterisation on chest computed tomography (CT). Lung cancer is one of the most common cancers worldwide, and CT-based screening is increasingly studied and implemented for early detection. This study investigates the performance of updated and widely accessible GenAI models for lung tumour detection using chest CT images.

Methods: This retrospective study analysed 60 publicly available chest CT cases randomly selected from Radiopaedia, including 30 normal cases and 30 cases with radiologist-confirmed lung cancer. CT image series were independently evaluated using ChatGPT-5.3 and Google Gemini 3. For each case, the models determined whether a lung tumour was present. If a tumour was detected, the models characterised the tumour by reporting tumour side, lung lobe, and number of lesions. Confidence level (low, moderate, or high) self-reported by the models and response time were recorded. AI responses were compared with radiologist-confirmed diagnoses to assess tumour detection and characterisation accuracy. Sensitivity, specificity, and overall accuracy were calculated.

Results: A total of 60 CT cases (30 cancer, 30 normal) were analysed. There was no statistically significant difference in age between the groups (cancer: 59.0 ± 6.6 years; normal: 45.0 ± 16.0 years; Mann–Whitney U test, $p = 0.056$). Gender distribution was identical in both groups (50% male, 50% female). ChatGPT demonstrated 90% sensitivity, 100% specificity, and 95% overall accuracy, whereas Gemini showed 100% sensitivity, 70% specificity, and 85% overall accuracy. Among true positive cases, ChatGPT correctly identified tumour side and lesion number in 100% of cases and lung lobe in 90%, compared with 100%, 100%, and 80%, respectively, for Gemini. Mean response times were 5.8 seconds for ChatGPT and 9.8 seconds for Gemini. Most responses were reported with moderate to high confidence, and no significant associations were observed between response time, confidence level, and detection accuracy.

Conclusion: Generative AI models demonstrated promising performance in lung tumour detection and characterisation on chest CT, with ChatGPT showing higher diagnostic accuracy than Gemini. These findings suggest that GenAI may facilitate rapid and reliable tumour screening while potentially reducing clinical workload in imaging interpretation.

8_Visualization of activity-dependent dendritic translation in hippocampal neurons

Johanna Rauhmeier

Department of Anatomy III (Cell Biology), AG Kiebler, LMU Munich, Germany

Purpose: Activity-dependent changes in the proteome of individual synapses enable persistent alterations in synaptic responsiveness. One key mechanism contributing to this process is the transport of mRNAs along the cytoskeleton from the soma of neurons towards distal subcellular compartments, where they can be locally translated. During transport, mRNAs are packaged together with RNA-binding proteins (RBPs) into ribonucleoprotein particles (RNPs). But the dynamic interplay between mRNA transport, RBP association and translational repression during transport remains insufficiently understood. Therefore, this project aimed to microscopically visualize local translation in primary cultured hippocampal neurons.

Methods: The SunTag reporter system was used to fluorescently mark individual nascent polypeptides being newly synthesized. The SunTag assay was combined with single-molecule inexpensive fluorescence in situ hybridization (smiFISH) targeting the reporter mRNA, allowing simultaneous visualization of translating and non-translating mRNAs. To relate observations to synaptic plasticity, the spatial relationship and ratio between translating and non-translating mRNAs was analyzed following activation of glutamatergic synapses. SunTag reporter constructs contained 3'-UTR elements with a Staufen2 binding site to investigate the role of untranslated regions. Additionally, Immunostaining targeting Staufen2 was performed.

Results: The experimental framework successfully enabled simultaneous visualization of translating and non-translating mRNAs in hippocampal neurons. Stimulation-dependent changes in translational events were assessed in relation to glutamatergic synapse activation. Analysis of the spatial relationship between mRNA translation events and synaptic sites is ongoing, and initial data support a stimulation-dependent modulation of local translation.

Conclusion: Together, these experiments provide a framework for understanding how dendritic mRNA translation is coordinated during synaptic plasticity, and highlight the role of Staufen2 and 3'-UTR elements in regulating local translation in neurons.

9_Neuronal Reprogramming as a Therapeutic Strategy: Neurogenin-2 Targets Patient-Derived Glioblastoma Cells

Diana Auer, Prof. Dr. Jovica Ninkovic[1], David Bühler[1], Polyxeni Moysidou-Tsiorva[1], Ecem Balcioglu[1], Arthur Wagner[2], Maria Goldberg[2]

[1] AG Ninkovic, Division of Cell Biology/Anatomy III, BMC, LMU Munich [2] Department of Neurosurgery, Klinikum rechts der Isar, TUM

Purpose: Glioblastoma (GBM) is the most aggressive malignant brain tumor, characterized by invasive growth, high recurrence rates, and remarkable cellular heterogeneity, resulting in a poor prognosis. Despite surgical resection, radiotherapy, and chemotherapy, residual tumor cells persist and drive recurrence. Rather than focusing solely on tumor cell elimination, our project investigates whether GBM malignancy can be reduced by redirecting tumor cells toward a post-mitotic, neuron-like identity through induction of a neurogenic transcriptional program mediated by Neurogenin-2 (Neurog2).

Methods: Two primary patient-derived GBM cell lines, NGL5 and NGL8, were transduced as dissociated single cells with a doxycycline (DOX)-inducible lentiviral Tet-ON construct encoding Neurog2 and GFP, the latter serving as a transduction marker. Control cells were transduced with a DOX-inducible GFP-only construct. Following expansion, cells were seeded onto 24-well plates, and doxycycline treatment was initiated one day later in neuronal differentiation medium. At 1, 2, and 3 weeks post-induction, cells were fixed and subjected to immunofluorescence staining for GFP, Ki67, DCX, and βIII-tubulin to assess transduction efficiency, proliferation, and neuronal marker expression.

Results: Preliminary analysis at one-week post-induction revealed increased βIII-tubulin expression in Neurog2-transduced NGL5 cells compared with GFP-only controls. DCX-positive cells increased from 21% in controls to 63.7% following Neurog2 expression, consistent with acquisition of a neuronal fate. Ki67 positivity was reduced in the Neurog2 condition, suggesting decreased proliferative activity. In contrast, NGL8 cells exhibited limited induction of neuronal markers and low GFP positivity, indicating reduced transduction efficiency and/or resistance to reprogramming.

Conclusion: These findings suggest that Neurog2 can promote early neuron-like features in patient-derived GBM cells, particularly in NGL5. The observed reduction in Ki67 positivity supports the notion that neuronal conversion may attenuate GBM proliferation. Future work should focus on improving neuronal conversion across heterogeneous GBM models and evaluating whether this reprogramming approach can serve as a complementary strategy to reduce malignancy in glioblastoma.

10_Plaque-Associated Perineuronal Net Alterations in a Mouse Amyloidosis Model

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Background: Alzheimer's Disease (AD) is a multifactorial neurodegenerative disorder characterised by protein aggregation, particularly extracellular β-amyloid (Aβ) plaques. Even before overt neurodegeneration becomes clinically apparent, aberrant neuronal network activity (including hypersynchrony, epileptiform activity, and disrupted oscillatory rhythms) is observed in AD patients and mouse models with Aβ pathology. These abnormalities may reflect impaired inhibitory circuitry and excitation–inhibition imbalance. A key structural component supporting inhibitory interneuron function is the presence of perineuronal nets, specialised extracellular matrix structures that surround inhibitory interneurons and help stabilise their signalling and synaptic inputs. Emerging evidence suggests that Aβ plaque accumulation may alter PNN coverage, potentially impairing inhibitory interneuron function even when interneuron cell numbers are preserved.

Purpose: This study aims to determine whether parvalbumin-positive (PV+) inhibitory interneurons show altered perineuronal net coverage near Aβ plaques. PV+ interneurons are of particular interest because they provide fast inhibition, generate gamma oscillations, and are strongly associated with PNNs, while showing early functional vulnerability in AD.

Methods: APPPS1 transgenic mice with extensive Aβ plaque pathology were compared with age-matched wild-type controls. Brain sections were stained using Methoxy-X04 for Aβ plaques, Parvalbumin for PV+ interneurons, and WFA (Wisteria floribunda agglutinin) for perineuronal nets. Stained sections were then imaged using an Olympus slide scanner, where compressed z-stacks were acquired for cell counting. Additionally, high-resolution confocal microscopy was performed, and images were reconstructed in 3D for detailed structural analysis of perineuronal net coverage.

Results: Preliminary analyses indicate a trend towards a reduced number of PV+ interneurons ensheated by perineuronal nets in APPPS1 mice. However, surface area, volume, and overall net coverage of PV+ interneurons remained similar in APPPS1 mice compared to controls.

Conclusion: Our data suggest that while there may be a modest reduction in the number of PV+ interneurons ensheated by perineuronal nets in APPPS1 mice, the structural properties of the remaining nets are largely preserved. This indicates that Aβ

pathology may preferentially affect the presence of perineuronal nets rather than their gross morphology. Future studies investigating perineuronal net composition will be important to determine whether specific structural components are selectively targeted, potentially preceding or contributing to more pronounced net degradation.

11_Apremilast-Mediated Stabilization of Intercalated Disc Integrity in Arrhythmogenic Cardiomyopathy

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Purpose: Arrhythmogenic cardiomyopathy (ACM) is a genetically inherited myocardial disorder characterized by impaired electromechanical coupling, progressive cardiomyocyte loss, and fibrofatty replacement, leading to malignant arrhythmias and sudden cardiac death, particularly in young individuals and athletes. Mutations in desmosomal genes such as desmoplakin (DSP) are central to disease pathogenesis, as they destabilize intercellular adhesion at the intercalated disc and compromise mechanical integrity and electrical conduction. While current therapeutic strategies primarly address symptomatic manifestations, pharmacological modulation of adhesion-related signaling pathways represents a promising strategy to directly target desmosomal dysfunction by reinforcing structural integrity at the intercalated disc. This study aimed to investigate whether apremilast, a phosphodiesterase-4 inhibitor elevating intracellular cAMP levels, can enhance intercellular adhesion and restore junctional integrity in DSP mutant murine model.

Methods: Cardiac tissue derived from wild-type and heterozygous DSP-mutant mice was treated with apremilast or maintained under control conditions. Desmosomal and junctional integrity at the intercalated disc was assessed using immunofluorescence staining and confocal microscopy. Key junctional proteins analyzed included desmosomal components (desmoplakin, desmoglein-2, plakoglobin), adherens junction protein N-cadherin, and gap junction protein Connexin 43. Quantitative image analysis, including skeletonization-based assessment using FIJI, was performed to evaluate intercalated disc fragmentation as a measure of junctional organization.

Results: Current quantitative analyses demonstrate a pronounced increase in intercalated disc fragmentation in DSP-mutant tissue compared to wild-type controls. Apremilast treatment markedly reduced fragmentation in mutant samples, decreasing N-cadherin-associated fragmentation from approximately 39% to 14% and Connexin 43 fragmentation from approximately 13% to 3%. Comparable, albeit less pronounced, effects were observed in wild-type tissue, indicating a substantial restoration of junctional integrity following apremilast treatment.

Conclusion: Apremilast-mediated elevation of cAMP levels effectively improves intercalated disc organization in DSP-mutant murine model supporting a mechanism-driven therapeutic approach targeting desmosomal adhesion.

12_Elucidating the impact of dietary fibre on temporal progression in Alzheimer's disease

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Purpose: Alzheimer´s disease is an irreversible neurodegenerative disorder characterized by amyloid-β plaques, neurofibrillary tangles and sustained neuroinflammatory responses, contributing to synaptic dysfunction and progressive cognitive decline (1). Evidence indicates a significant interaction between the gastrointestinal microbiome and the central nervous system, the gut-microbiota-brain axis, which has been linked to neurodegenerative processes, including Alzheimer´s disease (AD) (2-3). A recent pilot study from our laboratory investigated the effect of high-fibre diet on AD using inulin supplementation. In this context, inulin, a prebiotic dietary fibre, altered gut microbiome composition, reduced amyloid-β deposition and neuroinflammatory markers in a transgenic mouse model of Alzheimer´s disease (4). Considering these results, the present project validates and expands the pilot study through time-resolved profiling of disease progression.

Methods: Wildtype and 5xFAD mice were assigned to standard chow or an inulin-enriched diet and analysed at multiple ages (3, 4.5, 6, and 8 months old). MALDI mass spectrometry imaging was applied to detect amyloid-β plaques in sagittal brain sections. This allowed spatial profiling and composition analysis of amyloid-β depositions.

Results: Initial results from our follow-up study identified age-dependent alterations in Alzheimer´s pathology in wildtype and transgenic mice. At early disease stages, previous results were confirmed. 3-month-old mice receiving a high-fibre diet illustrated reduced amyloid-β deposition in the hippocampus and thalamus compared with mice receiving standard chow. Preliminary analysis indicates that amyloid-β accumulates with age in 5xFAD mice as expected. The effect of inulin seems to decrease at later time points. Only minor differences can be observed between standard chow and high fibre fed mice at ages 6 and 8 months.

Conclusion: These findings demonstrate that dietary fibre supplementation modulates temporal progression of Alzheimer´s disease in a transgenic mouse model. High-fibre diet may reduce amyloid-β accumulation and neuroinflammatory responses during early disease stages. However, over time, the diet does not sustainably influence amyloid-β deposition and neuroinflammation. Nonetheless, these findings emphasize the potential of dietary strategies to influence neurodegenerative processes via the gut-microbiota-brain axis by slowing amyloid-β deposition at initial disease stages.

13_Atherosclerotic Chemokine MIF is inhibited through allosteric transinhibition between CXCR4-CXCR3 Receptors

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Purpose: Atherosclerosis, the inflammatory buildup of plaques in arterial walls, is currently the leading cause of cardiovascular events and affects over 50% of the population over the age of 40. The paradoxically named atypical chemokine, Macrophage Migration Inhibitory Factor (MIF) is one of the most significant pro-inflammatory Chemokines in Atherosclerosis by attracting Monocytes and T-Cells into plaques through its cognate receptors CXCR4 and CXCR2. Recent research has proven that ligands of the CXCR3 receptor are able to inhibit MIF's migratory effect, raising questions as to how this happens and how this may be clinically applied to possibly inhibiting MIF's atherosclerotic effect while maintaining its cardioprotective signalling through CD74. Furthermore, it has been proven that CXCR4 and CXCR3 have the ability to dimerize with each other, implying the possibility of allosteric action as a mechanism of this inhibition.

Methods: To test this, VUF10661, a small molecule agonist of CXCR3 was placed in a chemokine cocktail with MIF when stimulating T-Cells for a 3D migration assay, as well as when measuring CXCR4-CXCR3 dimerization through proximity ligation assays. T-Cell 3D migration assays were specially chosen as a measure of functional effect as they effectively simulate the conditions necessary for cell migration in vivo. Furthermore, the proximity ligation assay allows us to view whether and to what extent receptor dimerization occurs with different stimulants.

Results: Though not all repeats have been completed, the data so far points towards an inhibition of MIF's migratory effect when VUF10661 is present, while dimerization stays low when looked at during a proximity ligation assay. Thereby, a likely mechanism of action is that the binding of CXCR3 ligands to CXCR3 causes conformational changes, preventing the dimerization with CXCR4 and thereby inhibiting its signalling pathway, possibly by preventing combined receptor internalisation or through an inhibited binding of downstream signal proteins.

Conclusion: In summary, though the exact mechanism of transinhibition has not been identified, the data speaks for allosteric effects between the CXCR4 and CXCR3 receptors, opening up new possibilities for the inhibition of MIF's inflammatory and atheroprogressive signalling.

14_Structure–function relationships in polysarcosine-based lipid nanoparticles for mRNA delivery

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Purpose: Lipid nanoparticles (LNPs) are widely used as non-viral delivery systems for mRNA therapeutics, enabling transient protein expression and forming the basis for next-generation vaccines and gene-based therapies. Despite their clinical relevance, structure–function relationships in polysarcosine (pSar)-based LNP systems remain insufficiently understood. This study aimed to identify structure–property relationships within pSar-LNP systems and to evaluate whether predictive models and design rules for formulation optimisation can be derived.

Methods: A dataset comprising 23 pSar-based LNP formulations and one PEG-LNP reference was analysed using partial least squares (PLS), self-validating ensemble models (SVEM), and machine learning approaches. Particle size, transfection efficiency, encapsulation efficiency, and zeta potential were evaluated as response variables. UMAP was applied to explore structural clustering, while descriptor-based machine learning models using RDKit and Mordred features were employed for predictive analysis.

Results: Particle size showed the most robust and consistent structure–property relationship. PLS analysis revealed a strong inverse correlation between polymerisation degree and particle size ($R^2 \approx 0.91$, $Q^2 \approx 0.89$), which was confirmed by SVEM, where polymerisation degree emerged as the most stable descriptor. In contrast, transfection efficiency, encapsulation efficiency, and zeta potential exhibited weak or inconsistent relationships across modelling approaches, with limited predictive performance and indications of overfitting in high-dimensional descriptor spaces ($p >> n$). Although machine learning models achieved high training accuracy, they failed to generalise reliably. SVEM further indicated a consistent formulation trend, suggesting an optimal parameter region at a polymerisation degree of approximately 59 in combination with specific structural descriptors.

Conclusion: Particle size represents the most reliable and interpretable response in pSar-based LNP systems, while functional endpoints remain highly model-dependent. These findings highlight limitations in current predictive approaches and emphasise the need for larger datasets, improved feature selection, and validation across biological contexts.

15_Preterm neutrophils lack full maturation at birth

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Purpose: Infection and sepsis remain critical challenges in preterm infants (gestational age < 37 weeks). As the first line of innate immune defense, neutrophils are essential for pathogen clearance. This study aimed to characterize neonatal neutrophil functional responses to immunological triggers. In particular, we validated proteomic data suggesting that immature neutrophils, which are predominant in preterm infants, possess diminished granule content compared to term neonates. Additionally, we ensured that isolation procedures from whole blood did not induce artifactual pre-activation.

Methods: Neutrophils from adults (N=4) and term neonates at day 3 of life (N=5) were isolated via density-gradient centrifugation and compared to whole blood samples. Subsequently, FACS-sorted CD49dpos (immNeu) and CD49dneg (matNeu) cells were stimulated in vitro with Lipopolysaccharide (LPS). Adults (N=6), term infants (N=6) and preterms (N=7) were included, and responses were assessed via flow cytometry and ELISA to quantify degranulation (Elastase 2, Lipocalin 2) in supernatants.

Results: Methodological validation confirmed no pre-activation, preventing CD49d upregulation before sorting. Functional assays demonstrated a developmental gradient, with adult and term neutrophils showing significant surface marker response and robust degranulation upon stimulation, consistent with a larger functional intracellular granular reservoir. In contrast, preterms' immNeu and matNeu fractions elicited a milder response to LPS, exhibiting a blunted functional immune response.

Conclusion: This study highlights the importance of characterizing neonatal immune cell development, that may help explaining preterm infant's higher risk of infection. Understanding gestational differences is crucial for refining clinical workflows and improving neonatal care.

Poster Abstracts

in the order of presentation

P1_A Systematic Review on Adherence Factors and Compliance in Patients with Head and Neck Squamous Cell Carcinoma after Tumor Board Recommendation

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Purpose: Head and neck squamous cell carcinoma (HNSCC) is the seventh most common malignancy globally, representing nearly 5% of all cancer diagnoses. The therapeutic trajectory is often demanding, involving aggressive surgery and prolonged adjuvant treatments. Identifying specific risk factors that impair therapy adherence is critical to developing targeted support strategies for high-risk patient groups.

Methods: A systematic review was conducted following the PRISMA guidelines. A comprehensive literature search was performed to identify retrospective studies focused on therapy adherence in HNSCC patients. Following a screening process, eight papers met the inclusion criteria for qualitative and quantitative synthesis. Statistical analysis included the calculation of weighted means to account for varying sample sizes across the included studies, with data variability reported as the range.

Results: The analysis demonstrated that age was not a significant risk factor for therapy adherence. In contrast, sex, ethnicity, tumor subsite, and clinical tumor stage were identified as significant determinants. Additionally, adherence was influenced by the therapy modality, geographical distance to the treatment center, and the patient's marital status.

Conclusion: Therapy adherence in HNSCC is influenced by a complex interplay of clinical and socio-demographic risk factors, which may have a cumulative negative impact when occurring simultaneously. Clinical attention should be prioritized for these specific risk groups to maximize adherence and improve overall patient outcomes.

P2_Association Between Time to Surgery and Postoperative Complications in Ankle Fractures: A Retrospective Cohort Study

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Background: Evidence regarding whether delayed surgical fixation of ankle fractures increases postoperative complications remains heterogeneous, partly due to varied definitions of delay and outcomes measured. This study investigated the association between delaying surgery beyond 7 days of hospital arrival and postoperative complications.

Methods: A retrospective cohort study was conducted using a prospectively maintained trauma database at Nottingham University Hospitals. 1,900 adult patients undergoing operative fixation for closed ankle fractures were included; pilon fractures and open fractures were excluded. Time to surgery was derived from arrival and theatre dates and patients were categorised into an early surgery group (≤7 days) versus a delayed surgery group (>7 days). The primary outcome was any postoperative complication. Univariable and multivariable logistic regression were used to estimate Odds Ratios (OR) and adjusted Odds Ratios (aOR) with 95% Confidence Intervals (CI), adjusting for age, sex, smoking, diabetes, obesity, hypertension, and fracture severity.

Results: Mean age was 46.9±19.1 years and 45.5% were male. Surgery occurred ≤7 days in 1,319 patients (69.4%) and >7 days in 581 (30.6%). Overall, 72 patients (3.8%) developed a postoperative complication, and rates were lower with early surgery (3.2% versus 5.2%; p=0.037). Early surgery was associated with reduced odds of complications on univariable analysis (OR 0.60, 95% CI 0.37–0.98; p=0.039) and after adjustment of patient comorbidities (aOR 0.58, 95% CI 0.35–0.95; p=0.031). Sensitivity analysis demonstrated similar findings (OR 0.62, 95% CI 0.38–1.01; p=0.056).

Conclusion: Early surgical fixation of closed ankle fractures (≤7 days from hospital arrival) is associated with significantly fewer postoperative complications compared to delayed surgery, even after adjusting for relevant comorbidities. These findings support timely operative management where clinically feasible.

P3_Functional Survey of Immunomodulators using in vitro Tumour Models of Cancer Immunotherapy

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Purpose: Immune checkpoint inhibitors (ICI) are the most widely used class of immunotherapies in the treatment of cancer. They have been shown to provide distinct benefits over traditional chemotherapy and/or molecular targeted therapy in a variety of cancer types. Despite this, patients who receive ICI therapy often experience unwanted tissue damage known as immune related adverse events (irAEs), which are debilitating and possibly life-threatening. Mechanisms driving irAE manifestation are largely unknown; clinicians tend to manage irAEs using empirical immunomodulators with no mechanistic basis to support their choices. Whilst the mechanisms of these immunomodulators in immune cells has been extensively studied, the potential for these drugs to affect cancer cell function has not. This study aims to investigate the impact that immunomodulators may have on cancer cells themselves. This is a relevant consideration to make when selecting the most appropriate immunosuppressive drug for patients experiencing irAEs, and requires systematic characterisation in vitro prior to integration with more complex immunomodulatory drug combinations.

Methods: A survey of the immunomodulators used in irAE treatment was conducted on melanoma cell lines in vitro, aiming to assess effects on cellular survival functions. LM-MEL-64, LM-MEL-1a, and A375 human melanoma cell lines were cultured and treated with immunomodulators of various drug classes (glucocorticoids, antimetabolites, calcineurin inhibitors, JAK inhibitors, mTOR inhibitors) with functional assays (MTS proliferation, scratch/migration, apoptosis and colony formation) then performed.

Results: Of the drug classes examined, glucocorticoids and calcineurin inhibitors did not demonstrate statistically significant dose-response effects on melanoma cell function. Notably, the anti-metabolite methotrexate demonstrated at least one instance of a statistically significant dose-response effect across all functional assays. Methotrexate exerted antiproliferative effects in LM-MEL-64 and LM-MEL-1a (One-way ANOVA $p=0.0012$ and $p=0.0042$ respectively), suppressed migration in LM-MEL-64 (Two-way ANOVA time x treatment interaction $p=0.0175$), and was pro-apoptotic in LM-MEL-1a (One way ANOVA $p<0.0001$).

Conclusion: Future in vivo work should prioritise the study of antimetabolites (particularly methotrexate), with findings potentially validating their use as a beneficial treatment option over other immunomodulators for patients experiencing irAEs.

P4_Development of a Whole Genome Sequencing Assay for Measles Virus

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Background: Measles remains a significant global health threat, causing periodic outbreaks despite widespread immunisation efforts. The high transmissibility of the virus, combined with gaps in vaccination coverage and reduced immunity in some populations, continues to challenge elimination efforts. Effective genomic surveillance is critical for monitoring viral transmission patterns, identifying co-circulating or emerging genotypes, and guiding timely public health interventions. Whole genome sequencing (WGS) plays a vital role in this process; however, many current methods rely on virus culturing to boost genome yield. This introduces genotype amplification bias, reduces sensitivity, and limits utility for direct sequencing from clinical samples particularly where viral loads are low or where genotype diversity must be preserved.

Methods: This study aimed to develop a robust WGS assay capable of capturing the full measles virus genome across a range of genotypes without the need for virus culturing. A broad-range primer set was designed to target conserved regions across the most prevalent outbreak-associated genotypes. Primer sequences were selected through multiple sequence alignments and bioinformatic analysis using tools such as Primer3 and WebLogo to ensure specificity and optimal coverage. The measles-mumps-rubella (MMR) vaccine strain was used as the template for assay development. Quantitative polymerase chain reaction (qPCR) was employed to quantify measles virus RNA in the template material. Amplification was conducted using conventional PCR with various primer pools, and products were assessed by gel electrophoresis to evaluate amplification efficiency and consistency across dilutions. Amplified products were then quantified, normalised, and prepared for sequencing.

Results: Gel electrophoresis revealed consistent amplification by the broad-range primers across multiple dilutions, supporting their potential for genotype-independent sequencing. Following PCR, sequencing was performed, and the resulting reads were analysed using BLASTn to assess query coverage and sequence identity. Phylogenetic analysis was conducted to contextualise the sequences obtained and evaluate their utility for molecular epidemiology. While the primers demonstrated broad utility, several regions of the genome exhibited reduced or absent coverage. Notably, the matrix-fusion non-coding region (M-F NCR), a complex and variable segment, was consistently underrepresented. These coverage gaps suggest that factors beyond primer design—such as reverse transcription efficiency or secondary RNA structures—may influence assay performance and genome recovery.

Conclusion: The developed WGS assay shows strong potential for comprehensive sequencing of the measles virus genome using a single primer scheme, without the

need for virus culturing. Its ability to amplify across multiple dilutions supports its potential application in clinical and surveillance settings, including samples with lower viral loads. With continued vaccine hesitancy globally, genome sequencing will play an increasing role in patient care, public health management and medical education. Future work should investigate the role of reverse transcription and RNA secondary structure in contributing to incomplete genome recovery. Continued refinement of this assay will be essential to improve accuracy, reliability, and inclusivity across diverse genotypes.

P5_LL-37-ATP5FA1 interaction as a mechanism of postoperative immunometabolic dysfunction in CD8⁺ T-cells

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Purpose: Sterile surgery triggers profound postoperative immunosuppression with pronounced mitochondrial dysfunction in CD8+ T-cells (CTL), rendering the patient susceptible for postoperative complications like hospital-acquired infections or wound healing disorders, increasing overall mortality, and healthcare costs. Here, the antimicrobial peptide LL-37 emerged as an interesting mediator: Due to lack of microbial targets, LL-37 interacts with mitochondria in a charge-dependent manner, reducing mitochondrial fitness and CTL function. However, specific mitochondrial interaction partners that might account for this phenotype and potential strategies alleviating CTL dysfunction are currently unknown.

Methods: CTL (healthy donors and cardiac surgery patients before (T1) or after (T2) surgery) were isolated by microbeads. LL-37 targets were identified by immunoprecipitation/proteomics. Candidate binding targets and their interactions with LL-37 were examined by PLA and knockdown (siRNA), respectively. Mitochondrial function was analyzed by JC-1 staining (mitochondrial membrane potential, $\Delta\Psi m$) and ATP-Synthesis capacity (seahorse). CTL function was assessed by confocal microscopy (co-localization TCR/mitochondria), cytokine secretion (ELISA) and proliferation (CFSE).

Results: LL-37-baited Co-IP identified ATP5FA1, an essential subunit for ATP synthase function, as a potential binding partner of LL-37 (n=10, p=0.015). Functional interaction was confirmed by PLA in vitro (incubation with recombinant LL-37). T2-CTL displayed significant increase of PLA signals (p=0.03, n=4), further corroborating a relevant functional interaction ex vivo. ATP5FA1 knockdown reduced mitochondrial ATP synthesis, collapsed $\Delta\Psi m$ (p=0.03, n=5) and impaired CTL function, recapitulating the LL-37-induced phenotype.

Conclusion: LL-37 exhibits a functional dichotomy: in sterile inflammation, it may contribute to immunosuppression through a direct interaction with ATP5FA1 rather than exerting its classical antimicrobial function. This mechanism contributes to postoperative CD8⁺ T-cell dysfunction and identifies LL-37 as a potential therapeutic target in immunoparalysis.

P6_Functional Analysis of INHBA in the Gene Regulatory Network of EGFR-Mediated Invasion in HNSCC

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Purpose: Head and neck squamous cell carcinoma (HNSCC) is associated with poor prognosis, particularly in recurrent or metastatic disease, where median survival remains below 11 months. Predictive biomarkers for response to immune checkpoint inhibitors and cetuximab-based therapies remain limited. We previously identified an EGFR-regulated gene network linked to tumour invasion in HNSCC, in which INHBA emerged as a central hub. INHBA encodes the βA subunit of Activin A, a secreted ligand of the TGF-β family. This study aimed to functionally characterize INHBA in HNSCC models.

Methods: Local invasion was assessed using three-dimensional spheroid models of FaDu and OSC-19 cells embedded in type I collagen and analyzed by phase-contrast microscopy. Invasive area and invasive distance were quantified using ImageJ. To investigate EGFR and Activin A signaling, spheroids were treated with epidermal growth factor (EGF), cetuximab, and the ALK4/5/7 inhibitors SB431542 (75 μM) and A83-01 (10 μM). In parallel, CRISPR–Cas9 was used to generate putative INHBA knockout clones, and Activin A protein levels were assessed by immunoblotting. Genomic validation and additional functional assays are ongoing. Downstream signaling and transcriptomic changes will be analyzed by immunoblotting and 3′ RNA sequencing.

Results: EGF (9 nM) significantly increased invasive area and invasive distance in FaDu and OSC-19 cells compared to serum-free controls ($p < 0.001$). This effect was reversed by cetuximab (66 nM), confirming EGFR-dependent invasion ($p < 0.001$). Co-treatment with A83-01 significantly reduced EGF-induced invasion in FaDu ($p = 0.0048$) and OSC-19 cells ($p < 0.001$), whereas SB431542 showed no significant effect. These findings support a contribution of Activin A signaling to EGFR-mediated invasion. Consistently, CRISPR-edited clones exhibited markedly reduced Activin A protein levels without complete loss of expression.

Conclusion: These data support a role for INHBA in EGFR-mediated invasion in HNSCC. The generated CRISPR–Cas9 clones provide a basis for further mechanistic studies, pending validation of knockout efficiency at genomic and functional levels.

P7_Galectin-mediated thromboinflammation in pancreatic ductal adenocarcinoma

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Purpose: Pancreatic ductal adenocarcinoma (PDAC) is a highly lethal malignancy characterized by late diagnosis, rapid progression, early metastatic spread, and resistance to therapy. With a median survival of less than 5 months, PDAC accounts for over 95,000 deaths annually in the European Union. PDAC also exhibits a pronounced inflammatory and procoagulant phenotype that promotes tumor progression, immune evasion, and metastasis. Galectin-9, an immunomodulatory lectin, has been implicated in PDAC progression through its effects on tumor-microenvironment interactions; however, its role in hematogenous metastasis, particularly in relation to platelet and neutrophil interactions, remains poorly defined.

Methods: Mouse PDAC cells expressing galectin-9 (KPCCtrl) or knock-out for galectin-9 gene (KPCLgals9-/-) were cultured as monolayers and incubated with washed mouse platelets. Platelet adhesion and procoagulant activity were assessed by immunofluorescence staining for GPIbβ and Annexin V to detect platelet binding and phosphatidylserine exposure, respectively. Lungs from mice intravenously injected with tumor cells (KPCCtrl) or knock-out for galectin-9 gene (KPCLgals9-/-), harvested 8 hours post-injection were cryosectioned, and stained to visualize tumor cells, platelets and neutrophils, using specific markers (GPIbβ and Ly6G) and tumor cell trackers. Both co-culture samples and lung sections were imaged using confocal microscopy, and quantitative analysis of fluorescence signals was performed using ImageJ software.

Results: Our data demonstrate that galectin-9 is a key regulator of tumor cell-platelet interplay in PDAC. Although galectin-9 does not affect platelet adhesion to tumor cells, it strongly enhances platelet procoagulant activity, indicating a specific role in platelet functional activation. In addition, galectin-9 enhances neutrophil recruitment to tumor cell-platelet complexes during the early stages of hematogenous metastasis. This process occurs without major changes in platelet adhesion but reflects a functional modulation of the tumor microenvironment, thereby linking neutrophil recruitment to platelet activation and procoagulant phenotype.

Conclusion: Galectin-9 enhances platelet procoagulant activity and neutrophil recruitment in PDAC, thereby promoting the formation of a thromboinflammatory niche that may facilitate metastatic seeding. Targeting galectin-9 may represent a therapeutic strategy to attenuate cancer-associated thromboinflammation and metastatic progression.

P8_Pro-apoptotic effects of tigecycline and death ligand (TRAIL) in colorectal and leukemic cancer cell lines

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Purpose: Colorectal cancer (CRC) remains a leading cause of cancer-related mortality worldwide, with rising incidence among younger populations. Despite therapeutic advances, resistance to apoptosis remains a major challenge. The tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) selectively induces apoptosis in malignant cells via activation of death receptors; however, intrinsic resistance limits its clinical efficacy. This study investigates whether tigecycline, a glycylcycline antibiotic with antiproliferative and mitochondrial effects, can sensitize cancer cells to TRAIL-induced apoptosis.

Methods: Human colorectal adenocarcinoma (HCT116, SW480) and leukemic (THP-1) cell lines were treated with varying concentrations of tigecycline, alone or in combination with TRAIL. Cell proliferation was assessed using WST-1 assays, and apoptosis was quantified by propidium iodide staining and flow cytometry. Expression of key apoptotic regulators was primarily analyzed by quantitative PCR, focusing on c-FLIP (CFLAR), while Western blot results for c-FLIP remained inconclusive due to poor antibody specificity.

Results: Tigecycline significantly reduced cell proliferation in a dose- and time-dependent manner across all cell lines. Combination treatment with tigecycline and TRAIL enhanced apoptosis, particularly in SW480 cells, as shown by increased sub-G1 populations. Mechanistically, tigecycline did not alter pro-caspase-8 levels but appears to promote apoptosis by reducing c-FLIP-mediated inhibition. Notably, qPCR revealed upregulation of CFLAR mRNA, suggesting a compensatory transcriptional response to c-FLIP protein depletion. These findings indicate that tigecycline enhances TRAIL sensitivity primarily through post-transcriptional modulation of apoptosis regulators. Additionally, tigecycline induced cell cycle arrest, reflected by reduced S-phase and G2/M populations. Bioinformatic analysis confirmed elevated CFLAR expression in colorectal and leukemic cancers, highlighting its role as a therapeutic barrier.

Conclusion: Tigecycline demonstrates significant potential as a sensitizing agent in TRAIL-based therapies by restoring apoptotic signaling in resistant cancer cells. Its dual role in inhibiting proliferation and modulating apoptosis-related pathways provides a strong basis for further investigation in targeted cancer treatment strategies.

P9_Effects of Tigecycline on Death Ligand (TRAIL) Induced Apoptosis in Hepatic Models

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Purpose: Hepatocellular carcinoma (HCC) is the most common primary liver tumor, accounting for over 90% of cases, and is the third leading cause of cancer-related deaths worldwide. Although there are potential treatment options such as transplantation, resection or immunotherapy, the 5-year survival rate is only 18%. Whilst liver transplantation has a low relapse rate, it is severely limited by the lack of donor organs. The more commonly performed surgical removal (resection), the tumor recurs in over 70% of cases. Indicating the urgent need for new therapeutic strategies. It was already shown that tigecycline has an antitumor effect on HCC cells. Building on this, we aim to investigate the potential of Tigecycline to enhance TRAIL-induced apoptosis in HCC cells. Tigecycline is a glycylcyclin antibiotic which has been reported to have anti-tumor effects in various cancer models.

Methods: To investigate the combined effect of Tigecycline and TRAIL, HCC cell lines (HepG2 and Huh7) were treated with individual compounds and in combination. Cell proliferation was analysed using a WST-1 assay, while a wound-healing scratch assay assessed cells' ability to migrate. Apoptosis signaling is determined by analyzing the DNA fragmentation (subG1). Relevant signaling markers (caspase-8 and PARP) were investigated by western blotting. Additionally, HCC morphology was characterized by HE staining and cFLIP expression was analyzed using bioinformatic tools.

Results: We found that Tigecycline has an antitumor effect on HCC cells, which can be observed by the reduced migration of cells under treatment. Also, the WST1 proliferation assay indicates that Tigecycline has a cytotoxic effect. However, we found no enhanced anti-proliferative effects in HCC cells with the combination of Tigecycline and TRAIL. Neither in the WST1 assay nor in the subG1 analysis. Further analysis of the involved molecular markers we found no activation of Caspase-8 but some increased cleavage of PARP, which indicates activation of the apoptosis signaling cascade. A key inhibitor for TRAIL-induced apoptosis is cFLIP. We analyzed the expression by bioinformatic tools (GEPIA3) and found no significant difference in the expression of cFLIP between HCC and normal tissue.

Conclusion: Tigecycline has cytotoxic effects on HCC cells but appears not to enhance TRAIL-induced apoptosis under the here investigated treatment conditions.

P10_TBX20 upregulation and contractile marker dysregulation in thoracic aortic aneurysm: stratification by valve phenotype and dysfunction

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Purpose: Phenotypic switching of vascular smooth muscle cells (VSMCs) from a contractile to a synthetic state plays a central role in aortic remodeling in thoracic aortic aneurysm (TAA). Yet how this process is shaped by valve morphology, valve dysfunction, and regional wall mechanics remains poorly defined. Using bulk and single cell RNA sequencing we identified TBX20 as potential as a candidate transcriptional regulator of this phenotypic transition. Here, we validate TBX20 alongside classical contractile markers (ACTA2, CNN1, TAGLN, MYH11) by RT-qPCR in TAA tissue stratified by valve phenotype and sampling location.

Methods: Aortic tissue samples were obtained from 80 patients undergoing elective surgical repair for TAA. Patients were divided into four groups based on valve morphology (bicuspid vs. tricuspid) and dysfunction (stenosis vs. insufficiency). As controls, 20 non-aneurysmal samples were collected from transplant recipients. Tissue specimens were sampled from both the inner and outer curvature of the ascending aorta to account for regional differences. Subsequently, total RNA was extracted from the samples, reverse-transcribed into cDNA, and analyzed using RT-qPCR with RPLP0 as housekeeping gene. Statistical analyses were conducted to compare aneurysmal and control tissues, as well as subgroup-specific differences using the ddCT-method.

Results: In TAA tissue, TBX20 was nearly twofold upregulated compared with controls (geometric mean FC 1.89, $p_{adj} < 0.0001$), accompanied by significant downregulation of ACTA2 (FC 0.64, $p_{adj} < 0.0001$) and CNN1 (FC 0.74, $p_{adj} = 0.0001$). MYH11 expression remained unchanged, whereas TAGLN was unexpectedly upregulated (FC 1.96, $p_{adj} < 0.0001$). Stratification by valve phenotype and dysfunction showed the most pronounced TBX20 induction in BAV patients with aortic stenosis (FC 3.99, $p_{adj} < 0.0001$), whereas TAV patients with aortic regurgitation showed attenuated effects across all markers. Paired comparison of outer vs. inner curvature revealed no regional differences for any of the five genes.

Conclusion: TBX20 is robustly upregulated in ATAA tissue alongside a partial loss of the contractile VSMC program, most pronounced in BAV with aortic stenosis. Regional outer vs. inner curvature differences are not detectable at the transcript level. These findings position TBX20 as a candidate driver of valve-dependent VSMC phenotypic modulation in ATAA.

P11_Identification of new pharmacological agents targeting TRPM7

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Purpose: TRPM7 is a ubiquitously expressed ion channel with a cytosolic kinase domain. TRPM7 regulates cellular uptake of divalent cations, including Ca2+, Mg2+, and Zn2+, thereby linking the cell's metabolic state to the cellular homeostasis of these cations. TRPM7 plays essential roles in the immune response, proliferation and differentiation, as well as in anoxic neuronal death, cardiac arrhythmia, and tumour progression. Therefore, TRPM7 represents a new therapeutic target. This work aims to explore the pharmacological modulation of the TRPM7 channel using agents selected from a previously conducted High Throughput Screening.

Methods: To assess the effects of pharmacological modulators, recombinant mouse TRPM7 was transiently expressed in HEK293 cells, and aequorin-based bioluminescence was used to monitor TRPM7-mediated Ca2+ influx. To evaluate inhibition of the TRPM7 channel, the extracellular Ca2+ concentration was increased from 0.5 to 5 mM by injecting CaCl2-containing Mg2+-free HEPES-buffered saline (HBS) in the absence or presence of inhibitors. To study activation of the TRPM7 channel, TRPM7-transfected cells were exposed to Mg2+-free HBS containing different concentrations of the putative agonists. The experiments were terminated by lysing cells with 0.1% (v/v) Triton X-100 in Mg2+-free HBS to measure total bioluminescence. For statistical comparison of EC50/IC50 values, GraphPad Prism was used.

Results: We examined three potential activators, of which only one, ralimetinib, acted as a TRPM7 agonist. We further tested ralimetinib using a dose-response approach and determined the EC50 to be x uM. We also evaluated two pending inhibitors and found that one of them, rotigotine, could block TRPM7 activity with an IC50 of x uM.

Conclusion: We identified two new pharmacological agents targeting the TRPM7 channel: Ralimetinib activated the TRPM7 channel, whereas rotigotine inhibited TRPM7. Further experiments are needed to provide mechanistic insights into the action of these compounds on TRPM7.

P12_Role of Bone marrow stromal antigen 2 (BST2) in megakaryopoiesis under Interferon-mediated stimulation

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Purpose: Bone marrow stromal antigen 2 (BST2), known as tetherin, is known to regulate membrane stability in antiviral defense, whereas such function might play a role in megakaryopoiesis, a process involving membrane reorganisation for proplatelet protrusion. In previous studies, it is discovered that BST2 is expressed in MKs, can be up-regulated by IFN/its mimetic Poly I:C and steady-state platelet production was not affected by BST2-KO, while MK membrane remodelling and platelet production are stimulated in acute poly I:C treatment with wild type mice. This study aims at analysing the morphological features of MK and MK progenitor cells in BST2-KO Genotype under IFN-mediated stimulation.

Methods: We use mouse model, in which BST2 is knocked out. Control mice (CRE-) and BST2-KO mice (CRE+) undergo daily injection with Poly I:C for 5 consecutive days, while the bones are harvested on the 6th day. The Sternum undergoes then a whole-mount staining of bone marrow megakaryocytes with vasculature. The samples are then imaged using confocal microscopy, enabling the three-dimensional reconstruction of megakaryocytes' localization and morphological appearance, such as MK and MKP cellularity, MK size and sphericity.

Results and Conclusion: Data analysis is currently ongoing. We expect that BST2 stabilizes the membrane dynamics in megakaryopoiesis and an increase in proplatelet formation and MKP activation in BST2-KO mice is to be observed. With this project, we aim at quantifying the morphological changes of interferon-induced BST2 expression in MKs and exploring the megakaryopoiesis regulatory pathway of IFN.

P13_ITGB4–Laminin-5 Modulation of EGFR-Driven Invasion in Head and neck squamous cell carcinoma

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Purpose: Head and neck squamous cell carcinoma (HNSCC) is a group of biologically similar cancers derived from the mucosal epithelium in the oral cavity, pharynx and larynx. HNSCC is a major global health burden, with approximately 890,000 new cases and 450,000 deaths annually. Despite therapeutic advances 5-year survival remains about 50–60%, with substantial morbidity characterized by locoregional recurrence rates of up to 30% and distant metastasis in up to 30% of patients. Integrin, beta 4 (ITGB4) is a mechanosensing adhesion receptor implicated in tumour invasion and upregulated in HNSCC, where it correlates with Epidermal Growth Factor Receptor/Mitogen-Activated Protein Kinase (EGFR/MAPK) activity. Together with Laminin-5 (LN5), its role in EGFR-driven Epithelial-Mesenchymal Transition (EMT) remains unclear. This study examines ITGB4–LN5–EGFR signalling in extracellular signal-regulated kinase (ERK) activation, EMT, and invasion.

Methods: KYSE-30 WT cells were cultured and seeded to form spheroids over 72 h. The spheroids were embedded in collagen, allowed to polymerize, and treated with EGF, cetuximab, defactinib, avutometinib (or a combination of those inhibitors) and LN5. After 72 h, spheroid morphology and behaviour were assessed by light microscopy and quantitative image analysis.

Results: EGF stimulation increased invasive area and migration distance in KYSE-30 WT spheroids compared to serum-free conditions. Co-treatment with LN5 further enhanced invasion, indicating a cooperative effect on tumour cell motility. Invasion was variably reduced by inhibiting EGFR with cetuximab or downstream signalling with defactinib and avutometinib, with the strongest suppression observed upon combined pathway targeting. Notably, LN5 partially attenuated the inhibitory effects of these agents, suggesting ECM-mediated resistance mechanisms. Unexpectedly, combined EGFR and Focal Adhesion Kinase (FAK) inhibition (cetuximab + defactinib) increased invasive area in one experimental set, suggesting paradoxical compensatory signalling or selection for a more invasive phenotype under dual pathway blockade.

Conclusion: Our findings support that EGFR and integrin signalling both contribute to ERK-associated invasion in KYSE-30 HNSCC cells, consistent with a partially integrated bifurcated model. However, the observed variability and paradoxical response to combined inhibition indicate that this integration is not strictly linear and likely involves compensatory signalling mechanisms, suggesting both ECM-mediated resistance mechanisms and, under dual pathway blockade, compensatory signalling or selection for a more invasive phenotype.

P14_Assessing the Hemocompatibility of Electrospun Thermoplastic Polyurethane (TPU)

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Purpose: Commonly used synthetic vascular grafts for aortic surgery are currently unable to mimic physiological behavior. Upholding physiological functions, specifically the “Windkessel effect” of the aorta, is essential to prevent long-term failure of vascular grafts. Electrospun thermoplastic polyurethane (TPU) combines mechanical stability as well as mimicking the original elastic properties of the aorta. To assess hemocompatibility of biomaterials, standardized assays are often used. These, however, only allow for a very limited amount of material to be tested and are rather expensive. For this reason, we present a newly developed customized testing kit for the standardized hemolytic assessment of biomaterials.

Methods: Electrospun TPU was cut into disks, sterilized using UV radiation, and put into contact with human blood for 24 hours at 37°C while being in orbital motion. Beforehand, the blood had been washed to only contain erythrocytes and a standardized solution to eliminate disrupting factors that might cause hemolysis and to better assess the damage done to the erythrocytes. Washing steps included adding a buffer solution relative to the blood volume, as well as centrifuging the compound. After the incubation period, the blood samples exposed to the materials were centrifuged, and the supernatant was used to assess hemolysis via microplate spectrometry at 405 nm by measuring the amount of free hemoglobin released from damaged erythrocytes. The results were then compared to other tested materials like polytetrafluoroethylene (PTFE) or polypropylene (PP).

Results: The newly developed assay was successfully established as well as validated and revealed that TPU only causes 0.25% - 0.9% of hemolysis, which falls into the range of acceptance for biomaterials according to a defined standard. Furthermore, TPU demonstrated superior performance compared to other tested materials, including clinically used biomaterials such as the Gore Pericardial Membrane, which exhibited hemolysis levels of up to 1.5%.

Conclusion: Electrospun TPU can be considered hemocompatible. If other aspects are further optimized, for example its activation of the coagulation cascade, electrospun TPU can be a promising material for vascular graft development in the future.

P15_Hydrogel injections promote the maturation of Müller cells in human iPSC-derived retinal organoids and thereby also benefit neuronal development and survival

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Purpose: Human induced pluripotent stem cell (hiPSC)-derived retinal organoids (hRO) are a powerful tool for modeling human tissue development and disease in vitro and reduce reliance on animal models. Müller glia cells are crucial for retinal structure and function, but in current organoid systems they often fail to mature, particularly lacking proper apical endfeet contacting the inner limiting membrane (ILM). We hypothesized, that adding a vitreous-like extracellular matrix, intended to correspond to the corpus vitreum, could promote inner retinal boundary formation and enhance Müller cell maturation.

Methods: hRO were generated from the IMR90-4 hiPSC line. At differentiation day 80 (D80) microinjections were performed into the hRO core using hydrogels composed of HyStem® or vitronectin. Phosphate-buffered saline (PBS) injections and non-injected organoids served as controls. Samples were collected at D80, D145 and D180 for further analysis. Müller cell maturation as well as neuronal development and survival was assessed using immunohistochemical staining for established molecular markers.

Results: We found enhanced Aquaporin4 (Aqp4) levels in gel-injected hRO at earlier time points (D145). We therefore hypothesize, that Müller cells mature faster in gel-injected hRO, compared to non- or PBS-injected controls. Gel-injection also promoted neuronal health, as demonstrated by increased neurofilament light chain (NFL) expression and higher calretinin positive cell counts. A shift in staining intensity can be detected for the transcription factor Sox2 that localized to nuclei of retinal precursor cells (low expression) and mature Müller cells (higher expression), but not to those of differentiated neurons.

Conclusion: Incorporating an artificial extracellular matrix scaffold that mimics the vitreus provides a structural anchoring site for the Müller glia cells allowing for the endfeet to form more reliably. This approach appears to promote a more physiologically accurate spatial organization of the retinal organoids.

P16_The role of Janus- and c-Jun-N-terminal-kinases in pemphigus signaling

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Purpose: Pemphigus vulgaris is a rare autoimmune disease characterized by autoantibodies directed against desmosomal proteins, primarily affecting the epidermis. The resulting loss of cell–cell adhesion leads to blister formation and reduced mechanical stability of the skin. Growing evidence suggests that these autoantibodies, through binding to desmosomal components, activate intracellular signaling pathways that ultimately result in desmosomal disassembly. Various protein kinases have been implicated as key mediators within these pathways; however, their individual contributions remain incompletely understood. The aim of this study was to investigate the role of JAK and JNK kinases in pemphigus signaling and to assess the effects of their pharmacological inhibition on desmosomal integrity.

Methods: To investigate the effects of these kinases on the pemphigus phenotype, an immunofluorescence-based analysis was performed using human keratinocytes. The monoclonal antibody AK23 has previously been established as a reliable tool to mimic the effects of pemphigus autoantibodies in vitro. For the experimental setup, cells were pretreated with the kinase inhibitors tofacitinib, baricitinib, and SP600125, followed by exposure to AK23. The resulting effects on key features characteristic of pemphigus, namely depletion of the desmosomal protein Dsg3 and retraction of keratin filaments from desmosomes, were assessed by confocal microscopy. These markers were quantified, and treated cells were compared with untreated controls.

Results: Baricitinib, a JAK1 inhibitor, showed no detectable effect on AK23-induced alterations. In contrast, pretreatment with tofacitinib, a JAK3 inhibitor, exerted a protective effect on keratin filament retraction; however, this effect did not extend to Dsg3 depletion. Inhibition of JNK signaling with SP600125 demonstrated a statistically significant protective effect on both keratin filament retraction and Dsg3 fragmentation. While the protective effect on Dsg3 did not fully restore baseline conditions, it was sufficient to attenuate AK23-induced alterations.

Conclusion: These findings suggest that JNK and JAK3, but not JAK1, contribute to pemphigus-associated signaling pathways. JAK3 appears to be primarily involved in mediating keratin filament retraction, whereas JNK affects both key hallmarks of the pemphigus phenotype. However, the mechanisms of kinase activation and additional pathway components remain to be elucidated.

P17_Investigating the effects of PKD inhibition on prostate smooth muscle contractility and cell viability

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Purpose: Benign prostatic hyperplasia (BPH) affects about 50% of men aged 50-59 years and over 90% of men in their nineties, with up to 40% developing lower urinary tract symptoms (LUTS). Key contributors to LUTS include hyperplastic growth of the prostate and increased smooth muscle tone. Current pharmacological treatments targeting the latter, including α1-adrenoceptors antagonists and phosphodiesterase-5 inhibitors, are limited by high discontinuation rates (up to 90% after one year), driven by suboptimal efficacy and side effects. This may in part reflect the contribution of non-adrenergic mechanisms to prostate smooth muscle contraction. Consequently, alternative molecular targets that modulate contractility are of considerable interest. Preclinical studies suggest that protein kinase D (PKD) is involved in vasoconstriction and the regulation of vascular tone. Given the similarities between vascular and prostatic smooth muscle contraction, a comparable role of PKD in the prostate is plausible. This study investigated the effects of the PKD inhibitor CID755673 on adrenergic contractility in human prostate tissue and on cell viability.

Methods: Adrenergic contractions were assessed in human prostate tissue obtained from holmium laser enucleation of the prostate (HoLEP) using organ bath experiments. Tissues were stimulated with phenylephrine (PE) or noradrenaline (NA) in the presence of CID755673 (10 µM; n=5 each). Cytotoxicity was evaluated using Cell Counting Kit-8 (CCK-8) assay in WPMY-1 human prostate stromal cells treated with CID755673 (0.3–30 µM) for 24, 48, and 72 hours.

Results: CID755673 significantly inhibited PE-induced contractions (p=0.0081), while inhibition of NA-induced contractions did not reach statistical significance. In WPMY-1 cells, CID755673 significantly reduced viability in a dose- and time-dependent manner, with more pronounced effects at higher concentrations (10 µM), although variability increased at later time points.

Conclusion: These findings suggest a role of PKD in the regulation of prostatic smooth muscle tone and highlight CID755673 as a candidate for further investigation. The organ bath results indicate possible agonist-dependent differences. Future studies should include additional contractility experiments using selective α1-adrenoceptor agonists (e.g. methoxamine) and non-adrenergic agonists (e.g. endothelin-1, thromboxane A2), increased sample sizes, and further characterization of cytotoxic and anti-proliferative effects in additional models.

P18_Glycinergic input to neurons of the vertical gaze center in monkey and human

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Purpose: The rostral interstitial nucleus of medial longitudinal fasciculus (riMLF) in the rostral midbrain plays a key role in generating vertical saccades. It contains excitatory premotor burst neurons showing a high frequency burst during saccades. They are ensheathed by perineuronal nets and hold the calcium binding protein parvalbumin. Burst neurons for upward saccades can be distinguished from those for downward saccades by the presence of another calcium binding protein, calretinin. In monkey during fixation or slow eye movements saccadic premotor burst neurons are inhibited by glycinergic input from pontine omnipause neurons. Here we investigated wether glycinergic input is present on up- and down-burst neurons within the riMLF in monkey and man.

Methods: Transversal 5µm paraffin sections of monkey and human brain (two cases each) were immunostained for different antigens. Double-immunohistochemical staining was performed with antibodies against aggrecan (ACAN) for identifying perineuronal nets and antibodies against calretinin (CR) to differentiate between up- and down-burst neurons. Adjacent sections were stained with glycine marker (GlyT2 transporter as a presynaptic marker in monkey and GlyR4 receptor as a postsynaptic marker in human).

Results: ACAN labelling identified a cell population with perineuronal nets in an area matching with riMLF. This group involves up-burst and down-burst neurons, which are intermingled without any apparent spatial organization. Both subsets receive glycinergic input in both species. However in monkey, the aggrecan and glycine labelled regions do not completely overlap: a medial portion of riMLF with less intense and more diffuse ACAN labelling revealed only few scattered glycinergic terminals not associated with neuronal cell bodies.

Conclusion: The study shows that as in monkey up- and down-burst neurons in the human riMLF are inhibited by glycinergic afferents most likely from omnipause neurons. However, in monkey a different organization of the riMLF is suggested by ACAN-based perineuronal net labelling and the distinct glycine input that spares the medial part, which may imply a different function. This suggests that in monkey the labelling of glycinergic afferents may be a more specific marker for burst neurons in riMLF.

P19_Cultivation of patient-derived xenograft cells of AML for ex vivo drug testing

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Purpose: Leukemia is a type of blood cancer which originates in hematopoietic tissues such as the bone marrow, where malignant cells proliferate and displace normal blood cell populations, which impair their physiological functions. Especially Acute Myeloid Leukemia (AML) predominantly affects elderly patients and is associated with a poor prognosis. Consequently, there is a strong need for the development of more effective therapeutic strategies. Patient-derived xenograft (PDX) models are used in preclinical research, as primary AML cells can be propagated in immunocompromised mice. However, cultivating patient-derived xenograft (PDX) cells to perform drug therapy in vitro remains challenging.

Methods: In this study, we compared the viability and proliferative capacity of PDX-derived AML cells (n=6) and AML or ALL cell lines (n=3) over a period of two weeks. Cell viability and proliferative capacity was assessed using trypan blue exclusion with a Neubauer chamber and flow cytometry-based analysis. Furthermore, the anti-leukemic effects of Venetoclax and a novel compound (Substance X) were evaluated after 24 and 48 hours of treatment in one AML PDX model.

Results: Our results demonstrate that PDX cells decline in viability during in vitro culture, whereas established cell lines maintain high viability and proliferative capacity. In addition, Venetoclax showed a stronger anti-leukemic activity compared to Substance X at both time points.

Conclusion: These results highlight the limitations of current in vitro culture conditions for maintaining PDX-derived AML cells and the continued reliance on in vivo models for proliferation. Therefore, developing improved culture conditions that more closely mimic the in vivo microenvironment, with the aim of reducing the reliance on animal models, is highly needed.

P20_Defining histological traits of paediatric hepatocellular carcinoma (HCC)

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Purpose: Hepatocellular carcinoma (HCC) is a malignant liver tumour rarely occurring in children and young adults, with great intratumoral heterogeneity and a lack of data to guide clinical treatment and predict prognosis. Unlike adult HCC, paediatric cases most often develop de novo in functionally and structurally healthy liver, underscoring fundamental biological differences that remain poorly understood. The main treatment for HCC to date is surgical resection of the tumour, as these tumours do not respond satisfactorily to chemotherapy. Consequently, prognosis largely depends on the success of resection, the stage of the tumour, and the presence of metastasis. Some mutations that influence the prognosis are known, but the key genomic alteration in HCC has not yet been identified or applied in clinical practice to predict therapeutic response. Increasing evidence suggests that aggressive tumour expansion and loss of cellular differentiation are key determinants of adverse outcome. However, the histopathological and molecular mechanisms underlying these processes in paediatric HCC remain insufficiently characterized.

Methods: First, we conducted scanning and histological examinations of hematoxylin & eosin-stained HCC tumour sections. This was followed by immunofluorescence staining on cryosections from nine paediatric HCC samples, six transitional samples (TLCT), five hepatoblastoma (HB) of high-risk type and three normal liver tissue samples (N). The sections have been processed using a rabbit anti-Ki67 antibody and a mouse anti-EpCAM antibody, followed by species-specific fluorescently labelled secondary antibodies. Then, fluorescent images were acquired and analysed using the EVOS™ M7000 imaging system.

Results: For the analyses, we plotted Ki-67 expression levels (%) across multiple clinical features, with particular emphasis on overall survival (OS) and event-free survival (EFS). Surprisingly, no statistically significant associations were detected between Ki-67 expression and any of the examined clinical parameters.

Conclusion: These findings suggest that there is no correlation between proliferation and clinical outcome. Given the current therapeutic limitation and poor prognosis of HCC, there is an urgent need to continue identifying meaningful parameters for improving clinical treatment.

P21_Targeted Gene Knockout in Primary Mouse T-Cells

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Purpose: This project aimed to generate targeted gene knockouts in mouse T-cells to investigate the function of integrin genes (Itga4, Itgal, Itgb1), which were specifically selected due to their known involvement in immune cell migration in the context of multiple sclerosis. To achieve a targeted gene knockout, a retroviral CRISPR-Cas9-based approach was employed using the plasmid pMSCV-sgRNA-EGFP-puro. This vector was chosen for its efficient delivery into primary murine T-cells, puromycin resistance for antibiotic selection, U6 promotor-driven sgRNA expression and EGFP reporter for visual identification of successfully transfected cells.

Methods: The experimental workflow involved cloning gene-specific single-guide RNAs (sgRNAs) into the plasmid through restriction digestion with BbsI, followed by dephosphorylation to prevent self-ligation, gel purification of the vector, oligonucleotide phosphorylation and annealing, and ligation. The plasmids were amplified into E.coli bacteria and then verified by PCR using the corresponding primers (Itga4-R, Itgal-R, Itgb1-R) and hu6-F. After successful verification, HEK cells were transfected to produce retroviral particles, which were then collected from the culture medium. Primary mouse T-cells were obtained from spleen tissue, then purified, and isolated using CD3/CD28 antibodies. These cells were transduced with the retrovirus, allowing stable genomic integration of the sgRNA construct. Puromycin selection ensured survival of only successfully transduced cells.

Results: Stable integration of the sgRNA construct into mouse T-cells was achieved, and successfully transduced cells were selected. In Cas9-expressing transgenic T-cells, the CRISPR-Cas9 system introduced targeted double-strand breaks at the targeted site. These breaks were predominantly repaired through error-prone non-homologous end joining, which is expected to result in a functional gene knockout. However, final validation via antibody staining was unsuccessful, likely due to insufficient primary antibody activity.

Conclusion: This study demonstrates a robust workflow combining molecular cloning, bacterial amplification, retroviral production, and primary T-cell manipulation to investigate gene function. Despite experimental limitations in final validation of a targeted gene knockout, the approach provides a solid framework for studying the role of integrin genes in T-cell-mediated immune responses relevant to multiple sclerosis.

P22_Construction of a retroviral sgRNA vector to analyze autoreactive CNS T cell activation in multiple sclerosis and retroviral overexpression of KLF2 to investigate antiinflammatory pathways in multiple sclerosis associated neuroimmune activation

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Purpose: Multiple sclerosis is a chronic autoimmune disease in which autoreactive T-cells drive CNS inflammation, demyelination, and neurodegenerative pathways. To dissect how specific genes regulate Tcell activation, migration, and function during neuroinflammation in multiple sclerosis, sgRNAs are retrovirally introduced into T-cells to enable targeted CRISPR-mediated gene modification. KLF2 is considered a potentially protective factor against neuroimmune inflammatory processes. Overexpression may lead to a significant reduction in inflammatory signaling pathways and may hold potential as a target for immunomodulatory therapy in multiple sclerosis.

Methods: For sgRNA vector generation, the pMSCVsgRNAEGFP plasmid containing the target-specific sgRNA cassette was digested with the appropriate restriction enzymes. The resulting 5'-3' overhangs were converted into blunt-ends by enzymatic blunting before ligation into the retroviral vector pLXSNNFAT6GFPneo. For KLF2 overexpression, murine RNA was isolated from donor tissue and reverse-transcribed to generate full-length KLF2 cDNA. The cDNA was amplified by PCR, and the primers were designed to include the sequences corresponding to the restriction enzyme sites required for cloning. The resulting PCR product was subsequently inserted into the retroviral expression vector pMSCVsgRNABFPpuro. For this purpose, the vector backbones were enzymatically digested using restriction enzymes to enable directional cloning and dephosphorylated to prevent self-ligation. The ligated constructs were introduced into competent ampicillin-resistant bacterial cells using high efficiency transformation. Positive clones were selected and confirmed by restriction enzyme digestion.

Results: Multiple ligation attempts failed to produce a correct construct, indicating that the chosen cloning strategy suffered from significant efficiency limitations. The most likely causes include inefficient bluntend ligation.

Conclusion: The cloning inefficiency highlights methodological limitations that prevented successful sgRNA vector and KLF2 construct generation. Moving forward, using advanced cloning approaches will be essential to establish a reliable system for studying T-cell activation pathways in multiple sclerosis.

P23_Low-Density Neutrophils – Friends or Foes in Neonatal Immunity: Optimization of assay conditions for LDN-T-cell Co-Culture

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Background: Perinatal infections and sepsis remain major causes of mortality in preterm infants possibly related to a bias of the immune system toward regulatory functions. Previous in-house CITE-seq data revealed an enrichment of low-density neutrophils (LDNs) with granulocytic myeloid-derived suppressor cell-like features, alongside a predominance of regulatory T-cell phenotypes in preterm infants <32 weeks of gestation. These findings suggest a suppressive immune landscape that may limit effective T-cell responses. However, functional assays to assess neonatal T-cell activation and its modulation by LDNs remain challenging due to limited volume and restricted availability of neonatal blood samples which often precludes the use of freshly isolated cells. Therefore, we aimed at optimization of stimulation conditions and readouts using cryopreserved samples to overcome these limitations.

Methods: Cryopreserved peripheral blood mononuclear cells (PBMCs) from six adult donors were thawed and cultured under baseline (IL-2 only) and stimulated (IL-2 plus stimulus) conditions. Stimulation was performed using either phorbol 12-myristate 13-acetate (PMA; n=3; 2h; 100 ng/mL) or anti-CD3/CD28 monoclonal antibodies (n=3; 14h, 20h, and 96h; 3 µg/mL anti-CD3 and 5 µg/mL anti-CD28). T-cell responses were assessed by flow cytometry at 14h, 20h, and 96h of culture, including proliferation (CellTrace Violet dilution; expansion index), cytokine production (intracellular IFN-y expression), and differentiation status (CD62L and CD45RA expression).

Results: T-cell proliferation increased markedly at 96h of culture upon anti-CD3/CD28 stimulation (mean expansion index: 6.3 vs. 1.0 at baseline), whereas minimal proliferation was observed at earlier time points. IFN-y expression peaked at 14-20h of culture. Overall, anti-CD3/CD28 stimulation induced stronger proliferative responses compared to PMA. Phenotypically, at baseline T cells were predominantly naïve (CD62L+CD45RA+: 62.5%), while prolonged stimulation promoted differentiation toward an effector memory phenotype (CD62L-CD45RA-: 24.6% vs. 9.0% at baseline).

Conclusion: Cryopreserved PBMCs retain robust functional responsiveness; however, T-cell activation dynamics vary substantially depending on stimulus and time point. These findings define critical parameters for measuring T-cell responses under conditions of limited samples availability and provide a foundation for future LDN-T-cell Co-culture assays in neonatal samples.

P24_Data-Driven Psychosis Phenotypes: Clinical Profiles and Longitudinal Outcomes

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Purpose: Psychosis is a clinically heterogeneous syndrome that is only partly captured by conventional diagnostic categories. Symptom-derived phenotypes may provide a complementary framework for describing clinical variation and prognosis. This analysis aimed to characterize data-driven psychosis phenotypes and assess differences in remission, longitudinal symptom change and functional outcomes.

Methods: The sample included 557 individuals with psychosis-spectrum disorders from three cohorts: MIMICSS, MUC and PRONIA. Patients had been assigned to one of three symptom-derived factors identified using non-negative matrix factorization of Positive and Negative Syndrome Scale (PANSS) and Scale for the Assessment of Negative Symptoms (SANS) items. Baseline sociodemographic, clinical and functional characteristics were compared across factors. Longitudinal analyses were restricted to PRONIA and used 9- and 18-month follow-up data. Outcomes included symptomatic remission according to Andreasen criteria, changes in symptom severity and global functioning. Between-factor differences were tested using ANOVA, Kruskal-Wallis or chi-square tests with false discovery rate correction for multiple comparisons, followed by post-hoc comparisons where applicable.

Results: Factor 2 was characterized by the highest positive and lowest negative symptom scores, fewer previous hospitalizations and shorter illness duration. Factor 1 showed the most pronounced negative symptom burden, whereas factor 3 demonstrated intermediate negative symptom levels and higher depressive symptoms. Across the full baseline sample, no significant factor differences were observed in sociodemographic characteristics or global functioning. Remission did not differ significantly between factors, with 58% of participants meeting criteria at 9 months and 62% at 18 months. Initially elevated positive symptoms in factor 2 converged with the other factors at 9 months and remained low at 18 months. Factors 1 and 3 showed higher negative symptom levels across follow-up, factor 1 improved consistently, whereas factor 3 improved at 9 months but deteriorated by 18 months. Changes in global functioning and depressive symptoms did not differ significantly between factors across follow-up.

Conclusion: Data-driven psychosis phenotypes captured meaningful baseline heterogeneity and differentiated symptom change, but did not clearly distinguish remission or functional outcomes. Positive symptoms appeared more changeable, whereas negative symptoms showed greater persistence, reflecting a known treatment challenge in psychotic disorders. These findings support transdiagnostic, symptom-based approaches and highlight negative symptoms as a key intervention target.

P25_Proteomic Profile of Transition to Psychotic Disorder in the Clinical High-Risk State

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Purpose: The aim of this project was to investigate differences in the proteomic profile of individuals who transitioned from the CHR status to psychosis (transitioners) and those who did not (non-transitioners) and hence investigate the proteomic signature of psychosis onset.

Methods: We analysed data collected within the multi-site PRONIA study (Personalised Prognostic Tools for Early Psychosis Management) (n = 221, including n = 110 CHR and n = 111 recent-onset depression). Transitioners and non-transitioners were compared on demographic, cognitive, social, psychopathological and functioning variables. Group differences in 277 proteins were then investigated using t-tests and linear regression with covariate correction. 57 proteins showed significant differences between individuals who transitioned and those who did not. After correcting for covariates that could possibly influence the measured protein concentrations, independent of transition status (storage length, plate), 27 proteins significantly differed between the groups. These 27 proteins then underwent protein-protein interaction network analyses in STRING and pathway analyses in g:Profiler.

Results: 11 of the 27 proteins demonstrated interactions amongst them, with several proteins involved in the blood coagulation cascade and the complement system. Pathway analyses highlighted the organisation of the extracellular components, suggesting involvement of significant proteins in neuroinflammation and the hyaluronan metabolic process.

Conclusion: These preliminary results offer insights into the biological pathways implicated in psychosis onset and highlight the promising use of proteomics in predicting transition to psychosis, either alone or in combination with clinical and neuroimaging data.

P26_Investigating childhood trauma and interacting risk and resilience factors to predict depression, psychosis, and high-risk individuals

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Purpose: Childhood trauma (CT) is common, and a transdiagnostic risk factor for mental health disorders. However, post-trauma outcomes vary across individuals in part due to multisystemic resilience mechanisms. Previous findings suggest that CT data alone are insufficient to distinguish between diagnostic groups such as recent-onset depression (ROD), recent-onset psychosis (ROP) and individuals at clinical high-risk for psychosis (CHR). Our study aimed to investigate risk and resilience factors interacting with childhood trauma experiences to determine if it is possible to predict which individuals develop psychosis versus depression following exposure to CT.

Methods: Our sample included 1083 individuals (ages 15 to 40) with ROD, ROP, CHR, and healthy controls (HC) from the multisite Personalised Prognostic Tools for Early Psychosis Management (PRONIA) study. We applied support vector machine learning classification models (L2-regularized logistic regression), within a nested 10-fold cross-validation structure to predict diagnostic and healthy control groups using NeuroMiner software. Features used to predict groups included data from the Childhood Trauma Questionnaire, Bullying Scale for Adults, Resilience Scale for Adults, the NEO Five-Factor Inventory, Coping Inventory for Stressful Situations, Multidimensional Scale of Perceived Social Support and the Level of Expressed Emotion Questionnaire.

Results: Models were able to differentiate clinical groups from healthy controls with high levels of accuracy (BAC= 85% for HC vs ROD; BAC= 88.1% for HC vs CHR; BAC= 81.2% for HC vs ROP). The most significant predictive features differentiating ROP and ROD (BAC=65.1%) included elevated overall childhood trauma, physical neglect, bullying stress, and sexual harassment predictive of ROP. Additionally, higher Task-Oriented Coping and Perception of Self Resilience contributed to ROP prediction, while higher Emotional-Oriented Coping and Neuroticism contributed to ROD prediction.

Conclusion: By integrating resilience factors, such as coping strategies and personality, together with childhood trauma, we demonstrated that a multisystemic approach allows for a more accurate classification and understanding of different psychiatric trajectories. These findings may provide and enhance detection of roadmaps for personalized, targeted prevention and intervention for psychopathology.

P27_Defining disease-relevant regulation of protein abundance in Rett Syndrome using spatial multiomics

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Purpose: Rett Syndrome is an X-linked neurological disorder affecting about 1 in 10.000 live born females worldwide. It is caused by mutations in the methyl CpG binding protein gene (Mecp2). Children with RTT apparently normal growth during the first 12–18 months of life, following which, a progressive neurological decline sets in. Symptoms observed in patients with RTT are very heterogenous and are usually attributed to cell-type specific molecular dysregulation within the brain. This study aimed to examine the underlying regulatory forces that contribute to the region-specific alterations of protein abundance within the RTT brain.

Methods: Liquid-chromatography coupled tandem mass spectrometry (LC-MS/MS) was performed for proteome analysis on neuronal populations isolated by laser capture microdissection (LCM) from the dentate gyrus (DG), cornu ammonis 1 (CA1), and cerebellar granule neurons (Cb) from Mecp2 knockout (Mecp2-/y) and wildtype (WT) mice. Transcriptomic data from the same regions were retrieved from publicly available datasets. Fold changes (Log2FC) for both mRNA and protein expression were calculated between Mecp2-/y and WT to correlate region-specific molecular dysregulation at both the transcriptomic and proteomic levels.

Results: Across all brain regions investigated, a moderate to weak correlation was observed between mRNA and protein changes. The discordance spanned at all hierarchical levels, ranging from whole proteome to significantly upregulated proteins to both targeted and untargeted pathways. At the same time, we observed upregulation of protein-degradation pathways in specific cell populations of RTT brains.

Conclusion: Our findings demonstrate a spatially resolved correlation between the transcriptome and proteome of RTT brains. Multi-omics data integration shows that protein degradation takes precedence in Cb, where the aforementioned correlation is weak. In the hippocampus, however, effects are more heterogenous. It therefore suggests that post-transcriptional mechanisms, such as altered protein stability, degradation, or complex formation, may play a major role in shaping the protein abundance landscape in RTT. While RTT is recognized as a transcriptional pathology, our results demonstrate a misalignment between transcriptomic alterations and functional proteomic consequences. This discrepancy necessitates a multi-omics approach, suggesting that future studies focused on cell-type-specific protein regulation are essential to reveal effective therapeutic targets for RTT and related complex disorders.

P28_In vitro characterization of oligodendrocyte progenitor cells

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Purpose: The mammalian brain is composed of an extraordinary cell type diversity, originated during embryonic development, which allows to perform very complex motor tasks and, in humans, high cognitive functions. Unfortunately, traumatic injuries or neurodegeneration cause the irreversible loss of neurons, leading to motor and cognitive dysfunction. Direct neuronal reprogramming is a promising avenue to replace lost neurons via the conversion of endogenous, non-neuronal cells into functional neurons without passing by a proliferative state. Among the cells present in the brain, oligodendrocyte precursor cells (OPCs) are of great interest: in fact, they are derived from radial glial cells, which give also rise to neurons during embryonic neurogenesis, are widespread throughout the central nervous system, and can proliferate both in homeostasis as well as following a disease. This last feature makes them a very attractive potential cell type to be targeted for reprogramming, because their depletion as consequence of their conversion into neurons would be compensated by the proliferation of non-targeted OPCs. Despite this, OPCs have been poorly investigated in direct reprogramming.

Methods: To investigate the possibility to reprogram OPCs into neurons, Masserdotti lab has been working to establish a protocol to isolate OPCs from the cortical gray matter newborn mice via Magnetic-activated cell sorting (MACS). Isolated cells were plated onto PLL-coated coverslips, fixed 24 hours later and their identity was assessed via immunofluorescence. Fabio Laredo, a PhD student in Masserdotti lab, performed the MACS sorting and seeded the cells. In the context of the Forschungsmodul, I joined Fabio in performing immunofluorescence to evaluate the expression of OPC markers and acquire the images. Then, I quantified the proportion of cells (DAPI+) expressing selected markers.

Results: This analysis showed that a very high proportion of cells express the OPC markers Sox10, Olig2, and PDGFRα across biological replicates, thus supporting the effectiveness of the MACS-based isolation of OPCs. Overall, these results pave the way to isolate OPCs for testing their direct neuronal conversion in vitro.

Conclusion: The results show that OPCs can be isolated from the cortical gray of neonatal mice and cultured, paving the way for experiments of direct neuronal reprogramming.

P29_synNotch-Mediated Spatial Control of Astrocyte-to-Neuron Reprogramming

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Purpose: Direct neuronal reprogramming of astrocytes is a promising avenue to replace neurons lost upon neurodegeneration or traumatic brain injury. This is achieved by the expression of specific reprogramming factors in non-neuronal cells, such as astrocytes. To date, the system lacks spatial control, making it difficult to predict or influence the generation of neuronal circuitry. Synthetic Notch (synNotch) – a Notch-based, controllable, cell-cell contact-dependent receptor – may provide a spatially controlled reprogramming system. This pilot project aims to assess whether such a system can be used for astrocyte-to-neuron conversion.

Methods: Primary cultures of mouse astrocytes were divided into two groups. The first group was transduced with a lentivirus encoding the membrane-bound GFP (green fluorescent protein) as the synNotch ligand; the second group with a lentivirus encoding a synNotch receptor fused to a tetracycline transactivator (tTA) and/or a lentivirus encoding either mScarlet (a red fluorescent protein (RFP)) or mScarlet and Neurog2 (the reprogramming factor used in this study) under the control of a tetracycline-responsive promoter (TET-OFF). Two days post-transduction, astrocytes were co-cultured in various combinations and treatments, including DAPT (a γ-secretase inhibitor repressing synNotch activation) and doxycycline (a TET-OFF inhibitor) to suppress transgene activation. Nine days post-transduction, the cells were fixed and analysed to evaluate under which conditions direct conversion occurred.

Results: Preliminary results suggest that ligand-mediated activation of the reprogramming factor can induce the conversion of mouse astrocytes, as the proportion of RFP-positive induced neuronal cells is higher than in the various negative controls (e.g., absence of ligand, mScarlet-only expression, or treatment with DAPT or doxycycline). However, some technical aspects need further investigation and improvement: for instance, membrane-bound GFP (the ligand) was barely expressed, background activity was observed, as some mScarlet-positive cells were detected in the absence of the ligand, and we found GFP-mScarlet double-positive cells.

Conclusion: This proof-of-concept project demonstrates the feasibility of a synNotch system for astrocyte-to-neuron conversion. Further experiments will be performed to improve the system and develop a second-generation system in which the ligand is bound to a substrate (e.g., fibrin) to induce spatially controlled astrocyte-to-neuron reprogramming.

P30_Analysis of genetically encoded sensors for Unfolded Protein Response

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Purpose: Unfolded protein response (UPR) is a safeguard mechanism triggered by misfolded proteins in the endoplasmic reticulum (ER). ER stress activates the PERK, IRE1α, and ATF6 pathways. ATF4 (PERK) and ATF6 are transcription factors that upregulate UPR target genes and regulate cell states through distinct signaling cascades. However, the kinetics and dynamics of UPR activation remain poorly understood, limiting insight into how cells balance survival and apoptosis. To address this, the Masserdotti lab is developing genetically encoded sensors for ATF4 and ATF6 that report UPR activation via fast-folding, fast-degrading nuclear fluorescent proteins (Achilles and mScarlet-i3). Here, I analyzed UPR kinetics and intensity over time by quantifying fluorescent protein expression.

Methods: Together with Deniz, PhD candidate in Masserdotti's lab, HEK-239T cells were transduced using two different lentiviral constructs. The first construct contains 5 repeats of the ATF6 binding site. This controls the expression of a synthetic gene in which the coding sequence of mScarletI3 has been engineered to localize into the nucleus (NLS) and to have a short half-life (using a PEST sequence). In the second construct, a strong promoter controls the expression of a transcribed-not-translated first exon of ATF4, fused to a fluorescent protein Achilles with a PEST and NLS signal. Cells were treated with Tunicamycin (1 µg/mL), serving as an ER stress inducer. Cell cultures were fixed after 1h, 4h, 6h and 24h, then stained with DAPI and antibodies against mScarletI3, Achilles, ATF4 and ATF6.

Results: We observed a continuous increase in the proportion of cells expressing mScarletI3 / ATF6 (normalised to DAPI) whereas the percentage in the control group showed no such increase. Analysis is ongoing to quantify the increase in intensity over time.

Conclusion: Although preliminary, the results suggest that the sensors can detect UPR within 6 hours from the treatment. More currently ongoing experiments may confirm this first observation and could reveal the extent of UPR activation by quantifying the intensity of the fluorescent proteins.

P31_Muscle Activity of Patients with RSA

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Purpose: Reverse shoulder arthroplasty (RSA) is a surgical procedure used primarily in patients with severe rotator cuff deficiency or advanced shoulder joint degeneration, where conventional treatments fail to restore function. In RSA, the natural anatomy of the shoulder joint is inverted, resulting in a medialization and distalization of the center of rotation. This alteration fundamentally changes the biomechanics of the shoulder, particularly affecting muscle function and joint kinematics. While musculoskeletal modeling approaches, such as the AnyBody Modeling System, are increasingly used to estimate muscle activity, there remains a lack of studies that integrate pre- and postoperative in vivo measurements in RSA patients. The aim of this study is to address this research gap by optimizing an existing musculoskeletal shoulder model and systematically evaluating changes in muscle activity and kinematics associated with RSA. Primary objectives include the assessment of kinematic and muscular activity pre- and postoperatively, as well as the comparison of muscle activation patterns between the operated shoulder, the contralateral side, and healthy control subjects.

Methods: Motion data were collected using inertial measurement units and processed within the AnyBody Modeling System to estimate muscle activity through inverse dynamics. Muscle activation patterns were analyzed across multiple movement tasks, including abduction, adduction, and anteversion. Furthermore, movement-specific muscle activity ratios were calculated to characterize coordination patterns between primary and secondary muscles. Correlations between model-based muscle activity and surface electromyography were assessed to evaluate model validity. In addition, range of motion and pain levels were recorded using standardized clinical questionnaires to complement the biomechanical analysis.

Results: The results demonstrate that RSA leads to significant alterations in both shoulder kinematics and muscle activation patterns. In particular, shifts in muscle recruitment strategies were observed, likely reflecting compensatory mechanisms due to the surgically altered joint geometry. Comparisons with healthy subjects and contralateral shoulders revealed distinct deviations, especially in movement-specific muscle coordination.

Conclusion: These findings provide novel insights into the functional consequences of RSA and contribute to closing the existing gap in pre- and postoperative biomechanical assessment. Moreover, the integration of experimental data with musculoskeletal modeling supports further refinement of simulation approaches and may enhance clinical evaluation and rehabilitation strategies for RSA patients.

P32_3D-Printed Resin Bone Models as Alternatives to Cadaveric Specimens in Biomechanical Screw Pull-Out Testing

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Purpose: Fracture fixation with bone screws is frequently complicated by implant loosening, particularly in periarticular fractures, yet biomechanical testing of primary stability of bone-screw constructs conventionally relies on cadaveric specimens, which are costly, ethically sensitive and subject to high inter-specimen variability. Synthetic bone replicas derived from imaging data offer a potential uniform and cost-effective alternative. This study investigates whether bone models printed from Rigid 10K and Grey Pro Resin via stereolithography (SLA) based on micro-CT data are mechanically comparable to native porcine tibial bone in axial screw pull-out testing.

Methods: Three porcine tibia bones were scanned using micro-CT, followed by deep learning segmentation in Dragonfly 3D World to differentiate cortical and trabecular structures. Bone models were then 3D-printed with Rigid 10K and Grey Pro Resin using a Formlabs Form 3 printer. Specimens were pre-drilled at two standardized anatomical sites in their respective groups: cortical bone only, and combined cortical-trabecular bone. All specimens were embedded and cortical screws were manually inserted. Mechanical testing was performed via axial pull-out using an Instron E10000 testing machine to measure the pull-out load until mechanical failure of the bone or the screw-bone interface occurred.

Results: Native bone displayed the highest cortical pull-out load (777 ± 151 N) compared to Rigid 10K (481 ± 136 N) and Grey Pro (447 ± 123 N). In combined cortical and trabecular bone, Rigid 10K achieved the highest observed pull-out load (1503 ± 460 N) across all groups (porcine combined pull-out load: 929 ± 143 N). Regarding stiffness, cortical Rigid 10K (647 ± 145 N/mm) and combined Rigid 10K (742 ± 135 N/mm) were the highest observed.

Conclusion: Rigid 10K and Grey Pro Resin partially replicate native bone pull-out behavior but show considerable mechanical deviations. Notably, Rigid 10K exceeded native bone pull-out loads in the combined cortical and trabecular configuration, which should be interpreted with caution given the small sample size (n=3) and high inter-specimen variability. Both materials show potential as bone replicas but require further systematic investigation, particularly regarding uncontrolled screw insertion torque.

P33_Investigations on Cyclodextrins as Excipients for LNP mediated RNA delivery

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Purpose: Lipid nanoparticle (LNP) formulations, as demonstrated by their success in vaccine applications, represent a promising platform for future gene therapy approaches. However, LNPs still face major stability issues during storage and transport. Considering observations on their stabilizing properties in freeze- and spray-drying, cyclodextrins (CDs) might improve on aforementioned problems. In this study, we investigated the impact of incorporating CDs as excipients into LNP formulations, with a particular focus on physiochemical characteristics and particle stability as well as the influence on their in vitro performance.

Methods: In a first instance LNPs were formulated according to the field's standards and supplemented with two types of cyclodextrins, 2-Hydroxypropyl-beta-cyclodextrin (HP-β-CD) and Methyl-beta-cyclodextrin (M-β-CD) at concentrations ranging from 0.1% (m/V) to 5% (m/V). Sucrose and lactose, commonly used excipients in the industry, served as standard controls. Afterwards those samples were subjected to a sequence of freeze-thaw cycles or storing at 7°C to mimic transport and storage conditions. Interactions between LNPs and CDs were analysed using dynamic light scattering (DLS) to assess immediate complex formation as well as its adaption over time. By employing a modified RiboGreen fluorescence assay we were able to measure possible RNA leakage from the particles following CD incorporation. In addition, cell culture experiments combined with flow cytometry were conducted to evaluate in vitro performance of the modified particles through potential changes in uptake or effect.

Results and Conclusion: In general, a time- and dose-dependent increase in particle size was detected with both kinds of CDs. Similar trends were observed in those samples undergoing freeze-thaw treatment. However, the addition of cholesterol attenuated these effects to some extent in both cases. Although in vitro results were inconsistent, the described deviations from the aspired particle size are expected to affect in vitro performance negatively. While the project provides initial insights into interactions between LNPs and CDs, further investigations - especially regarding in vitro performance - are required to assess the suitability of CDs as stabilizing components in LNP formulations. Among the tested conditions, low concentrations of HP-β-CD, particularly in combination with 0,025% (m/V) cholesterol, were identified as the most promising candidates for further testing.

P34_Does metabolism feed back the circadian clock in Bacillus subtilis?

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Abstract: All living beings are subject to daily, repetitive behavioural and physiological rhythms controlled by their circadian clock. This mechanism coordinates an endogenous, approximately 24-hour rhythm that governs key physiological processes such as the sleep-wake cycle, hormone regulation and metabolism. External cues can synchronise and modulate this rhythm. If its function is disrupted as a result, this can lead to disease. Whilst the influence of the circadian clock on metabolism in mammals has been well researched, it remains largely unclear whether and how metabolism influences the circadian rhythm of new models like bacteria. Although it is known that circadian clocks exist even in non-photosynthetic bacteria such as the Gram-positive model Bacillus subtilis, commonly found in soil-oscillates, and has been linked to the formation of biofilms. The relationship between the bacterium clock and its metabolism has not yet been sufficiently clarified. We are therefore investigating the question: Does the metabolism feed back the clock? In our experiment, we investigate the influence of various carbon sources on B. subtilis' internal clock. For that, we investigated the effect of four monosaccharides and two sugar alcohols, on growth, biofilm formation and activity. Our results reveal clear behavioural differences in B. subtilis between media containing sugar alcohols and those containing monosaccharides. Compared to sugar alcohols, monosaccharides induce stronger exponential growth. Furthermore, in media containing sugar alcohols, we observe a higher cell densities but reduced biofilm formation. The data from gene expression reporters suggest that no clear circadian rhythm is detectable under the conditions of the medium containing sugar alcohols, whereas this rhythm is maintained under the conditions of the medium containing monosaccharides. Overall, our results point to a modulation of the circadian clock by different carbon sources.

P35_Regulation of Insulin Secretion by Secretagogin and Calbindin D28k in pancreatic β-Cells

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Purpose: Insulin secretion in the pancreatic ß-cells of islets of Langerhans is the body's only mechanism for producing a hormone capable of lowering blood glucose levels. Insulin exocytosis is heavily dependent on calcium levels, as the fusion of the insulin-containing vesicles is triggered by an increase in the intracellular calcium concentration. Both Calbindin D28K and Secretagogin are calcium-binding proteins of the EF-hand family and may play various roles for the regulation of calcium-dependent cellular processes. Since our knowledge of insulin regulation directly affects our understanding of widespread diseases such as Diabetes Mellitus, a further detailed investigation of signal transduction pathways remains particularly relevant.

Methods: In order to investigate the relationship between insulin secretion and the aforementioned calcium binding proteins, we made use of INS-1 cells, a rat insulinoma ß-cell line, and compared these cells with genetically modified ß-cell variants. In our research, we first observed basal secretion by maintaining physiologically relevant conditions. Followingly, we performed glucose and KCl stimulations and collected samples at different time points. To measure insulin levels, we used the PTGlab ELISA-Kit and calculated the insulin concentrations from the standard curve based on the known standards.

Results: Our lab results revealed a possible connection between insulin secretion and the Calbindin D28k, as we were able to detect higher insulin levels in the ß-cell variants. We have also noticed a certain pattern, in which the insulin levels initially started lower than those of the the wild-type and went on to exceed the wild-type secretion after a prolonged KCl-stimulation. However, it is hard to make a certain statement, as our glucose stimulations are still ongoing.

Conclusion: The aforementioned results suggest that both Calbindin D28k and Secretagogin may influence the insulin secretion, however, in order to reach a certain conclusion, all experimental procedures should be completed first.

P36_A study of the binding of Calbindin-D28k to the glucose transporter isoform GLUT2 in rat pancreatic islet beta cells

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Purpose: Calbindin-D28k is a member of a family of calcium binding proteins with high affinity to Ca^{2+} that is expressed predominantly in the mammalian brain, kidney and pancreas. Among other functions, Calbindin acts as a calcium buffer in pancreatic β-cells, leading to decreased Ca^{2+} levels and, consequently, to reduced insulin release during the second (sustained) phase. In addition, Calbindin was revealed to have calcium sensor functions, interacting with several target proteins. Previous unpublished data (M. Gerstendörfer, Forschungsmodul last year) identified GLUT2, a critical transporter for glucose-stimulated insulin secretion, as a potential binding partner for Calbindin-D28k at elevated calcium levels. In this study, we investigated this interaction in rat pancreatic islet β-cells using Western Blot analysis.

Methods: Ins1 wildtype pathogenic rat pancreatic β-cells were cultured containing Calbindin-D28k. To isolate Calbindin-GLUT2 complexes, multiple co-immunoprecipitations were performed under high (1 mM) calcium concentrations. We used anti-Calbindin Cb38 antibodies followed by a Western Blot with an anti-GLUT2 antibody for the detection. We also performed immunoprecipitation with an anti-GLUT2 antibody and used an anti-Calbindin antibody for the detection.

Results: The Western Blots revealed a signal corresponding to the molecular weight of GLUT2 (57kDa) following the immunoprecipitation with the anti-Calbindin antibody. Furthermore, reciprocal immunoprecipitation with the anti-GLUT2 antibody, resulted in the detection of a signal at the molecular weight of Calbindin (27kDa). In addition, a strong signal of higher molecular weight (35 kDa) following immunoprecipitation with the anti GLUT2 antibody was detected. This signal was recognised by other mono- and polyclonal anti-Calbindin antibodies as well as by an anti-Calretinin antibody.

Conclusion: The aforementioned results suggest that Calbindin does indeed bind GLUT2 in rat pancreatic β-cells. Further research should investigate the effects of this complex on Glucose uptake and identify the molecule that produces the heavier signal of 35 kDa in the Western Blots.

P37_Influence of Calbindin-D28k Expression on Pancreatic β-Cell Morphology

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Background: Calbindin-D28k acts primarily as a calcium buffer. Calbindin knockout INS1 cells show a drastic change in morphology: they cease to build islets, become bigger, fusiform and generate pronounced extensions.

Purpose: Confirm calbindin as the cause of the altered phenotype and explore three possible explanations: structural integrity, cell motility and Cx36-mediated adhesion.

Methods: Lipofections were performed with a plasmid coding for a fluorescent calbindin fusion protein. Fluorescence-activated cell sorting is still ongoing. Immunofluorescence stainings were performed and visualized primarily in an LSM. ImageJ was used for colocalization analysis. Western blots to quantify connexin and confirm lack of calbindin in mutants. Cells were normally cultured in 5 mM glucose.

Results: Lipofections induced no morphological change. Cytoskeleton and calbindin in transfected mutants were moderately colocalized. Comparison between WT and knockouts showed clear differences in expression and organization of the cytoskeleton. WTs possessed more connexin than mutants under normal conditions, however, the relationship at higher glucose (11.1 mM) was inverted. Connexin antibodies possibly stained the nucleus center. Lack of dithiothreitol produced more connexin monomers at high glucose. Western blots confirmed calbindin absence in mutants.

Conclusion: A causal relationship between calbindin and morphology might still be confirmed. Colocalization supports the cytoskeletal-modulation-hypothesis, however, it does not equate to direct spatial interaction. The compromised structural integrity of the mutant cytoskeleton could indicate a change in motility and therefore phenotype, but could also serve as an explanation on its own. Results at normal glucose support connexin-mediated adhesion as another possible mechanism. The lack of morphological change in spite of more connexin in mutants at high glucose could be explained through the severity of the cytoskeletal modifications. WT cells possibly lower Cx-expression at high glucose to avoid glutotoxicity, mutants do the opposite maybe to avoid cytotoxic calcium levels through hemichannels, it being the greater danger due to lack of calcium buffering. Nuclear staining is either unspecific, attributable to paraformaldehyde, or detects some form of C-terminal truncated connexin acting as a transcription factor. Dithiothreitol interactions at high glucose possibly indicate a lesser reliance of connexons on disulfide bridges.

P38_Computational Docking of Calbindin-D28k to Identify Shared Interaction Motifs and Potential Binding Sites

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Background: Calbindin-D28k (CBD28k) is a calcium-binding protein occurring in e.g. neurons of the cerebellum, hippocampus in kidney tubules, the intestines and pancreas. Besides its Ca-buffer-function it has been lately hypothesized to have signalling functions by binding to cytosolic proteins like IMPase, RanBPM, Procaspase-3 and Insulin, peptides like Melittin and membrane proteins like GLUT2. Despite these known interactions significant gaps remain in our understanding of how and where exactly these proteins bind to CBD28k. Advancing the knowledge in the area is essential to understand its contribution to calcium-dependent signalling networks and to the regulation of neuronal, renal, and endocrine function.

Objective: This study aims at simulating the docking between CBD28k and its interaction partners, find the most probable interactions, analyse if the simulated complexes have shared interaction motifs with the previously described experimentally found complexes and determine if new potential bindings sites can be identified.

Methods: By retrieving experimental protein data from the Protein-Data-Bank and simulating the not experimentally identified structures or domains through ChimeraX-Modeller and the renowned AlphaFold2, thousands of docking-candidates were created with the help of cutting-edge sampler like HADDOCK2.5 or AlphaFold3. Furthermore, scorer PIsToN and dMaSIF chose the most probable samples and these were analysed by using software like ChimeraX or ParaView.

Results: Samples for the interaction between CBD28k and IMPase, RanBPM and Procaspace-3 could be created that have, according to the used scorer, significant results (e.g. IMPase: PIsToN=86.5%, dMaSIF=0.99 [higher-is-better]; Procaspase-3: PIsToN=85.8%, dMaSIF=1.06). These results contradict the past described interactions and show additional potential binding sites.

Conclusion: This study could represent a blueprint for other protein-protein-docking-simulations as it describes a protocol that optimizes the reliability of the results. In the future, computational docking in general may serve as a cost and time effective solution for an in depth understanding of how protein-complexes are structured. However, today's software cannot reliably produce very relevant samples and the scoring is not sufficiently significant to be trusted without additional experimentations.

P39_Interaction between IMPA1 and Calbindin in HN10E cells

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Purpose: Calbindin D28K is a highly preserved protein occurring in neuronal and endocrine cells. It has recently been shown that the activity of the inositol monophosphatase (IMPase) that is a therapeutically relevant target of the lithium therapy for patients with bipolar disorder is enhanced by Calbindin D28K (Berggård, Szczepankiewicz et al. 2002). At this stage it is not clear in which cells exactly the interaction takes place and if they play an important role concerning the pathology of bipolar disorders or other medical diseases. We studied whether Calbindin D28k interacts with IMPase in HN10E cells.

Methods: For this purpose, we used Co-Immunoprecipitations and Western Blots to proof the interactions. For this aim we variegated different antibody-combinations to increase the clarity of the results.

Results: First of all, we could prove that Calbindin D28k and IMPA1 occur in HN10E cells. Furthermore, with these techniques we could show that there seems to be an interaction between Calbindin D28K and IMPase in HN10E-cells, provable with a specific antibody combination for Co-IP and Western Blot. Moreover, experiments have shown that additional bands in the Western Blot could be attributed to the Protein A on the beads we used for the immunoprecipitation.

Conclusion: This result serves as a basis for further experiments concerning the interaction of Calbindin D28k and IMPase with other proteins and the physiological relevance of this interaction.

P40_ToppWrite - Towards a developmental writing model: Identification of cognitive predictors underlying writing skills in German

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Purpose: Understanding the development of text production skills is of central importance. The ability to bring thoughts and ideas into written form plays a key part in all school subjects and forms the base of written communication in everyday life, for example when writing e-Mails or messages, regardless of whether texts are produced by hand or digitally. As about 8% of German pupils are affected by reading- and writing disorders, it is important to search for tools to diagnose these disorders in an early stage of their development, in order to support them in their daily live. Despite this relevance, only a few studies to date have specifically examined the development of written text composition and spelling, as well as their mutual influence.

Methods: Topp-Write is designed as a longitudinal study which builds on the Topp-Spell study. The Topp-Spell study spans from preschool to third grade and includes four measurement points. Topp-Write continues this study from fourth to sixth grade. The aim is to identify specific predictors of spelling development and writing development, the relationship between handwriting and spelling and which shared and specific predictors exist for reading comprehension and text production based on the „Not-so-simple view of writing“ model (Berninger et al 2003).

Results: In the Topp-Spell study was found that recognizing phonemes in words plays a key part in early spelling development. Later on, the understanding of word structure and writing patterns is becoming more and more important.

Conclusion: Right now, we are at the first measuring point of the Topp-Write study (fourth grade). With the collected data, we hope to gain a deeper understanding of writing development in later years in order to develop new methods of early intervention and ways to support children and young adults with reading and writing disorders.

P41_Processing of thermal and visual information in Drosophila avoidance

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Purpose: The social behavior of the Drosophila melanogaster is guided by sensory cues such as visual and thermosensory input. A distant animal is detected as a small visual object devoid of a chemosensory signature, and is generally avoided. The neuronal connection between the cholinergic visual projection neuron LC10d and the GABAergic AOTU041 regulates visual object tracking levels. We seek to investigate which acetylcholine receptor of AOTU041 receives cholinergic input to influence the activity of LC10d.

Methods: To reduce the expression of the acetylcholine receptors, RNAi-based knockdown of each receptor specifically in the AOTU041 neuron type was made with the use of the UAS-Split-GAL4-System. The subtypes nAChR α1, nAChR α3 and mAChR B were investigated in this work. The vision-only-behavioral assay (2-Floor Assay) was used to investigate the behavior of naive males. The resulting videos were analyzed by 'Matebook' and quantitative behavioral data evaluated trough male centered heat-maps and other parameters.

Results: We found that each acetylcholine receptor tested has contributed somewhat to the activity of AOTU041. nAChR α1 and mAChR B show a similar outcome, with males showing higher tracking behavior and less avoidance. This points to an overall reduced activity of AOTU041 and, consequently, its inhibition of LC10d, suggesting that nAChR α1 and mAChR B constitute major cholinergic input pathways to AOTU041. Surprisingly, males with nAChR α3 knock down showed higher avoidance and less tracking of the females. These results point to a more complex circuit mechanism in cholinergic signaling in AOTU041.

Conclusion: The research project demonstrates the importance of AOTU041 regarding its modulation of visual information. Further experiments of knockdown of different combinations of acetylcholine receptors are necessary to investigate possible compensatory mechanisms of the neuronal circuit.

P42_Evaluation of Serum Replacement as an Alternative to Fetal Bovine Serum in HEK and Jurkat Cell Cultures

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Purpose: The use of Fetal Bovine Serum (FBS) for cell culture applications poses challenges. Due to batch-to-batch variability, contamination risks and its undefined composition, FBS may lead to altered, less reliable results in experimental outcomes. Chemically defined, animal-free serum replacement (SR) has been proposed as an alternative for FBS. However, there is a lack of understanding in regard to their ability in supporting various cell types. This study evaluates SR as a suitable substitute for FBS in adherent and suspension cell culture models.

Methods: HEK (adherent) and Jurkat (suspension) cells were exposed to SR in increasing concentrations (0%-25%-50%-75%-100%) using abrupt and gradual adaptation protocols. Cellular responses were assessed via growth curves (Neubauer chamber counting), post-thaw recovery experiments, scratch assays as well as qualitatively via morphology. For HEK cells Polylysine-coating was employed to assess and distinguish adhesion-dependent effects from influences of growth factor signaling. Additionally, metabolic activity was indirectly monitored through pH-dependent colour shifts of phenol red (pH-indicator) within the respective wells.

Results: SR induced dose-dependent alterations in both cell types. In HEK cells, higher SR concentrations resulted in reduced proliferation, recovery, attachment, morphological changes among others. Polylysine partially restored attachment yet did not fully restore growth behaviour. Similarly, Jurkat cells tolerated SR concentrations up to 50% but exhibited decreased proliferation, increased debris formation and signs of apoptosis at ≥75% SR. In migration assays, wound closure was delayed at high SR concentrations. Gradual adaptation seemed to partially overcome the aforementioned flaws.

Conclusion: In summary, SR does not fully mimic the functional complexity of FBS in neither adherent nor suspension cell cultures. Its limitations are cell type specific and become more apparent with increasing SR concentrations. Therefore, SR alone appears to be an unsuitable complete alternative for FBS. However, combining SR with FBS can reduce the amount of FBS required in cell culture. Overall, the study highlights the need for optimized, application-specific strategies and a framework for comparing serum-free systems.

P43_Clinically driven time-series decomposition for multimodal clustering of seizure onset and offset pattern characterization

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Purpose: Offset and onset patterns in wearable data are of significant importance to accurately identify the start and termination of seizures, are better tolerated and more suitable for long-term ambulatory monitoring, and help develop reliable tools for annotated datasets. Objective biomarkers for clinically driven decomposition and characterization of seizures outside hospital settings remain scarce. In this project, we applied time series decomposition with wearable data to try to identify physiological features and onset and offset patterns specific to seizure types.

Methods: Video EEG monitoring was used to record physiological signals from wearable devices worn by pediatric patients. Modalities recorded were accelerometry, electrodermal activity, heart rate, respiratory rate, and skin temperature. For each seizure, a window of 30 minutes was used on the seizure offset (15 minutes before and after) and aligned with timestamps that were annotated by a neurologist. Features of motor behaviour (movement amplitude, rhythmicity) and autonomic responses (EDA changes, heart rate variability shifts) were extracted for seizure timeslots. Previously mentioned features were compared across seizure types to identify type-specific signatures to be used as input for multimodal clustering and seizure classification based on machine learning.

Results: The preliminary analysis has shown differences in periictal wearable data depending on seizure type. EDA and heart rate have shown activation during seizure offset with some variation in onset latency. Features documented by accelerometry suggested potential differences in movement patterns across generalized tonic-clonic/focal-to-bilateral tonic-clonic, generalized/focal clonic, and generalized/focal myoclonic seizure types. Findings indicate that combining multiple modalities from wearable sensors could potentially help clinically accurate characterization of seizure types while using wearable data.

Conclusion: Overall, these findings suggest that the utilization of multimodal wearables that were analyzed in a clinically relevant way could help define seizure phenotypes. This could provide data for developing interpretable machine learning models to improve ambulatory monitoring practices of seizures, facilitate personalized therapy management strategies, and enhance safety protocols within epilepsy care.

P44_Clinical Characterization of a Pediatric Epilepsy Cohort for Neurocardiac Interaction Studies

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Purpose: Epilepsy is a chronic neurological disorder characterized by recurrent seizures and systemic alterations. While increasing attention has been given to neurocardiac interactions, especially cardiac seizure monitoring, baseline clinical characteristics remain essential for interpreting physiological findings. This study focuses on generalized tonic-clonic (GTC) and focal to bilateral tonic-clonic (FBTC) seizures, which are more likely to involve pronounced autonomic and cardiovascular changes. We aimed to characterize demographic and clinical features of a pediatric epilepsy cohort and explore associations with seizure-related variables, providing a foundation for subsequent heart-brain interaction analyses.

Methods: We conducted a retrospective analysis of pediatric patients admitted to the epilepsy monitoring unit at Boston Children's Hospital from February 2015 to February 2021. During admission, patients wore a wearable device and underwent continuous ECG and EEG monitoring. Seizure onset and offset were determined from EEG and video recordings by a board-certified epileptologist. Demographic data, clinical variables, and relevant medical history were collected from medical records and stored in REDCap. Descriptive statistics summarized baseline characteristics, and group comparisons explored differences between clinical subgroups, including GTC and FBTC seizures.

Results: The cohort showed heterogeneous clinical presentations across seizure types and patient characteristics, representing a broad spectrum of pediatric epilepsy (in total 55 patients with 125 seizures). Seizure onset times were not uniformly distributed across the 24-hour cycle, with a significant peak at 4:20. FBTC seizures had nearly twice the duration of GTC seizures, especially during clonic phases. No significant differences in seizure onset time distribution were observed by sex or seizure type.

Conclusion: This analysis provides a structured overview of baseline clinical and seizure-related characteristics in a pediatric epilepsy cohort. The early-morning predominance of seizure onset and longer FBTC duration highlight clinically relevant seizure patterns for subsequent physiological analyses. Although sample size limits statistical power and subgroup generalizability, these findings establish a foundation for future integrative studies of heart-brain dynamics, including EEG-ECG coupling and seizure-related autonomic changes.

P45_Development of an ECG Labelling Catalogue for Automated ECG Analysis in Sports Cardiology

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Introduction: Several underlying cardiac conditions can increase the risk of sudden cardiac death if left undetected. These conditions may lead to adverse events - for example, when previously untrained individuals participate in a marathon. While countries like Italy and Greece mandate routine cardiac screening for all athletes, Germany lacks standardised screening for recreational athletes, mainly due to high costs and limited expert interpretation availability. These challenges highlight the need for scalable, cost-effective AI-driven cardiac screening approaches. Recent advances in foundation models trained on large-scale ECG datasets show promise for automated classification and early detection of cardiac abnormalities in athletes. However, their performance and generalisability critically depend on large, consistently labelled datasets that capture athlete-specific cardiac adaptations. A major bottleneck remains expert-based ECG annotation, which is costly, time-consuming, and inherently prone to inter-observer variability.

Purpose: The project aimed to develop a standardised ECG labelling catalogue for athlete populations, providing consistent and reliable training data for the AI.

Methods: The labelling catalogue was developed based on European Society of Cardiology guidelines in close collaboration with cardiologists at LMU Hospital. We incorporated clinical expertise through expert interviews and real-world feedback from clinical practice. Representative ECG samples illustrating relevant abnormalities were selected, and the findings were compiled into a structured reference table to support expert annotation.

Results: The project resulted in a standardised ECG labelling catalogue with 30 anomalies, each defined and illustrated with an example. These labels were chosen based on the PhysioNet Challenge 2021, as initial tests in earlier stages were conducted using their data. The catalogue was verified by expert cardiologists and integrated into a web-based labelling tool for annotating ECG data from both amateur and professional athletes. The proposed approach is currently being evaluated in an ongoing study using real-world ECG data from both groups.

Conclusion: This work lays the foundation for reliable AI-assisted cardiac screening and demonstrates great potential for preventive medicine and sports cardiology. While automated screening could increase accessibility and reduce costs, challenges such as false negatives and missed diagnoses must be carefully managed.

P46_Investigating the Sensitizing Potential of the NK1R Antagonist Aprepitant on TRAIL-Induced Apoptosis in Colorectal Cancer Cell Models

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Purpose: Colorectal cancer remains a leading cause of cancer-related mortality when combining data for men and women, largely due to resistance against apoptosis-inducing therapies like the cytokine TRAIL. While TRAIL selectively targets malignant cells via death receptors DR4/DR5, clinical efficacy is often hindered by intrinsic or acquired resistance. The neurokinin-1 receptor (NK1R) and its ligand Substance P are frequently overexpressed in cancers, promoting anti-apoptotic signalling. This study investigated whether the NK1R antagonist Aprepitant can reduce cell viability and sensitize Colon Adenocarcinoma (COAD) cell lines to TRAIL-induced apoptosis to overcome these resistance barriers.

Methods: The COAD cell lines HCT116 and SW480 were used, with THP-1 as a hematopoietic comparative model. Proliferation and cell viability were assessed via WST-1 assays after 24- or 48-hour Aprepitant treatment. To quantify apoptosis, sub-G1 DNA fragmentation was measured using propidium iodide staining and flow cytometry following a sequential treatment protocol (24h Aprepitant pre-treatment, 16h TRAIL co-treatment). Downstream enzymatic activity was verified through Western blot analysis of PARP cleavage, while qPCR measured mRNA levels of the anti-apoptotic gene CFLAR (c-FLIP).

Results: Aprepitant exerted a dose-dependent anti-proliferative effect across all models. However, sensitization to TRAIL was cell-line dependent. A clear synergistic increase in DNA fragmentation and apoptosis was observed in SW480 cells under dual treatment. In contrast, HCT116 cells showed only marginal sensitivity and a modest trend toward sensitization. Western blot analysis confirmed PARP cleavage, indicating successful late-stage apoptosis. Interestingly, qPCR revealed a rise in CFLAR mRNA expression following treatment. We hypothesize this reflects a compensatory transcriptional feedback loop where cells attempt to counteract the depletion of functional protein levels.

Conclusion: Aprepitant successfully inhibits cell proliferation in COAD models, but its ability to sensitize cells to TRAIL is highly dependent on the specific genetic background of the cell line. While SW480 cells showed a clear synergy, other models showed more limited or merely additive responses. These data highlight that targeting the NK1R axis can lower the apoptotic threshold in certain resistant colorectal cancer environments, though further research is required to fully understand the determinants of sensitivity and the underlying compensatory mechanisms involving c-FLIP and NK1R expression.

P47_Effects of Tigecycline on TRAIL-induced apoptosis in pancreatic ductal adenocarcinoma (PDAC) models

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Background: Pancreatic ductal adenocarcinoma (PDAC), accounting for over 90% of pancreatic malignancies, remains one of the deadliest cancers worldwide, with a 5-year survival rate of approximately 13%. More than half of patients present with metastatic disease at diagnosis, and resistance to conventional therapies highlights a critical therapeutic gap, necessitating the development of novel treatment strategies. TRAIL (TNF-related apoptosis-inducing ligand) has been shown to selectively induce apoptosis in malignant cells but is often limited by resistance mechanisms. Tigecycline, a novel glycylcycline antibiotic, has demonstrated antitumor properties in several cancer entities.

Purpose: This study aims to investigate the effects of Tigecycline on TRAIL-mediated apoptosis in PDAC models, with a focus on understanding the underlying molecular mechanisms.

Methods: Human PDAC cell lines (MIA PaCa-2 and PSN-1) were treated with Tigecycline (10 µM, 24-48 h), TRAIL (20 ng/ml, 16 h), or a combination of both. Cell proliferation was assessed using WST-1 assays, and migration was analyzed via wound healing assays. Apoptosis was quantified by propidium iodide staining and flow cytometry (sub-G1 fraction). Western blot analysis was performed to evaluate apoptosis-related proteins, including caspases and cFLIP. Additionally, cFLIP expression was analyzed in patient datasets (GEPIA3) and validated in human PDAC tissue using immunofluorescence.

Results: Tigecycline alone reduced cell migration and proliferation, coinciding with a substantial G0/G1 cell cycle arrest. In both cell models, little to no apoptosis was observed following treatment with Tigecycline or TRAIL alone. However, pretreatment with Tigecycline markedly enhanced TRAIL-induced cytotoxicity in both cell lines, most prominently in MIA PaCa-2 cells. Mechanistically, the combination treatment activated the extrinsic apoptotic pathway, as evidenced by increased cleavage of caspase-8, caspase-3, and PARP. Importantly, we identified a reduction in cFLIP, a key apoptosis inhibitor, following Tigecycline treatment. Bioinformatic and histological analyses confirmed cFLIP expression in PDAC patient samples.

Conclusion: Tigecycline sensitizes PDAC cell models to TRAIL-induced apoptosis by targeting the key apoptosis inhibitor cFLIP. In addition, our data indicate the involvement of additional resistance mechanisms that require further investigation. Our findings suggest that Tigecycline could be used in combination with TRAIL or similar pro-apoptotic agents as a potential therapeutic strategy.

P48_Effects of autoantibodies on Desmoglein-2 and N-cadherin in human cardiac organoids

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Purpose: Cardiomyocytes are mechanically and electrically coupled through specialized cell–cell contact structures known as intercalated discs (ICDs), which consist of desmosomes, adherens junctions, and gap junctions, forming a functional network for coordinated cardiac contraction. Desmosomes are composed of three major protein families: desmosomal cadherins (desmoglein-2 [DSG2] and desmocollin-2), armadillo family proteins, and plakin proteins. Desmosomal structures in the heart are tightly interwoven with components of adherens junctions, such as N-cadherin (N-CAD). This hybrid junction is a hallmark of mature cardiac ICDs and is known as the area composita. Arrhythmogenic cardiomyopathy (ACM) is a hereditary heart disease characterized by ventricular arrhythmias, structural myocardial alterations, and an increased risk of sudden cardiac death. In over 50% of patients, mutations in desmosomal genes are identified, leading to desmosomal instability, cardiomyocyte loss, fibrofatty myocardial remodeling, and arrhythmogenesis. Recently, autoantibodies targeting ICD proteins, including DSG2, were reported in ACM patients and were considered relevant to ACM pathogenesis. To better understand this, we investigated the effects of autoantibodies on DSG2 and N-CAD using cardiac organoids, three-dimensional constructs derived from induced pluripotent stem cell (iPSC)-derived cardiomyocytes.

Methods: Immunostaining was performed on cardiac organoids treated with healthy control IgG (Ctrl-IgG) and ACM patient-IgG (ACM1-IgG). Tissue samples were incubated with primary antibodies against DSG2 and N-CAD. Secondary antibodies conjugated with Alexa 488, Cy3, and Cy5 were used for fluorescence-based detection. Various primary antibody concentrations and antigen retrieval buffers were tested to optimize staining conditions, and stained samples were analyzed using confocal laser microscopy.

Results: Staining was markedly improved when using a citrate antigen retrieval buffer (pH 6) compared to a Tris-EDTA buffer (pH 9). N-CAD was detectable in healthy control IgG-treated organoids, whereas DSG2 could not be detected. Therefore, it remains unclear whether ACM IgG affects DSG2 in this model.

Conclusion: A functional immunohistochemistry protocol for iPSC-derived cardiac organoid tissue was established. Further optimization of antibody concentrations is required to detect DSG2 in cardiac organoids.

P49_Gut microbiome alpha diversity and fasting GLP-1 in relation to depressive and anxiety symptom severity in an overweight/obesity cohort

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Purpose: Depression and anxiety are increasingly discussed within the microbiota-gut-brain axis, yet human studies often do not integrate gut microbiome features with plausible host endocrine signals, such as glucagon-like peptide 1 (GLP-1), a gut-derived peptide implicated in metabolic, homeostatic, and reward-related brain processes. This study tests whether gut microbiome alpha diversity is associated with fasting GLP-1, and whether fasting GLP-1 is associated with depressive and anxiety-related symptom severity at baseline in adults with overweight/obesity (BMI ≥ 25 kg/m²). Exploratory mediation analyses further evaluate indirect association patterns consistent with a candidate gut-microbial–endocrine–affective pathway.

Methods: This project is a secondary analysis of baseline cross-sectional data from an overweight/obesity cohort within the Leipzig clinical trials “GUT-BRAIN” and “MIFOOD”. Participants are included if they have processed baseline stool shotgun metagenomics data, fasting plasma GLP-1 measured after a 13–16 h fast, and baseline Beck Depression Inventory (BDI) and State-Trait Anxiety Depression Inventory – State version (STADI-S) state anxiety data. Shannon diversity is the primary microbiome exposure; Simpson index and observed richness are examined in secondary analyses. Confirmatory analyses use age- and sex-adjusted linear regression to test associations between alpha diversity and fasting GLP-1, and between fasting GLP-1 and depressive (BDI total score)/anxiety-related (STADI-S state anxiety score) symptom scores; exploratory mediation analyses assess indirect association patterns.

Results: Cohort assembly, variable harmonization, and analysis planning are complete. Approximately 165 participants are currently expected to meet final eligibility criteria, and final statistical analyses are ongoing. We expect the completed analyses to clarify whether broader gut microbial community structure is associated with fasting GLP-1 and whether GLP-1 is statistically linked to depressive and anxiety-related symptom burden at baseline.

Conclusion: By testing associations between gut microbial diversity, fasting GLP-1, and depressive and anxiety-related symptom burden in an obesity-related context, this study may help refine how endocrine pathways are incorporated into human gut-brain axis research. Given the cross-sectional design, findings will be interpreted as statistical associations rather than causal effects but observed association patterns could inform longitudinal or intervention-based follow-up studies of microbiome–GLP-1–affect pathways.

P50_Evaluation of Telehealth Services: Thematic Analysis of Patient and Clinician Perspectives

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Introduction: Telehealth usage has increased worldwide, especially over the course of the COVID-19 pandemic. This research was conducted at a large tertiary health service in Australia. Within this health service, pre-existing telehealth services were already present, with quality assurance research for evaluation and improvement embedded within these services. During the COVID-19 pandemic, there was an increased reliance on these telehealth services to support healthcare delivery during this time. In the post-COVID period, telehealth is now a common component of healthcare provision within this health service.

Purpose: The aims of this research were to explore patient perspectives on telehealth services, and clinician perspectives on features for successful telehealth utilisation.

Methods: Participants were patients and clinicians who took part in a telehealth consultation between 2018 and 2024. Data from the open-ended components of an opt-in voluntary survey following these consultations were analysed using Braun and Clarke's six phases of reflexive thematic analysis. Two thematic analyses were conducted, focusing separately on patient and clinician groups.

Results: The patient thematic analysis resulted in the conceptualisation of seven overarching themes reflecting patient perspectives: minimisation of impact, accessibility of healthcare services, avoidance of perceived or actual risk, technology affecting accessibility of healthcare, impacts to patient agency, operational factors impact access to telehealth and comparisons to expectations of a traditional clinical encounter. The clinician thematic analysis generated three overarching themes, reflecting their views on important factors for telehealth delivery: technological factors for effective healthcare provision, operational factors for an effective telehealth service and optimising telehealth consultations to meet traditional clinical expectations.

Conclusion: Findings from this research can be used to guide improvements within similar health services with pre-existing telehealth services. It can also provide areas of consideration and focus when developing telehealth services in other healthcare institutions.

NOTES

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