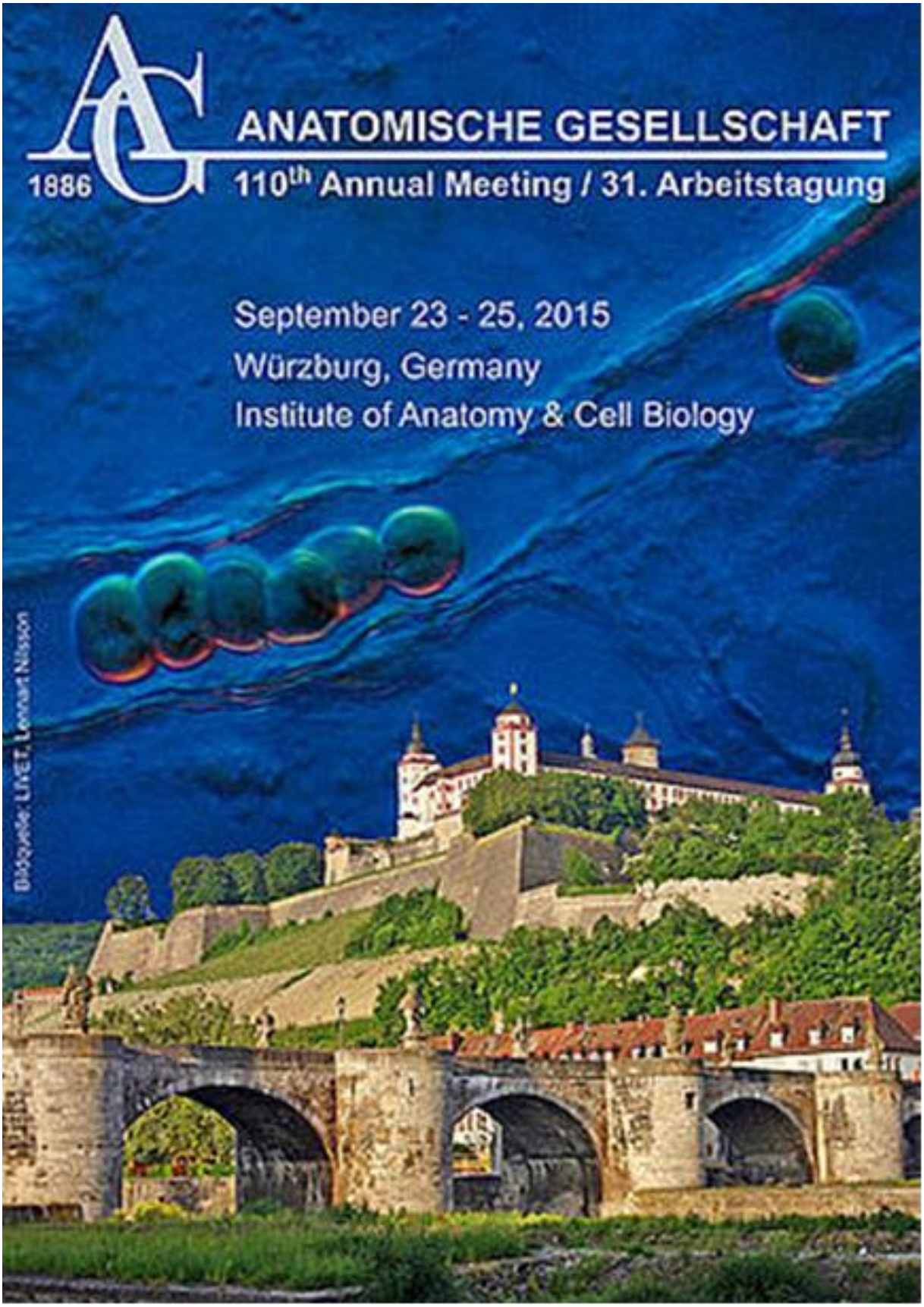
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Poster 1:

Titel:Visualising neovascularisation and tissue architecture of skin replacement materials and healing skin wounds

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Abstract:
Visualising the architecture of skin replacement material and the tissue architecture and vascular topology of skin grafts is essential for researching wound healing, and developing new materials and operative strategies. This presentation aims at demonstrating the potency of High resolution episcopic microscopy (HREM) as a tool for analysing skin replacement material and neovascularization and tissue remodeling in combined matrix-splitskin grafts. HREM volume data were produced from bovine collagen matrices, bovine matrices seed with keratinocytes and biopsies harvested from pigs with experimentally skin wounds that were covered in a one step operation with combined matrix/split skin grafts. HREM data proved to be of sufficient resolution and quality to permit precise analysis of the fiber architecture of native and seeded collagen matrices and healing skin grafts by using simple volume rendering algorithms. Blood vessels down to the size of capillaries can be traced. Topological analysis of the vessels with the aid of surface rendered 3D models is possible. In conclusion, we demonstrate that HREM is an excellent tool for studying wound healing.

Kategorie: Poster

Poster 2:

Titel:Vilip- an innovative literature research platform

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Abstract:
Introduction: A thorough literature research is usually the first step when dealing with a novel topic. Regarding the medical domain, a popular starting point for this task is the webpage PubMed, which has over 24Million publication in its database. Given certain keywords of interest, i.e. neurodegeneration, results are presented by PubMed in form of textual lists which can span over several hundred pages. Thus, getting a reasonable overview over published literature for a certain topic can be a very time consuming and challenging task. Objective: Development of an innovative software allowing for a swift visualized literature research. Methods and Results: The novel web platform VILIP (Visualized-literature platform) provides an easy to operate interface for visual-based literature research in the medical domain. In a first step, PubMed articles of interest are imported into a personalized database (for example by the student). During this import process, each publication is annotated with keywords and subsequently assigned to an anatomic, cellular or biochemical structure/item; this is done via drag-and-drop operations. Once all papers are imported, the visualization process is started. Given one or several search terms the domain-frequency of the papers are automatically visualized by an in-situ heat-map. This allows for a rapid overview of the amount of publications regarding a certain topic or biological structure. As in google-maps, VILIP allows for a smooth zoom between the top-down heat-map, the article-related abstract and finally the PDF file level. Conclusion: The VILIP platform provides a powerful and easy-to-use tool for rapid and time-effective literature research.

Kategorie: Poster

Poster 3:

Titel:Glycotyping of human neural stem cells and its descendants

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Abstract:
During brain development, radial glial cells represent a transient population of the neural stem cell (NSC) lineage. There is increasing evidence that these morphologically defined NSCs population itself is heterogeneous. This heterogeneity is indicated by the temporo-spatial expression of molecules, e.g. of those involved in cell cycle regulation, cell signalling, and cell recognition, suggesting their paramount importance for the generation of diverse neuronal and glial cell fates. Based on our morphological studies on human brain development, we investigated the role of cell surface molecules CD15, CD 56, and CD57 for the specification of human NSC/progenitor cell subpopulations. CD15 is expressed on a subset of RGCs during development, most abundantly in regions with increased neurogenic activity. Molecular characterisation of the CD15 glycosylated molecules gives evidence that neural cell adhesion molecules (NCAMs) are one of the main targets for CD15 glycosylation. Performing cell sorting experiments for CD15+ and CD15- cells, followed by clonal analysis, increased neurosphere formation of CD15+ cells can be observed by in vitro investigations using both fetal and iPS derived NSCs. Moreover, CD15+ cells show increased capacity for subsequent neuronal differentiation, correlated with glycosylation of NCAMs by the CD57/HNK-1 glycan. Hence, glycosylation of NCAMs by CD15 seems to be correlated with proliferation activity, followed by HNK-1 in course of a beginning neuronal differentiation. Further functional investigations are on the way to unravel mechanisms for the “when” and “why” of NSCs specification that are of outstanding interest for future cell based therapies of neurodegenerative diseases.

Kategorie: Poster

Poster 4:

Titel:Learning medical professionalism in the dissection course - qualitative analysis of a learning portfolio and an accompanying seminar

Autoren: Shiozawa T.(1),Banzahf M.(1),Glauben M.(1),Herrmann-Werner A.(2),Giese A.(3),Griewatz J.(3),Hirt B.(1),

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Abstract:
INTRODUCTION: Superior grades, broad knowledge and mechanical skills do not necessarily make a good doctor: professionalism has become an important issue in medical education. In gross anatomy, medical students are confronted with professional behavior when working on a cadaver. Tuebingen medical faculty introduced two instruments for self-reflection and documentation of professional development: a learning portfolio (Giese 2014) and a supportive seminar (Gahlen 2013). We asked if these instruments can support professional development in the dissection course and analyzed students' contributions. METHODS: In winter term 2013/14, 100 learning portfolio essays and the audio-recordings of 4 seminar discussions of students participating in the dissection course underwent a qualitative content analysis (Mayring 2003). RESULTS: The qualitative analysis of the seminar revealed 4 major categories, 68 main categories and 180 sub-categories. Students reflected on the difficulties at the beginning of the course, the impact and handling of the situation, and the medical profession. They discussed behavior in the dissection room, how to suppress emotions, and their ability for empathy. In the learning portfolios the students discussed habituation, what alleviated the situation, the influence of their teachers and prior experience in health care. All students expressed their respect to the body donor and his/her decision. SUMMARY: Students showed an amazing depth of reflection during the dissection course. Attributes of medical professionalism like respect, appraisal, compassion and communication could be documented. The seminar discussions yielded more depth than written essays. This let us conclude that the dissection course is suitable for teaching professional behavior in pre-clinical education.

Kategorie: Poster

Poster 5:

Titel:Reference genes for valid gene expression studies on rat dental-periodontal tissue by means of RT-qPCR with a focus on orthodontic tooth movement and periodontitis.

Autoren:Kirschneck C.(1),Proff P.(1),Fanghaenel J.(1),Roemer P.(1),

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Abstract:
BACKGROUND
To obtain valid results in relative gene/mRNA-expression analyses by RT-qPCR, a careful selection of stabile reference genes is required for normalization. Currently there is little information on reference gene stability in rat dental-periodontal tissues, especially regarding orthodontic tooth movement and periodontitis. We therefore aimed to identify the best selection and number of reference genes under these experimental as well as physiological conditions.
MATERIAL AND METHODS
In 7 male Fischer344-rats the upper left first and second molars were moved orthodontically for 2 weeks and in 7 more animals additionally subjected to an experimental periodontitis, whereas 7 animals were left untreated. Biopsies of defined size containing both molars (without crowns) as well as the adjacent periodontal and alveolar bone tissue were retrieved and RNA extracted for RT-qPCR analyses. Ten candidate reference genes were evaluated and ranked according to their expression stability by 4 different algorithms (geNorm, NormFinder, BestKeeper, comparative-ΔCq).
RESULTS
PPIB/YWHAZ were the most stabile reference genes for rat dental-periodontal tissue overall, in untreated animals and rats with additional periodontitis, whereas PPIB/B2M performed best in orthodontically treated rats with YWHAZ ranking third. Gene-stability ranking differed considerably between investigated groups. A combination of two reference genes was found to be sufficient for normalization in all cases.
CONCLUSIONS
The substantial differences in expression stability emphasize the need for valid reference genes, when aiming for meaningful results in relative gene expression analyses. Our results should enable researchers to optimize gene expression analysis in future studies by choosing the most suitable reference genes for normalization.

Kategorie: Poster

Poster 6:

Titel: Longitudinal change in thigh muscle strength prior and concurrent to a minimal clinically important worsening or improvement in knee function – Data from the Osteoarthritis Initiative

Autoren: Ruhdorfer A.(1),Wirth W.(1),Eckstein F.(1),

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Abstract:
Objective: Knee osteoarthritis is associated with reduced thigh muscle strength and functional limitations. Quadriceps strength, a potentially modifiable risk factor, is a stronger determinant of knee function than radiographic disease severity. However, the association of clinically relevant changes in knee function with concurrent or prior thigh muscle strength changes is unknown. Methods: 2675 Osteoarthritis Initiative participants (1485 women) with isometric strength measurements at baseline (BL), year 2 (Y2) and 4 (Y4) follow-up were divided into those with minimal clinically important (MCI) worsening in (WOMAC) knee function (i.e. worsening reaching or exceeding the MCI change threshold), MCI improvement, or without relevant change during Y2->Y4. Muscle strength changes, concurrent (Y2->Y4) and preceding (BL->Y2) function change, were compared between groups (ANCOVA). Results: Concurrent quadriceps strength loss in participants with functional worsening (-4.6% 95%CI [-6.8, -2.4]) and concurrent strength increase in those with functional improvement (+2.2% [-0.3, 4.7]) differed significantly (p=0.03; p<0.0001) from the change in participants without function change (-2.2% [-3.0, -1.4]). The strength increase in those with functional improvement was preceded by a greater strength loss (-7.7% [-10.3, -5.0]; p=0.02) compared with those without function change (-4.3% [-5.2, -3.4]). The preceding strength decrease in those with functional worsening (-4.5% [-6.9, -2.2]) did not differ from those without function change. No differences between groups were observed in hamstring strength. Conclusion: The findings suggest a positive concurrent (but not preceding) longitudinal association between quadriceps strength changes and knee function worsening/improvement.
Funding:PMU-FFF-R-13/05/055-RUH

Kategorie: Poster

Poster 7:

Titel:The glenoid joint revisited: clinical anatomy and pathology explored by dissection

Autoren: Eppler E.(1,2,3),Mathews S.(4),Burkhard M.(5),Franke I.(5),Bischofsberger H.(5),Harper G.(6),Qureshi F.(7),Bloch H.(8),Haeusler M.(4),Ullrich O.(5),Link K.(4,5),Ruehli F.(4),

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Abstract:
Modern shoulder surgery techniques such as Reverse Total Shoulder Arthroplasty (RTSA) during most recent years have strongly increased the demand for better knowledge of “the anatomy beyond the glenoid fossa” (e.g., Codsi et al. J Shoulder Elbow Surg 2007;16:84S-89S). The main aim of the present study is to further explore the topography of the scapula in light of modern surgical demands such as safe screw placement for baseplate fixation in the glenoid cavity. In an anatomical cadaver dissection study, we investigated 70 samples from the institutional body donation program of the University of Zurich. In succession to the dissection by a common surgical approach to the glenoid joint, measurements of the glenoid cavity were performed, particularly with relation to sexual dimorphism and individual body size. Furthermore, the topography of the suprascapular nerve and blood vessels traveling via the scapular notch and the distance to the glenoid cavity were explored with regard to the secure implantation particularly of the superior baseplate screw. From this, we aim at defining landmarks of safe zones for treatment planning. Furthermore, the humeral heads were inspected and classified with respect to the degree of osteoarthritis. The majority of the dissected joints presented with degenerative illness. These results are part of a larger study with the main focus on modern imaging and surgery of the glenoid joint. Supported by the Prof. Dr. med. Karl und Rena Theiler-Haag Foundation.

Kategorie: Poster

Poster 8:

Titel:Three-dimensional morphometrical investigation of the neurocranium of horses

Autoren: Lang A.(1),Ludwig M.(1),Wrede T.(2),Brucker P.(1),Gasse H.(1),

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Abstract:
Introduction: Considering the complete lack of stereotactic data on the equine head, attempts are made to elaborate craniometrical guide data for approaches to intracranial neuronal and vascular structures by means of a computer-assisted 3-d measuring device. Material and Methods: Skulls of 30 horses (6 weeks, n=2; 2-3.5 years, n=8; 7-9 years, n=10; 13-23 years, n=10) were cut in the median plane. The positions of osseous Points of Interest (POIs) outside and inside the neurocranium were transferred into a virtual three-dimensional coordinate system with the measurement device FaroArm® Fusion (Stuttgart, Germany). The growth-related shifts of POIs were analysed by determining angles within virtual geometrical triangles. Results: The greatest changes were found in specimens up to 2 years. They were located in the transitional region between Cranium and Facies. POIs at well-palpable extracranial landmarks (Orbita, Arcus zygomaticus) showed greater shifts of their positions than intracranial POIs. The metrical extent (length) of these shifts could not be deduced from the values of differences of angle-size alone. Instead, the angle sizes had to be interpreted in combination with the lengths of the sides of the triangles. Discussion/Conclusion: The method and the geometrical model of this pilot study yielded highly accurate and reproducible data. Intrinsic errors of other studies, which caused perspective distortions, were avoided. However, the applied method is very complex with regard to a large scale of different geometrical parameters.

Kategorie: Poster

Poster 9:

Titel: Knee pain is not related to alterations in the morphology or mri signal of the infra-patellar fat pad (ipfp) - a within-person and between- person analysis using data from the osteoarthritis initiative (oai)

Autoren: Steidle-Kloc E.(1),Doerrenberg J.(1),Wirth W.(1),Ruhdorfer A.(1),Eckstein F.(1),

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Abstract:
Objective: Obesity is a known risk factor for knee osteoarthritis which may in part be explained by endocrinological mechanisms. The infra-patellar fat pad (IPFP) represents an accumulation of intra-articular adipose tissue and may mediate inflammation and inflammation is known to influence knee pain. The direct relationship between IPFP volume and pain has not been explored. Methods: A between-knee, within-person design and a matched case-control design were used to explore the relationship between IPFP size and knee pain. 46 subjects from the Osteoarthritis Initiative (OAI) with unilateral knee pain, but the same radiographic stage (KLG 2 or 3), were studied. 43 subjects (OAI) with chronic pain over 4 years (numerical rating scale (NRS)>=4 and frequent pain) were compared with pain-free control subjects (NRS=<1, no or infrequent pain) who were matched 1:1 by age, BMI, and other factors. IPFP volume and MRI signal (i.e. inflammation) were analyzed using sagittal, fat-suppressed spin-echo MR images. Results: In 46 subjects with unilateral pain (67% female, 62.8±9.7 yrs, BMI: 30.0±4.7 kg/m²), IPFP volume was not significantly different between painful vs. pain-free knees (+0.18 cm³; +0.7%; p=0.64). In 43 knees with chronic pain (53% female, 60.7±9.0 yrs, BMI: 28.1±3.5 kg/m²), IPFP volume was not different compared to matched pain-free controls (-0.54 cm³; -2.1%; p=0.52). No significant differences were observed for MRI signal. Conclusions: Using both a within-person and between-person study design demonstrated that neither IPFP volume nor IPFP MRI signal are related to knee pain.

Kategorie: Poster

Poster 10:

Titel:The arterial blood vessels supplying the larynx of the minipig: gross anatomical and sem study with special regard to the glottis

Autoren: Kroll A.(1),Lang A.(1),Gasse H.(1),

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Abstract:
Introduction/Material and Methods Considering a possible role of the minipig as a model in human laryngology (e.g. for laser surgery or edema therapy), the arterial blood vessels of the larynges of 24 minipigs (2.5-60 months old) were injected with either latex rubber or epoxy resin (Biodur® E 20) via the abdominal aorta after euthanasia. Specimens injected with Biodur® were routinely processed for scanning electron microscopy (SEM). Preliminary Results From the Ramus laryngeus of the A. laryngea cranialis, one branch extended from its cranio-dorsal origin to reach the glottis cranio-ventrally, giving off branches to the ventral parts of both, the cranial and caudal fold. From the same origin, some other branches ran within the laryngeal wall in a caudo-ventral direction. One of it contributed most to the supply of the glottis, giving off branches (1) to the dorsal parts of both folds, (2) to the caudal margin of the caudal fold, and (3) to the ventral parts of the cranial and caudal fold. The involvement of a Ramus laryngeus caudalis of the A. thyroidea cranialis could not yet be clarified. No contribution of the A. thyroidea caudalis was found until now. Conclusion The cranial and the caudal folds of the glottis are not supplied separately by their proper blood vessels. As a common pattern, a four-directional supply to them via a dorsal, a caudal, a ventral, and a cranio-ventral approach was found. In general, the cranial fold was more sparsely supplied than the caudal fold.

Kategorie: Poster

Poster 11:

Titel:Applying CRM standards to body donation management in a modern clinical anatomy

Autoren:Barbian A.(1),Brzoska P.(1),Malenica D.(1),Barbian B.(1),Filler T.(1),

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Abstract:
Documentation of body donations meets stringent statutory standards in Anatomical Institutes worldwide. Due to respective local legislation1, the rights and privacy of living donors have to be separated from ethical and statutory requirements for deceased donors. Even greater need for strict documentation results from parallel administration of internal curricular dissecting courses and external advanced medical trainings.
We have designed a bilateral Customer-Relationship-Management (CRM) solution, which combines complying legal requirements as well as the needs of a broadly based Clinical Anatomy department with managing the requests of the different customer groups (Donors, Universities, Clinical Institutes and Industry). A comprehensive document management is included and covers the process from a living donor's first contact to the burial of the body donation. Thus, all archived documents relating to specific donors or events are easily accessible.
Additionally, using our CRM as a long-term archiving system, anatomical variations found in the dissection course can be monitored, accumulated and evaluated. Thus it can serve as a powerful analysis tool for clinical studies whilst intermeshing education and science for medical students.
Combining these different processes in transparent workflows provides a solid base for further expansion and (inter-)national cooperation. Furthermore, a digital tracking of single body parts via RFID can be integrated easily.

Kategorie: Poster

[1] exemplary source e.g. for Düsseldorf: https://recht.nrw.de/lmi/owa/br_text_anzeigen?v_id=532014100709213371 3#det315554

Poster 12:

Titel:Accessing the hypoglossal nerve with ultrasound - Visualizing the topology in body donators and healthy volunteers and diagnosing pathologies in a clinical setting

Autoren: Reissig L.(1),Meng S.(2),Tzou C.(3),Meng K.(4),Grisold W.(5),Weninger W.(1),

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Abstract:
Pathologies of the neck and skull base may affect the hypoglossal nerve and cause dysarthria, dysphagia, and ultimately atrophy of the tongue. We attempted to examine the feasibility of a direct visualization of the hypoglossal nerve in the neck of body donators with ultrasound. Based on these results we then aimed at evaluating the reproducibility of identifying the nerve in healthy volunteers and at testing the possibilities to diagnose hypoglossal nerve pathologies. Hence, the study had three parts: Firstly, identification of the nerve with ultrasound and ultrasound guided perineural ink injections along its extracranial course in 12 fresh, non-embalmed cadavers. This was, followed by anatomical dissection for confirming the correct identification of the nerve. Secondly, identification of the nerve in healthy volunteers with ultrasound and measuring of cross sectional areas for providing reference data. Thirdly, examination of the cross sectional appearance of the hypoglossal nerve in patients with tongue palsy. All three parts of our study provided highly significant results. Correct bilateral identification of the hypoglossal nerve was possible in all cadaver specimens (24/24) and all healthy volunteers (33/33). The cross sectional area ranged from 1.9 - 2.1 mm^2. Characteristic alterations of the hypoglossal nerve could be diagnosed in patients suffering form tongue palsy. As a consequence, our results show that, reliable and reproducible visualization of the extracranial segment of the hypoglossal nerve with ultrasound is feasible. Characteristic alterations in the appearance of the nerve permit the correct diagnosis of nerve pathologies.

Kategorie: Poster

Poster 13:

Titel:Ultrasound evaluation of an underestimated structure: the bicipital aponeurosis (ba)

Autoren: Moriggl B.(1),

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Abstract:
The BA reaches the antebrachial fascia and posterior margin of the ulna. Such expansions act via force transmission. The BA supports flexion of the elbow and reduces stress concentration at the enthesis. It increases the effectiveness of the biceps. A ruptured BA may result in tendon elongation and weakening of muscle function. This outlines the functional importance. Astonishingly, we lack reports on US-evaluation, literature even doubts visibility. M&M The investigation was performed in 100 Volunteers. All scans were done using 18 MHz (probe: LA435; MyLab25; Esaote, Italy). The BA was scanned in two planes. Scanning was done with and without isometric contraction. Results We could identify the BA in both planes in all subjects. The BA was characterized by two white lines enveloping a hypoechoic band. In 97/100 visibility was best during isometric contraction. In all longitudinal images, the BA was arose from the biceps belly, tendon or myotendineous junction. Due to the sparseness of the BA no measurements were taken (inherent measurement errors with pseudo-accurateness) Discussion and Conclusion In contrast to previous reports, US imaging of the BA is possible. What is illustrated here as the US representation of the BA is in fact its central main part. Importantly, visibility of the BA was best during isometric contraction (many of the MSK investigations are also done dynamically). With knowledge of the normal sono-anatomic appearance of the BA it we may be able to detect relevant alterations of that neglected structure, which has to be proven in clinical trials.

Kategorie: Poster

Poster 14:

Titel:Comparison of the fluid resuscitation rate with and without external pressure using two intraosseous infusion systems for adult emergencies

Autoren: Moebius R.(1),Hammer N.(1),Gries A.(2),Hossfeld B.(3),Bechmann I.(1),Bernhard M.(4),

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Abstract:
Introduction: Intraosseous infusion is recommended if peripheral venous access fails for cardiopulmonary resuscitation or other medical emergencies. The aim of this study, using body donors, was to compare a semi-automatic (EZ-IO®) device at two insertion sites and a sternal intraosseous infusion device (FASTR). Methods: Twenty-seven medical students were randomized into three groups using EZ-IO and FASTR. The following data were evaluated: attempts required for successful placement, insertion time and flow rates with and without external pressure to the infusion. Results: The first-pass insertion success of the EZ-IO tibia, EZ-IO humerus and FASTR was 91%, 77%, and 95%, respectively. Insertions times (MW±SD) did not show significant differences with 17±7 (EZ-IO tibia) vs. 29±42 (EZ-IO humerus) vs. 33±21 (FASTR), respectively. One-minute flow rates using external pressures between 0 mmHg and 300 mmHg ranged between 27±5 to 69±54 ml/min (EZ-IO tibia), 16±3 to 60±44 ml/min (EZ-IO humerus) and 53±2 to 112±47 ml/min (FASTR), respectively. Concerning pressure-related increases in flow rates, negligible correlations were found for the EZ-IO tibia in all time frames (c= 0.107-0.366; p≤0.013), moderate positive correlations were found for the EZ-IO humerus after 5 minutes (c=0.489; p=0.021) and strong positive correlations were found for the FASTR in all time frames (c=0.63-0.80; p≤0.007). Conclusions: The EZ-IO and FASTR appear to be effective intraosseous infusion devices, suitable for fluid resuscitation using a pressure bag. However, variations in flow rate may limit their reliability.

Kategorie: Poster

Poster 15:

Titel:The role of ehcographic measurements in determining the conversion from minicholecystoctectomy to classical cholecystectomy

Autoren: Motoc A.(1),Ilie A.(2),Jianu A.(2),Stana L.(2),Moise L.(2),Folescu R.(2),Ferencsik-Moldovan T.(3),

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Abstract:
Due to the progress made in the field of medicine in the past years, classical cholecystectomy has gradually been replaced by laparoscopic cholecystectomy and by cholecystectomy by mini-laparotomy. We established some pre-operative prognostic factors which might predict the conversion of cholecystectomy by mini-laparotomy (CM) to classical cholecystectomy (CC). The study was conducted for five years, between 2010 - 2014. The study group consisted of 100 patients who had undergone surgical cholecystectomy by: classical cholecystectomy, laparoscopic cholecystectomy, cholecystectomy by mini-laparotomy. Pre-operative echography is not just a diagnostic technique, but also as a pre-operative predictive conversion method for CM. The study shows that echography can be used as a standard technique for the classification of the operative risk as well as an exploration technique for CM. Due to the fact that it can be performed as an outpatient method, being an inexpensive investigative method, echography plays an important role in determining the pre-operative risk for the conversion of CM to CC. Several studies show extreme values of the conversion, values between 0.49% and 12%. In our study, the incidence of conversions has been situated at the lowest limits. In laparoscopic cholecystectomy, conversion is described as having lowest values of 1.76% and highest values of 20%. The present study reveals the following aspects: CM conversion is connected to the severity of the underlying disease, but it can also be the result of other associated disorders. The value of conversion is situated at the lower limit when compared to the values mentioned in other studies. Key words: mini-cholecystectomy, echography, conversion

Kategorie: Poster

Poster 16:

Titel:Minimally invasive approach to the iliac crest - functional and aesthetic outcome

Autoren: Stofferin H.(1),Zimmermann R.(2),Kuenzel K.(1),

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Abstract:
In hand surgery numerous free vascular bone grafts for treatment of scaphoid nonunion complicated by avascular necrosis have been described with generally similar favourable outcomes. Therefore careful selection of the harvesting site with regard to donor site morbidity is crucial. The aim of this retrospective study was to describe and evaluate our minimally invasive approach to the iliac crest, with special emphasis on the functional and aesthetic outcome. Two observers investigated the scars of 17 patients with a novel translated German version of the Patient and Observer Scar Assessment Scale (POSAS). Postoperative complications were investigated in patient files. The internal consistency of the POSAS (Cronbach's alpha = 0.86 and 0.83 respectively) and Inter-rater reliability of the observer scale were strong ($r = 0.85$, $p < 0.001$). Even a single observer evaluated the scars reliably ($r = 0.74$, $p < 0.001$). Median result in the POSAS overall was 15 (numerical score, 10 = normal skin, 70 = worst scar imaginable). We found no impact on range of motion, postoperative infections, postoperative haematoma or impairment of the lateral femoral cutaneous nerve. During our investigation the POSAS turned out to be a reliable and feasibly clinical tool for linear scar evaluation. We suggest a first evaluation of alternative approaches with similar methods, particularly with the POSAS, to substantiate the choice of donor sites. Consequently we consider the minimally invasive approach to the iliac crest a viable and low-risk option to harvest a vascularized bone graft with excellent patient satisfaction.

Kategorie: Poster

Poster 17:

Titel:Patient-satisfaction regarding the aesthetic aspect according to the type of cholecystectomy

Autoren: Ilie A.(1),Jianu A.(1),Stana L.(1),Motoc A.(1),Daescu E.(1),Selaru M.(2),Vilceanu A.(2),

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Abstract:
The aesthetic aspect is an important criterion for the patient which is why an increasing number of patients choose minimal-invasive surgical techniques. Laparoscopic cholecystectomy (LC) is recognised as being the surgical technique for cholecystectomy leading to the best results.The study group consisted of 100 patients who received surgical treatment. The conclusions regarding the quantification of the aesthetic results of cholecystectomy by mini-laparotomy (CM) were based on a questionnaire devised by the authors and applied the current study: the post-operative scar reflects the extension of the surgical trauma on the abdominal wall, this being the main element in determining post-operative motor inability, the least favourable aesthetic result, appears after classical cholecystectomy (CC), which is less and less accepted by patients; CM has superior aesthetic results versus CC; however, LC remains the surgical procedure with the best aesthetic results. A small incision in the abdominal wall is correlated with a high level of post-operative patient satisfaction bringing, at the same time, a number of beneficial effects in the patients' post-operative evolution, lowering the risk of post-operative infections, decreasing post-operative pain, shortening the hospitalisation period and the socio-professional reintegration period, with benefits both for the patient and for society.The authors consider that the minimum-invasive technique of CM can be regarded as an alternative to LC, both for the aesthetic results and for the post-operative evolution of the patients. Key words: cholecystectomy, post-operative scar, level of satisfaction

Kategorie: Poster

Poster 18:

Titel:Ultrasound and anatomical correlation of the radial nerve at the arcade of frohse

Autoren: Tinhofer I.(1),Reissig L.(1),Weninger W.(1),Grisold W.(2),Meng S.(1),

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Abstract:
Introduction: In this anatomical study we evaluated the feasibility of ultrasound (US) guided perineural injection of the deep branch of the radial nerve (DBRN) at the arcade of Frohse as potential therapy for nerve entrapment at this site. Methods: We examined 21 arms from 11 nonembalmed cadavers with US. Under US guidance, we injected ink into the DBRN perineural sheath beneath the arcade of Frohse. In subsequent anatomical dissection we evaluated the distribution of the ink. Results: It was possible to apply ink at the DBRN in 95%. In 80% the ink remained within the supinator and did not reach the DBRN segment proximal to the arcade. Conclusions: With US guidance, it is possible to apply injection fluid safely around the DBRN inside the supinator tunnel. Due to the limited extent of the fluid, a second injection proximal to the arcade should be considered in the clinical setting.

Kategorie: Poster

Poster 19:

Titel:The buccolingual topography of the mandibular canal

Autoren: Didilescu A.(1),Sandulescu M.(2),Rusu M.(3),

Adressen:(1)Embryology|Carol Davila University of Medicine and Pharmacy|Bucharest|Romania; email:andreea.didilescu@gmail.com; (2)Oral Implantology|Carol Davila University of Medicine and Pharmacy|Bucharest|Romania; (3)Anatomy|Carol Davila University of Medicine and Pharmacy|Bucharest|Romania

Abstract:
Damage of the inferior alveolar nerve in the mandibular canal (MC) may occur during mandibular surgical procedures. The aim of the present study was to assess the course of MC in the molar region of dentate patients, as referred to the lingual and buccal cortical plates, by Cone Beam Computed Tomography (CBCT). Thus, a sample of 60 patients (28 males) has been investigated. One hundred-twenty MCs were assessed using as landmarks the mandibular molars: third molar (M3), second molar (M2), and first molar (M1). Lingual, intermediary or buccal positions were assigned according to each landmark. There was a large range of topographic variants of MC's course as related to the cortical plates and molars. Three main topographic types were identified as follows: (a) 38.3% of canals were positioned lingually with respect to all three molars; (b) 15.8% of canals were placed lingually at M3 and M2, and in intermediary buccolingual position at M1; (c) 12.5% of all MCs were in intermediary position with regards to all three molars on that side. A higher variability of MC's course was recorded in females. Left-right asymmetry was present in 17 patients (M3), 12 patients (M2) and 14 patients (M1). However, no statistical significant association was found between left/right sides and MC's positions at each level. Knowledge of such details regarding topography of MC is important in assessment of potential risk of accidental nerve damage before local surgical interventions, such as endosseous implants placement.

Kategorie: Poster

Poster 20:

Titel:The innervation pattern of the crural diaphragm.

Autoren: Haenssgen K.(1),Herrmann G.(1),

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Abstract:
The crural part of the diaphragm plays an important role in maintaining the antireflux barrier at the esophagogastric junction. The poster presents the findings of an ongoing study investigating the neuronal structures of the crural diaphragm in a species which is anatomically similar to humans, the piglet. The aim of the study is to give an answer to the somewhat mysterious pattern of innervation involved in the control of the esophagastric junction, where the lower esophageal sphincter and the crural diaphragm are supposed to work together in order to establish the high pressure zone required to prevent gastroesophageal reflux. The classical view describes the vagus and phrenic nerve as providing separate innervation for the lower esophageal sphincter and the crural diaphragm, respectively. But there also is evidence for a purely peripheral mechanism at the level of the esophagogastric junction in cats. Other evidence comes from studies in ferrets where vagal sensory and motor neurons innervate both. A recent study in rats could neither confirm a co-innervation of motor endplates in the crural diaphragm nor the presence of vagal afferent endings. Our approach covers a wide range of methods, such as classical dissection and Sihler staining method. Motor endplates are visualized in relation to the arterial supply by applying the wholemount acetylcholinesterase staining. A possible motor co-innervation and possible vagal afferent endings are demonstrated using histochemical and immunohistochemical methods.

Kategorie: Poster

Poster 21:

Titel:Progesterone and estrogen receptors expression in ductal carcinomas

Autoren: Motoc A.(1),Sisu A.(1),Ilie A.(1),Jianu A.(1),Moise L.(1),Stana L.(1),

Adressen:(1)Department of Anatomy and Embryology|Victor Babes, University of Medicine and Pharmacy|Timisoara|Romania; email:anatomie@umft.ro;

Abstract:
The assessment of the ER (estrogen receptors) expression in the mammary carcinomas as a prognostic and especially predictive factors in the antiestrogenic endocrine adjuvant therapy represents the element of the traceability protocol in mammary neoplasm. We have studied the ER for 86 invasive ductal carcinomas. Ductal carcinomas in situ were positive for the ER in a percentage of 60% (three cases), one cribriform DCIS high positive (ER3+) and two solid DCIS - one of them weak positive (ER1+) and the other high positive (ER3+). DCIS with apocrine differentiation and one of the solid DCIS were negative. Out of the 86 invasive ductal carcinomas, a number of 18 (29%) cases were positive estrogen receptor, the rest being negative. Regarding the expression level of the ER expression, 2 carcinomas was weak positive (ER1+), 14 cases were moderate positive (ER2+) and 12 carcinomas were intense positive (ER3+). We studied 80 carcinomas. PR were positive in a percentage of 30% (24) and out of the positive cases, four (16.6%) were weak positive (PR1+), 13 (54.16%) moderate positive (PR2+) and seven (29.16%) intense positive (PR3+). Out of the in situ ductal carcinomas, only two (40%) have been moderately positive (PR2+), the cribriform type and one of the solid type. 14 out of 48 (29%) were PR positive. According to the preset quantification with an intensity and a percentage score, three cases have been quantified as being weak positive (PR1+), six moderate positive (PR2+), five intense positive (PR3+). Keywords: ductal carcinoma, progesterone, receptor

Kategorie: Poster

Poster 22:

Titel:The pleural cupula and its ligamentous connections – patterns/drawings in literature compared with fresh cadavers

Autoren: Hoermann R.(1),Brenner E.(1),Moriggl B.(1),Kuenzel K.(1),

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Abstract:
Background: In old and new anatomical literature there are many different descriptions of the ligaments and the connective tissue of the pleural cupula. But what is the real situation in humans? Is it truly so as shown in the drawn pattern? And what about functionality, is it possible in the described extent? Method: We dissected seven fresh cadavers and present several different views showing the pleural situation in the apex area in relation to the subclavian artery passing nearby and the brachial plexus to enlighten functionality and dependency. Documentation was done with photographs and film sequences. These films promote an increased understanding of the interaction of the tissues (ligaments, fat, and connective tissue) in this area. Results: The interaction and fixation of the pleural ligamentous system is more complex than it has been described in literature. The costo- and vertebro-pleural ligaments are branched in a special way and they are attached to various structures around. The subclavian artery is entirely covered in a triangle of collagenous fibers and has a connection to the trunks of the brachial plexus, too. Thus, there are also functional dependencies. Conclusions: As both the types of attachments and the kind in which the ligaments are attached to the surrounding tissue vary, it is impossible to describe a district fixation and a linear course. The interactions in movements, too, are more complex due to the branched attachments.

Kategorie: Poster

Poster 23:

Titel:Clinical and echographically correlations in a simple transposition of greater vessels

Autoren: Folescu R.(1),Sisu A.(1),Ilie C.(1),Grigoras M.(1),Haivas C.(1),Petrescu C.(1),Zamfir C.(2),Motoc A.(1),

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Abstract:
We present a case of a 6-weeks patient, male, Apgar score=10, weight=3,600gr., with an unsatisfactory growth, only 600 grams in 6 weeks. He was checked in our hospital service, where he presented: generalized cyanosis, bad general state, polipnea, wheezing, general oedema, bronchopneumonia, acute respiratory infection. Echography showed: atrioventricular concordance, ventricular-arterial discordance, greater vessels transposition, venae cavae are draining into the right atrium; right atrium is connected with right ventricle and from the late the aorta is outgoing. Left atrium is connected with left ventricle and from the late is going the pulmonary artery. There was a persistent arterial canal, with right-left shunt, funnel -shape, having the pulmonary end stenosed. Also there is a restrictive right-left shunt. It could be seen a peripherical stenosis of the left branch of the pulmonary artery, having an 8 mm diameter. It has been detected a patent foramen ovale, with a restrictive right-left shunt. The right coronary artery was seen very badly and was present an atrial situs solitus. Laboratory exams detected metabolic acidosis and a blood oxygen saturation of 65%. Also it was seen a severe hiponatremia. After one week, the patient suffered a heart attack and was declared dead. Keywords: atrium, stenosis, metabolic acidosis

Kategorie: Poster

Poster 24:

Titel:Idiopathic scoliosis – a clinical study to evaluate cross-relations with the stomatognathic system

Autoren:Fanghaenel J.(1),Hoesl H.(1),Proff P.(1),Roemer P.(1),Matussek J.(2),Grifka J.(2),Kirschneck C.(1),

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Abstract:
BACKGROUND
There is much controversy whether spinal deformities can affect the stomatognathic system. Muscular chains connecting both systems, however, establish an anatomical and functional relation and give reason to assume that transversal asymmetries of the spine - as seen in patients with idiopathic scoliosis - can cause deformities of the stomatognathic system and vice versa.
MATERIAL AND METHODS
In total, 144 patients with a mean age of 14.3 years (male/female=97/47) were prospectively recruited. 72 patients were diagnosed with idiopathic scoliosis and vertebral and orthodontic parameters of all patients were evaluated. The scoliosis was characterized by raster stereography (Formetric 4D®) and parameters of dental occlusion investigated by means of a clinical orthodontic examination and an analysis of orthodontic study models of the patients.
RESULTS
Mandibular midline shifts were significantly more prevalent in patients with idiopathic scoliosis (37.5%) than in the control group (13.9%; p=0.002). No significant relation could be established between the frequency of dental crossbites and the presence of a vertebral scoliosis (p=0.129). Severity, type (King 1983) and convexity of scoliosis did not significantly affect the parameters investigated.
CONCLUSIONS
A significant relation between the prevalence of idiopathic scoliosis and deformities of the stomatognathic system could be established. Patients with scoliosis showed an increased tendency for mandibular midline shifts, but not crossbites, whereas severity, type and convexity of scoliosis did have no significant effects. Future studies are needed to investigate possible compensatory mechanisms of the stomatognathic system during growth, which could account for the indifferent number of crossbites in both groups.

Kategorie: Poster

Poster 25:

Titel:Variations of the deep femoral artery and the circumflex femoral arteries with respect to the branches of the femoral nerve

Autoren: Claassen H.(1), Schmitt O.(2), Schulze M.(2), Wree A.(2),

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Abstract:
Four or five cm below the inguinal ligament, femoral artery (FA) gives off deep femoral artery (DFA) from its lateral or posterolateral side. Lateral (LCFA) and medial (MCFA) circumflex femoral arteries typically arise from the deep femoral artery. Among the lower extremities, evaluated during the gross anatomy course of Rostock Anatomical Institute in summer terms 2011 and 2012, three variants concerning the origin and course of these arteries were detected. Case 1: In a 81-year-old female, origin of DFA was located in cloth vicinity to the inguinal ligament. In addition, LCFA took off from FA instead from DFA. Branches of the femoral nerve passed before and behind LCFA. Case 2: In a 76-year-old male, LCFA derived from FA while origin of DFA was quite normal. Branches of the femoral nerve passed behind LCFA. Case 3: In a 90-year-old female, MCFA took off from FA while origin of DFA was quite normal. Branches of the femoral nerve passed before LCFA. Knowledge of variations of DFA or LCFA and MCFA is important when undertaking clinical procedures within the femoral region and in hip joint replacement. At the antero-lateral access to the hip joint, topography of lateral vastus and MCFA with respect to the branches of the femoral nerve have to be taken into account. Furthermore, DFA is an access point for invasive and diagnostic angiographic procedures. Complications like femoral arteriovenous fistula may occur during these procedures unless the anatomy of the femoral triangel is well understood.

Kategorie: Poster

Poster 26:

Titel:Morphological and histological aspects of the premaxilla

Autoren: Nimtschke U.(1),Vollmer R.(2),Schwab W.(1),

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Abstract:
The anterior region of the hard palate including the incisive canal and the passing neurovascular structures in combination with typical age-related changes of the maxilla in edentulous patients is from particular interest for implantologists. In the present study we try to summarize the topographic-anatomical details of the anterior palate region. Own immunohistochemical findings demonstrate the dense sensory innervation of the mucosa in the area of the incisive papilla. Periarterial autonomous nerve plexus could be further detected in blood vessels of the lamina propria. Individual sensory nerve fibers were found in close contact to the cells of the basal layer. These cells are assumed to be Merkel cells, because they expressed a specific and selective immune reactivity with antibodies against CK 20 and PGP3.5.The placement of dental implants in the area of anterior palate should be done without perforating the canal and hurting the nerve bundle. Implantation into the incisive canal itself can be done as an ultima ratio in highly atrophied maxillae and leads to complete numbness in the supplied region. For the patient the risk of unpleasant paresthesia of the palatal mucosa is reduced when the implants are placed in the region of the laterals and not in the central area. The area of the centrals and the incisive nerve should be especially be treated very gently in professions like singer, actor or cook.The dense innervation of the incisive papilla in combination with the expected function of Merkel cells as mechanosensors may be an explanation for the generally known sensitivity of this area to pain.

Kategorie: Poster

Poster 27:

Titel:Determination of location, number and shape of the greater palatine foramen in adult anatolian population

Autoren: Ortug A.(1),Uzel M.(2),

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Abstract:
Accurate knowledge of locations, numbers and shapes of the greater palatine foramen (GPF) and it's complex anatomy is a prerequisite necessity in performing a variety of anaesthesiological, dental and surgical procedures. The main aim of this study was to identify the GPF's locations, numbers and shapes via associating with gender and palatal indices among Anatolian population and compare with other populations results. Various metric assessments were observed on totally 97 sexed, dry craniums of different universities cranium collections. Thirty eight male craniums were observed and mean value of palatal indices was 86.28±10.75, and for 48 female craniums mean value for palatal indices was 81.06±10.56. Location of GPF were observed bilaterally and mostly found near the third upper molar both in males and females. Only one cranium was absent of GPF on one side. GPF was found oval on 62.8% of the right and 61.0% of the left sides of the male craniums; in female craniums it was oval on 66.0% of the right and 66.0% of the left sides. These results were compared with already existing anatomical data of other races and populations. Obtained results would have great clinical influence in localizing the palatine foramina toward better palatal area surgical approaches and anesthetics applications.

Kategorie: Poster

Poster 28:

Titel:Morphological variations of the superior cornu of thyroid cartilage in anatolian population

Autoren: Kopuz C.(1),Ortug G.(2),Ortug A.(3),

Adressen:(1)Department of Anatomy|Ondokuz Mayıs University|Samsun|Turkey; (2)Department of Anatomy|Bahcesehir University, Faculty of Medicine|Istanbul|Turkey; email:gurselortug@gmail.com; (3)Department of Anatomy|Istanbul Medipol University, School of Medicine|Istanbul|Turkey

Abstract:
Morphological variations of superior cornu of thyroid cartilage are rare and have not been previously described in Anatolian population. Posterior border of each lamina of thyroid cartilage projects superiorly as the superior cornu and attaches to the greater cornu of the hyoid bone by way of the lateral thyrohyoid ligament. Normal anatomy of laryngeal cartilages is responsible for its physiological function .The anomaly or displacement and ossification of superior cornua may cause pain , pharyngeal foreign body sensation or cervical dysphagia or odynophagia. The aim of this study was to investigate the morphological variations of the superior cornua of thyroid cartilage in Anatolian population. In this study, total 50 larynx specimens having no pathology or previous surgery in the related area were macroscopically examined. Size of the normal cornua and the main charecteristics of their shape were observed. Medially or posteriorly displaced type of cornu was the most common in the overall ratio. It has been found that the superior cornu of thyroid cartilage of Anatolian population has morphologically significant differences than other populations. It can be stated that morphological and morphometrical variations of the superior cornu are closely related to race, geographical factors and embryological development.

Kategorie: Poster

Poster 29:

Titel:The frequency of forms of the talus in modern russians population

Autoren: Khayrullin R.(1),Safiullina A.(1),

Adressen:(1)The Department of the Human Anatomy|Ulyanovsk State University|Ulyanovsk|Russian Federation; email:prof.khayrullin@gmail.com

Abstract:
At present time, the physical load on the musculoskeletal system of the human in general and of bones of the foot, in particular, has declined substantially. In physical anthropology to assume that the population standard for the identification of bones varies greatly and standard of one population cannot be adequately used for the other population. The classification of individuals of different demographic groups allow for anthropologists to create profiles of ethnic populations, based solely on the skeletal remains. In recent studies, forensic anthropologists and bioarchaeologists by using of passported bone collections, pay more attention to the evaluation form of the articular surfaces of bones and fragmented remains. Objective: To determine the frequency of different types of talus to form the basis of the classification of the upper articular surface. The objects of the study were 67 astragal bones of modern Russian population. Tali were classified on the basis of the two classifications, by Barnet [1954] and Arora et al. [1979]. It has been established that by first classification type 1 of talus was observed in 14.9%, 2th type in 58.2%, type 3 in 16.5% and type 4 in 10.4%. The bones of type 5 were not found. According to the second classification was observed following frequency of shapes of the articular surface: 32.8% of bones was type A, 20.9% type B, 29.8% type C, 16.4% type D, 17.9% E type, 25.4% type F, 15% type G and 41.7% type H. These frequencies were different from the data, obtained in other ethnic populations.

Kategorie: Poster

Poster 30:

Titel:Effect of surgical and natural menopause on proximal femur morphometry in obese women

Autoren: Sertel S.(1),Bamaç B.(2),Duran B.(3),Çolak T.(2),Memişoğlu K.(4),

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Abstract:
Objective of this study was to determine whether there is a change in proximal femur parameters of women which are subjected to menopause surgically and naturally. Method: In this study 10 parameters belonging to proximal femur of total 60 women cases were evaluated. Thirty of them have average age of 55.53±4.57 years, body mass index was 33.06±4.21 kg/cm², menopause age was 48.10±5.92 years and menopause years was 7.50±4.58 and subjected to natural menopause. Thirty women, average age was 56.10±6.87 years, body mass index was 33.33±3.76 kg/cm², menopause age was 48.00±4.64 years and menopause year was 8.10±7.29 who are subjected to surgical menopause who did not use hormone replacement were examined by radiography. Subject's antropometric measurements, body compositions, blood hormon analysis (FSH, LH, Estradiol, Progesteron) and bone mineral density (femur neck, femur total, lumbar t-score) were also evaluated. Results: We found that there was no difference between surgical and natural menopause with respect to proximal femur parameters ($p>0.05$). It was found that FSH levels are high in surgical menopause group and there were significant differences between groups ($p<0.040$). Conclusions: It was found that difference about low bone mineral density level and high FSH values in surgical menopause group do not have relationship with proximal femur morphology. We obtained these results even they do not have ovary.There was no difference between surgical menopause women and natural menopause women with respect to proximal femur morphometry.

Kategorie: Poster

Poster 31:

Titel:Anatomy of sigmoid colon - clinical and endoscopical view

Autoren: Wozniak S.(1),Woyton M.(2),Porwolik M.(1),Pula B.(3),Gworys B.(1),

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Abstract:
The paper was carried out on cadaveric analysis of 166 human fetuses (88 male and 78 female), aged from 122 to 213 days of gestation and body total length range 138 – 308 mm. The aim of this paper was to grouped the sigmoid colon according endoscopic (colonoscopic) value. Height of the mesentery and inflexions between divisions of the sigmoid colon were measured. We differentiate from 2 to 6 parts (divissions) of the sigmoid colon. Consequently we observed from 1 to 5 inflexions among them. The inflexions (angles) range from 20° to 160°, the sharp angle is difficult to force on colonoscopy (the boder between easy/difficult we established on 45°). The mean height of the mesentery was 10,24 mm (range 2,56 – 22,28 mm). In extremely difficult group very short mesentery (lower than 10,24 mm) and at least two inflexions equal or lower than 45° were present. When the mesentery was long (up to 10,24 mm) and two inflexions equal or lower than 45° were present the case was collected in difficult group. In moderate easy group we collected the cases with 1 inflexion with equal or lower angle than 45° (the height of the mesentery had not impact). The rest of the cases was grouped in the easy sigmoid colon group. In 9,0 % - 15 cases (12 m, 3 f) the extremely difficult, in 16,3 % - 27 cases (18 m, 9 f) the difficult, in 44,6 % - 74 cases (34 m, 40 f) moderate easy, in 30,1 % - 50 cases (24 m, 26 f) easy sigmoid colons were established.

Kategorie: Poster

Poster 32:

Titel:Evaluation of the median sacral artery in 30 cadaveric specimens

Autoren: Bamac B.(1),Colak T.(1),Ceylan .(2),Kurnaz S.(2),Gundogmus U.(3),Uzun I.(3),

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Abstract:
The median sacral artery (MSA) is a small artery that arises at the bifurcation of the aorta. It descends in the midline, anterior to the fourth and fifth lumbar vertebrae, sacrum and coccyx, ending in the coccygeal body. The MSA anatomy is important for prevention of intra-operative bleeding. Knowledge of the MSA helps the surgeon to operate more safely. Thirty adult (19 male and 11 female) abdominal aorta were obtained from the Ýstanbul Forensic Medicine Institute morgue. The MSA was cut where it emerged from abdominal aorta.We stained sections of formalin-fixed vessels with haematoxylin and eosin and examined diameter and tunica media thickness of the median sacral artery and their relationship to the gender, weight and height of the subjects. Measurements carried out in Kocaeli University, School of Medicine, Department of Anatomy. The mean MSA diameter in the males and females were 1315.06±291.18µm and 1389.31±243.06 µm, respectively. The mean tunica media thickness of the MSA in the males and females were 210.81±50.43µm and 256.35±31.41 µm, respectively. There is statistically differences in tunica media thickness of the MSA between males and females (p= 0.012). A comparison between the male and female showed no statistically significant difference for diameter of the MSA, height and weight. The tunica media thickness of the MSA was correlated negatively with height of the both genders (p= 0.003).

Kategorie: Poster

Poster 33:

Titel:Distribution Patterns of the Superior and the Inferior Labial Artery - Impact for Safe Upper and Lower Lip Augmentation Procedures

Autoren: Cotofana S.(1),Pretterklieber B.(2),Lucius R.(3),Frank K.(4),Haas M.(4),Schenck T.(5),Gleiser C.(6),Weyers I.(7),Wedel T.(3),Pretterklieber M.(2),

Adressen:(1)Paracelsus Medical University Salzburg & Nuremberg, Salzburg|Institute of Anatomy|Salzburg|Austria; email:sebastian.cotofana@pmu.ac.at; (2)Center of Anatomy and Cell Biology|Medical University of Vienna|Vienna|Austria; (3)Institute of Anatomy|Christian-Albrechts-University of Kiel|Kiel|Germany; (4)Institute of Anatomy|Paracelsus Medical University Salzburg & Nuremberg, Salzburg|Salzburg|Austria; (5)Department of Plastic Surgery and Hand Surgery|University Hospital rechts der Isar, Technische Universität München|Munich|Germany; (6)Institute of Anatomy|University of Tübingen|Tübingen|Germany; (7)Institute of Anatomy|University of Lübeck|Lübeck|Germany

Abstract:
Introduction: Injections of hyaluronic acid (HA)-based fillers is increasingly popular in response to the growing interest in physical appearance. Complications like upper/lower lip necrosis may arise as a result of direct injury, compression, or obstruction of the superior or inferior labial artery (SLA/ILA). To prevent these adverse effects a detailed knowledge of the topographic anatomy of the SLA/ILA is needed. However, to date there is no detailed description of the course of the SLA or the ILA within the upper and lower lip. Materials & Methods: Formalin embalmed specimens at 5 different anatomical centers (Salzburg/Austria, Tübingen/Germany/, Lübeck/Germany, Kiel/Germany, Vienna/Austria) were investigated based on a standardized central protocol. Each upper and lower lip was incised 1cm medial to the angle of the mouth (paramedian position, 4 incisions) and in the midline (median position, 2 incisions). The position of the SLA/ILA was recorded in the respective 6 locations. Results: In total 118 specimens (55.9% females) were included in this study. The most common location of both the SLA and the ILA was submucosal (83.3%). An intra-muscular course of both arteries was observed in 15.3% with a higher frequency in the upper/lower midline (18.6%/22.9%). In 1.7% and in 0.8% the SLA/ILA were found subcutaneously in the midline. Conclusion: Based on these data, the safest positions for HA-based filler application for upper and lower lip augmentation are in subcutaneous position off the median line. Injections deep into the lips should be therefore performed with caution in order to avoid vascular complications.

Kategorie: Poster

Poster 34:

Titel: Topography, syntopy and morphology of the human otic ganglion. A cadaver study

Autoren:Senger M.(2),Hans-Juergen S.(3),Angelov D.(2),

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Abstract:
The human otic ganglion (OG) is not readily accessible during ordinary anatomical teaching courses because of insufficient time and severe difficulties encounterd in the preparation. Accordingly, most anatomical descriptions of its location, relation with neighboring structures, size and shape are supported only by drawings, but not by photographs. The aim of this study was to present the OG with associated roots and branches in dissected anatomic specimens. Following cumbersome dissection and precise photo-documentation, a detailed analysis on location, syntopy and morphology was performed. We carried out this study in 21 infratemporal fossae of 18 cadavers and were able to identify the OG, the mandibular-, the inferior alveolar- and the lingual nerve in all of them. We found no significant variation regarding the location of the GO in the infratemporal fossa and its syntopy to the adjacent structures. An OG resembling the classic description was found only in 90,50% of the cases. All 3 roots (parasympathetic, sympathetic and sensory) could be identified only in 82,3% of the specimens. The established presence of ganglionic branches varied from 0% (communicating rami to the meningeal branch of the mandibular nerve, to the greater petrosal nerve and to the lingual nerve) to 90% (r. communicans to n. canalis pterygoideus). We conclude that precise knowledge on this enormous variety might be very helpful not only to students in medicine and dentistry during anatomical dissection courses, but also to head and neck surgeons, ear-nose-throat specialists and neurosurgeons when treating pathology of pre- and postganglionic fibers.

Kategorie: Poster

Poster 35:

Titel: Warfarin aggravates CKD induced neointimal hyperplasia and calcification in arteriovenous fistulas: The potential role for vitamin K2 to prevent AVF failure

Autoren: Kokozidou M.(1,2), Zaragatski E.(3),Grommes J.(3,4),Langer S.(3),Kennes L.(5), Tamm M.(5),Koeppel T.A.(3),Kranz J.(3),Hackhofer T.(3), Arakelyan K.(3),Jacobs M.J.(3,6), Schurgers L.J.(7)

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Abstract:
Warfarin aggravates CKD induced neointimal hyperplasia and calcification in arteriovenous fistulas: The potential role for vitamin K2 to prevent AVF failure Maria Kokozidou, Emma Zaragatski, Jochen Grommes, Stephan Langer, Lieven Kennes, Miriam Tamm, Thomas A Koeppel, Jennifer Kranz, Tina Hackhofer, Karen Arakelyan, Michael J Jacobs, Leon J Schurgers Objectives: Arteriovenous fistula (AVF) is the main vascular access type for hemodialysis patients and AVF failure is due to neointimal hyperplasia (NIH). Vitamin K antagonists (VKA) are given to lower thrombosis tendency, but possess side effects enhancing arterial calcifications. Methods: In this study we investigate the effects of VKA and vitamin K2 (K2) supplementation on NIH development and calcification in arteriovenous fistulas in our rat model. AVF was generated in 190 rats. Chronic kidney disease (CKD) was induced using adenine- enriched diet. Effects of CKD, VKA and K2 on AVF remodeling were evaluated using histology, morphometric analysis and immunohistochemistry. Results: Arterialization, CKD ($p<.001$) and VKA ($p<.0001$) significantly enhanced venous NIH. K2 supplementation additional to VKA reduced NIH in arterialized veins ($p<.05$) in healthy animals. Arterialization, CKD ($p<.005$) and VKA treatment ($p<.002$) increased calcification while K2 supplementation attenuated calcification in healthy and CKD animals. K2 enhanced matrix Gla protein (MGP) carboxylation in control ($p<.05$) and CKD ($p<.002$) animals. Conclusion: Our study shows that VKA treatment has detrimental effects on AVF remodeling. K2 supplementation reduced NIH and calcification indicating vasoprotective effects. In arterialized veins, K2 should be considered as therapeutic approach to prevent NIH and calcification.

Kategorie: Poster

Poster 36:

Titel:Three dimensional visualization and analysis of the revascularization of skin grafts - a pilot study

Autoren: Hejkrlik W.(1),Geyer S.(1),Tinhofer I.(1),Kamolz L.(2),Lumenta D.(2),Weninger W.(1),

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Abstract:
Neovascularization of skin grafts is essential for their functionality and healing. The pig is used as the preferable model organism to study the mechanisms triggering and orchestrating neovascularization. This study aimed at visualizing the neovascularization of a split-thickness skin graft (STSG)/artificial matrix – combination with a computer rendered reconstruction of the arterial system. Full skin defects were set in 2 pigs and covered in a one step operation with a combined STSG/matrix graft. Biopsies of the graft tissue were harvested at days 5, 15 and 28 after operation. Using the high-resolution episcopic microscopy (HREM) method and three-dimensional (3D) computer models, the topology and architecture of the tissues and arteries in the biopsies were analyzed. One biopsy harvested on day 28 appeared to be artificially damaged and useful analyses of tissues and vessels were impossible. Specimens harvested on day 5 showed that no blood vessel sprouts entered the graft. Distinct borders seperated the faszia, matrix and dermis. Specimen harvested on day 15 showed 6-13 almost vertically ascending arteries entering the matrix in a field of 1x1 mm2. The arteries had no anastomoses and formed only a few branches while ascending inside the matrix. Inside the dermal layer they ramified 0-6 times and formed between 3 and 10 arterio-arterial anastomoses. 1-6 final branches penetrated into the papillar stratum. The matrix was partially remodeled. Specimen harvested on day 15 showed a lower number of remodeled arteries with a thicker caliber.

Kategorie: Poster

Poster 37:

Titel:Cardiomyocyte loss is not involved in the transition from compensated hypertrophy to heart failure induced by pressure overload

Autoren: Schipke J.(1),Grimm C.(1),Sedej S.(2),Mühlfeld C.(1),

Adressen:(1)Institute of Functional and Applied Anatomy|Hannover Medical School|Hannover|Germany; email:Muehlfeld.Christian@mh-hannover.de; (2)Division of Cardiology|Medical University Graz|Graz|Austria

Abstract:
Left ventricular hypertrophy (LVH) in response to hypertension and increased afterload frequently progresses to heart failure. It is under debate whether the loss of cardiomyocytes contributes to this transition. To address this question, C57BL/6 wild-type mice were subjected to transverse aortic constriction (TAC) and developed compensated LVH after 1 week, which progressed to heart failure characterized by left ventricular dilation and reduced ejection fraction 4 weeks post-TAC. Quantitative design-based stereology methods were used to estimate number, mean volume and subcellular composition of left ventricular cardiomyocytes. The left ventricle volume as well as the cardiomyocyte mean volume increased progressively after TAC. This was in conjunction with elevated subcellular volumes of myofibrils and mitochondria and reflected the hypertrophic remodeling in response to mechanical overload. In contrast, the number of left ventricular cardiomyocytes remained constant 1 and 4 weeks post-TAC in comparison to sham-operated mice. We conclude that loss of cardiomyocytes is not implicated in the transition from compensated hypertrophy to heart failure induced by TAC in the murine heart.

Kategorie: Poster

Poster 38:

Titel:Protection of the dendritic tree of cultured hippocampal neurons by hspb5/alphab-crystallin during cellular stress: regulation by phosphorylation

Autoren: Glomb M.(1),Moron M.(1),Bartelt-Kirbach B.(1),Golenhofen N.(1),

Adressen:(1)Institute of Anatomy and Cell Biology|University of Ulm|Ulm|Germany; email:nikola.golenhofen@uni-ulm.de

Abstract:
HspB5/alphaB-crystallin is known to be upregulated and phosphorylated by cellular stress conditions as well as in neurodegenerative diseases. One hallmark of neurodegenerative diseases is the rarefaction of the dendritic tree leading to neuronal dysfunction. Our group identified a new function of HspB5, namely that HspB5 increases dendritic branching and thereby dendritic complexity of cultured hippocampal neurons. Thus, we hypothesized that one function of HspB5 in neurodegenerative diseases might be to maintain the dendritic architecture. In this study we overexpressed HspB5 in neuronal cultures, subjected them to cellular stress (heat shock) and investigated the complexity of the dendritic tree by MAP-2 staining of the dendrites with subsequent Sholl analysis. To assess the role of phosphorylation of HspB5 we used a non phosphorylatable HspB5 mutant as well as constructs simulating phosphorylation (amino acid exchange of serine by alanine or glutamate). Since HspB5 displays three phosphorylation sites at serine 19, 45 and 59 we generated in total seven phosphomimics simulating phosphorylation at exactly one, two or all three positions. We could show that heat shock led to a significant reduction of dendritic complexity which was rescued by HspB5 overexpression. Nearly the same effect was achieved by the triple-phosphomimic whereas the double- and single-phosphomimcis as well as the non-phosphorylatable mutant were less effective. Thus, HspB5 counteracted heat-shock induced rarefaction of the dendritic tree. Phosphorylation of HspB5 seems to play an important role in this process. However, the protective effect could not be attributed to one specific phosphorylation site.

Kategorie: Poster

Poster 39:

Titel:Comparative immunohistochemical study regarding the gabaergic innervation of the ciliary ganglion in different vertebrate species

Autoren:Schneider I.(1),Barnerssoi M.(1),Erichsen J.(2),Messoudi A.(1),Horn A.(1),

Adressen:(1)Institute of Anatomy and Cell Biology I|LMU|Munich|Germany; email:inca_schneider@hotmail.de; (2)School of Optometry and Vision Sciences|Cardiff Univeristy, UK|Cardiff (Wales)|United Kingdom

Abstract:
The vertebrate ciliary ganglion (CG) contains cholinergic parasympathetic postganglionic neurons, which project to the ciliary and the sphincter pupillae muscles to control lens accommodation and pupillary constriction, respectively. The avian CG contains additional postganglionic neurons innervating the choroid. Previous monkey studies showed that, besides the cholinergic input to the CG, gamma aminobutyric acid (GABA) may also play a role in neurotransmission through the ganglion. A subpopulation of CG neurons (approximately 20 percent) receives a dense GABAergic afferentation, whose function is unclear. To further explore whether a GABAergic innervation of the CG is a general feature in vertebrates, we investigated and quantified the CG of different species with differing visual capabilities: pigeon, rat, sheep, pig and human. By using double-immunofluorescence staining methods for glutamic acid decarboxylase (GAD) and choline acetyl transferase (ChAT) or synaptophysin (SynP), we confirmed that the CG of all species studied contain postganglionic neurons that are densely supplied by GAD-positive nerve endings. The numbers of GABA-recipient CG neurons, however, differed: 69 percent in pigeon (39 percent boutonal and 30 percent calyx-like endings), 52 percent in rat, 18 percent in pig, 3.5 percent in human and only 0.3 percent in sheep. Our findings indicate that the GABAergic innervation of a subpopulation of postganglionic CG neurons is a general property of all vertebrates. The inclusion of both terminal types in birds indicates a more general function of GABA in the CG. The differing size and proportion of the GABA-recipient populations did not permit making any correlation with specific properties of the visual system in a given species.

Kategorie: Poster

Poster 40:

Titel: Describing abstract artworks – Term usage and low-level image properties

Autoren: Hayn-Leichsenring G.(1),Lyssenko N.(1),Redies C.(1),

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Abstract:
One of the major challenges in aesthetics is the uncertainty of the terminology used in experiments. There are basically two possibilities to instruct participants: (A) to define for them what is meant by a specific term (e.g., beauty) or (B) to give no instructions and let the participants intuitively decide what terms they want to use. In this study, we used the latter approach and searched for terms that are intuitively used by participants for the description of abstract artworks. Since aesthetic perception might be based on the efficient processing of images with specific second-order image statistics (like self-similarity, complexity, anisotropy), we assumed that the perception of beauty and the classification of abstract artworks might also be affected by these properties. Therefore, we studied the correlation of descriptive terms with statistical image properties. Participants were asked to describe abstract paintings spontaneously using four or more adjectives. We found interactions of structure-describing terms with the second-order image properties. After that, we used the ten most frequently used terms to create five different rating scales (liking, interestingness, structure, complexity, friendliness). Another group of participants evaluated the same abstract paintings according to these rating scales. We found significant correlations among the scales (e.g., complex with liking and interesting) and between term scales and second-order image properties (e.g., complex/interesting with self-similarity and complexity). In conclusion, we found an interaction between subjectively used terms and objective image properties that might reflect principles of neural connectivity and function of the human visual system.

Kategorie: Poster

Poster 41:

Titel:Hsf1-deficiency affects cerebellar calbindin levels and locomotor function

Autoren: Ingenwerth M.(1),Estrada V.(2),Stahr A.(1), Müller HW.(2),von Gall C.(1),

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Abstract:
The cerebellum plays an important role in coordination and locomotion. Two major components have been identified to play a major role in Purkinje cell function, the calcium binding protein calbindin and the heat shock protein transcription factor HSF1. Both, calbindin and heat shock proteins are associated with ataxia. Therefore, we tested the hypothesis that there is an interconnection between HSF1 and calbindin in Purkinje cells using HSF1-deficient mice. The quality of locomotor function was monitored by a semi-automated gait-analysis system (Noldus CatWalk XT). Calbindin levels were analyzed qualitatively and quantitatively by immunohistochemistry and immunoblot, respectively. CatWalk gait analysis revealed significant changes in speed and stance parameters in HSF1-deficient mice as compared to WT-littermates. Moreover, calbindin levels were significantly decreased in Purkinje cells of HSF1-deficient mice as compared to WT mice. In summary, a specific loss of HSF1 leads to changes in locomotor function, associated with changes in cerebellar calbindin levels. These findings suggest a role of HSF1 in regular Purkinje cell calcium homeostasis.

Kategorie: Poster

Poster 42:

Titel:Mover is a novel calmodulin binding partner that regulates neurotransmitter release

Autoren: Arndt M.(1),Viotti J.(1),Akula A.(1),Wetzel F.(1),Dresbach T.(1),

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Abstract:
Neurotransmitter release is centered around an evolutionarily conserved set of proteins and mechanisms. We recently identified Mover, a member of a small set of presynaptic proteins that occur only in vertebrates. Here, we set out to characterize the features of this novel protein. Mover immunofluorescence varies strongly between types of synapses. Biochemical analysis reveals that Mover oligomerizes and binds to Calmodulin. The Calmodulin binding consensus site contains an amino acid, phenylalanine 206, that is also required for oligomerization and targeting of Mover to synaptic vesicles in cultured hippocampal neurons. Mimicking increased neuronal acitivity by Forskolin increases the expression of Mover, and overexpression of Mover downregulates synaptic vesicles recycling. To assess its role in vivo, we created a conditional knockout mouse line for Mover. Mover knockout mice have increased release probability in hippocampal, but decreased release probability in cerebellar mossy fibre terminals. In summary, we identified a novel Calmodulin binding parter that regulates presynaptic function differently at distinct synapses. We propose that one role of Mover is to downreglate transmitter release under conditions of increased neuronal activity.

Kategorie: Poster

Poster 43:

Titel:Tight junctions in the nerve fiber layer of the fish retina

Autoren: Garcia Pradas L.(1),Sroka A.(1),Gleiser C.(1),Wizenmann A.(1),Wolburg H.(2),Mack A.(1),

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Abstract:
The endfeet of Müller cells and the underlying basal lamina represent the interface between the retina and the vitreous humor in the vertebrate eye. However, these structures do not form a tight barrier. We have investigated the retina of fish because of its life-long continuous cell addition from a peripheral growth zone. Here, we studied more specifically the nerve fiber layer where new axons grow towards the optic nerve head in the functioning adult retina. Using freeze fracture electron microscopy, we discovered remarkable tight junctions in the retinal nerve fiber layer of the cichlid fish Astatotilapia burtoni. These tight junctions formed branching strands between myelin-like wrappings, likely formed by a population of glial cells in the nerve fiber layer. In contrast, the endfeet of Müller cells showed orthogonal arrays of particles known to represent aquaporin-4, likely involved in ionic homeostasis, and no tight junctions. We probed retinal tissue for the expression of aquaporin-4 and candidate claudins (cldn): cldn-1, -3, -5a, -5b, -9, -11, and -19. We could show the expression of all of these genes in retinal tissue by PCR analysis and confirmed some of them in the nerve fiber layer by immunocytochemistry. Aquaporin-4 immunoreactivity could be localized to Müller cells. Evans blue experiments suggested a leakiness in the peripherial but not the central retina. We speculate that the peripheral growth zone might have access to growth promoting substances derived from ciliary blood vessels whereas in the central retina, this might be prevented by the tight junctions.

Kategorie: Poster

Poster 44:

Titel:Localisation of synaptic proteins at the golgi apparatus

Autoren: Wittenmayer N.(1),Kamin D.(2),Ghelani T.(1),

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Abstract:
Synaptogenesis requires the coordinated formation and budding of transport vesicles from the Golgi apparatus, its transport along axons and dendrites and the insertion of synaptic proteins in nascent synaptic sites. Here we show by using nanoscopic image resolution the localisation of different synaptic proteins at the Golgi apparatus and in the soma of hippocampal neurons. During early synaptogenesis endogeneous and recombinant Bassoon localize at the trans-golgi network like its homologe Piccolo while Munc13-1 is more associated with the cis part of the Golgi apparatus. All characterized proteins localize in cluster at the Golgi lamellae with different cluster sizes. DAB- photoconversion of recombinant proteins and electron microscopy show different types of vesicles. Further investigations with electron microscopy and high resolution fluorescence microscopy will shed light on distinct types of vesicles which are generated during early synapse formation.

Kategorie: Poster

Poster 45:

Titel:Extraocular muscles are controlled by at least three neuronal populations in and around the oculomotor nuclei, which differ in their histochemistry and afferent transmitter input.

Autoren: Horn A.(1),Zeeh C.(2),Lienbacher K.(1),

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Abstract:
Extraocular muscles are highly specialized to perform different tasks, such as high speed contractions during saccades and fine eye alignment during fixation of a visual target. At least six different muscle fiber types of three main categories are known: singly-innervated twitch fibers (SIF), multiply-innervated non-twitch fibers (MIF) of the global layer and a mixed fiber type in the orbital layer. Only MIFs of the global layer are associated with palisade endings (PE) at the myotendinous junction. Tracer injections into different parts of the medial (MR) and inferior rectus muscle (IR) in monkey and immunostaining for different markers including choline acetyltransferase (ChAT), parvalbumin (PAV), calretinin (CR) and vesicular glutamate transporter 1 (vGlut1) revealed three populations of cholinergic motoneurons: 1. PAV- positive motoneurons within the oculomotor nucleus (nIII) innervating SIFs. 2. PAV-/CR-negative neurons in the peripheral C-group of nIII innervating MIFs 3. PAV-negative and CR-positive neurons in the C-group innervating primarily MIFs in MR. Only MR C-group neurons receive a selective vGlut1-input as the adjacent preganglionic of the ciliary ganglion in the Edinger-Westphal nucleus suggestive for a common input controlling the near response. The current data confirm the concept that SIF motoneurons generate eye movements, whereas MIF motoneurons contribute to gaze holding. The presence of an additional population of CR-expressing C group neurons giving rise to PE and multiple endings within the MR may point to a specialized role in vergence. Grant support: DFG HO 1639/4-4

Kategorie: Poster

Poster 46:

Titel:Srgap3 knockout mice display enlarges lateral ventricles, altered hippocampal architecture and are not able to solve the marble burying task

Autoren: Koschuetzke L.(1),Bertram J.(1),Pfannmoeller J.(2),Esche J.(1),van Diepen L.(1),Kuss A.(1),Bartsch D.(3),Lotze M.(2),von Bohlen und Halbach O.(1),

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Abstract:
Mutations in the SRGAP3 gene residing on chromosome 3p25 have previously been associated with intellectual disability in humans. To elucidate the roles of a deletion of SrGAP3 in the adult brain, we generated SrGAP3 knockout mice. About 10% of these mice developed a hydrocephalus and died shortly after birth, whereas the remaining mice survive but display a more than 15-fold enlargement of the lateral ventricles. This phenotype was accompanied by a reduction in the densities of cilia of ependymal cells in the third ventricle, indicating that the ventricular enlargement may be due to ciliopathy. Moreover, these mice display alterations in the hippocampal architecture including an increase in the thickness of the molecular layer of the dentate gyrus (DG). Concerning the DG, we observed a slight reduction in the number of proliferating cells, but the number of newly generated neurons was unaltered. The morphology and number of spines was not altered in the DG in the knockout mice, but adult granule cells displayed altered dendritic complexity and transcriptome analysis by RNA sequencing, using whole brain derived RNA extracts, showed characteristic alterations in the gene expression pattern of knockout mice. Despite these distinct alterations, SrGAP3 deficient mice were relatively inconspicuous in behavior seen in open-field-, nest building-, Morris water-maze-tasks. The SrGAP3 deficient mice, however, failed to solve the marble-burying test; a behavior that is e.g. seen in some animal models related to autism, supporting the view that SrGAP3 plays a role in neurodevelopmental disorders.

Kategorie: Poster

Poster 47:

Titel:The role of bcl11a/ctip1 and bcl11b/ctip2 in neocortical development

Autoren: Gaessler S.(1),Wiegreffe C.(1),Liu P.(2),Jenkins N.(3),Copeland N.(4),Britsch S.(1),

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Abstract:
It has been shown that both zinc-finger transcription factors Bcl11a and Bcl11b play important roles in the development of the neocortex. Bcl11a is necessary for migration and survival of upper layer cortical projection neurons, whereas Bcl11b is critical for correct differentiation of subsets of deep-layer neurons. Bcl11a is expressed by many projection neurons throughout the neocortex, while Bcl11b is restricted to deep layer projection neurons. Both genes are coexpressed to a large extent in deep cortical layers. It is not known whether Bcl11a and Bcl11b have redundant functions and can compensate for each other. Here we investigate forebrain-specific conditional Bcl11a/b compound mutant mice. Our phenotype analysis demonstrates a major shrinkage in cortical thickness, aberrant development of deep layer neurons, and indicate compensatory functions of Bcl11a and Bcl11b.

Kategorie: Poster

Poster 48:

Titel:Altered expression of sphingosine-1-phosphate receptor 5 in npc1 mouse brain

Autoren: Gläser A.(1),Wree A.(1),Bräuer A.(1),

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Abstract:
Niemann-Pick type C1 (NPC1) is a lysosomal storage disorder, induced by a mutation of the NPC1 gene, resulting in a malfunction of the transmembrane NPC1 protein. The autosomal-recessive neurodegenerative disease causes an intracellular accumulation of lipids (cholesterol, glycosphingolipids, sphingomyelin, sphingosine) in the endosomal-lysosomal system and a dramatic degeneration of cerebellar Purkinje-cells. Neurological symptoms are e.g. cerebellar ataxia, dysphagia, dysarthria, cataplexy and psychatric symptoms. In NPC1 mouse model a prospective therapy, comprising a combination of miglustat and allopregnanolone/cyclodextrin reduces intraneural lipid accumulation, delays onset of neurological symptoms and decreasing degeneration of Purkinje cells. According to the morphological analysis of NPC1 mouse brain (Maass et. al.) we performed gene expression analyses in NPC mouse brain subsequently. The family of sphingosine-1-phosphate receptors (S1PR1-5) belongs to G-protein-coupled receptors, activated by the signalling molecule sphingosine-1-phosphate (S1P). Interestingly, in NPC1 mouse model Speak et. al. described the frequency of natural killer cells was altered and phenocopied S1PR5 - deficient mice, accompanied by defects in S1P-level. Therefore we assume S1PR5 as a potential regulator of the sphingolipid metabolism in NPC1 mouse model. We performed expression analysis of brain tissues as well as liver and spleen via quantitative real-time PCR. In fact, the initial results exhibit considerable downregulation of S1PR5 in untreated NPC1-deficient mice compared with wild-type mice. Due to this promising outcomes we started analysing further gene expression of potential regulators of phospholipid metabolism such as lysophosphatidic acid receptors (LPARs), cannabinoid receptors (CNRs) and plasticity-related genes (PRGs).

Kategorie: Poster

Poster 49:

Titel:Accumulation of lamp-1 in hippocampal mossy fibers accompanying alterations of autophagy dynamics upon seizure-induced injury

Autoren: Rami A.(1),Niquet J.(2),

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Abstract:
We have previously reported that the dynamics of autophagy are altered by status epilepticus (SE) in the rat brain. We found a dramatic upregulation in the expression of LC3 in the hippocampus upon SE. However, the increase in LC3 expression might be caused by a reduction in lysosomal activity or by alterations in autophagosome-lysosome fusion leading to a cytosolic vesicular retention. In order to dissect this aspect, we monitored the spatial and temporal expression of LC3 and LAMP-1 in the hippocampus. The WB-analysis showed that the expression of LAMP-1 was slightly increased in hippocampal cells at 6, 24 h, and 48 h post-SE. However, immunofluorescence analysis showed dramatic spatial changes in LAMP-1 distribution within the hippocampus. LAMP-1 in controls was localised only in cytosol as dot like staining, however at 24 h post-SE LAMP-1 was not only highly expressed, but accumulated in mossy fibers. In parallel, we found few scattered LC3-positive-dots in neurites of dentate gyrus which co-localise with LAMP-1-positive structures. We conclude that SE not only increased autophagosomal abundance, but also lysosomal activities and a massive axonal accumulation of LAMP-1. This could support the hypothesis that the marked increased autophagosomal abundance in cytosol reflects an increase in the autophagic activity. Although LAMP-1 may have contributed to cell damage in the selective vulnerable hippocampal CA1-subfield, it is also possible that lysosomal/autophagic mechanisms in mossy fibers were compensatory and reflected an attempt to survive the epileptic insult by breaking down non-essential components.

Kategorie: Poster

Poster 50:

Titel:In vivo studies on intact and post-lesion glio-vascular connections: a multiphoton microscope study

Autoren: Toth L.(1),Szollosi D.(1),Kis Petik K.(2),Kalman M.(1),

Adressen:(1)Dept. of Anatomy, Histology and Embryology|Semmelweis University|Budapest|Hungary; email:tolacy@gmail.com; (2)Dept. of Biophysics and Radiation Biology|Semmelweis University|Budapest|Hungary

Abstract:
Multiphoton microscopy, an in vivo investigation method was used to study the glio-vascular connections in intact and laesioned mice. The study was performed with a Femtonics Femto2D-Inverted multiphoton microscope in the Dept. of Biophysics and Radiation Biology (INMIND 278850). For supravital labeling of astrocytes and vessels intravenously administered sulphorhodamine 101 (SR101) and FITC-conjugated dextran (70 kDa) were applied. Transgenic animals were also used: a green fluorescein-protein labeled fractalkin to visualize microglia, another strain had yellow fluorescent protein labeled endothelial cells. In the intact brain the astrocytes were stained with SR101 therefore gliovascular connections were visible. By making serial photos, a 3D reconstruction was available. A 20 minutes observation revealed that the glio-vascular connections are stable. No dynamic detaching/attaching of processes were observed, in contrast some opinion. Following lesions the blood-brain barrier becomes leaky. To find whether a gliovascular decoupling precedes or follows the leakage, we applied three types of lesions. Cryogenic lesion was performed with a dry ice cooled copper rod by contacting the brain surface for 20 sec. Combustion was performed by the laser beam of the multiphoton microscope as well as intravascular photocoagulation following intravenous injection of photosensitive dye Rose Bengal. These latter methods avoid a cryogenic damage of astrocytes and minimize the post-lesion delay to observation. Lesion of vessels was followed immediately by leakage. Within 20 minutes no astrocytic reaction was observed. In the transgenic mice the microglial cells were identified. They reacted to the direct laser combustion with swellings of processes.

Kategorie: Poster

Poster 51:

Titel:Spines slow down dendritic chloride diffusion and affect short-term ionic plasticity of gabaergic inhibition

Autoren: Mohapatra N.(1),Tonnesen J.(2),Vlachos A.(1),Kuner T.(3),Deller T.(1),Naegerl V.(2),Santamaria F.(4),Jedlicka P.(5),

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Abstract:
Chloride is important for regulating many cellular properties, from volume and pH to membrane voltage and excitability. Spatiotemporal changes of intracellular chloride concentration alter the electrochemical driving force for chloride across the neuronal membrane and thus affect the current flow through GABAA receptors and the efficacy of GABAergic inhibition. However, the impact of neuronal morphology on the diffusion and redistribution of intracellular chloride is not well understood. The role of dendritic spines in chloride diffusion in dendritic trees has not been addressed so far. Because measuring fast and spatially restricted chloride changes within dendrites is not yet technically possible, we used computational approaches to predict the effects of spines on chloride dynamics in morphologically complex dendrites. First, in all morphologies tested, including dendritic segments imaged by super-resolution STED microscopy in live brain tissue, spines slowed down longitudinal chloride diffusion along dendrites, where the increase in the tortuosity was proportional to spine density. Thus, our modeling predicts that the presence of dendritic spines retards chloride diffusion. Second, a KCC2-like chloride extrusion influences chloride diffusion to a much lesser extent than the presence of spines. Third, we predict that spine-dependent slowing of chloride diffusion affects the amount and spatial spread of changes in the reversal potential of the GABAergic conductance (EGABA), thereby altering homosynaptic as well as heterosynaptic short-term ionic plasticity at GABAergic synapses in dendrites. Altogether, our results suggest a fundamental role of dendritic spines in shaping chloride diffusion, which could be of relevance in the context of pathological conditions where spine densities and neural excitability are perturbed.

Kategorie: Poster

Poster 52:

Titel:The role of bcl11b in postnatal hippocampal mossy fiber development.

Autoren: Soi C.(1),Simon R.(1),Schwegler H.(2),Nullmeier S.(2),Copeland N.(3),Jenkins N.(3),Liu P.(4),Britsch S.(1),

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Abstract:
Mossy fibers connect dentate gyrus granule cells to the cornu ammonis 3 region in the hippocampus. The correct wiring of these two areas is fundamental for learning and memory. The molecular mechanisms that control mossy fiber development are not completely understood. We have shown that the transcription factor B-Cell CLL/lymphoma 11b (Bcl11b) is essential for the development of the dentate gyrus. Bcl11b mutant animals displayed a smaller dentate gyrus and Timm staining revealed a disorganized projection pattern of mossy fiber terminals. Furthermore spatial memory and learning were impaired in this mouse model. To investigate the mechanistic role of Bcl11b in mossy fiber outgrowth we employed a dentate gyrus specific cre mouse line that allows us to visualize and to manipulate mossy fibers through a channelrhodopsin-tdTomato fusion protein. Additional clarifications on whether Bcl11b acts cell-autonomously are provided by a mosaic deletion of this transcription factor in the dentate gyrus granule cells. Moreover in vivo electroporation is applied to observe Bcl11b specific effects on single mossy fiber axons.

Kategorie: Poster

Poster 53:

Titel:Smells like danger: pradator odor induced innate fear behavior in rats

Autoren: Storsberg S.(1),Schwegler H.(1),Wernecke K.(2),Vincenz D.(3),Goldschmidt J.(3),Kroeber A.(1),D`Hanis W.(1),Fendt M.(2),

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Abstract:
Innate defensive fear behavior (e.g. risk assessment and avoidance) is part of the behavioral system of prey animals in order to avoid or survive predator threats. The characterization of the underlying neuronal circuitry of predator odor-induced innate fear behavior is an important step towards understanding anxiety disorders in order to improve these mental conditions. In this study we use neuropharmacology, neuroanatomy, in vivo-imaging and behavioral studies to characterize this neuronal circuitry in naïve rats. Rats are exposed to predator odor or water in an open field paradigm. The behavior of the animals is recorded and/or measured via infrared sensors. During this test the brain activity can be monitored by SPECT to identify involved brain areas or microinjections can temporarily inhibit regions of interest. After testing the rats are transcardially perfused and the brains are immunhistochemically stained for c-fos to determine differences in the number of activated neurons. The behavioral tests show that rats avoid the odor quadrant significantly but after muscimol injections into the area of amygdalar olfactory cortex (AOC) this avoidance response is significantly reduced [K.E.A. Wernecke et al.]. However, exposure to fox urine seems not to affect c-fos expression in this area significantly. Although there are differences in the number of activated cells after exposure to odor compared to water. Further examination is required to clarify whether this is crucial for the specific reaction of the animal to the odor (e.g. avoid or approach) and if this might be depending on the intensity of the odor.

Kategorie: Poster

Poster 54:

Titel:Neuroanatomical investigation of sensory cross-activation in mice

Autoren: Landmann J.(1),Richter F.(2),Oros-Peusquens A.(3),Bechmann I.(1),

Adressen:(1)Institute of Anatomy|University Leipzig|Leipzig|Germany; email:Ingo.Bechmann@medizin.uni-leipzig.de; (2)Institute of Pharmacology, Pharmacy and Toxicology, Department of Veterinary Medicine|University Leipzig|Leipzig|Germany; (3)Institute of Neuroscience and Medicine (INM-4)| Forschungszentrum Jülich|Jülich|Germany

Abstract:
Functional MRI studies with pain-deficient mice (alpha2delta3KO) revealed sensory cross-activation (synesthesia) in unstimulated cortical areas traditionally considered unimodal (visual and auditory cortex), while pain-related areas were inhibited (Neely et al., 2010). As synesthesia remains a barely understood phenomenon, alpha2delta3KO mice provide the first feasible model to gain mechanistic insights. In characterizing alpha2delta3s role within calcium channels, we found modifications of the electrochemical properties of cortical neurons, suggesting an altered excitability in alpha2delta3KO animals. Immune histochemical and MRI analysis showed, lacking alpha2delta3, can cause some severe anatomical alterations mainly in white, but also in grey matter structures. Thereby, the differentiation in afferents and efferents revealed a massive disparity in projection and commissural fibers. L1-stainings exhibit a reduction of thalamocortical fibers reaching somatosensory/motor cortical areas, suggesting an insufficient transmission of the pain signal to cortical areas in alpha2delta3KO mice. Moreover, observed aberrant fibers nearby visual cortical areas may contribute to the described synesthesia. Additionally, we found variations in the intra- and intercortical connectivity, which may also account to synesthetic sensations. Alterations in thalamocortical and intra-/intercortical connectivity go along with the concept of hyperconnectivity for the development of synesthesia. Beyond, analyzing different neuronal populations being involved in the pain-deficiency and pain-induced synesthesia, revealed a dominance of excitatory neurons rather than interneurons, which argues against the concept of cortical disinhibition. Our data demonstrate various differences in the neuroanatomical connectivity of alpha2delta3KO mice which from a hodological point of view consisting with their observed synesthetic phenotype. Supported by the DFG Research Training School “InterNeuro”

Kategorie: Poster

Poster 55:

Titel:Studies on the function of aromatase in basolateral nucleus of amygdala using in vivo and in vitro approaches

Autoren: Bender R.(1),Zhou L.(1),Keller A.(1),Rune G.(1),

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Abstract:
Aromatase, the final enzyme of 17-beta-estrogen (E2) synthesis, is expressed in certain neurons and the produced E2 acts as a modulator of synaptic plasticity. Brain regions with substantial aromatase expression include the hippocampus and amygdala, both important for memory formation. Whereas considerable information exists about aromatase functions in hippocampus (e. g. Fester & Rune, Brain Res, 2014), less is known about its roles in amygdala. Here we demonstrate a strong expression of aromatase in basolateral nucleus (BLa), the sensory input region of the amygdala. We show that inhibiting aromatase function by systemic application of letrozole, which is also used clinically, results in a significant reduction of spine synapse density in BLa in vivo, as shown previously for the hippocampus (Vierk et al., J Neurosci, 2012). To study the mechanisms in more detail, we established organotypic cortico-amygdalar slice cultures, and show that these preserve the amygdalar anatomical organization and reproduce developmental features of the BLa. Moreover, when letrozole was applied to the culture medium, a similar reduction of spine synapse density was observed as in vivo. Taken together, our data provide evidence for a regulatory role of aromatase on synaptic function in BLa and suggest organotypic slice cultures of the amygdala as a suitable in vitro tool to study this role.

Kategorie: Poster

Poster 56:

Titel:Localization of slc35f1 in the forebrain and in cell culture

Autoren: Farenholtz J.(1),Endlich N.(1),Blumenthal A.(1),Kroemer H.(2),Endlich K.(1),von Bohlen und Halbach O.(1),

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Abstract:
The solute carrier (SLC) group of membrane transport proteins includes about 400 members organized into more than 50 families. The SLC family that comprises of nucleoside-sugar transporters is referred to as SLC35. One of the members of this family is SLC35F1. The function of SLC35F1 is still unknown, but it was already shown that SLC35F1 mRNA is highly expressed in fetal and adult brain. To clarify which cells in the brain express SLC35F1, we stained forebrains of mice and humans by immunohistochemistry. ¬We found that SLC35F1 is a neuron-specific protein that is highly expressed in a variety of different brain areas like the cortex, hippocampus, amygdala, thalamus, basal ganglia and hypothalamus. To get more insight into the role of SLC35F1 and its subcellular localization, we transfected glioblastoma cells with a plasmid expressing tGFP-labelled SLC35F1. As a member of the nucleoside-sugar transporter family we expected the localization of SLC35F1 in the rER. However, we found no colocalization of SLC35F1 with markers for the rER and the Golgi apparatus. Time-lapse microscopy of living cells revealed that SLC35F1 spots are highly dynamic and resemble vesicles. Staining with an antibody against □-tubulin showed a localization of SLC35F1 spots along microtubules. To identify the type of vesicle, colocalization studies were performed by superresolution microscopy. To some extent a colocalization of SLC35F1 with rab7 (late endosomes) and rab11 (recycling endosomes) was found. Our data show that SLC35F1 is highly expressed in different brain areas of mice and humans and seems to be associated with vesicles.

Kategorie: Poster

Poster 57:

Titel:Characterization of the axon initial segment in rodent serotonergic neurons in vitro and in vivo

Autoren:Tran J.(1),Schlueter A.(1),Schloss P.(2),Schultz C.(1),Lau T.(2),Engelhardt M.(1),

Adressen:(1)Institute of Neuroanatomy|Medical Faculty Mannheim, Heidelberg University|Mannheim|Germany; (2)Biochemical Laboratory|Central Institute of Mental Health|Mannheim|Germany; email:maren.engelhardt@medma.uni-heidelberg.de

Abstract:
Serotonin plays an important role in developmental events such as cell proliferation, neuronal migration, and differentiation. Neurons responsible for serotonergic projections are located in the raphe nuclei of the brain stem. Abnormalities in these serotonin-producing neurons are associated with developmental and psychiatric disorders. A key domain for normal neuronal function is the axon initial segment (AIS), normally spanning the first 20-50 Âµm of the proximal axon, depending on the cell type. Interestingly, despite the importance of serotonergic neuron function for brain development, no data on the molecular and structural characteristics of their AIS are currently available. We aimed to characterize the development of the AIS in serotonergic neurons in rodents at various developmental stages. Morphometric analysis of AIS position after immunofluorescence against AIS proteins (ankyrinG, Î²IV-spectrin) in tryptophan hydroxylase-2-positive neurons indicates that only a few cells form their AIS near the soma. The majority of serotonergic neurons establish their AIS up to 50Âµm from the soma, possibly indicating that the activity pattern of serotonergic neurons (tonic vs. phasic in principal neurons) plays a role for AIS location. This result was also observed in cultured stem and progenitor cells that were induced to differentiate into serotonergic neurons. Furthermore, undifferentiated stem and progenitor cells show differential protein expression patterns for ankyrinG with its small 55kDa isoform being the dominant one, and the essential 480kDa isoform missing almost entirely. In summary, our data indicate a significantly distal AIS position and ankyrinG-isoform composition in serotonergic neurons, whose function will require further analysis.

Kategorie: Poster

Poster 58:

Titel:Jacob/NSMF knock-out as a mouse model for Kallmann syndrome?

Autoren: Nullmeier S.(1),Spilker C.(2),Schumacher A.(3),Yuanxiang P.(2),Rodenstein C.(1),D'Hanis W.(1),Roskoden T.(1),Zenclussen A.(4),Kreutz M.(2),Schwegler H.(1),

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Abstract:
Jacob, a protein messenger encoded by NSMF gene, couples synaptic N-methyl-D-aspartate-receptor (NMDAR) activity to nuclear gene expression. Mutations of NSMF are considered causing Kallmann syndrome, a neurodevelopmental disorder characterized by hypogonadotropic-hypogonadism associated with anosmia or hyposmia. It has further been indicated that a knock-down of Jacob results in migration deficits of Gonadotropin releasing hormone (GnRH) positive neurons from the olfactory bulb to the hypothalamus during neuronal development. In the present study we investigated if a constitutive NSMF knock-out (ko) may cause a phenotype related to Kallmann syndrome in mice. We found, that male Jacob-ko, compared to wildtype littermattes, show normal testicular morphology and spermatogenesis. However, female Jacob-ko reveal a slight temporal shift in estrous cycle phases and lower numbers of primary and tertiary follicels. Further, male Jacob-ko mice display slightly reduced testosterone serum levels, whereas females have significantly reduced estradiol levels during the estrus phases. We did not find any evidence for anosmia in Jacob-ko, compared with wildtype mice. There was also no difference in the number and density of GnRH-positive neurons and fibers. Interestingly, we detected a reduced hippocampal long-term-potentiation (LTP) at CA1 synapses of Jacob-ko. While there is no evidence for a Kallmann phenotype, Jaco-ko mice present hippocampal alterations, which have to be investigated in further studies.

Kategorie: Poster

Poster 59:

Titel:Activity-dependent regulation of the cisternal organelle in the axon initial segment during murine visual system development and visual deprivation

Autoren:Schlueter A.(1),Rossberger S.(2),Del Turco D.(3),Deller T.(3),Schultz C.(1),Engelhardt M.(1),

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Abstract:
The cisternal organelle (CO) is a putative Ca2+-store localized in the axon initial segment (AIS) of principal neurons. The CO has been suggested to play a role in Ca2+ current regulation of the AIS, which is an axonal compartment crucial for action potential initiation. CO formation requires synaptopodin (synpo), an actin-associated protein. So far, it is unknown whether synpo/CO expression is activity-regulated during brain development. Moreover, the effect of synpo/CO presence and absence on AIS maturation has not been investigated. Here, we examined the impact of synpo expression on AIS maturation during murine visual cortex development under normal and visual deprivation conditions. AIS morphology was investigated using immunofluorescence for AIS-markers ankyrin-G and betaIV spectrin in synpo-deficient (KO) mice and in synpo-positive AIS of wildtype mice. Visual deprivation was utilized to study the effect of altered visual input on CO and AIS maturation. Dark rearing of mice for 28 and 35 days resulted in a significant increase of synpo cluster sizes and length of synpo-bearing AIS. Interestingly, these light-dependent modifications were irreversible after mice reached P28. In addition, developmental AIS length maturation was affected by the presence of synpo: In synpo KO mice, visual deprivation led to AIS shortening despite previous experiments showing AIS lengthening, indicating a potential role for synpo/CO in AIS remodeling. Taken together, these findings indicate that the morphological maturation of the CO is regulated in an activity-dependent manner and the presence of CO/synpo influences AIS morphological maturation in cortical neurons during visual system development.

Kategorie: Poster

Poster 60:

Titel:Foxg1 function in postnatal hippocampus and non-classical rett syndrome

Autoren: Hacker C.(1),Arumugam G.(1),Videm P.(2),Backofen R.(2),Vogel T.(1),

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Abstract:
The forkhead box transcription factor FoxG1 is known to influence forebrain development by determining regional brain specification as well as by regulating expansion of neuronal progenitors and timing of their differentiation. In the adult brain, FoxG1 is expressed in cortex and hippocampus. In the latter it is involved in postnatal neurogenesis in the dentate gyrus by influencing maintenance of the progenitor pool as well as survival and maturation of postmitotic neurons. In humans, haploinsufficiency of FoxG1 causes the congenital version of the Rett syndrome, a progressive neurologic developmental disorder. We use FoxG1 mutant mice to screen for global changes in mRNA expression after partial loss of FoxG1 protein in hippocampi of six week-old mice. Data analysis points to a specific function for FoxG1 in adult hippocampus besides its known involvement in dentate gyrus neurogenesis. We analyse transcriptional changes in the different CA-fields and show that especially the CA-1 field is influenced by lack of FOXG1 protein. Furthermore, data analysis shows altered expression of genes that have also been implicated in the classical form of the Rett syndrome and other autism spectrum disorders.

Kategorie: Poster

Poster 61:

Titel:Oxidative stress as a co-phenomenon or trigger during the formation of multiple sclerosis lesions

Autoren: Clarner T.(1),Draheim T.(1),Liessem A.(1),Wilms F.(1),Denecke B.(2),Wruck C.(3),Fragoulis A.(3),Kipp M.(4),Beyer C.(5),

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Abstract:
Lesion formation and progression in Multiple sclerosis (MS) is not well-understood. Reactive microglia are thought to contribute to overall tissue damage by oxidative burst. Signs of oxidative destruction such as oxidized phospholipids and malondialdehyde (MDH) in myelin, apoptotic oligodendrocytes, degenerating glia cells and neurons indicate the importance of oxidative injury for the pathogenesis of MS. Preventing or reducing oxidative stress and damage therefore might be a valuable therapeutic option to prevent the initiation and progression of demyelinating lesions. In this study, we have investigated oxidative stress-related parameters in the cuprizone mouse model for MS and their impact on lesion initiation and progression. WT-mice and mice showing reduced levels of oxidative stress (keap1-/-mice) were fed cuprizone for 1 week (lesion initiation) and 3 weeks (lesion progression). Oxidative stress was measured by in vivo luziferase assays, quantitative MDH-measurement and staining against 4-hydroxynonenal and dityrosin respectively. Axonal damage, oligodendrocyte loss and demyelination correlated to microgliosis and oxidative damage in WT-mice. Initial oligodendrocyte loss in keap1-/- animals was comparable to WT animals. However, microgliosis was ameliorated in early but not later lesions. Furthermore, axonal damage and demyelination was reduced in later lesions. Our results indicate that oxidative stress occurs during the initiation of lesions and later during progression. Early oxidative stress might be an important trigger of microglia activation and influence microglia activation state, leading to increased damage at later lesion stages. Further studies will have to show the influence and mechanisms of early occurring oxidative challenge on microglia activation and priming in vivo.

Kategorie: Poster

Poster 62:

Titel:Brain volume changes in a chronic activity-based anorexia rat model

Autoren: Frintrop L.(1),Seitz J.(2),Liesbrock J.(1),Baumann L.(1),Kas M.(3),Konrad K.(2),Herpertz-Dahlmann B.(2),Beyer C.(1),Tolba R.(4),

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Abstract:
Grey and white matter volume reduction has been found in anorexia nervosa (AN) patients and is linked to neuropsychological deficits. Activity-based anorexia (ABA) is a model that mimics behavioral and physiological aspects of AN including weight loss and hyperactivity. Adolescent female Wistar rats had 24h/day running wheel access and received 40% of their baseline daily food intake until a 25% weight reduction was reached. Animals were directly sacrificed (acute starvation) or kept for additional two weeks with reduced body weight (chronic starvation). The volumes of hippocampus, cortex and corpus callosum were quantitatively assessed in consecutive sections. Acute starvation only partially but chronic starvation completely disrupted the estrous cycle and impaired object recognition memory. Estrogen reduction correlated with the loss of memory function. Following acute starvation, only the cortex size was significantly reduced. In chronic ABA rats, the volumes of corpus callosum and cortex were significantly reduced compared to controls, whereas the hippocampus remained unchanged. Interestingly, the hippocampus volume in chronic ABA rats positively correlated with running wheel activity. The ABA animal model reflects distinct aspects of AN, such as amenorrhea and memory deficits, and mirrors volumetric brain changes as seen in humans. Cortical and the white matter region corpus callosum appear to be mainly affected. Hippocampus volume in ABA seems to be susceptible to activity induced hypertrophy, potentially eclipsing starvation induced volume loss as seen in AN patients. Future studies should focus on the underlying molecular changes at the cellular level and study the reversibility of disruptions by hormone substitution.

Kategorie: Poster

Poster 63:

Titel:Expression of ectonucleotidases in the prosencephalon of melatonin-proficient c3h and melatonin-deficient c57bl mice: spatial distribution and time-dependent changes

Autoren: Homola M.(1),Pfeffer M.(1),Fischer C.(1),Zimmermann H.(2),Robson S.(3),

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Abstract:
Extracellular purines (ATP, ADP and adenosine) are signaling molecules crucial for multiple physiological processes i.e. neurotransmission, neuromodulation, neural protection, nociception and wakefulness. Levels of extracellular purines are regulated by enzymes located at the cell surface referred to as ectonucleotidases. At physiological extracellular pH, NTPDase1, -2, -3, and ecto-5´-nucleotidase are regarded as the dominant ectonucleotidases in the brain. Our knowledge regarding the localization of these ectonucleotidases is incomplete. Moreover, time-dependent changes in their expression may strongly affect the availability of extracellular purines and thereby purinergic signaling. Using radioactive in situ hybridization, we analyzed the spatial and temporal mRNA distribution of the enzymes NTPDase1, -2, -3 and ecto-5′-nucleotidase in the prosencephalon of two mouse strains: melatonin-proficient C3H and melatonin-deficient C57Bl. Enzyme specific mRNA expression was located to hippocampus, striatum, medial habenula, and ventromedial hypothalamus. Surprisingly, NTPDase3 mRNA was discovered to be widely expressed in numerous brain regions. All ectonucleotidases investigated revealed prominent time-dependent expression patterns, which differed between the two mouse strains. In C3H, the mRNA expression of all four enzymes gradually increased during the day and peaked at night. Contrarily, in C57Bl, ecto-5′-nucleotidase revealed an opposite pattern. Interestingly, higher daytime activity of C57Bl compared with C3H was revealed using locomotor activity recordings suggesting involvement of melatonin in sleep regulation. Our results indicate that the expression of ectonucleotidases varies according to time and genotype and suggest an interplay between melatonin and purinergic signaling. These findings provide an important basis for further examination of the complexity of the purinergic system in the brain.

Kategorie: Poster

Poster 64:

Titel:An electron microscopic study of the monkey ciliary ganglion with emphasis on the gabaergic afferents

Autoren: Barnerssoi M.(1),May P.(2),Horn A.(1),

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Abstract:
The vertebrate ciliary ganglion (CG) is known as relay station in the parasympathetic pathways mediating pupillary constriction and accommodation. Postganglionic CG neurons receive a cholinergic input from the preganglionic Edinger-Westphal nucleus. A previous monkey study had identified a subpopulation of postganglionic CG-neurons that receives a GABAergic input demonstrated by glutamic acid decarboxylase (GAD) - immunostaining. GAD was found to colocalize with the cholinergic marker choline acetyltransferase (ChAT) in the CG terminals. To further explore the morphological properties of GABAergic nerve endings, we investigated the CG of three macaque monkeys by using electron microscopic techniques and post-embedding immunogold-labeling for GABA. Numerous terminals were found to contact dendrites and/or spines in the perisomatic neuropil. Three different terminal types were identified: The most prominent axon terminal type 1 (At1) displayed spherical vesicles, none or few dense-cored vesicles and clear asymmetric synaptic contacts. Axon terminal type 2 (At2), which displayed GABA-immunoreactivity, contained more pleomorphic vesicles and a higher number of dense-cored vesicles. The synaptic densities looked somewhat less asymmetric compared to At1. A rare third terminal type (At3) was characterized by its high number of dense-cored vesicles. Most somata displayed nearly exclusively GABA-positive or GABA-negative contacts. Approximately 25 percent of all CG neurons represented GABA-recipient cells. Here we confirm a direct synaptic input from GABAergic nerve endings to a subpopulation of postganglionic CG neurons in primates. This points to heterogeneity within the CG neuron population, as only a subpopulation would be modified by GABA as co-transmitter, whose function remains to be clarified.

Kategorie: Poster

Poster 65:

Titel:Comparison of axon initial segment development and plasticity in experimental models of rat hippocampal status epilepticus

Autoren:Katgely F.(1),Corcelli C.(1),Toellner K.(2),Schultz C.(1),Engelhardt M.(1),

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Abstract:
Recent studies have shown that the axon initial segment (AIS) - the site of action potential initiation - is dynamically regulated during sensory cortex development. However, little is known about AIS development in the hippocampus, an otherwise well-studied model system for synaptic plasticity. Therefore, we analyzed AIS maturation in hippocampal CA3 neurons at various time points (E14-P180) in rats utilizing a morphometric approach with triple-immunofluorescence for AIS markers (ankyrinG, Î²IV-spectrin, voltage-gated sodium channels) and confocal microscopy. Contrary to sensory cortical regions, where activity drives AIS maturation with periods of extreme elongation and shortening, we now observed an almost linear increase in length between embryonic stages and early adulthood, followed by a slight decrease up to P180. Overall, AIS length was extremely heterogeneous across all age groups, another significant difference to sensory cortical regions, where AIS length becomes homogeneous with adulthood. Recent studies in other labs suggest that altered excitation parameters (e.g. during status epilepticus (SE)), could have effects on AIS length and position in rodent hippocampus. Furthermore, the overall protein expression levels for AIS proteins seem significantly increased 60 days post SE. We therefore aimed at elucidating whether the increased protein expression in SE correlates with changes in AIS morphology. However, no significant changes in hippocampal AIS length were found between control and endpoints in an acute lithium-pilocarpine model. Interestingly, our data indicate that the time of recovery after SE may have an effect on overall AIS length, with AIS recovering to control lengths after at least 30 weeks post SE.

Kategorie: Poster

Poster 66:

Titel:Structural plasticity of the axon initial segment during early development of the mouse somatosensory cortex

Autoren: Jamann N.(1),Corcelli C.(1),Schultz C.(1),Engelhardt M.(1),

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Abstract:
The axon initial segment (AIS) is known to be a dynamic axonal compartment that can undergo structural remodeling to regulate neuronal activity. Recently, we demonstrated that the AIS undergoes a period of structural plasticity during visual cortex development. However, it is not known whether this dynamic regulation is a common developmental principle in other sensory cortices. Therefore we investigated the development of the AIS in a well-studied model for activity-dependent plasticity, the mouse barrel field in the primary somatosensory cortex (S1Bf). Using confocal microscopy, we quantified AIS-specific morphological changes in mice of different age groups (E20.5 - P180) in layers II/III and V after triple-immunofluorescence (ankyrinG, betaIV-spectrin, voltage-gated sodium channels). Additionally, we performed Western blot analysis to detect variations in expression levels of AIS-associated proteins. Furthermore, sensory deprivation experiments via whisker trimming were conducted. Our data demonstrate that AIS in S1Bf show an initial elongation in the first two weeks after birth. After the onset of â€œactive whiskingâ€• around P12, AIS length decreases in all layers to reach its mature length at P28. In adult S1Bf, AIS obtain a similar length across all layers. During this early development, the brain-specific isoforms of AIS proteins are dynamically regulated. Deprivation during early critical periods of cortical plasticity severely impairs normal AIS development at P15. Strikingly, a rescue effect for the structural maturation pattern of AIS was observed after restoration of sensory input. In summary, our findings indicate that the structure of AIS in the primary somatosensory cortex is regulated in an activity-dependent manner.

Kategorie: Poster

Poster 67:

Titel:Synaptic plasticity: a critical window for whole body vibration therapy following spinal cord injury (sc) in rats.

Autoren: Abdulla D.(1),Manthou M.(2),Pavlov S.(3),Jansen R.(1),Stein G.(4),Meyer C.(4),Semler J.(5),Schönau E.(5),Angelov D.(1),

Adressen:(1)Anatomical Institute|University of Cologne|Cologne|Germany; email:angelov.anatomie@uni-koeln.de; (2)Histology and Embryology|Aristotle University|Thessaloniki|Greece; (3)Anatomy, Histology, Embryology|Medical University Varna|Varna|Bulgaria; (4)Orthopedics and Traumatology|University of Cologne|Cologne|Germany; (5)Children's Hospital|University of Cologne|Cologne|Germany

Abstract:
Whole body vibration (WBV) in SCI patients improves walking and spasticity as well as bone and muscle mass. We showed previously that daily WBV started 14 days after SCI improves locomotor performance (rump height index; RHI) and restores synaptophysin expression in the ventral horn. Here, we extend these findings to include WBV started at 1 and 28 days after SCI as well as WBV started at 14 days but delivered twice a day. Intact animals and those receiving SCI but No WBV or passive hindlimb flexion-extension (PFE) served as controls. Following SCI and No WBV, synaptophysin levels fell to approximately one third of that in normal, intact animals. When WBV was started at 1 day after injury, compared to normal, synaptophysin levels were also low and not significantly different from animals with No WBV. However, starting WBV at 7 and 14 days resulted in significantly greater synaptophysin levels than in animals with No WBV. The highest synaptophysin values in the WBV14 group were complemented by improved body-weight support (RHI) and improved bladder function. None of the WBV treatments significantly reduced lesion-volume, or astroglial activation. Strikingly, starting WBV at 28 days resulted in synaptophysin levels that were significantly lower than in animals without WBV and increased microglial activation. We conclude that there is a critical window between 7 and 14 days after SCI during which WBV is beneficial for some outcomes; however, starting treatment earlier (1 day) provides no benefit, while starting treatment later (28 days) may be detrimental.

Kategorie: Poster

Poster 68:

Titel:Reactions of the rat musculoskeletal system to compressive spinal cord injury and whole body vibration therapy

Autoren: Schwarz A.(1),Pick C.(1),Harrach R.(1),Stein G.(2),Meyer C.(2),Schönau E.(3),Semler J.(3),Angelov D.(1),

Adressen:(1)Anatomical Institute|University of Cologne|Cologne|Germany; (2)Orthopedics and Traumatology|University of Cologne|Cologne|Germany; (3)Children's Hospital|University of Cologne|Cologne|Germany; email:angelov.anatomie@uni-koeln.de

Abstract:
Traumatic spinal cord injury (SCI) causes a loss of locomotor function with associated compromise of the musculo-skeletal system. Whole body vibration (WBV) is a potential therapy following SCI, but little is known about its effects on the musculo-skeletal system. Here, we examined locomotor recovery and the muskulo-skeletal system after thoracic (T7-9) compression SCI in adult rats. Daily WBV was started at 1, 7, 14 and 28 days after injury (WBV1-WBV28 respectively) and continued over a 12-week post-injury period. Intact rats, rats with SCI but no WBV (sham-treated) and a group that received passive flexion and extension (PFE) of their hind limbs served as controls. Compared to sham-treated rats, neither WBV nor PFE improved motor function. Only WBV14 and PFE improved body support. In line with earlier studies we failed to detect signs of soleus muscle atrophy (weight, cross sectional diameter, total amount of fibers, mean fiber diameter) or bone loss in the femur (length, weight, bone mineral density). One possible explanation is that, despite of injury extent, the preservation of some axons in the white matter, in combination with quadripedal locomotion, may provide sufficient trophic and neuronal support for the musculoskeletal system.

Kategorie: Poster

Poster 69:

Titel: Enteric phospho-alpha-synuclein expression is increased in patients with Parkinson’s disease

Autoren: Barrenschee M.(1),Boettner M.(1),Lange C.(1),Cossais F.(1),Zorenkov D.(2),Deuschl G.(3),Fritscher-Ravens A.(4),Ellrichmann M.(4),Wedel T.(1),

Adressen:(1)Institute of Anatomy|Christian-Albrechts-University Kiel|Kiel|Germany; email:m.barrenschee@anat.uni-kiel.de; (2)Department of Neurology|University Hospital Schleswig-Holstein, Campus Kiel|Kiel|Germany; (3)Department of Neurology|Christian-Albrechts-University Kiel|Kiel|Germany; (4)Experimental Endoscopy|University Hospital Schleswig-Holstein, Campus Kiel|Kiel|Germany

Abstract:
Parkinson's disease (PD) is associated with the presence of phosphorylated alpha-synuclein (p-alpha-syn) containing Lewy bodies (LBs) and Lewy neurites (LNs) as primary neuropathologic hallmarks in the central nervous system (CNS). Since the presence of LBs and LNs has been demonstrated previously in the enteric nervous system (ENS) of patients with PD, the aim of the study was to analyze p-alpha-syn positive structures in the ENS of patients with PD and controls. Colonoscopy biopsies were obtained from patients with PD and controls and processed for dual-label-immunohistochemistry for p-alpha-syn and the pan-neural marker PGP 9.5. Quantitative and morphometric analysis was performed to evaluate the presence and distributional pattern of p-alpha-syn positive structures in nerve fibers and neurons within the submucosal plexus. Frequency of p-alpha-syn positive LNs was comparable between PD and controls. Although p-alpha-syn positive (LBs) were detectable both in patients with PD and controls, total number and area of p-alpha-syn positive granula/ neuron were increased significantly in PD patients. Moreover, the number of small and larged sized p-alpha-syn positive granula was significantly higher in patients with PD compared to controls. The findings strengthen the hypothesis that the CNS pathology of increased p-alpha-syn in PD also applies to the ENS, if elaborated morphometry are applied. Although the mere presence of p-alpha-syn positive structures in the ENS should not be regarded as a criterion for the diagnosis of PD, the data provide the option for early in-vivio diagnosis of PD based on analysis of p-alpha-syn positive enteric neurons retrieved by colonoscopy biopsies.

Kategorie: Poster

Poster 70:

Titel: Hspb5/alphaB-crystallin increases dendritic branching and protects the dendritic tree during cellular stress in cultured rat hippocampal neurons

Autoren: Bartelt-Kirbach B.(1),Moron M.(1),Glomb M.(1),Beck C.(1),Weller M.(1),Golenhofen N.(1),

Adressen:(1)Institute of Anatomy and Cell Biology|University of Ulm|Ulm|Germany; email:britta.bartelt@uni-ulm.de

Abstract:
Small heat shock proteins (HspBs) are molecular chaperones that reportedly display also neuroprotective properties. To investigate their neuronal function, we overexpressed all HspBs known to be endogenously expressed in neurons by lentiviral transduction in cultured rat hippocampal neurons and assessed neuronal morphology thereafter. Neuronal cultures were fixed at day 14 in vitro, dendrites visualized by immunostaining for MAP-2 and the dendritic tree analyzed by Sholl analysis. HspB5 (alphaB-crystallin) overexpression resulted in a strong increase of dendritic complexity. We could show that this effect was dependent on phosphorylation since overexpression of a non-phosphorylatable HspB5-mutant (amino acid exchange of serine to alanine at all three phosphorylation sites) did not influence the dendritic tree. HspB5 is endogenously upregulated in neurodegenerative diseases which are characterized inter alia by rarefaction of the dendritic tree. To investigate if HspB5 might protect dendrites under stressful conditions we subjected cultured hippocampal neurons to heat shock. Interestingly, HspB5 prevented heat shock-induced degradation of dendrites. In conclusion, we identified a new function of HspB5 in regulation of dendritic complexity. HspB5 seems to play a role in long-term maintenance of dendrites and neuronal connectivity which is crucial for correct functioning of the brain.

Kategorie: Poster

Poster 71:

Titel:Visualization of neuron-intrinsic axonal ribosome transport

Autoren: Vogelaar C.(1), Müller K.(1),Nitsch R.(1),

Adressen:(1)Johannes Gutenberg-University Mainz, University Medical Center|Institute of Microanatomy and Neurobiology|Mainz|Germany; email:tineke.vogelaar@unimedizin-mainz.de

Abstract:
Unlike axons in the peripheral nervous system (PNS), axons in the central nervous system (CNS) are hardly able to regenerate. This is partly due to extrinsic factors, like lesion-induced scarring and accumulation of axon growth-inhibitory molecules. A great part, however, of CNS regeneration failure is caused by intrinsic factors, like neuronal atrophy, the lack of new growth cone formation and the inability of central neurons to spontaneously activate a regeneration-associated gene expression program. A new intrinsic aspect of axon regeneration is the localization of ribosomes and mRNA in the axon itself. This was shown for PNS axons of all developmental stages, including adult axons. Local treatment of the axons in a compartmented culture model with beta-actin siRNA reduced the formation of a new growth cone in vitro (Vogelaar et al, 2009). To date, however, most studies have been performed in vitro and not much is known about CNS axons. Only embryonic CNS axons are believed to contain ribosomes, however, adult CNS tissue can hardly be cultured.. We now created the RiboTracker mouse conditionally expressing tdTomato-tagged ribosomal protein L4, expressed in specific cell types when the mice are crossed with specific Cre lines. We are currently using the CamKIIalpha Cre mouse line for forebrain neurons, to study CNS axons. In parallel, we analysed Advillin Cre-crossed RiboTracker mice to study PNS axons. We will use PNS and CNS explant cultures, but also histological and in vivo imaging analysis to study and compare ribosome transport in various axon tracts.

Kategorie: Poster

Poster 72:

Titel:The magic marginal zone of the cerebral cortex

Autoren:Frotscher M.(1),Chai X.(1),Wang S.(1),Zhao S.(1),

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Abstract:
The marginal zone, future layer I of the cerebral cortex, is a cell-poor layer that contains the apical tuft of pyramidal neurons. Why do pyramidal neurons not invade this layer and give rise to the branches of the apical tuft? During development the marginal zone contains Cajal-Retzius cells synthesizing the extracellular matrix protein Reelin. Does Reelin prevent neurons from invading the marginal zone? Is Reelin involved in the formation of the apical tuft? Using in utero electroporation and live-imaging we here show that radial glial fibers as well as the leading processes of migrating neurons, future apical dendrites of pyramidal cells, start to branch as soon as they reach the Reelin-containing marginal zone. In contrast, in reeler mutants deficient in Reelin the number of branches is dramatically reduced, suggesting a role for Reelin in the branching of these processes. Moreover, in reeler mice numerous neurons invade the marginal zone. Live imaging of migrating neurons showed that migration by nuclear translocation was terminated when the nucleus reached the branches of the leading process in the Reelin zone, likely due to mechanical obstruction by the branches that were thinner than the main leading process. The results suggest an important role for Reelin in the branching of the apical tuft thereby terminating neuronal migration and preventing the immigration of neuronal cell bodies into the marginal zone. (Supported by Hertie Foundation and DFG: FR 620/12-1)

Kategorie: Poster

Poster 73:

Titel:The brain vessel wall is a potential source of microglia in health and disease

Autoren: Koeniger T.(1),Al-zuraiqi Y.(1),Erguen S.(1),Kuerten S.(1),

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Abstract:
Microglia are the predominant immune cells of the central nervous system (CNS). To date, several different hypotheses exist regarding the maintenance and expansion of microglia during health and disease. Only recently, new evidence was provided for the existence of a progenitor population within the CNS. These findings are intriguing, as outside of the CNS macrophage precursors have already been shown to reside in a stem-cell niche located in the adventitia of murine and human blood vessels. Here we adopted the mouse aortic ring assay (mARA), which is suitable to study adventitial macrophage precursors in CNS-associated blood vessels. Using this ex vivo model system, we examined the immunophenotype of potential microglial precursors as well as their differentiation towards mature microglia. We found that fragments of the mouse Circle of Willis showed comparable sprouting behavior in collagen matrices as explanted mouse aorta. Like in the mARA, a perivascular/ adventitial accumulation of macrophage/microglia-like cells could be observed after culture of the explanted tissue. Microglia-like cells were often seen to form proliferating clusters adjacent to the vessel wall (VW) and partly displayed known progenitor markers. Although the occasional transdifferentiation of pericytes into mature microglia has already been suggested, a possible contribution of VW-precursors to microglial homeostasis has not been addressed so far. Future research will have to verify the differentiation capacity of such progenitors as well as their contribution to the microglial pool under healthy conditions and in inflammatory CNS diseases such as multiple sclerosis.

Kategorie: Poster

Poster 74:

Titel:The role of bcl11b in the regulation of adult hippocampal neurogenesis

Autoren: De Bruyckere E.(1),Simon R.(1),Baumann L.(1),Fischer J.(1),Seigfried F.(1),Schwegler H.(2),Britsch S.(1),

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Abstract:
Adult neurogenesis occurs in the subgranular zone of the hippocampal dentate gyrus, generating new neurons throughout life. The proper generation, maturation and integration into the hippocampal circuitry of these new-born cells in adulthood is essential for the functions of the hippocampus in memory and learning. The molecular mechanisms regulating the adult neurogenesis in the hippocampus are not fully understood. Bcl11b/Ctip2, a Krueppel-like zinc finger transcription factor, is specifically expressed in postmitotic granule cell neurons of the dentate gyrus throughout development to adulthood. Using a conditional gene targeting in mice, we demonstrated the essential role of Bcl11b in postnatal development of the dentate gyrus. The expression of Bcl11b is maintained in adulthood raising the possibility of a function of this transcription factor in adult neurogenesis. Employing a tetracyclin-dependant mouse model we demonstrate an important role of Bcl11b in the regulation of adult neurogenesis. The ablation of Bcl11b only in adulthood leads to a reduced dentate gyrus area with a reduced number of granule cells, as well as an increase in apoptosis. We also report that the adult loss of Bcl11b leads to impairments in differentiation and maturation of new-born granule cells and deficit in spatial learning and memory behaviour. Together our data indicate a crucial role of Bcl11b in the regulation of adult hippocampal neurogenesis.

Kategorie: Poster

Poster 75:

Titel:Comparison of wild type and period-1 mouse vocal tract morphology by Âµ-ct

Autoren: Maronde E.(1),Bechstein P.(1),Schürmann C.(2),

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Abstract:
Ultrasonic vocalization serves social communication in mice. In our previous work we described both physical differences in the structure of such vocalisations as well as behavioural consequences of these differences between male mice deficient in the â€œcircadian clock geneâ€• period-1 (per-1) (N=8) and their corresponding wild type (N=9). In an attempt to identify the biological basis of the observed vocalization differences we analysed the vocal tract of these animals by micro-computer-tomography (micro-CT). Head length, vocal tract length, hyoid bone volume, cricoid cartilage volume, as well as the diameters of cricoid and thyroid were determined in 12-week-old male mice of both genotypes in fixed head preparations without contrasting. The dorso-ventral cricoid cartilage diameter was significantly different between per-1-deficient animals and the wild-type controls. Whether the difference in the dorso-ventral cricoid cartilage diameter contributes to the vocalization phenotype is discussed.

Kategorie: Poster

Poster 76:

Titel:Ips cells and neuronal differentiation of patients carrying mutation in a translation initiation factor

Autoren: Bertolessi Lourenco M.(1),Linta L.(1),Liebau S.(1),

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Abstract:
The eukaryotic initiation factor 2 (eIF2) is a protein complex acting in the initial part of the protein synthesis. eIF2 forms a complex with GTP and Met-tRNAMet, which then associates itself with the 40S subunit of the ribosome and, in a cap-dependent manner, scans the mRNA with the help of other factors to identify the staring codon and finally initiate translation. A eIF2 mutation was recently found to be responsible for intellectual disability in male patients. In those patients, signs of problems in nervous system development are accompanied by a broad spectrum of other symptoms such as obesity, microgenitalism and ataxia gait. This finding has motivated the present study in investigating why function disruption in a central player of protein translation has mainly impact in the nervous system development. Likewise Fragile X syndrome, this new reported mutation could lead to a post mitotic imbalance of neuronal mRNA translation control. On the other hand, early neuro development impairment could also explain patient symptoms. To understand more about the role of eIF2 in neuronal function, patient-derived iPS cells were generated and undirected neuronal differentiation was carried out aiming to trace any differences in both, gene expression and protein synthesis patterns. Results will provide an indication of possible interaction partners, as well as an overview of global translational changes, and protein families which are mainly affected by this mutation.

Kategorie: Poster

Poster 77:

Titel:Characterization of ischemia-induced blood-brain barrier breakdown in various models of experimental stroke

Autoren: Krueger M.(1),Bechmann I.(1),Immig K.(1),Reichenbach A.(2),Hartig W.(2),Michalski D.(3),

Adressen:(1)Institute of Anatomy|University of Leipzig|Leipzig|Germany; email:martin.krueger@medizin.uni-leipzig.de; (2)Paul Flechsig Institute for Brain Research|University of Leipzig|Leipzig|Germany; (3)Department of Neurology|University of Leipzig|Leipzig|Germany

Abstract:
Focal cerebral ischemia not only affects neuronal function but also vascular integrity, thereby allowing water and blood-borne molecules to enter the neuropil. This vascular injury is traditionally described by the metaphor of blood-brain barrier (BBB) breakdown. In the clinical setting, the described alterations lead to an increased risk of intracerebral bleeding and hemorrhagic transformation, predominantly associated with recanalization of occluded vessels, which then is assumed to induce a reperfusion injury. To investigate the fate of the cerebral vasculature after focal cerebral ischemia and reperfusion, we applied multiple immunofluorescence labeling and electron microscopy in a rat model of thromboembolic middle cerebral artery occlusion (eMCAO), and in mouse models of permanent (pMCAO) and transient (tMCAO) ischemia. Areas exhibiting BBB breakdown were identified by extravasation of intravenously applied FITC-albumin. Noteworthy, critical tight junction (TJ) proteins consistently remained detectable in areas of FITC-albumin leakage, in all animal models studied. However, application of the endothelial marker, Griffonia simplicifolia agglutinin I-B4, revealed structural alterations of the endothelium which were confirmed by electron microscopy. The observed ultrastructural pattern of endothelial degeneration was present in each of the animal models, including the reperfusion scenario. Four distinct stages of vascular damage were identified, ultimately leading to loss of endothelial cells and impaired vascular integrity. Our data suggest that ischemia-related BBB disruption is predominantly caused by endothelial degeneration. Thus, we propose a combination of vascular recanalization and endothelial protection as a promising neuroprotective approach.

Kategorie: Poster

Poster 78:

Titel:The Hippo/YAP-TAZ signaling pathway in neural stem cell biology

Autoren: Condurat A.(1),Menon V.(1),Thomas R.(1),Hindley C.(1),Pruszak J.(1),

Adressen:(1)Institut of Anatomy and Cell Biology|University of Freiburg|Freiburg|Germany; email: jan.pruszak@anat.uni-freiburg.de;

Abstract:
The Hippo signaling pathway at its core is represented by a highly conserved cascade of inhibitory kinases (including the eponymous Hippo) that converge on the transcriptional co-activator YAP and its paralog TAZ in the control of cellular proliferation and apoptosis. Responding to cellular density as well as mechanical cues, the associated signaling network closely integrates with other pathways including Wnt, MAPK and TGFbeta signaling, to name a few. The Hippo pathway has materialized as playing a key role in the sensing and integration of microenvironmental inputs, in stem cell maintenance and activation as well as tumorigenesis in various physiological and pathological contexts including hepatic, intestinal and epidermal tissues. Comparably, its role in neurobiology has remained poorly defined. While also providing a survey of Hippo/YAP-TAZ regulating processes as diverse as proliferation, apoptosis and dendritic field patterning in neurobiological models ranging from flies to neurological patients, we here present findings that implicate Hippo/YAP-TAZ in the maintenance of neural stemness in human pluripotent in vitro systems as well as in neural cancer lines. Moreover, we define a novel role for Hippo/YAP-TAZ signaling in the development of human and chick neural crest, with YAP expression in subpopulations consistent with pre-migratory neural crest character. We find YAP to be involved in promoting the transition from neuroepithelial progenitors to neural crest, a prominent example of physiological epithelial-to-mesenchymal transition. In neuroblastoma, a tumor of neural crest origin, RNA interference-mediated knockdown of YAP efficiently blocks tumor cell migration. Jointly, these concepts and data exemplify important functional roles for Hippo pathway members in neural development, stem cell and cancer biology.

Kategorie: Poster

Poster 79:

Titel:Neuroligins and bdnf in synaptic maturation

Autoren: Petkova A.(1),Gödecke N.(2),Korte M.(2),Dresbach T.(1),

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Abstract:
Nerve terminals are formed, modified, and eliminated during all stages of brain development. This includes the initial wiring of the brain, after adult neurogenesis, and during remodeling of synapses in regions undergoing structural plasticity. It is an emerging view that subtle changes in the properties of synaptic transmission - rather than a complete loss of function - may underlie some neurodevelopmental disorders. Mutations in the postsynaptic cell adhesion molecules Neuroligins (NLs) - in particular the isoforms NL1, NL3 and NL4 - have been implicated in autism spectrum disorders. In cultured neurons, NL1 mediates structural and functional maturation of presynaptic terminals, which may underlie autistic behaviors. But which transsynaptic signals allow NLs to regulate presynaptic maturation? Brain-derived neurotrophic factor (BDNF) is a secreted signaling molecule that mediates brain development, including synapse formation and maturation. Here, we tested if BDNF and Neuroligins cooperate to induce these events. We found that applying BDNF to neuronal cultures mimics the maturation-promoting effect of overexpressed NL1 and NL2. Moreover, inhibiting endogenous BDNF signaling reduced the effects of NL1 on presynaptic maturation and of NL2 on synapse formation. By studying BDNF-deficient cultures, we found that they failed to mature, and overexpressing NL1 and NL2 failed to induce presynaptic maturation. Interestingly, in cultured neurons from NL1-KO mice which also do not mature, applying BDNF reestablished structural and functional maturation. Our data introduce BDNF as a novel component in a pathway linking NL-induced synapse formation and presynaptic maturation.

Kategorie: Poster

Poster 80:

Titel:Fibroblast growth factor (FGF) and FGF receptor trafficking in human glioma cells

Autoren:Park J.(1),Irschick R.(1),Hausott B.(1),Claus P.(2),Klimaschewski L.(1),

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Abstract:
Fibroblast growth factor receptors (FGFRs) and their ligands are key regulators during development, regeneration and tumorigenesis in the brain. In human glioma cells, ligand binding activates intracellular signalling cascades resulting in cell proliferation. This is followed by endocytosis of the receptor/ligand complex and shuttling of receptor and ligand to the degradation and recycling compartment, respectively. In this study, we overexpressed fluorescently tagged FGFR1 in human glioma cells (U373) and treated the cells with fluorescently-labelled FGF2. Exogeneous FGF2-Cy5 was internalized into endosomal vesicles and translocated to the nucleus. Triple colocalization analysis of FGF2, FGFR1 and phosphorylated FGFR1 revealed a maximum of colocalization 1h after treatment. FGFR1 and FGF2 colocalized with transferrin, suggesting that receptor and ligand are both recycled back to the cell surface. Down-regulation of the negative inhibitor of receptor tyrosine kinase (RTK) signalling, Sprouty2, resulted in increased FGFR1/FGF2 recycling, reduced FGFR1 degradation and enhanced cell proliferation which could be blocked by AKT but not by ERK inhibitors. On the other hand, Sprouty2 overexpression decreased BrdU incorporation and cell proliferation. In conclusion, Sprouty2 modulates the strength and duration of FGFR1 signalling by interfering with FGFR1 trafficking. Supported by ÖKH and FWF - PhD program ‘Signal processing in neurons’.

Kategorie: Poster

Poster 81:

Titel:A novel cholinergic chemosensory cell in murine conjunctiva

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Abstract:
We recently identified a specialized cholinergic cell type in tracheal and urethral epithelium that utilizes molecules of the canonical taste transduction signaling cascade to sense potentially harmful substances in the luminal content. Upon stimulation, this cell initiates protective reflexes. Assuming a sentinel role of such cells at mucosal surfaces exposed to bacteria, we hypothesized their occurrence also in the conjunctiva and the lacrimal drainage system. Utilizing a mouse strain expressing eGFP under the promoter of the acetylcholine synthesizing enzyme, choline acetyltransferase (ChAT-eGFP), we observed a previously unidentified cholinergic cell in the murine conjunctiva. Evaluating whole mounts as well as serial sections of decalcified heads, singular cholinergic cells reaching the epithelial surface with slender processes were detected in fornical, but neither in bulbar nor palpebral epithelia. These cells were neither found in the lacrimal canaliculi, nor the lacrimal sac and the nasolacrimal duct. Cholinergic conjunctival epithelial cells are immunoreactive for cytokeratin 8 as well as for components of the canonical taste transduction signaling cascade (α-gustducin, phospholipase Cβ2 and TRPM5). They are approached by peptidergic sensory nerve fibers. The data show a previously unidentified cholinergic cell in murine conjunctiva with chemosensory traits presumably utilizing acetylcholine for signaling. In analogy to similar cells described in the tracheal and urethral epithelium, it might serve to detect bacterial products and to initiate protective reflexes such as lacrimation and blinking.

Kategorie: Poster

Poster 82:

Titel:Chemosensory cholinergic signaling network in the thymic medullary epithelium

Autoren: Soultanova A.(1),Panneck A.(1),Rafiq A.(1),Schuetz B.(2),Chubanov V.(3),Gudermann T.(3),Weihe E.(2),Krasteva-Christ G.(1),Mueller-Redetzky H.(4),Witzenrath M.(4),Voigt A.(5),Meyerhof W.(5),Kummer W.(1),

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Abstract:
Cholinergic signaling influences T cell maturation, and acetylcholine is endogenously synthesized in the thymus. Utilizing a reporter mouse strain that expresses GFP under the promoter of the acetylcholine synthesizing enzyme, choline acetyltransferase (ChAT), we detected cholinergic cells in the thymic medulla. Using additional reporter mouse strains and immunohistochemistry, we show that ChAT-positive cells co-express the bitter taste receptor Tas2r131 and the components of taste signaling cascade alpha-gustducin, phospholipase C beta 2 and the cation channel TRPM5. These thymic cholinergic chemosensory cells are different from the stellate medullary thymic epithelial cells (mTEC) involved in intrathymic negative selection of thymocytes in that they do not express autoimmune regulator (AIRE) and express cortical (8/18) instead of medullary (5/14) keratins. They are not approached by cholinoceptive sensory nerve fibers. Instead, they are in proximity to terminally differentiated (keratin 10-positive, Hassall-like bodies) mTEC carrying nicotinic acetylcholine receptors (alpha 3-subunit). In human newborn thymus, these cells closely surround or are integrated in the outer layer of the Hassall’s corpuscles. Similar cells in mucosal surfaces have been associated with detection of bacterial products. Hence, we quantified thymic mRNA expression of an array of genes involved in cholinergic and chemosensory transmission in streptococcal pneumonia-infected mice, which revealed 6-9fold up-regulation of TRPM5 and alpha-gustducin. In conclusion, we identified a novel chemosensory cholinergic cell type in the thymic medulla and hypothesize that there is a paracrine acetylcholine signaling between these cells and Hassall’s corpuscles, and that this signaling plays a role in bacterial pathogen detection and defense.

Kategorie: Poster

Poster 83:

Titel:Ultrastructural analysis of ectopic lymphoid organs in mp4-induced experimental autoimmune encephalomyelitis

Autoren:Grether N.(1),Bergwelt-Baildon M.S.(1),Wagner N.(2),Kuerten S.(2),

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Abstract:
Recent studies have shown that neogenesis of organized lymphoid structures occurs in the cerebral meninges of a subset of patients with multiple sclerosis (MS). The appearance of these structures was linked to an early disease onset and death, a faster transition to progressive MS and to more severe cortical pathology. Lymphoid organogenesis has also been described in other chronic autoimmune diseases, but the process itself, and how these newly formed structures can contribute to the disease pathogenesis has remained unclear. We have established a B cell-dependent mouse model of MS, the MP4-induced experimental autoimmune encephalomyelitis (EAE), in which we can reproducibly observe tertiary lymphoid organs (TLO) in the cerebellum in the chronic stage of the disease. In this study, we used light and electron microscopy to observe how these organs develop and transform during the course of EAE. In addition, we analyzed their cellular and ultrastructural composition, and the morphological aberrations that arise in the adjacent tissue. The data show that lymphoid organogenesis starts with the formation of a perivascular compartment, containing many neutrophil granulocytes, rather single cells and extracellular liquid. As disease progresses, the cellular composition changes. Only a few granulocytes, but many characteristic features of secondary lymphoid organs can be found. The extracellular liquid between the leukocytes is replaced by solid and organized structures, such as cellular extensions. Directly around the TLO, an edema can often be observed, in addition to single cells emigrating into the brain parenchyma and local circumscribed axonal damage.

Kategorie: Poster

Poster 84:

Titel:Glial reactivity and its role for retinal ganglion cell loss in glaucoma

Autoren:Seitz R.(1),Gruber R.(1),Meier E.(1),Fuchshofer R.(1),Tamm E.(1),

Adressen:(1)Institute of Human Anatomy & Embryology|University of Regensburg|Regensburg|Germany; email:Ernst.Tamm@vkl.uni-regensburg.de

Abstract:
Purpose: Glaucoma is a neurodegenerative disease characterized by axonal degeneration and subsequent apoptosis of retinal ganglion cells (RGC). The role of retinal glial cells during RGC-degeneration has been controversially discussed. Glial cells express neurotrophic factors, but can also secrete tumor necrosis factor-alpha (TNF-alpha) that augments apoptosis. Here we characterized the role of retinal macro- and microglia for RGC-damage in a transgenic mouse model (betaB1-CTGF) of glaucoma.
Methods: betaB1-CTGF mice and their wildtype littermates were investigated between 1-5 months of age. Changes in retinal glial cells were analyzed by immunohistochemistry on retinal wholemounts and meridional sections, real-time RT-PCR and immunoblotting.
Results: In betaB1-CTGF mice, axonal degeneration starts at p28. At this time microglial cells changed their morphology from a ramified to a reactive phenotype. The amount of reactive cells was significantly higher in transgenic than in wildtype animals. At 10 weeks of age, reactive microglial cells appeared to migrate from the outer retina towards the RGC-layer. In addition, Müller glia expressed increased amounts of GFAP, indicating their switch into a reactive state. Changes in microglia 117e9f8and Müller cells occurred in parallel to a significant increase of retinal amounts of mRNA for TNF-alpha. No changes were seen in retinal astrocytes.
Conclusion: Müller cells and retinal microglia, but not retinal astrocytes, react to optic nerve damage in glaucoma. The increased expression of TNF-alpha might indicate that reactive glial cells further augment RGC damage in glaucoma, a question that needs to be addressed in more detail in future studies.

Kategorie: Poster

Poster 85:

Titel:Mif operates on microglial polarization and facilitates brain angiogenesis

Autoren:Savaskan N.(1),Ghoochani A.(1),Yakubov E.(1),Buchfelder M.(1),Doerfler A.(2),Buccala R.(3),Eyüpoglu I.(1),

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Abstract:
Microglial cells in the brain tumor microenvironment are associated with enhanced glioma malignancy. They persist in an immunosuppressive M2 state at the peritumoral site and promote the growth of gliomas. Here, we investigated the underlying factors contributing to the abolished immune surveillance. We show that brain tumors escape pro-inflammatory M1 conversion of microglia via CD74 activation through the secretion of the cytokine MIF, which results in a M2 shift of microglial cells. Interruption of this glioma-microglial interaction through an antibody-neutralizing approach or siRNA-mediated inhibition prolongs survival time in glioma-implanted mice by reinstating the pro-inflammatory M2 to M1 shift in microglia. Moreover, MIF overexpression in glioma cells significantly increased angiogenesis while MIF knockdown displayed reduced vasculature. In addition, recombinant MIF application induced increased angiogenesis. Conversely, blocking the MIF receptor CD74 led to reduced vascularization. Furthermore, MIF increased ERK activation and induced VEGF A and B expression in endothelial cells. Hence, MIF-knockout mice revealed reduced vessel density in retina. Our data reveal that interference with the MIF signaling pathway affects microglial polarization. Furthermore, we found that MIF is a novel angiogenic regulator in tumor angiogenesis and in brain development.

Kategorie: Poster

Poster 86:

Titel:Modulation of formyl peptide receptor activity improved neuroinflammation in a mouse model of pneumococcal meningitis

Autoren: Kress E.(1),Schubert N.(2),Tauber S.(3),Pufe T.(1),Brandenburg L.(1),

Adressen:(1)RWTH Aachen University|anatomy and cell biology|Aachen|Germany; email:ekress@ukaachen.de; (2)RWTH Aachen|anatomy and cell biology|Aachen|Germany; (3)RWTH Aachen University|neurology|Aachen|Germany

Abstract:
Introduction: Bacterial meningitis is despite progress in research and the development of new treatment strategies still a cause of severe neuronal sequelae. The brain is protected from penetrating pathogens by the blood-brain barrier and the innate immune system. The invading pathogens are recognized by pattern recognition receptors including the G-protein coupled formyl peptide receptors (FPRs), which are expressed by immune cells of the central nervous system. Interestingly, FPRs show a broad spectrum of ligands including pro- and anti-inflammatory ligands. Here, we investigated the effects of AnnexinA1 and its mimetic peptide (Ac2-26) as potent anti-inflammatory ligand on the inflammation in a mouse model of pneumococcal meningitis. Methods: Therefore, wildtype, mFPR1 and mFPR2-deficient mice were intracerebral injected with Streptococcus pneumoniae D39 (type 2) as important meningitis pathogen. Subsequent, the different mice groups were treated with intraperitoneal injection of Ac2-26 (1 mg/kg body weight) two and 8 hour after infection. The degree of inflammation was analyzed in various brain regions by means of immunohistochemistry and real-time RT-PCR 30 h after infection. Results: The results showed a positive modulation of the innate immune response including decreased glial cell activation, reduced pro-inflammatory and increased anti-inflammatory cytokine expression compared to the non-infected control groups. Conclusion: Altogether, the results suggest that FPR1 and FPR2 play an important role in the innate immune responses against Streptococcus pneumoniae within the CNS. Furthermore, Ac2-26 could be applied as a new approached therapy for bacterial meningitis.

Kategorie: Poster

Poster 87:

Titel:Ceacam1 expression is increased in multiple sclerosis patients treated with natalizumab

Autoren: Rovituso D.(1),Lauer-Schmaltz S.(1),Bayas A.(2),Ulzheimer J.(3),Ergün S.(1, 4),Kürten S.(1),

Adressen:(1)Institute of Anatomy and Cellbiology - AG Neuroimmunology|University of Wurzburg|Wurzburg|Germany; email: damiano.rovituso@uni-wuerzburg.de; (2)Neurology|Klinikum Augsburg|Augsburg|Germany; (3)Neurology|Caritas Krankenhaus Bad Mergentheim|Bad Mergentheim|Germany; (4)Institute of Anatomy and Cellbiology, Lehrstuhl II|University of Wurzburg|Wurzburg|Germany;

Abstract:
The role of B cells in the pathogenesis of multiple sclerosis (MS) is still not fully understood. Recent studies report that the cell adhesion molecule CEACAM1 (CEA-related cell adhesion molecule-1) is expressed on peripheral human B cells. It was demonstrated that intrinsic CEACAM1 signalling was needed to generate an effective B cell response and to promote B cell survival. Furthermore, CEACAM1 and TIM-3 (T-cell immunoglobulin domain and mucin domain-3) were shown to dampen inflammatory processes and to restore or induce peripheral tolerance, respectively. To further elucidate the role of CEACAM1 and TIM-3 in MS we obtained peripheral blood mononuclear cells (PBMC) from RRMS patients (n = 20), healthy controls (HC, n = 22) and patients with neurological diseases other than MS (OND, n = 6). We compared the CEACAM1 and TIM-3 expression profile on B cell subsets and T cells by polychromatic flow cytometry. Additionally, we investigated CEACAM1 expression on B cell subsets during relapse (n = 7). We did not observe any differences between TIM-3 and CEACAM1 expression on T cells. However, our data demonstrate that CEACAM1 expression was significantly elevated on B cell subsets in RRMS patients in remission compared to HC or OND. Interestingly, we found CEACAM1 expression to be even further increased during relapse. We conclude that CEACAM1 expression on B cells might be crucially involved in the pathogenesis of MS and associated with disease activity, which warrants further investigations.

Kategorie: Poster

Poster 88:

Titel:Cd11c-positive cells from brain, spleen, lung, and liver exhibit site-specific immune phenotypes

Autoren: Immig K.(1),Gericke M.(1),Menzel F.(1),Merz F.(1),Krueger M.(1),Schiefenhövel F.(1),Hanisch U.(2),Biber K.(3),Bechmann I.(1),

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Abstract:
The brain’s immune privilege has been attributed to the lack of dendritic cells (DCs) within its parenchyma and the adjacent meninges. This view became challenged by the identification of cells expressing the DC marker CD11c in the meninges and choroid plexus in the brain of healthy mice. Using mice transcribing the green fluorescent protein under the promoter of CD11c, we identified an intraparenchymal and juxtavascular population of cells expressing CD11c. We now phenotypically compared brain derived CD11c+/CD45+ cells with CD11c+/CD45+ cells derived from lung, liver and spleen in healthy mice using flow cytometry. We found unique and site-specific expression patterns of the investigated CD11c+ cells for F4/80, CD80, CD86, CX3CR1, CCR2, FLT3, CD103 and MHC-II. Moreover, in the brain we observed the two known CD45 positive populations (CD45high and CD45int), whereas the other investigated organs exhibited homogeneous CD45high populations. Also, CD11c+ microglia were unique for their low MHC-II-expression. In order to test whether phenotypical differences are fixed by origin or develop due to environmental factors, we co-cultivated brain and spleen mononuclear cells on organotypic slice cultures from brain (OHSC) and spleen (OSSC). We show that ramification of MHC-II+ splenocytes in brain tissue correlates to the down-regulation of MHC-II. Brain mononuclear cells neither ramified nor up-regulated MHC-II in OSSCs. Thus, brain mononuclear cells remain MHC-II- within the environment of an immune organ. Our data confirm the view that intraparenchymal CD11c+ cells share established immunophenotypical characteristics of DCs from other organs but maintain their unique MHC-II expression.

Kategorie: Poster

Poster 89:

Titel:Effects of microglia-specific transforming growth factor-beta receptor type ii deletion on microglia pheontypes in vitro

Autoren: Zöller T.(1),Krieglstein K.(1),Spittau B.(1),

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Abstract:
Transforming growth factor beta 1 (TGFb1) has been shown to be a pivotal factor to regulate microglia functions and activation states in vitro and in vivo by promoting anti-inflammatory effects leading to resolution of microglia-driven neuroinflammation. We have recently shown that TGFb1 is an important endogenous regulator to keep microglia in a quiescent state and further induce a functional microglia phenotype involved in phagocytosis of apoptotic cells propagation o tissue repair. A prerequisite for TGFb1-mediated effects is the binding of TGFb1 to the TGF-beta receptor type II (TbRII), which forms a heteromeric complex and phosphorylates the TGF-beta receptor type I (TbRI). The activated TbRI itself phosphorylates the downstream mediators Smad2 and/or Smad3, which translocate to the nucleus to induce transcriptional regulation of TGFb1 target genes. Here, we demonstrate that primary microglia isolated from TbRIIflox/flox/Cx3cr1CreERT mice lack Smad2 phosphorylation as well as subsequent nuclear Smad2 translocation after stimulation with TGFb1. Moreover, classical TGFb1-induced target genes in primary microglia, such as Plasminogen activator inhibitor type 1 (Pai-1) and Transforming growth factor beta-induced (Tgfbi) were not upregulated after TGFb1 treatment of microglia from TbRIIflox/flox/Cx3cr1CreERT mice. Using flow cytometry, we provide evidence that TGFb1-signalling-deficient TbRIIflox/flox/Cx3cr1CreERT microglia display an expression pattern of CD36, CD86 and CD206, which was also observed after pharmacological inhibition of TbRI. Our data demonstrate efficient microglia-specific deletion of TbRII and introduce TbRIIflox/flox/Cx3cr1CreERT mice as a valuable tool to address the role of TGFb signalling for microglia functions and maintenance in vivo.

Kategorie: Poster

Poster 90:

Titel:Interferon influences (rodent) neocortical function

Autoren: Strauss U.(1),Reetz O.(1),Bräuer A.(2), Stadler K.(3),

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Abstract:
Pleiotrophic type I interferons (IFN-α and IFN-β) are therapeutically used and are produced by neocortical neurons in inflammation. Neuroinflammation as well as direct application of type I IFNs attenuate a main determinant of excitability of neocortical pyramidal neurons - the hyperpolarization activated cyclic nucleotide gated non-selective cation current I_h. The subunit HCN1 is a highly-specific target of type I IFNs, type I IFN receptors are present on neurons and modulation of HCN1 depends on the activation of the subsequent signaling cascade. The interaction does not involve the glial environment. I_h attenuation augments the excitability of neocortical pyramidal neurons by raising their input resistance but is not sufficient for the second IFN effect - enhanced action potential firing. For that, a simultaneous influence on additional molecular targets (I_{Nap}, I_{BK}, I_M) needs to be linked to type I IFNR activation by PKC as: *In silico* modulation of PKC-dependent ion channels reproduce in vitro findings, PKC activation augments neuronal excitability similar to IFN-β, blocking PKC activation prevented IFN-β effects. The findings are relevant for cortical network activity, because IFN-β slows neuronal resonance behaviour and surface EEG in rats. They constitute a major step towards understanding the interactions between immune- and central nervous system.

Kategorie: Poster

Poster 91:

Titel:Mitochondrial crossreactivity of an antiserum directed to the gram negative bacterium neisseria gonorrhoeae in choroid plexus and liver of the common marmoset monkey (callithrix jacchus)

Autoren: Reuss B.(1),Asif A.(2),Schroten H.(3),Ishikawa H.(4),Drummer C.(5),Behr R.(5),

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Abstract:
First trimester maternal infections with Neisseria gonorrhoeae (NG) increase the lifetime risk for the offspring to develop psychosis1,2. We have previously demonstrated that antibodies directed against NG (alpha-NG) cross-react with mitochondrial proteins Hsp60 and ATPB in human cell lines. To characterize an animal model for the in vivo relevance of these findings, we investigated now the cross-reactivity of alpha-NG with brain and liver samples, as well as embryonic tissues of Callithrix jacchus, a nonhuman primate. As revealed by immunohistochemical double-labelling, alpha-NG labels in the marmoset choroid plexus and liver intracellular organelles which were identified as mitochondria. Western blot analysis of whole cell protein extracts of adult and newborn liver and brain with alpha-NG revealed several strong bands of different molecular weights. Two-dimensional Western blot analysis with alpha-NG confirmed these findings revealing also several spots of different molecular weight and isoelectric points. In a next step these spots will be identified by mass spectrometric analysis in order to compare them with the findings in human cell lines. These results suggest the common marmoset monkey as a suitable animal model to test effects of immune activation against Neisseria gonorrhoeae on brain development, functioning and behavior. Such studies potentially will contribute to a better understanding of the role of pre- and perinatal bacterial infections in the etiology of neurodevelopmental disorders like schizophrenia. 1 Babulas et al., 2006, Am. J. Psychiatry 163, 927-929 2 Sørensen et al., 2009, Schizophrenia Bull. 35, 631-637 3 Reuss et al., 2015, J. Mol. Neurosci. (Epub ahead of print)

Kategorie: Poster

Poster 92:

Titel:Neuronal differentiation of human stem cells by striatal cell-conditioned media

Autoren: Engel C.(1),Koehler J.(1),Andressen C.(1),

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Abstract:
Neuronal loss caused by neurodegenerative diseases can hardly be regained by endogenous neurogenesis. Therefore the reconstruction of neural tissue and transplantation of neural progenitors is one therapeutic option to overcome neurodegeneration. Knowledge of intrinsic and extrinsic factors involved in proliferation and differentiation of stem cells into neuronal cells is a prerequisite for application of such therapies. Our studies are dealing with human retina-cells and induced pluripotent stem (IPS) cells which were cultivated with rat striatal astrocyte-conditioned media from embryonic day 13 and 19. Application of protein-specific ELISA and dot-blot technique showed that striatal cells secrete age-dependent concentrations of brain-derived neurotrophic factor (BDNF) and sonic hedgehog (SHH) which induced neural cell development. By means of immunofluorescence methods, monolayer cell cultures and cryostat section cuts of 3-dimensional neurospheres occurrence of cell type-specific intermediate filaments in different stages of differentiation could be investigated. Retina-cells under the influence of conditioned media showed augmented expression of DARPP-32 and Foxg1 revealing a tendency to dopaminergic commitment. Astrocyte-conditioned medium induced expression of neurofilaments like NF160 and neuronal specific class III beta tubulin in IPS cells. Investigation of neurospheres indicated morphological differences between inner layers –more neuronal differentiated cells – and outer layers – cells with progenitor properties –, pointing to the role of mechanical factors as well as cell-cell-interactions. Further studies shall uncover the signalling pathways inside the complex network of extrinsic and intrinsic factors which are necessary for neurogenesis and differentiation and thus development of cell-replacement therapies.

Kategorie: Poster

Poster 93:

Titel:Counteracting microvascular modifications in a murine oxygen-induced vaso-proliferative retinopathy model

Autoren: Jaszai J.(1),Rojo Arias J.(1),von Herrmanni F.(1),Kappert V.(1),Economopoulou M.(2),Morawietz H.(3),Chavakis T.(4),Funk R.(1),

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Abstract:
The postnatally developing murine retinal vasculature offers an excellent and easily accessible system for studying normal angiogenesis, and when it is challenged, also for pathologic vascularization. A particularly well-studied paradigm of the latter is the hypoxic stress response observed in the murine oxygen-induced retinopathy (OIR) model producing exuberant vasoproliferation mimicking pathognomonic signs of late severe forms of proliferative diabetic retinopathy (PDR). The consecutive hyper- and normoxia (relative hypoxia) applied in this model, after an initial vascular regression, lead to an increased release of vascular endothelial growth factor (VEGF) from hypoxic tissues triggering thus the formation of proliferative pathological epiretinal tufts. This study was undertaken to reveal the complex reactions of endothelial- (EC), perivascular- (PC) and glial cells in the context of the retinal vascular remodeling phenomenon with special emphasis on the microvessels of the superficial plexus in response to VEGF-Trap (Aflibercept) treatment. VEGF-Trap is a novel inhibitor of VEGF-receptor signaling acting through the quenching of VEGFR-ligands. Retinae from mice subjected to OIR (control) and such after receiving VEGF-Trap were compared. The results we have obtained with this model performing a detailed morphological analysis in retinal whole-mounts and in slice preparations by immunohistochemical methods show that a combined blockage of VEGFR-ligands by VEGF-Trap, a) counteracts the formation of abnormal epiretinal blood vessels, b) facilitates revascularization and c) promotes the normalization of microvascular network density, without adversely affecting the normal vascular architecture of the retina in normoxic animals.

Kategorie: Poster

Poster 94:

Titel: Optimizing amyloid beta detection in retinas of a double transgenic Alzheimer´s disease mouse model and of human subjects with dementia

Autoren:Löffler J.(1),Hempel S.(1),Valtink M.(1),Funk R.(1),Ader M.(2),Schroeder C.(3),Knels L.(1),

Adressen:(1)Department of Anatomy|TU Dresden, Medical Theoretical Center|Dresden|Germany; email:jana.loeffler@tu-dresden.de; (2)CRTD Center for Regenerative Therapies Dresden|TU Dresden|Dresden|Germany; (3)Department of Anatomy|TU Dresden Medical Theoretical Center, Max Planck Institute of Molecular Cell Biology and Genetics|Dresden|Germany

Abstract:
Objective: Beta amyloid (A-beta) plaques in brain and retina are a hallmark of Alzheimer´s disease (AD). The incidence of A-beta plaques in AD retina is controversially discussed, motivating us to optimize various staining protocols. We systematically analyzed brain and retina A-beta plaques of an AD mouse model (APPSwe/PS1ΔE9) and of human dementia post-mortem samples. Methods: Mouse and human brain and retina were analyzed in paraffin and cryosections. A-beta was stained by immunohistochemistry, varying formic acid (FA) pretreatment as well as dilutions and incubation times of three antibodies (A-beta 6E10, 4G8, 1-40/42), or with natural dyes (Congo red, curcumin, thioflavin S). Retinal A-beta staining required higher antibody concentrations. Optimized staining procedures using A-beta 1-40/42 or thioflavin S were then applied to paraffin sections of human dementia brain and retina samples. Results: Immunohistochemistry revealed that 70% FA treatment for 10 min is necessary and sufficient for antigen recovery without dissolving plaques. Both equally efficient antibodies 6E10 and 1-40/42 surpassed 4G8. A-beta was located surrounding and within blood vessels. Thioflavin S and curcumin were suitable for identifying A-beta in brain and retina, while Congo red failed to stain retinal plaques. A-beta deposition was detectable in both paraffin and cryosections with retinal morphology best preserved in mouse paraffin sections. The occurrence of A-beta plaques in the human retina was definitively demonstrated. Conclusions: Optimized immunohistochemical staining backed-up by natural dyes is effective for unequivocally identifying A-beta plaques in AD tissues. Natural dyes might be considered promising for fast amyloid detection in the retina.

Kategorie: Poster

Poster 95:

Titel:Recovery of function of the neurogenic hyperthrophied urinary bladder after spinal cord injury (sci) and whole-body vibration (wbv) therapy in rats is not associated with alterations of the intramural axonal density

Autoren: Scheer E.(1),Ozsoy U.(2),Stein G.(3),Meyer C.(3),Pavlov S.(4),Angelov D.(1),

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Abstract:
Recovery of lower urinary tract function is an important prognostic sign for functional recovery after spinal cord injury. In the present study we examined the effect of WBV on recovery of urine storage- and voiding bladder functions. Following compressive SCI at low-thoracic level, adult Wistar rats were subjected to WBV starting 7, 14, or 28 days after injury (WBV7, WBV14, WBV28 respectively). Intact rats, rats with SCI but no WBV training (sham therapy) as well as rats subjected to passive flexion and extension (PFE) of the hind limbs served as controls. Recovery of general locomotion was analyzed using video recordings of walking on a wooden beam and climbing an inclined ladder. The functional status of the bladder was assessed during each manual voiding i.e. 2 times daily. Only WBV14 had beneficial effects on general locomotion and bladder functions. Macroscopic observations and weight measurements revealed severe bladder hypertrophy in all SCI groups. The comparative analyses between recovery of urinary bladder function and bladder hypertrophy showed that the increased bladder mass was associated with worse bladder function. In contrast, the parallel analyses between recovery of bladder function and intramural axonal density revealed no correlations: despite obvious functional improvement (e.g. in group WBV14) there were no parallel alterations in the axon density in the bladder wall. We conclude that, despite evident postlesional hypertrophy of the bladder musculature and corresponding degrees of functional recovery, the innervation pattern of the bladder wall remains unchanged.

Kategorie: Poster

Poster 96:

Titel:Influence of a membrane-targeted bace1 inhibitor (tri-01) on app processing and cell survival in the retina of an alzheimer s disease mouse model

Autoren: Knels L.(1),Loeffler J.(1),Linning P.(2),Pietzsch J.(3),Simons K.(4),Knölker H.(5),Funk R.(1),Schroeder C.(1),

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Abstract:
Alzheimer’s disease (AD) is accompanied by retinal neurodegeneration with characteristic ß-amyloid plaques (Aß). Coincident with various early visual abnormalities described in humans and animal models, the appearance of pathologic ß-amyloid species in the retina precedes that in the brain. This may allow earlier diagnosis and therapy of AD. We examined whether the tripartite, membrane raft-targeted β-secretase (BACE1) inhibitor Tri-01 interferes with retinal β-amyloid formation and deposition. We cultured retinal explants from adult double transgenic Swedish APP/Psen1d9 mice (AD model) and wild type C57BL/6 mice (controls) in medium supplemented with Tri-01. Retina explants from Swedish APP/Psen1d9 mice exhibited enhanced APP expression with increased amyloid processing and Aß plaque accumulation, compared to wild-type mouse retina. APP cleavage products including CTFß and Aβ40/42 decreased during Tri-01 treatment. In contrast, levels of apoptosis and stress markers (AIF, Bax, Hsp70, HO-1), and of BACE1 were hardly affected by APP expression and processing or by Tri-01 treatment. Thus, Tri-01 appears to protect retinal explants from Aß accumulation. Compared to brain studies the retinal ex vivo model, intermediate between in vitro and in vivo systems, proved suitable for drug testing and facilitated monitoring, offering more complexity than cell culture models. Tripartite BACE inhibitors may hold promise as early topical medication against Aß induced retinal degeneration.

Kategorie: Poster

Poster 97:

Titel:Axonal density in the renal cortex after compression spinal cord injury (sci) and whole-body vibration (wbv) therapy

Autoren: Wöhler A.(1),Stein G.(2),Meyer C.(2),Pavlov S.(3),Angelov D.(1),

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(3)Department of Anatomy|Medical University Varna|Varna|Bulgaria;
email:angelov.anatomie@uni-koeln.de

Abstract:
In the present study we looked for correlations between objective functional (locomotor rating score and lower urinary tract status) and morphological (renal cortex thickness) parameters after SCI compression injury in rats. We performed compression SCI at low-thoracic level in adult female Wistar rats and subjected them to whole-body vibration (WBV) therapy. WBV training was performed daily starting 7, 14 and 28 days after injury and continued over a 12-week post-injury period. Intact rats (no SCI), rats with SCI but no WBV training (sham) and rats subjected to passive flexion and extension (PFE) of the hind limbs served as controls. Motor recovery was analyzed using the locomotor rating score of Basso, Beattie and Bresnahan (BBB). The bladder functional status was estimated 3 times a day (during manual voiding) according to a scoring table representing the degree of bladder filling. Both functional parameters showed significant differences between WBV-treated and control rats at 1-12 weeks after SCI. These correlated with clear morphological alterations in the wall of the neurogenic urinary bladder. However, macroscopic observations and weight measurements of the whole kidneys revealed no differences between intact and SCI-lesioned rats. In addition, estimation of the renal-cortex thickness in 25 Âµm thick transverse sections (HE-staining) as well as quantification of axonal density (immunofluorescence with ant-Beta-tubulin neuronal class III) also revealed no differences between intact and lesioned rats. We conclude that bladder emptying by the regular (3 times a day) manual expression preserved the kidneys from urine reflux and promoted unaffected renal function after SCI.

Kategorie: Poster

Poster 98:

Titel:Reactive changes in murine optic nerve astrocytes are mediated by growth factors and increasing substratum stiffness

Autoren: Dillinger A.(1),Mayer M.(2),Schneider M.(1),Weber G.(1),Goeppner C.(3),Tamm E.(1),Shamonin M.(2),Monkman G.(2),Fuchshofer R.(1),

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Abstract:
Purpose: Patients with primary open-angle glaucoma have a stiffer peripapillary sclera, reactive astrocytes and a remodeled lamina cribrosa. TGF-beta2 and its downstream mediator CTGF mediate the pathologic changes. Recently we developed a murine glaucoma model by overexpressing CTGF in the eye (beta-b1-CTGF). In this study, we investigate the glial lamina of beta-b1CTGF mice, and changes of astrocytes in response to CTGF and TGF-beta2 as well as increasing substratum stiffness. Methods: Tangential sections of the glial lamina of beta-b1-CTGF mice and wild-type littermates were labeled with phalloidin and stained against GFAP, CTGF and fibronectin. Murine optic nerve (ON) astrocytes from CD1 mice were isolated, cultured and characterized by GFAP staining. Astrocytes were treated with TGF-beta2 and CTGF or seeded on PDMS substrata with different stiffness (10, 30 and 60kPa). Cells were analyzed by Western blotting, real-time RT-PCR and immunohistochemistry. Wound healing assays were performed to analyze migration rate. Results: beta-b1-CTGF mice showed a massive increase in CTGF and GFAP in the glial lamina and an increase in fibronectin staining and phalloidin-labeled actin in the peripapillary sclera compared to their wild-type littermates. Murine ON astrocytes reacted on increased substratum stiffness by increasing reactivation and CTGF synthesis. TGF-beta2 and CTGF treatment led to an enhanced migration rate and an increase in extracellular matrix proteins. Conclusion: We conclude that remodeling of the lamina cribrosa and of the peripapillary sclera alter the biomechanical properties and thereby induce reactive changes in resident astrocytes. The reactivated astrocytes, in turn, contribute to the pathogenesis of glaucoma.

Kategorie: Poster

Poster 99:

Titel:Interaction of nanoparticles with neurons: a liaison with potential?

Autoren: Neubert J.(1),Braeuer A.(2),Glumm J.(1),

Adressen:(1)Anatomy, Institute of Cell Biology and Neurobiology| Charité - Universitätsmedizin Berlin|Berlin|Germany; email:jenni.neubert@charite.de; (2) Department of Anatomy|Universitätsmedizin Rostock AöR|Rostock|Germany

Abstract:
Originally, nanoparticles have been used as contrast agents in magnetic resonance imaging (MRI) and are of special interest for diagnostic and therapy of central nervous system (CNS) diseases. Furthermore, their composition including size, surface coating and charge and the resulting increased interaction with and accumulation by brain cells make them ideal tools to act at the molecular level. There is a growing body of evidence that nanoparticles can be used to influence neurite outgrowth at different levels. Particular focus lies on the use of superparamagnetic iron oxide nanoparticles (SPIOs) to specifically influence neuronal regeneration after injury due to their unique composition. In our previous study, we could already show that different types of clinically relevant SPIOs enhance neurite outgrowth of primary hippocampal neurons in neuron-glia cocultures, but not of neurons in monocultures, in a particle- and dose-dependent manner. On the basis of our results and those of other investigators, we analyzed which intracellular signaling pathways are activated and which cytokines and chemokines are secreted as a consequence of SPIO exposure leading to increased neurite outgrowth. The applied SPIOs were novel Very Small Iron Oxide Particles (VSOPs) or clinically approved ferucarbotran or ferumoxytol. We could show that the complex interaction of signaling molecules determines SPIO-induced effects and still remains challenging for the potential application of SPIOs to promote neuronal regeneration in vivo.

Kategorie: Poster

Poster 100:

Titel:Assessment of long-term effects in the peroxisomal compartment of the nucleus accumbens of ethanol-treated rats

Autoren: Islinger M.(1),Uhl A.(1),Pfarr S.(2),Sommer W.(2),Schultz C.(1),

Adressen:(1)Neuronatomie|Universität Heidelberg|Mannheim|Germany; email:markus.islinger@medma.uni-heidelberg.de; (2)Institut für Psychopharmakologie|Universität Heidelberg|Mannheim|Germany;

Abstract:
Prolonged ethanol exposure to the brain leads to alcohol addiction in humans. The behavioral changes induced by the alcohol abuse have to be reflected by neural adaptions at the molecular level, in particular, in brain regions as the nucleus accumbens (Ncl. acc.), which is involved in the regulation of conditioned rewarding effects. In brain tissue, peroxisomal catalase is estimated to oxidize up to 60% of ethanol. Thus, prolonged exposure to ethanol may interfere with basal catalase expression levels but also peroxisomal oxidases producing H2O2 required for this peroxidatic reaction. To assess potential peroxisomal changes in the Ncl. acc. in response to alcohol addiction, female SD rats were exposed to intermittent doses of ethanol vapor (150 – 250 mg/dl) for 7 weeks triggering spontaneous alcohol preference. Analysis of control and treated rats revealed that peroxisomes in the Ncl. acc. exhibit significant heterogeneity. While astrocytes express substantial levels of catalase, the enzyme is hardly detectable in neurons. Nevertheless, both cell types harbor considerable amounts of peroxisomes as shown by Pex14 staining. In response to the ethanol treatment peroxisome numbers remained stable. Likewise, catalase levels showed no long-term alterations in order to adapt to the continuously elevated ethanol levels. However, catalase-driven ethanol degradation depends on H2O2 supplied by peroxisomal oxidases, whose status is currently assessed. If peroxisomal oxidases or ROS producing CYP2E1, involved in an alternative ethanol degradation pathway, are induced to cope with prolonged alcohol exposure, the inability to induce catalase expression might render neurons vulnerable to the increased H2O2 levels.

Kategorie: Poster

Poster 101:

Titel:Polyglutamine aggregation in Huntington's disease and Spinocerebellar Ataxia type 3: similar mechanisms in aggregate formation

Autoren: Seidel K.(1),Siswanto S.(1),Fredrich M.(1),Bouzrou M.(1),Brunt E.(2),van Leeuwen F.(3),Kampinga H.(4),Korf H.(1),Rueb U.(1),den Dunnen W.(5),

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Abstract:
Polyglutamine diseases are characterized by the expansion of a polymorphic glutamine sequence in disease specific proteins and exhibit aggregation of these proteins. This is combated by the cellular protein quality control system, consisting of chaperone mediated refolding as well as proteasomal and lysosomal degradation pathways. Our recent study in the polyglutamine disease spinocerebellar ataxia type 3 suggested a distinct pattern of protein aggregation and protein quality control dysregulation. To corroborate these findings we have investigated immunohistochemically stained 5µm sections from different brain areas of Huntington's disease and spinocerebellar ataxia type 3 patients. Irrespective of disease and brain region, we observed peri- and intranuclear polyglutamine aggregates. A subset of neurons with intranuclear inclusions bodies exhibited signs of proteasomal dysfunction, up-regulation of HSPA1A and re-distribution of DNAJB1. The extent of the observed effects varied depending on brain area and disease protein. Our results suggest a common sequence, in which formation of cytoplasmic and nuclear inclusions precede proteasomal impairment and induction of the cellular stress response. Clearly, impairment of the protein quality control is not the primary cause for inclusion formation but rather a consequence that might contribute to neuronal dysfunction and death. Notably, the inclusion pathology is not directly correlated to the severity of the degeneration in different areas, implying that different populations of neurons respond to polyglutamine aggregation with varying efficacy and that protein aggregation outside the neuronal perikaryon (e.g. axonal aggregates) or other effects of polyglutamine aggregation, which are more difficult to visualize, may contribute to neurodegeneration.

Kategorie: Poster

Poster 102:

Titel:Densities of acetylcholine receptors in hemiparkinsonian rat striatum following botulinum neurotoxin-a injection

Autoren: Klawitter F.(1),Schmitt O.(1),Hawlitschka A.(1),Cremer M.(2),Zilles K.(2),Wree A.(1),

Adressen:(1)Institute of Anatomy|Rostock University Medical Center|Rostock|Germany; email:andreas.wree@med.uni-rostock.de; (2)Institute of Neuroscience and Medicine INM-1|Forschungszentrum Jülich|Jülich|Germany;

Abstract:
Injection of 6-hydroxydopamin into the rat medial forebrain bundle causes a degeneration of dopaminergic neurons in the substantia nigra pars compacta mimicking important aspects of Parkinson´s disease. These include an overactivity of cholinergic interneurons in the striatum. Recently, we developed a therapeutic option for experimental 6-OHDA-induced Hemiparkinsonism in the rat by intrastriatal injections of 1 ng botulinum neurotoxin-A (BoNT-A) following the hypothesis that BoNT-A massively reduces the release of acetylcholine in the striatum. Thus, BoNT-A inhibits apomorphine-induced rotation behavior of unilaterally 6-OHDA-lesioned rats up to 3 months completely. In order to explored the molecular mechanisms beyond the observed behavioural effects of 6-OHDA-lesioned rats subsequently treated with BoNT-A, we here evaluated the striatal receptor densities of the cholinergic transmitter system. Using quantitative in vitro receptor autoradiography striatal muscarinergic (M1, M2, M3) and nicotinergic (N) acetylcholine receptors (AChR) were studied. Dopaminergic deafferentation leads to a massive reduction of the striatal NAChR density, striatal BoNT-injection has no effect on NAChR. Dopaminergic deafferentation leads to a reduction of striatal M1, M2, and M3 receptor densities, striatal BoNT-injection has little or no effect on those receptors. We conclude that the the pathological behaviors of hemiparkinsonian rats at least partly can be explained be lesion-induced changes in cholinergic receptors, however, the therapeutic effect of striatal BoNT-application in hemiparkinsonian rats cannot be explained by BoNT-induced changes on AChR.

Kategorie: Poster

Poster 103:

Titel:Anti-inflammatory effects of aldosterone on microglia in relation to neurodegenerative diseases

Autoren: Bast B.O.(1),Wilms H.(2),Arnold P.(1),Lucius R.(1),Rickert U.(1),

Adressen:(1)Institute of Anatomy|Christian-Albrechts-University of Kiel|Kiel|Germany; email:bo.bast@web.de; (2)Department of Neurology|Texas Tech University|Lubbock,TX|USA

Abstract:
Microglia can lead to chronic neuroinflammation and neuronal necrosis, which gives them an important role in specific neurodegenerative diseases, as Multiple Sclerosis (MS), Alzheimer's Disease (AD), and Parkinson's Disease (PD). Those diseases play a major role in the aging society of today. Therefore there evolved a widespread research field, to find possible drugs, to stop such neuroinflammatory processes. Aldosterone is a naturally produced steroid hormone of the adrenal cortex, which mainly induces homeostatic and renal effects. Knowing of the existence of mineralocorticoid receptors (MCR) on microglia, aldosterone might be able to influence microglia cell functions, possibly via anti-inflammatory effects. This study assesses the anti-inflammatory effects of aldosterone in an in vitro assay using LPS-activated rat microglia. Therefore we incubated microglia with aldosterone (200nM) with or without LPS (5ng/ml) for 3, 6, and 24 hours. To analyze the effects we examined the inflammatory molecules nitric oxide (NO), iNOS, IL-6, IL-1 beta, TNF-alpha, and COX2, using various methods such as Griess-assay, qPCR, and ELISA. Furthermore we analyzed various signaling pathways, using western blotting. Analyzing the results, we were able to demonstrate that 200nM aldosterone has a highly significant effect on microglia, decreasing NO-release, and the mRNA level of most pro-inflammatory mediators mentioned above, and a decrease in protein levels (TNF-alpha, IL-6). Moreover, this effect increases with the duration of stimulation. Our results indicate that aldosterone has an anti-inflammatory effect on microglia, which leads to the conclusion that it might be a potential drug in the therapy of neurodegenerative diseases in the future.

Kategorie: Poster

Poster 104:

Titel:Reduction of formyl peptide receptors activity decreased inflammation and improved neuropsychological behaviour in a mouse model of alzheimer disease

Autoren: Brandenburg L.(1),Brandt E.(2),Welter J.(2),Samer S.(2),Kress E.(2),Pufe T.(3),

Adressen:(1)Antomy and Cell Biology|RWTH Aachen University|Aachen|Germany; email:lbrandenburg@ukaachen.de; (2)Anatomy and Cell Biology|RWTH Aachen University|Aachen|Germany; (3)Anatomy and Cell Biology|RWTH Aachen Unversity|Aachen|Germany

Abstract:
The main component of the amyloid plaques in the Alzheimer brains is amyloid-beta 1-42 (Abeta1-42). Furthermore, a massive increase of glial cells (astrocytes and microglia) can be detected in the brain of affected individuals. It is assumed that the chemotactic G-protein coupled formyl peptide receptor (FPR) modulates uptake and/or signal transduction of Abeta1-42 in glial cells. The murine FPR gene family has at least six members in contrast to only three in humans. The two most important members, mFPR1 and mFPR2, are in the focus of our work. We assume that mFPR1/2-mediated gliosis is critically involved in neuroinflammation and neurodegenerative processes of the Abeta1-42-affected brain. To confirm this hypothesis, we used wildtype (WT), mFPR1- or mFPR2-deficient mice for stereotactic injection of oligomeric or fibrillary Abeta1-42 into the hippocampus formation. Furthermore, intraperitoneally injection of the proinflammatory FPR agonist fMLF or the FPR antagonists Boc-FLFLF in a mouse model of Alzheimer disease (AD) was performed about 20 weeks. Our results showed a changed microglial cell density in the hippocampus of FPR-deficient mice one week after fibrillary Abeta1-42 stereotactic injection. An injection of the FPR antagonist boc-FLFLF in a mouse model of AD about 20 weeks reduced significantly glial cell activation and improved neuropsychological behaviour in the Morris Water Maze. Altogether, our results suggest that the FPRs play an essential role in Abeta1-42-induced inflammation and glial cell activation in the course of Alzheimer disease.

Kategorie: Poster

Poster 105:

Titel:Effect of intra-striatal 6-ohda lesion on extra-striatal structures in the mouse

Autoren: Becker B.(1),Demirbas M.(1),Beyer C.(1),Kipp M.(2),

Adressen:(1)RWTH Aachen University|Institute of Neuroanatomy|Aachen|Germany; email:bbecker@ukaachen.de; (2)Ludwig-Maximilians-University|Department of Anatomy II|Munich|Germany

Abstract:
Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by progressive loss of dopaminergic neurons in the substantia nigra. This results in the onset of motor and non-motor manifestations. Non-motor symptoms, such as cognitive decline, psychiatric disturbances and sleep difficulties, are not well-investigated in established PD animal models. It is currently discussed whether these manifestations are affected by pathological changes of extra-striatal structures. Objective: Characterization of extra-striatal manifestations in the 6-hydroxydopamine (6-OHDA) PD animal model. Methods: Intra-striatal lesions were induced by unilateral stereotactic injections of 6-OHDA in adult male mice. 3 weeks post-surgery lesion induction was verified by behavioural testing. Loss of tyrosine hydroxylase (TH) fibres plus microglia and astrocyte activation were quantified by means of design-based stereological approaches in nigro-striatal and extra-striatal regions. Results: Successfully induced lesions revealed reduced TH-positive fibre density in the dorsal and central part of the striatum accompanied by a massive retrograde loss of TH-positive neurons in the substantia nigra. In contrast, the ventral tegmental area was only marginally affected. A substantial loss of TH-positive fibres was observed in the cortical cingulate and motor area. Furthermore, signs of microgliosis were evident within the striatum and thalamus but not in the examined cortical regions. Conclusion: These results demonstrate that intra-striatal injections of 6-OHDA lead to pathological changes in extra-striatal structures including cingulate-, motor cortex and thalamus possibly influencing non-motor symptoms. Further studies can help to investigate underlying mechanisms contributing to functional sequelae in this PD animal model.

Kategorie: Poster

Poster 106:

Titel:Inflammasome activation in the sod1(g93a) mouse model for amyotrophic lateral sclerosis (als) and in human als patients

Autoren: Johann S.(1),Heitzer M.(1),Kanagaratnam M.(1),Goswami A.(2),Weis J.(2),Troost D.(3),Beyer C.(1),

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Abstract:
Amyotrophic lateral sclerosis (ALS) is characterized by the degeneration of motoneurons in the cerebral cortex, brainstem and spinal cord. Neuroinflammation plays an important role in the pathogenesis of ALS and involves the activation of microglia and astrocytes. Intracellular inflammasome complexes are part of the innate immunity as they sense and execute host inflammatory responses. The NLRP3 inflammasome is currently the most fully characterized inflammasome activated in numerous disease with an inflammatory background. NLRP3 is critical for the activation of caspase 1 and the processing and release of IL1beta and IL18. In this study, we investigated the expression and cellular localization of NLRP3 components and cytokines in the spinal cord of SOD1(G93A) mice which serves as animal model for ALS and in post-mortem tissue of ALS patients. NLRP3 activation was moderately detectable in SOD1 mice at a pre-symptomatic stage and increased in symptomatic animals. Immunofluorescence labelling and biochemical analysis revealed that astroglia but not microglia were the major source of NLRP3. Conforming data were obtained in human ALS samples. Our findings suggest that activation of inflammasomes precede neurodegeneration in SOD1 mice and that NLRP3 activation in astrocytes could become a promising target of therapeutic intervention in ALS.

Kategorie: Poster

Poster 107:

Titel:The influence of honokiol on microglia and astrocytes

Autoren:Heimke M.(1),Wilms H.(2),Lucius R.(1),Rickert U.(1),

Adressen:(1)Department of Anatomy|Christian-Albrechts-University of Kiel|Kiel|Germany; email:marvinheimke@googlemail.com; (2)Department of Neurology|Texas Tech University|Lubbock,TX|USA

Abstract:
Honokiol is a bioactive compound isolated from the bark of the Magnolia tree, which is used in traditional herbal medicine in China for treatment of several diseases e.g. gastrointestinal disorders, anxiety and allergic disease.
Recent studies have not only shown anti-cancerous and neuroprotective effects, but also potential anti-inflammatory properties.
Since neuroinflammation is known to play an important role in the pathogenesis of several neurodegenerative diseases, such as Parkinson's Disease (PD), Multiple Sclerosis (MS) and Alzheimer's Disease (AD), potential anti-inflammatory drugs are one approach of treating those conditions.
In this study we used an *in-vitro* model of neuroinflammation with LPS pretreated primary microglia and astrocytes and investigated the influence of Honokiol treatment on pro- and anti-inflammatory mediators. First, we investigated the metabolic activity via MTT assay, followed by measuring of nitric oxide (NO) synthesis using Griess reagent.
Furthermore, we investigated the transcription of the cytokines IL-6, IL-1beta, TNF-alpha and IL-10 and of the enzymes iNOS and COX-2 via qPCR as well as the protein secretion of IL-6 and TNF-alpha via ELISA. The influence of Honokiol treatment on possible intracellular signaling pathways was determined via Western Blot and immunofluorescence staining.

Our findings suggest that Honokiol is able to decrease the gene expression and protein secretion of pro-inflammatory metabolites in activated central glia and increase the anti-inflammatory cytokine IL-10. Finally, we here describe the detection of the transcription factor Krüppel-like factor (KLF) 4 in astrocytes.

Kategorie: Poster

Poster 108:

Titel:Regenerative capacity of the olfactory epithelium in niemann-pick disease type c1

Autoren: Meyer A.(1),Guenther R.(1),Lehmann S.(1),Brueckmann H.(1),Schmitt O.(1),Wree A.(1),Witt M.(1),

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Abstract:
Niemann-Pick disease type C1 (NPC1) is a neurovisceral lipid storage disorder characterized by a deficiency of the NPC1 gene function. Olfactory impairment is one of the earliest symptoms in neurodegenerative disorders. Previous findings confirm severe morphological and immunohistochemical alterations in the olfactory system of NPC1(-/-) mutants compared with healthy controls. A combination of a substrate-reduction therapy (SRT) with miglustat and byproduct therapy (BPT) with allopregnanolone/cyclodextrin has been shown to delay the onset of neurological symptoms. We investigated the replacement capacity of the olfactory epithelim (OE) in adult untreated NPC1(-/-) and in two different therapy approaches: one group with a combination of SRT and BPT and one with cyclodextrin only. Using BrdU to label dividing cells, we detected a significant proliferation increase of 75 ±22% in NPC1(-/-), 161% ±22% in SRT/BPT NPC1(-/-) and 331% ±14% in cyclodextrin NPC1(-/-), indicating a high regenerative potential of olfactory basal cells in NPC1. Surprisingly, we also detected a massive therapy-induced proliferation in both treated control groups of 325% ±29% in SRT/BPT WT and 331% ±17% in cyclodextrin WT compared with untreated controls. In addition, we estimated the total number of mature olfactory receptor neurons (ORNs) in the main OE using Olfactory Marker Protein (OMP). Stereological analyses showed a dramatic decrease of OMP+ cells in the OE of NPC1(-/-) (47% ±18%) and significantly higher rates in both treated NPC1(-/-) groups (SRT/BPT 68% ±15%; cyclodextrin 83% ±27%). Interestingly, the OMP+ rates do not completely reflect the highly increased proliferation rates of basal cells.

Kategorie: Poster

Poster 109:

Titel:Behavioral characterisation of hemiparkinsonian rats repetitively intrastriatally injected with botulinum neurotoxin-a and analysis of acetylcholine-dependency of prior results

Autoren: Hawlitschka A.(1),Eilhard M.(2),Wree A.(1),

Adressen:(1)Institute of Anatomy|Medical Faculty; University of Rostock|Rostock|Germany; email:alexander.hawlitschka@uni-rostock.de; (2)Department of Neurology|Medical Faculty; University of Rostock|Rostock|Germany

Abstract:
Recently we showed that intrastriatal injections of 1 ng botulinum neurotoxin-A inhibits pathologic apomorphine-induced rotation behavior of hemiparkinsonian rats up to 3 months completely and inhibits them significantly up to 6 months. In order to investigate whether it is possible to prolong the suppression of apomorphine-induced rotations of a single BoNT-A treatment, we injected 1 ng BoNT-A again into the right striatum 6 months after the first application. Indeed, the second BoNT-A injection led to a further reduction of the meanwhile reverted apopmorphine-induced rotation rate. This experiment supplied evidence for the theoretical possibility of intracerebral administration of BoNT-A for treatment of motor symptoms of PD especially bradykinesia of PD patients over long time. Assuming that the observed beneficial effect of BoNT-A results from a reduction of pathologic increased striatal acetylcholine content, we wanted to prove this theory by application of a cholinesterase inhibitor, which should increase the striatal acetylcholine content again and should lead to an abrogation of the supression of the apomorphie-induced rotation behaviour. Donepezil is a well known cholinesterase inhibitor which passes the blood brain barrier. We used 6-OHDA hemilesioned rats whose pathologic apomorphine-induced rotation behavior was successfully treated by an intrastriatal administration of 1 ng BoNT-A. Indeed, subsequent donepezil injections led to an increase of apomorphine-induced rotation behavior of these rats. Nevertheless, also after sham-donepezil injections the apomorphine-induced rotation rates were increased. We draw the conclusion that systemic donepezil injection is not qualified to proof that the BoNT-A effects caused by an reduction of striatal acetylcholine

Kategorie: Poster

Poster 110:

Titel:The influence of rasagiline, a clinically effective drug in parkinson's disease, on microglia and astrocytes in vitro

Autoren: Rickert U.(1),Wilms H.(2),Arnold P.(1),Spreu J.(1),Lucius R.(1),

Adressen:(1)Department of Anatomy|Christian-Albrechts-University of Kiel|Kiel|Germany; email:u.rickert@anat.uni-kiel.de; (2)Department of Neurology|Texas Tech University|Lubbock,TX|USA

Abstract:
Parkinson's Disease (PD) is a chronically, progressive neurodegenerative disorder, characterized by imbalance of neurotransmitters such as low dopamine- and increased acetylcholine- and glutamate levels, mainly resulting in muscle dysfunctions. Causal is the selective degeneration of dopaminergic neurons in the substantia nigra. To the earliest drugs tried in PD belong inhibitors of the enzyme monoamine oxidase B (MAO-B), which is in the brain mainly localized in glia cells near the dopaminergic synapses. Its inhibition arrests dopamine degradation in PD and elevates dopamine levels. Different studies have shown, that the selective and irreversible MAO-B inhibitor rasagiline (Azilect) has a proven neuroprotective effect. To evaluate if the well known neuroprotection is at least in part mediated via influence on microglial and astrocytic cell functions, we investigated the possible anti-inflammatory potential of rasagiline on primary central glia cells in vitro. We used an in vitro-model of brain inflammation, consisting of activated microglia and astrocytes, which had been pretreated with lipopolysaccharide (LPS). First, we measured the synthesis of nitric oxide (NO, Griess reagent). Furthermore we investigated proinflammatory cytokine and enzyme gene expression of TNF-alpha, IL-6, IL-1beta and MMP-9 (qPCR) as well as protein secretion of TNF-alpha and IL-6 (ELISA) in rasagiline-treated microglia and astrocytes with or without LPS. Finally, we investigated the intracellular signaling mechanisms triggered by rasagiline exposure using western blotting. We here could show that rasagiline is able to significantly inhibit gene expression and secretion of proinflammatory metabolites in activated central glia cells, probably triggered by MAP kinase signaling pathways.

Kategorie: Poster

Poster 111:

Titel: Embroidered collagen-hybrid scaffolds for ligament tissue engineering

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Abstract:
Tissue engineering of an ACL implant might overcome some of the limitations associated with the current ACL substitution techniques and could present a novel approach for ACL reconstruction. The aim of this study was to develop and optimize a tissue engineered embroidered collagen-hybrid scaffold for ligament reconstruction. 1. Survival, adherence and distribution of lapine ACL cells was analyzed on the scaffold. 2. A technique for directed seeding of the scaffold with the lapine ACL cells was developed for co-culturing the cell types of the ACL enthesis. A collagen-based cell barrier was created to initially separate cell types 3. Functionalization strategies of the scaffold were elaborated to optimize cell growth. Porous embroidered scaffolds were generated using the embroidering technique and resorbable polymer threads consisting of polylactic acid (PLA, multifilament) and poly(lactic-co-caprolacton) (PLA-CL, monofilament) or a combination of both materials. The colonization success, distribution and vitality of primary lapine ACL cells in the scaffold was determined using vitality stainings. The scaffolds were functionalized using fluor/argon-plasma and stabilized collagen foams. The embroidering technique allowed the combination of resorbable polymer threads in the scaffold and the adaption of biomechanical properties comparable to that of the lapine ACL. Embroidered scaffolds were biocompatible and functionalization using argon plasma and collagen foams led to increased cell adherence. A spheroid-based seeding technique allowed directed seeding and a collagen thread-based barrier was suitable for cell separation. First experiments using mechanostimulation were performed for further optimization. In future, biomechanic properties have also to be determined during scaffold degradation.

Kategorie: Poster

Poster 112:

Titel:The role of ceacam1 in endothelial barrier function .

Autoren: Bömmel H.(1),Kleefeldt F.(1),Ghavampour S.(1),Wagner N.(1),Ergün S.(1),

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Abstract:
Ceacam1 (Cc1) is essential for the structural and functional integrity of the endothelial barrier. Cc1âˆ’/âˆ’ mice exhibit small plaque-like lesions in the aorta accompanied by impaired endothelial integrity. One of the earliest steps of atherosclerosis initiation is endothelial dysfunction defined by increased leukocyte-endothelial interaction, vessel permeability and altered endothelial glycocalyx. The aim of this study was to analyze the role of Ceacam1in these processes. Ex vivo analyses revealed increased adhesion of the monocytic cell line (THP1) to aortic wall explants of Cc1âˆ’/âˆ’ in comparison to WT mice. This effect was confirmed in vitro as adhesion of monocytes to cultured Cc1âˆ’/âˆ’ myocardial endothelial (Myend) cells was also elevated. Electron microscopic studies showed a reduced endothelial glycocalyx in Cc1âˆ’/âˆ’ aortae probably increasing the accessibility of adhesion molecules. Interestingly, treatment of WT Myend cells with anti-Ceacam1 antibody mCC1 increased their basal and VEGF-mediated adhesion to THP1 cells suggesting a cross talk between Ceacam1 and VEGFR-2 signaling. No such effect was seen when mCC1 Fab fragments were used instead of mCC1. Importantly, the endothelial permeability of Cc1âˆ’/âˆ’ aorta was significantly enhanced as it was analyzed by Evans-blue deposition in vivo as well as by fluorescently labeled dextran deposition in aortic wall explants ex vivo in comparison to WT aorta. In vitro Cc1âˆ’/âˆ’ Myend cells revealed increased leakiness for both dextran and monocytes in comparison to WT Myend cells. Taken together, our data identify Ceacam1 as relevant factor regulating the endothelial barrier and protecting macrovessels against development of atherosclerosis.

Kategorie: Poster

Poster 113:

Titel:The role of ceacam1 in lymph node metastasis of prostate cancer

Autoren: Pfeiffer V.(1),Vix P.(2),Tilki D.(3),Ergün S.(1),

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Abstract:
The carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1) is recognized as a tumor suppressor gene due to its downregulation in solid tumors like colon, breast and prostate cancer (PCA), although in some tumors like melanoma CEACAM1 was found to be upregulated. Tissue sections from human PCA of various Gleason Stages and corresponding lymph nodes were stained for CEACAM1, the epithelial cell marker Cytokeratin and the Prostate-specific-Antigen (PSA). Furthermore, using experimental tumor models, lymph nodes and PCA tissues were analyzed for CEACAM1 and PSA expression. Remarkably, CEACAM1 expression was found in sinus endothelial and fibroblastic reticular cells of human lymph nodes of patients with an early stage of PCA, while these lymph nodes were diagnosed to be tumor cell free. Correspondingly, our analyses revealed the lack of tumor cells in these lymph nodes by immunostaining for Cytokeratin and PSA. These findings were further confirmed by results obtained from mouse lymph node tissue of experimentally grown tumors. Furthermore, we observed CEACAM1 expression in newly formed blood vessels of human and mouse lymph node tissue. Additionally, in human PCA prostate tissue the majority of tumor cells showed a downregulation of CEACAM1, whereas we located metastasized tumor cells with upregulated and downregulated CEACAM1 expression in the associated lymph nodes. Taken together, our data identify CEACAM1 as an early marker for lymphatic metastasis of PCA even before tumor cells arrived in the sentinel lymph nodes. Whether upregulation of CEACAM1 in lymph node sinus endothelial cells is beneficial for tumor cells or not remained to clarified.

Kategorie: Poster

Poster 114:

Titel:Re-transforming the malignant tumor microenvironment to increase therapeutic response in systemic cancer therapy

Autoren: Henke E.(1),Rosow L.(1),Schuetze F.(1),Veitl S.(2),Vorlova S.(3),Wax J.(2),Kuhn A.(2),Roehrig F.(2),Wartenberg M.(4),Rosenwald A.(4),Erguen S.(2),

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Abstract:
The tumor microenvironment is formed by the tumor’s vasculature, various tumor associated cells like fibroblasts, macrophages and lymphocytes and by an abundant extracellular matrix (ECM). These components are strongly influenced by the malignant signaling within the tumor and differ often substantially in their function from their respective counterparts in non-normal tissue. The microenvironment not only supports tumor growth, but also protects the tumor from therapeutic agents. We evaluated both the angiogenesis inducing VEGF-pathway and ECM-modifying lysyl oxidases (LOXs) as pharmacological targets aiming to improve drug delivery in various tumor models. VEGF-inhibition improved in all models the defective tumor vasculature. However contrary to widely accepted models this did not consistently improve drug delivery, but in some tumors VEGF-inhibition reduced overall drug supply leading to therapeutic failure. On the other hand LOXs crosslink ECM components thereby increasing its stiffness and its physical barrier function, which protects tumor cells from exposure to cytotoxic drugs. LOX inhibition enhanced in all tested tumor models permeability, consequently improving drug delivery and response. Combination of anti-VEGF and LOX inhibition synergistically improved drug delivery and response in both anti-VEGF responsive and refractory tumors. We demonstrate that the biological effects of microenvironment-targeted intervention are strongly context dependent and vary from tumor to tumor. However, effects of these interventions on physical properties like tissue stiffness or drug permeability appear to be more predictable and vary less between different tumors. Our results indicate the prospect to develop novel promising and widely applicable strategies to improve therapeutic efficacy in cancer treatment.

Kategorie: Poster

Poster 115:

Titel:Loss of desmoglein 3 promotes p38mapk-dependent keratinocyte migration

Autoren: Rötzer V.(1),Hartlieb E.(1),Winkler J.(1),Walter E.(1),Schlipp A.(1),Sardy M.(2),Spindler V.(1),Waschke J.(1),

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Abstract:
The desmosomal transmembrane adhesion molecule desmoglein 3 (Dsg3) is required for strong keratinocyte cohesion. Recently, we have shown that Dsg3 loss of function, either by siRNA silencing or by peptides interfering with Dsg3 binding, increases the activity of p38MAPK. Here, we further investigated the role of Dsg3-dependent p38MAPK suppression. Dsg3-deficient mice display recurrent skin erosions which spontaneously heal. In lysates from wound biopsies and from perilesional areas, p38MAPK activation was detectable compared to control animals. Similarly, in skin of pemphigus patients suffering from impaired cell cohesion due to autoantibodies targeting Dsg3, p38MAPK activity was increased in areas of epidermal blistering. This led us to speculate that Dsg3 regulates wound repair in a p38MAPK-dependent manner. Indeed, accelerated migration was detected in human keratinocytes after silencing of Dsg3 and in mouse keratinocytes derived from Dsg3-deficient mice compared to controls with normal Dsg3 levels. Scratch-wounded keratinocyte monolayers exhibited p38MAPK activation and loss of Dsg3 in cells lining the wound edge. Importantly, migration was efficiently blocked by inhibition of p38MAPK both in control and Dsg3-deficient keratinocytes. These data indicate that Dsg3 prevents a switch from an adhesive to a migratory keratinocyte phenotype via p38MAPK inhibition. Thus, in wounding conditions loss of Dsg3 adhesion may foster wound closure by allowing p38MAPK-dependent migration.

Kategorie: Poster

Poster 116:

Titel:Lysophosphatidic acid selectively influences excitatory transmission in the hippocampus

Autoren: Kieselmann O.(3),Battefeld A.(3),Stadler K.(3),Singh B.(4),Henneberger C.(4),Zhang P.(3),Aoki J.(5),Chun J.(6),Grantyn R.(4),Nitsch R.(2),Strauss U.(3),Bräuer A.(1),

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Abstract:
In recent years, great progress has been made in the analysis of the molecular machinery involved in the clathrin-mediated endocytosis of synaptic vesicles and evidence shows that phospholipids such as lysophosphatidic acid (LPA) regulate vesicle recycling independently of receptors. Here we show a receptor-dependent mechanism of LPA, specifically controlling glutamatergic neurotransmission. Genetic and pharmacological analysis demonstrated LPA-induced signaling on differentiated hippocampal neurons mediated by presynaptically expressed LPA2-receptor and Gi-coupling. Changes in extracellular LPA concentration mediate inositol (1,4,5) trisphosphate (IP3)-induced Ca2+ release (IICR), in turn activating P/Q-type calcium channels. Our results show that this signaling modulates the spontaneous vesicle release probability, as well as the rate of clathrin-independent vesicle recycling. Our data propose that, on differentiated primary neurons, LPA influences excitatory neurotransmission through the IICR.

Kategorie: Poster

Poster 117:

Titel:Culturing in aerosol - a new dimension in cell and tissue culture technology

Autoren: von der Ruhr J.(1),Seid K.(1),Neckel P.(1),Hirt B.(1),Just L.(1),

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Abstract:
In conventional culture systems, cells and tissues are mainly kept in cell culture medium (submerged cell culture) or at the interface between air and culture medium (air/liquid culture). We developed a principally new culture technique by which the cultivated cells are continuously surrounded and supported with aerosols of culture medium. This concept provides an efficient nutrient and gas supply to cells and allows to culture tissue constructs with less restrictions in shape and size. Using this aerosol based technology we were able to demonstrate the proliferation and specific differentiation of various mesenchymal and neural cells in a nebulous environment. The successful long-term cultivation however strongly depends on the amount and the manner of aerosol generation, the distribution of aerosol droplets and on the design of the culture chamber. This method offers novel possibilities in the engineering of complex three-dimensional cell and tissue constructs. In addition, it is particularly suited for the pharmacological testing of aerosol bound bioactive substances, such as drugs, toxins, virus particles, or synthetic nanoparticles.

Kategorie: Poster

Poster 118:

Titel:In situ molecular anatomy within the human cardiac stem niche: facts and hypotheses

Autoren: Rusu M.(1),Vrapciu A.(1),Hostiuc S.(2),Dermengiu D.(2),

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Abstract:
Until recently the heart has been regarded as a postmitotic organ. Recent publications have shown that cardiomyocytes are generated in the adult mammalian heart. At the date there are two hypotheses, of cardiac stem/progenitors (CSCs) differentiating to cardiomyocytes (CMs) and of CMs origin from the pre-existing ones. We aimed at evaluating the cardiac stem niche in human adult. There were used postautopsic cardiac samples from seven donor cadavers, adequately preserved. Immunohistochemistry on paraffin-embedded samples used alpha-smooth muscle actin (Î±-SMA), CD10, CD34, CD117/c-kit, CD133, CD146, Stro-1, Isl-1, cytokeratin 7 (CK7) and Ki67. Flattened or hypertrophied epicardial cells expressed Ki67, Î±-SMA, CK7, CD10 and c-kit. Immediate submesothelial epicardial cells had similar phenotypes; there were also scarcely found subepicardial CD133+ cells and c-kit+ myotubes. Epicardial and subepicardial Î±-SMA+ muscle layers were found, lying over and distinctive of the cardiac muscle layer. Isolated cardiac stromal rounded cells were positive for all antibodies, except CD146. Expression of Ki67, CK7, CD34 and CD146 was assessed in endothelial cells. Periendothelial cells, such as pericytes, expressed Î±-SMA, CK7, CD34, c-kit and CD146. Perivascular cells were found expressing all antibodies, except CD133. Adipocytes, uni- and multilocular, were found positive for c-kit, CK7, CD10, CD146 (rarely). Although Stro-1 expression was found in all cell types here, it should be regarded with caution. These results are likely indicating three distinctive niches supplying the heart with CSCs, two intrinsic and one extrinsic: the epicardial niche, the vascular/perivascular niche, and the hematopoietic bone marrow.

Kategorie: Poster

Poster 119:

Titel:Ceacam1 affects uptake of endothelial-derived microvesicles

Autoren:Huebner A.(1),Wagner N.(1),Erguen S.(1),

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Abstract:
The carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1) is a transmembrane protein expressed in various cells, including endothelial cells. Endothelial CEACAM1 is important for structural and functional integrity of blood vessels. A protective involvement of CEACAM1 in atheriosclerosis has also been discussed. Microvesicles (MV), small membrane coated vesicles, are shed from surface membranes of most cell types. Accumulating evidence point to a role of MVs in intercellular communication, under physiological and pathological conditions. Therefore, as diverse cargo (signaling molecules, mRNA/miRNA etc.) transporting vehicles, endothelial-derived MVs could contribute to atheriosclerosis. In order to investigate participation of MV and CEACAM1 in atheriosclerosis, we generated myocardial-derived endothelial cell lines (MyEnds) from wildtype (wt) and CEACAM1 knock out (CC1-/-) mice (MyEndswt, MyEndsCC1-/-). Uptake of calcein-loaded MyEndswt/MyEndsCC1-/--MVs by either MyEnd cell line was observed to occur more efficient in the presence of CEACAM1. Next, we investigated MV-dependent cell-cell interactions using MV-treated MyEnds and human monocytes (THP1). MyEnd-derived MVs generated in the presence of TNFalpha were able to augment monocyte binding on MyEnds. This implies that endothelial MV assembly takes place according to stimuli (e.g. inflammatory cytokines) during their formation and is therefore a specific process. We hypothesize that CEACAM1 influence in arteriosclerosis could be due to an altered response of endothelial cells to MVs of different cellular origin e.g. endothelial cells and/or leukocytes. Further studies are necessary to reveal the exact mechanism of MV uptake including the involvement of adhesion proteins in this process.

Kategorie: Poster

Poster 120:

Titel:Treatment with sodium-selenite as potential protection against the consequences of mechanical injury in bovine joint cartilage.

Autoren:Preusse-Prange A.(1),Behrendt P.(2),Haefelein K.(1),Grodzinsky A.(3),Kurz B.(1),

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Abstract:
Osteoarthritis is the most common degenerative joint disease. Traumatic joint injury can induce a subform of Osteoarthritis called post-traumatic osteoarthritis.
It has been shown that sodium-selenite-treatment has a curative or preventive effect on the course of various diseases (cancer, coronary artery disease).
Furthermore, a selenite deficiency is known to induce degenerative processes in articular joints (Kashin-Beck disease).
The aim of our study was therefore to investigate whether sodium-selenite-treatment reduces the effects generated by mechanical injury.
Articular cartilage explants were collected from femoro-patellar grooves of 2-year-old cattle,
randomly divided into groups, and incubated in standard culture medium with/without sodium-selenite (0.1 µg/ml). After equilibration half of the pre-treated and non-pre-treated explants were subjected to a single load compression (50% strain, velocity 1mm/s, held for 10s) using a computer controlled compression device**.**
After 4 days in standard culture medium (with/without sodium-selenite) explants were embedded for histological analysis or frozen for mRNA isolation.
Glycosaminoglycane (GAG) release was determined photometrically (DMMB-test) in culture supernatants. Gene expression analysis of known matrix degrading enzymes (ADAMTS-5, MMP- 3) and the amount of apoptotic cells (nuclear blebbing and tunnel) were determined.
Sodium-selenite reduced significantly injury-dependent apoptosis but not the GAG-release. Transcription levels for MMP-3 and ADAMTS- 5 were not affected. Our study shows that sodium-selenite has potential cell protective properties against mechanical injury in joint cartilage. To clarify the exact mechanisms further investigations must be performed.

Kategorie: Poster

Poster 121:

Titel:Chronic nrf2 activation in hepatocytes results in tumourigenesis

Autoren: Schenkel J.(1),Fragoulis A.(2),Streetz K.(3),Pufe T.(1),Wruck C.(1),

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Abstract:
Hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCC) occurs in the background of the pro-oxidative environment found in chronic liver disease. Nrf2 and its cellular repressor Keap1 is well established as the major regulators of oxidative stress defence with anti-carcinogenic effect and is known to be activated during chronic liver disease. In contrast, somatic mutations of the Nrf2 gene (NFE2L2) leading to constitutive activation of Nrf2 by disrupting the Nrf2 Keap1 interaction are found in various carcinomas. Recently, analysis of somatic mutations of HCC reveals an interaction of the Nrf2/Keap1 pathway with the Wnt/beta-catenin pathway, which is also involved in HCC development and progression. However, the molecular mechanisms of this interplay leading to HCC development are unknown. Here we show that chronic activation of Nrf2 in hepatocytes spontaneously induces HCC formation and CCC up to large hepatic cysts via epithelial–mesenchymal transition. Specifically, constitutive Nrf2 signalling in the liver leads to beta-catenin up-regulation via an antioxidant response element within the beta-catenin promoter and to nuclear translocation of beta-catenin. Consequently, beta‑catenin target gene SOX9 are constantly up-regulated in Nrf2 active livers inducing EMT of hepatocytes. Our data establish a previously unexpected oncogenic role for an Nrf2-beta-catenin interplay in liver cancer development. This study provides a new explanatory approach for the fact that chronic liver diseases and NFE2L2 mutations lead to cancer development.

Kategorie: Poster

Poster 122:

Titel:Gelsolin affects the differentiation of human corneal fibroblasts into myofibroblasts

Autoren:Schroeder H.(1),Wittmann J.(1),Hampel U.(1),Garreis F.(1),Milczarek A.(1),Schob S.(1),Braeuer L.(1),Paulsen F.(1),Schicht M.(1),

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Abstract

Introduction: Gelsolin (GSN) is known to be an actin filament severing and capping protein that contributes to cytoskeletal remodeling during growth and apoptosis. TGF-β, a secreted multifunctional protein, is known to induce the expression of GSN and to play a role in cellular differentiation.

Objective: The objective of this study is to investigate the influence of recombinant Gelsolin (r-GSN) on the differentiation of human corneal fibroblasts into myofibroblasts with regard to better understand epithelial wound healing processes.

Methods: Human corneal fibroblasts were obtained from human corneal tissue in the context of transplant surgery. Primary cells were cultured and subsequently stimulated with TGF-β and/or r-GSN. Additional knockdown experiments with GSN targeted siRNAs were used in order to determine the influence of endogenous GSN *in vitro*. Differentiation was analyzed by determination of cellular actin by means of Western blot analysis, immunohistochemistry and RT-qPCR.

Results: GSN influences the TGF-β dependent differentiation of corneal derived human fibroblasts into myofibroblasts *in vitro*. These effects are enhanced after combination of TGF- β and r-GSN. In contrast, the knockdown of GSN using siRNA leads to a decreased cellular differentiation, which is reversible by application of r-GSN.

Conclusion: Our results reveal that GSN affects the differentiation of human corneal fibroblasts into myofibroblasts and thereby may possibly contribute to wound healing processes of the ocular surface *in vivo*.

Kategorie: Poster

Poster 123:

Titel:Anti-inflammatory and barrier-stabilizing effects of anthocyanidins on the brain microvascular endothelial cell line cend

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Abstract:
Delphinidin, one of the major anthocyanidins present in berry fruits, has been shown to possess strong antioxidant and anti-inflammatory effects. Tumor Necrosis Factor alpha (TNF alpha) induces inflammatory cytokine production and impairs blood-brain barrier (BBB) integrity. We examined the effects of delphinidin on barrier properties in mouse cerebral microvascular endothelial cells (cEND) after TNF alpha treatment. The expression of proinflammatory cytokines, monocyte chemotactic protein-5 (MCP-5/Ccl7) and Ccl12 as well as tight junction protein claudin-5 and occludin were determined by quantitative real time PCR and Western blot. The effects of delphinidin were compared with effects of potential anti-inflammatory agent, synthetic glucocorticoid dexamethasone. Delphinidin significantly suppressed the TNF alpha - induced expression and secretion of Ccl7 and Ccl12 in cEND, which was comparable with the effects of dexamethasone. Interestingly, delphinidin induced the expression of claudin-5 in cEND, which resulted in lower permeability and higher electrical resistance of endothelial monolayer treated with delphinidin. In conclusion, TNF alpha induces inflammatory cytokine production at the BBB and destroy the barrier properties. Addition of delphinidin attenuated these effects to the extent comparable with dexamethasone. These data indicate that delphinidin has a therapeutic potential for endothelial inflammation in the brain.

Kategorie: Poster

Poster 124:

Titel:Optimized Human Intervertebral Disc De- and Rezellularization using Allogeneic Disc Cells or Mesenchymal Stromal Cells

Autoren:Zhao H. (1,2), Kohl B. (1),Schulze-Tanzil G.(2),

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Abstract:
Objective: Intervertebral disc (IVD) degeneration is a frequently encountered, clinically important disorder in the aging population. The IVD consists of a mostly fibrocartilaginous extracellular matrix (ECM) occupied by nucleus pulposus cells (NPCs) and annulus fibrosus cells (AFCs). So far, there is no artificial scaffold manufactured from either natural, synthetic or composite polymers that can mimic all aspects of IVD unique biomechanics. An allogenic native IVD tissue ECM devoid of immunogenic cell components could present an versatile tissue engineering-based approach.
Methods: IVDs were obtained during spine surgery in 6 patients. Mesenchymal stromal cells (MSCs) and IVD cells were respectively isolated from 6 different human femoral heads or IVDs. The decellularization protocol was based on mechanical/physical treatment (6 freeze-thaw cycles), detergents (2% SDS and Triton X-100) and enzymatic decellularization (0.25% trypsin). Scaffolds were subsequently analyzed for effective cell-removal and ECM alterations by histology and biochemical assays. Moreover, we adopted an innovative way for recellularization preconditioning, utilizing bovine serum albumin (BSA) to decrease SDS toxicity. Afterwards, MSCs (chondrogenically induced or undifferentiated) and human IVD cells were dynamically reseeded on the cell-free ECM scaffolds in vitro for 14 days. Recellularized scaffolds were analyzed using vitality assays to detect cyto-compatibility of the ECM, histology and biochemical assays for measurements of DNA content, glycosaminoglycans (GAG), and total collagen. Statistical analysis was performed using the ordinary one-way ANOVA and Tukey's test (n=6). $P<0.05$ was considered significant.
Results: After decellularization, HE, Alcian blue (AB) and DAPI stainings revealed few discernible nuclei in the decellularized scaffolds compared to the native tissue. After 14 days recellularization, live-dead cells assay demonstrated that the majority of MSCs and IVD cells survived after 14 days of culture; HE, AB and DAPI stainings indicated that the recolonized cells were more evenly distributed on the surface of the scaffolds than in the inner part for both MSCs and IVD cells. The inner part of the scaffold was only poorly infiltrated by cells. Scaffolds recellularized with IVD cells contained significantly more DNA than all other groups ($p<0.01$). There was a significantly increased total collagen content in the chondrogenically induced MSCs group ($p<0.01$) compared with native IVD, cell-free and IVD cell seeded scaffolds; meanwhile, the GAG content in the native tissue was significantly higher compared to the other groups except for the induced MSCs group ($p<0.05$).
Conclusion: Our modified decellularization protocol was effective to prepare mostly cell-free IVD-derived scaffolds. These decellularized IVD scaffolds are suitable for further tissue engineering applications, as they proved their cyto-compatibility by successful recolonization with MSCs and IVD cells.

Kategorie: Poster

Poster 125:

Titel:In vitro effects of sex hormones and retinoic acid derivates in human meibomian gland epithelial cells.

Autoren: Garreis F.(1),Schroeder A.(1),Abrar D.(1),Hampel U.(1),Fischer M.(2),Paulsen F.(1),

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Abstract:
Meibomian gland dysfunction (MGD) is considered the most common cause of dry eye disease. MGD is caused primarily by terminal duct obstruction due to hyperkeratinization of the ductal epithelium and an increase in meibum viscosity. Sex hormones and retinoic acid derivates are well-known risk factors of MGD. However, the molecular mechanisms that underlie this process are unknown. The effect of dihydrotestosteron (DHT), estradiol (β-Est) and all-trans retinoic acid (ATRA) in an immortalized human meibomian gland epithelial cell line (HMGEC) was evaluated. Ultrastructural morphology, Sudan III lipid staining, cell proliferation as well as vitality assays were performed. Expression of markers of keratinization (hornerin, involucrin and CK6), proliferation (CK5 and CK14) and lipid synthesis (fatty acid synthase and stearoyl-CoA desaturase) were analyzed by realtime RT-PCR and western blot. Furthermore, MGD-associated calcium regulation was investigated by fura-2-based microfluorimetry. In HMGEC ATRA decreases gene expression of proliferation markers (CK5 and -14) and increases gene expression of keratinization markers (HRNR, IVL and CK6). Additionally, ATRA inhibits cell proliferation. DHT and β-Est induce gene expression of keratinization markers but do not influence cell proliferation. Interestingly, HMGEC cultivated in serum and without serum show significant differences in the gene expression. ATRA but not DHT and β-Est induce intracellular calcium influx.In HMGEC DHT, β-Est as well as ATRA alter gene expression of MGD associated markers and promote keratinization process. Further studies are necessary to analyze (hyper) keratinization processes in cultivated HMGEC in detail.

Kategorie: Poster

Poster 126:

Titel:Selenite partly inhibits the pro-inflammatory effects of tumor necrosis factor alpha in meniscal tissue

Autoren:Haefelein K.(1),Preusse-Prange A.(1),Behrendt P.(2),Kurz B.(1),

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Abstract:
Introduction: Chronic joint inflammation can lead to cartilage destruction and meniscal degeneration. Since protective effects of selenite on hyaline cartilage are well described, but little is known about the effects on meniscal tissue, we investigated the influence of sodium-selenite on menisci in a simulated inflammation in vitro-model by using the pro-inflammatory cytokine tumor necrosis factor alpha (TNF-alpha). Material and methods: Meniscal explant disks (3 mm diameter x 1mm thickness) were isolated from 2-year-old cattle. After 3 days of TNF-alpha- (10ng/ml) and sodium-selenite-treatment (low-dose 6,7ng/ml; high-dose 100ng/ml) glycosaminoglycane (GAG) release (DMMB assay), nitric oxide (NO) production (Griess assay), gene expression of matrix-degrading enzymes (quantitative RT-PCR) and number of cells showing signs of apoptosis (nuclear blebbing) were determined. Results: TNF-alpha induced a significant release of GAG as well as production of NO. Low-dose-selenite significantly decreased the TNF-alpha-induced GAG release almost entirely and the TNF-alpha-induced NO production by one third. TNF-alpha increased transcription levels significantly of matrix metalloproteinase (MMP)-3 and a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS)-4 22.7-fold and 9.1-fold, respectively, whereas Aggrecan transcription levels decreased TNF-alpha-dependent (0.54). Low-dose-selenite decreased significantly the TNF-alpha-induced MMP-3 increase by 40%. Low-dose-selenite showed a tendency to reduce the significant 4.5-fold TNF-alpha-induced increase of apoptosis, whereas high-dose-selenite showed no effect. Conclusions: Our study shows that sodium-selenite in a low-dose can partly inhibit the inflammatory effects of TNF-alpha on meniscal tissue. To further investigate the molecular mechanisms of the protective qualities of selenite in the meniscus future studies are required.

Kategorie: Poster

Poster 127:

Titel:Influence of tensile strain and growth and differentiation factors on extracellular matrix production of mesenchymal stem cells

Autoren: Bernhardt C.(1),Heimann M.(1),Rauschenbach C.(2),Mazurek S.(2),Arnhold S.(1),

Adressen:(1)Institute of Veterinary Anatomy, Histology and Embryology|Justus Liebig University Giessen|Giessen|Germany; email:Carolin.Bernhardt@vetmed.uni-giessen.de; (2)Institute of Veterinary Physiology and Biochemistry|Justus Liebig University Giessen|Giessen|Germany

Abstract:
Tendon injuries are a common health problem in sport horses that cause long convalescence time and often are followed by relapses. Because of the poor healing capacities of the cell arm tendon tissue one way of treatment is the implantation of mesenchymal stem cells (MSC) into tendon defects. The injected stem cells are supposed to help rebuild functionally working tissue and so lower the rate of relapses. These multipotent mesenchymal stem cells can be isolated from different tissues. Most commonly used sources are bone marrow and adipose tissue. A capability for multilineage differentiation characterizes these cells. To improve the effectiveness of stem cell treatment we look for ways to predifferentiate MSCs into tenogenic direction so they may take over extracellular matrix production after implantation. To this end we examine the effects of different treatments in vitro on adipose tissue derived MSCs. We compare the effects of cyclicly applied biomechanical strain, which is supposed to simulate the natural effect of load on tendon tissue, with the effects of different media components as well as growth and differentiation factors on the cells. The changes in gene expression and extracellular matrix production are evaluated by quantifying RT-PCR, western blot analysis and immunofluorescence staining. So far we observed that biomechanically induced cells orientate themselves parallel to strain direction and elongate. Cells cultivated with differentiation medium form three dimensional cell structures that resemble tendon tissue after one week of cultivation. Preliminary PCR results suggest a higher extracellular matrix production under the influence of GDF 7.

Kategorie: Poster

Poster 128:

Titel:Changes in gene expression and morphology in a dry eye mouse model

Autoren:Schroeder A.(1),Garreis F.(1),Hampel U.(2),Funke S.(3),Paulsen F.(1),

Adressen:(1)Department of Anatomy II|Friedrich Alexander University Erlangen-Nuernberg|Erlangen|Germany; email:antje.schroeder@fau.de; (2)Department of Anatomy II|Friedrich Alexander University Erlangen-Nuernberg|Erlangen|Germany; (3)Experimental Ophthalmology|Johannes Gutenberg University|Mainz|Germany

Abstract:
Purpose: Hyperkeratinization of the meibomian gland ductal epithelium is thought to be a central mechanism in the development of meibomian gland dysfunction (MGD), the main cause of evaporative dry eye. So far, the underlying pathological mechanisms are unknown. By establishing a dry eye mouse model we analyzed changes in morphology and gene expression in tissues of the lacrimal system. Methods: For dry eye mouse model pumps filled with 0,9% NaCl (control) or scopolamine (dry eye) were implanted subcutaneously in female C57/BL6 mice. Dry eye mice were housed under low humidity and constant air flow, controls under standard conditions. After 10 days tear fluid collection, Schirmer tests and fluorescein measurements were performed and eyes, lacrimal and meibomian glands were collected. Custom made arrays were used to analyze cytokine and MGD associated gene and protein expression. Morphology was determined by HE-staining. Results: Schirmer tests and fluorescein staining revealed a significant decrease in tear fluid as well as corneal damage in dry eye mice. Changes in cytokine expression pattern between both groups could not be observed. Even so, gene expression pattern did not differ significantly in meibomian and lacrimal glands. HE sections showed no morphological difference. Slight differences concerning tear-related proteins could recently be shown by proteomic analysis. Conclusion: Even if the investigated dry eye mouse model apparently did not show any changes in the expression pattern in meibomian or lacrimal glands, it could be demonstrated that a dry eye phenotype could be induced in mice, providing a potential model for therapeutic approaches.

Kategorie: Poster

Poster 129:

Titel:Silica-collagen-nanocomposits and mesenchymal stem cells for bone tissue engineering in the systemic diseased bone

Autoren: Baulig N.(1),Heimann M.(1),Hanke T.(2),Wenisch S.(3),Arnhold S.(1),

Adressen:(1)Department of Veterinary Anatomy, -Histology and -Embryology|University of Giessen|Giessen|Germany; email:nadine.baulig@vetmed.uni-giessen.de; (2)Institute of Material Science|TU Dresden|Dresden|Germany; (3)Department of Veterinary Clinical Sciences, Small Animal Clinic c/o Institute of Veterinary Anatomy, -Histology and -Embryology|University of Giessen|Giessen|Germany

Abstract:
Osteoporosis is one of the most important diseases from elderly patients with a rapidly increasing prevalence. It is defined by loss of bone mass and deterioration of the bone microarchitecture with a high risk of pathological fractures. Because of the still existing lack of efficient and cost-effective treatment of these fractures further research in this field is absolutely essential. Bone tissue engineering by combining MSCs and a new silica - collagen – nanocomposition (B-30) seems to be a promising therapeutic approach to improve the healing tendency of systemic diseased bone by covering critical sized bone defects. The aim of this study is to investigate the interaction between MSCs and this novel biomaterial. Thus, we compared MSCs from different species under two different culture conditions - a threedimensional static pellet culture and a non – static rotation culture. We investigated the cell - adherence, - proliferation and - differentiation capacity on the scaffolds using the MTT-Test, different staining procedures, scanning and transmission electron microscopy as well as life cell imaging. Furthermore, using RT-PCR we examined the cell characteristics including the expression of RANKL and OPG, which are known to play a key role in osteoporosis bone metabolism. The results show, that cells from all species are able to attach, proliferate and differentiate on B-30 under both culture conditions but to some extent with distinct characteristics. Our studies reveal, that the combination of stem cells and B-30 seems to be an auspicious way of bone tissue engineering if further modified and investigated.

Kategorie: Poster

Poster 130:

Titel:Tissue fixation disturbs the epitope availability for two anti-angiotensin ii receptor type i antibodies in ihc

Autoren: Pryymachuk G.(1),El-Awaad E.(2),Barham M.(1),Pietsch M.(2),Neiss W.(3),

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Abstract:
The angiotensin II type 1 receptor (AGTR1) is abundantly present in healthy liver and is described as a membrane protein. However, little is known about its exact distribution in hepatocytes and cholangiocytes. Difficulties in the detection of AGTR1 arise due to the poor specificity of several literature-known primary antibodies (Herrera, M., et al., Hypertension, 2013; 61:253-258). We have characterized the polyclonal anti-AGTR1 antibody sc-31181 mapping an epitope of 15-25 amino acids (AA) at the C-terminal region (AA 300-350) of AGTR1 for immunohistochemistry (IHC). For this purpose, we used HEK293 cells transiently transfected with an expression vector for Strep tag II-tagged AGTR1 as well as cryosections from murine, rat, porcine, feline and human liver. The plasma membrane of transfected HEK293 showed strong colocalization of Strep-tag II and AGTR1, while no staining was observed in both sham- and untransfected HEK293. All unfixed liver cryosections showed three distinctive types of staining patterns: diffusely distributed signals in interlobular arteries; honeycomb-like structures in cholangiocytes and tram tracks surrounding hepatocytes. In addition, detection of AGTR1 by IHC and Western blotting was dose-dependently reduced when sc-31181 was pre-incubated with increasing concentrations of the respective blocking peptide sc-31181p. The staining patterns were dramatically hampered by paraformaldehyde or methanol fixation in both transfected HEK293 and cryosections. A similar behavior was observed with another polyclonal antibody (ab59018) recognizing an internal sequence (AA 227-240) of AGTR1. We conclude that identification of AGTR1 in IHC does not only depend on epitope specificity of primary antibodies but also on tissue fixation and processing.

Kategorie: Poster

Poster 131:

Titel:Modulation of cross talk between cancer stem cells and fibroblasts in tumor microenvironment co-cultures by curcumin

Autoren: Buhrmann C.(1),Kraehe P.(1),Goel A.(2),Shakibaei M.(1),

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Abstract:
Objective: The tumor microenvironment is essential for up-keeping and promoting tumor cell proliferation, invasion and metastasis, which are all important factors for tumor malignity. In a 3D-co-culture model we investigated the crosstalk between colorectal cancer (CRC) cells with stromal fibroblasts (MRC-5) and the anti-cancer effects of curcumin or/and 5-Fluorouracil (5-FU), especially on epithelial-to-mesenchymal transition (EMT) and cancer stem cell (CSC) survival. Methods: High density tumor microenvironment mono-cultures of CRC cells HCT116 or co-cultures of HCT116 and MRC-5 were cultured with/without curcumin or/and 5-FU. Results: In high density tumor microenvironment co-cultures, synergistic cross talk between HCT116 and stromal fibroblasts, markedly increased tumor-promoting factors (NF-kappaB, MMP-13), TGF-beta3, enhanced CSC survival (characterized by up-regulation of CD133, CD44, ALDH1) and up-regulation of EMT-factors (increased vimentin and Slug, decreased E-cadherin) compared to HCT116 mono-cultures. These synergistic cross talk effects were even more pronounced in the presence of 5-FU, but decreased in the presence of curcumin or anti-TGF-beta. Finally, curcumin induced biochemical changes to mesenchymal-epithelial transition (MET), thereby sensitizing HCT116 to 5-FU treatment. Conclusion: Activation of CSCs, EMT and tumor-promoting factors in tumor microenvironment co-cultures was mediated, at least in part through TGF-beta. Modulation of this functional cooperation in co-culture by curcumin might be a potential therapy for CRC and suppress metastasis.

Kategorie: Poster

Poster 132:

Titel:Short-term stimulation of primary human epithelial cell proliferation by two different transient viral vector systems

Autoren: Donau J.(1),Lindemann D.(2),Funk R.(1),Valtink M.(1),

Adressen:(1)Anatomy|TU Dresden|Dresden|Germany; email:jennifer.donau@mailbox.tu-dresden.de; (2)Virology|TU Dresden|Dresden|Germany

Abstract:
Objective: Ectopic overexpression of Human Papillomavirus type 16 E6/E7 genes (E6E7) or Simian Virus 40 T-antigens (SV40Ts) leads to permanent proliferation in primary cells. In contrast, transient proliferation may be achieved by transgene expression from episomes of integrase-deficient, lentiviral vectors (IDLVs) or transgene-encoding mRNA delivered by enzymatically inactive Prototype Foamy Virus (PFV) particles. Methods: Human retinal pigment epithelium (RPE) cells were transduced in vitro with IDLVs and comparatively by PFV-mediated mRNA-transfer, for expression of either E6E7 or SV40Ts. Growth curves were recorded by calculating cumulative population doublings to determine transgene-induced proliferation. Uninfected cells, cells transduced with transgene-free vector particles and cells stably transduced with integration-competent lentiviral vectors for permanent transgene expression served as controls. Background integration of episomes was determined by recording mean fluorescence intensity of the marker gene EGFP. After transient transduction, senescent cells were identified by assaying ß-galactosidase. Results: Transduction with IDLVs encoding for either of the transgenes led to permanent stimulation of proliferation. E6E7 mRNA-transfer could stimulate proliferation and overcome cytotoxic side effects of PFV particle transduction, while SV40Ts mRNA-transfer-mediated stimulation failed to counteract cytotoxic effects. Conclusions: IDLVs show an integrase-independent integration capacity and are therefore not suitable for induction of transient proliferation. However, the mRNA-transfer system is capable of increasing proliferation of RPEs via transient delivery of E6E7 but not SV40Ts transcripts. Optimizing PFV particles by pseudotyping to overcome cytotoxic side effects of viral vector transduction may render PFV-mediated mRNA-transfer into a useful tool for transient stimulation of primary cell growth even with low-potential proliferation factors.

Kategorie: Poster

Poster 133:

Titel:The role of isoprostanes in the activation of vascular wall-resident stem cells

Autoren: Bauer J.(1),Benndorf R.(2),Frantz S.(3),Ergün S.(1)

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Abstract:
The vascular wall has been described to harbor local stem cells but less is known about the role of these cells in the context of myocardial infarction (MI). Isoprostanes are free radical-catalyzed products of unsaturated fatty acids and independent and cumulative marker of cardiovascular diseases. The aim of this study was to explore the role of cardiac vessel wall-resident stem cells under MI conditions and the influence of isoprostanes in this context. Using a murine model of acute MI, the expression pattern of stem cell as well as inflammatory markers was analyzed by immunostaining on paraffin sections of mouse heart tissue. These studies revealed an altered Post-MI expression of CD34, CD44 and c-Kit within the adventitia of coronary blood vessels of the infarcted area. Furthermore, immunhistochemical analysis revealed the presence of highly proliferative Ki67(+)/CD44(+)-cells in the vascular adventitia immediately after MI. A part of these cells was also positive for the inflammatory markers IL-10 and iNOS, respectively. As analyzed by ex vivo cardiac angiogenesis assay, in vivo application of isoprostanes significantly reduced the sprouting capacity of cardiac tissue pieces accompanied by an isoprostane-dependent modulation of the amount of cardiac CD34(+) and CD44(+) cells. In summary, our results indicate that the coronary vascular adventitia serves as an immediate reservoir for CD34(+) and CD44(+) stem cells and a subset of CD44(+) coronary vessel-derived cells display an inflammatory phenotype under MI conditions. The activation/mobilization of these stem cells is affected by isoprostanes, which might affect cardiac angiogenesis under hypoxic conditions such as MI.

Kategorie: Poster

Poster 134:

Titel:Egfr-dependent regulation of the human na-d-glucose cotransporter sglt1

Autoren:Veyhl-Wichmann M.(1),Gorboulev V.(1),Erguen S.(1),

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Abstract:
Expression of the Na-D-glucose cotransporter1 (SGLT1) and the epidermal growth factor receptor (EGFR), a receptor tyrosine kinase associated with cell proliferation and survival, is increased in many tumours of epithelial origin. EGFR binds to SGLT1 and stabilizes its expression to promote glucose uptake independent to its kinase activity. Here, we characterized SGLT1-EGFR interaction in detail applying the *Xenopus laevis* oocyte expression system. The affinity of transport of alpha-methylglucose (AMG), a SGLT-specific substrate, was significantly increased in the presence of co-expressed EGFR (SGLT1: K_m ~ 0,470 mM ± 0,052 mM; SGLT1 + EGFR: K_m ~ 1,7 mM ± 0,23 mM) implicating a direct protein interaction. Transport affinities of the organic cation transporter1 and the concentrative nucleoside transporter1 were not modulated by coexpression with EGFR.
The dependency of SGLT1-mediated transport on phlorizin, a specific SGLT1 inhibitor, remained unchanged in the presence of EGFR. However, after EGFR-activation, the influence of phlorizin on SGLT1 transport activity was significantly decreased, due to reduced affinity of phlorizin (SGLT1: IC_{50} ~ 50 nM ± 19 nM; SGLT1 + EGFR: IC_{50} ~ 1,3 µM ± 0,32µM). This implies that the phlorizin binding site within the SGLT1-EGFR complex is modulated by EGFR activation. Nevertheless, EGFR-activation did not alter observed decreased AMG transport affinity despite of reduced phlorizin affinity.
Long term EGF incubation induced EGFR internalization (unpublished data) and the release of interacting SGLT, resulting in SGLT1-typical transport properties.
Our data suggest that SGLT1-EGFR interaction, its regulation and influence on glucose metabolism might be a novel target in cancer therapy.

Kategorie: Poster

Poster 135:

Titel:Extracellular calcium as a modulator of osteogenic differentiation of human mesenchymal stromal cells via connexin 43

Autoren: Wagner A.(1),Mazurek S.(2),Arnhold S.(3),Wenisch S.(4),

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Abstract:
Calcium plays an important role in bone remodeling. It is known that extracellular calcium ions (Ca2+) promote osteogenic differentiation of stromal cells. Furthermore, calcium has the capability to stimulate Connexin 43-mediated gap junctional communication. By means of an in vitro approach we aim to elucidate the question whether extracellular calcium stimulates osteogenic differentiation via the gap junctional protein Connexin 43. For this approach, mesenchymal stromal cells, isolated from human cancellous bone were cultured at different calcium concentrations (0; 1.8; 10; 20 mmol l-1) on tissue culture plates (TCP) in osteogenic medium and in basal medium without any osteogenic supplements. After 21 days of cultivation, cell responses to the different conditions were evaluated by Life-Cell-Imaging, von Kossa-Staining and quantitative RT-PCR. Furthermore, immunohistochemistry and Lucifer Yellow dye uptake were performed in order to study spatial distribution of connexin 43 and the appropriate gating mechanism in vitro . The results show, that high extracellular calcium concentrations stimulate Connexin 43 expression as well as the expression of the osteogenic marker Bone Sialoprotein. Moreover, cell migration and mineralization of the extracellular matrix were more pronounced when the cells were cultured in combination with high extracellular calcium concentrations. The extracellular calcium in turn induces opening of connexin 43 based hemichannels as shown by the uptake of Lucifer Yellow. Based upon the results, it can be concluded, that increasing levels of extracellular calcium stimulate osteogenic differentiation via the gap junctional protein Connexin 43.

Kategorie: Poster

Poster 136:

Titel:3d-printed strontium doped scaffolds enhance angiogenesis during critical size bone fracture regeneration

Autoren:Heigl T.(1),Diederichs S.(1),Kloss K.(1),Bergmann C.(1),Pape H-C.(1),Lichte P.(1),Sönmez T.(1),Fischer H.(1),Pufe T.(1),Tohidnezhad M.(1),

Adressen:(1)Institut für Anatomie und Zellbiologie|Uniklinik RWTH Aachen|Aachen|Deutschland; email:theigl@ukaachen.de

Abstract:
Background:
Large bone defects still challenge the orthopaedic surgeon. Vascularity at the fracture site has an important influence on the healing procedure. Vascular endothelial growth factor (VEGF) and it`s receptor (VEGFR2) are potent inducers of angiogenesis during fracture healing. Aim of the present study was the investigation of critical size fracture (CSF) healing in VEGFR2-luc mice using tailored scaffolds.
Methods:
CSFs were performed and stabilized in mouse femur using an external fixator. The fracture was bridged using a 3D printed scaffold with defined porosity to promote regeneration. The beta-tricalciumphosphate (beta-TCP) and strontium doped beta-tricalciumphosphate (beta-TCP+Sr) scaffolds were investigated for their regenerative potential. The expression levels of VEGFR2 were monitored non-invasively via in vivo bioluminescence imaging for 2 months. Subsequently, a histological endpoint analysis to assess the scaffold induced tissue regeneration was performed.
Results:
Bioluminescence signal levels of VEGFR2 expression were significantly higher in the beta-TCP+Sr group when compared to the beta-TCP, control and sham group. Both types of scaffolds significantly enhanced new bone formation when compared to the sham group. The beta-TCP+Sr scaffolds showed a significantly greater regenerative potential.
Conclusions:
This standardized defect model mimics a clinically relevant situation to study the regenerative effects of biomaterials on bone. Additionally, the usability of our method for longitudinal fracture healing studies is affirmed. Moreover, it could be shown that strontium does have an enhancing effect on bone regeneration. Consequently, strontium doped scaffolds might be a useful addition in the surgeon’s spectrum of methods.

Kategorie: Poster

Poster 137:

Titel:Differential claudin expression in the endolymphatic sac and duct

Autoren: Runggaldier D.(1),Neckel P.(1),Wolburg H.(2),Mack A.(1),Hirt B.(1),Gleiser C.(1),

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Abstract:
The endolymphatic sac (ES) and the endolymphatic duct (ED) form an extension of the membranous labyrinth in the inner ear and are thought to be involved in the regulation of the endolymphatic ion and fluid homeostasis. It is widely believed that its dysfunction might lead to inner ear diseases such as Meniere's disease (MD). However, little is known about the epithelial barrier that separates the endolymph fluid space from the surrounding extracellular fluid space. In this study we identified and characterized tight junction molecules expressed in the ES and ED. A qPCR screen for claudin family members revealed the specific mRNA expression of claudin 3, 4, 6, 7, 8, 10 and 16. By using immunhistochemical analysis of whole mount preparations and tissue sections of the ES and ED we could further confirm the protein expression of the identified claudins in specific parts of the endolymphatic epithelium. Further, the evaluation of the subcellular localization of claudin 3 showed differences in the subcellular distribution in the ES and ED. The anti-diuretic hormone (ADH) is suggested to be involved in inner ear fluid and ion homeostasis. We could observe an effect of ADH on the subcellular claudin distribution which could provide a potential regulation mechanism of the epithelial barrier.

Kategorie: Poster

Poster 138:

Titel:Identification of cholinergic chemosensory cells in mouse tracheal and laryngeal glandular ducts

Autoren: Krasteva-Christ G.(1),Soultanova A.(2),Schuetz B.(3),Papadakis T.(2),Weiss C.(2),Deckmann K.(2),Chubanov V.(4),Gudermann T.(4),Voigt A.(5),Meyerhof W.(5),Boehm U.(6),Weihe E.(3),Kummer W.(2),

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Abstract:
In the last years, specialized cholinergic chemosensory (â€œtasteâ€•) epithelial cells were identified in several organs beyond the gustatory system, e.g. urethra, thymus, thyroid gland, heart, auditory tube, airways and lung. In the airways, nasal solitary chemosensory and tracheal brush cells are important for sensing of potentially dangerous substances incl. bacteria, and for initiation of protective reflexes. Although the ciliated duct is lined by respiratory epithelium, the presence of brush cells has not yet been described. Utilizing two different reporter mouse strains for expression of choline acetyltransferase (ChAT), the synthetizing enzyme of acetylcholine (ACh), we investigated for the presence of cholinergic cells in the submucosal glands of the murine larynx and trachea. Cholinergic cells were observed in the ciliated glandular ducts and were neither found in the collecting ducts nor in alveolar and tubular segments of the glands. Expression of ChAT in tracheal gland ducts was confirmed by in-situ-hybridization. The cholinergic duct cells showed expression of brush cell marker proteins, villin and cytokeratin-18, and were immunoreactive for components of the taste transduction cascade (Galpha-gustducin, transient receptor potential melastatin-like subtype 5 channel = TRPM5, phospholipase Cbeta2), but not for carbonic anhydrase IV. Furthermore, these cells expressed the bitter taste receptor Tas2r131, as demonstrated utilizing an appropriate reporter mouse strain. Our study identified a previously unrecognized presumptive chemosensory cell in the duct of the airway submucosal glands that likely utilizes ACh for paracrine signaling. We propose that this cell participates in infection-sensing mechanisms and initiates responses assisting bacterial clearance from the lower airways.

Kategorie: Poster

Poster 139:

Titel:A valvular adrenomedullin/intermedin/calcitonin gene-related peptide signaling system in the mouse and human heart

Autoren: Pfeil U.(1),Bharathala S.(2),Murtaza G.(3),Mermer P.(1),Boening A.(4),Kummer W.(5),

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Abstract:
Heart valves are highly organized structures with an endothelial lining and a connective tissue matrix containing different types of valvular interstitial cells (VIC). These VIC play an important role in maintaining the structural integrity of the heart valve, thereby affecting heart valve function and extracellular matrix remodelling. Activation of fibroblasts and differentiation to contractile myofibroblasts is a key step in the onset of fibrotic disorders. Accumulating evidence suggests an important role of the calcitonin receptor-like receptor (CRLR) pathway in preventing heart damage under several pathological conditions. Here we investigated the presence of a CRLR signaling pathway in human and mouse heart valves by immunofluorescence, NADPH-diaphorase histochemistry, RT-PCR, and laser-assisted microdissection with subsequent RT-PCR. Mouse and human heart valves expressed mRNAs for adrenomedullin (AM), intermedin (IMD), calcitonin gene-related peptide (CGRP), and for their receptor components CRLR and receptor activity-modifying proteins (RAMP) 1-3. Immunofluorescence analysis showed AM, IMD, and CRLR positive VIC, whereas CGRP-immunoreactivity was restricted to nerve fibers at the valve root and some endothelial cells lining the heart valves. Demonstration of NOS activity by NADPH-diaphorase histochemistry showed different results in mouse and human aortic valves. In mouse, staining was limited to the endothelial cell layer surrounding the valve leaflet with a more prominent staining of the aortic side, whereas in human, smooth muscle cells and VIC display NOS activity. Our results demonstrate the presence of an intrinsic ADM/IMD/CGRP signaling pathway in murine and human heart valves suggesting an involvement in regulation of valvular extracellular matrix production and turnover.

Kategorie: Poster

Poster 140:

Titel:Influence of dendritic polyglycerol sulfates on knee osteoarthritis: an experimental study in the rat model

Autoren: Schneider T.(1),Welker P.(2),Licha K.(2),Haag R.(3),Schulze-Tanzil G.(4),

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Abstract:
Background: Anti-inflammatory nanoparticular compounds could represent a strategy to diminish osteoarthritis (OA) progression. The present study was undertaken to prove the up-take of nanoparticular dendritic polyglycerol sulfates (dPGS) by rat-derived articular chondrocytes and to answer the question of whether dPGS could modulate knee joint inflammation and cartilage degradation in a rat OA model. Methods: dPGS uptake and cytotoxicity was assessed in cultured primary rat-derived articular chondrocytes. Subsequently, OA was induced in the right knee joints of 12 male Wistar rats by medial collateral ligament and meniscus transection. Unoperated left knees remained as controls. Six weeks post surgery six rats were either treated daily (14 days) with 30 mg/kg dPGS (s.c.) or a similar volume of PBS. Animals were analyzed clinically for gait alterations. Explanted knee joints were studied histologically using OA scores according to Mankin (1971) & Glasson et al., (2010). Liver, spleen and kidneys were analyzed for degenerative changes due to dPGS accumulation. Results: dPGS was rapidly taken up by the chondrocytes. Whereas no significant clinical signs of OA could be detected, at the histological level, all operated rat knee joints revealed features of OA in the medial compartment. The values produced by both OA score systems were lower in rats treated with dPGS compared with saline-treated animals. Synovitis score did not significantly differ between the groups. The analyzed organs revealed no degenerative changes. Conclusion: The results indicate overall biocompatibility and first signs of chondroprotective properties of dPGS in the osteoarthritic knee joint.

Kategorie: Poster

Poster 141:

Titel:Aqp4 formation into orthogonal arrays of particles is independent from aqp4 anchoring via the dystrophin-associated protein complex in the rat and human cochlea.

Autoren: Wagner A.(1),Gleiser C.(2),Garcia Pradas L.(1),Wolburg H.(3),Mack A.(1),Hirt B.(1),

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Abstract:
Aquaporin-4 (AQP4) is the primary water channel expressed in the epithelial supporting cells (SCs) of the cochlea. The maintenance of water homeostasis via AQP4 during auditory sensory transduction is essential for hearing. AQP4 is a component of orthogonal arrays of particles (OAPs), which are seen in cell membranes by freeze-fracture electron microscopy. In contradiction to the glia cells in the CNS and retina the distribution of AQP4 does not completely coincide with distribution of OAPs in the SCs of the cochlea. The biological significance of OAP formation by AQP4 is unknown, though it has been proposed that the dystrophin-associated protein complex (DAPC) play a central role in the formation of AQP4 into OAPs in glia cells. The present study was initiated in order to resolve the role of the DAPC for the AQP4 formation into OAPs in the rat and human cochlea. Through a combination of real-time PCR, immunohistochemical analysis and immunoprecipitation, we demonstrated that AQP4 is anchored to the membranes of the SCs in the rat and human cochlea by all transmembrane, intra- and extracellular members of the DAPC. AQP4 and the DAPC members were also expressed in Claudius cells which are avoid of OAPs and therefore it seems that the formation of AQP4 into OAPs is independent from the AQP4 anchoring via the DAPC in the cochlea. These findings provide new indications for the function and significance of the AQP4 formation and anchoring mechanism.

Kategorie: Poster

Poster 142:

Titel:Heterogeneity in the human adult dental pulp stem niche

Autoren: Patroi E.(1),Manoiu V.(2),Didilescu A.(3),Rusu M.(4),

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Abstract:
Adult stem cells (SCs) are found in most tissues throughout the human body. The SCs niches, firstly described by Schofield (1978), house heterologous cell types as well as committed SC progeny which join the niche to regulate homeostasis. Dental stem cells are novel targets as a source of stem cells for research as they could be the most viable alternative to the current population since it is only now that umbilical cord blood cryopreservation is gaining momentum. We performed a combined study of adult dental pulp SCs, by immunohistochemistry and transmission electron microscopy (TEM). There were used primary antibodies against CD10, CD31, CD34, CD44, CD117/c-kit, CD105, Ki67, Stro-1, and nestin. Stromal networks were built up by fibroblastoid cells which expressed, c-kit, nestin, CD10 and CD44, but not CD34 or CD45. Ki67 expressing cells were scarce. In the pulp mantle the expression of CD105 and Stro-1 was heterogeneous, suggesting a mixed population of signet ring-like mesenchymal SCs and committed progenitors. In TEM there were confirmed the pulp stromal networks. These were embedding quiescent SCs, some of which were seemingly derived from pericytes. Cells with long and thick prolongations with an almost exclusive content of intermediate filaments and mitochondria were assumed being progenitor cells constantly neighboring or contacting SCs. Thus, the dental pulp stem niche equally houses stem and progenitor cells, these later building stromal networks. They are difficult, if not impossible, to be distinguished by specific markers, although nestin expression could indicate osteogenic progenitors. Project POSDRU/159/1.5/S/141531 (author #1).

Kategorie: Poster

Poster 143:

Titel:Changes in gene expression during neuroendocrine differentiation of pca cell line lncap reveal new microrna target genes

Autoren: Wiesehoefer M.(1),Szczyrba J.(1),Wennemuth G.(1),

Adressen:(1)Department of Anatomy|University Clinic Essen|Essen|Germany; email:marc.wiesehoefer@uk-essen.de

Abstract:
Prostate carcinoma (PCa) is still a leading cause of cancer related death in men worldwide. This tumor entity contains foci of neuroendocrine transdifferentiation, resulting in an increase of androgen-independent neuroendocrine-like (NE) tumor cells, whose number significantly correlates with tumor aggressiveness and a lower survival rate. NE-like tumor cells do not respond to common PCa therapies and secrete, according to normal NE cells, a variety of diverse neuropeptides which have mitogenic effects on adjacent cancer cells. However, the mechanism of neuroendocrine transdifferentiation and a possible role of microRNAs during this process have not been clarified yet. MicroRNAs are small non-coding RNAs which posttranscriptionally regulate gene expression and which are involved in tumor development and progression as oncogenes or tumor suppressors. To investigate the expression changes of mRNAs and microRNAs and their role in neuroendocrine transdifferentiation, we differentiated LNCaP prostate cancer cells by androgen deprivation and performed Micro-Array analysis, obtaining highly modified mRNA and microRNA expression profiles for transdifferentiated LNCaP cells compared to untreated LNCaP cells. These Micro-Array results have further been validated for the most deregulated mRNAs and microRNAs via qRT-PCR and analyzed with different algorithms to predict new targets for the deregulated microRNAs involved in neuroendocrine transdifferentiation. In subsequent luciferase reporter assays we could confirm TGF-beta2, an induced mRNA, as a new target of miRNA-148a, which is downregulated during neuroendocrine differentiation. Our data demonstrate wide changes in mRNA and microRNA expression during neuroendocrine transdifferentiation of LNCaP cells and confirm new mRNA-microRNA interactions with potential roles in NE-transdifferentiation of prostate carcinoma.

Kategorie: Poster

Poster 144:

Titel:Pemphigus autoantibodies induce blistering in cultured human conjunctiva

Autoren: Vielmuth F.(1),Waschke J.(1),Spindler V.(1),

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Abstract:
Pemphigus vulgaris (PV) is a severe autoimmune disease in which autoantibodies directed against the desmosomal adhesion molecules desmoglein (Dsg) 1 and 3 lead to flaccid blisters of the skin and the squamous epithelia of the oral cavity. An ocular involvement in PV is also reported and is most frequently diagnosed as conjunctivitis. However, in pemphigus, infections typically occur as superinfection secondary to split formation. To test the hypothesis that, similar to the epidermis, the conjunctiva also is affected directly by autoantibody-induced intraepithelial separation, we used human conjunctiva biopsies acquired during surgical procedures or from body donors. The conjunctiva samples expressed the desmosomal plaque proteins desmoplakin and plakoglobin. In addition, all desmocollin isoforms (Dsc1-3) as well as Dsg1-3 were detectable. In a next step we took surgical biopsies into culture for up to 12h. Incubation of specimens with IgG-fractions of pemphigus vulgaris patients (PV-IgG) for 12h caused blistering in the suprabasal layers of the conjunctiva, resembling the effects of PV-IgG in the epidermis. Concomitantly, a reduction of Dsg1 and 3 levels was detectable. Next, we examined the activation of p38MAPK and its downstream target MK2, which is a central pathomechanism in PV. Interestingly, both molecules were clearly activated in our conjunctiva model, indicating similar mechanisms underlying blister formation in the epidermis and in the conjunctiva. Taken together, our data demonstrate a model system for investigations on human conjunctiva and indicate that the ocular involvement observed in PV patients is based on conjunctival blistering.

Kategorie: Poster

Poster 145:

Titel:The localization of alpha-adducin phosphorylated at a side typical for pka is functionally linked with the integrity of endothelial adherens junctions under inflammatory conditions

Autoren: Kugelmann D.(1),Waschke J.(1),Radeva M.(1),

Adressen:(1)Institute of Anatomy and Cell Biology, Department I|University of Munich|Munich|Germany; email:Mariya.Radeva@med.uni-muenchen.de

Abstract:
Adducins tightly regulate actin dynamics which is critical for endothelial barrier function. We reported previously that alpha-adducin is required for establishment of microvascular endothelial barrier properties. Here, we further investigated the role of adducin phosphorylation for endothelial barrier regulation by using microvascular human dermal and myocardial murine endothelial cells. Transendothelial electrical resistence (TER) measurements verified that endothelial barrier reorganization can be effectively modulated by altering Ca2+ concentration. Thus, in a first attempt junctional remodeling was induced by a Ca2+-switch assay. Ca2+-depletion reduced TER whereas Ca2+-repletion led to recovery of endothelial barrier properties reflected in increased TER. Interestingly, the Ca2+-dependent increase in TER was significantly reduced after siRNA-mediated alpha-adducin downregulation. Furthermore, immunostaining revealed that the peripheral localization not only of alpha-adducin but also for alpha-adducin phosphorylated at a side typical for PKA (pSer 481) is functionally linked with integrity of endothelial adherens junctions. Ca2+-depletion disturbed the linear distribution of vascular endothelial (VE)-cadherin, alpha-adducin and alpha-adducin (pSer 481) along cell junctions, whereas Ca2+-repletion restored the junctional localization pattern. Similarly, the endothelial breakdown induced by inflammatory mediators such as thrombin, LPS and TNFα was also paralleled by remarkable reduction of alpha-adducin and alpha-adducin (pSer481) at cell junctions. Taken together, our results indicate that alpha-adducin and its phosphorylation by PKA are maybe involved in remodeling of endothelial junctions and may also be compromised in endothelial barrier dysfunction under inflammatory conditions.

Kategorie: Poster

Poster 146:

Titel:Carl von kupffer: pioneer of liver anatomy

Autoren: Kurz B.(1),Luellmann-Rauch R.(1),Tillmann B.(1),

Adressen:(1)Anatomisches Insitut|CAU|Kiel|Germany; email:bntill@t-online.de

Abstract:
Internationally, the name Carl von Kupffer is associated with the anatomy of the liver. During his working period in Kiel (Germany) von Kupffer published his studies about the stellate cells in the liver ("Über Sternzellen der Leber") in the Archiv für mikroskopische Anatomie (1876). Due to the fact that he used different staining techniques but found putatively similar distributional patterns of stellate cells in the tissue von Kupffer was labouring under a misapprehension by thinking that he found one new type of cells. Today we know that these are two distinct cell types: the Kupffer cells (liver macrophages) and the stellate cells (also formerly Ito cells). The term "Kupffer'sche Sternzelle" (Kupffer's stellate cell) which is still often found in the text books, must be revised. The present medical historical work is a reminder of von Kupffer's achievements, the terminology, and the relevance of his findings regarding the functional anatomy and pathology of the liver. Interestingly, only four of von Kupffer's 66 publications deal with the structure of the liver. Von Kupffer's main research areas were comparative embryology and neuroanatomy. Additionally, von Kupffer's work as a pioneer in marine biology is being highlighted.

Kategorie: Poster

Poster 147:

Titel:Walther Flemming: founder of cytogenetics

Autoren: Kurz B.(1),Luellmann-Rauch R.(1),Tillmann B.(1),

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Abstract:
Despite his epochal findings the name of the anatomist Walther Flemming (1843-1905) is mostly unknown to scientists and physicians. Therefore, this medical historical presentation is a reminder of Walther Flemming's achievements and their relevance to modern cell biology and cytogenetics. Flemming was the first scientist showing the correct order of events in cell division; he coined the term "mitosis" and defined the term "chromatin" and is therefore seen as a founder of modern cytogenetics among experts. For his studies on cellular division Flemming introduced a new method by studying living tissues (for example gills or epithelium of the tail of larval salamanders). Additionally, Flemming discovered the germinal center in lymphatic organs and was the first who described a functional connection between mitosis and wound healing or epithelial regeneration. When studying spermatogenesis in the salamander he discovered the process of meiosis without using this term. Flemming identified adipose tissue as a sort of connective tissue and the intracellular lipid droplets as a product of the cellular metabolism. In his free time he also established a butterfly collection with over 4,000 specimens which he left to the Zoology Museum, Kiel, Germany.

Kategorie: Poster

Poster 148:

Titel:Expression and function of gpx-1 during endochondral ossification

Autoren: Roemer P.(1),Proff P.(1),Kirschneck C.(1),

Adressen:(1)Orthodontics|University Medical Centre Regensburg|Regensburg|Germany; email:piero.roemer@ukr.de

Abstract:
Objective: Chondrogenesis is an integral part of endochondral bone formation, by which the midline cranial base is developed. Reactive oxygen species (ROS) are required in chondrogenic differentiation and antioxidant enzymes regulate their levels. The aim of this study was to localize the antioxidant enzyme glutathione peroxidase 1 (Gpx1) at the spheno-occipital synchondrosis, as well as its effect on ROS challenge and its expression pattern in the course of differentiation. Materials and Methods: Gpx1 was semiquantified in immunohistochemically stained sections of spheno-occipital synchondroses of rats. The effect of Gpx1 on ROS-induced apoptosis was investigated by manipulating the expression of Gpx1 in ATDC5 cells. The temporal pattern of Gpx1 expression was determined during chondrocyte differentiation for 21 days in vitro. Results: Proliferating chondrocytes exhibited the greatest Gpx1 immunoreactivity and hypertrophic ones the lowest ($P = 0.02$). Cells transfected with Gpx1-siRNA had the highest apoptotic rate, while cells overexpressing Gpx1 the lowest one ($P < 0.001$). Gpx1 was significantly increased on days 10 ($P = 0.02$) and 14 ($P = 0.01$). Discussion: Hypertrophic chondrocytes have the lowest Gpx1 activity in the spheno-occipital synchondrosis. Gpx1 is implicated in the ROS-induced apoptosis in chondrocytes. Its expression was not constitutive during chondrogenic differentiation.

Kategorie: Poster

Poster 149:

Titel:Adiponectin regulates embryonic lipid metabolism in rabbit blastocysts

Autoren: Schindler M.(1),Pendzialek M.(1),Grybel K.(1),Guerke J.(1),Fischer B.(1),Navarrete Santos A.(1),

Adressen:(1)Department of Anatomy and Cell Biology|Martin Luther University Halle-Wittenberg Faculty of Medicine|Halle (Saale)|Deutschland; email:maria.schindler@medizin.uni-halle.de

Abstract:
We have recently shown that a maternal diabetes mellitus leads to a strongly increased level of intracellular lipid droplets in blastocysts. Also, adiponectin levels in embryos and mothers were increased. Adiponectin is a 26kDa peptide hormone. Its main function is maintenance of energy homeostasis. Several studies point to an important role of adiponectin in early embryo lipid metabolism. The object of current study was to find a potential link between adiponectin and the disturbed embryonic lipid metabolism in a diabetic pregnancy. Rabbit blastocysts were investigated under in vivo diabetic conditions and after in vitro culture with adiponectin (1µg/ml). Expression of molecules involved in lipid metabolism were analysed by qPCR and Western Blot. Adiponectin regulated p38MAPK phosphorylation in vivo and in vitro. A significant increased phosphorylation of acetyl CoA carboxylase (ACC) was detected, accompanied by an increased expression of CPT1, which is the key enzyme of beta-oxidation. Furthermore, expression of fatty acid transporters, FATP4 and CD36, was upregulated by adipoenectin. We show that a maternal diabetes mellitus leads to alterations in embryonic lipid metabolism very early in development and that adiponectin is a determining factor. Therefore, the observed increased intracellular lipid accumulation under diabetic developmental condition could be caused by the compensatory increased adiponectin levels.

Kategorie: Poster

Poster 150:

Titel:Investigating the role of atoh8 in developmental myogenesis, regeneration and myopathies

Autoren:Balakrishnan-Renuka A.(1),Boeing M.(1),Satya Srirama K.(1),Guettsches A.(2),Otto A.(3),Patel K.(3),Vorgerd M.(2),Brand-Saberi B.(1),

Adressen:(1)Anatomy and Molecular Embryology|Ruhr University Bochum|Bochum|Germany; (2)Neurologische Klinik und Poliklinik||Bochum|Germany; (3)School of Biological Sciences|University of Reading|Reading|United Kingdom

Abstract:
Multitudes of individuals are affected by skeletal muscle disorders in the form of embryonic and postnatal developmental defects, myopathies and volumetric muscle losses. Many of such situations become life threatening to the patient. Better understanding of the factors involved in the process of skeletal muscle development and regeneration will be crucial in improving the treatment methods for these issues. A bHLH transcription factor, ATOH8, has recently been identified to play a role in the development of skeletal muscles in vertebrates. ATOH8 has previously been implicated in the specification and differentiation of cell lineages in neurogenesis and in the development of kidney, pancreas and retina. We have shown that this protein is substantial for the regulation of myogenic progenitors during embryogenesis and myoblast differentiation in vitro. Furthermore, our clinical investigation showed that ATOH8 is expressed in the regenerating skeletal muscles of myopathic patients. In order to determine the exact dynamics of ATOH8 expression during skeletal muscle regeneration, we analyzed the co-expression of the protein and well studied myogenic markers (Pax7, Myogenin) in murine satellite cells in vitro. The results showed that the activated and proliferating satellite cells express ATOH8, whereas quiescent satellite cells and the cells that proceed towards terminal differentiation do not express the protein. Preliminary studies on ATOH8 knockout mice showed that these animals have reduced body weight and skeletal muscle cross-sectional area, compared to the wild-type animals. We have also observed that the efficiency of reprogramming in ATOH8 knockout adult fibroblasts is significantly lower than in wild-types.

Kategorie: Poster

Poster 151:

Titel:Connexin-mediated intercellular signalling via gap junctions is required for primitive endoderm formation

Autoren: Woersdoerfer P.(1),Frank E.(1),Klaus W.(2),

Adressen:(1)Institute of Anatomy and Cell Biology|Universität Würzburg|Würzburg|Germany; email:philipp.woersdoerfer@uni-wuerzburg.de; (2)Life & Medical Sciences Institute (LIMES)|University of Bonn|Bonn|Germany

Abstract:
A long-standing question in developmental biology is the role of gap junctional communication during early embryogenesis. Connexin(Cx)43 and Cx45 are expressed in mouse embryonic stem (ES) cells as well as in blastocyst stage embryos and contribute to formation of functional gap junctions. To elucidate the role of connexins during early lineage segregation and morphogenesis, we generated Cx43/Cx45 double deficient ES cells. These ES cells were cultured in floating three-dimensional aggregates, so called embryoid bodies (EBs). The EBs recapitulate early developmental steps, like primitive endoderm (PrE) formation as well as gastrulation-like events and can, therefore, serve as an in vitro model system for early embryonic development. Whereas pluripotency features appear to be unaffected by Cx43/45 ablation we found that the expression of these Connexins is required for the establishment of an organized layer of PrE, the initial step during EB differentiation. Defective PrE formation leads to a block in subsequent differentiation events e.g. germ layer specification. Lentiviral overexpression of either Cx43 or Cx45 rescues the observed phenotype, indicating both the specificity of the observation and a redundant function. Viral overexpression of the Oculodentodigital Dyplasia associated mutant Cx43 G138R in Cx43/Cx45 deficient ES cells indicates that functional gap junctional communication is required. We present evidence that intercellular transfer of Ca/IP3 is required for the formation of primitive endoderm and hypothesize that Calcineurin/NFAT signaling might be involved in downstream transcriptional regulation.

Kategorie: Poster

Poster 152:

Titel:Sox17 expression in precursors of primordial germ cells in the rabbit embryo.

Autoren: Pueschel B.(1),Viebahn C.(1),

Adressen:(1)Department of Anatomy and Embryology|Georg-August-University of Goettingen|Goettingen|Germany; email:bpuesch@gwdg.de

Abstract:
The precursors of primordial germ cells segregate early from the somatic cell lineage during embryonic development in all animal phyla. A combination of signals from extraembryonic and embryonic tissues specifies the area where primordial germ cell differentiation is initiated in mammals. Many molecular details of this process have been uncovered in the mouse and some of the key players were detected in other mammals as well. In the human, the Sry-related transcription factor Sox17 appears to be a key regulator during PGC specification - at least in vitro - acting upstream of Blimp1. Because this seems not to be the case in mice we analyzed the expression of Sox17 in the developing rabbit embryo to see whether Sox17 is an early germ cell marker in other mammals as well. A comparison of Blimp1 and Sox17 expression in in situ hybridized rabbit embryos revealed matching distribution of positive cells in the peripheral epiblast at the posterior margin of the embryonic disc, which – according to growth factor expression analysis – may also be considered to belong to extraembryonic parts of the embryo. We hypothesize that – similar to the situation in man - Sox17 may indeed be expressed in precursors of rabbit primordial germ cells. Whether Sox17 is acting upstream of Blimp1 in rabbit as well will be subject of future experiments.

Kategorie: Poster

Poster 153:

Titel:Tbx3 knockdown in somatic cells leads to decreased reprogramming efficiency

Autoren: Klingenstein M.(1),Raab S.(1),Achberger K.(1),Kleger A.(2),Liebau S.(1),Linta L.(1),

Adressen:(1)|Neuroanatomy and developmantal biology|Universität Tübingen|Tübingen|Germany; email:moritz.klingenstein@uni-tuebingen.de; (2)University Ulm|Internal medicine 1|Ulm|Germany

Abstract:
Objectives: The inner cell mass of early embryos can be isolated as embryonic stem cells (ESCs) and have the potential to proliferate and to differentiate into all three germ layers. The overexpression of specific factors leads to a reprogramming of somatic cells to induced pluripotent stem cells (iPSCs) which are like the ESCs pluripotent and have a high proliferative potential. T-box transcription factor 3 (TBX3) is involved in various differentiation and pluripotency processes in stem cells. TBX3 interacts with various pluripotency factors and in murine pluripotent stem cells depletion of Tbx3 activates differentiation. In this setup we want to show the influence of TBX3 knockdown while reprogramming human fibroblasts and keratinocytes to iPSCs. Methods & Results: Our somatic cells source were human foreskin fibroblasts and keratinocytes from plucked hair. We created inducible TBX3 knockdown lines for both cell types. For the reprogramming process the somatic cells were transduced with a lentivirus which contains the four reprogramming factors OCT4, KLF4, SOX2 and c-MYC. The infected cells were placed on feeder cells until little stem cell colonies appear after about four weeks. To compare the reprogramming efficiency we performed an alkaline phosphatase staining. In the knockdown lines we saw a significantly reduced reprogramming efficiency compared to the normal cell lines. Conclusion: TBX3 is not only important for differentiation but also plays a crucial role in the pluripotency network. Especially it seems to be indispensable in the reprogramming progress of somatic cells to iPSCs.

Kategorie: Poster

Poster 154:

Titel:Visualisation of subtle phenotype abnormalities of prenatally lethal mouse embryos produced in the dmdd project.

Autoren: Reissig L.(1),Geyer S.(1),Rose J.(1),Mohun T.(2),Wilson R.(2),Adams D.(3),Weninger W.(1),

Adressen:(1)Center for Anatomy and Cell Biology|Medical University of Vienna|Vienna|Austria; email:lukas.reissig@meduniwien.ac.at; (2)Developmental Biology|The Francis Crick Institute|London|UK; (3)Experimental Cancer Genetics|Wellcome Trust Sanger Institute|Camebridge|UK

Abstract:
The mouse is a popular biomedical model organism. The “Deciphering the Mechanisms of Developmental Disorders” (DMDD) project aims at screening the phenotype of 14.5 days old homozygous mouse embryos, which carry pre- or perinatally lethal gene defects. For this purpose, it makes use of the “High Resolution Episcopic Microscopy“ (HREM) method, which has proved to permit detection of a broad variety of abnormalities that escape visualization with alternative imaging methods. In this poster I am presenting new examples of recently detected subtle phenotype abnormalities, on the tissue and small structural level, which require HREM data resolution and quality for detection. Some of the abnormalities have only minor influence on intra-uterine development, some might be lethal.

Kategorie: Poster

Poster 155:

Titel:Gastric h+/k+-atpase and shh signalling during left-right patterning in the chick

Autoren: Pieper T.(1),Viebahn C.(1),Tsikolia N.(1),

Adressen:(1)Department of Anatomy and Embryology|University of Goettingen|Goettingen|Germany; email:Nikoloz.Tsikolia@med.uni-goettingen.de

Abstract:
Ciliary flow is a widely accepted mechanism in left-right (LR) symmetry breaking in vertebrate embryos such as Xenopus, zebrafish and mouse; as a downstream effector of ciliary flow nodal is expressed asymmetrically in the lateral plate mesoderm. In the chick, however, mechanisms leading to LR-patterning remain to be elucidated since, instead of ciliary flow, asymmetrical node morphogenesis prior to notochord formation is involved in LR patterning. Because the activity of the gastric H+/K+-ATPase ATP4a in Xenopus leads to specific positioning of motile cilia in the gastrocoel roof plate we set out to reassess its suggested role in LR patterning in the chick. ATP4a α-subunit mRNA showed a symmetrical expression pattern at stages 4 and 5; We treated embryos at stages 3, 4 and 5 with the pharmacological ATP4a-inhibitor SCH28080; in all cases, the experimental embryos showed robust left-sided nodal-expression. In a second line of experiments, we tested sonic hedgehog (shh) signaling (which is also known to be involved in LR patterning in connection with the presence of monocilia) using pharmacological inhibition and the novel early nodal expression domain (which is closely related to asymmetrical node morphogenesis) as a read out: Administration of cyclopamine immediately prior to LR asymmetry (at stage 3 or 4) did indeed randomize heart looping and completely suppressed the initiation of nodal expression. According to these results, ATP4a does not appear to play a causative role in LR patterning in the chick but monocilia or ciliary proteins may still be involved in this process via their functional connection to shh signalling.

Kategorie: Poster

Poster 156:

Titel:Function of the draxin-netrin interaction in vivo

Autoren: Zhu M.(1),Gao X.(2),Soellner C.(3),Hirt B.(1),Wizenmann A.(1),

Adressen:(1)Anatomy|University of Tübingen|Tübingen|Germany; email:ZhuMengbai <shandianlanzmb@hotmail.com>; (2)Institute for Developmental Biology|Max Planck|Tübingen|Germany; (3)Developmental Biology|Max Planck|Tübingen|Germany

Abstract:
During the development of the nervous system axons navigate towards their target area with the help of guidance cues in their environment. The correct establishment of these connections is an essentail step to a functional brain. Netrin is one of the main guidance cues and can attract neurones to their destinations like the commissural axons of the spinal cord towards the ventral midline (1). Draxin, a repulsive guidance cue seems to counteract Netrin attraction (2). Gao et al.'s investigations suggested that Draxin directly binds to Netrin (3). They identified a small area within the Draxin protein responsible for the binding to Netrin. This region is conserved across vertebrates including chick, mouse and human indicating a conserved function of this region. Expression analysis in zebrafish and chick embryos has shown that Draxin expression mainly located to the dorsal spinal cord just opposite to Netrin's ventral expression (2,3). To test the function of the Draxin-Netrin interaction in vivo, we overexpressed Draxin and Draxin lacking the Netrin binding region in chick spinal cord. So far our results support a direct binding of Draxin to Netrin. These experiments will help to understand how this interaction is affecting Netrin signaling. (1) Kennedy et al., Cell 78, pp425; 1994; (2) Islam et al., Science, Vol 323, pp388; 2009; (3) Gao et al., Cell Reports, in press

Kategorie: Poster

Poster 157:

Titel:Reprogramming of human keratinocytes shows mesenchymal-to-epithelial-transition (met)

Autoren: Raab S.(1),Klingenstein M.(1),Linta L.(1),Liebau S.(1),Kleger A.(2),

Adressen:(1)|Neuroanatomy and Developmental Biology|University of Tuebingen|Tuebingen|Germany; email:stefanie.raab@uni-tuebingen.de; (2)University Ulm|Internal Medicine I|Ulm|Germany

Abstract:
Objectives: Induced pluripotent stem cells (iPSCs) have like embryonic stem cells (ESCs) a high proliferative potential and can differentiate into all germ layers. Reprogramming of somatic cells to iPSCs with the overexpression of the four Yamanaka factors is a well-established method. In the developing embryo Epithelial-to-Mesenchymal-Transition (MET) occurs. This process describes the travelling of cells from the early epiblast to form the endoderm and mesoderm and later to build up the internal organs. This process can also be reversible, then called EMT and occurs e.g. in the reprogramming of mesoderm derived fibroblasts to iPSCs. The reprogramming of cells from ectodermal origin, like keratinocytes was not analyzed until now with respect to MET/EMT transition. Methods and Results: Human hair derived keratinocytes were transduced with a lentivirus to undergo iPSC formation. RNA samples were taken at different time points while reprogramming and expression analysis using fluidigm technologies was performed. Genes involved in the development of the three germ layers as well as important genes of the pluripotency network were selected. The results show increased expression of genes representative for primitive streak with the highest expression at day 18. Conclusion: During reprogramming somatic ectodermal cells, here keratinocytes from plucked hair, show similar gene expression profiles like mesodermal cells. Therefore they transit through a similar state to get pluripotent. We can also show that independent of the reprogramming source, cells need to acquire an MET-like intermediate state short before entering the pluripotent state.

Kategorie: Poster

Poster 158:

Titel:Ceacam1 induces b-cell survival and is essential for protective antiviral antibody response

Autoren: Singer B.(1),Khairnar V.(2),Duhan V.(2),Beauchemin N.(3),Goethert J.(4),Lang P.(5),Lang K.(2),

Adressen:(1)Anatomy|University Hospital Essen, University Duisburg-Essen|Essen|Germany; email:bbsinger@gmx.de; (2)Immunology|University Hospital Essen, University Duisburg-Essen|Essen|Germany; (3)Biochemistry, Medicine and Oncology|Rosalind and Morris Goodman Cancer Centre|Montreal, Quebec|Kanada; (4)Hematology (WTZ)|University Hospital Essen, University Duisburg-Essen|Essen|Germany; (5)Gastroenterology, Hepatology and Infectious Diseases|Heinrich-Heine-University|Düsseldorf|Germany

Abstract:
B cells are essential for antiviral immune defence because they produce neutralizing antibodies, present antigen and maintain the lymphoid architecture. Here we show that intrinsic signalling of CEACAM1 is essential for generating efficient B-cell responses. Although CEACAM1 exerts limited influence on the proliferation of B cells, expression of CEACAM1 induces survival of proliferating B cells via the BTK/Syk/NF-ÎºB-axis. The absence of this signalling cascade in naive Ceacam1(-/-) mice limits the survival of B cells. During systemic infection with cytopathic vesicular stomatitis virus, Ceacam1(-/-) mice can barely induce neutralizing antibody responses and die early after infection. Thus, we conclude that CEACAM1 is a crucial regulator of B-cell survival, influencing B-cell numbers and protective antiviral antibody responses.

Kategorie: Poster

Poster 159:

Titel:Cd103+ conventional dendritic cells are in contact to a new antigen-uptaking interstitial macrophage-like cell population around the airways

Autoren: Hoffmann F.(1),Berger J.(1),König P.(2),

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Abstract:
Although dendritic cells (DCs) are important in asthma, data of DC localization in the lung is patchy and largely based on FACS analyses. Since cell localization is important for access to antigen, we aimed to localize DC and macrophage (MÎ¦) subtypes in the murine lung in steady state and after intratracheal application of house dust mite (HDM), ovalbumin (OVA) or both by multicolor immunohistochemistry on precision cut lung slices. Furthermore, we wanted to determine the antigen-uptaking populations. We were able to identify CD11b+ and CD103+ conventional (c)DCs, alveolar macrophages (AMÎ¦s) and interstitial macrophages (IMÎ¦s) at the same time. CD11b+ and CD103+ cDCs were localized between airway and pulmonary artery and around blood vessels in the interstitium, but CD103+ cDCs were rarely found in the epithelium itself. Interestingly, in the steady state CD103+ cDCs were often found in contact with a previously unrecognized cell population around the airways that resembles IMÎ¦s. To investigate functional differences between the DC and MÎ¦ populations, antigen uptake was examined after administration of labeled OVA. During the first hours after the antigen challenge AMÎ¦s were the main antigen-uptaking population in the alveolar lumen while few cDCs took up antigen in the interstitium around the airways. Unexpectedly, most of the OVA around the airways was taken up by the new IMÎ¦-like population (IMÎ¦L). As a similar population has been described to induce tolerance in the gut via cross-talk with CD103+ cells, we speculate that our novel antigen-uptaking IMÎ¦L cell population may similarly regulate tolerance in the lung.

Kategorie: Poster

Poster 160:

Titel:Pro-inflammatory stimuli induce Nrf2/are signalling in macrophages mediated by ROS

Autoren: Fragoulis A.(1),Schenkel J.(2),Pufe T.(2),Wruck C.(2),

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Abstract:
Objectives: Oxidative stress has been implicated in a variety of inflammatory diseases. Nuclear factor-erythroid 2 (NF-E2)-related-factor-2 (Nrf2) is a transcription factor maintaining cellular defence against oxidative stress. This study investigates the effects of pro-inflammatory stimuli on the Nrf2/ARE signalling cascade in macrophages. Methods: Nrf2 activation in response to different pro- and anti-inflammatory stimuli was studied via promoter studies using RAW 264.7 cells and primary murine macrophages. Therefore we used LPS, peptidoglykan, zymosan, TNF-alpha, IL-1beta and IL-6 as pro-inflammatory, and IL-4 and IL-10 as anti-inflammatory stimuli. Kinase inhibitors, antioxidants and diphenyliodonium chloride as NADPH-oxidase inhibitor were used to elucidate signal transduction. Expression of the Nrf2 target genes HO-1 and NQO1 was studied by qRT PCR. Western Blot analysis for HO-1 was performed. ROS production in stimulated cells was investigated using the H2DCF-DA and lucigenin reagents. Results: Treatment of macrophages with pro-inflammatory stimuli showed increased Nrf2 activity but not the treatment with the anti-inflammatory cytokines IL-4 and IL-10. Nrf2 induction was dependent on NADPH-oxidase, ERK and p38 kinase activity. Treatment mediates an increase of HO 1, which is known to act anti-inflammatory due to carbon monoxide production and NF-kappaB inhibition. Conclusion: These data demonstrate an anti-oxidative and anti inflammatory role of Nrf2 during inflammatory processes. Pro-inflammatory stimuli seem to promote the resolution of inflammation at an early stage of acute inflammation by Nrf2 induction. The inhibitor studies revealed ROS as a potential signalling molecule in this Nrf2 activation.

Kategorie: Poster

Poster 161:

Titel:Nk cells in postmenopausal breast cancer of obese mice

Autoren: Mattheis L.(1),Jung J.(1),Kielstein H.(1),Spielmann J.(1),

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Abstract:
Background and Aims Obesity is a widespread disease having a strong impact on onset, prognosis, progression, and treatment of various cancers including postmenopausal breast cancer. Although the underlying mechanisms are poorly understood, it is known that essential functions of natural killer (NK) cells such as targeting tumor cells are disturbed in obese individuals. Thus, the aim of the present study is the investigation of NK cell functionality of obese mice in a postmenopausal breast cancer model. Methods 48 female mice (BALB/c) received either a standard chow or a high fat diet for up to 13 weeks. Thereafter, mice were ovarectomized or sham-operated and syngeneic 4T1-Luc2 mouse mammary tumor cells were injected into the fat pad of the mammary gland. Tumor progression and metastasis were weekly visualized by bioluminescence life imaging. After 3 weeks, blood, tissues and tumors were collected and analyzed. Different techniques such as flow cytometry, luminex, and real-time PCR aimed to analyze numbers, activity and physiological properties of NK cells. Results Body weight, visceral fat amount and blood adipokine levels were significantly increased in diet-induced obese BALB/c mice. As expected tumor burden was increased in the obese animals as compared to their lean littermates. Interestingly, the NK cell functionality was subset-specifically altered in the obese mice with breast cancer. Conclusion In summary, the postmenopausal breast cancer model helps to understand molecular mechanisms regulating NK cell functionality in obese individuals.

Kategorie: Poster

Poster 162:

Titel:Acute lung injury in the aging lung

Autoren: Brandenberger C.(1),Kling K.(1),Lopez-Rodriguez E.(1),Muehlfeld C.(1),

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Abstract:
Introduction: Pulmonary inflammatory diseases such as pneumonia or acute lung injury are associated with increased morbidity and mortality in the elderly. However, little is known about effects of aging on lung function and inflammation in acute lung injury. Methods: In the current study we investigated lung function and histopathology in young (2-3 months) and old (18-19 months) male C57BL/6 mice. The mice were intranasally dosed with 2.5 mg lipopolysaccharide (LPS)/kg body weight. Twenty-four hours later, lung function was tested with a rodent FlexiVent and lung compliance, tissue elastance and tissue dampening were assessed. Afterwards the animals were sacrificed and the lungs processed for histopathological analysis. Results: Pulmonary function testing revealed that old animals have decreased tissue elastance and tissue dampening compared to young animals. No differences were apparent in lung compliance. Both, tissue elastance and dampening are increased after LPS administration which is probably caused by edema. Pulmonary histophathology showed inflammatory cell infiltrates, mostly neutrophils, in the lung parencyma as well as in the peri-bronchiolar and peri-vascular area of LPS exposed animals. The cell infiltration apeared more pronounced in old compared to young LPS exposed mice. Conclusion: These data give evidence that lung function is affected by age and acute lung injury, probably contributing to an increased mortality in inflammatory lung disease in the elderly. Enhanced pulmonary neutrophils in old LPS exposed mice furthermore indicate a greater inflammatory response with advanced age.

Kategorie: Poster

Poster 163:

Titel:Comparison of chemokine expression patterns in freshly isolated human glioblastoma-associated macrophages/microglia and in vitro polarized human macrophages

Autoren: Hattermann K.(1),Sebens S.(2),Helm O.(2),Mentlein R.(1),Mehdorn H.(2),Held-Feindt J.(2),

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Abstract:
Background: Tumor-associated microglia/macrophages (TAMs) account for up to 30% of the total tumor mass of human glioblastomas. Glioblastoma TAMs are reported to show distinct characteristics of mainly the M2 macrophage polarization type probably favouring glioblastoma progression. Chemokines and their corresponding receptors are key drivers of leukocyte migration and invasion and they are also well known to promote tumor progression. Thus, we wanted to investigate the expression of chemokines / receptors in TAMs freshly isolated from glioblastomas in comparison to in vitro polarized M1 and M2 macrophages. Methods: TAMs from fresh human glioblastoma samples were enriched by CD11b-Magnetic Cell Separation (MACS), M1 and M2 polarized macrophages were obtained by incubation of human peripheral blood monocytes with 50 ng/ml GM-CSF or M-CSF for 7 days, respectively. The transcription of the chemokines/-receptors CXCL12-CXCR4-CXCR7, CXCL16-CXCR6 and CX3CL1-CX3CR1 as well as M1 and M2 markers were analysed by quantitative PCR. Results and conclusion: The M1 and M2 marker expression profile of freshly isolated TAMs from human glioblastomas showed similarities and differences in comparison to respective polarized macrophages emphasizing an “intermediate”-state. However, the chemokine / receptor expression patterns are partly distinct (elevated or reduced) from those observed in the in vitro polarized macrophages. As they may influence on tumor cells and TAMs, chemokines/receptor are promising targets for future therapeutic approaches.

Kategorie: Poster

Poster 164:

Titel:Comparative analysis of tight, adherens and gap junctions in the human sertoli cell line fs1 and the human seminoma like cell line tcam-2 prior to co-culture experiments

Autoren:Brehm R.(1),Schumacher V.(2),Schorle H.(3),Nettersheim D.(3),Ngezahayo A.(4),Begandt D.(4),Dilger N.(4),Schnepel N.(1),Gaehle M.(1),Hambruch N.(1),Rode K.(1),Wilhelm J.(5),Kliesch S.(6),Weidner W.(7),Bergmann M.(8),Fink C.(8),

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Abstract:
Sertoli cells form the blood-testis barrier (BTB) which is composed of tight junctions (TJ), adherens junctions (AJ), and gap junctions (GJ). Alterations in BTB assembly have been associated with the pathogenesis of human testicular carcinoma in situ (CIS), which represents the non-invasive precursor of seminoma and non-seminoma. The TJ protein claudin11 (Cldn11) constitutes the major functional component of the human barrier so far and GJ proteins, like connexin43 (Gja1) might be important regulators for BTB formation. To investigate whether changes in intercellular adhesion and communication between Sertoli cells, between tumor cells and between Sertoli and tumor cells could play a role in the neoplastic progression of CIS cells to invasive malignancy, a cell culture model has been developed using the human Sertoli cell line FS1 and the human seminoma-like cell line TCam-2. Prior to co-culture experiments, both cell lines have been further characterized to identify differentially expressed genes/proteins using descriptive methods like histology (morphology), RNA-Microarrays, RT-PCR, immunofluorescence (IF) and Western blot (WB) focusing on BTB components like claudin11 (Cldn11), N-cadherin (Cdh2), ZO-1 (Tjp1), connexin43 (Gja1), connexin45 (Gjc1) as well as on GJ coupling (Lucifer Yellow dye transfer experiments). In addition, data were compared with corresponding human testicular biopsies. Results show e.g. that only FS1 cells express claudin11. Moreover both cells are functionally coupled by GJ formed by connexin43 in FS1 cells and connexin45 in TCam-2 cells. These results describe initial starting points to elucidate alterations concerning cell-cell contacts during co-culture experiments.

Kategorie: Poster

Poster 165:

Titel:Extravillous trophoblast invasion in differently polarized endometrial epithelial cell lines

Autoren:Krings O.(1),Buck V.(1),Flensberg F.(1),Classen-Linke I.(1),

Adressen:(1)Institute of Molecular and Cellular Anatomy|RWTH Aachen University|Aachen|Germany

Abstract:
The receptive phase of the human endometrium during the menstrual cycle and in preparation for embryo implantation is characterized by a less polarized luminal and glandular epithelium. To proof the concept that a change in polarity facilitates the invasion of trophoblast cells, three differently polarized endometrial epithelial cell lines - HEC-1-A, Ishikawa and RL95-2 - were co-cultured with the extravillous trophoblast cell line AC-1M88. Two different co-culture methods, on coverslips or in Ibidi culture inserts, were used. Main advantage of the latter was that initially cells were cultured separately and could then, after withdrawal of the culture-insert, be confronted via a defined cell-free gap. The strongest invasive behaviour of the trophoblast cells was obtained by confrontation with the weakly polarized RL95-2 cell line in comparison with the moderately polarized Ishikawa and the highly polarized HEC-1-A cell line. The formation of desmosomes and adherens junctions which was shown by desmoplakin 1/ 2 and beta-catenin immunofluorescent staining was most apparent in the co-cultures with RL95-2 cells, where HLA-G positive trophoblast cells displayed distinct cellular protrusions. In conclusion, it could be shown that the invasiveness of trophoblast cells depends on the polarity of the epithelial cell lines used in confrontation assays. This refers to the importance of the cyclic change in polarity and differentiation of endometrial cells in the receptive period of the menstrual cycle. Further studies will help to improve our understanding of endometrial receptivity and may contribute to higher implantation rates in assisted reproductive technology.

Kategorie: Poster

Poster 166:

Titel:Nestin expressing progenitor cells are present in the vasculature of the epididymis and regulated during postnatal development and hypoxic exposure

Autoren: Reckmann A.(1),Mietens A.(1),Middendorff A.(1),

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Abstract:
Vascular smooth muscle cells (VSMCs), distinguished by the expression of the neuronal stem cell marker nestin, may represent stem cell-like progenitor cells for tissues in various organs. In previous studies we found that nestin-expressing VSMCs in the testis are the progenitors of testosterone producing Leydig cells and drive development of pulmonary hypertension in the lung. Data on nestin in the epididymis however are missing. Expression and localization of nestin in the epididymis were investigated using immunohistochemistry, 3D-morphological analyses, Western-Blot and qPCR in Nestin-GFP and WT mice. The potential role of nestin was tested during postnatal development and under hypoxic conditions. Nestin was found in a subpopulation of VSMCs in the vasculature of the epididymis. As compared to adult normoxic controls significantly higher nestin expression was observed in VSMCs during early postnatal development and in adult epididymis between day 2-4 of hypoxic exposure, but not at later time points. Interestingly, nestin-expressing cells were shown to indicate proliferating cells in the vasculature of the epididymis. Our data suggest a role of nestin in development and tissue repair in the vasculature of the epididymis.

Kategorie: Poster

Poster 167:

Titel:Claudin-3 and -10 show distinct distribution patterns during decidualization and trophoblast invasion

Autoren:Schumann S.(1),Buck V.(2),Classen-Linke I.(2),Wennemuth G.(1),Gruemmer R.(1),

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Abstract:
To establish a successful pregnancy, embryo implantation requires profound changes in the endometrium, including epithelial-mesenchymal transition of the luminal epithelium and stromal-epithelial transition of the stromal cells resulting in decidualization. Claudins, members of the tight junction protein complex, regulate paracellular permeability and seem to play a role during these epithelial and stromal changes. In murine estrous phase endometrium, luminal and glandular epithelium exhibited claudin-3 immunostaining, whereas claudin-10 only was detectable in glandular epithelium. On day 4.5 of pregnancy (dpc), claudin-3 was concentrated at the most apical part of the lateral membrane of the epithelium adjacent to the blastocyst. In the stromal compartment, claudin-10 was induced in the primary decidual zone on 4.5 dpc, whereas claudin-3 expanded considerably from 6.5 dpc onwards in endothelial cells of the decidual sinusoids, as well as in antimesometrial decidual cells. Moreover, trophoblast giant cells revealed a nuclear claudin-3 staining, whereas claudin-10 exclusively was detectable in decidual cells. In human endometrial epithelium, claudin-10 was identified in addition to claudin-3. Both proteins were not detected in human first trimester decidual cells, but claudin-3 was shown in vascular endothelial cells and human extravillous trophoblast cells, corresponding to murine trophoblast giant cells. In summary, we demonstrated a sophisticated claudin signature during decidualization in mice pointing to a role in decidual angiogenesis and regulation of trophoblast invasion. Moreover, claudin-3 was located in murine trophoblast giant cells as well as in human extravillous trophoblast cells and thus may have an impact on invasion capacity of trophoblast cells in both species.

Kategorie: Poster

Poster 168:

Titel:Trophoblast-endometrial interaction in vitro as a model for early human implantation

Autoren: Buck V.(1),Roesing B.(2),Neulen J.(2),Leube R.(1),Classen-Linke I.(1),

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Abstract:
A basic requirement for human embryo invasion which comprises penetration of endometrial epithelial cells (EECs) by trophoblast cells is the appropriate preparation of the endometrium. Its cyclic differentiation leads to a short receptive period called window of implantation (WOI). Previously, we observed an altered distribution of adhering junctions along lateral membranes of glandular human EECs during the WOI. In a 3D confrontation culture, gland-like endometrial adenocarcinoma spheroids with a junction distribution similar to EECs during the WOI were more strongly invaded by the extravillous trophoblast cell line AC-1M88 than highly polarized epithelial cell lines. Aim of the current study was to apply the 3D confrontation cell culture system on primary EECs. Primary human EECs from scratch biopsies of women undergoing assisted reproductive technology (ART) were cultured up to 12 days in vitro (DIV 12) in Matrigel. During DIV 1-4 glandular fragments were reorganized to new gland-like EEC structures. EEC polarity and lumen formation was shown by desmoplakin 1/2 and ZO-1 staining using confocal microscopy. After confrontation with AC-1M88 cells HLA-G-positive trophoblast cells could be identified in between primary EEC structures. Taken together the newly established culture tools - primary culture of small biopsy fragments and trophoblast invasion assay - are a valuable advancement in developing a monitoring system to characterize endometrial samples of ART patients. Comparing the degree of in vitro receptivity with available clinical parameters may help to improve the outcome of ARTs in the future.

Kategorie: Poster

Poster 169:

Titel:Androgen-dependent regulation of cgmp pathways in a subpopulation of prostatic smooth muscle cells

Autoren: Kuegler R.(1),Mueller D.(1),Tasch S.(1),Tjahjono Y.(1),Kaschtanow A.(1),Mietens A.(1),Wagenlehner F.(2),Ellem S.(3),Resbridger G.(3),Middendorff R.(1),

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Abstract:
Our previous data showed that expression of cGMP pathway components is very low in the prostate compared to other androgen-dependent organs, but is dramatically upregulated in case of androgen depletion (Müller et al. 2011). This data is of special interest, since inhibitors of the cGMP-hydrolyzing enzyme phospodiesterase 5 (PDE5) are now regularly used for treatment of benign prostate hyperplasia (BPH). The cellular localization of cGMP-related enzymes and the mechanisms in the prostate underlying this medication is still a matter of debate. In prostate tissue of mouse, rat and man, PDE5 was shown to be highly expressed in interstitial and vascular smooth muscle cells (SMCs), but not in epithelial cells of the gland. 3D-analyses revealed - independently of age - a periglandular inhomogeneous bandage-like distribution of interstitial smooth muscle cells in rodents. In androgen deprivation models, an increase of PDE5, correlating with an increase of SMCs surrounding disturbed glands, was observed. Using aromatase-knockout and -overexpressing mice it was shown that only glandular, but not vascular smooth muscle cells are affected by changes of hormone levels. Time lapse-imaging of in vivo treated prostatic glands and ducts allowed to visualize the occurrence of spontaneous contractions and essential effects of the PDE5 inhibitor sildenafil only in terminal glands, whereas noradrenaline showed dramatic effects in both structures. Data, showing relevant PDE5 effects and their androgen-dependent regulation only in a subpopulation of prostatic SMCs, might be important for use of PDE-5 inhibitors as a possible block buster for therapy of BPH. Grant: DFG-IRTG Giessen-Monash (Melbourne, Australia)

Kategorie: Poster

Poster 170:

Titel:To what extent can human testicular cancer cells actively shape their immunological microenvironment?

Autoren:Klein B.(1),Schuppe H.(2),Weidner W.(2),Kliesch S.(3),Indumathy S.(4),Loveland B.(5),Hedger M.(4),Loveland K.(6),Bergmann M.(1),

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Abstract:
Human testicular germ cell tumours commonly feature abundant infiltrating immune cells, most previously identified as T cells and macrophages. In our study, the cytokine microenvironment of these cancers has been surveyed for the first time, revealing significantly increased expression of proinflammatory cytokines relative to healthy tissue, as well as cytokines associated with B cells, whose presence can further be confirmed by immunohistochemistry. These ex vivo results suggest an exceptional involvement of B cells in the immunopathology of testicular cancer. For further analysis, an in vitro model was developed to assess the interaction between immune and testicular cancer cells in more detail. TCam2 cells (human seminoma-derived line) were co-cultured with human peripheral blood mononuclear cells (PBMC) to interrogate responses to their co-localization. Data from nine independent experiments using PBMCs from eight different donors indicate that seminoma cell growth is unaffected by direct or indirect contact with PBMC, at least in short-term. However, cytokine expression profiles of co-cultured TCam2 cells show significantly increased production of the pro-inflammatory cytokines IL1-beta, IFN-gamma, TNF-alpha, TGF-beta1 and CCL5. These outcomes resemble the ex vivo data and highlight the potential for neoplastic human germ cells to promote immune cell infiltration and to actively shape the cytokine microenvironment in germ cell tumours. Flow cytometry is used to assess the activation status of co-cultured immune cells and the proportions of distinct immune cell subpopulations in co-culture, as TCam2 cells might serve as feeder cells through a naturally high production of IL6 that can specifically enhance B cell viability.

Kategorie: Poster

Poster 171:

Titel:Epididymitis: ascending infection restricted by segmental boundaries

Autoren: Stammler A.(1),Hau T.(1),Bhushan S.(1),Meinhardt A.(1),Jonigk D.(2),Lippmann T.(2),Pilatz A.(3),Schneider-H. I.(1),Middendorff R.(1),

Adressen:(1)Institute of Anatomy and Cell Biology|Justus-Liebig-University Giessen|Giessen|Germany; (2)Institute of Pathology|Hannover Medical School|Hannover|Germany; (3)Department of Urology, Pediatric Urology and Andrology|Justus-Liebig-University Giessen|Giessen|Germany; email:Ralf.Middendorff@anatomie.med.uni-giessen.de

Abstract:
The epididymal duct is a continuous, unbranched tube, coiled into segments that are divided by connective tissue septa. Epididymal segmentation has never been investigated in the context of epididymitis even though clinical data indicate that swelling predominates in the cauda region according to sonographic analysis. We analyzed segment-specific changes in the epididymal duct during epididymitis in a mouse model and in men. In the mouse epididymitis model (three days post-infection, injection of bacteria into the lumen of the vas deferens) two E. coli strains were tested: an uropathogenic strain CFT073 and a fecal non-pathogenic strain NPEC470, as well as two control groups, PBS sham-treated and untreated mice. Segmentation was verified by ex vivo injection of dye into the interstitial space of untreated mouse epididymides. Histological findings were compared with specimens from epididymitis patients (n = 10) (control: samples from patients without epididymitis, n = 16). In the mouse model and in patients, E. coli was restricted to the distal cauda segment associated with damage of the epithelium and muscle layer. Ductal constriction occurred in the non-infected upstream segments of infected area associated with specific morphological alterations, representing a putatively protective mechanism preventing luminal ascent of bacteria. The caput region was found to be unaffected in patients and the mouse model. We show for the first time that luminal ascent of bacteria is strictly gated by epididymal segment boundaries and demonstrate the impact of epididymal segmentation for infectious invasion during epididymitis. Supported by grants from State of Hessen (LOEWE-MIBIE) and DFG (KFO 181)

Kategorie: Poster

Poster 172:

Titel:The testicular expression of katnb1 during human spermatogenesis

Autoren: Pleuger C.(1),Fietz D.(1),Hartmann K.(1),Weidner W.(2),Kliesch S.(3),O Bryan M.(4),Dorresteijn A.(5),Bergmann M.(1),

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Abstract:
Microtubule-severing proteins like katanin are key factors for the regulation of microtubule dynamics. Katanin consists of a p60 enzymatic subunit (encoded by KATNA1) and a p80 regulatory subunit (encoded by KATNB1). The p80 subunit is responsible for targeting the p60-mediated severing. Particularly during spermatogenesis, microtubule-modifying proteins are essential for mitotic and meiotic divisions. A missense mutation in the highly conserved WD40 domain of the Katnb1 gene causes defects in spermatogenesis and infertility in male mice. Homozygous Katnb1-mutants (called -Taily') show reduced sperm counts and an impaired sperm morphology. This phenotype is comparable with the human oligoasthenteratozoospermia (OAT) syndrome. The expression pattern of KATNB1 during human spermatogenesis was analysed on mRNA (RT-PCR, RT-qPCR and in situ-hybridization) and protein level (immunohistochemistry). In normal spermatogenesis (n=43), KATNB1 mRNA was exclusively expressed in pachytene spermatocytes and quantitatively reduced in maturation arrests at primary spermatocyte (n=7) and spermatogonia level (n=4) by RT-qPCR. The KATNB1 protein was detected in the Golgi complex of pachytene spermatocytes, co-localized with Golgin A2 (a Golgi-specific protein). Additionally a co-localisation with pericentrin was detected in the cleaving centrosome immediately before the first meiotic division. The p80 subunit was also detected in dictyosomes in early round spermatids. Our data indicate an involvement of the p80 subunit in the formation of spindle apparatus in primary spermatocytes, and in manchette and flagellum formation in early round spermatids. Our data correspond to the results reported in the mouse, and suggest the Taily mouse model to be suitable to analyse the human OAT phenotype.

Kategorie: Poster

Poster 173:

Titel:Components of a functional sulfatase pathway are present in the human testis

Autoren: Hartmann K.(1),Fietz D.(1),Wapelhorst B.(1),Kliesch S.(2),Weidner W.(3),Bergmann M.(1),

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Abstract:
Steroid synthesis in the testis might not only occur via de novo synthesis, but also by re-activation of sulfated steroids by steroid sulfatase (STS) called â€œsulfatase pathwayâ€• . Recently, we detected SOAT (Sodium-dependent Organic Anion Transporter) a transporter for sulfated steroids in primary spermatocytes and early round spermatids. To overcome the blood-testis-barrier (BTB), influx and efflux carriers expressed by Sertoli cells are required. We analysed the testicular mRNA expression of two Organic Anion Transporting Peptides (OATP2B1, OATP3A1), three efflux transporters (Multidrug Resistance-related Proteins, MRP1 and MRP4 and Breast Cancer Resistance Protein, BCRP), and involved enzymes i.e. StS and sulfotransferases (SULT1E1, SULT2A1) employing RT- and qPCR- techniques, RT-PCR following laser assisted cell picking (LACP) and in situ hybridyzation (ISH). Protein expression of relevant targets was performed by immunohistochemical analyses. So far, we successfully detected STS, OATP2B1 and OATP3A1 in Sertoli cells and pachytene spermatocytes and MRP1 exclusively in Sertoli cells on mRNA and protein level. SULT1E1 was present in interstitial Leydig cells. Our data suggest a comprehensible route for sulfated steroid hormones - presumably synthesized in Leydig cells - to overcome BTB via Sertoli cells. Expression of inward transporting proteins and STS in germ cells suggests that these cells could also be targets for sulfated steroids passing the Sertoli cells through MRP1 mediated efflux. Taken together with previous data localizing androgen and estrogen receptors in Sertoli cells and the latter also in germ cells we assume a functional sufatase pathway within the human seminiferous epithelium. Funded by DFG-FOR1369 BE 1016/10-1, FI 1927/1-2.

Kategorie: Poster

Poster 174:

Titel:Loss of connexin 43 in sertoli cells and its effect on the expression of claudin-3, -5 and -11 and blood-testis barrier integrity in mice

Autoren: Heinrich J.(1),Gerber J.(1),Hansmann F.(2),Gasse H.(1),Brehm R.(1),

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Abstract:
Connexin43 (Cx43) is the predominant testicular gap junction (GJ) protein. Within the seminiferous epithelium it connects adjacent Sertoli cells (SC) as well as SC and germ cells (GC). In cases of impaired spermatogenesis, Cx43 expression has been shown to be altered in men and several animal species. Amongst other functions, Cx43 is supposed to play a role in blood-testis barrier (BTB) formation and dynamics. Additionally other junctional proteins, like adherens junctions (AJ) and tight junctions (TJ), are involved in the establishment of this barrier. The aim of the present study was to investigate the expression pattern of different TJ proteins of the murine BTB using SC-specific knockout mice (SCCx43KO). Male SCCx43KO mice are infertile due to an arrest of spermatogenesis. TJ molecules claudin-3, -5 and -11 were examined using immunohistochemistry and Western Blot, and RT-PCR/qRT-PCR. Additionally, BTB was functionally analyzed using hypertonic glucose fixation. Adult WT and SCCx43KO mice synthesized claudin-3 and -11 proteins with claudin-11 protein being increased in SCCx43KO mice. Claudin-5 protein was synthesized in adult WT mice, but seems to be down-regulated in SCCx43KO mice. Moreover, both genotypes expressed claudin-3, -5 and -11 on mRNA level. Functional data indicated an effective BTB in adult SCCx43KO mice despite the loss of Cx43 in SC. Further investigations are required to quantify murine protein and mRNA data. First results demonstrate that different members of the claudin family show an altered expression in SCCx43KO mice, which possibly leads to a BTB dysfunction and to an impaired spermatogenesis in adult mutants.

Kategorie: Poster

Poster 175:

Titel:Uroplakins show a nycthemeral rhythm in mouse urothelium

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Abstract:
The urine bladder urothelium provides a permeability barrier to protect the body from toxic urinary substances while being highly flexible throughout the micturition cycle in order to accommodate significant changes in surface area. The apical surface of urothelial umbrella cells is covered by two-dimensional crystals (plaques) consisting of uroplakins (UPKIa, UPKIb, UPKII and UPKIIIa). UPKs are essential for bladder epithelial physiology by regulating membrane permeability and conferring barrier stability. A molecular clockwork in the urinary bladder is crucial for rhythmicity of micturition. However, little is known about nycthemeral changes in the composition of urothelial plaques. Therefore, we analysed immunoreactivity (Ir) and mRNA expression of uroplakins in C57Bl/6 mice kept in 12h light/12h dark cycles at every 4 h. In parallel, mice were kept in metabolic cages to assess urine secretion over time. Ir of all uroplakins underwent a significant time-of-day dependent fluctuation whereas mRNA levels were constant. This finding suggests a posttranscriptional regulation of rhythmic uroplakin protein expression. Ir of UPKIa, UPKIb, UPKII and UPKIIIa peaked around late daytime thereby preceding the peak in urine voiding at early nighttime. Ir of UPKIIIa, UPKIa, UPKIb, UPKII, and UPKIIIb was lowest at mid-night preceding the nadir in urine voiding at late night. These observations suggest a specific time-of-day dependent rearrangement of urothelial plaques correlated with urine bladder function.

Kategorie: Poster

Poster 176:

Titel:Light- and electron microscopic immunodetection of Âµ-opioid receptor (mop) in peripheral nerve

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Abstract:
Opioid receptors (OPs) are produced in perikarya of pseudounipolar sensory neurons, and transported to peripheral axonal terminals, where their presence and functionality has been conclusively documented. Under pathological conditions (e.g. nerve constriction), mu-OP (MOP) agonist application to the injured nerve induces antinociception, indicating localization of functional MOPs also along axonal membranes. Information on the presence of MOP in membranes of unharmed nociceptive axons is lacking. Ultrastructural immunodetection of MOP using polyclonal antibodies is hampered by high unspecific labeling and low axonal MOP levels in intact peripheral nerve. We applied a monoclonal rabbit-antibody (RabMAb) for light- and electron microscopic MOP-immunodetection in rat sciatic nerve. Additionally, we studied sciatic nerves of mice expressing a MOP-mcherry fusion protein (MOP-mcherry knock-in mice). RabMAb yielded superior specific immunolabeling in CNS areas, and faint but clearly recognizable labeling in sciatic nerve. Granular immunofluorescence was detected in narrow fibers/fiber bundles, colocalized with sensory fiber marker calcitonin-gene related peptide. Schwann cell labeling, which was seen using polyclonal MOP antibodies, was absent. Mcherry immunolabeling in knock-in mice gave identical results, with enhanced signal-to-noise ratio compared to RabMAb reactions. Preembedding mcherry-immunogold electronmicroscopy provided evidence of specific labeling in non-myelinated fiber bundles of knock-in mice compared to wildtype, with numerous silver/gold particles localized on or near axonal membranes. Analysis of immunoelectron microscopic RabMAb detection is ongoing. The availability of specific detection methods combined with reliable ultrastructural information opens new possibilities to study MOP in sciatic nerve under basal and pathological conditions.

Kategorie: Poster

Poster 177:

Titel:Involvement of enteric glial cells in diverticular disease

Autoren: Leuschner S.(1),Cossais F.(1),Barrenschee M.(1),Lange C.(1),Egberts J.(2),Becker T.(2),Boettner M.(1),Wedel T.(1),

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Abstract:
Background: Besides enteric neurons, enteric glial cells (EGC) have been recognized as essential mediators of intestinal motility functions. Motility disorders are associated with decreased expression of the EGC marker S100b and decreased EGC number. Calcium response mediated by connexin 43 (Cx43) plays an essential role in the regulation of intestinal motility by EGC. Diverticular disease (DD) is frequently associated with impaired intestinal motility and characterized by an enteric neuropathy. However, whether changes in EGC markers expression occur in DD remains unclear. Therefore, we aimed to characterize the expression of EGC markers and of Cx43 in DD and controls. Material and Methods: Expression of glial markers S100b, GFAP and Sox10 and of Cx43 was analyzed by quantitative PCR performed on mRNA samples from tunica muscularis and myenteric ganglia (distal colon) harvested by laser microdissection (LMD) in patients with DD and controls. The distributional pattern of S100b and Cx43 was additionally assessed by immunohistochemistry in colon tissue of patients with DD and controls. Results: Expression of S100b was slightly increased at mRNA and protein levels in DD. No major changes in mRNA expression were observed for the other markers analyzed. Cx43 immunoreactivity was decreased in 5 out of 9 patients with DD compared to controls. Conclusions: These preliminary results do not support previous results showing decreased S100b in patients with DD and suggest that DD is associated with limited alterations of EGC network as compared to enteric neurons. Further experiments are required to fully characterize potential impacts of EGC in DD.

Kategorie: Poster

Poster 178:

Titel:Connectivity of sensory nerve fibers and cholinergic brush cells in the urethral epithelium

Autoren: Schulz L.(1),Papadakis T.(1),Bodenbenner M.(1),Deckmann K.(1),Kummer W.(1),

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Abstract:
Urethral brush cells (UBC) use components of the taste transduction cascade to detect uropathogenic bacteria or harmful substances. Upon stimulation, these cells release acetylcholine which is likely to activate sensory nerve fibers in the direct surrounding, thereby evoking defense mechanisms such as reflex micturition and, potentially, neurogenic inflammation. Here we aimed to determine the structural connectivity between UBC and such axons, and the equipment of intraepithelial axons with pro-inflammatory neuropeptides and the nicotinic receptor alpha3 subunit (chrna3). Pre-embedding immunoelectronmicroscopy utilizing ChATBAC-eGFP mice showed that UBC form desmosomal adhesions with epithelial cells. Neither ultrastructural nor deep sequencing data suggest gap junction coupling to neighboring cells. In comparison to urethral neuroendocrine cells, UBC are sparsely innervated. Deep sequencing data reveal expression of elements of the synaptic vesicle fusion machinery, but direct UBC-nerve fiber contacts with synaptic morphology have not been observed yet. UBC are approached up to 600 nm by varicose nerve fibers with dense core vesicles. Immunohistochemistry revealed a dense innervation of the urethral epithelium with nerve fibers containing SP and/or CGRP which only partially coexpress chrna3. The urethral epithelium is densely innervated by at least three subtypes of sensory nerve fibers. Deep sequencing data support the hypothesis that UBC express a synaptic vesicle fusion machinery to release transmitters, but up to now, we were not able to locate classical synapses. Intraepithelial spread of excitation via gap junctions, as described in sinonasal epithelium, appears to be unlikely. The ultrastructural findings suggest an additional sensory role of the non-cholinergic urethral neuroendocrine cells.

Kategorie: Poster

Poster 179:

Rubrik: 11.Pheripheral and vegetative nervous system

Titel:Postnatal development of the enteric glial network and modulation by butyrate

Autoren: Cossais F.(1),Boudaud M.(2),Kermarec L.(2),Durand T.(2),Chevalier J.(2),Neveu I.(2),Naveilhan P.(2),Neunlist M.(2),

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Abstract:
INTRODUCTION: Gastrointestinal (GI) functions continue to mature after birth. This maturation is characterized by modifications of enteric neurons and is regulated by microbiota-derived short chain fatty acids, such as butyrate. Although enteric glial cells (EGC) are central regulators of GI functions, postnatal maturation of EGC phenotype and its regulation by butyrate remain to be characterized. MATERIAL & METHODS: EGC proliferation and phenotype were assessed by immunohistochemistry and RT-qPCR in colonic myenteric plexus of rat pups between 1 and 36 days after birth. Impact of age upon ATP-induced calcium response in EGC was analyzed. Impact of butyrate on EGC phenotype and proliferation was further analyzed in EGC culture in vitro and by performing butyrate enemas in vivo. RESULTS: We showed that the EGC network continues to set up after birth and this maturation was characterized by increased mRNA and protein expressions of the glial markers GFAP and S100b. EGC calcium response to ATP was significantly modified as a function of age. Butyrate enemas inhibited the proliferation of EGC in vivo and in vitro but had no impact on glial markers expression. Finally, we showed that EGC express the butyrate transporters MCT1, MCT2, GPR41, and GPR109A. Butyrate treatment increases acetylation of H3K9, activates pERK and increases the proportion of EGC in G1 phase. CONCLUSION: These results demonstrate that the EGC network continues to mature after birth and that EGC proliferation can be modulated by butyrate. The mechanisms responsible for EGC maturation remain to be identified.

Kategorie: Poster

Poster 180:

Titel:Decreased expression of snare-complex proteins in diverticulitis and diverticulosis

Autoren: Lange C.(1),Barrenschee M.(1),Boettner M.(1),Cossais F.(1),Egberts J.(2),Becker T.(2),Wedel T.(2),

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Abstract:
Background and aims: The enteric nervous system controls intestinal motility by communication with smooth muscle cells via neurotransmitters. An intact neurotransmitter release machinery requires SNARE (soluble N-ethylmaleimide-sensitive-factor attachment receptor) proteins for fusion of synaptic vesicles with the pre-synaptic membrane. As diverticular disease is associated with enteric neuropathy and impaired intestinal motility, we analyzed SNARE proteins and synaptophysin to clarify a putative synaptic vesicle apparatus disturbance. Material and methods: In colonic samples obtained from patients with diverticulitis (n=9), diverticulosis (n=14) and controls (n=10) site-specific gene expression analysis was performed for SNAP-25, synaptobrevin, and synaptophysin by RT-qPCR analysis on mRNA samples extracted from tunica muscularis (TM) and myenteric ganglia harvested by laser microdissection (LMD). Protein expression was assessed and quantified by immunohistochemistry on full-thickness sections of patients and controls. Results: mRNA expression of SNAP-25 and synaptophysin was decreased in the TM of patients with both diverticulitis and diverticulosis compared to controls. In myenteric ganglia of patients with diverticulitis transcription of all three genes was reduced compared to controls. Immunoreactivity of all studied proteins was decreased within myenteric ganglia of patients with diverticulitis compared to controls. Immunoreactivity of synaptophysin was also reduced within myenteric ganglia of patients with diverticulosis compared to controls. Conclusion: Our data provide evidence for an impaired neurotransmitter release machinery at gene and protein expression level in diverticulitis and during early stages of diverticula formation. These findings add further evidence for a primary enteric neuropathy contributing to the pathogenesis and disturbed intestinal motility in diverticular disease independent from inflammatory events.

Kategorie: Poster

Poster 181:

Titel:Brush cell released acetylcholine induces neurogenic inflammation

Autoren:Jurastow I.(1),Nandigama R.(2),Wiederhold S.(3),Deckmann K.(3),Scholz P.(4),Altmüller J.(5),Reeh P.(6),Kummer W.(3),Krasteva-Christ G.(2),

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Abstract:
We recently demonstrated that tracheal brush cells (BC) initiate protective reflexes to bacterial and bitter tasting substances utilizing cholinergic signaling. These effects were dependent on activation of cholinoreceptive sensory nerve fibers. Here, we explored ACh-release and subsequent release of calcitonin related-gene peptide (CGRP) from nerve fibers innervating the trachea leading to neurogenic inflammation in the airways. Expression of taste receptor (Tas2R) 108 and all key members of the taste transduction cascade was detected in all investigated tracheal BC as determined by deep sequencing. Isolated BC responded to the bitter substance denatonium (1mM) with an immediate increase in [Ca2+]i, while ACh-biosensor cells, positioned near BC, showed a delayed increase in [Ca2+]i. In addition, ACh was released also from intact tracheal slices as confirmed by confocal [Ca2+]i-imaging. Atropine eliminated the response in ACh-biosensor cells. Taste transduction signaling cascade inhibitors (U-73122/TPPO) abolished the responses of BC to denatonium and subsequent responses of ACh-reporter cells. Applied at the tracheal surface, denatonium led to a release of CGRP from sensory nerve fibers as measured by Sandwich-ELISA . Inhalative tracheal challenge of anesthetized spontaneously breathing mice with denatonium evoked extravasation of Evans blue from subepithelial blood vessels. Saline application had no effect on blood vessel leakage. In conclusion, the canonical taste transduction signaling cascade is essential for denatonium-mediated activation of tracheal brush cells in vivo. The subsequent release of ACh leads to activation of CGRP-containing tracheal nerve fibers and thereby stimulates microvascular plasma extravasation.

Kategorie: Poster

Poster 182:

Titel:Innervation of pulmonary trunk in human and mice

Autoren: Rafiq A.(1),Deckmann K.(1),Papadakis T.(1),Bodenbenner M.(1),Kummer W.(1),

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Abstract:
The innervation of pulmonary trunk and main pulmonary arteries plays an important role in the pathogenesis of pulmonary arterial hypertension (PAH). This has been shown in First-in-Man studies, where denervation proximal to the bifurcation causes normalization of pulmonary artery pressure in patients not responding to classical therapy. The mechanisms underlying this effect are unclear. Here we investigated the extent and precise neurochemical characteristics of pulmonary trunk and artery innervation in vascular whole mounts and sections using wild type and transgenic reporter mouse strains demonstrating general autonomic and cholinergic nerve fibers. Antibodies were directed against the catecholaminergic marker enzyme tyrosine hydroxylase (TH), neuropeptide Y (NPY), calcitonin gene-related peptide (CGRP; mainly sensory neurons) and vasoactive intestinal peptide (VIP). Interestingly, only the pulmonary trunk is densely innervated while the bifurcation and main pulmonary arteries nearly lack innervation. At least three neurochemical types of axons were distinguished: Noradrenergic with NPY (sympathetic), CGRP-immunoreactive (sensory), and VIP-immunoreactive (parasympathetic). Rank order of frequency is TH/NPY > CGRP >>> VIP. Cholinergic nerve fibers are absent. In very preliminary experiments, a rich adrenergic innervation comprising of TH-, TH/NPY-immunoreactive nerve fibers was observed at the media adventitia junction of the human pulmonary trunk. Adventitial layers were also innervated by nerve fibers immunoreactive for substance P and TH. In conclusion, the pulmonary trunk receives a spatially restricted specific autonomic and sensory innervation. We propose that trunk innervation plays an important role in development of PAH by regulating compliance and triggering remodeling.

Kategorie: Poster

Poster 183:

Titel:50b11 dorsal root ganglion cells as a peripheral sensory neuron model for sphingolipid and neurotrophin signaling

Autoren:Srikantharajah K.(1),Haberberger R.(2),Schaefer K.(1),Matusica D.(3),

Adressen:(1)School of Computer Science and Microsystems Technology|University of Applied Sciences, Kaiserslautern|Kaiserslautern|Germany; email:kagithiri.srikantharajah@outlook.com; (2)Department of Anatomy and Histology, and Centre for Neuroscience|Flinders University|Adelaide|Australia; (3)School of Computer Science and Microsystems Technology|Flinders University|Adelaide|Australia

Abstract:
Neurotrophins and their receptors play a key role in the development of neuropathic pain, and the ability to modulate their signalling provides some of the most promising targets for dis-covery of novel therapeutics to relieve neuropathic pain. We have recently identified that the biolipid sphingosine-1-phosphate (S1P), its receptors and its enzymes; sphingosine kinase-1 and -2 (SphK1 and 2) also play important roles in nociceptive signaling. To establish whether neurotrophin signalling regulates sphingosine kinase activity, we characterized the immortal-ized 50B11 cell line generated from embryonic rat dorsal root ganglia (DRG) as a peripheral sensory neuron model for the study of nociceptive signaling. Here, we show that 50B11 cells express the neurotrophin receptors TrkA and p75NTR, as well as the transient receptor potential vanilloid family-1 (TRPV-1) receptor (characteristic of a peptidergic nociceptors), in response to forskolin and nerve growth factor (NGF) (n=4). The neurotrophin brain derived neurotrophic factor (BDNF) was also expressed and its relative mRNA expression increased in response to NGF but not forskolin (n=5). More importantly, 50B11 cells expressed SphK1 and 2, and their expression levels were differentially regulated in response to the activator of nociceptors, capsaicin. In addition, TrpV1, TrkA and p75NTR receptor expression increased significantly in response to capsaicin. In summary the DRG cell line 50B11 provides a suitable peripheral sensory neuron model for the study of neurotrophin receptor and sphingosine kinase associated nociceptive signaling events, and may provide a high-throughput model for drug screening against these target proteins.

Kategorie: Poster

Poster 184:

Titel:Cxcr7 is expressed in astrocytes of the diseased cns

Autoren: Puchert M.(1),Pelkner F.(1),Angelov D.(2),Boltze J.(3),Wagner D.(3),Fluegel A.(4),Streit W.(5),Engele J.(1),

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Abstract:
It is well documented that in the central nervous system, the chemokine SDF-1/CXCL12 and its alleged primary receptor, CXCR4, are indispensable for proper brain development, and are upregulated following brain inflammation and injury. By contrast, information on the function of the previously identified second CXCL12 receptor, CXCR7, in the injured CNS is still sparse. Interestingly, our previous work demonstrated that CXCR7 is expressed by cultured cortical astrocytes, and represents the active signalling receptor in these cells. Since in culture, astrocytes reportedly exhibit reactive traits, we now asked whether CXCR7 is also expressed in reactive astrocytes of the diseased brain. To this end, we determined astrocytic CXCR7 expression in histological sections of the spinal cord of rats with experimental autoimmune encephalomyelitis (EAE) and compression injury as well as in sections of the cortex of rats with middle cerebral artery occlusion (MCAO) and of the hippocampus of Alzheimer`s patients. We found that under all these pathologies CXCR7 is prominently expressed by astrocytes whereas CXCR7 expression is rather marginal in spinal cord and brain astrocytes of healthy individuals. Moreover, when we treated cultured cortical astrocytes with the pro-inflammatory cytokine IFN-γ, which typically increases during CNS disorders, we found an upregulation of CXCR7, whereas CXCR7 was downregulated following treatment with the anti-inflammatory cytokine, IFN-β. Collectively, these findings identify CXCR7 expression as a crucial step of astrogliosis which seems to be tightly controlled by cytokines.

Kategorie: Poster

Poster 185:

Titel: The effect of electric stimulation of the medial forebrain bundle on prepulse inhibition. A pilot study in Alzheimer´s disease

Autoren: Panther P.(1),Zaele T.(2),Voges J.(1),Kühne M.(2),Heinze H.J.(2),Kupsch A.(1,2),Nullmeier S.(3),

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Abstract:
Prepulse inhibition of acoustic startle response (PPI) is an operational measure of sensorimotor gating reported to be affected in a variety of neuropsychiatric disorders. Monoaminergic alterations are known to be involved in diseases like Morbus Parkinson or schizophrenia, but may also affect PPI processing. Additionally, a target specific influence of deep brain stimulation (DBS) on PPI has been shown in animal studies. On the other hand, DBS of monoaminergic projections such as the medial forebrain bundle (MFB) could be a possible treatment target for improvement of motivational learning and mood in diseases like Alzheimer´s disease. Here we investigated the influence of different stimulation settings on PPI in three Patients with Alzheimer´s disease (age 72±2.5, duration of symptoms 5.2±0,7 years) treated with experimental DBS of the MFB. PPI was tested frequency dependent: no stimulation, 20Hz, 60Hz or 130Hz. The amplitude was set below occurrence of side effects (pulse width of 90µs). The active contacts were chosen by using tractography of the MFB. The prepulse (85dB) was given 30ms, 60ms and 100ms before presentation of the pulse (103dB).Our three patients showed a frequency dependent pattern of PPI with a DBS-induced reduction of PPI at 20Hz and 130Hz, but a DBS-induced improvement of PPI at 60Hz when compared to results without stimulation. In conclusion PPI is frequency dependent modulated by DBS of the MFB, suggesting that sensorimotor gating can be influenced by electric stimulation of this fiber tract.

Kategorie: Poster

Poster 186:

Titel:Sex matters in hippocampal synaptic connectivity

Autoren: Brandt N.(1),Fester L.(1),Anstoetz M.(1),Rune G.(1),

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Abstract:
Sex matters in hippocampal synaptic connectivity Sexual steroids, which are synthesized in the brain and function in a paracrine manner, are defined as neurosteroids. In final neurosteroid synthesis testosterone is either converted to 17beta-estradiol by activity of aromatase or is irreversibly metabolized to 5alpha-dihydrotestosterone (DHT) by activity of 5alpha-reductase. Our recent findings pointed to a role of 17beta-estradiol in female hippocampal plasticity since inhibition of estradiol synthesis results in a loss of spine synapses in females but not in males, whereas spine synapses are lost in “male” hippocampal cultures but not in “female” cultures in response to inhibition of dihydrotestosterone synthesis, indicating a sex-specific role of sexual neurosteroids. Synthesis of neurosteroids is regulated by Gonadotropin releasing hormone (GnRH). In female hippocampal neurons GnRH upregulates 17beta-estradiol synthesis and increases synapse density via activation of aromatase. This effect was not found in neurons originating from males, very likely due to the higher degree of phosphorylation of aromatase in “male” than in “female” neurons. Taken together maintenance of hippocampal connectivity requires sex-specific neuronal sex steroid synthesis while its plasticity is controlled by GnRH, which regulates sex neurosteroid synthesis in a sex-dependent manner.

Kategorie: Poster

Poster 187:

Titel:Synaptic pruning and microglia in phenylketonuria

Autoren: Schlegel G.(1),Horling K.(2),Schulz S.(2),Vierk R.(2),Ullrich K.(3),Santer R.(3),Rune G.(2),

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Abstract:
The metabolic disease Phenylketonuria is caused by mutations in the gene phenylalanine hydroxylase, leading to the dysfunction of the enzyme and subsequently to elevated levels of phenylalanine in plasma and liquor. Untreated, children develop a severe mental retardation. As learning and memory are strongly associated with the hippocampus, we analysed synaptic connectivity in the Pahenu2 mouse, which is an approved model for the disease. Stereological counting of the synapse density at different developmental stages revealed a disturbed synaptic pruning in the mutants. Neuronal activity, as indicated by LTP and PPF, microglia activity, and C3 mRNA were consistently reduced. In order to find out whether disturbed synaptic pruning is due to elevated levels of phenylalanine we tested the effects of the amino acid in hippocampal slice cultures. High doses of phenylalanine induced synapse loss in the slices, reduced neuronal activity but had no effect on microglia and C3 complement. Our findings suggest an involvement of immune system in Phenylketonuria.

Kategorie: Poster

Poster 188:

Titel:Evidence for circadian control of energy metabolism in murine retina

Autoren: Wolloscheck T.(1),Vancura P.(1),Spessert R.(1),

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Abstract:
The energy metabolism of the mammalian retina has to comply with daily changes in energy demand and its impairment contributes to diabetic retinopathy - one of the most common causes of blindness in Europe and USA. To gain a view of the regulation of the energy metabolism of the retina, in the present study the transcriptional control of Pgc-1alpha (Peroxisome proliferator-activated receptor gamma coactivator 1-alpha) - a transcriptional regulator of energy metabolism - and its target gene (Cpt-1alpha) carnitine palmitoyltransferase-1alpha - a key regulator of mitochondrial beta-oxidation - has been investigated. Both genes were found to undergo daily regulation with elevated values during daytime under light-dark conditions and constant darkness. Furthermore, expression of both genes was modulated in the db/db mouse - a model for diabetic retinopathy. The data of the present study suggest that circadian control of retinal energy metabolism involves transcriptional regulation of mitochondrial beta-oxidation and might be impaired in diabetic retinopathy.

Kategorie: Poster