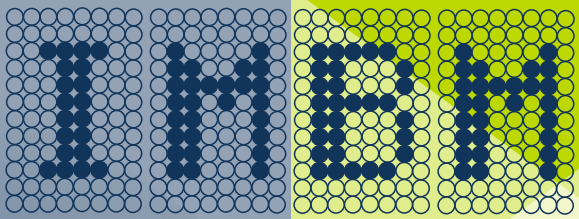
INSTITUTE OF MOLECULAR BIOMEDICINE
Faculty of Medicine, Comenius University, Bratislava



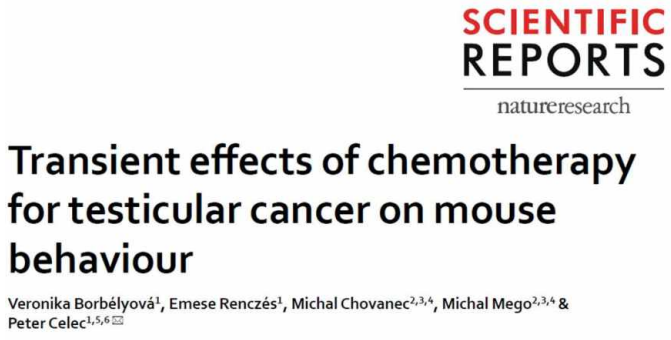
2020

IMBM 2020

1 research institute
11 years
1 professor
5 associate professors
7 postdocs
15 PhD students
12 diploma thesis students
13 bachelor students
6 APVV grants
1 KEGA grant
4 VEGA grants
4 UK grants
31 CC/IF publications
1128 SCI citations

SCIENTOMETRIC DATA

NUMBER OF CC/IF PUBLICATIONS: 33
OF THESE WITH FIRST/LAST AUTHORS FROM IMBM: 20
CUMULATIVE IF: 109,9



SCIENTIFIC REPORTS
nature research

Transient effects of chemotherapy for testicular cancer on mouse behaviour

Veronika Borbélyová[1], Emese Renczés[1], Michal Chovanec[2,3,4], Michal Mego[2,3,4] & Peter Celec[1,5,6]

[1]Institute of Molecular Biomedicine, Faculty of Medicine, Comenius University, Bratislava, Slovakia.

frontiers in Endocrinology

ORIGINAL RESEARCH
published: 07 October 2020
doi: 10.3389/fendo.2020.570560

The Role of Estrogen in Anxiety-Like Behavior and Memory of Middle-Aged Female Rats

*Emese Renczés[1], Veronika Borbélyová[1], Manuel Steinhardt[1], Tim Höpfner[1], Thomas Stehle[1], Daniela Ostatníková[2] and Peter Celec[1,3,4]**

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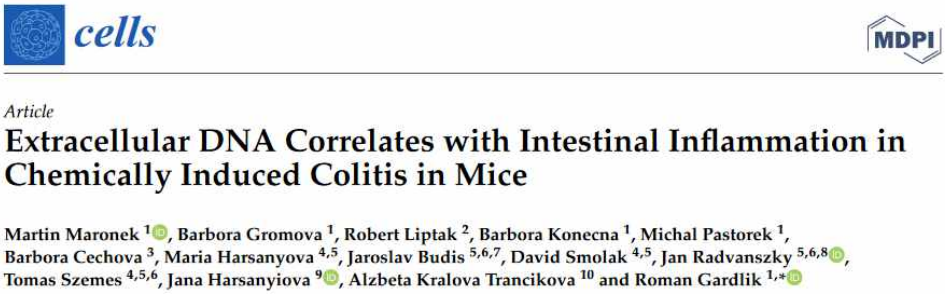

cells

MDPI

Article

Extracellular DNA Correlates with Intestinal Inflammation in Chemically Induced Colitis in Mice

Martin Maronek [1], Barbora Gromova [1], Robert Liptak [2], Barbora Konecna [1], Michal Pastorek [1], Barbora Cechova [3], Maria Harsanyova [4,5], Jaroslav Budis [5,6,7], David Smolak [4,5], Jan Radvanszky [5,6,8], Tomas Szemes [4,5,6], Jana Harsanyiova [9], Alzbeta Kralova Trancikova [10] and Roman Gardlik [1,*]

Research Article
DILI, Autoimmune, Cholestatic and Genetic Diseases

JOURNAL OF HEPATOLOGY

Altered aryl-hydrocarbon-receptor signalling affects regulatory and effector cell immunity in autoimmune hepatitis

Marta Vuerich[1,†], Rasika Harshe[1,†], Luiza Abrahão Frank[1,†], Samiran Mukherjee[1], Barbora Gromova[1,2], Eva Csizmadia[1], Imad A.M. Nasser[3], Yun Ma[4], Alan Bonder[5], Vilas Patwardhan[5], Simon C. Robson[1,5], Maria Serena Longhi[1,*]

[1]Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; [2]Institute of Molecular Biomedicine, Faculty of Medicine, Comenius University, Bratislava, Slovakia; [3]Department of Pathology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; [4]Institute of Liver Studies, Department of Inflammation Biology, School of Immunology and Microbial Sciences, Faculty of Liver Sciences and Medicine, King's College London, London, UK; [5]Division of Gastroenterology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-020-19692-y OPEN

Endogenous antisense RNA curbs CD39 expression in Crohn's disease

Rasika P. Harshe[1,5], Anyan Xie[2,5], Marta Vuerich[1,5], Luiza Abrahão Frank[1], Barbora Gromova[1,3], Haohai Zhang[1], Rene' J. Robles[2], Samiran Mukherjee[1], Eva Csizmadia[1], Efi Kokkotou[2], Adam S. Cheifetz[2], Alan C. Moss[2], Satya K. Kota[4], Simon C. Robson[1,2,5] & Maria Serena Longhi[1,5]✉

biomolecules

MDPI

Review

Deoxyribonucleases and Their Applications in Biomedicine

Lucia Lauková [1], Barbora Konečná [2], Ľubica Janovičová [2], Barbora Vlková [2] and Peter Celec [2,3,4,*]

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3 Institute of Pathophysiology, Faculty of Medicine, Comenius University, 81108 Bratislava, Slovakia
4 Department of Molecular Biology, Faculty of Natural Sciences, Comenius University, 81108 Bratislava, Slovakia

scientific reports

OPEN

Dynamics of salivary markers of kidney functions in acute and chronic kidney diseases

Alexandra Gaál Kovalčíková[1,2], Kristína Pavlov[1,3], Róbert Lipták[1,4], Marianna Hladová[1], Emese Renczés[1], Peter Boor[5], Ľudmila Podracká[2], Katarína Šebeková[1], Július Hodosy[1], Ľubomíra Tóthová[1] & Peter Celec[1,4]✉

THE YEAR 2020 AT IMBM
The view of the head of the institute

People do not need a doctor until they are ill. A pandemic is needed to discover the role of science in our life. More physicians and nurses will be useless without an effective treatment or prevention. The year 2020 was a difficult year for all of us, but a crisis also opens doors and changes the most solid paradigms. Hopefully, the society will understand the value of research in biomedicine and beyond.

Thousands of labs all over the world changed their focus to SARS2 and Covid, so did we. But we did not have to change much. Saliva as a diagnostic fluid has been a research topic since the start of our institute. So, after establishing salivary marker of oxidative stress, measuring testosterone and other steroids in thousands of samples, we now try to find a way how to detect the viral RNA in saliva that can be collected non-invasively using LAMP, but also using established qPCR protocols in wastewater. We study neutrophils and their reactivity in patients with rheumatoid arthritis, but the same extracellular traps produced by the immune cells seems to be important for the pathogenesis of Covid.

We did not have to change much in our research focus. However, the new projects are extremely short and demanding. They require more people in the lab, not less.

With all the lockdowns, quarantines and home schoolings this might really be a challenge.

We have two new associate professors - congratulations! We have finally published again more than 30 papers in a year. Thanks to very productive students and their research stays abroad - I would name Martin Marônek with already 4 such papers and Barbora Gromová with publications in Journal of Hepatology or Nature Communications. These are reasons to celebrate.

RNA vaccines, recombinant viral vaccines, enormous amounts of molecular testing… The crisis forces molecular biomedicine to use its full potential. I hope at least the next generation of this institute will participate in the upcoming revolution in medicine with targeted and personalized treatments and even more, with extremely sensitive and simple screening of the most serious diseases.

I am looking forward…

Peter Celec


QIAGEN

RESEARCHERS AT IMBM

PROFESSORS

KATARÍNA ŠEBEKOVÁ, assoc. prof., MD, DrSc

CC/IF publications - 154, SCI citations - 2827, H-index - 31

metabolic syndrome, diabetes mellitus, advanced glycation end products, clinical biochemistry, pathogenesis of renal diseases

katarina.sebekova@imbm.sk

PETER CELEC, assoc. prof., MD, Ing, MSc, DrSc, MPH

CC/IF publications - 226, SCI citations - 2939, h-index - 30

extracellular DNA, testosterone, salivary biomarkers, sepsis

peter.celec@imbm.sk

PETER BOOR, prof., MD, PhD

CC/IF publications - 184, SCI citations - 4581, h-index - 41

renal fibrosis, nephropathology, immunopathomechanisms, models of renal diseases, imaging

boor.peter@gmail.com **pboor@ukaachen.de**

JÚLIUS HODOSY, assoc. prof., MD, MSc, PhD, MPH

CC/IF publications - 89, SCI citations - 1036, H-index - 20

sex steroids, oxidative stress, animal models of diseases, sleep apnea syndrome traumatic brain injury

hodosy@gmail.com

ROMAN GARDLÍK, assoc.prof., MD, MSc, PhD

CC/IF publications - 71, SCI citations - 685, h-index - 14

inflammatory bowel disease, animal models, extracellular DNA, microbiome

roman.gardlik@imbm.sk

ĽUBOMÍRA TÓTHOVÁ, assoc.prof., MSc, PhD

CC/IF publications - 77, SCI citations - 644, h-index - 15

salivary markers, oxidative stress, urinary tract infections, experimental nephrology, bacteriophages

lubomira.tothova@imbm.sk

POSTDOCS

BARBORA VLKOVÁ, MSc, PhD

CC/IF publications - 45, SCI citations - 628, h-index - 12

extracellular DNA, non-invasive prenatal diagnostics, pneumonia, sepsis, molecular pathology

barbora.vlkova@imbm.sk

JANKA BÁBÍČKOVÁ, MSc, PhD

CC/IF publications - 33, SCI citations - 424, h-index - 12

phage display, sex steroids, inflammatory bowel disease, extracellular DNA, experimental nephrology

jana.babickova@gmail.com

MICHAL PASTOREK, MSc, PhD

CC/IF publications - 24, SCI citations - 248, h-index - 11

neutrophil biology, autoimmune diseases, tumor hypoxia, extracellular DNA, molecular chaperones

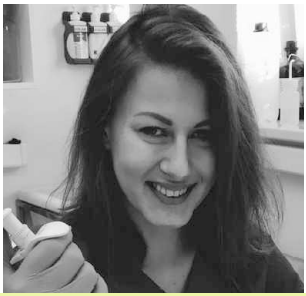
michal.pastorek@imbm.sk

VERONIKA BORBÉLYOVÁ, MSc, PhD

CC/IF publications - 20, SCI citations - 73, h-index - 5

animal models of autism spectrum disorder, effects of prenatal testosterone on postnatal behavior, metabolic syndrome, menopause

veronika.borbelyova@imbm.sk



BARBORA KONEČNÁ, MSc, PhD

CC/IF publications - 22, SCI citations - 125,
h-index - 6

extracellular DNA, extracellular vesicles,
pregnancy complications,
quantitative real-time PCR

barbora.konecna@imbm.sk

EMESE RENCZÉS, MSc, PhD

CC/IF publications - 18, SCI citations - 72,
h-index - 5

sex hormones,
behavioral penotyping in rats and mice,
mental disorders, autism

emese.domonkos@imbm.sk

MÁRIA SUCHOŇOVÁ, MSc, PhD

CC/IF publications - 4, SCI citations - 35,
h-index - 3

optics, optical spectroscopy, biomedical physics,
laser-induced breakdown spectroscopy,
imaging methods in medicine

maria.suchonova@imbm.sk

PHD STUDENTS AT IMBM

Melinda Csongová, MSc
Ľubica Janovičová, MSc
Martin Marônek, MSc
Katarína Kmeťová, MSc
Lucia Mihalovičová, MSc
Miriam Pillerová, MSc
Veronika Šarayová, MSc
Alena Potočárová, DVM
Dávid Miláček, MSc
Jakub Janko, MSc
Kristína Macáková, MSc
Nadja Ivašková, MSc
Jakub Szabó, MSc
Barbora Gromová, MSc

MASTER STUDENTS AT IMBM

Diana Drobná, B.S.
Tanzeel Ahmed
Johan Filo
Andrej Kirn
Alexander Jančuška
Zuzana Sliacka
Kristína Lichá, B.S.
Michaela Vašeková, B.S.
Andrej Feješ, B.S.
Emil Bečka, B.S.
Gergő Borka, B.S.
Michaela Budovcová, B.S.

BACHELOR STUDENTS AT IMBM

Letícia Hudecová
Lucia Mosná
Lucia Grácová
Alžbeta Jančovičová
Adam Polák
Daniel Králik
Martina Belišová
Diana Papová
Karolína Kováčová
Dana Görčiová
Aneta Krajníkova
Ivana Slivková
Jakub Villant

MASTER STUDENTS WHO SUCCESSFULLY DEFENDED THEIR THESES

Drobná Diana, MSc
Gromová Barbora, MSc
Zuzana Sliacka, MSc

BACHELOR STUDENTS WHO SUCCESSFULLY DEFENDED THEIR THESES

Karolína Kováčová, B.S.
Gergő Borka, B.S.
Andrej Feješ, B.S.
Dana Görčiová, B.S.
Emil Bečka, B.S.

OTHER COLLEAGUES

Henrieta Rácová, Ingrid Simonová, Ingrid Klobušická, Mária Turoňová, Barnabáš Borbély, Darina Mackovičová, Darina Skuráková

RESEARCH TOPICS AT IMBM 2020

1/ EXTRACELLULAR DNA IN ACUTE KIDNEY INJURY

2/ DEVELOPMENT OF AUTISTIC SYMPTOMS THROUGHOUT LIFESPAN

3/ GENE x ENVIRONMENT INTERACTION IN AUTISM

4/ 24-HOUR HOME-CAGE MONITORING: AN IMPROVED APPROACH FOR BEHAVIORAL PHENOTYPING IN MICE

5/ INHIBITION OF NEUTROPHIL EXTRACELLULAR TRAPS AND SEVERITY OF INTESTINAL INFLAMMATION

6/ SEX DIFFERENCES IN CIRCULATING EXTRACELLULAR DNA AND DNASE ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN REMISSION

7/ DNA IN PLASMATIC EXOSOMES

8/ WASTEWATER

9/ PLASMA ACTIVATED WATER

10/ SARS-CoV-2 VIRUS INDUCES THE FORMATION OF NETs

11/ ROLE OF NETs IN RHEUMATOID ARTHRITIS

12/ FORMATION OF NETs DURING FEVER

13/ MITOCHONDRIAL COMPONENTS AS NETs INDUCERS

14/ LOOP-MEDIATED ISOTHERMAL AMPLIFICATION FOR THE DETECTION OF SARS-COV-2 IN SALIVA

15/ ASYMPTOMATIC HYPERURICEMIA ASSOCIATES WITH CARDIOMETABOLIC RISK INDICATORS IN OVERWEIGHT/ OBESE BUT NOT IN LEAN ADOLESCENTS

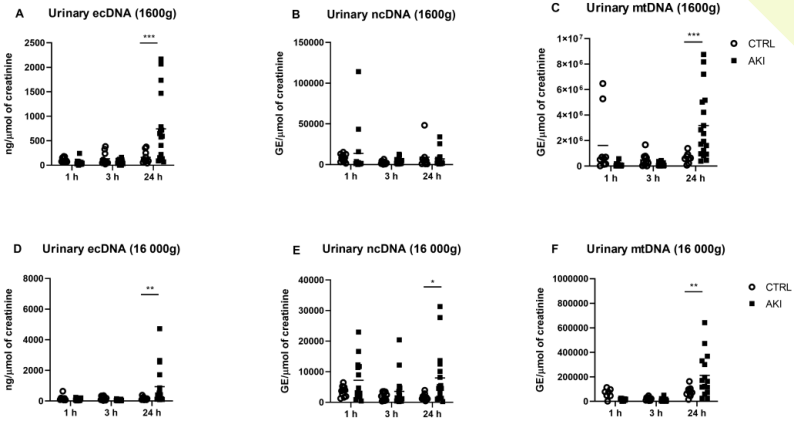
EXTRACELLULAR DNA IN ACUTE KIDNEY INJURY

What is known?

Acute kidney injury (AKI) is a clinical syndrome characterized by rapid decrease of kidney function and resulting retention of nitrogenous waste products, acid-base and electrolyte balance and other homeostasis impairments. Currently, the diagnosis of acute kidney injury is most often based on the rise in serum creatinine concentration. However, there is a time gap between the causative kidney insult and this rise, which means the loss of a potential therapeutic window. New markers of AKI, which would provide earlier detection or prediction of kidney damage before the deterioration of function are challenging. Studying the role of extracellular DNA (ecDNA) in AKI pathogenesis or as a potential biomarker is promising.

What is new?

The time dynamics of ecDNA in plasma and urine through the progression of acute kidney injury was described. The plasma ecDNA showed significant rise of mitochondrial DNA within 1 hour, and nuclear DNA within 3 hours after the model induction. Urinary ecDNA is increased between 3 and 24 hours after induction of AKI. Although not specific, the ecDNA and/or its fractions either in plasma or urine might have the potential of early AKI markers. In case the urine ecDNA to be increased within 12 hours (not yet studied in our experiment), we would obtain an early and non-invasive marker of AKI. Also, our initial findings need to be confirmed for consistency by other models of AKI.



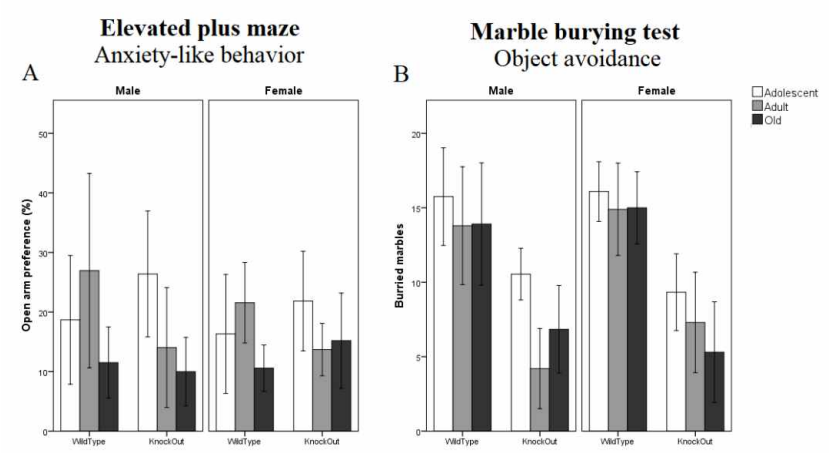
DEVELOPMENT OF AUTISTIC SYMPTOMS THROUGHOUT LIFESPAN

What is known?

Incidence of Autism Spectrum Disorders (ASD) has been shown increasing tendency over the last decades with 4-fold higher prevalence in males than in females. Despite obvious sex differences in etiopathogenesis of ASD, most of the experiments are conducted only in males. The focus is often placed on core features of ASD, such as impaired sociability and excessive repetitive behavior. However, the extended symptoms, such as anxiety or avoidance, are neglected. To establish an appropriate animal model of ASD, the heterogeneity as well as the sex- and age-specific manifestations of ASD should be considered.

What is new?

The main goal of our study was to describe the sex-specific behavioral phenotype of Shank3 mutant mice, and to follow up the development of ASD-like symptoms from adolescence through adulthood to old age. Our results indicate that anxiety-like phenotype in both female and male ASD mice manifests in adulthood, but not in adolescence or at old age (A). However, object avoidance is obvious in ASD mice throughout the lifespan, regardless to sex (B).



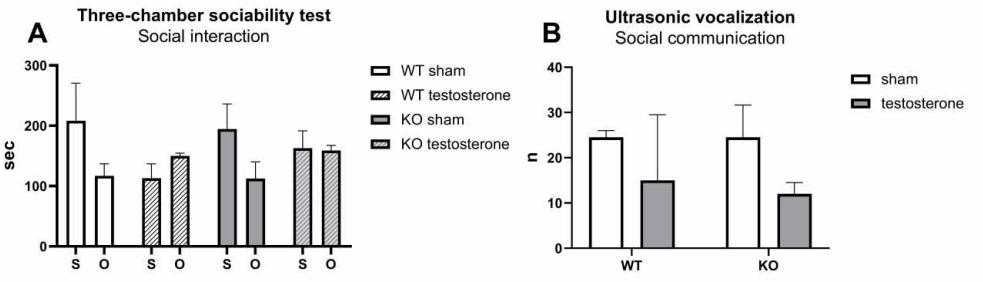
GENE x ENVIRONMENT INTERACTION IN AUTISM

What is known?

Although progress has been achieved in diagnostics of ASD, its etiology is still unknown. Besides genetic factors, the role of endocrine and environmental risk factors have been presumed. According to the Extreme Male Brain Theory, we hypothesized that absence of testosterone during the sensitive period of brain development in females, unlike the males, is protective against ASD.

What is new?

Our study aimed to examine the role of gene x environment interactions in etiopathogenesis of ASD. Our results show that neonatal testosterone exposure may diminish social-partner preference (A) and decrease ultrasonic vocalization (B) in wild-type (WT) as well as in female Shank3 mutant mice (KO). It indicates that testosterone excess during early development may cause deficits in social interactions and social communication in females regardless of genetic predisposition.



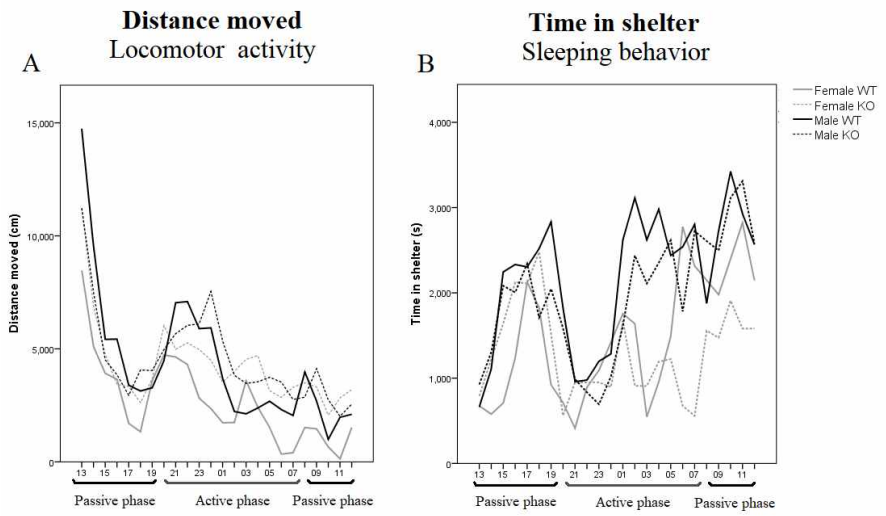
24-HOUR HOME-CAGE MONITORING: AN IMPROVED APPROACH FOR BEHAVIORAL PHENOTYPING IN MICE

What is known?

Despite the fact that rodents are nocturnal animals, most of the experiments, including behavioral testing, are conducted during the day, which is the passive phase for the animals. In addition, the behavioral tests are often affected by novelty-induced stress, which might be avoided using a home-cage monitoring system applied for long-term observation. For the consistent and reliable data, the behavioral phenotype of the animals should be monitored under an undisturbed condition throughout the whole light-dark cycle.

How can we move further?

We aimed to describe a comprehensive behavioral phenotype of mice using the PhenoTyper home-cage monitoring system from Noldus, EthoVision. We constructed an ethogram demonstrating the dynamical changes in several behavioral parameters throughout the day. Our data indicate that locomotor activity, exploratory-, feeding-, sleeping-, as well as anxiety-like behavior are changing not only between but also within the active and passive phase of the day. These results should be considered to avoid technical variability, and to improve reproducibility of behavioral data.



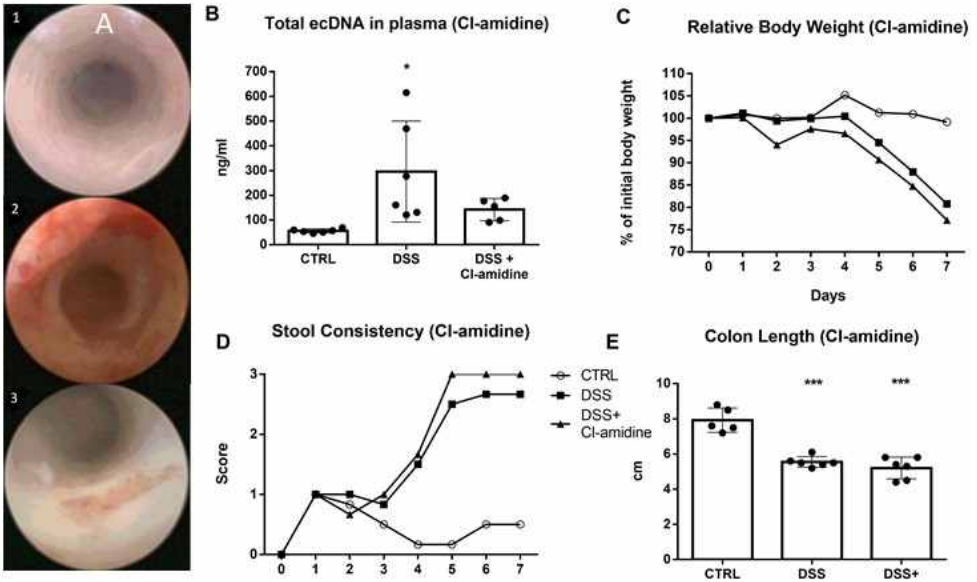
INHIBITION OF NEUTROPHIL EXTRACELLULAR TRAPS AND SEVERITY OF INTESTINAL INFLAMMATION DISEASE

What is known?

One of the immune stimulants in colitis may be ongoing neutrophil extracellular traps (NETs) production or increasing concentration of extracellular DNA (ecDNA) during intestinal inflammation.

What is new?

Endoscopic visualization (A) of the colonic mucosa showed visibly alleviated intestinal inflammation after administration of NETs inhibitor (Cl-amidine). Cl-amidine treatment led to a decrease of the concentration of ecDNA in plasma (B). However, in view of the clinical symptoms of colitis such as weight loss (C), rectal bleeding (D) or shortening of the intestine (E), treatment with Cl-amidine colitis mice did not lead to their recovery.



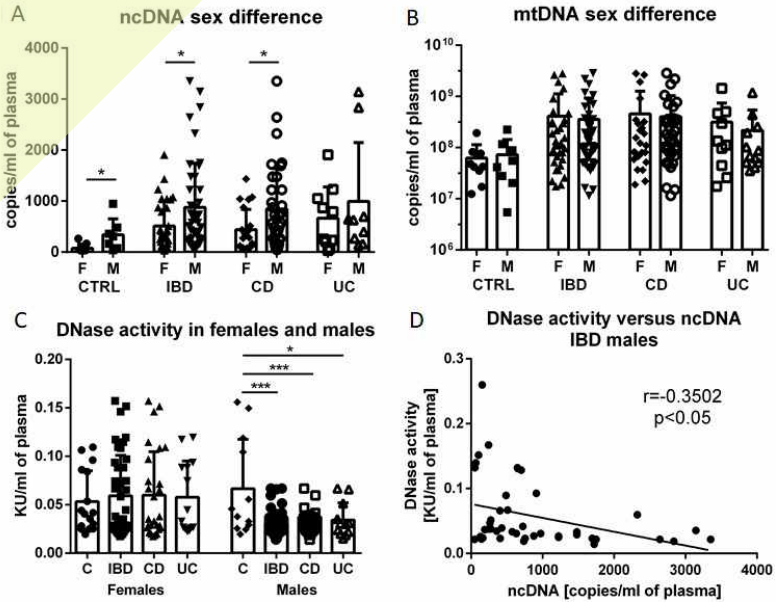
SEX DIFFERENCES IN CIRCULATING EXTRACELLULAR DNA AND DNASE ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN REMISSION

What is known?

EcDNA and its variants (nuclear - ncDNA or mitochondrial - mtDNA) together with the enzyme deoxyribonuclease (DNase) can be a potential biomarker of inflammatory bowel disease (IBD) activity.

How can we move further?

Circulating ncDNA levels in men with IBD were increased compared to healthy controls (A), but no sex difference was found in mtDNA in either group (B). DNase activity was lower in male IBD patients, including Crohn's disease (CD) and ulcerative colitis (UC) compared with healthy controls (C). Sex difference in circulating ncDNA levels were possibly associated with lower DNase activity in males (D).y.



DNA IN PLASMATIC EXOSOMES

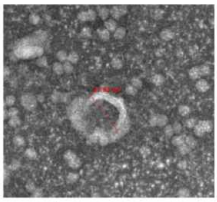
What is known?

Exosomes are the smallest subset of extracellular vesicles produced by each cell. Their role in the body is not yet fully understood. They are interesting for us mainly because it is believed they contain DNA, therefore exosomes are also a form of extracellular DNA, which is one of the main topics at our Institute.

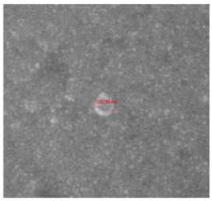
What is new?

We were able to isolate exosomes from human plasma according to relevant publications and separate them from non-vesicular compartments. We tested the isolated vesicles with transmission electron microscopy, nanoparticle tracking analysis and western blot. Most importantly we showed that not every plasma exosome carries DNA. We also know that mitochondrial DNA is much more abundant in comparison to nuclear DNA. An important finding was that 60-75% of the exosomal DNA is located on the surface of the vesicle. In the coming year, we would like to use our new flow cytometer to confirm our findings.

Exosomes by transmission electron microscope

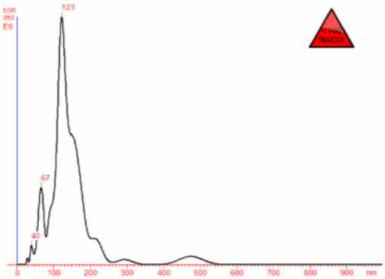


Ø 97,83 nm



Ø 130,39 nm

Size profile of plasmatic exosomes

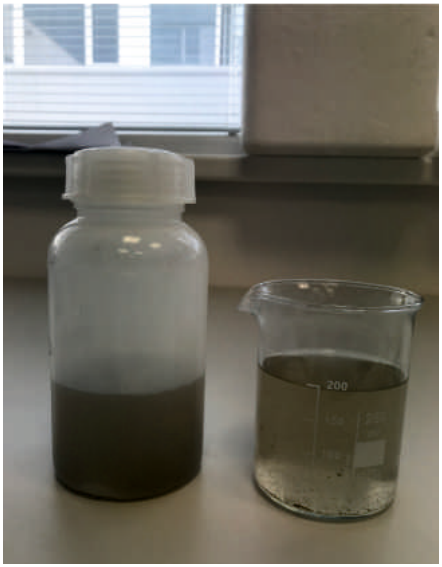


Particle Size / Concentration

WASTEWATER

What is known?

Wastewater is an important source of information about the population. It is possible to monitor the usage of pharmaceuticals, drugs, pesticides etc. It was published that wastewater also contains fragments of DNA. For the environment, it is important to degrade the substances that could be harmful for humans, animals and plants.



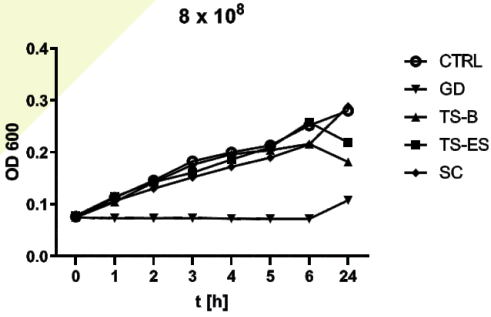
What is new?

We have established cooperation with the Department of Environmental Engineering of STU. They approached us with a proposal for wastewater monitoring for the presence of SARS-CoV-2. The aim was to monitor the presence, or dynamics, with respect to the number of infected inhabitants in the area. The Department of Molecular Biology PRIF UK is also involved in the project. Wastewater is also interesting in terms of the total human DNA, its form, dynamics and origin. In addition, there are other substances in the wastewater that can have an adverse impact on the environment. Therefore, we plan to monitor the impact of wastewater drinking on endocrine and metabolic functions as well as on behavior in rats in the coming period.

PLASMA ACTIVATED WATER

What is known?

Inactivation of microorganisms using plasma activated water offers an original alternative to standard approaches, which are prone to induce resistance in the target organisms. The main mechanisms of cold plasma sterilization relate to the production of reactive species and their interaction with the microorganisms without damaging the host tissues. These properties make plasma an attractive tool for medical applications, e.g. wound healing, treatment of ulcers and some skin diseases.



What is new?

In cooperation with assoc. prof. Zdenko Machal from the Department of Environmental Physics from FMFI UK, the antimicrobial effect of plasma activated waters was studied in in vitro and in vivo experiments.

First, the effect of four different types of plasma activated water was tested to inactivation of uropathogenic E. Coli bacteria. Following, the plasma activated water with high content of hydrogen peroxide (GD PAW), which showed the highest antimicrobial effect (Fig. 1) was used in animal model of urinary tract infection and chemical induced colitis in mice. The plasma activated water did not reduce the number of bacteria in the homogenates of the bladders in case of urinary tract infection in mice (Fig. 2). In animal model of colitis, bowel lavage using plasma activated water did not improve the symptoms of colitis, but improved the overall antioxidant capacity of intestines (Fig.3 a, b).

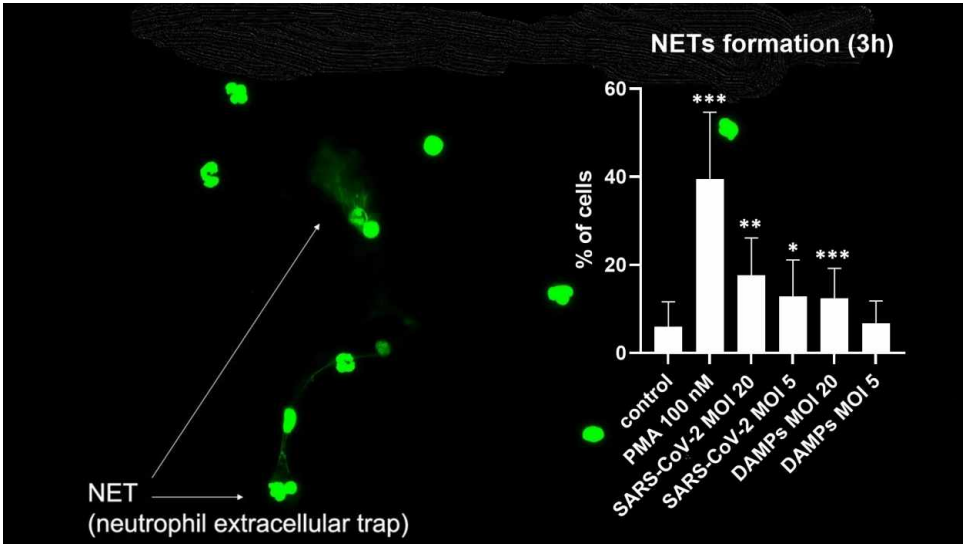
SARS-CoV-2 virus induces the formation of NETs

What is known?

Covid-19 was the most discussed disease of the last year and at its peak, hundreds of teams were investigating its pathomechanism. Among others, deregulation of immune response and NETs (neutrophil extracellular traps) formation were found to be associated with the severity of SARS-CoV-2 infection. And while it's known that age is the dominant factor determining survival, the underlying reasons are not fully understood.

What is new?

Thanks to the grant support, we were able to analyze neutrophils in presence of SARS-CoV-2 virus and observed that both active and heat-inactivated viruses were able to induce formation of NETs. These findings are currently utilized in ongoing experiments, where we compare neutrophils from donors of all age groups in their capacity to induce NETs as a response to stimuli ranging from damage associated molecular patterns (DAMPs) to virus itself.



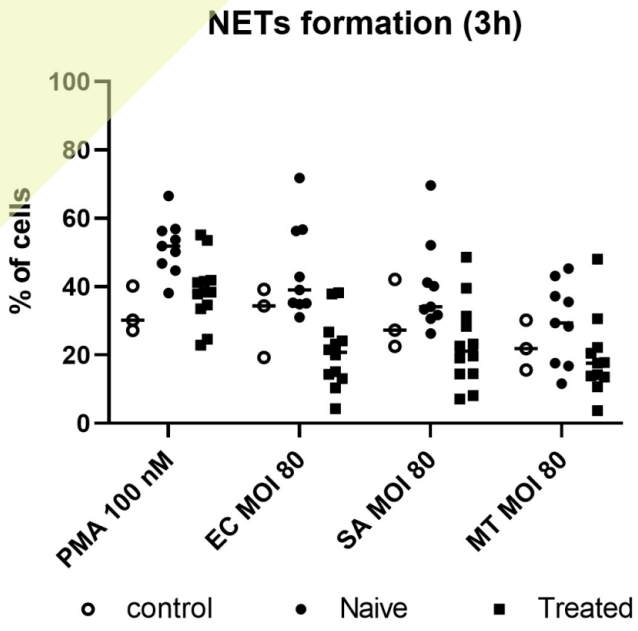
Role of NETs in rheumatoid arthritis

What is known?

While the knowledge of autoimmune diseases pathology is expanding, its pathomechanisms are still not fully understood and rheumatoid arthritis (RA) is no exception. Presence of autoantibodies against citrullinated peptides is one of the features of this disease and since NETs (neutrophil extracellular traps) contain citrullinated proteins, their role in RA onset is widely discussed.

What is new?

Our analysis revealed that neutrophils of naive RA patients are more prone to form NETs when compared to the control patients with arthrosis and, interestingly, NETs formation in RA patients undergoing biological therapy is lower than in naive patients. Whether increased NETs formation in naive RA patients is a cause or a consequence of the disease remains to be determined.



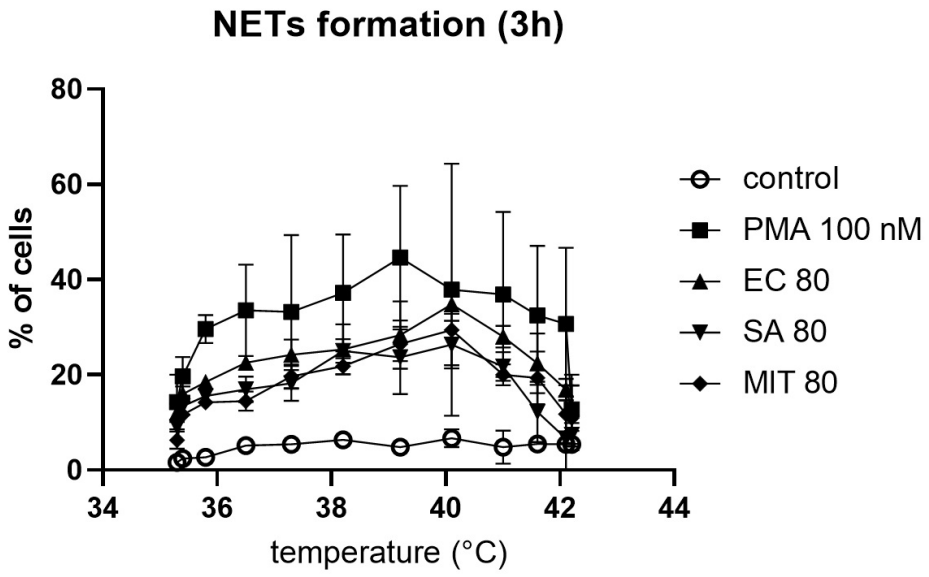
FORMATION OF NETs DURING FEVER

What is known?

Fever is an evolutionary old response of vertebrates to the infection that integrates the activation of both adaptive and innate immune systems. It is known that increased temperature potentiates neutrophil migration to the site of infection, but there is little evidence on its effect on NETs (neutrophil extracellular traps) formation.

What is new?

Twe have observed that formation of NETs in response to bacteria and mitochondria is increased during fever and peaks at 40°C, but interestingly, decreases when the temperature rises too high (>41°C) or gets too low (<36°C).



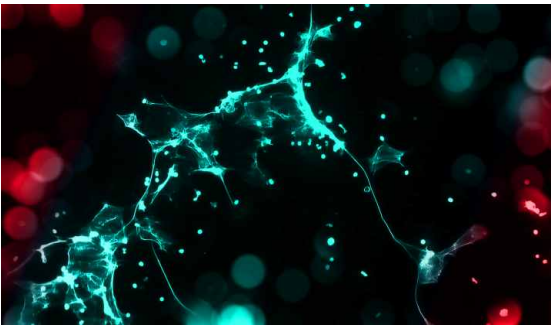
Mitochondrial components as NETs inducers

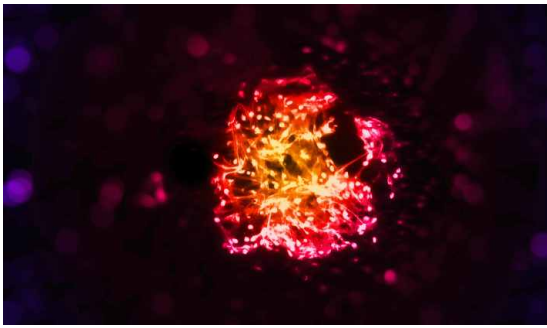
What is known?

Formation of NETs (neutrophil extracellular traps) was first described as a response of neutrophils to bacteria, but soon after, it became apparent that their distant endosymbiotic cousins mitochondria are able to induce their formation as well.

What is new?

We have aimed to identify components of mitochondria that are the most potent in inducing NETs formation. We found that mitochondrial proteins, but not DNA are key components that stimulate neutrophils and protease treatment attenuates their formation.





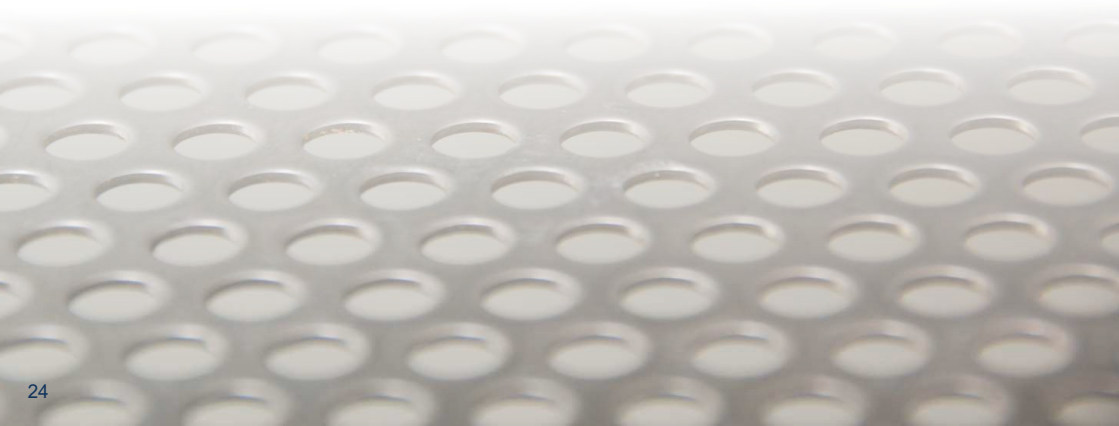
LOOP-MEDIATED ISOTHERMAL AMPLIFICATION FOR THE DETECTION OF SARS-COV-2 IN SALIVA

What is known?

SARS-CoV-2 is the strain of virus responsible for ongoing COVID-19 pandemics. Currently, nasopharyngeal swabs and real time RT-PCR are used for the standard detection of the viral RNA. In the clinical practice testing is crucial, ideally with a result within one or two hours. An alternative to RT-PCR is loop-mediated isothermal amplification coupled with reverse transcription (RT-LAMP) that is easy to perform, quick and does not require a thermal cycler. Also, collection of saliva is non-invasive, pain-free and does not require trained personnel. Saliva as a diagnostic fluid and RT-LAMP as the analytical method is a promising approach for a rapid point of care diagnostics.

What is new?

Whole saliva, as well as saliva collected using Salivette collection tubes interfered with the RT-LAMP analysis. Neither Chelex-100, nor protease treatment of saliva prevented the inhibitory effect of saliva. With the addition of the ribonuclease inhibitor, the sensitivity of the RT-LAMP assay was 12 copies per reaction of RNA in Salivette® saliva samples and 6 copies per reaction of RNA in whole saliva samples (Figure 1). Our finding shows that it is possible to combine the use of saliva and RT-LAMP for SARS-CoV-2 RNA detection without RNA extraction which was confirmed on a small set of correctly diagnosed clinical samples (Figure 2). Further studies should prove whether this protocol is suitable for point of care testing in the clinical setting.



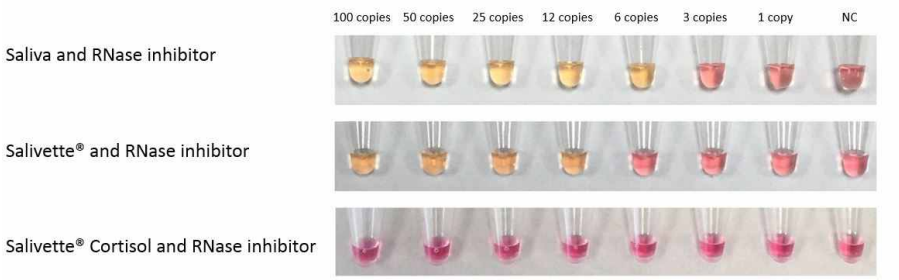


Figure 1: Effect of RNase inhibitor on RT-LAMP on saliva samples with a serial dilution of the EDX SARS-CoV-2 RNA Standard as the RNA template performed with Yan et al. (S-123) primer mix. Yellow color - positive result - presence of RNA, pink color - negative result - absence of RNA. NC – negative control

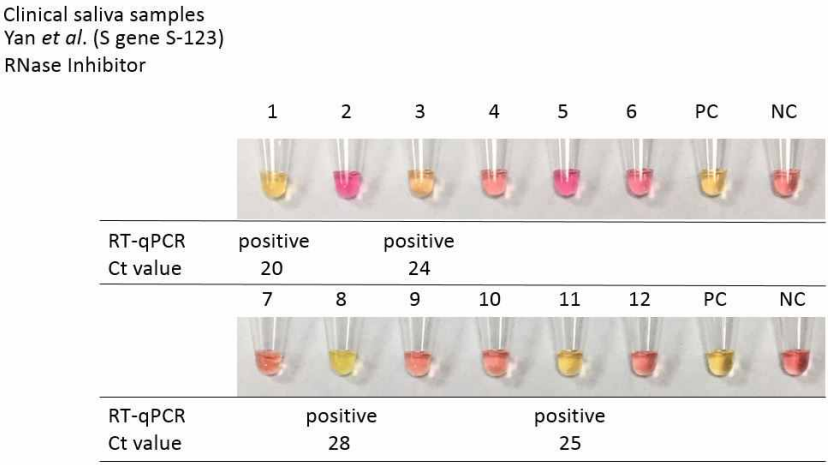


Figure 2: The RT-LAMP on clinical saliva samples performed with Yan et al. (S-123) primer mix and RNase inhibitor. Yellow color - positive result - presence of RNA, pink color - negative result - absence of RNA. PC – positive control, NC – negative control

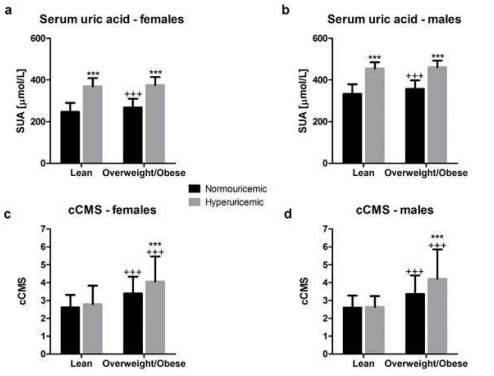
ASYMPTOMATIC HYPERURICEMIA ASSOCIATES WITH CARDIOMETABOLIC RISK INDICATORS IN OVERWEIGHT/ OBESE BUT NOT IN LEAN ADOLESCENTS

What is known?

In overweight/obese adolescents, asymptomatic hyperuricemia is associated with increased prevalence of metabolic syndrome, its components, and a higher cardiometabolic risk. Whether similar associations exist in lean hyperuricemic adolescents is unknown.

What is new?

Analysis of data from 2 424 adolescents aged 16-19 years showed that more than a half of adolescents with asymptomatic hyperuricemia are lean. Lean and obese hyperuricemic adolescents present similar serum uric acid (SUA) concentrations (Figure). In overweight/obese hyperuricemic adolescents, continuous cardiometabolic risk score (cMSS) is increased; while lean hyperuricemic adolescents present similarly low cardiometabolic risk as their normouricemic peers. In lean subjects, hyperuricemia generally remains undiagnosed, unless there is a reasonable indication to analyze SUA concentration. Whether in lean subjects asymptomatic hyperuricemia will have clinical consequences in later life remains unclear.



***: p<0.001 vs normouricemic subjects of the same body frame;

+++: p<0.001 vs lean subjects in the corresponding SUA category

Summer School of Biomedicine For High School Students and University Students

In 2020, we organized a summer school for both, high school and university students. Within the summer school of biomedicine, students had an opportunity to learn the basic methods of biomedical research and experience research work in the laboratories of the Institute of Molecular Biomedicine by participating in our ongoing projects. We assume that summer school improved the overall readiness of students to successfully complete their university studies and their work in biomedical research. Our long-term goals also include the reintegration of Slovak students studying abroad and the integration of foreign students into biomedical research, thus, the summer school at IMBM was a good opportunity to reach these goals.

Alumni of Summer School of Biomedicine 2020

Rateb Alzeer, Gergő Borka, Patrik Boskovič, Martina Brozová, Michaela Budovcová, Leonid Chernivetskiy, Klaudia Cisárová, Gauri Deák, Rebeka Démuthová, Renáta Dominiková, Andrej Feješ, Johan Filo, Lucia Grácová, Barbora Gromová, Lukáš Hajdúch, Letícia Hudecová, Ján Hunák, Nadja Ivašková, Alžbeta Jančovičová, Terézia Jurášová, Veronika Kašová, Jiwon Kim, Terézia Kolenová, Karolína Kováčová, Aneta Krajníková, Ema Kubovská, Lukáš Lahučký, Marek Lamos, Barbara Lechnická, Alexandra Lesayová, Kristína Lichá, Kristína Macáková, Maximilián Marton, Zuzana Matulová, Matúš Mlynár, Lucia Mosná, Miroslava Orgoňová, Diana Papová, Jakub Petrus, Adam Polák, Evelína Šťastná, Matej Šteňo, Taha Torabpourshiraz, Aneta Uherčíková, Michaela Vašeková, Alžbeta Vitteková, Milan Žiak

CONFERENCES

An active participation in scientific conferences is an indispensable element for our work. At conferences we have the opportunity to present the results of our experiments, to discuss with experts and to establish new cooperation. In 2020, we actively attended or participated online at the following scientific conferences:

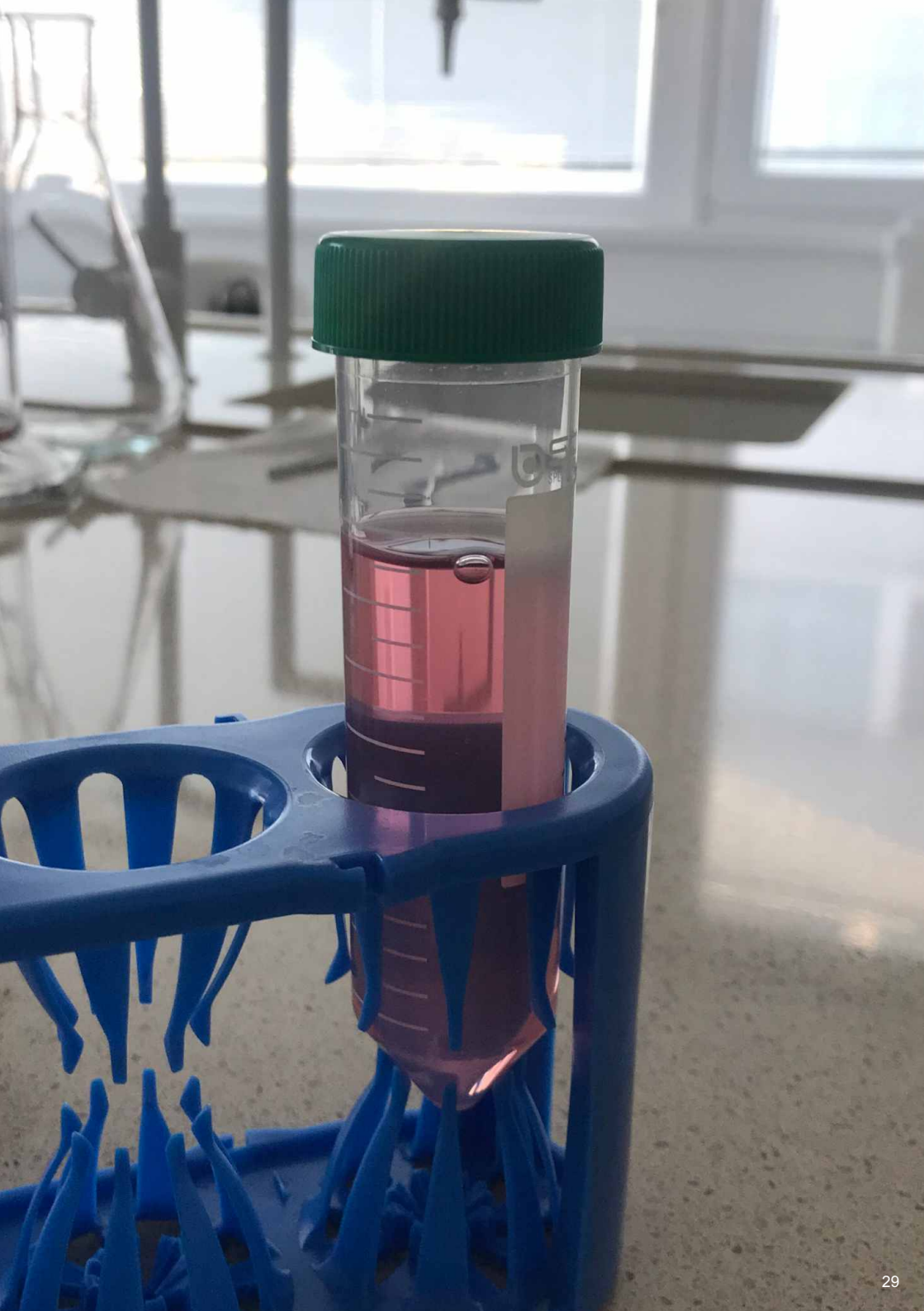
LVII. BRATISLAVA ONCOLOGY DAYS, 01.-02.10.2020, Bratislava, Slovakia
(Veronika Borbélyová, Emese Renczés, Michal Chovanec, Michal Mego, Peter Celec)

96th PHYSIOLOGICAL DAYS, 04.-06.02.2020, Martin, Slovakia
(Peter Celec, Veronika Borbélyová, Alena Potočárová, Dávid Miláček)

DAYS OF PRACTICAL OBESITOLOGY AND METABOLIC SYNDROME, 16.-18.07.2020, Demänovská dolina, Slovakia
(Lucia Mihalovičová, Veronika Šarayová, Dávid Miláček)

PRACTICAL PEDIATRICS - 60th PEDIATRIC DAYS. Invited lecture: Kovács' memorial Lecture, 25.-26.6.2020, Bratislava, Slovakia
(Katarína Šebeková)

XV. SCIENTIFIC CONFERENCE OF DOCTORAL STUDENTS, Comenius University, Medical Faculty, 04.-18.5.2020, Bratislava, Slovakia
(Lucia Mihalovičová, Veronika Šarayová, Dávid Miláček, Alena Potočárová)



FOREIGN STAYS

BARBORA KONEČNÁ
Beth Israel Deaconess Medical Center/Harvard Medical School Boston, MA, USA, Department of Surgery, October 2019 - April 2020 working on neutrophil activity in various conditions

ĽUBICA JANOVIČOVÁ
Beth Israel Deaconess Medical Center/Harvard Medical School Boston, MA, USA, Department of Surgery, October 2019 - December 2020 working on origin extracellular DNA in plasma and its structure

MONIKA JANÍKOVÁ
Beth Israel Deaconess Medical Center/Harvard Medical School Boston, MA, USA, Department of Surgery, November 2020 - present, working on origin extracellular DNA in plasma and its structure

MARTIN MARÔNEK
Università degli Studi di Roma "Tor Vergata", Facoltà di Medicina e Chirurgia, Dipartimento di Medicina dei Sistemi, Rome, Italy, March 2020 – August 2020, October 2020 – December 2020, working on the effect of NETs on intestinal wound healing

MIRIAM PILLEROVÁ
University of Wisconsin-Milwaukee, Milwaukee, WI, USA, Department of Psychology, February 2020 - September 2020, working on the necessity of glycogenolysis in dorsal hippocampal astrocytes for object memory consolidation

INVITED LECTURES

Veronika Borbélyová

Autism Spectrum Disorder, Summer School Viva La Science, 19.8.2020, Nitra, Slovakia

Emese Renczés

Sex differences in brain and behavior, Summer School Viva La Science, 19.8.2020, Nitra, Slovakia

Katarína Šebeková

Cardiometabolic risk in adolescents with asymptomatic hyperuricemia, Practical Pediatrics - 60th Pediatric Days, Kovács' memorial lecture, 25.-26.6.2020, Bratislava, Slovakia

EDUCATION ACTIVITIES 2020

IMBM is a research institute, but it is also important to participate in the educational process. Beyond institutional meetings, seminars and courses we prepared the lectures, seminars and practical courses at the Faculty of Medicine and Faculty of Natural Sciences, Comenius University in Bratislava:

FACULTY OF MEDICINE:

Physiology
Pathophysiology
Pathology
Introduction to Science

FACULTY OF NATURAL SCIENCES:

Molecular Endocrinology
Basics of Theoretical and Experimental Medicine

Progress in Molecular Biology
Advanced Methods in Molecular Biology
Behavioral Genetics
Special Genetics
Basics of Clinical Medicine

PRIZES

Dávid Miláček, MSc
1st place winner in poster section within congress Days of practical obesitology and metabolic syndrome
Demänovská dolina, Slovakia

Veronika Šarayová, MSc and Lucia Mihalovičová, MSc
3rd place winners in poster section within congress Days of practical obesitology and metabolic syndrome
Demänovská dolina, Slovakia

Dávid Miláček, MSc
2nd place winner at XV. Science conference of Ph.D. students within section of clinical research
Faculty of Medicine UK, Slovakia

SCHOLARSHIPS

Monika Janíkova, MSc
scholarship for research stay for 8 months at Harvard Medical School, Boston
(funded by National Scholarship Programme of Slovak Republic)

Veronika Šarayová, MSc
scholarship for research stay for 6 months at IRCCS Instituto Centro San Giovanni di Dio Fatebenefratelli, Italy
(funded by National Scholarship Programme of Slovak Republic)

Lucia Mihalovičová, MSc
Scholarship of Ľudmila Sedlárová - Rabanová

Lucia Mihalovičová, MSc
scholarship for research stay for 10 months at L'Institut de Recherche en Cancérologie de Montpellier, France
(funded by National Scholarship Programme of Slovak Republic)

Martin Marônek, MSc
scholarship for 5 months at Università degli Studi di Roma "Tor Vergata" (funded by Erasmus+ programme, EACEA, European Commission); scholarship for 2.5 months at Università degli Studi di Roma "Tor Vergata"
(funded by the National Scholarship Programme of Slovak Republic)

Miriam Pillerová, MSc
scholarship of Ľudmila Sedlárová - Rabanová

Miriam Pillerová, MSc
scholarship for research stay for 10 months at University of Wisconsin-Milwaukee, Milwaukee, WI, USA
(funded by National Scholarship Programme of Slovak Republic)

Miriam Pillerová, MSc
scholarship "Hlavička" from SPP foundation

COOPERATIONS

Institute of Physiology, Faculty of Medicine, Comenius University in Bratislava, Bratislava, Slovakia
(Daniela Ostatníková, prof., MD, PhD)

Department of Paediatrics, National Institute of Children's Diseases and Faculty of Medicine, Comenius University in Bratislava, Bratislava, Slovakia
(Ľudmila Podracká, prof., MD, CSc; Alexandra Gaál Kovalčíková, MSc, PhD)

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Comenius University in Bratislava, Bratislava, Slovakia
(Diana Vavrincová-Yaghi, MSc, PhD)

Department of Environmental Engineering, Slovak Technical University in Bratislava, Bratislava, Slovakia
(Tomáš Mackuľák, assoc. prof., PhD; Miroslav Gál, assoc. prof., PhD)

2nd Department of Oncology, Faculty of Medicine, Comenius University and Translational Research Unit, National Cancer Institute, Bratislava, Slovakia
(Michal Mego, prof., MD, PhD; Michal Chovanec, assoc. prof., MD, PhD)

Department of Dental Hygiene, Faculty of Health Care, University Prešov, Slovakia
(Eva Kovaľová, assoc. prof., MD, PhD)

1st Department of Internal Medicine, Medical Faculty, Comenius University, Bratislava, Slovakia
(Emoke Steňová, assoc. prof., MD, PhD)

National Institute of Rheumatic Diseases, Piešťany, Slovakia (Vanda Mlynáriková, MD)
2nd Gynecology and Obstetrics Clinic, Faculty of Medicine, Comenius University, Bratislava, Slovakia
(Jozef Záhumenský, assoc. prof., MD, PhD)

Department of Environmental Physics, Astronomy, Earth Physics and Meteorology, Faculty of Mathematics, Physics and Informatics, Comenius University, Bratislava, Slovakia
(Zdenko Machala, prof., PhD)

Department of Physiology, First Faculty of Medicine, Charles University, Prague, Czech Republic
(Vladimír Riljak, assoc. prof., MD, PhD; Jaromír Mysliveček, prof., MD, PhD)

Department of Anesthesia, Beth Israel Deaconess Medical Center/Harvard Medical School Boston, Massachusetts, USA
(Maria Serena Longhi, MD, PhD)

Department of Surgery, Beth Israel Deaconess Medical Center/Harvard Medical School Boston, Massachusetts, USA
(Barbara Wegiel, PhD)

Department of Surgery, Beth Israel Deaconess Medical Center/Harvard Medical School Boston, Massachusetts, USA
(Carl J Hauser, MD)

Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy
(prof. Giovanni Monteleone)

Institute of Experimental Medicine, Faculty of Medicine, University of Pavol Jozef Šafárik, Košice, Slovakia
(Alojz Bomba, MD, CSc; Ľuboš Ambro, MSc, PhD)

Institute of Biology and Ecology, Faculty of Science, University of Pavol Jozef Šafárik, Košice, Slovakia
(Vlasta Demečková, PhD)

PUBLICATIONS

1. Renczés E, Marônek M, Gaál Kovalčíková A, Vavrincová-Yaghi D, Tóthová L, Hodosy J. Behavioral Changes During Development of Chronic Kidney Disease in Rats. Front Med (Lausanne), 6:311, 2020.

2. Renczés E, Borbélyová V, Keresztesová L, Ostatníková D, Celec P, Hodosy J. The age-dependent effect of pre-pubertal castration on anxiety-like behaviour in male rats. Andrologia, 52(7):e13649, 2020.

3. Renczés E, Borbélyová V, Steinhardt M, Höpfner T, Stehle T, Ostatníková D, Celec P. The Role of Estrogen in Anxiety-Like Behavior and Memory of Middle-Aged Female Rats. Front Endocrinol (Lausanne), 11:570560, 2020.

4. Borbélyová V, Renczés E, Chovanec M, Mego M, Celec P. Transient effects of chemotherapy for testicular cancer on mouse behaviour. Sci Rep, 10(1):10224, 2020.

5. Riljak V, Laštůvka Z, Mysliveček J, Borbélyová V, Otáhal J. Early postnatal hypoxia induces behavioral deficits but not morphological damage in the hippocampus in adolescent rats. Physiol Res, 69(1):165-179, 2020.

6. Kovalčíková AG, Pavlov K, Lipták R, Hladová M, Renczés E, Boor P, Podracká Ľ, Šebeková K, Hodosy J, Tóthová Ľ, Celec P. Dynamics of salivary markers of kidney functions in acute and chronic kidney diseases. Sci Rep, 10(1):21260, 2020.

7. Vrablicova Z, Tomova K, Tothova L, Babickova J, Gromova B, Konecna B Liptak R, Hlavaty T, Gardlik R: Nuclear and Mitochondrial Circulating Cell-Free DNA Is Increased in Patients With Inflammatory Bowel Disease in Clinical Remission. Front Med (Lausanne), 7; 593316, 2020

8. Franzè E, Laudisi F, Di Grazia A, Marônek M, Bellato V, Sica G, Monteleone G.: Macrophages produce and functionally respond to interleukin-34 in colon cancer. Cell Death Discov, 6(1):117, 2020

9. Marônek M, Link R, Ambro L, Gardlik R: Phages and Their Role in Gastrointestinal Disease: Focus on Inflammatory Bowel Disease. Cells, 18;9(4):1013, 2020

10. Marônek M, Link R, Monteleone G, Gardlík R, Stolfi C: Viruses in Cancers of the Digestive System: Active Contributors or Idle Bystanders? Int J Mol Sci, 21(21):8133, 2020

11. Laudisi F, Marônek M, Di Grazia A, Monteleone G, Stolfi C: Repositioning of Anthelmintic Drugs for the Treatment of Cancers of the Digestive System. Int J Mol Sci, 21(14):4957, 2020

12. Džunková M, Lipták R, Vlková B, Gardlík R, Čierny M, Moya A, Celec P: Salivary microbiome composition changes after bariatric surgery. Sci Rep, 10(1):20086, 2020

13. Harshe RP, Xie A, Vuerich M, Frank LA, Gromova B, Zhang H, Robles RJ, Mukherjee S, Csizmadia E, Kokkotou E, Cheifetz AS, Moss AC, Kota SK, Robson SC, Longhi MS: Endogenous antisense RNA curbs CD39 expression in Crohn's disease. Nat Commun, 11(1):5894, 2020

14. Vuerich M, Harshe R, Frank LA, Mukherjee S, Gromova B, Csizmadia E, Nasser IAM, Ma Y, Bonder A, Patwardhan V, Robson SC, Longhi MS: Altered aryl-hydrocarbon-receptor signalling affects regulatory and effector cell immunity in autoimmune hepatitis. J Hepatol, S0168-8278(20)30454-2, 2020

15. Borbélyová V, Janišová K, Mysliveček J, Riljak V: Sex-related differences in locomotion and climbing of C57Bl/6NTac mice in a novel environment. Physiological Research, 68 (Suppl 3):S353-S359, 2019

16. Murden S, Borbélyová V, Laštůvka Z, Mysliveček J, Otáhal J, Riljak V: Gender differences involved in the pathophysiology of the perinatal hypoxic-ischemic damage. Physiological Research. 68(Suppl 3):S207-S217, 2019

17. Šebeková, K., Gurecká, R., Csongová, M., Koborová I., Šebek, J. Elevated blood pressure-associated cardiometabolic risk factors and biomarkers in 16–23 years old students with or without metabolic abnormalities. J Hum Hypertens; 178(8):1243-1253, 2020

18. Šebeková, K.; Gurecká, R.; Csongová, M.; Koborová, I.; Šebek, J. Sex Differences in Association of Elevated Blood Pressure with Variables Characterizing Cardiometabolic Risk in Young Subjects with or Without Metabolic Abnormalities. Int. J. Environ. Res. Public Health, 17, e3612, 2020

19. Šebeková K, Gurecká R, Podracka L. Asymptomatic Hyperuricemia Associates with Cardiometabolic Risk Indicators in Overweight/ Obese but Not in Lean Adolescents. Diabetes Metab Syndr Obes:13 3977–3992, 2020

20. Uher T, Bohm A, Urban L, Tothova L, Bacharova L, Musil P, Kyselovic J, Michalek P, Vachalcova M, Olejnik P, Hatala R: Association of apelin and AF in patients with implanted loop recorders undergoing catheter ablation. Bratisl Med J, 121(7):484-487, 2020

21. Dusinska M, Sojka M, Horvathova M, Alacova R, Vecera Z, Mikuska P, Coufalik P, Krumal K, Capka L, Docekal B: Six-week inhalation of CdO nanoparticles in mice: The effects on immune response, oxidative stress, antioxidative defense, fibrotic response, and bones. Food Chem Toxicol, 136:110954, 2020

22. Gyurászová M, Gurecká R, Bábíčková J, Tóthová Ľ: Oxidative Stress in the Pathophysiology of Kidney Disease: Implications for Noninvasive Monitoring and Identification of Biomarkers. Oxid Med Cell Longev, 5478708 eCollection, 2020

23. Homolová J, Janovičová Ľ, Konečná B, Vlková B, Celec P, Tóthová Ľ, Bábíčková J: Plasma Concentrations of Extracellular DNA in Acute Kidney Injury. Diagnostics (Basel), 10(3):152, 2020

24. Konečná B, Vlková B, Repiská G, Tóthová Ľ: Transfection of maternal cells with placental extracellular vesicles in preeclampsia. Med Hypotheses, 141:109721, 2020

25. Ferenczyova K, Kalocayova B, Kindernay L, Jelemensky M, Balis P, Berenyiova A, Zemancikova A, Farkasova V, Sykora M, Tothova L, Jasenovec T, Radosinska J, Torok J, Cacanyiova S, Barancik M, Bartekova M: Quercetin Exerts Age-Dependent Beneficial Effects on Blood Pressure and Vascular Function, But Is Inefficient in Preventing Myocardial Ischemia-Reperfusion Injury in Zucker Diabetic Fatty Rats. Molecules, 25(1):187, 2020

26. Kollarova M, Puzserova A, Balis P, Radosinska D, Tothova L, Bartekova M, Barancik M, Radosinska J: Age- and Phenotype-Dependent Changes in Circulating MMP-2 and MMP-9 Activities in Normotensive and Hypertensive Rats. Int J Mol Sci, 21(19):7286, 2020

27. Radošinská J, Jasenovec T, Púzserová A, Krajčír J, Laceková J, Kučerová K, Kalnovičová T, Tóthová Ľ, Kovačicová I, Vrbjar N: Vitamin C supplementation promotes whole blood rheology in healthy humans. Cardiology Lett, 29(4):248–255, 2020

28. Konečná B, Gaál Kovalčíková A, Pančiková A, Novák B, Kovaľová E, Celec P, Tóthová Ľ: Salivary extracellular DNA and DNase activity in periodontitis. Appl Sci, 10(21):7490, 2020

29. Konecna B, Radosinska J, Kemenyova P, Repiska G. Detection of disease-associated microRNAs - application for autism spectrum disorders. Rev Neurosci.;31(7):757-69. 2020

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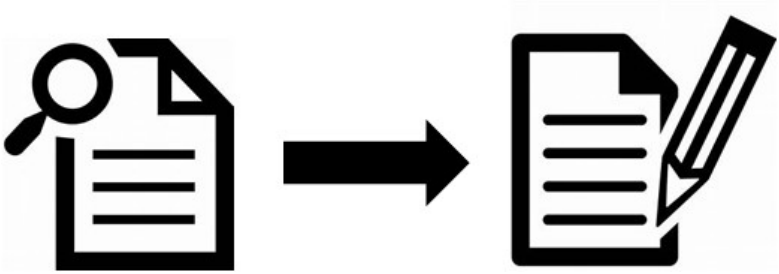

GRANT PROJECTS

APVV GRANTS

APVV-17-0505
BIOLOGICAL ASPECTS OF EXTRACELLULAR NUCLEIC ACIDS IN COLONIC INFLAMMATION
Roman Gardlík
2019-2021

APVV-18-0287
NON-INVASIVE YET UNUSED MARKERS OF RENAL FUNCTION: PROBLEMS, CAUSES AND OPPORTUNITIES
Ľubomíra Tóthová
2019-2022

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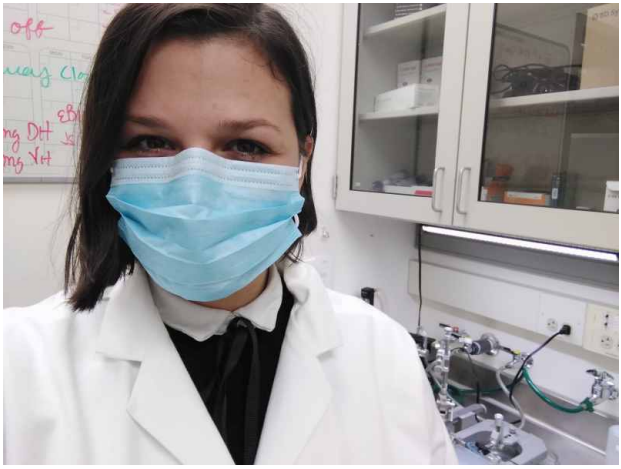

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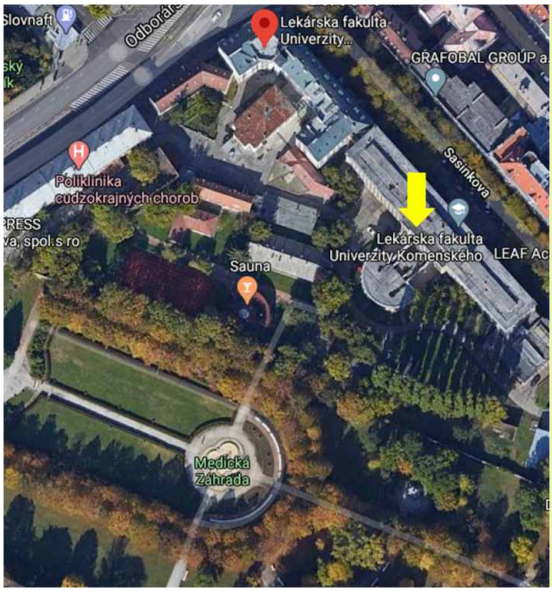

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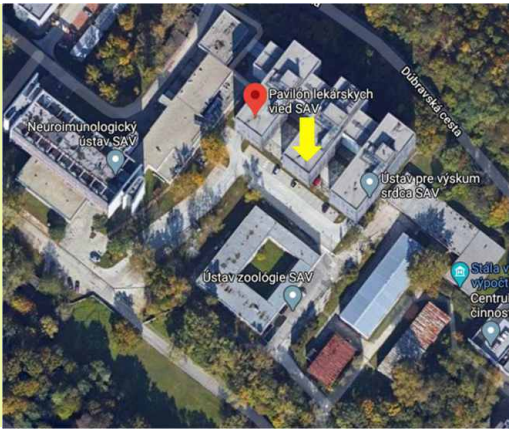

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