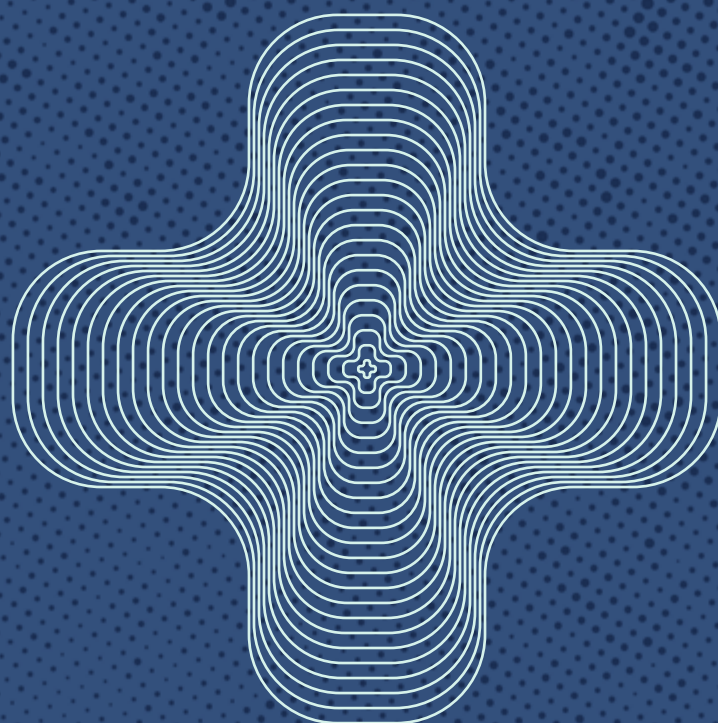


**MED+PECS**

# BOOK OF ABSTRACTS



**MedPECS – Medical Conference  
for PhD Students and  
Experts of Clinical Sciences**

20 May 2023  
Szentágotthai Research Centre

Medical Conference for PhD Students  
and Experts of Clinical Sciences  
20th of May 2023

Book of Abstracts



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# Presidential Welcome Speech

The Medical Conference for PhD Students and Experts of Clinical Sciences (MEDPECS2023) held in Pécs at 20th May, 2023 is the result of a trustful collaboration of the Doctoral Student Association and the Szentágotthai János Research Centre. It is an event designed to empower the next generation of medical researchers and cultivate their passion for scientific exploration. This conference serves as a platform for young scholars to showcase their innovative research, exchange ideas, and forge connections with fellow peers and renowned experts in the field. This conference aims to nurture the intellectual curiosity and scientific acumen of PhD students in medical science. By providing a supportive environment, we encourage these budding researchers to push the boundaries of knowledge, challenge prevailing notions, and contribute to advancements that shape the future of healthcare.

Throughout the conference, participants had the opportunity to present their research findings through oral presentations and interactive poster sessions and I hope our keynote lecture also offered invaluable guidance and inspiration to help PhD students navigate their academic journey.

In addition to the scientific program, I sincerely believe that the networking sessions at our conference was able to facilitate meaningful connections among peers and mentors, fostering collaboration and future research opportunities.

I extend a warm welcome to all the talented PhD students who joined us for this exceptional gathering, and I hope they will join us next year also.



**Márton BALOGH**

president

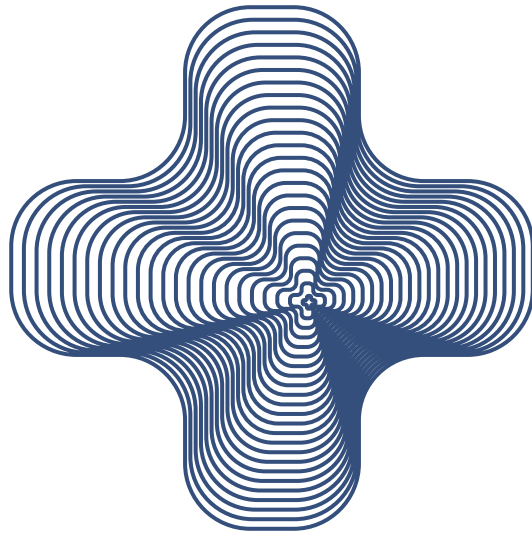
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# COVID-19





## Assessment of COVID-19 Antibody Response Using Magnetic Bead-Coupled S-Protein in Flow Cytometry

Roland Hetenyi<sup>1,2,3</sup>, Daniel Hanna<sup>1,2,3</sup>, Krisztián Bányai<sup>4</sup>, Janos Nacsa<sup>3</sup>, Balázs A. Somogyi<sup>4</sup>, Ferenc Jakab<sup>4</sup>, Edina Szabó-Meleg<sup>2,5</sup>

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**Introduction:** The COVID-19 pandemic caused by the SARS-CoV-2 virus has resulted in a global health crisis. The development of effective diagnostic tools to assess the immune response is crucial in controlling the spread of the virus or assessing vaccine efficacy.[1] One such approach involves the use of magnetic bead-coupled S-protein in flow cytometry to assess the COVID-19 antibody response. Magnetic bead-based flow cytometry offers advantages over ELISA, including increased sensitivity and specificity, reduced background noise, and quantitative analysis of the antibody response. [2]

**Aim:** To evaluate the use of magnetic bead-coupled S-protein in flow cytometry as a comparative approach to ELISA for the assessment of COVID-19 antibody response.

**Methods:** Magnetic beads were coupled with S-protein and incubated with serum samples to capture COVID-19-specific antibodies, and flow cytometry was used for quantitative analysis of the resulting bead-coupled S-protein-antibody complexes. Results were compared with those obtained from commercial anti-SARS-CoV-2 QuantiVac IgG ELISA diagnostic assays.

**Results:** Magnetic bead-coupled S-protein in flow cytometry offers comparable detection of COVID-19-specific antibodies to standard anti-SARS-CoV-2 ELISA assays, detecting antibodies in 1:100 and 1:400 serum dilutions with high agreement to commercially available diagnostic assays.

**Conclusions:** The use of magnetic bead-coupled S-protein in flow cytometry represents a novel and effective approach for the assessment of COVID-19 antibody response. This approach offers high sensitivity and specificity, making it a valuable tool in the development of diagnostic assays and in assessing the immune response to COVID-19.

### References:

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2. Xiangyu Yao, et al., A highly sensitive bead-based flow cytometric competitive binding assay to detect SARS-CoV-2 neutralizing antibody activity. *Frontiers in Immunology*, 2022. 13.

**Acknowledgment:** The research was performed in collaboration with the National Laboratory of Virology and Flow Cytometry Core Facility of University of Pécs. The project 2020-2.1.1-ED-2020-00100 and RRF-2.3.1-21-2022-00010 was sponsored by the National Research, Development, and Innovation Office of Hungary.

*Keywords:* COVID-19, antibody, S-protein, magnetic bead, flow cytometry

## **SARS-CoV-2 induces targeted apoptosis of monocytes in human PBMC**

**Daniel Hanna<sup>1,2,3</sup>, Roland Hetenyi<sup>1,2,3</sup>, Janos Nacsa<sup>3</sup>, Balázs A. Somogyi<sup>4</sup>, Ferenc Jakab<sup>4</sup>, Edina Szabó-Meleg<sup>2,5</sup>, Krisztián Bányai<sup>4</sup>**

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**Introduction:** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus responsible for the coronavirus disease 2019 (COVID-19) pandemic. SARS-CoV-2 primarily targets the respiratory system, but it can also cause systemic inflammation and affect multiple organs. Monocytes are a type of white blood cell that plays a critical role in the immune response, including the detection and elimination of viruses. Recent studies have shown that SARS-CoV-2 can induce programmed cell death, or apoptosis, specifically in monocytes present in human peripheral blood mononuclear cells (PBMCs). Understanding the mechanisms of selective monocyte death by SARS-CoV-2 could provide insights into the pathogenesis of COVID-19 and lead to the development of novel therapeutic strategies.

**Aim:** While investigating the effects of SARS-CoV-2 on human PBMCs, we observed a byproduct of the virus's ability to induce targeted apoptosis of monocytes. We aimed to further explore this phenomenon.

**Methods:** PBMCs obtained from healthy human donors were isolated and incubated with UV-inactivated SARS-CoV-2 at varying concentrations, using both purified and unpurified forms of the inactivated virus. The induction of apoptosis specifically in monocytes was evaluated using flow cytometry and microscopy.

**Results:** Our flow cytometric and microscopic findings demonstrate that high viral titers of purified, UV-inactivated SARS-CoV-2 induce targeted apoptosis of monocytes in human PBMCs. In contrast, unpurified UV-inactivated virus induced apoptosis in every cell in whole blood.

**Conclusions:** Unpurified SARS-CoV-2 isolates are not suitable for downstream immunological experiments with live human blood cells. Purified SARS-CoV-2 induces a concentration (virus titer) dependent destruction of monocytes in PBMC. Selective monocyte death induced by purified UV-inactivated SARS-CoV-2 may contribute to COVID-19 pathogenesis, highlighting the importance of monocytes in the immune response. Further studies are required to fully understand the implications of selective monocyte death in the context of COVID-19.

**Acknowledgment:** The research was performed in collaboration with the National Virology Laboratory, and Flow Cytometry Core Facility, University of Pécs. The project 2020-2.1.1-ED-2020-00100 and RRF-2.3.1-21-2022-00010 was sponsored by the National Research, Development, and Innovation Office of Hungary.

*Keywords: SARS-CoV-2, Monocyte, PBMC, apoptosis, cell death*



## The Alterations of Serum N-glycome in Response to SARS-CoV-2 Vaccination

Dalma Dojcsák<sup>1</sup>, Csaba Váradi<sup>1</sup>, Zsófia Kardos<sup>2</sup>, Miklós Szabó<sup>2</sup>, Csaba Oláh<sup>2</sup>, Zsolt Körömi<sup>2</sup>, Béla Viskolcz<sup>1</sup>

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**Introduction:** The global pandemic of coronavirus disease 2019 (COVID-19) has affected millions of people worldwide and caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). One of the main strategies to control the pandemic, was the use of vaccination against the SARS-CoV-2 virus, reducing the duration of infection time.

Glycosylation is a chemical modification of proteins by the covalent attachment of carbohydrate chains after translation, serving as an important signal in the quality control of protein synthesis. Recent studies suggest that serum glycosylation can be significantly altered in patients after SARS-CoV-2 infection and the analysis of serum N-glycome might be significant in the surveillance of COVID-19.

Glycans are complex carbohydrates consisting of multiple monosaccharide units with no fluorophore group requiring multistep sample preparation and high-resolution separation methods for their sensitive and reliable quantitative analysis. One of the most efficient separation technique in quantitative glycomics is the ultra-performance liquid chromatography (UPLC) combined with fluorescence and/or mass-spectrometric detection.

**Aim:** Our goal was analysis of clinical samples to identify potential glycosylation-based alterations in serum samples of SARS-CoV-2 infected and/or mRNA vaccinated patients using ultra-high-performance liquid chromatography (UHPLC).

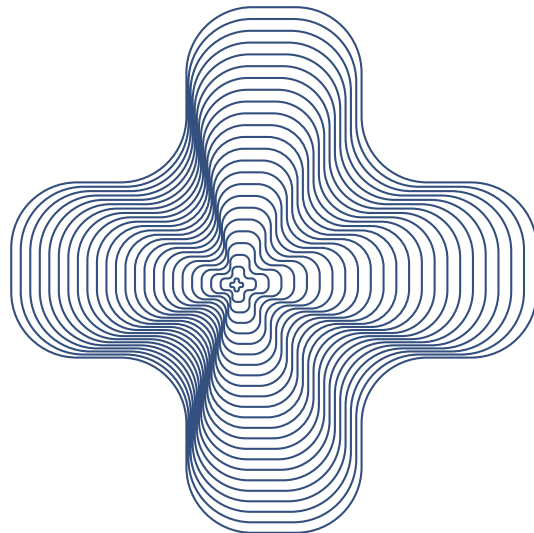
**Methods:** The anti-SARS-CoV-2 IgG positivity of the samples was determined across the patient groups by anti-SARS-CoV-2 IgG ELISA immunoassay. Glycans from the serum samples were released by PNGase F digestion based deglycosylation followed via fluorescent derivatization and hydrophilic solid phase extraction. Each individual patient samples were relatively quantified by UHPLC with fluorescence detection.

**Results:** Our results suggest the increase of non-fucosylated-sialylated glycan species in both post-COVID and post-Vaccinated patients. In case of the fucosylated and sialylated structures there was no significant increase in response to vaccination while higher fucosylation values were found in post-COVID patients.

**Conclusions:** In this study, total serum N-glycome was analyzed in patients after SARS-CoV-2 infection and/or after mRNA vaccination in order to identify potential glycosylation based alterations using hydrophilic-interaction liquid chromatography.

*Keywords: SARS-CoV-2, serum protein glycosylation, liquid chromatography*

# HEALTH SCIENCES



## Treatment outcomes and mortality of patients with tuberculosis at DOTS facilities in Abuja, Nigeria: a 2 years retrospective study

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**Background:** Millions of people are affected by Mycobacterium tuberculosis (MTB) worldwide despite being preventable and curable. Clinical and public health benefits of successful Tuberculosis (TB) therapy include decreased transmission, complications, and patient death. TB is known to have killed millions of people globally, making it the most contagious disease in the world. One of the ways to comprehend the care TB patients received from healthcare providers at the course of treatment is to monitor the outcome of the treatment TB patients receive. During the investigative period, factors associated with successful treatment of tuberculosis and death rate was investigated among those who received treatment for two years in the capital city of Nigeria.

**Methods:** We constructed a 2 years retrospective cohort of patients enrolled on TB treatment using data from 11 randomly selected tuberculosis facilities registers from all levels of healthcare. In order to assess the relationship between categorical variables, descriptive statistics were provided on frequency tables and inferential statistics with chi-square were used to measure the TB treatment outcomes. The limit for significance was 5%. A difference was deemed significant when it reached p value of 0.05.

**Results:** Out of a total of 928 records of patients retrieved in the process all of whom have been diagnosed of Pulmonary TB(PTB), only 921 had complete information. Outcomes of treatment are as follows: 338(36.7%) cured, 233(25.3%) treatment completed, 12(1.3%) treatment failed, 44(4.8%) died, 123 (13.4%) loss to follow up, 117(12.7%) not evaluated, 8(0.9%) removed from register and 46(5.0%) transferred. Of the 921 TB patients who had treatment outcomes, 571(62.0%) had successful outcomes. Analysis base on health facility, site of disease, AFB5, AFB month6, gene expert, HIV status and institution are statistically significant at 5% confidence level, while sex, age, treatment regimen, referred, registration group, AFB (month2/3), HIV care and support are not significant.

According to the baseline characteristics of TB patients by the survival status of being alive or dying, the following characteristics are found to be significant: referred and HIV status, whereas year, sex, age, health facility, treatment plan, site of the disease, registration group, AFB(month5), AFB(month6), gene expert.

*Keywords: Tuberculosis, treatment outcomes, DOTS, survival rate, Nigeria*

## Significance of postural parameters in shoulder pain in case of adolescence swimmers

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**Introduction:** The typical 'swimmer's posture' is described in the literature as being characterised mainly by sagittal plane deviations, which, in addition to the protrusion of the head and shoulders, is characterised by increased thoracic kyphosis. In this sport, the most common musculoskeletal complaint is shoulder pain, one of the aetiological factors of which is poor posture. In our study, we aimed to assess postural abnormalities in adolescence swimmers and to investigate the effects of changes in our implemented prevention program on the occurrence of pain.

**Materials and methods:** The study involved swimmers aged 12-19 years (n=54), divided into 2 groups (intervention and control group). Posture was analysed using the PostureScreen mobile application, which allowed us to describe the participants' posture along objective parameters (TAA - total anterior angulation, TLA - total lateral angulation, SF - scull flexion, CVA - cervicovertebral angulation, ATK - angle of thoracic kyphosis). The test was performed at the beginning and end of the programme. The exercise programme used consisted of progressively sequential exercises, which lasted 3x8 weeks. The presence and intensity of pain was assessed using the Swimmers Functional Pain Scale (SFPS). Statistical analysis significance level  $p < 0.05$

**Results:** There was no difference between the anthropometric and training load values of the two groups. The posture scores of the group that participated in the exercise program showed a significant improvement compared to the control group ( $p < 0.05$ ). A significant change in pain scores was also detected between the two groups ( $p < 0.05$ ). Pain scores of the intervention group decreased from 71.8% to 34.3%, while shoulder pain scores of the control group only changed from 77.2% to 72.7%.

**Conclusion:** According to international researches, an intervention programme can improve swimmers' posture and reduce shoulder pain at the same training load. However, very few studies have investigated total body posture and its changes in relation to an intervention programme in the context of the swimmer's shoulder. Detailed research into the relationship between postural anomalies and injury incidence provides an opportunity to explore algorithms which could support more targeted and effective work by sport practitioners. Swimming without pain may be particularly important for athletes, as a key elements of a long-term athletic career.

*Keywords: swimming, shoulder pain, body posture*

## Changes in Lipid Profile and Glucose marker after 10 weeks of Yoga Intervention among Medicine Students: GSY Study

Shalini Chauhan<sup>1,2</sup>, Ann Mary Babu<sup>1</sup>, Sachal Sadiq Bokhari<sup>3</sup>, Carla Schreiber<sup>4</sup>, Dr Zsófia Nagy<sup>1,5</sup>, Dr Viktoria Prémusz<sup>1,6</sup>, Dr István Karsai<sup>1,2</sup>

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**Introduction:** Evidence states that generally, medical students have a high level of stress. Studies have valid explanations to show the challenges faced by education institutions to provide specific students with emotional support and different stress management techniques. Increased level of stress can lead to increase level of glucose in the body, and hence increase level of glucose can lead to cardiovascular risk. One of the successful techniques for achieving relaxation by breathing and postural exercise is Yoga. Yoga is the most effective anxiolytic tool for centuries in India.

**Aim:** The current study aimed to highlight the effect of a 10-week yoga intervention on the lipid profile and glucose markers in blood samples of medical students.

**Methods:** Medical students of the University of Pécs (N=37, age  $21.84 \pm 2.67$  years, BMI  $22.56 \pm 3.85$  kg/m<sup>2</sup>) participated in a 10-week yoga intervention. Pre- and post-training assessments were completed by taking blood samples to assess the information for glucose markers (fasting plasma glucose (FPG), glycohemoglobin (HbA1c, HbA1c-IFCC) and lipid profile (total cholesterol (TC), triglyceride (TG), High-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C)). The distribution of the data is analyzed by the Shapiro-Wilk test. Paired T-test or Wilcoxon Signed Ranks Test was applied to analyze mean differences between pre- and post-data. SPSS 27 was used for the analyses where the level of significance was set at  $p \leq 0.05$ .

**Results:** There were 80 % of females participated in the current research. About 62% of the total have never practiced yoga before this intervention. The baseline blood marker parameters of the test sample fell within the normal range (i.e. FPG  $4.87 \pm 0.47$  mmol/l, TC  $4.41 \pm 0.83$  mmol/l). Glucose parameters decreased due to intervention, but not significantly. ( $p \geq 0.05$ ). Lipid parameters decreased as well except for non-HDL and TGC, where a drop in HDL-C ( $-0.05$ ) could indicate a serious lifestyle risk that we couldn't counter with yoga. Based on Wilcoxon Signed Ranks Test significant difference was found only by pre-post HDL mean difference ( $Z = -2.806$ ,  $p = 0.005$ ).

**Conclusion:** The findings suggest that yoga can improve the glucose parameters. However, This study only tested on sample size, it is suggested that not only yoga but also other lifestyle parameters like Diet have to be supported with larger sample size.

*Keywords: Yoga, Medical Student, Glucose, Lipid Profile*

## **Baseline survey of pastoralist pregnant mothers who attended integrated maternal mobile outreach in Moyale Sub-County, Kenya**

**Dahabo Adi Galgalo<sup>1</sup>, Viktória Prémusz<sup>1,2,3</sup>, Ákos Várnagy<sup>1,3,4</sup>, Ibrahim Kontoma<sup>5</sup>, Annamaria Pakai<sup>6</sup>, József Bódis<sup>2,3,4</sup>, Kálmán András Kovács<sup>3,4</sup>**

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**Introduction:** World Health Organization (WHO) recommend antenatal care (ANC) with a minimum of eight contacts to reduce perinatal mortality and improve women's experience of care. Some of these recommendations are nutritional interventions, maternal and fetal assessment, preventive measures, interventions for common physiological symptoms, and health system interventions to improve the utilization and quality of ANC.

**Aim:** This study aimed to explore baseline information on past-antenatal care among pastoralist pregnant mothers in Moyale sub-County, Kenya.

**Methods:** A retrospective data review of baseline data of 237 pregnant mothers was conducted. Baseline data from the outreach program were entered into Microsoft Excel and transferred to IBM SPSS 27.0. The mean was calculated for continuous variables, frequency, and proportions for categorical variables.

**Results:** A total of 237 women entries were reviewed with a mean age of  $25.54 \pm 5.677$  years, a median weight of 55.00 kg (34-87), and 99.6% illiterate. The median commuting distance to the health facility was 14.00km (8-74). Regarding contraceptive pills, only 77(33.0%) have received information on their use but only 4(2.0%) have ever used them. During the previous pregnancy, 66 (27.0%) attended antenatal care of which all were checked for weight and blood pressure but only 33 (14.0%) were tested for urine and blood test and 12(5.1%) for stool for ova, cysts and parasites. Of 152 who responded on who assisted them during birth, 17 (7.0%) by health care workers and 135 (93.0%) by traditional birth attendance.

**Conclusion:** Antenatal care captures early diagnosis of preventable conditions that can affect birth outcomes. This study shows an urgent need to bring antenatal care close to the pastoralist community. Therefore, the County government should avail mobile outreach ANC services at all levels, especially for mobile pastoralist communities.

*Keywords: antenatal care, early diagnosis, pastoralist, pregnant women, WHO*



## **Effectiveness of return to work programs for workers with disability after occupational injury: A scoping review**

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**Introduction:** Occupational injuries can lead to disability, and the implementation of Return To Work (RTW) programs can be crucial to managing disability and improving job outcomes. However, the effectiveness of RTW programs in assisting disabled workers to return to work and maintain employment still needs investigation.

**Aim:** This scoping review aims to identify and synthesize the available evidence on the effectiveness of RTW for workers with a disability after occupational injury.

**Method:** A scoping review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines. Electronic searches were performed on Web of Science (WoS), PubMed, and Scopus to identify relevant studies published between 2012 and 2022. Studies were considered for inclusion if they met one of the following criteria: return to work (RTW), social security, occupational injury, and the research designs include a case report, randomized clinical trial, observational study, and cohort. The inclusion criteria were studies that reported on the effectiveness of RTW programs for disabled workers. A total of 8 observational studies were included in the review.

**Results:** The key findings of this scoping review suggest that RTW programs can have a range of outcomes, including improved physical functioning, return to work rates, occupational outcomes, and productivity. Rehabilitation programs within RTW programs can improve various outcomes for disabled workers with occupational injuries.

**Conclusions:** The scoping review highlights the potential benefits of RTW programs for workers with a disability due to occupational injury. However, further research is needed to identify the specific elements or components of RTW programs that are most effective in assisting disabled workers to return to work and maintain employment.

*Keywords: Return To Work, disability, occupational injury, rehabilitation*

## **A digital intervention to improve parental health literacy and reduce non urgent visits to pediatric emergency departments: a randomized clinical trial**

**Tatiana Scheuer Becker<sup>1</sup>, Diego Andrade<sup>1</sup>, József Betlehem<sup>1</sup>**

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**Introduction:** Health literacy represents a critical determinant of health at a population level and can be defined as people's ability to manage and cope with their health in everyday life<sup>1</sup>. In a pediatric context, studies have found a relationship between low parental health literacy and negative results in child's health outcomes, such as a bigger frequency of consults to emergency departments in non urgent situations<sup>2,3</sup>.

**Aim:** This research aims to improve parental health literacy as well as reduce non urgent visits to pediatric emergency departments.

**Method:** To accomplish that, it's proposed the development of an online educational platform and the conduction of a randomized clinical trial where intervention group will receive monthly content from this platform. Within 1+1 years of follow-up, frequency of non urgent visits to emergency departments among intervention and control groups will be compared together with pre and post intervention evaluation of parental health literacy skills.

**Expected Outcomes:** The main expected outcome is a frequency reduction of visits to emergency departments within the intervention group, besides a potential improvement in health literacy in this group. A better usage of health systems and also better children' and parents' healthcare are expected as a consequence of this study, mainly because of the accessibility and replicability of the training program developed for it.

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*Keywords: Health literacy, Pediatrics, Non urgent visits, Emergency Department*

## Attitude of the university students towards disability – differences between the nurses and the coaches

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**Introduction:** The health-conscious lifestyle is important for everyone especially for the disabled people. There are many benefits of the physical activity and it can be done in many ways. The disabled ones can do physical activity in many ways, such as physiotherapy, recreational sport activities and even in the competitive sport they can find their place. In order to be carried out safely and to achieve the adequate effect, it is necessary to cooperate with the proper specialist. In the rehabilitation, the disabled ones work almost exclusively with specialists in health sciences, and in the competitive sport, they typically work with sports specialist or coach.

**Aim:** In our study, we sought an answer for the question of what kind of attitude students participating in sports professional training and health science training have towards people with disabilities.

**Method:** 47 coach and 86 nurse students filled out our questionnaire which was based on the MAS questionnaire. We used Mann-Whitney U test for the statistics.

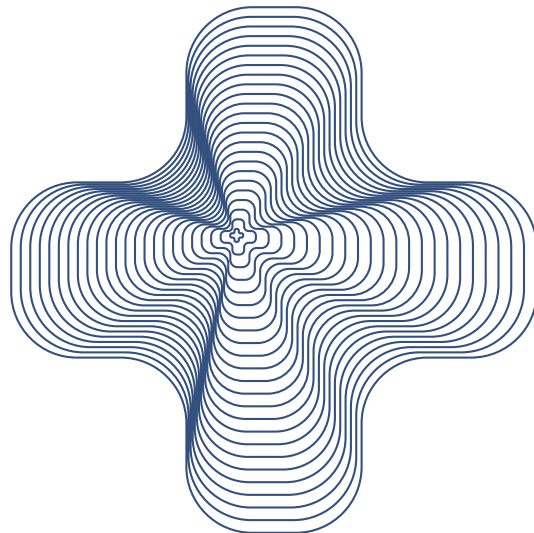
**Results:** The results of the research indicate that the individual training centers adequately provide their students with their own professional knowledge and psychosocial skills. The research highlighted that there is no separate course for people with disabilities in the health sciences training area, in contrast to the sports science training area. Based on the results of the MAS, that students studying at the Faculty of Health Sciences have significantly more positive attitude towards people with disabilities,  $U=-7,473$ ,  $p=0,000$ . We found an equally significant difference women have a much more positive attitude than male students ( $U=-4,537$ ,  $p=0,000$ ).

**Conclusion:** Taking into account the results, we consider it important that the university education imparts knowledge to the students about rehabilitation and sports opportunities for people with disabilities. Furthermore, it is important for both professional groups that directly promote the support of people with disabilities to approach their work with the right attitude, therefore the transfer of knowledge on the subject must be of particular importance. As a further research opportunity, the topic should be assessed on a wider scale, also by interviewing those who are already actively working.

Supported by the ÚNKP-22-2 New National Excellence Program of the Ministry for Culture and Innovation from the source of the National Research, Development and Innovation Fund.

*Keywords: attitude, disability, coach students, nurse students, education*

# **INTERDISCIPLINARY MEDICAL SCIENCES I.**



## A new potential therapeutic target in inflammatory retinopathy

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

**Methods:** Inflammation was induced by bacterial lipopolysaccharide in mice. Maxadilan was administered by intravitreal injection. Optical coherence tomography was used to follow the changes in thickness of all retinal layers. Change of ganglion cell number was evaluated after toluidine blue staining. Electroretinography provided functional information. Expression level of forty different types of cytokines was also analyzed.

**Results:** Our data show that maxadilan is able to prevent the decrease of the outer nuclear layer, outer plexiform layer, inner nuclear layer, inner plexiform layer and the photoreceptor layer. In addition, it improves the functional outcome. Significant ganglion cell degeneration was observed in inflamed group. However, ganglion cell number remained similar to control group after maxadilan treatment. Based on our results, PAC1 receptor-mediated signaling pathways significantly influence the level of several cytokines and chemokines (such as MIG, MIP2, G-CSF and C5/C5a) .

**Conclusions:** The specific, exogenous PAC1 receptor agonist maxadilan prevents the morphological and functional damage in inflammatory retinopathy. Based on our results PAC1 receptor is a new possible therapeutic target in this disease.

**Acknowledgement:** Supported by the ÚNKP-22-2-I-PTE-1459 New National Excellence Program of the Ministry for Culture and Innovation from the source of the National Research, Development and Innovation Fund.

*Keywords: inflammatory retinopathy, PACAP, PAC1 receptor*

## Early versus Delayed Nutrition in Patients After Upper Gastrointestinal Bleeding: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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**Introduction:** Despite lack of evidence, patients are kept nil by mouth for 48 to 96 hours after upper gastrointestinal bleeding (UGIB) due to fear of rebleeding. However, many trials have demonstrated the benefits of early enteral nutrition (EEN) after UGIB.

We conducted a meta-analysis of randomized controlled trials to evaluate the safety and outcomes of EEN compared to delayed enteral nutrition (DEN) after UGIB.

**Methods:** The protocol was registered on PROSPERO in advance (CRD42022372306). Five databases (PubMed, Embase, CENTRAL, Scopus, and Web of Science) were searched on the 10th of November 2022 to identify randomized controlled trials that met our eligibility criteria. In-hospital and 30-day outcomes were pooled separately. Mortality rate, rebleeding rate, and length of hospital stay were the primary outcomes. The pooled risk ratio (RR), mean difference (MD), and the corresponding 95% confidence interval (CI) were calculated using a random effects model.

**Results:** A total of 10 trials with 1,051 patients were included in the analysis. Comparing the two groups, 7-day mortality showed no significant difference (RR=1.23, CI: 0.72 - 2.10), while there was a clear tendency for a decrease in 30-day mortality in the EEN group (RR=0.57, CI: 0.31 – 1.04). As for 7-day and 30-day rebleeding, there was no statistically significant difference between the two groups (RR=1.05, CI: 0.63 – 1.74 and RR=1.16, CI: 0.59 – 2.26, respectively). In addition, our analysis showed that the EEN group needed a reduced length of hospital stay compared to the DEN group (MD= - 1.22, CI: -2.43 to -0.01).

**Conclusion:** Compared with DEN, EEN appears to be a safe intervention and could reduce the length of hospital stay without increasing the risk of complications regarding rebleeding or mortality after upper gastrointestinal bleeding.

*Keywords: Early nutrition, Early refeeding, Delayed nutrition, Delayed refeeding, Meta-analysis, Statistics, Gastrointestinal bleeding*



## Analysis of genetic elements and epigenetic changes in the molecular pathomechanisms of sepsis

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**Introduction:** Sepsis is a life-threatening multi-organ failure caused by an uncontrolled response to infection. There is no causal therapy currently available for the clinical treatment of sepsis, however, it is a serious clinical problem in terms of its occurrence and mortality. The primary goal of our work is to reveal the molecular pathology of Gram-negative (lipopolysaccharide; LPS) sepsis and to create a transgenic animal model that can be used in pharmacological research. Intense intravascular coagulation is observed in the LPS-induced sepsis model. As a result, we focused on the identification and functional analysis of DNA elements and epigenetic factors important in the genetic and epigenetic regulatory cascade of Serpin proteins which are protease inhibitors involved in blood coagulation.

**Methods:** We used the LPS-induced mice sepsis model for our work. After 3, 6, 12, and 24 hours of treatment with LPS total RNA was purified from the livers of the treated mice and the gene expression changes were measured by new-generation sequencing (RNA-Seq). Confirmation of the RNA-Seq data was performed by reverse transcription quantitative PCR. Important genetic elements in the transcription of the miRNA-155 gene (the gene's promoter and four potential enhancers) were fused with the Luciferase reporter gene, then the recombinant plasmids were introduced into eukaryotic cells and Luciferase activity was measured. The actual expression of the Serpina5 protein was investigated using immunohistochemistry.

**Results:** Based on the RNA-Seq analysis, miRNA-155 and Serpin family members showed the highest gene expression increase in the sepsis model. At the same time, the expression of the Polycomb Repressive Complex 1-2 (PRC1-2) genes were significantly reduced. During the functional analyses, in transient expression experiments, the promoter and some of the enhancers showed a sepsis-specific function. The increased expression of the Serpin protein as a result of LPS treatment was also confirmed by immunohistochemistry.

**Discussion:** Serpin genes are kept switched off by PRC1-2 proteins. miRNA-155 directly affects the level of the Jarid2 subunit of the PRC2. As a result of sepsis, the synthesis of Polycomb proteins decrease, which can be explained by the increased level of miRNA-155. The identification of a sepsis-dependent enhancer helps to develop an animal model that allows the investigation of the effectiveness of sepsis therapies.

*Keywords: Epigenetics, sepsis, coagulation, Serpins, miRNA-155*

## Morphological and Chemical Characterization of the Surface of Orthopedic Implant Materials

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**Introduction:** Hip and knee replacements are one of the most frequently used medical implants, that can significantly improve patients' quality of life. Long term success and biointegration of these prostheses depend on several factors, like bulk and surface characteristics, construction and biocompatibility of the material. The applied surgical technique, the general health condition and life-quality of the patient are also determinant factors. Medical devices used in orthopedic surgeries have different surfaces depending on their function inside the human body. Surface roughness of these implants determines the interaction with the surrounding tissues. Numerous modifications have been applied in the recent decades to improve a specific property of an implant.

**Aim:** Our goal was to compare the surface characteristics of typical implant materials used in orthopedic surgery and traumatology.

**Methods:** Morphological and chemical structure of Vortex plate anodized titanium, cemented THR (total hip replacement) stem high nitrogen REX steel (SS), uncemented THR stem and cup titanium (Ti) alloy with titanium plasma spray coating (TPS), THR CoCrMo alloy head, cemented cup and uncemented acetabular liner HXL and UHMWPE and TKR (total knee replacement) femoral component CoCrMo alloy (Sanatmetal Ltd, Hungary) discs were examined. Visualization and elemental analysis were made by scanning electron microscopy (SEM) and energy dispersive spectroscopy (EDS). Surface roughness was determined by atomic force microscopy (AFM) and profilometry.

**Results:** SEM and AFM revealed the morphological and roughness features of the examined materials. TPS Ti presented the highest Ra value ( $25 \pm 2$  nm), followed by CoCrMo alloy ( $535 \pm 19$  nm), Ti ( $227 \pm 15$  nm) and stainless steel ( $170 \pm 11$  nm). The roughness of the HXL and UHMWPE surfaces was in the same range,  $147 \pm 13$  nm and  $144 \pm 15$  nm, respectively. EDS confirmed typical elements on the investigated prosthesis materials: Vortex plate Ti (Ti, O, P); TPS Ti (Ti, O, Al); SS (Fe, Cr, Ni, C) CoCrMo (Co, Cr, Mo), HXL (C, Al, Ni) and UHMWPE (C, Al).

**Conclusions:** The results indicate that the surface of prosthesis materials have significantly different features and the applied investigation methods are suitable for their characterization. Contact angle measurements and in vitro cell culture testing are further planned to test their surface energy characteristics and biocompatibility.

*Keywords: chemical composition, orthopedic implants, roughness, stainless steel, titanium*

## Microalbuminuria in healthy Hungarian children

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**Introduction:** Although microalbuminuria is known as an independent predictive and prognostic marker of cardiovascular morbidity and mortality, there are only few studies about the incidence and reference range of microalbuminuria in childhood.

**Aims:** to investigate the difference of microalbuminuria between healthy children with normal weight and overweight/obesity (OW/O). Furthermore our aim was to evaluate urinary albumin/creatinine ratio (U-ACR) in relation to the children's age and gender.

**Participants and methods:** Children were recruited from elementary and secondary schools from three towns (Nagykanizsa, Pécs, Zalaegerszeg) in Hungary. The study design was approved by the National Medical Research Council (ETT TUKEB 4536-2/2012/EKU). Altogether n=805 children (n=419 boys) aged 3 to 16.8 years were participated to collect random morning urine samples. Among these children n=183 (22.7 %) were overweight or obese. Urinary albumin concentration was determined by immunoturbidimetry and urinary creatinine concentration (Jaffe method) was also measured and used U-ACR to compensate for the variations in the concentration of random urine samples. Statistical analysis was performed using non-parametric (Wilcoxon signed-rank) test.

**Results:** U-ACR was significantly higher in children with normal weight compared to children with OW/O (12.02±33.46 vs 11.52±38.56 mg/g, p=0.036). This difference was present only among girls (14.38±28.98 vs 10.17±21.34 mg/g, p=0.025), but not in boys. U-ACR was significantly higher in normal weight girls than in normal weight boys (girls: 14.38±28.98 vs boys: 9.92±36.89 mg/g, p=0.004). Three different groups were created by ages (1. childrens <10 years, 2. childrens 10-<12 years, 3. childrens >12 years old). In the 2nd group there was also a significant difference between the two sexes among children with normal weight (girls: 15.31±27.2 vs boys: 6.55±5.79 mg/g, p=0.022).

**Conclusions:** a significant difference of U-ACR was found between normal weight and OW/O children. In accordance with the literature our results confirm that U-ACR are significantly higher in girls which can be explained by the lower muscle mass and urinary creatinine excretion of them. These are preliminary results, and further investigations are needed especially to establish age- and sex-specific reference values for microalbuminuria in healthy children.

**Funding:** National Research, Development and Innovation Fund of Hungary. Project No. TKP2021-EGA-10.

*Keywords: microalbuminuria, overweight, obesity*

## The effect of a small neuropeptide in glaucomatous rat model

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**Introduction:** Glaucoma is a leading cause of blindness worldwide. A major risk factor of glaucoma is elevated intraocular pressure (IOP). 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. PACAP acts through three receptors, of which PAC1 receptor has been shown to play the most important role in protection. Accordingly, the present study aimed to examine the possible neuroprotective effects of PAC1-specific PACAP fragment eye drops.

**Materials and Methods:** Throughout the control analysis, the retinal morphology with optical coherence tomography (OCT) and functionality with electroretinography (ERG) was examined. Hypertension was induced by polystyrene microbeads injection into the anterior chamber of SD rats, PBS receiving rats served as controls. Animals received either Systane or PACAP fragment (1 µg/drop) containing eye drops for four weeks. The IOP changes were monitored for eight weeks. After eight weeks the OCT and ERG examinations were repeated. Samples were processed for immunohistochemical and molecular analysis.

**Results:** Microbeads injection significantly increased the IOP in the glaucomatous groups, however, PACAP fragment treatment decreased the IOP after 4 weeks. OCT and ERG results suggested severe retinal degeneration and functional decay in the glaucomatous vehicle-treated group. In contrast, the PACAP fragment-treated group had a control-like retinal morphology. We assessed cell-specific changes through immunofluorescence and western blot analysis in the glaucomatous vehicle-treated group. The PACAP fragment-treated glaucomatous group had a preserved retinal structure, and functionality, and was preserved in a control-like condition.

**Conclusion:** Based on our results, we provide evidence that PACAP fragment eye drops treatment is neuroprotective in glaucoma, providing the basis for future therapeutic administration.

**Acknowledgment:** ÚNKP-22-3-II-PTE-1402, FK129190, K135457; National Brain Research Program NAP2017-1.2.1-NKP-2017-00002; MTA-TKI-14016; PTE AOK-TANDEM; GINOP-2.3.2-15-2016-00050 “PEPSYS”; EFOP-3.6.2-16-2017-00008; “The role of neuroinflammation in neurodegeneration: from molecules to clinics”; and Higher Education Institutional Excellence Programme of the Ministry of Human Capacities in Hungary: 20765/3/2018/FEKUTSTRAT, 2020-4.1.1-TKP2020—FIKP III. Project No. TKP2020-IKA-08, 2020-4.1.1-TKP2020.

*Keywords: retina, PACAP fragment, glaucoma*

## **PACAP contributes to the maintenance of endotoxin fever through the regulation of pyrogenic cytokines and cyclooxygenase-2**

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**Introduction and Aim:** Pituitary adenylate cyclase-activating polipeptide (PACAP) signaling is involved in various inflammatory processes. A common manifestation of systemic inflammation is fever, which is usually induced in animal models with the administration of bacterial lipopolysaccharide (LPS). A role for PACAP signaling was suggested in LPS-induced fever, but the underlying mechanisms of how PACAP contributes to febrile response have remained unclarified.

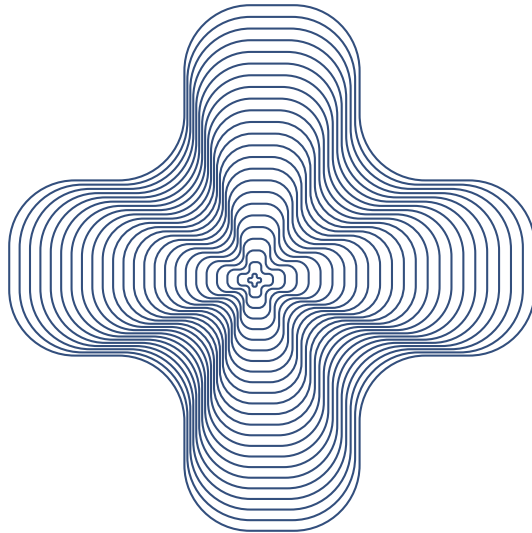
**Methods:** We administered LPS (120 µg/kg, intraperitoneally) to mice with the Pacap gene, i.e., the gene encoding the PACAP protein, either present (Pacap<sup>+/+</sup>) (n=15) or absent (Pacap<sup>-/-</sup>) (n=14) and measured their thermoregulatory responses, serum cytokine levels, and tissue cyclooxygenase-2 (COX-2) expression.

**Results:** We found that the LPS-induced febrile response was attenuated in Pacap<sup>-/-</sup> mice compared to their Pacap<sup>+/+</sup> littermates starting from ~120 min postinfusion. Administration of LPS resulted in amplification of COX-2 mRNA expression in the lungs, liver, and brain of the mice in both genotypes at 210 min postinfusion. In the LPS-treated groups, the upregulation of the COX-2 mRNA in Pacap<sup>-/-</sup> mice was significantly attenuated in the liver, whereas it was augmented in the lungs and the brain compared to Pacap<sup>+/+</sup> mice. Serum concentration of the pyrogenic cytokines interleukin (IL)-1α and β were significantly increased in Pacap<sup>+/+</sup> mice in response to LPS compared with saline, whereas the change was not significant between the treatment groups in Pacap<sup>-/-</sup> mice. In case of IL-1α and β, the intergenotype difference between the LPS-treated groups was also significant. The serum concentrations of IL-6, IL-10, and TNFα were higher in LPS-treated than in saline-treated mice of both genotypes, however, the rise in IL-10 was significantly attenuated in Pacap<sup>-/-</sup> mice compared to Pacap<sup>+/+</sup> mice.

**Conclusion:** PACAP signaling is necessary for normal fever maintenance. Our results suggest that PACAP contributes to the later phases of LPS-induced fever by modulation of COX-2 protein expression in the periphery and the brain, as well as by augmentation of pyrogenic cytokine levels in the circulation. These findings advance the understanding of the crosstalk between PACAP signaling and the “cytokine-COX-2” axis in systemic inflammation, thereby open up the possibilities for new therapeutic approaches.

*Keywords: PACAP, thermoregulation, COX-2*

# **INTERDISCIPLINARY MEDICAL SCIENCES II.**





## **Transcriptomic profiling of *Streptococcus mutans* during planktonic growth, biofilm formation and interaction with human oral keratinocytes**

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Dental caries is a common chronic oral disease that affects the health of adults and children and arises from a homeostatic imbalance between the host and microbiota. *Streptococcus mutans* is a principal etiological agent of dental caries and occasionally in sub-acute bacterial endocarditis. Applying in vitro human cell line models is a commonly used method for simulating host-microbe interactions, among these human oral mucosa contribute significantly to host defense against pathogens. In this research, we aim to develop tractable experimental model systems to characterize *S. mutans* virulence factors. To fulfill this aim *S. mutans* planktonic cells were cultivated in Brain heart infusion broth and collected at different time points. After establishing the bacterial growth curve, biofilm was developed and evaluated by crystal violet staining. Stages of biofilm formation were further characterized by fluorescence microscopy and 3D digital microscopic imaging. To determine *S. mutans* antibiotic susceptibility against erythromycin broth microdilution method was performed, and biofilm eradication was followed by crystal violet staining. To characterize gene expression profiles at different time points, RNA was extracted. cDNA synthesis was carried out by RevertAid First Strand Synthesis Kit, and an expression study was performed with SYBR-Green fluorescence in StepOne qRT-PCR. The fold change of gene expression level was calculated according to the  $2^{-\Delta\Delta Ct}$  method. The frozen stocks of the TR146 cell line were seeded in flasks, with Dulbecco's modified eagle-free medium supplemented with 10% fetal bovine serum. The cells were maintained until 70–80% confluence at 37 °C, 5% CO<sub>2</sub>, and then the cells were passages using 0.05% trypsin EDTA. The antibiotics susceptibility test of planktonic *S. mutans* against erythromycin revealed sensitivity at 0.015 µg/ml concentration. Not surprisingly, the same concentration of antibiotics was less effective against biofilms. Microscopic examination of biofilm cell viability revealed elevated cell death after 48h incubation. Until now, expression profiles of biofilm-forming (GtfB, GtfC, GtfD, GbpB, and Ftf), quorum sensing (ComAB and ComCDE), and stress response (VicRK) genes activity were determined at different time points in planktonic growth and biofilm development. We hope that the presented data contributes to deepening our knowledge of *S. mutans* diseases causing ability.

*Keywords: Streptococcus mutans, Biofilm formation, Transcriptional profiling and In vitro human cell line model*

## Optimization of passive transfer trauma mouse model of complex regional pain syndrome to investigate the chronic phase

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**Background and aims:** Complex regional pain syndrome (CRPS) is a chronic pain condition characterized by persistent pain, sudomotor and vasomotor abnormalities, and trophic changes. The pathophysiological mechanisms are unclear, but complex neuro-immune-vascular interactions and neuroinflammation are suggested. Since the therapy is unsatisfactory, it is crucial to understand the pathomechanisms to identify potential drug targets and key mediators. Previously, we established a passive transfer trauma mouse model, whereas animals were treated daily with purified IgG fractions from CRPS patients to mimic the main symptoms of CRPS. Since our model was limitedly suitable for studying the chronic phase of CRPS, the aim of the present study was to develop a prolonged model.

**Methods:** Experiments were performed using female C57BL/6 animals. Plantar skin-muscle incision was done on day 0 and 1 ml of IgG fraction was injected on each treatment day originating from CRPS or Healthy volunteers. Treatment was administered either daily; only the first 4 days, or every 4th or 3rd day after the first 4 days of injection. The touch sensitivity of the hind paws was measured by a dynamic plantar aesthesiometer.

**Results:** Daily treatment of CRPS IgG significantly decreased the mechanonociceptive thresholds compared to the controls during a 13-day long experiment, whereas treatment given on the first 4 days together with every 4th or 3rd day caused also significantly higher mechanical hyperalgesia in the CRPS groups until day 25. However, only the first 4 days given IgG treatment was not effective.

**Conclusions:** Autoantibody-mediated processes may play a significant role in the early phase of CRPS development, but more frequent treatments may be sufficient to prolong the symptoms in the chronic phase.

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*Keywords: Chronic, autoantibody, pain, Autoimmune, hyperalgesia*

## Fractalkine receptor (CX3CR1) mediates chronic restraint stress-induced pain behaviour in a mouse model

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**Background and aims:** Microglia activation is involved in neuroinflammation and related chronic pain. The microglia-surface fractalkine receptor (CX3CR1) plays a role in mood disorders, stress, and inflammatory pain, but its relevance in stress-induced pain conditions such as fibromyalgia is unknown. Therefore, we studied the involvement of CX3CR1 in a chronic restraint stress-induced pain model.

**Methods:** Male and female fractalkine receptor-deficient (knockout: KO) and C57Bl/6J wildtype (WT) mice were restrained for 6 hours daily for two weeks. Mechanonociceptive threshold and cold tolerance were determined weekly. IBA1-microglia, and GFAP-astrocyte immunohistochemistry was performed to determine cell number and morphological changes due to immobilization in stress- and pain-related brain regions.

**Results:** Immobilisation stress induced significant (15-20%) mechanical hyperalgesia was present in male and female WTs but did not develop in the KO animals. The cold tolerance drop due to stress (60-70%) was significantly smaller in the CX3CR1 KO animals. Stress-induced IBA1+microglia cell number increase in the hippocampus CA3 region in male animals in both genotypes. Meanwhile, significant activation score elevation was present only in WT female and male animals, but not in KOs. No GFAP+ astroglia number elevation was present in either group in the CA3 region. Astrocyte activation score elevation was present in female WT mice, but not KO after 2 weeks of stress.

**Conclusions:** According to our results, both CX3CR1 influence chronic stress-induced pain in mice, in which neuroinflammation (microglia and astrocyte activation), and consequent central sensitization, might be involved. These outcomes suggest the possible use of CX3CR1 antagonists in stress-induced pain syndromes.

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*Keywords: CX3CR1, Fractalkine receptor, stress-induced pain*

## Examination insight of cannabimimetic compounds in basil varieties

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One of the significant discoveries of recent decades is that the human body has a so-called endocannabinoid system (ECS), which involves the whole organism. It is a regulatory system, its operation is essential for homeostasis, for maintaining the internal balance of the body. The ECS consists of receptors, internally produced molecules (endocannabinoids) and enzymes that synthesize and break down these molecules. The known and studied receptors of the system are the CB1 and CB2 receptors, but endocannabinoids also activate additional receptors, and the phenomenon has become the focus of research these days.

In addition to active substances derived from the Cannabis plant, cannabimimetic compounds can also act on the endocannabinoid system as agonists, antagonists, or enzyme inhibitors. It can be said that essential oils are complex mixtures of volatile organic compounds that contain tens or hundreds of active ingredients, the largest number of which are monoterpenes and sesquiterpenes. Terpenes are potential sources of modulators of the internal lipid system, including the ECS.

Members of the genus *Ocimum* proved to be suitable plants for the detection of cannabimimetic compounds. Mapping the effects of agro-technological conditions and recording botanical characteristics is a possibility.

*Keywords: endocannabinoid system, cannabimimetic compounds, basil, GC-FID*

## The stress-relieving effect of *Withania somnifera* and other adaptogenic plants: a systematic review and meta-analysis

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**Background:** Stress is a substantial inherent of life, however, chronic stress might become debilitating, and might be the breeding ground for several diseases through overbalancing the hypothalamic-pituitary-adrenal axis [1]. The use of adaptogenic plants to relieve stress is a common practice [2], with the theoretical foundation being that their effect on stress is related to the decrease in cortisol level [3].

In our investigation, we hypothesized that adaptogens normalize cortisol level in stress, and we conducted a systematic review and meta-analysis based on the results of randomized, double-blind, placebo-controlled trials (RCTs).

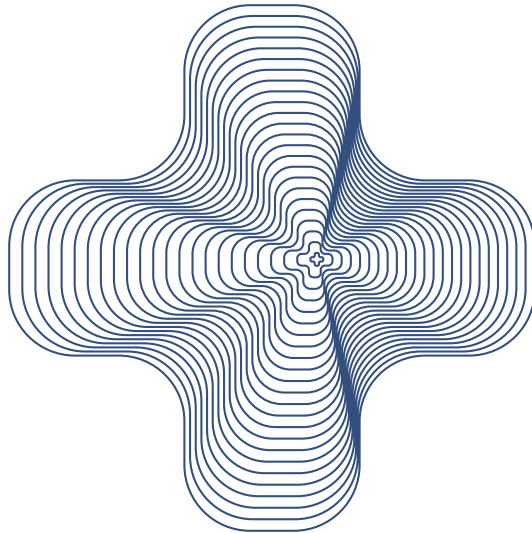
**Methods:** Our systematic review and meta-analysis was performed in accordance with the PRISMA guidelines, conducting a systematic search in 5 databases. To assess the risk of bias in the RCTs included in our study, we used the Cochrane risk-of-bias tool. The primary outcomes were the mean Perceived Stress Scale (PSS) score, mean serum or saliva cortisol level, and mean ACTH level of mentally stressed healthy adults assigned to intervention and placebo groups at baseline, if available during, and necessarily after treatment. The level of evidence was assessed by using the GRADEpro Guideline Developmental Tool.

**Results:** Twenty-five studies [4]-[28] on nine different adaptogenic herbs met the eligibility criteria. Clinical trials on *Bacopa monnieri*, *Eleutherococcus senticosus*, *Eurycoma longifolia*, *Gynostemma pentaphyllum*, *Lepidium peruvianum*, *Ocimum sanctum*, *Panax ginseng*, *Rhodiola rosea*, and *Withania somnifera* were included in our systematic review. We conducted a meta-analysis on the long-term effect of *Withania somnifera* supplementation on the serum cortisol level and on the Perceived Stress Scale (PSS) score. As a result of the treatment, the serum cortisol level showed a clinically relevant and statistically significant decrease in the intervention group compared to the placebo group [4][7][9][15][23]. Also, we found a clinically relevant, however, not statistically significant decrease of the PSS score [7][9][23].

**Conclusion:** *Withania somnifera* treatment clinically improved stress in stressed healthy adults, thus, this therapy can be a useful tool in stress management. As demonstrated in case of this plant, adaptogens might have a cortisol level normalizing effect, however, further studies are needed to generalize these findings.

*Keywords: stress, adaptogens, cortisol, Withania somnifera, Perceived Stress Scale*

# MENTAL HEALTH





## Compliance through the psychological well-being of patients with polycystic ovary syndrome

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**Introduction:** Polycystic ovary syndrome (PCOS) is a multi-systematic disease with a genetic predisposition, manifesting in increased risks for various metabolic diseases and its comorbidities, such as infertility, hyperandrogenism, insulin resistance, type 2 diabetes, cardiovascular diseases and certain types of cancer. Apart from the physiological consequences, patients also often suffer from psychological consequences, such as depression, anxiety and a lower quality of life (Márki et al., 2014). Despite of the high prevalence of these psychological comorbidities, the usual treatment of PCOS patients focuses only on the physical symptoms of this disease, and neglects their mental well-being.

The psychological status of patients has proven to influence their adherence and cooperation with medical advice. PCOS patients often loose the sense of control above their health, become passive, and feel that they are unable to change their situation. This often leads to abandoning lifestyle changes, such as physical activity and diet, which would be crucial for improving several PCOS symptoms.

**Aim and Methodology:** A recent study aimed to explore the relation of PCOS with depression, anxiety, satisfaction with life, self-efficacy as well as the risk perception of patients, by using standardised psychological questionnaires.

**Results:** 389 PCOS patients participated in the study. Analysing data of women with and without PCOS, statistically significant difference was observed in their values of depression [ $t(95.62)=-4.959$ ,  $p<0.001$ ], and satisfaction with life [ $t(99.40)=3.062$ , where  $p<0.05$ ]. No significant difference was found related to their values of anxiety or self-efficacy. In terms of risk perception, using The Health-Related Quality of Life Questionnaire for Women with Polycystic Ovary Syndrome developed by Cronin et al. (1998), among the 26 symptom bothers, most of PCOS respondents ranked esthetical problems more bothering than long-term metabolic consequences or the possible onset of cancer. This may be explained by the lack of information and low level of risk perception of PCOS patients.

**Conclusions:** The result of the research project suggests that screening and prevention of depression should be part of PCOS treatment, and patients need accurate information about the long-term risks associated with this condition in order to benefit from preventive care, improve their compliance with medical advice and to achieve a sustainable lifestyle change.

*Keywords: PCOS, compliance, risk perception, psychological well-being*

## The Jungian Self in existential bibliotherapy

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**Introduction:** Bibliotherapy appeared in the early 19th century as a treatment for the mentally ill. As an applied literary discipline, it is based on the theoretical findings of narratology, reception theory and hermeneutics. Especially the latter is applicable in the field of existential bibliotherapy, which focuses on the fears rooted in the individual's existence.

**Aim:** In a four-semester reading course at the University of Pécs in 2020–2022 with my students we interpreted premodern, modern and postmodern literary works with the aim of exploring the unknown spiritual regions, fears, and general anxiety that everybody can experience from time to time.

**Method:** The selected literary works reflected the Jungian archetypes, thus suitable for the symbolic mapping of the inner world of the human soul. I chose excerpts for each course related to an existential theme or archetype. After the questions about liking and feelings, we approached the character of the protagonist and tried to identify him or her with one of our acquaintances or relatives, which was followed by creative writing to achieve a kind of Self-reading. Life maps and narratives completed by the end of the fourth semester resulted strong emotions and realizations.

**Results:** Existential bibliotherapy is usually a brief dynamic therapy, maintaining a focus on the clients' issues. The literary work in this process is normally a "spring board". With my students we have developed a long-lasting hermeneutic dialogue with literary works that served as world models for us. This process can be exemplary for bibliotherapy with a hermeneutic approach based on the Jungian archetypes.

**Conclusions:** Looking for the root of fears, we also discussed the topic of Satan. The group members projected the Jungian archetype of the "trickster" onto people in their immediate environment, who once caused them personal harm. At the same time we have not reached the more unknowable, numinous regions of the soul and the experience of non-existence and emptiness. The Jungian Self and its deconstructive postmodern critical reinterpretations, the therapeutic methods built around the symbol of the Black Sun by James Hillman and Stanton Marlan, hold unexploited opportunities for the deepening of existential bibliotherapy with a hermeneutic approach.

*Keywords: Existential bibliotherapy, hermeneutics, fears, Self, Black Sun*

## A new way to assess Theory of Mind deficits in bipolar I patients

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**Introduction:** Theory of mind (ToM) is an ability to understand other individual's beliefs, emotions, intentions, and desires, and it is a crucial skill in navigating and functioning in social world. ToM impairment was found in several studies, and more and more data confirm that it can be a state-dependant trait marker of the bipolar I disorder, because impairment is apparent in euthymic state, and also in first-degree relatives. However, most of the ToM tests are not sensitive enough to detect subtle individual differences, which would be necessary for an individualized treatment plan. Short Story Task (SST) is a new way to sensitively assess individual differences in ToM performance. The aim of the study was to test the feasibility of SST in patients with bipolar disorder.

**Method:** We recruited 31 persons (11 male, 20 female) with bipolar I disorder and 31 healthy individuals (15 males and 16 females) as a control group. We used SST to evaluate ToM performance. SST uses a Hemingway novel, which shows the patient a social situation similar to reality, where the reader has to guess complex social situations where the motivation of characters and the causality of events are not explicitly written down.

**Results:** In the explicit mental state reasoning questions the control group (CG) (M=8.06) had significantly higher ( $p < 0.001$ ) scores than the persons with bipolar I disorder (BG) (M=5.03). Subjects in CG (M=8.03) also outperformed ( $p = 0.006$ ) the BG (M=6.55) significantly in the comprehension questions. The performance in the spontaneous mental state inference question was equal (M=0.23) in the experimental groups, but only a few responded this. The explicit ToM was not influenced by age, gender or education but group ( $t = -3.503$ ,  $p < 0.001$ ), comprehension score ( $t = 2.864$ ,  $p = 0.006$ ), and spontaneous mentalizing ( $t = 2.846$ ,  $p = 0.006$ ) significantly predicted the explicit ToM performance.

**Conclusions:** As we know, we firstly used the STT to assess ToM deficits in euthymic bipolar I. patients. In our study primarily explicit ToM was found to be deficient in bipolar I. disorder, which corresponds well with the ToM literature in bipolar disorder. Contrary to our hypothesis we couldn't reveal impairments in spontaneous ToM, and we found that patients living with bipolar disorder also exhibited deficits in comprehension. Overall we found that Short Story Task is a suitable tool for measuring ToM in bipolar patients.

*Keywords: Bipolar, mentalization, euthymic, theory of mind, literature*

## Russian-Ukrainian war: first reactions of the people in the health care field and the local population

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**Introduction:** On 24 February 2022, Russia attacked Ukraine, starting a war between the two countries. The negative impact of the war on mental health can hardly be underestimated. There are likely to be immediate effects, as well as effects that will be felt over a longer period of time, even decades and across generations.

**Aim:** The aim of this study is to assess the initial reactions to the war among those working and studying in the health care field and among the local population in order to conduct further useful research on the subject regarding the results.

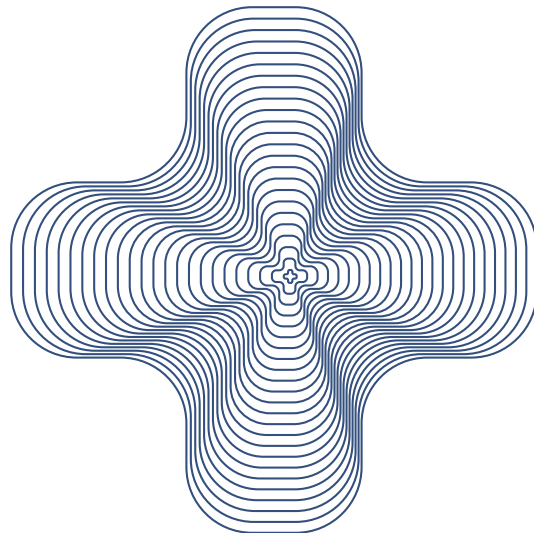
**Method:** Data was collected online between 18 March 2022 and 8 September 2022. A questionnaire survey was used to measure the psychological symptoms experienced in relation to the war, the coping methods used and the importance of distance from the border.

**Results:** 116 people completed the questionnaire, the vast majority of whom were women (86, 74%). The mean age was  $M=35$  years ( $SD=13.4$ ; min = 19 years; max = 76 years). The great majority of the sample consisted of people with tertiary education or who were in higher education, and half of the sample were people working or studying in the health care field (59 people, 51%). Exploratory factor analysis was used to create 4 factors based on symptoms; these were labelled as vulnerability, fatigue, anger and hopelessness. Based on the resulting factors, cluster analysis was used to examine the patterns of these symptom groups in the sample. Four distinct patterns were found, which showed a trend-like correlation with the gender of the respondents and the coping style used. There was no significant role of health care professions or distance from the border in the pattern of symptoms.

**Conclusion:** Among the first emotional reactions to war, feelings of helplessness, anger, hopelessness and fatigue were observed among both the health care professions and the local population. Distance from the border did not play a role in the development of symptoms, suggesting that the psychological burden of war affects the whole population of Hungary due to the constant media exposure. In consideration of the results, an effective intervention should be developed to provide useful help to maintain the mental health of those affected.

*Keywords:* Russian-ukrainian war, mental health, health care workers

# NEUROSCIENCES



## Resting-state functional connectivity correlates of mental fatigue

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Mental fatigue arises during prolonged cognitively-taxing tasks, leading to performance decrements or time-on-task effects (ToT) and declines through rest or incentives. Although mental fatigue is ubiquitously experienced in daily life and its adverse consequences are documented in a variety of settings, its neurocognitive correlates remain uncertain. This study used the prolonged version of the psychomotor vigilance task (PVT) to induce fatigue and resting-state functional MRI (rs-fMRI) to investigate functional connectivity (FC) correlates of the ToT effect and the motivation effect (monetarily rewarding participants after fatigue induction) in 74 young healthy adults. Fatigue scores (change in median reaction times between the blocks of PVT) were extracted as a measure of overall performance. Fatigue-resistant (n=25) and fatigue-sensitive (n=24) subjects were separated based on fatigue scores. A data-driven, multi-variate pattern analysis (MVPA) was used to derive suitable seeds (3) for later seed-to-voxel analysis -post hoc analysis- to analyse FC patterns. Behaviourally, subjects showed strong ToT drops in performance, as assessed by increasing reaction times as the test progressed. Extra monetary reward positively affected PVT performance in fatigued subjects. Our rs-fMRI results showed changes in FC in task-related brain regions and non-related regions. MVPA and subsequent post hoc analysis revealed associations between mental fatigue and reward processing, and patterns of RsFc in brain areas linked to different networks, such as somatomotor, dorsal attention, ventral attention, frontoparietal, basal ganglia, and default mode. Additionally, we found that networks that are anti-correlated at rest become less anticorrelated, meaning that “highly segregated networks become less segregated”, as a function of fatigue.

*Keywords: Mental fatigue, psychomotor vigilance task, motivation, resting-state fMRI, basal ganglia, default mode network*



## **The effect of high concentration sucrose consumption on posttraumatic stress-like changes in mice**

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A healthy diet helps to maintain the anatomical and functional integrity of neurons in the brain. Nutritional deficiencies at the cellular level are implicated in several neuropsychiatry disorders, among others posttraumatic stress (PTSD). On the other hand, consumption of sucrose has been associated with improved mental alertness, reaction time, memory, attention, and ability to solve mathematical problems, as well as a reduction in fatigue, both in healthy individuals and patients. Prior research in rats found that sucrose consumption may have a beneficial effect on the stressed brain. However, transgenic mice strains would be appropriate for examining the molecular background, although the positive effect of sucrose in mice has yet to be explored thoroughly. Thus, we examined how different sucrose solutions influenced the trauma-induced freezing behavior. A short electric foot-shock was used as trauma, and the symptoms were detected 24h (recent) or 14 days (remote) later in the trauma context and with trauma cues. First, the mice were habituated for three days to 2%, 16%, or 32% sucrose, which did not influence their freezing behavior. Then, after the trauma, half of the mice got sucrose, while the other half-drunk tap water for 24 hours. Exposing mice to 16% and 32% sucrose significantly reduced freezing behavior 24 hours but not 14 days after trauma. However, 2% sucrose concentration have been non-effective. Therefore, we conclude that consuming much energy immediately following trauma may change recent but not remote fear memories. More research is essential to elucidate the details (e.g., the necessary time window, mechanism). Our results may provide novel insight into the energetic regulation of neuro-psychiatric disorders and point to a low-cost, widely accessible therapy option.

*Keywords: Post-traumatic stress disorder, Metabolic disorder, Sucrose, Fear memory, and Freezing*

## Task-related Mental Fatigue in Problematic Internet- and Excessive Smartphone Use: an fMRI study

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**Introduction:** Recent questionnaire studies found that the extent of Problematic Internet use (PIU) and excessive smartphone use (ESU) have a long-term impact on mental fatigue. The effect of PIU and ESU on task-related mental fatigue (MF) has not been investigated. Similarly, the underlying neural background of MF in PIU and ESU is not well understood. The investigation of MF with functional Magnetic Resonance Imaging (fMRI) is essential in these conditions.

**Methods:** Psychomotor Vigilance Task (PVT) was applied to induce MF during task-based fMRI. Blood-oxygen-level-dependent analysis was implemented to investigate changes in brain activation during the PVT. Self-reported questionnaires were used to assess PIU, ESU, and the extent of subjective mental fatigue (SMF). Mean changes in reaction time during the PVT were measured to get an objective data of subjects' MF.

**Results:** The extent of PIU and ESU independently predicted the degree of SMF. No associations were found between the mean reaction time changes during the PVT and the extent of PIU and ESU. In addition, no associations were found between the extent of ESU, and the changes in brain activation during the PVT. Brain activation increases in regions related to attentional processes (the left precuneus) and executive control functions (the left medial and superior frontal gyrus) were associated negatively with the extent of PIU.

**Discussion:** Our findings highlight the impact of PIU on subjective mental fatigue. Consistent with previous findings, we confirmed the altered functioning of executive brain areas in PIU and found some attentional regions which activation changes during a cognitively demanding task is related to the extent of PIU.

*Keywords: Problematic Internet use, excessive smartphone use, task-induced mental fatigue, Psychomotor Vigilance Task, blood-oxygen-level-dependent analysis*

## **Futile reperfusion shapes hemoglobin content after spreading depolarization in mice**

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**Intro:** Spreading depolarizations (SDs) restrain cerebral perfusion and worsen tissue outcome after acute ischemic stroke (AIS). Our recent study has confirmed that SDs are crucial for the evolution of reperfusion failure after AIS. Here we show that the SD-related futile reperfusion is accompanied by diminished tissue hemoglobin content and neuronal necrosis.

**Methods:** Male (n=6) C57BL/6 mice were anesthetized with isoflurane (0.6-0.9%). A baseline of 10 min was followed by a transient (45 min) bilateral common carotid artery occlusion (2VO) and a subsequent 60 min reperfusion. Cerebral blood flow (CBF) and hemoglobin concentration variations were captured using green light reflectance and laser speckle contrast imaging. Image analysis and signal processing were performed with custom-made MATLAB algorithms. Neuronal necrosis was evaluated by Hematoxylin-eosin staining.

**Results:** In some mice (n=4) SDs (n=6) occurred spontaneously in response to AIS induction. The SD invaded cortical area displayed futile reperfusion (CBF<60% in 78±11% of total cortical area) and profound hemoglobin concentration decline (-10.77±3.7 mM). In contrast, cortical hemispheres devoid of SD (n=6) showed optimal reperfusion (CBF>60% in 97±3% of total cortical area) and negligible hemoglobin concentration changes (-1.02±3.39 mM). In concert, SD occurrence and futile reperfusion were associated with neuronal necrosis 24 hours after AIS.

**Discussion:** We assume that SDs have a fundamental role in the development of adverse neurological outcomes despite successful recanalization in AIS patients. We propose the pharmacological blockade of SD evolution to improve CBF after recanalization. Our future perspective is to investigate the effects of SDs on the capillary no-reflow phenomenon.

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*Keywords: Spreading depolarization, acute ischemic stroke, reperfusion failure*

## Association between serum periostin level and poor collaterals in the hyperacute phase of ischemic stroke

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**Introduction:** Periostin is a 93-kDa secreted N-glycoprotein that mediates cell-matrix interactions and cell functions in the extracellular matrix [1]. It is expressed at low level in human tissues, but can be rapidly upregulated by various pathophysiological signals in disorders such as acute ischemic stroke (AIS) [2,3].

**Aim:** The aim of our research was to measure the serum periostin level in the hyperacute phase of ischemic stroke in order to reveal its predictive power in identifying patients with poor collateral network (Alberta stroke programme early CT score (ASPECT) < 6).

**Methods:** Our prospective study included a total of 122 patients with acute ischemic stroke admitted to hospital within 6 hours after onset. Stroke severity was assessed by using the National Institutes of Health Stroke Scale (NIHSS) scores, while the early ischemic changes were evaluated by calculating ASPECT score on admission. An unfavorable outcome was defined as the modified Rankin Scale (mRS) > 2 at 90 days follow-up. Blood samples were collected on admission immediately after CT scan and not later than 6 hours after symptom onset. Biomarker concentrations were measured using ELISA-based kits. Patients with an ASPECT score < 6 on admission were considered to have a poor collateral network.

**Results:** The admission concentration of serum periostin was significantly higher in patients with unfavorable outcome than in patients with favorable outcome on 90-day follow up (615 ng/L, IQR: 443–1070 vs. 390 ng/L, 260–563,  $p < 0.001$ ). In a binary logistic regression model, serum periostin level measured within 6 hours after stroke onset was a significant predictor for ASPECT < 6 status on admission (OR, 5.911; CI, 0.990–0.999;  $p = 0.015$ ).

**Conclusion:** In the hyperacute stage of AIS, we found a relationship between the systemic concentration of periostin and the quality of the collateral network, which can serve as a surrogate marker during the planning of neurointervention.

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*Keywords: hyperacute ischemic stroke, periostin, ASPECT, collaterals*

## Negative effects of maternal smoking on retinopathy of prematurity

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**Introduction:** Premature birth can be associated with a series of disorders affecting the quality of future life. One of these conditions is a neurovascular disease of the retina, which called retinopathy of prematurity (ROP). The oxygen-induced retinopathy (OIR) is a well-established model of ROP characterized by vessel abnormalities such as vasoobliteration and neovascularization. It is known that there are several factors which can result premature birth, such as smoking during pregnancy. Our aim of this study was to examine the vulnerabilities of maternal smoking on OIR with immunohistochemical and molecular biological methods.

**Materials and Methods:** Pigmented strain of laboratory mice (C57BL/6) were used in this experiment. During the pregnancy mice had to smoke two times a day for 30 minutes in a special chamber. To induce retinopathy pups were exposed to 75% oxygen +/- 2% from postnatal day (PD) 7-12 then returned to room air. On PD17, after anaesthesia, animals were decapitated, and the retinas were removed for histological and biochemical analysis. Isolectin GS-IB4 was used to label the endothelial cells of the retinas, then a computational tool was used for further quantitative analysis of the retinal vascular networks. VEGF, HIF1- $\alpha$ , iNOS, Erk, and pErk antibodies were detected and quantified by western blotting of pooled retinas distributed by treatment groups.

**Results:** Our computational analysis of retinal vasculature showed quantitative changes in several parameters (such as vessel density, branching index, total number of junctions) as well as in case of the protein expressions examined by western blotting. Two primary angiogenic factor, HIF-1 $\alpha$  and VEGF showed elevated levels in the retinas exposed to nicotine during the smoking process compared to the samples affected by ROP alone.

**Conclusion:** Based on our results we showed that maternal smoking caused a greater degree of retinal damage in ROP, thus prevention and screening of this disease can be considered essential in preterm infant care.

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*Keywords: Retinopathy, prematurity, smoking*

## The protective effect of PACAP1-38 in diabetic retinopathy

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**Introduction:** Nowadays, obesity and type 2 diabetes mellitus (T2DM) have become a global problem. Diabetic retinopathy (DMR) is often the first symptom of T2DM, and the leading cause of vision loss in the elderly age. The protective effect of the pituitary adenylate cyclase-activating polypeptide (PACAP1-38) has been demonstrated in several ophthalmic diseases. The aim of our study was to prove the protective effects of PACAP1-38 in type 2 diabetic retinopathy (T2DMR) in animal model.

**Materials and Methods:** A T2DMR animal model was induced in Wistar rats by injection of streptozotocin and high-fat food diet. Animals were treated with PACAP1-38 eye drops twice daily for 16 weeks. We have four study groups: control+placebo; control+PACAP1-38; diabetes+placebo and diabetes+PACAP1-38. Oral glucose tolerance test (OGTT), C-peptide Elisa assay and the changes in the fasting glucose level were used to test the T2DM model. During the experiment, body weight of the animals, changes in the visual function by electroretinography (ERG) and the total retinal thickness (TRT) by optical coherence tomography (OCT) were measured. We also performed vascular network analysis on post-mortem retinal samples by trypsin digestion.

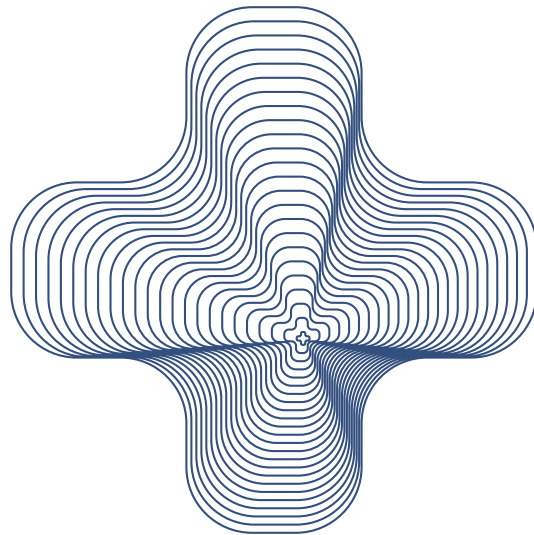
**Results:** Oral glucose tolerance test, C-peptide Elisa, and fasting glucose level changes confirmed the formation of our diabetic model. Based on the ERG examinations we found that, both wave parameters (a- and b-waves) were dramatically reduced in the diabetes+placebo group. However, this reduction was slighter in the case of PACAP 1-38 treatment. Our ERG results were also correlated with the OCT results, where the total retinal thickness was decreased mostly in the diabetes+placebo group. In the diabetes group convoluted and constricted vessels, and microaneurysms were observed. PACAP1-38 treatment moderated the vasoconstriction in the peripheral areas of the retina and also reduced acellular capillary formations.

**Conclusions:** Based on our results, we found that PACAP1-38 treatment has retinoprotective effect in T2DMR and could be a promising pharmacological target in different retinopathies.

*Keywords: Diabetes, PACAP1-38, retinopathy*



# POSTER SESSION I.



## Modifications of the gastrointestinal microbiome have crucial role in the control of social behavioural processes

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**Introduction:** Bidirectional communication between the gut microbiota and the central nervous system have been considered being the so-called microbiota Gut-Brain Axis [1]. The disruption of gut-brain crosstalk has been implicated in the development of various neurological and psychological diseases, among others autism spectrum disorder, therefore, changes in the microbiome community are supposed to influence the regulation of behavioural processes and the health status of the individual [2].

**Aim:** The aim of the present study was to assess and elucidate the effects of qualitative and quantitative alterations of the gut microbiome on social behavioural responses in adulthood.

**Method:** The impact of the alterations on the social behaviour were examined in adult male Wistar rats. Animals have been divided into six groups - 1. antibiotics treated; 2. antibiotics and probiotic treated; 3. probiotic treated; 4 valproic acid treated; 5. valproic acid and probiotic treated; 6. control groups. As antibiotics treatment, rats were given broad spectrum antibiotic mixture dissolved in their drinking water for 4 weeks. Probiotic treated groups daily received our probiotic mixture (containing beneficial bacterial species) with their food for 14 days. Valproic acid treated groups were created as pregnant rats received a single dose of valproic acid on the 12.5th day of gestation and then their pupils were used in the experiments. Social behavioural test was conducted following the respective modifications of the microbiota.

**Results:** Our findings demonstrate significant group-differences in the social behavioural test. Abnormal behavioural phenomena were identified among the antibiotics treated animals, similar to those seen in the valproic acid treated rats. However, this antisocial behaviour was stopped existing after the probiotic treatment in the above groups.

**Conclusions:** The present findings well demonstrate that the gastrointestinal microbiome plays important role in the organisation of social behavioural processes, and also substantiate that our specific probiotic mixture can attenuate both the antibiotics and the valproic acid generated antisocial behavioural symptoms.

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*Keywords: microbiome, antibiotics, social behaviour, autism spectrum disorder, microbiota gut-brain axis*

## **Social inference in temporal lobe epilepsy: preliminary findings with the Hungarian “The Awareness of Social Inference Test - Short Version (TASIT-S)”**

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**Introduction:** Successful social interactions rely on the correct interpretation of social signals. Theory of Mind (ToM) refers to our ability to represent mental states other than ours and to explain behavior with these mental states. It is now well established that temporal lobe epilepsy (TLE) is accompanied by deficits in ToM, however, clinical, psycho-social and cognitive factors influencing the impairment are barely investigated.

**Aim:** Most of the previously used measures of ToM in TLE lack ecological validity. To overcome this limitation, our aim was to investigate 1) ToM in TLE with both multimodal and verbal neuropsychological tests and 2) the relationship between subjective social-cognitive skills and objective test performance.

**Methods:** Seven patients with TLE and 7 HCs matched by age, gender and education participated. We applied the multimodal “The Awareness of Social Inference Test - Short Version (TASIT-S)”, which has 3 subtests. In the Emotion Evaluation subtest (EE), participants indicate the emotional state of a demonstrator. The Social Inference Minimal subtest (SIM) assesses ToM for sincere and sarcastic exchanges, while the Social Inference Enriched subtest (SIE) focuses on the comprehension of lies and sarcasm. As a verbal measure of ToM, we used the Faux pas Recognition test (FPR). To explore subjective perspective-taking skills the Four Item Mentalizing Index (FIMI) was included.

**Results:** Results show no significant differences between patients and HCs in the EE and SIE subtests. In the SIM subtest, we found a trend toward group differences for the total score ( $U=10.5$ ,  $p=.071$ ) and for the sarcasm interpretation alone ( $U=11.5$ ,  $p=.074$ ) with patients performing below HCs. Surprisingly, the FPR test did not differentiate between the groups. The FIMI score of patients showed a strong positive correlation with sarcasm comprehension in SIM [ $r(5)=.817$ ,  $p=.025$ ].

**Conclusions:** Overall, our results indicate no ToM deficits in TLE. These findings are unexpected, since previous studies have reported group differences both with the FPR and TASIT. According to the positive relationship between subjective perspective-taking skills and sarcasm interpretation, it is plausible that the ability to resolve ambiguity between discourse content and paralinguistic cues might be of great importance for patients in everyday social interactions.

**Acknowledgements:** GD was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences

*Keywords: Temporal lobe epilepsy, Social inference, Theory of mind, TASIT-Short, Faux pas recognition*

## One in Four Patients with Gastrointestinal Bleeding Develops Shock or Hemodynamic Instability: A Systematic Review and Meta-analysis

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**Background:** Hemodynamic instability and shock are associated with untoward outcomes in gastrointestinal bleeding. However, there are no studies in the existing literature on the proportion of patients who developed these outcomes after gastrointestinal bleeding. We aimed to meta-analyze the available data to determine these proportions in different bleeding sources.

**Methods:** The protocol was registered on PROSPERO in advance (CRD42021283258). A systematic search was performed in three databases (PubMed, Embase, and CENTRAL) on 14th October 2021. Pooled proportions with 95% confidence intervals (CI) were calculated with a random-effects model. A subgroup analysis was carried out based on the time of assessment (on admission or during hospital stay). Heterogeneity was assessed by Higgins and Thompson's  $I^2$ . The Joanna Briggs Institute Prevalence Critical Appraisal Tool was used for the risk of bias assessment.

**Results:** We identified 11,589 records, of which 220 studies were eligible for data extraction. The overall proportion of shock and hemodynamic instability in general gastrointestinal bleeding patients was 0.25 (CI: 0.17–0.36). In non-variceal bleeding, the proportion was 0.22 (CI: 0.14–0.31), whereas it was 0.25 (CI: 0.19–0.32) in variceal bleeding. The proportion of patients with colonic diverticular bleeding who developed shock or hemodynamic instability was 0.12 (CI: 0.06–0.22). The risk of bias was low, and heterogeneity was high in all analyses.

**Conclusion:** One in five, one in four, and one in eight patients develop shock or hemodynamic instability on admission or during the hospital stay in the case of non-variceal, variceal, and colonic diverticular bleeding, respectively.

*Keywords:* gastrointestinal bleeding; hemodynamic instability; shock; meta-analysis; statistics, review

## Emergence of NDM-5 producing *Escherichia coli* ST361 in Baranya County, Hungary

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**Introduction:** Between February and June 2022, 12 NDM-5 producing *E. coli* strains were isolated from patients treated at six different wards of the Clinical Center of University of Pécs. As this type of pathogen has not been encountered here earlier, the aim of our study was to determine the genetic relatedness of these isolates and to compare them to NDM-5 producing *E. coli* recovered elsewhere.

**Materials and methods:** Isolates were identified by MALDI-TOF MS. The antibiotic susceptibility was determined and interpreted based on the EUCAST standards. The production of NDM carbapenemase was confirmed by NG-Test CARBA-5 test. The isolates were compared by PFGE. Whole genome sequencing was performed using Illumina NovaSeq platforms and assembled by CLC Genomic WorkBench v20. Resistome was identified by ResFinder4.0. and core genome MLST by Ridom SeqSphere+. A plasmid carrying the NDM carbapenemase was conjugally transferred into *E. coli* J53RAZ.

**Results:** NDM-5 producing *E. coli* were recovered from 2 blood, 1 respiratory, 1 bedsore, 3 urine and 5 rectal swab samples of 12 patients treated at the University Hospital, Pécs. Another NDM-5 producing *E. coli* bloodstream isolate was recovered from a patient treated in a secondary care hospital in Baranya County. Although apparent epidemiological links could not be established, all 13 isolates belonged to ST361 forming a single cgMLST cluster with 0-4 allelic differences, while they did not cluster with ST361 strains isolated abroad, or NDM-5 producer *E. coli* isolated elsewhere in Hungary. All isolates were resistant to all beta-lactam, beta-lactamase inhibitors, fluoroquinolones, variably susceptible to aminoglycosides, tigecycline, eravacycline, cefiderocol and uniformly susceptible to colistin. All isolates exhibited identical PFGE pattern. All *E. coli* ST361 isolates harboured blaNDM-5, blaCMY-145, tet(A), mph(A), aadA1, aadA2, dfrA12, sul1 and catA1 genes. blaNDM-5 was conjugally transferred to *E. coli* J53RAZ, resulting in a single plasmid containing derivative. The approximately 120 kb sized IncFII plasmid carried the blaNDM-5 in an IS26 bracketed, 9594 bp long region containing other resistance genes in a Class I integron.

**Conclusions:** Emergence of NDM-5 producing *E. coli* ST361, a rare sequence type in a region of Europe, where the rate of carbapenemase producing Enterobacterales is still low, highlights the importance on continued molecular typing-based surveillance.

*Keywords: Escherichia coli, Bacterial susceptibility and resistance*

## Production and purification of nuclear receptors for studying their interactions in a microfluidic chamber with fluorescence spectroscopy

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**Introduction:** Nuclear receptor-mediated signaling is one of the most important signaling pathways in medicine, with about 10% of drug substances acting on nuclear receptors. To study their interactions, pure receptor proteins are required, which allow to quantify the extent of receptor dimerization and cofactor binding by *in vitro* titrations.

**Aim:** Our research aims to quantify the interactions of nuclear receptors by the utilization of fluorescent protein-tagged nuclear receptor proteins and fluorescence microscopy titration using a microfluidic chamber.

**Materials and methods:** The sequences of HaloTag-GFP-RAR and HaloTag-mScarlet3-RXR proteins were designed, and introduced into the pOptiVec expression vector. The sequence of GFP-RAR was cloned into the pFN29A bacterial expression vector as well. Final constructs were transfected into CHO-DG44 cells or transformed into BL21(DE3)-RIL competent cells. The recombinant proteins were purified using the HaloTag Protein purification system or Nickelate affinity chromatography. Purified fractions were examined by SDS-PAGE and Western blot analyses.

**Results:** The transfection of CHO-DG44 cells was successful with both vectors, however, the cells containing the pOptiVec-HaloTag-GFP-RAR vector died after a couple of days after transfection. Therefore, the GFP-RAR sequence was cloned into the pFN29A vector for bacterial expression. CHO-DG44 cells containing pOptiVec-HaloTag-mScarlet3-RXR vector were able to produce recombinant mScarlet3-RXR protein, however, the subsequent analysis of HaloTag purification showed additional proteins in the purified fraction. Further analysis of this fraction showed that those proteins also contain the HaloTag, which suggests that the protein was either truncated during translation or degraded by the host cell. The same phenomenon was observed for the GFP-RAR protein produced in *E. coli* cells.

**Conclusion:** Protein mScarlet3-RXR was successfully expressed in the CHO-DG44 cell line, while the GFP-RAR was produced in BL21(DE3) cells. However, for having proteins with proper purity, further optimization of the expression conditions, or the utilization of additional purification methods are needed.

*Keywords: Protein production, Nuclear receptor, Protein purification*



## The complex relationship of glucose and neural activity in the light of limbic forebrain glucose-monitoring neurons

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**Introduction:** The glucose, in addition to be the primary energy source of the brain cells, is also known to change the activity of some special chemosensory (so called glucose-monitoring /GM/) neurons which change their firing frequency in response to the change of concentration of D-glucose in the local intracerebral extracellular space or in the systemic circulation. The dysfunction of these neurons was proved to be present in the regulatory background in various nutritional and metabolic diseases [1].

**Aim:** The main goal of the present experiments was to further investigate the involvement of the GM neural cells in the organization of feeding and metabolism related regulatory processes, among others, to examine the firing rate changes of the forebrain GM neurons after long-term sugar feeding in laboratory rats.

**Methods:** The activity changes of GM neurons were recorded during local intracerebral or peripheral, systemic administration of D-glucose by means of the multibarreled microelectrode technique along and after 4-week sugar drinking treatment (0,04 g saccharose /ml).

**Results:** The registered neural activity of the 8 GM (out of recorded 283) neural cells was in close interrelationship with the fluctuations of blood glucose levels and varied depending on the examined brain area. The long-term sugar treatment appeared to have minor altering effects, but to prove whether significant changes exist, more data, obtained in future experiments, are needed.

**Conclusions:** Our findings further expand the view of the variety of known characteristics of the GM neurons that interconnect along the brain axis to form a well-organized system of chemosensory cells, the so called GM neural network, which appears to represent one of the most important constituents of the adaptive central feeding and metabolic control processes [2].

**Acknowledgment:** PTE ÁOK KA 2013/34039/1; EFOP-3.6.1-16-2016-00004; EFOP-VEKOP; TKP2.

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*Keywords:* glucose-monitoring, neurons, microelectrophysiology, homeostatic network

## Development of an impedance-based cell measuring plate

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**Introduction:** The University of Pécs Cellular Bioimpedance Research Group is working on a development of a new type of impedance-based cell testing method which is compatible with the previously developed bioimpedance device and can be suitable for continuous monitoring of cellular mechanisms.

**Aim:** The aim of this study to develop an impedance-based cell culture plate that could be used for future research to examine the progression of NAFLD in human hepatic cell cultures, and the results can be translated into the research group's NAFLD clinical research.

**Method:** The custom-made plate is coated with a hand-painted, graphene-based conducting material, and the connection to the four-channel impedance measuring instrument is ensured by silver wires. The validation of the hand-made plates were performed by measuring the impedance of a series of physiological saline solutions with different concentrations. The validating impedance measurements were carried out using the self-developed four-electrode technique developed by Vizvari et al. [1]. The developed system is an innovative solution to eliminate contact impedance due to the agility of the ions compared to the two electrode measurements known so far. Electrical impedance spectroscopy measurements allow us to study the parameters of biological systems such as cell growth, displacement, and changes in the state of the membranes in a non-destructive way [2].

**Result:** As a result of our development, an impedance-based, graphene-coated cell culture plate was prepared and validated. During the validation, we have demonstrated that the method we have developed is sufficiently sensitive, furthermore it can be used in a wide frequency range, so it is therefore suitable for further cellular testing, such as to investigate the process of inducing NAFLD in human hepatic cells.

**Conclusion:** In addition to demonstrate the self-developed cell testing method, we also present the early results of an impedance measurement of HepG2 human cells.

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*Keywords: bioimpedance, non-alcoholic fatty liver disease, graphene*

## **Examination of the TIGIT-CD226-CD112-CD155 Immune Checkpoint Network during a Healthy Pregnancy**

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Although the possible role of immune checkpoint molecules is well known in the field of tumor and transplantation immunology, their significance in the case of human pregnancy is still not clarified. Despite the significant amount of information about the TIGIT and CD226 immune checkpoint receptors regarding immune therapies, much less research has been conducted to study these surface molecules and their ligands (CD112 and CD155) throughout the three trimesters of human pregnancy.

Immune cell subpopulations were separated from heparinized venous blood and the surface expression of immune checkpoint molecules were analyzed by flow cytometry. The levels of the soluble immune checkpoint molecules were measured by ELISA.

Significant changes were observed in the percentage of the monocyte subpopulations and the surface expression of the CD226 receptor in the case of CD4<sup>+</sup> T and NKT cells. An elevated granzyme B content was measured in the intermediate and non-classical monocyte subsets as pregnancy proceeded. Moreover, an important relationship has been revealed between the surface expression on NKT cells and the serum level of soluble CD226 molecule in the third trimester of pregnancy.

Our findings further confirm the importance of immune checkpoint molecules in immunoregulation during pregnancy. CD226 could be a significant regulator, especially in the case of CD4<sup>+</sup> T and NKT cells, and possibly contribute to the maternal immune tolerance mechanisms in the late phase of pregnancy.

*Keywords: immunology, pregnancy, T cells, flow cytometry, immune checkpoint*

## Examination of retinoprotective compound in type 2 diabetes mellitus

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**Introduction:** Nowadays, type 2 diabetes mellitus (T2DM) is considered as a global pandemic, nearly 250 million people are affected by this disease. A common complication of T2DM is diabetic retinopathy (DMR), which is a leading cause of vision loss. Based on numerous studies it is known that pituitary adenylate cyclase-activating polypeptide (PACAP) also has a protective role in various ophthalmological diseases, including DMR in case of type 1 diabetes mellitus. The aim of our research was to demonstrate the possible protective role of a short PACAP fragment in a DMR rodent model.

**Materials and Methods:** Two-month-old male Wistar rats have been used in this experiment. Type 2 diabetes was induced with the combination of low-dose streptozotocin (STZ) (30mg/ttkg) and high-fat diet. Eight weeks after STZ injection the model was validated by fasting oral glucose tolerance test (OGTT) and C-peptid ELISA test. A group of rats was treated topically two times per day for 16 weeks with a selective PAC1 receptor PACAP fragment (1µg/drop). Four experimental groups were created: control+systane, control+PACAP fragment, diabetes+systane, and diabetes+PACAP fragment. Animals have been monitored during the whole experiment to track the progression of the disease. Body weight, skinfold thickness, intraocular pressure, electroretinography (ERG), and optical coherence tomography (OCT) measurements were carried out.

**Results:** With fasting oral glucose tolerance test (120 mins), the development of diabetes was justified. Using ELISA test, we found that the level of C-peptide in the diabetic group was almost the same compared to the control once. Increased ketone level with the progression of the disease was observed in the diabetic group. Body weight and skinfold thickness measurements showed no significant differences between the control and the diabetic group. Significant differences could be detected in visual function between the two groups at 16 weeks (in the case of a-wave, b-wave and OP amplitudes), where the diabetes PACAP fragment treated group was similar to the control groups. OCT measurements were correlated with the data of the ERG test, thus a greater reduction was detectable in the total retinal thickness in the diabetic+systane group compared to the diabetic+PACAP fragment group.

**Conclusions:** In summary, the specific PACAP fragment, had a retinoprotective role in T2DM.

*Keywords: diabetes, retinopathy, PACAP fragment, protection*

## **Involvement of the centrally projecting Edinger–Westphal nucleus in a mouse model of migraine.**

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**Background:** Urocortin1 (UCN1)-immunoreactive neurons of the centrally projecting Edinger-Westphal (EWcp) nucleus are recruited by acute pain stress. The EWcp projects to several pain sensitive centers including the spinal trigeminal nucleus (SpV), that plays a key role in the protopathic afferentation in migraine. Interestingly, the EWcp is involved in the regulation of the circadian rhythm, hormonal changes, stress exposure, pain and inflammation, that are known to induce migraine in susceptible individuals. Therefore, here we aimed at investigating the possible role of EWcp nucleus in the neurobiology of migraine.

**Methods:** A calcitonin gene-related peptide (CGRP) injection model of migraine was applied in C57BL6J mice. Light-dark box test was performed to validate the migraine-like state. In the EWcp, the neuronal activity was measured by FOS immunohistochemistry, and the Cgrp receptor and Ucn1 mRNA as well as UCN1 peptide expression was tested by RNAscope in situ hybridization combined with immunofluorescence. In the SpV, we searched for urocortinergic fibers juxtaposed to corticotropin-releasing hormone receptor (Crhr1 and Crhr2) mRNA expressing cells.

**Results:** CGRP treatment increased the time spent in the dark compartment of the light-dark box device suggesting the development of migraine-like state associated with photophobia in mice. The number of FOS positive neurons, the magnitude of Ucn1 mRNA expression and UCN1 peptide content in the EWcp/UCN1 neurons was increased upon CGRP treatment. We proved the presence of Cgrp receptor mRNA in the EWcp. Crhr1 and Crhr2 mRNA-containing SpV cells were seen to receive urocortinergic afferentation.

**Conclusion:** EWcp urocortinergic neurons are recruited by CGRP-induced migraine-like state. The increased Ucn1 mRNA expression and UCN1 peptide content of EWcp neurons in migraine, moreover, their possible connection to CRHR1 and/or CRHR2-positive SpV cells strongly suggest their regulatory role in headache control.

*Keywords: TRPA1, UCN1, CGRP, EWcp, Migraine*

## **Antiproliferative activity of Novel Cyclic C5-Curcuminoid derivatives against Lung cancer cells**

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Curcumin and its derivatives have shown very promising results as tumor suppressants. The purpose of this study is to investigate the cytotoxic effect of novel cyclic C5-curcuminoid analogues and to test their DNA cleavage ability and antioxidant capacity. Using cell viability assay (XTT) we studied the effect of selected substances in different concentrations on two lung cancer cell lines (PC-9, A549) to determine their IC<sub>50</sub> value. An Agarose-gel electrophoresis method using Supercoiled pBR322 DNA was done to investigate the interaction between these compounds and the plasmid DNA. The DPPH assay was done to screen the antioxidant capacity of some derivatives using. Some of the cyclic C5-curcuminoid derivatives have shown very promising results, hence the IC<sub>50</sub> value was lower than 5 mikrom. Non of the cyclic C5-curcuminoid derivatives cleaved the DNA, moreover they could protect the plasmid DNA from being cleaved under special circumstances (UV irradiation at 254nm). In the applied DPPH assay, Curcumin reacted with DPPH as an effective antioxidant as expected, where the other tested cyclic C5-curcuminoid derivatives did not exhibit any antioxidant activities. The experimental results encourage further work to get better insight into the mechanisms behind the cytotoxic activity.

*Keywords: Curcuminoids, cytotoxicity, DNA cleavage, antioxidant activity*

## Investigation of paracetamol metabolism related enzyme activities in the small intestine of streptozotocin-induced hyperglycemia in rat

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**Introduction:** After therapeutic dose, the paracetamol is converted—in the liver, in the enterocytes of the small intestine and in the kidney—into inactive paracetamol  $\beta$ -D-glucuronide and sulphate, and a minor fraction is formed into a reactive metabolite, N-acetyl-p-benzoquinone imine (NAPQI), and less than 5% of it is excreted in the urine unchanged. The importance of the small intestine can be emphasized, because this is the site of the absorption. The NAPQI is produced by a CYP3A4, CYP2E1, CYP1A2, and cyclooxygenase (COX)-mediated enzymatic transformation and it is inactivated by a conjugation with glutathione. [1] Pathologic conditions, e.g., hyperglycemia and diabetes, can influence the activities of the conjugative and possibly the oxidative enzymes too. [2]

**Aim:** The present investigation was designed to study the effect of streptozotocin-induced hyperglycemia on the rat intestinal enzyme activity.

**Methods:** Experimental diabetes was induced by intravenous administration of streptozotocin (STZ) at a dose of 65 mg/kg 1 week before the experiment. Spectrophotometric method was used to determine CYP3A4 and COX activity in the small intestine from microsomes and HPLC method was used to determine CYP2E1 activity from small intestine homogenate.

**Results:** There was a significant enzyme activity elevation in the intestinal COX enzymes, but there was a decrease in the activity of the intestinal CYP3A4 enzymes, and the CYP2E1 enzyme activity was practically changeless.

**Conclusions:** These data suggest that streptozotocin-induced hyperglycemia influence the intestinal activity of the investigated enzymes. According to these results, we would like to continue the examination of the oxidative transformation of paracetamol in control and STZ treated rats.

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*Keywords:* small intestine, enzyme activity, CYP, COX, streptozotocin



## Prevalence and legitimacy of online pharmacy market participants accessed via search engine query results in Hungary and Sweden

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**Introduction:** A rapid proliferation of online pharmacies has been observed during the past decades. Thousands of internet pharmacies are accessible on the web, yet illegitimate vendors overwhelm the market of online pharmaceuticals.

**Aim:** A representative sample of 600 search engine results (SER) in Hungary and Sweden was evaluated to document legal and illegal pharmacies accessible from each region. Methods: We utilized Google Trends to determine the most searched for active pharmaceutical ingredients (APIs) in three categories: Abused substances (A: alprazolam and clonazepam), Prescription medications (B: amoxicillin and pantoprazole) and Over-the-counter (C: ibuprofen and paracetamol). Apify search engine scraper was used to collect the first 50 SERs for each API, by translating “Buy API” search query into Hungarian and Swedish. SER links were manually evaluated and categorized, legal online pharmacies were verified using national drug authority listings.

**Results:** A sum of 600 SER links were documented and evaluated. In the Hungarian dataset 31,7% (n/N=95/300) of the links referred individuals to websites offering medicines for sale, with 26,3% (n=79) leading to legitimate websites and 5,3% (n=16) to illegal vendors. Search engine redirection was observed in 10 links (3,3%). The prevalence of internet pharmacy links in SERs was 16%, 26% and 53% for API category A, B and C respectively. The ratio of links referring to legitimate online pharmacies was lowest (7%) for A category APIs, 19% for prescription medicines, and highest (53%) in case of OTC products. The number of SER links directing to legal pharmacies were similar (n=70, 23,3%) in Sweden, however the prevalence of illegal pharmacy links was significantly higher (n=107, 35,5%). Search engine redirection was six-fold (61 links 20,3%). The ratio of links referring to legitimate online pharmacies was like the Hungarian dataset for the three API categories (9%, 24% and 37%), but surprisingly high A category API links have led to illegal websites in Sweden (69%) compared to Hungary (9%).

**Conclusion:** Illegal online pharmacies are accessible from Hungary, but significantly more prevalent in Sweden. Action is required to combat illegal medicine sales and preventing patients consuming potentially dangerous medicines.

**Acknowledgement:** Supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences (BO/00238/20/5) and the Hungarian Scientific Research Fund (OTKA FK\_22-143684)

*Keywords: Europe, illegal websites, patient safety*

## **Ingenuity Pathway Analysis (IPA) of microRNAs associated with lung cancer and regular physical activity**

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**Introduction:** Regular physical activity has long been known to reduce cancer risk and improve treatment efficiency in lung cancer (LC) patients. Numerous studies have shown that miRNAs are actively released into the circulation as signaling molecules during exercise and are involved in cancer pathology regulation<sup>1</sup>. Moreover, it is known that miRNAs could modulate fundamental biological processes by regulating gene expression<sup>2</sup>. However, the exact mechanisms that link LC and exercise are not well understood.

**Aim:** Therefore, the exact role of regular physical activity in LC may be further understood by identifying miRNAs associated with LC and exercise.

**Method:** In the current work, miRNA expression data sets associated with LC and exercise were collected using IPA to screen for inversely regulated miRNAs. Then, a dynamic evaluation of pathway activity was performed depending on gene dysregulation level.

**Results:** Our analysis identified several miRNAs co-regulated by LC and exercise that were mainly involved in apoptosis, cell cycle, and cell viability. These miRNAs, which are downregulated in LC but upregulated by regular exercise could serve as miRNA-targeted therapeutics for lung cancer treatment or as a biomarker.

**Conclusions:** The results provide novel potential mechanisms and molecular targets that need to be explored in future studies and assist in improving the understanding the role of regular physical activity in LC prevention.

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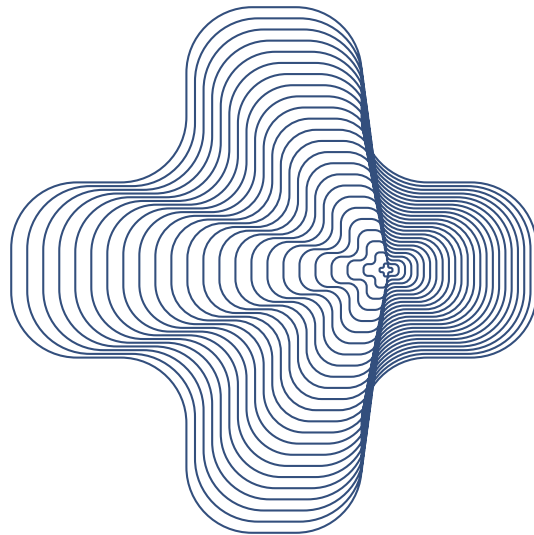
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*Keywords: lung cancer, exercise, miRNA, biomarker, miRNA therapy*

## POSTER SESSION II.



## TrxR inhibition, a potential treatment of Angiomyolipoma and Lymphangioliomyomatosis?

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**Introduction:** Angiomyolipoma (AML) and lymphangioliomyomatosis (LAM) are rare diseases characterized by tuberous sclerosis (TSC) gene mutations. The mutation of TSC1 or 2 genes results in the activation of the mammalian target of rapamycin pathway (mTOR) leading to intense proliferation. mTOR inhibitor, rapamycin is an FDA-approved drug for the treatment of LAM and AML, however, in some patients, the adverse effects can force discontinuation of the treatment. As no other drugs are available to replace rapamycin, deterioration of the patient's condition can ensue, and the alternative treatment can only be lung transplantation in LAM and nephrectomy or angioembolization in AML.

**Aims:** Our previous study showed that mitochondrial function is also affected by TSC mutation. In the present study, we aimed to target mitochondria in TSC mutant cells and identify a potential new drug combination that reduces proliferation and induces apoptosis.

**Methods:** AML and LAM cell lines were treated with rapamycin and auranofin either alone or in combination. To investigate the effects and mechanism of action of mono- and combined drug treatments on TSC wild-type control and TSC mutant cells, cell proliferation assay, mitochondrial staining, electron microscopy, enzyme activity assays (Thioredoxin reductase and Caspase), Western-blot and Cell Stress Protein Array were performed.

**Results:** The study revealed that the inhibition of proliferation and the induction of apoptosis are more effective in the case of auranofin and rapamycin combination treatment than mono-treatment by either drug.

**Conclusions:** TrxR activity is an important regulator of diseases triggered by TSC mutations, combining the two clinically approved drugs rapamycin and auranofin could improve therapeutic efficacy.

*Keywords: TSC mutation, mTOR, TrxR, Angiomyolipoma, Lymphangioliomyomatosis*

## Protective and risk factors in the mental health of patients with Polycystic Ovary Syndrome (PCOS)

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**Introduction:** Polycystic ovary syndrome (PCOS) is a multi-systematic disease with a genetic predisposition, manifesting in increased risks for various metabolic diseases and its comorbidities, such as infertility, hyperandrogenism, insulin resistance, type 2 diabetes, cardiovascular diseases and certain types of cancer (Márki et al., 2014). Apart from the physiological consequences, patients also often suffer from psychological consequences, such as depression, anxiety and a lower quality of life.

**Aim:** This currently on-going research project aims to better understand this complex disease. The research project is uncovering which challenges women with PCOS may face in terms of their psychological well-being, as well as which conditions may serve as protective and risk factors among the PCOS population in relation to how challenging they find their situation. The goal of the research is to contribute with valid information to the development of intervention programs that would target the prevention and screening of mental health problems in PCOS.

**Methodology:** The research project includes a comparative study of the mental health of PCOS patients, patients suffering from other chronic disease and a healthy sample of age-matched women. The parameters monitored among others are depression, anxiety, satisfaction with life and quality of life. Based on the available data from recent studies, we expect PCOS patients to demonstrate higher values of depression, anxiety and lower levels of quality of life and satisfaction with life, compared to healthy women (Mohácsi et al., 2015). In comparison with women suffering from other chronic diseases we expect a lower level of depression, but a higher level of anxiety among PCOS patients (Márki et al. 2014).

The second part of the research project aims to study the PCOS population itself, aiming to identify protective and risk factors for the appearance and for the severity of psychological problems experienced. Based on the results of earlier studies we expect the level of education, as well as relationship and sexual satisfaction to appear as protective, while the number of children, as well as lower levels of resilience and self-efficacy to appear as risk factors (Cipkala-Gaffin et al., 2012). We also analyse the impact of temperament and character, as well the impact of coping mechanisms on the psychological well-being of women with PCOS.

*Keywords: PCOS, psychological problems, protective and risk factors*

## **Needle stick injuries among healthcare workers in Indonesian teaching hospital: Examining social security program coverage and possible outcomes**

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**Introduction:** Needle stick injuries (NSIs) are a significant occupational hazard among healthcare workers (HCWs) worldwide, including in Indonesian teaching hospitals. NSIs can result in serious consequences such as exposure to blood-borne pathogens and transmission of infectious diseases. The lack of adequate social security program coverage for HCWs who experience NSIs can further complicate the situation by delaying access to prompt medical treatment and increasing the risk of disease transmission. However, little is known about the extent of social security program coverage for HCWs who experience NSIs in Indonesia.

**Aim:** This study aims to investigate the coverage of social security programs for HCWs who experienced NSIs and explore the possible outcomes of these incidents, including the incidence of infectious diseases and associated costs of treatment.

**Method:** We conducted a retrospective review of medical records for 87 HCWs who experienced NSIs in two Indonesian teaching hospitals. We analyzed the data to determine the extent of social security program coverage and assessed the outcomes of NSIs, including the incidence of infectious diseases and associated costs of treatment.

**Results:** Our findings showed that only 43% of HCWs who experienced NSIs had social security program coverage. Additionally, HCWs without social security coverage were more likely to delay seeking treatment, experience higher rates of infectious disease transmission, and incur higher costs of treatment. The most common infectious disease transmitted through NSIs was Hepatitis B.

**Conclusions:** The findings of this study emphasize the need for increased coverage of social security programs for HCWs who experience NSIs in Indonesian teaching hospitals. By providing adequate coverage, HCWs can receive prompt medical treatment and minimize the risk of infectious disease transmission. Furthermore, this study provides insights into the potential costs associated with NSIs and emphasizes the importance of implementing effective prevention strategies to reduce the incidence of these incidents. Overall, this research sheds light on the challenges faced by HCWs in Indonesia and emphasizes the need for policy interventions to improve the working conditions and well-being of HCWs in this context.

*Keywords: needle stick injuries, occupational accident, social security, healthcare workers*

## Long-term knowledge retention in physiology and microbiology at the University of Pécs, Medical School

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**Introduction:** Students' knowledge, when tested months after university examinations, can be considerably lower than the results of the original examinations. Various studies of medical students have found 48-80% retention rate in preclinical, theoretical subjects after few months retention interval. However, studies have described significant individual differences in the extent of forgetting between students [1].

**Aim:** Our main aim was to examine medical students' retention rates of knowledge in theoretical subjects at the Medical School, University of Pécs.

**Methods:** Repetitions of the exact exams that the students had previously passed were carried out. For third-year medical students, we repeated the final exam in physiology, while for fourth-year medical students we repeated the microbiology final exam. Both exams were written and included only multiple choice questions. The conduct of the repeated tests were identical to the original exams - using a "Clickers" system for the physiology exam and paper-based for the microbiology exam. Students did not know anything about the content before the retests – during the recruitment they were told about a general knowledge test regarding medicine. Retention rates were defined as the percentage of the score on the retest to the score on the original exam.

**Results:** 27 medical students repeated the physiology exam, while 23 students completed the retest in microbiology voluntarily with mean retention rates of 72,7% and 78,6%, respectively. Most of the students had a retention interval of one semester, however, a few students completed these subjects one or two years earlier. Comparing the results in this regard, we found that the mean retention rate with one semester interval was 77,7% (N=41), with three semesters was 67,1% (N=7) and with five semesters was 57,7% (N=2). For individual students with one semester interval, the retention ranged from 54,5% to 97,2%. When the students initially took the course exams, all students passed the investigated exam. After the retention interval, 36 students (72%) fell below the passing level of 60%.

**Conclusions:** The retention rates for one semester interval are comparable to results other studies have found in other countries, at first glance they show above-average retention. On the other hand, the high (imaginary) failing rate at the retests draws attention to a significant amount of forgetting. Medical educators should be more aware of this common phenomenon.

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*Keywords: learning, knowledge retention, physiology, microbiology*



## Values and health behaviour

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**Introduction:** The health status of a society is important, so a healthy youth is a worthwhile investment for Hungarian society (Barabás, 2006). Health behaviour refers to a set of health-related behaviours that can be active or passive (Szakály, 2016; Domrádi, 2019). By raising awareness and developing health behaviours, many diseases can be prevented, as evidenced by the doubling of non-communicable diseases (NCDs) and cardiovascular diseases compared to the 1990s (Domrádi, 2019). The negative, proven effects of health status on the population are manifested at the individual level and also have an impact on the health care system.

**Aim:** Our main aim is to demonstrate the role of values in improving health, thus demonstrating the importance of health education in education and training institutions.

**Method:** Our data collection method was interviewing, using a validated attitude questionnaire (IRVS Value List, WHO WBI-5), extended with own questions, completed by 380 people in total. Data were processed using SPSS 24.0 statistical software.

**Results:** Health ranked first (4.83) for importance and third (4.16) for implementation. Wilcoxon signed rank test results show that the importance of the value system is significantly more frequent ( $T = 54851$   $Z = -12.310$   $p < .000$  (1-tailed)  $r = .631$ ) (Mdn = 108) than the implementation of values (Mdn = 99), respondents care about values but do not act on them.

**Conclusion:** Education for healthier lifestyles should be promoted and preferred, regardless of age, taking into account needs and circumstances. We consider it important to develop a preventive approach and to create an inclusive educational environment.

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*Keywords: IRVS, health, university students, value*

## Regulation of lipopolysaccharide biosynthesis

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**Introduction:** More than 70% of all Gram-negative bacterial surfaces are covered by lipopolysaccharide molecules. While these molecules are barriers and provide structural integrity, they are also virulence factors, determine the thermosensitivity and biofilm forming ability of Gram-negative bacteria. Lipopolysaccharide biosynthesis is under the regulation of bacterial two-component systems.

**Aim:** This project demonstrates the connection between the biosynthesis of lipopolysaccharides and bacterial two-component systems, suggesting new possible targets on Gram-negative bacteria.

**Materials and methods:** Whole genome of two *Shigella sonnei* species were sequenced by IonTorrent PGM. De novo assembly of genomes were performed by SPAdes v3.1 [1] and scaffolds of the draft genome were reordered by Mauve [2] software and MeDuSa web server [3]. Closest relatives were found by phylogenetic analysis of 16S rRNA, *adk*, *fumC*, *gyrB*, *mdh* and *purA* sequences by BLASTn [4]. Lipopolysaccharide biosynthesis genes were identified using KEGG database [5]. Bacterial two-component system contributors were identified using KEGG and literature data.

**Results:** Hotspots in lipopolysaccharide biosynthesis were identified. A network between bacterial two-component system contributors and lipopolysaccharide biosynthesis enzymes were described. A possible target of *gmhD* by Closantel was tested by negative result.

**Conclusion:** Bacterial two-component systems can play a role in the regulation of LPS biosynthesis by controlling the expression of genes involved in the biosynthesis, while the testes Closantel had no effect on the expression of *gmhD*.

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**Keywords:** *Shigella sonnei*, lipopolysaccharide, bacterial two-component system

## Suppression of ZG16B production is a molecular mechanism of rexinoid-based chemoprevention

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Prevention of breast cancer is feasible using low-dose rexinoid-based synergistic combinations. Expression profiling of normal breast epithelial cells identified ZG16B (PAUF) as a gene suppressed by combining bexarotene with the adrenergic inhibitor carvedilol (Bex+Carv). ZG16B is overexpressed in a number of cancers, including mammary tumors. We hypothesized a pro-tumorigenic role for ZG16B in breast cells, whereas its suppression may constitute a preventive effect by the synergistic combination.

As previously established, low-dose Bex+Carv treatment inhibits HER2-induced breast cancer in transgenic mice. Immunohistochemical analysis showed reduced ZG16B levels in healthy mouse mammary tissue sections, as well as in xenografts of MDA-MB-231 breast cancer cells in vivo. To characterize its effect, ZG16B was cloned and expressed as a cleavable fusion protein with EGFP and used as a supernatant enriched in ZG16B. Proliferation of breast cells was stimulated by soluble ZG16B in normal and ER-positive, but not in triple negative breast cancer cells. In contrast, anchorage-independent colony formation increased in all tested cell lines upon ZG16B, but reduced by Bex+Carv treatment. Gene ontology analysis of ZG16B-treated immortalized breast epithelial (HME-hTert) cells revealed its role in extracellular matrix interactions, focal adhesion and PI3K signaling. ZG16B reduced cell attachment and induced a phenotypic shift characteristic of epithelial-mesenchymal transition (EMT). Furthermore, ZG16B stimulated cell migration in all tested cell lines, which was blocked by inhibitors of PI3K and Akt. The cohort of genes classified by their induction by ZG16B and their suppression by Bex+Carv delineated cellular functions of extracellular matrix organization, motility and adhesion. Conversely, exposure of Bex+Carv-pretreated cells to ZG16B blunted the anti-proliferative and anti-migratory effects of the chemopreventive combination.

Taken together, our data indicate that ZG16B is a major regulator of the extracellular microenvironment of breast cells and its production is suppressed by the chemopreventive combination of Bex+Carv. Furthermore, ZG16B and Bex+Carv treatments inversely regulate proliferation, migration and EMT, suggesting that suppression of ZG16B may be a part of the chemopreventive program induced by Bex+Carv, and thus a relevant preventive and therapeutic target in breast cancer.

*Keywords: Chemoprevention, ZG16B, Breast cancer, Rexinoid, Synergy*

## Hypervirulent *Klebsiella pneumoniae* causing bloodstream infection in Hungary

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**Introduction:** Hypervirulent *Klebsiella pneumoniae* (hvKP) cause serious infections that can be disseminated, such as pyogenic liver abscesses, endophthalmitis, osteomyelitis, and bacteremia in healthy young people (1). No data is available from Hungary on the incidence of bloodstream infections caused by hvKP.

**Aim:** Our aim was to investigate whether hvKP were recovered from blood samples of patients treated in 2020-2022 at the Clinical Center of University of Pécs.

**Materials and methods:** 157 non-repeat isolates recovered from blood culture of 157 patients, identified as *K. pneumoniae* were screened by string test for hypermucoviscosity and by PCR for the presence of *iucA*, *rmpA* and /or *rmpA2*, i.e. genes characteristic to hvKP (1). The antibiotic susceptibility of strains identified as hvKP were tested by disc diffusion (2). Their genetic relatedness was established by pulsed field gel electrophoresis and whole genome sequencing on Illumina NovaSeq platform. Multi-locus sequence type (MLST), resistance, virulence gene content, capsular and O serotype and plasmid incompatibility type were predicted from the whole genome sequence data using Kleborate (3) on PathogenWatch (4).

**Results:** Three of the 157 isolates were identified as hvKP (2%). They exhibited different PFGE patterns and belonged to three different MLST types (ST5, ST893-SLV and ST86). They were all susceptible to the antibiotics tested. None of them had acquired resistance traits. They had K2, K20 and K39 capsular types. Beyond the genes responsible for capsule hyperproduction (*rmpA/A2*) they possessed two or three siderophore genes. Two of them carried a plasmid of the classical hypervirulence type.

**Conclusions:** To the best of our knowledge, our study identified first hypervirulent *Klebsiella pneumoniae* isolated from bloodstream infections in Hungary. Identification of these isolates, two of which are members of the known hypervirulent clones, is alarming. Further surveillance and monitoring is required to determine the incidence of hvKP in the country.

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**Keywords:** *Hypervirulent Klebsiella pneumoniae*, *Bloodstream infection*, *Molecular typing*

## The risk factors of acute pancreatitis progression into recurrent acute pancreatitis and chronic pancreatitis

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**Introduction:** Acute pancreatitis (AP) can progress to recurrent acute pancreatitis (RAP) or chronic pancreatitis (CP).

**Aim:** This systematic review and meta-analysis aimed to identify risk factors associated with this progression.

**Methods:** The protocol was registered on PROSPERO (CRD42022368931). A comprehensive search was conducted in three (Medline, Embase, Cochrane) databases on October 25th, 2022. Articles reporting AP – RAP or RAP – CP patient groups comparisons and risk factors associated with AP progression into RAP or CP were included. Pooled odds ratios (OR) with 95% confidence intervals (CI) were calculated using the random effects model. Heterogeneity was evaluated using the  $I^2$  statistic. The risk of bias assessment was performed using the Quality in Prognostic Studies (QUIPS) tool.

**Results:** A total of 71 articles were included in the meta-analysis, and several risk factors were identified for the progression of AP into RAP and CP. We found the following risk factors of AP recurrence: younger age, male gender, smoking, alcoholic etiology, hypertriglyceridemia, diabetes mellitus, pseudocyst, etc. The pooled OR for the male gender was 1.45 (95% CI: 1.29-1.64,  $I^2=24%$ ), for smoking was 1.45 (95% CI: 1.16-1.81,  $I^2=62%$ ), for alcoholic etiology was 1.76 (95% CI: 1.38-2.25,  $I^2=81%$ ), for hypertriglyceridemia was 2.45 (95% CI: 2.07-2.90,  $I^2=9%$ ), for diabetes mellitus was 1.49 (95% CI: 1.24-1.80,  $I^2=0%$ ), for pseudocyst was 2.19 (95% CI: 1.52-3.15,  $I^2=0%$ ). We also found risk factors of RAP progression into CP, which were the following: male gender, alcoholic etiology, alcohol consumption, smoking, etc. The risk of bias was low in the majority of the included studies.

**Conclusion:** Our study identified multiple modifiable risk factors which can be treated to prevent the progression of pancreatitis.

*Keywords: acute pancreatitis, recurrence, chronic pancreatitis, progression, risk factors*

## Time dependency and risk factors of splanchnic vein thrombosis development in early-phase acute pancreatitis: a systematic review and meta-analysis

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**Introduction, Aim:** Splanchnic vein thrombosis (SVT) is a complication of acute pancreatitis (AP). However, there is limited information about the risk factors and time course of SVT in the early phase of AP, our objective was to investigate these factors.

**Methods:** A systematic search was conducted on 27.10.2022, in four medical databases (Embase, PubMed, Scopus, Cochrane). Inclusion criteria were appropriate imaging in adult patients with AP and reliable reporting of imaging timing. Exclusion criteria were co-occurrence or recent history of malignant disease and recent surgical interventions. Pooled proportion of patients affected by SVT was calculated with 95% confidence intervals (CI), and subgroup analyses were performed for diagnosis timing and disease characteristics. The JBI tool was used to assess the risk of bias, and the GRADEpro tool for the level of evidence.[1,2] The protocol was prospectively registered in PROSPERO, CRD42022367578.[3]

**Results:** Data from 15 eligible studies and 1,979 patients were pooled; the proportion of patients with SVT in the early phase of AP (within 11 days after symptom onset/5 days after admission) was 0.16 (CI 0.08-0.29). The occurrence was lowest 0-3 days after symptom onset at 0.05 (CI 0.00-0.45), it increased almost five-fold to 0.23 (CI 0.02-0.79) between 3-11 days. Disease factors influencing SVT occurrence were severity (mild 0.14 (CI 0.04-0.39), moderate 0.23 (CI 0.09-0.47), severe 0.31 (CI 0.15-0.54),  $p=0.21$ ), etiology (alcoholic 0.31 (CI 0.13-0.58), biliary 0.12 (CI 0.04-0.3),  $p=0.03$ ), and pancreatic necrosis (absent 0.11 (CI 0.05-0.25), <30% 0.25 (CI 0.11-0.47), >30% 0.5 (CI 0.29-0.72),  $p=0.01$ ).

**Conclusion:** One in six patients develops SVT in the early phase of AP. A severe disease course, alcoholic etiology, and pancreatic necrosis increase the risk of SVT. This risk increases with the duration of AP; therefore, looking for and diagnosing SVT with imaging is important in the management of AP.

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*Keywords: splanchnic vein thrombosis, acute pancreatitis, early phase, imaging, risk factors*



## High-affinity streptavidin redirected universal CAR T cells targeted with biotinylated trastuzumab can eliminate HER2+ tumors in vitro, but toxic in vivo

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**Introduction:** Cancer therapies based on CAR-T cells have made breakthroughs in treating hematological malignancies but are less effective against solid tumors. The main reason for this is that they usually target a single antigen, and therefore not suitable for tumors with high heterogeneity. The universal chimeric antigen receptor (UniCAR) characterized in this present research is able to bind biotinylated antibodies specific to different epitopes through its high-affinity streptavidin monomer domain (mSA2), thus enabling the parallel detection of several tumor antigens with the administration of appropriate antibodies.

**Aim:** In our project, we produced our own UniCAR construct and executed a thorough comparative study both with in vitro assays and in vivo animal experiments to evaluate its selective target recognition and cell activation capacities and the evoked cytotoxic effect compared to a classical second-generation anti-HER2-CAR construct.

**Method:** UniCAR-T cells were prepared by retroviral transduction and their activation and cytotoxic efficacy was investigated in the presence of biotin-trastuzumab (BT) at a concentration of 10 µg/ml using conventional immunological assays. The targets were HER2 immobilized on the plate surface and expressed in the membrane of MDA-HER2 breast tumor cells. Subsequently, the efficacy of UniCAR-T cells against tumors was investigated in subcutaneous xenotransplanted NSG mice with MDA-HER2 cells in the presence of a BT linker.

**Results:** We found that in the presence of BT, UniCAR-T cells recognized both molecular and cell surface HER2, indicated by significant interferon-gamma secretion and target cell lysis. The response was comparable to that of conventional anti-HER2-CAR-T cells used as positive controls. In the absence of a linker and target, no activation occurred. To our surprise, mice treated with UniCAR + BT developed serious side effects shortly after starting therapy, compared to mice treated with UniCAR-T cells alone. Significant T cell infiltration as well as native biotin were detected in lung sections of the dead animals.

**Conclusion:** It is hypothesized that the adverse reaction was caused by synergism between UniCAR-T cells that bind directly to biotin, which is natively found in the body, and to HER2 via biotin-trastuzumab. Based on this, in our further experiments, we plan to test the in vivo applicability of the UniCAR concept with another linker molecule not expressed in mammals (e.g. FITC).

*Keywords: CAR T cells, immune cell therapies, solid tumors, UniCAR T cells*



## **Anthropomorphic versus Non-anthropomorphic: Which will be a potential prospect?**

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With the owner of the combination of incredible functions, the hand is considered an essential component of the human body. It can be seen from the fact that there are many cases in which this integral part is missing. When the hand is amputated or lost, a prosthetic device can play an important role in rehabilitation. For many people, a hand with anthropomorphic or non-anthropomorphic design can improve the ability to manage daily activities, as well as maintain body balance. By considering the advantages and disadvantages of the two aforementioned types of design based on three elements, namely: grasping mechanism, flexibility in manipulation and demand capacity, the paper aims to determine the future superiority of biomedical engineering for two categories of prosthetic hand designs. How can these hands be controlled, and which one could effectively replace a real hand will be figured out in this article. Thus, some useful insights are provided for better prosthetic hand design and development.

*Keywords: prosthetic hand, anthropomorphic, non-anthropomorphic, biomedical, superiority*

## Epidemiological disease burden of unspecified female infertility in Hungary during the last decade

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**Introduction:** Infertility affects more than 185 million people worldwide, of which 120 million are women. Prevalence ranges widely, with lower incidence in developed countries and higher rates in developing ones. Unintended childlessness is a major problem at both individual and societal levels in the majority of European countries. It can also place an increased burden on the women and couples concerned, as well as on health care and health insurance systems.

**Aim:** The aim of our quantitative, descriptive and cross-sectional study is to analyze the epidemiological disease burden of female infertility in Hungary between 2010 and 2019.

**Methods:** Data were derived from the financial database of the Hungarian National Health Insurance Fund Administration (NHIFA), for the years 2010 and 2019. The database included the annual number of patients, number of cases, and prevalence of the health care utilization per 100,000 population according to age groups. The following health insurance treatment categories were included in the study: general practice care, home care, in-, and outpatient care, medical imaging, laboratory diagnostics and pharmaceuticals. Patients with female infertility, unspecified were identified with the following code of the International Classification of Diseases 10th revision: N97.9.

**Results:** The highest number of patients were found in outpatient care (2010: 22,456; 2019: 26,160), followed by pharmaceuticals (2010: 15,341; 2019: 15,914) and laboratory diagnostics (2010: 10,352; 2019: 12,797). Based on the number of patients related to outpatient care the prevalence among women was 439.7 in 2010, while it was increased up to 512.3 per 100,000 inhabitants in 2019. Age-specific prevalence was the highest within the age group of '30-39 years women' (1,767.4). It was followed by the 20-29 years (996) in 2010. In 2019 the prevalence was remarkably increased in the '30-39' (2,248.6) and '40-49' age groups (792.3). The mean age of the patients in outpatient care was 33.5 years in 2010 and 35.4 years in 2019.

**Conclusions:** The most significant increase in the number of patients was in chronic inpatient care (14.4 times), general practice (2.2 times), and inpatient care (1.5 times) as well. The mean age increased by 3.3 years in the study period, furthermore, the '40-49' age group became the second most affected group with infertility.

*Keywords: female infertility, infertility, prevalence, epidemiology, Hungary*

## Health insurance utilisation indicators for the treatment of hip osteoarthritis

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**Introduction:** Hip osteoarthritis is a degenerative disease with an estimated prevalence of nearly 1.5% of the total population and 15-25% of the population over 65 years. Health services utilization related to hip osteoarthritis represents a significant burden for the society and health care systems.

**Aim:** The aim of our study is to investigate health insurance utilization indicators in the care of hip osteoarthritis in Hungary.

**Methods:** Data were derived from the financial database of the National Health Insurance Fund Administration (NHIFA) of Hungary for the year 2018. The data analysed included annual patient numbers, prevalence per 100 000 population in acute inpatient care, health insurance costs calculated for age groups and sex for all types of care. The following health insurance treatment categories were included into our study: general practice care, home care, in- and outpatient care, medical imaging, laboratory diagnostics, pharmaceuticals and medical aids. Patients with hip osteoarthritis were identified with the code M16 of the International Classification of Diseases, 10th revision.

**Results:** The highest national patient numbers were found in outpatient care: 69,311 men, 148,375 women, in total 217,686 patients, followed by general practice care (63,551 men, 138,030 women, in total 201,581 patients), and pharmaceuticals (29,071 men, 68,618 women, in total 97,689 patients). Based on patient numbers in acute inpatient care, the prevalence per 100,000 among men was 91,9, among women 124,9, in total 109,1 patients. In 2018, the NHIFA spent 13.49 billion HUF (49.93 million USD/42.31 million EUR) on the treatment of hip osteoarthritis. 36.8% of costs was spent on the treatment of male, 63.2% on female patients. Acute inpatient care (62.7% of total health insurance costs in men, 51.0% in women), outpatient care (14.6% in men, 20.0% in women) and chronic inpatient care (8.2% in men, 11.2% in women) were the main cost drivers. The average annual treatment cost per patient was 1,156,605 HUF (4,280 USD/3,627 EUR) in men and 1,337,344 HUF (4,949 USD/4,194 EUR) in women.

**Conclusions:** The prevalence of hip osteoarthritis was 1.36-times higher in women compared to men. Acute inpatient care was the major cost driver in the treatment of hip osteoarthritis. Global increase in prevalence is largely attributable to ageing society, increased physical work load and obesity.

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*Keywords: health insurance utilisation, hip osteoarthritis, epidemiology, cost, Hungary*

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