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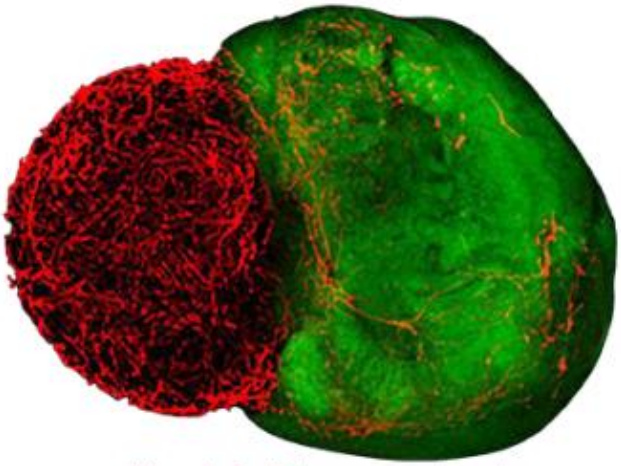

Vascularized Neuro-mesodermal
Assembloid

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am Institut für Anatomie und Zellbiologie
der Universität Würzburg

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an abstract of interest

please use the alphabetical list of

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Poster 1:

Title:
Induction of small heat shock protein HspB5/alphaB-crystallin by celastrol

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Abstract:
We previously identified enhancement of neuronal dendritic complexity as a new function of the small heat shock protein HspB5/alphaB-crystallin. As rarefaction of the dendritic tree is common in many neurodegenerative diseases, upregulation of HspB5 might be neuroprotective and a suitable target for developing new therapeutic approaches. Therefore, we conducted a literature search to identify promising chemical compounds already known to induce other Hsps, e.g. Hsp70. We selected four compounds (arimoclomol, geranylgeranylacetone (GGA), curcumin and celastrol) for testing their effect on HspB5 in cultured rat hippocampal neurons.
First, cultured neurons were treated up to 72h with different concentrations of the selected compounds and toxicity was assessed by LDH assay. Subsequently, the highest sublethal concentrations were used and HspB5 as well as Hsp70 protein amount was measured by western blot.
Of the four compounds, only celastrol (0.5µM) reliably increased the HspB5 amount while arimoclomol, GGA and curcumin did not. This HspB5 increase peaked 24h after single treatment with a subsequent decrease to control levels within 7 days. For evaluation of the effect of a long-term celastrol application the concentration was reduced. Recurrent treatment every 24h with 0.125 or 0.25 µM celastrol resulted in a strong, lasting HspB5 increase. Immunofluorescent staining of the cultures revealed that HspB5 was induced in neurons as well as in glia.
In conclusion, celastrol is able to induce the small heat shock protein HspB5 in rat hippocampal neurons and is therefore a promising candidate for further analysis of a possible neuroprotective activity.

Poster 2:

Title:
Influence of propionic acid and Air-Liquid-Interface Cultivation (ALI) on the metabolism of the intestinal porcine epithelial cells (IPEC-J2)

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Abstract:
The impact of the microbiome on human health is an area of increasing interest. Short chain fatty acids (SCFAs), the main metabolites produced by bacterial fermentation of dietary fibre in the gastrointestinal tract, support epithelial integrity and exhibit anti-inflammatory effects, which are potentially clinically relevant for different disorders like Colitis ulcerosa, Crohn's disease and Multiple Sclerosis.
Air-liquid cultured (ALI) intestinal porcine epithelial cells (IPEC-J2) have shown to be a highly valuable model system. We investigated the effect of propionic acid and glucose on the cell metabolism with a Seahorse analyzer but also the FFAR expression with immunostaining and western blot analysis.
Reduction of glucose leads to a collapse of epithelial integrity, which presumably can be explained by ATP depletion. ALI cultivation was shown to ameliorate this effect, thus exerting a protective effect. NDUFA4, which is a subunit of cytochrome C oxidase, was detected for the first time in porcine cell and is regulated by glucose. In addition, extracellular flux analysis demonstrated reduced extracellular acidification (ECAR) by ALI and by the addition of propionate. We detected FFAR2 and FFAR 3 in IPEC-J2 via western blot analysis and immunofluorescence staining, but no significant differences were found with or without propionic acid.
A reduced ECAR in ALI cultures indicate an oxidative-orientated metabolic phenotype combined with a reduced anaerobic glycolysis. Our results emphasise the essential role of ALI cultivation to improve cell culture model quality and the potential positive benefits of propionic acid.

Poster 3:

Title:
Thermosensitive TRP channels in the human meibomian gland

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Abstract:
Hyperevaporation of the tear film is the leading cause of Dry Eye Disease (DED), often caused by a dysfunction of the Meibomian Gland (MGD), for which there are no pharmacological treatment options.
The transient receptor potential (TRP) channels are new pharmacological targets in various fields. They play an important role in the calcium regulation of cells and take part in several signaling pathways. This study was conducted to investigate the properties of temperature-sensitive TRPs in the Meibomian gland (MG).
The expression of thermosensitive TRP channels was analysed in immortalized human meibomian gland epithelial cells (hMGECs), murine and human MG tissue by RT-PCR, western blot and immunofluorescence. Planar Patch-clamping and fluorescence calcium imaging (fura-2) were performed to verify the functional activity of TRPV1 and TRPM8 in hMGECs. Finally, Oil Red O staining was performed on hMGECs to investigate a possible link between the activation of TRPV1 and TRPM8 and the lipid synthesis.
The RT-PCRs, western blots and Immunofluorescence revealed the expression of TRPV1, TRPV3, TRPV4 and TRPM8 in the MG on gene and protein level. RT-PCRs also showed the expression of TRPV2 but not TRPA1. Planar Patch-clamping and fura-2 calcium assays verified the activity of TRPV1 and TRPM8 in the hMGECs. Oil Red O staining showed a statistically significant increase in lipid expression after TRPV1 activation and decrease after TRPM8 activation.
Thermosensitive TRP channels are expressed and functionally active in the MG and could be a promising new target for the treatment of DED.

Poster 4:

Title:
Period-1 inactivation alters behavioral and morphological phenotypes in C3H mice

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Abstract:
Period genes and their protein products are known to be involved in the regulation of the circadian clock. As timing is very important for the development of complex traits, the dysregulation of the circadian clock can lead to downstream effects in complex systems.
We used a broad range of methods to investigate Period1 knockout mice (Per1-/-) in terms of changes in behavioural and morphological traits in comparison to wild-type C3H-animals.
Period-1-deficiency caused reduced overall body size and -weight, smaller appendicular bones (femur and tibia) and reduced bone volume and density in femur, tibia and skull. Period-1-deficient animals also displayed significantly smaller inner organs. One particular difference in the larynx of Period-1-deficient mice, namely reduced cricoid cartilage diameter and volume may explain previously observed alterations in ultrasonic vocalizations.
In summary Period1-deficiency in mice leads to a complex phenotype involving changes in innate behaviour, at least partly associated with significant morphological alterations compared to wildtype controls.

Poster 5:

Title:
Cyclosporine distinctly damages proximal tubules, tacrolimus the filtration barrier in calcineurin inhibitor nephrotoxicity

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Abstract:
Calcineurin inhibitors (CNI) are the backbone for immunosuppression after solid organ transplantation. Although successful in preventing kidney transplant rejection, their nephrotoxic side effects notoriously contribute to allograft injury despite attempts to optimize their application, often with additional medications. Complex renal parenchymal damage occurs for cyclosporine A (CsA) as well as for the currently favoured tacrolimus (Tac). We asked whether CsA and Tac exert distinct damage patterns during onset stages CNI nephropathy. We combined multiomics analysis with histopathology from rat kidneys exposed to continuous CNI delivery.
CsA and Tac were administered chronically in Wistar rats using osmotic minipumps for 4 weeks. Large scale electron microscopy, confocal, stimulated emission-depletion and 3D-structured illumination microscopy were used for pathology. Standard biochemistry, RNAseq, proteomic and phosphoproteomic technology was performed to identify molecular alterations.
Damage forms varied strikingly. Both drugs caused significant albeit differential damage in vasculature and nephron. The glomerular filtration barrier was more affected by Tac than by CsA, showing prominent deteriorations in pore endothelium and podocytes along with impaired VEGF/VEGFR2 signaling and podocyte-specific gene expression. By contrast, proximal tubule epithelia were more severely affected by CsA than by Tac, revealing lysosomal dysfunction and enhanced apoptosis and necrosis along with impaired proteostasis and oxidative stress.
We conclude that pathogenetic alterations in renal microenvironments are specific for either treatment. Should this translate to the clinical setting, CNI choice should reflect individual risk factors for renal vasculature and tubular epithelia. As a step in this direction, we share products identified from multiomics for differential pathognomonic biomarkers.

Poster 6:

Title:
The multi-kinase inhibitor Midostaurin mitigates loss of intercellular adhesion and skin blistering in pemphigus vulgaris

Authors:
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Abstract:
The multi-kinase inhibitor Midostaurin has proven its efficacy in treating a specific form of acute myeloid leukemia. In this study, we delve into the exploration of Midostaurin's potential applications in treating pemphigus vulgaris (PV).
To unravel the impact of autoantibodies from PV patients (PV-IgG) and Midostaurin on intercellular adhesion, we conducted keratinocyte dissociation assays. Additionally, we employed immunostaining and transmission electron microscopy in an ex-vivo model to investigate alterations in the desmosomal ultrastructure. Moreover, we utilized atomic force microscopy (AFM) to explore the effects at the single molecule level.
Keratinocyte dissociation assays confirmed that PV-IgG derived from patients leads to the loss of intercellular adhesion. However, this effect was mitigated by the administration of Midostaurin. Similarly, in an ex vivo model, co-injection of Midostaurin and PV-IgG successfully prevented the formation of blisters in the epidermis. Additionally, Midostaurin demonstrated its efficacy in averting PV-IgG-induced reduction in both desmosome number and size on an ultrastructural level. AFM experiments revealed that Midostaurin reversed the reduced binding probability of desmoglein (Dsg) 3 caused by PV-IgG whereas the interaction forces of Dsg3 remained unaffected by both PV-IgG and Midostaurin treatment.
Midostaurin emerges as a promising candidate for a novel treatment option for pemphigus vulgaris. However, further detailed investigation is necessary to elucidate the precise mechanisms through which Midostaurin prevents the loss of adhesion and rearrangement of desmosomal proteins in response to PV-IgG.

Poster 7:

Title:
Solitary chemosensory cells in the respiratory tract of man

Authors:
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Abstract:
Specialized sensory epithelial cells sensing noxious chemicals and initiating protective reflexes are found along the mammalian respiratory tract. Studies in mice suggested the presence of at least two populations: 1) neuroendocrine cells (marker: PGP9.5), 2) solitary cholinergic chemosensory cells (SCCC) (brush or tuft cells; markers: GNAT3, PLCβ2, TRPM5, POU2F3). In humans, a positional and sensory signaling pathway focused inventory of SCCC is yet missing.
Single- and multiple-labelling immunofluorescence with relevant marker antibodies was performed on human vallate papillae (positive control) and respiratory tract (nose, trachea, lung) obtained from anatomy body donors and organ donors. Pig trachea and lung were studied for comparison; TRPM5-eGFP reporter and C57BL6/J mice served as reference. Publicly available scRNAseq data were analyzed in silico.
PLCβ2-antisera labelled cells in human taste buds, but not in the respiratory mucosa; TRPM5-, POU2F3- and GNAT3-positive cells were not found. Accordingly, in silico-analysis revealed minimal expression of these markers in human airway epithelial cells, opposite to mice. Guided by scRNAseq data, LRMP-antibodies (lymphoid-restricted membrane protein) were used and labelled cells in taste buds and rare slender epithelial cells along the entire airways with predominance in bronchioli (0.323 cells/mm; trachea: 0.004). Multiple-immunolabeling established them as separate entity, distinct from ciliated, secretory, neuroendocrine cells and ionocytes. In pig, the distribution is similar to human. In mice, LRMP was also localized specifically to brush cells, which in this species were restricted to extrapulmonary airways.
These data identify chemosensory cells in human and pig airways with predominant intrapulmonary (bronchioli) localization, substantially different from mice.

Poster 8:

Title:
Identification of WNT7-specific frizzled receptors

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Abstract:
Paracrine activation of the WNT/β-catenin signaling pathway in brain endothelium by WNT7 ligands (WNT7A and WNT7B) essentially regulates blood-brain barrier formation and maintenance. Receptors of the frizzled family (FZD1-10) transduce WNT signals into the cell. So far, it is unknown which FZD isoforms mediate WNT7 signaling in brain endothelial cells. Although expressed at high levels in brain endothelium, FZD4 has been shown not to interact with WNT7, whereas FZD8 expressed at low levels does bind to WNT7. Binding of WNT7 to the other eight FZD isoforms has not been determined yet and is currently being investigated by us.
Expression constructs of all ten FZD ectodomains as well as the known WNT7 receptor RECK have been cloned as IgG Fc fusion constructs. Once secreted, active WNT7 ligands have a very short half-life and become inactivated, unless bound to a receptor. Therefore, purified recombinant FZD- and RECK-Fc fusion proteins will be added to the medium of HEK293 cells expressing WNT7A or WNT7B to stabilize newly secreted WNT ligand by soluble receptor-ligand complex formation. Potentially formed receptor-ligand complexes will be purified from the conditioned media using protein A agarose beads and analyzed by Western blotting.
Western blot analysis revealed expression and secretion of all cloned Fc fusion constructs. Gaining a better understanding of the FZD isoform requirements for WNT7/β-catenin signaling in brain endothelium, will help to further elucidate the molecular mechanisms of blood-brain barrier formation and maintenance and may be beneficial for the development of drugs modulating blood-brain barrier function.

Poster 9:

Title:
Alternative splicing in mechanically stretched podocytes as a model of glomerular hypertension

Authors:
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Abstract:
Alterations in pre-mRNA splicing play an important role in disease pathophysiology. The role of alternative splicing (AS) in hypertensive nephropathy (HN) has not been investigated. The purpose of the Sys_CARE (Systems Medicine Investigation of AS in Cardiac and Renal Diseases) project is to identify AS events that play a role in the development and progression of HN.
Cultured mouse podocytes were exposed to mechanical stretch for 3 days under low and high stretch conditions. Subsequently, mRNA and proteins were analyzed by RNA-Seq and LC-MS/MS. Enrichment analysis identified proteins which were classified according to the related biological processes. Splicing and transcript expression were evaluated with bioinformatical tools (e.g. rMATS).
Proteomic analysis identified a total of 135 and 424 significantly regulated proteins under low and high stretch conditions, respectively, compared to unstretched conditions. Transcriptomics confirmed that higher mechanical stress leads to more differentially expressed genes. Most of the genes/proteins with decreased intensity upon stretch were actin-associated proteins. In contrast, the up-regulated proteins were associated in clusters affecting mRNA processing and splicing. By RNA-Seq, we identified over 1000 different splicing events including all types of AS events. We screened for candidates that showed an AS event in multiple tools, were found in proteomics, were podocyte-specific, or showed altered expression in glomerulopathies. Based on these criteria, we initially focused on Myl6 and Shroom3.
The mechanical stretch of cultured podocytes provides an excellent model to simulate hypertensive nephropathy. In addition, RNA-Seq analysis identified AS events that could be associated with the development of HN.

Poster 10:

Title:
Calebin A, Inflammation and Colorectal Cancer: How are they linked?

Authors:
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Abstract:
Tumor malignancy and progression are crucially driven by components of the tumor microenvironment (TME). Although curcuma longa component Calebin A has been shown to suppress colorectal cancer (CRC) cell growth, its impact on the TME-induced epithelial-to-mesenchymal transition (EMT), which is related to tumor progression and metastasis, require further investigation.
We investigated CRC cell lines (HCT116, RKO) in monolayer and 3-dimensional (3D) in vitro TME-culture models exposed to Calebin A and/or a FAK inhibitor or cytochalasin D (CD).
TME-induced viability, proliferation, and invasiveness of CRC were abrogated by Calebin A, comparable to FAK inhibitor or CD. Furthermore, Calebin A, similar to FAK inhibitor or CD, dramatically suppressed TME-stimulated EMT-related transcription factor Slug, expression of EMT-associated biomarkers, and significantly down-regulated TME-induced stimulation of NF-κB, TGF-β1, and FAK signaling pathways. Finally, it was shown that Calebin A was able to inhibit TME-induced functional association between NF-κB and Slug, disturbing the synergistic interaction between the two transcription factors and preventing initiation of EMT and tumor cell migration.
For the first time, we reported that Calebin A attenuates TME-stimulated EMT and migration via NF-κB/Slug axis, TGF-β1, and FAK signaling, suggesting that it is an interesting novel agent for CRC management.

Poster 11:

Title:
Phospholipase Cd1 and Cd3 double-mutant mice develop cardiac fibrosis due to aberrant NFAT signalling and epicardial cell reactivation

Authors:
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Abstract:
Cardiac fibrosis and adverse cardiac remodelling represent major complications after myocardial infarction. Various signalling mechanisms in cardiomyocytes have been implicated in adverse cardiac remodelling, but post-infarction epicardial cell activation and regulation remains poorly understood. Here we describe a heart defect in a viable mouse mutant that completely lacks PLCd1 enzyme and expresses a novel truncated isoform of PLCd3. Double-mutant mice develop severe cardiac fibrosis without preceding cardiac infarction, leading to early death.
Using immunohistology and qPCR, we examined cardiac remodelling and lesion formation in double-mutant mice at different stages of the disease. We generated a cell culture model to study intracellular distribution and function of truncated PLCd3 expressed in mutant epicardial-derived cells.
We show that the fibrotic lesions mainly originate from the epicardium, where aberrant proliferation is detectable in young double-mutant mice. We also show that immortalised epicardium-derived cells from double-homozygous mutant mice exhibit enhanced calcineurin/NFAT signalling in vitro. Truncated mutant PLCd3 shows perinuclear localisation as opposed to membrane localisation of full-length PLCd3, possibly causing the reduced calcium and NFAT signalling observed in double-mutant epicardial-derived cells in vitro.
We show that combined loss of PLCd1 and PLCd3 activities causes proliferation and invasion of epicardial cells into non-infarcted myocardial tissues. Our data suggest that increased NFAT signalling in PLCd1 and PLCd3 in double-mutant mice might cause loss of epithelial integrity and enhanced invasive potential of epicardial cells in vivo. Similar molecular mechanisms might be involved in the initiation and regulation of post-infarction cardiac fibrotic remodelling and scarring.

Poster 12:

Title:
Genetic analysis of Bcl11a in murine cerebellar development

Authors:
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Abstract:
The zinc-finger transcription factor Bcl11a has been previously shown to be essential for cortical projection neuron development. Among other neuron types, Bcl11a is also expressed in cerebellar Purkinje cells (PC). Mutations of BCL11A in humans are associated with cerebellar hypoplasia, suggesting this factor to play a role in cerebellar development. Yet, cellular and molecular mechanisms through which Bcl11a controls cerebellar development are undetermined.
To investigate functions of Bcl11a in cerebellar development, we generated mice with a hindbrain-specific mutation of Bcl11a (Bcl11aflox/flox; En1-Cre). Phenotype analysis was carried out using standard histological and molecular techniques. To systematically identify candidate target genes of Bcl11a we employed microarray-based differential transcriptome analyses on laser-microdissected PC from homozygous Bcl11a mutant and control mice at P4, respectively. Phenotype analysis at P30 revealed that loss of Bcl11a resulted in a reduction of cerebellar PC-density by 36.7% as compared to controls. Mutant PC appeared hypoplastic with smaller dendritic trees. Using transcriptomic analysis, we found 210 differentially expressed genes in the Bcl11a mutants, of which 13 were chosen for further analysis after validation by RT-qPCR and in-situ-hybridization. Among these are genes with previously reported functions in PC development as well as genes associated with neurodevelopmental disorders involving cerebellar development. Genetic analysis of mice with hindbrain-specific mutation of Bcl11a demonstrates for the first time a role of this transcription factor in cerebellar PC development. Cell-type specific identification of candidate target genes will provide an experimental basis for the further characterization of Bcl11a-dependent regulatory pathways in cerebellar development.

Poster 13:

Title:
The efferent tear ducts as an entry point for SARS-CoV-2

Authors:
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Abstract:
Our aim was to investigate whether SARS-CoV-2, the cause of the COVID-19 pandemic, can enter the efferent lacrimal drainage system via the ocular surface and tear film. The relatively large mucosal surface area and long tear contact time, raises the possibility that this pathway contributes to the initiation of systemic infection. We looked for expression of ACE2, the main receptor for SARS-CoV-2, as well as cofactors such as TMPRSS2 and other enzymes such as cathepsin B, trypsin, furin, neuropilin1, neuropilin2, elastase1, TMPRSS11D and CD147 which also play a role in SARS-CoV-2 infection, in this system.
Human tissue samples of the efferent tear ducts (fundus lacrimalis, corpus lacrimalis, ductus nasolacrimalis) from body donors and matched positive controls were analysed by RT-PCR, Western blot and immunohistochemistry. It is not known whether the respective body donors were Sars-Cov-2 positive at any time; they were negative when they entered the institute.
The expression of the main receptor studied, ACE2, cofactors such as TMPRSS2 and other enzymes such as cathepsin B, trypsin, furin, neuropilin1, neuropilin2, elastase1, TMPRSS11D and CD147 were detected at the gene and protein level. ACE2 showed double bands at 50 and 60 kDa, which was unusual for the antibody used, but confirmed by other scientific work.
The results show the presence of all analysed receptors in the efferent lacrimal drainage system, which could be detected by each of the methods used. With an average tear passage time of 3 minutes and a relatively large mucosal surface area, the lacrimal drainage system could therefore be considered as a portal of entry and conduit for SARS-CoV-2.

Poster 14:

Title:
In vivo pathway of endocytosed albumin in renal proximal tubular cells

Authors:
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Abstract:
The neonatal Fc receptor (FcRn) is responsible for the transport of immunoglobulin G (IgG) and albumin across cells and is expressed in endothelial and epithelial cells, including renal proximal tubular (PT) cells. The transcytosis of albumin in the PT is essential for maintaining albumin homeostasis and preventing albuminuria. Since FcRn binds its ligands at pH 6.0, the albumin is most likely endocytosed by the scavenger receptor megalin. The intracellular route of endocytosed albumin however remains unknown.
The pathway of endocytosed albumin was visualized by injecting intranvenously nanogold-labeled albumin into wild-type mice and FcRn-/- littermates. Animals were in vivo perfusion-fixed 10 seconds, 1 and 5 minutes after albumin-nanogold administration. Using transmission electron microscopy, we examined proximal tubular profiles of S1 and S2 segments and compared the albumin-nanogold distribution to analyze the role of FcRn in transcytosis of albumin.
The filtration, endocytosis and transcytosis of albumin-nanogold was observed to occur faster than initially expected. Already 10 seconds after the injection, albumin-nanogold was detectable in the basolateral space of cells from the S1 and S2 segments. Absence of FcRn did not abolish transcytosis but moderately decreased efficiency. A significant increase in albumin-nanogold was observed in lysosomes of proximal tubule cells from wild type compared to FcRN -/- mice.
In conclusion, transcytosis is a extremly rapid cellular process. FcRn mediated trancytosis is involved in this pathway but not exclusive. Other endocytosis receptors such as megalin may perform transcytosis as well.

Poster 15:

Title:
Impact of the extracellular vesicles treatment on the myogenic differentiation capacity of skeletal muscle stem cells

Authors:
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Abstract:
Improving skeletal muscle regeneration has received much attention to overcome muscle wasting as in muscular dystrophy and degenerative myopathy. Several reports have introduced muscle stem cells (SCs) as an alternative therapeutic approach to enhance muscle regeneration however, the effect of molecules delivered by SCs including extracellular vesicles (EVs) on myogenic differentiation (MD) is not fully elucidated. This study evaluates the impact of EVs on MD capacity of SCs of mice.
C2C12 mouse myoblasts were cultivated in serum free-medium for 72 h under culture conditions. The supernatant was processed for EVs extraction using ultracentrifugation (100.000 g for 2h) and ultrafiltration methods. Quantification of EVs using nanoparticle tracking analysis was performed. Detection of EVs specific tetraspanins markers using western blot and Immunohistochemistry were carried out. The effect of EVs treatment on MD capacity of C2C12 after 72 h in SFM compared to control was assessed. Detection of myosin heavy chain and myotubes formation indicative of MD potential using Immunohistochemistry, morphometric analysis and RT-qPCR were analysed.
We were able to define SCs secreted EVs by using both methods. The data show the expression of EVs markers including CD9, CD63 and CD81 expression. The analysis revealed increases in MHC expression, and increases in myotubes number and length indicative for MD following 1 % EVs particles treatment compared to the control.
The data point out an enhanced MD by using ultracentrifugation and ultrafiltration derived EVs particles. The data provide a platform to investigate molecular components of EVs and their biological effect in regenerative medicine.

Poster 16:

Title:
Investigation of NRF2 on skin regeneration and ageing under influence of PRGF stimulation

Authors:
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Abstract:
Platelet-Released-Growth-Factors (PRGF) support regeneration and healing of tissue and are used widely in the clinic. NRF2 is a well-studied regulator of epithelial repair that is activated by oxidative stress and targets Antioxidative-Response-Elements (AREs) found in genes like HO-1 and NQO1. In this study, keratinocyte cell cultures are used to characterize the PRGF-NRF2 interplay and effect on 2D tissue regeneration and gene expression after PRGF short and long-term stimulation.
The PRGF-NRF2 interaction is characterized by Western-Blotting, Dual-Luciferase-Reporter Assays and RT-PCR/qRT-PCR. We use 2D scratch assays to compare PRGF induced tissue regeneration with known NRF2 activators like Sulforaphan. Gap-Closure-Rates are determined using software based analytics (Incucyte). CRISPR-CAS9 generated NRF2-knock-outs are used to support functional and transcriptional analytics and categorize first results in cell lines.
Stimulation with PRGF revealed improved cell viability and proliferation after stimulation, as well as complete gap closure in 2D scratch assays in HaCat cell culture. We could identify increased translocated NRF2, ARE activity, as well as HO-1 expression that indicate a PRGF-NRF2 interaction on transcriptional level. Further experiments with human primary keratinocytes and the respective knock-outs are required to frame the pilot-study results and answer the question if PRGF activates NRF2.
Our study design is a great opportunity to investigate the hypothesized biochemical activation of NRF2 by PRGF and its mechanistic contribution to dermal regeneration and ageing. It is planned to transfer our findings from 2D to a 3D multilayer skin model that allows further characterization.

Poster 17:

Title:
Generation of a human induced pluripotent stem cell (iPSC) line from urinary cells of a patient suffering from chronic kidney disease.

Authors:
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Abstract:
Chronic kidney disease (CKD) is a major public health burden associated with a drastically reduced quality of living and life span that lacks suitable, individualized therapeutic strategies. To address this, we wanted to establish an induced, pluripotent stem cell (iPSC) line, reprogrammed from urinary cells of a CKD patient, as non-invasive source.
We isolated urinary cells from a dialysis patient suffering from CKD with underlying hypertension and diabetic nephropathy. The cells were reprogrammed using the non-integrating Stemgent® StemRNA™ 3rd Gen Reprogramming Kit for Reprogramming Urine Derived Progenitor Cells. The generated iPSCs were picked, further expanded and cryo-conserved. For characterization, we performed immunofluorescence microscopy and RT-qPCR for pluripotency marker expression. Pluripotency was further analyzed by directed differentiation. iPSCs were karyotyped, tested for HIV, HPV and mycoplasma contamination and a Single-Tandem-Repeat (STR)-analysis for donor matching was performed.
The iPSC line shows a typical morphology and a positive expression of pluripotency markers OCT3/4, SOX2 and NANOG. The cells can differentiate into all three germ layers as revealed by RT-qPCR and immunofluorescence staining for OTX2, SOX17 and TBTX after directed differentiation. The cells are free of any contamination and virus infection. They exhibit a typical male karyotype of 46,XY. STR-analysis showed a perfect match with the donor cells at all 21 tested sites.
We established an iPSC line that shows all relevant characteristics of iPSCs. This iPSC line can be used for individualized in vitro disease modelling, treatment development or drug screening and for differentiation towards specific cell types or whole organoids.

Poster 18:

Title:
Tracheal brush cells modulate immune responses during airways inflammation through TRPM5 channel activation

Authors:
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Abstract:
Tracheal brush cells (BC) are specialized epithelial cells in the lower respiratory tract that have been proved to be able to detect bacterial signaling molecules and to initiate protective early immune responses. Here, we address the hypothesis that BC activation impacts later immune responses in a Trpm5-dependant manner.
Trpm5-/- and Trpm5+/+ mice were either intratracheally infected with P. aeruginosa or treated with denatonium. Immunohistochemistry and FACS were used for analyses of immune cells recruitment in bronchoalveolar lavages (BAL), tracheae and lungs of these mice. Plasma levels of selected cytokines were quantified using an ELISA assay.
Previously, we have demonstrated that BCs are crucial for neutrophils recruitment after short term activation by denatonium (30 min) and P. aeruginosa infection (4 h). Here, we show that 24 h after BC activation with denatonium or 48 h and 72 h after P. aeruginosa infection Trpm5+/+ mice were able to limit neutrophils infiltration. Higher neutrophils counts were observed in lungs, BAL, tracheae of Trpm5-/-compared to Trpm5+/+ mice. Elevated levels of IL-1α, CCL7 and CCL12 were detected in plasma of infected Trpm5-/- but not in Trpm5+/+ mice. Moreover, BC activation led to a significant increased recruitment of alveolar macrophages and DCs with higher percentages of CD86+ DCs in a Trpm5-dependent fashion.
BCs contribute significantly in shaping immune responses during airway inflammation.

Poster 19:

Title:
Generation of complex 3D cardiac organoids from human

Authors:
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Abstract:
The heart is the first fully functional organ during development and is affected by various diseases and congenital defects. Human-induced pluripotent stem cell (hiPSC)-derived cardiomyocytes offer a promising platform for studying cardiac development and disease in vitro. Here, we present a protocol for generating self-assembled, chambered human iPSC-derived 3D cardiac organoids Differentiation of 3D aggregates of hiPSCs into cardiac tissue was directed by modulating the WNT and BMP4 signaling pathways. It was essential to determine the optimal time frames for pathway activation and inhibition, as well as perfect concentrations of small molecules used. After a specified growth period, the cardiac organoids were analyzed using RT-PCR, immunofluorescence, and electron microscopy. Moreover, calcium imaging was performed Cardiac organoids exhibit a functioning myocardium, which displays differences in sarcomere structure and beating frequency between early and mature organoids. The myocardium is surrounded by mesenchymal tissue interspersed with a branching vascular network. Moreover, endothelial-lined chambers can be observed. The vascular network gives rise to hematopoietic progenitor cells and cell types derived thereof such as erythrocytes and macrophages. We further modulated ß-adrenergic receptors in several cardiac organoids, both wild-type (WT) and LemD2 knockout (KO), using Isoproterenol and Propranolol and observed changes in beating frequency induced by the molecules.
In this study, we have successfully developed a protocol for generating self-assembling, chambered human iPSC-derived 3D cardiac organoids which display robust spontaneous beating. The organoid model also contains a branched vascular network with different hematopoietic cell types associated to the vascular system. We will utilize this model to investigate LemD2-associated dilated left ventricular cardiomyopathy.

Poster 20:

Title:
Modulation of Nrf2 in the tumor immune microenvironment (TIME) to affect tumor characteristics

Authors:
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Abstract:
The regulatory status of nuclear factor-erythroid 2 related factor 2 (Nrf2) affects both hepatocellular carcinoma cells and tumor-associated macrophages (TAMs). It is known that the inflammatory state of TAMs is influenced by Nrf2, which is a crucial factor for tumor progression. However, the specific mechanisms involved are still unclear. To investigate this effect, a realistic co-culture model combining TAMs and tumor cells is required.
Non-alcoholic steatohepatitis-derived hepatocellular carcinoma cells (N-HCC25) spheroids and multicellular spheroids (MCT) consisting of N-HCC25 cells and bone marrow-derived macrophages (BMDMs) were used. In these models, the influence of Nrf2 on both BMDMs and tumor cells was investigated. Spheroid formation, growth characteristics and invasion behavior were investigated. Supernatants were analyzed by ELISA. Cell distribution, proliferation and extracellular matrix components were immunohistochemically analyzed. Gene expression was compared between monolayers and spheroids by RT-qPCR. A flow cytometry study was conducted.
We were able to show that the use of spheroids has advantages over the 2D-monolayer culture in terms of increased tumor marker gene expression. Interestingly, Nrf2 hyper-activation in N-HCC25 cells inhibited spheroid formation. Moreover, Nrf2-KO BMDMs within MCTs decreased VEGF secretion into the supernatant. Immunohistochemical studies confirmed the localization of BMDMs and proliferating cells. The amount of BMDMs incorporated into the MCT was determined by flow cytometry.
Multicellular and tumor spheroids appear to better reproduce the in vivo situation of a tumor than classical 2D-monolayer cultures. This enhances the possibilities to study the direct interactions between different cell types as a function of Nrf2 activity.

Poster 21:

Title:
Starvation in Mice Induces Liver Damage Associated with Autophagy

Authors:
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Abstract:
Anorexia nervosa (AN) induces widespread organ dysfunction by severe malnutrition. Starvation-induced liver enzyme increases are widely reported in AN patients. The underlying pathophysiology is not yet fully understood, despite its potential importance for explaining clinical symptoms. Therefore, we aimed to investigate to what extent liver damage occurs in an AN-mouse model, and what are the potential underlying mechanisms.
Female mice received 40% of their baseline food intake until a 25% weight reduction was reached. To mimic chronic starvation, body weight loss was maintained for two additional weeks. The animals had access to a running wheel throughout the whole experiment. Serum levels of the liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured spectrophotometrically. Histochemical stainings and immunohistochemistry were used to analyze liver fat content, cell proliferation, apoptosis, macrophage numbers, and autophagy in the murine liver.
We observed lower liver fat contents in the livers of starved animals compared to control animals and an increase in AST and ALT in the livers of chronically starved mice. Additionally, cell proliferation decreased while apoptosis remained unchanged. This was paralleled by a decreased density of F4/80+ macrophages and an increased autophagosomal-related staining intensity.
The observed liver changes induced by starvation may be associated with increased autophagy. Whether autophagy is the primary underlying mechanism of starvation-induced liver damage remains unknown and should be investigated in further research.

Poster 22:

Title:
Quantitative lipidomic analysis of tafazzin-knockdown mouse hearts give new insights in BTHS cardiomyopathy

Authors:
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Abstract:
Barth syndrome (BTHS) is a complex metabolic disorder caused by mutations in the mitochondrial tafazzin gene (Taz), impacting the synthesis of cardiolipin in mitochondria. So far, a comprehensive analysis of the complete lipid profile in BTHS hearts, specifically comparing young and older animals, has not been conducted. Hence, this study aimed to comprehensively profile the lipids in BTHS hearts and compare the profiles between young and older animals.
BTHS mouse model hearts from both wild-type (WT) and Taz knockdown mice (Taz-KD) at 10 and 50 weeks of age were collected for lipid extraction and the samples were then subjected to mass spectrometric analysis using a triple quadrupole mass spectrometer (FIA-MS/MS; QQQ triple quadrupole).
Statistically significant lipid composition differences were observed between the Taz-KD and WT groups, indicating genotype-dependent alterations in most analyzed lipid species. Loss of tafazzin function resulted in significant changes in the myocardial lipidome, affecting both young animals without cardiomyopathy and older animals with heart failure. Notable alterations were found in sphingomyelin, ceramide, and hexosylceramide, plasmalogen lipid species.
Our study employed high-throughput tandem mass spectrometry to examine lipid classes and individual lipid species in the Taz-KD BTHS model at 10 and 50 weeks of age. We discovered that SM, Cer, and HexCer, known to be implicated in cardiovascular disease, also contribute to the development of cardiomyopathy in BTHS. These findings offer potential avenues for the diagnosis and treatment of BTHS, presenting new possibilities for therapeutic approaches.

Poster 23:

Title:
Role of peroxisomes in compensatory metabolic adaptation in heart failure

Authors:
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Abstract:
An inherited defect in mitochondrial cardiolipin biogenesis causes a substantial alterations in cardiac metabolism in Barth syndrome (BTHS). Peroxisomes locate in close proximity to mitochondria and share many metabolic pathways. The role of peroxisomes in compensatory responses to changes in the metabolism is currently only poorly understood. Therefore, the objective of this project is to investigate the modifications in peroxisomal compartment, and their structural interactions with mitochondria in BTHS. By analyzing these aspects, we aim to gain a comprehensive understanding of how peroxisomes adapt to the altered metabolic conditions in BTHS and potentially contribute to the compensatory mechanisms in the disease.
To explore the impact of peroxisomal effects, MEF cells obtained from both wild-type (wt) and Taz-Kd (Taz knockdown) samples subjected to immunofluorescence, western blotting, quantitative PCR, and enzyme activity assays
Our findings demonstrate that Barth syndrome (BTHS) exhibits an imbalance in redox homeostasis, which is compensated by the upregulation of enzymes involved in reactive oxygen species (ROS) detoxification, including catalase. Inhibition of catalase function using 3-AT resulted in the loss of catalase activity in Taz-Kd cells, rendering them more sensitive to this loss. Immunofluorescence results supported these observations. Additionally, we identified the upregulation of key enzymes, Fatty Acyl-CoA Reductase 1 (FAR1) and Glyceronephosphate O-Acyltransferase (GNPAT), in TAZ KD cells. These enzymes are crucial for plasmalogen synthesis and are preferentially oxidized in the presence of ROS.
The modulation of peroxisomal metabolisim could potentially alleviate the defects in the mitochondria. Plasmalogens emerge as a promising therapeutic target in the treatment of BTHS. Upregulation of peroxisomal catalase can help reduce the ROS burden on cells

Poster 24:

Title:
The Role of Peroxisomes in Atherosclerosis: Insights from CEACAM1-Deficient Bone Marrow-Derived Macrophage (BMDM)

Authors:
Anggi Muhtar Pratama (Institute of Anatomy and Cell Biology, Graduate School of Life Sciences, Würzburg), Heike Bömmel (Institute of Anatomy and Cell Biology, Anatomical Society, Würzburg), Süleyman Ergün (Institute of Anatomy and Cell Biology, Anatomical Society, Würzburg), Srikanth Karnati (Institute of Anatomy and Cell Biology, Anatomical Society, Würzburg); anggi-muhtar.pratama@uni-wuerzburg.de

Abstract:
Atherosclerosis, a chronic inflammatory disease associated with severe cardiovascular complications, has been linked to the absence of CEACAM1, an immunoglobulin superfamily glycoprotein. While peroxisomes in macrophages are believed to play crucial roles in atherosclerosis by influencing lipid metabolism, reactive oxygen species (ROS) regulation, and inflammation, the specific role of peroxisomes in bone marrow-derived macrophages (BMDMs) from CEACAM1-deficient mice remains unknown. This study aimed to investigate the role of peroxisomes and their associated signaling and immune response in CEACAM1-deficient BMDMs. BMDMs were isolated and cultured from wild-type and CEACAM1-deficient mice for a duration of 3 days. The peroxisomal compartment was analyzed using techniques such as immunofluorescence, electron microscopy, quantitative PCR (qPCR), and Western blotting.
The mRNA levels of peroxisomal membrane formation proteins (PEX3, PEX16, and PEX19) and peroxisomal β-oxidation enzyme (ACOX1) were significantly upregulated in CEACAM1-deficient BMDMs. Moreover, CEACAM1-deficient BMDMs exhibited elevated protein levels of catalase (an antioxidative enzyme) and Glyceronephosphate O-acyltransferase (GNPAT), responsible for ether lipid synthesis. These findings were further supported by immunofluorescence results. Collectively, these results indicate an increased involvement of peroxisome markers in maintaining ROS and lipid homeostasis in the absence of CEACAM1 in BMDMs.
The loss of CEACAM1 in BMDMs leads to a significant upregulation of peroxisome markers, suggesting a potential association between peroxisomes and CEACAM1 in the metabolic pathways involved in atherosclerosis. Further research is necessary to fully comprehend this relationship and its implications for the progression of atherosclerosis.

Poster 25:

Title:
Long cellular protrusions interconnect distant cells in the gastrulating chick embryo

Authors:
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Abstract:
Development and persistence of multicellular organisms require fine-tuned information processing based both on intracellular processes and communication between its cellular units. The main approach of this communication is based on study of signalling pathways modulated by receptor-ligand interaction. During embryonic development ligands, also known as morphogens, are secreted from local sources and form gradients, thus regulating fate and behaviour in nearby cells. Complementary approaches are based on more global and robust types of regulation, like distribution of mechanical tensions or electrical fields. However, growing evidence supports the existence of an additional, initially overlooked layer of regulation – cell-to-cell communication by intercellular processes.
We made use of light as well scanning and transmission electron microscopy to study ultrastructural features of the mesodermal compartment in gastrulating chick embryos. For scanning electron microscopy, embryos were fractured transversally to reveal insight into all germ layers.
Our analysis reveals that virtually all mesoderm cells in the late gastrula and early neurula are interconnected by long cell processes. Crucially, the basement membrane of the epiblast is penetrated by similar filopodia-like processes which are formed by both epiblast and mesodermal cells and able to form direct intercellular contacts between the two germ layers. Our data reveal several morphological subgroups of cell processes and suggest a variety of their functions in embryonic development.
We discuss our findings in context of current models of developmental regulation.

Poster 26:

Title:
Peroxisomes in megakaryocytes and platelets?

Authors:
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Abstract:
The presence and functional role of peroxisomes in megakaryocytes and platelets, as well as their significance in vascular cell biology, remain largely unknown. Only one article has described the presence of “peroxidase-like” activity, potentially representing catalase, at the ultrastructural level in platelets and megakaryocytes. Consequently, our objective is to address the following research questions: a) Are peroxisomes abundant in platelets? b) Are there specific differences in peroxisomal composition between mouse and human platelets? c) Do platelets possess any peroxisomal antioxidative enzymes?
Human Megakaryoblast (MEG-01) cells were cultured, platelets were isolated and compared with human apheresis platelets that were obtained from the Department of Transfusion Medicine at the University Hospital, Wurzburg. To address the species-specific differences, platelets were also isolated from mouse blood. To explore the peroxisomal proteins in platelets, all these preparations were subjected to immunofluorescence, qPCR, and Western Blotting
Our findings demonstrate the abundance of peroxisomes in megakaryocytes and platelets. We successfully detected various peroxisomal mRNAs and proteins in megakaryocytes, platelets isolated from human and mouse blood, as well as platelets derived from an apheresis model. Notably, platelets exhibited high levels of peroxisomal biogenesis protein 14 (PEX14p), peroxisomal lipid transporter (ABCD3), plasmalogen biosynthesizing enzymes (GNPAT, AGPS), and the ROS defence enzyme catalase (CAT).
These novel findings provide the first evidence of abundant peroxisomes in platelets, along with the presence of peroxisomal proteins involved in diverse metabolic pathways. This analysis is crucial in investigating the potential involvement of platelet peroxisomes in inflammatory diseases and the initiation of transfusion-associated adverse events during ex vivo storage.

Poster 27:

Title:
Biofabrication of blood vessels from hiPSC-derived mesodermal progenitor cells

Authors:
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Abstract:
An intricate blood vessels network is essential for artificially generated tissues. However, the generation of vascular networks using biofabrication remains a challenge. The objective of this work is to biofabricate a vascular system using hiPSC-derived mesodermal progenitor cells (hiMPCs).
Different bioinks were used to print hiMPCs either in a shape free approach or in tubular geometry using in-gel bioprinting. Cell viability and morphogenesis were evaluated using life-dead staining, H&E staining, immunofluorescence analyses, tissue clearing and electron microscopy.
Initially, shape-free bioprinting was performed. Different bioinks were used and supplemented with collagen type 1 and sacrificial gum. Cells survived, differentiated, and underwent morphogenesis resulting in small vessel-like structures. Afterwards, vascular network formation by angiogenic sprouting was observed.
To generate larger vessel-like tubes (up to 3.5mm), in-gel printing was performed. Different bioinks supported cell viability, proliferation, differentiation, and migration to a varying extent. Under ideal conditions, the lumen of bioprinted tubes was lined by CD31+ endothelial cells like in the vascular intima and were circularly surrounded by SMA+ smooth muscle-like cells mimicking the vascular tunica media. Additionally, micro vessels formed within the wall of the printed tube.
We demonstrate that bioprinting of hiMPCs is suitable for the biofabrication of large as well as small/micro vascular structures. However, the success strongly depends on the composition of the bioinks. Furthermore, printing of tubular structures resembling larger vessels is possible using an in-gel printing approach. Human iMPCs were able to survive this process and retain their differentiation capacity.

Poster 28:

Title:
Large Scale production of Blood Vessel Organoids as building blocks for Biofabrication

Authors:
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Abstract:
Organoids are 3D-tissue models that recapitulate organ development, morphogenesis, and fulfill some tissue-specific functions. Our group has previously developed a blood vessel organoid (BVO) model that mimics aspects of embryonic vasculogenesis and angiogenesis. Here, we explore a strategy to significantly scale-up the generation of BVOs using custom-made agarose molds. This will enable their use as building blocks for larger artificial tissues created through biofabrication techniques.
Custom-made agarose molds fit into one well of a 12-well plate and are designed to have multiple microwells (159 wells/mold) to allow the mass production of organoids with an ideal size for bioprinting applications while reducing labor and costs. We experimented with different initial seeding numbers of cells per microwell and carefully analyzed the effect on the differentiation outcome. Subsequently, the extrusion of BVOs into ring-shaped molds was tested to demonstrate their feasibility for bioprinting applications and the assembly of large, vascularized tissues.
An initial seeding density of 40t cells/mold and the ideal microwell diameter of 700 µm resulted in the generation of BVOs with an optimal size for bioprinting applications. Immunofluorescence analyses and tissue clearing demonstrated the presence of a comparable blood vessel network within each generated organoid. After extrusion under realistic bioprinting conditions, the organoids survived, maintained their vascular network, and produced a continuous, branched vascular network through angiogenic sprouting. Printing BVOs at high density resulted in organoid fusion and the generation of stable vascularized tissue rings with a diameter of 8 mm.
The use of custom-made aggrewell-like agarose molds is a viable method for large-scale production of BVOs. The method will enable their use as building blocks to produce large vascularized connective tissue structures using biofabrication techniques.

Poster 29:

Title:
T cell microRNAs and their impact on myelodysplastic neoplasms

Authors:
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Abstract:
Myelodysplastic neoplasms (MDS) are a group of hematopoietic disorders resulting in non-functional blood cells. The immunological influence on the disease is largely unexplored. The combination of the immunological influence, in the form of T cells, and the fine regulators of biological processes, microRNAs, are the subject of the present work.
For the analysis of the microRNA expression pattern of flow cytometrically sorted T cells from MDS and non-MDS bone marrow samples a microRNA microarray was used. To explore the biological function of differentially expressed microRNA candidates, they were overexpressed in primary CD8+ T cells. These T cells were then analyzed with regard to their proliferation and CD107a degranulation behavior in co-culture with the MDS cell line MDS-L.
Array analysis showed that miR-1281, hsa-miR-1825 and hsa-miR-5571-5p, among others, are downregulated in CD8+ and CD4+ T cells of MDS bone marrow compared to non-MDS samples. These selected candidates were successfully overexpressed in primary CD8+ T cells. The proliferation behavior after stimulation with IL-2 and anti-CD3 could not reveal any significant differences between transfected and non-transfected CD8+ T cells. Likewise, the CD107a degranulation behavior in the presence of the MDS-L cell line did not show any differences.
The array analysis revealed differences in the microRNA expression pattern of the examined T cells. In the experiments used here, the candidates selected for further analysis showed no influence on the proliferation and CD107a degranulation behavior of isolated primary CD8+ T cells, which leaves their exact function in the T cells still open.

Poster 30:

Title:
Desmosomal hyper-adhesion protects keratinocytes from pemphigus autoantibody-induced loss of intercellular adhesion without changing antibody binding and Dsg3 interaction partners

Authors:
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Abstract:
In pemphigus, autoantibodies against the desmosomal cadherins desmoglein (Dsg)1 and 3 cause loss of keratinocyte cohesion. Interestingly, keratinocytes acquire a strong adhesive state, referred to as hyper-adhesive, in which they are protected from pemphigus autoantibody-induced loss of cell cohesion. In hyper-adhesive keratinocytes, desmosomal cadherins are Ca2+-independent but the underlying mechanism is largely unknown. We recently observed that Dsg3 is important for acquisition of desmosomal hyper-adhesion. Additionally, pemphigus autoantibody-mediated direct inhibition of Dsg3 interactions was reduced. Here, we investigated whether changes in direct inhibition of Dsg3 interactions are caused by changes in autoantibody binding or Dsg3 interaction partners.
Keratinocyte dissociation assay, Immunofluorescence, Atomic force microscopy (AFM)
Using AFM, Dsg3-dependent interactions revealed a similar binding frequency under both hyper-adhesive and non-hyper-adhesive conditions. Next, we applied antibodies specific for Dsg2, Dsg3 or desmocollin (Dsc)3, respectively. However, only AK23, a monoclonal anti-Dsg3-antibody, significantly reduced binding frequencies under all conditions indicating that predominantly homophilic Dsg3 interactions are present. As we previously recognized that blocking potential is epitope-dependent, we further used AK23, and measured Dsc3-dependent interactions. However, AK23 did not change binding frequency of Dsc3 interactions under both adhesive states, indicating that no heterophilic Dsc3-Dsg3 interactions were measured. Finally, we also checked whether binding of pathogenic antibodies was different in both adhesive states using immunostaining, which, however, was not the case.
Taken together, the data indicate that protective hyper-adhesiveness in pemphigus is caused neither by changes in Dsg3 interaction partners nor by altered binding of the pemphigus autoantibodies.

Poster 31:

Title:
Regeneration in the equine dental pulp

Authors:
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Abstract:
The silicate enriched diet of horses causes massive dental wear. Therefore, continues production of subocclusal dentin is essential to avoid pulpal exposure. Concurrently, a lifelong dental eruption is required to ensure the teeth's functionality. Both, dental pulp, and periodontal ligament are required to remain in an active and regenerative status to avoid pulpal exposure by continued dentin production and maintain dental eruption even in aged horses. The aim of the present study was to identify equine pulpal and periodontal medicinal signaling cells (MSCs) and determine their niches within the respective tissues.
Therefore, we developed a method to isolate equine MSCs from the dental pulp and periodontal ligament (PDL). Isolated MSCs were characterized via flow cytometry and trilineage differentiation. Furthermore, immunofluorescence-staining for CD90 in equine pulpal and periodontal tissue samples were established.
The cells mainly were positive for the surface markers CD44 and CD90 and negative for MHCII, CD11a/18 and CD45. CD90-positive cells were found especially in the odontoblastic layer and perivascular region of the PDL.
The finding of a CD90-positive cell population in the odontoblastic layer of the equine dental pulp supports the hypothesis that the equine odontoblasts represent a regenerating cell population rather than being postmitotic cells with limited regenerative capacities. Though this should be confirmed by further investigations. As a next step, it would be appropriate to compare equine teeth with teeth which have to cope with similar conditions like rats' incisors by using different markers for odontoblastic differentiation.

Poster 32:

Title:
Effect of shock waves on the adipogenic differentiation of mesenchymal stem cells

Authors:
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Abstract:
Mesenchymal stem cells are already widely used for therapeutic applications, including the treatment of musculoskeletal disorders. Extracorporeal shock waves are also a known therapeutic intervention to cure or alleviate these diseases.
Here, we investigated the influence of focused shock waves on the three-lineage differentiation of equine MSCs. Using transmission electron microscopy (TEM), we found marked morphological changes at the subcellular level. These were characterised by the absence of large fat vacuoles after shock wave treatment compared to untreated conditions. Furthermore, they did not reappear after further cultivation of the cells.
In order to verify and confirm these results, cells from four donors were further examined by investigating the proliferative capacity using MTT proliferation assays in combination with SRB analysis. In a further series of experiments, adipogenic differentiation was assessed and quantified by Oil red-O staining. Specific marker expression was analysed by RT-qPCR for the expression of LPL, PPaRg, beta Actin and FAB4). Our data provide evidence that adipogenic differentiation was significantly reduced after shock wave treatment compared to the negative control. This was specifically demonstrated by SRB, MTT and Oil-Red-O staining analysis.
However, quantification of specific adipogenic marker expression by RT-qPCR revealed inter-individual differences, which cannot conclusively explain the cause of the observed effect on cell morphology after shock wave treatment. This interesting phenomenon requires further analysis.

Poster 33:

Title:
Influence of melanocortin receptors in human meibomian glands

Authors:
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Abstract:
Meibomian glands are specialized sebaceous glands that produce meibum, a lipid-rich secretion that forms a protective layer on the tear film. Dysfunction of these glands is a primary cause of dry eye disease and treatment options for this condition are limited. Previous studies have indicated that α-/β- melanocyte-stimulating hormones (α-/β-MSH), which are ligands of the melanocortin receptors (MCR), play a role in regulating lipid production and glandular differentiation in sebaceous glands.
To investigate MCR expression in human meibomian glands, immunohistochemistry and RT-PCR analyses were conducted on both human meibomian glands and an immortalized human meibomian gland epithelial cell line (ihMGECs). The ihMGECs were stimulated with α-/β-MSH and an MCR antagonist (JNJ-10229570), and the effects on viability, lipid production, and MCR response were evaluated. Additionally, qPCR analyses were performed to assess the impact of α-/β-MSH on gene expression levels of MCRs and lipogenesis markers.
The study confirmed the expression of MCRs in human meibomian glands. Stimulation with α-/β-MSH did not affect cell viability but led to a dose-dependent increase in cAMP levels and lipid production ($p<0.001$). However, simultaneous administration of the MCR antagonist significantly reduced this effect ($p=0.005$). Moreover, treatment with α-/β-MSH resulted in a significant increase in the expression of lipogenesis markers and MCRs.
These findings suggest that α-/β-MSH positively influences meibum production by modulating the expression of MCRs and lipogenesis markers in ihMGECs. Considering the impact of α-/β-MSH on glandular secretion, it should be explored as a potential treatment and for understanding changes in meibum production.

Poster 34:

Title:
Methysticin and L-Sulforaphane activate the Nrf2/ARE pathway in MLO-Y4 osteocytes: in vitro study

Authors:
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Abstract:
Oxidative distress-induced osteocyte death plays a crucial role in the pathogenesis of skeletal diseases. A master regulator in the cellular response to elevated oxidative stress levels is the transcriptional factor nuclear factor erythroid 2-related factor 2 (Nrf2). However, the effects of phytopharmaceutical Nrf2 induction by Methysticin and L-Sulforaphane on the Nrf2/antioxidant response element (ARE) pathway in osteocytes have not yet been fully elucidated.
Murine MLO-Y4 and transfected MLO-Y4-SIN-lenti-ARE osteocytes were used. Methysticin and L-sulforaphane were used as Nrf2 stimulants. Oxidative stress was induced by H2O2. Cytotoxicity was evaluated using the CytoTox-Glo™ Assay. Time- and dose-dependent ARE induction was assessed using the Monoluciferase Assay and CyQUANT™ Assay. Nrf2 targets' (Ho-1, Nqo1, Txnrd1) mRNA and protein levels were assessed after Nrf2 induction by RT-qPCR and immunofluorescence staining. The protein expression of osteopontin and osteocalcin was evaluated by immunofluorescence staining.
Methysticin and L-Sulforaphane induced ARE activity time- and dose-dependent, increasing antioxidant marker gene and protein expression. L-Sulforaphane pretreatment resulted in elevated protein levels of osteopontin and osteocalcin and decreased the cell death rate induced by H2O2 compared to no pretreatment. Methysticin increased osteopontin expression and did not affect the H2O2-induced cell death rate.
Methysticin and L-Sulforaphane enhanced the expression of antioxidant genes through the Nrf2/ARE pathway in osteocytes. L-Sulforaphane increased the protein expression of osteocyte-associated osteogenic markers and effectively prevented H2O2-induced osteocyte death. Methysticin marginally increased osteopontin expression and showed no preventive effect. Thus, Nrf2 inducers reduced oxidative stress, and L-Sulforaphane enhanced osteogenesis effects in osteocytes.

Poster 35:

Title:
Loss of Desmocollin 1 alters proliferation and differentiation in reconstructed human epidermis

Authors:
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Abstract:
Desmosomes are mediators of strong cell cohesion, but the layer-specific patterning of desmosomal adhesion molecules, desmoglein (DSG) 1-4 and desmocollin (DSC) 1-3, in the human epidermis suggest additional functions with regard to signalling and epidermal differentiation, which is only partially understood. The DSC1 isoform is particularly interesting as its expression correlates with the onset of keratinization and therefore terminal differentiation.
The influence of DSC1 on epidermal differentiation was addressed by silencing DSC1 in normal human epidermal keratinocytes (NHEK) by lentiviral transduction. To investigate the differentiation behaviour of human epidermal keratinocytes, 3D reconstructed human epidermis (3D-RHE) was cultivated at the air-liquid interface for 6 and 12 days and tissue sections analysed by immunohistochemistry. Additionally, RNAseq of 3D-RHEs after 6 days was performed to identify targets leading to changes in proliferation and differentiation in DSC1 knock-down 3D-RHEs.
Loss of cell-cell adhesion was detected in dispase-based dissociation assays of DSC1 knock-down cells. Knock-down of DSC1 in 3D-RHEs was confirmed and expression of differentiation markers was grossly normal. Histology revealed significantly reduced thickness of 3D-RHE sections with DSC1 knock-down after 6 days of cultivation as a result of reduced spinous layer area. Immunostainings for Ki67 showed reduced proliferation in knock-down 3D RHEs after 6 days. RNAseq analysis demonstrated alterations in pathways involving TGF-beta or TNF-alpha signalling and interferon responses, suggesting a paracrine regulation of keratinocyte proliferation dependent on the presence of DSC1.
Our data indicate that DSC1 modulates cell cohesion, as well as proliferation and differentiation of keratinocytes in 3D-reconstructed human epidermis.

Poster 36:

Title:
Investigation of nanoscale deformation of collagen in the human broad ligament of the uterus using small-angle X-ray scattering and histology

Authors:
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Abstract:
Pelvic floor disorders, such as uterine prolapse, impact the quality of life of one-third to one-half of elderly women. Molecular alterations, mediated by ageing and hormonal fluctuations, driving the weakening of uterine support structures are understudied. The broad ligament connects the uterus to the lateral pelvic walls and is characterized as peritoneal fold. Our objective was to examine the distribution of collagen within the broad ligament and its nanoscale behavior under loading conditions to enhance our understanding of uterine prolapse.
Broad ligaments were procured post-mortem from women (66±22 years) following ethics guidelines. Samples (15×15 mm^2) were stretched biaxially while simultaneously assessing collagen fiber orientation and d-spacing using small-angle X-ray scattering (SAXS) (MiNaXS beamline P03/PETRA III, DESY). At each deformation (0%, 5%, 10%, 15%, 20%), a 1×1 mm^2 map of SAXS measurements was generated. Adjacent tissue was prepared for histology to evaluate collagen, elastin, proteoglycan, and cellular properties in multiple planes.
SAXS showed two orthogonal orientations of collagen fibrils. Collagen fibril strain and alignment increased with tissue strain, while fibril thickness decreased (all $p<0.05$). Preliminary histological confirmed multiple main orientations of crimped collagen fibers. The broad ligament was cell rich and included small blood vessels.
Histological evaluation confirmed the SAXS findings and corresponds to fiber distribution in peritoneum. Fibril strain in the broad ligament was lower than strain reported for tendons, likely due to the higher alignment of collagen in tendons. These findings may contribute to our understanding of uterine prolapse and the development of biomechanical models of uterine support structures.

Poster 37:

Title:
Characterization of immortalized human lacrimal gland epithelial cells in 2D and 3D cell culture models

Authors:
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Abstract:
Research on the human lacrimal gland (LG) is limited by the scarcity of material and the lack of a human lacrimal gland epithelial cell line. To facilitate mechanistic understanding and translational research in dry eye disease, we set out to establish a human lacrimal gland epithelial cell line.
We established three SV40 immortalized epithelial cell lines from a female human lacrimal gland. We characterized the cell lines at the genomic and protein level using RNA sequencing, RT-PCR and immunofluorescence staining. We also analyzed their epithelial character using scanning electron microscopy and a transwell diffusion assay and further characterized them in a 3D cell culture model.
We successfully selected three immortalized human single cell clones with characteristics of human lacrimal gland epithelial cells (hLGECs). Typical transcription factors such as PAX6 and FOXC1 were expressed and immunostaining showed their localization in the nucleus. We also showed expression of the LG markers AQP5, CSTB, CST6, and MYL9 and the tear proteins lactoferrin and lysozyme. The ability to form an epithelial cell sheet was confirmed morphologically and by a Fitc-dextran transwell diffusion assay. A 3D growth model showed the formation of spheroids that continuously expressed marker genes for lacrimal gland epithelial cells.
In this project, three cell lines with the characteristics of hLGECs were established. In the future, these three cell lines will be included in larger studies as they can be expanded to large cell numbers and will contribute to a better understanding of dry eye disease and the underlying molecular disease mechanisms.

Poster 38:

Title:
Purification of RECK-associated proteins from brain endothelial cells using combined in situ chemical crosslinking and affinity chromatography

Authors:
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Abstract:
Reversion-inducing cysteine-rich protein with kazal motifs (RECK) is a multidomain, GPI-anchored cell surface protein with a variety of functions. Initially identified as a metalloprotease inhibitor and tumor suppressor, more recent genetic studies in mice revealed RECK as an essential regulator of the WNT7/β-catenin pathway in brain endothelium, controlling developmental brain angiogenesis and blood-brain barrier formation. So far, RECK has been shown to directly interact with several metalloproteinases, GPR124, and WNT7A/7B. Here, we sought to identify novel RECK binding partners in brain endothelial cells using combined in situ chemical crosslinking and affinity chromatography.
The Reck gene of the murine brain endothelial cells line bEnd.3 was knocked out (CRISPR/Cas9) and functionally replaced with a doxycycline-inducible biotin acceptor peptide (BAP)-RECK fusion construct tuned to endogenous expression levels. To induce BAP-RECK biotinylation (bRECK), the cells were additionally transduced with the BAP-specific biotin ligase BirA. Large scale cultures of the cells were treated with the cell-permeable, thiol-cleavable chemical crosslinker DSP to stabilize protein-protein interactions in situ. Crosslinked bRECK protein complexes were isolated from cell lysates using streptavidin agarose beads. bRECK binding partners were specifically eluted by cleaving the crosslinker using DTT. Eluates were subjected to protein identification by mass spectrometry.
Mass spectrometry analyses identified the known RECK binding partners GPR124 and ADAM10 as well as several previously unknown RECK-associated cell surface proteins.
We successfully established a brain endothelial cell model and protocol for isolation of RECK-associated proteins. The newly identified RECK interactions will be analyzed biochemically and functionally in follow up studies.

Poster 39:

Title:
Ionocytes in the Murine Urethral Epithelium

Authors:
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Abstract:
Objective: Mucosal epithelia of different organs can contain three types of rare epithelial cells, namely tuft (brush, cholinergic chemosensory) cells, neuroendocrine cells, and ionocytes. In the urethra, neuroendocrine cells are well established, and we previously reported the presence of tuft cells based on a hypothesis-driven approach. We aimed to provide an inventory of rare cells in the urethra by an unbiased approach.
Methods: A publicly available single-cell sequencing data (GSE145865) of mouse urethral epithelial cells was reanalyzed using the Seurat package in R focussing on specific ionocyte marker genes, including *Forkhead Box I1 (Foxi1), Barttin CLCNK Type Accessory Subunit Beta (Bsnd), and ATPase H+ transporting V1 subunit B1B2 (Atp6v1b1b2)*. The results guided selection of primers and antibodies for further RT-PCR, immunofluorescence and immune electron microscopy. To distinguish ionocytes from other rare cell types, we utilized a tuft cell reporter mouse strain (*Trpm5*-eGPF, n=4 of each gender and antibody; total n=16) and antibodies against the neuroendocrine cell marker serotonin.
Results: Unbiased scRNA-seq data analysis revealed well separated clusters of neuroendocrine cells and ionocytes, and only few tuft cells. Ionocytes represented 0.49% of the total urethral epithelial cell population. Their markers were *Foxi1, Bsnd, Atp6v1b1b2, Atp6v1g3,* and *Clcnkb,* but not *Cftr*. In urethrae of *Trpm5*-eGFP mice immunolabelled with antibodies against serotonin (neuroendocrine maker) and BSND or Atp6v1b1b2, more than 90 % of rare cells (n=6,584 cells) were positive for only one marker. Single-positive cells appeared in equal proportions. Ultrastructurally, ionocytes (BSND-immunoreactive) showed no bundles of stiff microvilli, a characteristic feature of brush and neuroendocrine cells, at their lumenal surface. In the basal region, long and thin (<0.1 µm) finger-like protrusion extended between neighbouring cells. Stereological point counting analysis revealed a higher volume density of mitochondria compared to other epithelial cells.
Conclusions: This study establishes ionocytes as a third rare cell type in the urethral epithelium. Its ultrastructure is consistent with a high capacity of ion transport.

Poster 40:

Title:
Soluble VE-cadherin disrupts endothelial barrier function via VE-PTP/RhoA signalling

Authors:
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Abstract:
Increased levels of soluble Vascular endothelial (VE)-cadherin fragments (sVE-cadherin) have previously been linked with inflammation-induced loss of endothelial barrier function. We tested whether sVE-cadherin is critically involved in the onset of endothelial barrier dysfunction.
Application of recombinant human sVE-cadherin (extracellular domains EC1-5) on human microvascular endothelial cells *in vitro* and in a rat model *in vivo* induced loss of endothelial barrier function and reduced microcirculatory flow. sVE-cadherin^{EC1-5} led to decreased localization of VE-cadherin at cell borders. Additionally, sVE-cadherin^{EC1-5} perturbed VE-protein tyrosine phosphatase (VE-PTP)/VE-cadherin interaction. VE-PTP inhibitor AKB9778 blunted all sVE-cadherin^{EC1-5}-induced effects *in vitro* and *in vivo*. Downstream effects involve VE-PTP-dependent RhoA activation which was attenuated by AKB9778. Rho-kinase inhibitor Y27632 blocked sVE-cadherin^{EC1-5}-induced loss of endothelial barrier function.
sVE-cadherin disrupts endothelial barrier function by dismantling the VE-cadherin complex at cell borders via VE-PTP-dependent RhoA activation. This uncovers a pathophysiological role of sVE-cadherin in the context of endothelial barrier dysfunction in inflammation.

Poster 41:

Title:
Anatomical analysis of a hallux valgus foot pair in comparison to a normal one

Authors:
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Abstract:
Hallux valgus foot deformity is a common and progressive clinical problem characterized by lateral deviation of the hallux and medial deviation of the first metatarsal bone.
Among the lower extremities, evaluated during the gross anatomy course of Rostock Anatomical Institute in the summer term of 2022, a comparative analysis was conducted between a foot pair with hallux valgus and a quiete normal foot pair.
In case 1, an 87-year-old female exhibited valgus positioning of the hallux on both sides, along with varus position of the first metatarsal bone. The sesamoids were oriented laterally, and the toes showed a splayfoot arrangement. Within the muscles acting on the big toe, the abductor hallucis had become a flexor and the flexor hallucis brevis had transformed to an adductor.
In case 2, a 78-year-old female displayed only a slight lateral deviation of the big toe with the sesamoids in their normal position. The insertions of the abductor hallucis and flexor hallucis brevis remained unchanged.
The etiology of hallux valgus is multifactorial. High-heeled shoes are certainly known to contribute to this significant toe deformity, and a positive family history is often observed. Other intrinsic factors include general ligament laxity, anatomical variations of the first metatarsal bone, flat feet, and a shortened Achilles tendon or calf muscle. Recent research has also indicated that additional tendons of the extensor hallucis longus can predipose individuals to hallux valgus deformity.
Further studies will examine the potential impact of muscle and tendon variations on the deviation of the big toe.

Poster 42:

Title:
Transcutaneous vagus nerve stimulation as a treatment option for adjuvant brain metastasis prevention and brain cancer therapy

Authors:
Niklas Frank (Department of Anaesthesiology, Intensive Care, Emergency and Pain Medicine, University hospital Würzburg, Würzburg), Michiaki Nagai (Cardiology and general medicine, Hiroshima Asa Citizens Hospital, Hiroshima), Carola Y. Förster (Department of Anaesthesiology, Intensive Care, Emergency and Pain Medicine, University hospital Würzburg, Würzburg); foerster_c@ukw.de

Abstract:
Breast cancer brain metastasis (BCBM) is associated with poor prognosis and, insufficient treatment options. Blood-brain barrier (BBB) transmigration plays a key role in BM. Preventive therapeutic strategies are urgently wanted, eg by targeting inflammation.
Transcutaneous vagus nerve stimulation (tVNS) has gained prominence in the treatment of various clinical disorders. Recent studies consistently show better cancer prognosis, independent of confounders such as cancer stage and treatments.
For tVNS application we use the cutaneous distribution of afferent vagus nerve fibers in the auricle (tragus, cymba concha, ABVN) for stimulation and monitor of HRV and inflammatory markers. Previous studies indicate that tVNS mediates anti-inflammatory effects and increased BBB integrity. Our own clinical studies showed that i) tVNS-mediated beneficial effects on blood pressure control and in addition, that ii) tVNS results in afterload reduction in acute HF patients.

To extend this line of investigation we design an analysis of expression of cellular markers of tVNS-induced anti-inflammatory effects in endothelial cell lines from mouse brain and myocard to establish tVNS as a novel adjuvant anti-inflammatory therapy to prevent BCBM and associated cardiac complications.
In the present study, we test the hypothesis that restoring BBB function through tVNS administration and reducing barrier leakage by scavenging pro-inflammatory mediators will restore barrier function, decrease neuroinflammation, maintains the neuro-cardiac axis and by this slows cognitive decline . tVNS is thus highly suitable as a treatment option for adjuvant brain metastasis prevention and brain cancer therapy and might be potentially preventive against cardiooncologic complications resulting from cancer treatments.

Poster 43:

Title:
Predictive molecular pathology after long-term formalin fixation: a study on tissue from body donors in the gross anatomy course

Authors:
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Abstract:
While the feasibility of histo-morphological investigations on long-term formalin-fixated (LTFF) tissue has been proven in the past, there is currently only limited knowledge regarding the applicability of molecular methods on LTFF tissue.
In a pilot study, 57 tissue samples were collected from from body donors in the gross anatomy course at the Ulm University (WS 2019/20 and 20/21). Of these, 11 involved tumor entities which were tested for their suitability for molecular pathological methods. The post mortem interval until fixation lasted on average 2.5 days (min/max: 1-6 days). Fixation was performed with formalin-based solution (0,9L of 30% formaldehyde solution/body) according to the method of Tutsch (1975). The average storage time was 9.8 ± 3.4 months (min/max: 7-18 months). Molecular analysis was performed on biomarkers of different tumor entities according to pathological routine diagnostics. Methods used included DNA isolation, pyrosequencing, fluorescence in situ hybridization, analysis of methylation, clonality, and mutation.
In general, an investigation of long-term formalin-fixed tissue with molecular pathological methods was possible, nevertheless samples showed significant variability in their quality and evaluability. Pyrosequencing was successful in all investigated samples. Methylation analyses were partially not feasible, or it had not been possible to isolate enough DNA for it.
The use of LTFF tissue samples from body donors opens up new approaches in research and education: It is conceivable that these samples could be used for genetic studies or biobanks. Sample collection during the gross anatomy course performed as a “pathological ward round” and its histopathological work-up are an integral part of medical students’ anatomy education in Ulm. Tumor diagnoses made during donors' lifetimes could be confirmed or even specified.

Poster 44:

Title:
VALIDATION OF AUTOMATED ANALYSIS OF CARTILAGE TRANSVERSE RELAXATION TIME (T2) USING CONVOLUTIONAL NEURAL NETWORKS (CNNs) IN KNEES WITH AND WITHOUT MRI CARTILAGE DAMAGE – ON BEHALF OF THE OA-BIO CONSORTIUM

Authors:
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Abstract:
Cartilage T2 is thought to reflect cartilage composition (hydration, collagen), mechanical properties, and early alterations in osteoarthritis. We aimed to clinically validate a CNN-based, fully automated analysis method for measurement of laminar cartilage T2, in knees with and without MRI cartilage damage.
Multi-echo spin-echo (MESE) MRIs from a public image repository were used (the OAI). U-Nets for automated femoro-tibial cartilage segmentation were trained on 92 MESE MRIs of healthy reference subjects, with manual segmentation completed. These U-Nets were then applied to 741 radiographically normal knees of the OAI incidence cohort (full sample), 123 of which had manual cartilage segmentation (subsample). Differences (Cohen D) in T2 were compared between knees with vs. without cartilage damage (MOAKS score >0).
Of 741 knees studied, 333 displayed medial and/or lateral cartilage damage. Medially, superficial cartilage T2 was longer in knees with than in those without damage, using manual/automated analysis of the subsample (Cohen D 0.63/0.58), or automated analysis of the full sample (0.70). Deep cartilage T2 did not differ between these groups with either method. Laterally, T2 was longer in knees with cartilage damage, in superficial and deep layers, in the sub- and full sample; Cohen D values were similar for manual vs. automated analysis.
A fully automated CNN-based analysis method identified comparable differences in laminar cartilage T2 between knees with vs. without MOAKS cartilage damage as quality-controlled, manual cartilage segmentation. This approach shows great potential for compositional cartilage analysis in large samples and clinical trials focusing on early osteoarthritis.

Poster 45:

Title:
Vascular coloured latex injection as a feasible facilitator of dissection and deeper learning of anatomy of the hand

Authors:
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Abstract:
Understanding the vascular anatomy of the hand is challenging for medical students and residents. Nevertheless, a comprehensive knowledge of anatomy is essential for good results at hand surgery. The best teaching method is careful dissection of human cadaveric specimens. Injection of the vascular system with coloured latex to allow arteries and veins to appear more prominently should result in a substantial facilitation of the dissection process for students and teachers.
In a pilot study, four specimens had undergone coloured latex injection at the sites of radial and ulnar artery and veins for subsequent dissection. A survey among students and medical residents confirmed the feasibility of anatomical dissection and study between hands with and without latex injection. As a next step, the method was applied in a postgraduate training setting.
Tissue penetration of latex was excellent in all specimens and clearly improved malleability and vascular identification. The technique was fast and easy to apply in a postgraduate educational training workshop for anatomy teachers with varying levels of experience.
We consider that injection of coloured latex, reaching small calibric vessels, and giving tissues a greater malleability and flexibility, allows facilitated dissections and exposure and makes them suitable for improved anatomy and surgery teaching. The method is fast, easy and affordable to establish in various teaching settings, be it in a dissection course, in a training course for surgical specialties, or a postgraduate training setting as recently applied in a workshop for anatomists with varying levels of experience.

Poster 46:

Title:
Features of clinical anatomy of facial ligaments

Authors:
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Abstract:
Understanding of the mechanism of facial aging is inextricably linked with the analysis of the structure, position and relationship of the ligaments of the face. We conducted an anatomical study in order to describe in detail the zygomatic, masticatory and mandibular ligaments.
The study was carried out by the method of layered dissection of the fresh cadavers. A total of 30 heads, 15 heads of each sex, were selected for the study. The main inclusion criteria were the absence of surgical interventions and injuries in the lateral region of the face.
The zygomatic ligament was most pronounced in all observations and was represented by dense connective tissue cords, while in a number of observations the main part of the ligament was represented by tendon fibers coming from the muscle fibers of the zygomatic major muscle. The masseteric ligaments and the mandibular ligament were represented by connective tissue coming from the parotideomasseteric fascia. In addition, unlike all the others, it was only in the course of the fibers of the zygomatic ligament that it was possible to unequivocally state their interweaving into the skin. The remaining bundles were lost, weaving into the thickness of the SMAS.
The zygomatic ligament should be considered not an osteocutaneous ligament, but an osteomusculocutaneous ligament, such an understanding makes it possible to better assess the role of the zygomatic major muscle in the mechanism of aging. The group of ligaments, including the masticatory and mandibular ligament, should also be considered not osteocutaneous, but fascio-SMAS ligaments.

Poster 47:

Title:
An hitherto unknown variation of the arterial supply of the liver – new insights into vitelline artery development

Authors:
Silke D. Storsberg (Institute for Anatomy, Brandenburg Medical School, Neruppin), Sandra Petzold (Institute of Anatomy, Otto-von-Guericke-University, Magdeburg), Karin Fischer (Institute of Anatomy, Otto-von-Guericke-University, Magdeburg), Anja Oelschlegl (, Leibniz-Institute for Neurobiology (LIN), Magdeburg), Sven Schumann (Institute for Microscopic Anatomy and Neurobiology, Johannes Gutenberg-University, Mainz); sven.schumann@uni-mainz.de

Abstract:
Knowledge of arterial variations of the abdominal organs is of great clinical importance in visceral surgery and interventional radiology. Additionally, vascular variations can give insight into the embryonic development of the vascular system.
An hitherto unknown combination of vascular variations in the arterial supply of the liver was observed in a Caucasian female body donor during routine dissection course.
Here, we described the combination of a replaced common hepatic artery and an aberrant right hepatic artery branching from the superior mesenteric artery and an aberrant left hepatic artery arising from the left gastric artery.
This pattern of arterial variations gives insights into the differentiation of the vitelline arteries. Clinicians should be aware of hepatic artery variations to avoid bleedings or ischemia during abdominal surgery or interventional radiology.

Poster 48:

Title:
Arteriovenous Anastomoses of the Hoyer Grosser type in the subungual region of human fingers

Authors:
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Abstract:
Arteriovenous anastomoses of the Hoyer Grosser type are specialized vascular structures that regulate dermal blood flow. Their core element is a thick-walled channel, the Sucquet-Hoyer canal. Investigating the complexity of the SHC can enhance the understanding of the physiology and function of Hoyer Grosser's Organs (HGOs), and can assist in the diagnosis and management of dermal pathologies. This study, therefore, aims to characterize SHCs that occur in the subungual region and to provide information on their frequency and complexity.
8 biopsies were harvested from the subungual tissue of the 1st and 4th fingers of embalmed corpses. Employing the High-Resolution Episcopic Microscopy (HREM) technique, digital volume data with voxel dimensions of 1.5×1.5×1.5µm3 were produced and the SHCs of the HGOs were manually segmented. Then their numbers were counted in comparable volumes and their tortuosity (τ Value) was calculated.
On average, about 4 HGOs were located beneath an area of 2x2mm2. The average tortuosity of their SHC was 3.68 (1.11 to 10). 27 (81.8%) SHCs were single channels connecting dermal arteries and veins while 6 (18.2%) arose as single channels but split into two tributaries, which joined different veins. 69% of the HGOs were located in the lower 50% depth of the dermis.
Our objective and comprehensive characterizations of the SHCs located in the subungual region of fingers revealed considerable variability in their complexity. Since we hypothesize that complexity reflects function, we suggest to distinguishing between simple and complexly formed HGOs when studying HGO physiology.

Poster 49:

Title:
Three dimensional-CT reconstructive evaluation of the shoulder joint bone-to-bone spacing values in non-European population

Authors:
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Abstract:
Accurate measurement of physiological bone-to-bone spacing values for the shoulder joint facilitates a better understanding of anatomical structures. Our aim was to establish physiological reference values of the supraspinatus outlet area (SOA), available supraspinatus outlet area (ASOA), acromiohumeral distance (AHD), and coracohumeral distance (CHD) values in a normal Chinese population sample.
A total of 96 Chinese patients without any shoulder disorders were retrospectively included in the study. The SOA, ASOA, AHD, CHD, were quantitatively measured using 3D-CT reconstruction techniques. The correlation between the anatomical parameters were assessed using Pearson correlation coefficient.
We found that the SOA (men: 957.62 ± 158.66 mm2; women: 735.87 ± 95.86 mm2), ASOA (male: 661.35 ± 104.88 mm2; female: 511.49 ± 69.26 mm2), and CHD (men: 11.22 ± 2.24 mm; women: 9.23 ± 1.35 mm) were significantly higher in men than that in women ($p < 0.001$). Interestingly, both SOA and ASOA were linearly correlated with AHD, CHD (R: 0.304 - 0.494, $p < 0.05$).
In a normal Chinese population sample, SOA and ASOA was positively correlated with the AHD or CHD values. Individual consideration should be given to different geographical populations when establishing anatomical structures of the shoulder joint bone-to-bone spacing values in non-European population.

Poster 50:

Title:
Skull morphology and brain size in crested chicken (Gallus gallus f.d.) with cerebral hernia

Authors:
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Abstract:
Crested chicken show abnormalities in their anatomy of the skull, endocranium and brain (including cerebral hernia) and can be appropriate model systems for neuroanatomical evolution, brain-skull integration and craniofacial and brain deformities.
Here, we give a detailed macroscopic and microscopic description of the skull of crested chicken with and without cerebral hernia, including ontogenetic aspects and an allometric analysis of their brain size.
In total, 109 chicken of two different strains of Padovana chicken were hatched together. All animals were x-rayed weekly during growth. Nine juvenile and 22 adult skulls were processed for histology and morphological descriptions, further 20 individuals for the brain analysis.
At hatching, all chicks were already crested, a distinctive bony protuberance was firstly shown at an age of 4 weeks. Juvenile chicken exhibit either an open neurocranium or a protuberance. In the adult skull, foramina of different sizes can be found in the frontal bone. Besides, several peculiarities can be observed in the os mesethmoidale, os nasale, orbit and cranial fossae. The brain of Padovana with cranial protuberances looks like drawn in length with the shape of an hour-glass. Padovana with protuberance showed significant larger encephalisation indices than plain-headed breeds, topped only by another crested chicken breed.
Investigations on chicken with cerebral hernia may facilitate the understanding of skull and brain dysplasia and may provide meaningful insights into cerebral hernia development. Additionally, crested breeds, combined with standard chickens, form a promising comparative system for investigating the emergence of novel brain and skull morphologies.

Poster 51:

Title:
The interincisive suture in humans – fact or fiction?

Authors:
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Abstract:
Detailed knowledge of palatine sutures is of great clinical importance in dental surgery and orthodontics, for example during treatment of a cleft palate. While the incisive suture, which separates the incisive bone from the palatine process in newborns, is extensively described in anatomical literature, the interincisive suture, which lies in the midline of the incisive bone, is poorly characterized in humans.
Using an Ultra-High Resolution CT Scanner (UHR CT), we analyzed occurrence and morphology of the human interincisive suture both in prenatal and postnatal macerated dry skulls, as well as in patients of different sexes and ages.
We were able to visualize the interincisive suture both in prenatal and postnatal human individuals. Our results provide new insights into the development of the palate. Clinicians should be aware of the interincisive suture during orthodontic treatment or surgical intervention. The interincisive suture appears as a continuous structure in the maxilla across all examined images. Therefore, its appearance should be known and taken into consideration in the treatment planning of orthodontic or surgical interventions.

Poster 52:

Title:
Bilateral insertion of axillary arches at the medial epicondyle of the humerus via a chondroepitrochlearis muscle

Authors:
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Abstract:
9% of the central European population features at least unilaterally an anatomic variation named as axillary arch. This report aims to present a very rare variation of an axillary arch, which bilaterally inserts at the medial epicondyle of the humerus.
Both axillae of a non-embalmed and unharmed female body donor (82-year-old) were bilaterally exposed by carefully anatomic dissection during a study examining the frequency of axillary arches. After identifying axillary arches, the entire antero-medial brachium was also dissected to fully expose the identified variation.
Both axillae showed a largely identical situs. A muscular axillary arch split from the latissimus dorsi muscle. It crossed the axillary neurovascular bundle and joined the tendon of a chondroepitrochlearis muscle at the level of the proximal humerus. The tendon of the chondroepitrochlearis muscle then inserted at the medial epicondyle. Upon abduction and external rotation of the arm, the axillary arched compressed the axillary neuromuscular bundle.
While a high proportion of the central European population features axillary arches, a chondroepitrochlearis muscles is a very rare variation. We provide the first documentation of a bilaterally existing chondroepitrochlearis muscles, which are joined by muscular axillary arches. The detection of this situation in merely one out of 200 body donors reflects the very rare existence of chondroepitrochlearis muscles.

Poster 53:

Title:
Histomorphological Fundamentals of the Human Clitoris: Distribution and Density of Different Sensory Corpuscles

Authors:
Michael Wolf-Vollenbröker (Institute for Anatomy I, University of Düsseldorf, Medical Faculty, Düsseldorf), Lea Piermaier (Institute for Anatomy I, University of Düsseldorf, Medical Faculty, Düsseldorf), Dan mon O'Dey (Department of Plastic, Reconstructive, and Aesthetic Surgery, Hand Surgery; Center for Reconstructive Surgery of Female Gender Characteristics, Luisenhospital Aachen, Aachen), Timm Joachim Filler (Institute for Anatomy I, University of Düsseldorf, Medical Faculty, Düsseldorf); wolfvoll@hhu.de

Abstract:
The understudied human clitoris acts as an outstanding sensory organ of the female outer genitalia and is involved in forming and supporting sexual arousal. The morphological basis of this pronounced sensitivity lies in the composition of various sensory elements. This study aimed to reveal the occurrence, distribution and density of these corpuscles.
Four entire human external female genital organs were collected from body donors, fixed in 4% formaldehyde, divided medianly, and sectioned in craniocaudal direction into 5mm slices. These were histologically processed, stained, and digitalized. Subsequently, we counted the different sensory corpuscles regarding their hosting tissues to gain an amount per area.
The histological examination shows a broad spectrum of sensory corpuscles: (1) Genital corpuscles are found mainly in the area of the clitoral erectile tissue itself and in the cutaneous parts of the labia. (2) Ruffini-like corpuscles, (3) Vater-Paccini- and (4) Golgi-Mazzoni-bodies can be observed mainly adjacent to the clitoral tunica albuginea. The results were listed in density per tissue (corpuscle/µm2).
The presentation of the corpuscles distribution per tissue area allows a more detailed interpretation of the complex sensory processes and presents the role of the different tissue/organ parts concerning their functional contribution to the sensitivity of the external female genitalia.

Poster 54:

Title:
Goblet cell staining and mucin preservation in the mucosa of different segments in the porcine intestine: effects of Carnoy's fixative and modified alcian blue/periodic acid Schiff and mucicarmine staining

Authors:
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Abstract:
Carnoy's fixative is specifically designed for the preservation of mucins. Different staining techniques show the goblet cells indirectly through fixation and/or chemical interaction with the mucins. Two of these stainings are Alcian Blue (at pH 2,5)/Periodic Acid Schiff stain [AB/PAS], and Mucicarmine stain. In our study we compared both stains for the detailed examination of goblet cells and the mucous layer in three porcine intestinal segments (jejunum, ileum, and colon) fixed with Carnoy's fixative.
Tissue samples of the jejunum and ileum (both with areas containing Peyer’s patches) and from the colon were taken from 12 piglets aged 42 days/56 days. From every sample 4 slides with each two 5 µm thick slices were prepared and histochemically stained. Morphometric measures of goblet cells and mucous thickness were performed in the regions of jejunal and ileal villi and crypts, colon crypts, and on the dome epithelium of the Peyer’s patches.
The AB/PAS stain differentiates between neutral and acid mucins in the tissue. Acidic mucins are stained (dark)blue with AB, and neutral mucins are stained magenta/red with PAS. A combination of acidic and neutral mucins stains the tissue in different variations of purple. Mucicarmine stains the goblet cells pink or magenta. A thick two-layer mucosal coat was absent on the domes of the Peyer’s patches.
Both staining methods allow good evaluation of mucin-rich cells/goblet cells in the tissues. First results demonstrate in the young piglets a marked reduction of the mucus layer of the dome epithelium due to the missing goblet cells in the follicle associated epithelium.

Poster 55:

Title:
Lunate fossa (fossa lunata). An anatomical landmark of the wrist

Authors:
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Abstract:
The lunate fossa is often the starting point of a cystic swelling called a "ganglion". To make the anatomy of this region more relevant to the needs of clinicians and more accessible to students, we propose to introduce the term lunate fossa (Fossa lunata) on the dorsal side of the wrist just distal to the os lunatum.
The easily located fossa will help in the examination of the wrist to more easily understand the anatomy of the wrist and facilitate the examination of patients with wrist injuries when an injury to the lunate (Os lunatum) is suspected.
We propose the term lunate fossa (Fossa lunata) for the triangular depression on the dorsal side of the wrist located between the tendons of the extensor carpi radialis brevis (Musculus extensor carpi radialis brevis) on the radial side and the extensor digitorum muscle for the index finger (Musculus extensor digitorum) medially. The base of this fossa is formed by the distal part of the radius and its floor by the scaphoid and lunate, which interact in the plane synovial scaphoid-lunate joint.
1. We propose the term lunate fossa for the triangular depression on the dorsal side of the wrist, located between the tendons of the extensor carpi radialis brevis (musculus extensor carpi radialis brevis) radially, and the extensor digitorum for the index finger (musculus extensor digitorum) medially.
2. Its base is formed by the scaphoid and the lunate, which interact in the planar synovial scaphoid-lunate joint.

Poster 56:

Title:
Annuloplasty of the Mitral Valve - Accuracy of Anterior Leaflet Sizers

Authors:
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Abstract:
A method for selecting the appropriate size of a mitral annuloplasty ring is to define the dimensions of the anterior leaflet with a sizer. Our study aims to evaluate whether in vivo selection of sizers is accurate and whether sizer dimensions reflect the true dimensions of the anterior leaflet.
Mitral valves of 50 non-embalmed human hearts were examined. Simulating intraoperative conditions, the left atrium was exposed, different sizers (Edwards Lifesciences) were placed at the anterior leaflet and the best fitting was selected. The mitral valves were then excised and straightly mounted on a cork sheet. In this position, again the best fitting sizer was selected and important valve dimensions were measured.
The selected sizers varied from 26 to 36. 24 fitted for 6, 28 for 10, 30 for 15, 32 for 13, 34 for 6 and 36 for 2 leaflets. In 9 cases the sizer selected in situ was smaller than the sizer selected when assessing the anterior leaflet of the mounted valve. The length of the annulus segment of the anterior leaflet and its height were 20% on average, its surface area 30% and the distance between the commissures was 27% greater than the dimension of the corresponding sizer.
Our results show that, when performing annuloplasties, there is an 18% chance to select sizers, which are smaller than required. Also, there is an obvious discrepancy between the dimensions of fitting sizers and the true dimensions of the anterior leaflets of the mitral valve.

Poster 57:

Title:
On a specific proprioceptive layer in the outer eye muscles

Authors:
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Abstract:
The extraocular muscles differ from the rest of the skeletal muscles. Constantly in use, they show an almost tireless activity requiring advanced sensory feedback. The role of their proprioception (e.g., muscle spindles) in humans has been discussed scarcely in the scientific literature and is very controversial. We assumed a specific distribution pattern of muscle spindles could explain the contradictions.
The entire contents of 7 orbits of our body donors underwent a histological process. In addition, the individual eye muscles were dissected, sectioned, and examined separately under the microscope for a topographical counting of muscle spindles.
We could confirm the earlier described varying numbers of muscle spindles in the respective muscles. A new observation is a significantly enhanced equipment of the outer (orbital) muscle layers with numerous muscle spindles and multiple muscle cells embodying central cell nuclei chains paired with a similarly high number of elastic fibers, defining a specific functional lamella. Furthermore, we found no evidence of a muscle spindle apparatus in one eye.
The observed distribution of muscle spindles allowed us to draw a map of the extraocular eye muscles. The next step is to look at the outcome of strabismus operations regarding the distribution of sensorimotor feedback.
The single observation of an eye (parallel eye not available) with obvious unknown propriosensing requires further investigation. Most animal species' eye muscles function without muscle spindles. To our knowledge, there is only one similar old description for humans.

Poster 58:

Title:
On the Lumbar Okada Space

Authors:
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Abstract:
Our goal was to examine the facet joint space, its recesses, and its relationship to supposed lumbar Okada spaces. We hypothesized that weak points in the elastic parts of the joint capsule could explain the formation of synovial cysts and other cystic formations along the ligamentum flavum and may be the reason for leakage during therapeutic injections.
We analyzed the transarticular flow of the facet joints T12 to L5 from six body donations and detected five extra-articular leakages through computed tomography. In addition, we examined the connecting retrodural spaces, earlier radiologically assumed to be lumbar Okada spaces, histologically in serial sections. We applied immunohistochemistry to determine the internal surfaces.
CT revealed in the upper capsule extravasation, where the agent spread toward the intervertebral foramen and the epidural space. In the center of the joint most leakage was present due to small clefts in the ligamentum flavum. The inferior recess of the joint showed abnormal contrast distribution dorsal paraspinal, presenting Okada spaces. Histology revealed spaces in the transition zone of a ligamentum flavum that have a synovial lining with synoviocytes.
These results suggest that injections might open irregular pathways through intervals in the ligamentum flavum. Two different principles characterize the Okada space formation mechanism and facet joint cysts. Cysts can develop at the upper and middle joint recess, likely the Okada space's origin. In our specimen, Okada spaces are epithelialized clefts with synoviocytes located inside the ligamentum flavum, and we observed a connection to the joint space.

Poster 59:

Title:
Evaluating virtual reality-based anatomy courses in addition to traditional anatomic teaching methods: lessons from the first semester of the Medical Curriculum Vienna

Authors:
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Abstract:
This study aimed to evaluate virtual reality (VR) teaching approaches in anatomy complementing traditional anatomic methods at the beginning of the Medical Curriculum Vienna (MCV). In the MCV first semester students of human medicine and dentistry are introduced to the skeletal system. These students participated in practical VR courses that were implemented in addition to traditional lectures and practical lessons of osteology. Advanced anatomic classes take place in the fourth to sixth semester of the MCV in the form of dissection courses.
At the Division of Anatomy, Medical University of Vienna, 760 first semester students of human medicine and dentistry were educated in a hybrid teaching setting. Both VR headsets (Oculus/Meta Quest 2) with software and human bone specimens were provided, allowing the students to prepare for oral exams. Following their practical courses, students were encouraged to fill in questionnaires comparing the value of VR and traditional anatomic teaching methods. Results of these student evaluations are presented in this study using tools of descriptive statistics. The majority of the participants in this cohort prefer bone specimens compared to VR methods for studying osteology.
The present study indicates that VR applications have the potential of complementing traditional educational methods, such as lectures and practical seminars, for teaching first semester students basic anatomy and osteology – although students prefer human bone specimens preparing for their oral osteology exams.

Poster 60:

Title:
On the importance of hands-on dissection courses for student's learning experience

Authors:
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Abstract:
The COVID pandemic made it necessary to teach the dissection courses of medical students partially online. This raises the research question if online teaching can be an acceptable replacement for hands-on courses.
A cross-sectional study was conducted which investigates evaluation results from two cohorts of students. One cohort with mostly hybrid teaching (388 students) whereas the other cohort took the first part of the course in presence and the second part was carried out in completely digital form (230 students). Students gave self-reports about their learning experience both in closed (40 Likert scale items) and free-form questions.
To analyze the Likert scale responses students were grouped by k-means clustering. Gap statistics suggested existence of three clusters in the first cohort which can be interpreted in the following manner: One cluster (45%) consists of students who prefer the digital format, mostly because of flexibility. The two other clusters showed preference for traditional teaching. A smaller cluster (12%) consisted of very motivated students who aimed at getting best insights by hands-on dissection courses while a larger cluster (43%) was formed by students who feared to miss important information in the digital format due to limited quality of video transmission especially for the learning of spatial topographical relations. The second cohort showed three similar clusters as well, but the preference for hands-on courses was even stronger.
Further analysis of the free form answers and factor analytic statistical analysis gave evidence that hands-on dissections courses are the optimal teaching method for macroscopical anatomy.

Poster 61:

Title:
New perspectives in arterial blood supply of the facial skin

Authors:
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Abstract:
Our aim is to evaluate the blood microperfusion of the SMAS in the zygomatic and infraorbital regions. We did this from a new perspective, integrating blood supply of the SMAS with its colagen and muscular fibers. We used new immunohystochemical techniques, never worked on this area.
Our Study group consists of 16 specimens, collected from 9 male and 7 women donors. The donors have been undertaken different surgical manouvras for benign formations in corresponding regions. To achieve our scope we related blood vessels identification by I-CAM 2 Imunohystochemical marker with the other components of SMAS. For collagen we used Anti-colagen III Antibody and for muscles Anti-MyH2x10 marker. We applied this markers on the same hystologic plates.
Our results highlight different calitative and quantitative relations between the existing colagen fibers, muscle fibers and arteries, in each region. Also, the directon, density and shape of the blood vessels differs by region.
Morphologic aspects, stratigraphy and regional anatomy of the superficial blood supply of the facial skin have important functional and clinical significances. The research topic must be continued on large groups of patients and correlated with the ultrastructural aspects of the SMAS.

Poster 62:

Title:
The muse from the Pharynx

Authors:
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Abstract:
Our aim is to highlight the modification which take place within oropharyngeal istmus during phonation and their functional significance.
We conducted a CCBT study on a group of 25 subjects. 9 of them are beginers in opera singing, another 7 have 7 years, in average of practicing opera singing and the other 8 are professionals, with more than 15 years of experience. each of them have been asked to perform three states: mimiting fonation, phonating on letter "O" and phonating on letter "I". We measured the oro-pharyngeal istmus dimensions on the CBCT images taken while subject war phonation each of the three states.
We found significant differences in contraction of oro-pharyngeal istmus muscles between the three phonatory states. Also, the most experienced subjects shown the most important morphologic changes of the oropharyngeal istmus during the three phonatory states.
The experienced opera singers are adapting much faster and more appropriate when passing from a phonatory state to another. This happens probably because they develop neurologic reflexes for this. This reflexes are directly related to the type of voice, gender, age and anatomical particularities.

Poster 63:

Title:
Is the tricuspid valve tricuspid?

Authors:
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Abstract:
Detailed anatomic descriptions of the macroscopic morphology of the tricuspid valve and awareness of norm variations are the basis for successful reconstructive surgery. Our study aims to provide detailed macroscopic descriptions of leaflet morphology of the tricuspid valve to enhance anatomic knowledge and to aid the repair of tricuspid valve pathologies.
Tricuspid valves of 50 non-embalmed human body donors (26 female, 24 male) were excised, mounted and classified according to the classification system proposed by Hahn R.T. et al.
16 (32%) tricuspid valves were classified as type I (anterior, posterior and septal leaflet), 2 (4%) as type II (unification of leaflets), 0 as type III (2 anterior leaflets), 11 (22%) as type IIIb (2 posterior leaflets), 11 (22%) as type IIIc (2 septal leaflets) and 10 (20%) as type IV (bipartition of leaflets).
Our results demonstrate the high variability in the morphology of the tricuspid valve. Since only type I can be considered as truly tricuspid, the majority of our collective was either quadricuspid, pentacuspid, or bicuspid. Interestingly, the frequency of the observed types does not match with the original findings of Hahn et al. This might be caused by the unequal patient collective and the multicentric set up used by Hahn and coworkers. We therefore suggest to launch single centered large-scale studies based on a randomized and comparable sample to provide precise information on tricuspid morphology.

Poster 64:

Title:
Novel techniques for hernia surgery require a subtle revisiting of the topographic anatomy of the ventral abdominal wall

Authors:
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Abstract:
The classic concept related to the ventral abdominal wall fascial system does not fully reflect the anatomical complexity as identified by enhanced visualization tools in modern hernia surgery. To avoid misguidance during hernia repair, the topographic anatomy of the ventral abdominal wall was reassessed.
Systematic stepwise dissection of the ventral abdominal wall was performed in formalin fixed body donors to describe and characterize the multi-layered fascial system. Selected regions were processed for large-scale histological examinations.
The obliterated umbilical arteries and urachus are encased within a matrix of adipose and loose connective tissue forming a triangular sheath extending from the umbilicus to the urinary bladder. This vesicoumbilical fascia is covered by parietal peritoneum at the dorsal side, lateral borders and partially at its ventral aspect due to peritoneal folding. Along the midline, the vesicoumbilical fascia is connected to the extraperitoneal tissue. The dorsal lamina of the rectus sheath extends anterior to the vesicoumbilical fascia and fades out at the arcuate line/zone. The transversalis fascia below the arcuate line/zone is bilaminar and splits up at the midline ensheathing a "fatty triangle".
The ventral abdominal wall exhibits multi-layered fascial structures not properly considered in current anatomical textbooks. Therefore, a reappraisal of the topographic peculiarities of the ventral abdominal wall anatomy is required. Moreover, detailed knowledge of the abdominal fascial system is mandatory for safe implementation of novel techniques in hernia surgery.

Poster 65:

Title:
Proprioceptors of the human pericardium

Authors:
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Abstract:
Proprioception describes the unconscious and conscious perception of the spatial tensile state of tissues, in which sensors generate impulse patterns to be processed in the central nervous system. Previous literature on the presence and distribution of proprioceptors has focused on the musculoskeletal system, while viscera have yet to be considered. Due to a lack of knowledge regarding sensory receptors of the heart, we studied the entire human pericardium to describe the presence, density, and distribution pattern of proprioceptors.
We used eight in situ fixed human pericardial specimens to create a three-dimensional map based on histological and immunohistological identification of proprioceptors in the pericardium.
We discovered a substantial number of Ruffini-like corpuscles close to all eight pericardia and identified three receptor-localization classes depending on the pericardial sublayers. Cluster analysis revealed that they dispose of in a specific pattern with the highest concentration around the largest ventricular diameter and the perivascular pericardial turn-up. No gender-specific differences were observed.
To the best of our knowledge, we present the first analysis of proprioceptive entities in the human pericardium. Our findings suggest that the pericardium is subject to proprioceptive control. Ruffini-like corpuscles sense lateral thrusts between the pericardial sublayers, and their distribution pattern enables the detection of differentiated dilation of the contiguous heart. The sensory feedback is most robust during pronounced displacements, such as those occurring at the largest diameter of the heart and during substantial volumetric oscillations at the rise of the large vessels. Therefore, it seems that the pericardium exhibits a new function.

Poster 66:

Title:
Biomechanical analysis of external fixators for the initial treatment of pelvic instability

Authors:
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Abstract:
Pelvic ring instabilities present complex orthopaedic injuries associated with high-velocity trauma or falls, affecting mostly young individuals, or fragility fractures in the elderly. Treatment involves damage control resuscitation to control bleeding and prioritise interventions, while emergency reduction using external fixators provides temporary stability and facilitates mobilisation. However, there is a lack of consensus regarding the optimal treatment and the most stable external frame configuration for specific injuries.
To provide an overview of the topic, a systematic review of previous biomechanical research on external pelvic fixators was conducted, indicating that mostly type C injuries have been studied. External fixation designs differed vastly in terms of device type and configuration, pin size and geometry. Loading protocols and measurement devices also varied considerably and inconsistent definitions of failure were determined.
Subsequently, a loading protocol was devised, and implemented in a sample of 27 pelves afflicted with type C fractures to assess the impact of various pin configurations on biomechanical stability under physiologic loading in double-leg stance. In line with the literature, the best choice for the insertion and stability of the pin at the anterior inferior spina iliaca was chosen. Measurement data was obtained by a universal testing machine and digital image correlation.
The preliminary research outcomes indicate that the choice of pin configuration may not have a significant impact on the overall stability of unstable pelves with type C fractures.
Further findings derived from this experimental study are elucidated.

Poster 67:

Title:
Experiences with student response systems in large group anatomy teaching.

Authors:
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Abstract:
Formative assessment is known to aid learning in several ways, it strengthens the memory traces of new knowledge, it discloses misconceptions and stimulates metacognition.

In this light we would like to share our experiences with student response systems in large group anatomy teaching.
We incorporated different question types in anatomy lectures and question-and-answer sessions for undergraduate students in medicine (Radboudumc) and technical medicine (University of Twente) using Mentimeter. These questions served the purpose of assessing student's understanding of the subject, improving interaction and involvement and evaluating the lectures.

To collect student's opinion on the use of Mentimeter during anatomy teaching, short evaluating questions were used at the end of each lesson. Additionally, a group discussion was conducted to collect teacher's experiences and opinions on the use of Mentimeter in anatomy teaching.
Student's feedback regarding the use of Mentimeter during anatomy teaching was positive. They reported increased engagement and motivation. They appreciated the opportunity to easily and accessibly assess their understanding of the subject.

Mentimeter also positively impacted overall teaching experience. Teachers observed heightened student involvement and more interaction. The real-time data provided valuable insights for refining teaching approaches and identifying areas that required further attention during the lessons and coming classes.
The integration of Mentimeter in large group anatomy teaching offers substantial benefits. These systems improve student engagement, facilitate formative assessment, and provide valuable feedback to both students and teachers.

Further research is warranted to investigate the effects of incorporating these systems on summative testing.

Poster 68:

Title:
Lactic acid-based fixatives as non-toxic and non-carcinogenic substitutes for body embalming – a pilot study by means of murine corpses

Authors:
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Abstract:
Formaldehyde is widely used for embalming, although having only limited approval as a biocide due to its cancerogenic properties. Denaturation by formaldehyde hardens most soft tissues and stiffens articulations limiting its use for surgical education. Therefore, formaldehyde-free ethanol (EtOH) is often used as an embalming fixative for advanced trainings, though lacking sufficient antimicrobial long-term effects. As an alternative, food preservatives might be promising as these are well known to inhibit bacteria and mold growth. Thus, we investigate in this project whether food preservatives are suitable for anatomical embalming needs.
Various food preservatives were initially tested for preservative effects in histology, with lactic acid (LA) demonstrating the most promising results. To further systematically investigate the suitability of ethanolic LA (LA-EtOH) for embalming, we compared LA-EtOH to current standards for dissection courses (i.e., ethanolic formaldehyde, FA-EtOH) and surgical trainings (i.e., EtOH) by means of murine corpses.
Mice were embalmed by transcardial perfusion with subsequent immersion postfixation and stored analogous to the condition in dissection courses, with repetitive exposure to room air. To assess microscopic preservation, histological samples were taken at specific storage times. For microbiological analysis, tissue samples were taken before and after embalming, and microbial load was assessed qualitatively and quantitatively, respectively. Alterations in organ coloration were documented.
In comparison to FA-EtOH, LA-EtOH-embalmment resulted in similar tissue integrity, but without denaturation effects, and good long-term antimicrobial effects. Only EtOH-embalmed specimens possessed early mold growth.
Based on our results, LA has the potential to prospectively substitute harmful formaldehyde for anatomical embalming.

Poster 69:

Title:
Vocalis muscle arrangement - a way for contraction to influence vocal oscillatory properties.

Authors:
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Abstract:
Objective
The aim of our study was to re-evaluate the arrangement of muscle fibers in the vocalis muscle and to compare it with current functional models of the vocalis muscle contraction. The vocalis muscle is disposed in a crossed pattern, with the conus elasticus acting as an intramuscular tendon. This means that the stiffness of both the vocalis muscle and conus changes during contraction.
Methods
We performed a literature search in the PUBMED and MEDLINE databases and in the Google Scholar database aggregator using the search terms: "vocalis muscle", "muscular fibers", "thyroarytenoid", "vocal fold histology", "vocal fold", "vocal cord", "adduction", "glottis shape", "multi-mass model", "vocal model", "body-cover", "airflow", "vocal register". Illustrations were drawn from the results showing the histological aspects of the vocalis muscle and the influence of the contractile models.
Results
The muscle fibers of the vocalis muscle are arranged to exert both an antero-posterior shortening and a transverse latero-lateral tension on the conus elasticus, since there are muscle fibers that attach directly to it. The increased stiffness of the conus increases the difference between wave propagation in the lower and upper mucosal halves during oscillation. This allows for more contraction states to produce the same acoustic result but with wider register selection.
Conclusion
The muscular arrangement of the vocalis muscle is functionally relevant as it can control oscillations in the mucosal layer of the vocal fold, traditionally considered a separate entity in models of vocal oscillations, this explains discrepancies between the predicted and observed response in vocal oscillations.

Poster 70:

Title:
Alteration of gut microbiota and brain parameters after refeeding in an anorexia nervosa rat model

Authors:
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Abstract:
The gut microbiota composition is causally involved in the regulation of body weight and eating behavior. Through the gut-brain axis, microbiota play a role in psychiatric disorders including anorexia nervosa (AN). Previously, we showed microbiota changes to be associated with brain volume and astrocyte reductions after chronic starvation in an AN animal model. Here, we analyzed the reversibility of these changes after refeeding.
The activity-based anorexia (ABA) model is a well-established animal model that mimics several symptoms of AN such as body weight loss, endocrine disruptions, and increased physical activity. Fecal samples were analyzed using 16S rRNA gene amplicon sequencing. Brain parameters such as volume and GFAP-positive astrocytes were measured in the cerebral cortex and corpus callosum.
Significant alterations in the microbiome were observed after starvation. After refeeding, including the normalization of food intake and body weight, α- and β-diversity as well as the relative abundance of specific genera were largely normalized in starved rats. Brain parameters appeared to normalize alongside microbial restitution with some aberrations in the white matter.
We confirmed microbial dysbiosis during chronic starvation and showed a high degree of reversibility after refeeding. Thus, microbiome alterations in the ABA model appear to be mostly starvation-related. These findings support the usefulness of the ABA model in investigating starvation-induced effects on the microbiota-gut-brain axis to help comprehend the pathomechanism of AN and potentially develop microbiome-targeted treatments for patients.

Poster 71:

Title:
Human skeletal muscle organoids recapitulate fetal myogenesis and sustain uncommitted PAX7 myogenic progenitors

Authors:
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Abstract:
Objective: In vitro culture systems that structurally model human myogenesis and promote PAX7^{+} myogenic progenitor maturation have not been established. The study aimed to develop and validate a novel skeletal muscle organoid system for investigating human myogenesis and muscular dystrophy pathogenesis.

Methods: A comprehensive growth factor supplementation / reduction protocol to first drive differentiation towards paraxial mesoderm through application of the GSK3 inhibitor CHIR99021, BMP inhibitor LDN193189 and bFGF and subsequent sequential stimulation with WNT1A, SHH, FGF and HGF was applied to Matrigel-embedded human induced pluripotent stem (iPS) cells. In addition, organoid cultures from three Duchenne muscular dystrophy (DMD) patient-derived iPS cell lines were performed. Immunohistochemical and scRNAseq analyses were applied to map the organoid developmental stages in detail.

Results: Human skeletal muscle organoids contain paraxial mesoderm and neuromesodermal progenitors and develop into organized structures reassembling neural plate border and dermomyotome. Culture conditions instigate neural lineage arrest and promote fetal hypaxial myogenesis towards limb axial anatomical identity, with generation of sustainable uncommitted PAX7 myogenic progenitors and fibroadipogenic (PDGFRa+) progenitor populations equivalent to those from the second trimester of human gestation. Single cell comparison to human fetal and adult myogenic progenitors reveals distinct molecular signatures for non-dividing myogenic progenitors in activated (CD44^{High}/CD98^{+}/MYOD1^{+}) and dormant (PAX7^{High}/FBN1^{High}/SPRY1^{High}) states.

Conclusion: Our organoid approach provides a robust 3D in vitro developmental system for investigating human skeletal muscle tissue morphogenesis and homeostasis.

Poster 72:

Title:
Quantum sensor for intracellular potential distribution

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Abstract:
Objective: In this work, we propose to develop a quantum sensor which is able to measure inner charge and potential of a cell utilizing quantum capacitive coupling between the device and biological material.

Methods: Here, we aim at measuring the electric stray fields of cells based on the Coulomb interaction with electrons in a nanoscale quantum device. As the electric stray fields of a cell rapidly decay with distance, it is important to place a sensor in close vicinity to the cell. Hence, we will craft our sensors in a two-dimensional sheet of carbon-based graphene, which is non-invasive to biological materials.

Results: The very first measurements performed at low-temperatures point that the quantum capacitance is dominant at certain magnetic field intervals, where quantum Hall effects can be observed. This can be directly observed at the entrance and exits of the quantized Hall plateaus, where the inner contact potential presents extreme potential oscillations compared to the normal (metal-like) phase.

Conclusion: Our initial experiments and numerical calculations point out that, capacitive coupling between the biological material and semi-conductor-based quantum sensor may pave the path to develop bio-sensing devices which promise a higher resolution and sensitivity. These devices, may have an important impact in improving diagnosis like Röntgen, MRI and similar physics base devices.

Poster 73:

Title:
Effects of microglia driven inflammation on glioblastoma cells

Authors:
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Abstract:
Tumor-associated macrophages, microglia, and astrocytes build up to 30-40% of tumor mass in glioblastoma, affecting migration, proliferation, and apoptosis. Several aspects of the tumor microenvironment, and cell-cell interactions have been linked to challenges in the treatment of glioblastoma, but therefore also offer a potential target for new therapeutic strategies.
In this work, the influence of differently activated murine BV2 microglia (via classical, alternative or acquired deactivation) by LPS, CBD, IL-1ß, IL-4, IL-6, or IL-10 was investigated on the human glioblastoma cell lines LN229 and U138.
Treatment with supernatant of conditioned BV2 cells led to significantly increased formation of multicellular tumor spheroids of LN229 and U138 glioblastoma cells in most cases. During collective migration, a significantly reduced mean speed of LN229 cells was found after treatment with supernatants of BV2 cells, independent of activation type. Furthermore, BrdU and Ki67 staining showed influences of supernatants on the proliferative capacity of U138 cells. In fluorescence-activated cell sorting measurements no effect of BV2 conditioned medium was detected on the cell cycle.
Altering the activation state of microglia cells affected all measurement parameters, but in a heterogeneous manner. Thus, additional research, taking e.g. tumor subtypes, etc. into account, should be conducted to elucidate
the heterogeneous response to differentially activated microglia.

Poster 74:

Title:
FLIM-FRET Analysis Reveals PRG5 Multimerization at the Cellular Level

Authors:
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Abstract:
Plasticity related gene 5 (PRG5) is a membrane protein predominantly found in neurons and is involved in cellular processes such as growth cone guidance, migration, and spine formation. Overexpression of PRG5 induces membrane protrusions, including filopodia in non-neuronal cell lines. Moreover, PRG5 contributes to the induction of spines in immature neurons and regulates the density and morphology of spines in mature neurons. The understanding of spine formation is vital as disruptions in spine appearance are associated with neurological disorders. Although the importance of PRG5 in neuronal function is evident, the precise mechanisms through which it induces membrane protrusions and orchestrates cellular responses remain unresolved. We hypothesise that multimerization of PRG5 is required for its function.
We aim to investigate this further using innovative techniques like Fluorescence Lifetime Imaging using Förster Resonance Energy Transfer (FLIM-FRET) which is a powerful technique that utilizes fluorescence lifetimes to detect and quantify energy transfer between fluorescent molecules. FLIM-FRET enables specific visualization of PRG5 multimerization at the plasma membrane and tracks temporal changes in cellular lifetimes. Notably, this effect is observed in non-neuronal cells and primary hippocampal neurons, with a primary localization of PRG5 multimers within small neuronal protrusions.
Unravelling the complexities of the role of PRG5 in membrane protrusion formation and signal transduction is crucial for advancing our understanding of neuronal development and addressing neurological disorders linked to spine abnormalities.

Poster 75:

Title:
Heterogeneous immune cell distribution in murine meninges

Authors:
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Abstract:
Three layers of meninges surround the central nervous system (CNS): The dura mater, the arachnoid mater and the pia mater. The arachnoid mater contains the subarachnoid space that is laced with a multitude of blood vessels. Recently, the meninges have been strongly implicated in the recruitment of immune cells. Previous work from our group demonstrated a profound region-specific heterogeneity in meningeal morphology and blood vessel distribution. Therefore, we hypothesize that peripheral immune cells accumulate in the meninges in specific regional patterns under neuroinflammatory conditions.
The morphology of human meninges from various CNS regions was assessed by (immuno)histochemical analysis in post-mortem tissue. Mice were subjected to a 3-week-long intoxication with Cuprizone (Cup) and subsequent experimental autoimmune encephalomyelitis (EAE) induction. The mice were perfused, and the intact skulls were collected and decalcified. Overall morphology and immune cell distribution within the meninges were assessed by (immuno)histochemical analysis of CD3-positive T-lymphocytes and Ly-6G- and Ly-6C-positive neutrophils.
Meningeal morphology and blood vessel distribution demonstrated high region-specific heterogeneity in human meninges. In the neuroinflammatory murine model, the accumulation of neutrophils and lymphocytes in the meninges was observed. A detailed analysis of the immune cell distribution indicated that the number of lymphocytes exceeded that of neutrophils. While the neutrophils demonstrated an even distribution over the meninges, the lymphocytes predominantly accumulated near the cerebellum and the brainstem.
Our findings indicate a heterogeneous immune cell distribution pattern in the murine meninges under neuroinflammatory conditions, hinting at potentially heterogeneous recruitment routes of immune cells into the brain parenchyma.

Poster 76:

Title:
Characterization of isoform-specific expression and function of Bcl11a in the central nervous system

Authors:
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Abstract:
The zinc-finger transcription factor Bcl11a plays important roles in neural development and it is well established that different isoforms are generated from the Bcl11a gene locus. However, the biological significance of the different isoforms remains unclear. Studies in humans suggest that BCL11A mutations differentially affecting isoform expression lead to varying clinical symptoms. To systematically explore expression and putative functions, we developed tools that allow isoform-specific analysis in mice.
We developed several molecular tools, including isoform-specific antibodies, FLAG-and Myc-tagged expression constructs to characterize Bcl11a isoform expression in cell culture and different brain regions of developing mice. To test in vivo functions in cortical neurons, we overexpressed Bcl11a isoforms using in utero electroporation.
Our findings show that Bcl11a isoforms exhibit spatiotemporal expression differences at the tissue and subcellular levels. In vivo overexpression of Bcl11a isoforms in wildtype brains differentially affects neuronal polarization and positioning, suggesting functional differences of Bcl11a isoforms. Bcl11a isoforms have overlapping but also differential spatiotemporal expression and function in forebrain development. The developed tools will be useful to further improve our understanding of Bcl11a function and its associated disorders.

Poster 77:

Title:
Stimulation of autophagy in hippocampal neurons by Neuropeptide Y

Authors:
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Abstract:
Neuropeptide Y (NPY) is one of the most abundant peptides in the brain. On the behavioral level, NPY promotes resilience to stress by reducing anxiety and fear memory generalization via NPY-positive hippocampal interneurons in the hippocampus. However, its cellular functions in the hippocampus are less well described. NPY was recently found to induce autophagy in primary hypothalamic and cortical co-cultures. Here, we investigate whether NPY modulates autophagy in hippocampal neurons.
Here we investigate autophagic dynamics in neuronal primary cultures of the rat hippocampus, in organotypic hippocampal slices cultures (OHSCs) from mice and in the mouse hippocampus in vivo by using western blot and immunocytochemistry for autophagy markers such as LC3. Treatment of hippocampal primary cultures with NPY induced autophagy for up to 24h. In organotypic hippocampal slice cultures, NPY altered LC3 expression in a dynamic time- and subregion-specific way. In vivo NPY-injections into the dentate gyrus of adult mice increased LC3 levels specifically in the DG hilus, a region containing NPY-positive interneurons. Chemogenetic silencing of local NPY neurons led to reduced LC3 intensities within these neurons 24h later. These alterations were accompanied by an increased mossy fibre area, indicating structural plasticity.
NPY regulates autophagy in the hippocampus in a dynamic and region- as well as neuron-subtype specific way. Potentially, NPY may shape structural plasticity of the mossy fibre system and other functional domains via autophagy modulation and thereby can potentially link cellular events to the observed behavioral effects of NPY.

Poster 78:

Title:
Neither cerebrospinal fluid nor blood serum of Alzheimer’s patients contain Antibodies to the Amyloid-β-clearance factor low-density-lipoprotein-receptor-associated-protein Lrpap-1

Authors:
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Abstract:
In the brains of Alzheimer's disease (AD) patients, β-amyloid (Aβ) accumulates in senile plaques, leading to neurodegeneration and cognitive decline. This depends on impaired Aβ-clearance over the blood brain barrier by the LDL-receptor-related-protein-1, and its regulator, the low-density-lipoprotein-receptor-associated-protein-1 (Lrpap1), expression of which is reduced in brain samples of AD-patients. In this context a previous in vitro finding, that antibodies directed to the Gram positive bacterium Listeria monocytogenes can interact with Lrpap-1, and by this increase β-amyloid levels in human neuroblastoma cell lines, seemed to us to be of importance.
To further clarify the in vivo relevance of such a mechanism, we analysed now the presence of antibodies binding to Lrpap1 in cerebrospinal fluid and blood serum samples from either AD-patients or from healthy controls using a commercial multiprotein array and other proteomic methods.
In contrast to our expectations antibodies interacting with Lrpap-1 could not be detected in either AD-patients liquor or serum samples, however were highly abundant in blood serum of healthy controls.
Therefore, in conclusion, the results of the present study are contradictory to a direct role of autoantibodies to Lrpap1 in AD-pathogenesis. This suggests also that the previously reported lower levels of Lrpap1 in AD-patients brains are probably not caused by an antibody dependent mechanism.

Poster 79:

Title:
Insights from in vitro studies: lipocalin 2 as modulator of the blood-brain barrier integrity and immune cell invasion in multiple sclerosis

Authors:
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Abstract:
The pathogenesis of multiple sclerosis (MS) includes vascular inflammatory processes with invading immune cells into the CNS. Endothelial cells mainly determine the integrity of the blood-brain barrier (BBB). Recent studies have identified lipocalin 2 (LCN2) as a protective molecule in MS animal models. Here, we aimed to investigate the impact of LCN2 on BBB integrity and immune cell invasion in the context of MS.
Endothelial cell cultures (bEnd3) were subjected to inflammatory conditions by stimulating with tumor necrosis factor alpha (TNF ALPHA, 60 ng/mL) and/or LCN2 (1 µg/mL) for 6 h. Gene and protein expression levels of chemokines, tight junctions, and adherens junctions were analyzed using RT-qPCR and immunofluorescence staining. Additionally, an immune cell migration assay was performed to evaluate the impact of LCN2 on immune cell traversal across the endothelial cell barrier.
LCN2 treatment reduced the expression of chemokines induced by TNF ALPHA. Furthermore, LCN2 treatment effectively prevented the re-localization of tight junction proteins, thereby preserving barrier properties under inflammatory conditions. Importantly, LCN2 treatment resulted in a reduction in immune cell migration through the endothelial cell barrier in vitro.
These findings suggest that LCN2 plays a crucial role in modulating BBB integrity and immune cell invasion in MS. LCN2 treatment attenuated the expression of endothelial chemokines, maintained tight junction integrity, and inhibited immune cell migration across the endothelial barrier. Understanding the mechanisms by which LCN2 influences BBB integrity may provide new approaches for novel therapeutics targeting immune cell invasion and preserving BBB integrity in MS.

Poster 80:

Title:
Ion Channels in Motoneurons of the Human Trochlear Nucleus

Authors:
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Abstract:
Extraocular muscles contain at least 6 different muscle fiber types, which based on their innervation pattern are divided in: 1. Singly-innervated muscle fibers (SIF) contacted by a central en plaque endplate, which respond with a twitch after stimulation. 2. Multiply innervated fibers (MIF) targeted by multiple en grappe endplates distributed along the entire muscle fiber, which respond with tonic contraction, when stimulated. In monkey, motoneurons of SIFs and MIFs lie separated and show different histochemical features including the ion channel profile. Here, we identified the MIF and SIF motoneurons in human trochlear nucleus (nIV) and studied them for fast voltage-gated potassium channels and HCN channels both important for high firing rates.
Thin (5µm) paraffin midbrain sections of three human controls were immunostained for aggrecan (ACAN) and choline acetyltransferase (ChAT) to identify MIF and SIF motoneurons. Neighbouring sections were treated with antibodies against Kv1.1, Kv3.1b, HCN1,2 and 4 channels, respectively. Three populations were found: Putative MIF motoneurons lacking ACAN-positive perineuronal nets (1) mainly in the periphery of nIV and putative SIF motoneurons with strong (2) and weak ACAN-labelling (3) intermingled within nIV. MIF motoneurons are smaller than SIF motoneurons. Both motoneuron groups express similar strong Kv1.1 immunoreactivity, whereas Kv3.1b is stronger in SIF motoneurons. HCN1,2,4 channels are expressed in MIF and SIF motoneurons. Interestingly, internuclear neurons lack HCN1 channels as verified in the abducens nucleus
The findings provide the neuroanatomical basis for investigations of differential vulnerability of motoneuron types in clinical cases, e.g. amyotrophic lateral sclerosis.

Poster 81:

Title:
Distribution of IgSF9b at GABAergic and glutamatergic synapses in mouse and human brain

Authors:
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Abstract:
Alterations in synaptic connections between GABAergic inhibitory neurons play an important role in the development of psychiatric and neurodegenerative diseases. However, the underlying molecular mechanisms are still not fully understood. In mice, the cell adhesion protein IgSF9b was recently identified as a component of GABAergic synapses, and it was found that deletion of IgSF9b normalizes anxiety related behaviour in a mouse model of anxiety disorders. Additionally, genetic studies have shown that variants of IgSF9b are associated with the development of several disorders in humans, such as schizophrenia or depression. To elucidate the functional role of IgSF9b in the CNS, we analyzed the regional and synaptic distribution of IgSF9b both in the mouse and human brain.
We performed immunostaining for IgSF9b in 12 different brain regions in mice and human body donors. Additionally, we analyzed the co-localization of IgSF9b with GABAergic and glutamatergic synaptic markers in the regions with the highest expression of IgSF9b.
Contrary to prior evidence in cell cultures, our results in mice indicate that IgSF9b is not exclusively localized at GABAergic synapses. The results in the human brain provide a complementary analysis to the investigations in the mouse brain and will facilitate translational research on IgSF9b between both species.
The current experiments form an important basis for further investigations into the role of IgSF9b in the development of psychiatric disorders. The investigation of the specific molecular composition of GABAergic and glutamatergic synapses in combination with the analysis of psychiatrically relevant circuits offers a potential opportunity for the development of more specific therapeutic interventions.

Poster 82:

Title:
Profile of ion channels and transmitter-related molecules in saccade burst generator neurons in a post-mortem case of opsoclonus

Authors:
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Abstract:
The saccadic burst generator in the brainstem includes burst neurons, which provide high frequent bursts to the motoneurons during a saccade. Between saccades burst neurons are inhibited by the glycinergic omnipause neurons (OPN), which have to be disinhibited for evoking a saccade. This circuit is further controlled by the cerebellar vermis and underlying caudal fastigial nucleus. An imbalance of the action of burst neurons and OPNs has been suggested to cause saccadic oscillations, such as opsoclonus, which may be due to alterations in membrane biology of involved neurons.
Here we studied the profile of fast-voltage gated potassium channels Kv1.1 and Kv3.1b mediating fast firing properties and hyperpolarization-activated inward mixed cation channels (HCN) mediating post-inhibitory rebound (PIR) properties in the OPNs in controls and an opsoclonus case in post-mortem tissue. Further, the expression of GABA-related proteins and glycine receptor were studied in OPNs and the cerebellum.
We found expression of Kv1.1. and Kv3.1b, HCN1, HCN2 and HCN4 and Cav3.2 and Cav3.3 channels in OPNs of controls that was not qualitatively different in the opsoclonus case. Immunostaining for the GABA-synthetizing enzyme glutamate decarboxylase (GAD) revealed an unexpected low GABA-input to OPNs in human compared to monkey that was accompanied by the lack of GABA A receptor expression. The GABA-input appeared reduced in the opsoclonus case. The GAD-staining pattern in the cerebellar cortex was normal, including the density of Purkinje cells, however an unusual somatal expression was found in neurons in the fastigial nucleus.
In conclusion fast firing and PIR properties of OPNs appear not to be affected in the opsoclonus case, however a decreased GABA input may render omnipause neurons hyperexcitable. An investigation of the burst neurons is still pending.

Poster 83:

Title:
Role of synaptic lipid modulated cortical excitability in motor control - importance for brain disorders

Authors:
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Abstract:
Bioactive synaptic lipids like lysophosphatidic acid (LPA) modulate synaptic homeostasis and excitation and inhibition (E/I) balance in cortical networks. Disruption of the plasticity-related gene-1 (PRG-1) protein, which regulates synaptic LPA levels, leads to increased glutamatergic release probabilities, higher neuronal excitability and consequently to a shift in cortical network E/I-balance. On the behavioral level, shifted E/I-balance results in hyperlocomotion, reduced sensorimotor gating and stereotypic behaviors - typical phenotypes of psychiatric disorders related to the dopaminergic system. Since PRG-1 is expressed at different levels of the motor control network (motor cortex, striatum, cerebellum) we aimed to analyze the effect of E/I-balance shifts at different motor control levels.
Effects of synaptic lipid-induced E/I shifts were analyzed in Prg-1-/- mice and in mice with cell-type specific Prg-1 deletion (dopamine receptor (D)1-expressing neurons, D2-expressing neurons, Adora2a-expressing neurons and Purkinje neurons) in specific brain regions involved in motor control. Mice were analyzed on the electrophysiological, morphological and on the behavioral level. PRG-1 is highly expressed in D1- and D2- expressing medium spiny neurons (MSNs) in the dorsal striatum. Systemic Prg-1-/- mice were significantly better in the rotarod experiment and had reduced anxiety levels, implicating improved motor control and higher impulsivity compared to control littermates.
Comparing the systemic Prg-1-/- mice to our conditional lines gave us a first hint that the increased motor control but not impulsivity in Prg-1-/- mice is mediated via synaptic lipid signaling in D2-expressing MSNs.

Poster 84:

Title:
The influence of bilingualism on gray matter volume in the course of aging

Authors:
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Abstract:
With aging, “brain reserve” may help preserve cognitive functioning. One factor influencing brain reserve is bilingualism, which was associated with higher gray matter volume (GMV) in the inferior frontal gyrus (IFG) and the inferior parietal lobule (IPL). This potential of bilingualism as variability factor between subjects was now assessed to understand its relevance for intraindividual aging trajectories.
We included 200 subjects (87 monolinguals) from the 1000BRAINS cohort. Trajectories of GMV decline in bilateral IFG and IPL were analyzed in mono- and bilinguals over two time points (mean interval: 3.6 years). For each region of interest, mixed Analyses of Covariance were conducted to assess (i) GMV differences for language groups (monolinguals/bilinguals) and (ii) GMV change over time in the two language groups. Corresponding analyses were performed for the two factors of GMV, surface area and cortical thickness.
There was higher GMV in bilinguals compared to monolinguals in the IPL, with a steeper GMV decline in bilinguals within the left IPL. Additionally, bilinguals showed greater surface area in the bilateral IPL and a steeper cortical thickness decline within the left IPL.
With the frontal part of the language network (IFG) showing no longitudinal effect, bilingualism might influence individual aging trajectories especially in posterior language-relevant brain regions (IPL). However, a steeper GMV decline in bilinguals’ left IPL argued for a reduction of this effect with aging. With aging theories suggesting posterior brain regions to decline earlier, our results might hint at potential for influencing aging effects in the brain through external factors.

Poster 85:

Title:
Microglia Affect Proliferation, Differentiation, and Apoptosis of Striatal Neural Progenitors

Authors:
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Abstract:
The striatum mainly comprises morphologically similar medium-sized spiny projection neurons (MSNs). However, there is a distinct division within the striatum known as stiosome and matrix compartments. While all MSNs originate from the lateral ganglionic eminence (LGE), the striosomal neurons are born during a specific time window before the matrix neurons. In order to examine molecular cues involved in lineage specification, we investigated the properties of neural precursor cells isolated from S13 and S19 rat LGE focusing on the role of direct and indirect regulation of proliferation, differentiation and apoptosis by homeostatic and reactive microglia. The contribution of microglia-derived soluble factors or direct microglia-NPC cell interaction was analysed using microglia-conditioned medium or direct cocultures with primary microglia, respectively. S13 and S19 LGE-derived NPCs were characterized with respect to proliferation, apoptosis and differentiation using immunocytochemistry and volumetric analysis by neurosphere formation assays.
Under homeostatic conditions, S13 and S19 NPC proliferation is positively regulated by microglia-secreted factors but not by direct interaction. In contrast, LPS-stimulated microglia mediate antiproliferative effects on NPCs accompanied by increased apoptosis. Additionally, the direct and indirect presence of homeostatic microglia resulted in increased numbers of neurons exhibiting higher ramifications. However, these effects are abrogated by reactive microglia treatment.
Our data indicate that microglia are involved in the regulation of proliferation, apoptosis and differentiation of striatal NPCs. These effects seem to be rather a result of microglia-secreted factors than driven by direct cellular interactions. Taken together, our results further underline the importance of microglia during CNS development.

Poster 86:

Title:
Advancing Tract-Tracing in the Postmortem Human Brain: Visualization of Fiber Tracts and Cortical Connectivity in the Occipital Lobe

Authors:
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Abstract:
In recent years, the study of intralobar fibers in the human occipital lobe has gained renewed interest. However, uncertainties persist regarding their cortical origin and terminations, which cannot be adequately addressed through fiber-dissection and diffusion-weighted imaging studies alone.
To overcome these limitations, we employed our newly developed rotating field tracer electrophoresis (RFTE) setup, designed to enhance the diffusion of polar lipophilic tracers in the fixed postmortem human brain. Furthermore, we utilized our optimized staining protocol that effectively minimizes signal deterioration typically observed with lipophilic dyes in cryostat sections. These methodological improvements allow for practical and scalable application of our approach.
Our investigation revealed a network of short association fibers connecting the calcarine cortex to various gyri within the occipital lobe, including the cuneus and inferior, middle, superior occipital, lingual, and fusiform gyri. These fiber bundles include the transverse fascicle of the lingual gyrus of Vialet inferiorly, the calcarine stratum medially, and the transverse fascicle and the proper stratum of the cuneus of Sachs superiorly. Notably, we successfully traced the projections from the primary visual cortex to layers 2, 3, and 4 in the prestriate cortex. We also observed infra- and supragranular feedback projections originating from layers II, III, and VI. These findings represent the first experimental confirmation of such connections in the human brain over longer distances and align with previous studies conducted in macaque monkeys.
By achieving this level of analysis our study brings us closer to the level of detail observed in non-human primate studies.

Poster 87:

Title:
The effect of BV-2 cell-derived exosomes on primary mouse astrocytes

Authors:
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Abstract:
Exosomes are small extracellular vesicles released by cells as a form of cell-cell-communication. In recent years, they have become increasingly important in the context of inflammatory diseases. After inflammatory insults, microglia-astrocyte interactions are altered and may lead to the progression of inflammation and disease. In this study, we investigated the effect of BV-2 cell-derived inflammatory exosomes on primary mouse astrocyte function.
BV2-cells were stimulated with lipopolysaccharides (LPS) for 24h. Cell culture supernatants were ultracentrifuged at 100.000 x g. Isolated exosomes were characterized by western blotting and nanoparticle tracking analysis (NTA). Exosomes were used for stimulation of primary mouse astrocytes with a focus on inflammatory cytokines and activation markers.
Proinflammatory stimulation of BV-2 cells was confirmed by increased expression of M1 markers. Successful isolation of exosomes was shown by the presence of the exosome markers CD9 and CD81. Following exosome stimulation, astrocytes were activated in a proinflammatory manner, displayed by an increased C3, LCN2 and CXCL10 expression.
We show that in the context of neuroinflammation, microglia-derived exosomes influence astrocytes towards a proinflammatory activation state. Thus, paracrine microglia-astrocyte communication may contribute to local inflammatory processes in the brain, but released exosomes may also affect peripheral organ function. Further studies will include proteomic analysis of the exosome content to pinpoint the transported molecules and their interacting and signaling mechanisms in activated astrocytes.

Poster 88:

Title:
Morphological subtypes of neocortical somatostatin-expressing interneurons in mice

Authors:
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Abstract:
Somatostatin-expressing cells make up the second most abundant group of cortical GABAergic interneurons. They provide lateral inhibition between pyramidal cells, as well as exerting inter- and translaminar inhibition on other interneuron subtypes, i.e. VIP and and PV cells. Thus SST cells play an important role in shaping cortical circuitry. As with other interneuron subtypes, SST cells are heterogeneous in their morphological and electrophysiological characteristics.
In this study, we analyzed the morphological characteristics of two major SST cell subtypes, namely: Martinotti and non-Martinotti cells. While there is a general understanding about the gross morphological differences between these two subtypes, a quantitative analysis of their morphological differences does not exist. Consequentially, for this study, we generated 3D models of biocytin-filled SST positive cells from the mouse barrel cortex using Neurolucida-based neuronal tracings and quantitatively compared morphological parameters of their somata, dendrites and axons.
We were especially interested in axonal parameters such as axonal branching and bouton distribution with respect to cortical layering.
Our aim is to enhance the classification of different interneuron subtypes based on their morphology, in order to provide a better understanding of each of the SST subtypes.

Poster 89:

Title:
Activation of tracheal brush cells induces TRPV1-mediated neurogenic inflammation

Authors:
Mohamed Ibrahem Elhawy (Institute of Anatomy and Cell Biology, Saarland University, Homburg), Firat Biradli (Institute of Anatomy and Cell Biology, Saarland University, Homburg), Gabriela Krasteva-Christ (Institute of Anatomy and Cell Biology, Saarland University, Homburg); mohamed.elhawy@uks.eu

Abstract:
We recently reported a positive connection between bitter taste signaling in brush cells (BCs) and the induction of neurogenic inflammatory response in murine tracheae. Such protective reactions involved two main aspects: an increased plasma extravasation and recruitment of neutrophils (PMNs) to the site of BC activation. Here, we characterize the ability of tracheal BCs to induce an innate immune response after depletion of transient receptor potential vanilloid 1 (TRPV1)-positive neurons.
TRPV1-expressing neurons were depleted by s.c. injections of resiniferatoxin (RTX), an ultrapotent TRPV1 agonist, in Trpm5+/+ mice. After 10 days, mice were i.v. injected with Evans Blue (EB), as a marker for the vascular permeability and challenged with the bitter taste receptor agonist denatonium intratracheally. Immunofluorescence staining was used to estimate plasma extravasation and recruitment of PMNs in murine tracheae.
Activation of BCs with denatonium induced a dose-dependent increased extravasation of plasma and PMN recruitment. RTX injection caused a complete depletion of TRPV1-expressing neurons in the sensory ganglia. Additionally, RTX-treated mice lacked peptidergic sensory neurons in the trachea. In mice with depleted TRPV1+ neurons, inflammatory responses to the activation of BCs were completely abolished.
Neurogenic inflammation in murine tracheae induced by BC activation through bitter agonists or bacterial products depends on transmission to TRPV1+ sensory neurons.

Poster 90:

Title:
Investigating the role of interneuron populations in whisking behavior through chemogenetics

Authors:
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Abstract:
Barrel cortex (wS1) of rodents is a favorable model for the investigation of the roles of neuronal subtypes in the processing of sensory information. We aim to investigate the role of interneuron populations in whisking behavior using texture discrimination task and chemogenetic manipulation in freely moving mice.
We established a novel texture based 2 choice task on T-maze to determine texture discrimination threshold of mice. With the help of bilateral Gq-DREADD expression in wS1, distinct groups of interneurons are aimed to be activated via CNO.
To show that surgery and IP injections on mice do not have a negative effect on their texture discrimination capacity, sham injections were performed.
A paired t-test on the highest 3 scores pre- and post-OP showed that surgery did not change animals' success rates in texture discrimination ($t(14) = 1.101$, $p = 0.46$). A one-way ANOVA revealed that there was no difference in animals' performance with IP injection of CNO and saline compared to no IP injection condition ($F(2,23) = 0.142$, $p = 0.87$).
Textured T-maze come out as a reliable measure for the discrimination capacity of mice. Furthermore, it can be safely combined with chemogenetic manipulation since neither intracranial surgery nor IP injection of CNO impaired mice's performance. We will start with bilateral Gq-DREADD expression in both PVcre+ and VIPcre+ mice to figure out the role of PV and VIP neurons in texture discrimination via CNO administration.

Poster 91:

Title:
The effect of interleukin 11 on plasticity-relevant proteins in murine hippocampal cells

Authors:
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Abstract:
Proinflammatory interleukins such as interleukin (IL-6) or TNFalpha are discussed as biomarkers for stress-induced anxiety disorders such as depression or anxiety disorders. They can affect neuronal metabolism and function and have been shown to regulate neuronal plasticity and synaptic transmission by targeting receptors and transporters within the synaptic membrane. Here, we investigate whether interleukin 11 (IL-11), another member of the IL-6-like protein family, alters the protein expression of plasticity-relevant proteins in hippocampal neurons of the mouse.
Hippocampal primary neuron cultures derived from mouse at E18 were either incubated with IL11 or hyper-IL6 as a preactivated IL-6 form on DIV21 or left unstimulated as controls. After 24h of incubation, cells were lysed for western blot analysis of proteins relevant for synaptic transmission and synaptic plasticity in the hippocampus.
Stimulation by IL-11 or the activated form of IL-6 activated the Jak/STAT pathway by STAT phosphorylation in hippocampal neuron cultures. The expression analysis of selected postsynaptic receptors and presynaptic transporters revealed a trend for a downregulation of the vesicular GABA transporter (VGAT). Possible differences in the intracellular distribution of VGAT (soma vs. neurites) are currently under way using immunofluorescence staining and qPCR analysis.
While the current evidence suggests only minor or highly specific effects of IL-11 on neuronal plasticity markers, other cell-types such as microglia or astrocytes may serve as mediators of IL-11 modulation on neurons as well. This hypothesis is currently tested by IL-11 stimulation of organotypic slice cultures of the hippocampus.

Poster 92:

Title:
The role of endothelial Tgf-BETA signaling and microglia in laser-induced choroidal neovascularization

Authors:
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Abstract:
Neovascular age-related macular degeneration (nAMD) is amongst the leading causes of blindness worldwide and characterized through development of choroidal neovascularization (CNV). We recently showed that developmental deletion of endothelial transforming growth factor receptor 2 (Tgfbr2) in mice promotes formation of CNV concomitant with an accumulation of myeloid cells. Here, we investigated the interaction of endothelial and microglia cells and the role of endothelial Tgf-BETA signaling and microglia cells in CNV development using a mouse model of nAMD.
Adult B6.Cdh5-Cre-ERT2.Tgfbr2fl/fl mice (Tgfbr2ΔEC) and Tgfbr2fl/fl control littermates (controls) were treated with Tamoxifen eye drops. Activation of cre and subsequent deletion of Tgfbr2 was monitored via mtmg cre reporter mice and PCR. Microglia was depleted in a subset of Tgfbr2ΔEC and control animals by feeding PLX5622 chow. CNV development was induced via a NdYAG-Laser (150 mW, 100 ms, 100 µm). CNV formation was documented by funduscopy and fluorescein angiography. CNV area and the number of accumulating microglia was determined using immunohistochemical staining against Collagen IV and IBA-1.
Tamoxifen treatment reliably activated Cdh5-Cre and led to deletion of Tgfbr2. Following laser treatment, Tgfbr2ΔEC mice developed significantly larger CNVs compared to controls. Additional depletion of microglia in Tgfbr2ΔEC resulted in significantly less microglia cells near CNV lesions, concomitant with a significantly reduced CNV area.
Our study demonstrates that both, endothelial Tgfbr2 and microglia in Tgfbr2ΔEC influences the size of CNV. Thus, targeting endothelial and/or microglia cells represent promising strategies to counteract CNV development in patients suffering from nAMD.

Poster 93:

Title:
The effect of dihydropyridines on mitochondrial stress in human neurons, oligodendrocytes and astrocytes

Authors:
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Abstract:
Multiple sclerosis (MS) is a chronic neuroinflammatory disease caused by an autoimmune response against central nervous system (CNS) antigens. Mitochondrial damage is observed during MS-associated stress responses, resulting in myelin loss and neurodegeneration. Current therapy is mainly effective in earlier inflammation-driven disease stages, but lack efficacy in progressive MS. The dihydropyridine (DHP) nimodipine promoted remyelination in a mouse model of MS, but the cellular mechanism needs further investigation.
In this project we tested stress-modulating effects of DHPs on different CNS cell types, with a focus on mitochondrial protection and regeneration. We treated human oligodendrocytes, neurons and astrocytes with different DHPs in the presence or absence of mitochondrial stress responses and investigated cellular responses using qPCR, immunofluorescence, and Western blot.
We found that under mitochondrial stress conditions, nimodipine treatment upregulated the mitophagy regulator PTEN-induced kinase 1 (PINK1) in human oligodendrocytic, neuronal, and astrocytic cell lines in vitro. We also found that different other DHPs induced different PINK1 regulation and stress responses in these different cell lines.
Our data show that in human oligodendrocytic, neuronal, and astrocytic cell lines, some DHPs exhibit previously unknown protective effects by modulating mitochondrial signaling pathways. Based on our observed protective effects, nimodipine or other DHPs may represent future therapeutic options to alleviate myelin loss and neurodegeneration during late phases of progressive MS.

Poster 94:

Title:
Reelin impacts the neuronal cholinergic signal transmission and posttranscriptional protein modifications

Authors:
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Abstract:
Named after the reeler-mutant mouse, the extracellular matrix protein reelin exerts many key functions in both the developing and the adult brain of mammals. While reelin is mainly secreted by Cajal-Retzius and regulates neuronal cell migration cells during embryonal development, it is predominantly expressed by interneurons and modulates synaptic transmission in the maturated and adult brain. Previous work has already shown that reelin has a great impact on neurophysiological processes such as learning and memory formation by modulating both excitatory glutamateric as well as inhibitory GABAergic neuronal signaling.
By using primary neurons, tumor cell lines, and rodent brain slices we want to further investigate reelin-modulated neuronal signaling by focusing on the cholinergic system. Although cholinergic projections modulate neurons in various brain regions including the hippocampus, the impact of reelin on the cholinergic system has so far not been examined. By using the calcium-imaging technique we want to elucidate reelin-induced changes in acetylcholine-evoked calcium signals within neurons followed by a detailed investigation of the underlying molecular mechanisms of action by using proteomics, western blotting and immunofluorescent staining.
Our preliminary results show a significant and receptor-subtype specific reduction of acetylcholine-induced calcium signals in the presence of reelin when compared to control. Furthermore, a reelin-induced increase in nuclear pCREB was observed.
Identifying the underlying molecular mechanisms will complement our knowledge of reelin’s action in both the developing and the mature brain and contribute to a better understanding of the interplay between posttranslational protein modifications, their intracellular pathways and neuronal signaling processes.

Poster 95:

Title:
The spine apparatus organelle regulates lesion-induced homeostatic plasticity at hippocampal mossy fiber synapses

Authors:
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Abstract:
Neurological diseases often result in denervation of brain regions due to demyelination, traumatic injury, or cell death. However, the molecular and structural mechanisms underlying lesion-induced reorganization of denervated brain regions are still insufficiently understood. Here, we investigated the effects of a partial denervation on hippocampal CA3 pyramidal neurons and granule cells to elucidate the role of the spine apparatus organelle.
We performed an entorhinal cortex lesion (ECL) in mouse organotypic entorhino-hippocampal tissue cultures and studied denervation-induced homeostatic plasticity of granule cells, CA3 pyramidal neurons and their synaptic connection – the mossy fiber synapse – by employing single and paired whole-cell patch-clamp recordings. Furthermore, we investigated the role and function of the spine apparatus organelle by performing a synaptopodin-co-immunoprecipitation and a subsequent transcriptome analysis.
Lesion-induced denervation caused a homeostatic strengthening in excitatory neurotransmission in the investigated cell types and specifically at the mossy fiber synapse. These functional changes were accompanied by structural and molecular adjustments. Moreover, homeostatic changes depended on the presence of the spine apparatus organelle – an organelle that seems to be associated with ribosomes and synaptic mRNAs.
Our findings suggest a close association between the spine apparatus organelle and local protein synthesis, highlighting its essential role in lesion-induced homeostatic synaptic plasticity in hippocampal neurons.

Poster 96:

Title:
PRG3 and PRG5 C-Termini: Important Players in Early Neuronal Differentiation

Authors:
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Abstract:
The functional importance of neuronal differentiation of the transmembrane proteins' plasticity-related genes 3 (PRG3) and 5 (PRG5) has been shown. Although their sequence is closely related, they promote different morphological changes in neurons. PRG3 was shown to promote neuritogenesis in primary neurons; PRG5 contributes to spine induction in immature neurons and the regulation of spine density and morphology in mature neurons. Both exhibit intracellularly located C-termini of less than 50 amino acids. Varying C-termini suggested that these domains shape neuronal morphology differently. These findings prompted us to investigate the involvement of the varying C-terminal domains of PRG3 and PRG5 in stages of neuronal differentiation during which neurite outgrowth happens.
We generated mutant EGFP-fusion proteins in which the C-termini were either swapped between PRG3 and PRG5, deleted, or fused to another family member, plasticity-related gene 4 (PRG4), that was recently shown to be expressed in different brain regions. We subsequently analyzed the influence of overexpression in immature neurons.
Our results point to a critical role of the PRG3 and PRG5 C-termini in shaping early neuronal morphology.
Both PRG3 and PRG5 play a pivotal role in neuronal differentiation. Particularly the C-terminal domains of both proteins are important for growth. However, the results suggest that the C-terminus alone might not be sufficient for promoting the morphological effects induced by PRG3 and PRG5. This is extended by the fact that other, yet unidentified, domains of PRG3 or PRG5 not located in the C-terminal domains are essential for the establisment of certain neuronal differentiation steps.

Poster 97:

Title:
Immunomodulation by resident neural stem cells suppresses chronic inflammation

Authors:
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Abstract:
Multiple sclerosis (MS) is triggered by the peripheral autoreactive immune cell - activated myeloid cell interplay. Neural stem/progenitor cells (NSPCs) are capable of contributing to repair processes and regulating immune responses in the central nervous system (CNS). However, a potential immunomodulatory role of endogenous NSPCs in MS disease initiation and progression remains unclear.
Here, we reveal a latent immunomodulatory function of endogenous NSPCs that reduces the pro-inflammatory properties of CNS-resident myeloid cells, thereby preventing the initiation of experimental autoimmune encephalomyelitis (EAE), a mouse model of MS.
NSPC-targeted conditional depletion of inhibitor of DNA binding (Id) 2/3 proteins altered the cellular composition and secretory profile of the subventricular zone (SVZ) stem cell niche during EAE. Id-depleted NSPCs increased vascular barrier properties and reduced microglial activation in the SVZ. Thus, Id-depleted NSPCs successfully alleviated the vulnerability of the niche to peripheral inflammation and prevented early activation of resident myeloid cells. This in turn resulted in a reduced accumulation of chemotactic cues in the cerebrospinal fluid, suppressing autoreactive T cell infiltration, demyelination, and relapsing paralysis.
Our results highlight the functional significance of endogenous NSPCs as signal mediators between CNS and peripheral immune system, and uncover their potential as therapeutic targets for CNS inflammatory diseases.

Poster 98:

Title:
Effects of the cannabinoids 2-Arachidonylglycerol and WIN 55,212-2 on primary isolated astrocytic cultures and astrocytic-microglial co-cultures

Authors:
Franziska Vieregge (Institute for Anatomie and Cell Biology, Martin-Luther-Universität Halle-Wittenberg, Halle), Tim Hohmann (, , Halle), Chalid Ghadban (, , Halle), Candy Rothgänger-Strube (, , Halle), Urszula Hohmann (, , Halle), Faramarz Dehghani (, , Halle); vieregge.franziska@t-online.de

Abstract:
Various Cannabinoids have been shown to mediate neuroprotective and anti-inflammatory effects via microglia and astrocytes. After neuronal injury or inflammatory events, subsequent activation of microglia leads to their morphological and functional changes. The release of proinflammatory cytokines and the stimulation of microglia and astrocytes exacerbate the neuronal damage.
The aim of this study was to evaluate the effects of co-incubation of the neuroprotective cannabinoids WIN 55,212-2 (WIN, a synthetic cannabinoid) and 2-Arachidonylglycerol (2-AG), the most abundant endogenous cannabinoid in the brain, on glia cell response.
Primary astrocytic and microglial co-cultures and astrocytic cultures were used. Both cannabinoids were applied alone or in combination and astrocytic wound healing was assessed in a scratch-wound assay by live cell imaging. Furthermore, the effects of cannabinoids were investigated on morphological changes of glia cells. To study the effects on proliferation, the cell cycle was assessed by flow cytometry. Lastly, the expression of pro- and anti-inflammatory cytokines on mRNA and protein level and in addition the nitrite oxide secretion were analyzed after LPS stimulation and treatment with cannabinoids.
We observed no effects of the cannabinoids on astrocytic wound closure in mixed glial cultures nor in isolated astrocytic cultures. Cannabinoid WIN alone reduced the LPS-mediated increase in nitrite oxide secretion in astrocytic and microglial co-cultures while 2-AG alone and the co-incubation of WIN and 2-AG had no decreasing effect.
Cannabinoids modulate glial cell function, affect their reactivity, phenotype polarization and migration. Both cannabinoids used here appear to specifically impact each glia cell type and contribute to shifting the balance towards a neuroprotective microenvironment.

Poster 99:

Title:
Ocular surface changes differ significantly in oxaliplatin - and diabetes induced polyneuropathy

Authors:
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Abstract:
Chronic peripheral polyneuropathies (PN) are among the most common diseases of the peripheral nervous system. Patients suffer from loss of sensory function and sensory pain that begins in the lower extremities. Often PN is associated with diabetes or oxaliplatin treatment, but since only a proportion of patients get PN, other factors must be additionally causative.

In this study, we examined streptozotocin-induced (DPN) and Ox-treated (OPN) mice with PN. Because the cornea is one of the most sensitive innervated organs and can be examined noninvasively, we compared the morphologic changes of the periphery with the anterior segment of the eye to better understand the pathomechanisms of the disease.

In both PN mice, swollen mitochondria in the spinal nerves were the main finding in the periphery. In the eye, there were significant changes between the two groups. In OPN, there was a significant change in 7 proteins in the tear film that differed from DPN tear film. In the conjunctiva, the number of goblet cells was significantly decreased, with changes in apical secretory vesicles. In DPN, the number of goblet cells in the eyelid was significantly increased, with unchanged apical secretory vesicles. The lacrimal gland showed differences in morphology, the rER was smaller and the area covered by apical vesicles was significantly larger.

We found significant differences between the groups. They showed pronounced early morphologic and molecular changes in and around the eye. Therefore, an ocular surface analysis can contribute to a better understanding of PN and could be used for an early diagnosis.

Poster 100:

Title:
mGluR5 dependent mitochondrial translocation of PKCδ: A mechanism raising astrocytic oxidative metabolism in response to neuronal activity.

Authors:
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Abstract:
A major contribution to brain metabolism, synaptic activity imposes high demands of local energy production on astrocytes. However, the (an)aerobic pathways and fuel for generation of energy equivalents in astrocytes are still debated. Also, mechanisms to ensure rapid metabolic adaptation to bouts of neuronal activity have not been sufficiently explored.
To investigate a possible influence of synaptic activity on glial mitochondrial activity, we stimulated primary astrocytes with glutamate and applied fluorescent immunocytochemistry with anti-protein kinase Cδ (PKCδ), anti- pyruvate dehydrogenase (PDH) and anti-phospho-PDH antibodies and object-oriented image analysis.
Glutamate induces mitochondrial translocation of protein kinase Cδ (PKCδ) and subsequent activation of the mitochondrial enzyme pyruvate dehydrogenase (PDH) - the point-of-no-return in the utilization of carbohydrates. Using luminometric ATP assay and subtype-specific inhibitors of PKC and mGluR5, we demonstrate that the enormous initial drop in intracellular ATP following glutamate application is dramatically counteracted by the described mGluR5/PKCδ-dependent mitochondrial activation. In glutamate-stimulated acute brain slices, pharmacological inhibition of metabotropic glutamate receptor 5 (mGluR5), the receptor inducing PKCδ translocation, decreases ATP recovery in astrocytes.
We show a mechanism in astrocytes linking extracellular glutamate to upregulation of oxidative phosphorylation. Collectively, our findings suggest that astrocytes possess a ´standby´ potential for oxidative phosphorylation that can be activated by extracellular glutamate and the mGluR5/PKCδ/PDH axis, indicating targets for pathologies involving excess glutamate.

Poster 101:

Title:
Modulation of glial inflammatory reactions by Gpr55

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Abstract:
The mechanisms of neuroinflammation play a crucial role in the pathogenesis of various neurodegenerative diseases. Cannabinoids have been shown to be protective by affecting the activation state of microglia, nevertheless, the underlying molecular mechanism are still poorly defined. Modulating the activity of the orphan cannabinoid receptor Gpr55 was shown to influence inflammation in vivo and to exert neuroprotection in lesioned organotypic hippocampal slice cultures.
In the present study primary astrocytic and astrocytic-microglial mixed cultures were used and their response to stimulation with Gpr55 ligands CID 16020046 and Cannabidiol (CBD) was evaluated. The presence of gpr55 was proven by using RT-qPCR and toxic effect of both ligands examined with MTT assay and propidium iodide staining. Proliferation and nitric oxide secretion were measured in presence or absence of Gpr55 antagonists. The influence on cell proliferation was verified with BrdU staining.
The expression of gpr55 at the mRNA level revealed approximately 19-fold higher expression in astrocytes compared to microglia and both cannabinoids showed no toxic effects. BrdU staining demonstrated that pre-incubation with CID 16020046 significantly diminished the number of BrdU-positive cells in comparison to LPS alone. Moreover, an LPS-mediated increase in NO production was significantly reduced by pretreatment with CID16020046 and CBD in mixed astrocytic-microglial cultures but not in primary astrocytes.
These results provide evidence for the involvement of Gpr55 in various aspects of microglial and astrocyte activation in the context of an inflammatory response. Gpr55 thus may represent a promising target for the development of therapeutic concepts in neurodegenerative diseases with a neuroinflammatory background

Poster 102:

Title:
Inducible CSF1R-dependent microglia depletion in vivo

Authors:
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Abstract:
Microglia are the resident immune cells of the central nervous system (CNS) and function in multiple ways to facilitate proper development as well as homeostasis of essential functional CNS systems during adulthood. Moreover, establishment of neuronal circuits and regulation of synaptic connections has been shown to be influenced by microglia. However, our current understanding of how microglia influence development, differentiation and maturation of CNS cell types such as neurons, astrocytes, and oligodendrocytes is limited and adequate tools are needed in order to address these questions.
In the current study, we have successfully established a transgenic mouse model (Cx3cr1CreERT2/EFYP/Csf1rflox/flox) for inducible microglia depletion upon chow-based tamoxifen administration. Flow cytometry, immunohistochemistry, and transcriptomics have been used to validate our transgenic in vivo depletion model.
Tamoxifen chow given to Cx3cr1CreERT2/EFYP/Csf1rflox/flox mice resulted in subsequent deletion of the Csf1 receptor in Cx3cr1-positive microglia leading to approximately 95% loss of the parenchymal microglia population when compared to control chow-treated mice. Loss of microglia resulted in astrogliosis as evidenced by increased numbers of GFAP-positive. Analysis of transcriptomic data from depleted brains further verified our observations.
Taken together, we introduce an elegant chow-inducible microglia depletion model which is of utmost interest for further studies addressing the role of microglia during development, maintenance and disease models of the CNS.

Poster 103:

Title:
Retinal degeneration in a mouse model for the peroxisomal disorder ACDB5-deficiency

Authors:
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Abstract:
The ACBD5-deficiency is an inherited peroxisomal disorder caused by a disrupted acyl-CoA binding-domain containing protein 5 gene. ACBD5 is a multifunctional, peroxisomal membrane protein involved in the import of very long-chain fatty acids into the organelles but is also a tethering protein facilitating membrane contacts between the endoplasmic reticulum and peroxisomes. ACBD5-deficient patients were first discovered in a genetic retinopathy screen and therefore retinal degeneration is considered one of the disease hallmarks. To unravel its pathologic mechanism, retinae of Acbd5-deficient mice (Acbd5-/-) were investigated.
Retina sections or tissue homogenates of three month- and one year-old Acbd5+/+ and Acbd5-/- mice were analysed by confocal immunofluorescence, block face scanning electron microscopy and immunoblotting, respectively.
Acbd5-/- mice developed a progressive retinopathy with a moderate decline in outer nuclear layer thickness. A closer investigation revealed primarily reduced numbers in cone photoreceptor cells but less in rods. In addition, the retinae showed signs of inflammation documented by microglia migrating into the subretinal space and activated astroglia in the ganglion cell layer. At the subcellular level, lysosomal accumulations were observed in the outer plexiform layer. The pathology in the optic retina was accompanied by a degeneration of the retinal pigment epithelium (RPE) presented by declined cell numbers, increased binucleated cells and cell membrane distortions. Of note, RPE cells exhibited increased levels of phagocytized cone opsin but not rhodopsin supporting the hypothesis of a primarily cone photoreceptor pathology.
Peroxisomal metabolic alterations in the Acbd5-/- retina appear to lead to specific changes in lipid species primarily affecting cone photoreceptor cells.

Poster 104:

Title:
Differently increased Volumes of Multiple Brain Areas in NPC1 Mutant Mice Following Various Drug Treatments

Authors:
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Abstract:
Human Niemann-Pick disease, type C1 (NPC1, MIM 257220) is a inherited lysosomal storage disease characterized by a progressive neurological degeneration that causes disability and premature death. A murine model Npc1−/− displays a rapidly progressing form of Npc1 disease which is characterized by weight loss, ataxia and increased cholesterol storage.
Npc1−/− mice receiving a combined therapy of miglustat (MIGLU), the neurosteroid allopregnanolone (ALLO) and the cyclic oligosaccharide 2-hydroxypropyl-β-cyclodextrin (HPßCD) showed prevention of Purkinje cell loss, improved motor function and reduced intracellular lipid storage. In order to evaluate possibly different alterations of different brain areas caused by pharmacotherapy, here, using stereological methods, fresh volumes of various brain structures were calculated in sham- and drug-treated wild type and mutant mice.
Although therapy of Npc1−/− mice with MIGLU, HPßCD and combination of MIGLU, HPßCD and ALLO resulted in prevention of body weight loss, reduced total brain weight was not positively influenced. Compared with the respective wild types, in all treatment strategies, fresh volumes of some brain structures, that were significantly reduced in Sham-treated Npc1−/− mice, normalized after the pharmacotherapies, best seen in the dentate gyrus and the CA1 area. The respective volumes in the wild type mice were not significantly altered by either therapy.
In conclusion, measurements of fresh volumes of brain areas in Npc1−/− mice can monitor region-specific changes and response to treatment that correlate, in part, with behavioral improvements in this mouse model.

Poster 105:

Title:
Probiotics prevent increase of gut-associated lymphatic tissue after food restriction in an anorexia nervosa animal model

Authors:
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Abstract:
Anorexia nervosa (AN) is a severe and often chronic eating disorder that leads to alterations in the gut microbiome and significant diversity shifts. This, in turn, influences appetite and body weight regulation, gut permeability, inflammatory reaction, and gut-brain interactions.
We used a translational activity-based anorexia (ABA) rat model which mimics the main characteristics of AN, such as loss of body weight or increased physical activity. The present study examined the effect of chronic food starvation, multistrain probiotic supplementation and refeeding on the structure of the gut and gut-associated lymphatic tissue (GALT).
Our results indicate that ABA had an atrophic influence on intestinal morphology and increased the formation of GALT in the small bowel and colon. Higher formation of GALT in ABA rats appeared to be reversible upon application of a multistrain probiotic mixture and refeeding of the starved animals.
We report that starvation increased GALT volume in the ABA model. Our results underscore the potential role of gut inflammatory alterations in the underlying pathophysiology of AN. Increased GALT might be linked to already described gut microbiome alterations which we have previously demonstrated. These results also emphasize a putative role of the microbiome-gut-brain axis in the pathophysiology of AN, and point to probiotics as potentially beneficial addendum in the treatment of AN.

Poster 106:

Title:
Glial cell changes in the corpus callosum and hypothalamus in chronically-starved mice

Authors:
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Abstract:
Anorexia nervosa (AN) is characterized by emaciation, hyperactivity, and amenorrhea. Imaging studies in AN patients have revealed severe reductions in grey and white matter volume, which correlate with the severity of neuropsychological deficits. However, the cellular basis for the observed brain atrophy is poorly understood. Although distinct hypothalamic centers, including the arcuate nucleus (ARC) are critically involved in regulating feeding behavior, little is known about potential hypothalamic modifications in this disorder. Since glia e.g. astrocytes and microglia influence neuronal circuits, we investigated the glial changes underlying pathophysiology of starvation in the corpus callosum (CC) and hypothalamus.
Female mice were given a limited amount of food once a day and had unlimited access to a running wheel until a 20% weight reduction was achieved (acute starvation). This weight reduction was maintained for two weeks to mimic chronic starvation. Immunohistochemistry was used to quantify the density of astrocytes, microglia, and the staining intensity of neuropeptide Y (NPY), a potent orexigenic peptide.
After chronic starvation, the densities of GFAP+ astrocytes and IBA1+ microglia in the CC and ARC were decreased. In contrast, microglia distribution in the ARC increased in density after acute starvation. In addition, the staining intensity of NPY was increased after acute starvation indicating an increased orexigenic signaling.
Chronic starvation induced glial cell changes in the CC and ARC in a mouse model of AN suggesting that glia pathophysiology may play a role in the disease.

Poster 107:

Title:
Regional heterogeneity and inflammatory properties of human meninges

Authors:
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Abstract:
The central nervous system (CNS) is covered by three layers of meninges: dura mater, arachnoid mater and pia mater. According to recent studies, they are involved in the recruitment of immune cells into the CNS, but the underlying mechanisms, as well as regional heterogeneity, have barely been addressed. We hypothesize that the meninges, especially the arachnoid mater, can contribute to the establishment and maintenance of a proinflammatory meningeal compartment and show region-specific heterogeneity in morphology and gene expression.
Human arachnoid fibroblast cultures were derived from meningeal biopsies, treated with interferon GAMMA (IFN-GAMMA) or lipopolysaccharide (LPS), and gene expression levels of proinflammatory genes were analyzed by quantitative real-time PCR. Furthermore, we collected post-mortem meningeal material of distinct CNS regions for (immuno-)histochemical analysis of overall meningeal morphology and spatial distribution of blood vessels. Differential gene expression was analyzed by next-generation sequencing.
Cultured meningeal fibroblasts upregulated expression of proinflammatory genes in response to IFN-GAMMA or LPS treatment. Histologic sections revealed distinct morphological differences in the thickness and structure of meninges depending on the sampled region. Meningeal blood vessels showed a higher density and larger caliber within the depth of the sulci than on the top of the gyri. Next-generation sequencing analyses pointed toward a strong molecular divergence between the sampled meningeal regions.
Our findings suggest that arachnoid fibroblasts can induce a proinflammatory environment in the meninges and demonstrate a distinct regional heterogeneity of meninges on the histological and gene expression level. Future studies will concentrate on the regional specificity of functional meningeal properties.

Poster 108:

Title:
Towards a light-mediated gene therapy for the eye - retinal transgene expression through photoactivation of caged ethinylestradiol and the inducible Cre/lox system

Authors:
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Abstract:
Increasingly, retinal pathologies are being treated with virus-mediated gene therapies. To be able to target viral transgene expression specifically to the pathological regions of the retina with light, we established an in vivo photoactivated gene expression paradigm for retinal tissue.
Based on the inducible Cre/lox system, we discovered that ethinylestradiol is a suitable alternative to Tamoxifen as ethinylestradiol is more amenable to modification with photosensitive protecting compounds, i.e., ‘caging.’ Identification of ethinylestradiol as a ligand for the mutated human estradiol receptor was supported by in silico binding studies showing the reduced binding of caged ethinylestradiol. Caged ethinylestradiol was injected into the eyes of double transgenic GFAP-CreERT2 mice with a Cre-dependent tdTomato reporter transgene followed by irradiation with light of 450 nm.
Photoactivation of eyes injected with caged ethinylestradiol significantly increased retinal tdTomato expression compared to controls. Successful photoactivation was also achieved in retinal neurovasculature using Tie2-CreERT2 mice.
Photoactivated transgene expression was robust, reproducible, easily implemented, without obvious toxicity, and flexible in different genetic backgrounds. We thus demonstrated a first step towards the development of a targeted, light-mediated gene therapy for the eyes.

Poster 109:

Title:
Where does transcranial magnetic stimulation stimulate neurons? A Multi-scale computational modeling study of human brain anatomy

Authors:
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Abstract:
Transcranial magnetic stimulation (TMS) is a powerful non-invasive tool for brain stimulation that is increasingly used in neuroscience research and clinical treatment. However, the limited understanding of the factors influencing neuronal responses to TMS has hindered its efficacy.
In this study, we used a multi-scale computational modeling approach with ~380,000 simulations to evaluate the influence of neuronal properties, cortical morphology, and stimulation parameters on the elicited neuronal responses to TMS.
We found that the precise spatial distribution of neuronal activation patterns was contingent upon the rotating angle of the cells along their longitudinal somatodendritic axis. Previous studies have overlooked this parameter, since they primarily focused on neuronal orientation relative to the cortical surface. Additionally, our study demonstrated the effects of gyral shape, as TMS activated more neurons in mushroom-shaped compared to sinusoidal-shaped gyri. We also found that neurons at the sulcal wall have a lower activation threshold when exposed to the same electric field (E-field) than neurons at the gyral crown. However, this effect is counteracted by the weaker E-field in the sulcal wall that requires stronger stimulation intensities.
These findings represent significant advancements in unravelling the impact and interplay of various morphological and functional factors on neuronal responses to TMS, encompassing neuronal, cortical, and stimulation parameters. This knowledge is pivotal for achieving a comprehensive understanding of the intricate neuronal mechanisms underlying TMS, thereby facilitating the development of more effective stimulation protocols in the future.

Poster 110:

Title:
Implication of miRNA in the eating disorder Anorexia nervosa

Authors:
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Abstract:
Anorexia nervosa (AN) is a chronic eating disorder characterized by pathological low body weight and multifactorial pathophysiology, including endocrine dysfunctions, functional/morphological brain alterations, and intestinal malfunction. Nowadays, the role of miRNAs is extensively discussed in psychological, neurodegenerative, and inflammatory diseases. Therefore, we aimed to analyze the expression levels of miRNAs to investigate their implications in AN.
We evaluated miRNA levels in the blood serum of AN patients in the acute status upon hospital admission (AN, n=20) and age-matched healthy controls (HC, n=19) using next-generation sequencing. Within the patient group, we further differentiated two subgroups based on their body weight one year after discharge into good prognosis vs. bad prognosis. We compared the miRNA expression levels between the experimental groups and correlated them with clinical parameters like age, body weight, levels of inflammatory cytokines and clinical questionnaires.
We identified a total of 220 significantly deregulated miRNA candidates in AN. Correlations with clinical data revealed that a high number of miRNAs were associated with body weight, inflammation, depression, and anxiety behavior. Comparison between the experimental groups demonstrated different expression patterns, categorizing the deregulated miRNAs as potential biomarkers for the acute starvation state or as having a prognostic potential e.g. for body weight development after treatment.
miRNAs are pathologically altered in AN and hold great potential as biomarkers to better classify patients into high- and low-risk groups for chronic progression of AN. Future research should focus on determining the specific cells and tissues expressing these miRNAs and identifying their targets.

Poster 111:

Title:
Unlocking the Power of NAD: Boosting Neuronal Protection in ALS with NMNAT2 and Caffeine

Authors:
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Abstract:
Nicotinamide adenine dinucleotide (NAD) is essential for mitochondrial metabolism and involved in cellular processes. It acts as a signaling molecule and contributes to DNA repair, gene regulation and neuron protection, among others. NAD is de-novo-synthesized by NMNAT. NMNAT2 deficiency and low NAD levels can cause reduced energy production and neuronal degeneration. However, it has been found that caffeine can enhance the expression of NMNAT2, thereby potentially mitigating these effects.
The study investigated metabolic deregulation in the NAD-pathway in ALS using in-vitro and in-vivo experiments with the wobbler mouse model. The research included gene and protein expression analyses, metabolite analysis, in-vitro tests with nicotinamide riboside (NR) and caffeine supplementation on primary motor neurons, and evaluation of muscle strength in mice.
We found that all three isoforms of NMNAT, crucial for NAD synthesis, are downregulated in the cervical spinal cord of Wobbler mice during the clinical stage (p40), leading to reduced NAD levels. However, compensating for the NAD deficits through NAD and caffeine supplementation in the culture medium of motoneuronal cells from Wobbler mice (p20 and p40) resulted in a phenotype similar to wild-type mice. Moreover, supplementing the animal model with caffeine but not with NR through drinking water slightly delayed the decline in strength in homozygous Wobbler animals.
Our project revealed a key pathological factor: reduced NMNAT2 expression and insufficient NAD supply in the spinal cord. This imbalance disrupts cellular redox balance and increases oxidative stress. Therefore, supplementing this metabolite holds promise as a potential therapeutic approach for ALS.

Poster 112:

Title:
GFAP deficiency increases age-related loss of retinal ganglion cell axons

Authors:
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Abstract:
Glial fibrillary acid protein (GFAP) is a major intermediate filament component of astrocytes and contributes significantly to their biological functions. In human and experimental glaucoma, astrocytes show signs of reactivity, distinct morphological changes and an increased immunoreactivity for GFAP. Several studies in animal models of glaucoma reported on an association of the reactive phenotype with severe axon loss. In this study we aimed to investigate how a complete deficiency of GFAP influences retinal ganglion cell (RGC) survival with increasing age.
12-week-old and 12-month-old GFAP deficient (GFAP-/-) mice and their wildtype (WT) littermates were analyzed in this study. IOP was measured prior to sacrifice. RGC somata and ON axons were quantified. Immunofluorescence staining against Glutamine Synthetase (GS) and Connexin 43 (Cx43) was carried out to visualize changes in astrocyte and Müller Cell reactivity.
No differences regarding IOP and axon numbers were found in 12-week-old mice. IOP in 12-month-old GFAP-/- mice was significantly higher than in WT mice (WT:12.24 ± 2.97 mmHg, GFAP-/-: 15.66 ± 2.62 mmHg, n = 22, p = 0.04). ON axon numbers in GFAP-/- mice were lower than in WT animals (WT: 48324 ± 3777, GFAP-/-: 40876 ± 2615, n = 9, p = 0.0002), as were RGC numbers (WT: 2469 ± 181 RGC/mm2, GFAP-/-: 2087 ± 282 RGC/mm2, n = 9, p = 0.003). Immunofluorescence staining against GS and Cx43 indicated higher macroglial reactivity in GFAP deficient mice.
We conclude that GFAP is required for maintenance and survival of RGC and that GFAP deficiency contributes to RGC loss with age.

Poster 113:

Title:
Molecular Case Study of a GALC Mutation Causing Infantile Krabbe Disease

Authors:
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Abstract:
Krabbe disease is a rare lysosomal disorder affecting the white matter of the central and peripheral nervous system. It is characterized by neurodegeneration and the most common form is the infantile Krabbe disease, which is usually diagnosed within the first year of life and has a high morbidity and mortality. This autosomal recessive disease is caused by mutations in the GALC gene, which encodes the lysosomal enzyme galactocerebrosidase. This study presents a structural approach towards a galactocerebrosidase variant found as homozygous mutation in the GALC gene of a patient with infantile Krabbe disease.
To investigate the effects of this mutation on protein structure, a homology model of human galactocerebrosidase was build. Thereafter, the structural stability of the mutant enzyme and the wild type was analyzed in several all-atom molecular dynamics (MD) simulations with protonation states corresponding to cytosolic pH (pH 7). Since galactocerebrosidase is subcellularly localized in the lysosome (pH 4.5-5.5), we performed additional MD simulations with protonation states corresponding to pH 4.5.
Differences in protein flexibility between the wild type and the mutated enzyme were observed at acidic lysosomal pH but not at neutral pH. Similarly, we detected effects of the mutation on the size of the substrate binding pocket at pH 4.5, although the mutation site itself is not part of the active site/binding site of the enzyme.
Overall, our MD simulations shed light on how this mutation affects the structure of human galactocerebrosidase in the acidic environment of the lysosome.

Poster 114:

Title:
Rocuronium induced global cerebral hypoxia - a new minimal invasive rat model

Authors:
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Abstract:
Severe global cerebral hypoxia can lead to significant disabilities. No model to date addresses hypoxia as independent factor on the brain. To investigate this condition, we developed a minimally invasive rat model that employs rocuronium, a well characterized muscle-blocking agent commonly used in surgeries to induce respiratory insufficiency by paralyzing striated muscles.

In our study, 14 rats underwent 12 minutes of hypoxemia, achieving an oxygen saturation of approximately 60% as measured by pulse oximetry. Subsequently, sugammadex was administered to immediately counteract the effects of rocuronium. 24 hours after the procedure blood and brain tissue was sampled for molecular biology studies.

The examination of 14 rats receiving anesthesia alone (control) compared to rats that underwent hypoxia revealed significant morphological alterations in the hippocampus (reduced cell count in the CA1 region) and cerebellum (decreased Purkinje cells). Additionally, significant changes in mRNA levels of hypoxia markers were observed in the blood (Hif2α, Il1β, Tgf1β, Tnfα, S100b, cspg2), hippocampus (Il1β, Tnfα, S100b, cspg2), and cerebellum (Hif1α, Tnfα, S100b, cspg2). It was particularly notable that the effect was more pronounced in females over males.

Despite the existence of various animal models for studying hypoxia, there is a need for an endogenous model that specifically examines the independent impact of hypoxia on the brain. Our developed model fills this gap by successfully inducing hypoxemia and subsequent global cerebral hypoxia. With the observed morphological and biochemical changes, this model holds promise for investigating potential therapeutic and preventative interventions for global cerebral hypoxia.

Poster 115:

Title:
Nutrition dependent morphology changes in gut immune system of the domestic pig, sus scrofa

Authors:
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Abstract:
Across species, the gut is a fragile ecosystem strongly influenced by nutrition.
This study focuses on morphological adaptions of the gut immune system due to food-related changes in the microbiom.
As a proxy for respective adaptions, the amount of γδ T-lymphocytes and the pattern recognition receptor TLR5 were investigated.
Jejunal tissue samples containing also Peyer's patch follicles (PP) of 8-9 weeks old pigs, fed with different food mixtures were taken.
We assessed changes in γδ T-lymphocytes numbers, their distribution within villi and crypts, as well as the general distribution of TLR5 in the jejunum using immunohistochemistry. Using microscopy T-lymphocytes were counted in the epithelium and lamina propria.
Generally, more T-cells were found within villi than crypts. Regarding rye/soy fed pigs this villus/crypt difference was statistically significant.
The lowest cell number was detected in the epithelial layers as well as in the lamina propria of crypts and villi in rye/rape-fed animals.
Contrastingly, rye/soy-fed pigs showed the highest average cell amount and highest variance. No significant differences between treatments were detected.
TLR5 expression was verified in muscular cell layers, blood vessel walls and in the center of PP. Interestingly, the TLR5 signal in epithelial layer of crypts and villi was concentrated at apical cell pole.
Both higher cell numbers and variances in soy-fed animals may point to an immune reaction of some individuals to soy, which is widely fed to factory-farmed pigs. To further evaluate this observation, immune factors such as cytokines in the gut of differentially treated animals will be analyzed.

Poster 116:

Title:
The neglected excretory duct system of the human prostate

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Abstract:
In comparison to other glands, shockingly little is known about the duct system of the human prostate. We aimed to clarify the 3D structure and the characteristics of the excretory duct system of the human prostate.
We used contrasted microCT imaging (using phosphotungstic acid (PTA)), Dragonfly 2020.2 software (Object Research Systems) for 3D reconstruction and histological analysis of the same human prostates.
PTA-contrasted microCT imaging allowed the identification of the branching excretory duct system of the human prostate with surprisingly intense periluminal PTA-accumulation.
Through 3D reconstruction of the microCT images we could show the spatial orientation of these ducts connecting the predominantly peripherally localized glands to the colliculus seminalis.
After establishing a PTA-washout for the microCT-prostates (making the tissue usable for histological work-up) and planning and comparing histological sectioning with the scans, we could confidently identify human prostatic duct structures histologically.
The highly PTA-contrasted walls of the ducts could be characterized as dense layers of collagen fibers with smooth muscle cells in-between, both orientated longitudinally.
Interstitial smooth muscle cells of the prostate contract spontaneously and single glands of the prostate contract forcefully in response to norepinephrine (already shown by us). Therefore, we postulate that the thick longitudinally organized collagen layers of the excretory duct system in the human prostate act as a protector to keep the ducts patent while the glands are compressed to excrete the prostatic fluid.
Methodologically, the combination of contrasted microCT imaging (3D structures) with succeeding histology of the same tissue enables to clarify underlying cellular structures.

Poster 117:

Title:
Compartments in human lymph nodes up to 15 years of age

Authors:
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Abstract:
The histology of normal human lymph nodes in different ages until adulthood is largely unknown. However, this knowledge is of relevance for intranodal desensitization and for comparison to lymphoma.
Superficial inguinal lymph nodes (LN) of 25 children of different ages were obtained from the legal medicine department at necropsy and were studied by routine histology and immunohistochemistry for T and B lymphocytes. We assessed the occurrence of the different compartments of the lymph nodes qualitatively. Several sections per LN were evaluated with the focus on follicles, HEV and the localization of T and B lymphocytes.
Already in LN of children of less than 1 month of age cortex and medulla were identifiable. Lymph follicles were not seen after H & E staining. Using immunohistochemistry some areas of follicular accumulated CD20 positive B lymphocytes were detected. Also, numerous CD3 positive T lymphocytes were seen in the cortex. In sucklings cortical primary lymph follicle were visible and high endothelial venules as typical structures for the T cell area are present. Secondary follicles were found frequently in toddlers and rarely in sucklings. From toddlers onwards the structure of LN was comparable with that of LN of adolescence.
The LN structure in newborns and sucklings seems somewhat immature. The knowledge of LN structure in postnatal development is essential to identify pathology like lymphoma in children. The structural elements for an intranodal desensitization are already given in human children.

Poster 118:

Title:
Advanced maternal age alters embryo – maternal communication during the preimplantation period – insights from the rabbit model.

Authors:
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Abstract:
The reproductive potential in women declines with age. Molecular mechanisms involved in age-related infertility and their impact on embryo-maternal-interaction during early pregnancy are still not completely understood. The insulin/insulin-like growth factors-(IGF-)system plays a pivotal role in the embryo-maternal crosstalk, connecting maternal insulin/IGF with embryonic metabolism. Our aim was to analyse the insulin/IGF-system and lipid metabolism on day 6 of pregnancy in reproductive young and old rabbits.
A total of 50 young (16-20 weeks) and 31 old (<108 weeks) sexually mature, female rabbits and their blastocysts were investigated at day 6 post coitum. Target genes expression of the insulin/IGF-system and lipid metabolism were quantified by qPCR, western blot and ELISA in maternal blood, endometrium and blastocysts. Blastocysts were morphological stages and separated in embryoblast (EB) and trophoblast (TB).
In reproductive old rabbits, a lower number of embryos was observed at day 6 of pregnancy. The insulin and IGF serum levels were reduced, accompanied by a paracrine upregulation of IGF1 and its receptors in the endometrium in reproductive old rabbits. In blastocysts, IGF1 and IGF2 levels were reduced in both compartments, EB and TB.
In addition, in the endometrium of old females changes of fatty acid metabolism were observed, indicated by an increased beta-oxidation, fatty acid binding and transport, as well as lower level of fatty acid synthesis. The embryonic fatty acid uptake and beta-oxidation were increased in EB and TB, too.
Advanced maternal age has a decisive effect on maternal and embryonic insulin/IGF-signalling and lipid metabolism, correlating with a higher embryo loss during the preimplantation period.

Poster 119:

Title:
Splenic compartments differ in their T cell receptor repertoire -already in the naive state

Authors:
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Abstract:
The immunological compartments of the spleen are well described, but details of their T cell receptor (TCR)-repertoire (TCR-R) are still unknown.
We isolated the T cell zone (TCZ), B cell zone (BCZ) and germinal centers (GCs) by laser-microdissection of murine splenic cryosections and performed next-generation sequencing to study the TCR-R. We focused on the CDR3β region of the TCR - being the most variable region and responsible for a diverse TCR-R- and developed analysis tools, like the coding diversity index (CDI). It describes the heterogeneity of nucleotide coding of the CDR3β amino acid sequences. Usage of different nucleotides leads to high values, while homogenization tends towards 0.
T cells occur in all compartments. Yet, the pattern of the TCR-R differs, already in the naïve state: For example, the number of different clonotypes – meaning a set of T cells bearing identical CDR3β chains – strongly differs, leading to a less diverse and more homogenous repertoire within the BCZ. 7 days after antigen challenge with sheep red blood cells the number of different T cell clonotypes decreased especially in the TCZ. Only now the CDI of the TCZ reaches the level of the naïve BCZ. For the GC we found a restricted repertoire which was equally homogenic compared to the BCZ.
T cells are present in all compartments of the spleen, but their TCR-R differs already in the naïve state and shifted upon antigen challenge. These detailed observations of the TCR-R might help to understand early processes in immunological diseases.

Poster 120:

Title:
Tracheal brush cells contribute positively to the phagocytosis of Pseudomonas aeruginosa by dendritic cells

Authors:
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Abstract:
Activation of tracheal brush cells (BCs) was previously linked to enhance the survival of mice infected with Pseudomonas aeruginosa (P. aeruginosa). Here, we describe the role of BC activation for the recruitment of immune cells using a mouse Trpm5-DREADD model.
The DREADD-agonist clozapine N-oxide (CNO) was applied intratracheally to stimulate BCs in Trpm5-DREADD mice. Immune cell profiling of blood, bronchoalveolar lavage fluid (BALF), tracheae and lungs was performed via FACS-analysis. Phagocytosis assays were performed using bone marrow derived dendritic cells (BMDCs) exposed to supernatants from Trpm5+/+ or Trpm5-/- tracheae stimulated with denatonium. BMDCs were infected with the cystic fibrosis P. aeruginosa strain NH57388A for 1 h and their phagocytic capability was estimated by quantifying numbers of phagocytosed bacterial cells.
BC activation in the Trpm5-DREADD model enhanced the recruitment of neutrophils in BALF and tracheae of CNO-treated mice compared to the control group (not expressing DREADD). Blood count of neutrophils remained unchanged. Remarkedly, numbers of the main type of antigen-presenting cells, dendritic cells (DCs), were increased in BALF and lungs of Trpm5-DREADD mice. Phagocytosis of P. aeruginosa was enhanced in DCs treated with supernatants from Trpm5+/+ after BC activation.
BC activation impacts the innate and adaptive immune responses and plays an important role in eliminating P. aeruginosa infection.

Poster 121:

Title:
The mitochondrial protease PARL is required for spermatogenesis

Authors:
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Abstract:
Spermatogenesis is a fundamental but highly specialized process that is crucial for sexual proliferation and male infertility is an increasing clinical problem that affects millions of patients worldwide. The severe changes germ cells undergo during meiosis make spermatogenesis an energy demanding process, so it is not surprising that mitochondrial defects have been shown to be involved in causing spermatogenic arrest, leading to infertility. The mitochondrial protease PARL is involved in the maintenance of several mitochondrial functions and is mostly known for its association with neuronal degeneration and Parkinson´s disease. With this study we aimed to shed more light onto the question how mitochondrial defects, specifically those caused by a deficiency of PARL, lead to male infertility.
Using immunhistological stainings, western blots, RT-qPCR and electron microscopy our research revealed a so far unknown role of PARL in the maintenance of spermatogenesis.
We show that PARL deficiency in mice leads to a defect in respiratory chain complex IV that causes a severe deficit in complex IV function and ATP production resulting in a complete arrest of spermatogenesis during prophase of meiosis I. Crucially, our results show that the downstream responses to a loss of PARL vary between tissues. While PARL is known to affect respiratory chain function in the brain, the defect in complex IV, described here, seems to be unique to germ cells and did not occur in other tested tissues.
Our results highlight the importance of mitochondrial function to spermatogenesis and provide new insights in cell-type-specific responses to mitochondrial defects.

Poster 122:

Title:
The role of resident macrophages in the immune response to bacterial infection of the murine epididymis

Authors:
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Abstract:
The epididymis faces contrasting immunological challenges (tolerance towards sperm, defense against pathogens). Accordingly, the epididymal regions (initial segment (IS), caput, corpus, cauda) show striking differences in their immune responses during infection. We have previously shown that resident leukocytes shape distinct immunological environments along the duct. CX3CR1+ macrophages constitute the major leukocytes population with region-specific specializations in phenotype and morphology. We hypothesize that CX3CR1+ macrophages play a crucial role in epididymal immune regulation.
This study aims at depleting CX3CR1+ macrophages using Cx3cr1CreERT2Rosa26iDTR mice to analyze the consequences under physiological and pathological conditions. Uropathogenic E. coli (UPEC) were injected into the vas deferens and disease progression of acute bacterial epididymitis was compared between macrophage-depleted and wild type (WT) mice. The extent of macrophage depletion, leukocytic infiltration, and histopathology were assessed by flow cytometry, immunofluorescence staining and Masson-Goldner staining.
Depletion of CX3CR1+ macrophages resulted in loss of intraepithelial macrophages, which recovered within 30 days. Interstitial macrophages remained unaffected. The loss of macrophages resulted in epithelial damage and extravasation of spermatozoa under physiological condition.
After UPEC infection, immune responses varied in WT and macrophage-depleted mice. The distal region of WT mice showed leukocyte infiltrations and tissue damage which was not evident in IS and caput. Contrastingly, macrophage-depleted mice showed an earlier onset of inflammation with tissue damage in all regions.
We established a model for targeted depletion of intraepithelial CX3CR1+ macrophages within the epididymis that suggest a pivotal role of CX3CR1+ macrophages in maintaining epithelial integrity and controlling the magnitude of the immune response.

Poster 123:

Titel:
The role of Nrf2 and it´s over-activation in endochondrale ossifikation

Autoren:
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Abstract:
Diseases with intrinsic oxidative stress, such as osteoporosis, often worsen bone healing due to excessive toxic radicals. The nuclear factor erythroid 2-like factor 2 (Nrf2) has been identified as a key transcriptional regulator of antioxidant expression. In this work, we investigated how Nrf2-overactivation (Col2-Cre::Keap1loxP/loxP mice) can affect bone growth.
Postnatal Col2-Cre::Keap1loxP/loxP mice were used to study skeletal development using total skeleton staining with Alcian blue and Alizarin red. Histology and immunohistology were used to analyze picked target proteins in the growth plate. Micro-CT (µCT) was used to determine the length of the femur and growth plate.
Preliminary results show Cre+-animals (overactivation of Nrf2) have a shorter spine and tend to have shorter extremities than Cre--controls. µCT analysis verified the size difference in femurs of Nrf2—overexpressed animals.
These data suggest that sustained activation of Nrf2 slows chondral ossification. The extent to which this effect affects fracture healing, in which chondral ossification plays an important role, will be investigated in further experiments.

Poster 124:

Titel:
From a Single Villous Tree to Whole Placentome – Quantitative Imaging of the Placental Villous Architecture by Micro-CT

Autoren:
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Abstract:
OBJECTIVES: A full quantification of small villous tips has been achieved previously by 3D-Microscopy. However, the imaging of a single villous tree in its entirety or a whole placentome still remains a challenge. Our objective was, at first, to use Micro-CT to create 3D images of such specimens without using any contrasting agents. The second objective was to quantify the branching structure of the resulting images.

METHODS: Whole placentomes, blocks corresponding to a single villous tree or a free-floating single villous tree were dissected from freshly delivered placentas. Subsequently, they were fixed and embedded in paraffin according to standard laboratory protocols.

For Micro-CT measurements, the paraffin-embedded samples were processed as per the previously published protocol to replace the paraffin by air selectively from the intervillous space. The specimens were measured either by a GE phoenix v|tome|x s 240 or a Scanco MicroCT 42 with an isotropic voxel size of 50 µm or better. ITK-SNAP and Fiji/ImageJ were used for image processing and analysis.

RESULTS: Fig. 1 shows (A) a projection of the reconstructed volume of a single free-floating villous tree, (B) a projection of the 3D volume of a segmented villous tree block, (C) a projection of the 3D volume of a segmented placentome and (D) quantitative measures of the branching pattern of villous block by means of Sholl analysis. Herein the intersection points of projected concentric circles of increasing radius with the underlying tree structure are measured. The profiles show that the normal villous tree has a pronounced branching pattern than the villous tree of a FGR sample.

CONCLUSION: We show that a single villous tree as well as a whole placentome can be visualized by Micro-CT without using any contrasting agents. Further, we were able to extract a quantitative measure of the branching pattern by means of Sholl analysis.

Poster 125:

Titel:
Neurogenesis in the postnatal Enteric Nervous System: New-born Neurons throughout life – and beyond?

Autoren:
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Abstract:
Objective: Neural progenitor cells from the postnatal enteric nervous system (ENS) are a promising source for cell-replacement therapies. Yet, the regulation of proliferation and neurogenesis in the ENS-progenitor cell pool remains poorly characterized, particularly in postnatal development and aging. With this study, we entered uncharted territories by systematically mapping neural proliferation and neurogenesis in the murine and human ENS throughout life and beyond.
Methods: We investigated the proliferative and neurogenic potential of murine ENS-progenitors throughout postnatal life using BrdU-incorporation and immunohistochemistry. We carried out proteomic/secretomic profiling combined with a cross-over cell culture paradigm to identify signaling mechanisms involved in age-related loss of enteric neurogenesis. Moreover, we applied our protocols on human *post mortem* intestinal resectates.

Results: Proliferation in the murine ENS decreased markedly *in vivo* within the first postnatal days and was virtually absent afterwards. Yet, after isolation, ENS-progenitors were capable of considerable proliferation and neurogenesis *in vitro* even at senile stages. We were able to partly rescue the age-related effect on proliferation and neurogenesis by subjecting aged ENS-progenitors to media conditioned by juvenile ENS-cells. To elucidate the underlying mechanisms, we carried out proteomic/secretomic analyses indicating the regulation of signaling cascades including WNT and IGF pathways. Additionally, we used this knowledge to successfully establish an isolation protocol for vital human ENS-progenitors from anatomical body donors.

Conclusion: Despite the decreasing neurogenesis in the postnatal ENS *in vivo*, quiescent ENS-progenitors still persist and can be expanded in culture even at senile stages. Our proteomic analyses unravel previously uncharted regulatory signaling networks that likely drive the age-related loss of neurogenic capacity deepening our understanding of the cellular homeostasis of the postnatal ENS. Moreover, we provided pioneering evidence for the persistence of vital ENS-progenitor cells in humans beyond death rendering anatomical body donors a novel source for research in neurogastroenterology.

Poster 126:

Titel:
Psychobiological Responses and Emotional Dynamics in the Transition from Face-to-Face to Online Anatomy Education

Autoren:
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Abstract:
Objective: To scrutinize the ramifications of transitioning from traditional in-person anatomical education to online learning from a psychobiological standpoint, this investigation delved into potential differentials in physiological stress parameters exhibited by students participating in online learning versus those engaged in face-to-face instruction. The study aimed to ascertain whether these physiological measures could be delineated as conceivable variables mediating the connection between the learning experience and emotions associated with academic achievement. Further, the objective of this research project was to systematically investigate the feasibility of enhancing students' psychobiological stress responses within the framework of digital anatomical online learning, while concurrently assessing the manner in which heightened physiological parameters align with distinctive attributes of the learning encounters within a digital learning environment.

Methods: A cohort of healthy first-year medical students (n = 104) engaged in a conventional practical course on Microscopic Anatomy, delivered through one of three modalities: conventional in-person instruction, passive online learning devoid of interactive components, or an iteration of online learning enriched with interactive and activating didactic elements.

Results: A substantial reduction in Heart Rate Variability was discerned in the in-person learning setting, pointing to an increase in stress responses within this pedagogical environment ($\eta^2 = 0.421$, $P < 0.001$). Moreover, participants partaking in face-to-face instruction exhibited significantly elevated levels of cortisol ($\eta^2 = 0.115$, $P = 0.032$). Notably, augmented sympathetic nervous system activation correlated exclusively with the discrete positive emotion of enjoyment within the in-person learning condition ($r = 0.365$, $P = 0.043$). It was also possible to demonstrate that students participating in the interactive version of online learning exhibited a statistically significant reduction in Heart Rate Variability ($p < 0.001$, partial $\eta^2 = 0.381$), accompanied by a marked increase in salivary cortisol levels ($p < 0.001$, partial $\eta^2 = 0.179$), and intensified salivary alpha-amylase activity ($p < 0.001$, partial $\eta^2 = 0.195$), in contrast to those engaged in passive online learning.

Conclusion: Collectively, these findings shed light on the intricate physiological dynamics underlying the transition of a conventional face-to-face practical course in Microscopic Anatomy to an online learning environment. The transfer of an in-person practical course in Microscopic Anatomy to an online learning environment is associated with diminished sympathetic nervous system influences, increased vagal cardiovascular modulations, and reduced cortisol concentrations. Further, these outcomes illustrate that the physiological arousal of students engaged in online learning can be elevated through the strategic incorporation of interactive and activating teaching methods. Moreover, the findings underscore discernible associations between heightened physiological responses and fundamental components of the learning experience, such as enhanced cognitive engagement and sustained attention.