The Association of Hungarian PhD and DLA Candidates

Science and Innovation Conference

Programme and abstracts book

29-30 of January

Agenda

29th of January

9:00-9:30

Opening ceremony:

Prof. Dr. Péter Ferdinandy – Vice-rector of Semmelweis University and dr. *Szabolcs Bozsányi* short presentation about the Medical and Health Sciences Section of The Association of Hungarian PhD and DLA Candidates (DOSZ)

9:30-10:30

First plenary lecture:

INNOVATIVE R&D PRACTICE – SCIENTIFIC AND BUSINESS CAREER AT Semmelweis University - *Prof. Dr. Ferdinandy Péter*

10:30-12:00

Clinical sciences I.

Clinical sciences II.

12:00-13:00

Second plenary lecture:

Aktuális kérdések a koronavírussal kapcsolatban - Dr. János Szlávik

13:00-14:30

Theoretical medical sciences I.

Theoretical medical sciences II.

14:30-16:00

Surgical sciences

16:00-17:00

Third plenary lecture:

The Cancer Moonshot Actions at the European Center in Lund, Sweden *Johan Malm and György Marko-Varga*

Agenda

30th of January

9:30-10:30

Fourth pleanry lecture:

3D printing in medicine - *Dr. Dániel Végh, Dr Imre J. Barabás és Dr. Palkovics Dániel*

10:30-12:00

Neurological sciences

12:00-13:00

Fifth plenary lecture:

Diagnosis and treatment of facial pain and involuntary movements - Neurosurgical treatment for trigeminal neuralgia and hemifacial spasm - *Prof. Dr. Takamitsu Fujimaki*

13:00-14:30

Translational and interdisciplinal sciences

14:30-16:00

Psychological sciences

16:00-17:00

Round table discussion:

A közösségi média szerepe és jövője az orvoslásban és kutatásban - *Mariann Forgács (CEO- Be Social) és dr. András Kulja (videoblogger and surgeon - Fonendoszkóp)*

17:00-18:00

Sixth plenary lecture:

The Terminator- Robot invasion in the operating room - *Dr. Zsolt Garami*

18:00-18:30

Closing ceremony and announcement of the results:

Prof. Dr. Péter Ferdinándy and *Prof. Dr. Zoltán Benyó* and the *dr. Sándor Erdős*

29 of January (Friday) - Schedule

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10:30-10:45 Balázs Koncz
10:45-11:00 Bozsányi Szabolcs
11:00-11:15 dr Piros Éva Anna
11:15-11:30 Flink Lili Borbála
11:30-11:45 Márk Félix Juhász
11:45-12:00 Szentpéteri Szófia
12:00-12:15 Tamás Linkner

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10:30-10:45 Benjamin Tamás Papp
10:45-11:00 Dr Markóth Csilla
11:00-11:15 Dr. Kulin Dániel
11:15-11:30 dr. Ocskay Klementina
11:30-11:45 Dr. Szadai Leticia
11:45-12:00 Vivien Telek

13:00-14:30 Theoretical sciences I.

13:00-13:15 Ádám Diós
13:15-14:30 Balogh Gergő Mihály
13:30-13:45 Combi Zsolt
13:45-14:00 Domonkos Czárán
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14:15-14:30 Halász Hajnalka Emese
14:30-14:45 Mark Kantor

13:00-14:30 Theoretical sciences II.

13:00-13:15 Baráth Barbara
13:15-14:30 Dr. Antali Flóra
13:30-13:45 Dr. Tóth Noémi
13:45-14:00 Orsolya Mózner
14:00-14:15 Péter Sasvári
14:15-14:30 Varga Rita
14:30-14:45 Dr. Schranc Álmos István

29 of January (Friday)

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14:30-14:45 Ali Alkhayer
14:45-15:00 Barth Anita
15:00-15:15 Constantinos Voniats
15:15-15:30 Dr. Szécsényi-Nagy Balázs
15:30-15:45 Dr. Szécsi Balázs
15:45-16:00 Ganna Stepanova
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30 of January (Saturday) - Schedule

10:30-12:00 Neurological sciences

10:30-10:45 Dr. Jason Sparks
10:45-11:00 dr. Nádró Bíborka
11:00-11:15 Horváth Dorottya
11:15-11:30 Keller Dávid
11:30-11:45 Patkó Evelin
11:45-12:00 Szenasi Annamaria

13:00-14:30 Translational and interdisciplinal sciences

13:00-13:15 Beáta Szeitz
13:15-13:30 dr. Bartha Áron
13:30-13:45 Longauer Beáta
13:45-14:00 Nardos Abebe Werissa
14:00-14:15 Stier Ágnes
14:15-14:30 Uhljar Luca Éva

14:30-16:00 Psychology sciences

14:30-14:45 Mittly Veronika
14:45-15:00 Dr. Módis László
15:00-15:15 Dr. Erdős Sándor
15:15-15:30 Matuz András
15:30-15:45 Oláh Barnabás
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Scientific committees

Chief patron: Prof. Dr. Péter Ferdinandy

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Prof. Dr. Zoltán Rakonczay - *President*
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Dr. Domonkos Ádám Tárnoki

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29 of January (Friday)

Clinical sciences I. 10:30-12:00

Balázs Koncz, SZTE, Klinikai Orvostudományok Doktori Iskola; Balogh Gergő Mihály, SZTE

Blindspot in immune recognition - a consequence of T cell positive selection?

One of the most important functions of the human immune system is to differentiate between self and nonself peptides. It is widely accepted that nonself peptides highly dissimilar to human proteins are more immunogenic. But does high dissimilarity go hand in hand with immunogenicity? The adaptive immune recognition is mediated by the binding of peptide-HLA complexes by T cells. Positive selection of T cells in the thymus is a fundamental step in the generation of a responding T cell repertoire: only those T cells survive, which recognize human peptides presented on the surface of cortical thymic epithelial cells. We propose that while the positive selection of T cells is essential for optimal immune function, the process results in a lack of immune response to a large fraction of nonself peptides because it is mediated by self ones. To test our hypothesis, we focused on amino acid motifs of peptides in contact with T cell receptors. We found that motifs rarely or not found in the human proteome are unlikely to be recognized by the immune system. Peptides carrying these motifs were especially dissimilar to human proteins, even more than most immunogenic ones. Importantly, we present this result on two independent T cell activation datasets and provide direct evidence by analyzing SARS-CoV-2-specific TCR-sequencing data.

Supervisor: Dr. Manczinger Máté, SZTE-ÁOK

Dr. Bozsányi Szabolcs, SE, Klinikai Orvostudományok Doktori Iskola

Multispektrális LED-alapú eszköz használata melanoma malignum és seborrhoeás keratosis kvantitatív elkülönítésére

This abstract is encrypted.

Supervisor: Prof. Dr. Wikonkál Norbert, Semmelweis Egyetem, Bőr-, Nemikórtani és Bőronkológiai Klinika

dr Piros Éva Anna, SE, Rácz Károly Doktori Iskola; dr Szalai Klára, SE

IL-17 gátlóval kezelt pikkelysömörös páciensek kardiovaszkuláris státuszának felmérése, a kezelés hatékonyságának vizsgálata

Title of the presentation: Assessment of the cardiovascular state of moderate-to-severe psoriatic patients treated with IL-17 inhibitors and the effectiveness of treatment Éva Anna Piros MD1, Klára Szalai MD1, Péter Holló MD, DSc1 1:Department of Dermatology, Venereology and Dermatooncology, Semmelweis University, Budapest, Hungary

Introduction: Psoriasis is a chronic, immune-mediated autoinflammatory disorder. It mainly affects the skin and joints (arthritis psoriatica), but the systemic inflammation has a great impact on the cardiovascular system. Based on the scientific literature among moderate-to-severe psoriatic patients increased arterial intima media thickness was observed compared to non-psoriatic healthy controls. Vascular ultrasound examinations are reproducible, inexpensive, non-invasive, and based on nonionizing radiation. Therefore, these examinations are perfectly suitable for cardiovascular screening to evaluate the state of the vasculature and monitor changes induced by the applied therapy. Aim: Assessment of the effect of IL-17 inhibitor (secukinumab, ixekizumab) therapies among moderate-to-severe psoriatic patients on vascular wall thickness by high-resolution mode B ultrasound examinations and on cardiovascular risk assessement scales (ASCVD and Framingham). Materials and Methods: Adult (≥18 years) patients with moderate-to-severe psoriasis are enrolled in this study, receiving IL-17 inhibitors (secukinumab or ixekizumab). The study is conducted in the Department of Dermatology, Venereology and Dermatooncology of the Semmelweis University, Budapest, Hungary. Before the initiation of the therapy and after 6 months we measured the intima media thickness of the carotid and brachial arteries on both sides and also determined the cardiovascular risk with the usage of Framingham and ASCVD scales.

Results: Up to now 15 patients completed the study. All in the observed parameters we found significant improvements. The cumulate amelioration of the intima media thicknesses in the carotid and brachial arteries (both sides) is 22.73% ($p=0.0001$). Improvement in the cardiovascular risk assessment scales was 6.5% in the case of Framingham, and 23.57% in the case of ASCVD scales ($p<0.05$). Discussion: Based on the available literature and our study so far, biologic therapies, in this case IL-17 inhibitors, not only lead to remarkable improvement in skin symptoms, but they can also slow down the progression of atherosclerosis by improving endothelial function, reducing the increased cardiovascular morbidity-mortality rate associated with the disease.

Supervisor: Prof. Dr. Holló Péter, Semmelweis Egyetem

Flink Lili Borbála, SZTE, Klinikai Orvostudományi Doktori Iskola; Dr. Bozó Renáta, SZTE

Determination of serum periostin in psoriasis

Psoriasis is a multifactorial, chronic, inflammatory skin disease characterized by keratinocyte hyperproliferation, altered basement membrane composition and massive infiltration of immune-cells. Examination of the lesional skin has revealed important mechanisms in the pathology, and this knowledge has led to successful targeted therapies, that are symptomatic, but not curative. Periostin is an extracellular matrix protein and is expressed by both epidermal keratinocytes and dermal fibroblasts. It interacts with several integrin molecules and also plays role in fibrosis and wound repair. Data suggest that periostin is critical for the induction of epidermal hyperplasia in both atopic dermatitis (AD) and psoriasis. In plaque-type psoriasis lesions elevated periostin was detected in the tissue compared to normal skin. It has also been shown that serum levels of periostin are increased in patients with AD and psoriasis. Based on these results we aimed to see whether serum levels of periostin could be correlated to disease severity, activity related to treatments, and gender. Patients were diagnosed with psoriasis by a dermatologist and their psoriasis area severity index (PASI) scores were determined. We collected blood samples from both treated and untreated male and female psoriatic patients (n=62) and also from healthy volunteers (n=18). Serum periostin levels were measured by sandwich enzyme-linked immunosorbent assay (ELISA). Data are normalized to control and are presented as mean ± standard error of mean and analyzed by two-sample t-test. $P < 0.05$ was considered statistically significant. Our results confirmed the previous observation that periostin is increased in the serum of psoriatic patients. It is important, that treatment did not affect the serum periostin level, indicating that periostin is not disease activity dependent. Gender also did not make a difference among patients in the measured elevated periostin levels. When we compared the serum periostin levels among untreated patients with severe versus mild disease based on PASI scores, we could not detect any difference between the two groups. Our data indicate that periostin is a disease related marker in psoriasis, however it is independent of disease severity and activity.

Supervisor: Prof. Dr. Bata-Csörgő Zsuzsanna, Szegedi Tudományegyetem, Általános Orvostudományi Kar, Bőrgyógyászati és Allergológiai Klinika

Márk Félix Juhász , PTE, Gyógyszertudományok Doktori Iskola
Márk Félix Juhász, PTE, Gyógyszertudományok Doktori Iskola

Age-dependent association of pancreatic family history with recurrent and chronic pancreatitis, idiopathic ethiology and risk factors: secondary analysis of an international cohort of 2345 acute pancreatitis patients.

"Background: In pediatric acute pancreatitis (AP) a family history of pancreatic diseases is a well-established prognostic factor for higher rate / earlier onset of recurrent AP (ARP) and chronic pancreatitis (CP). Adult guidelines also highlight its importance, but currently no clinical evidence is available.Objective: To examine the prognostic role of pancreatic family history for ARP/CP and observe possible underlying mechanisms. Methods: We conducted a secondary analysis of the Hungarian Pancreatic Study Group's (HPSG) multicenter, international, prospectively collected registry of AP patients, both children and adults. We compared those with a positive family history of pancreatic diseases to those without, in different age groups, and analysed trends of accompanying factors. Chi-square and Fisher exact tests were used.Results: We found a higher rate of ARP/CP in the positive pancreatic family history group (35.5% vs 25.8%, p=0.0032), peaking at 6-17 years. Idiopathic AP peaked in childhood in the positive group(75% 0-5 years, 60% 6-11 years) and was consistently 15-25% in the negative group. A significantly higher rate of alcohol consumption / smoking was found in the positive groups at 12-17 years (62.5% vs 15.8%, p=0.0127), 18-29 years (90.9% vs 58.1%, p=0.0493), 42-53 years and overall. We found no significant differences in diabetes/hyperlipidemia. Conclusion: Positive family history most likely signifies genetic background in early childhood. In adolescence and early adulthood there is a strong association with alcohol and smoking – clinicians should be aware and apply intervention if necessary. A positive pancreatic family history is not a prognostic factor for ARP and CP in adults.

Supervisor: Andrea Párniczky PTE ÁOK Transzlációs Medicina Intézet Supervisor: Andrea Párniczky, PTE ÁOK Transzlációs Medicina Intézet

Szentpéteri Szófia, SE, Klinikai Orvostudományok Doktori Iskola

Examination of Interleukin 1 and Toll-like receptor 4 gene single nucleotid polimorphisms in medication-related osteonecrosis of the jaw

Introduction: We examine the single nucleotid polimorphism of interleukin 1A, 1B (IL-1A, IL-1B) and Toll-like receptor 4 (TLR4) gene in development and prognosis of medication-related osteonecrosis of the jaw (MRONJ). Methods: In our study we apply DentiGen Parodontitis Test in investigation of polimorphism IL-1A and IL-1B (IL-1A-889, IL-1B+3953). The genetic samples were evaluated DNA-hybridization technic. TLR4 single nucleotid polimorphisms (rs4986790, rs4986791) are determined from blood sample with Sanger-technique. In our investigation we made examination in patient group and control group. In the patient group was MRONJ diagnosted. In control group the patient didn't suffer from MRONJ. The role of gene polymorphism in development of the disease is examined by comparing the genetic results of patient group and control group. The investigation of gene polymorphism in prognosis of the disease is based on treatment-induced stage improvement, recovery and the relapses following the treatment. Results: During our investigation 150 genetic examination were performed for determine IL-1A and IL-1B polimorphisms. 91 patients are suffering from MRONJ and 59 patients are in control group. In patient group 51 (56,04%) patients carry unfavourable allelic variant, in control group 22 (37,28%) patients have unfavourable allelic variant. We didn't find any association (p=0,498) between the unfavourable polimorphism and the development of the MRONJ. In patient group were used surgical therapy in 79 cases. In this group were detected stage improvement in 78 (98,73%) cases, recovery in 67 (88,15%) cases and relapses in 33 (49,25%) cases. 49 patients have unfavourable allelic variant from 79 patients treated with surgical therapy. We haven't found any connection between the examined polymorphism and the stage improvement (p=0,382) or recovery (p=0,561). Significant association (p=0,022) was detected between the relapses and the carrying of unfavourable allelic variant. To date, 26 sample have been collected for determine TLR4 polimorhisms. The samples are being processed. Summery: We found significant association between relapses of MRONJ and the carrying of interleukin 1A and 1B polimorphism.

Supervisor: Vaszilkó Mihály dr. , Semmelweis Egyetem Arc-Állcsont-Szájsebészeti és Fogászati Klinika

Tamás Linkner, DE, Molecular Cell- and Immune biology doctoral school; Dr. Zsófia Szojka, DE

Analysis of changes in the cellular proteome and transcriptome in the early time-points following HIV transduction, and the role of HIV-2 Vpx.

The human immunodeficiency viruses (HIV-1 and HIV-2) share a similar genomic and organizational structure. These viruses rely on host cell machinery for replication, and compared to HIV-1, responses of the host cell to HIV-2 infection is understudied. One of our aims was to characterize the remodeling of the cellular proteome and transcriptome at very early time-points (0-2 hours), following transduction of HEK-293T cells by HIV-1 and HIV-2 pseudovirions, using mass spectrometry and transcriptomic analysis. Secondly, we wanted to elucidate the role of the viral protein X accessory protein of HIV-2 (Vpx), which is present only in HIV-2 and its predecessor, the simian immunodeficiency virus of sooty mangabeys (SIV/smm). The function of Vpx has not yet been thoroughly characterized. In our previous studies, HIV-2 Vpx was responsible for dampening the infectivity of HIV-1 in dual transduction assays. We therefore set out to elucidate the function of this accessory protein, and reveal its cellular interaction partners using pull-down immunoprecipitation, as well studying the transcriptomic changes induced upon transfection of the cells with this protein utilizing transcriptomic analysis techniques. Our results indicate that in the first 2 hours of transduction, 7 proteins were significantly downregulated by HIV-2, and 5 by HIV-1. Among these proteins were the Non-POU domain-containing octamer-binding protein (NONO), heterogeneous nuclear ribonucleoprotein A1 (hnRNPA1) and Heat shock protein family member D member 1 (HSP60), all of which were shown to augment viral replication in the late-phase of infection. Expression level of genes involved in mRNA splicing, transport, DNA repair and cytoskeletal reorganization was also differentially altered. In regards to Vpx, pull-down immunoprecipitation assay showed that wild-type Vpx interacted with proteins involved in splicing, packaging of pre-mRNA, nuclear export and translation, while transcriptomic analysis is underway. Our findings may shed light on the role of HIV-2 Vpx, and highlight the differential changes in the cellular proteome and transcriptome in the early-phase of HIV-1 and -2 lentiviral transduction.

Supervisor: Dr. Mohamed Mahdi, Department of Biochemistry and Molecular biology, University of Debrecen, Faculty of Medicine, Debrecen, Hungary

Clincal sciences II. 10:30-12:00

Dr. Benjamin Tamás Papp, SZTE, Klinikai Orvostudományok Doktori Iskola

Negative trade-off between neoantigen repertoire breadth and the specificity of HLA-I molecules shapes antitumour immunity

The human leukocyte antigen class I (HLA-I) genes shape our immune response against pathogens and cancer. Certain HLA-I variants can bind a much wider range of peptides than others, a feature that could be favorable against a range of viral diseases. However, the implications of this phenomenon on cancer immune response is unknown. In this paper, we quantified peptide repertoire breadth (or promiscuity) of a representative set of HLA-I alleles, and found that cancer patients that carry HLA-I alleles with high peptide binding promiscuity are characterized by significantly worse prognosis after immune checkpoint inhibitor treatment. This trend can be explained by a reduced capacity of promiscuous HLA-I molecules to discriminate between human self and tumour peptides. In summary, HLA-I peptide binding specificity shapes neopeptide immunogenicity and the self-immunopeptidome repertoire in an antagonistic manner.

Supervisor: Dr. Manczinger Máté, SZTE ÁOK bőrgyógyászati és allergológiai klinika

Dr Markóth Csilla, DE, Laki Kálmán Doktori Iskola

Nem infektív eredetű cryoglobulinaemiás glomerulonephritis

Markóth Csilla1, Trinn Csilla1, Bidiga László, Ujhelyi László1, Mátyus János1 1DE KK Belgyógyászati Intézet A Épület, Nephrológiai Tanszék 2DE KK Pathológiai Intézet

Bevezetés: A cryoglobulin hidegben kicsapódó fehérje. Az esetek 5-20 %-ban alakul ki veseérintettség, döntően membranoproliferatív glomerulonephritis (MPGN). Leggyakrabban II-es típusú cryoglobulinaemiával találkozunk, főként infekció (HCV) következményeként, ritka az egyéb típusú és eredetű.

Beteganyag, módszer: Klinikánkon 2015. január óta (527 betegnél) végzett vesebiopszia közül a cryoglobulinaemiás MPGN betegek adatainak részletes retrospektív feldolgozása. Eredmények: A MPGN betegek 12%-ában (7/56) igazolódott nem infekcióhoz társuló cryoglobulinaemiás GN. A 7 esetből 1 betegnél I-es, 3 betegnél II-es, 3 betegnél III-as típusú cryoglobulinaemiát mutattunk ki. A komplementrendszer mindenkiben érintett volt. A vesebiopszia indikációja legtöbbször (4/7) nephroso-nephritis volt. Extrarenális tünet közül bőrtünetek, ízületi panaszok 4 esetben voltak jelen. A háttérben 4 betegnél igazolódott immunbetegség, csontvelővizsgálattal 3 betegnél mutattunk ki hematológiai teendőt nem igénylő monoklonális gammopathiát. Egy betegnél korábban, míg másik betegünknél a kivizsgálás során MALT lymphoma igazolódott. Minden esetben steroidot, 4 betegnél cyclophosphamidot adtunk, emellett 2 betegünknél a gyors vesefunkció-romlás, kiterjedt extrarenalis tünetek miatt plazmaferezis (PF) kezelést végeztünk. Terápia refrakteritás miatt 2 beteg, további 3 hematológiai alapbetegség progressziója alapján rituximabot kapott. Később egyikük Waldenström betegség kialakulása miatt PF mellett kemoterápiás kezelésben is részesült. Fentiek mellett a vesefunkció javult, a korábban vesepótló kezelésre szoruló betegnél átmeneti javulás után ismét dialízis igényű veseelégtelenség alakult ki, míg egy másik beteg kezelése során HD bevezetése vált szükségessé. Következtetés: Nephroso-nephritis, hypocomplementaemia, MPGN gyanúja esetén cryoglobulin meghatározás szükséges. Pozitív esetben, amennyiben HCV vagy egyéb infectio kizárható elsősorban Sjögren syndromára vagy lymphoproliferatív betegségre, MGRS-re kell gondolnunk. A hatékony B sejt/plazmasejt ellenes kezelés alapvető fontosságú a vesefunkció hosszútávú megőrzése érdekében.

Supervisor: Dr Mátyus János, Debreceni Egyetem KK Belgyógy. Int. Nephrológiai Tanszék

Dr. Kulin Dániel, SE, Doctoral School of Theoretical and Translational Medicine ; Dr. Antali Flóra, SE

Preclinical validation of reliability of a novel remote-patient-monitor platform, SCN4ALL

Preclinical validation of reliability of a novel remote-patient-monitor platform, SCN4ALL

Photoplethysmography-based contour analysis of the digital arterial volume pulse (DVP) incorporated into a telemedicine system can be optimal tools for remote monitoring of various patients; however, the method has certain limitations. Our data shows that DVP analysis by SCN4ALL is a reliable method to track cardiovascular status. We analyzed nine parameters derived from the DVP and its second derivative (SDDVP). First, the repeatability of measurements were assessed by detecting artificial signals. Secondly, under standardized conditions test–retest reliability of human measurements were evaluated in healthy individuals.

SCN4ALL analyzed each parameter with high accuracy (coefficients of variation (CVs) < 1%). Test–retest reliability of most parameters (heart rate, left ventricular ejection time index, stiffness index, reflection index, b/a,) was satisfactory (CVs < 10%) in healthy individuals. However, aging index and d/a parameters, derived from the SDDVP showed higher variability. Our results highlighted that in some cases SDDVP parameters can be interpreted with limitations due
to (patho)physiological variations of the DVP.

As to conclude: SCN4ALL system is proven to give reliable results in steady-state conditions and healthy individuals.

Supervisor: Dr. Miklós Zsuzsanna PhD, Semmelweis Egyetem Transzlációs Medicina Intézet

Dr. Ocskay Klementina, PTE, Gyógyszertudományok Doktori Iskola

The protective effect of albumin in acute pancreatitis – a prospective, international, multicenter registry analysis of 1149 patients

Introduction: Acute pancreatitis (AP) is a frequent disease with significant morbidity and mortality. Hypoalbuminemia is an independent risk factor for severe AP and in-hospital mortality based on small retrospective cohort studies. Aims: Our aim was to assess clinical outcomes and inflammatory markers of patients with lower-than-normal albumin levels in a prospectively collected, large, multicenter cohort. Materials and methods: The Hungarian Pancreatic Study Group (HPSG) enrolled patients with AP from 12 countries from 2012 to 2018 in the Acute Pancreatitis Registry. Patients were divided into low and normal albumin groups, the cutoff being 35 g/L. Laboratory parameters were measured in the first 48 hours. Chi-square test and Mann-Whitney-U test were used. Results: The analyzed cohort comprised of 1149 patients (57% males, average 56.7 years, 6% severe and 20% moderately severe cases). The 218 patients in the low albumin group were older ($p=0.005$) and more had alcoholic etiology (30.2% vs 23.4%, $p=0.03$). The low albumin group had lower amylase, lipase, eGFR and total protein ($p<0.001$ in all comparisons), but higher C-reactive protein, white blood cell and procalcitonin levels ($p<0.001$, $p=0.017$ and $p<0.001$). The development of organ failure (kidney, heart and respiratory) and local complications (peripancreatic fluid, necrosis and pseudocyst) were more frequent ($p<0.001$ and $p=0.016$). Low albumin patients had higher mortality (6.4% vs 2.9%, $p<0.001$), more severe disease course ($p<0.001$) and longer hospital stay (average 8.9 vs 12.0 days, $p<0.001$). Conclusion: On-admission hypoalbuminemia is associated with more severe inflammation, higher mortality, more severe cases, complications and longer hospital stay..

Supervisor: dr. Párniczky Andrea, Transzlációs Medicina Intézet, PTE ÁOK; Heim Pál Országos Gyermekgyógyászati Intézet

Dr. Szadai Leticia, SZTE, Klinikai Orvostudományok

DIAGNOSTIC APPROACHES FOR PATIENTS WITH BRAFV600 MELANOMA: IMMUNHISTOCHEMISTRY OR PCR?

Leticia Szadai MD Department of Dermatology and Allergology, Albert Szent-Györgyi Health Center, University of Szeged, Hungary.

Keywords: melanoma, BRAF V600E, immunohistochemistry (IHC), polymerase chain reaction (PCR)

Aims: The analysis of B-raf proto-onkogene, serine/threonine (BRAF) mutation status is important regarding the diagnostics of the disease and the BRAF-inhibitor therapy. Nowadays, the gold standard assessment of BRAF mutation are the DNA-based PCR techniques. However, recently the testing of immunhistochemical BRAF antibody became available, which would help the detection of BRAF mutations. Our aim was to investigate the results of the assessments of immunhistochemical BRAF mutated protein and to understand its role in the melanoma diagnostics. Methods: We included 49 patients with primary and metastatic melanoma in our pilot study. We examined the FFPE (formalin-fixed, paraffin-embedded) samples of these patients for Sanger sequencing (PCR) and for immunohistochemistry (IHC) analysis and assessed the BRAF mutation status from the results of PCR and IHC. Results In 18 cases out of 49, BRAF mutation was found. The VE1 antibody showed a sensitivity of 94.4% with a specificity of 82%. The positive predictive value was 81% and the negative predictive value was 95%. The overall concordance rate was 71.4% between the PCR and IHC VE1 staining on BRAF status. Conclusions: The results from our study compared to the literature validate the high sensitivity and specificity of the BRAF VE1 antibody. Our data support the use of the immunohistochemichal VE1 antibody staining for the BRAF V600E mutation screening and IHC can be a potentially alternative to PCR testing.

Supervisor: Dr. Németh István Balázs, SZTE-ÁOK Bőrgyógyászati és Allergológiai Klinika

Vivien Telek, PTE, Clinical Medical Sciences

A novel treatment on endoplasmic reticulum stress regarding in situ perfused rat model

Authors: Vivien Telek1, Luca Erlitz1, Ibitamuno Caleb1, Tibor Nagy1, Mónika Vecsernyés2, Bálint Balogh2, György Sétáló Jr.2, Gábor Jancsó1, Péter Hardi1 and Ildikó Takács1Affiliations: [1] Department of Surgical Research and Techniques, Medical School, University of Pécs, Hungary[2] Department of Medical Biology and Central Electron Microscope Laboratory, Medical School, University of Pécs, Hungary BACKGROUND: Ischemia-reperfusion injury (IRI) can cause insufficient microcirculation of the transplanted organ and results in worse graft survival rate. Next to mitochondria, the endoplasmic reticulum (ER) is also a target organelle in the first steps of ischemic injury and due to changed conditions, it cannot maintain the proper protein folding capacity and it will cause the ER stress which can lead to cell death. OBJECTIVE: This study aimed to investigate the effect of different doses of an anti-diabetic drug, Pioglitazone (Pio), on ERS and histopathological changes, using in-situ perfusion rat model. METHODS: 60 male Wistar rats were used, that were divided into six groups. Control group, vehicle-treated group and four Pio treated groups were established (10, 20, 30 and 40 mg/kg Pio was given). The rats were perfused through inferior vena cava and we made a small incision on the infrarenal abdominal aorta which served as an outflow. The outflowed perfusate was removed from the abdominal cavity by suction. After the experiment, kidneys and livers were collected and put immediately on liquid nitrogen. Levels of the endoplasmic reticulum stress markers (XBP1s and XBP1u and Caspase 12) were analyzed by Western blot and histopathological changes were evaluated by hematoxylin-eosin staining. RESULTS: Histopathological findings were correlated with the Western blot results and show a protective effect of the higher dosages of Pio in in situ perfusion rat model. In our study, Pio could reduce ERS, and the most effective dosage was the 40 mg/kg Pio in case of kidney samples. According to the histopathological results, in the 40 mg/kg Pio group the kidney's structure was correlated to the control group's samples. After the analyzation of liver samples, based on our results, the 10 and 20 mg/kg Pio groups decreased the caspase 12 level compared to the untreated but operated group (KH). The pattern of the kidney samples returns when analyzing XBP1s and XBP1u, and the significantly effective doses of Pio are the 30 and 40 mg/kg. To analyze the data we used one way ANOVA with Bonferroni correction. CONCLUSIONS: Consequently, we recommend Pio for further experiments on the field of ischemia-perfusion-reperfusion research because of its anti-inflammatory, antioxidant and ERS reducing activity, which can moderate the ischemic damages and prevent cell death.

Supervisor: Takács Ildikó MD PhD habil., Surgical Research and Techniques

Theoretical sciences I 13:00-14:30

Ádám Diós, DE, Doctoral School of Molecular Cell and Immune Biology

Optimalization of biosensor regeneration for new anti-transglutaminase antibody serology assay

Coeliac disease (CeD) is a chronic, systemic immune disorder with autoimmune features where ingestion of gluten induces antibody production against gliadin peptides and a self antigen, transglutaminase 2 (TG2). The detection of TG2 autoantibodies is the gold standard of CeD diagnosis. The TG2 based serologic assays have prominent sensitivity and specificity values, however have certain limitations as well, for example that concentration of antibodies is only given in arbitrary units. We are optimizing a biolayer interferometry based real time, label free, quantitative method which enables to detect the absolute concentration of TG2 antibodies from a drop of blood or serum within 5 minutes, which could be a new level in CeD patient health care. The hardest point of the assay optimalization is the regeneration of the biosensors in order make them reusable and in this way to lower the costs of the testing. The antibody-targeted surfaces of TG2 are discontinous multidomain epitopes, which are extremely sensitive for conformational changes. If we utilize biotin tagged recombinant human TG2 we can permanently immobilize the protein to Streptavidin biosensors. However the removal of the patient antibodies from the surface of TG2 after the measurement will disrupt the epitope surfaces. Common methods by utilizing acidic or alkaline solutions or chaotripc agents cause irreversible damage to the protein. To prevent or treat that effect we tested different compounds and found that reducer agents can improve the conservation of the epitope surfaces while changes in the ionic strength or adding compounds which assist in the refolding of the protein have only modest effect. Another possibility is to utilize Glutation-S-Transferase (GST) tagged recombinant human TG2 antigen which we can transiently immobilize to anti-GST sensors, but here we have to clean the surface properly to always assure the consistent reload of the antigen. For that purpose we tested multiple reagents and found that 100mM glycine pH 2.5 + 0.1% sodium-dodecil-sulfate (SDS) treatment can ensure the most proper surface cleaning before the next measurement. The method is now ready for the measurement of real patient samples and sensors can be reused 2-3 times for new assays.

Supervisor: Prof. Dr. Ilma R. Korponay-Szabó, Department of Pediatrics

Balogh Gergő Mihály, SZTE, Klinikai Orvostudományi Doktori Iskola

Mutagenic mechanisms of the innate immune system can generate novel, potentially immunogenic peptides in SARS-CoV-2

The prerequisite of adaptive immune recognition of viruses is the binding of foreign peptides to HLA molecules on the surface of infected cells. T cells can recognize only these viral peptides, leading to their activation. Since the beginning of the COVID-19 pandemic, more than 300 thousand viral genomic sequences have been registered, containing thousands of different mutations. We show that a large fraction of these mutations is associated with the activity of APOBEC cytidine deaminases and reactive oxygen species. These processes result in C>U and G>U mutations in viral RNA leading to the destruction of the virus. We also show that these mutations are likely to potentiate the HLA-binding of the affected peptides. Our results suggest that novel, potentially immunogenic peptides are frequently generated in the SARS-CoV-2 proteome, potentially preventing the immune evasion of the virus. This mechanism might have implications in COVID-19 epidemiology and vaccination.

Supervisor: Dr. Manczinger Máté, Bőrgyógyászati és Allergológiai Klinika

Combi Zsolt, DE, Laki Kálmán Doktori Iskola

Új generációs vas tartalmú gyógyszerkészítmények hatása a valvuláris kalcifikáció folyamatára

Háttér: A kalcifikált aorta billentyű betegség (CAVD: Calcified Aortic Valve Disease) kialakulásában fontos szerepet játszik a dohányzás, az előrehaladott életkor, a 2-es típusú diabétesz, a magas vérnyomás. A folyamat hátterében, a billentyűk szövetének nagy hányadát alkotó, valvuláris interstitialis sejtek (VIC) oszteoblaszt irányú transzdifferenciálódása áll. A mineralizáció során a szívbillentyűk megvastagodása, elcsontosodása figyelhető meg, melynek következtében, részben vagy teljesen megszűnik fiziológiás funkciójuk. Célkitűzés: Olyan vas tartalmú gyógyszerkészítmények vizsgálata, melyek jelentősen csökkenthetik a valvuláris kalcifikációban kulcsszerepet játszó biomarkerek hatását. Módszerek: Szívbillentyű transzplantáción átesett betegek szövetanyagából izolált, interstitiális sejteken modelleztük a betegek pathológiás állapotát. A VIC sejtek in vitro kalcifikációs kísérleteihez különböző koncentrációjú foszfátot (1,5-3,0 mmol/L) és kalciumot (1,5-2,0 mmol/L) tartalmazó növekedési médiumot használtunk. A vas valvuláris mineralizációra kifejtett hatásának vizsgálatát két gyógyszerkészítmény, az F1 és F2 eltérő koncentrációival (10-500 µmol/L) vizsgáltuk. A szívbillentyű sejteken képződő hidroxiapatit kristályok kvalitatív szemléltetésére, Alizarin Red S és ALP (alkalikus foszfatáz) festéseket végeztünk. A kvantitatív elemzés során, a sejtek felülúszójából, kalciumot, a sejt lizátumokból pedig intracelluláris foszfáttartalmat mértünk. A betegségre jellemző csontspecifikus fehérjék (Pit1, OC: oszteokalcin) és transzkripciós faktorok (RUNX2, SOX9) expresszióját Western Blot segítségével vizsgáltuk. Eredményeink látványosabbá tételére, immunfluoreszcens (RUNX2; SOX9) festéseket kiviteleztünk, melyeket STED nanoszkóp segítségével értékeltünk. Eredmények: Kísérleteink azt bizonyítják, hogy az általunk vizsgált, két vas tartalmú gyógyszerkészítmény dózisfüggő módon csökkenti, az extracelluláris mátrixban képződő kalcium-foszfát depozitumok mennyiségét, amit az oszteoblaszt specifikus fehérjék (pl: oszteokalcin) expressziójának csökkenésében is megfigyeltünk. Következtetés: Az ígéretes in vitro eredmények alapján, in vivo és ex vivo kísérletekkel tervezzük a hatásmechanizmus pontosabb felderítését, és személyre szabott, klinikai terápiák kidolgozását.

Supervisor: Prof. Dr. Balla József, Debreceni Egyetem Általános Orvostudományi Kar Belgyógyászati Intézet

Domonkos Czárán, SE, Molekuláris orvostudományok; Ádám Horváth 1,2, Péter Sasvári3, Afrodité Németh3, Éva Wisniewski3, Zsuzsanna Helyes1,2, 1University of Pécs, 2Szentágothai Research Centre, 3Semmelweis University

REDUCED SYMPTOMES OF ARTHRITIS IN ARHGAP25 KNOCKOUT MICE AND THE POSSIBLE MECHANISMS BEHIND IT

Introduction ARHGAP25 is a GTP-ase activating protein expressed mostly in leukocytes. Through the inhibition of Rac activity it has a central role in regulating different neutrophilic functions including phagocytosis, superoxide production and migration. In this study, we investigated functional changes as well as the possible reasons which may lead to reduced arthritic symptoms in ARHGAP25 knockout mice. Methods Wild type (WT) and ARHGAP25 knockout (KO) mice were treated with either arthritic (K/BxN) or control (BxN) serum. Clinical score, ankle thickness (measured with caliper) and hind paw volume (using a plethysmometer) were followed for 8 days after treatment. Articular function was investigated with horizontal grid test. Touch sensitivity was measured with dynamic planar aesthesiometry. Neutrophil myeloperoxidase (MPO) activity was measured in vivo, after intraperitoneal administration of Na-luminol. Superoxide production measurement of neutrophils was carried out using the Cytochrome C reduction assay. Results After arthritic serum treatment, ARHGAP25 KO mice showed decreased signs of arthritis (ankle thickness, clinical score and function of the limbs) compared to WT. Hyperalgesia of KO mice after 6 and 8 days of serum treatment was significantly reduced compared to WT. We observed a reduction of MPO activity in KO mice 1 day after treatment, however, after 2 days there were no difference compared to WT. Investigating superoxide production after different stimuli, we did not find significant differences between KO and WT bone marrow derived neutrophils. Conclusion Our result suggest that ARHGAP25 deletion significantly mitigates the symptoms of rheumatoid arthritis (ankle and hind paw swelling, joint function and hyperalgesia). These changes cannot be explained by the altered MPO, or superoxide production of ARHGAP25 knockout neutrophils. In further experiments, we turn to the examination of possibly changed cytokine environment or altered macrophage functions in the KO animals to reveal the role of ARHGAP25 in rheumatoid arthritis. Supporting grants: János Bolyai Research Scholarship, ÚNKP-20-5-SE-2, NKFIH FK_18/128376 The research was performed in collaboration with Animal imaging core facility at the Szentágothai Research Centre of the University of Pécs

Supervisor: Dr. Csépányi-Kömi Roland, Semmelweis Egyetem

Dr. HeténYi Roland, PTE, Interdiszciplináris Orvostudományok Doktori Iskola

Cellular internalization of Thymosin beta-4

Background: Hypoxic heart disease is a predominant cause of disability and death worldwide. As adult mammals are incapable of cardiac repair, achieving regeneration is crucial. An alternative to stem cell therapy can be reprogramming via regulatory pathways using peptides or miRNAs. Thymosin β4 (TB4), a 43 amino-acid G-actin sequestering peptide promotes myocardial cell survival and coronary angiogenesis after infarction in adult mammals. Objective: However, the precise cellular and molecular alterations induced by TB4 that promote cell survival and resistance to cardiac damage, and the mechanism of cellular uptake are not well understood. By means of reviewing the key signalling pathways and utilizing methodology, we investigated the internalization process. Methods: Therefore, TB4 was chemically labelled with a bright, photostable dye, ATTO488, then the location of the fluorescent labelling was analysed by Western blot. Previous data claimed crucial significance to an intact C-terminus, thus TB4 was required to be labelled in close proximity to the N-terminus. We hypothesized that TB4 enters these cells via receptor-mediated endocytosis, therefore ATTO-TB4 was utilized in a time-lapse cytochemistry with C2C12 cells. Cardiac cells were also studied with immunohistochemistry whether they internalize TB4 expressing T7 phages in vitro. Results: Western blot analyses clearly demonstrated that centrally located amino groups are prone to conjugation chemistry, while the uptake most likely occurs via receptor-mediated endocytosis. Conclusion: This research targets key instances in the peptide's interactome and a consequential intelligence gained on internalization processes.

Supervisor: Dr. Bock-Marquette Ildikó, PTE ÁOK, Biokémiai és Orvosi Kémiai Intézet, PTE SZKK

Halász Hajnalka Emese, DE, Molekuláris Sejt- és Immunbiológiai Doktori Iskola

The role of neutrophil granulocytes in skeletal muscle inflammation and regeneration

Background: The skeletal muscle is permanently exposed to physical damage but in normal condition the tissue is able to repair itself in a very efficient way. Neutrophils enter traumatized tissue firstly and act as professional phagocytic cells. Like macrophages, neutrophils also form a heterogeneous population, they can contribute to inflammation and to repair as well. The myeloid-specific deletion of Mcl-1 anti-apoptotic protein in mice leads to dramatic reduction of neutrophil counts. In these mice we observed a delayed skeletal muscle regeneration. Objective: Our aim is to investigate the role of neutrophils during a sterile muscle injury in order to understand better the molecular mechanisms and immunological pathways in tissue regeneration. Methods: The muscle injury is induced by cardiotoxin (CTX) injection in tibialis anterior muscle. The muscle isolation and processing are performed on different consecutive days after injury. The regeneration is monitored by analysing satellite cells, fibro/adipogenic progenitors (FAPs) and infiltrating immune cells with flow cytometry. Results: The phenotypic analysis of wild type (WT) and Mcl-1 KO mouse strains showed splenomegaly in Mcl-1-KO mice and increased number of myeloid progenitor cells in the bone marrow and spleen. We compared two types of experimental models (CTX and barium-chloride injection) for muscle regeneration. The CTX-injury induced inflammation was associated with eosinophilic infiltration. This prolonged eosinophil migration can be detected for several days in Mcl-1 KO mice. The numbers of inflammatory Ly6C+ monocytes and resolving F4/80+ macrophages were reduced in Mcl-1 KO mice compared to WT mice. The muscle regeneration was followed by measuring the FAPs and satellite cells with flow cytometry. The high number of these cells at day 7 post injury in Mcl-1 KO mice may refer to delayed regeneration. Conclusion: These preliminary results show that the myeloid-specific deletion of Mcl-1 anti-apoptotic protein affects the neutrophil and monocyte/macrophage counts too. In the absence of neutrophils the muscle regeneration takes more time than in normal condition. Next, we would like to restore the delayed repair with transferring neutrophils from MHC-compatible mice by adoptive cell transfer.

Supervisor: Dr. Gogolák Péter, Debreceni Egyetem, ÁOK, Immunológiai Intézet

Mark Kantor, SE, Theoretical and Translational Medicine

Animal models of human preeclampsia – advantages and limitations for investigating cerebrovascular autoregulation

Background Hypertension in pregnancy - preeclampsia - is affecting ~8% of pregnancies and is a leading cause of both maternal and fetal morbidity and mortality. Unfortunately, the underlying mechanisms are still unclear. Thus, many animal models have been developed, which share many of its features, but do not include the complete spectrum of symptoms present in this human disease. The increased systemic pressure in preeclampsia imposes a great challenge to the mechanisms contributing to the autoregulation of cerebral blood flow. Objective Thus, we aimed to elucidate whether the available animal models are suitable to study the adaptation of cerebral autoregulation in preeclampsia. Methods We have reviewed the literature (PUBMED) regarding the animal models of preeclampsia. Results In general, animal models of preeclampsia can be divided into 4 groups: 1) spontaneous, 2) surgically induced, 3) pharmacologically induced and 4) transgenic. Model 1: The Dahl salt-sensitive rat is a genetic model of kidney disease and hypertension (PMID: 25904684). Model 2: The reduced uterine perfusion pressure (RUPP), rat elicited with a combination of aortic constriction and occlusion of the uterine-ovarian arteries (PMID: 31669926). Model 3: Inhibition of nitric oxide synthase in rats by L-NAME at different gestational stages, which leads to preeclampsia-like symptoms (PMID: 7909994). Model 4: Overexpression of the VEGF antagonist sFlt-1 via the administration of viral vectors results in pregnancy-specific proteinuria and hypertension in rats (PMID: 12618519). Conclusion Preeclampsia is a disease unique to humans. Although several animal models exist and some of them have placental lesions, none of them is ideal, thus extrapolation of the findings to human preeclampsia must be made with caution. Moreover, the effect of high systemic pressure on the mechanosensitive mechanisms contributing to the adaptation of cerebral autoregulation providing protection against stroke has not yet been addressed. Therefore, at first, comparison of such adaptation should be studied in young and old pregnant rats, which would help to better understand the effects of preeclampsia on the brain. Support: OTKA132596, K_19

Supervisor: Akos Koller, Institute of Translational Medicine, Faculty of Medicine; Department of Morphology and Physiology, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary

Theoretical sciences II. 13:00-14:30

Baráth Barbara, DE, Klinikai Orvostudományok Doktori Iskola; Ozsváth Xénia Erika, DE

Hőstressz hatása a makro-és mikro-reológiai paraméterekre sertésben

A klímaváltozás következtében, főként a nyári időszakban, jelentős környezeti hőmérséklet emelkedés figyelhető meg. A komfortzónánál magasabb környezeti hőmérséklet hatással van a reológiai paraméterekre. A tartósan magas hőmérséklet hatására megváltoznak a vörösvérsejt-membrán mechanikai tulajdonságai. A kísérlet célja annak vizsgálata volt, hogy e negatív hatások vitaminokkal és mikroelemekkel kiegészített diétákkal mérsékelhetők-e. Vizsgálatainkba 24 egészséges, ártány, Danbred sertést vontunk be (9/2019/DEMÁB). Az állatokat 4 csoportba osztottuk (n=6/csoport). Az 1. csoport a termoneutrális zónában (20℃) kontroll tápot fogyasztott: TC), A 2. csoport hő-stressznek (30 °C) kitett, de a kontroll diétát fogyasztó csoport (HC) volt. A 3. és a 4. csoportban (HT1 és HT2) az állatok ugyancsak 30°C-on voltak elhelyezve, de a kontroll táp két lépcsőben, kétféle vitaminnal és mikroelemmel (C-és E-vitamin, Zn és Se különböző koncentrációban) kiegészített. Vérvételek a hőmérséklet emelése előtt, majd azt követően 1 és 3 héttel történtek. A mintákból teljes vér (TVV) és plazmaviszkozitást (PV), vörösvérsejt deformabilitást, membrán stabilitást, ozmotikus deformabilitást, vörösvérsejt aggregatiot és hematológiai paramétereket mértünk.A TVV értékek a HC csoportban szignifikáns emelkedést mutattak. A PV a HT1 csoportban jelentősen csökkent az alap mérésekhez viszonyítva. A vörösvérsejt szám a 3. hétre a TC, HC, HT1 csoportnál szignifikánsan emelkedett, a HT2 csoportban csökkent. Minden csoportban hematokrit emelkedés volt. Az EI 3Pa értékek a kísérlet végére minden csoportban csökkentek, a vitaminnal és mikroelemekkel dúsított táppal etetett csoportokban az első héten a deformabilitás javult. Az ozmotikus deformabilitásnál a TC és HT2 csoportokban az EI min értékek csökkentek, míg az Omin értékek emelkedtek. Az aggregatiós index a HT1 csoportban jelentősen emelkedett, valamint az aggregatiós folyamat felgyorsult. A HC csoportban ezek ellenkezőjét tapasztaltuk. A vizsgálatok azt mutatják, hogy a magas környezeti hőmérséklet jelentősen befolyásolja a makro- és mikro-reologiai paramétereket, azonban e változások vitaminnal és mikroelemekkel kivédhetőek. Eredményeink alapján paraméterenként eltérő, hogy melyik vitamin dózis és ásványi anyag koncentráció lehet a legmegfelelőbb.

Supervisor: Dr. Deák Ádám, DE-ÁOK Sebészeti Műtéttani Tanszék

Dr. Antali Flóra, SE, Elméleti és Transzlációs orvostudományok; Dr. Kulin Dániel, SE

Verification of the photoplethysmography-based Pulse Rate Variabilty (PRV) analysis and determination of its compatibility with the results of ECG-based Heart Rate Variability (HRV) analysis

This abstract is encrypted.

Supervisor: Dr. Miklós Zsuzsanna, Semmelweis Egyetem, Transzlációs Medicina Intézet

Dr. Tóth Noémi, SZTE, Multidiszciplináris Orvostudományok Doktori Iskola

Investigating the role of the reverse Na+/Ca2+ exchanger in the sinus node pacemaking

This abstract is encrypted.

Supervisor: Dr. Nagy Norbert, SZTE ÁOK Farmakológiai és Farmakoterápiai Intézet

Orsolya Mózner, SE, Doctoral School of Molecular Medicine

Interactions of Potential Anti-COVID-19 Compounds with the wild type ABCG2 multidrug transporter and its common variant

This abstract is encrypted.

Supervisor: Dr. Balazs Sarkadi, Semmelweis University

Péter Sasvári, SE, Molekuláris Orvostudományok; Domonkos Czárán, Éva Wisniewski, Afrodité Németh, Kitti Nagy, Domonkos Czárán, SE

Optimalization of the BioID method for ARHGAP25 in COS-7 cells

Background The novel Rac-specific GTPase activating protein, ARHGAP25 is the participant of several phagocyte-related processes and there is an increasing number of new discoveries signalling the importance if said protein in tumour cells. However, we still cannot declare that we completely understand its intracellular behaviour either in physiological conditions or in tumor cells. Moreover, recent studies suggest that it contributes to the Wnt/β-catenin pathway, however the ways in which it can interact are not yet known. We need to develop a working method to examine its intracellular interactions more profoundly if we wish to understand it at a deeper level. Objective The development and optimization of an in-vivo protein interaction screening method in different cell lines.
Methods As more classical approaches seemed unsuccessful and raised some technical difficulties, we decided to use a new approach called BioID. This is a distance-dependent method based on biotin-transfer, during which our bait protein (ARHGAP25) is fused with a genetically modified prokaryotic biotin protein ligase enzyme (BirA). By expressing said fused protein in eukaryotic cells, it is able to biotinylate neighbouring proteins within the radius of 10-15 nm in a distance-dependent manner. Due to the great affinity of streptavidin to the covalently bound biotin, potential protein partners can be easily isolated with conventional methods. In our case, we used COS-7 cells to refine and optimise our method and we detected our proteins using mass spectroscopy. Results We have successfully constructed the BirA-ARHGAP25 plasmid, which was analysed by sequencing. By introducing a new type of control, we managed to reduce the number of potentially false positive results which provided us 29 proteins likely to be partners of ARHGAP25. Conclusion By refining our method, we could reduce the number of false results which is a stepping stone in understanding our target and we were able to detect new potential partners of ARHGAP25 which were never published before. This project was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences, and the ÚNKP-20-5-SE-2, as well as the NKFIH FK_18/128376 grants.

Supervisor: Dr. Roland Csépányi-Kömi, Semmelweis University

Varga Rita, SE, Elméleti és Transzlációs Orvostudományok Doktori Iskola; Jedlovszky-Hajdú Angéla, SE

Electrospun nanofibrous scaffolds for tissue engineering

Tissue engineering is one of the most intensively studied fields of medicine. A novel direction in medicine is the regeneration of damaged tissue by culturing cells on a host artificial matrix and implanting it back to the damaged area to induce the generation of new, healthy tissue, trying to restore its original structure and function. For this, there is a constant need for new materials, to which cells can adhere and proliferate on. Fibrous hydrogel membranes prepared by electrospinning would be ideal materials mimicking the native soft tissue with their high water content and fibrous structure. Poly(amino acid) based hydrogels are emerging materials aiming for bio-medical applications. Their peptide like structure can be easily degraded by enzymes thus their biodegradability is ensured. With time, the scaffold degrades, and the cells syntesize a new extracellular matrix, and produce a functioning tissue. Hence our aim was to synthesize poly(aspartic acid) fibers by electrospinning to induce regeneration in the damaged tissue, and restore its original function. In our research we prepared cross-linked poly(aspartic acid) polymers with hydrolysis, which contain disulphide bonds and 1,4-diaminobutane as cross-linkers. FTIR was used to confirm the chemical structure. We tested the biocompatibility of the meshes using MG63 human osteoblast-like cell line. Cell viability was assessed 24 and 72 hours after cell seeding with WST1 reagent. Crosslinked poly(aspartic acid) nanofibers were prepared, the hydrogel form prevented the dissolving in water via cross-linkers. During the test of cell viability we found that cells can adhere and proliferate on these membranes. Hence we have observed, that the artificial tissues are non-toxic for the cells, but we need more experiments to prove, that they are really suitable as scaffolds for tissue engineering. The use of this type of biodegradable implant can be a huge step forward towards tissue regeneration, because the poly(aspartic acid) mesh has desirable chemical, mechanical and biological properties. This research was supported by NKFIH FK 124147, EFOP-3.6.2-06-2017-00006, by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences and also supported by the ÚNKP-20-5-SE-9 new national excellence program of the Ministry of Human Capacities.

Supervisor: Dr. Jedlovszky-Hajdú Angéla, Semmelweis Egyetem, Biofizikai és Sugárbiológiai Intézet, Nanokémiai Kutatócsoport

Dr. Schranc Álmos István, SZTE, Elméleti Orvostudományok Doktori Iskola

Exaggerated ventilator-induced lung injury in an animal model of type two diabetes

Background and aim: While ventilator-induced lung injury (VILI) develops following prolonged mechanical ventilation in normal lungs, pulmonary disorders may facilitate adverse symptoms. Since type two diabetes (T2DM) facilitates atelectasis development, exaggeration of VILI can be anticipated. Therefore, we aimed at characterizing whether T2DM modulates VILI, and we also characterized how T2DM therapy affect adverse pulmonary changes. Methods: Rats were randomly assigned into one of the three groups: a model of untreated T2DM received a low dose of streptozotocin with high-fat diet (T2DM, n=8); a model of T2DM where this treatment was supplemented by metformin therapy (MET, n=8); and a control group (CTRL, n=8). VILI in each animal was induced by ventilating the rats with high tidal volume (VT=23 ml/kg) for four hours. Arterial and venous blood samples were analyzed to measure the arterial partial pressure of oxygen (PaO2), oxygen saturation (SaO2) and the intrapulmonary shunt fraction (Qs/Qt) in every two hours. Airway and respiratory tissue mechanics were assessed by forced oscillations. Level of injury was determined lung histology samples. Results: Significant worsening of VILI was observed in PaO2, SaO2 and Qs/Qt in T2DM group, without differences in the respiratory mechanics. These functional changes were also reflected in the lung injury score. Animals in the MET group showed no difference to rats in the CTRL group. Conclusion: Impairment of the gas exchange without significant mechanical changes suggest that untreated diabetes exaggerates VILI via destructing the alveolar-capillary barrier. Controlled hyperglycemia with metformin may reduce the manifestations of respiratory defects during prolonged mechanical ventilation.

Supervisor: Prof. Dr. Peták Ferenc, SZTE ÁOK Orvosi Fizikai és Orvosi Informatikai Intézet

Surgical sciences 14:30-16:00

Ali Alkhayer, SZTE, Doctoral School of Clinical Medicine; József Piffkó, Emil Segatto, SZTE

Three-dimensional short-term changes of the facial soft tissue after bimaxillary surgery of skeletal class III patients: a prospective study

Background Soft tissue adaptation and normal skeletal relationships have the greatest importance during orthognathic surgery. Therefore, our prospective study aimed to perform an extensive evaluation of the post-operation soft tissue changes in various morphological regions of the face after bimaxillary surgery of skeletal class III patients using a three-dimensional handheld structured-light scanner. Methods Our sample consisted of 12 patients (6 males and 6 females), with a mean age of (22±2.17 years, range 19.6-24.5) with skeletal class III malocclusion requiring bimaxillary osteotomy as the second step of their comprehensive treatment. The three-dimensional facial images were acquired one week before surgery (T0) and 6 months after surgery (T1) using a 3D handheld structured-light scanner (Artec EvaTM; Artec Group, Luxembourg). 20 landmarks, 13 linear and 6 angular measurements were located and measured directly on the facial images using Artec Studio V.12 software. The pre-and post-surgical measurements were compared and the significant changes were evaluated using the Wilcoxon signed-rank test. Three-dimensional deviation analyses were done for 7-morphological regions of the face using (GOM Inspect Software, Capture 3D, Inc., Santa Ana, CA). Results We found statistically significant increases in the nasal and nasal base width, nasal tip angle, upper lip height, and the lower lip angle after bimaxillary surgery. We also found significant decreases in the lower lip height and the Inter-labial angle. Soft tissue changes in most of the facial regions were also observed after bimaxillary surgery. Conclusions Three-dimensional soft tissue changes in most of the facial regions were observed after bimaxillary surgery of skeletal class III patients, especially in the middle third of the face, the nose, and the upper lip compared to the other facial structures. This must be taken into account in the course of treatment planning and that patients must be informed accordingly. Further investigations with larger sample size and appropriate controls are necessary for a more accurate evaluation of soft tissue response after bimaxillary surgery. Keywords: Orthognathic Surgery; Facial Soft tissue; Three-Dimensional Imaging

Supervisor: Assoc. Prof. Emil Segatto, Craniofacial Unit, Department of Oral & Maxillofacial Surgery, Faculty of Medicine, University of Szeged

Barth Anita, DE, Egészségtudományok Doktori Iskola

Factors affecting the access to the kidney transplant waiting list in the East Hungarian region

Kidney transplantation is the best available treatment choice for patients suffering from end-stage renal disease (ESRD), however not all ESRD patients have equal access to it. The aim of the study was to measure the factors that may influence the access to kidney transplant waiting list in the East Hungarian region. A total of 254 renal failure patients between 18 and 75 years old from eight dialysis centres participated in the study. The factors associated with access to waiting list were identified by univariate descriptive analysis and multivariate logistic regression analysis where the outcome variable was the placement on the kidney transplant waiting list. Our findings demonstrates that patients registered on the waiting list were younger (OR=0.96, 95% CI: [0.94-0.98]), male (OR=0.54, 95% CI: [0.30-0.98]), economically active (OR=0.53, 95% CI: [0.29-0.98]) and had greater knowledge in the field (OR=1.17, 95% CI: [1.03-1.33]). It can be sad that disparity exist in access to kidney transplant waiting list in Hungarian aspect. Key words: end-stage renal disease, kidney transplantation, access to waiting list, barriers

Supervisor: Dr. Nemes Balázs, DE ÁOK Sebészeti Intézet Szervtranszplantációs nem Önálló Tanszék

Constantinos Voniatis, SE, Doctoral School of Theoretical and Translational Medicine; Száva Bánsághi, SE

Establishing the correlation between the applied amount of alcohol-based handrub and hand hygiene effectiveness

Introduction: Hand hygiene is the most practical measure to prevent hospital-associated infections. Yet, it is only effective if the applied alcohol-based handrub (ABHR) covers the entire hand surface. The most commonly used hand hygiene protocol written by the World Health Organization does not mention an exact amount of handrub, as it may depend on the hand size. Some guidelines agree that 3 ml of ABHR should be applied. Nevertheless, handrub dispensers provide only 1.2–1.5 ml ABHR per stroke. The study aims to clarify how the amount of ABHR affects hand hygiene effectiveness. Methods: 57 surgical residents were voluntarily involved in this study. During their 2-weeks surgical practice, their hand hygiene performance was recorded daily, using the Semmelweis System, an automated hand hygiene technique monitoring device. The Semmelweis Scanner employs digital imaging and AI-based image processing to objectively determine which areas of the hand were properly covered by ABHR. The volume of ABHR applied was changed daily, from 1 ml to 3 ml (1, 1.5, 2, 2.5, and 3 ml portions was tested), in a random order. Participants were blinded, they did not know the amount received. Two questions were asked along each hand hygiene event: whether the applied handrub was enough to perform hand hygiene, and weather the ABHR drop off from their hands Results: A total of 441 measurements were recorded. Participants did not cover 5.63% of their hand surface on average when 1 ml ABHR was provided. In contrast, applying 3 ml handrub, the average missed hand surface was decreased to 0.72%. The study was blinded with respect to ABHR volume, yet participants could tell fairly accurately when they got more or less volume. In the case of 1 ml, only 1 person replied that the amount was more than enough (1.2%), while this ratio increased to 25% in the case of 3 ml ABHR. As the volume was increased, more and more participant noticed that ABHR was dripping off from their hand (15.9% vs. 65.6% in the case of 1 ml and 3 ml, respectively) Conclusion: The applied ABHR amount had a significant, measurable effect on hand hygiene performance. More handrub resulted in better coverage, which was quantified objectively. Further increasing ABHR amount may not result in an additional increase, as dripping became more significant at larger volumes, however, this phenomenon needs further investigation. Equal volumes were perceived quite differently by participants, leading to the conclusion that variance in hand size should be taken into consideration in future volume– coverage studies. Acknowledgement: C.V. is supported by the ÚNKP-20-3-II-SE-29, S.B. is supported by the ÚNKP-20-3-II-SE-24 New National Excellence Program of the Ministry for Innovation and Technology from the source of the National Research, Development and Innovation Found.

Supervisor: Andrea Ferencz, Department of Surgical Research and Techniques, Heart and Vascular Centre, Semmelweis University

Dr. Szécsényi-Nagy Balázs, SE, Mentális Egészségtudományok Doktori Iskola; Dr. Imre László, SE

Császármetszések arányának változása Magyarországon 2010-2019 között, figyelemmel az ellátó intézmények méretére és kitekintéssel az Európai Unió tagállamainak hasonló adataira

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Supervisor: DR. GAÁL PÉTER, Semmelweis Egyetem Egészségügyi Közszolgálati Kar

Dr. Szécsi Balázs, SE, Elméleti és Transzlációs Orvostudományok Doktori Iskola

A donorgondozás új lehetőségei: pajzsmirigyhormonok szerepe a szívátültetésben

Háttér: A végstádiumú szívelégtelenség jelenleg egyetlen definitív kezelése a szívtranszplantáció. Sajnos a szívátültetéshez szükséges allografto k száma messze nem haladja meg a transzplantációs várólistán helyet foglaló betegek számát. Megfigyelések alapján súlyos, egész szervezetet érintő stressz hatására egyes endokrin funkciók szuppresszálódnak. Célkitűzés: Kutatásunk során a neuroendokrin rendszer szerepét vizsgáltuk a szívtranszplantációt követő túlélésben. Módszer: Retrospektív, megfigyeléses vizsgálatunk 2011 és 2019 között a Semmelweis Egyetem Aneszteziológiai és Intenzív Terápiás Klinikán, valamint a Városmajori Szív- és Érgyógyászati Klinikán szívtranszplantáción átesett betegek perioperatív adatait dolgozta fel. A vizsgált paraméterek elsősorban a halálozási mutatók, egyes endokrin funkciók, illetve a United Network for Organ Sharing (UNOS) pontszám kiszámításához szükséges adatok voltak. Adataink elemzését általános leíró statisztikával, többváltozós Cox-regressziós analízissel, Kaplan-Meier görbével és Log-rank teszttel végeztük. Eredmény: Összesen 308 beteget vontunk be kutatásunkban, melyből 80 fő (26,0%) nő és 228 fő (74,0%) férfi volt. A donorok életkorának mediánja 57,8 év volt (IQR 25-75= 48,9-63,7). Pajzsmirigyhormon szubsztitúcióban összesen 99 donor (32,1%) részesült a transzplantációt megelőzően. Az operációt követő 30 napon belül 33 (10,7%), 1 éven belül 58 (18,8%), 2 éven belül pedig 63 (20,5%) recipiens hunyt el. Többváltozós Cox-regressziós analízissel azon recipiensek túlélése, akik tiroxin kezelés alatt álló donortól kapták az allografto t szignifikánsan nagyobb volt, mint azon recipienseké, akik az allografto t tiroxin kezelés alatt nem álló donortól kapták. Ez az összefüggés a 30 napos (Hazard Ratio {HR}=0,27; 95% Confidence Interval {CI}=0,10-0,77; p=0,014), az 1 éves (HR=0,44; 95% CI=0,23-0,85; p=0,014), valamint a 2 éves (HR=0,44; 95% CI=0,24-0,83; p=0,011) túlélés esetében is szignifikánsnak és függetlennek mutatkozott. Többváltozós modelljeinket az összesített UNOS pontszámra adjusztáltuk. Következtetés: A szívátültetés komplex feladatai közül a donorgondozásnak kiemelkedő jelentősége van, ugyanis meghatározó szereppel bír a transzplantáció kimenetelére. Eredményeink alapján donorgondozás során megfontolandó lehet a pajzsmirigyhormon szubsztitúció, ugyanis a recipiens túlélését pozitívan befolyásolhatja.

Supervisor: Dr. Székely Andrea PhD, Semmelweis Egyetem, Városmajori Szív- és Érgyógyászati Klinika

Ganna Stepanova, SE, Theoretical and Translational Medicine

STRAIN-DEPENDENT COMPLEMENT EXPRESSION IN UUO murine MODEL OF RENAL FIBROSIS

Renal fibrosis develops in chronic kidney diseases and represents a significant health concern due to the exponentially increasing number of patients. However, progression rates vary among patients, presumably due to genetic variation. We have previously described the strain-dependent progression of renal fibrosis in TGF-beta transgenic mice, being C57B/6J (B6) mice resistant (Nephrol Dial Transplant Plus 2011, 4 (S2): 421-429). Yet, the events of early renal fibrosis development in various common laboratory mouse strains has not been simultaneously tested. Here we compared the rate of fibrotic development due to unilateral ureter obstrucion (UUO) in C57B/6J (B6), Balb/cJ (BalbC), CBA/J(CBA), and FVB/NJ (FVB) mice. Although renal complement-3 (C3) expression has been described in several experimental and human kidney diseases, we hypothesize that altered local complement expression might strongly depend on genetic variability of the mice. Six-week old B6, CBA, BalcC, and FVB male mice underwent UUO surgery of the left kidney (n=3-6/strain). Contralateral (unobstructed) kidneys served as controls. Mice were investigated 24 hours post-surgery for mRNA expressions and histological evaluation. Statistical significance was evaluated using a one-way analysis of variance (ANOVA). Level of significance was set to $p<0.05$. Although the histological evaluation did not show any apparent signs of fibrotic events at 24 hrs post-UUO surgery, C3 gene expression was induced in all strains to various degrees. As a marker of tubulointerstitial fibrosis, TGF-beta and CTGF mRNA expressions were increased in CBA and BalbC strain, respectively. Gene expressions for c-Fos and STAT3 also showed a different expression pattern being more elevated in the BalbC strain. Further investigation of individual pathways in each strain will follow. We conclude that genetic background determines the expression rate of renal complement system components, growth factor, and transcription factors in the UUO model of kidney fibrosis. Altered renal complement expression could, through paracrine/autocrine effects, influence chronic kidney disease progression.

Supervisor: Dr. Gabor Kokeny, none

Syed Rehan Iftikhar Bukhari, SE, Clinical Medicine; Dr. Berkes Istvan, SE

Clinical and experimental analysis of return to competition and repeat rupture for anterior cruciate ligament reconstructions in Hungarian elite athletes

ABSTRACT Background and Purpose: The occurrence of anterior cruciate ligament sports injuries has much increased due to an increased trend towards sports and fitness activities in population. ACL injury is most common in elite athletes involved in contact sports like soccer, rugby etc. ACL reconstruction surgery (ACLR) followed by an intensive rehabilitation program is recommended to restore normal knee function and to allow subsequent return back to sports after an ACL tear. ACL reconstruction is usually performed by using patellar tendon (PT) and hamstring tendon (HT) grafts, while the rehabilitation includes exercise and physiotherapy sessions aimed to improve the bone and soft tissue health; the combination of both treatments could bring athletes back to their previous level of sport activities. Early return to sports after an ACL injury is the biggest challenge for both athletes and their health care providers. Literature says that the average time frame for elite athletes to return back to sports after ACL tear is around 6-9 months, depending upon the expertise of the surgeon and the physiotherapist. Psychological factors also play an important role for the fast recovery. Studies reporting the role of rigorous rehabilitation after ACLR are emerging in the literature, but the data have not yet been comprehensively synthesized. The purpose of this systematic review is to provide a summary of current evidence to assist the rehabilitation professionals in recognizing, and addressing factors which may have been unrecognized in literature as having significant influence on the rehabilitation outcomes, mainly focussing on early return to sports after ACLR Methodology: A literature review has been conducted using PubMed, Medline, and Cochrane Database with results of peer-reviewed articles and randomized control trials published in English language using subject headings and free-text terminologies. Subject-specific search was based on the terms rehabilitation, early return to sport, and anterior cruciate ligament reconstruction. 72 relevant articles were selected, among which 40 highly relevant articles were reviewed and included in the study after the search and consultation with experts and rating of study quality. Result: Review of the current literature resulted in the understanding that a successful rehabilitation program for early return to sport after ACLR mainly works on five principal criteria, including psychological factors, performance or functional tests, neuromuscular strength and integration tests, time, and modifiable and non-modifiable risk factors. Conclusion: Challenges to successful return to previous level of sports activity following ACLR are multifactorial. Recent systematic review suggests an EBM paradigm shift in postoperative rehabilitation and return-to-sport training after ACLR that should be focused on the management of neuromuscular deficits in athletes that commonly persist after surgical reconstruction and standardized rehabilitation protocols post-surgery. Level of Evidence: Level 2b – Descriptive Review Keywords: Rehabilitation, Anterior cruciate ligament (ACL) injury, Anterior cruciate ligament reconstruction (ACLR), Return to sport, Evidence based guidelines.

Supervisor: Prof. Dr. Berkes Istvan, Semmelweis University

30 of January (Saturday)

Neurological sciences 10:30-12:00

Dr. Jason Sparks, PTE , Elméleti Orvostudományok D95, Neuroendokrinológia és Neurohisztológia

Investigation of systemic amyloid deposition in the absence of endogenous PACAP and its receptor

Introduction: PACAP (pituitary adenylate cyclase activating polypeptide) is a neuropeptide expressed in many organs that has been shown to have general cytoprotective, anti-inflammatory, and antiapoptotic effects. However, we only have little data on its role in the aging process. Aim: In our previous experiments, we observed accelerated systemic senile amyloid deposition in PACAP KO mice. The aim of the present experiment was to investigate the effect of partial PACAP deficiency in PACAP heterozygous (HZ) mice and PACAP receptor inefficiency in PAC1 receptor KO animals on amyloid deposits. Methods: In our experiment, we sampled more than 20 organs from PACAP HZ (n = 4) 12-18 months and 1-year-old PAC1 receptor wild (n = 9) and KO (n = 2) mice. Haematoxylin-eosin and Congo red staining were used to examine the amyloid deposits. The amyloid content of the organs was rated on a scale of 0 to 3 according to severity. Results: In our histopathological analysis, the same or more severe deposits were observed in HZ mice with partial PACAP deficiency as in PACAP KO mice. The organs most severely affected were the kidneys, spleen, liver, skin, thyroid, trachea, esophagus, and intestines. No signs of amyloid deposits were found in any of the PAC1 receptor WT and KO mice. Conclusions: Based on our results, we can say that systemic amyloidosis develops not only due to the complete but also partial absence of PACAP, in contrast, the lack of its receptor does not lead to pathological protein deposits.

Supervisor: Prof. Dr. Reglődi Dóra, PTE ÁOK Anatómiai Intézet

dr. Nádró Bíborka, DE, Egészségtudományok Doktori Iskola

AZ ALFA-LIPONSAV KEZELÉS EMELI A SZÉRUM PROGRANULIN SZINTJÉT DIABETES NEUROPATHIÁBAN

AZ ALFA-LIPONSAV KEZELÉS EMELI A SZÉRUM PROGRANULIN SZINTJÉT DIABETES NEUROPATHIÁBAN Nádró Bíborka Dr., (1) Sztanek Ferenc Dr., (1) Lőrincz Hajnalka Dr., (1) Szentpéteri Anita Dr., (1) Molnár Ágnes, (1) Seres Ildikó Dr., (1) Páll Dénes Prof. Dr., (1) Paragh György Prof. Dr., (1) Harangi Mariann Dr., (1) 1Debreceni Egyetem ÁOK Belgyógyászati Intézet, Anyagcsere Betegségek Tanszék Bevezetés: A progranulin (PGRN) egy számos sejttípus, köztük az idegsejtek és a leukociták által termelt glikoprotein. Pleiotróp növekedési faktor-szerű fehérjeként a PGRN részt vesz a sebgyógyulás és az idegsejt regeneráció folyamatában. Direkt módon kötődik a tumor nekrózis faktor-alfa (TNFα) receptor 1 és 2-höz, melyen keresztül anti-inflammatorikus hatást fejt ki. Az antioxidáns hatású alfa-liponsav (ALA) egy a diabeteses neuropathiában elterjedten alkalmazott gyógyszer, mely javítja az idegvezetést és csökkenti a neuropathiás fájdalmat. Kitűzött célok: Az ALA kezelés PRGN szintre kifejtett hatását korábban nem vizsgálták. Módszerek: Ötvennégy 2-es típusú diabeteses beteget vontunk be a vizsgálatba. A szérum PGRN, aszimmetrikus dimetilarginin (ADMA), ICAM-1, VCAM-1, oxidált LDL és TNFα szinteket ELISA módszerrel határoztuk meg. Az idegvezetési sebességet az áramérzet küszöbérték (current perception threshold; CPT) teszt segítségével mértük. Az autonóm funkció értékelésére a Ewing féle standard kardiovaszkuláris reflexteszt értékek (CAS) átlagát alkalmaztuk. Eredmények: A szérum PRGN szintje szignifikánsan emelkedett (33,3±7,2 vs. 36,2±7,9 ng/ml, $p<0,05$) a 6 hónapos, napi 600 mg ALA kezelés hatására, míg a szérum ADMA szintje szignifikáns mértékben csökkent. A CPT és CAS értékek szignifikáns mértékben javultak az ALA kezelés hatására. Szignifikáns negatív korrelációt találtunk az ADMA és PRGN szint változás között, míg szignifikáns pozitív korreláció igazolódott az ICAM-1 és VCAM-1, valamint a PRGN szintek között. Értékelés: Eredményeink alapján az ALA kezelés alkalmazása emeli az idegvezetési sebességet diabeteses neuropathiában. A szérum PRGN szint emelkedése az ALA kezelés endothel funkcióra, valamint neuron gyulladásra és regenerációra kifejtett kedvező hatására utalhat.

Supervisor: dr. Harangi Mariann, Debreceni Egyetem ÁOK Belgyógyászati Intézet, Anyagcsere Betegségek Tanszék

Horváth Dorottya, DE, Molekuláris Orvostudomány Doktori Iskola

Neuroimmune communication in the epidermal compartment of human skin

The immune system is strongly linked to the nervous system within the human organism, to the point that in many diseases they cannot be discussed as separate entities. Specifically, some inflammatory skin diseases such as atopic dermatitis and psoriasis have been reported to be intensified by stress, and, interestingly the skin lesions in these diseases sometimes resolve after nerve injury. The putative cause underlying this empirical observation is that sensory nerves secrete neuropeptides and other mediators that are important members of neuro-immune communication. Neuropeptides play a key role in skin immunity, the inflammation process, and wound healing. Inside the epidermis, the only dedicated resident immune cells under steady-state are the antigen-presenting cells called Langerhans cells (LCs). LCs are anatomically associated with neurons that produce Calcitonin Gene-Related Peptide (CGRP), supporting the hypothesis that neuropeptides possibly play a role in cutaneous inflammation. Previous reports have shown that CGRP reduces LC antigen-presentation to a Th1 clone while simultaneously, enhancing antigen-presentation for Th2 clones. Cytokine secretion after chicken ovalbumin challenge was shifted towards a Th2 profile since IL-4 was increased while IFNγ production was decreased. While these results are interesting, they were carried out in mouse models, therefore we decided to investigate the role of neuropeptides on human monocyte-derived LCs. In this project, we aim to discover the communication between LCs and neurons located in the skin. As a first, we utilized RNA sequencing from LCs samples from five donors and we detected the expression of neuropeptide receptor genes. We found a high expression of the CGRP receptor and its coreceptor RAMP1 and neurotensin receptor (SORT1) and the Brain Natriuretic peptide receptor (NPR1). These results were validated with q-PCR in monocyte-derived LCs. We also determined the effect of all three neuropeptides on the differentiation of LCs with flow cytometry and found that NPR1 activation had significantly increased the differentiation of LCs. Building on these results we plan to validate the expression of NPR1 with Western blot, as well as elucidating the signal transduction pathways initiated by these peptides.

Supervisor: Szöllősi Attila Gábor, Debreceni Egyetem Immunológiai Intézet

Keller Dávid, SE, Szentágothai János Idegtudományi Doktori Iskola

Involvement of a novel thalamo-preoptic neuronal pathway in social interaction

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Supervisor: Dobolyi Árpád, Department of Anatomy, Histology and Embryology, Semmelweis University

Patkó Evelin, PTE, Elméleti Orvostudományok Doktori Iskola

Investigation of PACAP1-38 eye-drops treatment in glaucoma

Patko E1, Szabo E1, Vaczy A1, Molitor D1, Csutak A2, Reglodi D1, Atlasz T1,3 1Dept. of Anatomy, MTA-TKI PACAP Research Group, University of Pecs, Medical School, Pecs, Hungary 2Dept. of Ophthalmology, University of Pecs, Medical School, Pecs, Hungary 3Dept. of Sportbiology, University of Pecs, Pecs, Hungary Introduction: Approximately 4.5 million people worldwide are blind due to glaucoma, which makes it the second most common cause of irreversible blindness. This progressive condition develops by the blockage of the aqueous humor drainage system leading to intraocular hypertension. Progression of the condition causes the loss of the retinal ganglion cells and their axons. PACAP has shown protection against retinal degenerations in several diseases, such as excitotoxicity, hypoxia, or diabetic retinopathy. Also, we proved that PACAP passes through ocular barriers and so, retinoprotection can be achieved also by eye drops. Accordingly, the aim of the present study was to examine the possible neuroprotective effects of topically administered (eye-drops) PACAP in glaucoma. Methods: We used 20 adult, male Sprague-Dawley rats for this study. Polystyrene microbeads (10µl, 10µm) were injected into the anterior chamber of the right eyes with 33G Hamilton syringe, while the control group received the same volume of PBS serving as a control. After the microbeads injections, we treated the eyes with PACAP1-38 eye-drops for 4 weeks. Intraocular pressure (IOP) was monitored with tonometer and retinal morphological changes were followed with Optical Coherence Tomography. Results: In the PACAP1-38 treated group we observed a lower IOP and less severe damage in the retinal thickness and GCL compared to the microbeads injected, control animals. Conclusion: Based on our results, we proved that the topical administration of PACAP is neuroprotective in glaucoma, providing the basis for future therapeutic administration. Supports: NKFIH129190, Bolyai Scholarship, NAP 2017-1.2.1-NKP-2017-00002, GINOP-2.3.2-15-2016-00050 “PEPSYS”, MTA-TKI 14016, EFOP-3.6.2-16-2017-00008, EFOP 3.6.1-16.2016.00004, Centre for neuroscience, PTE AOK-TANDEM 2019 Grant, “The role of neuro-inflammation in neurodegeneration: from molecules to clinics”. Higher Education Institutional Excellence Program of the Ministry of Human Capacities in Hungary, within the framework of the FIKPII. TUDFO/47138-1/2019-ITM FIKP program.

Supervisor: Dr. Atlasz Tamás, Pécsi Tudományegyetem Természettudományi Kar

Szenasi Annamaria, SE, Elméleti és Transzlációs orvostudományok

Traumatic brain injury impairs flow-dependent responses of middle cerebral arteries

Traumatic brain injury (TBI) is a major health problem worldwide due to its high mortality (35–40%), and morbidity (headache, brain edema, cognitive, behavioral, and communicative disabilities). Each year more than 1.7 million people in the United States and another 2.5 million patients in the European Union suffer TBI. Our previous studies showed that mechanotransduction of two hemodynamic factors, pressure and flow are importantly involved in the autoregulation of blood flow, which may become inefficient after TBI. Indeed, previously we have shown that TBI diminishes pressure-induced myogenic constriction. In the present study we hypothesized that TBI effects also flow-induced constrictor response of isolated cerebral arteries. TBI was induced in anaesthetized rats by Marmarou's weight drop model, then middle cerebral arteries (MCA) were isolated and transferred into pressure-flow chamber. Inflow and outflow pressures were controlled and measured. The internal diameter was continuously measured by a videomicroscopy equipped with a microangiometer and recorded digitally by PowerLab system (AD Instruments). Data are mean±SEM. The active (242,2±6,1 µm) and passive (277,9±8,8) diameters ($p<0.05$) of isolated MCA of control rats were obtained (n=39), indicating that a substantial myogenic tone developed in response to pressure (Δ-35,7 ±2,7 µm, $p<0.05$). Arachidonic acid (AA), after an initial dilation (+6±3 and +9±2,5 µm) elicited dose dependent constrictions (-9±2,1 and -20±3,2 µm) of MCA of control rats. Step increases in flow elicited gradual constrictions of MCA of control rats (from max.: 229,3±6,6 to 191±6 µm, Δ-38,3 ±0,6 µm, $p<0.05$), which was eliminated after TBI (from 227,3±14,1 to 227,4±13,3 µm). U46619, a thromboxane A2(TXA2)/prostaglandin H2 (PGH2) receptor (TP receptor) agonist elicited similar constrictions of MCA of control and TBI rats (max.: Δ-66,1 ±0,7 µm vs. Δ-49 ±4 µm) rats, which were eliminated by SQ 29,548 a TP receptor antagonist. CYP-450 metabolite 20-HETE elicited similar constrictions of MCA in control (Δ-18 ±0,9 µm and TBI rats (Δ-15 ±0,1 µm) which were eliminated by HET0016, an inhibitor of CYP-450. Paxilline (an inhibitor of potassium channel blocker) inhibited flow-induced constrictions of MCA of control (max.: Δ-37,5 ±3 µm vs. max.: Δ-2,8 ±1 µm, $p<0.05$), whereas did not affect responses of MCA after TBI (max.: Δ-0,1 ±1,6 µm vs. Δ-2,5 ±3 µm). These findings suggest that 1) flow-induced constrictor response of MCA depends on AA-metabolites acting on TP receptors, 2) constrictor responses to TP agonist remain intact after TBI, 3) thus TBI interferes primarily with the flow sensing mechanisms of the vascular wall, which 4) likely leads to diminished autoregulation of cerebral blood flow. OTKA:K108444

Supervisor: Koller Ákos, Institute of Translational Medicine, Faculty of Medicine; Department of Morphology and Physiology, Faculty of Health Sciences, Semmelweis University, Budapest, Hungary

Translational and interdisciplinal sciences 13:00-14:30

Beáta Szeitz, SE, Pathological Sciences

Addressing the clinical heterogeneity of small cell lung cancer through proteomics: Relationship between proteomic profiles and in vitro cell line characteristics.

Background: Small cell lung cancer (SCLC), representing ca. 15% of all lung cancers, is an especially aggressive malignancy, characterized by high metastatic potential and fast development of drug resistance. While personalized treatment of patients with lung adenocarcinoma is already part of clinical practice, SCLC is still treated as a single disease, although recent `omic` studies suggest the presence of biologically distinct subtypes. Just recently, a review article published by Rudin et. al (doi: 10.1038/s41568-019-0133-9) outlined a new model of SCLC subtypes defined by the relative gene expression of four key transcription factors (ASCL1, NEUROD1, POU2F3, YAP1). Objectives: To supplement the current information on SCLC heterogeneity, our aim is to further characterize the aforementioned molecular subtypes on the proteome level, by analyzing both the cellular proteome and the secretome of SCLC cell lines using mass spectrometry-based shotgun proteomics. Methods: 26 patient-derived cell lines were grown and characterized by defining their molecular subtypes (as proposed by Rudin et. al), their in vitro growth pattern and response to targeted therapy (Venetoclax). The harvested cell pellets and the secreted proteins were then subjected to nanoLC-MS/MS analysis using label-free quantification, followed by data pre-processing and statistical analyses. Results: The in-depth proteomic analysis identified 9566 proteins in the cell pellet and 6425 proteins in the secretome. Consensus clustering on the pre-processed data revealed a strong relationship between cellular proteomic profiles and molecular subtypes. ANOVA tests outlined proteins potentially involved in subtype-specific processes (1085 and 56 proteins with FDR < 0.05 in the pellet and secretome, respectively). Additionally, we have identified 125 and 19 proteins in the pellet and secretome, respectively, that could be associated with the cell line's response to Venetoclax therapy (correlation test FDR < 0.05). Conclusions: Our proteomic data provides further evidence of SCLC heterogeneity and is a valuable resource to identify novel subtype-specific diagnostic and prognostic markers. We believe that the results will contribute to the development of a new SCLC classification.

Supervisor: Dr. Melinda Rezeli, Division of Clinical Protein Science & Imaging, Department of Biomedical Engineering, Lund University, Lund, Sweden

Dr. Bartha Áron, SE, Patológiai Tudományok

TNMplot: egy webes alkalmazás a normál, tumoros és metasztatikus adatok transzkriptom szintű összehasonlítására

Bevezetés: Az elmúlt két évtizedben hatalmas mennyiségű, online is elérhető adatvált elérhetővé a rosszindulatú tumorok kutatásához. Ezek részben RNS szekvenálási adatokat (TCGA, TARGET, GTEx),részben gén chip alapú vizsgálatokat (NCBI-GEO) tartalmaznak. Jelenleg nincs olyan felhasználóbarát, könnyen elérhető platform, amely lehetővé teszi ezen adatbázisokon belül és ezek között a normál, tumoros és áttétes génexpressziós adatok nagy mintaszámon alapuló összehasonlítását. Célkitűzés: Egy olyan webes felület létrehozása, amelynek felhasználásával összemérhetőek a normál, tumoros és áttétes génexpressziós adatok. Módszerek: Munkánk során két génexpresszió mérésére alkalmas eszköz, a génchip, illetve az RNS szekvenálás adataira támaszkodtunk. A génchip adatokat az NCBI-GEO adatbázisban elérhető adatok alapján dolgoztuk fel, összesen 3180 vizsgálatot felhasználva, melyekből manuálisan választottuk ki a megfelelőnek ítélt mintákat, amelyeket a MAS5 algoritmus segítségével normalizáltunk. Az RNS szekvenálási adatokat a TCGA, a TARGET valamint a GTEx adatbázisaiból töltöttük le. A három adatbázisból összesen 23 418 minta szekvenálási adatát tudtuk felhasználni, amelyeket a DESeq2 algoritmus segítségével normalizáltunk. Az adatok kiértékeléséhez Mann-Whitney U vagy Kruskall-Wallis tesztet alkalmaztunk. Eredmények: A 3180 génchip alapú vizsgálatból összesen 33 520 minta került bevonásra, melyből 453 áttétes, 29 376 tumoros és 3691 normál típusú, összesen 38 féle szövet típusból. A TCGA adataiból 11010 mintát használtunk fel (394 áttétes, 9886 tumoros, 730 normál) amely 33 szövet típust reprezentál, a TARGET –ből 1193 minta került felhasználásra (1 áttétes, 1180 tumoros, 12 normál) 5 féle szövet típusból, míg a GTEx-ből 11 215 normál mintát sikerült kinyerni melyek 51 féle szövet típusba vannak sorolva. Összegzés:Munkánk során létrehoztunk egy adatbázist, mely összesen 56 938 minta transzkriptom-szintű adatait tartalmazza. A létrehozott web platform lehetővé teszi az adatbázis korlátlan felhasználását, amellyel elérhetővé válik a normál, tumoros és metasztatikus szövetek génexpresszió szintű összehasonlítása. Az oldal elérhető a https://tnmplot.com/ felületen.

Supervisor: Prof. Dr. Győrffy Balázs, Semmelweis Egyetem, Bioinformatika Tanszék

Longauer Beáta, PTE, Interdiszciplináris Orvostudományok Doktori Iskola

Az A22 hatása a MreB fehérje polimerizációjára

Háttér: A bakteriális fertőzések kezelésében egyre nagyobb problémát jelent a növekvő antibiotikum rezisztencia, a multirezisztenssé váló baktériumok. A jelenleg használt antibiotikumok jelentős részének a bakteriális sejtfal a támadási pontja. A sejtfal szintézis irányításában alapvető jelentősége van a citoszkeletonnak is. Az eukarióta aktin bakteriális megfelelője az MreB fehérje. Hiányában, hasonlóan a fentebb említett antibiotikumok okozta hatáshoz, a sejtek morfológiája megváltozik, sejtlízis következhet be. Az MreB funkció az A22 segítségével specifikusan gátolható. Ez a kis méretű molekula roncsolja a MreB citoszkeletont, ezzel morfológiai elváltozásokat és a kromoszómaszegregáció meghibásodását okozva. Irodalmi adatok arra utalnak, hogy az A22 kezelés hatására a MreB depolimerizálódik, ami a fehérje diffúz elhelyezkedését okozza a citoplazmában, és a pálcaalak illetve az életképesség elvesztéséhez vezet. Ezen kívül gátolja a sejtmozgást, a felületre való kitapadást, és a biofilmképződést, tehát mindazokat a folyamatokat, amik a bakteriális fertőzéshez szükségesek. Célkitűzés: Célom, hogy feltárjam az A22 MreB-re gyakorolt közvetlen és közvetett hatásait, leírjam, hogyan befolyásolja a MreB polimerizációját, depolimerizációját, hogyan változik, illetve változik-e a MreB lokalizációja a szer hatására. Módszerek: Kísérleteinkben fluoreszcens mikroszkópiai és spektroszkópiai mérések mellett szedimentációs teszteket és steady-state ATP-áz esszét is végeztünk. Eredmények: Polimerizációs tesztjeinkben A22 hatására a MreB polimerizációjának gyorsulását tapasztaltuk, amit a szedimentációs tesztek is megerősítettek, hiszen az A22 már polimerizáló só nélkül is indukálja a monomerek összeépülését. Viszont hatására csak kisebb fragmentumok képződnek, amit mikroszkópos vizsgálataink támasztanak alá. Az ATP-áz esszék viszont azt mutatják, hogy az A22 gátolja az ADP leválását a filamentumról. Következtetés: Az A22 a MreB fehérje polimerizációjának sebességét gyorsítja, viszont egy ADP kötött állapotot tart fent, meggátolva annak ATP-re való kicserélődését, és így a filamentum további növekedését. Ezáltal a baktériumsejtek nem képesek fenntartani a pálca alakot, nem tudják a MreB irányította sejtfunkciókat ellátni, és végső soron a sejtek életképtelenek lesznek.

Supervisor: Prof. Dr. Nyitrai Miklós, PTE-ÁOK Biofizikai Intézet

Nardos Abebe Werissa, DE, Health Sciences ; Peter Piko, DE

Impact of Genetic Factors on the Age of Onset for Type 2 Diabetes Mellitus in Addition to the Conventional Risk Factors

Background: It is generally accepted that the early detection of type 2 diabetes mellitus (T2DM) is important to prevent the development of complications and comorbidities, as well as premature death. The onset of type 2 diabetes mellitus results from a complex interplay between genetic, environmental, and lifestyle risk factors. Aims: Our study aims to evaluate the joint effect of T2DM associated single nucleotide polymorphisms (SNPs) on the age of onset for T2DM in combination with conventional risk factors (such as sex, body mass index (BMI), and TG/HDL-C ratio) in the Hungarian population. Methods: This study includes 881 T2DM patients (Case population) and 1415 samples from the Hungarian general population (HG). Twenty-three SNPs were tested on how they are associated with the age of onset for T2DM in the Case population and 12 of them with a certified effect on the age of T2DM onset were chosen for an optimized genetic risk score (GRS) analysis. Testing the validity of the GRS model developed was carried out on the HG population. Results: The GRS showed a significant association with the age of onset for T2DM ($\beta = -0.454$, $p = 0.001$) in the Case population, as well as among T2DM patients in the HG one ($\beta = -0.999$, $p = 0.003$) in the replication study. The higher the GRS, the earlier was the T2DM onset. Individuals with more than eight risk alleles will presumably be diabetic six and a half years earlier than those with less than four risk alleles. Conclusion: Our results suggest that there is a considerable genetic predisposition for the early onset of T2DM; therefore, in addition to conventional risk factors, GRS can be used as a tool for estimating the risk of the earlier onset of T2DM and stratifying populations at risk in order to define preventive interventions.

Supervisor: Prof.Dr. Roza Adany, University of Debrecen

Stier Ágnes, SE, Egészségtudományi Doktori Iskola; Dr Páldy Anna, NNK

Epidemiology of melanoma in Hungary: morbidity, mortality, and spatial distributions

This abstract is encrypted.

Supervisor: Dr. Páldy Anna, Nemzeti Népegészségügyi Központ

Uhljar Luca Éva, SZTE, Doctoral School of Pharmaceutical Sciences

Development of antibiotic-loaded electrospun nanofibers

Background: Nanofibrous mats have numerous advantages and are used in more and more fields. Electrospinning is the most cost-effective method for the production of nanofibers. Nanofibers can be considered as drug delivery systems with various active pharmaceutical ingredients incorporated. Ciprofloxacin is a worldwide-used, broad-spectrum antibiotic with low water-solubility and therefore its bioavailability is poor. Objective: Nanofibers were fabricated with the polymer, polyvinylpyrrolidone (PVP) to earn higher solubility and better bioavailability. Methods: For the production, needle and needleless electrospinning methods were used. The fiber size and morphology were observed by scanning electron microscopy (SEM). Physicochemical properties were characterized by X-ray powder diffraction (XRPD), differential scanning calorimeter (DSC), and Fourier-transform infrared spectroscopy (FTIR). Results: The results proved the amorphous state of the CIP inside the nanofibrous mats. The solubility, in vitro dissolution rate, and in vitro diffusion were remarkably higher in the case of the nanofibers compared with the CIP powder or the physical mixture of the two components. The solubility of the CIP demonstrated a significant increase both in water (pH 6.3) and phosphate buffer solution (pH 7.4). In addition, fast-dissolving formulations were developed. Additionally, in vitro diffusion from pH 6.8 to pH 7.4 also showed a notable increase. Conclusion: The solubility and in vitro diffusion of CIP increased by formulated it nanofibers. Fast-dissolving formulations were developed which can be further investigated. Acknowledgments: This project was supported by the Gedeon Richter's Talentum Foundation, Gedeon Richter Plc. Also, the Ministry of Human Capacities, Hungary grant, TKP-2020, and EFOP 3.6.3-VEKOP-16-2017-00009 are acknowledged.

Supervisor: Rita Ambrus, Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged

Psychology sciences 14:30-16:00

Mittly Veronika, SE, Mentális Egészségtudományok Doktori Iskola

Állatasszisztált terápiák lehetséges szerepe a klinikai javulásban és az életminőség javításában

Bevezetés: Bármely mozgásszervi vagy mentális betegség jelentős biopszichoszociális terhet ró a betegekre, amely az életminőség romlását is magában hordozza. Ennek mérséklésében lehet segítségünkre a betegek rehabilitációja ill. a kezelés során alkalmazott állatasszisztált terápia foglalkozások, amely habár nemzetközileg igen elterjedt és elfogadott terápiás lehetőség, Magyarországon még megerősítésre szorul a kiemelkedő szerepe a betegek gyógyulásában. Betegek és módszerek: Prospektív, randomizált, kontrollált vizsgálat során a Dél-pesti Centrumkórház Rehabilitációs Centrum tervezetten 120 betege részesül min. 3 héten át tartó, heti 1 órás kutyaterápiás foglalkozásban 2018 októbere óta. Az első kutyaterápia előtt illetve az utolsó foglakozás után betegeink egy átfogó pszichés és fizikális állapotukat felmérő kérdőívcsomagot töltenek ki. A terápia során a csoportösszetételre reflektálva állítjuk össze a feladatokat, amelyeknek célja a mozgásfejlesztés, kognitív funkciófejlesztés és pszichés támogatás. Eredmények: A beavatkozás hatására eddigi szignifikáns eredményeink alapján a betegek életminősége szubjektív megítélése javult, a betegségükkel való megküzdés az állatasszisztált terápia nyújtotta kapaszkodókkal könnyedebbé vált, motivációjuk erősödött a rehabilitációs programban. Mindemellett a terápiás kutyával történő foglalkozások valóban mérsékelik a betegek állapot szorongását ill. pozitív hatást gyakorol mindennapjaikra. Továbbá megfigyelésünk szerint az állatasszisztált terápia megfelelően beilleszthető a betegek rehabilitációs programjába kiegészítve az egyéb kezelések hatását. Következtetések: Az állatasszisztált terápiának, mint kiegészítő kezelésnek helye van a rehabilitációban, javasolt megfontolni az egészségügyben történő széleskörű alkalmazását. Folytatva kutatásunkat fő célunk a fentiek statisztikai módszerekkel történő igazolása is. Kulcsszavak: rehabilitáció, állatasszisztált intervenció, kutyaterápia, életminőség, megküzdés

Supervisor: Purebl György, Semmelweis Egyetem Magatartástudományi Intézet

Dr. Módis László, DE, Egészségtudományok Doktori Iskola

Biopsychosocial and spiritual investigations in primary Sjögren syndrome

Primary Sjögren syndrome (pSS) is an autoimmune exocrinopathy, characterized by the lymphocytic infiltration of the salivary and lacrimal glands. PSS is the most frequent systemic autoimmune disease besides rheumatoid arthritis, affecting 0.3–3% of the population. The main clinical hallmarks of the disease are particular antibody profile, sicca symptoms and systemic manifestations. Growing evidence suggest that beyond the biological traits of the disease psychological burden is present, moreover, it may have a serious effect on the disease course. Our purpose in the research is to identify certain psychological and mental properties, which may pave the way to understand the impact of the mental health on pSS and vice versa. We also aim to reveal correlations between the data gained through medical treatment (e.g. antibody levels) and the psychological phenomena. Accordingly, social and spiritual questionnaires are also involved in the research and the correlation profile mentioned above. The experiment happens through questionnaires and inventories. Among psychological variables we wish to establish results of the personality profile in pSS with the Temperament and Character Inventory, which lets us conclude to certain neurobiological background of the disorder (neurotransmission). Furthermore, we obtain information about depression, anxiety, self-esteem and the body image of pSS patients. Adding the social and spiritual phenomenal dimension, data about the social support and spiritual transcendence of the patients are also going to be collected. Hence, the image about pSS could be more complex in correspondence to the biopsychosocial model of the WHO completed with a spiritual dimension. This may lead to holistic therapeutic approach hopefully not only in pSS, but in further rheumatic and autoimmune disorders in general.

Supervisor: Prof. Dr. Bugán Antal, DE ÁOK Magatartástudományi Intézet

Dr. Erdős Sándor, SE, Rácz Károly Klinikai orvostudományok

Virtuális valóság hatása pszichológiai és fiziológiai változókra kemoterápiában részesülő gyermekeknél

Bevezetés A gyermekkori daganatos betegségek kezelése során az alapbetegség elleni harc mellett fontos szerepe van a gyermekek általános jóllétét célzó beavatkozásoknak. A virtuális valóság (VR) egy 360°-os mesterséges környezet, melynek immerzív hatását egyre több vizsgálatban használják fel az orvostudományban. Pilot vizsgálatunkban a VR beilleszthetőségét vizsgáltuk a gyermekonkológiai centrumok mindennapjaiba illetve a VR pszichológiai és fiziológiai hatását térképeztük fel kemoterápiás kezelés közben. Módszerek A kutatásunkba 10-18 év közötti, kemoterápiás kezelést kapó gyerekonkológiai betegeket vontunk be (n=23). A kísérlet során ismételt méréses elrendezést alkalmaztunk, ahol minden gyermek részt vett mind a kísérleti (VR), mind a kontroll kondícióban. A vizsgálatban pszichológiai és fiziológiai változókat (szívfrekvencia, vérnyomás, bőrimpedencia - EDA) mértünk a foglalkozás előtt és után közvetlenül. A pszichológiai változókat egy egyedileg összeállított, 11-pontos Likert skálákat tartalmazó kérdőívvel vizsgáltuk, ami olyan változókat mért, mint a hangulat, szorongás, türelem. A gyermekek a VR foglalkozáson Gear VR/Oculus Go eszközön futó Night Sky játékkal játszhattak 20-30 percen keresztül, míg a kontroll kondícióban egy mobil applikációval játszhattak. A statisztikai elemzés során lineáris kevert modellezést alkalmaztunk. Eredmények A VR foglalkozás szignifikánsan jobban javította a gyermekek hangulatát a kontroll kondícióhoz képest ($p = 0,042$). Továbbá mindkét kondíció során szignifikánsan csökkent a szorongás ($p=0,017$), azonban nem találtunk szignifikáns interakciós hatást az alkalom és a kondíció között. A türelem illetve hányinger esetében nem találtunk szignifikáns hatást. Egy gyerek esetében észleltük kinetózis tüneteit. A fiziológiai változók esetén nem találtunk szignifikáns interakciós hatást. Következtetések A VR felhasználhatóságát illetően kedvező tapasztalatunk volt mind a családok, mind a személyzet részéről. Eredményeink alapján a VR kedvezőbb hatással van a gyermekek hangulatára, mint egy mobilapplikáció. Annak megállapítására, hogy ez mennyiben tulajdonítható a VR újszerűségének vagy specifikus tulajdonságainak további vizsgálatok szükségesek, azonban addig is biztonságosan használható a gyermekek kezelése során.

Supervisor: Dr. Horváth Klára, II. Sz. Gyermekgyógyászati Klinika

Matuz András, PTE, Elméleti Orvostudományok Doktori Iskola

Estimating and detecting mental fatigue based on heart-rate variability: a machine learning approach

Background: Rapid detection of mental fatigue (MF) as well as reliable predictions regarding its consequences have significant implications for medical work and safety monitoring. Previous studies suggest that heart-rate variability (HRV) is a potential biomarker of MF. Objective: We aimed to effectively detect MF and predict its subjective consequences via machine learning algorithms trained on HRV data. Methods: The data of three MF experiments (n = 85) utilizing different cognitive tasks lasting approx. 1-2 hours were analyzed. In each experiment, 37 HRV indices were calculated for the pre-experiment resting interval and two task-related 4-min intervals: the first 4-min of the tasks („Non-fatigued" state) and the last 4-min of the tasks („Fatigued state"). Supervised classification methods with 5-fold stratified cross-validation (5-CV) were trained on task-related HRV data to detect MF. In addition, various regression models based on pre-experiment resting HRV were applied to predict the level of subjective fatigue induced by the cognitive tasks. Results: Using the best set of features, the highest classification performance was achieved by logistic regression (sensitivity = 81.1%, AUC = .86). The best model to predict post-experiment subjective fatigue was the lasso regression model (5-CV R2 of .33, permutation test $p < .001$). Conclusions: In line with previous studies, we found that MF detection with machine learning based on HRV data is effective. In addition, our results suggest that pre-experiment HRV data could be used to predict the potential increase in subjective fatigue induced by prolonged task performance. Acknowledgements: Supported by the ÚNKP-20-3-II-PTE-876 New National Excellence Program of the Ministry for Innovation and Technology and the National Research, Development and Innovation Office (NKFIH K120012).

Supervisor: Csathó Árpád, Department of Behavioural Sciences

Oláh Barnabás, DE, Egészségtudományok Doktori Iskola; Rádi Bence Márk, Debreceni Egyetem

Understanding students' perspectives on interventions to improve mental health in medical school: a qualitative study

Background: Multiple evidence suggests that medical students have been at increased risk of developing mental health problems. Setting-based innovations to improve the mental health of medical student could improve their resilience as future doctors, hereby increasing the quality of future care in the health care system. While there has been an abundance of quantitative studies on student mental health, their in-depth perspective on the issue has been of much less interest. Objectives: This study aims to improve our understanding of the perspectives of both Hungarian and foreign medical students of the University of Debrecen on the major sources of student anguish in a hierarchical manner, stratifying those into organizational, community and individual level problems upon which interventions can be designed. Methods: Semi-structured interviews were conducted with 13 Hungarian and 13 foreign medical students at years I-VI in four focus groups. Interviews were audio-recorded, transcribed and content-analyzed by two independent coders using NVivo and manual checking. The total length of the recording was 480 minutes, the total word count of the interviews was 62,499 words. Results: Organizational level problems were related to standards in examination (clearer requirements, scheduling, standardization, objectivity), the quality of teaching (study materials, resources, teacher's enthusiasm, practical education), and systematic information on studies. Foreign students suggested teacher-led mentoring program for freshmen, community-based interventions like events to facilitate integration, and expressed more openness towards participating in self-help groups, than Hungarians did. Individual level problems consisted of students not being properly prepared and helped to adapt to university requirements. They expressed their need for early availability of study skills training, time and stress management courses, yet another desire was expressed for better career guidance. Conclusions: A wide range of interventions would be needed to improve the mental health of medical students, primarily at the organizational level to help them proceed with their studies. The need for organized social support and help to improve individual skills for studying was also uncovered. Keywords: medical students, well-being, mental health interventions, focus group SUPPORTED BY THE ÚNKP-20-3 NEW NATIONAL EXCELLENCE PROGRAM OF THE MINISTRY FOR INNOVATION AND TECHNOLOGY FROM THE SOURCE OF THE NATIONAL RESEARCH, DEVELOPMENT AND INNOVATION FUND.

Supervisor: Dr. Kósa Karolina, DE-ÁOK Magatartástudományi Intézet

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Páciens elégedettség értékelése az egészségügyi ellátással kapcsolatban - Kvalitatív tartalomelemzés

Háttér: Az egészségügyi és kórházi ellátással kapcsolatos online blogok és vélemények száma az utóbbi években folyamatosan növekszik. A szociális médián megjelenő panaszok fontos forrása lehet a páciens elégedettségét befolyásoló, egészségügyi ellátásban megjelenő problémák és orvosi hibák azonosításában. A többféle információforrás azonosítása és vizsgálata implikációkat jelenthet a kórházi ellátás és páciens elégedettségének javítására. Célkitűzés: A kutatás célja egy interneten található online fórumhoz - blog formájában - beérkezett, egészségügyi tapasztalatokatban rejlő problémák azonosítása és értékelése. Donabedian egészségügyi ellátás minőségét leíró keretrendszere került felhasználásra a tartalomelemzés során felmerülő témák azonosítására. Módszerek: Egy egészségügyi elltással kapcsolatos, páciens tapasztalait megosztó interneten található fórum adatait nyertük a kvalitatív tartalomelemzéshez. Az összesen 1662 blog közül random mintavétellel 346 blog került kiválasztásra és analizálásra. A korábbi szakirodalommal összhangban, egy kódrendszer került kialakításra a panaszok tartalmainak analizálása érdekében. Eredmények: A blogok legnagyobb része egy specifikus tapasztalatról (92,8%) számolt be. Az írók 90,2%-a volt elégedetlen és az írások 53,46%-a páciensektől származott. A páciensek 60,48%-a azonosított egy specifikus klinikát vagy kórházi osztályt és a panaszok jelentős része orvoshoz kapcsolódott (78,3%). A Donabedian modellben, a struktúra és folyamat dimenzióban lévő emberi faktorok, az ellátáshoz való hozzáférés (36,41%) és kivizsgáláshoz (30,34%) kötődő problémák jelentek meg leggyakrabban a panaszokban. Az eredmények dimenzió a panaszok 53.75%-ban került azonosításra. Következtetés: A struktúra, folyamat és eredmények dimenzióra bontott Donabedian modell megfelelően azonosította a páciens elégedetlenségében rejlő problémákat. Ezeknek a minőségi indikátoroknak a monitorozása és fejlesztése hozzájárulhat az egészségügyi ellátás javulásához, a páciens elégedettségének növeléséhez és az erőforrások megfelelő allokálásához.

Supervisor: Prof. Dr. Kósa karolina, DE ÁOK Magatartástudományi Intézet

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Pesticide Health Risks Perception, Knowledge and their Utilization and Management among Extension Officers in Hungary and Ethiopia: A comparative study

Background: Intensive use of pesticides threatens human health worldwide caused several types of acute and chronic diseases by disrupting normal endocrine function and immune systems in the body. Objective: This study aimed to investigate pesticide use, knowledge, and perception of health risks and their management among extension officers providing advisory service for farmers in Hungary and Ethiopia. Methods: A cross-sectional study was conducted using a structured survey questionnaire. Descriptive analysis and multivariable ordinal logistic regression model fitted to control confounding factors and ascertain the independent predictors of outcome variables was applied in SPSS Version 25. Crude and adjusted odds ratios (AORs) were calculated to assess the strength of association between outcome and explanatory variables. The significance of statistical associations was accepted at 5% significance level. Results: A total of 326 respondents (92 from Hungary and 234 from Ethiopia) have participated in the study. Malathion (85%) and glyphosate (97%) were the most frequently reported pesticides from Ethiopian and Hungarian officers, respectively. Based on the WHO classification, 70% of pesticides from Ethiopia, and 60% reported from Hungarian were moderately hazardous. The study indicated that 92% of Hungarian and 66% of Ethiopian respondents had good knowledge of pesticide products, respectively. Forty-seven percent and 7% of Hungarian plus 77% and 41%of Ethiopian respondents deemed pesticides risky and experienced pesticide poisoning among farmers in the past, respectively. In multivariate analysis, we found that officers' nationality was negatively and significantly associated with perceived health risk of pesticide (AOR=0.49, 95%Cl: 0.27-0.89, $p<0.05$), poor knowledge about pesticide (AOR=0.15, 95%Cl: 0.06-0.40, $p<0.001$) and experience of pesticide poisoning among agricultural workers (AOR=0.08, 95%Cl: 0.03-0.22, $p<0.001$). Conclusions: A considerable proportion of extension officers reported that there is unsafe use of pesticides, poor utilization of PPE by farmers, inadequate training and pesticides risk-aware attitude is still insufficient. This impairs the quality of advisory service provided by them and a threat to pesticide applicators and community.

Supervisor: Balázs Ádám, University of debrecen

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