
# DocDay 2024

Abstract Book

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## Talk Session I

### Zach David

Abstract ID: 119464

# Residual mitral leaflet length identifies left ventricular outflow tract obstruction in hypertrophic cardiomyopathy

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Background/Aims: Due to its dynamic character, identification of left ventricular outflow tract obstruction (LVOTO) in hypertrophic cardiomyopathy (HCM) often requires extensive exercise testing. Structural alterations of the mitral valve (MV) are not affected by dynamic properties and influence LVOT gradients. The residual portion of the MV extending beyond its coaptation (RML) has been postulated as a necessity to exhibit LVOTO. This study aims to assess the effect of RML length on predicting the likelihood of LVOTO in HCM patients. Methods/Results: This is a cross-sectional analysis from the Graz HCM Registry, a prospective single-center cohort study enrolling consecutive HCM patients. Blinded investigators performed post-processing echocardiographic analyses to characterize the MV. Among 120 HCM patients (43% women, mean age 56<U+00B1>15 years), LVOTO was present in 49 patients (41%). HCM patients with LVOTO (oHCM) exhibited more pronounced end-diastolic interventricular septum thickness (2.2<U+00B1>0.4 cm vs. 1.9<U+00B1>0.5 cm; p<0.001) and higher left ventricular ejection fraction [60% (56-63) vs. 56% (52-64); p=0.021] than those without LVOTO (nHCM). Moreover, oHCM patients showed longer anterior (27.9<U+00B1>3.6 mm vs. 24.4<U+00B1>4.7 mm; p<0.001), posterior (23.7<U+00B1>4.3 mm vs. 20.4<U+00B1>4.7 mm; p<0.001), and residual mitral leaflets [12.2 mm (10.0-13.4) vs. 5.9 mm (3.0-9.0); p<0.001). Multivariable logistic regression analysis revealed RML length as an independent predictor of LVOTO [OR=1.60 (95% CI 1.29-1.99)], adjusting for covariates. ROC analysis showed an AUC of 0.87 (95% CI 0.81-0.93) for RML length to identify LVOTO among HCM patients. RML length ?9.2 mm demonstrated 88% sensitivity and 75% specificity in identifying LVOTO. Conclusion: oHCM exhibited longer RML than nHCM patients. Moreover, RML length showed high diagnostic accuracy in identifying LVOTO among HCM patients. Prospective studies are needed to evaluate the added value of RML length in the diagnostic work-up of HCM patients.

**Erdo?an Yusuf Ceyhun**

Abstract ID: 119383

# Development of Novel Dual Reporter System to Visualize Intracellular Signaling around AMPK-Activity

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AMP-activated protein kinase (AMPK) acts as a master regulator of cellular bioenergetics by phosphorylating a diverse set of targets within the cell. Changes in cellular energy status, Ca2+ levels or redox status are defined upstream regulators of this kinase activity. Investigating the regulation around the AMPK-activity at single cell level would require co-imaging with single fluorescence protein (FP) and/or Frster Resonance Energy Transfer (FRET)-based biosensors. However, this kind of multi-spectral co-imaging is challenging, as it requires co-expression of biosensors in different colors as well as complex filter layouts to avoid spectral limitations. In this study, we present novel tools that report the essential quality of information in a simpler experimental setup, overcoming the issues posed by existing approaches. Here, we introduce a new separation of phases-based activity reporter of kinase (SPARK) based AMPK reporter, dubbed SPARK-AMPK, which reports the kinase activity by the formation of bright fluorescent clusters. Furthermore, we incorporated single-FP based Ca2+ biosensor GCaMP or the H2O2-sensitive HyPer into our SPARK-AMPK design to create a novel dual-modality reporter system. These new reporters permit probing signaling crosstalks in cell of interest by live-cell fluorescence microscopy. We employed well-established agonists, inhibitors, and protocols to induce AMPK activity, including energy stress, Ca2+ mobilization and oxidative challenge. The results show that our novel reporters can report how Ca2+ signaling and oxidative stress intersect and influence AMPK activity in cultured cells at the single cell level. We anticipate that our next-generation dual reporter approach could open up new avenues of research into understanding the intricate interplay between different secondary messengers and kinase activity in different cellular contexts.

**Rathner Thomas**

Abstract ID: 118867

# Role of NAD+ metabolism in diabetes-induced atherosclerosis

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Background: Atherosclerosis is an inflammatory disease and a main contributor to cardiovascular disease. The coenzyme NAD+ is of central importance in metabolism. It was shown that NAD+ depletion induces proinflammatory response and is associated with the progression of atherosclerosis. NAD+ precursors, such as nicotinamide mononucleotide (NMN), have been shown to replenish NAD+ levels in several tissues. Methods: The aim of this study was to demonstrate the effect of NMN supplementation on the development of atherosclerosis. 8-week-old C57BL/6J male low density lipoprotein receptor knockout (Ldlr-/-) mice were fed a chow diet (n=12) or a WD containing 1.25% cholesterol (n=12). After 8 weeks of diet, half the mice from each diet were supplemented with NMN in the drinking water (500mg/kg/day). We performed GTTs, lipid measurements, leukocyte isolation, NAD+ measurements, WB, RTqPCR and histology of the aortic root and arch. Results: Oil red O staining showed distinct atherosclerotic lesions in the WD-fed group. NMN treatment in WD group significantly reduced atherosclerosis in the aortic root. Expression of NAD+-producing enzymes (Nampt, Nmnat1) and NAD+-consuming (Parp1, Cd38, Sirt3) in spleen leukocytes were upregulated in WD group and NMN treatment blunted the expression. The protein expression of the NAD+-dependent deacetylase SIRT3 was significantly reduced. Acetylation of its mitochondrial target MnSOD was significantly increased following WD. Moreover, NMN treatment blunted the WD-induced increase in gene expression of the downstream SIRT3 target, the proinflammatory NLRP3-inflammasome. There were no significant changes in expression of NAD+ metabolic enzymes in bone marrow. Conclusion: These results suggest that WD-feeding promotes atherosclerosis development, leukocyte NAD+ depletion, and impaired SIRT3 activity in Ldlr-/- mice. NMN supplementation replenished NAD+ levels and significantly attenuated the development of atherosclerosis in WD-fed mice.

## Talk Session II

### J<e4>ger Vanessa

Abstract ID: 119302

# Functional characterization of plasma membrane rupture mediator Ninjurin1 in lung adenocarcinoma

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Background/Aims Despite recent therapeutic advances, lung cancer is still the leading cause of cancer-related deaths worldwide. The introduction of immunotherapy improved patient outcomes, but it often fails to provide long-term remission. Triggering inflammatory cell death in cancer cells, thereby altering the tumor immune microenvironment (TIM) may be a strategy to boost the responses to immunotherapy. Plasma membrane rupture (PMR) is the final event of lytic/inflammatory forms of cell death, such as necroptosis, which are associated with release of damage-associated molecular patterns (DAMPs) that propagate inflammation and subsequently influence the TIM. Initially, PMR was thought to be a passive event, but recent studies identified Ninjurin 1 (NINJ1) as a key mediator. Deregulation of NINJ1 has been implicated in different cancers, but its role in lung cancer is not well understood. Therefore, the aim of this study is to comprehensively characterize the role of NINJ1 in lung cancer.

Method/Results Performing CRISPR/Cas9-mediated modulation of NINJ1 in lung cancer cell lines, we could confirm that changes in NINJ1 expression levels affect the release of DAMPs from the tumor cells. Bioinformatic analysis of publicly available datasets revealed reduced immune cell infiltration in NINJ1 low tumors. Decreased NINJ1 levels also correlated with shorter patient survival. For further functional characterization of NINJ1 in vivo, we used a unique murine lung cancer model which allows CRISPR-mediated somatic targeting of NINJ1 specifically in the tumor cells. Our preliminary analysis of this model confirmed a tumor-suppressive role of NINJ1 in lung cancer development.

Conclusion Our studies highlight an important role of NINJ1 in shaping the TIM in lung cancer and suggests that it functions as a tumor suppressor. This highlights the great potential of modulating regulators of lytic death to improve immune therapy in lung cancer patients.

**Balihodzic Amar**

Abstract ID: 119211

# BCL-XL plays a role in determining lung cancer cell fate upon chemotherapy

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Background/Aims

Lung cancer (LC) is the leading cause of cancer-related deaths. Despite advancements in targeted therapies, many patients do not benefit due to the emerging resistance. Thus, chemotherapy, such as cisplatin, is still used in LC treatment. However, it often induces senescence rather than apoptosis and there is growing evidence that senescent cells may contribute to cancer progression. BCL-XL, a pro-survival member of BCL-2 protein family, is one of the major regulators of apoptosis and often deregulated in LC. Hence, we aim to evaluate the role of BCL-XL in determining the cell fate upon treatment of LC cells with cisplatin and test if it represents a target to eliminate senescent cells.

Methods/Results To study if/how BCL-XL is involved in life-death decision in LC cells upon chemotherapy, I generated a CRISPR-based endogenous BCL-XL reporter system to monitor changes in the transcriptional levels of BCL-XL upon different treatments. Using this unique reporter system in LC cell lines, we observed that sub-lethal concentrations of cisplatin, leading to cell cycle arrest, strongly induce BCL-XL mRNA expression. We also confirmed this observation on a protein level. Furthermore, we found that the increase in BCL-XL was independent of the cellular p53 status, which is mutated in about 50% of lung tumors. Intriguingly, we observed that the induction of BCL-XL renders the LC cells entirely dependent on the pro-survival protein and that blocking it shifts the cellular fate upon chemotherapy towards apoptosis. To identify the molecular regulators mediating the induction of BCL-XL in response to chemotherapy, we are currently applying whole-genome CRISPR screening in our BCL-XL reporter LC cell lines.

Conclusion BCL-XL induction in response to low doses of chemotherapy might represent a key mechanism how cancer cells protect themselves from the induction of apoptosis and might represent an <U+0091>Achilles heel<U+0092> of cells entering chemotherapy-induced senescence.

**Ermakov Mikhail**

Abstract ID: 118978

# Mutational analysis of HPV-induced and HPV-independent penile squamous cell carcinoma

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Background: Penile squamous cell carcinoma (SCC) is a rare, but lethal malignancy, that arises after transforming human papillomavirus (HPV) infection or independent of HPV in the background of lichenoid dermatoses. Genetic events accompanying penile carcinogenesis are poorly understood. We performed a comparative study of genetic alterations in HPV-induced and HPV-independent penile SCC in a large cohort of 156 patients from a low incidence country. Materials and Methods: DNA was extracted from microdissected, FFPE tumor tissues, and analyzed for the presence of 32 HPV genotype-specific DNA using the LCD-Array Kit (CHIPRON, Germany) and for mutations in hot spot regions of 50 cancer genes by Ion Torrent Next-Generation Sequencing. Immunohistochemical overexpression of p16INK4A in HPV-induced SCC served as a surrogate marker for a transforming HPV infection. Results: 51% (79/156) SCC were classified as HPV-induced, 49% (77/156) SCC arose independent of HPV. Only 28/79 (35%) of HPV-induced penile SCC, but 69/77 (90%) of HPV-independent SCC carried somatic mutations (Chi-sq; $p< 0.001$). PIK3CA, FGFR3 and FBXW7 mutations occurred in both groups in similar numbers. Mutations in TP53 (44/77; 57%), CDKN2A (35/77; 45%) and HRAS (13/77; 17%) occurred exclusively in HPV-independent SCC, with a frequent co-occurrence of TP53 and CDKN2A mutation (28/77; 36%). More than one mutation per gene was characteristic for HPV-independent SCC in 14/77 (18%) compared to 3/79 (4%) HPV-induced SCC (Chi-sq; $p< 0.001$). The total number of mutations in HPV-induced penile SCC (47 mutations) was significantly lower than in HPV-independent (143 mutations; Welsh test; $p<0.001$). Conclusion: Somatic gene mutations significantly differ in HPV-induced and HPV-independent penile SCC. While mutations in tumor suppressor genes (TP53 and CDKN2A) drive HPV-independent penile carcinogenesis, the oncogenic action of HPV is sufficient for HPV-induced SCC.

## Poster Session I

### Lazzeri Isaac

Abstract ID: 119462

# Unveiling Prostate Cancer Transcription Factor Activity via Liquid Biopsy

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Background/Aims Transcription Factors (TFs) play a pivotal role in the orchestration of gene expression. Their binding to genes<U+0092> regulatory regions, such as promoter and enhancer sites, can facilitate or hinder the recruitment of the RNA polymerase modulating so the transcription process and causing nucleosome displacement and phasing. Patterns derived by open or closed chromatin states due to TFs binding can be observed and multiple features extracted from circulating free DNA (cfDNA).

Method/Results Utilizing cfDNA from high-coverage prostate cancer samples, we present novel feature extraction methods based on fragmentomics and coverage-based signals. To address coverage and tumor fraction variations, we introduce an in-silico dilution method, ensuring consistent coverage and tumor fraction across samples. Through the analysis of the extracted features with unsupervised and semi-supervised machine learning methods we defined prostate cancer clusters, highlighted differentially active transcription factors and conducted enrichment analysis to unveil underlying biological processes.

Conclusion Our findings reveal multiple differentially active transcription factors associated with the androgen receptor signaling pathway, which are generally linked to different castration-resistant prostate cancer subtypes. These insights offer potential applications for non-invasive monitoring of prostate cancer progression and personalized therapeutic guidance.

**Cosic Mujkanovic Nejra**

Abstract ID: 119458

# Myeloperoxidase alters lung cancer cell function to benefit their survival

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Background: Neutrophils are an abundant immune cell type in non-small cell lung cancer that accounts for 85% of all lung cancer cases. Some of the cytoplasmic granule components of neutrophils, such as myeloperoxidase (MPO), are considered to contribute to tumour development, but the involved mechanisms are unknown. MPO is a heme-containing peroxidase and converts hydrogen peroxide and chloride ions to hypochlorous acid (HOCl). Upon neutrophil activation, MPO is secreted into the extracellular milieu where it can modify proteins, lipids, or internalise into neighboring cells. While MPO has both pro- and anti-tumour properties, most of the evidence suggests that it supports tumour initiation and progression. Reports demonstrated that MPO can influence proliferation, apoptosis and migration of cancer cells. Previous studies in our laboratory showed that MPO-deficient mice (MPO KO; C57BL/6 MPO-/-) have up to 40% reduced tumour size compared to MPO wild-type mice (C57BL/6 MPO+/+). To further understand the role of MPO in the setting of lung cancer, we aimed to investigate whether MPO can alter the function of tumour cells in vitro. Methods: Changes in proliferation, apoptosis and MPO activity were assessed using flow cytometry. ECIS-system for changes in migration. MPO uptake by cancer cells was analysed with western blot and fluorescence microscopy. Results: MPO treated human lung cancer cells show increased proliferation and reduced apoptosis and migration when compared to untreated cells. We found that MPO internalises A549 cells and preserves its enzyme activity as we detected HOCl after exposing cells to MPO. Blocking MPO internalisation with heparin or additional treatment with an MPO specific inhibitor (ABAH) reduced or abolished MPO effects on lung cancer cell function. Lastly, MPO WT mice treated with ABAH developed smaller tumours when compared to vehicle treatment. Conclusion: MPO might support tumour progression by altering lung cancer cell function.

**Alihod<U+009E>i? Dina**

Abstract ID: 119457

# Investigating the contribution of TET2 mutant human clonal hematopoiesis to atherosclerotic plaque formation in a novel LDL-R/ApoE double knock-out mouse model.

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Background: Clonal hematopoiesis of indeterminate potential (CHIP) is characterized by the presence disproportionately expanded hematopoietic clones carrying cancer associated mutations in individuals without a frank hematological malignancy. CHIP increases with age and is associated with increased risk of hematological cancer and atherosclerosis (AS) and cardiovascular disease. Ten-eleven translocation 2 (TET2) is an epigenetic regulator catalyzing DNA demethylation and the second most frequently mutated gene in CHIP. Murine CHIP models indicate a direct connection between TET2 deficiency in myeloid cells and increased atherosclerotic plaque size. However, the mechanistic contribution of TET2-mutant human hematopoietic cells to AS formation and cardiovascular disease has not been investigated due to the inherent resistance of immunocompromised NOD-SCID gamma (NSG) mice to form AS plaques. Recently, double knock-out of LDL-receptor and ApoE in NOD-SCID mice has been shown to be sufficient for the generation of AS. Therefore, combining (i) genome engineered human TET2 deficient immune system mimicking clonal hematopoiesis with (ii) this novel LDL-R/ApoE double KO atherosclerotic mouse model will allow for the first time to investigate the effect of CHIP mutation on the atherosclerotic plaque development in a human setting. Hypothesis: We hypothesize that human TET2 deficient hematopoietic cells increase atherosclerotic plaque formation in a novel atherosclerotic mouse model. Methods: We will employ CRISPR-Cas9 base editing to induce TET2 loss -of-function (LOF) mutation in primary human CD34+ HSPCs. The engineered TET2 deficient cells will be xenotransplanted into a unique LDL-R/ApoE knock-out atherosclerotic mouse model generated on NOD-SCID gamma background. After. Atherosclerotic plaques formation upon western type diet in the aorta of mice will be analyzed. Mutant human cells in the plaques will be investigated by immunohistochemistry, DNA- and RNA- sequencing.

**Miknevicius Povilas**

Abstract ID: 119453

# The influence of probiotics on chemotherapy side effects

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Background/Aims: Intestinal mucositis is a commonly encountered side effect in cancer patients receiving chemotherapy. However, intestinal mucositis remains a common adverse effect for which no effective preventive strategies are available. The aim of this study was to assess the outcomes of probiotic supplementation on CTx-induced IM in a CRC liver metastasis rat model. The aim of this study was to assess the outcomes of probiotic supplementation on CTx-induced IM in a CRC liver metastasis rat model.

Method/Results: Six-week-old male Wistar rats received either a multispecies probiotic or placebo mixture. On the 28th experiment day, rats received FOLFOX CTx. At study completion, Ileum and colon tissue samples were collected to investigate mucin composition. Also, Tight junction protein expression, inhibition of inflammation and cell apoptosis was studied by Western blot. The increased intestinal permeability caused by FOLFOX was ameliorated in probiotic group. Furthermore, probiotic supplementation mitigated CTx-induced histological changes in the gut and promoted intestinal cell regeneration.

Conclusion: This study shows that multispecies probiotic supplementation is effective in reducing FOLFOX-induced IM by inhibiting apoptosis and inflammation, also maintaining intestinal permeability and mucus barrier.

**<d6>zkaya Erdem**

Abstract ID: 119439

# Genome engineered TET2 loss-of-function mutations increase stem cell self-renewal in human hematopoietic stem and progenitor cells

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Background and Aim: Ten<U+0096>eleven translocation 2 (TET2) is an epigenetic regulator catalyzing DNA demethylation. Genomic studies have identified somatic TET2 loss-of-function (LOF) mutations across hematologic malignancies. Precise DNA Base editing (BE) is a new CRISPR-based application allowing for modification of single nucleotides without inducing double strand breaks (DDB) and DDB-induced apoptosis of fragile hematopoietic stem and progenitor cells (HSPCs). BE can be used to introduce in-frame STOP codons via C?T transitions, thereby leading to gene KO and mimicking (LOF) mutations. Here, we employ BE to mimic TET2 LOF and investigate its effect on HSPC function and engraftment into immune-compromised mice.

Methods and results: BE mRNA with sgRNAs were used to precisely introduce C?T transitions for the formation of premature in-frame STOP codons leading to successful TET2 LOF mutation in HSPCs. Functional studies investigating differentiation and colony-forming potential were performed and engraftment of engineered cells into NSG mice was analyzed. Competitive advantage of TET2 LOF HSPCs was assessed over time in transplanted mice. Mutated cells showed increased colony forming and self-renewal potential. In vivo experiments revealed TET2 mutations induced myeloid skewing and selective outgrowth of mutant over wild-type cells, resulting in shortened overall survival of transplanted mice.

Conclusion: CRISPR/Cas9-BE can be used to mimic LOF mutations such as TET2 in primary HSPCs. This low toxicity approach has negligible effects HSPC viability and should become the preferred method for leukemia disease modeling.

**Telebar-<U+008E>bulj Vito**

Abstract ID: 119355

# Tunable Chemoimmunotherapy: Combining Iontronic Local Drug Delivery with Immune Checkpoint Inhibition

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Iontronic devices as a tool for local administration of chemotherapeutics were shown to provide consistent long-term delivery of drugs and maintenance of a high local concentration at the tumor site. While immunologic cell death (ICD) facilitated by chemotherapeutics can stimulate the immune system to combat cancer, it is often hindered by the immune-evading abilities of cancerous cells. Therefore, we aim to combine the iontronic local delivery of ICD-inducing drugs with immunotherapy, specifically immune checkpoint inhibitors.

We aim to utilize the local chemotherapy delivery capabilities of the ELectroPHoretic Implants (ELPHIs) in combination with systemic immunotherapy in an in vivo mouse tumor flank model. We hypothesize that the immunogenic response facilitated by ICD-inducing drugs will be enhanced when combined with immunotherapy, enabling the immune system to overcome the immune-evading abilities of cancerous cells. This ELPHI-chemoimmunotherapy should elicit a more effective reduction in local and distal tumors.

Our objectives are to implant ELPHI devices into one mouse flank and, after sufficient recovery, introduce tumor cells into both flanks. Investigating the timing between delivering chemo drugs and administering systemic immunotherapy treatments will be essential for finding the most effective treatment profile. We will follow the changes of the immune cells in both tumors and the release of ICD markers via flow cytometry and immunohistochemistry (IHC). We will specifically track the activation status and exhaustion of the cells most commonly involved in the anti-tumor immune response (dendritic and T-cells).

We expect to establish a reliable and effective platform for chemoimmunotherapy treatment of cancers, emphasizing the tunability in the timing of the two treatments. The low systemic burden of the local drug delivery could prove essential in enhancing the immune response of immune cells.

**Vejzovic Djenana**

Abstract ID: 119349

# Identifying metastatic sarcoma on an extracellular vesicle level

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Background/Aims EWSR1 is the most common gene involved in fusion-associated translocations. They mainly occur in pediatric sarcomas and define depending on the fusion partner their own histological subtype. Although disease defining, the expression of these fusion transcripts does not give any insight into the metastatic potential or prognosis of the patient. Detection of metastasis often occurs when tumors are too advanced, and therapy is not curative anymore. Extracellular vesicles (EVs) are found in all tissues and body fluids and are emerging as key mediators in cancer progression and metastasis. Tumor-derived EVs have unique protein profiles and harbor the oncogenic information from their originating cells, providing a potential, non-invasive platform for detecting metastatic signatures.

Method/Results EVs from patient-derived EWSR1-sarcoma cell lines with different phenotypes (primary vs. metastasis) were isolated by either sequential ultracentrifugation (UC) or tangential flow filtration (TFF) of cell culture supernatants. Primary and metastatic cell lines, were established from the same patient to enable direct comparison between originating tumor and distant spread. Western blot and ExoView confirmed the expression of EV-specific markers in UC-EVs, whereas cryo-electron microscopy revealed vesicular structures. In addition, EV-associated RNA was analyzed by RT-qPCR (Real-time quantitative PCR) in UC-EVs verifying presence of EWSR1- fusion transcripts. To generate protein profiles, quantitative proteomics by mass spectrometry was performed using TFF-isolated EVs. A total of 354 quantifiable proteins could be detected in both samples, 46 were unique to metastasis-derived EVs and 69 other proteins were found exclusively in primary-tumor EVs, enabling clear differentiation between the two.

Conclusion These results set the stage for the development of EV-based detection of metastatic sarcoma, urgently needed to improve management of this lethal malignancy.

**Chaida Panagiota**

Abstract ID: 119324

# The role of RAS signalling aberrations in the development of myeloid sarcoma

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Myeloid sarcoma (MS) is an extramedullary manifestation of acute myeloid leukemia. It is a rare manifestation with a largely unknown molecular pathogenesis. We previously highlighted a potential role of aberrant RAS-signalling in MS by identifying a functionally relevant expression loss of the RAS-MAPK/ERK inhibitor RKIP in a subset of MS cases. Mutations modifying RAS occur in ~10-25% of AML cases and are drivers of leukemogenesis. In this project, we hypothesize that RAS-modifying mutations are relevant for MS development. Initially, we studied 34 primary MS patient specimens by next-generation sequencing (NGS) covering 49 genes recurrently mutated in myeloid leukemias. Importantly, 18/34 (53%) had one or more mutations in RAS (NRAS or KRAS) or RAS-modifying genes (PTPN11, CBL, NF1), most frequently affecting NRAS codon 12. We then performed genome editing by CRISPR/Cas9 in the myeloid leukemia cell line K562 and introduced a heterozygous NRAS-G12D mutation. Functional experiments revealed that K562-NRAS-G12D showed an increased potential for migration and invasion in-vitro. This could be validated in-vivo by showing increased invasion of K562-NRAS-G12D into chicken embryo chorioallantoic membranes. These preliminary data suggest that RAS-modifying mutations are frequent events in MS and might be functionally involved in MS development. We further plan to validate these results by increasing the cohort size of primary MS patient specimens and extending the functional characterization of RAS mutations in MS. Therefore, we will validate the data in a series of additional myeloid leukemia cell lines, healthy CD34+ hematopoietic stem- and progenitor samples and primary leukemia patient specimens.

**Eberhard Anna**

Abstract ID: 119269

# Examining Cancer using Urinary Cell-Free DNA Analysis Workflows

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Background Urinary cell-free DNA (ucfDNA) holds the potential to improve the accuracy of liquid biopsy approaches by proximal sampling However, due to its extremely high fragmentation, ucfDNA is an extremely challenging analyte. In this study, we assessed various workflows for ucfDNA across three caner types: metastatic prostate cancer (mPCa), metastatic colorectal cancer (mCRC), and metastatic breast cancer (mBCa). Methods Matching blood and urine specimen were collected from 135 mPC, 36 mCRC, and 27 mBC patients. cfDNA was extracted using the QIAsymphony Circulating DNA Kit. For mPC samples shallow whole genome sequencing (sWGS) was used to infer genomewide copy number alterations and tumor fractions (iTF). mCRC samples were analyzed using a hybrid-capture based approach enriching for 17 genes. For mBC a high-resolution 4plex amplicon approach (SiMSen-Seq) targeting 11 PIK3CA hotspots mutations. Results Our data demonstrated that sWGS as well as hybrid capture based enrichment is feasibly inucfDNA. Using an iTF cut-off of 4%, tumor-derived cfDNA could be detected 54/135 (40.0%) of urine samples from mPC patients, of which 23 (42.6%) had also ctDNA detected in corresponding plasma with highly concordant copy number profiles. In addition, in 23/135 (23.7%) ctDNA was detected in plasma only. In mCRC patients, sequence analysis revealed a full concordance between urine and plasma for putative germline variants. However, since the use of <50ng input material led to high signal-to-noise ratio, we adjusted the limit of detection for ucfDNA to 0.5% at which tumor-derived DNA was detected in only one patient. In mBC patients, SiMSen-Seq library analysis failed in most urine samples, and no PIK3CA mutation could be detected, most likely due to the fact that the amplicon size of SiMSen-Seq is optimized for cfDNA from plasma. Conclusion Due to the high fragmentation and low concentrations, ucfDNA workflows need to be optimized and adopted. Yet, our data shows that multiple a

**Berton Franziska**

Abstract ID: 119254

# Pattern of venous thromboembolism (VTE) in patients with cancer treated with immune checkpoint inhibitors (ICI)

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Background: Patients with cancer treated with ICI are at substantial VTE-risk, yet clinical risk profiles are unclear. Our aim was to identify risk factors for VTE during ICI-therapy to support the development of specific thromboprophylaxis strategies. Methods: Consecutive adult patients treated with ICI at the Medical University of Graz were included in this retrospective cohort study and followed for the occurrence of VTE during ICI-therapy (AUTRICHE-register-based). Statistical analyses were conducted in competing risk analysis, accounting for all-cause mortality as competing event. Results: Overall, 417 patients were included [non-small cell lung cancer (41%), renal cell carcinoma (16%) and melanoma (15%)]. Over a median follow-up of 26.4 months, 37 VTE occurred [cumulative incidence: 12.2% (95% confidence interval [CI]: 8.7-16.4)]. VTE-risk was increased after ICI-initiation compared to the period from cancer-diagnosis to ICI-start (transition-hazard-ratio (HR): 3.30, 95%CI: 1.95-5.57). Similar incidences and no significant differences in risk were observed according to demographics, comorbidity burden, cancer-type and -stage. The Khorana-score did not predict VTE-risk (subdistribution-HR [score ?2]: 0.88, 95%CI: 0.45-1.72). Baseline levels of routine laboratory parameters including C-reactive protein (CRP) did not predict VTE-risk, yet early increases in CRP (2-fold increase within 3 months of ICI-initiation) were associated with a significantly higher VTE-risk (adjusted subdistribution-HR: 2.31, 95%CI: 1.06-5.02), with a cumulative incidence of 22.9% in patients with an early CRP-flare. Conclusion: A substantial burden of VTE among ICI-treated patients was observed, characterised by homogenously high risks according to patient- and cancer-characteristics. Longitudinal trajectories of inflammatory biomarkers might identify patients at very high VTE risk.

**Moritz Jennifer**

Abstract ID: 119175

# Flowcytometry-based leukemic cell enrichment followed by mutational analysis for optimized comprehensive detection of residual disease in acute myeloid leukemia

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Acute myeloid leukemia (AML) is a malignant clonal disorder of myeloid progenitor cells associated with poor prognosis due to high relapse rates. Relapse is caused by trace amounts of chemoresistant leukemic cells in the bone marrow persisting beyond complete hematologic remission. Detection of these persistent cells as measurable residual disease (MRD) is therefore of high clinical impact for optimizing disease outcome. In contrast to other hematologic malignancies no uniform MRD detection method is available for all AML patients. Measurement of MRD is either performed by qPCR-based detection of leukemia-specific genetic aberrations, which is available for less than half of the patients, or multicolor flow cytometry (MFC) analysis, which is hampered by low sensitivity and poor standardization. Given its prognostic relevance, novel approaches for MRD detection in AML are clearly needed. Based on these clinical needs, we recently developed a novel two-step method of MRD detection consisting of MFC-based leukemic cell enrichment using antibodies against surface markers highly expressed on leukemic cells, followed by mutational analysis of recurrently mutated genes in AML using next generation sequencing (NGS). We have now optimized this approach by using a combinatorial antibody panel against the surface markers CD117, CD312, CD123, CLL1 and TIM3 labeled with the same fluorochrome for leukemic cell enrichment. Preliminary results show on average a 70-fold enrichment of cells using this method. In this project, we will therefore set up a pilot study involving 90 AML patients undergoing intensive chemotherapy. Status of MRD will be determined by our proposed method and compared to conventional MRD detection methods. Our method is hypothesized to be non-inferior to conventional techniques in terms of sensitivity and specificity to predict relapse, but to allow a uniform approach in the vast majority of AML patients.

**Zupo Antonella**

Abstract ID: 119117

# Distinct chemokine receptor expression profiles in the development and early progression of follicular lymphoma

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Follicular lymphoma (FL) is one of the most frequent non-Hodgkin<U+00B4>s lymphoma and represents a heterogeneous disease. Progression of disease within 24 months (POD24) is the most accurate predictor of worse clinical outcome but specific parameters useful for risk stratification before start of therapy are lacking. The role of chemokine receptors (CRs) in the development of various lymphoma entities has been identified as crucial. Thus, we aimed to comprehensively study CR expression profiles in FL.

We investigated of 17 well-characterized chemokine receptors (CCR1<U+0096>CCR10, CXCR1<U+0096>CXCR5, CX3CR1 and XCR1) in a cohort of FL patients with POD24 (n=14) and without POD24 (n=57) by RQ-PCR. Non-neoplastic tonsils (n=5) served as non-malignant controls.

The chemokine receptor expression profile of FL substantially differed from that of tonsils, with higher expression of CCR1, CCR6, CCR7, CXCR5 and CX3CR1 in this lymphoma entity. Furthermore, an at least 2.5-fold higher expression of CCR8, CCR10, CXCR1, CXCR2 and CX3CR1 was detected in grade 3a-b FLs compared to grade 1-2. Interestingly, CCR4 and XCR1 exhibited an at least four fold higher expression in POD24-FLs compared to non-POD24 FLs. Relating the CR expression levels to clinical data of our FL cohort, high levels of CCR3, CCR4 and CCR7 correlated with poor lymphoma-specific survival.

Overall, our results indicate that a distinct chemokine expression profile might be implicated in the development and early progression of FL. Thus, several receptors could serve as clinically useful prognostic markers for risk stratification and/or as potential novel therapeutic targets for lymphoma therapy.

**Telebar-Zbulj Franciska**

Abstract ID: 119088

# Beyond Conventional Methods: ELPHIs for Local and Distal Tumor Treatment

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Administering chemotherapeutics locally and long time periods is a promising method to boost the potency of established drugs. Iontronic tools enable continuous delivery, creating high local drug concentrations at the tumor site over days. Our previous results demonstrate that this profile significantly reduces tumor size compared to conventional drop casting methods in in vitro and in vivo models. In addition, a local and prolonged release of chemotherapy inducing immunologic cell death (ICD), can be used for not only the treatment of local tumors, but also for metastases, when combined with immunotherapy.

Our goal is to address local and distal tumors through the extended operation of ElectroPHoretic Implants (ELPHIs) in vivo. We aim to develop implantable ELPHI devices for murine in vivo studies, hypothesizing that precise timing of chemotherapy and ICD induction will lead to efficient local and distal tumor reduction, diminished systemic burden, improved overall survival, reduced recurrence, and enhanced immunologic response.

Our initial objective is to create a library of potential cancer treatment substances suitable for ELPHI administration. Subsequently, we plan to implant ELPHI devices in a mouse flank, assessing the foreign body response (FBR) through immunohistochemistry (IHC) and flow cytometry. Using a mouse model with a controlled immune response, we will introduce tumor cells near the ELPHI implant site and at a distant site, followed by ELPHI-chemo treatment. Pharmacokinetic studies employing HPLC-MSMS will assess implant performance, optimizing local drug concentrations while minimizing systemic effects.

Anticipated outcomes include estimating FBR and implant performance in vivo, accompanied by a more active and viable immune response. These pivotal steps set the stage for combinational treatments with immune checkpoint inhibitors, potentially synergizing with ICD chemotherapies, advancing tumor treatment at both local and distal levels.

**Gollmer Johannes**

Abstract ID: 119299

# Molecular alterations in human diabetic heart disease

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Background/Aims: Diabetes mellitus (DM) can facilitate molecular and structural alterations in the human myocardium as well as in coronary arteries. Ischemic heart disease (IHD) due to coronary artery disease (CAD) with systolic heart failure is common in diabetic patients. Heart failure (HF) due to diabetic induced alterations, in the absence of CAD, often with hypertrophy and diastolic dysfunction is termed diabetic cardiomyopathy. Since data evaluating the proposed mechanisms of the diabetes induced alterations from rodent studies in human myocardium are sparse, we aimed to provide a comprehensive analysis of human diabetic myocardium.

Methods/Results: We studied LV samples of 8 subjects with T2D, preserved ejection fraction (EF) (63?5%) and no history of ischemic heart disease (Db-pEF), 7 subjects with T2D, reduced EF (26?9%) and ischemic heart disease (Db-ICM), and 15 non-diabetic individuals with normal EF. Label-free proteomics identified 1168 proteins with 146 differentially expressed in Db-ICM, and 66 in Db-pEF. Bulk RNA sequencing revealed 1795 differentially expressed genes (DEG) in Db-ICM and 527 in Db-pEF, with only 128 commonly regulated. Pathway analysis found enrichment of inflammation and extracellular matrix remodelling in Db-ICM or Db-pEF. Single nucleus RNAseq showed no differences in cell frequencies between the groups. However, analysis of DEG in cardiomyocytes of diabetic hearts unmasked enrichments in many pathways related to rodent diabetic cardiomyopathy e.g. insulin resistance, fatty acid oxidation, oxidative phosphorylation and oxidative stress.

Conclusion: We present the first comprehensive atlas of molecular and cellular alterations in the human diabetic heart, confirming many pathomechanisms previously proposed in animal studies.

**Riahi Zina**

Abstract ID: 119275

# Extracellular vesicle singalling upon NAD+ replenishment during exercise in cardiometabolic disease

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Dysregulation of NAD+ metabolism has emerged as a common driver of cardiometabolic (CM) disorders. An age-/disease-related decline in NAD+ levels can lead to inadequate response to physical activity, therefore reducing its therapeutic efficacy. Here we investigate if NAD+ replenishment improves the compliance to exercise and enhances its beneficial metabolic effects in CM syndrome. Mechanistically, we focus on exerkines<U+0097>molecules released by skeletal muscles during exercise, both soluble and within extracellular vesicles (EVs)<U+0097> as mediators of interorgan communication and whether supplementing NAD+ accentuates this crosstalk. To investigate the in vivo impact of NAD+ replenishment combined with exercise in CM syndrome, Fischer rats fed a free choice diet are subjected to 16 weeks of endurance exercise training. To boost systemic NAD+ levels, a subgroup of rats will receive daily injections of NAM, a NAD+ precursor. To identify muscle-derived exerkines , we will isolate EVs from tissue and plasma after exercise. To investigate the EV content, we will perform miRNA-sequencing and untargeted proteomics, aiming to identify potentially novel exerkines. To this end, we set up protocols for isolation and comprehensive characterization of EVs (nano particle tracking, electron microscopy, and western blot), and started training of the first rat cohort. To evaluate whether cellular NAD+ status impacts exerkine release and improves responses in tissues involved in metabolic homeostasis (i.e. liver, AT), we will incubate primary cell models of rats with isolated plasma/muscle-derived EVs and analyze downstream effects such as lipolysis, FA oxidation, glucose metabolism, lipid and glycogen content, and mitochondrial function. In sum, this project will define EVs and EV-associated exerkines as mediators of exercise-related health effects in dependence of NAD+ levels in CM syndrome.

**Michenthaler Helene**

Abstract ID: 119243

# MULTI-OMICS IN ONE ASSAY: QPRO-SEQ TO DECIPHER CHROMATIN AND TRANSCRIPTIONAL LANDSCAPES OF FASTING IN ADIPOSE TISSUE

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Adipose tissue (AT) plays a central role in the regulation of systemic energy homeostasis through its endocrine function and storing excess lipids. These lipids are released at the onset of fasting, upon which AT globally rewires its gene expression (GE) program. But the regulatory determinants are not well understood. Key players of the fasting response are specific transcription factors (TFs) that bind to promoter and enhancer regions. Enhancer RNAs (eRNAs) are short and unstable RNAs, that are generated from TF-bound enhancers that are actively involved in transcription. This study aimed to identify TF networks and eRNAs that coordinate the immediate-early response to nutrient withdrawal in mouse white AT over a fasting period of 3 and 6 hours. Quick precision nuclear run-on sequencing (qPRO-seq) allows for detection of nascent RNA transcripts in genes, promoters, and enhancers. Data were analyzed and visualized using various bioinformatics tools and R scripts. Validating our method, we found genes involved in lipolysis to be upregulated after six hours of fasting, including Pnpla2 and Hsl, while genes involved in lipid storage, including Gk, were downregulated already after three hours of fasting. We detected more than 250 fasting activated enhancers that were annotated to the respective nearest genes, resulting in overrepresentation of various pathways, such as fatty acid oxidation and regulation of lipase activity, depending on duration of fasting. Motif enrichment analysis of fasting selective enhancers identified several known adipose tissue-relevant TFs, such as members of the KLF family (KLF3, KLF1) and E2F3 as well as previously undescribed players, like regulatory factor RFX5. In future experiments, we will focus on verification of super enhancer clusters, TF networks, and downstream pathways. Since AT is very heterogenous and undergoes extensive remodeling upon fasting, approaches like single-nuclei ATAC-seq are envisioned.

**Verma Daksh**

Abstract ID: 119230

# Cardioprotective effects of exercise in rats with diet-induced cardiometabolic syndrome

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The obesity epidemic is a major cause of the rising incidence of cardiovascular and metabolic diseases. Often linked to a sedentary lifestyle and increased intake of hypercaloric diets, obesity disrupts metabolic regulation and impairs the function of several organs, particularly the heart. Regular physical activity is a powerful intervention for combating obesity and improving cardiometabolic health.

We hypothesize that regular exercise attenuates cardiometabolic (CM) syndrome in rats fed a free-choice diet (FCD). To this end, we employed a diet-induced obesity rat model that recapitulates key features of excessive fat and sugar consumption typically observed in human dietary habits. Six-month-old F344 female rats were subjected to ad libitum access to a free-choice diet (FCD) regimen, comprising a standard chow and a high-fat/high-cholesterol diet, along with fructose-enriched and regular drinking water, within a single cage for 16 weeks. Half of the rats fed FCD were subjected to a running protocol on a treadmill (5 days per week for 16 weeks), while a subset of rats that received the standard diet (SD) alone served as a healthy control.

Preliminary results show that feeding sedentary rats with FCD increased body weight gain and elevated systemic blood pressure compared with SD. However, rats subjected to FCD in combination with exercise training on a treadmill were protected from FCD-induced body weight gain and hypertension, even though exercised rats supplemented with FCD had a comparable total caloric intake to the sedentary FCD group.

In the future, we will evaluate the positive impact of regular exercise training in combination with a caloric restriction mimetic on the cardiometabolic phenotype of rats fed FCD and study the mechanisms underlying these beneficial effects.

**Reynders Michelle**

Abstract ID: 119177

# Liver-adipose tissue communication through mTORC1

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Background: Mammalian target of rapamycin complex 1 (mTORC1) serves as a nutrient-sensing hub responsible for the switch between anabolism and catabolism. While much is known about the regulation of mTORC1 within an organ, little is known about its regulation through inter-organ communication. Our research focuses specifically on the regulation of adipose tissue mTORC1 in response to signals from the liver. Aims: We studied the role of mTORC1 within the liver-adipose tissue axis using different dietary regimes and knockout mice. Our main aim was to investigate whether adipose mTORC1 could be regulated by nutrient-specific diets, and if so, if this regulation is mediated by the hepatokine fibroblast growth factor 21 (FGF21), which is expressed in the liver and travels to the adipose tissue. Results: Feeding a ketogenic diet strongly activates mTORC1 in adipose tissue and, to a lesser extent, in liver. One possible explanation for this might be an increased secretion of the hepatokine fibroblast growth factor 21 that occurs under this diet. Our research has shown that mice, injected with recombinant FGF21, show activation of mTORC1 in adipose tissue, similar to what is seen under a ketogenic diet. To further look into this, we fed a ketogenic diet to Fgf21 knockout mice, which resulted in increased adipose mTORC1 activity, regardless of the loss of FGF21. However, further research into this is needed as we found that an increased expression of FGF15, which is expressed in ileum and travels to liver and adipose tissue, can (partly) compensate for the loss of FGF21. Thus, we will feed a ketogenic diet to Fgf15/21 double knockout mice and expect them to lose the ketogenic diet-induced ability to upregulate adipose mTORC1 activity. Conclusion: Ketogenic diet activates adipose tissue mTORC1, possibly through liver-adipose signaling via the hepatokine FGF21. Furthermore, when FGF21 signaling is lost, FGF15 can (partly) compensate for this loss.

**Pammer Anja**

Abstract ID: 119118

# Measures of HDL-related Functions and Mortality in Acute Heart Failure Patients

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High-density lipoprotein (HDL), a dynamic and multifunctional lipoprotein, plays a crucial role in maintaining vascular health and preventing cardiovascular diseases. However, functional impairment of HDL has been linked to an increased risk of recurrent cardiovascular events, particularly in patients with acute heart failure (AHF). In a study involving 315 AHF patients, we investigated whether alterations in HDL metabolism, composition, and function were associated with HF mortality. We assessed the anti-inflammatory and antioxidant properties of HDL and changes in HDL composition and metabolism in this cohort. Our findings revealed that patients who died within 3 months of AHF diagnosis had significantly lower levels of paraoxonase 1 (PON1), lecithin-cholesterol acyltransferase (LCAT), and cholesterol ester transfer protein (CETP) activity. Additionally, they exhibited lower levels of apolipoprotein A-I (apoA-I) and apoM than survivors. After adjusting for established risk factors, PON1 and LCAT activities remained significantly associated with 3-month mortality. These results underscore the importance of HDL functionality in AHF and suggest its potential role as both a therapeutic target and a biomarker for predicting mortality risk.

**Grgic-Mustafic Renata**

Abstract ID: 118795

# A novel method of congenital heart disease screening in new-borns using phonocardiography

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Background: Auscultation of the heart is a standard clinical examination and screening method for congenital heart disease. It is physician skill level and heart rate dependent,especially in neonates. Automated detection of heart murmurs by using phonocardiography is due to limited accuracy not in clinical routine use yet. The aim of this pilot study was to determine the diagnostic ability and accuracy of a novel self-developing algorithm in detection of heart murmurs out of phonocardiograms in neonates. Methods: A prospective observational pilot study was conducted on 40 preterm and term neonates. Auscultations by a paediatrician and phonocardiograms were performed within 12 hours of echocardiography in neonates. Phonocardiograms were analysed for detection of murmurs offline with a new self-learning algorithm in two runs. Sensitivity and specificity of detection of murmurs with pathological echocardiography by auscultation and by phonocardiography during a first self-learning run and a consecutive second run were analysed and compared. Results: Out of 40 included neonates, 36 neonates (gestational age: 36 <U+00B1>3 weeks, birth weight: 2572 <U+00B1>847g) were analysed. 23 (64 %) neonates had pathological and 13 (36%) normal findings in echocardiography. Sensitivity and specificity of auscultation were 17% and 100%, respectively. The new algorithm showed in first run a significantly higher 70% sensitivity and lower 77% specificity for detecting murmurs in neonates with pathological echocardiography. After the self-learning run, in the second run sensitivity improved significantly to 83% and specificity to 85%. Conclusion: Phonocardiography with the self-learning algorithm showed higher sensitivity but lower specificity than auscultation and an improvement in detection of heart murmurs in neonates with pathological echocardiography. Present data suggests that further improvement of correct detection of murmurs with underlying cardiac disease might be achieved in a larger study.

**Tandl Veronika**

Abstract ID: 118934

# Body Composition Influences on Serum Anti-Mllerian Hormone (AMH) Levels in Adult Males Imply Hemodilution

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A negative relationship between body mass index (BMI) and serum Anti-Mllerian hormone (AMH) levels has been previously reported. Whether this is because of an adverse effect of adiposity on AMH production or the hormone<U+0092>s dilution in a higher blood volume that accompanies larger body size (<U+0093>hemodilution<U+0094>) is not yet clear. Blood volume can be estimated by body weight, body surface area (BSA) or lean mass (LM). Of note, adipose tissue is poorly perfused and adds relatively little to the overall blood volume. To investigate a possible hemodilution effect, we analyzed the relationships between serum AMH levels and different body size and composition parameters in adult males. We used data of 382 adult, male participants of the ongoing, prospective BioPersMed study cohort. Body parameters used include height, weight, waist circumference, BMI, waist-to-hip ratio, body surface area (BSA) and estimated lean mass (eLM). Of 278 participants, dual energy X-ray absorptiometry (DXA)-derived body composition data, including fat mass (FM) and LM, were available. We performed univariate and multivariate regression models with potential confounders (age, follicle-stimulating hormone, and estradiol) included as additional predictors. In the fully adjusted models, weight (R2=0.201; ?=-0.002; p=0.0022), BSA (R2=0.206; ?=-0.231; p=0.0006) eLM (R2=0.206; ?=-0.006; p=0.0006) and LM (R2=0.197; ?=-0.006; p=0.003) significantly predicted AMH. In an age adjusted model that challenged FM and LM against each other by including them both as predictors, only LM remained significant (R2=0.061; ?=-0.007; p=0.0035). In adult males, weight, BSA, eLM and LM (proxies of blood volume) better predicted serum AMH levels than measures of adiposity <U+0096> suggesting hemodilution is at least partly responsible for the observed inverse relationship between AMH concentrations and BMI. Thus, hemodilution should be considered for normalization in future studie

**Ellmeier Elena**

Abstract ID: 120715

# Evaluating the role of succinate sensing via GPR91 in T cell-mediated anti-tumor immunity

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Cancer cells create an unfavorable tumor microenvironment (TME) for infiltrating immune cells by depleting essential nutrients or by secreting high levels of immunomodulatory products. These molecules dampen the pro-inflammatory potential of tumor-associated leukocytes, favoring tumor growth. The metabolite succinate (SUC), an intermediate of the tricarboxylic acid cycle, accumulates within tumor cells due to intracellular metabolic rewiring. Cancer cells actively secrete SUC in the TME, where it may interact with its cellular receptor, succinate receptor 1 (SUCNR1/GPR91), on the surface of tumor-associated macrophages, promoting an anti-inflammatory phenotype that favors immune evasion by the tumor. Of note, the impact of extracellular SUC on the functionality of CD4+ and CD8+ T cells, two major players in anti-tumor immunity, is poorly understood, and it is unclear whether tumor-derived SUC can modulate T cell-mediated anti-tumor immunity. This project aims to investigate the effect of extracellular SUC on CD4+ and CD8+ T cells in vitro and in vivo. Our hypothesis is that SUC released by cancer cells may affect T cell anti-tumor potential upon uptake or through the interaction with GPR91 on the T cells surface. In preliminary experiments, we first confirmed that GPR91 is expressed on human and murine T cells. We then showed that, in vitro, SUC boosts the release of interleukin-5 (IL-5), IL-13, and IL-4 by murine and human T helper 2 (Th2) cells, without affecting the polarization of other Th subsets. Finally, we confirmed such observation in a mouse tumor model, where systemic SUC injection increases IL-4 production by T cells in the TME. Overall, our preliminary data indicate that T cells may indeed sense extracellular SUC, supporting our experimental hypothesis. Our work may strengthen previous data on tumor-infiltrating macrophages, confirming that targeting SUC uptake or GPR91 may represent a new approach to boost anti-tumor immunity and limit tumor growth.

**Joshi Aaroh Anand**

Abstract ID: 119927

# beta-defensin 1 is a mediator in ultraviolet-induced healing of atopic dermatitis lesions

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Atopic dermatitis (AD) is a prevalent inflammatory skin disorder, with Staphylococcus aureus (S. aureus) playing a pivotal role in its pathogenesis through the secretion of various virulence and adhesive factors. Ultraviolet-based phototherapy, encompassing UVA and UVB treatments, represents a viable therapeutic approach for AD. This modality is known to influence the expression of host-derived antimicrobial peptides (AMPs), molecules possessing both antimicrobial and immunomodulatory properties. Through literature research, we identified the upregulation of the peptide beta-defensin 1 (Defb1) in healed AD lesions. Intriguingly, our investigations revealed that Defb1 was upregulated following UV irradiation, both ex-vivo and in vivo in mice. Topical application of Defb1 demonstrated a notable reduction in inflammation in a novel in-house AD mouse model. This effect was independent of its antimicrobial activity on S. aureus. This anti-inflammatory activity was further substantiated in a mouse model of contact dermatitis, where S. aureus was not implicated. RNA-sequencing data suggested potential involvement of genes related to dendritic cell docking to lymphatic vessels and trafficking, in the observed anti-inflammatory effects. Ongoing studies involve elucidating this mechanism by blocking downstream mediators identified by bulk-RNA sequencing analysis.

**Reiter Bernhard**

Abstract ID: 119461

# Immune cell characterization of pulmonary hypertension associated with chronic lung diseases

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Chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis (PF) are highly heterogeneous severe chronic lung diseases (CLD) associated with a decreased quality of life and increased mortality. The presence of pulmonary hypertension (PH) in CLD, which is characterised by a progressive remodelling of the pulmonary arteries (PA) is associated with worse patient prognosis. In the idiopathic form of PH the immune system has been shown to have an important role, however, its involvement in CLD-PH is much less clear. PA were isolated from human COPD (n = 11), PF (n = 7) and control lungs (n = 6). The immune cell characterization was performed using several multicolour flow cytometry panels and analysed bioinformatically.

Principal component analysis (PCA) revealed an altered immune cell profile in the PAs of COPD and PF compared to control-PAs. The strongest separation from the control immune profiled was observed for COPD-PAs. PF-PAs were more heterogeneous and partially overlapped with the COPD-PA, indicating overlaps in the immune profile, but separated from the control-PA in PC3. The separation of the PC1 is mainly driven by lymphocyte populations and macrophages, while the PC3 is driven by monocytes and neutrophils. Deeper analysed revealed an increased presence of CD4 and CD8 lymphocytes and monocytes, while neutrophil granulocytes and macrophages were decreased in both diseases. Work is ongoing to determine immune cell localization and association of immune cell signatures with
clinical and histological parameters.

Our initial data indicates that there is a separation between control and CLD-PA, and by understanding the immune system in PA of CLD we can lay the foundations for future immunomodulatory PH treatments.

**Pacher Christian**

Abstract ID: 119447

# Impact of microplastics on the human gut <U+0096> A series of bioreactor experiments

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Microplastic particles (MPs), plastic fragments smaller than 5mm, have been detected in ecosystems around the world. Accumulating in the food web, those particles can even enter the human body. While research has begun to investigate the ecological consequences of microplastic pollution, the effects on the human gut microbiome are still largely unknown. In this study, ex-vivo experiments were conducted using a bioreactor model inoculated with stool samples from healthy donors to investigate the effects of various plastic types on the gut microbiome. Cultures were grown under semi-continuous feeding conditions with regular medium exchange over the course of five days, and MPs were used as a possible stressor for the microbiome in mixed size classes, including polystyrene (PS), polypropylene (PP), low-density polyethylene (LDPE), and poly(methyl methacrylate) (PMMA). The used amounts of MPs reflect the quantity that people consume according to literature-calculations, and higher amounts to test dose dependent effects. Readouts included continuous measurements of pH inside the cultures and cell counting using a bacterial cell counter with viable and total cell staining. The presence of MPs did not significantly affect the viable or total cell count of the stool cultures, nor did it affect the viability of the cultures. However, a highly significant decrease in pH was observed in all cultures containing plastic compared to control cultures. This pH drop may result from alterations in the metabolism of the gut bacteria or from a changed composition of bacteria. Future investigations will include 16s-rRNA sequencing to assess changes in bacterial composition. Furthermore, the study intends to explore the effects plastic particle size on the gut microbiome. The study's outcomes will shed light on the complex and dynamic relationship between microplastics and the gut microbiome and pave the way for further research in this critical field.

**Radic Nemanja**

Abstract ID: 119421

# Biglycan modulates pulmonary arterial smooth muscle cell physiology

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Background Pulmonary arterial hypertension (PAH) is a chronic lung disease characterized by increased mean pulmo-arterial blood pressure and pulmonary vascular resistance. These hemodynamic changes are accompanied by vascular remodeling and deposition of extracellular matrix (ECM) components. In our previous work we have shown that biglycan (BGN), a component of the ECM, is more abundantly transcribed in PAH PAs. However, the mode of action of BGN during pulmonary vascular remodeling is unknown. Therefore, we aim to investigate the role of BGN in orchestrating cellular expansion and immune processes associated with PAH.
Methods We used our previously published single cell RNA dataset, derived from isolated pulmonary arteries (PA) from healthy and PAH lungs to investigate the transcription of BGN and downstream interaction partners in all cell clusters (GSE228644). Furthermore, pulmonary arterial smooth muscle cells (PASMC) isolated from healthy and PAH PAs were treated with siRNA for BGN and assessed for proliferation and apoptosis as well as phenotype markers. Results In PAH PAs BGN transcripts are increased in all subsets of the SMCs. In addition, we identified an altered transcript profile for the receptors TLR-2/4 and P2X4/7, which have been shown to bind BGN, in SMCs and macrophages. BGN depletion in healthy and PAH PASMCs lead to reduced proliferation, while concurrently increasing apoptosis. Furthermore, ?-SMA transcription is elevated in healthy and reduced in PAH PASMCs depleted of BGN. However, the transcription of the fibrosis markers Col1A1 and Col4A5 is increased in both groups. Conclusion We demonstrate that depletion of BGN in PASMCs inhibits proliferation via the promotion of apoptosis. Furthermore, depletion alters PASMC phenotype as shown by a shift in transcript levels of contractility and fibrosis markers. Altogether our data suggests a crucial role for BGN in the modulation of vascular remodeling and PAH-associated cellular expansion.

**Myronenko Oleh**

Abstract ID: 119380

# Soluble transferrin receptor (sTfR) as a potential marker of pulmonary hypertension associated with chronic obstructive pulmonary disease (COPD)

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Background. Despite smoking-induced iron loading in the lungs of COPD patients, systemic non-anemic iron deficiency (ID) is observed in 40-50% of cases. In turn, ID is associated with an increase of mean pulmonary artery pressure (mPAP). Therefore, biomarkers of altered iron homeostasis in COPD may provide important diagnostic/prognostic tools and therapeutic opportunities for pulmonary hypertension (PH). We aimed to characterize the profiles of systemic circulating iron levels and iron-associated factors of COPD patients with and without PH.

Methods. Blood serum samples from COPD patients were obtained from Graz biobank and divided into 4 groups: COPD (mPAP ? 24 mmHg, n=6), COPD-PHlow (mPAP = 25-34 mmHg, n=7), COPD-PHhigh (mPAP ? 35 mmHg, n=7) and healthy controls (n=10). The validation cohort included blood samples from patients that underwent right heart catheterization at LKH Uniklinik Graz: COPD without PH (n=11), COPD-PHlow (n=24) and COPD-PHhigh (n=35). All the groups were age- and gender-matched. Total iron, ferritin, transferrin, soluble transferrin receptor-1 (sTfR) levels were measured with the particle-enhanced immunoturbidimetric assay (Roche Diagnostics Inc.). Multiple group comparisons were performed with the Kruskal-Wallis H test. Correlations were calculated with the Spearman<U+00B4>s rank test. SPSS software (IBM SPSS Inc.) was used for statistical analysis. A p-value < 0.05 was considered significant.

Results/conclusions. In the screening and validation cohorts, levels of total serum iron, ferritin, transferrin, hemoglobin and red cell distribution width were comparable between all groups, but sTfR was significantly lower in COPD-PHhigh, compared to COPD without PH ($p<0.05$), and, in the screening cohort, was correlated with mPAP. In the validation cohort, sTfR did not differ between the comparison groups, and was correlated with mPAP ($R=0.475$, $p=0.004$) only in COPD-PHhigh patients, suggesting that it may be a potential biomarker of severe PH in COPD.

**Schaffer Anja**

Abstract ID: 119330

# Clusters of lung clearance index trajectories and survival in people with cystic fibrosis

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Background: Progressive muco-obstructive lung disease impairs lung function, i.e. ventilation in small airways, and leads to premature death in people with Cystic Fibrosis (pwCF). Serial measurements of lung clearance index (LCI), a biomarker of ventilation inhomogeneity, may predict survival in pwCF. We aim to examine LCI clusters and the associated risk of death or lung transplantation (LTx) in pwCF. Methods: We performed a retrospective, longitudinal analysis in a cohort of pwCF aged >5 years and at least one LCI measurement. LCI was measured using a nitrogen multiple-breath washout (MBW) setup during clinical routine visits in Bern (Switzerland) between 1986 and 2006. Preliminary analyses include descriptive statistics. We aim to apply latent classes analysis (LCA) from unobserved patterns of the indicator variables FEV1 and LCI and link these classes to the compound outcome risk of death or LTx in pwCF until 12/2018. Results: In total, 268 pwCF were eligible and 259 (135 females) were included contributing 3158 person-years and 2787 LCI measurements in total. Mean age was 15.7 <U+00B1> 0,9 years at study entry. The median of visits per patient was 11 (interquartile range (IQR) = 5.0-19.0) units. Median LCI was 18.40 (IQR = 13.8-24.6) units. LCA models with the fewest number of classes that best fits the data remain to be selected. In 106 (40.9%) pwCF the primary outcome occured: 59 patients received LTX and 47 died. Conclusion: Our preliminary analyses suggest that the dataset is correctly setup and sufficiently large for LCA. We will explore if pwCF who died or received LTX belong to specific LCI clusters. However, the dataset seems not large enough for stratification into training and test sets for internal validation.

**Faimann Isabella**

Abstract ID: 119320

# Effects of Environmental Enrichment on Microbial Community Composition and Behaviour in Mice and Zebrafish

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The microbiota-gut-brain axis denotes the bidirectional communication between visceral organs and the brain. The gut microbiota are an important component of this communication, for example, by regulating the activity of the local and systemic immune system and by secreting bacterial metabolites able to reach distant organs. Environmental enrichment (EE) is a husbandry method known to provide enhanced somatosensory, locomotor and cognitive stimulation. It improves rodent and fish behavior, alters neuronal plasticity, and promotes stress resilience. The aim of the current work is to investigate, whether the beneficial effects of EE are mediated via the microbiota-gut-brain axis. Four-week-old C57BL6/J mice were co-housed for four weeks in order to homogenize their microbiome. Afterwards the mice were split into EE and standard environment (SE) housing. Similarly, nine-week-old AB zebrafish were kept in EE and SE housing. Following differential housing, the open field test (OFT) was conducted in both species to asses anxiety-like behaviour. In addition, mouse boli were analyzed with 16S Illumina sequencing in order to determine differences in the intestinal microbial community composition. In the OFT we found that EE-housed animals entered the central zone of the test arena significantly more often than animals in SE indicating reduced anxiety. 16S sequencing showed unique microbiome signatures developing over time in SE and EE. Furthermore, we found significant changes in the microbiome of female EE mice compared to SE-housed females after 9 weeks of differential housing. In conclusion, we found an EE-induced reduction of anxiety-like behaviour and changes to the microbiome, which might be linked. In future experiments, we want to assess causality by using antibiotics models and stool transplantation experiments.

**Esparta Olaya**

Abstract ID: 119274

# Are gdT and pDC driving vascular remodelling?

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Pulmonary arterial hypertension (PAH) is a cardiovascular disease characterised by a high mean pulmonary arterial pressure of >20 mmHg at rest and a low survival rate. It is associated with chronic inflammation, lung vascular remodelling and vasoconstriction that ultimately leads to heart failure and death. Immune cell infiltration is a hallmark of PAH, and emerging evidence suggests that gamma-delta T (gdT) and plasmacytoid dendritic cells (pDC), with pro-inflammatory and cytotoxic effects, could play a crucial role in the transition to a chronic inflammatory environment. Therefore, we aim to investigate how gdT and pDC cell populations interact with each other and with the structural cells from all layers of the pulmonary arteries (PAs) and might potentiate vascular remodelling in PAH. We use methods such as cell isolations via magnetic beads, co-culture, multi-colour flow cytometry, in combination with fluorescent microscopy and qPCR, to characterise the two cell populations and understand the cell-crosstalk between them and structural cells. Cell isolation from healthy buffy coats resulted in over 90% purity. Flow cytometry of immune cells co-cultured with human primary pulmonary arterial smooth muscle cells (hPASMC) revealed significant differences in the activation marker CD25 in gdT cells. hPASMC did not show evident morphological changes with fluorescent microscopy, however, qPCR revealed a downregulation in extracellular matrix components in the presence of immune cells. Further experiments need to be performed in order to validate these findings. So far, these preliminary results are promising, but ongoing experiments with human pulmonary arterial endothelial cells (hPAEC) and adventitial fibroblast are necessary to fully elucidate the role of gdT and pDC in PAH.

**Brandl Katharina**

Abstract ID: 119236

# Antigen Presentation and Immunopathology in Heart Failure

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Background: Heart failure, characterized by the heart<U+0092>s inability to meet the metabolic demands of the body, is affecting an estimated 64 million individuals worldwide. A myocardial infarction (MI), causing the necrotic death of cardiomyocytes, can lead to heart failure. Necrotic cardiomyocytes trigger acute inflammation which may initiate a persistent adaptive immune response. Emerging data indicate that upregulated self-antigen presentation and persistent anti-heart autoimmunity contributes to the development of heart failure. The role of non-immune cells, including cardiomyocytes, in these self-antigen presentation pathways are unknown. Hypothesis: Self-antigen presentation by cardiomyocytes, as well as anti-heart autoimmunity, may maintain and exacerbate the adaptive immune response to ischaemic myocardial injury. Approach/methods: Antigen-presentation pathways will be explored by single cell sequencing analysis with focus on cardiomyocyte and myocardial immune cells obtained from patient samples, including male and female individuals of different ages, with ischaemic or dilated cardiomyopathy. To decipher the effect of cardiomyocyte-intrinsic antigen-presentation, type-1 and type-2 MI will be induced in mice, using isoproterenol-HCl administration, and a novel minimal invasive left descending artery ligation technique, respectively. Assessment of cardiac injury, inflammation and fibrosis, as well as heart function will be performed by immunohistochemistry and in vivo imaging. Flow Cytometry will be used for the characterization of dendritic and T-cell populations in hearts, lymph nodes and blood. Furthermore, a possible therapeutic benefit of blocking antigen-presentation in post-MI cardiac immunopathology after ischaemic damage will be investigated in mice. Conclusion: This study will unveil novel targets to improve myocardial health in heart failure patients by preventing anti-heart autoimmunity.

**Mittl Barbara**

Abstract ID: 118734

# The urogenital microbiome of children and adolescents with neurogenic bladder disorder

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Introduction: The earlier assumption of sterile urine has long been proven wrong, but the urobiome in children and adolescents has only been less researched. This is very important in patients with neurogenic bladder dysfunction, e.g. meningomyelocele, as repeated antibiotic administration and intermittent catheterization can lead to a high number of urinary tract infections. The aim of the study is to analyze the urobiome of child and adolescent patients with neurogenic bladder disorder in comparison to healthy children and adolescents. Patients and Methods: Catheter urine has been collected prospectively from 27 patients with neurogenic bladder disorder and from 27 other age- and gender-matched patients without diseases of the urogenital system. The urobiome was analyzed using 16S rRNA gene sequencing. Results: 15 girls and 12 boys per group were included in the study. The mean age of patients in both groups was 11 years (range 0<U+0096>18 years). The evaluation of the microbiome showed a significantly higher alpha diversity (Observed Species, Shannon Index, Inverse Simpson Index and PD Whole Tree) in the group of control patients compared to the patients with neurogenic bladder disorder. The -diversity also showed a significant difference taking into account the gender differences in both groups with a p-value of < 0.001 (PERMANOVA based on Bray-Curtis, Jaccard, UniFrac and weighted UniFrac). While Proteobacteria were very dominant among the phyla in the group of patients with neurogenic bladder disorder, Firmicutes and Bacteroidetes were increasingly detected in the control group. Conclusions: Patients with neurogenic bladder dysfunction show significant changes in the physiological urobiome. Proteobacteria were particularly dominant here as typical bacteria that cause urinary tract infections. However, further studies are needed to analyze the possibility of a positive influence on the urobiome, for example through the use of probiotics.

**Wolfschluckner Vanessa**

Abstract ID: 118078

# Metabolomic Alterations of Volatile Organic Compounds and Bile Acids as Biomarkers of Microbial Shifts in a Murine Model of Short Bowel Syndrome

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Background: The study aimed to comprehensively investigate the intestinal microbiome and metabolome in a murine model of Pediatric Short Bowel Syndrome (SBS), a rare condition characterized by the extensive loss of the small intestine, resulting in the need for parenteral or enteral supplementation to meet nutritional requirements. Method: To achieve this, we conducted a 60% proximal small bowel resection compared to a sham operation in C57BL/6 mice. Four weeks after the surgery, we analyzed the microbial communities in various intestinal segments (jejunum, ileum, colon) and stool through 16S rRNA gene sequencing and assessed bile acids in serum and stool, as well as volatile organic compounds (VOCs) in fecal headspace using LC-MS and GC-MS techniques. Results: The study found that the ?-diversity of the different intestinal segments did not significantly differ between the two groups. However, the ?-diversity showed significant variations between the sham and SBS mice. In the jejunum of SBS animals, there was a significant increase in Faecalibaculum, while the ileum of SBS mice exhibited a significant reduction in Lactobacillus and Sporosarcina. In the colon of SBS mice, there was a significant decrease in Ruminococcaceae and a significant increase in Proteobacteria, including Faecalibaculum and Escherichia-Shigella. Furthermore, the study revealed that serum levels of deoxycholic, taurocholic, and taurochenodeoxycholic acid were significantly higher in the SBS group. Among the 29 VOCs tested, hexane, isoflurane, and pentane were significantly higher in the SBS group, while pyrrole was significantly lower. Conclusion: Overall, the research demonstrated that SBS leads to substantial alterations in the murine intestinal microbiome and metabolome, impacting serum bile acids and fecal volatile organic compounds.

**Connolly Sally**

Abstract ID: 117989

# Transcriptional regulation of Langerhans cell fate and function

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Langerhans cells (LCs) are central to the maintenance of tolerance within the epidermis. LCs are seeded prenatally from embryonic precursors and are replenished throughout life by circulating precursors, such as monocytes. TGF-? family ligands are key in shaping the differentiation trajectory of circulating precursors into LCs. While several master transcriptional regulators involved in LC differentiation have been identified, the complex interplay of these proteins and how initial signals are relayed remain poorly understood. Following a microarray screen, we have identified several transcription factors rapidly induced and repressed during the early stages of LC differentiation. Lentiviral-mediated gain and loss-of-function experiments of these transcription factors reveals their role in LC commitment and differentiation. Moreover, we show that several of these transcription factors are dependent on canonical TGF-?-ALK5 signaling.

**Hodl Isabel**

Abstract ID: 117322

# Altered cellular immune response to vaccination against SARS-CoV-2 in patients with B-cell depleting therapy

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Background: B-cell depleting therapies result in diminished humoral immunity following vaccination against COVID-19, but our understanding on the impact on cellular immune responses is limited. Here, we performed a detailed analysis of cellular immunity following mRNA vaccination in patients receiving B-cell depleting therapy. Methods: We analyzed T-cell responses in autoimmune patients treated with B-cell depleting therapy and healthy controls after receiving their first two mRNA vaccinations against COVID-19. We isolated PBMCs and stimulated them with a peptide pool covering the spike protein in vitro. Reactive T-cells were determined by IFN? ELISpot assay and staining for effector cytokines by flow cytometry. Anti-SARS-CoV-2 spike receptor-binding domain antibody assays were performed to elucidate B-cell responses. To complement our cellular analysis, we performed immunophenotyping for T- and B-cell subsets. Results: In this work, we show that SARS-CoV-2 vaccination using mRNA vaccines elicits cellular T-cell responses in patients under B-cell depleting therapy. Some facets of this immune response, including TNF? production of CD4+ T-cells and GzmB production of CD8+ T-cells, however, are distinctly diminished in these patients. Consequently, it appears that the finely coordinated process of T-cell activation with a uniform involvement of CD4+ and CD8+ T-cells as seen in HCs is disturbed in autoimmune patients. In addition, we observed that immune cell composition does impact cellular immune responses as well as sustainability of anti-spike antibody titers, a fact that also holds true for healthy individuals. Conclusion: Our data suggest disturbed cellular immunity following mRNA vaccination in patients treated with B-cell depleting therapy. Immune cell composition may be an important determinant for vaccination efficacy.

**Ujcic Kaja**

Abstract ID: 119387

# Effects of Placenta-Derived Factors on Maternal Thrombopoiesis

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Background During pregnancy major adaptations of the maternal blood composition take place in order to support the developing fetus and combat immunological and hemostatic challenges. Simplified, pregnancy represents a hypercoagulation state with platelets being important players in its pathophysiology. During gestation platelet count decreases while their activation increases. Moreover, platelets are involved in the pathogenesis of obstetrics disorders such as preeclampsia (PE). The placenta is secreting signalling entities that through maternal circulation reach distant organs and induce adaptations of their function. Literature suggests platelets are reprogrammed by the placenta-derived factors. However, there is a lack of evidence regarding pregnancy-induced alterations of megakaryocytes (MK) and thrombopoiesis. We hypothesize that placenta-derived factors affect maternal thrombopoiesis. Methods/Results MEG-01 cell line is differentiated into MK-like cells. The maturation is confirmed by marker expression, ploidy and changes in the morphology. Primary cord blood-derived CD34+ hematopoietic stem cells (HSCs) are isolated and will be differentiated into MKs in vitro. Pregnancy-specific factors are collected from placental villi explants and blood of different pregnancy cohort groups and introduced to the cellular models. Subsequently, cells undergoing thrombopoiesis in vitro will be examined (number, transcriptome, proteome, morphology, ploidy, platelet production, differentiation/proliferation potential) in order to analyse the effects of placenta-derived factors on thrombopoiesis. Additionally, levels of thrombopoietin (TPO) in blood of non-pregnant vs. pregnant women will be examined. Conclusion Thrombopoiesis can be modelled in vitro using MEG-01 cell line or primary HSCs. Pregnancy-specific factors obtained from blood or placental explants can be introduced into the model. We expect to observe (in vivo-like) cellular alterations upon the treatment.

**Skerjanz Julia**

Abstract ID: 119426

# Revealing TRPC1 as a key player in ER Ca2+ dynamics and potential Ca2+ leak channel

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Background: Transient receptor potential canonical proteins (TRPC1-7) are a group of calcium (Ca2+) permeable cation channels that exhibit a significant presence in the brain. Among the seven isoforms, TRPC1 stands out for its role in hippocampal physiology and pathophysiology via the regulation of cellular Ca2+ homeostasis. A peculiar feature of TRPC1 is its targeting to the ER membrane, where it can potentially physically associate with other proteins (inositol trisphosphate receptor; IP3R) involved in Ca2+ release mechanisms or function as a Ca2+ leak channel on its own. The engagement of TRPC1 in the ER Ca2+ efflux could potentially affect the extent of Ca2+ signaling within the cell, influencing various cellular processes. Aim: Study the role of TRPC1 in ER Ca2+ dynamics. Methods: In this study we conducted confocal microscopy, FRET microscopy (with ER-targeted D1ER) and Ca2+ imaging (with cytosolic R-GECO) in transiently transfected HEK293 and HEK IP3R KO cells. Results: We confirmed TRPC1 channels cellular targeting to the ER membrane via confocal microscopy. FRET experiments showed a significantly lower Ca2+ efflux via IP3R after application of carbachol (CCh) when TRPC1 was present, as opposed to control cells without TRPC1. When introducing various mutations in TRPC1, we observed alterations in the channel's activity with the most prominent changes observed in the D582K mutant. The presence of the D582K mutation restored Ca2+ release levels to match those observed in control cells. Ca2+ imaging measurements validated those findings. Moreover, a TRPC1-R-GECO fusion enabled us to detect local Ca2+ fluctuations in close vicinity to TRPC1. Conclusions: TRPC1 is targeted to the ER and affects ER Ca2+ release mechanisms. This indicates that TRPC1 potentially acts as a Ca2+ leak channel in the ER.

**Baron Jasmin**

Abstract ID: 118843

# Preserving the native lipid environment of TRPC3 using novel nanodisc systems

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TRPC3 is a lipid-sensitive and calcium-permeable ion channel predominantly expressed in excitable cells. It plays a role in diseases such as cardiac hypertrophy and dementia. Recent experiments using photoswitchable activators revealed that TRPC3's calcium selectivity depends on ligands, indicating significant changes in the channel's pore structure. Previous attempts to study TRPC3 with ligands only yielded a closed conformation, failing to provide insights into the structural determinants of calcium selectivity. We hypothesized that the lipid environment around TRPC3 is an important key feature in channel function and that previous purification procedures disrupted the lipid environment resulting in a closed and non-functional TRPC3. The aim of our study is to purify TRPC3 under near-native conditions which will allow us to resolve the structure in the active conformation. To achieve this goal, we used new lipid nanodisc systems, stabilized by a novel small-molecule glycoamphiphile DDDG, which retains the natural environment of the protein. Results: We successfully extracted and purified TRPC3 using DDDG nanodiscs, with extraction efficiency, yield, and purity comparable to the gold standard detergent DDM. Negative stain electron microscopy confirmed the integrity of the nanodiscs and the preservation of TRPC3's lipid environment.

**Stursa Lea**

Abstract ID: 114035

# Accuracy of palatal orthodontic mini-implants placed using fully digital planned insertion guides: A cadaver study

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Digital workflows have become integral in orthodontic diagnosis and therapy, reducing risk factors and chair time with one-visit protocols. Development in imaging procedures, especially widespread of cone beam computed tomography (CBCT), enabled a better preoperative planning of surgical procedures and by using a certain orthodontic software, insertion templates for orthodontic mini-implants (OMIs) and digitally created orthodontic appliances can be CAD/CAM (computer-aided design and computer-aided manufacturing) fabricated without any analogue in-between-steps. This study assessed the transfer accuracy of fully digital planned insertion guides for OMIs compared with freehanded insertion. Cone-beam computed tomography (CBCT) datasets and intraoral surface scans of 32 cadaver maxillae were used to place 64 miniscrews in the anterior palate. Three groups were formed, two using printed insertion guides (A and B) and one with freehand insertion (C). Postoperative CBCT datasets were superimposed with the planning model, and accuracy measurements were performed using orthodontic software. Statistical differences were found for transverse angular deviations (4.81<U+00B0> in A vs. 12.66<U+00B0> in B and 5.02<U+00B0> in C, p = 0.003) and sagittal angular deviations (2.26<U+00B0> in A vs. 2.20<U+00B0> in B and 5.34<U+00B0> in C, p = 0.007). However, accurate insertion depth was not achieved in either guide group; group A insertion was too shallow (?0.17 mm), whereas group B insertion was deeper (+0.65 mm) than planned. Outsourcing the planning and fabrication of computer-aided design and computer-aided manufacturing insertion guides proved beneficial for certain indications, with commercial templates showing superior accuracy compared with in-house<U+0096>fabricated insertion guides.

**Sand Tamara Sophia**

Abstract ID: 119455

# SPACE-, QISS- and 4D-Flow-MRA at 3T in Comparison to CE-MRA for Evaluation and Quantification of the Thoracic Aorta after Therapy <U+0096> a Pilot Study

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Purpose: After treatment of thoracic aortic diseases, a CE-MRA is one of the diagnostic standard methods for further follow up and treatment decisions. The purpose of the study was to compare the image quality and diagnostic accuracy of the flow related MRA-sequences: SPACE-, QISS- and 4D-Flow-MRA, with the CE-MRA. Methods: 7 patients (57<U+00B1>19y, 2 men) were selected for the prospective study. The examination was done with SPACE-, QISS- and 4D-Flow-MRA in addition to the CE-MRA. The 4D-Flow-MRA was analysed with the software cvi42. Results: None of these flow related MRA-sequences can replace the CE-MRA-sequences in total. If there is no contraindication of contrast agent application, the CE-MRA is the first MRA-sequence that should be aquired. When a short-term follow-up is indicated, especially the 4D-Flow-MRA could add useful information about the hemodynamic. The QISS-sequence had unacceptable inhomogeneities and signal loss. The acquisition time was uncomfortable for our patient cohort as well. In general the results of the SPACE-MRA were better than these of the QISS-MRA, although the diameter measurement was more precise in the QISS-MRA, but only if there was no signal loss in the segment. The evaluation of a mural thrombus was more reliable with SPACE-MRA than with QISS-MRA. The main problem of the SPACE-MRA is, that it is not a 3D-sequence. There is a quality loss in the MPR and 3D reconstruction (reduced reliability of diameter measurement). 4D-flow offers information about intravascular flow, pressure, wall shear stress and energy loss. Discussion: CE-MRA should be the sequence of first choice. The SPACE-MRA seems to be the first sequence to choose, if the use of contrast agent is not possible. The QISS-MRA is not recommended for these cases. The 4D-Flow shows promising results regarding hemodynamic parameters without invasive diagnostic tools and should be added to routine screening and follow up protocols to get more data for decision making.

**Habersack Andreas**

Abstract ID: 118490

# A 3D ultrasound approach to assess muscle-tendon lengthening behavior in vivo during walking <U+0096> a reliability study

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Background Gaining information about adaptations in gastrocnemius medialis (GM) muscle and Achilles tendon lengthening behavior in response to treatments is important to develop efficient therapies. Various ultrasound (US) approaches have been developed to measure these tissue lengths in static conditions. However, measuring muscle belly and tendon length changes during walking seems to be of clinical importance and is nowadays usually only estimated using musculoskeletal models. Moreover, literature investigating the lengthening of muscle-tendon unit while walking is scarce and there are drawbacks to be considered. Therefore, we developed an US approach, that can be used to directly assess the GM muscle-tendon-unit (MTU), muscle belly and tendon lengthening behavior in three-dimensional (3D) space during overground walking. The aim of this study was to evaluate the reliability of this approach. Methods Altogether 10 participants were included in the study. To evaluate the intra- & inter-day reliability of the approach, two US measurement sessions were performed on two different days. By combining 2D US, 3D motion capture, and vector algebra, the tissues<U+0092> lengths were assessed throughout gait cycles. The Intra- and inter-day reliability of the examiner was determined using coefficients of variation (CoV), standard errors of measurement (SEM), minimal detectable changes (MDC95), and intraclass correlation coefficients (ICC). Results The approach showed excellent intra- as well as inter-day reliability with small SEM (?0.73 mm) and CoV (?1.9 %), MDC (?2.1 mm), and excellent ICC (?0.95). Conclusion The proposed 3D US approach can be used reliably by one rater to assess the GM MTU, muscle belly, and Achilles tendon lengthening behavior during overground walking. Therefore, this study supports its potential as useful tool for investigations of the effects of training interventions or therapeutical treatments on GM muscle and Achilles lengthening behavior in the future.

**Loh Satinee Xuying**

Abstract ID: 118813

# Immobilisation of enhanced PETase onto Iron Oxide Nanoparticles for Microplastics Capture

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Background Microplastics are widespread pollutants that pose health risks to all organisms. Thus, urgent action is needed to remove them. Recent research focuses on biological plastic degradation, particularly PETase from I. sakaiensis. While improved variants exist, none are yet suitable for industrial use. Our aim is to immobilise PETase on magnetic iron oxide nanoparticles (IONPs) to capture microplastics from wastewater <U+0096> an approach often overlooked in favour of better biodegradation. This prevents their release into the environment and enables various methods of treatment, including chemical and biological degradation. It ensures that the products of degradation, some of which are toxic, are contained and can be used for re-synthesis of polyethylene terephthalate (PET).

Method Our goal is to enhance PETase binding affinity to PET with computational guidance. Molecular dynamics simulations of PETase-PET will assess binding energies for different mutations. The best mutant will be transformed and then expressed in E. coli, with the enzyme then being immobilised onto IONPs. Protein expression will be optimised for high enzyme yield, with different growth media, incubation time and lysis conditions being tested. Enzyme concentration will be verified using BCA assay and UV/vis spectroscopy. Enzyme activity will be checked by p-nitrophenyl acetate assay with UV/vis spectroscopy at 405nm. Immobilisation conditions will also be optimised for microplastics separation effectiveness. This will be evaluated by taking absorbance measurements of the reaction mixture, with UV/vis spectroscopy. The enzyme-nanoparticle complex (ENC) will be mixed into the reaction mixture with PET microplastics. After a fixed duration, the ENCs are retrieved with a magnet, and the supernatant collected for calculation of remaining PET concentration. ENCs will be characterised using IR spectroscopy, SEM and DLS. Finally, all processes will be scaled up for use in wastewater treatment plants.

**Mandl Spela**

Abstract ID: 121110

# Open questions on the maturation and quaternary structure of the human lysosomal ?-mannosidaseHUMAN LYSOSOMAL ? -MANNOSIDASE

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Human lysosomal ?-mannosidase (hLAMAN, EC 3.2.1.24) is a part of the GH38 zinc-dependent aspartic glycosidase gydrolases. It catalyzes the cleavage of ?-1,2, ?-1,3, and ?-1,6 mannosidic linkages in N-linked glycoprotein degradation. Mutations causing a total or partial loss of hLAMAN enzyme activity lead to autosomal recessive disease alpha-mannosidosis (MANSA), a lysosomal storage disorder, characterized by a spectrum of symptoms ranging from mild skeletal abnormalities and myopathy to severe prenatal loss. Current treatments like bone marrow transplantation (BMT) and enzyme replacement therapy (ERT) are limited and can lead to serious complications, highlighting the need for novel therapeutic approaches.

hLAMAN is synthesized as a single-chain precursor undergoing proteolytic cleavage into three major peptides during the transport to lysosomes. The enzyme is cleaved into three peptides: 70 kDa (ABC peptide), 42 kDa (D), and 13/15 kDa (E). The 70 kDa peptide is subsequently cleaved into three additional peptides labeled A, B, and C, which are connected by disulfide bonds. The underlying mechanisms governing the proteolytic cleavage of the enzyme remain elusive, particularly given that the enzymatic activity is retained in the precursor form.

The goal of this work is to elucidate the quaternary structure of hLAMAN, involving the expression of wild-type and defective variants in P. pastoris , followed by purification and enzymatic activity assessment. SDS-PAGE and western blot analyses of the expressed protein revealed bands at 70 kDa, 45 kDa, and 35 kDa, corresponding to different peptides. Furthermore, we would like to explore the link between reported missense mutations and enzyme maturation, paving the way for understanding MANSA at a molecular level.

**Suppan Ena**

Abstract ID: 119276

# Fetal hemoglobin and cerebral tissue oxygenation during immediate postnatal transition

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Introduction: Concentration of fetal hemoglobin (HbFc) in human neonates determines oxygen carrying capacity of blood and the position of oxyhemoglobin dissociation curve. Near-infrared spectroscopy enables the measurement of regional cerebral tissue oxygen saturation (rScO2) and in combination with measurements of pulsatile arterial oxygen saturation (SpO2), the calculation of cerebral fractional tissue oxygen extraction (cFTOE). Methods: We aimed to investigate the impact of HbFc on rScO2, cFTOE and SpO2 in neonates during the first 15 minutes after birth. Patients were stratified in two groups based on their gestational age (preterm and term). Blood analyses provided total blood hemoglobin (Hb) and HbFc measurements. Correlations between HbFc, Hb and rScO2, cFTOE and SpO2 in each minute were analyzed. Results: Ninety term and 19 preterm neonates without medical support were included. HbFc was significantly higher in preterm neonates, whereas there were no significant differences in Hb between the groups. In preterm neonates, we found positive correlations of both HbFc and Hb with rScO2 and negative correlations of HbFc and Hb with cFTOE in the first minutes after birth. In contrast, there were no significant correlations between the same parameters in term neonates. Correlations between HbFc or Hb and SpO2 were either insignificant, negligible or very low in both preterm and term neonates. Discussion/Conclusion: In preterm neonates higher HbFc were associated with higher rScO2 and lower cFTOE in the first minutes after birth. This phenomenon could not be confirmed in term neonates and might reflect an immature autoregulation of oxygen delivery to the brain or lower oxygen consumption in preterm neonates in the first minutes of immediate postnatal transition.

**Rath Anna Maria**

Abstract ID: 119217

# The effects of maternal milk feeding styles during early infancy on infants<U+0092> anthropometric parameters including body composition: a longitudinal cohort study

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Background Obesity is a global health problem whose multifaceted nature is more and more understood by the concept of metabolic programming, particularly during early life. Infant feeding practices play a significant role, with responsive feeding supporting self-regulation, while concerns about infant weight often lead to controlling feeding styles. Our study aim is to investigate the effect of maternal feeding styles on infant body composition in this critical early phase.

Methods The Investigation on the effect of maternal feeding styles on infant body composition during the exclusive milk feeding period was part of the “Health perception Lab” at the FH Joanneum University of applied sciences Graz. A prospective longitudinal cohort study was conducted from 2013 - 2015. Data was collected from 54 healthy mother infant dyades from 24 weeks of gestation up to 16 weeks postpartum and during 3 Follow ups time points (1 year/ 3 years/ 6 years). Maternal feeding styles were measured using the Infant milk feeding questionnaire (IMFQ) and infants body composition was analyzed using a PEA POD, an Air Displacement Plethysmography (ADP) system.

Results In the healthy, well educated, mostly breastfeeding cohort it could be shown that the feeding styles are loading low in all dimensions and were relatively stable over time in the first 16 weeks p.p.. “Concern for weight” was significantly associated with all other factors (“monitor feeding”, “feeding routine”, “encourage feeding”, “limiting intake”) at the time point 14-16 weeks p.p.. In regards to body composition the Fat free mass Index was associated with “concern for weight” (p=,027) and “limiting intake” (p=,020) and the Fat mass Index was negativ associated with “encourage feeding” (p=,027) at 14-16 weeks p.p..

Conclusion As early as 14-16 weeks p.p in the exclusive milk feeding period associations between maternal feeding styles and infant body composition can be seen in a healthy mostly breastfeeding cohort.

**Brunner Elke**

Abstract ID: 119163

# Benign vocal fold lesions: sex, age, and critical reflection. A retrospective observational study in a treatment seeking population.

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Benign vocal fold (VF) lesions are structural alterations within the mucous membrane of the VFs. They primarily result from mechanical stress and trauma to the VFs due to vocal misuse and lead to hoarseness and limited voice capacity. The lesions have a high clinical prevalence, but epidemiological studies focusing on them are rare. The purpose of this investigation was to provide current European data on five typical lesion types (VF nodules, polyp, cyst, contact granuloma, Reinke<U+00B4>s edema).

A retrospective study was performed in an Austrian voice center. Data were collected from all patients diagnosed with one of the aforementioned VF lesions over a 13-year period. Video recordings of the initial laryngoscopies were subjected to a blinded review process with regard to the diagnosis. The included patients were classified according to sex, age, lesion type and the side affected, and the data were analyzed statistically.

In a total of 535 patients, VF polyps were found most frequently, followed by Reinke<U+00B4>s edema and nodules. Each of the lesion types was significantly related to sex. Female sex was associated with VF nodules, cysts and Reinke<U+00B4>s edema, whereas male sex was a risk factor for VF polyps and contact granulomas. Except VF cysts, each of the diagnoses was also significantly related to age. VF nodules were predominantly found in young patients, VF polyps in middle aged, Reinke<U+00B4>s edema and contact granulomas in later adulthood. Females and males differed in terms of the side predominantly affected (bilateral, right or left VF).

The lack of a universally accepted classification framework limited the comparability of the results with previous studies. Prophylactic voice care education is required for all populations. A non-binary view of benign VF lesions would open new perspectives for phoniatric research.

**Embacher Stefan**

Abstract ID: 118898

# Within-host mathematical models for antibody kinetics to improve infectious disease study design

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Background/Aims Immunity against infectious diseases is strongly driven by antibodies. The evaluation of interventions reducing the burden of infection, such as vaccination, need to be evaluated through clinical studies. Being able to describe antibody kinetics, the change in antibody concentration over time, is crucial in optimizing the design of immunization trials. This includes determining the sample size and sampling times to accurately describe the underlying kinetics. In our research we try to answer the question of when and how often to measure antibodies. Methods We conducted a systematic review, with the main objective of identifying studies that use mathematical or statistical models to describe antibody kinetics and in which context they have been used in study design. The sampling frequency depends on the number of parameters in the model, while approaches to determine the optimal sampling schedule utilize characteristics of the Fischer information matrix. One of the most commonly used criteria, D-optimality, finds the sampling schedule, which maximizes the determinant of the Fischer information matrix. Results Despite the relatively high number of included publications (270), none considered models for study design. A range of models are employed to account for the longitudinal structure of the data. These models include fundamental statistical approaches and more sophisticated statistical techniques like nonlinear mixed effects models. Mathematical models are also frequently used, mostly in the form of deterministic within-host compartmental models. Using an implemented model, we found that frequency and timing of sampling influence the estimates and the variability of the underlying parameters. Conclusion The limited use of mathematical models regarding study design, highlights the need and importance of basic research. Through our work, we aim to provide a framework, which can be actively used in practice to improve infectious disease study design.

**Oeffl Nathalie**

Abstract ID: 118626

# Standard values of subcostal aortic and pulmonary artery velocity time integrals in infants

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Background: Subcostal views are an easily accessible option to investigate the heart, especially in neonates and infants where cardiac structures are in proximity to the ultrasound probe as well in emergency assessment of critically ill patients. They are further useful under special conditions such as pneumothorax where echo imaging is limited to subcostal views only. Normative values of subcostal view measurements remain scarce. To quickly identify hemodynamic impairment and to support clinical decision making, the aortic and pulmonary velocity time integrals (VTI) are well established transthoracic echocardiographic parameters to estimate left and right heart function. We aim to establish normative values of subcostal aortic and pulmonary VTI in a pediatric age group. We herein report preliminary study results. Methods: The target population are neonates and infants composed of a healthy study group and a validation study group of children suffering from cardiac shunt lesions, pulmonary hypertension or low cardiac output. Echocardiography is performed following a detailed study protocol for subcostal views and collected data is compared to existing normative parameters of parasternal views. Results: In this ongoing study we have included 300 pediatric patients to date. Our preliminary data clearly shows that subcostal aortic VTI and pulmonary VTI values are in good correlation with already existing parasternal VTI normative values. Conclusion: In this study we confirm that using subcostal views during echocardiography provide a good imaging quality and are easily accessible. By establishing VTI normative values for this vulnerable population, the practical approach to investigate cardiac function from subcostal view will gain increasing clinical value.

**Me<e7>ani Renald**

Abstract ID: 117466

# Pilots with Type 1 diabetes mellitus flying commercial airplanes: A brief review of the evidence and future considerations for diabetes technology in aviation medicine

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BACKGROUND: Several countries allow pilots with insulin-treated diabetes mellitus to operate commercial flights. However, new diabetes management technologies necessitate discussions on their effectiveness and safety in-flight conditions.

RESULTS: Continuous subcutaneous insulin infusion (CSII) from the late 1970s has been found to improve glycemic control and decrease hypoglycemic episodes. CSII is now widely supported for patients as young as one year of age. CSII aims to mimic natural insulin secretion patterns, leading to equal or superior glycemic control compared to multiple daily injections. CSII reduces hypoglycemia, and sensor-augmented pumps can suspend insulin delivery when hypoglycemia is imminent. Austria, the UK, and Ireland allow insulin-treated pilots to fly under the ARA.MED.330 protocol which necessitates strict and frequent capillary blood glucose monitoring. Diabetes technology is not yet approved for use in the cockpit. Recently, a 2023 study from Garden et. al showed continuous glucose monitoring (CGM) as a valid alternative to self-monitored blood glucose for pilots. On the other hand, there is evidence that cabin pressure changes can cause insulin pumps to release excess insulin. This phenomenon is attributed more to the fluid-gas physics and the bubbles of nitrogen and oxygen physically dissolved in the insulin solution than to any minor dysfunction of the pump. There is also the issue that current CGM devices are not approved for use above 5,500 meters in altitude. These systems may not function properly in situations with low air pressure, sudden decompression, or other extreme flight scenarios.

CONCLUSION: AID systems' efficiency in real flight conditions remains unassessed. Studies are needed to evaluate them under varied physiological conditions, including cabin pressure changes and their effect on insulin delivery and blood glucose levels. The results could impact licensing protocols for pilots using diabetes technology.

**Eichinger Michael**

Abstract ID: 115792

# Effect of Pre-operative Intravenous Crystalloids on Post-Induction Blood Pressure <U+0096> Methods abstract

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Background and Aims: Hypotension during surgery directly impacts patients' postoperative outcomes and complications. A decrease in blood pressure measurements secondary to anaesthetic drugs is an expected scenario in most surgical cases. Moreover, hypovolemia secondary to fasting in the pre-operative period may facilitate post-induction hypotension, which can be compensated by fluid bolus pre-operatively. We aim to conduct a randomized intervention cohort study using pre-operative fluid therapy to assess its effect on blood pressure during the post-induction period.

Methods We conduct a randomized intervention cohort study using pre-operative fluid therapy to assess its effect on blood pressure post-induction. The intervention group will receive a balanced crystalloid solution bolus within 60 (+/-15) minutes before induction of anaesthesia. The control group will be treated according to the current clinical standard of care. We will compare the time-weighted average (TWA) mean arterial pressure (MAP) under 65 mmHg during the first 20 minutes after anaesthetic induction or until surgical incision (whichever comes first).

Results and Discussion Post-induction hypotension mainly depends on age, pre-existing arterial hypertension, and diabetes mellitus. One simple but potential intervention to attenuate blood pressure drops might be the administration of a pre-operative fluid bolus. Since there is no consensus on using pre-operative fluid treatment to prevent post-induction hypotension, we conduct this study to answer this question. We expect an advantage of the intervention group regarding the primary endpoint compared to the control group.

Conclusion This appropriately powered study will answer the utility of a pre-operative fluid bolus administration, which might improve perioperative outcomes through a simple intervention.

**Schweiger Leyla**

Abstract ID: 115579

# Relevance of cardiac biomarkers in patients with peripheral arterial disease (PAD)

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Title: Cardiac Biomarkers' Relevance in Peripheral Arterial Disease (PAD) Patients Author: Dr. Leyla Schweiger Affiliation: Division of Angiology, Department of Internal Medicine, Medical University of Graz, Austria Objective: Critical limb ischemia (CLI), characterized by ischemic rest pain with or without tissue loss or infection, represents an advanced stage of lower extremity artery disease (LEAD) associated with high mortality and morbidity rates. Early diagnosis and aggressive treatment are essential to prevent complications. This study explores the potential of cardiac biomarkers, such as Pro-BNP and Troponin T, extensively studied in cardiovascular contexts, to aid in risk stratification for CLI patients. Methods and Results: This retrospective cross-sectional study, conducted at the Medical University of Graz, obtained approval from the International Review Board. Patient data were collected retrospectively without requiring patient consent. The study included all patients admitted to our outpatient clinic for peripheral artery disease (PAD) from 2000 to 2020, totaling 1782 patients, without any exclusion criteria. Patients were categorized into CLI and non-CLI groups following established guidelines. Current statistical analysis aims to identify elevated cardiac biomarkers and assess whether the N-terminal Pro-BNP to Troponin I ratio is increased in CLI patients. This investigation seeks to determine the potential of these markers for identifying high-risk CLI patients in the future. Conclusion: Timely identification of PAD patients at risk of progressing to CLI and requiring amputation is imperative. With suitable risk stratification tools, even with limited resources, we can expedite optimal therapy for high-risk patients, ultimately improving their outcomes. Authors' disclosures: No conflicts of interest to report.

**Schreiber Nikolaus**

Abstract ID: 114999

# Biomarkers of alcohol abuse potentially predict delirium, delirium duration and mortality in critically ill patients

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Objective: Carbohydrate-deficient transferrin (CDT) and the ?-glutamyltransferase-CDT derived Anttila-Index are established biomarkers for sustained heavy alcohol consumption. We hypothesized that these parameters may have a potential role to predict delirium and mortality in critically ill patients.

Design: Prospective observational study

Patients: 343 consecutive patients admitted to our medical intensive care unit (ICU) between February and November 2022

Measurements and Main Results: During ICU stay 35% of patients (n=121) developed delirium. CDT levels and Anttila-Index were significantly higher in critically ill patients with ICU-delirium compared to patients without delirium (p=0.011, p=0.001 respectively). CDT above 1.7% (aOR 2.06, 95% CI 1.10 - 3.84, p=0.023), CDT per percent increase (aOR 1.26, 95% CI 1.03 - 1.60, p=0.036, AUROC 0.75), and Anttila-Index per unit increase (aOR 1.28, 95% CI 1.04 - 1.60, p=0.023, AUROC 0.74) remained significant predictors for delirium development in Sequential Organ Failure (SOFA)-score, mechanical ventilation, age, and albumin adjusted regression models. Anttila-Index (aOR 1.70, 95% CI 1.21-2.51, p=0.004) and CDT were also found to be predictive of delirium duration of more than 5 days (aOR 1.34, 95% CI 1.04-1.84, p=0.042). Most importantly, Anttila-Index above 4 (aHR 2.20, 95% CI 1.21 - 4.00, p=0.010), Anttila-Index per unit increase (aHR 1.36, 95% CI 1.05 - 1.74, p=0.018) and CDT per percent increase (aHR 1.19, 95% CI1.01 - 1.40, p=0.034) were independent predictors of hospital mortality in adjusted Cox-proportional-hazard-models.

Conclusion: Higher levels of CDT and particularly the derived Anttila-Index are not only specific biomarkers for sustained heavy alcohol consumption, but are also associated with development of delirium, longer delirium duration, and higher mortality in critically ill patients.

**Wolfgruber Stella**

Abstract ID: 112439

# Antiviral Activity of Zinc Oxide Nanoparticles against SARS-CoV-2

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Background/Aims The highly contagious virus SARS-CoV-2 primarily spreads through respiratory droplets, aerosols, and contaminated surfaces. In addition to antiviral drugs, effective decontamination of surfaces and personal protective equipment (PPE) is essential to mitigate the spread of infection. Conventional approaches including ultraviolet radiation, vaporized hydrogen peroxide, heat and liquid chemicals possibly damage materials or lack comprehensive disinfection capabilities. Consequently, alternative material-compatible and sustainable methods, such as nanomaterial coatings, are needed. This study aimed to investigate the antiviral activity of two novel zinc-oxide nanoparticles (ZnO-NP), ZnO-NP-45 and ZnO-NP-76, against SARS-CoV-2 using cell culture-based virus neutralization assays.

Methods and Results The nanoparticles were synthesized using an environmentally friendly, highly efficient method. To characterize the ZnO-NPs, their hydrodynamic sizes and zeta potentials were evaluated using dynamic light scattering (DLS). Primary particle sizes and elemental composition were further determined by scanning transmission electron microscopy (STEM) and energy-dispersive X-ray spectroscopy (EDX). Their antiviral activity was evaluated by pre-treating SARS-CoV-2 particles in suspension with increasing ZnO-concentrations and subsequent infection of Calu-3 cells. Inactivation of the two SARS-CoV-2 variants Delta and Omicron by a factor of more than 106 was shown after treatment with ZnO-NP-45, which was more active than ZnO-NP-76.

Conclusion The findings of this study clearly demonstrate a high antiviral activity of ZnO-NP against SARS-CoV-2, which is based on adsorption and an additional not yet defined antiviral effect. The outcomes of this research may form the basis for the development of an antiviral coating for PPE and filters to improve protection and reduce the transmission of pathogens such as SARS-CoV-2.

**Kolland Michael**

Abstract ID: 112230

# Cardiac troponin kinetics in haemodialysis patients are heavily dependent on haemodialysis modality <U+0096> a randomized cross-over trial

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Background During hemodialysis (HD), diagnosis of acute myocardial infarction (AMI) is challenging, since HD patients less often present with typical symptoms or EKG changes, thus, the diagnosis heavily relies on cardiac troponins (cTn). However, the effect of HD modalities on cTn kinetics during HD is not well described. We aimed to determine intradialytic cTn kinetics in different dialysis modalities in HD patients. Methods In this randomized controlled crossover trial, asymptomatic, clinically stable patients were randomized to a sequence of low-flux HD, high-flux HD, hemodiafiltration (HDF), and medium cut-off (MCO)-HD, which are all routine treatment approaches. Blood was drawn predialytic, after 1 hour, and immediately after HD. The primary outcome was the relative change of high sensitivity cTn from baseline to after 1 hour of HD treatment for different dialysis modalities. Secondary outcomes included absolute and relative changes of cTn after 1 hour and after treatment. Results Nineteen patients (47.4% female) with a mean age of 65.5<U+00B1>13.4 years and a median of 19 months (min.3, max.165) on dialysis were included. Relative changes of cTnT after 1h were greater with MCO-HD (LSM -21.9 decrease; 95% CI -27.3 <U+0096> -16.6%) than with low-flux (LSM +2.2 increase; 95% CI -3.2 <U+0096> 7.5%, p<0.001), high-flux (LSM -6.8 decrease; 95% CI -12.2 <U+0096> -1.5%, p<0.001) and HDF (LSM -21.2 decrease; 95% CI -26.6 <U+0096> -15.7%, p=0.81) (p-values referring to difference to MCO-HD). LSM for absolute changes with MCO-HD were -21.2 (95% CI -27.6 <U+0096> -14.8 pg/mL), -6.4 (95% CI -12.8 <U+0096> -0.0 pg/mL) for high-flux, -20.2 (95% CI -26.8 <U+0096> -13.7 pg/mL) for HDF and +2.3 (95% CI -4.1 <U+0096> 8.6 pg/mL) for low flux HD after one hour. There were no significant effects observed for cTnI. Conclusions Depending on HD modality, ?cTnT in stable HD patients, without any clinical evidence of myocardial ischemia, significantly exceeds guideline-recommended diagnostic thresholds.

**Andorfer Andrea**

Abstract ID: 119294

# The role of Mindful Self-Compassion in psychiatric rehabilitation

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Background and aims: The importance of mindful self-compassion (MSC) for physical and mental health has been confirmed in numerous studies. However, there are still few studies that address the effectiveness of MSC in clinical psychiatric patients. Method: In order to improve understanding of the underlying principles of the effectiveness of an adapted 6-week MSC training program in a psychiatric rehabilitation facility, this paper analyzes two clinical trials (Study 1: n=200; Study 2: n=170). In both studies, the Self-Compassion Scale (SCS), the Short-Form Health Survey 12 (SF-12), and the Brief Symptom Inventory (BSI-18) were completed by all participants at the beginning and end of therapy. Both studies included MSC as the intervention method and progressive muscle relaxation (PMR) as treatment as usual. Each intervention took place weekly for 75 minutes per group. Results: Linear mixed models show that exercise frequency matters most. In Study 1, exercise frequency moderated symptom decline, particularly in the MSC intervention group. In addition, we observed improvements in five of six SCS subscales in the MSC group compared to the PMR group. In addition, MSC was found to be more beneficial in terms of psychiatric symptom reduction among individuals with lower levels of education in Study 2. Conclusion: Both interventions (MSC and PMR) have the potential to improve people's psychological well-being. Further research is needed to better understand the relationship to potential influencing factors and to allow for individualized indication.

## Talk Session III

### Waked Pamela

Abstract ID: 119450

# The role of sex hormones in Systemic Sclerosis

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Background: Systemic sclerosis (SSc) is a rare chronic autoimmune disease that primarily affects connective tissues, leading to fibrosis and vascular abnormalities in multiple organs. Notably, SSc exhibits a higher prevalence in females, with a female to male ratio exceeding 3:1, however affected males often present a more severe phenotype. This gender-based difference in disease manifestation suggests the potential influence of sex-related factors in SSc development. Despite this, limited studies have explored sexual dimorphism at a hormonal level. Therefore, our aim is to investigate this gender disparity in disease manifestation and identify the role of sex hormones in SSc.

Method and results: Utilizing the Fra-2 transgenic mouse model, an established model for SSc studies, we conducted a comprehensive investigation into the influence of sex on disease phenotype. A comparative analysis between male and female Fra-2 mice revealed a more severe phenotype in females compared to males. To explore the role of sex hormones in disease manifestation, we conducted castration experiments. Surprisingly, ovariectomy did not exacerbate the disease in females, while orchiectomy worsened the phenotype in males. Further experimentation involved testosterone replacement in castrated mice, resulting in a notable amelioration of the phenotype in males. This improvement was evidenced by enhanced lung function, reduced fibrosis, and a more favorable vascular phenotype in the lungs. Intriguingly, testosterone replacement exhibited no significant phenotypic improvement in females.

Conclusion: These findings suggest a potential association between testosterone levels and disease severity in male Fra-2 mice, highlighting the importance of sex hormones in SSc pathology. It also paves the way for further investigations into hormonal levels in SSc patients and potentially hormonal therapies in these patients, with the ultimate goal of improving the outcome of the disease.

**Syarif Ayu Hutami**

Abstract ID: 119448

# Deciphering Compartmentalized Immune Responses in Chronic Obstructive Pulmonary Disease (COPD)

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Introduction: Chronic obstructive pulmonary disease (COPD) is characterized by chronic inflammation and remodeling in various lung compartments, including the airways, parenchyma, and pulmonary arteries . However, the extent to which the inflammatory profiles are distinct across these compartments remains unknown. Therefore, our aim is to investigate the different immune profiles in different lung compartments in COPD.

Methods: Multi-color flow cytometry was performed on freshly isolated airways, parenchyma, and pulmonary arteries samples obtained from end-stage COPD patients (n = 15) and control lungs (n = 5). Independently, spatial transcriptomics was conducted on fresh frozen lung sections from end-stage COPD patients (n = 5) and healthy donors (n=3).

Results: Flow cytometry analysis revealed distinct immune compositions in COPD compared to controls, with increased CD4+ T cells and CD19+ B cells across all compartments. These populations drove the separation between COPD patients and controls in Principal Component Analysis (PCA), particularly in the parenchyma and pulmonary artery. Spatial transcriptomics analysis identified that COPD lungs were characterised by enriched biological processes including inflammatory responses associated with TNF-?, IL-1, and IFN-?, shared across lung compartments. Remarkably, compartment-specific pathways were identified: extracellular matrix organization in the airways, intrinsic apoptotic signaling pathways in the parenchyma, and a response to hypoxia in the pulmonary artery.

Conclusions: This multi-level analysis is the first to elucidate distinct immune compositions in different lung compartments in COPD. It identifies immune populations distinguishing COPD from controls and reveals globally upregulated inflammatory responses shared across lung compartments. The findings provide insights into compartmentalized immune responses and global inflammatory patterns in COPD.

**Pahernik Svetlana**

Abstract ID: 119363

# Phenotypic changes of eosinophil granulocytes in aging

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Introduction: During aging, the functionality of the immune system progressively declines as it gradually deteriorates in a process termed immunosenescence. This leads to chronic inflammation, increased susceptibility to infections, and heightened risks of cancer and autoimmunity - factors notably contributing to the morbidity and mortality of the older population. While adaptive immune changes have been extensively studied, the role of the innate immune system, particularly eosinophils, in immunosenescence remains largely unexplored.

Objective: This study aims to investigate the hypothesis of a functionally compromised, proinflammatory, and metabolically impaired eosinophil phenotype in older individuals and explore dysregulated cellular pathways that may be pharmacologically targeted.

Methods: Circulating eosinophils were isolated from donors of three different age groups (<25 years, 35-45 years, >55 years). High-quality RNA was successfully obtained from 30 donors (RIN >8) and sent to RNA sequencing. The raw sequencing reads have been processed and analysed by us to uncover potential molecules of interest. Subsequently their expression in eosinophils was confirmed by qPCR.

Results: Preliminary analysis suggests a potential role of NAAA, FIGN and FOLR3 in aged eosinophils. Furthermore, we observed that the gene expression pattern of eosinophils seems to be influenced by sex.

Conclusion: This ongoing research aims to uncover the molecular mechanisms underlying the potentially compromised functionality of aged eosinophils. The findings may shed light on the contribution of eosinophils to age-associated disorders. Specifically, we further plan to investigate the role of NAAA in promoting inflammatory responses and explore its pharmacological modulation in the context of eosinophil aging.

## Talk Session IV

### Demjaha Rina

Abstract ID: 119246

# Serum NfL levels and cognitive performance in persons with multiple sclerosis

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Introduction: Serum neurofilament light (sNfL) is a robust biomarker to indicate neuro-axonal damage in various neurologic conditions including multiple sclerosis (MS). Cognitive impairment (CI) is a frequent feature in MS with a huge impact on quality of life and social functioning. It is still not clear if sNfL correlates with or even predicts CI in MS. This study aims to elucidate the association between sNfL and CI in persons with MS (pwMS).

Methods: 186 pwMS (112 female; mean age=39.6<U+00B1>10.4; mean disease duration=10.6 years; median EDSS=1.5 (IQR=2.75)) and 49 healthy controls (HC) (35 females; mean age=33.4<U+00B1>10.7) underwent clinical examination, neuropsychological (Brief Cognitive Assessment for MS-BICAMS) and 3T brain-MRI assessment, including T2-hyperintense lesion load and normalized brain volumes calculations. sNfL was quantified by single molecule array (Simoa SR-X). We calculated sNfL Z-scores corrected for age and body-mass-index; Symbol Digit Modalities Test (SDMT) Z-scores corrected for age and education; Verbal Learning Memory Test (VLMT) and Brief Visuospatial Memory Test (BVMT) T-scores corrected for age.

Results: In this cross-sectional analysis, 48 pwMS showed CI in at least one BICAMS test and 38 in SDMT (M=-0.2<U+00B1>1.1); 6 in VLMT (M=56.2<U+00B1>9.5) and 20 in BVMT (M=54.3<U+00B1>12.7) in comparison to no CI in HC (p<0.001). Baseline sNfL Z-scores (M=0.73<U+00B1>1.27) were unrelated to BICAMS sub-tests, including the SDMT, VLMT and BVMT (all p>0.05, n.s.) both in pwMS and HC.

Conclusion: In this cross-sectional analysis, sNfL was unrelated to CI in pwMS. Longitudinal analyses investigating the relation of sNfL dynamics and MRI metrics with cognitive decline are currently ongoing.

**Leber Stefan**

Abstract ID: 117750

# Aneurysm Wall Enhancement of Coiled Intracranial Aneurysms is Associated with Aneurysm Recanalization

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Background/Aims Wall enhancement of untreated intracranial aneurysms on MRI is suspected to predict aneurysm instability. Wall enhancement or enhancement of the aneurysm cavity in coiled intracranial aneurysms are discussed controversially in the literature regarding potential healing mechanisms or adverse inflammatory reactions. Our aim was to compare occurrence of aneurysm wall enhancement and cavity enhancement between completely occluded intracranial aneurysms and recanalized aneurysms after initially complete coil embolization.

Methods In this single centre cross-sectional study, we evaluated intracranial aneurysms after successful coil embolization for aneurysm recanalization, wall enhancement and cavity enhancement with 3-Tesla MRI. We then compared the incidence of wall enhancement and cavity enhancement of completely occluded aneurysms to aneurysms with recanalization by Chi2- Test and performed a multivariate linear regression analysis with recanalization size as independent variable.

Results We evaluated 59 patients (mean age 54.7 years +/- 12.4, 48 women) with 60 intracranial aneurysms and found a significantly higher incidence of wall enhancement in coiled aneurysms with recanalization (n=38) compared to completely occluded aneurysms (n= 22, p= 0.036). In addition, there was a significantly higher incidence of wall enhancement in aneurysms with recanalization larger than 3 mm (p= 0.0033). In a multivariate linear regression analysis wall enhancement (p= 0.010) and increase of overall aneurysm size after embolization (p< 0.001) were significant predictors for recanalization size (corrected R2= 0.430, CI 95%).

Conclusion The incidence of aneurysm wall enhancement is significantly increased in coiled intracranial aneurysms with recanalization and associated with recanalization size.

**Liebhauser Martin**

Abstract ID: 116804

# Implant Breakage after Shoulder Arthroplasty: A systematic review of data from worldwide arthroplasty registries and clinical trials

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Background: Implant breakage after shoulder arthroplasty is a rare complication. Specific data of complication rates and implant breakage are available in detailed arthroplasty registries, but due to the rare occurrence and possibly underestimated value rarely described in published studies. The aim of this systematic review was to point out the frequency of implant breakage. We hypothesized that worldwide arthroplasty registry datasets record higher rates of implant breakage than clinical trials. Methods: PubMed, MEDLINE, EMBASE, CINHAL, and the Cochrane Central Register of Controlled Trials database were utilized for this systematic review according to the PRISMA guidelines on July 3rd, 2023. Study selection, quality assessment, and data extraction were conducted according to the Cochrane standards. The breakage rate per 100,000 observed component years was used to compare data from national arthroplasty registries and clinical trials. Results: Data of 5 registries and 15 studies were included. Rates of implant breakage after shoulder arthroplasty were reported with 0.06-0.86% in registries versus 0.01-6.65% in clinical studies. The breakage rate per 100,000 observed component years was 10 in clinical studies and 9 in registries. There was a revision rate of 0.09% for registry data and 0.1% for clinical studies within a 10-year period. The most frequently affected component in connection with implant fracture was the glenoid insert. Conclusion: Clinical studies revealed a similar incidence of implant failure compared to data of worldwide arthroplasty registries. These complications arise mainly due to breakage of screws and glenospheres and there seems to be a direct correlation to loosening. Periprosthetic joint infection might be associated with loosening of the prosthesis and subsequent material breakage. We believe that this analysis can help physicians to advise patients on potential risks after shoulder arthroplasty.

## Poster Session II

### Habacher Hermann

Abstract ID: 119016

# Establishing the Wnt and p53 pathway intersection as a novel drug target

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Background/Aims: Canonical Wnt signaling is involved in the orchestration of cell fate during embryogenesis and tissue maintenance, whereas p53 acts as a guardian by mediating stress response, cell cycle arrest and apoptosis. Dysfunction of both pathways has been closely associated with cancer, as for example colorectal cancer (CRC) with Wnt hyperactivation causing ?-catenin accumulation in the nucleus in early stages and a frequent p53 inactivation in later development. A crosstalk between both pathways is proposed but a direct interaction of ?-catenin and p53 is still elusive. The study is aimed to reveal the molecular details of the direct binding between p53 and ?-catenin. The structure of the ?-catenin-p53 complex will be solved to gain cues for rational drug design. The interacting domains on both proteins should be determined including a potential modulation via posttranslational modifications. Finally, the functional relevance of this novel Wnt/p53 pathway intersection will be assessed by cell-based assays.

Results: NMR and fluorescence polarization consistently indicate a strong interaction between ?-catenin and p53. Our experiments showed that four N-terminal armadillo repeats of ?-catenin are sufficient to bind p53. Within p53, the transactivation domain (TAD) interacts with ?-catenin and its phosphorylation enhances binding. Finally paramagnetic relaxation enhancement (PRE) NMR experiments provide proper distance information between these proteins capable of solving a first model of the ?-catenin-p53 complex.

Conclusion: By providing strong evidence of a physical interaction of ?-catenin and p53 we propose a model of an interaction dependent stabilization of these proteins. A subsequent release of p53 and ?-catenin may has crucial effects on cell fate.

**Trapp Elisabeth Katharina**

Abstract ID: 119007

# Multigene panel analysis in breast and ovarian cancer

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Introduction: Breast and ovarian cancer are the most common female cancers. In Austria about 5500 patients are diagnosed with and about 1600 die from breast cancer each year. Ovarian cancer ranks third place with about 700 newly diagnosed and 500 patients dying from it each year. In 5-10% of all breast and 10-15 % of all ovarian cancers have a hereditary background (1, 2) Mostly one of the two risk genes BRCA1 and BRCA2 are affected, but many other risk genes can promote a hereditary tumor syndrome. Hence, multigene analysis, which in most cases is initiated at diagnosis or in genetic high-risk families, should complete routine genetic counseling.

Methods: All patients counseled in Genetics out-patient clinic of the University Department of Gynecology and Obstetrics in cooperation with the Institute of Genetics at the Medical University of Graz between 2007-2020 were evaluated, if they had an analysis of the panel genes ATM, PTEN, RAD50, RAD51D, RAD51C, TP53, STK11, NBN, CDH, MSH6, MSH2, MLH1 CHEK2, PALB2, BRIP1 and SMO. Subsequent data analysis were analyzed with SPSS.

Results: 449 patients were tested for the multigene panel.142 patients (31.6%) met the guideline criteria for genetic testing based on family history, even before being diagnosed with cancer. Over one third (33.9%) (n=152) had either a pathogenic mutation or an unclassified variant (UV). At least one unclassified variant was detected in 111 patients (24.7%). 43 patients (9.6%) were tested positive for a pathogenic mutation. The most common of these was found in the CHEK2 gene, which occurred in 15 cases (3,3%). In all pathogen mutation carriers 25 patients (56.8%) were diagnosed with breast cancer and three with ovarian cancer (6.8%).

Conclusion: More than one third of the patients with a highly positive family history or high-risk tumor history were tested positive for either a pathogenic mutation or an unclassified variant in the panel genes.

**Kostmann Sarah Madelaine**

Abstract ID: 118959

# Evaluation of efficacy of comprehensive genomic tumour profiling (CGP) from liquid and/or tissue biopsy in patients with locally advanced and/or metastatic carcinoma

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Background/Aims:Molecular profiling plays an increasingly important role to find individualized targeted therapies, especially for patients with advanced or treatment refractory malignant disease. The decreasing costs and turnaround time of next generation sequencing methods paired with the rapidly growing arsenal of available genome-targeted drugs, have significantly raised the impact of molecular profiling (MP) for treatment selection in clinical practice. To date, numerous studies evaluated the clinical benefit of treatments selected through genetic profiling. The results remain inconclusive. SOUND aims to evaluate the utility of comprehensive MP of ctDNA for personalized, cancer-agnostic treatment matching and to investigate the efficacy of MP-matched therapy in this salvage setting. Method/Results:SOUND is a multicenter phase II trial. Adult patients with locally advanced or metastatic carcinoma, who have exhausted all evidence-based therapies and have an ECOG performance status of 0-2 are eligible. At study enrollment, a mandatory liquid-biopsy for the analysis of ctDNA is obtained from all patients. A tissue biopsy will be tested in study patients who consent to tissue biopsy or for whom a tissue biopsy (not older than 3 months) is available. Additionally, available tissue will undergo an immunohistochemical test for HER2, NTRK and PD-L1. MP of ctDNA and tumor tissue DNA is performed using the FoundationOne<U+00AE>Liquid CDx and the FoundationOne<U+00AE> CDx panel analysis tools. All patient cases including the molecular reports, actionable molecular targets (AMT) and MP-guided treatment recommendations are reviewed weekly in a virtual multidisciplinary molecular tumor board. The study is ongoing. To date (November 14th, 2023) 128 of 200 planned patients are enrolled. Conclusion: The SOUND study is the largest prospective study in Austria exploring the treatment strategy and outcomes of CGP-driven targeted treatment in patients with advanced or metastatic cancer.

**Dobri? Nina**

Abstract ID: 118821

# Comparison of ctDNA profiles from HR+/HER2-low and HR+/HER2-0 advanced breast cancer patients

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Background/Aims: Despite the substantial progress in systemic treatment of hormone receptor-positive breast cancer, a significant proportion of patients have dismal prognosis. A meaningful proportion of these patients have HER2-low disease. Circulating tumor DNA (ctDNA) profiles between HER2-low and HER2-0 have not yet been comprehensively investigated. We hypothesize that we will be able to establish and differentiate between the mutational profiles from plasma samples of HR+/HER2-low and HR+/HER2-0 advanced breast cancer patients.

Method/Results: 92 plasma samples from 83 metastatic breast cancer patients (HR+/HER2-low, n=62; HR+/HER2-0, n=30) were collected before starting 1st line or 2nd line treatment. Tumor fractions were assessed using an untargeted aneuploidy screening and expressed as z-scores (mFAST-SeqS). The mutational landscape of ctDNA was established using a 77-gene panel (AVENIO ctDNA Expanded). Tumor fractions, the number of somatic variants and variant allele frequencies (VAF) were compared between HER2-low and HER2-0 patients. HER2-low patients had significantly higher z-scores compared to HER2-0 patients. The highest and the average VAF did not differ significantly between the two groups. HER2-low patients had a median of 3 detected variants, with a median of 2 clonal and 1 subclonal variants. HER2-0 patients presented with a median of 4 variants, including a median of 3 clonal and 1 subclonal variants. In contrast to previous reports, PIK3CA mutations were more prevalent in HER2-0 patients compared to HER2-low patients. TP53 mutations were identified at the same extent in HER2-0 and HER2-low patients.

Conclusion: Our results suggest a significant difference in the tumor fractions in plasma between HER2-0 and HER2-low patients. Moreover, the mutational landscape of our cohort revealed differences from previous reports, indicating that further investigations are needed to elucidate and establish the distinct features of HER2-low breast tumors.

**Santiso Ana**

Abstract ID: 118762

# Functional characterisation of B cells in NSCLC

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The presence of tumor-infiltrating B-cells correlates with survival of patients presenting several types of solid tumors, including patients with non small cell lung cancer (NSCLC). However, both anti- and pro-tumorigenic functions have been described for B-cells present in the tumor microenvironment (TME). The specific phenotype and function of B cells present in a tumor might ultimately depend on the specific cellular and signaling context within the TME. Identifying and characterizing pro- and anti-tumorigenic B-cell phenotypes could be key to modulating B-cell responses in the TME towards anti-tumor immunity.

We integrated high-dimensional protein and RNA expression data from human B cells obtained from lung, blood, and tumor samples to identify B cell subpopulations TME of non- NSCLC patients. The analysis of clinical samples involved surface marker screening and validation using flow cytometry to assess the differential expression of protein surface markers on B cells within the TME. Additionally, single-cell RNA sequencing was conducted on sorted B cells from matched tumor and lung samples. Multiplex immunofluorescence (mIF) was employed to assess the spatial localization of B cells in both tumor and adjacent lung regions of FFPE patient samples, providing insights into the spatial expression of selected protein markers.

Four distinct subtypes of B cells could be identified in TME of NSCLC patients: Plasma cells, memory B cells, germinal center (GC) B cells, and naive B cells. We successfully detected and validated the differential expression of 11 markers on B cells within the TME, when compared with B cells from the lung and/or PBMCs. Notably, the surface marker CD55 exhibits differential expression at both mRNA and protein levels. mIF data revealed increased CD55 expression localized around the GC area of tertiary lymphoid structures (TLSs).

**Kindler Oliver**

Abstract ID: 118609

# Influence of age on the tumor microenvironment in a cohort of non-small cell lung cancer

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Introduction: Immune Checkpoint Blockade (ICB) led to better outcomes in non-small cell lung cancer (NSCLC) but only a subset of patients benefits from current treatment regimens. Different molecular subtypes show diverse responses to treatment. Additionally, age is suggested to be an important factor in ICB response. It was reported that the survival advantage of ICB in comparison to conventional therapy was only modest in patients aged over 75. To evaluate the influence of age on the immune environment (IE) in lung cancer, a thorough characterization was performed in patients with untreated NSCLC. Methods: To characterize the immune environment, flow cytometry and multiplex immunohistochemistry were used. Additionally, TCR sequencing and RNA sequencing were performed. The findings were validated in public datasets. Results: Higher infiltration of T cells in older patients was found, which could be mainly attributed to CD4+ T cells. Validation in the TCGA-LUAD cohort additionally revealed higher abundance of regulatory T cells. No difference was found regarding T cell clonality and Tumor Mutational Burden (TMB). Additionally, public single-cell RNA sequencing data revealed less effector molecule expression in CD8+ T cells in older patients. Conclusion: Higher regulatory T-cell infiltration is associated with treatment failure of ICB. Further research on the biochemical mechanisms of regulatory T cells in ICB response of elderly lung cancer patients is warranted.

**Lueger Anna**

Abstract ID: 118474

# Myeloperoxidase creates an immunosuppressive tumor microenvironment in non-small cell lung cancer by altering T cell function

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Background: The tumor microenvironment (TME) of non-small cell lung cancer (NSCLC) involves high infiltration of immune cells, including neutrophils. These neutrophils contribute to the complexity of the TME by releasing myeloperoxidase (MPO) upon activation and degranulation. In the presence of H2O2, MPO generates HOCl, a highly reactive molecule that can cause damage to proteins, lipids and DNA. In this study, we investigated the functional role of MPO in the NSCLC and its effect on T cells within the TME. We hypothesize that MPO in the TME may alter T cell activation and function, ultimately leading to an immunosuppressive TME. Methods: We studied MPO knock-out mice in a flank tumor mouse model. Additionally, we conducted in vitro experiments using recombinant MPO treatments to analyze the impact of MPO on T cells. Results: MPO knock-out mice exhibited reduced tumor growth compared to WT controls. This decrease in tumor growth was accompanied by an increase in lymphocyte populations, including natural killer cells (NKs) and CD8+ T cells. Furthermore, MPO knock-out mice demonstrated enhanced expression of IFN-? by T cells. In vitro experiments also revealed that CD8+ T cells treated with MPO exhibited reduced proliferation and production of IFN-?. Conclusion: Our findings indicate that the deletion of MPO promotes an anti-tumorigenic immune environment in a mouse tumor model, characterized by an increase in CD8+ T cells and heightened expression of IFN-?. Additionally, MPO negatively affects function of anti-tumor T cells, supported by in vitro experiments demonstrating decreased proliferation and IFN-? expression of CD8+ T cells after MPO treatment. These results suggest that MPO contributes to tumor growth and exhibits an immunosuppressive role in NSCLC. Consequently, MPO might serve as a potential target for lung cancer therapies, aiming to counteract its immunosuppressive effects in NSCLC.

**Bayer Christian**

Abstract ID: 117788

# Unlocking Precision in Pancreatic Cancer Treatment: Controlled Release Strategies of Hydrogel-Bound Chemotherapeutics via Iontronic Devices

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Background/Aim: Chemotherapy's limited effectiveness in treating cancer is often due to challenges in drug delivery efficiency and systemic toxicity. We focus on challenging cancers, like Pancreatic Adenocarcinoma (PAAD), which often occurs near critical blood supply structures. Surgical resection is often unfeasible until the tumor is a manageable size, making tumor shrinkage a promising strategy for making PAAD patients eligible for surgery.This study aims to use iontronic devices to deliver a specific trigger molecule with spatiotemporal accuracy into a drug-loaded hydrogel, setting off a "click-to-release" (C2R) reaction that releases the chemotherapeutic drug directly at the tumor site. By implementing the bioSWITCH concept locally, our goal is to position potent pharmaceutical agents near the tumor, optimizing their anti-cancer impact through precise targeting.

Methods/Results: We conducted tests on the C2R system components across different cancer cell lines to identify IC50 concentrations and assess toxicity levels. Simultaneously, we determined trigger molecule delivery rates using different ion exchange membranes. Following this, we tested the iontronic-controlled C2R of potent chemotherapy drugs and hydrogel prototypes in a 2D cell culture setup and a 3D in vivo tumor model using the chick chorioallantoic membrane (CAM). We developed a C2R mechanism using iontronic devices to trigger controlled release of a potent prodrug. Initial proof-of-concept experiments were performed in vitro on tumor cells. The prodrug exhibited biocompatibility when bound, but the introduction of the trigger molecule through iontronics led to an interaction, resulting in drug release. Significantly, we achieved precise control over system activation and deactivation, effectively influencing cancer cell death.

Conclusion: These results underscore the potential of this approach and provide a basis for further preclinical investigations into a novel therapy strategy for PAAD.

**Leoni Marlene**

Abstract ID: 116844

# The role of chemokine receptor expression in the progression of brain metastases in different cancer types- A retrospective study

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BACKGROUND: Lung cancer, Renal Cell Carcinomas, Colorectal Adenocacrinomas and Malignant Melanomas are the most common cancers in industrial countries and the leading cause of cancer-related mortality. Especially the development of brain metastases is accompanied by a poor prognosis. Since all of these malignant tumors are able to progress in form of metastasis into the brain, it is important to elucidate the causes and events in the development of metastases. METHODS: This thesis aimed to find out if the chemokine receptor expression is different between the primary tumors and brain-specific metastases of these four tumorentities. Differences in the expression of the most well-characterized chemokine receptors (CCR1- 10, CXCR1-7, XCR1 and CX3CR1) were detected by RT-qPCR. Furthermore, the chemokine receptor expression in tumor tissues was compared to the chemokine receptor expression in the surrounding non-neoplastic tissues. RESULTS: In lung cancer the mRNA expression of CCR6 was significantly lower in metastases compared to the primary tumors, as was the expression for CCR9. The chemokine receptor expression was also lower in metastases compared to the primary tumors for CXCR4 and CXCR6. In Renal Cell Carcinomas there is a higher expression of CCR8,6 and 9 in the metastases. In colorectal carcinomas there is a significant higher expression of CXCR6 in the metastases. In Malignant Melanomas three CC chemokine receptors showed a decreased expression in tumor tissues in relation to control tissues as well as to metastases. Comparing CC chemokine receptor expression in melanomas and their surrounding skin tissue, significantly elevated levels of chemokine gene products were detected in melanoma<U+0091>s surrounding tissue ($p < 0.05$). Overall, CXCR4 was expressed in lower levels in all samples compared to controll tissue.

CONCLUSION: The mRNA expression profile for some chemokine receptors is different in brain-specific metastases of NSCLC compared to the primary tumors

**Nussbaumer Gunther**

Abstract ID: 113993

# Gliomatosis cerebri in children: A poor prognostic, highly infiltrative phenotype of pediatric-type diffuse gliomas with a distinct molecular profile

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Background: Gliomatosis cerebri (GC), a radiology-defined highly infiltrating glioma, is no longer considered a distinct tumor type since the 2016 World Health Organization (WHO) classification of tumors of the central nervous system (CNS). So far, neither prognostic factors, nor molecular GC-associated features have been firmly established. We conducted a multinational retrospective study of 104 children and adolescents with GC, providing comprehensive radiological, clinical and (epi-)genetic characterization. Results: Within a median follow-up of 15.5 months (range, 2.3<U+0096>138.8), 93 patients (89.4%) had died, four (3.8%) were lost to follow-up and seven (6.8%) were alive with stable/progressive disease. Median progression free- (PFS) and overall survival (OS) were 8.6 (interquartile range, 4.3<U+0096>14.0) and 15.5 months (10.9<U+0096>27.7), respectively. Available histopathological grading correlated significantly with median OS: CNS WHO grade II: 47.8 months (25.2<U+0096>55.7); grade III: 15.9 months (11.4<U+0096>26.3); grade IV: 10.4 months (8.8<U+0096>14.4). In GC with high-grade features, combined radio-chemotherapy achieved the longest PFS (median 9.6 months [5.7<U+0096>14.0]). By DNA methylation profiling (n=49), most tumors were classified as pediatric-type diffuse high-grade glioma (pedHGG), H3-/IDH-wildtype (n=31/49, 63.3%) with enriched subclasses pedHGG_RTK2 (n=19), pedHGG_A/B (n=6), and pedHGG_MYCN (n=5), but only one pedHGG_RTK1 case. Within the pedHGG, H3-/IDH-wildtype subgroup, recurrent alterations in EGFR (n=10) and BCOR (n=9) were identified. Additionally, we observed structural aberrations in chromosome 6 comprising complex genomic rearrangements with large areas of loss or gain/amplification in 16/49 tumors (32.7%). Conclusion: Our representative pediatric GC cohort provides evidence that GC has a strong predilection to arise on the background of specific molecular features (especially pedHGG_RTK2, pedHGG_A/B, EGFR- and BCOR mutations, chromosome 6 rearrangements).

**Steiner Jakob**

Abstract ID: 112311

# Myxoid liposarcoma (MLS) <U+0096> Size, grading and location in a large monocentric cohort

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Purpose or Learning Objective: Soft tissue sarcomas are a heterogeneous group of neoplasms with different malignant potential and prognosis. With 10-15 % of diagnosed sarcoma, liposarcoma accounts for the second most malignancies. Myxoid liposarcoma with round cell sarcoma is among the most common ones. Its distinct radiological features make it an important differential for soft tissue tumors.

Methods or Background: For this study, we retrospectively identified patients in our university clinic and national sarcoma center with postoperative histologically proven myxoid liposarcoma (MLS) from 1998 <U+0096> 2021.

Results or Findings: Sixty-two patients treated and diagnosed with MLS at our institution were identified. The mean patient age at presentation and diagnosis was 50.8 years (19-82, 14.5). 73 % of patients were under the age of 60. There was a male predominance with 57.1 % (36 male). Distribution was shown to be more peripheral compared to a central location, with 83 %. The lower limb was more likely to be the tumor side with 78 % in the thigh, lower leg, and gluteal. The thigh was mainly the primary tumor location in male and female patients (53 %; 61 %). G2 was the most common histological grading with 39.7 % (G1 38.1 %, G3 22.2 %). MRI was the primary imaging modality in most cases, with 92.1 % (58). Three cases were imaged with computer tomography alone (4.7%). In one case, no imaging data were available. Maximum radiological diameter averaged 12.4 cm and was more extensive in the male cohort with 13.4 cm (12.4 cm). G1 tumors were smaller than G2 and G3 tumors at diagnosis, with an average of 10.4 cm (14.2; 14.9).

Conclusion: Myxoid liposarcoma outside specialized centers can be a challenging for clinicians, radiologist, and pathologist. Our data shows that most tumors in the lower limb affect the thigh. Higher grading was present in larger tumor size. Within our cohort, there were no significant differences in gender distribution or features, though th

**Klocker Eva Valentina**

Abstract ID: NA

# Histopathological features and prognosis of early lobular breast cancer

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Background: Invasive lobular breast cancer (ILC) is the second most common histological subtype in breast cancer. Te aim of this study was to analyze clinico-pathological features and their impact on overall survival (OS) and diseasefree survival (DFS) of early ILC patients treated at our institution. Methods: We collected clinico-pathological features of 344 early ILC patients diagnosed and treated between 2006 and 2021. We stratifed the tumors according to hormone receptor (HR) and HER2 status. As DFS we defned the time between diagnosis and occurrence of metastasis, locoregional disease, second breast cancer, or death from any cause. Results: Te mean age of patients was 63.2 (25th percentile: 52; 75th percentile: 74). 334 patients (97,1 %) were hormone receptor positive (HR+), 26 (7,6 %) were HER2 positive (HER2+) and<U+00A0>6 (1,7 %) were triple negative. In HER2+ disease, 24 patients (92,3 %) were HR+. Tere was no signifcant difference in OS and DFS between HR+ and HER2+ disease or between the ER+/PR+ and the ER+/PR- group. OS and DFS were signifcantly reduced in triple negative ILC ($p < 0.0001$, respectively). Ki-67 ? 15 % and larger tumor size were signifcantly associated with shorter DFS and OS. Conclusions: In our analysis 97,1 % were HR+. Larger tumor size and Ki-67 ? 15 % as well as triple negative subtype of ILC had a signifcantly adverse impact on DFS and OS. In the HER2+ subgroup, there was no diference in OS and DFS, either due to targeted treatment efect or the lack of dependence of ILC on HER2 signaling, which remains to be studied.

**PHAN THI THANH HUYEN**

Abstract ID: 119835

# PPAR-? SIGNALING TRIGGERS A METABOLIC SWITCH DURING BRONCHIOLAR REGENERATION

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Aberrant repair, regeneration and remodeling of injured lung epithelia are associated with idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease and asthma. Dysregulation of energy homeostasis often leads to the development of metabolic syndromes. Central obesity, type 2 diabetes, hypertension and elevated blood triglyceride levels have been associated with reduced lung function in several epidemiological studies. We are interested in the link between metabolism and lung regeneration. Our data show that peroxisomal proliferator activated receptor-? (PPAR-?) signalling is essential for lung regeneration after Naphthalene(NA)-induced airway injury (Kanti et al., 2022). PPAR-? is a nuclear receptor that regulates genes involved in energy metabolism and inflammation. Using in situ hybridisation, we found that PPAR-? target genes were selectively upregulated in the bronchiolar epithelium during repair. PDK-4 is one of those downstream genes. In a canonical pathway, PDK4 inhibits pyruvate dehydrogenase complex (PDC)<U+0092>s activity by phosphorylation, thereby inducing metabolic reprogramming towards fatty acid oxidation. Pharmacological activation of PPAR-alpha signalling enhanced bronchiolar epithelial regeneration after NA injury (Kanti et al., 2022). We hypothesize that PPAR-? signalling triggers a metabolic switch during bronchiolar regeneration.

Using a powerful combination of RNAscope<U+0099> in situ hybridization and immunofluorescence, we aim to delineate which bronchiolar cell type(s) undergoes a metabolic shift during lung repair. In addition, we are now establishing an experimental system for CRISPR/Cas9-mediated PDK ablation in vivo and performing pharmacological inhibition of PDK(s) during NA-induced lung injury to investigate the metabolic requirements during airway regeneration. Air-liquid interphase culture of human bronchial epithelial cells (HBEC) is also used to study the effect of PDK inhibition on HBEC differentiation.

**Kulovic-Sissawo Azra**

Abstract ID: 119451

# The link between circulating neprilysin and metabolism during pregnancy

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Background: During pregnancy, the female organism undergoes profound vascular and metabolic adaptations, which are orchestrated by an interplay of bioactive, regulatory molecules. Neprilysin is a protease that exists in both membrane?bound and soluble form (sNEP). Soluble NEP circulates in the bloodstream and degrades a wide range of bioactive peptides including peptides involved in glycemic control (insulin B chain, GLP-1) and in vascular tone regulation (angiotensin, ANP, BNP). Objective: The substrate specificity of neprilysin suggests a potential involvement in metabolic and vascular adaptions during pregnancy. However, the link between sNEP and metabolism in pregnancy has not yet been investigated. Methods: Serum sNEP, longitudinally collected from metabolically healthy pregnant women (n=98, trial number NTC05496712), was measured at three visits throughout gestation (gestational age: 12.5<U+00B1>0.7, 20<U+00B1>0.8, 33<U+00B1>1.6 weeks) and post-partum (2<U+00B1>1.2 days after delivery) using a commercially available sandwich ELISA. Clinical and anthropometric measurements were determined and the association of sNEP and metabolic characteristics elucidated. Results: Circulating sNEP levels showed large individual differences, with individual levels remaining constant over gestation (n= 80). After delivery, however, sNEP concentration decreased (n=80, p=0.0001). At all visits in pregnancy, sNEP showed a positive correlation with non-fasting GLP-1 (Spearman, n=83, r=0.372, p=0.001), and systolic blood pressure (Spearman, n=56, r=0.321, p=0.02) at early stages of pregnancy, but did not correlate with maternal age, pre-pregnancy BMI, or insulin resistance. Conclusion: The decrease in sNEP post-partum as compared to levels throughout pregnancy suggests a particular way of sNEP regulation and release in gestation. During pregnancy, sNEP may be involved in metabolic and cardiovascular adaption to pregnancy, with circulating sNEP levels showing massive individual differences.

**Filelfi Sebastian Lucio**

Abstract ID: 119444

# Lymphatic senescence in humans: study of the depletion of the lymphatic network of the lower limb in the cadaver and in the living.

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The hypothesis of the proposed study is that the senescence of the lymphatics implies the numerical reduction of the lymphatic collectors of the leg, a possible explanation of the dependent oedema often found in the elderly. No studies approached the ageing of lymphatic collectors of the legs in humans. Recent articles have shown that the use of fluoroscopy with indocyanine green allows the study of the lymphatic collectors (number, location) in the cadaver, while older, less applicable methods implied the use of mercury and then of radiopaque resins. The study consists of a first investigation carried out on cadavers, with the observation of morphological variations, and a second one, in which the anatomical and functional alterations of the lymphatics of the leg are evaluated in living subjects. Inclusion criteria: Observations will be performed in one lower leg of cadavers of two age groups: 50-60 y.o. and 70-80 y.o. (5 for the first and 5 for the second group), including both males and females. Exam technique: 0.05 mL of ICG solution will be intradermally injected by using a 1-mL syringe with a 30-gauge needle. The injections sites will be at the web space between the first and second toes, and at two points of the lateral aspect of the foot (well established for paramount study of lymphatic collectors). Immediately after the injections, gentle hand massage will be applied at each injection site and then to the lower limb. Expected results In accordance with the scientific literature, an age related reduction of the network of lymphatic collectors of the lower legs of cadavers. In living subjects we expect an age related reduction of the number and function of lymphatic collectors, with possible their permeability. The obtainable advantage is that of contributing to the understanding of the physiopathology of dependent edema in the elderly, being able to optimize the pharmacological and physical therapeutic approaches.

**Wojcik Gabriela**

Abstract ID: 119435

# Exploring the Role of Lipids in Lung Fibrosis: Understanding the Complexities

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Background/Aims: The damage to the lung structure during lung fibrosis is connected to the intensive changes in extracellular matrix (ECM). Fibroblasts (PDGFR?+ cells) are the main responsible cell type, which are producers of collagen, the main ECM ingredient. In Idiopathic Pulmonary Fibrosis (IPF), fibroblast persistent collagen production, via TGF?1-SMAD2/3 pathways, have the major role in lung fibrosis development. Abnormal changes in metabolism of Fatty acids (FAs), the components of the complex lipids, are connected to the IPF pathology, especially in the fibrotic fibroblasts. Yet, there is no established connection between lipids and collagen. One of the downregulators of FAs influx is Angiopoietin-like 4 (ANGPTL4), inhibitor of lipoprotein lipase. We hypothesized that modifications in lipid metabolism during the lung fibrosis development influence the fibroblast populations, therefore influencing lung fibrosis. Methods/Results: We attempted to validate our hypothesis by examining the human, animal, and in vitro cell culture. In the bleomycin model, popular lung fibrosis model, ANGPTL4 colocalizes with the PDGFR?+ cells, which was similar in donor and IPF tissues. ANGPTL4 KO animals showed lowered collagen deposition and higher lipid droplet (LDs) content after BLM treatment, compared to controls. In vitro treatment of human parafibroblasts (hPFs) with physiological mix of FAs with/without presence of TGF? showed that FAs could lower the collagen expression. Currently, we are analyzing the reports from the lipidomics of animal and human lung tissue. Conclusion: In summary, our results suggest the strong influence of the lipid metabolism on lung fibrosis, however additional tests are needed.

**Klaczynski Michaela**

Abstract ID: 119428

# Preeclampsia modifies the miRNA cargo of fetoplacental-endothelial derived small extracellular vesicles

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Background: Preeclampsia (PE) affects 3-8% of pregnant women worldwide and poses a significant risk to maternal and perinatal health. Fetal complications of PE include thrombocytopenia and neutropenia, indicating an underdeveloped innate immune system in utero. Placental small extracellular vesicles (sEVs) are known to be mediators of immune cell communication and are altered in PE; therefore, we aim to elucidate the contribution of placental sEVs to the immune cell fate decisions.

Methods: Conditioned media from primary placental endothelial cells (ECs) from term (T, n=6), gestational age-matched preterm (PT, n=6) and PE (n=5) pregnancies were used to isolate sEVs by differential ultracentrifugation. The presence of EC-sEVs was determined by size and concentration using Nanoparticle Tracking Analysis (NTA). The miRNA and proteomic cargo was characterized using miRNAseq and nanoLC-MS/MS.

Results: ECs from all groups secreted sEVs of heterogeneous size; however, up to 2.5 times higher concentrations of sEVs were released into the conditioned media from ECs of the PT and PE groups. Furthermore, miRNAseq revealed seven dysregulated miRNAs (fold change < 2, p= < 0.05) in the PE cohort, including upregulation of hsa-miRNA-145-5p and hsa-miR-143-3p. The upregulated miRNAs were subjected to functional enrichment analysis, which revealed specific interactions with 620 target genes. Notably, this analysis suggested a potential upregulation of the INF-gamma pathway in the target cell. Proteomic analysis of EC-sEVs identified 1272 proteins; but no significant changes were observed between the groups.

Conclusion: Preliminary results of this study suggest that regardless of the pathological state of the ECs, the secreted EV protein cargo remains unaltered and only the miRNA cargo is affected by PE. Bioinformatic analysis of the upregulated miRNAs in PE revealed INF-gamma signaling as a potential regulatory pathway in the hematopoietic stem cell fate.

**Xu Ruonan**

Abstract ID: 119414

# P53 regulation of lipid-associated macrophages upon fasting in liver disease

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Fatty liver is a major stepping stone to chronic liver disease progressing to cirrhosis and non-alcoholic steatohepatitis (NASH), the latter of which being strongly associated with infiltration of immune cells such as monocyte-derived lipid-associated macrophages (LAMs). Using life-style interventions like intermittent fasting (IF) can be effective at reversing early states of fatty liver. However, how IF affects NASH and the corresponding hepatic immune cell landscape is still elusive.

Previous work in our lab showed a strong remodeling of the LAM population in adipose tissue of high-fat diet (HFD)-fed mice after 3 weeks of IF and that this was largely dependent on parenchymal p53 signaling.

Consistent with other studies, preliminary data in livers from this cohort showed that macrophage numbers were increased in HFD-induced obese mice. Interestingly, both IHC staining data and gene expression showed that macrophages were strongly decreased after 3 weeks of IF. Furthermore, we observed a reduction of lipid accumulation and liver fibrosis by IF, as shown with H&E staining and marker gene expression. As Mmp12 is a prominent LAM marker, we next asked whether LAM abundance is changed in Mmp12 knock out mice fed an HFD and subjected to IF. Interestingly, macrophage abundance was similar to wildtype controls and we observed a trend towards increased macrophage and LAM marker gene expression.

Based on these results, we will investigate dietary NASH models (CDAHFD) to delineate the dynamic effects of IF on lesion-associated LAMs during disease progression and in dependence of hepatocyte p53 and LAM Mmp12 signaling. For this we will use global (single nuclei RNA-seq and spatial transcriptomics) as well as focused (histology, gene expression, in vitro experiments) approaches in NASH model with and without p53 and LAM deficiency.

Overall, we plan to unravel the interaction of LAMs with hepatic p53 signaling and IF during the progression of liver disease.

**Kamali Simsek Nil<fc>fer**

Abstract ID: 119406

# Influence of plasma membrane composition on feto-placental endothelial cell function <U+0096> investigation of ROS levels and plasma membrane purification

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BACKGROUND Piezo1, a mechanosensitive Ca2+-permeable ion channel, is a key player in endothelial function and may be altered in preeclampsia (PE), a pregnancy disorder associated with oxidative stress. Piezo1 is embedded in the fpEC plasma membrane (PM) and its activation is regulated by the structure/composition of the PM. It mediates vasodilation through inducing nitric oxide synthase, which is regulated by the resting membrane potential (RMP). Preliminary data show that the RMP of PE feto-placental endothelial cells (fpECs) is significantly higher. The study aims to investigate whether higher RMP in PE is associated with reactive oxygen species (ROS) and to establish a protocol to isolate pure PM for downstream analysis. METHOD CellROX Green Reagent was used to measure ROS levels in control and PE fpECs (n=3/group) and was measured by using flow cytometry. Density gradient ultracentrifugation (n=4) and Minute<U+0099> Plasma Membrane Protein Isolation kit (n=2) were applied for PM isolation. Protein yield was measured by BCA assay. To determine purity of PM samples, different organelle marker proteins such as Na+/K+-ATPase (PM), CALR (endoplasmic reticulum (ER)), TGN46 (golgi), and MTCO1 (mitochondria) were tested. RESULTS No significant difference (p = 0.38) in ROS levels was found between control and PE samples (0.14<U+00B1>0.09 and 0.29<U+00B1>0.13, respectively, mean <U+00B1> SD). PM protein yield was 7-2000 <U+00B5>g using ultracentrifugation and 7-33 <U+00B5>g using the kit. While PM marker was increased and ER marker was reduced, other organelle membrane markers were enriched when ultracentrifugation method was used. CONCLUSION We conclude from the pilot study that cellular ROS levels do not correlate with RMP of fPECs, therefore, other pathways such as apoptosis and senescence will be investigated to find an explanation for the RMP difference between the groups. We are working on optimizing the protocol for fpECs-PM isolation in order to minimize organelle membrane contamination.

**Stevanov Dr. Marina**

Abstract ID: 119394

# The impact of the inflammatory ratios neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-tolymphocyte ratio (PLR) on abdominal aortic aneurysm growth

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Background: Abdominal aortic aneurysm (AAA) is a life-threatening disease associated with high morbidity, and also high mortality in the event of aortic rupture, where the inflammatory process may has a crucial role in AAA growth and substantially influences many determinants of aortic wall remodeling. Objective: This study could contribute to better decision making in the management of AAA by suggesting possible targets for new medical treatments to slow AAA progression. Primary endpoint of the study is impact of neutrophil-to-lymphocyte ratio (NLR) on aneurysm growth. Secondary endpoints are impacts of monocyte-to-lymphocyte ratio (LMR) and platelet-tolymphocyte ratio (PLR) on aneurysm growth. We designated these markers as promising because of a clear association of inflammatory biomarkers and ratios with the expansion of abdominal aortic aneurysms. Method: Routine preoperative blood samples was drawn on admission before surgical intervention. After that the NLR, MLR, PLR was calculated and analysed from laboratory results. The aneurysm volumes was measured digitally on-screen from current computed tomography angiography (CTA) images and from one previous investigation. Difference in aneurysm<U+00B4>s volume for that time period difference is calculated (?V/ V/ ?t) and the growth rate of the aneurysm will be determined. Results/Conclusion: Statistics and data analysis are still being conducted. After we have soon the statistical data, we will be able to present the results and conclusion of the study.

**Jeremic Dusan**

Abstract ID: 119379

# Impact of potassium channel regulator in pulmonary arterial hypertension

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Background: Pulmonary arterial hypertension is a devastating disease that can be life-threatening. One of the hallmarks of PAH is the remodelling and thickening of the vessel wall in the small pulmonary arteries (PA). It is well established that potassium channelopathies play an important role in the pathobiology of PAH. Therefore, we investigated a previously described voltage-gated potassium channel regulator (KCNRG) in PAH to better understand the mechanisms of potassium channel regulation in health and disease. Materials and methods: Quantitative polymerase chain reaction (qPCR) for KCNRG was performed on lung homogenate, laser-captured microdissected (LCM) PAs, and pulmonary arterial smooth muscle cells (PASMCs) from healthy subjects and patients with idiopathic pulmonary arterial hypertension (IPAH). Western blot was employed to analyze the protein content of KCNRG of donor and IPAH PASMCs. A patch clamp was performed for the recording of potassium current in HEK293 cells. Cells were transfected with either Kv1.5 plasmids with or without KCNRG. Results: Levels of KCNRG mRNA in whole lung homogenate remained comparable between donors and IPAH patients. However, KCNRG mRNA in LCM PAs and PASMCs was increased in IPAH. In HEK293 cells KCNRG significantly reduced the Kv1.5 current Conclusions: The presence of KCNRG functionally inhibited Kv1.5 by decreasing its current. Together with the increased expression of KCNRG in remodeled PAs, our data suggest that the KCNRG-Kv1.5 regulatory axis may play a role in the pathology of PAH.

**Kie<df>ling Mara**

Abstract ID: 119368

# CaMKII-mediated hypertrophic and inflammatory signaling in hypertensive heart disease

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Background/Aims Ca2+/calmodulin-dependent protein kinase II (CaMKII) plays a dual role in driving both adaptive and maladaptive remodeling in the myocardium by selectively phosphorylating Ca2+ cycling proteins and regulating transcriptional signaling. Evidence suggests that the decisive factor influencing the direction of downstream effects lies in the subcellular spatio-temporal activation pattern of CaMKII, yet the precise tipping point from adaptation to dysfunction remains elusive. Thus, we aim to characterize localized CaMKII activity in a clinically-relevant animal model of hypertensive heart disease at early and late stages of remodeling and determine the influence of persistent low-grade inflammation. Methods/Results Dahl salt-sensitive rats were fed a high-salt diet (8% NaCl) for 5 or 10 weeks to model early and late hypertensive effects, respectively. Age-matched low-salt-diet-fed (0.3% NaCl) rats served as normotensive controls. Spleens, kidneys and hearts from hypertensive rats showed significant hypertrophy ($p<0.0001$). Immunocytochemistry revealed marked shifts in the localisation of CaMKII activation between hypertensive and control groups at both time-points. Immune-inflammatory signaling was evident through transcriptional upregulation of interleukin-6 ($p=0.019$) and its receptor ($p=0.0095$), as well as follicular structures in mediastinal lymph nodes indicating B cell maturation. Immunoblotting and a caspase-1-activity assay further suggested the activation of the NLRP3 inflammasome. Conclusion Our findings support the existence of a putative link between subcellular CaMKII activation and inflammatory signaling in cardiomyocytes. Understanding the molecular mechanisms by which CaMKII intersects with inflammatory pathways may pave the way for innovative therapeutic strategies aimed at attenuating cardiac inflammation, preventing adverse remodeling, and ultimately improving outcomes for individuals afflicted by hypertensive heart disease.

**Dohr Katrin**

Abstract ID: 119339

# Effect of inflammation on endothelial cells of female Fabry Disease patients

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Fabry Disease (FD) is an X-chromosomal, lysosomal storage disorder with pathogenic variants in the GLA-gene leading to reduced or absent ?-Galactosidase A (?Gal) activity. Consequently, glycosphingolipides, primarily globotriaosylceramide, accumulate in tissues causing chronic inflammation, affecting the endothelium of the heart, kidney and brain. Due to X-inactivation, the presentation of FD in female patients may range from asymptomatic to severely affected. We hypothesized that endothelial cells (EC) of asymptomatic to mildly affected female FD-patients show different gene and protein expression compared to healthy female controls. Furthermore, FD-EC are already primed in vivo through persistent inflammation, showing reduced reaction to inflammation in vitro. Endothelial colony forming cells (ECFC) were isolated from female FD-patients and age-matched female controls and treated with 20ng/ml TNF? for 19h to induce inflammation. Expression of endothelium-relevant genes (vWF, IL-6, NOS3, VEGFA, F5, PROZ) was determined using RT-qPCR. ?Gal activity was determined fluorometrically. Proteomics were analyzed using nano HPLC-Q-TOF. ECFC of female FD-patients had decreased vWF-gene expression (FC=-2.2, 0.025) compared to control ECFC. TNF? treatment increased expression of VEGFA (FC= 1.91; p=0.014) and IL-6 (FC=3.25; p=0.016) and decreased expression of F5 (FC 1.65; p =0.035) in FD, whereas in controls it increased VEGFA- (FC=2.21; p=0.032) and IL-6 expression (FC=6.33; p=0.018). Upon inflammation, proteomics showed reduced expression of cell-adhesion molecules (ICAM1, VCAM1 and SELE) in FD patients compared to controls. TNF? treatment decreased ?Gal activity in both FD-patients (-19.9%, p=0.023) and controls (-32.4%, p=0.041). Primary ECFC of female FD-patients show an altered gene and protein expression profile and a different response to (re)inflammation compared to control ECFC. These results implicate altered endothelial function prior to onset of clinical symptoms.

**Stockner Alina**

Abstract ID: 119335

# Targeting the adipose tissue to treat heart failure with preserved ejection fraction

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Obesity is a main driver of heart failure with preserved ejection fraction (HFpEF), the predominant form of heart failure with diastolic dysfunction (DD) as the main clinical manifestation. Because obesity is associated with lipid accumulation in the heart the crosstalk between the white adipose tissue (WAT) and the heart is an emerging target for potential therapeutic interventions. In obesity, enhanced rates of lipolysis are linked with excessively available fatty acids, thereby causing lipotoxicity with detrimental effects on the myocardium. We hypothesize that interventions targeting lipolysis in WAT interrupt the fat-heart crosstalk, and effectively mitigate HFpEF induced by obesity and hypertension. Toward this end, we induced HFpEF in C57BL/6 mice by a combination of high-fat diet (HFD) and the nitric oxide synthase inhibitor L-NAME. A subset of mice with HFpEF was treated with Atglistatin (ATGLi) to inhibit adipose triglyceride lipase (ATGL), the rate-limiting enzyme of lipolysis, while mice fed standard chow served as control. Pair-fed animals and a group of mice that received HFD ad libitum were regularly weighed and subjected to cardiometabolic phenotyping and inflammatory profiling at the end of the feeding protocol. Mice fed HFD and L-NAME ad libitum developed obesity, hypertension and DD <U+0096> a hallmark of HFpEF. ATGLi treatment reduced obesity and improved DD, but failed to reduce blood pressure in mice with HFpEF. Furthermore, ATGLi supplementation lowered the levels of pro-inflammatory cytokines IL-6, TNF-? and IL-1? in WAT, indicating reduced obesity-induced inflammation. Taken together, results show that ATGLi improves several hallmarks of HFpEF. Future experiments will aim to elucidate mechanisms by which ATGLi exerts its beneficial cardiometabolic effects.

**Michaelis Simon**

Abstract ID: 119326

# Cerebrospinal fluid ferritin status in patients undergoing routine lumbar puncture <U+0096> first results

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Background/Aims Iron plays an important role in various pathways of the brain metabolism. Furthermore, a disturbance of the brain iron homeostasis is associated with neurodegenerative diseases, such as Parkinson's disease and Alzheimer<U+0092>s disease. However, the processes of iron transport from the systemic circulation to the brain across the blood-brain-barrier and the blood-cerebrospinal fluid (CSF)-barrier are not fully elucidated yet. Particularly, data about possible involvement of the iron-storage protein ferritin in the iron-transport across these barriers are scarce. Hence, the aim of this study was the assessment of the behavior of ferritin in the CSF in relation to the respective serum-ferritin levels.

Methods/Results Overall, 309 patients undergoing routine lumbar puncture were included in the study. Ferritin and albumin were measured in parallel in the serum and CSF using standard laboratory methods (electrochemiluminescence immunoassay and bromcresol green method). The ratios between the CSF- and serum-values for ferritin and albumin were calculated (QFerr and QAlb). QFerr showed a median of 0.057 (interquartile range 0.031-0.122). No statistically significant correlation between QFerr and QAlb was observed (Spearman<U+0092>s rho -0.099, p=0.082). Statistically significant correlations between ferritin in serum and CSF (Spearman<U+0092>s rho 0.411, p<0.001) and also between QFerr and serum-ferritin (Spearman<U+00B4> rho 0.882, p<0.001) were detected.

Conclusion The concentration of ferritin in the CSF is independent of the overall barrier function. A concentration-dependent transport mechanism for ferritin from the systemic circulation to the brain might be possible. In case of low serum-ferritin concentrations, the cerebral iron supply might be maintained by an upregulated ferritin transport across the CSF-barrier.

**Schwegel Nora**

Abstract ID: 119313

# Prognostic impact of echocardiographic functional parameters in patients with chronic heart failure

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Background Left ventricular ejection fraction (LVEF) provides only poor prognostic value in heart failure with reduced ejection fraction (HFrEF) and fails to give prognostic information in patients with an LVEF <35%.

Methods and results We enrolled 205 patients with HFrEF in a prospective single-center cohort study. All patients underwent a standardized echocardiographic examination. LVEF and left ventricular global longitudinal strain (LV GLS) were assessed using a vendor-independent post-processing software, blinded to patient<U+0092>s characteristics. Tricuspid annular plane systolic excursion (TAPSE), E/e<U+0092>, left atrial volume index (LAVI), and peak tricuspid regurgitation velocity (TRVmax) were measured during the examination. Univariate significant parameters were included in a multivariable COX-regression model comprising all patients (n=205) and a subgroup with LVEF <35% (n=81), respectively. The mean observation time was 56.3<U+00B1>8.3 months. The composite endpoint of unplanned hospitalization due to worsening heart failure (WHF) and death of cardiovascular cause occurred in 52 patients (25.4%): 45 patients (22.0%) had a WHF event and 7 patients (3.4%) died due to a cardiovascular cause. Age, LVEF, LV GLS, TAPSE, LAVI, TRVmax, atrial fibrillation, creatinine, and NT-proBNP met significance in univariate analysis. However, in a multivariable regression model only TAPSE and NT-proBNP remained independent prognostic parameters (HR TAPSE 0.91 (95%CI 0.84-0.98), p=0.013; NT-proBNP/1000 1.12 (95%CI 1.03-1.21), p=0.007). In patients with LVEF <35% only TAPSE remained as predictive parameter for the composite outcome (HR 0.89 (95%CI 0.80-0.98), p=0.019).

Conclusion Though HFrEF is considered as primarily a left ventricular pathology, left ventricular parameters provide poor prognostic value. TAPSE is found the best prognostic echocardiographic parameter for WHF and cardiovascular death in patients with HFrEF, especially when LVEF is lower than 35%.

**Zoidl Philipp**

Abstract ID: 119395

# The influence of tramadol on platelet function

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Background Tramadol is one of the most important opioids. In addition to the opioid effect, there is also an analgesic mechanism via the inhibition of the reuptake of serotonin. Serotonin also has an influence on blood clotting. While the bleeding risk of SNRIs in the psychiatric context as a consequence of serotonin-dependent reduced platelet aggregation is well known, interestingly, only few studies with contrary results can be found on the question of the influence of tramadol on this.

Methods/ Results The aim of our study was to quantify the effect of tramadol on platelet aggregation in an ex vivo study using optical aggregometry (LTA) on whole blood. After signing an informed consent form, 14 healthy volunteers (4 Female, median age 33,2y) donated 40 ml of blood. All volunteers stated that they were not taking any anticoagulants. A baseline platelet function was measured then tramadol was added in increasing concentrations (500, 1500, 4500 and 9000 ng/ml, which is considerably higher than the therapeutical plasma level of 100 - 1000ng/ml). The light transmittance was measured after the addition of ADP and the result described as % of maximum aggregation. We calculated the difference in per cent to the initial value of the respective test subjects. As these differences were normally distributed, an ANOVA test could be performed with SPSS. Tramadol in supratherapeutic doses caused a dose-dependent inhibition of platelets stimulated with 10 <U+00B5>M ADP. (c0 [0ng/ml]: 89,63% [85,89 <U+0096> 93,42%], c5 [9000 ng/ ml]: 85,81% [47,34 <U+0096> 88,16%], p < 0,05).

Conclusion Although a relatively small group of patients was tested in this study, we were able to confirm our hypothesis. Effects occur at doses considerably higher than the recommended plasma concentrations; further studies with larger numbers of cases should investigate whether these effects are also present at clinically relevant doses.

**Eichlseder Michael**

Abstract ID: 119433

# Association of changes in serum neurofilament light chain concentrations and postoperative cognitive dysfunction <U+0096> study design of a prospec-tive observa-tional study

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Introduction Postoperative cognitive dysfunction (POCD) occurs in approximately one third of the patients aged 65 and older who undergo major surgery. The pathogenesis of POCD is only partly understood and multifactorial. Serum neurofilament light chain (sNfL), a promising biomarker indicating neuro-axonal injury, has been associated with postoperative delirium. However, the relation between sNfL and POCD in the non-cardiac perioperative setting has not been studied until now. Therefore, we aimed to test the primary hypothesis that an increase in postoperative sNfL concentrations is associated with POCD one month after surgery.

Methods We will measure sNfL using a single molecule array (Simoa) preoperatively and on the third post-operative day in 180 patients undergoing major non-cardiac surgery at the Medical Uni-versities of Graz and Vienna. Neurocognitive testing, using the telephone version of the Mon-treal Cognitive Assessment, will be done preoperatively and one month, three months and one year after surgery. Furthermore, we eval-uate associations between perioperative sNfL kinet-ics and depth of anaesthesia (using bispectral index), intraoperative blood pressure and markers of perioperative inflammation (C-reactive protein, Interleukin-6, Procalcitonin).

Results Study enrollment started in July 2022 and 139 patients (mean age 72<U+00B1>5 years, 24% fe-male) have been included so far. POCD occurred in 17% of the patients who completed the 30 day follow up.

Discussion It was previously shown that patients with postoperative delirium have significantly elevated sNfL concentrations, indicating axonal damage. Interestingly, there was no significant change in sNfL val-ues when anaesthesia without surgery was performed. Furthermore, recently pub-lished data suggests an association between sNfL and POCD in cardiac surgery patients with cardiopulmonary bypass. Our study will allow for additional insights in the pathophysiology of POCD and its association with sNfL.

**Haidegger Melanie**

Abstract ID: 119305

# Frequency and risk factors of recurrent cerebrovascular events after recent small subcortical infarcts

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Background Cerebral small vessel disease (CSVD) is an important cause of (lacunar) ischaemic stroke, brain haemorrhage and dementia. Recent small subcortical infarcts (RSSI) are the neuroimaging hallmark feature of acute lacunar stroke. Data on long-term follow-up and recurrent cerebrovascular events (CVE) of RSSI patients is scarce. Methods This study retrospectively included consecutive ischaemic stroke patients diagnosed with an RSSI at University Hospital Graz between 2008 and 2013. Clinical and MRI parameters were compared between patients with and without recurrent CVE. Imaging features of CSVD such as lacunes, white matter hyperintensities (WMH), microbleeds and enlarged perivascular spaces and were rated on MRI. We also calculated a quantitative CSVD sum score combining different MRI features. Multivariable Cox regression adjusted for age, sex, vascular risk factors and MRI features was performed. Results We analysed 332 consecutive patients (mean age 68 years, 35.8% women). The mean follow-up time was 5.4 years (range: 0-14). A recurrent ischaemic CVE occurred in 70 patients (20.1%), an intracranial haemorrhage in 26 patients (7.8%). Diabetes (HR 2.36, 95% CI 1.44-3.88), presence of WMH (HR 1.87, 95% CI 1.06-3.29) and microbleeds (HR 2.13, 95% CI 1.25-3.66) at baseline MRI were related to recurrent ischaemic CVE, while only microbleeds increased the risk for haemorrhagic CVE (HR 2.87, 95% CI 1.22-6.75). The CSVD score was higher in patients with recurrent ischaemic (HR 1.27, 95% CI 1.04-1.55) and haemorrhagic cerebrovascular events (HR 1.48, 95% CI 1.05-2.05). Conclusion RSSI patients have a substantial risk for recurrent CVE during a mean follow-up period of more than 5 years. Our findings further highlight the importance of a structured secondary prevention protocol and control of risk factors in patients with RSSI and coexisting chronic CSVD features on MRI as the rate of recurrent CVE is particularly high in this subgroup.

**Maget Alexander**

Abstract ID: 119287

# Microbial and metabolic changes in depressive patients after probiotic supplementation

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The connection between gut microbiome and psychiatric entities has been a topic of interes in recent years. Via the microbiome-gut-brain axis different bidirectional pathways between microbiota and central nervous functions have been identified. Relevant factors include inflammation, intestinal and blood-brain-barrier permeability, and neuronal signaling via vagal stimulation. Depression is one of the most impactful psychiatric disorders, so additional ways of treatment are of high medical and economic interest. Interventions targeting the microbiome could be a well-tolerated addition to the treatment of affective disorders. In this study, we aimed to enrichen the knowledge on whether probiotic supplements would influence depressive symptoms in psychiatric patients and how they would alter composition and metabolic activity of the microbiome. During the PROVIT study, 82 subjects who were currently in-patients at a psychiatric ward received either a probiotic supplement (<U+0093>OMNi-BiOTiC<U+00AE> Stress Repair<U+0094>) or placebo for 28 days. We assessed clinical symptoms of depression using the Hamilton Depression Scale and the Beck Depression Inventory-II. Consequently, a whole genome SHOTGUN sequencing of 54 of these subjects using a NovaSeqSP 500 (PE250bp) cycle flow cell with a sequencing depth of 8,2 to 10 millions per sample was performed. Evaluation of the differentially abundant species, functions, and KEGG orthologies was conducted using linear discriminant analysis in conjunction with effect size (LEfSe) on the Huttenhower lab Galaxy server. To find species connected to probiotic use, MaAsLin2 analysis was performed, however, no notable species, functions, or KEGG orthologies were discovered. While Piphilin analysis indicated an upregulation of several relevant metabolites like thiamine, tryptophane, and interleukin-17, we did not find these alterations with our current analysis. We could not find evidence in support of probiotic supplementation for depression.

**Petracco Giulia**

Abstract ID: 119285

# Sex-dependent Effects of Environmental Enrichment in a Mouse Model of Ulcerative Colitis

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Background: Ulcerative colitis, a chronic inflammatory bowel disease, is often associated with mental health disorders exacerbated by chronic stress. Environmental enrichment (EE) has been shown to alleviate stress and inflammation in mice, therefore we hypothesized that it may mitigate the adverse behavioral and neurobiological outcomes associated with experimental colitis.

Methods/Results: Male and female mice were co-housed in groups of 20, before being divided into experimental groups<U+0097>one in conventional small cages (standard environment, SE) and the other in an enriched environment (EE; large cages containing various items) for 8 weeks. In both SE and EE subgroups experimental colitis was induced by using dextran-sulfate sodium (DSS; 1-1.5% w/v in drinking water), followed by behavioral testing and inflammation assessments of all groups. Results showed that male DSS-treated, EE-housed mice lost less weight, had a lower disease activity index (DAI) and presented reduced colonic inflammation compared to DSS-treated, SE-housed male mice. In contrast, DSS-treated females in EE exhibited more severe symptoms than corresponding females in SE, hinting at sex-dependent EE effects. Both male and female DSS-treated mice, irrespective of housing condition, displayed reduced locomotion in the open field test. DSS-treated males in SE showed less anxious behavior in the elevated plus maze compared to untreated SE males, an effect not observed in EE conditions. DSS-treated females displayed increased anxiety-like behavior and impaired social behavior regardless of housing.

Conclusion: In conclusion, EE appears to provide partial protection against experimental colitis in males, but exacerbates colonic inflammation in females. Further experiments will clarify whether sex hormones or other biological pathways contribute to the observed sex-dependent effects of EE.

**Fink Andrea**

Abstract ID: 119173

# Clinical characteristics, osteoporosis management and risk of refractures, complications and mortality among patients following treatment of osteoporotic hip fracture

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Background: Osteoporotic fractures are a major public health issue affecting every third postmenopausal woman and every fifth men aged 50 years and above. Most commonly the fractures are localized at the hip and carry an increased risk of refracture and premature mortality. Aim of the study is to explore the clinical characteristics and osteoporotic management as well as to determine risk factors of refracture, complications and mortality among patients following surgical treatment of osteoporotic hip fractures. Method/Results: A retrospective cohort-study of patients with osteoporotic hip fracture who underwent surgical treatment at the department of orthopaedics and trauma in Graz between January 2019 and December 2020 was conducted. Three dependent (refracture within two years, postoperative complication, death for any reason within two years) and a number of independent variables (e.g. general health status, specific lab values, surgical treatment, osteoporotic treatment) were defined and gathered through retrospective review of medical records. In total 661 patients with osteoporotic fracture were included in the study. The mean age was 81.2 years and 69.0% were female. The osteoporotic fracture was located in 49.4% of cases at the femoral neck, and most commonly treated with intramedullary nails (52.6%). 78.7% of patients suffered on a vitamin D3 deficiency. A systemic osteoporosis therapy was initiated in 1.05% of patients. 11.5 % of patients experienced postoperative complications and 16.2% a re-fracture within two years. Results of the multivariate regression analysis will be added until January 2024. Conclusion: Osteoporotic hip fractures are predominantly age-related, female and most commonly localized at the femoral neck. Most patients were not appropriately treated in respect of systemic osteoporotic therapies. The high refracture und mortality rate highlight the importance of adequate interventions especially in patients at high risk.

**Kinsky Rudolf Maximilian**

Abstract ID: 118868

# The Biomechanical Stability of a Novel Bioabsorbable Magnesium Alloy (ZX00:Mg-Zn-Ca) Bone Anchor for Rotator Cuff Repairs. A Human ex-vivo Study

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Abstract Background Aims: The purpose of this study was to ascertain the primary ex-vivo biomechanical stability of a novel bioabsorbable magnesium alloy (ZX00: Mg-Zn-Ca) bone anchor in human cadaveric proximal humeri, indicated in the reconstruction of the rotator cuff. Methods: 20 human Thiel-embalmed cadaveric humeri were prepared and freed from soft tissue. One 5.7 x 20.5-mm ZX00 anchor and one 5.5 mm x 16.3 mm Arthrex Titanium FT Corkscrew control anchor were inserted into the footprint of the supraspinatus tendon, 15 mm apart. The humeri were mounted onto a material testing machine and following a 40 N preload, cyclic loading was performed over 400 cycles. If the construct remained intact, ultimate load to failure was measured using an increasing axial load of 1 mm/s, ultimate load to failure and mode of failure were recorded. Results: No difference was found in ability to withstand cyclic loading, mode or load to failure strengths between ZX00 and control anchors. The maximum tractional force loaded for the ZX00 anchors had a median of 257.4 N (range 165.3 - 328.2). The corresponding value for the Arthrex Titanium FT Corkscrew anchors averaged 239.9 N (range 118.9 <U+0096> 306.7). Conclusion: ZX00 alloy anchors appear to provide adequate initial biomechanical stability when compared to an industry standard control in a cadaveric rotator cuff repair model. Keywords: Shoulder Injuries, Rotator Cuff Tear Arthropathy, Absorbable Implants, Experimental Implants, Magnesium, Alloys

**Tomic Josip**

Abstract ID: 118310

# Preclinical application of Mg- based bioresorbable material for orbital floor reconstruction in an animal model

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Introduction Orbital floor fractures are also known as blowout fractures that frequently result form blunt trauma to the face. The repair of orbital floor fractures is performed using titanium mesh, and bioresorbable polymers, each with its advantages and disadvantages. Magnesium materials provide advantages such as reduced implant weight and improved load transfer.

Material and Methods Six Tyrolean mountain sheep were included in this preclinical study. The surgical repair of the orbital floor was performed with the newly developed ZX00 magnesium implants between January 2023 and February 2023. The suitability of ZX00 magnesium implants was evaluated based on their intraoperative biomechanical behavior, and postoperative outcomes. Outcome measures included surgical complications and were assessed using regular examininations. Data analysis included descriptive statistics to identify factors accociated with good biomechanical and surgical performance. The sheep were monitored for a period of 12 weeks at the animal husbandry facility. Relevant parameters were assessed, including the gas volume of the magnesium implants.

Results This animal pilot study included a total of 6 sheep that underwent surgical intervention for controlled fractures in the orbits. No animal death or drop-out occurred prior to study termination. Fracture severity and location were similar in all study animals. Regarding surgical outcomes, sheep had three sheep had no surgical complications, such as infection, enophthalmus, exophthalmos, infection or bleeding at the last follow-up. Imaging studies showed that the magnesium orbital floor plates were present at the last follow up (postoperative week 12) and resorption over time, allowing for the restoration of the orbital floor's natural anatomy. No complications, such as infection, plate fractures or migration, were observed during the study period.

Conclusion In conclusion, this animal study demonstrates the suitability of magnesium orbital

**Lodron Julia**

Abstract ID: 120721

# Mental health, cognitive function and stress-related biomarkers in patients with Long COVID

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Background: Coronavirus disease 2019 (covid-19) has spread across the world since December 2019. The phenomenon of Long COVID, system duration > 4 weeks, has raised significant concerns about its impact on individuals, who often experience a range of mental health challenges including anxiety and depression. It is unclear to what extend reduced mental health before acute infection influences the disease process.

Aim: As a part of the overall study, we investigate the influence of pre-existing reduced mental health parameters such as anxiety and depression on developing Long-COVID. We also investigate the influence of a prolonged disease to cognitive functioning.

Method: This is a longitudinal, prospective, single-centre, observational cohort trial, including participants newly tested positive for SARS-CoV-2 infection by real-time quantitative polymerase chain reaction (qPCR) and reporting symptoms of acute COVID-19. A combination of clinical assessments, questionnaires, cognitive function tests and biomarker analysis is used. All study assessments are performed within a time period of six month after acute infection.

Results: First interim analysis is currently conducted. Data from a subgroup of 98 participants, including patients suffering from Long COVID matched to a health control group, will be presented on Doctoral Day 2024.

Conclusion: The results of this study will have implications for both clinical practice and public health interventions. This study contributes to understand the role of mental health as a risk factor for Long COVID. Thus, more targeted approaches to clinical and public health care interventions can be developed. Therefore, further research on interventions is necessary.

**Rijksen Marc**

Abstract ID: 120661

# Influence of protective factors on health outcome in acute and post-acute COVID-19

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The global impact of the COVID-19 pandemic on health has been substantial, resulting in diverse outcomes among infected individuals. While various risk factors have been identified, it is widely unknown why some people recover from the infection and return to usual health, while others continue to experience COVID-19 related symptoms. Up to now, little attention has been paid to protective factors in studies on the clinical course of disease after SARS-CoV-2 infection, such as resilience. This research aims to explore the influence of protective factors on health outcomes during both acute and post-acute (symptom duration ? 4 weeks) phases of COVID-19.

Through a prospective cohort study design including questionnaires, blood samples, cognitive tests, and psychological interviews, the study seeks to identify associations between protective factors and health outcomes.

The research primarily focuses on the role of resilience on physical outcomes such as symptom duration and number of newly developed symptoms during infection. Additionally, the connection between resilience and mental health outcomes will be determined considering confounding variables such as pre-existing health conditions, lifestyle choices and socio-economic factors.

Preliminary data, based on a six-month observation period of 244 individuals through regular questionnaires and additional insights from a subgroup of 98 people, will be presented on a poster in early 2024. Based on the analysis of resilience, it may lead to interventions supporting protective factors against COVID-19 and other viral diseases.

**Holter Magdalena**

Abstract ID: 120565

# Assessing patient activation in patients with macular edema

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Introduction

For patients suffering from a chronic disease engagement in their own health management is necessary to facilitate a better health outcome. It can be assessed by the Patient Activation Measure<U+00AE> (PAM) survey, which demonstrated to be a reliable and valid measurement tool in many different populations. The main objective is to investigate the psychometric properties of the German PAM survey<U+00AE> in patients with macular edema using item response theory (IRT).

Methods

Outpatients with macular edema participated in this questionnaire-based cross-sectional study. Patient activation was assessed by the PAM<U+00AE> survey. Self-rated health, self-efficacy, quality of life and general mood were measured as well. Questionnaires were read aloud to participating patients by interviewers.

PAM<U+00AE> data were analyzed with a generalized partial credit model. Further psychometric properties were explored by Cronbach<U+0092>s ? and trait-trait correlations.

Results

554 patients were included in the final analysis. 317 (57%) patients suffered from a macular edema due to diabetes, 224 (40%) due to retinal vein occlusion and 13 (2%) exhibited both types. The study sample showed a mean overall activation score of 74.1 (SD:13.7). All items showed ceiling effects. Test information is highest for low to middle ability range. Empirical reliability from the IRT model and Cronbach<U+0092>s ? were 0.75. The PAM<U+00AE> survey showed a Spearman correlation of 0.54 (p<.001) with self-efficacy, 0.51 (p<.001) with quality of life and 0.34 (p<.001) with general mood.

Discussion

Patient activation can be assessed with the PAM<U+00AE> survey in patients with macular edema. Results indicate that it is a reliable and valid measurement tool for this population.Patients with low patient activation are identified. Measurement quality deteriorates for those with high activation ability level, as PAM<U+00AE> items offer little information to distinguish between them.

**EBERL Anna-Sophie**

Abstract ID: 119476

# Incidence, types and predictors of AF recurrence after AF ablation with pulsed field ablation. A single centre experience.

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Background: Pulsed field ablation (PFA) is an emerging method for atrial fibrillation (AF) ablation. However, there is little data about incidence, types, and predictors of AF recurrences after PFA for AF ablation.

Methods: We report our single-centre experience with PFA for AF ablation using the Farapulse<U+00AE> system. Each procedure was performed under unconscious sedation with propofol and fentanyl. Before transeptal puncture 70IU/kg of unfractionated heparin were administered, for an ACT level >300sec during the entire procedure. Isolation of pulmonary veins was started after administration of 1mg of atropine with 8 applications per vein (4 in basket, 4 in flower configuration). Afterwards all veins were checked for entrance- and exitblock to confirm isolation during sinus rhythm. If needed, additional ablation was performed.

Results: In total, 165 patients were analysed. Mean age was 62<U+00B1>9 years, 40% were female. Mean CHADS-VASc Score was 2<U+00B1>1. In total 62% had paroxysmal AF, 38% persistent AF. In 84% (n=123) first pass isolation of all veins was possible. In addition to PVI, in 6% of patients cavo-tricuspid isthmus (CTI) was blocked, in another 6% the posterior wall was isolated during the first procedure. Mean procedure duration was 61<U+00B1>28 minutes, mean x-ray time 21<U+00B1>10 minutes. During 146 procedures, only one catheter associated complication was documented (vascular). Twenty-five patients (17%) had recurrence of dysrhythmia after a blanking period of 3 months after a mean follow-up period of 283<U+00B1>158 days. Mean time to recurrence was 128<U+00B1>114 days. Patients with recurrences suffered significantly more often from diabetes (OR 4,419 (1,096-17,8220; p<0.05)). There was no statistically significant difference in baseline data, except the type of AF (p<0,05).

Conclusion: AF ablation with PFA is associated with high success rate, and acceptable procedure duration and complication rates. RCTs are needed to further evaluate this new method.

**Baumann Petra Martina**

Abstract ID: 119410

# Development of short-, medium- and long-term solutions to import raw CGM data in a multitude of formats for clinical research.

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Background/Aims Continuous glucose monitoring (CGM) provides more detailed information on glycaemic control than blood glucose (BG) measurements because they provide glucose data every 5-15 minutes in real-time. In addition to the individual benefit for each person living with diabetes and healthcare professionals in daily routine and clinical care, CGM data are also relevant for research.

For many retrospective studies, participants provide real-life data by sending records manually or by granting third-party access to their user accounts on the respective manufacturer<U+0092>s website. Thus, data arrive at the site in multiple formats and importing, harmonising and validating can take (much) longer than anticipated. Sometimes, data may even have to be excluded from further statistical analysis.

Method/Results CGM data typically arrive as CSV, sometimes as XLSX or TXT files. Moreover, there are different table formats within the respective file formats: differing numbers of header rows to be excluded, different places where the anonymised participant ID can be found, or different column names in German or English. To deal with this, we came up with short-, medium- and long-term solutions. We first developed and tested project-specific R scripts to import the current data quickly within one project. With every new project, we aimed at re-using and adapting these scripts and only develop new scripts if necessary. We then collected all scripts into a library for 10+ different file and data formats. Finally, we switched to Python and started to develop a general parser which will be able to import CGM data in any format in the future. The parser is work in progress but has already proven successful with all previously used CSV files.

Conclusion Our approach balances project demands and the desire for leaner long-term solutions. The short and medium-term solutions in R enabled timely work and, since they had been validated, are used to evaluate the new Python program.

**List Wolfgang**

Abstract ID: 119303

# Prospective randomized intraindividual comparison of digital and manual marking of the axis in refractive surgery for myopic astigmatic eyes with toric phakic intraocular lenses

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Aims/Background: Refractive errors such as myopia, hyperopia, and astigmatism can be permanently corrected by surgical refractive procedures. In cases where keratorefractive laser is not feasible, phakic intraocular lenses (pIOLs) can be implanted. Toric pIOLs require precise alignment to achieve optimal astigmatic correction. This study aims to compare the outcomes of digital axis marking using the Callisto eye system with manual axis marking for toric pIOL implantation in terms of visual and refractive outcomes and pIOL rotation stability. Methods/Results: This prospective, randomized, controlled, intraindividual study involves 20 patients aged 20 to 60 years with a significant refractive astigmatism (?0.5 D). The study includes two groups differentiating in the sequence of axis marking. The mean alignment error 3 months postoperatively did not differ between the groups <U+0096> in the digital marking group 2.8<U+00B1>3.1 degrees (0 to 10) and 3.6<U+00B1>4.0 degrees (0 to 11) in the manual marking group, respectively (p=0.537). Change in best corrected visual acuity (BCVA) in digital marking was logMAR -0.06<U+00B1>0.07 (0.1 to -0.1) with a total sum of change -1.2 and logMAR -0.07<U+00B1>0.07 (0.1 to -0.2) with a total sum of change -1.3 in manual marking. Residual refractive error in the digital marking group was SE -0.04<U+00B1>0.26 dpt (-0.25 to +0.25) <U+0096> occurring in 3 eyes; and in the manual marking group SE -0.21<U+00B1>0.5 dpt (-1.0 to +0.25) <U+0096> occurring in 5 eyes. Residual refractive astigmatism was 0,63<U+00B1>0,18 dpt (0,5-0,75) in digital marking (N=2) and 0.5<U+00B1>0 dpt (0,5-0,5) in manual marking (N=2). In one eye following digital marking a postoperative realignment by rotation of the pIOL was necessary. Discussion: This study could demonstrate that digital axis marking and manual axis marking show comparable results regarding postoperative axis alignment error and visual and refractive outcomes.

**Wegscheider Thomas**

Abstract ID: 119297

# Rapid Response Systems (RRS) in the in-hospital emergency management: Selected results of a RRS pre-implementation analysis

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Background Up to 20% of all hospitalized patients are affected by critical events during their hospital stay(1). RRS aim to avoid critical events by detecting and treating patients at risk early. In 2015 a RRS has been implemented at the Department of Ophthalmology at the University Hospital of Graz.

Method The RRS implementation was preceded by a pre-implementation analysis using a tablet-based offline questionnaire survey. During a two-week survey period, hospital staff answered questions about their satisfaction with their preparation for emergency situations and their knowledge and skills in the area of Basic Life Support (BLS).

Results 112 people took part in the survey. 91 data sets were analyzed. 56% came from senior nursing staff, 2.2% of whom had special training in anesthesia care, 20.9% from nursing assistants, 5.5% from medical-technical staff, 3.3% from technical and 6.6% from administrative staff, 2.2% from residents and 5.5% from specialists. 2.2% rated their BLS knowledge as “Very good”, 21.9% as “Good”. 63.7% stated that they had “fair” knowledge in this area, 9.9% rated their BLS knowledge as “poor” and 2.2% as “very poor”. No one rated their BLS skills as “Very good”, 19.8% rated them as “Good”, 65.9% as “Average”, 13.2% as “Poor” and in one case as “Very poor”. 15 participants rated their employer as providing “very good” preparation. 40 staff members rated their employer’s efforts to prepare them for emergency situations as “good”, 27 as “average”, 8 as “poor” and one as “very poor”.

Conclusion There is a need for emergency medicine training programs for in-hospital personnel. Accordingly, the RRS implementation was accompanied by such a program.

Literature 1. Jones D, Bellomo R. Introduction of a rapid response system: why we are glad we MET. Crit Care. 2006;10(1):121. doi:10.1186/cc4841.

**Medic Nika**

Abstract ID: 119172

# Evaluation of tear evaporation rates measured with the VapoMeter: Fit for the routine?

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Tear film plays an important role in the pathology of dry eye disease (DED). Since evaporation accounts for up to 40% of tear loss, there have been many efforts made to measure the tear evaporation rate (TER). TER measurement is not standardised. We have decided to perform evaporation measurements with the VapoMeter (Delfin Technologies, Finland) because of its ease of use in comparison to other devices.

We hypothesise that TERs in DED patients is higher than those in healthy individuals, and that TER correlates with other tear film and ocular surface parameters. Our aim is to determine the TER in a routine clinical setting with a method, which is simple, practical and comfortable for the patient.

According to the available data, the average TER values in spontaneous blinking eyes are by 45% lower in the control group (126 g/m2/h) compared to the DED patients (231 g/m2/h). Similarly, the average TER in opened eyes is by 46% lower in the control group (137 g/m2/h) compared to the DED patients (254 g/m2/h). TER in closed eyes is lower by 41% in the control group (59 g/m2/h) compared to the patients group (100 g/m2/h).

Our interim analysis showed higher TER values in DED patients compared to the healthy controls. A detailed analysis of the correlation between TER values and other DED parameters will be performed, including eye blinking pattern (EBP). An incomplete EBP suggesting weaker closing of the eyelids is often observed in DED patients. If this will be observed in our patients, it could explain the higher TERs in closed eyes in the patient group compared to healthy individuals.

**Mihalic Zala Nikita**

Abstract ID: 118797

# Neutrophil proteome atlas in first trimester pregnancy

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Objectives: Pregnancy is an immunological challenge for mother and fetus, and the establishment of immune tolerance at the feto-maternal interface is essential for normal pregnancy development. Our study aims to elucidate neutrophil subpopulations, functions and interactions in decidua basalis (DB) of first trimester pregnancies. Methods: Using multiplex flow cytometry we evaluated neutrophil subpopulations in DB in comparison to DP and blood from first trimester elective abortion samples. To evaluate whether neutrophil function is modulated at the feto-maternal interface we measured NETosis, ROS production and degranulation of healthy blood neutrophils after stimulation with tissue explant supernatants. Further, to investigate tissue localisation we performed imaging mass cytometry. Results: Preliminary data suggest abundant neutrophil infiltration in DB, whereas there is very low infiltration of neutrophils in DP. We identified 58 differentially expressed surface proteins on neutrophils infiltrating DB in comparison to blood neutrophils and neutrophils infiltrating DP. In addition, we selected 30 surface, which were further validated on higher number of samples (N=9). Neutrophils in tissue exert different phenotype in comparison to blood and cluster into three distinct subtypes. We could confirm that tissue supernatants stimulate neutrophils into activated state, which resulted in more ROS production and NET formation. Conclusion: Our study comprehends a detailed picture of the immune landscape and specific surface protein expression pattern at the feto-maternal interface in the first trimester pregnancy, with the focus on neutrophils. Further, it reveals the role of neutrophils in maintaining immune tolerance at this critical state. To our knowledge, this is the first study that focuses on the specific subpopulation of neutrophils infiltrating DB as well as their function and interaction with other cell populations.

**Krenn Cornelia**

Abstract ID: 118528

# User-centered customization options in consumer health information materials on type 2 diabetes mellitus - an analysis of modifiable features in different types of media

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Background: Communicating understandable health information to consumers is challenging as they have varying health statuses, prior disease knowledge, personal abilities, information needs and preferences. However, comprehensible consumer health information is essential in health care as they form the basis for informed shared decision-making. Aim: The aim of our research was to analyze different consumer health information materials (CHIMs) on type 2 diabetes mellitus regarding user-centered customization options. We hypothesized that current CHIMs offer limited opportunities to tailor the information to meet specific needs and preferences of consumers. Methods: To obtain a representative sample of currently used modifiable features, we searched different media types, such as websites, apps, videos, and printed/printable media. We sequentially analyzed blocks of randomly selected CHIMs (one from each of the predefined media types) until data saturation of extracted modifiable features was reached. Results: In our representative sample of 114 CHIMs, we identified a total of 24 modifiable features, which we grouped into five main categories: (1) language, (2) text, (3) audiovisual, (4) presentation, and (5) medical content. Videos provided the most customization options (95%), while we could not determine any possibilities for users to adjust printed/printable formats. We could identify any form of customization in 47% of websites and 26% of apps. Overall, almost 65% of the included CHIMs did not offer any customization option. Conclusion: We conclude that current CHIMs are mainly offered with a <U+0091>one-size-fits-all<U+0092> approach, i.e. presenting content statically. We suggest that CHIMs can be improved by offering greater opportunities for users to adjust them according to their needs. In a next step, we will develop a toolbox describing user-centered customization options available for different CHIMs, intended to inform developers of CHIMs about these possibilities.

**Tsiountsioura Melina**

Abstract ID: 118380

# Anti-coagulatory and anti-oxidative effects of powdered fruit, vegetable and berry juice concentrates.

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Introduction Micronutrients are involved in many important functions of the human body and an adequate intake is necessary for optimal health. They could be supplied either by the intake of food or through supplements. The aim of this in-vitro study was to examine the anti-coagulatory as well as the anti-oxidative properties of four supplements, namely a fruit, a vegetable and a berry powder concentrate, and a powder concentrate containing a combination of the three (FVB). Method Dried extracts were resuspended with NaCl solution, left in an ultrasonic bath, rotated for 30 min in a rotary shaker, and centrifuged. Their anti-oxidative properties were estimated via their capability to attenuate the Cu2+-induced oxidation of low-density lipoprotein (LDL). The anti-coagulatory properties of the concentrates were estimated via thrombelastometry (TEM) and platelet aggregation measurements, performed in whole blood samples. Thrombin generation was assessed by using calibrated automated thrombogram (CAT). Results The berry concentrate most efficiently impeded the Cu2+-induced LDL oxidation and thus, possessed the highest antioxidant capacity, followed by the FVB concentrate. The vegetable and fruit concentrates had only low antioxidant capacities. Correspondingly, the berry concentrate exerted the most efficient anticoagulant action. The TEM-value Coagulation time was significantly prolonged from 218<U+00B1>18 to 249<U+00B1>23s (P=0.017) and the Impedance Aggregation value Amplitude was significantly decreased from 13<U+00B1>1.7 to 4.3<U+00B1>1.5ohm (P=0.017) by the berry concentrate. CAT measurements revealed that the berry concentrate is able to inhibit the thrombin activity in plasma samples. The fruit, vegetable and FVB concentrate affected all the coagulation parameters to a much lesser degree. Conclusion Our in-vitro study indicates that particularly the berry concentrate has potent anti-coagulatory as well as anti-oxidative properties. A clinical trial is underway for assessing in vivo effects.

**Pfurtscheller Daniel**

Abstract ID: 115803

# Arterial Blood Pressure and Cerebral Oxygenation during the Immediate Neonatal Transition after birth <U+0096> A Prospective Observational Study

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Background and Aims: The aim of this study was to investigate the influence of arterial blood pressure on cerebral tissue oxygenation index (cTOI) and cerebral fractional tissue oxygen extraction (cFTOE) in preterm and term neonates during the immediate neonatal transition after birth.

Methods: For this purpose, we conducted a prospective observational study. Neonates received oscillometric blood pressure measurements at minutes 5, 10, and 15 after birth , and continuous cTOI monitoring with near-infrared spectroscopy and continuous monitoring of arterial oxygen saturation (SpO2) with pulse oximetry during the first 15 minutes after birth. cFTOE was calculated out of cTOI and SpO2 . Preterm neonates receiving respiratory support and term neonates without medical support (control group) were analyzed. cTOI and cFTOE at minutes 5, 10, and 15 were correlated to systolic (SABP), diastolic (DABP), and mean arterial blood pressure (MABP) in both groups.

Results: In the 24 included preterm neonates (gestational age 34.4 weeks (33.7 - 35.1)) requiring respiratory support, cTOI correlated positively with DABP at minute 5 and with MABP and SABP at minute 15. cFTOE correlated negatively with all blood pressure values at minutes 5, 10 and 15. In the 51 included stable term neonates (gestational age 38.7 weeks (38.4 - 39.0)), blood pressure values did not correlate with crSO2 nor cFTOE at any time point (Table1).

Conclusion: In compromised preterm neonates requiring respiratory support, crSO2 and cFTOE were associated with arterial blood pressure at different time points during the first 15 minutes after birth, while no such associations were observed in stable term neonates.

**Lederer-Hutsteiner Thomas**

Abstract ID: 115559

# Prevalence and correlates of internet-related addictive behaviour among Styrian pupils

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Background: The ubiquitous availability of Internet-based applications through mobile digital devices is associated with ever-increasing hours of use, especially among adolescents and young adults. The increasing societal concern is related to the addictive dimension of their excessive use, as well as to other associated health impairments such as sleep disorders, myopia, obesity, anxiety disorders, etc. The aim of this dissertation project is to provide evidence-based support for policy planning processes, which are in Austria currently severely complicated by a lack of data.

Aims: For this purpose, an accurate prevalence estimate and an analysis of the risk and protective factors associated with internet-related addictive behaviour will be conducted.

Methods: A secondary data analysis is carried out on the basis of an existing data set from a representative survey in spring 2022 of almost 3,000 pupils in Styrian schools from 7th grade onwards (x-sample, 2023). The sample is based on a stratified and gender-balanced one-stage cluster sample. 201 school classes were randomly selected. The online survey, which was supervised by teachers, was finally carried out in 175 classes, which corresponds to a participation rate of 87.1%. The questionnaire as the main material contained a set of existing screening instruments and self-constructed items representing all outcome and predictive constructs within this dissertation project.

Results: Prevalences are high, not only for Internet-related addictive behaviour (about one third), but also for anxiety (about one fourth) and sleep impairments (about one fifths with moderate or strong clinical relevance), indicating a widespread unstable psychosocial constitution within the target group examined.

Conclusion: In short, the findings show a clear need not only for addiction-based policy planning and decision-making processes at the level of prevention and care, but also for turning it into a public health issue.

**Benedikt Martin**

Abstract ID: 112257

# Impact of the SGLT2-inhibitor Empagliflozin on inflammatory biomarkers in acute myocardial infarction <U+0096> a post-hoc analysis of the EMMY trial

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Inflammation plays a crucial role in the formation and progression of atherosclerotic plaques. Among others, cytokines (interleukins [IL]) and acute phase reactants (c-reactive protein) are involved in the inflammatory atherosclerotic process. The recently published EMMY trial was the first clinical trial worldwide showing significant reduction in NT-proBNP levels in patients after AMI for empagliflozin compared to placebo independent of diabetic status. However, data about the potential impact of SGLT2-inhibitors on inflammatory biomarkers in ACS are scarce.

The EMMY trial was a 1:1 randomized, multicentre, investigator-initiated, double-blind, and placebo-controlled trial investigating potential effects of the SGLT2-inhibitor empagliflozin on structural as well as functional cardiac parameters and heart failure biomarkers in patients with acute coronary syndrome compared to placebo. In this post-hoc analysis, we performed a complete analysis of the inflammatory biomarkers in all patients participating in the EMMY trial with available frozen samples. In addition, inflammatory biomarker were analysed on the background of structural and functional cardiac parameters, biomarkers, baseline characteristics and treatment effects.

At baseline elevated levels of inflammatory biomarkers were observed in both groups but without significant differences between the groups. From baseline to week 26, a significant decline in inflammatory parameters was observed in both groups, but no significant differences in IL-6 (p=0.475), hs-CRP (p=0.457), neutrophils (p=0.796), leukocytes (p=0.637), and neutrophil-lymphocyte ratio (p=0.577) decline was observed between groups. Neither structural or functional cardiac parameters nor eGFR, NTproBNP or troponin showed significant interactions with inflammatory parameters.

Trajectories of inflammatory biomarkers (hs-crp, IL-6, leukocytes, neutrophils, NLR) showed a pronounced decline after MI but were not different between the groups.

## Talk Session V

### Pichler Alexander

Abstract ID: 119328

# Tryptophan recovery index as a new biomarker for fitness

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Introduction The maximal oxygen uptake (VO2max) and maximal power output (Pmax) are commonly used parameters to evaluate the endurance fitness status. A connection between exercise and the kynurenine pathway (KP), which describes the metabolism of unused tryptophan, has already been reported. However, a potential association of the KP with endurance fitness levels remains unknown.

Methods In this study, adolescent competitive athletes performed an exhaustive incremental exercise test. Blood samples were taken before, directly after, and 30 minutes after the end of exercise. Tryptophan (Trp), kynurenine (Kyn) and kynurenic acid (KA) serum levels were determined by high-performance liquid chromatography (HPLC).

Results Forty-four male and 27 female athletes (median age: 16 years) were recruited. During exhaustive exercise tests, Trp initially declined and then increased 30 minutes after discontinuing exercise. Similar findings were observed for Kyn, whereas KA levels behaved inversely. After incremental exhaustive exercise the relative increase of Trp concentrations, termed the tryptophan-recovery-index (TRI), showed a highly significant positive correlation with VO2max and Pmax (r=0.468 and 0.491, p-values <0.001). There was a significant gender-difference with higher levels of all metabolites at all measured time points in male participants.

Discussion In the present study, a highly significant correlation was found between the TRI and the maximal oxygen uptake in well-trained athletes. The implementation of TRI can therefore be suggested as a biomarker for physical fitness.

Reference Pichler, A., Meinitzer, A., Enko, D., Schober, P., Singer, G., Castellani, C., Herrmann, M., Holasek, S. J., Till, H. and Windhaber, J. M. (2022) <U+0093>Tryptophan recovery index as a new biomarker for fitness<U+0094>, EXCLI Journal, 21, pp. 888<U+0096>896. doi: 10.17179/excli2022-4889.

**Falb Thomas**

Abstract ID: 119282

# The impact of intraretinal cystoid fluid and foveal anatomy on visual acuity in macular edema

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Background/Aims: Optical Coherence Tomography (OCT) has been a major game changer as a diagnostic procedure in retinal pathologies. With OCT, high-resolution in vivo images of the retina can be obtained and measured. Measurements within these images can be used as biomarkers to predict retinal functionality and outcomes after treatments. Aim of this study is to evaluate the association between intraretinal cystoid fluid (IRC) and retinal functionality in patients with macular edema due to retinal vein occlusion (RVO) or diabetic maculopathy (DMP), and to explore a potential impact of the foveal gap (FG) of inner retinal layers upon this association. Methods: Patients, who were newly diagnosed with RVO or DMP and scheduled for treatment through intravitreal injections (IVI) with anti-VEGF were included into the study. Best corrected visual acuity was done through Early Treatment of Diabetic Retinopathy (EDTRS) Charts by masked investigators before treatment and after resolution of IRC, or at the latest, 6 months after first treatment. For statistical analyses, IRC height was grouped as ?350<U+00B5>m and >350<U+00B5>m, foveal gap (FG) was grouped as ?200<U+00B5>m and >200<U+00B5>m. Results: 61 patients successfully finished the study. Mean age was 67.26 years, mean IRC height was 269.98<U+00B5>m, successfully read EDTRS letters changed from 37.66 at baseline towards 46.54 at endvisit. Mean EDTRS letters at baseline were 39.68 for IRC ?350<U+00B5>m vs. 31.85 for IRC >350<U+00B5>m and 33.14 vs. 39.09 for FG ?200<U+00B5>m and >200<U+00B5>m respectively. Mean EDTRS letters at endvisit were 49.26 for IRC ?350<U+00B5>m vs. 41.14 for IRC >350<U+00B5>m and 45.07 vs. 47.48 for FG ?200<U+00B5>m and >200<U+00B5>m respectively. Conclusion: Visual acuity was worse with higher intraretinal cystoid fluid height and smaller foveal gap at baseline and endvisit.

**Pichlsberger Melanie**

Abstract ID: 118619

# Testing of wound dressing materials for colonization with mesenchymal stromal cells

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Background/Aims: Healing of chronic wounds is still a challenge in medical care. A promising approach for the improvement in wound management are stem cell-based therapies and in particular the use of degradable wound dressings populated with stem cells. The aim of this study was to compare natural fish skin material (FS) with electrospun synthetic polycaprolactone/polylactide (PCL/PLA) materials regarding to their suitability as carriers for colonialization with mesenchymal stem/stromal cells (MSC).

Method/Results: FS and PCL/PLA were seeded with MSC derived from the human amniotic membrane or from adipose tissue. Due to anti-adhesive properties, the PCL/PLA has to be pretreated by consecutive incubation in 70% ethanol, ethanol/culture medium 1:1, and pure culture medium to allow successful seeding of cells. In contrast, FS material was easy to handle, as it immediately absorbed the applied cell suspension. After the incubation period for 3 and 8 days in vitro, cell growth, infiltration, proliferation and apoptosis of the MSC were assessed using histological examinations. MSC adhered to and infiltrated both FS and PCL/PLA, and showed a multilayered cell growth on day 3 and day 8. Most cells remained at the apical surface of the materials. FS and PCL/PLA displayed a similar percentage of proliferating cells (detected by anti-Ki 67) during whole incubation time. Interestingly, hardly any apoptotic cells were observed on FS, whereas PCL/PLA showed an increase of Caspase-8 positive apoptotic cells from day 3 to day 8 (13.7 <U+00B1> 0.9% versus 26.9 <U+00B1> 1.8% apoptotic cells). On day 8, the total cell number of MSC decreased on PCL/PLA as opposed to FS.

Conclusion: This study showed that both PCL/PLA and FS may be used as promising skin substitutes in wound healing. Due to the easy handling and the anti-apoptotic properties, FS may be more suitable for therapeutical treatment than PCL/PLA, but this has to be confirmed in future pre-clinical and clinical studies.

## Talk Session VI

### Toledo-Marcos Juan

Abstract ID: 119434

# Structural Targeting of STIM1-Orai Interface: Crafting Peptide Inhibitors for CRAC Channel

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Calcium ions serve as pivotal intracellular messengers in eukaryotic cells, impacting cell proliferation, growth, muscle contraction, immune cell activation, and apoptosis. The calcium-release activated channels (CRAC) at endoplasmic reticulum-plasma membrane junctions involve Orai1 and STIM1. STIM1 binding to Orai1, particularly at the C-terminus, activates store-operated Ca2+ entry (SOCE). In 2013, the NMR structure revealed the interaction between Orai1 C-terminal peptide and STIM1 coiled-coils, providing a basis for designing potential SOCE inhibitors. This PhD project aims to develop potent peptide inhibitors of CRAC at the STIM1-Orai interaction level. Various STIM1-based ?-helical macrocyclic peptides and the Orai C-terminal peptide were synthesized. In this sense, the characterization of the binding of STIM1-based macrocycles and the Orai C-terminal peptide was conducted using 1H-NMR and isothermal titration calorimetry, showing evidence of binding. Furthermore, the synthetic Orai C-terminal peptide successfully inhibited SOCE in HEK cells after optimizing peptide formulation for cell penetration. However, the concentration required for inhibition remains impractical for pharmacological use. Ongoing efforts involve improving the peptide sequence for enhanced binding. Work is underway to express and purify the STIM1 domain involved in binding with Orai, providing insights into the interaction's structure and strength. A binding assay using microscale thermophoresis (MST) is in progress, showing promising preliminary results. In conclusion, while macrocycles bind to interacting partners and the Orai C-terminal peptide inhibits SOCE, further experiments are crucial for understanding and enhancing the interaction for potential pharmacological applications. These findings contribute to knowledge in cellular signaling pathways and may lead to targeted therapies for conditions influenced by aberrant calcium signaling.

**Spiegl Benjamin**

Abstract ID: 118148

# GCparagon: Evaluating and correcting GC biases in cell-free DNA at the fragment level

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Analyses of cell-free DNA (cfDNA) are increasingly being employed for various diagnostic and research applications. Many technologies aim to increase resolution, e.g., for detecting early-stage cancer or minimal residual disease. However, these efforts can be confounded by inherent base composition biases of cfDNA analyses, specifically the over- and under-representation of Guanine (G) and Cytosine (C) rich sequences. For sequencing data there is currently no universally applicable tool available to correct these effects for individual cfDNA fragments.

We present GCparagon, a two-stage algorithm for computing and correcting GC biases in sequencing data of cfDNA samples. In the initial step, length and GC base count parameters are determined. Here, our algorithm minimizes the inclusion of known problematic genomic regions, such as low-mappability regions, in its calculations. Expected fragment attribute distributions are simulated for each processed genomic interval. GCparagon uses observed and expected values to compute weights for cfDNA fragments to counterbalance the observed distortion of cfDNA attributes. Correction weights are output as a correction matrix in compressed text format. In an optional second step, these weights can be added as alignment tags to each sequence read alignment of the input binary alignment map (BAM file). Both the GC bias matrix and the tagged BAM file can be used for downstream analyses. Parallel computing allows for a GC bias computation in less than a minute and bias correction in less than 30 minutes for 0.1-60x whole genome sequenced cfDNA samples.

We show that GCparagon greatly improves the analysis of regulatory regions, which often have specific GC compositional patterns. GCparagon is therefore suitable to contribute to the establishment of standardized cfDNA applications.

**Reindl Marco**

Abstract ID: 119090

# Magnetic molecularly imprinted polymers as devices to remove limonin selectively from lemon juice

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Lemon juice, a popular fruit beverage rich in nutrients, faces taste deterioration due to the bitterness of limonin, prompting juice manufacturers to seek alternatives to the non-economic, time-intensive resin adsorption technique for the reduction of the limonin content. The demand for an efficient, cost-effective, and resource-saving approach has grown, especially considering limonin's potential anti-inflammatory properties, making its removal crucial for both the food and pharmaceutical industries.

Building on previous success in synthesising fructose-binding molecularly imprinted polymers (MIPs), we aim to merge MIP selectivity with the superparamagnetic property of iron oxide nanoparticles (IONPs) to streamline limonin removal. Successful silica and IONP functionalisation with amine and carboxyl groups has laid the groundwork for IONP@MIPs synthesis. Initially, acryloyl chloride is employed to introduce acryl groups onto IONP surfaces, allowing direct MIP synthesis on the nanoparticles. Limonin and methacrylic acid create a pre-polymerisation complex, initiating free radical polymerisation using ammonium persulfate and N,N,N?,N?-Tetramethyl ethylenediamine. MIP specificity to limonin stems from non-covalent interactions with the functional monomer, methacrylic acid.

Comprehensive IONP@MIP characterisation involves Fourier-transform infrared spectroscopy for nanoparticle composition analysis; dynamic light scattering and transmission electron microscopy for morphology and dimensions. HPLC will assess IONP@MIP performance and adsorption capacity in limonin solutions and lemon juice matrices. Based on published results, an expected adsorption capacity between 25 and 35 mg/g should sufficiently deplete limonin from lemon juice.

The ultimate goal is to scale up this system for industrial application, offering a superior method for limonin removal from lemon juice and an efficient means of obtaining limonin for medical applications concurrently.

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