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ABSTRACTS

Tartalom

SS1.Anatomy-Physiology-Pathophysiology session

AGE-DEPENDENT CHARACTERISTICS OF PRIMARY AFFERENT DEPOLARIZATION IN THE SPINAL CORD OF RATS AND MICE

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Keywords: primary afferents, projection neurons, spinal cord, dorsal root potential
Aims: Previous morphological findings from our laboratory indicate that the local axon collaterals of projection neurons (PN) of the dorsal horn show close appositions with IB4 positive primary afferent terminals. Since PN terminals release glutamate, we assume that they may participate in the development of glutamate-induced primary afferent depolarization (PAD).
To test our hypothesis we're planning selective optogenetic activation of dorsal horn PNs after retrograde viral transfection with channelrhodopsin. However, PAD was previously primarily studied in rats and young mice, so we felt it necessary to confirm the existence of PAD in adult mice that we plan to use for the optogenetic experiments.
Methods: During my study trip to our collaboration partners in Portugal, I worked with preparations made from the lumbar spinal cord of adult mice. PAD evoked by stimulation of adjacent roots was measured as dorsal root potentials recorded with a suction electrode at the L4 dorsal root.
Results: Based on our preliminary results, PAD can only be evoked/detected in mediansagittally hemisected lumbar spinal cord preparations of adult mice.
Conclusion: We assume that age- and species-related characteristics are behind our observations. We will use our results in the planning of optogenetic experiments.

ALTERATIONS IN DENDRITIC IMPULSE PROPAGATION CAUSED BY ATROPHY IS COMPENSATED BY ALTERED MEMBRANE PROPERTIES IN NEOCORTICAL NEURONS OF THE TG2576 MOUSE MODEL OF ALZHEIMER'S DISEASE

Nguyen Nhan, Ervin Wolf, Attila Somogyi (University of Debrecen, Medical School, Debrecen, Hungary)

Introduction: Neurons in the Tg2576 mouse model of Alzheimer's disease, overexpress the human pathological amyloid precursor protein, dendrites show atrophy, and these morphological alterations are accompanied by biophysical alterations of neuronal membranes. Our research group has published that effects of atrophy on dendritic impulse propagation are tended to be compensated by parallel changes in membrane resistance and capacitance of affected neurons.
Now, we aimed to confirm these findings on compensation by using morphofunctional matrices (MFM), a newly developed method of our research group. Elements of MFMs give percentages of total dendritic surface area with similar distances from the soma and with synapses, whose postsynaptic potentials (PSPs) have similar voltage- or current transfers or delays while traveling to the soma.
Methods: We utilized 3-D reconstructed morphology of layer 3 neocortical pyramidal neurons from 12-month-old wild-type (WT) and Tg2576 mice. Segmental cable models of 29 WT and 29 TG neurons were created by matching their membrane properties to electrophysiological data. Voltage- and current transfers and delays of PSPs, mimicked by current injections in various dendritic points of model neurons, were computed and MFMs of WT and TG neurons were calculated. Based on these MFMs, we used cluster analysis to divide the 58 neurons into two groups. Morphofunctional similarity of WT and TG neurons was then quantified by homogeneity and similarity indices, which measure degree of separation of WT and TG neurons in the two clusters. If WT and TG

neurons were morphofunctionally significantly different, MFMs of WT and TG neurons would be separated in the two clusters. However, such a separation could not be detected, indicating morphofunctional similarity of WT and TG neurons. To prove compensation of atrophy by altered membrane properties in TG neurons, imaginary TG' model neurons were created with morphology of TG neurons but with membrane resistances and capacitances of WT neurons. Therefore, TG' cells represented neurons with dendritic atrophy but without compensation. Following simulation of dendritic signaling in 29 TG' cells, MFMs were calculated, cluster analysis and quantification of separation of WT and TG' cells were performed and compared with the degree of separation between WT and TG neurons.
Conclusion: WT and TG neurons were found to be morphofunctionally more similar than WT and TG' neurons, confirming the compensation phenomenon and validity of MFM method.

THE FUNCTIONAL AND MORPHOLOGICAL DAMAGE TO EDINGER-WESTPHAL NUCLEUS OBSERVED IN A PARKINSON'S DISEASE MODEL CANNOT BE REVERSED BY BENZERAZIDE-LEVODOPA TREATMENT

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Keywords: UCN1, EWcp, rotenone, levodopa/benzerazide, Parkinson
Introduction: Parkinson's disease (PD) is a neurodegenerative disease, wtih symptoms divided into motor and non-motor groups. Our research group focuses on the ethiology of mood disorders among the non-motor symptoms. We have seen in previous studies that neurodegeneration occurs in the main neuropeptide expression site of urocortin-1 (UCN1) called central projectional Edinger-Westphal nucleus (EWcp) in PD models and that Ucn1 mRNA expression is reduced, which is associated with mood disorders.
Aim: The aim of this study was to investigate whether anti-PD therapy reverses the functional-morphological changes seen in the nucleus. We hypothesized that treatment would have no signifficant effect on the amount of UCN1 and its mRNA.
Methods: Compared to oil treated control group we induced PD-like state by 6 weeks of rotenone treatment. Half of the animals injected with rotenone were also treated with benzerazide/levodopa which is the treatment used in PD. Rotarod, open field and sugar preference tests were used to verify the efficacy of the model and therapy. Functional morphological studies were performed on EWcp sections using a combination of immunfluorescence labeling and RNAscope in situ hybridization.
Results: Animal's locomotion and mood were severly impaired during rotenone treatment. Motor symptoms improved with benzerazide/levodopa, in contrast to anxiety and depression-like state. We reproduced the previously observed UCN1/EWcp neuronal death, which was not affected by therapy. Surviving cells had higher levels of UCN1 peptide and lower levels of Ucn1 mRNA, which were unaffected by drug treatment.
Conclusion: The opposite change of the UCN1 peptide and its mRNA indicates that the release of the neuropeptide from the cells is inhibited. This phenomenon may be due to a PD-like state and energetic deficit induced by rotenone. Our Results suggest that benzerazide/levodopa treatment is ineffective in treating mood-realated non-motor symptoms, suggesting that impairment of EWcp contributes to mood disorders in PD.

THE ROLE OF EXTRACELLULAR DNA AND NEUTROPHIL EXTRACELLULAR TRAPS IN MURINE MODEL OF ACUTE LIVER FAILURE

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Keywords: extracellular DNA, neutrophil extracellular traps, acute liver failure
Aims: The aim of our study was to analyse and compare total extracellular DNA concentration and formation of neutrophil extracellular traps in murine model of acute liver failure (ALF). Further we aimed to clarify the role of toll-like receptor 9 (TLR-9), which is important for signalling and activation of NETosis and the enzyme peptidyl deaminase 4 (PAD 4) initiating chromatin decondensation.
Methods: Acute liver failure was induced by intraperitoneal administration of 200 mg/kg thioacetamide to three groups of mice: wild type (WT), PAD 4-deficient and TLR- 9-deficient mice.

Results: We observed a trend of increased ecDNA concentration in all ALF mice compared to controls. This result correlated with an increased DNase activity and nuclear DNA concentration, but not mitochondrial DNA. The result from noetic cell number analysis was variable.
Conclusion: Despite the high variability in values and mortality of the animals, we found increased extracellular DNA and absent NETosis in mice with acute liver failure.
Supports: Supported in part by the grant of the Ministry of Education, Science, Research and Sport of the Slovak Republic VEGA 1/0649/21 and the grant of the Agency for Research and Development APVV-21-0370.

NEUROECTODERMAL STEM CELLS IMPROVE THE FUNCTIONAL AND MORPHOLOGICAL OUTCOME AFTER CHRONIC SPINAL CORD INJURY VIA MULTIPLE MECHANISMS

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Keywords: stem cell, regeneration, spinal cord injury
Aims: Spinal cord contusion injury leads to severe tissue loss and subsequent deficit of motor, sensory and vegetative functions below the lesion. In this study we investigated whether transplantation of neuroectodermal stem cells into the injured rat spinal cord is able to induce morphological and functional improvement in a chronic spinal cord injury model.
Methods: Mouse embryonic clonal neuroectodermal stem cells were grafted intraspinally five weeks after a thoracic spinal cord contusion injury performed in SD rats. Control animals underwent contusion injury without stem cell transplantation. Functional tests and detailed morphological analysis were performed to evaluate the effects of grafted cells.
Results: Grafted animals showed significantly better functional recovery compared with control animals. Morphologically, the contusion cavity was significantly smaller, and the amount of spared tissue was significantly higher in grafted animals than in controls. Retrograde tracing studies showed a statistically significant increase in the number of FB-labelled neurons rostral to the injury. The extent of functional improvement was related to the amount of inhibitory factors around the cavity and microglial reactions in the injured segment. Five days after transplantation the majority of grafted cells appeared to survive, formed clusters and a small proportion of the cells differentiated into neurons and astrocytes. Ten days after grafting the majority of the grafted cells appeared as nonviable fragments in microglia/macrophage cells.
Conclusions: These data suggest that grafted neuroectodermal stem cells are able to induce morphological and functional recovery after chronic spinal cord contusion injury despite the limited survival of transplanted cells.

A NEW POTENTIAL THERAPEUTIC TARGET IN INFLAMMATORY RETINOPATHY

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Keywords: retinal inflammation, PAC1R, PACAP
Retinal inflammation may lead to visual impairment, even blindness in most severe cases. Pituitary adenylate cyclase activating polypeptide (PACAP) is a neuropeptide, which has strong neuroprotective and general cytoprotective effects. It is also found in the eye and it is involved in several ocular processes. Three receptors can be distinguished, however the specific PAC1 receptor plays the key role in its protective mechanisms.
Our aim was to investigate the effectiveness of a specific, exogenous PAC1 receptor agonist agent, maxadilan, in inflammatory retinopathy.

Inflammation was induced by bacterial lipopolysaccharide in mice. Maxadilan was administered by intravitreal injection. Optical coherence tomography was used to follow the changes in thickness of all retinal layers. Change of ganglion cell number was evaluated after toluidine blue staining. Electroretinography provided functional information. Expression level of forty different types of cytokines was also analyzed.
Results: Our data show that maxadilan is able to prevent the decrease of the outer nuclear layer, outer plexiform layer, inner nuclear layer, inner plexiform layer and the photoreceptor layer. In addition, it improves functional outcome. Significant ganglion cell degeneration was observed in the inflamed group. However, ganglion cell number remained similar to control group after maxadilan treatment. Based on our Results, PAC1 receptor-mediated signaling pathways significantly influence the level of several cytokines and chemokines (such as MIG, MIP2, G-CSF and C5/C5a).
Conclusion: The specific, exogenous PAC1 receptor agonist maxadilan prevents the morphological and functional damage in inflammatory retinopathy. Based on our Results PAC1 receptor is a new potential therapeutic target in this disease.

EXAMINATION OF PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE (PACAP) IN PATIENTS WITH ATRIAL FIBRILLATION UNDERGOING PULMONARY VEIN ISOLATION

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Keywords: PACAP, atrial fibrillation, pulmonary vein isolation, electroanatomical mapping
Introduction: PACAP is a multifunctional neuropeptide having cardioprotective effects. Recently we showed that plasma PACAP level increases in myocardial infarction and decompensated heart failure (HF), while it decreases in compensated chronic HF. The aim of the present study was to examine the changes of PACAP levels in patients with atrial fibrillation (AF) undergoing pulmonary vein isolation(PVI).
Material and Methods: We collected blood samples from patients (n=20) with AF undergoing PVI from the femoral vein at the beginning of the procedure, the left atrium before the ablation, the femoral vein at the end of the procedure, and the cubital vein on the first postoperative day. ELISA was used to measure the endogenous PACAP level. Patients were divided into intact(n=11) and scarred(n=9) left atrial groups based on the left atrial voltage map created by electroanatomic mapping system.
Results: We detected significantly higher PACAP levels in left atrial and post-operative femoral vein samples compared to peripheral blood samples collected at the beginning of the procedure and 1 day after the procedure. We found a significantly larger increase in PACAP levels in femoral vein blood samples immediately after surgery in patients with scarred left atrium compared to patients with intact atrium.
Conclusions: We found significant differences between PACAP levels of blood samples from the atrium and peripheral veins. Elevated PACAP levels in atrial samples may be due to myocardial cells and/or neurons. After the procedure, we found elevated PACAP levels in peripheral blood samples, although the dynamics of the elevation varied depending on myocardial scarring.

SFS1.HIGHLITED SESSION

ORTHOGNATIC SURGERY FOR CRANIOFACIAL DEFORMITIES

Prof. Chung. H. Kau (USA)

No abstract available.

ARTIFICIAL INTELLIGENCE IN RHEUMATOLOGY AND IMMUNOLOGY

Dr. Zoltan Szekanecz

No abstract available.

SS2.RADIOLOGY

RADIOGENOMIC ANALYSIS OF NSCLC

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Background: Biological and immunotherapies are becoming more and more frequent therapeutic choices in lung cancer treatment. In all cases a biopsy is necessary to verify the genetic features of said tumor prior to starting treatment. Due to these genetic variabilities, research of radiogenomic markers is becoming popular. The aim of our study is to identify radiomic traits in close correlation with these genetic mutations, which are the basis of targeted treatment now and in the future.

Methods: From the patient database of the Thoracic Surgery Unit of the National Institute of Oncology, 187 patients were selected. These patients were diagnosed with non-small cell lung cancer (NSCLC) and following resection, molecular pathological analysis was performed using the specimens. These patients were sorted into categories based on their EGFR, KRAS mutations and PD-L1 expressions.

Results: There were 53 patients without genetic mutation, 50 patients showed EGFR positivity, 69 were KRAS positive and 82 patients had a PD-L1 expression over 50%. Our patient population is sorted and non-representative of the NSCLC group, therefore the ratio of mutations alters from those of the NSCLC group. Naturally, multiple mutations can be present within one specimen. In the 187 selected cases the earliest, preoperative native CT was obtained as the basis of segmentation. The tumors were segmented on non-contrast images using an open-source program, Slicer-3D. Following tumor segmentation, the image file containing radiomic information together with the file containing the mask (segmentation starting point and coordinates) were sent to our colleagues at SZTAKI for analysis using a safe storage interface. Clinically relevant mutations and mutation-combinations are to be appointed together with clinicians and pathologists.

Conclusion: Although the analysis and software-learning is still in progress, we aim in our study to find links between radio morphology and mutation status in close coherence with NSCLC and current drug targets used in treatment.

ELEVATED BLOOD LIPID LEVELS DO NOT PREDICT THE INCIDENCE OF ARTERIAL PLAQUES IN ELDERLY MONOZYGOTIC TWINS DISCORDANT FOR NON-ALCOHOLIC FATTY LIVER DISEASE

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Keywords: NAFLD, atherosclerosis, twins, ultrasound

Introduction: Elevated blood lipid levels are considered to be a risk factor for both non-alcoholic fatty liver disease (NAFLD) and arterial plaque formation. The development of these pathologies can be strongly influenced by the individual genetic background of the patients. We hypothesized that the elevated blood lipid levels of patients with NAFLD have an accelerating effect on arterial plaque formation. Because genetic background can have a major impact on both of these pathologic changes, we investigated monozygotic twins discordant for NAFLD.

Methods: We investigated 60 elderly monozygotic twins from the population based Hungarian Twin Registry (30 pairs, age ±SD: 66.1±5.8 years, 23% male), who were discordant for NAFLD. The twins underwent blood sampling and laboratory analysis, ultrasonographic fatty liver assessment by measuring liver to kidney ratio based on attenuation, and ultrasonographic carotid and femoral atherosclerotic plaque assessment (Samsung RS85).

Results: Twins with NAFLD had significantly higher glutamate pyruvate transaminase (GPT), ApoA1 and ApoB apolipoprotein, low density lipoprotein (LDL), and serum cholesterol levels ($p<0.05$). The number, type, and localization of carotid and femoral artery plaques did not show any significant correlation with the presence of NAFLD.

Conclusions: NAFLD and the presence of carotid or femoral atherosclerotic plaques did not share the presumed common genetic background with high plasma lipid levels based on our relatively small cohort of discordant MZ twins. Blood lipid levels although might play a role in the individual differences in NAFLD severity.

THE IMPACT OF NOVEL RECONSTRUCTION ALGORITHMS ON CALCIUM SCORING: RESULTS ON A DEDICATED CARDIAC CT SCANNER

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Keywords: cardiovascular risk; coronary artery calcium score; coronary artery disease; image reconstruction.

Aims: We aimed to assess the reliability of coronary artery calcium score (CACS) measurements with an advanced adaptive statistical iterative reconstruction (ASIR-CV) and model-based adaptive filter (MBAF2) designed for a dedicated cardiac CT scanner by comparing them to the gold-standard filtered back projection (FBP) calculations.

Methods: We analyzed non-contrast coronary CT images of 404 consecutive patients undergoing clinically indicated CCTA. CACS and total calcium volume were quantified and compared on three reconstructions (FBP, ASIR-CV, and MBAF2+ASIR-CV). Patients were classified into risk categories based on CACS and the rate of reclassification was assessed.

Results: Patients were categorized into the following groups based on FBP reconstructions: 172 zero CACS, 38 minimal (1–10), 87 mild (11–100), 57 moderate (101–400), and 50 severe (400<). Overall, 19/404 (4.7%) patients were reclassified into a lower-risk group with MBAF2+ASIR-CV, while 8 additional patients (27/404, 6.7%) shifted downward when applying stand-alone ASIR-CV. The total calcium volume with FBP was 7.0 (0.0–133.25) mm3, 4.0 (0.0–103.5) mm3 using ASIR-CV, and 5.0 (0.0–118.5) mm3 with MBAF2+ASIR-CV (all comparisons $p < 0.001$).

Conclusion: The concomitant use of ASIR-CV and MBAF2 may allow the reduction of noise levels while maintaining similar CACS values as FBP measurements.

FOLLOW-UP EXAMINATION OF WHITE MATTER MICROSTRUCTURAL CHANGES CAUSED BY TRAUMATIC BRAIN IJNURY WITH DTI.

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Aims: Traumatic brain injuries are the leading cause of death in developed societies. Pathological components of diffuse axonal injury (DAI) such as microbleeds can be visualized with modern MRI modalities. Susceptibility-weighted imaging (SWI) is sensitive modality for these associated microbleeds. In our previous research, we examined the differences in the diffusion parameter of DAI-associated microbleeds after trauma with diffusion

tensor imaging. In our present research, we investigated the evolution of these parameter deviations. **Methods**: 13 Mayo severe-moderate cranial trauma patients with a negative history of psychiatric, neurological or previous cranial trauma were taken after the trauma and 1-year follow-up, furthermore recordings of 16 persons with a history of TBI older than 5 years were compared with the recordings of age-matched control patients. The white matter was reconstructed by probabilistic tractography, and the perilesional white matter was examined in areas concentrically every 2 mm up to 20 mm from the center of the microbleeds. The mean diffusion parameters of the sectional voxels of the spheroids and white matter obtained during tractography were recorded.

Results: The significant ($p<0.005$) perilesional diffusion parameter differences on the recordings immediately following the trauma still show significant differences on the one-year follow-up recordings compared to the recordings of the control group. The perilesional diffusion parameters of the group with an anamnesis of more than 5 years of TBI also remain significantly preserved.

Conclusion: Differences in derived diffusion parameters that can be detected in the environment of white matter microbleeds caused by TBI are maintained over time.

HERITABILITY OF ANATOMICAL STRUCTURES ASSOCIATED WITH OBSTRUCTIVE SLEEP APNOEA IN TWINS USING MRI IMAGING

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Introduction: In addition to predisposing factors, anatomical features have a role in the development of obstructive sleep apnoea(OSA). The aim of our study was to investigate the genetic and environmental determinants of the soft tissue structures associated with upper airway obstruction on MRI scans in twins and study the influence of environmental factors on the measured structures.

Methods: 55 adult twin pairs (33MZ, 22DZ, median age and Q1-Q3: 53(44-63.75)years) from the Hungarian Twin Registry underwent head and neck MRI(Philips Ingenia 1.5T). Cephalometric, soft tissue and adipose tissue structures were measured. Carotid and femoral artery US(Samsung RS85) and whole-body composition measurements (OMRON BF500) were obtained.

Results: Strong genetic determination was found for the anteroposterior diameter of the tongue and the thickness of submental adipose tissue. Parapharyngeal fat-area, pharyngeal wall thickness and the smallest diameter of the posterior airways were strongly determined by environmental factors. We found a significant association between parapharyngeal fat area and body weight, waist circumference and metabolism($p<0.05$) in discordant MZ twin pairs. The thickness of submental adipose tissue showed a correlation with a lower muscle percentage($p<0.05$). There were inverse correlations between carotid intima-media thickness and parapharyngeal fat, tongue volume and submental fat thickness($p<0.05$).

Conclusions: We found significant association between anatomical structures potentially involved in upper airway obstruction and obesity-related markers.

These Results might provide a better understanding of the genetic and environmental background in the development of OSA.

EXPLORING THE INTERPLAY OF GENETIC AND ENVIRONMENTAL FACTORS ON THE MORPHOLOGY OF THE LIMBIC CORTEX AND HIPPOCAMPAL SUBFIELDS: INSIGHTS FROM AN MRI TWIN STUDY

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Introduction: The Hippocampus and limbic system are vital for memory, emotions, and learning, and linked to disorders like anxiety and schizophrenia. While genetic influence on total brain volume is known, heritability of specific limbic and Hippocampal subfield structures remains unclear. This twin MRI analysis explores the genetic and environmental influences on these critical brain regions, bridging neurology and psychiatry.

Material and Methods: A total of 118 healthy adult twins were enrolled from the Hungarian Twin Registry, including 86 monozygotic and 32 dizygotic twins, with a median age of 50 ± 27 years. Participants underwent high-resolution three-dimensional T1-weighted MRI to assess the volume and grey matter thickness of limbic cortex structures, such as the anterior cingulate gyrus(ACg), middle cingulate gyrus(MCg), and posterior cingulate gyrus(PCg), parahippocampal gyrus(PHg), and Entorhinal area (Ent). Additionally, the volume of the Hippocampus and its subfields, including Cornu Ammonis (CA)1, CA2, CA3, CA4, Dentate Gyrus (DG), and strata radiatum/lacunosum/moleculare (SR/SL/SM), was measured using an automated quantitative analysis tool (volBrain). Genetic modeling was performed to decompose the variance of traits into genetic, shared environmental, and unshared environmental components while adjusting for age and sex.

Results: The limbic cortical and hippocampal compartments exhibited strong genetic influences. After adjusting for age and sex, heritability estimates were as follows: total limbic cortex volume (76.6%, 95% CI: 0.609-0.865), Entorhinal area volume (60.9%, 95% CI: 0.383-0.766), ACg volume (67.4%, 95% CI: 0.474-0.807), MCg volume (61.1%, 95% CI: 0.387-0.767), PCg volume (69.4%, 95% CI: 0.503-0.821), parahippocampal gyrus volume (72.7%, 95% CI: 0.548-0.842), total hippocampal volume (77.1%, 95% CI: 0.617-0.869), CA1 volume (72.3%, 95% CI: 0.544-0.839), CA2/3 volume (48%, 95% CI: 0.215-0.679), CA4 and DG volume (65.7%, 95% CI: 0.448-0.797), and SR/SL/SM total volume (81.6%, 95% CI: 0.687-0.895).

Environmental factors substantially influenced the phenotypic variance of CA2/3, Entorhinal area, and PCg volumes. Shared environmental factors accounted for 45.7% (95% CI: 0.239-0.632), 56.6% (95% CI: 0.372-0.713), and 65% (95% CI: 0.481-0.773) of the variance in these volumes, respectively. Non-shared environmental factors accounted for 54.3% (95% CI: 0.368-0.761), 43.4% (95% CI: 0.287-0.628), and 35% (95% CI: 0.227-0.518) of the variance in these volumes, respectively.

Conclusion: Our study demonstrated a strong genetic influence on the limbic system's cortical grey matter and hippocampal volume compartments.

Additionally, we observed a noteworthy impact of shared environmental factors on the volume of the CA2/3, Entorhinal area, and PCg. These findings emphasize the potential involvement of environmental factors in neurodegenerative disorders such as Alzheimer's disease, schizophrenia, and Parkinson's disease.

OPTICALLY GUIDED HIGH-FREQUENCY ULTRASOUND IS A NEW IN VIVO TOOL IN THE DIAGNOSIS OF SKIN CANCERS

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Aims: Skin cancer is a pressing health concern, with basal cell carcinoma (BCC) being the most prevalent among Caucasians and melanoma's incidence on the rise. Histological subtype (HST) identification and treatment planning often require invasive biopsies. We explored the early detection potential of optically guided high-frequency ultrasound (OG-HFUS) imaging for aggressive BCC HSTs and compared OG-HFUS with multispectral imaging (MSI) for melanoma Breslow thickness (BT) estimation.

Methods: Clinical assessments, dermoscopy, and 33 MHz OG-HFUS imaging were

performed on 62 BCC patients, identifying 15 aggressive and 47 low-risk HST cases. In 79 primary melanoma patients (mean BT: 1,631±1,745), we compared optically guided 33 MHz HFUS and MSI prototype with histology-established BT, categorizing into three tumor thickness groups.
Results: OG-HFUS distinguished aggressive BCC HSTs through irregular shape ($p<0.0001$), ill-defined margins ($p<0.0001$), and non-homogeneous echoes ($p=0.004$). Our risk algorithm outperformed macroscopic and dermoscopic evaluation, exhibiting higher sensitivity (84.6% vs. 31.9%) and specificity (92.3% vs. 75.5%) in discriminating aggressive from low-risk HSTs. HFUS-measured tumor thickness showed stronger correlation with histological BT than MSI (HFUS: r: 0.9706, p:<0.0001; MSI: r: -0.6788, p:<0.0001). HFUS displayed elevated sensitivity (93.42%) and specificity (96.71%) in differentiating tumor thickness, surpassing MSI (sensitivity: 58.44%, specificity: 79.22%).
Conclusions: OG-HFUS effectively identifies aggressive BCC subtypes, aiding early treatment decisions. Moreover, HFUS surpasses MSI in noninvasively predicting BT, holding potential for surgical margin selection in melanoma surgery.
Support: This study received support from Dermus Ltd., University of Latvia, Semmelweis University, and Roswell Park Comprehensive Cancer Center.

SFS2. HIGHLITED SESSION

SERENDIPITY OR PERSISTENT DRUDGERY; RESEARCH IN LIGHT AND SHADOW

Sánticsné Prof. Dr. Pintér Erika

No abstract available.

SS3.CARDIOLOGY

THE BACKGROUND OF PULSE ARRIVAL TIME (PAT) OSCILLATIONS IN HEALTHY YOUNG ADULTS

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Keywords: photoplethysmography, pulse arrival time, respiratory sinus arrhythmia, fast Fourier transformation, breathing pattern
Aims: For the monitoring and follow-up of cardiovascular diseases, parameters such as pulse arrival time (PAT) are of increasing importance. Obtained from simultaneous ECG-PPG (photoplethysmogram) recordings, measured at different reference points, oscillating PAT-values are related to blood pressure, also stiffness. Our aim was proving the correlation between said PAT-oscillations and breathing.
Methods: We analysed 4x5-minute ECG-PPG records of ten healthy volunteers (average: 26,5years) from our database, with the following breathing patterns: spontaneous, single- and double-paced with metronome at 4500ms (222.2mHz), using 1:2 and 1:1 inhalation:exhalation ratio. Applied PPG reference points: extrapolated base point, 1/3 and 2/3-amplitude height, peak, derivative peak. The spectra of RRI and corresponding PAT-series showing respiratory sinus arrhythmia (RSA) were computed by fast Fourier transformation, then compared with normalized cross-correlation.
Results: At each breathing pattern, group averages of the maximum correlation of RSA-PAT did
not show significant differences by Friedman-test, neither did the frequency-shift of the spectra. The lowest correlation was obtained at the peak (median= 0.79; IQR=0.12; Friedman $p<0.001$; Wilcoxon $p<0.001$). Furthermore, frequency-shift was not detected.

Conclusions: Among the reference points, the highest correlation value was measured at T1/3 height, while the lowest cross-correlation was obtained at the peak, caused by the temporal uncertainty of the peak detection. Overall, an excellent correlation of RSA-PAT was proved, with negligible frequency shift in the spectra.
In healthy volunteers, PAT oscillation shows a strong cross-correlation with RSA for all studied reference points and breathing patterns. Our research can facilitate choosing optimal reference points in PAT-measuring in smart devices.

USE OF A NEW NON-CONTRAST-ENHANCED BOOST CARDIAC MR SEQUENCE BEFORE ELECTRICAL CARDIOVERSION OR ABLATION OF ATRIAL FIBRILLATION – A PILOT STUDY

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Keywords: atrial fibrillation, ablation, pulmonary vein anatomy, left atrial thrombus, cardiac magnetic resonance imaging, BOOST sequence
Aims: We aimed to compare the efficacy of a new non-contrast-enhanced cardiac MR (CMR) sequence (BOOST) with transesophageal echocardiography (TEE) for left atrial appendage (LAA) thrombus detection and to evaluate the usefulness of BOOST images for planning radiofrequency catheter ablation (RFCA) compared with left atrial (LA) contrast-enhanced CT.
Methods: Patients with atrial fibrillation undergoing either electrical cardioversion or RFCA were enrolled. Participants underwent pre-procedural TEE and CMR scans. Patients scheduled for RFCA also had pre-procedural LA contrast-enhanced CT. In such cases, the operating physician was asked to subjectively define the CT and CMR scan quality on a scale of 1-10 (1 = worst, 10 = best) and comment on CMR's usefulness in RFCA planning.
Results: Seventy-one patients were enrolled. In 94%, both TEE and CMR excluded, and in 1 patient, both modalities reported the presence of LAA thrombus. In 1 patient, TEE was inconclusive, but CMR excluded LAA thrombus. In 2 patients, CMR could not exclude the presence of thrombus, but in 1 of those cases, TEE was also indecisive. The quality of the LA contrast-enhanced CT scans was better compared with the image quality of the CMR BOOST sequence [8 (7-9) vs. 6 (5-7), $p<0.0001$]. Still, the CMR images were useful for procedural planning in 91% of cases.
Conclusions: The new CMR BOOST sequence provides appropriate image quality for ablation planning. The sequence might be useful for excluding larger LAA thrombi; however, its accuracy in detecting smaller thrombi is limited.

REMOTE MANAGEMENT OF PATIENTS WITH CARDIAC IMPLANTABLE ELECTRONIC DEVICES DURING THE COVID-19 PANDEMIC

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Keywords: remote monitoring; chronic heart failure; cardiac implantable electronic devices; COVID-19
Aim: Remote monitoring (RM) is the newest function of cardiac implantable electronic devices (CIEDs). In our observational retrospective analysis, we aimed to assess whether telecardiology could be a safe alternative to routine outpatient examinations during the COVID-19 pandemic.
Methods: The in- and outpatient visits, the number of acute cardiac decompensation episodes, the RM data from CIEDs, and general condition were examined via questionnaires (KCCQ, EQ-5D-5L).
Results: Regarding the enrolled 85 patients, the number of personal patient appearances was significantly lower in the year following the pandemic outbreak compared to the previous year (1.4 ± 1.4 and 1.9 ± 1.2, $p = 0.0077$). The number of acute decompensation events was five before and seven during lockdown ($p = 0.6$). Based on the RM data, there was no significant difference in heart failure (HF) markers (all related $p > 0.05$); only patient activity increased after restrictions were lifted compared to that before the lockdown ($p = 0.03$). During restrictions,

patients reported increased anxiety and depression compared to their previous state ($p < 0.001$). There was no subjective change in the perception of HF symptoms ($p = 0.7$).
Conclusion: Based on the subjective perception and CIED data, the quality of life of patients with CIED did not deteriorate during the pandemic, but their anxiety and depression intensified. Telecardiology may be a safe alternative to routine inpatient examination.

INVESTIGATION OF THE EFFECTS OF DANICAMTIV, A NOVEL CARDIAC MYOSIN ACTIVATOR IN VIVO

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Keywords: danicamtiv, myosin activator, HFrEF, diastolic dysfunction
Introduction: Enhancing myocardial contractility is another possible way to treat heart failure with reduced ejection fraction (EF). Danicamtiv (DAN) is a novel cardiac myosin activator capable of augmenting left ventricular (LV) systolic function.
Aim of the study: To characterize the effects of DAN on systolic and diastolic function in vivo with echocardiography.
Material and Methods: Experiments were performed on anaesthetised rats (n=14). DAN was administered intravenously, at a dose of 2 mg/kg amd continuous 3-lead ECG monitoring was performed. Systolic and diastolic function was assessed by echocardiography, before and after DAN administration. Data are indicated as mean±SEM. Statistics: paired t-test, $p<0.05$.
Results: DAN reduced end-systolic diameter (2.9±0.2 vs. 3.8±0.1 mm, $p<0.001$), whereas end-diastolic diameter remained unchanged. The LVEF (89.4±1.0 vs. 79.8±1.2%, $p<0.001$), fractional shortening (63.6±1.5 vs. 50.6±1.3%, $p<0.001$), stroke volume (290.6±20.3 vs. 243.9±10.1µL, $p=0.01$), and cardiac output (72.5±5.0 vs. 61.4±3.0mL/min, $p=0.03$) increased significantly. LV strain improved, supporting the positive inotropic effect of the drug. Systolic duration (106.0±3.3 vs. 88.6±1.8ms, $p=0.0001$) and systolic ejection time (87.1±3.1 vs. 72.3±1.5ms, $p<0.001$) prolonged, whereas diastolic duration (133.0±4.7 vs. 152.2±4.2ms, $p=0.008$) decreased. Early (E) diastolic transmitral filling (TF) velocity decreased (645.9±29.2 vs. 720.9±11.9mm/s, $p=0.01$), since late (A) TF velocity increased (506.9±37.8 vs. 379.2±19.0mm/s, $p=0.003$) resulting in a decrease in the E/A ratio. Continuous ECG monitoring did not reveal any proarrhythmic effect.
Conclusion: DAN improves LV contractility without any proarrhythmic effects, but the diastolic dysfunction (DD) provoked by DAN should be taken into consideration. Close monitoring DD seems to be essential during the future clinical application.

FEATURE SELECTION IDENTIFIES ACTIVE RELAXATION AS THE MOST INDICATIVE ASPECT OF LEFT VENTRICULAR FUNCTION FOR PROTEOMIC PERTURBATIONS IN A COHORT OF MALE AND FEMALE RATS IN VARIOUS STAGES OF MYOCARDIAL REMODELING AND REVERSE-REMODELING

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Keywords: aortic banding, myocardial hypertrophy, reverse remodeling, proteomics, active relaxation
Introduction: Pressure overload (PO) and myocardial remodeling impair left ventricular (LV) function, whilst pressure-unloading (PU) therapies can lead to reverse remodeling and restore LV structure and function. Ethical limits on repeated myocardial sampling restrict investigation into pressure unloading therapies' ability to induce reverse remodeling at the molecular level.
Methods: Aortic banding (AB) was performed to induce PO in male and female rats. Debanding (DB) the aorta in a subset of the animals resulted in PU at week 6. The morphological and functional aspects of LV remodeling and reverse remodeling were assessed through echocardiography and pressure-volume analysis at weeks 6 and 12. LC-MS/MS was used for proteomic measurements on LV samples, and bioinformatic feature selection identified myocardial proteomic alterations tightly linked to selected LV parameters.
Results: Functional and morphological characteristics of myocardial hypertrophy developed and regressed irrespective of sex. Of the 3343 proteins identified, 416 demonstrated a significant association with changes in Tau (a robust parameter of LV active relaxation) due to myocardial remodeling and reverse remodeling in the AB and DB groups, respectively. Tau far outperformed other LV parameters in showing a strong relationship with LV proteomic alterations. Gene ontology biological process (GO:BP) analysis of the 416 proteins demonstrated the role of specific regulatory mechanisms influencing myocardial remodeling. Changes in active relaxation showed a strong correlation with proteins governing cellular functions in myocardial reverse remodeling.
Conclusions: Parameters of active relaxation may be the best metrics to assess the extent of myocardial remodeling and reverse remodeling in experimental and clinical studies.

LONG-TERM PROGNOSIS OF FUNCTIONALLY NON-SIGNIFICANT CORONARY STENOSES WITHOUT REVASCULARISATION

Dora Klettner, Zsolt Piroth (Gottsegen National Cardiovascular Centre Budapest, Hungary)

Introduction: Fractional flow reserve (FFR) is the gold standard for revascularisation decisions with a cut off value of 0.80. We studied the outcome of coronary arteries (target vessels, TV) that were not revascularized because of a negative FFR at our centre between January 01, 2016, and June 30, 2017.
Our aims were 1) to find the relationship between risk factors (gender, age, hypertension, dyslipidaemia, diabetes, smoking), previous percutan coronary intervention (PCI) of the TV (>6 months before), indication for coronary angiography (acute (ACS) or chronic coronary syndrome (CCS)), location of stenosis and the FFR value, and 2) the relationship between the above parameters and clinical outcome, the endpoint being a composite of TV revascularisation (TVR) and TV-related myocardial infarction (TVMI).
535 lesions of 447 patients were followed for a median of 49.7 months. Follow-up was complete in 93.5%. Significantly lower FFR values were observed in men ($p=0.015$) and in left anterior descending (LAD) arteries ($p<0.0001$). During follow-up 12 TVMI and 8 FFR-guided TVR occurred. Another 5 lesions underwent TVR without FFR measurement due to obvious morphological progression of stenosis. Thus, 25 out of 535 FFR negative lesions had an endpoint. ACS indication ($p=0.021$) and previous TV PCI ($p=0.027$) were significantly predictive of clinical outcome. We found significantly lower FFR values in men and in LAD arteries in an FFR negative population. ACS indication and previous TV PCI were predictors of clinical events related to TV with a functionally non-significant stenosis. The incidence of adverse clinical events (TVR, TVMI) associated with non-revascularised vessels with a non-significant FFR was only 1.1% per year. Our Results indicate that FFR is an adequate method to choose lesions the revascularisation of which can be safely deferred and treated by medical therapy alone with good clinical outcome.

RETROSPECTIVE RECLASSIFICATION OF AORTIC STENOSIS SEVERITY BY HYBRID AVA METHOD IN TAVR PATIENTS

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Keywords: aortic stenosis, TAVR, hybrid AVA
Background: Echocardiography may underestimate aortic valve area (AVA) due to the elliptic shape of left ventricular outflow track (LVOT) and therefore may misclassify the degree of aortic stenosis (AS). Using CT derived LVOT area in the continuity equation (hybrid-AVA) may provide more accurate estimates of AS and reclassify desease severity.
Aims: To assess the reclassification rate of AS using hybrid AVA in different subgroups of AS.
Methods: We enrolled 241 patients (121 males, mean age: 77.9±8.2 years) with severe native valve AS who underwent transcathether aortic valve replacement (TAVR) in our tertiary cardiovascular center. Patients were divided into high-gradient (HG), low-flow low-gradient (LFLG), and normal-flow low-gradient (NFLG) AS. Hybrid AVA was calculated by combining CT-based LVOT area with echo Doppler parameters.
Results: The echo-LVOT diameter (20.2±1.9 mm) was significantly smaller than the minimum (21.8±2.9 mm), maximum (28.9±3.3 mm) and mean (25.4 ± 2.9 mm) CT-LVOT diameter (p<0.0001 for all). Echo-LVOT area was smaller than CT-LVOT area (324.3±62.2 mm2 vs 497.0±116.4 mm2; p<0.0001), and echo-AVA was smaller than hybrid-AVA (0.6±0.2 cm2 vs 0.9±0.3 cm2; p<0.0001). Implementing the hybrid method 72 patients (29.9%) were reclassified to moderate AS, 37 patients (21.5%) in the HG group, 26 patients (47.2%) in the LFLG group, and 9 patients (64.3%) in the NFLG group.
Conclusions: Using CT-based measurements resulted in one third of our population being reclassified from severe to moderate AS, which was most pronounced in patients with low-flow AS.

IMPACT OF HIGH-POWER AND VERY HIGH-POWER SHORT-DURATION RADIOFREQUENCY ABLATION TECHNIQUES ON PROCEDURE CHARACTERISTICS AND FIRST-PASS ISOLATION DURING PULMONARY VEIN ISOLATION

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Keywords: atrial fibrillation, high-power RF-ablation, first pass isolation
Aims: High-power short-duration (HPSD) radiofrequency ablation has been proposed as a method for producing rapid and effective lesions for pulmonary vein isolation (PVI). We aimed to evaluate the procedural characteristics and the first-pass isolation (FPI) rate of HPSD and very high-power short-duration (vHPSD) ablation compared to low-power long-duration (LPLD) ablation technique.
Methods: 156 patients with atrial fibrillation (AF) were enrolled and assigned to LPLD, HPSD, or vHPSD PVI. The energy setting was 30W, 50W, and 90W in the LPLD, HPSD, and vHPSD groups, respectively.
Results: Bilateral PVI was achieved in all cases. Compared to the LPLD group, the HPSD and vHPSD groups had shorter procedure times (85 [75-101] min, 79 [65-91] min, and 70 [53-83] min), left atrial dwelling times (61 [55-70] min, 53 [41-56] min, and 45 [34-52] min), total RF ablation time (1567 [1366-1761] sec, 1398 [1021-1711] sec, and 336 [247-386] sec) (all p-values < 0.01). The use of HPSD (OR=2.72, 95% CI 1.15-6.44, p=0.023) and vHPSD (OR=2.90, 95% CI 1.24-6.44, p=0.014) ablation techniques were associated with a higher probability of bilateral FPI. The 9-month AF-recurrence rate was lower in case of HPSD and vHPSD compared to LPLD ablation (10, 8 and 36%, p=0.0001). The presence of FPI was associated with a lower AF-recurrence rate at 9 months (OR=0.09, 95% CI 0.04-0.24, p=0.0001).
Conclusion: both HPSD and vHPSD RF ablations shorten procedure time and RF time and result in a higher rate of FPI compared to LPLD ablation. Moreover, the use of HPSD and vHPSD ablation increased the acute and mid-term success rate. No safety concerns were raised for HPSD or vHPSD ablation.

SFS3. HIGHLIGHTED SESSION

NOVEL ASPECTS IN SURGERY

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No abstract available.

SS4. SURGERY

THE SURGICAL TREATMENTS OF PRIMARY BONE TUMORS

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Key words: osteosarcoma, chondrosarcoma, endoprosthesis
Introduction: Primary bone tumors are rare conditions, but in the case of malignancies can be life threatening without early diagnosis and appropriate therapy.
Methods: Data was analysed from patients diagnosed with primary bone tumors and tumor-like lesions between 2012 and 2022. The main aspects were gender, age, dignity, bone localisations, surgical Methods, possible recurrences and complications, the use of chemo- or radiotherapy. I observed the five-year survival.
Results: From all 130 cases analysed 56% had a chondrogenic tumor, 20% had tumor-like lesions and 17% had osteogenic tumors. We also diagnosed 6 patients with osteoclastoma and 3 with Ewing-sarcoma. In the case of benign and borderline tumors, observation or excochleation/marginal resection with allogenic spongyoplasty as a treatment was enough. In our Clinic 9 limb salvage surgeries and 7 amputations were performed due to malignancies. Concernig bone localisation, long bones and metatarsals were most frequently affected. The five-year survival rate of chondrosarcoma was 100%, but in the case of osteosarcoma, it was 75%. Complications and tumor recurrence were minimal occurrence.
Conclusions: The number of the diagnosed patients is increasing year by year parallel to the incidence of malignancies and the surgical procedures. Limb salvage surgeries are an effective method in the treatment of bone sarcomas combined with neoadjuvant and adjuvant chemotherapy. The incidence of osteochondroma and chondrosarcoma was equal. The five-year survival is better in chondrosarcomas than osteosarcomas.

TREATMENT OF OPTIC PATHWAY GLIOMAS AT THE UNIVERSITY OF DEBRECEN

Ruzsa-Kis-Schubert Kinga, Fekete Gábor (Department of Neurosurgery, University of Debrecen)

Keywords: optic pathway glioma, children, chemotherapy, surgery
Aim: Optic pathway gliomas (OPG) are benign lesions affecting mainly children and young people. Despite modern chemotherapeutic treatments and surgical procedures, there is no gold-standard treatment for satisfactory cure of this disease that offers an adequate quality of life. Our study aimed to investigate how the Results obtained with chemotherapy procedures described in the literature are similar or different from those we have found in patients who have undergone surgery, and to choose the optimal treatment for the patient.
Methods: We included 22 patients who underwent surgery. Based on the patients' pre- and postoperative deficits, we aimed to assess their quality of life before and after surgery. We wanted to compare this with the data available in the relevant literature on chemotherapy and radiotherapy treatments. To do this, we had to distinguish between unavoidable complications of surgery and those that can be avoided, and between deficits that can be corrected and those that cannot. These aspects then were compared with those described in the literature.
Results: Ultimately, we found that radiotherapy procedures only have a justification if the disease is diagnosed in young adulthood, but the average age of our patients was well below this. When comparing chemotherapy treatment with surgery, we found that a higher percentage of patients improved with chemotherapy (21% for the former, 17% for the latter), while a higher percentage of patients' condition remained unchanged with surgery

(66% surgery, 39% chemotherapy) and a higher percentage of patients deteriorated with chemotherapy (40%) than with surgery (17%).

A NEW TRANSCRANIAL DOPPLER OUTCOME MEASURE FOR TRANSCAROTID ARTERY REVASCULARIZATION SUCCESS

Gaal, Anna; Izygon, Jonathan; Lumsden, Alan; Bavare, Charudatta; Garami, Zsolt (Department of Neurology, Semmelweis University Budapest Hungary, Vascular Ultrasound Lab, Department of Cardiovascular Surgery, Methodist DeBakey Heart & Vascular Center, Houston Methodist Hospital, Houston, Texas)

Background: Transcarotid artery revascularization (TCAR) is a hybrid technique for carotid artery revascularization that relies on proximal carotid occlusion with flow reversal for distal embolic protection. Intraoperative Transcranial Doppler (TCD) monitoring can be used to help guide cardiovascular surgeons during the TCAR. Studies showing an association between improved MCA flow and executive functioning after carotid revascularization indicate that measurement of MCA peak systolic acceleration (PSA) in carotid interventions may be an important outcome measure. We evaluated the MCA waveform for PSA before and after TCAR intervention.
Aim: The purpose of this study is to investigate whether flow improvement in the MCA can be used as a new outcome measure for carotid interventions such as the TCAR.
Methods: A total of 12 patients (7 male; average age 77) who required and underwent TCAR were observed with TCD (NovaSignal Los Angeles, CA; Spencer) monitoring.
Waveform data was acquired with DigiView (Digisonics inc.). Using the "Measure" function, PSA was calculated for the MCA before and after carotid stenting intraoperatively in TCAR cases. Results were confirmed by carotid duplex measurements.
Results: PSA (dv/dt) increased after successful (patent carotid on duplex) TCAR operation for every patient. The average increase in peak acceleration was 439.583 cm/s. Average PSA was 368±182 at baseline and 807±316, post procedure. A paired 2-tailed T-Test was used to analyze the difference between pre- and post-stent waveforms and found that the two groups were significantly different ($p < .05$).
Discussion: We investigated the justifiability of PSA as a measure of improvement of blood flow to the brain. After successful TCAR, we found that PSA significantly increased ($p < .05$) and this trended with patency of carotid. Thus, after undergoing carotid revascularization, we may use the peak acceleration of the waveform to determine improved flow of blood to the brain.

EFFECT OF CYP3A GENOTYPE IN RENAL TRANSPLANT PATIENTS ON TACROLIMUS MEDICATION

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Keywords: pharmacogenetics; precision medicine; tacrolimus; organ transplantation; cytochrome P-450 CYP3A
Aim: Tacrolimus is an essential component of post-transplant immunosuppressive therapy to inhibit graft rejection. Its use is overshadowed by its renal toxicity, extremely narrow therapeutic range, and wide inter-individual variability regarding its metabolism.Our aim was to consider the potential incorporation of CYP3A genotyping into the immunosuppressive protocol.
Methods: In our project, CYP3A4 and CYP3A5 genotyping was performed on blood samples from kidney transplant recipients (N=39) since Feb 22, 2021. Based on genotype combinations and literature data, recipients were classified as extensive metabolizers (EM), intermediate metabolizers (IM) and poor metabolizers (PM). Daily tacrolimus doses were normalized to body weight and tacrolimus blood levels were normalized to daily doses.
Results: Data from 9 EM, 26 IM and 4 PM subjects were pooled. At the time of the third monthly follow-up, statistically significantly higher values for mean normalized doses and significantly lower values for mean

normalized blood levels were found for the EM group compared to both IM and PM subjects. Furthermore, we found a significant negative correlation between normalized tacrolimus blood concentrations and GFR values of the recipients. In the sixth month control data, we found statistically significant higher GFR values in EM individuals compared to the PM group ($p<0.05$).
Conclusions: Based on population allele and genotype frequencies our study group was a representative sample of Caucasian ethnicity. Our Results seem to support the justification of CYP3A genotyping, its inclusion in a preoperative protocol requires further continuation of our project and consideration of practical aspects.

RECONSTRUCTION OF PELVIC FLOOR DEFECT WITH RECTUS ABDOMINIS MUSCLE FLAP AFTER PELVIC EXENTERATION

Elisabeth Garcia, Ariella Kondor (Department of Surgery),Gábor Pavlovics (Department of Surgery) , Ákos Pytel (Department of Urology)

Aims: Pelvic exenteration (PE) may become necessary in case of locally advanced pelvic cancer or extended necrosis after irradiation. This procedure involves the removal of organs such as the bladder, rectum and the genitourinary structures. The reconstruction of the perineum is a challenging task. The greater omentum is the most common option to cover the defect. However, sometimes it is not available because of its former removal. Our aim was to find another method to achieve good Results which requires the cooperation of a team of healthcare professionals.
Methods: In the Department of Surgery, Pécs we used vertical rectus abdominis muscle flap in four cases during the last 5 years to cover the perineum. after pelvic exenteration. One patient had locally advanced bladder carcinoma, which infiltrated the rectum and the abdominal wall also. Three patients underwent pelvic irradiation because of cervix carcinoma and developed extended necrosis of multiple organs in the pelvis.
Results: The outcomes of this procedure are prosperous because we did not have any flap-related complications. The patient with bladder carcinoma died of the tumor. The three women are in complete remission and their quality of life has improved significantly after the operation.
Conclusion: The Vertical Rectus Abdominis Myocutaneous (VRAM) flap is commonly used in breast reconstruction. However, based on our experiences the muscle flap can also be a fair choice for pelvic defect coverage, if we preserve the inferior epigastric artery.

THE IMPACT OF 3D MODELS ON THE PREOPERATIVE SURGICAL PLANNING OF CARDIAC SURGERIES

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Keywords: 3D imaging, visualization, unique anatomy, reduced operative risk
Aim: The objective is to achieve better visualization and transparency by using 3D modeling software and 3D printing from standard imaging studies of the surgical area, especially in cases with significantly deviated or unique anatomy compared to normal anatomy. This will allow for the creation of more precise surgical plans.
Methods: In the past year, we created preoperative 3D models of the surgical area for 30 patients. We used MR, CT, and cardiac ultrasound images of the patients for the planning process, which were processed using the 3D Slicer, Autodesk Fusion 360, and Meshmixer software. The printing was done using the Flashforge Adventurer 3 3D printer and PLA filament. Among the 30 patients, we selected cases with extreme deviations from normal anatomy or cases where proper visualization was crucial for surgical reasons.
Results: The surgical plans based on the preoperative 3D models were accurately followed in all cases, and the intraoperative images corresponded precisely to the modeled surgical area. The 3D models played a crucial role in planning the incisions, and in no case was there a need for conversion. They also assisted in identifying optimal cannulation sites for extracorporeal perfusion, which were successfully followed in every case, and in assessing operability.
Conclusion: 3D models created from various imaging studies provide better visualization of the target structures, their relationship with the surrounding anatomy, and the prospective surgical area. This facilitates the development of more precise surgical plans, leading to more effective and safer surgeries.

INVESTIGATION OF THE EFFECTIVENESS OF PREHOSPITAL AMPUTATION DEVICES ON CADAVERS

Jozsef Farkas, Peter Gedei, Szilard Rendeki, Norbert Wiegand, Peter Maroti, Ferenc Molnar, Balint Nagy, Dora Keresztes, Peter Kiss, Ivett Jonas, Krisztina Szekely, Mark Ughy, (University of Pecs, Medical School, Dept. of Anatomy Pecs, Hungary, University of Pecs, Medical School, Medical Skills Education and Innovation Centre, Pecs, Hungary)

Amputations take place in the operating rooms. Circumstances may necessitate on-site amputation to save lives. There are no evidence-based guidelines neither for the execution of the amputation, nor for the instruments to be chosen. There is no widely accepted criteria for the standardized characterization of amputation devices. The present study aimed to examine the effectiveness of commercially available cutting tools used by emergency services, as on-site amputation tools. Five tools (Holmatro type hydraulic cutter, with two cutting attachments, reciprocating saw, hacksaw, gigli saw) were used to carry out amputations on cadavers (locations: brachial, antebrachial, femoral and crural regions). During the experiment, the required time and the number of attempts to detach limbs were recorded. With the help of post amputation CT scan-based 3D models the proximal cut surfaces were analyzed. Based on the cut surface quality, an Amputation Index (AI) was determined for each device in each examined region. Amputation Score (AS) was calculated based on the time required for cutting, the number of cutting attempts and the AI. With the help of AS, the usability of the used devices was determined. Based on our scoring system, the reciprocating saw turned out to be the most effective tool.
We recommend the consideration and further investigation of the reciprocating saw as a possible on-site amputation device, as well as the introduction of the Amputation Score as an objective and quantitative indicator in the future characterization of on-site amputation devices.

SS5. PREVENTIVE MEDICINE, HEALTH SCIENCES

PSYCHOLOGICAL BACKGROUND OF SEXUAL QUALITY OF LIFE OF WOMEN LIVING WITH ENDOMETRIOSIS: THE DIFFERENT ROLES OF SELF-ESTEEM AND ATTACHMENT

Luca Felföldi, Boróka Gács (Department of Behavioural sciences, University of Pécs)

Keywords: endomteriosis, pain, sexual quality of life, attachment, self-esteem

Aims: In our research, we examine (1) how painful intercourse and everyday pain affect the quality of the relationship; (2) the psychological factors that can positively influence the quality of sexual life of women living with endometriosis, and (3) the relationships between self-esteem and attachment style.
Methods: We conducted a cross-sectional online questionnaire research, for which we used the "Experiences in Close Relationships " (ECR-RS), the "Relationship Assessment Scale " (RAS-H) and the "Rosenberg Self-esteem Scale" (RSES-H) questionnaires in addition to recording data about demographics and pain. The questionnaires were filled out by 195 women (average age=32).
Results: Based on our Results, everyday and sexual pain show a strong negative correlation with the quality of sexual life and the quality of the relationship. Furthermore, both avoidant and anxious attachment negatively correlate with relationship quality and sexual satisfaction. Higher self-esteem has a protective effect on the quality of the relationship, but does not affect sexual satisfaction. When everyday pain and sexual pain are compared, we see differences: sexual pain only has an effect on sexual satisfaction, while everyday pain affects sexual satisfaction, confidence and attachment. Predictors of lower relationship quality include lower sexual satisfaction, avoidant attachment, and severe everyday and sexual pain.
Conclusions: Pain has a serious negative effect on both the relationship quality and sexual quality of life of women living with endometriosis, so appropriate treatmen is of utmost imporatance. Secure attachment and higher self-esteem can function as psychological protective factors.

ASSOCIATIONS BETWEEN PERSONALITY TRAITS AND CHRONOTYPE WITHIN A COMPLEX RESEARCH FRAMEWORK

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Keywords: Personality, Chronobiology Disorders, Sleep

Aims: Diurnal preference influences various aspects of life, including mental health and academic performance. Our work aimed to demonstrate the relationship between personality traits and chronotypes using our own database. We also intended to investigate the parameters in the context of the Halo bias.

Methods: Participants received a psychological test battery and also complete a daily events reflection questionnaire. This battery includes the Big Five Inventory and the Munich Chronotype Questionnaire. Furthermore, portable Dreem2 EEG polysomnography recordings were conducted during the seven-day study. The correlation between personality and chronotype was analyzed while controlling for age. The halo factor's influence on personality traits was calculated using factor analysis.

Results: Among the five personality factors, agreeableness ($r=-0.27$, $p<0.001$) and conscientiousness ($r=-0.28$, $p<0.001$) showed significant correlations with morning diurnal preference. We also found a weaker association with openness ($r=0.21$, $p=0.02$), which predicted evening chronotype. Subsequently, we calculated and substracted the distorting effect of the Halo factor on the five personality traits using confirmatory factor analysis. We observed that the influence of agreeableness and conscientiousness became insignificant, while the effect of openness augmented ($r=0.314$, $p<0.001$).

Conclusions: Our findings contribute novel insights to the current state of science by revealing that the relationship between agreeableness and conscientiousness traits was explained by the Halo factor. Meanwhile, this latent factor "masked" the effect of openness on chronotype.

ASSESSMENT OF ANOREXIA NERVOSA ACCORDING TO THE DSM-5 ALTERNATIVE PERSONALITY MODEL USING THE SCID-5-AMPD DIAGNOSTIC INTERVIEW SYSTEM

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Keywords: anorexia nervosa, endophenotype, personality disorder, pathological personality traits, SCID-5-AMPD

Aims: Our aim is to facilitate effective and targeted therapy for anorexia nervosa (AN) by identifying personality traits and endophenotypes that aid diagnosis and identification of psychotherapeutic targets.

Methods: AN patients aged 18-45 years (N=14 female patients in the current study) completed online questionnaires on personality traits (PID-5), eating disorder (EDI-1), emotion regulation style, mentalization (MZQ), dissociation (DIS-Q), current emotional and mood state (SCL-90, PHQ-9), and past traumatic events (CTQ) after MINI and SCID-5-AMPD interview. Results were compared with a matched healthy control sample.

Results: Apart from AN, the most common comorbidity was depressive episode, and anxiety disorders were also present. In the SCID-5-AMPD interview, high scores were obtained for several domains describing personality dysfunction in the AN group. Among self-report questionnaires, we observed significant differences in scores on the SCL-90-R and CTQ in the AN patients compared to healthy controls.

Conclusion: Based on the Results of our study, the AN group showed more severe personality trauma, especially in the functional domains of identity and intimacy, and more psychological distress and childhood traumatization. The above may help to identify personalised psychotherapeutic treatment targets in AN patients, which may significantly improve effectiveness and reduce the time spent in therapy.

THE CORRELATION BETWEEN METABOLIC SYNDROME, GUT-MICROBIOME AND DIET THERAPY

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Keywords: obesity, atherosclerosis, gut-microbiome, metabolism, dysbiosis

Introduction: Metabolic syndrome is a combination of metabolic factors such as obesity, high blood pressure, impaired fasting glucose, high triglyceride levels, and low HDL cholesterol levels and its rapidly growing problems worldwide. The relation between the gut microbiome and its effect on human metabolism is recognised. There are severe roles of the gut microbiome for example it is physical barrier and most of the metabolic processes in humans are catalyzed by enzymes encoded by microbial genes.
Methods: For literature search PubMed, Elsevier, Nature was used with the following Keywords: obesity, atherosclerosis, gut-microbiome, metabolism, dysbiosis
Results: The healthy gut microbiota is predominantly constituted by the phyla Firmicutes and Bacteroidetes. This is followed by the phyla Actinobacteria and Proteobacteia. An increased ratio of Firmicutes/Bacteroidetes is often associated with obesity, and if this ratio settles back the result would be weight loss, as confirmed by animal experiments. Bacteroides population is inversely proportional to body weight. 1 There was a correlation between the gut microbiome, subclinical atherosclerosis and intima-media thickness (IMT). The result was an increased Firmicutes/Bacteroidetes ratio in the group with high IMT values (IMT>0.9).2
Discussion: More and more studies and clinical trials show that gut-microbiome and its diversity have a relevant effect on the functioning of the human body. Dysbiosis of the microbiome does not mean an immediate illness, minor fluctuations can occur, its composition and metabolic activity can be easily influenced by diet, environment, and medications.
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2 Szabo H, Hernyes A, Piroska M, Ligeti B, Fussy P, Zoldi L, Galyasz S, Makra N, Szabo D, Tarnoki AD, Tarnoki DL, Association between Gut Microbial Diversity and Carotid Intima-Media Thickness. Medicina (Kaunas, Lithuania), 2021;57(3), 195

MONITORING OF EATING/SWALLOWING DIFFICULTIES AND SPEECH DEVELOPMENT IN PATIENTS WITH SMA I

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Keywords: SMA, atrophy, dysphagia, speech development, stimulation
Introduction: In Hungary, 10-12 children are born with SMA annually due to a defective gene. Amongst others, this condition effects the orofacial and laryngopharyngeal muscles as not to receiving sufficient nerve impulses Results in gradually deterioration.
Aim: While gene modification and replacement therapies have increased their survival rate, addressing their functional impairment has become increasingly urgent. I carried out their swallowing and speech rehabilitation as a member of the complex paediatric rehabilitation team.
Method: I applied a somatic-oral/intraoral form of basal stimulation known in physical education by stimulating sensorimotor reflexes in 8 SMA type I patients. Both mechanical and thermal stimuli activate the primary trigeminal sensory pathway. Stimulation is initiated externally in the frontal, temporal and buccal areas. I linked the movements to the orofacial region and stimulated the orofacial muscles, palatum and alvelolum within the oral cavity, including tongue exercises. It took 30-45 minutes a day for 1 month.
Result: Significant improvement could be observed. After 1 month, 2 children have started to speak and 8 out of 8 children have had their initial heavy drooling decreased to a minimal amount. They all started to use their facial muscles more intensively and their nonverbal communication became more expressive. All 8 children have improved. The Results were objectified using FIM scale: average input score was 37, average output score was 44.
Conclusion: Although the number of cases is low and follow-up time is short, the therapy used has proved to be effective. The doctor-therapist team regarded it as a basis for speech and swallowing development.

WS5. DANONE SYMPOSIUM

THE COMPLEX THERAPY FOR SWALLOWING AND SPEECH

No abstract available.

SS6. INTERDISCIPLINARY, PATHOLOGY

ASSESSING MOLECULAR SUBTYPES OF MEDULLOBLASTOMAS USING IMMUNOHISTOCHEMICAL, MOLECULAR, AND HISTOLOGICAL CLASSIFICATION

Nour Kurdi, Judit Bedekovics (Department of Pathology, University of Debrecen)

Keywords: immunohistochemistry, medulloblastoma, next-generation sequencing, WNT, SHH
Aims: To assess the efficiency of an established IHC algorithm and customized NGS panel in samples from 15 patients with medulloblastoma (MB) to establish molecular subtypes as an alternative method to gene expression and methylation profiling Methods.
Methods: Patient group consists of 15 patients (10 male, 5 female). FFPE tissue blocks were collected from the archives of Department of Pathology, University of Debrecen. 4 um thick tissue sections were used for IHC stains including β-catenin (clone 14), GAB1 (clone BSB-155), YAP1 (clone 2F12) and p53 (clone DO-7). Next-generation sequencing (NGS) was performed in selected cases. For NGS library preparation, an RNA-based Archer FusionPlex custom gene panel (Archer DX, Boulder, CO, USA) was applied. Sequencing was performed on the MiSeq System (MiSeq Reagent kit v3). 5% variant allele frequency was used as the cut-off value.
Results: Histological subgrouping revealed 12 classic, 2 nodular desmoplastic, and 1 anaplastic variant case. IHC analysis identified 1 WNT-activated, 3 SHH-activated, 7 non-WNT/non-SHH-activated, and 4 indeterminate cases. CTNNB1 mutation was detected in the IHC-defined WNT-activated case whereas all three IHC-defined SHH-activated cases carried non-subgroup defining mutations.
Conclusions: Eleven out of the fifteen MB cases could be classified using the IHC algorithm, while four showed indeterminate molecular Results. The clinically unique WNT-activated subgroup could be identified with both IHC Methods and molecular sequencing.

THE CLINICAL RELEVANCE OF EZH2 MUTATION-BASED LIQUID-BIOPSY TEST IN FOLLICULAR LYMPHOMA

Laura Kiss, Ákos Nagy, Csaba Bödör (Department of Pathology and Experimental Cancer Research, Semmelweis University)

Keywords: follicular lymphoma, liquid-biopsy, EZH2
Introduction: Follicular lymphoma (FL) is the most common indolent non-Hodgkin's lymphoma. Investigating the molecular background of FL revealed that mutations of the EZH2 epigenetic regulatory gene are present in 25% of the cases. Further evaluation of these mutations has clinical relevance due to their gain-of-function nature, making this molecular aberration the first precision oncological target in FL. The heterogeneous disease course raises the need for an effective disease monitoring system. An emerging option is the minimally-invasive liquid-biopsy (LB).
Aims: In parallel to studying spatial heterogeneity we also aimed to compare the quantitative indicators of the LB test with the standard tissue biopsies (TB). In addition, the study focuses on the correlation between EZH2 variant allele frequency (VAF), EZH2 mutation status and clinical/histological indicators.
Methods: Pretreatment paired LB and TB samples were collected from 117 patients. To characterize the EZH2 mutation status, samples were tested by droplet digital PCR method.
Results: By testing paired TB and LB samples the mutation frequency proved to be 38%. The proportion of cases that harbored a mutation by only one of these techniques was 5% and 7% for TB and LB, respectively. Higher histological grade was significantly associated with mutant EZH2 status and higher VAF. We also identified that EZH2 wild-type clones infiltrated the bone marrow more frequently.
Conclusions: Our Results suggest that parallel testing of TB and LB samples yields a higher EZH2 mutation frequency in FL, thereby expanding the group of patients who may be eligible for the EZH2 inhibitor therapy.

DEVELOPMENT OF METHYL-SELENOCYSTEINE ANTITUMOR THERAPY IN HEPATOCELLULAR CARCINOMA CELL LINES

Alexandra Pop, Barbara Mátyási, Adrián Pesti, Andrea Reszegi, András Kiss (Department of Pathology, Forensic and Insurance Medicine, Semmelweis University)

Keywords: selenium, hepatocellular carcinoma, antitumor effects, sorafenib, combination therapy
Introduction: Hepatocellular carcinoma (HCC) is the fourth most common malignancy worldwide. The cytotoxic effect of selenium compounds on tumor cells provides the opportunity to treat cells highly resistant to cytostatics. Methyl-selenocysteine (MSC) is a natural selenium compound primarily metabolized by KYAT 1.
Aims: We aimed to monitor the antitumor effect of MSC on different HCC cell lines. Our goal was to investigate its effects in combination with traditional chemotherapeutic agents and detect main molecular mechanisms.
Methods: We used Huh7 and HepG2 hepatoma cell lines for our study. We applied two keto acid analogs to stimulate MSC. The antiproliferative effect of MSC, α-keto acids, and sorafenib in monotherapy and in combination treatment was determined using the Alamar Blue Assay technique. We used Wes Simple to analyze protein levels of main signaling pathways, proliferation, and EMT markers.
Results: After 72 hours of treatment in both cell lines, the addition of α-keto acid increased the cytotoxic efficiency of MSC. In HepG2, after triple-combination treatment, markedly increased inhibition of proliferation was detected compared to sorafenib monotherapy. However, we could not prove this with Huh7. Triple combination treatment reduced the activity of PI3K/AKT/mTOR and MAPK/ERK pathways at the protein level. It may explain the success of combination therapy by simultaneously inhibiting several signaling pathways.
Conclusions: Our Results highlighted the possibility of combined use of selenium compounds and traditional chemotherapeutic agents, especially in late-diagnosed, therapy-resistant tumors. In tumors of different aggressiveness, it is necessary to identify molecular mechanisms to enable personalized, successful therapy in HCC patients.

LOW-GRADE ONCOCYTIC TUMOR OF THE KIDNEY – CLINICAL, PATHOLOGICAL, AND GENETIC FEATURES

Fanni Sánta, Boglárka Pósfai, Levente Kuthi (University of Szeged Albert Szent-györgyi Medical School, Department of Pathology)

Keywords: oncocytic, kidney tumors
Introduction: Low-grade oncocytic tumor of the kidney (LOT) is a provisional entity categorized as "other oncocytic tumor" in the current WHO classification scheme. In this study, we investigated the clinical, morphological, immunohistochemical, and genetic characteristics of LOT.
Methods: LOTs were collected from 6 pathology departments in Hungary. We recorded the demographic, pathological, and survival data. The immunophenotype of the tumors was characterized by CA9, CK7, CK20, CD10, CD117, AMACR, PAX8, GATA3, FH, and SDHB. By the expression of mismatch repair proteins, we defined the microsatellite status. Whole exome sequencing was carried out in 5 cases.
Results: We identified 12 LOTs in 7 males and 5 females. The median age was 74 (51-83 years). The median tumor size was 33.5 mm (18-105 mm). All LOTs were kidney-confined (10 pT1 and 2 pT2). The growth pattern was solid, and the tumors were composed of eosinophilic tumor cells having mild nuclear atypia and perinuclear halos. All cases harbored a CK7-positive and CD117-negative immunophenotype, furthermore, PAX8, GATA3, FH, and SDHB were diffusely positive in all LOTs. The mismatch repair proteins were retained, indicating a microsatellite stable status. The whole exome sequencing revealed mutations of the TSC1, TSC2, mTOR, and PIK3CA genes. Cancer-specific death was not recorded.
Conclusion: LOT was a rare neoplasm (0.42%), with an excellent clinical course, and it mainly affected old males. LOTs had a unique immunophenotype (CK7+, CD117-, GATA3+), that could be used to discriminate LOTs from other renal neoplasms with eosinophilic cytoplasm. The presence of the mutations of the mTOR/PIK3CA pathway supports that LOT can be a distinct renal tumor entity.

EXAMINATION OF NON-CONVENTIONAL DYSPLASIAS IN IBD-ASSOCIATED COLORECTAL ADENOCARCINOMA PATIENTS

Panna Szaszák, Bence Kővári, Anita Sejben (Department of Pathology, University of Szeged)

Keywords: inflammatory bowel disease, non-conventional dysplasia, IBD-associated neoplasia
Aims: Knowledge on the development, morphology, and clinical importance of neoplasms associated with inflammatory bowel disease (IBD) is currently limited. In the last few years, several new morphological variants of IBD-associated dysplasias have been described. The aim of our study was to re-evaluate our IBD-associated carcinoma cases, and to retrospectively identify so-called non-conventional dysplasias.
Methods: We re-evaluated a total of 28 cases of IBD-associated adenocarcinomas, diagnosed between 2010 and 2022. We recorded the patients' sex, age at diagnosis of IBD and neoplasia, type of IBD, type of specimen (biopsy [n=8]/surgical specimen [n=20]), histological type, grade, localization, stage, and overall survival.
Results: The mean age at carcinoma diagnosis was 47 years in the conventional, and 50 years in the non-conventional dysplastic group. The male:female ratio was 13:2 in the conventionalis group, and 10:3 in the non-conventional group. Conventional dysplasia was observed in 15, and non-conventional dysplasia in 13 patients. They were detected combined in 9 patients. Alltogether, 25 non-conventional dysplasia foci were identified, that were identified as: hypermucinous (n=9), goblet cell deficient (n=6), serrated NOS (n=6), and traditional serrated adenoma-like dysplasia(n=4). The majority of non-conventional dysplasias were associated with ulcerative colitis (n=12).
Conclusions: The recognition of IBD-associated non-conventional dysplasias may be important in the future, because they may appear as flat lesions endoscopically, have a higher rate of aneuploidy, and are more frequently associated with high-risk carcinomas. Therefore, closer follow-up of these patients is necessary, and patients may benefit from random biopsy samples.

ANALYSIS OF THE FIRST HUNGARIAN PRIMARY IMMUNODEFICIENCY COHORT

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Objective.Genetic analysis of the heterogenous diseases group of primary immunodeficiency (PID) has been greatly improved since the introduction of whole exome sequencing (WES). We aimed to collect and analyze the PID Results of our laboratory in samples from 2019 to 2022 tested by WES in order to measure diagnostic efficiency. In addition, we performed a bioinformatic reanalysis according to the most recent gene list of International Union of Immunological Societies (IUIS).
Methods.The cohort contained data from 162 PID patients. In case of negative result, a bioinformatic reanalysis was done using the 2022 gene list of IUIS. Pathogenicity analysis was performed by the ACMG guidelines. Pathogenic/likely pathogenic (P/LP) gene variants with were grouped into the disease groups of IUIS.
Results. Of the tested 162 samples, in 31 cases we did find variations associated with the phenotype. Among positive cases, 7 novel mutations were detected. Significant secondary findings were detected in 16 samples. Diagnostic efficiency was shown to be 19.1%. No novel diagnosis could be achieved by the bioinformatic reanalysis.
Conclusion. Diagnostic efficiency was shown to be in line with the international data. Seven novel disease causing mutations were found. The detected P/LP variants could be grouped into all but two
IUIS disease categories. Bioinformatic reanalysis led to no novel diagnosis.

TESTING OF DOPAMINE-COUPLED POLYPEPTIDE NANOPARTICLES ON THE MODEL OF THE BLOOD-BRAIN BARRIER

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Keywords: polipeptide nanoparticles, alanine, glutathione, dopamine, brain-targeting
The central problem in the current treatment of brain disorders is to reach suitable drug amount to the brain due to the presence of the blood-brain barrier (BBB). Polypeptide nanoparticles (NPs) are versatile platforms for drug delivery combined high functionality with good biocompatibility. The key to the efficient brain delivery of NPs is the specific targeting of cerebral endothelial cells that form BBB.
Aims: The aim of our reserach was to test dopamine-coupled three-armed polypeptide (3-PLG-dopa) NPs on the cell culture model of the BBB and to investigate whether the combination of glutathione and alanine as BBB targetig ligands can promote the efficient transfer of these NPs across the BBB into midbrain organoids.
Methods: The size and surface charge of NPs were determined by dynamic light scattering. The cellular uptake and BBB penetration of NPs were quantified by spectrofluorometer. The visualization of nanocarrier uptake into endothelial cells and organoids was investigated by confocal laser microscopy.
Results: We demonstrated that physico-chemical properties of NPs was ideal and the tested NPs not decreased the cell viability. Cellular uptake of targeted nanocarriers coupled with dopamine showed significantly better uptake compared to the non-targeted group. In the permeability assays, the presence of ligands promoted significantly higher penetration of NPs across the BBB and increased their internalization into organoids.
Conclusion: The glutathione-alanine ligand combination has been shown to be suitable for BBB targeting of 3-PLG-dopa nanocarriers, and our Results may contribute to the development of more efficient drug delivery systems targeting the brain.

SS7. PULMONOLOGY AND COVID

DOES EOSINOPHIL CELL COUNT PREDICT MORTALITY IN VENTILATED AND ECMO TREATED COVID-19 PATIENTS?

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Keywords: eosinophil cell count, mortality, COVID-19, ECMO, ICU
Aim: A Chinese study showed that a decrease in eosinophil count is associated with mortality in critically ill COVID-19 patients. However, it is not known whether eosinophil count is predictive for mortality in patients treated with extracorporeal membrane oxygenation (ECMO). Our aim is to characterize and compare the association between mortality and eosinophil cell count in ECMO-assisted and mechanically ventilated patients.
Methods: We retrospectively reviewed the mortality data, eosinophil white blood cells count and its change during ICU stay of critically ill patients who were hospitalized in our COVID-19 ICU between March 1, 2020 and Feb 28, 2022. We studied patients undergoing ECMO (n=62), and artificially ventilated patients (non-ECMO; n=330).
Results: Surviving COVID-19 patients lab tests showed a significant increase in eosinophil cell count between their admission and last day of care in both ECMO supported patient group (0.36±0.84% and 2.85±3.4%) and non-ECMO group (0. 42±0.74% and 3.78±3.97%). The increasing tendency in eosinophil cell count reduced the probability of death (OR: 0.38; $p<0.02$ in the ECMO group and OR: 0.55; $p<0.001$ in the non-ECMO group). All patients in the ECMO-assisted group who had a significant reduction in eosinophil cell count died.
Conclusion: Our Results confirmed that a decreasing eosinophil count has a high predictive value for mortality in critically ill COVID-19 patients.

HUNGARIAN TWIN STUDY ON COVID-19 INFECTIONS AND VACCINATION STATUS

Gergely Szabó 1, Márton Piroska 1, Ádám Domonkos Tárnoki 1, Dávid László Tárnoki1 (1Medical Imaging Centre, Semmelweis University, Budapest, Hungary)

Keywords: COVID, online survey, vaccination willingness
Introduction: SARS-CoV-2 has resulted a devastating pandemic with serious social, economic and health disruptions globally. There have been over 750 million confirmed cases including almost 7 million deaths reported

to WHO. Considering the high transmission and pathogenic potential of the virus, it is crucial to examine the characteristic of the disease and the willingness to vaccination, understanding more the genetic susceptibility and the phenotype influenceability by external factors. We aimed to identify genetic and environmental factors and detect the vulnerable groups.
Methods: We performed a questionnaire based online survey to inquire about the impact, symptoms, and severity of COVID-19 disease in Hungarian twins among the members of the population based Hungarian twin registry.
Results: From July 2022 to April 2023, 813 twins filled the questionnaire form (608 female, 205 male subjects, 74,7% women; 460 monozygotic, MZ and 353 dizygotic, DZ twins, age range 19-84 years). 26 (16,3%) out of 160 MZ pairs, and 20 (21%) out of 95 DZ pairs were discordant for COVID vaccination. Getting vaccinated (C: 62.6%, 95%CI, 48.0-74.7%; E: 37.4%, 95%CI, 25.3-52.0%), undergoing COVID infection (C: 45.8%, 95%CI, 30.3-59.3%; E: 54.2%, 95%CI, 40.7-69.7%) were influenced by environmental factors. Vaccination willingness at the time when the vaccine first became available was not influenced by heritable factors. The feeling of being a test subject in the vaccination campaign (27.3%, 95%CI,11.1-42.2%) and the opinion on that the vaccination should be obligatory (60.7%, 95% CI, 49.0-70.3%) was a heritable trait.
Conclusion: More MZ was concordant in opinion of vaccination than DZ twins. COVID infection severity, willingness and opinion on the COVID vaccination was influenced by environmental factors which underlines the importance of external communication channels.

EOSINOPHIL COUNT INCREASES DURING PULMONARY EXACERBATION IN PATIENTS WITH CYSTIC FIBROSIS

Márton Falus, Zoltan Örlős, Zsuzsanna Miklos, Ildiko Horvath (National Korányi Institute for Pulmonology)

Keywords: cystic fibrosis, eosinophils, blood biomarkers
Background: Blood eosinophil counts are used as predictive biomarkers in several chronic airway diseases, but their potential role is not well elucidated in cystic fibrosis (CF).
Aims: The aim of our study was to evaluate blood eosinophil numbers during pulmonary exacerbation (PEx) of patients with CF and compare those with values obtained from stable patients.
Methods: Blood cell counts of forty patients with PEx and 41 stable patients visiting our CF center in 2022 were collected retrospectively from the hospital health care data. For patients with PEx values were collected both at admission and discharge. Data are given as mean+ SD. Within group difference was assessed by paired t-test and between group difference was tested by paired t-test.
Results: Absolute blood eosinophil count was lower at admission of patients with PEx (1.61+ 1.67 G/l) than that in stable CF patients (2.58+-2.34 G/l). In patients with PEx eosinophil numbers increased significantly during treatment as measured at the time of discharge (4.24+ 2.32 G/l). All patients were in better condition at discharge than at admission.
Conclusion: Blood eosinophil numbers change profoundly in relation to exacerbations in CF patients. This observation highlights their important role even in a typically neutrophilic airway inflammation, further studies are required to learn about the potential predictive role of these cells in the outcomes of CF exacerbations.

PARTICIPATION OF ABDOMINAL AND CHEST BREATHING IN DIFFERENT POSITIONS DURING A COMPLETE BREATHING CYCLE

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Keywords:optimal breathing, respiratory frequency, COVID-19, cardiorespiratory function, athletes
Aims: In COVID-19 disease the position of patients significantly affected the mortality rate. Thus, we aimed to measure the participation of abdominal and thoracic breathing in different positions during resting conditions. We hypothesized that abdominal (AB) and thoracic breathing (TB) participate differently in the respiratory cycle.
Method: Using plethysmography respiratory belts changes in the circumference of the chest and abdomen cavities were measured in young men and women (n=14; age:21.3±1.8 years) during calm inhalation and

exhalation. The following positions were used: standing (St), sitting (Si), supine (Su), prone (Pr), and all on fours (Af).
Results: Respiratory frequency (1/min) did not change significantly in different positions (Si: 15.0, St: 15.2, Su: 14.7, Pr: 14.9, Af: 13.8). However, the percent ratio of AB and TB changed significantly. AB gradually increased while TB gradually decreased in the following order: Si: 62/38%, St: 65/35%, Su: 75/25%, Pr: 61/39%, Af: 55/45%. For example, AB was significantly higher than TB in the Su position, while there was no significant difference between AB and TB in the Af position.
Conclusion: While maintaining a constant respiratory frequency, different positions significantly affect the participation of AB and TB during complete respiration. Therefore, Optimizing the participation of AB and TB breathing may improve the breathing of patients and athletes.

THE MEASUREMENT OF EXHALED CARBON MONOXIDE IN NON-SMOKERS, ELECTRONIC-SMOKERS, TRADITIONAL SMOKERS AND HOOKAH-SMOKERS

Saba Seyfi (University of Debrecen, Debrecen, Hungary)

Introduction: New generation tobacco products, including use of water-pipe (hookah) and heated tobacco products, gain increasing popularity in young people with limited information about their health effects.
Objectives: Our aim was to compare the levels of exhaled carbon monoxide (CO) and carboxyhemoglobin (CO-Hb%) in non-smokers, smokers of traditional cigarettes, heated tobacco products and hookahs in young adults. We also analysed the acute effect of smoking on these variables.
Methods: Levels of exhaled CO were measured in 14 non-smokers, 32 traditional smokers, 23 heat-not-burn product (IQOS) smokers, and 16 hookah smokers at baseline and immediately after smoking. The age of participants was 23 ± 3 years (mean± SD). 59% of them was male. A timeline of acute effect of smoking was determined in 22 participants measuring exhaled CO before and 15, 30, 60, and 90 minutes after smoking. CO-Hb% was calculated by the instrument. Data are presented as mean± SD.
Results: Baseline levels of exhaled CO and CO-Hb% were significantly higher in smokers compared to non-smokers ($p<0.001$). Exhaled CO and CO-Hb% level of non-smokers was 1.69±0.75 ppm and 0.92±0.12, respectively. Exhaled CO and CO-Hb% levels after smoking were higher than those of non-smokers both in traditional smokers (9.41±4.1 ppm; $p^{<}0.001$ and 2.18±0.63, $p^{<}0.001$, respectively) and in HTP smokers (3.50±1.26, $p^{<}0.001$ and 1.26±0.24, $p^{<}0.001$, respectively). The exhaled CO and CO-Hb% level after smoking in hookah-smokers were higher compared to all other groups (27.60±3.07 ppm, $p^{<}0.001$ for exhaled CO and 5.03±0.49, $p^{<}0.001$ for CO-Hb%). The time-slope in hookah smokers was much higher than those of the other groups, indicating much higher concentrations of carbon monoxide in hookahs compared to other types of cigarettes.
Conclusion: This study provides evidence for acute health effects of new generation tobacco products and can help policy-makers to raise awareness of communities and specifically young adults regarding the impact of different types of cigarettes on body health and false believes regarding the so called 'safer cigarettes'. Further studies are required to assess the health effects of smoking in young people.

WS1. How to present?

Prof. Dr. Kinga Karlinger Prof. Dr. Galuska László

No abstract available.

WS2. What is the biophysics of the future according to young people?

Prof. Dr. Mátyus László, Dr. Nyitrai Miklós, MSc PhD DSc

No abstract available.

WS3. Statistics workshop: Personalized medicine and the statistical paradox of the "average" patient

Dr. Johanna Takács, PhD, MSc

No abstract available.

WS4. Minimally invasive analgesia in spine surgery

Dr. László Entz

No abstract available.

WS5. Spirometry driver licence

Prof Dr. Horváth Ildikó

No abstract available.

WS6. HMAA Buffalo exchange program session

Dr. Marcel Pop

No abstract available.

PS1. Multidisciplinary poster session

TREATMENT OF PEDIATRIC ARTICULAR SURFACE FRACTURES WITH ABSORBABLE PLGA IMPLANTS

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Keywords: intra-articular fracture, absorbable implants, pediatric, PLGA, osteosynthesis

The incidence rate of articular injury is rising. With the help of imaging techniques, we classify the severity of the fracture and possible dislocations. Therapeutic interventions include the use of absorbable implants. The paper aims to present the surgical correction and post-operative treatment of articular surface fractures with absorbable implants in three children. Affected areas are discussed as follows: lateral condyle of the femur, patella, and radial head.

1)A nine-year-old girl heard a sharp sound accompanied by pain after taking a careless step. Slight swelling of the knee was observed with the patella in place. Diagnostics revealed a broken piece of the femur's lateral condyle located at the lateral recess. Under general anesthesia, an arthrotomy was performed. The fragment was cleaned and reattached with absorbable nails. Postoperatively, a brace was applied for six weeks.

2)A 15-year-old boy was admitted due to a fall during ice skating, leading to rotational torsion of the knee. X-ray and CT imaging identified the osteochondral fracture of the patella. Based on these findings, an arthroscopy with arthrotomy was performed.

3)A 17-year-old girl fell while snowboarding, resulting in swelling of the proximal forearm. Imaging diagnostics confirmed the radial head fracture. Closed-fracture repositioning with absorbable implants was performed.

The use of biodegradable implants eliminates the need for re-anaesthesia and reoperation, reducing the risks of complications such as infections. It also allows for earlier initiation of rehabilitation including physiotherapy. The cost efficiency of the method is further increased by a minimized hospital stay.

FUNCTIONAL-MORPHOLOGICAL ANALYSIS OF CORTICOTROPIN-RELEASING HORMONE-CONTAINING NEURONS IN THE ROTENONE MODEL OF PARKINSON'S DISEASE

Bence Pytel, Zsombor Márton, Balázs Ujvári, László Á. Kovács, Tamás Gaszner, Nóra Füredi, Viktória Kormos, Balázs Gaszner (University of Pécs Medical School, Department of Anatomy)

Keywords: EWcp, rotenone, rat, CRH

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder with motor (tremor, rigor, hypokinesia) and non-motor (e.g. depression, anxiety) symptoms. Our group investigates the background of mood disorders as a non-motor symptom of PD. We have previously found a correlation between damage to urocortin-1 (UCN1)-containing cells of the centrally projecting Edinger-Westphal nucleus (cpEW) and mood disorders in the rotenone model of PD, in the rat. An inverse correlation between corticotropin-releasing hormone (CRH) and UCN1 expression levels has been previously found, raising the question of what changes occur in the major CRH-containing systems in the PD rotenone model.

Therefore, we aimed to investigate functional morphological changes in the CRH neurons of the hypothalamic paraventricular nucleus (PVN), central amygdala (CeA) and the bed nucleus of stria terminalis (BNST).

Six weeks of subcutaneous rotenone treatment was applied to induce a PD-like state. Control rats received vehicle injections. Half of the treated rats also received levodopa/benserazide anti-PD therapy. The animals' locomotion was analyzed by rotarod test, the anhedonia by sucrose preference, and anxiety level by open field test.

Morphological changes were assessed by a combination of RNAscope in situ hybridization and immunofluorescence.
Results: The rotenone-induced motor deficits improved on levodopa/benserazide treatment, in contrast to non-motor symptoms. Rotenone treatment did not induce remarkable CRH neuron death in any of the regions studied. In rotenone-treated animals, Crh mRNA levels were reduced in the PVN and CeA, which were not reversed by levodopa/benserazide treatment. The FOSB neuronal activity of CRH neurons was reduced by rotenone treatment in the CeA and BNST, but not in PVN.
Conclusion: No CRH neuron death occurs in the rotenone model of PD. The change in CRH neuronal function may be interpreted as a compensatory mechanism due to cpEW/UCN1 neuronal death, which may be the result of an inverse relationship between the two systems.

WITH ARTIFICIAL INTELLIGENCE-ASSISTED HEPATODIAGNOSING MILD AND MODERATE HEPATIC STEATOSIS IN NON-ALCOHOLIC FATTY LIVER DISEASERENAL INDEX

Boglárka Zsély, Zita Zsombor, Aladár Dávid Rónaszéki, Róbert Stollmayer, Bettina Budai, Gabriella Győri, Pál Maurovich-Horvat, Novák Pál Kaposi (Semmelweis University, Medical Imaging Centre Budapest Hungary)

Introduction: Early recognition and staging of fatty liver disease are vital to therapy. This study aims to evaluate artificial intelligence-calculated hepatorenal index (AI-HRI) as a diagnostic method for hepatic steatosis.
Methods: We prospectively enrolled 102 patients with clinically suspected non-alcoholic fatty liver disease (NAFLD). All patients had a quantitative ultrasound (QUS), including AI-HRI, ultrasound attenuation coefficient (AC), and ultrasound backscatter-distribution coefficient (SC) measurements. The ultrasonographic fatty liver indicator (US-FLI) score was also calculated. The magnetic resonance imaging fat fraction (MRI-PDFF) was the reference to classify patients into four grades of steatosis: none < 5%, mild 5–10%, moderate 10–20%, and severe ≥ 20%. We compared AI-HRI between steatosis grades and calculated Spearman's correlation (rs) between the Methods. We determined the agreement between AI-HRI by two examiners using the intraclass correlation coefficient (ICC) of 68 cases. We performed a receiver operating characteristics (ROC) analysis to estimate the area under the curve (AUC) for AI-HRI.
Results: The patient cohort's mean AI-HRI was 2.27 (standard deviation, ±0.96). The AI-HRI was significantly different between groups without (1.480 ± 0.607, $p < 0.003$) and with mild steatosis (2.155 ± 0.776), as well as between mild and moderate steatosis (2.777 ± 0.923, $p < 0.018$). AI-HRI showed a moderate correlation with AC (rs = 0.597), SC (rs = 0.473), US-FLI (rs = 0.5), and MRI- PDFF (rs = 0.528). The agreement in AI-HRI was good between the two examiners (ICC = 0.635, 95% confidence interval (CI) = 0.411–0.774, $p < 0.001$). The AI-HRI could detect mild steatosis (AUC = 0.758, 95% CI = 0.621–0.894) with fair and moderate/severe steatosis (AUC = 0.803, 95% CI = 0.721–0.885) with good accuracy. However, the performance of AI-HRI was not significantly different ($p < 0.578$) between the two diagnostic tasks.
Conclusion: AI-HRI is an easy-to-use, reproducible, and accurate QUS method for diagnosing mild and moderate hepatic steatosis.

A TWIN STUDY EXAMINING THE VOLUME OF SUBCORTICAL GREY MATTER STRUCTURES

David Strelnikov1, Amirreza Alijanpourotaghsara1, Arsalan Vessal1, Marton Piroska1, Laszlo Szalontai1, Bianka Forgo2, Zsofia Jokkel1, Alíz Persely1, Anita Hernyes1, Lajos Rudolf Kozak1, Adam Szabo1, Pal Maurovich-Horvat1, David Laszlo Tarnoki1, Adam Domonkos Tarnoki1 (1 Medical Imaging Centre, Semmelweis University, Budapest, Hungary, 2 Department of Radiology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden.)

Keywords: brain, subcortical, volumetry, heritability, twin

Aim: To examine the genetic and environmental influences on six subcortical brain volumes; the amygdala, caudate nucleus, pallidum, putamen, thalamus, and nucleus accumbens, and four general brain volumes; total intracranial volume, grey matter, white matter, and CSF volume in twins.
Methods: 120 healthy adult twins from the Hungarian Twin Registry (86 monozygotic and 34 dizygotic; median age 50±26.5) underwent brain MRI. Two automated pipelines (CAT12 and volBrain) were used to calculate subcortical and general brain volumes from three-dimensional T1-weighted images. Age- and sex-adjusted monozygotic and dizygotic intra-pair correlations were calculated and the univariate ACE model was applied. Pearson's correlation test was used to compare the Results obtained by the two pipelines.
Results: Age- and sex-adjusted heritability estimates for the four general brain volumes were 0.78-0.93 and 0.89-0.94 using CAT12 and volBrain, respectively. Heritability estimates, using CAT12 for the amygdala, caudate nucleus, pallidum, putamen, and nucleus accumbens were between 0.76-0.95. The thalamus was more strongly influenced by common environmental factors (C=0.49-0.74). Heritability estimates, using volBrain were between 0.73-0.92 for the nucleus accumbens, pallidum, putamen, right amygdala and right caudate. The left caudate, left amygdala and thalamus were more strongly influenced by common environmental factors (C=0.49-0.86). A strong correlation between CAT12 and volBrain (r=74-94) was obtained for all volumes.
Conclusion: The majority of examined subcortical volumes appeared strongly heritable. The thalamus was more strongly influenced by common environmental factors. Our Results underline the importance of identifying relevant genes responsible for the variation in subcortical structure volume and associated diseases.

RADIOLOGICAL ASSESSMENT OF POST-COVID SYMPTOMS

Janka Fejes, Adam Domonkos Tarnoki, David Laszlo Tarnoki (Semmelweis University, Department of Medical Imaging, Budapest)

Introduction: In addition to acute complications caused by COVID-19 the long-term effects of the disease have been in the focus of clinical studies. One of the factors most influential in determining patients' life quality is the residual pulmanory changes following COVID-19 pneumonia.
Aims: Our aim is to assess the prelavence and temporal changes of CT-findings of the lungs in patients recovering after COVID-19 to better understand the effects of post- COVID syndroms.
Methods: CT-scans (Philips Ingenia Core 64) of the chest of 47 patients (28 men, 19 women, 63.5±27.5 years of age) recovered from COVID-19 were taken and evaluated retrospectively at the Medical Imaging Center of the Semmelweis University. For each patient, two follow-up CT-scans were made at 136 days apart on average. The left, the right and the total involevements, as well as the prelavence and temporal changes of radiologic abnormalities of the lung parenchima were assessed, including ground glass opacity, consolidation, crazy paving, reticulation, bands, fibrosis.
Results: All patients had bilateral lung involvements. The most frequent morphological changes at the first follow-up CT were ground-glass opacity (89%), consolidation (53%), parenchymal bands (42%), fibrotic changes (21%) and reticulation (17%). Patients with fibrosis were significantly older than the ones without (72.4 vs. 62.1 years of age, $p<0.05$). During the follow-up examinations the number of consolidations and crazy pavings have reduced in a statistically significant way, however, ground glass opacity, reticulation, bands and fibrosis have shown no significant change. We have found no relationship between the lung involvement and the fibrotic changes.
Conclusions: Our Results confirm the most frequent morphological changes of COVID pneumonia published in clinical studies, however, fibrotic changes and reticulation seemed to appear more frequently (17-21%) at elderly patients, which was independent of lung involevement in our relative small sample size. The persisting reticulation, bands and fibrotic changes examined during the follow-up CT's suggest that they may have existed prior to COVID pneumonia.

SKIN COLORS DO NOT INTERFERE WITH OXYGEN SATURATION MEASUREMENTS WITH PULSE OXIMETER

Darina Deák (Semmelweis University Department of Morphology and Physiology Budapest)

Objective: Previous report claimed that patients with darker skin were not treated properly due to the false reading of pulse oximeter. Thus we tested the hypothesis that the pulse oximeter will show a higher oxygen

saturation (SpO2) compared to the real value in subjects with darker compared to lighter skin tones by measuring hemoglobin SpO2 with a pulse oximeter in healthy students of different skin colors.
Patients and Methods: 42 (30 women and 12 men), aged 18-37, healthy Hungarian and foreign students of Semmelweis University participated in the research. The heart rate and SpO2 were measured with a finger-clipped pulse oximeter. Photos of the students' fingers were taken, and the skin color was evaluated by the Fitzpatrick scale. In addition, the students filled out a questionnaires assessing their general health conditions (1: no symptoms; 2: mild complaints; 3: severe complaints) and general physical conditions (1: no physical activity; 6: 6 per week/day).
Results: Majority of the students reported to be healthy (83.3%) and doing regular physical activity (83.3%). There was a negative, weak, but significant relationship between Fitzpatrick scale value and oxygen saturation (rho(25)=-0.318; p=0.04).
Conclusions: Thus in healthy individuals, the pulse oximeter did not measure higher values with darker, compared to those with lighter skin colors. Thus, our Results questioning the Conclusions of previous reports that skin pigmentation influenced the SpO2 measured by the pulse oximeter and thus the care of Covid-19 patients.

INVESTIGATING DENTAL BIOMEDICAL WASTE MANAGEMENT AT SEMMELWEIS UNIVERSITY THROUGH WASTE AUDITS

Dóra Irinyi, Imola Monos, Virág Palotai, Kinga Volford (Semmelweis University Faculty of Dentistry), Fanni Andrea Vass (Semmelweis University Faculty of Dentistry, Department of General Dental Preclinical Practice), Csilla Erdei (Semmelweis University Faculty of Dentistry, Department of General Dental Preclinical Practice), Emese Mester (Dental Hygienist and Environmental Engineer), Krisztina Márton (Semmelweis University Faculty of Dentistry, Department of General Dental Preclinical Practice),Tamás Demeter (Semmelweis University Faculty of Dentistry, Department of General Dental Preclinical Practice)

Introduction: Dental biomedical waste (BMW) generation and disposal is known to contribute significantly to the environmental burden of healthcare systems. The aim of this study was to assess the composition of daily generated BMW and waste segregation awareness at Semmelweis University Faculty of Dentistry.
Methods: Waste audits were conducted three times in one of the university dental educational centres to assess and analyse the complete daily production of BMW generated during dental care. The audits took place on Tuesdays with two-week intervals between each, in order to reduce the possibility of bias. Analysed waste has been separated into 49 categories, and each fractions were weighed using kitchen scales. Generated data of the three audits were averaged and analysed.
Results: The average daily amount of generated BMW in the dental centre is .
Ratio of PPE among total BMW
Ratio of SUP among total BMW
Ratio of mismanaged waste among total BMW
Conclusions: Excessive use of SUP and PPE together with overproduction, inappropriate collection and/or mismanagement of dental BMW has negative economical and planetary health consequences. Switching to sustainable procurement strategies, raising awareness and educating staff members and dental students may help mitigate these effects.

ASSESSMENT OF HEARING-RELATED QUALITY OF LIFE IN UNILATERAL HEARING LOSS

Nóra Szalai, Dr. Beáta Bencsik, Dr. Judit Szigeti F., Fatime Csontos, Prof. Dr. László Tamás, Dr. Anita Gáborján (Department of Otorhinolaryngology, Head and Neck Surgery, Semmelweis University)

Keywords: unilateral hearing loss, single sided deafness, quality of life
Aims: Unilateral hearing loss (UHL) or single sided deafness (SSD) is a condition characterized by the inability to hear in one ear. The aim of this study is to develop a Hungarian self-assessment hearing-related quality of life

questionnaire for UHL/SSD patients to analyse the main complaints, and the effectiveness of the available rehabilitation options.
Methods: The questionnaire is structured to measure hearing-related quality of life from three main aspects: physical, psychological and social. The Speech, Spatial and Qualities of Hearing Scale, The Abbreviated Profile of Hearing Aid Benefit, and the Nijmegen Cochlear Implant Questionnaire were partially included in the questionnaire. The Tinnitus Handicap Inventory is also integrated into the questionnaire since tinnitus often causes complaints in UHL/SSD presumably affecting the quality of life.
Results: Our questionnaire contains 30 questions that can be scored on a 6-point Likert scale from never to always. The questionnaire is available for completion in a paper-and-pencil manner, online and by telephone. Reaching out for testing has already been initiated on 40 patients.
Conclusions: Based on preliminary Results, the physical aspect (speech perception, sound localization) of hearing-related quality of life causes the main problem in UHL/SSD compared to other psychological and social aspects.

INVESTIGATION OF ORGAN-SPECIFIC INFLAMMASOME ACTIVITY IN HEART FAILURE

Artur Toth, Zsofia Onodi, Dávid Nagy, Tamás Radovits, Mihály Ruppert, Zoltan Varga (Department of Pharmacology and Pharmacotherapy, Semmelweis University, HCEMM-SU Cardiometabolic Immunology Research Group, Semmelweis University)

Keywords: inflammasomes, heart failure, lung circulation, inflammation
Aim: Inflammasomes are important mediators of inflammation. Heart failure (HF) has been shown to be associated with enhanced inflammasome activity in left ventricle. However, there is lack of data on inflammasomesin other HF-affected organs such as right ventricle, lung or liver. Therefore, our aim was to examine the expression of inflammasome components from the ventricles and the lung tissue to identify prognostic markers and therapeutic targets.
Methods: Pressure-overload HF was induced by transversal aortic constriction. Based on the clinical symptoms we classified the animals into severe/decompensated and mild/compensated groups. Inflammasome priming (ie. expression of inflammasome proteins [eg. AIM2, NLRP3, pro-IL-1β]) were assessed with immunoblot analysis.
Results: In severe HF, the inflammasome priming was significantly increased in the right ventricle, and showed a strong tendency from the left ventricle (eg. AIM2: p=0.005 and p=0.16, respectively). From the mild/compensated HF, inflammasome priming was less pronounced. Similar changes were seen in lung samples; in severe HF, the priming was significantly enhanced (eg. NLRP3: p=0.003).
Conclusion: Enhanced priming was demonstrated in severe HF from heart ventricles and lung. We observed significant difference in inflammasome activity between the right and left ventricle as well. NLRP3 and AIM2 expression might be promising protein as future biomarkers.

PS2. Multidisciplinary poster session

SUBJECTIVE AND QUANTITATIVE ASSESSMENT AND FOLLOW-UP OF OLFACTORY FUNCTION IN PATIENTS WITH PAROSMIA AFTER COVID-19 INFECTION AND THE ROLE OF THERAPEUTIC ADHERENCE

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Introduction: SARS-CoV-2 infection can be associated with long-term complications that affect quality of life, such as quantitative and qualitative changes in olfactory function. While a suitable tool for the assessment of olfactory impairment has long been available, a modified version of the Sniffin' sticks test (SSParoT) for the quantitative evaluation of distorted sense of smell was only developed during the pandemic, with still very limited experience worldwide.

Aim: To evaluate subjectively and quantitatively the baseline status of patients with parosmia and the change in their olfaction. This prospective study focuses on the investigation of the relationship of each parameter with each other and with therapeutic adherence.
Methods: 23 patients with parosmia (9 males, 14 females, mean age 43.33 and 40.57 years) were evaluated with Sniffin' sticks and SSParo Test at the first examination and at the 3 month follow-up. Subjective parameters were also recorded. Between the two examinations, patients were offered olfactory training. An olfactory journal was used to assess therapeutic adherence. Measured values (TDI-Threshold, Discrimination, Identification, HR-Hedonic Range, HD-Hedonic Direction) were compared with subjective sensation and adherence.
Results: 11 patients completed at least 50% of the training, 12 less. The following baseline paramteres were recorded during the first examination: $TDI_{average}$ 25,75 ($TDI_{50\%>}$:26,64, $TDI_{50\%<}$:24,91), $HR_{average}$ 1,52 ($HR_{50\%>}$:2,29, $HR_{50\%<}$:0,68), $HD_{average}$ 0,44 ($HD_{50\%>}$:0,63, $HD_{50\%<}$:0,23). The $TDI_{average}$ of patients with better compliance during control was 26.73 (p=0.226), while that of patients with less compliance was 31.1 (p=0.006) compared to baseline. The control $HR_{average}$ and $HD_{average}$ of the group exercising above 50% were 2 and 1.045 (p=0.001 and p=0.117 vs baseline), while those exercising less, were 2.5 and 0.583 (p=0.691 and p=0.851 vs baseline). Spearman's rank correlation was used to measure correlation. There is a probable correlation between HR change and training and HD change and training ($r_{\Delta HR}$=0,363, p=0,089 és $r_{\Delta HD}$=0,395, p=0,062). Subjective change is not correlated with change in HR, HD or TDI. HR and TDI and HD and TDI are independent variables.
Conclusion: the olfactory training method can be used to improve olfaction even in cases of distorted olfaction.

PULMONARY ASPECTS OF POST-COVID SYNDROME

Békési Lajos Erik (University of Debrecen, Department of Pulmonology, Derecske, Hungary)

Introduction: Nowadays, the end of the Covid-19 pandemic can be observed, at the same time, the long-term complication of the infection, the Post-Covid syndrome, comes into focus.
Objective: The aim of my study was to examine the quality of life, respiratory function values, and symptoms of these patients.
Methodology: Health care data of 238 patients visiting our Post-Covid Outpatient Center in 2021 were included in this retrospective study. Respiratory function Results, chest CT findings, number of days spent in hospital, COPD Assessment Test (CAT) Results, and those of our locally developed Post-Covid quality of life questionnaire were obtained. Patients were divided into two groups and Mann-Withney U-test was used to examine the relationship between quality of life and the other variables. Kruskal-Wallis test was used to examine the respiratory function Results and their relationship to gender, age, number of hospital days and the degree of chest CT abnormalities in the acute phase.
Results: Deterioration of quality of life was not significantly related to the FEV1 value, DLco, FEV1/FVC, length of hospitalization or abnormalities seen on chest CT. FEV1 values did not show significant correlation either with the degree of CT abnormalities, CAT score and age. FEV1/FVC was not associated with CT abnormalities, hospital days, sex, age and CAT scores. The relationship between Dlco reduction and lung damage, however, was significant. Several patients were diagnosed with COPD, asthma, sarcoidosis, pulmonary fibrosis, and lung cancer.
Conclusion: As a result of the follow-up, we got a broader picture of the manifestations and course of the Post-Covid syndrome.

CHANGES OF NEURON-SPECIFIC ENOLASE AND S100B SERUM CONCENTRATION UNDER CARDIAC ARREST

Ábel Papp1, Christopher Kristály1, L. Levente Horváth1, Laura Béri1, Bálint Kittka2, Tamás Nagy3, Zsófia Nagy3, Zoltán Vámos1 (1Department of Anaesthesiology and Intensive Care, 2 Heart Institute, 3Laboratory Medicine, University of Pécs)

Keywords: NSE, S100β, peri-arrest
Background: Neuron-specific enolase (NSE) and astroglial protein S100β are associated with outcomes following resuscitation from cardiac arrest. We tested whether NSE and S100β serum concentrations are associated with cardiac arrest time. We hypothesized that NSE and S100β serum concentration reversible changes as a function of time under a short arrest period.

Methods:25 patients were included with severe aortic valvular stenosis and without previous neurological disorders. Cardiac arrest (CA) was performed by temporary implanted VVI pacemaker activity, during percutaneous catheter aortic valve implantation (TAVI). Blood samples were taken 20 minutes before CA (0.), 8. second (I.), and 15. second (II.) under, then 20 minutes after the return of spontaneous circulation (ROSC). NSE/S100β were measured by conventional laboratory testing Methods.
Results: NSE increased from 0. to II., then decreased to ROSC (0.: 20.05±2.6ug/l vs. II.: 30.17±3ug/l vs. ROSC: 18.70±1.17ug/l, $p<0.05$). S100β increased 0. to I. then not changed until II., then increased to ROSC (0.: 55.56±7.59ng/ml vs. I.:97.78±18.18ng/ml vs. II.: 97.65±18.84ng/ml vs. ROSC: 149.41 ± 23.21ng/ml, $p<0.05$).
Conclusion: During the peri-arrest period, NSE serum concentration shows an inverse "U" shape, although S100β elicits a logarithmic trend. In the future, we aim to explore how these neurobiomarkers could serve as valuable diagnostic indicators in cases of cerebral hypoperfusion.

THERAPEUTIC USE OF PARASITES IN THE TREATMENT OF IBD

Diana Húsvéthová (First Surgical Clinic of Comenius University and University Hospital in Bratislava)

Keywords: IBD, gut microbiome, parasite-derived products, parasites, hygiene hypothesis; Aims: discovering the newest alternative less invasive Methods of IBD treatment,
Methods: data analysis,
Results: this thesis describes the hygiene hypothesis, mechanisms of how the gut microbiota influences the host immune system, and includes Results from various clinical studies on the use of parasites and their products in the treatment of IBD,
Conclusion: proper formation of the immune system requires some kind of contact with parasites within the gut microbiome.

BALANCING BEHAVIOUR. EXPERIENCES OF THE DEVELOPMENT AND APPLICATION OF THE MINDIET PROGRAM IN HUNGARY.

Roland Kasek (Institute of Behavioural Sciences, Semmelweis University, Selye János Doctoral College for Advanced Studies, Semmelweis University); Réka Bogdányi, (Selye János Doctoral College for Advanced Studies, Semmelweis University); Emese Fejes (Selye János Doctoral College for Advanced Studies, Semmelweis University)

Keywords: behavioural medicine, health development, health restoration, illness prevention
Aims: Poor lifestyle choices – induced by psychosocial discomfort and maladaptive coping – directly contribute to the pathogenesis of metabolic syndrome, hence most major causes of preventable deaths including cardiovascular and oncological diseases. The rapid surge in stress-related mental disorders during the past few years – mainly caused by the pandemic and control measures – indicates future increase of somatic decay at an unprecedented scale unless coping mechanisms and lifestyle choices improve quicker.
Methods: Enhancing metacognitive abilities and self-control, developing time perspective and self-consciousness, increasing habitual control and proactive behaviour promotes better quality of life and resilience, hence reverses the self-sustaining somatic decline and restores the healthy mental – and consequently metabolic – balance in mentally healthy clients.
Results: Contrary to symptomatic treatments – which promise rapid and effortless Results while their quickly transient effect diverts subjects towards increasingly radical and invasive attempts, intensifying the psychological discomfort that induced their perceptible issues – the MINDiet Program offers behavioural development that Results in somatic improvement measured in medical data (eg. body composition ratio, metabolic age, blood pressure), and quality of sleep amongst other client-specific factors.
Conclusion: In a set of selected cases of increasingly complex psychobiological background, recent advancements, general experiences and medical evidences in the development and application of the MINDiet Program in Hungary are discussed.

QUANTITATIVE PROTEOMICS ON LASER MICRODISSECTED EARLY-STAGE MELANOMAS REVEALS A MITOCHONDRIAL INVOLVEMENT IN THE DISEASE PROGRESSION

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Keywords: Melanoma, Proteomics, Tumor Biology.

Aims: Approximately 50% of melanoma-related deaths were early stage at the moment of diagnosis. There are no novel biomarkers with prognostic values at the early identification of the advanced melanoma attributes, therefore, we investigated the main driver mechanisms of the progression of early-stage melanomas.

Methods: We analyzed a cohort of 12 primary melanomas with < Breslow level 1.6 mm divided into recurrent and non-recurrent within five years after surgical intervention. Tumor and stromal compartments in each tissue section were isolated and collected using laser-capture microdissection and submitted to quantitative proteomics.

Results: In the progression group of melanomas, the mitochondrial translation, especially 39S ribosomal proteins were upregulated in tumor cells ($p<0.05$). On the contrary, proteins from immune system response were downregulated ($p<0.05$). Interestingly, when analyzing the stromal components, a similar pattern was observed. These Results shed light on the not well-understood tumor-stroma interaction, revealing a possible phenotype transferring from cancer cells to their microenvironment.

Conclusions: In summary, by separating tumor and stromal components, our Results added an additional layer of information to enrich our analysis. The bioinformatics analysis highlighted that mitochondrial functions might play a role in melanoma pathogenesis.

MYELOID NEOPLASMS WITH EOSINOPHILIA AND ABNORMALITIES OF PDGFRA OR PDGFRB

Anna Nagy, Hajnalka Andrikovics, András Kozma, András Bors (DPC Molecular Genetics Laboratory) Viktor Lakatos, Judit Reichardt, János Dolgos, Sándor Fekete, Zoltán Mátrai, Gábor Mikala, István Vályi-Nagy, Péter Reményi (DPC – Department of Hematology and Stem Cell Transplantation) Piroska Pettendi (Jász-Nagykun-Szolnok County Heténi Géza Hospital-Operating Institute) Márk Plander (Vas County Markusovszky University Teaching Hospital)

Keywords: hypereosinophilic syndrome, PDGFRA, PDGFRB

Aims: The WHO-classified myeloid neoplasms with eosinophilia and recurring genetic abnormalities are rare, but they are common differential diagnostic questions. Their clinical manifestation can range from asymptomatic isolated eosinophilia, through various organ system failure, to severely progressive acute hematologic malignancies. We attempted to get an overview of the Hungarian patient pool having myeloid neoplasms with eosinophilia and abnormalities of PDGFRA or PDGFRB.

Methods and Results: We used the hospital's patient documentation and the EESZT system to collect data retrospectively. The cytogenetic and molecular genetic testing were implemented in the laboratory of the DPC. From 2004 with RNS based PCR technique (FIP1L1::PDGFRA), and from 2016 FISH technique (PDGFRA, PDGFRB). In total 16 patients were identified, from which 13 patients (11 PDGFRA and 2 PDGFRB) had sufficient clinical data. The median age at diagnosis was 44 (25-61). The follow up time was 37 (1-225) months. In all 13 cases Imatinib therapy was started, but in 3 cases trial for quitting therapy was attempted, all of them resulting in the relapse of the patient. In 2 cases patients had hematopoietic stem cell transplant. The 5-year survival proved to be 77%, while the 10-year survival was 69%.

Conclusions: The clinical findings of myeloid neoplasms with eosinophilia and abnormalities of PDGFRA or PDGFRB in our population was consistent with the literature. Moreover, for a stable condition continuous Imatinib therapy is necessary.

THE RISK FACTORS OF ACUTE PANCREATITIS PROGRESSION INTO RECURRENT ACUTE PANCREATITIS AND CHRONIC PANCREATITIS. A SYSTEMATIC REVIEW AND META-ANALYSIS

Endre-Botond Gagyi, Mahmoud Obeidat, Edina Tari, Szilárd Váncsa, Dániel Veres, Péter Hegyi, Bálint Erőss (Center for Translational Medicine, Semmelweis University, Budapest, Hungary)

Introduction: Acute pancreatitis (AP) can progress to recurrent acute pancreatitis (RAP) or chronic pancreatitis (CP).
Aim: This systematic review and meta-analysis aimed to identify risk factors associated with this progression.
Methods: The protocol was registered on PROSPERO (CRD42022368931). A comprehensive search was conducted in three (Medline, Embase, Cochrane) databases on October 25th, 2022. Articles reporting and risk factors associated with AP progression into RAP or CP were included. Pooled odds ratios (OR) with 95% confidence intervals (CI) were calculated using the random effects model. Heterogeneity was evaluated using the I^2 statistic. The risk of bias assessment was performed using the Quality in Prognostic Studies (QUIPS) tool.
Results: A total of 71 articles were included in the meta–analysis, and several risk factors were identified for the progression of AP into RAP and CP. We found the following risk factors of AP recurrence: younger age, male gender, smoking, alcoholic etiology, hypertriglyceridemia, diabetes mellitus, pseudocyst, etc. The pooled OR for the male gender was 1.45 (95% CI: 1.29-1.64, I^2=24%), for smoking was 1.45 (95% CI: 1.16-1.81, I^2=62%), for alcoholic etiology was 1.76 (95% CI: 1.38-2.25, I^2=81%), for hypertriglyceridemia was 2.45 (95% CI: 2.07-2.90, I^2=9%), for diabetes mellitus was 1.49 (95% CI: 1.24-1.80, I^2=0%), for pseudocyst was 2.19 (95% CI: 1.52-3.15, I^2=0%). We also found risk factors of RAP progression into CP. The risk of bias was moderate in the majority of the included studies.
Conclusion: Our study identified multiple modifiable risk factors which can be treated to prevent the progression of pancreatitis.

CHANGE IN THE FERTILIZATION ABILITY OF SPERM CELLS WITH ADVANCING AGE

Csongor Etele Veress, Dr. Miklós Szűcs (Department of Urology and Andrology, University of Debrecen, Kenézy Gyula Campus)

Keyword: HBA, Age, HB-MaSC
Aims: Infertility is a worldwide problem regardless of the level of development of countries. It affects 8-12% of couples of reproductive age, and according to literary data, 20-40% of these cases can be attributed to male-related issues. In developed countries, the age at which couples choose to have children has significantly shifted towards the mid-30s in the last 50 years, which has been proven to decrease fertility in women. However, there is not as much international consensus regarding age-related changes in male fertility. Conventional sperm analysis tests widely used alone are not capable of assessing fertility, thus necessitating the performance of functional tests for this purpose. The aim of our research was to examine the correlation between age and values of sperm concentration (a conventional test) and Hyaluronan Binding Assay (HBA) and its derived index, Hyaluronan Bound Matured Sperm Count (HB-MaSC), which are functional tests.
Methods: Based on the data of 422 male patients previously seen at an andrology outpatient clinic, the patients were divided into seven groups according to age, and for each of the three test parameters, the dispersion and mean values were determined within each age group. These obtained data were subjected to statistical analysis using two-way ANOVA and Tukey's test due to multiple variables, aiming to determine significant differences.
Results, **Conclusion**: According to the graphs generated as a result of these analyses, there were no significant differences in sperm concentration, HBA, and HB-MaSC values among the age groups. Since the study encompassed samples from patients between the ages of 22 and 52, we plan to conduct a similar study in the future focusing on older patients.

PS3. Multidisciplinary poster session

DIGITAL PROCESSING OF ISTVÁN APÁTHY'S SCIENTIFIC HISTOLOGICAL COLLECTION

Levente Lászlófy, Zoltán Fekécs, Gergely Osváth, Antal Nógrádi (Department of Anatomy, Histology and Embryology, Laboratory of Neural Regeneration Szeged, Hungary, Babeș-Bolyai University, Zoological Museum, Kolozsvár, Romania)

István Apáthy (1863-1922), professor of zoology at the Franz Joseph University of Kolozsvár was an outstanding neuroscientist of his time, who became world-famous for his innovations in microtechnology and neuroscience. He developed a number of innovations in histological microtechnology which were far ahead of his time. His modification of the sectioning apparatus (microtome) and his special staining techniques led to the discovery of „neurofibrils" (the precipitated form of the much later descibed neurofilaments and neurotulules) and the visualisation of neuronal structures with an unprecedented clarity. To mark the 100th anniversary of the move of the Franz Joseph University from Kolozsvár to Szeged and the death of István Apáthy, we started a collaboration between the University of Szeged and the Babeş-Bolyai University in Kolozsvár to explore István Apáthy's scientific legacy. The Department of Anatomy, Histology and Embryology of the University of Szeged, in cooperation with the Zoological Museum of the Babeş-Bolyai University, is determined to explore and create a digital archive of István Apáthy's scientific histological collection. Our aim is to make the future digital archive available for those scientist, who would like to get an insight into István Apáthy's nearly forgotten scientific heritage.
In Kolozsvár, the slides are being cleaned, catalogued and macroscopically photographed under the supervision of Gergely Osváth, at the Museum of Zoology. The most important specimens in the collection will be digitised by the members of the Szeged team through the use of a high-resolution slide scanner or a special digital camera mounted on a research microscope, depending on the characteristics of the slides.
According to the primary survey of the collection in Kolozsvár, more than 10,000 sections can be linked to the 30 years scientific activity of István Apáthy's laboratory. Categorisation of these specimens identified by the year of preparation is already in progress. Our preliminary experience has shown that approximately half of the sections can be digitised with a slide scanner, while the rest have to be photographed individually by using a research microscope. The scientific evaluation and archiving of the already digitised samples is under progress.

COMPARISON OF PLGA AND METAL IMPLANTS IN PEDIATRIC ANKLE FRACTURE MANAGEMENT.

Nudelman Hermann, Aba Lőrincz, Tamás Kassai, Marcell Varga, Gergő Józsa (Division of Surgery, Traumatology and Otorhinolaryngology, Department of Paediatrics, Clinical Complex, University of Pécs, Hungary, Department of Thermophysiology, Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary, Department of Pediatric Traumatology, Péterfy Hospital, Manninger Jenő National Trauma Center, Budapest, Hungary)

Keywords: pediatric, ankle, fracture, PLGA, osteosynthesis, absorbable screw
Objective: To evaluate the effects and outcomes of ankle fracture treatment with absorbable implants compared to metal screws.
Patients and Methods: A total of 129 patients were under observation, with distal tibial fracture types ranging from Salter-Harris II-IV, in a retrospective review. Patients were treated with poly L-lactide-co-glycolic acid (PLGA) absorbable screws in group A. Group B included patients treated with metal screws. The extremities were placed in a cast for six weeks after surgery and were utilized for another 6-8 weeks. Patients were followed up for 12-30 months and were evaluated accordingly.
Results: Results were examined in several aspects such as age, gender, open or closed surgery, mechanism of injury, length of hospitalization, and type of fracture. Radiographic images show proper callus formation in all patients throughout the follow-up period. The length of hospitalization and complications were lower in group A.
Conclusion: In pediatric cases, the application of absorbable implants presents excellent Results for the treatment of ankle fractures. It does not disturb the growth plate and does not require reoperation. For this reason, it

reduces the burden on the patient and the healthcare provider, while simultaneously decreasing the risk of complications such as infections or problems due to general anesthesia.

A SELF-DEVELOPED TOOL FOR MEASURING REACTION TIME (CERVELOX)

Marcell Kákonyi, Marianna Matányi (The Department of Paediatrics, Semmelweis University, Budapest, Hungary)

Keywords: reaction time, diagnostic equipment, neurologic deficits, children
Aims: The aim of our study is to investigate whether statistical analysis of multiple reflex time measurement data from different reflex pathways can be used as an additional diagnostic tool for certain neurological disorders.
Methods: The study is performed using a self-developed device consisting of head-mounted LED lights, push buttons, and a microcomputer controlling them. The speed of right (RR) and left (RL) hand responses to a stimulus from the right visual field and the speed of right (LR) and left (LL) hand responses to a stimulus from the left visual field (reflex time) are measured.
Results: We included preschool and primary school children (N=62, boys: 50%, age (mean±SD) 7.9±2.1 years). The study population was divided into 3 age groups (5-6, 7-8, 9-11). For RR, RL, and LR reflex times, a significant difference was found between the mean reflex time of the two smaller age groups and the mean reflex time of the largest age group. All reflex time parameters showed a significant inverse correlation with age.
Conclusions: In healthy children, reflex time decreases with age. The instrument is suitable for accurately measuring reaction time across different stimulus pathways. In some neurological pathologies, the measured reaction times may differ from the healthy mean values for the age group.

EXAMINATION OF THE FACTORS IN SERUM AND AMNIOTIC FLUID THAT AFFECTS THE PLACENTATION IN PHYSIOLOGICAL PREGNANCIES

Sikovanyecz János Sebestyén, Németh Gábor, Sikovanyecz János, Vincze Márió (Department of Obstetrics and Gynecology University of Szeged SZTE)

Keywords: placentation, Laeverin, Galecetin-13, HLA-G
Aims: Examination of the factors (Laeverin, Galectin-13, HLA-G) in serum and amniotic fluid and compare with maternal datas (BMI, age, and gestational age in the moment of sampling) and with each other. Aim to investigate further in either the physiological and pathological placentation to understand pathologies as preeclamptic pregnancy or IUGR.
Methods: Blood sampling and amniotic fluid sampling with amniocentesis between the gestational week 18 and 22. ELISA analysis with 75 maternal serum and amniotic fluid samples from physiological pregnancies. Sample Comparing made by SPSS statistics softver. For correlation we used Pearson Correlation formula. The signification limit was 0.05 level.
Results: Negative significal correlations were found in serum between HLA-G levels and Galectin-13 levels (n=49, p=0,01), and between Galectin-13 levels and Laeverin levels (n=43, p=0,02) also in serum. Didn't succeed to find any significal correlation between the levels of the factors and the maternal datas.
Conclusions: These significations in the serum were negative. This means higher Galectin-13 serum level connects with lower HlA-G level and higher Galectin-13 level connects with lower Laeverin level. These Results could work as a normal database for further examinations with pathological cases.

THE ROLE OF MRI IN THE STAGING OF RECTAL CANCER - ANALYSIS OF 9 YEARS' DATA

Elisabeth Garcia, Ariella Kondor (Department of Surgery), Ivett Hegedűs (Department of Pathology), Nándor Faluhelyi (Department of Medical Imaging)

Keywords: rectal cancer, MRI, staging, mesorectal fascia, CRM
Aims: The treatment of locally advanced rectal cancer is challenging. The therapeutic decision is made by a multidisciplinary oncoteam based on the staging examinations. The necessity of neoadjuvant therapy depends on the local extension of the tumor determined by CT or recently by MRI. Our aim was to prove that not the T3 stage

itself, buadt the involvement of mesorectal fascia (MRF) by the tumor determines if neoadjuvant chemoradiotherapy is necessary.
Methods: MRI for staging of rectal cancer was used at first in 2014 in the Department of Surgery, Pécs. Until 2022 December 218 patients underwent this examination. In 110 patients, the mesorectal fascia (MRF) was not involved by the tumor according to the MRI, so primary operation was performed. We compared the Results of CT and MRI examinations with the pathological outcomes.
Results: T stage was predicted accurately in 55% by CT and in 50% by MRI. CT rather underscored, MRI rather overscored it. Our Results showed low specificity (39% with CT and 25% with MRI), but higher sensitivity (72% with CT and 83% with MRI). Negative predictive values were 66% with CT and 67% with MRI, positive predictive values were 46% with CT and 44% with MRI. The ratio of R1 resection caused by circumferential resection margin (CRM) involvement was 6,5%.
Conclusions: MRI can predict reliably the CRM positivity, which determines the necessity of neoadjuvant chemoradiotherapy. However, neither CT nor MRI examination can presume adequately the T and N stages.

VIRTUAL 3D VASCULAR MODEL STUDY IN LAPAROSCOPIC COLORECTAL SURGERY - A PRESENTATION OF A RANDOMIZED CONTROLLED TRIAL

Olivér Geletey, Tamás Sztipits, Imre J. Barabás (National Institution of Oncology, Budapest, Hungary)

Introduction: Laparoscopic right hemicolectomy and complete mesocolic excision (CME) are increasingly accepted and recommended as the standard surgical treatment for right colon tumors. During surgery, precise preoperative mapping of the variable branches of the arterial (AMS) and superior mesenteric vein (VMS) located in the root of the mesentery is key, as this is where the central lymph node dissection occurs.
Aim: Our aim is to investigate the role and applicability of a CT angiography-based virtual vascular model - depicting the AMS/VMS branch system in high detail - for preoperative planning and intraoperative orientation.
Methods: 40 patients are planned to be included in the study. Patients undergoing surgery will be randomized in a 1:1 ratio. For study group (A), a virtual 3D model of the AMS/VMS branch system will be obtained along with a targeted CT scan. For the control group (B), no model will be created. CT and 3D model images are obtained by the surgeon before surgery and are available during surgery. Surgery is performed by designated surgeons at the OOI Centre for Tumour Surgery in a standardised way. During surgery, we record the time of AMS/VMS branch care, total operating time, rate of vascular injury, intraoperative blood loss, specimen quality, number of arterial nodes removed, rate of postoperative complications and length of hospital stay. The surgeon rates the model on a scale of 0-10.
Preliminary Results: 22 patients were randomized by the time of abstract submission, 13 patients in the 3D group and 9 in the control group. Based on the Results so far, there is no difference in surgical blood loss and vascular injury so far.
The operative time is shorter in the control group, but the difference is not significant (164 ±20min vs 154 ±50min; p=0.65).
More lymph nodes were removed in the 3D group (44,4 vs 38,6; p=0.53) but the difference is not significant here either. A strong positive correlation was found between BMI and length of surgery (p=0.78). Surgeons rated the models positively.
Conclusion: No Conclusion can be drawn from the preliminary data of this study due to the small number of cases. Based on the data so far, the study has good efficacy and no patients dropped out of the study. Our primary objective at the present is to provide a technical demonstration of the trial.

EFFECT OF BGP-15 ON THE REGENERATION OF MICROVASCULAR ANASTOMOSES IN RATS

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Hungary, 3Department of Anatomy, Histology and Embryology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary)

Keywords: microvascular anastomosis, BGP-15, tensile strength, hematology, hemorheology
Aim: Vascular anastomosis is a widely used technique in many fields of surgery. Regeneration of the vessel wall post-op is crucial to restore vascular function and improve tissue survival. In the literature, BGP-15 has been shown to reduce oxidative stress and preserve cellular integrity in various pathologies. Here, we examined whether BGP-15 has beneficial effects on the regeneration of arterial microvascular anastomoses.
Methods: Microvascular anastomosis was performed on the right femoral artery of fourteen male Wistar rats. We used eight-stitched end-to-end microsurgical technique (10/0 polyamide-6). We measured the blood flow before, after surgery, and on the termination day to assess anastomosis patency. A subcutaneous cannula was also inserted on animals in the drug-treated group (n=7) for local BGP-15 administration. Every week, we monitored changes in hematology and hemorheology by lateral tail vein blood sampling. On the 21st day, animals were sacrificed for tensile strength and histological examination of the arteries.
Results: All anastomoses were performed successfully without major difference in blood flow values. We found that BGP-15-treated anastomoses retained significantly more tensile strength, corroborated by thicker vessel walls in histology analysis. In addition, there was a noticeable increase in red blood cell aggregation index despite a fall in the number of cells. White blood cells, platelet count, and red blood cell deformability slightly fluctuated, conforming to physiological post-operative reactions.
Conclusion: Local treatment of BGP-15 improved tensile strength of arterial anastomoses. After systemic absorption, the drug could modify the laboratory Results which encourages further investigation.

PREDICTORS OF DISEASE REMISSION IN RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS ALONGSIDE THE TAPERING OF BIOLOGICAL THERAPY

Bianka Horváth (University of Szeged Szent-Györgyi Albert Faculty of Medicine, Szeged, Hungary)

Introduction: In rheumatoid arthritis (RA) and ankylosing spondylitis (AS) patients who are in stable remission on biological therapy, identification of patients suitable for dose reduction or permanent discontinuation of therapy without a flare-up of disease has become an important issue. As potential predictive biomarkers we investigated two plasma factors: S100A12, an inflammatory mediator and proposed biomarker for unstable remission in juvenile RA and platelet factor-4 (PF-4), which is released from activated platelets and activates neutrophil.
Methods: In this prospective, controlled, multicenter study in Hungary, we recorded the clinical parameters of 55 RA and 58 AS patients in sustained remission after dose reduction, and of 47 RA patients and 35 AS patients in dose-maintenance control groups, over a period of 3-4 years. Using ELISA, we measured the plasma levels of S100A12 and PF-4 in 30 RA and 31 AS patients undergoing dose-reduced anti-TNF and anti-IL6 therapy.
Results: Plasma levels of S100A12 at baseline were significantly higher in RA patients who later experienced relapse than in those who remained in remission (mean: 136.5375 vs 46.8636 ng/ml). A biomarker elevation was also observed in AS relapse vs remission (mean: 68.252 vs 41.0026 ng/ml, p=0.44). There was no difference in PF-4 biomarker levels between relapsing and remission patients.
Discussion: The elevated plasma level of S100A12 may correlate with the extent of inflammation in patients with RA, which cannot be clinically measured by other means. Therefore, it can be a predictive biomarker in the planning of biological therapy tapering.

SS8. MOLECULAR MEDICINE SESSION

IMAGING BY TOUCHING: BIOMEDICAL APPLICATIONS OF SCANNING PROBE MICROSCOPY

Prof. Dr. Miklós Kellermayer (Dean, Semmelweis University)

No abstract available.

EFFECT OF CYP3A GENOTYPE IN RENAL TRANSPLANT PATIENTS ON TACROLIMUS MEDICATION

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Keywords: pharmacogenetics; precision medicine; tacrolimus; organ transplantation; cytochrome P-450 CYP3A
Aim: Tacrolimus is an essential component of post-transplant immunosuppressive therapy to inhibit graft rejection. Its use is overshadowed by its renal toxicity, extremely narrow therapeutic range, and wide inter-individual variability regarding its metabolism.Our aim was to consider the potential incorporation of CYP3A genotyping into the immunosuppressive protocol.
Methods: In our project, CYP3A4 and CYP3A5 genotyping was performed on blood samples from kidney transplant recipients (N=39) since Feb 22, 2021. Based on genotype combinations and literature data, recipients were classified as extensive metabolizers (EM), intermediate metabolizers (IM) and poor metabolizers (PM). Daily tacrolimus doses were normalized to body weight and tacrolimus blood levels were normalized to daily doses.
Results: Data from 9 EM, 26 IM and 4 PM subjects were pooled. At the time of the third monthly follow-up, statistically significantly higher values for mean normalized doses and significantly lower values for mean normalized blood levels were found for the EM group compared to both IM and PM subjects. Furthermore, we found a significant negative correlation between normalized tacrolimus blood concentrations and GFR values of the recipients. In the sixth month control data, we found statistically significant higher GFR values in EM individuals compared to the PM group ($p<0.05$).
Conclusions: Based on population allele and genotype frequencies our study group was a representative sample of Caucasian ethnicity. Our Results seem to support the justification of CYP3A genotyping, its inclusion in a preoperative protocol requires further continuation of our project and consideration of practical aspects.

EFFECTS OF MICRODOMAIN-FORMING LIPIDS ON THE MEMBRANE LOCALIZATION AND GATING OF VOLTAGE-GATED ION CHANNELS

Bence Cs. Szabó, Tamás Kovács, Florina Zakany (Department of Biophysics and Cell Biology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary)

Aims: The gating of ion channels and their distribution between membrane microdomains such as lipid rafts and ceramide platforms strongly depend on lipid composition of the cell membrane. The level of the lipid raft constituent cholesterol (CHOL) influences these functionally relevant parameters of the KV1.3 voltage-gated potassium channel by modifying its pore domain (PD), which might carry pathophysiological relevance through controlling lymphocyte activation and neuronal functions. The HV1 voltage-gated proton channel has a unique structure by having only a voltage-sensor domain (VSD) without a PD. Although recent studies suggested a connection between HV1 and diseases with increased CHOL levels such as breast and colorectal cancers, CHOL actions on HV1 gating have not been investigated before. Furthermore, the effects of C16-ceramide (Cer) and

C16-glycosylceramide (GCer), two other membrane microdomain-forming lipids, have not been previously examined on KV1.3 or HV1 in spite of the importance of these lipids and channels in neurodegenerative and lipid storage disorders.

Methods: We investigated the consequences of loading the cell membrane with CHOL, Cer or GCer on the localization and gating of KV1.3 or HV1 applying confocal microscopy and two-electrode voltage-clamp fluorometry (TEVCF). For microscopy, we transfected HEK cells with Kv1.3- and HV1-encoding plasmids, while GFP-GPI transfection and anti-ceramide antibodies were used for the visualization of lipid rafts and ceramide platforms, respectively. During quantitative image processing Pearson correlation coefficients were determined between KV1.3 or HV1, raft and ceramide platform markers in control and lipid-loaded samples to quantify their colocalization. TEVCF measurements performed on channels expressed in Xenopus laevis oocytes enabled simultaneous measurements of ionic currents and characterization of VSD and PD movements during the gating process after labeling a cysteine residue introduced into the VSD with TAMRA-MTS. By determining steady-state activation (G-V curves) and fluorescence-voltage relationship (F-V curves) we can identify the intramolecular target of lipids.

Results: Cer treatment significantly decreased the strongly positive Pearson coefficient between markers of KV1.3 or HV1 and lipid rafts, while increased that between channels and ceramide platforms, suggesting a relocalization of these channels from lipid rafts to ceramide platforms. In contrast, GCer treatment significantly increased the colocalization of channels with lipid rafts without modifying that with ceramide platforms referring to enhanced lipid raft localization. Distinctive effects of Cer and GCer were further corroborated by TEVCF measurements for KV1.3. While both treatments shifted G-V curves towards more positive membrane potential values, only Cer induced similar changes in the F-V curve and GCer exerted no significant effects on VSD movements, suggesting that Cer modulates KV1.3 function through affecting the VSD, whereas GCer targets directly the PD. TEVCF examination of HV1 is in progress.

Conclusion: The intrinsic membrane components CHOL, Cer and GCer affect the gating of KV1.3 and HV1 channels possibly through modifying their preferential localization in various membrane microdomains, which could contribute to the pathomechanism of diseases with altered lipid levels.

EFFECT OF MUTATIONS IN PROTEIN ARGININE METHYLTRANSFERASE 5 ON TUMORIGENESIS

Mihály Székely, Attila Makai, Klaudia Tóth, Ilka Keller, Dániel Horváth, Evelin Major, Ádám László Ungvári, Beáta Lontay (Department of Medical Chemistry, University of Debrecen, Debrecen, Hungary)

Abstract: Over- and under-activation of enzymes, triggered by mutations and abnormal post-translational modifications, is a major cause of tumorigenesis. Protein arginine methyltransferase 5 (PRMT5) catalyzes the dimethylation of histone proteins, thus altering gene expression. It is regulated by RhoA-activated kinase (ROK) and myosin phosphatase (MP) via its Thr80 phosphorylation. Mutations of Thr80 have been identified in several tumor types.

We aimed at investigating the effect of mutations in PRMT5 Thr80 biochemically.

We transfected tsA201 cells with plasmids encoding Flag-tagged wild-type and Thr80 mutant PRMT5 and purified them by Flag affinity chromatography. By mass spectrometry analysis, a new phosphorylation site, Ser74, was described for Thr80 mutant proteins under ROK treatment. To investigate the mutation's effect on enzyme activity, overexpressed proteins were bound to affinity gels. In vitro ROK kinase assay was conducted on PRMT5 and then examined for phosphorylation by Western blotting.

While WT PRMT5 showed no increase in the phosphorylation of Ser amino acid residues upon ROK treatment, an increase was detected in Thr80 mutants. The mutant PRMT5 showed clear PRMT5 Ser phosphorylation by in vitro ROK enzyme activity assay, which was reduced by the addition of MP. We analyzed the amount of histone substrates bound by WT and mutant PRMT5 proteins and found that ROK induced mutant PRMT5 to bind significantly more histone substrates, which was not altered by further phosphorylation. We validated our Results with lung cancer tissue samples and observed a grade-dependent correlation in the phosphorylation.

Mutations in tumors may regulate PRMT5 activity by increasing the amount of substrate bound by the enzyme, which may be due to spatial structural changes and exposure of new activating phosphorylation sites.

INVESTIGATING THE PRODUCTION AND ROLE OF LEUKOTRIENE B4 IN NEUTROPHIL

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Keywords: neutrophil granulocytes, leukotriene B4, neutrophil swarming, fluorescent probes

Introduction: It is well established that leukotriene B4 (LTB4) plays an important role in the initial steps of inflammation and wound healing as a chemoattractant, but little is known about its endogenous release pattern and its role in neutrophil swarming. We aim to better understand these processes and to decipher how LTB4 mediates neutrophil migration and swarming.

Methods: We inserted a green fluorescent protein into the endogenous receptor of LTB4 to generate a fluorescent biosensor (GEM-LTB4) in which the presence of LTB4 induces a fluorescence intensity change. Our sensor was optimized and characterized using a GEM-LTB4-expressing stable HEK293A cell line. Murine neutrophil granulocytes were stimulated with fMLP and the secretion of LTB4 was assessed using GEM-LTB4. We also generated a transgenic zebrafish line expressing GEM-LTB4 and assayed the production of LTB4 in response to sterile wounding. Furthermore, we investigated the LTB4 production and intracellular Ca2+ levels in neutrophils in response to the calcium ionophore Calcimycin.

Results: Using GEM-LTB4, we detected LTB4 waves produced by individual murine neutrophils in response to fMLP. In parallel, we detected pseudopodia formation towards the source of LTB4 production in surrounding neutrophils. Following sterile wounding in transgenic zebrafish expressing GEM-LTB4, we measured variable amounts of endogenous LTB4 release. LTB4 production was enhanced by Calcimycin.

Conclusions: We have created a novel fluorescent biosensor which allows us to investigate the spatiotemporal pattern of endogenous LTB4 release both in vitro and in vivo. Using GEM-LTB4 we also assessed the effect of intracellular Ca2+ level changes on neutrophil-derived LTB4 production.

ANTIBIOTICS OF THE FUTURE ARE PRONE TO BACTERIAL RESISTANCE

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Keywords: antibiotic resistance, microbiology, evolution, WHO critical priority pathogens

Aims: The rapid spread of multi-resistant pathogens will lead to a global health problem by 2050. Thus we examined whether recently-developed antibiotics can be effective in the long term, or whether resistance to them can evolve easily.

Methods: We selected 13 recently-developed antibiotics from five different mode of action families. We also included one control antibiotic to each antibiotic family. Using high-throughput laboratory evolution, we investigated whether resistance to these antibiotics develops through spontaneous mutations in the laboratory. For this, I used a sensitive and a multi-resistant strain of E.coli, K.pneumoniae, A.baumannii and P.aeruginosa. Next, to assess the molecular mechanisms behind the evolved resistance we sequenced the whole genome of laboratory evolved populations. After, to test the impact of the evolved resistance on virulence we used a greater wax moth larva model (Galleria mellonella).

Results and Conclusions: We found that recently-developed antibiotics are as prone to resistance evolution in Gram-negative pathogens as clinically employed antibiotics. The molecular mechanisms of resistance overlap with those found in commonly used antibiotics. As a consequence, these mechanisms are already prevalent in natural bacterial pathogens, indicating that resistance can rapidly emerge through selection of pre-existing bacterial variants. Additionally, resistance to new peptide-based antibiotics enhances bacterial virulence, raising concerns. However, certain combinations of antibiotics and bacterial strains are less prone to developing resistance, emphasizing the potential of narrow-spectrum antibacterial therapies that could remain effective. Our comprehensive framework could be used to assess the future health risks associated with bacterial resistance to new antibiotics.

A NEW FLUORESCENCE PHOTOAFFINITY LIGAND-BASED TECHNIQUE FOR THE D3 DOPAMINE RECEPTOR

Dárius Leszkó, Susanne Prokop (Kísérletes Orvostudományi Kutatóintézet, Budapest, Hungary)

Introduction: Immunohistochemistry is commonly used for protein labeling in scientific studies. However, the lack of selective antibodies against important proteins poses a challenge. Our research group recently demonstrated the effectiveness of fluorescent ligands in labeling previously challenging target proteins, addressing some of the technical limitations of immunohistochemistry (Prokop et al. Nat Commun 2021). Nevertheless, fluorescent ligand-treated samples have a short lifespan and are less resistant to repeated washing steps. To overcome the reversible binding issue of fluorescent ligands, we aimed to develop novel covalently coupled compounds in collaboration with Prof. György Miklós Keserű's group. Our goal was to create photoactivatable compounds capable of covalently binding to target proteins.
Methods: We focused on the D3 dopamine receptor (D3R), a protein of significant neuropsychiatric importance. HEK 293 cells expressing hemagglutinin-labeled D3R were treated with a photoactivatable fluorescent ligand. The efficiency of covalent binding was assessed using three UV light sources with varying power. The fluorescence signal was analyzed using confocal and epifluorescence microscopy techniques.
Results: Two new photoactivatable compounds successfully enabled selective labeling of D3R. Both a partial agonist and an antagonist-based fluorescent ligand irreversibly bound to the receptor. The efficiency of covalent receptor labeling was found to rely heavily on the duration and intensity of UV exposure. By manipulating these parameters simultaneously, we achieved diverse and efficient protein labeling. Moreover, our method proved suitable for analyzing tissue proteins.
Summary: Covalently bound photoactivated ligands expand the range of fluorescent ligand-based microscopy tools and facilitate the study of previously challenging-to-label proteins.

POSSIBLE ROLE OF THE TRPA1 IN A MOUSE MODEL OF CHRONIC ALCOHOL CONSUMPTION

Izabella Török, Ammar Al-Omari, Viktória Kormos (Department of Pharmacology and Pharmacotherapy, Pécs, Hungary)

Keywords: alcohol, addiction, Edinger-Westphal nucleus, urocortin1
Aims: The centrally projecting Edinger-Westphal nucleus (EWcp) contributes to control of alcohol consumption by its urocortin1 (UCN1) and cocaine- and amphetamine-regulated transcript (CART) co-expressing peptidergic neurons. UCN1/CART/EWcp is the primary seat of central transient receptor potential ankyrin1 (TRPA1) cation channel. We hypothesized that ethanol and its metabolites, may directly activate TRPA1 ion channels in the EWcp, thus may play a role in alcohol consumption.
Methods: Free-choice dark-phase mouse model of chronic alcohol (10% ethanol) consumption was performed involving male Trpa1 knock-out (KO) and wild type (WT) mice for 3 months. Alcohol preference was measured. Trpa1, Cart and Ucn1 mRNA expression was quantified by RNAscope in situ hybridization.
Results: Decreased Ucn1 and Cart mRNA density was found in the control KO group with lower initial alcohol preference, which is consistent with the literature data that low Cart and Ucn1 expressing mouse strains have lower alcohol preference. The mRNA expression of all three genes tested was significantly reduced upon chronic alcohol exposure which may explain the lower alcohol preference in WT mice at the end of the experiment. In contrast, Ucn1 mRNA levels were unchanged and Cart mRNA expression was reduced to a lesser extent in KO mice, which may explain the increased alcohol preference in the KO animals at the end of the experiment.
Conclusions: Decreased Trpa1, Ucn1 and Cart mRNA expression upon chronic alcohol treatment, associated with reduced alcohol preference strongly suggests the regulatory role of this ion channel in alcohol consumption.

SFS4. HIGHLITED SESSION

LATEST ADVANCES IN ORAL MEDICINE

Dr. Lászlóffy Csaba -The All-on-4® treatment concept - transforming people's lives for 25 years

No abstract available.

SS9.PAEDIATRICS, ANAESTHESIOLOGY-EMERGENCY SESSION

NEW DIRECTIONS IN ELECTROCHEMOTHERAPY

Dr. Lázárné Dr. Oláh Judit (University of Szeged, Szeged, Hungary)

No abstract available.

THE PAST AND PERSPECTIVES OF NUCLEAR MEDICINE

Prof. Dr. Galuska László

No abstract available.

CORRELATION BETWEEN SARS-COV-2 INFECTION AND CHILDHOOD AUTOIMMUNE THYROIDITIS

Papp Sára1, Herczeg Vivien2, Tóth-Heyn Péter2 (1 Semmelweis University, 2 Semmelweis University, Pediatric Center, Bókay street Unit)

Keywords: SARS-CoV-2, Thyroiditis, autoimmune

Aim: To investigate the prevalence of post SARS-CoV-2 infection thyroid abnormalities and autoimmune thyroiditis in childhood.

Methods: Patients from the Long Covid clinic were examined between 24th March 2021 and 23rd March 2022; 300 children were included. We registered their age, sex, thyroid hormone levels (TSH,T3,T4), presence of autoantibodies (anti-thyreoglobulin-ATG, anti-thyreoidea-peroxidase-ATPO). We also analyzed ultrasound findings, and drug administration. Patients with abnormalities were invited for follow-up exams.

Results: The mean age of the children was 12.35±3.83 years, male:female ratio was 136:167. Twenty-three cases (7,7%) with deviation in thyroid related values were found. Autoantibody elevation was found in 19 children (6,3%), out of them 5 had TSH alteration. Four children had isolated TSH elevation. ATPO positivity was found in 16, ATG positivity in 14 cases. Twenty-two children were submitted to ultrasound imaging, and 12 of them showed inflammatory changes. Metothyrin was prescribed to one child and two had to start L-Thyroxine therapy. During our follow-up study, 17 patients showed permanent disturbances, and 5 transient changes were found. Two children's ultrasounds changed from negative to positive and one child had to start L-thyroxine therapy during the follow up period.

Conclusion: The observed 6,3% autoantibody positivity is considered to be high, suggesting the relationship between SARS-CoV-2 with and autoimmune thyroiditis. To establish if these disturbances are related to SARS-CoV-2, further clinical research is required.

RETROSPECTIVE ANALYSIS OF THE USE OF VISCOELASTIC HEMOSTATIC ASSAY (CLOTPRO) IN AN ACADEMIC EMERGENCY DEPARTMENT

Viktória Hahn, Gabriella Anna Rapszky, Judit Imecz, Péter Vass, Csaba Varga, Bánk Gábor Fenyves (Department of Emergency Medicine of Semmelweis University)

Keywords: viscoelastic hemostatic assay, viscoelasticity, hemostasis, point-of-care, emergency department
Aims: We aimed to analyse retrospective data of patients who had a viscoelastic haemostatic assay (VHA - ClotPro) performed at the emergency department (ED). We aimed to identify unique characteristics of ED VHA use regarding target patient population, indications, and therapeutic decisions.
Methods: We included patients for whom a VHA test was ordered between 07/15/2019 – 12/31/2021 at the ED of Semmelweis University. We collected demographic, laboratory, clinical, and VHA data. Correlations between VHA findings and laboratory Results, demographic characteristics and therapeutic interventions were analysed.
Results: Data of 381 patients (178 (43.7%) female) were processed. We found significant correlation between EX test clotting time (CT) and INR values, EX maximal clot firmness (MCF) and fibrinogen levels, EX MCF and platelet count, FIB MCF and fibrinogen levels, and IN CT and activated partial thromboplastin time (all p-values < 0.05). Of 63 patients who had a hemorrhagic event while on novel oral anticoagulant (NOAC) therapy, only 26 (41.3%) had a NOAC-specific RVV or ECA test. Patients with prolonged EX CT had higher likelihood of receiving prothrombin complex concentrate (PCC) or fresh frozen plasma (FFP) (OR=3.12; 95% CI=1.99-4.88). In the prolonged EX CT cohort, patients with high INR value were more likely to receive PCC/FFP therapy than patients with normal or unknown INR (79.1% vs. 36.5%).
Conclusions: VHA Results correlate well with conventional laboratory tests, making it a reliable diagnostic tool. Data suggest positive correlation with optimal therapeutic decisions. Further analysis is necessary to establish patient-oriented outcomes of VHA use.

CLINICAL AND MICROBIOLOGICAL OUTCOMES AND FOLLOW-UP OF SECONDARY BACTERIAL AND FUNGAL INFECTIONS AMONG CRITICALLY ILL COVID-19 ADULT PATIENTS TREATED WITH AND WITHOUT IMMUNOMODULATION

Martin Rajmon, Márk Di Giovanni, Bálint Gergely Szabó (Semmelweis University, Budapest, Hungary)

Introduction: Nearly 10% with COVID-19 require admission to an intensive care unit. Our aim was to assess clinical and microbiological outcomes of secondary infections among critically ill COVID-19 adult patients treated with/without immunomodulation.
Methods: A single-centre prospective observational cohort study was performed between 2020–2022 at a dedicated center. Diagnosis and severity classification was established by respiratory SARS-CoV-2 PCR and the WHO criteria, respectively. Eligible patients were included consecutively at admission, follow-up was done per protocol +30 days post-inclusion. Bloodstream-infections (BSI), ventilator-associated bacterial pneumonia (VAP) and COVID-19-associated invasive pulmonary aspergillosis (CAPA) were defined according to international guidelines. Patient stratification was performed by immunomodulatory therapy administration (dexamethasone, tocilizumab, baricitinib/ruxolitinib). Primary outcome was any microbiologically confirmed major infectious complication, secondary outcomes were invasive mechanical ventilation (IMV) requirement and all-cause mortality.
Results: Altogether 379 adults were included. At baseline, 249/379 (65.7%) required IMV, 196/379 (51.7%) had cytokine storm. At +30 days post-inclusion, rate of any infectious complication was 151/379 (39.8%), IMV requirement and all-cause mortality was 303/379 (79.9%) and 203/379 (53.6%), respectively. There were no statistically significant outcome differences after stratification. BSI, VAP and CAPA episodes were mostly caused by Enterococcus faecalis (27/124, 22.1%), Pseudomonas aeruginosa (26/91, 28.6%) and Aspergillus fumigatus (20/20, 100%). Concerning the primary outcome, Kaplan–Meier analysis showed similar probability distributions between treatment subgroups (118/299, 39.5% vs. 33/80, 41.3%, log-rank p=0.22), and immunomodulation was not retained as its independent predictor in logistic regression.
Conclusion: Secondary infections among critically ill COVID-19 adult patients possess a relevant burden, irrespective of immunomodulatory treatment.

COMPARABILITY OF THE EFFECTS OF SARS-COV-2 INFECTION ON CONVENTIONAL AND VISCOELASTIC COAGULATION MONITORING RESULT

János Domonkos Stubnya1, Diána Rohács1 (1Deparment of Anaesthesiology and Intensive Therapy, Semmelweis University)

Keywords: SARS-CoV-2, Viscoelastic Coagulation Monitoring

Aims: The laboratory method widely used for monitoring anticoagulation with low molecular weight heparin (LMWH) is antiXa measurement. Among the viscoelastic tests, we can utilize the RVV test in the ClotPro© system. Our study aimed to investigate the comparability of conventional and viscoelastic coagulation monitoring in patients treated with LMWH based on their COVID status.

Methods: In our observational study, we performed parallel laboratory antiXa activity and bedside RVV tests on 40 patients. The antiXa activity was determined using the Innovance© Heparin Assay. Additionally, we recorded the SARS-CoV-2 status of the patients.

We conducted various statistical analyses to examine the relationship between heparin levels and RVV test clotting time.

Results: In COVID-19-negative patients, a relatively strong correlation was found between the laboratory-measured antiXa activity and RVV clotting time. However, no such correlation was observed in COVID-19-positive patients. There was a significant difference in the maximum clot stability between COVID-19-positive and negative patients.

Conclusions: No reliable linear correlation between antiXa activity and viscoelastic RVV clotting time in COVID-19-positive patients can be established. The differences observed between the two groups may be attributed to the hypercoagulable state of COVID-19-positive patients, supported by the significant difference in MCF values.

MT1. MTT Session

A BREATHTAKING STORY

Mihály Anna, Dr. Mihály András Imréné, Dr. Csada Edit, Dr. Barna Katalin

No abstract available.

SPATIOTEMPORAL CHANGES AND INTRATUMORAL HETEROGENEITY OF MOLECULAR SUBTYPE MARKERS IN PRIMARY AND BRAIN METASTATIC SMALL CELL LUNG CARCINOMA

Ildikó Krencz, Dániel Sztankovics, Fatime Szalai, Dorottya Moldvai, Titanilla Dankó, Bálint Scheich, Anna Sebestyén, Judit Pápay (Department of Pathology and Experimental Cancer Research, Semmelweis University)

Keywords: small cell lung carcinoma, subtypes, brain metastasis, heterogeneity, phenotype transition

Aims: Small cell lung carcinoma (SCLC) has recently been classified into 4 subtypes based on the expression of ASCL1, NeuroD1, POU2F3, and YAP1. These advances in molecular subclassification may help to overcome the unmet need for targeted therapies and improve survival. However, limited information is available on how the expression of these subtype markers changes during tumor progression. Therefore, the aim of our study was to compare the expression of these markers in primary and brain metastatic SCLCs.

Methods: Immunohistochemical analysis of ASCL1, NeuroD1, POU2F3, and YAP1 was performed on 120 SCLCs, including 10 paired samples (primary-primary, primary-metastatic, and metastatic-metastatic pairs). The H-score method was used to evaluate the immunohistochemical reactions, and the samples were classified into subtypes.

Results: In primary SCLCs, the proportion of ASCL1-high, NeuroD1-high, and ASCL1-high/NeuroD1-high subtypes was 20%, 14%, and 22%, respectively. Low expression of all markers was observed in 20% of the cases. In brain metastases, there was a significant increase in the proportion of multiple subtypes, with a rate of ASCL1-high/NeuroD1-high and ASCL1-high/NeuroD1-high/YAP1-high subtypes increasing to 24% and 18%, respectively.

However, the proportion of quadruple-negative cases remained almost unchanged. The subtype of the paired samples matched in only one-third of the cases.
Conclusion: Our Results indicate that the expression of subtype markers may change during disease progression, and subtype analysis of the primary SCLC may not provide accurate information about the characteristics of the recurrent/metastatic tumor. Therefore, repeated sampling and subtyping may be necessary for subtype-specific targeted therapy.

CLINICAL CHARACTERISTICS AND SURVIVAL OF NSCLC PATIENTS WITH KRAS MUTATION

Fanni Tószegi (1), Lilla Tamási (2), Andrea Bíró (2), Balázs Csoma (2) (1: Semmelweis University Faculty of Medicine, 2: Semmelweis University Department of Pulmonology)

Keywords: NSCLC, PD-L1, KRAS-mutation, Kaplan-Meier method, PFS
Introduction: Despite recent advances in the treatment of advanced non-small-cell lung cancer, there remains a need for effective treatments for progressive disease. There have been several attempts to come up with targetted therapy against KRAS mutant NSCLC in the past decades. Among the new molecules, there are promising ones, but their use in the clinical practice is not yet widespread.
Aims: to compare the efficacy of 5 different treatments and to examine the connection between PD-L1 expression and progression-free survival, and to characterize the population treated at the Department of Pulmonology
Methods: For this study, we enrolled 102 patients with NSCLC harboring KRAS mutation between Aug 28, 2020, and Feb 28, 2022. Data from the University's database (eMedsol) were used to carry out descriptive statistics. For survival analysis, Kaplan-Meier method was used.
Results: Most patients had advanced (stage IIIB: 9,8%) or metastatic (70,6%) disease at the time of the diagnose. Also, most of them are either current (52%) or former (36%) smokers. As a result, 54% had COPD. Besides basic supportive care, patients were treated with one of the following 5 different combinations of therapies: surgery+chemo; platium-based chemo doublet; chemo-immunotherapy; platinum-based chemo+bevacizumab; and mono-immunotherapy. The progression-free survival was significantly higher in the surgery+chemo group. No significant correlation was found between PD-L1 expression and PFS.
Conclusions: surgery is the most effective treatment of NSCLC. There is a great need for new targetted therapies in NSCLC harbouring KRAS-mutation.

IN VITRO VALIDATION ASSAYS FOR RECOMBINANT BACTERIAL PROTEIN BIOMARKERS

Sara Vago-Szincsak1, David Dora2, Zoltan Lohinai1,3 1Translational Medicine Institute, Semmelweis University; 2 Department of Anatomy, Histology and Embryology, Semmelweis University; 3 Pulmonary Hospital of Torokbalint

Keywords: lung cancer, biomarker, recombinant proteinAims: In the preliminary study, our research team identified microbiota-related proteins that potentially influence oncotherapy outcomes. We aim to use recombinant proteins to investigate the role of potential bacterial proteins in the anti-tumor immune response.
Methods: We searched appropriate Methods, such as in vitro translation and protein expression in E.coli, to produce recombinant proteins with bacterial protein expression units.
We screened n=17 colorectal cancer cell lines in the ATCC database for in vitro and in vivo experiments that are appropriate based on cell line adherency and 3D cell culturing.
Results: We identified and selected n=3 critical potentially relevant bacterial proteins in the clinics for further in vitro validation studies. Coupled transcription-translation with E. coli extract or expression in E. coli B21 strain with pET28a vector Methods are appropriate for producing recombinant proteins to study the effects in the anti-tumor immune response. Verification of protein expression will be performed with western blot and quantification with NanoOrange protein quantification kit.
Conclusions: These Methods can be used to precisely and efficiently investigate the role of biomarkers expected from clinical samples in predicting lung cancer treatment outcomes.

COVID19 INFECTION IN LUNG TRANSPLANTED PATIENTS

Peter Leo Jalsovszky (1), Viktoria Varga (2), Lorincz Polvika (2), Edit Hidvegi (2), Ildiko Madurka (3), Ferenc Renyi-Vamos (4), Veronika Muller (2), Aniko Bohacs (2) (1: Semmelweis University Faculty of medicine 2: Semmelweis University Department of Pulmonology 3: National Institute of oncology Department of Anesthesiology and Intensive care 4: National Institute of oncology Department of Thoracic surgery)

Keywords: Lung transplant, COVID19 infection, SARS-CoV2 virus, Hungary
Aims: To analyze the Hungarian lung transplanted and COVID19 infected population's data and draw Conclusion about the severity and the runoff of the illness, the therapy and the response to the therapy. In addition, the evaluation of lung function parameters after the infection in survived patients.
Methods: Retrospective review of the Hungarian lung transplanted, COVID19 infected patient's documentary between 2019 December and 2022 December (source: database of the Semmelweis University's Department of Pulmonology: emedsol and EESZT), and the statistical analysis of the received data (with exscel and GraphPad Prizm 8.01 program).
Results: In this interval there were 69 infections in 68 patients (Cause of the LuTx: COPD:21, CF:19, ILD:20, PAH:3, other reason:5). The average age±SE was: 48,61±1,6, the gender distribution was: male:37, female:31. Taken to hospital: 41 (59,4%), got to intensive unit: 12 (17,4%) patients. Of the infected group deceased: 13 (18,8%), suffered from severe residual symptoms: 3 (4,4%), cured: 56 (76,8%) patients. The deceased patient's age were higher: 57,2 then the cured: 46,6 (p=0,01). The patients got favipiravir: 4, remdesivir: 23, baricitinib: 3, and antybody therapy: 3. In survival group, the average of the respiratory function parameters did not change significantly: FVC before: 81,84, after: 80,57, FEV1 before: 79,2, after:78,27 (p=0,43).
Conclusions: The Hungarian lung transplanted COVID19 infected population got to the hospital and intensive care unit more often and the mortality was higher than the average population, especially among the elderly. With appropriate expertise and therapy, the biggest part of the patients will be cured without the loss of function.

ANALYSIS OF GUT MICROBIOTA COMMUNITY FUNCTIONAL PROFILES AND CARDIOPULMONARY EXERCISE TESTING (CPET) IN EARLY-STAGE LUNG CANCER

Zoltan Lohinai1,2 (1. Translational Medicine Institute, Semmelweis University; 2. Pulmonary Hospital of Torokbalint, Torokbalint

Keywords: Cardiopulmonary exercise testing (CPET), Gut microbiome, Lung cancer Cardiopulmonary exercise testing (CPET) can be used to assess the overall functional and metabolic capacity. Physical activity may affect the gut mucus layer integrity. It can alter the abundance of butyrate, a short-chain fatty acid (SCFA) that regulates the proliferation of epithelial cells in the Gut.
Aims: We analyze the associations between CPET parameters and gut microbiota functional profiles in early-stage lung cancer patients.
Methods: We used shotgun metagenomic sequencing to include Gut microbiota pre- and post-surgical samples of 15 early-stage lung cancer patients. We analyzed microbiome metabolic pathways using MetaCyc and their associations with post-surgery CPET parameters.
Results: Overall, n=337 bacterial species and n=498 MetaCyc pathways were identified.
We showed a significant difference in bacterial functional profiles before compared to after lung resection cases (P = 0.047, R2 = 6.4%, PERMANOVA). Differentially abundant MetaCyc (n=22) pathways were analyzed with CPET parameters.
Interestingly, an increase in VO2 max coincides with an increase in certain species and the "GABA shunt" pathway, suggesting that treatment outcomes might improve by enriching butyrate-producing species.
Conclusions: We showed a possible association of Gut microbiota community functional profiles that might be associated with cardiopulmonary exercise testing (CPET) parameters following lung resection surgery

THE CLINICAL PRESENTATION OF LYMPHANGIOLEIOMYOMATOSIS

Krisztina Guth, Anikó Bohács

Introduction: Lymphangioleiomyomatosis (LAM) is a rare cystic disease affecting mainly the interstitium of the lungs, and mostly occurs in women of reproductive age. The most common symptoms are shortness of breath that increases with exertion, coughing, and obstructive-restrictive ventilation disorder The most common symptoms are exertional dyspnea, cough, and obstructive-restrictive ventilatory impairment. Based on the non-specific symptoms and respiratory function data, LAM can be misdiagnosed as obstructive lung disease. Recurrent spontaneous pneumothorax and chylothorax are common pulmonary complications of LAM. For symptomatic treatment in LAM, bronchodilators can be used, and the progression of the disease can be slowed down by inhibiting LAM cell growth with mTOR inhibitors. In cases of lung involvement causing respiratory failure, lung transplantation can be the ultimate solution, however, the disease can return in the new organ too.
Aim and objective: Retrospective analysis of clinical, functional, and radiomorphological data, complications, and pharmacotherapy of LAM patients under care at Semmelweis University (SE) Department of Pulmonology. Analyzing the impact of modern pharmacotherapy on respiratory function parameters and investigating the relationship between HRCT score and respiratory function value.
Methods: Respiratory function tests were performed using whole-body plethysmography, and the Results of the forced expiratory volume in the first second (FEV1) are presented as a percentage of the reference value (%). Manual examination was conducted to determine the number and distribution of cysts on chest HRCT images.
Results: Results: Between 2013 and June 2023, a total of n=24 LAM patients with an average age of 41.25±6.8 years at the time of diagnosis were under care at the SE dept. of Pulmonology. At the time of diagnosis, their average FVC value was 75.14±17.94%, and FEV1 was 60.6±19.42%. The diagnosis was confirmed based on histological examination in n=17 (70.8%) cases and on clinical-radiological findings in n=7 (29.2%) cases.
Angiomyolipoma was confirmed in n=12 (50%) patients. A negative correlation between FEV1 and HRCT score was confirmed (R=0.81, R2=0.65). Symptomatic treatment with bronchodilators were administered to n=17 (70.8%) patients. The respiratory function of n=15 (62.5%) patients treated with mTOR inhibitors did not deteriorate, indicating that the therapy slows down the progression of LAM. Lung transplantation was performed in n=4 (23.53%)cases.
Conclusion: In cases of therapy-resistant obstructive disorders in young and middle-aged women, LAM should be considered in the differential diagnosis. The diagnosis can be confirmed by histological samples, typical radio-morphological abnormalities, and the presence of other organ manifestations, such as renal angiomyolipoma. Similar to international literature Results, clinical experiences also confirm the beneficial effects of mTOR inhibitor therapy.

SS10. CLINICAL SCIENCES

TISSUE TRANSGLUTAMINASE 2 REGULATES THE MITOCHONDRIAL FUNCTIONS IN SZ95 SEBOCYTES

Heba Yousef Hussein Mustafa1, Dóra Kovács1, Zouboulis Christos C.2, Andrea Szegedi1, Dániel Törőcsik1, Kinga Fedor-Lénárt1 (1 Department of Dermatology, University of Debrecen, Hungary, 2 Departments of Dermatology, Venereology, Allergology and Immunology, Dessau Medical Center, Dessau, Germany)

Keywords: mitochondria, sebocytes, tissue transglutaminase, lipid storage, SLC25A21
Aims: This study aims to investigate the role of tissue transglutaminase 2 (TG2) in regulating mitochondrial functions in SZ95 sebocytes. Specifically, we aimed to determine whether the absence of TG2 affects lipid storage and mitochondrial dysfunctions.
Methods: We used wild-type (WT) and permanent TG2 knockout (KO) SZ95 sebocyte cell lines generated through the CRISPR/Cas9 method. We conducted microarray measurements, protein studies, and reactive oxygen species (ROS) detection assays to investigate the effects of TG2 on mitochondrial gene expression, protein levels, and ROS production.
Results: Our microarray analysis revealed significant differential expression of mitochondria-associated genes in TG2 KO cells compared to WT cells. We confirmed that the solute carrier SLC25A21 was expressed significantly

lower at the protein level in TG2 KO sebocytes. Additionally, we observed a significant decrease in the protein expressions of mitochondrial oxidative phosphorylation complexes, including complex I-NDUFB8, III-UQCRC2, and V-ATPSA, in TG2 KO sebocytes. Our ROS measurements indicated elevated levels of ROS in TG2 KO sebocytes, further supporting mitochondrial dysfunctions.
Conclusion: Our findings suggest that the absence of TG2 leads to defective functions of the mitochondrial electron transport chain and ATP synthesis at multiple points. These Results warrant further investigation to determine the implications of TG2 in disease pathogenesis and the development of therapeutic strategies.

UTILIZING TRANSCRIPTOMIC ANALYSIS TO VALIDATE PROTEOMIC SIGNATURES ASSOCIATED WITH PROGRESSION IN MELANOMA

Elmar Gregor Lutz (Department of Dermatology, Venereology, and Dermatooncology, Semmelweis University)

Aim: To validate initial findings using a larger transcriptomic dataset with clinical data to identify patterns of gene up-regulation, down-regulation, and dysregulation in melanoma.
Methods: Two Methods were utilized using larger gene sets identified from the preliminary study and TCGA transcriptome data. The first approach created a gene set signature, and individual melanoma samples of TCGA were scored by ssGSEA analysis. Focusing on the primary tumors, gene expression scores were created for progression, and overall survival time was compared for differences. The second approach investigated pathways associated with progression in primary tumors and metastasis formation in melanoma using GSEA analysis.
Results: Similarities between the utilized approaches, suggesting that proteomic data derived from even a small number of patients was robust enough to identify differentially regulated pathways, similar to large transcriptomic analyses.
Conclusion: Single protein level data obtained from observational cohorts is difficult to validate on the transcriptomic level in a larger cohort, but pathway-level analysis of transcriptomic data is a potentially beneficial approach.

CARDIOVASCULAR SCREENING OF MODERATE TO SEVERE PSORIATIC PATIENTS: THE DERMATOLOGISTS' POINT OF VIEW

Mária Veronika Kolonics(1), Éva Anna Piros MD, PhD(1), Noémi Ágnes Galajda MD(1), Andrea Lukács MD(1), Bernadett Hon-Balla MD(1), Borbála Vattay MD(2), Bálint Szilveszter MD, PhD(2), Fanni Rencz MD, PhD(3), Ákos Szabó(3), Péter Holló MD, PhD(1)((1) Department of Dermatology, Venereology and Dermatooncology, Semmelweis University, 1085 Budapest, Hungary(2) Heart and Vascular Center, MTA-SU Cardiovascular Imaging Research Group, Semmelweis University, 1122 Budapest, Hungary (3) Department of Health Economics, Corvinus University, 1093 Budapest, Hungary)

Keywords: psoriasis, cardiac CT, dermatology, cardiovascular risk, guidelines
Aims: To assess the cardiovascular risk of moderate to severe psoriatic patients by using laboratory tests, cardiovascular risk estimating calculators and medical imaging tools (peripheral arterial ultrasound and native cardiac CT), while monitoring dermatological status (PASI, DLQI) of the patients.
Methods: 44 patients with moderate to severe psoriasis treated with biologics (PASI≥10, DLQI≥10) without any cardiac complaint, with prior negative ECG and echocardiography were enrolled from the Department of Dermatology, Venerology and Dermatooncology, Semmelweis University. Native cardiac CT, peripheral arterial ultrasound and laboratory tests for atherogenic lipids were conducted. According to the CT scan results, high (CACS>0) and low (CACS=0) cardiovascular risk cohorts were created for the data analysis. CT scan results were compared to non-psoriatic age, sex and comorbidity matched controls. ASCVD, HeartScore and Framingham risk calculators were used.
Results: The native cardiac CT scans showed a significantly higher calcified plaque burden in the psoriatic cohort compared to non-psoriatic controls. In the high-risk psoriatic group higher disease activity, elevated levels of CRP,

atherogenic lipids and glucose, greater cardiovascular risk scores, and slightly more biological therapy switches were observed.

Conclusions: According to our results, moderate to severe psoriatic patients need further examinations than recommended by the latest guidelines to screen asymptomatic but cardiologically affected patients. support: ÚNKP-20-3-I., Semmelweis University 250+ Excellence PhD grant EFOP-3.6.3.-VEKOP-16-2017-00009.

DELAYED INTRALESIONAL DELIVERY OF NUCLEOSIDE-MODIFIED M-RNA ENCODING A COMBINATION OF CYTOKINES AND GDNF PROMOTES FUNCTIONAL RECOVERY FOLLOWING SPINAL CORD INJURY

Levente Lászlófy, László Gál, Krisztián Pajer, Tamás Bellák, Annamária Marton, Rebeka Kristóf, Zoltán Fekécs, Drew Weissman, Dénes Török, Csaba Vizler, Paulo J.C. Lin, YingK. Tam, Norbert Pardi, Antal Nógrádi (Department of Anatomy, Histology and Embryology, Albert Szent-Györgyi Medical School, University of Szeged Szeged Hungary, Department of Biochemistry, Biological Research Center, Hungarian Academy of Sciences, Szeged, Hungary, Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania USA, Acuitas Therapeutics, Vancouver, Canada)

Abstract: Spinal cord injury Results in irreversible tissue damage followed by limited recovery of function. Our earlier study has shown that a cocktail with recombinant human (h) interleukin-10 (hIL-10), interleukin-6 (hIL-6), macrophage inflammatory protein 1-alpha (hMIP-1-alpha) and glial cell line-derived neurotrophic factor (hGDNF) loaded via osmotic pump is able to induce neuroprotection and functional recovery following spinal cord contusion injury (at the level of thoracic 10 vertebra) in a rat model. Based on these Results intraspinal delivery of mRNA-LNPs encoding a combination of cytokines (hIL-6, hIL-10, hMIP-1-alpha) and hGDNF was applied at the level of thoracic 10 vertebra 7 days after contusion injury.

The mRNA-LNPs were administrated 7 days after contusion injury directly into the lesion cavity. The functional analysis showed that the therapeutic proteins encoded by mRNAs enhanced the coordinated movement in the treated group relative to controls. Similarly, administration of mRNA-LNPs resulted in significantly smaller lesion area at the epicentre of the injury and significantly greater amount of spared tissue. Analysis of supra- and propriospinal connections with the retrograde tracer Fast Blue indicated that the treatment led to higher the number of connections between the segments caudal to the lesion and various cranial parts of the CNS. Astrocytes, microglial cells and neurons also expressed each therapeutic protein after mRNA-LNP injection up to 5 days in the injured spinal cord.

These Results demonstrate that the delayed treatment with mRNA-LNPs which encode a combination of therapeutic proteins is able to induce morphological and functional improvement after spinal cord contusion.

ANALYSIS OF PACAP AND OTHER BIOACTIVE FACTORS IN PLASMA SAMPLES FROM WOMEN WHO HAD ABORTIONS

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Keywords: miscarriage, pregnancy, PACAP, cytokines

Pituitary adenylate cyclase activating polypeptide (PACAP) is an anti-inflammatory and anti-apoptotic protein. Its neuroprotective and general cytoprotective effects have been demonstrated in numerous in vivo and in vitro studies. The neuropeptide is known to play an important role in the regulation of female reproductive system.

Previously, PACAP has been detected in the placenta, umbilical blood samples, amniotic and follicular fluid, and its levels have been observed to increase during pregnancy and lactation in plasma and human milk samples.
Our aim was to compare the plasma PACAP levels of women who underwent induced abortion (healthy pregnant group; n=44) and spontaneous abortion (n=28) with ELISA and analyse the changes of different bioactive factors (IL-1α,IL-1β,IL-1RA,IL-2,IL-6,IL-8,IL-10,IL-17α,MCP-1,FGF2,GCSF,IP-10,PDGF,VEGF) using Luminex method.
Significantly lower PACAP levels were detected in the plasma of spontaneously aborting women at 9-13 weeks of gestation, and significantly lower IL-8, FGF-2 and higher MCP-1 levers were measured in these women compared to the healthy pregnant group. In case of spontaneous abortion, we found a significant negative correlation between PACAP and gestational age, and plasma PACAP levels showed a positive correlation with VEGF and a negative correlation with IL-1β levels. In healthy pregnant group, who underwent induced abortion, PACAP also showed a moderate significant positive correlation with plasma IL-8 and IL-10 concentrations.
Our findings suggest that PACAP associated with different cytokines, chemokines and growth factors may play an important role in the regulation of implantation, placentation, and trophoblast migration. Our future goal is to further elucidate the role of PACAP in various reproductive disorders and prenatal pathological conditions.

EVALUATION OF MORCELLATOR EFFICIENCY DURING TRANSURETHRAL BIPOLAR PROSTATE ENUCLEATION

Daniel Kovacs, Zoltan Kiss (Department of Urology, University of Debrecen)

Keywords: BPH, morcellation, minimal invasiveness, uroflowmetry, IPSSIntroduction: A number of minimally invasive techniques have been developed for the surgical treatment of BPH, among which transurethral bipolar prostate enucleation with physiological saline is considered a low morbidity, safe and effective surgical procedure. During surgery, the prostate lobules are enucleated then lobules are resected or morcellated. In our study, we investigated the effectiveness of morcellation versus the resection.
Method: In our study 350 cases of transurethral bipolar prostate enucleation were performed, of which 93 cases were treated with morcellator. During the retrospective study, data were collected on patients' age, BMI, preoperative PSA, uroflowmetry values, prostate size, residual urine volume and IPSS. We examined resectated volume of the prostate, velocity of resection and operative time. At 1, 3, 6 and 12 months follow-ups, we examined the rate of PSA reduction, uroflowmetry values and IPSS questionnaire Results.
Results: A significant reduction in operative time was observed with the use of the morcellator compared to resection: 45 min (IQR: 30-70) and median resectate volume was 58 g (IQR: 22-69). A significant increase in Qmax was observed during control uroflowmetry: preoperative median Qmax: 8 ml/s (IQR: 5.9-11.45), 1st postoperative median Qmax: 18.7 ml/s (IQR: 13.8-26.5), $p<0.001$. IPSS questionnaire Results showed significant improvement: preoperative median IPSS: 22 (IQR: 15-25), 1st month control median IPSS: 9 (IQR: 6-14), $p<0.001$.
Conclusion: Based on our Results, we conclude that the TUEB with morcellation reduces the opreative time, is a safe and effective method that combines the advantages of anatomical enucleation during open prostatectomy with minimal invasiveness.

EVALUATING THE ROLE OF FOLLICULAR T-HELPER SUBSETS AND FOLLICULAR T-REGULATORY CELLS IN THE PATHOMECHANISM OF ENDOMETRIOSIS

Marija Andreeska (University of Debrecen, Department of Obstetrics and Gynaecology, Debrecen, Hungary)

Problem statement: Endometriosis is an oestrogen-dependent, benign gynaecological disease, largely defined by the presence of endometrial- like tissue in an ectopic location (outside of the uterus). Previous studies have demonstrated increased number and activation of B-lymphocytes and excessive production of autoantibodies in endometriosis, which may suggest the importance of follicular T-helper (TFH) subsets and follicular T-regulatory (TFR) cells in the pathomechanism of the disease. In the present study, we analyzed the distribution of the circulating TFH subsets and TFR cells in endometriosis, and their role in its development.
Patients and Methods: Eleven patients with endometriosis and 9 healthy controls were enrolled in our study. Peripheral blood lymphocyte subgroups were quantified by flow cytometry. Beside ICOS+ PD-1+ CD4+CXCR5+ activated TFH cells, the following TFH subsets were determined within CD4+CXCR5+ TFH cell population: Th1-like

TFH1 (CXCR3+CCR6−), TFH1/17 (CXCR3+CCR6+), Th2-like TFH2 (CXCR3−CCR6−) and Th17-like TFH17 (CXCR3−CCR6+) cells. Moreover, we assessed the ratio of circulating CD127−CD25+ CD4+CXCR5+ TFR cells, as well.
Results: We found no difference in the percentages of activated circulating TFH cells and TFR cells in endometriosis patients compared to controls. Among the circulating TFH subsets, we observed the same cellular distribution in endometriosis as in healthy individuals.
Discussion and Conclusion: Although over-activation of B-cells as well as autoantibody production could be potentially linked to an altered TFH cell activation and function; our Results suggest that in the pathogenesis of endometriosis, an enhanced cTFH-B cell interaction may not play an important role.

SS11. PHYSIOLOGY

SELECTIVE NA+/CA2+ EXCHANGER INHIBITION DECREASES VENTRICULAR ALTERNANS IN CANINE AND RABBIT CARDIAC MUSCLE

Gergő Bitay (Department of Pharmacology and Pharmacotherapy, University of Szeged)

Keywords: heart, electrophysiology, alternans, arrhythmia, sudden cardiac death
Aims: The action potential (AP) and intracellular Ca2+ homeostasis of the heart are simultaneous phenomena that interact with each other on multiple levels. Due to this, the electrical integrity and the contractile function of the heart is secured. During everyday life the heart rate varies between a large interval, which the heart can accommodate. Nevertheless, during tachycardia, after reaching a certain threshold the electrical and intracellular Ca2+ stability gets compromised and so called alternans occur. During alternans, the AP duration oscillates in a 'long-short-long' fashion, whereas the intracellular Ca2+ release level oscillates in a 'large-small-large' way, beat-to-beat. The occurrence of alternans is considered to be a reliable predictor of sudden cardiac death. Despite this, no specific pharmacological intervention is available to combat alternans. According to previous studies, the Na+/Ca2+ exchanger may play an important role in the formation of alternans. Our goal was to examine the role of the selective Na+/Ca2+ exchanger inhibitor ORM-10962 on the formation of alternans.
Methods: For our experiments we used canine papillary muscle tissue, isolated left ventricular cardiomyocytes as well as rabbit hearts. The action potentials were measured with standard microelectrode technique, the Ca2+ releases from the sarcoplasmic reticulum transients were recorded using fluorescent optical Methods. Voltage mapping was performed using optical mapping method.
Results: The AP and Ca2+ transient were created using high frequency outer electrical stimuli. 1 µM ORM-10962 significantly decreased the AP and Ca2+ transient alternans in canine cardiac muscle. The effect was predominant at 25% of the repolisation phase. The selective Na+/Ca2+ inhibition also increased the postrepolarisation refracterity. Arrhythmia mapping performed on rabbit heart showed synchronised (concordant) alternans, which also reduced due to selective Na+/Ca2+ inhibition.
Conclusions: The inhibition of the Na+/Ca2+ decreases the amplitude of the ventricular alternans. Because of this, it could be a promising antiarrhythmic method to prevent arrhythmias due to alternans.

THE ROLE OF INTRAAMYGDALOID OXYTOCIN ON REINFORCEMENT IN VALPROATE-INDUCED AUTISM RAT MODEL

Bálint Turcsán, Kristóf László (University of Pécs Medical School, Pécs, Hungary)

Autism spectrum disorder is a neurodevelopmental disorder affecting around 1.5-2% of children, and its incidence shows an increasing tendency. Its treatment is currently not resolved. In autism research, we used the widely accepted valproate-induced rodent model. Our previous Results showed that intraamygdaloid oxytocin has anxiolytic effect and increases the number and length of social interactions in rats showing autistic signs. In the present study, we sought an answer to whether intraamydaloid oxytocin has any effect on reinforcement in valproate-induced autism rat model.

Methods: bilateral guide cannulae were implanted above the central nucleus of the amygdala using the stereotaxic technique in male autistic and neurotypical Wistar rats. We investigated the effect of intraamygdaloid oxytocin and oxytocin receptor antagonists in conditioned place preference test.
Results: valproate-treated rats that received 10 ng of oxytocin spent significantly more time in the treatment quadrant in the test phase of the conditioned place preference paradigm. A pre-administered 20 ng oxytocin receptor antagonist blocked the positive reinforcing effect of 10 ng oxytocin. The 20 ng oxytocin receptor antagonist alone did not affect the time spent in the treatment quadrant.
Conclusions: our Results show that oxytocin has a positive reinforcing, rewarding effect on rats showing autistic signs and that this effect is oxytocin receptor specific.

HEMOKININ-1 IS INVOLVED IN AGING-RELATED MOTOR COORDINATION AND MUSCLE STRENGTHS CHANGES IN MICE

Simon Dávid Vince (Department of Pharmacology and Pharmacotherapy, University of Pécs, Pécs, Hungary)

Key words: tachykinin, hemokinin-1, ageing, motor coordination, muscle strengths
Aims: Motor coordination problems and consequent bone fractures in older age significantly reduce quality of life. Hemokinin-1 (HK-1), member of the tachykinin family, plays important regulatory role in the central nervous system and the periphery. It is present in high concentrations in the cerebellum as well as in bone- and muscle tissues. We investigated its involvement in motor coordination and muscle strengths in young (3-4-month-old) and old (12-month-old) C57BL/6 wild-type and HK-1-deficient (Tac4 gene-deficient) male mice.
Methods: Motor coordination was assessed in the rotarod test, where mice have to walk on an accelerating drum, while in the static rod test, they are placed on ends of rods of different thicknesses and time spent to turn and reach the end of the rod is measured. Muscle strenghts was assessed in the horizontal bar test, where the animals have to grip the bars with their forelegs and climb out to the edge of the stand, and in the grid test, in which the time spent upside down on a metal grid was measured.
Results: We did not find significant differences between wild-type and gene-deficient young animals in any of the tests. We found remarkable deterioration of motor coordination in the static bar and rotarod tests in the 12-month-old groups, which was more severe in the Tac4 gene-deficient animals compared to the wild-types. Muscle strengths was also significantly reduced in old animals. There was no difference between old wild-type and gene-deleted animals in the grid test, but aged Tac4 gene-deficient animals showed significantly improved performance in the horizontal bar test compared to their wild-type counterparts.
Conclusion: Our Results show that HK-1 is involved in aging-related motor coordination and muscle strengths changes, but the effects are likely due to different mechanisms. Identification of its targets and signalling pathways may open new drug developmental perspectives. Support: Eötvös Loránd Research Network (Chronic Pain Research Group), Pécs, National Brain Research Program 3.0, National Research, Development and Innovation Office - OTKA K138046 and OTKA FK137951, TKP2021-EGA-16, János Bolyai Research Scholarship of the Hungarian Academy of Sciences (BO/00592/19/5), and ÚNKP-21-5 new National Excellence Program of the Ministry for Innovation and Technology (ÚNKP-22-5-PTE-1447), Project no. RRF-2.3.1-21-2022-00015 has been implemented with the support provided by the European Union.

INVESTIGATING THE ROLE OF PLASMA MEMBRANE CALCIUM ATPASE PROTEINS DURING TISSUE INJURY

Nada Mohamed Al-Sheraj (Department of Physiology, Semmelweis University)

Keywords: plasma membrane calcium ATPase; tissue damage; zebrafish; calcium signal; CRISPR
Aims: Calcium signals are among the earliest signaling events triggered by epithelial wounding. They are essential in mediating the very first tissue-protective responses including leukocyte recruitment and wound closure. Despite the importance of these signaling events, little is known about their molecular regulation. In seeking regulators of these Ca2+ signaling patterns, we turned our attention to plasma membrane Ca2+-ATPases (PMCA).
Methods: Using Western blot we first identified zebrafish PMCA4 as the major PMCA isoform in the tail fin of the larvae. Zebrafish PMCA4 is orthologous to human PMCA4, but its function has not yet been described in detail. To investigate the role of this ATPase, we expressed the zebrafish PMCA4 in HEK293A cells. Our measurements

showed that fish PMCA4 is capable of similar cellular Ca2+ export as its human counterpart. We then moved to in vivo experiments in zebrafish larvae. In order to measure Ca2+ level changes, we created transgenic fish lines expressing GCaMP7s. Using spinning disk confocal microscopy, we could then follow in real-time the Ca2+ level changes after wounding.
Results: To delineate the role of PMCA4 in wound-induced Ca2+ signaling, we used morpholino oligonucleotides to transiently knock it down. We observed that this resulted in diminished wound-induced oscillatory Ca2+-signaling and an increase in the Ca2+ levels measured at the wound margin. Furthermore, we also confirmed our Results using CRISPR/Cas9-mediated full PMCA4 knockout animals.
Conclusions: Our Results so far provide opportunities for a more detailed understanding of tissue-injury induced Ca2+ signaling, and for mapping the role of the PMCA4 protein in the process.

NIMODIPINE EXERTS A NEUROPROTECTIVE EFFECT AGAINST SPREADING DEPOLARIZATION INDEPENDENT OF CEREBRAL CIRCULATION

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Keywords: neuroprotection, nimodipine, spreading depolarization
Aims: Nimodipine is an L-type voltage gated Ca2+ channel (VGCC) antagonist and a potent cerebral vasodilator. In preclinical models of cerebral ischemia, nimodipine mitigates the deleterious impact of spreading depolarizations (SDs). It remains to be explored whether the beneficial effect of nimodipine is achieved by the improvement of perfusion, or a potential direct action on the nervous tissue. Here we evaluate direct nimodipine action on SD in live brain slice preparations.
Materials: Coronal brain slices prepared from C56BL/6 mice (n=16) were perfused with artificial cerebrospinal fluid (aCSF). First, we determined the kinetics of nimodipine (10 µM) saturation with liquid chromatography-tandem mass spectrometry and found that 30 min incubation leads to full saturation of brain slices. Accordingly, 30 min nimodipine incubation, low glucose aCSF (5 mM) and transient anoxia (1 min) were applied to elicit SD. Intrinsic optical signal imaging was used to analyse SD features, TTC staining was carried out to assess tissue injury.
Results: Nimodipine reduced the focal area of SD (3.38±0.88 vs. 2.37±0.94 %, control vs. nimodipine), decreased the total cortical area affected by SD (39.88±22.42 vs. 17.12±8.63 %, control vs. nimodipine) and curtailed the propagation velocity of SD (1.59±2.29 vs. 0.19±0.79 mm/min, control vs. nimodipine). Furthermore, nimodipine reduced the tissue injury by elevating the number of TTC stained particles (3.52±1.52 vs. 4.48±1.45 particle/1000 µm2, control vs. nimodipine).
Conclusion: Taken together, nimodipine exerted direct neuroprotection against the detrimental effect of SD, irrespective of its vascular action.
Support: OTKA K134377 and K134334, HCEMM, NAP3.0

IMPACT OF TREADMILL TRAINING AND CALORIC RESTRICTION ON THE ROLE OF ALPHA-MELANOCYTE STIMULATING HORMONE (ALPHA-MSH) IN ENERGY BALANCE IN MIDDLE-AGED MALE WISTAR RATS

Eszter Kőrösi (Institute for Translational Medicine, University of Pécs, Pécs, Hungary)

Key words: caloric restriction, treadmill training, obesity, alpha-melanocyte-stimulating hormone, hypermetabolism
Aims: Middle-aged obesity is a world-wide problem, which can be observed also in rodents. Therefore, age-related regulatory changes may contribute to its development. Hypermetabolic mediators e.g. cholecystokinin or alpha-melanocyte stimulating hormone (alpha-MSH) show weak responsiveness in middle-aged animals. Previous studies demonstrated that life-long caloric restriction (CR) restored the efficacy of CCK in middle-aged rats. We aimed to test the hypothesis that a 12-week CR or training intervention would improve the efficacy of alpha-MSH in middle-aged male Wistar rats.

Methods: The 12-week treadmill training or 30% CR started at 9 months. We determined the density of alpha-MSH in the arcuate nucleus (ARC) with immunohistochemistry. Other rats were implanted with a guide cannula for intracerebroventricular (ICV) injections under ketamine+xylazine anesthesia. We tested the hypermetabolic/hyperthermic responses to an ICV injection of 5 µg alpha-MSH. Oxygen consumption, core- and tail skin temperatures were recorded in an OxyletPro indirect calorimeter also using thermocouples linked to a Digi-Sense Benchtop Thermometer (Cole-Parmer). Ethical considerations were fully observed (BA 35/66-6/2020). Data are presented as mean±SEM. SPSS was used for statistical analysis.
Results: Neither the training nor the CR affected the density of alpha-MSH in the ARC. However, the CR increased the hypermetabolic/hyperthermic responses to alpha-MSH.
Conclusions: The effects of aging proved to be stronger than those of our 12-week interventions on the expression of alpha-MSH in the ARC. However, CR increased the hypermetabolic/hyperthermic responsiveness to alpha-MSH. We plan to investigate the effects of the treadmill training on the central hypermetabolic/hyperthermic efficacy of alpha-MSH, as well.

VEKLURY® (REMDESIVIR) FORMULATIONS INHIBIT INITIAL MEMBRANE-COUPLED EVENTS OF SARS-COV-2 INFECTION DUE TO THEIR CYCLODEXTRIN CONTENT

Kitti Kurtan, Tamas Kovacs, Florina Zakany (Department of Biophysics and Cell Biology, University of Debrecen

Keywords: SARS-CoV-2, remdesivir, cyclodextrin, cholesterolAims: Veklury® (remdesivir), formulated as powder or solution, is well-established in COVID-19 therapy. Besides the same amount of poorly soluble remdesivir, both formulations contain high, but different amounts (3 vs. 6 g) of the solubilizing agent, sulfobutylether-beta-cyclodextrin (SBECD). CDs, through their cholesterol-depleting ability, can disrupt lipids rafts and thus alter the membrane localization of various proteins such as raft-resident ACE2 and TMPRSS2 that mediate viral uptakes. We examined how different CDs and Veklury® formulations affect the association of ACE2 and TMPRSS2 with lipid rafts, as well as the ACE2 binding and cellular uptake of SARS-CoV-2 spike proteins.
Methods: To evaluate colocalizations we determined Pearson correlation coefficients using confocal microscopy images of HEK cells stably expressing ACE2 and TMPRSS2 (HEK/ACE2+TMPRSS2). For the examination of ACE2 binding we used time-correlated flow cytometry, while trimer internalizations were quantified using confocal microscopy and quantitative 3D image analysis on HEK/ACE2+TMPRSS2 and Calu-3 lung adenocarcinoma cells.
Results: Different CDs and Veklury® formulations significantly reduced the association of ACE2, TMPRSS2 and lipid rafts. In both HEK/ACE2+TMPRSS2 and Calu-3 cells, CDs and Veklury® formulations dose-dependently reduced ACE2 binding of wild-type, delta and omicron spike proteins, and similarly inhibited the uptake of these spike trimers. Remdesivir alone had no effects on these parameters.
Conclusions: According to its twice higher CD content, Veklury® solution is more effective in inhibiting the initial cellular steps of SARS-CoV-2 infection highlighting not only the therapeutic potential of CDs but potential invivo differences in the efficacy of the two Veklury® formulations.
Support: OTKA FK143400, ÚNKP-22-4-II-DE-69

WS7.

LIABILITY OF DOCTORS, IN THE LIGHT OF RECENT JUDICIAL DECISIONS

Dr. György Kovács LL.M; Ph.D.

No abstract available.

Notes

EDITOR'S NOTE:

All abstracts available to the Editorial Office as of August 25, 2023 are included in this edition of the Archives of the Hungarian Medical Association of America.

The help of the Program Dr Beáta Kőrösi and Lili Schwieters is appreciated in forwarding and editing the abstracts they received. No alterations in content were carried out.

With questions or suggestions, please contact the Editor at ssomkuti@abington-repromed.com.

Thank you,
István Somkúti MD PhD

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