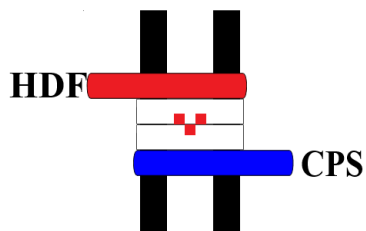


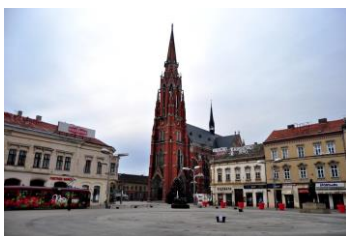
16th Annual Meeting of Croatian Physiological Society with International participation Osijek, September 28-30, 2023.

HRVATSKO DRUŠTVO FIZIOLOGA



CROATIAN PHYSIOLOGICAL SOCIETY

PROGRAM AND BOOK OF ABSTRACTS



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Program for 16th Annual Meeting of Croatian Physiological Society with International participation Osijek, September 28-30, 2023.

Thursday, September 28nd 2023

12:00 – 18:00 Registration (Hall Faculty of Medicine Osijek)

12:00 – 12:15 Opening ceremony, welcome (*lecture room P1, ground floor*)

12:15 – 14:10 Session 1 – Neurophysiology and cerebral circulation – Chairs: Aleksandra Dugandžić, Ferenc Bari

25' Invited speaker: Akos Koller (Budapest, Hungary): Novel concept and mechanisms of the autoregulation of cerebral blood flow. Role of arachidonic acid pathway

25' Invited speaker: Nikola Habek (Zagreb, CRO): Uroguanylin in the Brain - New Kid on the Block?

25' Invited speaker: Eszter Farkas, Anna Törteli, Réka Tóth, Ferenc Bari, Ákos Menyhárt (Szeged, HU): Reperfusion failure after acute ischemic stroke

25' Invited speaker: Ferenc Bari (Ferenc Bari, Viktória Péter, Ákos Menyhárt, Eszter Farkas, László Janovák, Szeged, HU): How could be nanomedicine helpful in stroke therapy?

15' **Sibel Akyol, Berkay Sen** (Istanbul, Turkey): Comparative Analysis of Proinflammatory and Anti-inflammatory Cytokines in Brain Tissue of Juvenile Offspring of Chronic Alcoholics

14:10 -14:20 short intersession break

14:20 - 16:00 Session 2 – Sport physiology – Chairs: Lana Ružić, Akos Koller

25' Invited speaker: Vladimir Ivančev (Split, CRO): Physiological markers of functional status - possibilities of functional diagnostics

25' Invited speaker: Helena Lenasi, N Potočnik, L Kralj (Ljubljana, SLO): Exercise and skin microcirculation

15' Invited lecture: **Dragan Mirkov** (Beograd, SRB): The Rate of Force Development Scaling Factor: The new kid in the block?

15' **Ines Mrakovčić- Šutić**: The influence of intense physical activity on perforin and granulysin expression

10' **Luka Kolar**, M Stupin, A Stupin, P Šušnjara, I Jukić, Z Mihaljević, N Kolobarić, I Drenjančević (Osijek, CRO): Consumption of functional food enriched with n-3 PUFAs and antioxidants enhances microvascular reactivity and reduces oxidative stress in competitive athletes

10' **Lana Kralj, H Lenasi** (Ljubljana, SLO): Wavelet analysis of laser Doppler microcirculatory signals: current position in the field

16:00 – 16:30 coffee break

16:30- 18:10 Session 3 – General physiology – Chairs: Helena Lenasi, Ivana Jukić

25' Invited speaker: Dora Zelena (Pecs, HU): Vasopressin as a social hormone

15' Szonja Decker, D Deák, T Horváth, A Koller (Budapest, HU): Contribution of abdominal and chest breathing in different body positions to the breathing cycle

15' Martina Mihalj (Osijek, CRO): The rationale for introducing low salt diet for the management of Th17-mediated skin disorders

15' Martina Vulin, A Muller, I Drenjančević, P Šušnjara, Z Mihaljević, A Stupin (Osijek, CRO): Effects of dietary salt intake on vascular endothelial function in healthy pregnant women during third trimester of uncomplicated pregnancy.

15' Darina Deák, S Decker, J Takács, A Koller (Budapest, HU): Effect of skin color on the pulse oximeter measurement of oxygen saturation in humans

15' David Ivanov, Drapšin M, Mihajlović A, Tapavički B, Lendak D (Novi Sad, SRB): Did we underestimate prognostic value of routine biomarkers in the early stage of COVID-19?

18:15 - 19:45 E - Poster session #1 - (lecture room P1, ground floor) Chairs: Ana Stupin, Hrvoje Lalić – 6 min per poster

1. Tanja Grubić Kezele, A Stari, L Vidović, D Repac Antić (Rijeka, CRO): Physical and psychosocial limitations short before and short after COVID-19 pandemic in individuals with multiple sclerosis.
2. Babić A, A Zelić Kerep, A Lelas, J Knežević, L Desnica, N Duraković, R Vrhovac, D Pulanić, D Batinić, Hrvoje Lalić (Zagreb, CRO): Plasma cytokine profiling in patients with chronic graft-versus-host disease.
3. Justić H, Barić A, Šimunić I, Radmilović M, Ratko Martina, Škokić S, Dobrivojević Radmilović M (Zagreb, CRO): Dual role of bradykinin receptor type 2 in mouse retinal ischemia.
4. Anja Barić, D Smilović, H Justić, S Škokić, M Dobrivojević Radmilović (Zagreb, CRO): The effects of bradykinin type 2 receptor deficiency on microglia activation and survival after cerebral ischemia in mice.
5. Dora Uršić, Kibel A, Jukić I, Drenjančević I (Osijek, CRO): Ongoing study: Effect of consumption of chicken meat enriched with carnosine on microvascular function and immune system in patients with chronic coronary artery disease.
6. Dijana Dumančić, A Stupin, M Kožul, V Šerić, A Kibel, N Goswami, B Brix, Ž Debeljak, R Scitovski, I Drenjančević (Osijek, CRO): Hyperventilation-provoked response of heart rate variability and baroreceptor sensitivity in young, healthy individuals after a short term high salt diet.
7. Dora Jarai, A Koller (Budapest, HU): Role and potential mechanisms of walnut consumption-induced improvement of endothelial function in cardiovascular diseases.
8. Petar Šušnjara, Z Mihaljević, A Stupin, N Kolobarić, I Drenjančević (Osijek, CRO): Health benefit of the consumption of functionally enriched eggs in healthy young subjects.
9. Aleksandra Popović, J Drljača Lero, D Miljković, M Popović, A Klačnja, V Karan Rakić, I Čapo, M Ljubković (Novi Sad, SRB; Split CRO): Karnozin EXTRA® inhibits growth, survival, and migration of human glioblastoma cells through inducing mitochondrial dysfunction.

PROGRAM

10. Božena Ćurko Cofek, T Grubić Kezele, M Tota, N Starčević Čizmarević, S Ristić, V Barac-Latas (Rijeka, HRV): Sex-related differences in zinc, metallothionein I/II, and estrogen receptor-alpha interaction in iron-overloaded EAE rats.
11. Domagoj Jakovac, M Ratko, I Marolt Banek, I Lapić, A Dugandžić (Zagreb, CRO): Physiological role of systemic uroguanylin in mouse salivary glands.
12. Jasna Aladrović, Miljković J, Shek Vugrovečki A, Blažević SA, Lisičić D, Gojak T, Šikić D, Beer Ljubić B, Pađen L (Zagreb, CRO): Lipid indices in abdominal fat and ovaries in *Podarcis siculus* and *Podarcis melisellensis*.
13. Martina Ratko, V Crljen, M Tkalčić, A Mažuranić, P Bubalo, P Škavić, I Banovac, A Dugandžić (Zagreb, CRO): Guanylate cyclase C expression in the human brain.
14. Vedrana Karan Rakić, A Klačnja, A Popović, Dj Djilvesi, M Karan, S Maricic Prijic, M Drapsin (Novi Sad, SRB): Intraoperative neurophysiological parameters in patients with radiculopathy and myelopathy.
15. Verner Marijančić, G Starčević-Klasan, S Peharec, T Grubić Kezele (Rijeka, CRO): Association of spinal curvatures with BMI, body composition and muscular endurance of trunk muscles in college students.

Osijek sightseeing, free time

PROGRAM

Friday, September 29th 2023

9.00.–17.00. Registration

9:00 - 10:20 Session 4 – Cell physiology and immunology – Chairs: Vilma Dembitz, Helena Lenasi

25' Invited speaker: Ivona Žura-Žaja, N Poljičak Milas, S Milinković Tur, A Shek Vugrovečki, M Vilić, N Žura, I Butković, J Miljković, P Prgomet, L Rodman, S Vince (Zagreb, CRO): Morphometry as a method in the assessment of cell morphology in veterinary medicine

15' Peter Balogh, X Jia (Pecs, HU): Serosal lymphoid organoids – shapes and functions

15' D Simon, S Erdo-Bonyar, A Bajnok, A Varnagy, K Kovacs, E Mezosi, Timea Berki (Pecs, HU): The maternal tolerance development during pregnancy and the immunological background of infertility.

15' Peter Engelmann, Ko Bodó, CBrotzki da Costa, P Németh (Pecs, HU): Injury-induced regeneration in earthworms: cells, molecules and beyond

10' Nikolina Kolobarić, P Šušnjara, A Stupin, A Matić, I Drenjančević: N-3 PUFAs and Microcirculation: Unravelling the Prostanoids Connection

10:20 -10:50 Coffee break

10:50 – 12:20 Session 5 – Physiology in clinical settings: endocrinology, metabolism. Chairs: Aleksandar Kibel, Ana Shek Vugrovečki

25' Invited speaker: Ivan Čavar (KCvitković, A Sesar, T Kelava, A Sućur, I Čavar): **Concentrations of selected inflammatory cytokines in aqueous humor and serum of diabetic patients**

15' Zoltán Kellermayer, S Tahri, MME de Jong, N Papazian, C Fokkema, R Hoogenboezem, MA Sanders, L Boon, C Den Hollander, A Broijl, P Sonneveld, T Cupedo (Pecs, HU): Control of 5TGM1 myeloma growth in C57Bl/6 mice is associated with an activated bone marrow NK cell response

20' Invited lecture: Ivana Šutić: Changes in the concentration of matrix metalloproteinases 2 and 9 residents near the waste disposal centers

20' Invited lecture: Josipa Josipović (Zagreb, CRO): Multiple renal arteries and hypertension- physiological aspects

10' A Zrilić, T Režić Palaversa, A Majić, S Marušić, M Cigrovski Berković, Lana Ružić (Zagreb, CRO): Thyroid function and short-and middle-term outcomes of SARS_CoV patients

12:30 - 13:30 Lunch (catering)

13:30 -13:40 Taking conference participants photo (in front of the Faculty of Medicine building)

PROGRAM

13:40 -14:50 Session 6 Immunology – Chairs: Ines Mrakovčić-Šutić, Martina Mihalj

25' Invited speaker: Vilma Dembitz (Zagreb, Croatia): The role of stearyl-CoA desaturase in acute myeloid leukemia.

15' Tomislav Smoljo, B Tomic, H Lalić, V Dembitz, D Visnjić

(Zagreb, CRO): Bone marrow stromal cells decrease differentiation of acute myeloid leukemia cells induced by low-dose cytarabine

15' Ivana Krajina (Osijek, CRO): Short term low salt diet changes inflammatory parameters in mild to moderate psoriasis vulgaris

15' Ana Marija Masle, A Kibel, K Selthofer Relatić, A Stupin, Z Mihaljević, P Šušnjara, Ž Breškić, N Kolobarić, B Juranić, V Šerić, I Jukić, G Kralik, I Drenjančević

(Osijek, CRO): Microvascular endothelium function response to n-3 polyunsaturated fatty acids, vitamin E, selenium and lutein enriched functional food in patients with acute coronary syndrome

15:00 -16:30 CPS Assembly (*lecture room P1, ground floor*)

Guided sightseeing, English, meeting point

20:00 –23:00 Conference Dinner - Hotel Waldinger

<https://www.bing.com/search?pc=W099&q=hotel+waldinger+osijek&form=BW MFDF>

Saturday, September 30th 2023

9:00 - 10:30 E-Poster session #2- (lecture room P1, ground floor) Chairs: Zrinka Mihaljević, Ivana Šutić – 6 min per poster

1. Martina Kos, A Stupin, P Šušnjara, T Nađ, M Damašek, I Drenjančević, S Pušeljić, I Jukić (Osijek, CRO): Essential arterial hypertension attenuated endothelium-dependent microvascular response in pediatric patients
2. Lea Gvozdanović, Štefek, Ž Dragila, Z Mihaljević, V Adam Nesek (Našice, CRO): The diagnostic accuracy of calprotectin in patients with suspected sepsis.
3. V Đambić, I Drenjančević, Zrinka Mihaljević, A Kibel (Osijek, CRO): The role of adenosine A1 and A2a receptor in cerebral blood vessels of Sprague-Dawley rats exposed to hyperbaric oxygen.
4. Erna Davidović Cvetko, D Pejić, I Lovrić, D Jozinović (Vukovar, CRO). Correlation of explosive muscle strength and body composition in young adults: difference between athletes and non-athletes.
5. N Šantek, T Režić Palaversa, I Kirac, B Vilč, Lj Mayer, M Šoštarić, A Mrzljak, Maja Cigrovski Berković (Zagreb, CRO): Retrospective analysis of breathing exercise intervention in patients with type 2 diabetes scheduled for abdominal cancer surgery and how it affects patients' outcomes.
6. Shek Vugrovečki Ana, Miljković J, Aladrović J, Pađen L, Šikić D, Gojak T, Lisičić D, Blažević SA (Zagreb, CRO): Oxidative Stability of Muscle Tissue in a Free-Living Lizard Podarcis siculus from two different locations – a Pilot Study.
7. Ivana Potočnik, N Potočnik (Ljubljana, SLO): The effect of endurance exercise on arterial blood pressure in trained type 1 diabetic patients compared to healthy controls.
8. Marta Pongrac, Radmilović Marina (Zagreb, CRO): The role of bradykinin receptor type 2 in murine cerebral glucose metabolism.
9. Tina Zavidić, G Laškarin (Rijeka, CRO): Can measuring pulse wave velocity alert us to the need for early treatment of prediabetes and metabolic syndrome?
10. Patrik Debeljak, S Brnić, V Brnić, K Jordan, S Grazio, F Grubišić (Zagreb, CRO): Impact of Personalized Kinesitherapy on Lymphedema Management in Women with Breast Cancer After Surgical Treatment and Adjuvant Radiotherapy – A Retrospective Reanalysis
11. Lucija Faj, J Aleksic, K Radović, MO Knezevic, D Cabarkapa, VD Cabarkapa, MD Mirkov (Osijek CRO, Beograd, SRB): Reliability of a low-cost, high-speed camera-based method for assessing Selected kinematic variables in the unilateral countermovement jump.
12. Jasna Aladrović, B Beer-Ljubić, A Kostelić, L Pađen (Zagreb, CRO): Nutritional lipid quality indices in goat's milk regarding lactation period.

10:30 Closing remarks, awards

11:00 Excursion to Vukovar and Lunch in Vukovar (Vukovar watertower <https://vukovarskivodotoranj.hr/en/home/>; Museum of Vučedol culture <https://vucedol.hr/>)

PROGRAM

Additional information:

The **16th Annual symposium of the Croatian Physiological Society with international participation**, will be held on **28-30 September 2023** in Osijek, Croatia at the **Faculty of Medicine Osijek** (J. Huttlera street 4).

Croatian Chamber of Physicians (Hrvatska liječnička komora) will credit participation at the congress as: International congress, 20 points for active participation and 12 points for passive participation.

Additional information regarding the symposium is available on the CPS website (www.hdf.hr). We ask that all interested to attend to register as soon as possible.

Registration fee: 25 euros for non-member of Croatian Physiological Society, sponsors and accompanying persons, **payment account: HR112360001101865173 (Croatian Physiological Society)**, **Payment description: registration fee for [Your name and surname]**

Abstracts information:

Write a summary in English, up to 300 words.

Format: structured (Introduction, Materials and methods, Results, Conclusions)

Font: Time New Roman, 12, spacing 1.5, without paragraph indentation.

Title and authors, example:

Peric P¹, Ivic I². How to write a scientific structured summary

1- Faculty of Medicine South, 2- Faculty of Medicine North

E-Poster display: posters will be displayed as **e-posters**, orientation portrait.

Faculty of Medicine Osijek:

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BOOK OF ABSTRACTS

How could be nanomedicine helpful in stroke therapy?

Ferenc Bari¹, Péter V¹, Menyhárt A^{2,3}, Farkas E^{2,3}, Janovák L⁴

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²*Hungarian Centre of Excellence for Molecular Medicine – University of Szeged Cerebral Blood Flow and Metabolism Research Group, Szeged, Hungary*

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⁴*Department of Physical Chemistry and Materials Science, Faculty of Science and Informatics, University of Szeged, Hungary*

Introduction: Effective pharmaceutical treatment of central nervous system damage due to stroke is hampered by a number of factors. Following successful recanalization, the putative neuroprotective compound must be delivered to the damaged brain area in an effective concentration so that its harmful systemic side effects are minimized. Recently nanotechnology-assisted drug delivery offers some improvement in targeted therapies. There are a number of nanomedical approaches that aim to get the drug across the blood-brain barrier or to achieve an effective drug concentration only at the site of injury.

Methods: We constructed and tested chitosan nanoparticles as drug carriers, which release nimodipine – L-type voltage gated Ca²⁺ channel blocker, known as vasorelaxant, FDA approved drug- in response to decreasing pH typical of cerebral ischemia. We have performed several experiments to evaluate this nanomedical approach to deliver nimodipine selectively to acidic ischemic brain tissue. In rodent model of global cerebral ischemia and related cortical spreading depolarization resulted in marked drop of tissue pH (from 7,4 to 6,8 or so).

Results: We have provided evidence that the administered nanoparticles release their cargo in acidic tissue environment, which reliably delineates sites at risk of injury. Therefore, tissue pH-targeted drug delivery is expected to enrich sites of ongoing injury with the therapeutical agent, without the risk of unfavorable off-target effects. We also report on our current work using infrared laser light to activate nimodipine packaged in nanocarriers. In doing so, we present the optimization of a polymer containing gold nanorods and drug as well as the results of our baseline measurements leading to effective drug release.

Conclusion: We are convinced that nanomedical approaches for effective drug delivery already used in oncology, dermatology or other medical fields can be effectively adopted to the stroke therapy.

Concentrations of selected inflammatory cytokines in aqueous humor and serum of diabetic patients

Cvitković K, Sesar A, Kelava T, Sućur A, Ivan Čavar

Faculty of Medicine, University of Mostar, Mostar, Bosnia and Herzegovina

Introduction: This study aimed to investigate the aqueous humor and serum levels of selected inflammatory cytokines in diabetic patients, implicating their role in the pathogenesis of diabetic eye complications.

Methods: A total of 65 patients (27 males and 38 females) who underwent cataract surgery were recruited into the study. The study group consisted of 30 cataract patients with type 2 diabetes mellitus, and this group was divided into two subgroups: 14 patients with diabetic retinopathy (DR group) and 16 patients without DR (NDR group). The control group consisted of 35 non-diabetic cataract subjects.

Results: Patients in the DR group had significantly higher aqueous humor concentrations of interleukin (IL)-1 β , IL-6, IL-8, IL-10, monocyte chemotactic protein (MCP-1) and VEGF. Likewise, serum concentrations of IL-1 β , IL-6, IL-8, IL-12, TNF- α and IFN- γ were significantly higher in the DR group as compared to the controls. Aqueous humor concentrations of IL-1 β , IL-8, MCP-1 and VEGF were significantly higher in the DR group as compared with the NDR group.

Conclusion: Our findings support the hypothesis that chronic inflammation and a disturbance of the immune system play important roles in the pathogenesis of diabetic cataract and DR.

The role of stearoyl-CoA desaturase in acute myeloid leukemia

Vilma Dembitz

Introduction: Identification of specific and therapeutically actionable vulnerabilities in acute myeloid leukaemia (AML) is needed to improve patients' outcome. These features should be ideally present in many patients independently of mutational background.

Methods and Results: Here we identify *de novo* fatty acid (FA) desaturation, specifically stearoyl-CoA desaturase (SCD) inhibition, as a therapeutic vulnerability across multiple AML models *in vitro* and *in vivo*. We use the novel clinical grade SCD inhibitor SSI-4 to show that SCD inhibition induces AML cell death *via* pleiotropic effects, and sensitivity is based on their dependency on FA desaturation regardless of mutational profile. SSI-4 efficacy is enhanced by driving FA biosynthesis *in vitro* while stroma confers protective effects that extend to *in vivo* models. SCD inhibition increases DNA damage and its combination with standard DNA damage-inducing chemotherapy prolongs survival in aggressive murine AML models.

Conclusion: Our work supports developing FA desaturase inhibitors in AML while stressing the importance of identifying predictive biomarkers of response and biologically validated combination therapies to realize their therapeutic potential.

Reperfusion failure after acute ischemic stroke

Eszter Farkas^{1,2}, Törteli A^{1,2}, Tóth R^{1,2}, Bari F³, Menyhárt A^{1,2}

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Introduction: Despite successful recanalization to treat acute ischemic stroke, reperfusion failure associated with poor functional outcomes develops in half of the patients. The cause of reperfusion failure remains the subject of intensive research. Here, we explore the possibility that spreading depolarization (SD), a potent ischemic injury mechanism is a significant contributor and reliable predictor of reperfusion failure.

Methods: Young adult male and female C57BL/6 mice (n=69) were anesthetized with isoflurane (0.6-0.9%) and prepared for transcranial optical imaging. After 10 min of baseline, incomplete global forebrain ischemia was induced by transient (45 min) bilateral common carotid artery (CCA) occlusion, followed by 75 min reperfusion. SD and cerebral blood flow (CBF) changes were visualized with intrinsic optical signal imaging and laser speckle contrast imaging. To block SD, the irreversible NMDA receptor antagonist MK801 was applied (0.3 mg/kg, i.p., n=29). Neurological deficit was evaluated at baseline and post-ischemia with a composite Garcia Neuroscore scale. Collaterals of the circle of Willis were examined after loading the vasculature with carbon black ink. Ischemic neuronal injury was evaluated in hematoxylin-eosin-stained brain sections.

Results: SD emerged after ischemia onset in one or both hemispheres under a perfusion threshold (CBF drop to 21.1±4.6 vs. 33.6±4.4 %, SD vs. no SD). The failure of later reperfusion (44.4±12.5 %) was invariably linked to previous ischemic SD. In contrast, reperfusion was adequate (98.9±7.4 %) in hemispheres devoid of SD during ischemia. CBF reduced below the perfusion threshold of SD, when the P1 segment of the posterior communicating artery was absent in the circle of Willis. SD occurrence and the linked reperfusion failure were associated with poor neurologic function, and greater neuronal necrosis. The inhibition of SD with MK801 significantly improved reperfusion.

Conclusion: SD occurrence during ischemia impairs later reperfusion, prognosticating poor functional outcomes. The underlying mechanism of reperfusion failure due to SD must be sustained vasoconstriction mediated by arachidonic acid metabolites. The increased likelihood of SD occurrence is predicted by inadequate collaterals.

Uroguanylin in the Brain - New Kid on the Block?

Nikola Habek

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Department of Neuroscience, University of Zagreb School of Medicine
Croatian Institute for Brain Research, University of Zagreb School of Medicine*

Uroguanylin (UGN) is a member of the guanylin peptide (GP) family, known for its regulatory role in electrolyte and water transport within the intestine through the activation of guanylate cyclase C (GC-C), the only known receptor for GP. In our research, we have showed the expression of UGN within distinct cerebral regions, which is regulated by feeding, challenging the conventional belief that the brain does not express UGN.

We have detected the expression of GC-C in the midbrain and hypothalamus, while our investigations have unveiled additional brain regions where GC-C is expressed, notably in neurons located within the cerebral cortex, amygdala, Purkinje cells, and the deep nuclei of the cerebellum. Expression analysis also showed that GC-C is absent in astrocytes. Our findings demonstrate that UGN induces hyperpolarization of Purkinje cells, resulting in a decrease in firing rates. Additionally, in astrocytes, UGN prompts an elevation in intracellular Ca^{2+} concentration through a GC-C/cGMP independent signaling pathway, which was unreported in the brain.

Furthermore, we have observed that the effects of UGN action on the hypothalamus, specifically in relation to diet-induced thermogenesis and brown adipose tissue (BAT) activation following a meal, exhibit sex-dependent characteristics. These effects are discernible in male WT animals but not in female mice, as well as in GC-C KO animals of both sexes. Our investigations extended to healthy volunteers, revealing that BAT activation post-meal is sex, age, and body mass index dependent. The role of UGN in the regulation of BAT assumes paramount importance in the development of innovative therapeutic approaches for addressing conditions such as obesity, metabolic syndrome, and diabetes mellitus.

Physiological markers of functional status - possibilities of functional diagnostics

Vladimir Ivančev

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Introduction: Functional capability is an individual's ability to perform ordinary daily activities. Functionality is based on motor skills such as balance, coordination, body awareness, agility, reaction time, strength, endurance. Functional capability can be determined on the basis of an evaluation of rehabilitation potential. Strength is based on local neuromuscular status, but endurance includes lots of factors cardiovascular, respiratory, metabolic, hormonal and local muscle too. This review gives diagnostic methods which provide possibility to measure and determinate parameters of interest.

Methods: Lots of diagnostical methods give different parameters regarding functional capacity. Some of them are used into ordinary clinical practice, but the others are mostly part of scientific measuring tools. Clinical exercise testing is based on monitoring of cardiovascular and respiratory parameters giving some extrapolated metabolic data and conclusions. Cardio-pulmonary exercise testing (CPET), VO₂ kinetics, infrared spectroscopy (NIRS) gives lots of cardiorespiratory and muscle parameters.

Results: There are many diagnostics and measuring tools of interest but mostly all of them have some limitations. Some of them could be used in the resting state and specific body position, the others could be used during effort but need specific protocol or ergometers.

Conclusion: Contemporary clinical and scientific diagnostics have reached some higher level, but dynamic of progress does not give more accurate data from cell level. Measuring tools we use depends on financial issues, availability and correctly decision what we really wants to measure.

Novel concept and mechanisms of the autoregulation of cerebral blood flow. Role of arachidonic acid pathway

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Healthy functioning of the brain requires a precise regulation of cerebral blood flow (CBF), which however have to comply with the limited space available in the cranium. The latter requirement is ensured by the autoregulation of CBF, i.e. relative independence from systemic blood pressure. Logically, for many years, the pressure-sensitive myogenic response of arterial wall was assigned to be responsible to play a pivotal role. Yet in vitro studies showed that the myogenic responses of cerebral arteries of different sizes do not generate sufficient constrictions. In addition, in vivo increases in pressure are accompanied by increases in blood flow. Yet the idea that increases in flow affect the vasomotor tone of cerebral vessels was not well known. Earlier studies showed flow-sensitive dilation and/or constriction or both, but – due to methodological difficulties - no clear picture emerged. Importantly a decade ago we have demonstrated that there is a flow-sensitive mechanism, which elicit constrictions of small isolated cerebral arteries. This talk focuses on the effects of hemodynamic forces (both pressure and flow) on the vasomotor tone of cerebral vessels and the underlying cellular and molecular mechanisms, highlighting the role of arachnoid metabolism particularly the role of cytochrome P450 4A enzyme, which convert arachidonic acid to constrictor prostaglandins. Then a novel concept of autoregulation of CBF is proposed, suggesting that in the arterial cerebrovascular tree pressure- and flow-induced constrictions together maintain an effective autoregulation, and that adaptation or impairment of these mechanisms may protect from or contribute to the development of cerebrovascular disorders, such as headache, disruption of blood brain barrier, brain edema, Alzheimer disease and vascular dementia.

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Exercise and Skin Microcirculation

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Dynamic exercise profoundly impacts skin microcirculation, as skin is importantly involved in thermoregulation. It has been established that thermoregulatory mechanisms during exercise differ from the ones during resting since in exercise, the majority of perfusion is redirected to the working skeletal muscles. Even exercise of short duration, as in cardiopulmonary testing on a cycloergometer, induces alterations in skin blood flow consistent with establishment of thermal homeostasis. Yet, the exact mechanisms regulating the redistribution of blood flow, are not clear. Moreover, the time profile as well as the extent of vasodilation significantly differ between glabrous and non-glabrous skin sites, respectively. In humans there is a lack of appropriate methods to directly investigate the mechanisms involved in cutaneous microvascular regulation. One of the approaches to study the complex interplay between various mechanisms regulating microcirculation is decomposition of the signals obtained by laser Doppler fluxmetry, the gold standard for skin microcirculation assessment, into basic frequency spectra, each of them corresponding to specific physiological influence: endothelial NO-independent (0.005– 0.0095 Hz), endothelial NO-dependent (0.0095-0.021 Hz), neurogenic (0.021–0.052 Hz), myogenic (0.052–0.15 Hz), respiratory (0.152–0.4 Hz), and cardiac (0.4–2.0 Hz), respectively. It has already been demonstrated that skin blood flow undergoes the greatest changes in the early recovery to exercise exhibiting distinct characteristics of a transient phenomenon that cannot be evaluated by classical mathematical tools for signal decomposition. Wavelet analysis (WA) has gained increasing importance as an alternative to classical fast Fourier transformation. Accordingly, the talk will present some of the main features of skin microcirculation dynamics in exercise and recovery and potential mechanisms involved with particular emphasis on endothelial component that has been shown to play a major role in early recovery, as evaluated by WA. Also, other mechanisms involved in skin microvascular adjustments during short-lasting submaximal exercise and its recovery will be presented.

The Rate of Force Development Scaling Factor (RFD-SF): The New Kid on the Block

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The most frequently applied muscle function test has been based on exerting maximum force against fixed resistance as fast as possible. The primary outcome variables in this test are peak muscle force (F_{max}) and the maximum gradient of the force-time trace (RFD). However, maximum isometric contractions are rarely involved in daily activities. Nevertheless, it has been shown that when brief isometric contractions are performed at submaximal levels, a robust linear relationship between F_{max} and RFD_{max} exists. Studies have shown that the slope of this relationship (introduced as the rate of development scaling factor: RFD-SF) could be used as a reliable and valid measure of neuromuscular quickness, providing insights into the ability to modulate motor unit firing rate with change in contraction intensities.

Furthermore, the current literature review indicates that the RFD-SF is relatively invariant, not dependent on muscle group and function, and is not influenced by sex or fatigue. Conversely, the RFD-SF scaling factor increases with power training in young individuals and decreases with the severity of symptoms in Parkinson's disease or multiple sclerosis. Also, it was able to detect interlimb asymmetries. It should be noted that only a few trials within two submaximal intensities (30 and 70% of F_{max}) of isometric contractions are sufficient to obtain a reliable and valid RFD-SF, which makes this test easily applicable even in frail populations (elderly, patients in early-stage recovery after injuries or those with neurological disorders). Considering all this, the advantage of the RFD-SF to a standard approach based on F_{max} and RFD assessments is clear and should not be questioned. However, due to the limited number of studies on athletes, the correlation to athletic performance should be further evaluated in the future.

Vasopressin as a social hormone

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Social interactions between conspecifics are the basis of survival and reproduction. Moreover, disturbed social contact in humans may be both the symptom and trigger of different mental disorders including autism or schizophrenia. Vasopressin, a water-regulatory neurohypophyseal peptide, is synthesized and secreted widely in the brain, and has long been implicated in social behaviour. Moreover, vasopressin may program the development of social brain in sex-specific manner. Indeed, in rodents, the males have higher vasopressin synthesis and fibre density on many critical brain areas contributing to sex-specific regulation of social play, social recognition, and sociosexual motivation. Due to these roles the lack of vasopressin may induce autism- and schizophrenia-like symptoms observable already in pups by disturbed social communication. Drugs targeting the vasopressin system are currently being tested for their efficacy to restore social functioning, but more emphasis should be given to sex-specific drug development.

Morphometry as a method in the assessment of cell morphology in veterinary medicine

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Various physiological, environmental (*e.g.* radiofrequency electromagnetic radiation) and pathological factors can affect structure of body cells (*i.e.* spermatozoa or erythrocytes). Impaired morphology of cells can significantly disrupt their functions. Therefore, knowledge about physiological differences in cell morphology related to species, breed, age, gender, and environmental factors, is necessary for making a correct diagnosis. Morphometry is a computerized version of planimetry, and at the same time the simplest form of imaging cytometry, which refers to the measurement of different cellular structures and their display in a two-dimensional form. This method detects certain cell abnormalities, classify them in certain groups or subpopulations using statistical analysis (principal component, and cluster analysis according to morphometric variables). Spermatozoa morphology is one of the most important indicators in determining male fertility potential. In human medicine due to the heterogeneity of spermatozoa, the proportion of morphological defects in spermatozoa is determined. Computer-assisted analysis of spermatozoa morphology greatly improve the assessment of spermatozoa morphology and it enables a more objective and reliable measurement method for routine semen analysis and studying of male infertility. Along with spermatozoa, erythrocytes are very sensitive to pathological conditions under which morphological transformations of the typical healthy cells (biconcave discoid shape) can change. In veterinary medicine erythrocytes are anucleated only in mammals but also differ greatly in morphology and size among domestic mammals. Consequently, morphometry as a method should be routinely used in medicine and specially in veterinary medicine in the setting of certain diagnoses, disease prognosis and health status monitoring, but further research is needed before its implementation.

Comparative Analysis of Proinflammatory and Anti-inflammatory Cytokines in Brain Tissue of Juvenile Offspring of Chronic Alcoholics

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Introduction: The effect of alcohol on immune responses, infection and inflammatory processes has not been fully understood. Research on how these connections change during pregnancy is limited, and results vary. Although studies have shown that alcohol consumption affects the mother and causes fetal alcohol syndrome, no obvious information has been found about its effects on the immune system in the newborn and juvenile period. The study was planned to investigate how mothers' consumption of alcohol during pre-pregnancy, pregnancy and lactation affects the immune responses in the brain tissue of juvenile rats.

Methods: 12 weeks old Wistar albino female rat (200-220 gr, N=45) were divided to non-alcoholic pregnant (Control) (G1) (N: 15) and alcoholic pregnant (G2) (n: 30); G2a) Group that sacrificed at the end of pregnancy (N:15) and G2b) Group that continues to live after pregnancy (N:15). 30 %-ethanol was applied to the G2 group by gavage twice a day 8 g/kg, at 9 a.m. and 6 p.m., four weeks before mating. This procedure lasted throughout pregnancy and until the end of lactation. Among the newly born rats, males were selected as second generation subjects, 61st day after birth groups: J1 (control) (N:15) and J2 (alcohol) (N:15). J1 and J2 groups were sacrificed on day 61 and brain tissue was taken. TNF α , IL-2, IL-4, IL-10, IFN- γ and IL-12 cytokines from brain tissue were tested by ELISA. For statistical analysis, ANOVA, Tukey and Tamhane tests were used.

Results: A significant increase in TNF α and IL-2, a very significant increase in IFN- γ , IL-4 and IL-10, and a slight increase in IL-12 was observed compared to G1 and G2a groups. A significant increase in TNF α , IFN- γ ve IL-4, and a slight increase in IL-2 and IL-12 was observed compared to J1 and J2 groups. There was no significant increase in IL-10. A slight increase in TNF α , a very significant increase in IFN- γ and IL-12, and a significant increase in IL-4 was observed compared to G2a and J2 groups. There was no significant increase in IL-2 and IL-10.

Conclusion: The results suggest that alcohol triggers anti-inflammatory and pro-inflammatory responses, affecting immune responses. The greatest effects of prenatal alcohol consumption are on inflammatory responses in the brain tissue.

Serosal lymphoid organoids – shapes and functions

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Introduction: In contrast to the extensive knowledge of the lymphoid tissues responsible for the immunological protection of the intestinal mucosa, the adipose-associated lymphoid tissues of the serous surface are scarcely studied. Recent data indicate that, in addition to contributing to the recirculation of the “fluid” exudate compartment of the abdominal, thoracic and pleural cavities, the lymphoid formations of the serous membranes provide sites for local immune responses and act as distribution foci.

Methods and Results: Using a spontaneous high-grade B-cell lymphoma (Bc.DLFL1) from a BALB/c mouse with restricted nodal and extranodal dissemination, we incidentally discovered that the omental as well as mesenteric fat streaks contain partially organized lymphoid territories, in addition to the diffuse compartments (denoted earlier as milky spots [MS]). Using whole-mount immunohistology combined with cell tracing we found that these sites could efficiently immobilize both normal and malignant B cells following intraperitoneal administration. We identified a special variant with a more complex structure (foliate lymphoid aggregate/FLAg) containing specific stromal architecture, with gp38⁺ reticular fibroblasts, fibronectin, high endothelial venules expressing peripheral lymph node addressin (PNAd), but lacking follicular dendritic cells. The homing mechanisms to FLAgs comprise surface-attracted as well as blood-borne pathways, latter involving L-selectin:PNAd interaction. Following surface adhesion the segregation of B-cell lymphoma subtypes within FLAgs is determined by homeostatic chemokine domains, thus A20 centroblastic lymphoma cells congregate at the periphery, whereas Bc.DLFL1 extrafollicular B-cell lymphoma cells accumulate at the center. Following adhesion to serosal lymphoid aggregates, intraperitoneal cells egress into the mesenteric lymphatic capillaries, thus these lymphatics may simultaneously perform mucosal and serosal drainage for both B cells towards the mesenteric lymph nodes.

Conclusion: Our findings indicate that the adipose-associated serosal lymphoid tissues encompass a broad spectrum of structural variants, which have important roles in the local as well as the systemic lymphocyte distribution, and may influence local immunological competence.

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Effect of skin color on the pulse oximeter measurement of oxygen saturation in humans

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Introduction: To test the hypothesis that the pulse oximeter will show a higher oxygen saturation compared to the real value in subjects with darker skin tones compared to lighter ones, because it was reported that due to the false reading of pulse oximeter dark skin patients were not treated properly during Covid-19. Thus, we aimed was to measure hemoglobin oxygen saturation with a pulse oximeter in healthy students of different skin colors.

Methods: 42 (30 women and 12 men), aged 18-37, healthy Hungarian and foreign students of Semmelweis University, Faculty of Health Sciences participated in the research. The heart rate and oxygen saturation were measured with a portable, finger-clipped pulse oximeter, according to the protocol, on the index finger of the left hand. We took a photo of the students' fingers against a white background, based on which the skin color was evaluated according to the Fitzpatrick scale. In addition, the students filled out a questionnaire assessing a three-level general health condition (1: no symptoms; 2: mild complaints; 3: severe complaints) and a six-level general physical condition assessment (1: no physical activity; 6: 6 per week/day) Who.

Results: 83.3% of the students felt healthy at the time of the measurement. 83.3% of students are doing physical activity regularly. There was a negative, weak relationship between Fitzpatrick scale value and oxygen saturation ($\rho(25)=-0.318$; $p=0.04$).

Conclusions: The data of this study showed that the pulse oximeter did not measure higher oxygen saturation in healthy individuals with darker skin color compared to those with lighter colors. Importantly, our results question the conclusions of previous reports that skin pigmentation influenced the oxygen saturation measured by the pulse oximeter and thus the care of Covid-19 patients.

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Contribution of abdominal and chest breathing in different body positions to the breathing cycle

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Introduction: Previous report showed that the body position of patients with COVID-19 disease significantly affected the mortality. Thus we hypothesized that the proportional participation of abdominal (AB) and thoracic breathings (TB) to the respiratory cycle is different. Thus, we aimed to measure the participation of AB and TB in different positions during resting conditions.

Methods: Using plethysmography respiratory belts, changes in the circumference of the chest and abdomen cavities were measured in young men and women (n=14; age:21.3±1.8 years) during inhalation and exhalation in resting conditions. The following positions were used: standing (St), sitting (Si), supine (Su), prone (Pr), and all on fours (Af).

Results: In different positions, the percent ratio of AB and TB was significantly different. AB gradually increased while TB gradually decreased in the following order: Si: 62/38%; St: 65/35%; Su: 75/25%; Pr: 61/39%; Af: 55/45%. For example, AB was significantly higher than TB in the Su position, while there was no significant difference between AB and TB in the Af position. During the measurements the respiratory frequency did not change significantly.

Conclusions: These data show that the different body positions significantly affected the participation of abdominal and thoracic breathing during complete breathing cycle. Thus, optimizing the participation of abdominal and thoracic breathing may improve the efficacy of respiration of patients and mortality.

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Injury-induced regeneration in earthworms: cells, molecules and beyond...

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Introduction: Recent years have brought several proceedings to understand the phylogeny of regeneration and gain insights its developmental origin applying different animal models. In this regard, most annelid species have enormous capacity to regenerate their lost segments, but still several molecular and cellular aspects are unexplored in this animal group. To this end, we aimed to evaluate the anterior and posterior segment restoration in *Eisenia andrei* earthworms with a special emphasis on the immunobiological and epigenetic processes.

Methods and Results: Following segment amputations, we observed the EdU positive cells to trace cell-proliferation kinetics in the 2nd and 4th week of regenerating blastema. Dividing cells are increased at 2 weeks and decreased at 4 weeks of regeneration compared to intact animals. Several immune-related target gene levels were monitored by real-time PCR in the regenerating segments. Certain immune response-related genes (eg. *lysenin*, *lysozyme*) showed a decreased pattern, while other genes (*scavenger receptor*, *beta-catenin*) evidenced a gradual increase during the regeneration period. In addition, DNA methylation levels of regenerating blastema were observed applying the 5-methylcytosine (5mC), 5-hydroxymethylcytosine (5hmC) and N6-methyladenine (6mA) specific monoclonal antibodies. By means of dot-blot assays we measured higher 5mC levels on 1st week of anterior regeneration and a 5hmC peak on the third week, while 6mA levels did not change significantly. Blastema formation and the number of EdU⁺ cells were monitored following the depletion of immune-competent cells (eg. coelomocytes). Indeed, coelomocyte depletion seriously impaired the blastema formation, and consequently decreased the proportion of EdU⁺ cells during both anterior and posterior regeneration.

Conclusion: During earthworm regeneration, we observed first, characteristic events at different biological levels. Notably, cellular, molecular, and epigenetic changes highlight the segment restoration of *Eisenia* earthworms that can aid our understanding of the regeneration physiology across metazoan animals.

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Did we underestimate prognostic value of eosinophil and platelet count in COVID-19?

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Various biomarkers like certain complete blood cell count parameters and derived ratios including neutrophil–lymphocyte ratio (NLR) are commonly used to evaluate disease severity. Our study aimed to establish if baseline levels of complete blood cell count-derived biomarkers and CRP, measured before any treatment that can interfere with their values, could serve as a predictor of COVID-19 clinical presentation. We retrospectively analyzed the laboratory data of 200 consecutive patients without comorbidities who had a positive SARS-CoV-2 test and denied usage of medications prior to blood analysis. They visited a COVID-19 ambulance between October and December 2021. Participants underwent a physical exam, oximetry measurement, laboratory analyses and a chest X-ray based on which they were triaged for inpatient or outpatient care and followed by their initial clinic physician until the end of treatment. Participants were classified into groups: a) patients without pneumonia vs. patients with chest X-ray-verified pneumonia and (b) non-hospitalized patients vs. hospitalized pneumonia patients requiring oxygen therapy (severe form of COVID-19); Patients who developed pneumonia and those who required hospital treatment with oxygen therapy had significantly lower values of platelet and eosinophil counts and higher values of CRP. Multivariate regression analysis extracted older age, elevated CRP and lower eosinophil count as significant independent predictors of pneumonia ($p = 0.003$, $p = 0.000$, $p = 0.046$, respectively). Independent predictors of hospitalization were higher CRP ($p = 0.000$) and lower platelet count ($p = 0.005$). There was no significant difference in the NLR and platelet–lymphocyte ratios (PLR) between examined groups. Individual CBC parameters may be better as predictors of the development of pneumonia and severe COVID-19 compared to CBC-derived ratios such as the NLR, PLR if other variables such as sex and age are not taken into account, which is not uncommon.

Multiple renal arteries and hypertension- physiological aspects

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Objective : The significance of multiple renal arteries (MRAs) in arterial hypertension (AH) is not fully understood. Lower perfusion pressure due to longer length and narrower caliber of MRAs could cause segmental hyperreninemia sufficient to result in renin-dependent systemic hypertension. Sympathetic renal nerve activity might be affected by hyperreninemia as well. The aim of the study was to examine the characteristics of young adult hypertensives in relation to the existence of MRAs that were diagnosed during evaluation for secondary arterial hypertension.

Design and method: 32 patients underwent routine evaluation for secondary hypertension and target organ damage. Patients were divided into two groups, one with MRAs and the other without MRAs. Data were presented as mean +standard deviation and compared by the Independent-Sample t-test.

Results: The mean age was 38 years, and 13 patients were diagnosed with MRAs. There were more men in the MRAs group, otherwise, there were no significant differences in baseline characteristics between the groups (BMI, smoking, family history). None of them were diagnosed with secondary endocrine hypertension or renal artery stenosis. MRAs group showed significantly higher values of office SBP/DBP ($p < 0,012$) and 24-hour SBP/DBP ($p < 0,001$), and nonsignificantly higher values of heart rate. Although nonsignificant, direct renin concentrations were slightly higher in the MRAs group, while insulin levels were higher in the non-MRAs group. Dyslipidemia was diagnosed in most patients, without significant differences between groups. Electrocardiographic and echocardiographic changes suggesting hypertensive heart remodeling were found in 55% of patients in MRAs compared to 32% in non-MRAs, there were no significant differences in NTproBNP levels. A nonsignificant reduction in glomerular filtration rate was noticed in the MRAs group, while there were no significant differences in 24-hour albuminuria ($p = 0,308$; $p = 0,614$).

Conclusion: The significance of MRAs in arterial hypertension is a matter of debate. In our study of young patients with arterial hypertension and MRAs, we observed features of more severe hypertension with already existing hypertensive target organ damages. Proper medical treatment with antihypertensive agents is crucial. Future studies will answer the question about interventional therapeutic procedures' role in preventing cardiovascular complications.

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Intraoperative neurophysiological parameters in patients with radiculopathy and myelopathy

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Introduction: Degenerative disease of cervical spine are increased. Clinical signs can be in the form of radiculopathy, myelopathy or both. During anterior cervical discectomy and fusion (ACDF) we used intraoperative neurophysiological monitoring (IONM) that provide us insight in function of somatosensory and motor system.

Methods: This study included 30 patients who underwent ACDF. Patients were divided in two groups, 15 patients with clinical signs of radiculopathy and 15 with clinical signs of myelopathy. During surgery Somatosensory (SSEP) and Motor evoked potentials (MEP) were registered.

Results: There were statistically significant difference ($p < 0,05$) in latencies and amplitudes of SSEP of right and left median nerve. Difference is also found in amplitudes ($p < 0,05$) but not between latencies ($p > 0,05$) of SSEP of left and right tibial nerve ($p < 0,05$). In four patients with clinical signs of myelopathy SSEP of tibial nerve could not be registered. Statistically significant difference ($p < 0,05$) in threshold MEP were found.

Conclusion: Patients with clinical signs of myelopathy had longer latencies and lower amplitudes of SSEP in comparison with patients with radiculopathy. Also in these patients threshold to elicit MEP was significantly higher. These results were consistent with clinical severity and time to recover after surgery. IONM can provide us not only with useful insights on functional status of long tracts in spinal cord, but also with important information regarding prognosis.

Control of 5TGM1 myeloma growth in C57Bl/6 mice is associated with an activated bone marrow NK cell response

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Multiple myeloma is a malignancy of plasma cells, and despite recent therapeutic advances, it is still an incurable disease. Myeloma cells, just like normal plasma cells, reside mainly in the bone marrow, where they are in constant interaction with their local microenvironment. Signals from the microenvironment influence myeloma cell survival and response to therapy, and therefore disease prognosis. Deciphering the exact cellular and molecular components participating in the immune response against multiple myeloma are critical for a better understanding of disease pathogenesis. Therefore, using the 5TGM1 murine transfer model of multiple myeloma we compared the bone marrow immune response to malignant cells in myeloma-permissive KaLwRij mice and myeloma-resistant C57Bl/6 mice. KaLwRij and C57Bl/6 mice received 10⁶ 5TGM1-GFP murine myeloma cells intravenously. 3 weeks later, bone marrows and spleens were harvested and analyzed with flow cytometry, single cell RNA sequencing, and bulk mRNA sequencing.

Transfer of 5TGM1 cells led to the development of unrestrained and disseminated myeloma in all injected KaLwRij mice. In contrast, only a subset of C57Bl/6 mice developed myeloma, which was usually restricted to the bone marrow. Transcriptomic and flow cytometric analyses revealed an activated bone marrow NK cell and CD8⁺ T cell response in C57Bl/6 mice with a restrained tumor, while this was absent from KaLwRij mice and the small number of C57Bl/6 mice with an unrestrained tumor. Transcriptomic data indicated the role of IFN γ in tumor containment, and antibody-mediated neutralization of IFN γ increased incidence and outgrowth of myeloma in C57Bl/6 mice. Our findings that a fully functional immune system is capable of controlling myeloma progression, and that this tumor control is mediated via IFN γ . Furthermore, we suggest using C57Bl/6 mice as 5TGM1 recipients to study the immune response against myeloma in a genetically modifiable mouse strain.

Consumption of functional food enriched with n-3 PUFAs and antioxidants enhances microvascular reactivity and reduces oxidative stress in competitive athletes

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Introduction: Due to the increased need for micronutrients, athletes often take additional supplements containing, among others, n-3 polyunsaturated fatty acids (n-3 PUFAs), selenium, lutein and vitamin E. However, there are no studies that examined the intake of these micronutrients in the form of functional food on cardiovascular health. The present study aimed to investigate the impact of enriched hen eggs with n-3 PUFAs, selenium, lutein, and vitamin E on microvascular endothelial function, oxidative stress, and microvascular response to acute exhausting exercise (AEE).

Methods: In this randomized interventional study, 31 competitive athletes were divided into two groups: Control group (n=14) and Nutri4 group (n=17). The Nutri4 group consumed three enriched eggs and Control three regular eggs daily for a duration of 3 weeks. Prior to and after the dietary intervention, body mass index, body composition, blood pressure, serum lipid levels, free fatty acid profiles, and oxidative stress biomarkers were measured. Before and after protocol in pre- and post-AEE sessions, endothelium-dependent (PORH and AChID) and endothelium-independent responses (SNPID) of skin microvascular blood flow were assessed.

Results: After consuming enriched eggs, the Nutri4 group showed significant enhancements in both PORH and AChID, without changes in Control. In the Nutri4 group, there was a decrease in the formation of hydrogen peroxide and peroxynitrite in peripheral blood mononuclear cells, as well as a decrease in serum concentration of 8-iso prostaglandin F₂α. Conversely, these factors remained unchanged in the control group. Both PORH and AChID were reduced after AEE before and after the dietary interventions. However, the responsiveness range of PORH to AEE (ΔPORH) increased following the consumption of enriched eggs.

Conclusion: Three-week consumption of enriched hen eggs resulted in improved endothelium-dependent microvascular reactivity and reduced oxidative stress in competitive athletes. Also, microvascular adaptation to the AEE was improved after consumption of Nutri4 eggs.

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N-3 PUFAs and Microcirculation: Unravelling the Prostanoids Connection

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Introduction: Previously, we have demonstrated that the short-term intake of n-3 PUFAs enriched food leads to a shift towards anti-inflammatory prostanoids and increased resolvins serum levels. Furthermore, acetylcholine-induced vasodilatation was significantly improved following the n-3 PUFAs dietary protocol. Understanding how dietary interventions may influence the balance between vasodilator and vasoconstrictor prostanoids and the subsequent changes in microcirculation and vascular function is of great interest.

Methods: Participants were divided into two groups: control group (N = 21) and n-3 PUFAs group (N = 19). Dietary protocol included consumption of three hard-boiled eggs per day for three weeks. Correlation analysis was performed on the previously obtained and described data including: a) measurement of skin microvascular blood flow in response to iontophoresis of acetylcholine (ACh) and sodium nitroprusside (SNP) assessed by laser Doppler flowmetry (MoorVMS-LDF, Axminster, UK); and b) serum concentrations of leukotriene B4, B5 and prostaglandin E2, E3 were measured by commercially available ELISA kits (BioRad PR 3100 TSC, Bio-Rad Laboratories, CA, USA).

Results: A significant positive correlation between prostaglandin E2 serum concentration and SNP-induced vasodilatation ($r=0.489$, $p=0.011$) was found in n-3 PUFA group. In the control group this endothelium-independent vasodilatation negatively correlated with serum concentration of leukotriene B4 ($r=-0.478$, $p=0.018$).

Conclusion: Previously described improvement in ACh-induced vasodilation and a significant decrease in serum prostaglandin E2/E3 concentration ratio, alongside the positive correlation between SNP-induced vasodilation and serum prostaglandin E2 levels implies that n-3 PUFA metabolites might also enhance endothelium-independent vasodilation via PGE2, a known vasodilator. Correlation with leukotriene B4 in control group, a pro-inflammatory lipid mediator that was significantly increased following the dietary protocol, indicates that increased inflammation may impair endothelium-independent vasodilation responses. These results support the idea that enriched egg consumption may positively influence vascular function through the regulation of prostanoids.

Short term low salt diet reduces inflammation in mild to moderate psoriasis vulgaris, as assessed by PASI score

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Introduction: Psoriasis vulgaris is an autoimmune disease characterised with low grade chronic systemic inflammation. Increased sodium content in lesional and non lesional skin in psoriasis patients who had PASI > 5 has been found to be elevated.

Materials and methods: The study was designed as a prospective cohort study. Participants suffering from mild to moderate psoriasis, measuring PASI > 5 at baseline, were included. All participants have been assigned to the same study protocol. Clinical evaluation with PASI has been

Results: Twenty patients suffering from mild to moderate psoriasis were recruited to participate in the study (11 [55%] female, 9 [45%] male). 24-hour natriuresis validated that participants maintained the LS diet protocol. Mean age of the subjects was 47.7 ± 15.44 years. Average reduction in sodium intake calculated from 24-h sodium excretion was $51\% \pm 30$. PASI values after 2 weeks of LS diet decreased significantly compared to the values at baseline (PASI: baseline 9.5 ± 5.4 vs. LS diet 7.9 ± 5 ; $p < 0.001$). No statistically significant changes were observed in DLQI or hsCRP values. Furthermore, SBP and DBP decreased significantly after LS diet, compared with baseline measurements.

Conclusion: A 2-week LS diet led to clinical improvement in subjects with psoriasis, as seen in the decrease of PASI values after a short-term LS diet compared with baseline measurements. Thus, reduction in dietary salt intake could benefit psoriasis patients.

Wavelet analysis of laser Doppler microcirculatory signals: current position in the field

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Laser Doppler flowmetry (LDF) has long been considered a gold standard for non-invasive assessment of skin microvascular dynamics. Due to the laser Doppler (LD) microcirculatory signal's complex biological and physiological context, using spectral analysis is advisable to extract as many of the signal's properties as feasible.

Spectral analysis can be performed using either a classical Fourier transform (FT) technique, which has the disadvantage of not being able to localize a signal in time, or wavelet analysis (WA), which provides both the time and frequency localization of the inspected signal. To date, WA of LD microcirculatory signals has revealed six characteristic frequency intervals, ranging from 0.005 to 2 Hz. Each of these relates to a specific physiological influence that modulates the skin microcirculatory response: endothelial nitric oxide (NO)-independent, endothelial NO-dependent, neurogenic, myogenic, respiratory, and cardiac. WA thus provides a more thorough analysis of LD signals measured in healthy and diseased subjects, but some limitations remain. As a more accurate assessment of human skin microcirculation may better enhance the prognosis of diseases characterized by microvascular dysfunction, the search for improvements in analytical methods is also crucial from a clinical perspective.

In this talk, we summarize and discuss the advantages of WA in relation to the gold-standard FT. In addition, we briefly present the current limitations of the technique as well as possible future improvements.

Microvascular endothelium function response to n-3 polyunsaturated fatty acids, vitamin E, selenium and lutein enriched functional food in patients with acute coronary syndrome

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Introduction: Acute coronary syndrome (ACS) is an acute atherothrombotic event in coronary arteries and the leading cause of death at global level. High levels of low-density lipoprotein cholesterol increase oxidative stress and inflammation, and lead to the development of endothelial dysfunction. To examine the influence of hen eggs consumption, enriched with n-3 polyunsaturated fatty acids (n-3 PUFAs), lutein, vitamin E and selenium on indicators of microvascular function, oxidative stress and the level of inflammatory mediators in patients after ACS.

Methods: Adult subjects of both sexes with ACS were randomized into a control group (regular hen eggs) and a Nutri4 group (functionally enriched eggs) and underwent a three-week supervised dietary protocol. Before and after the diet, changes in the values of post-occlusive reactive hyperemia (PORH), iontophoresis of acetylcholine (AChID) and sodium nitroprusside (SNPID) were determined using the laser doppler blood flow measurement method in the skin microcirculation, which are indicators of microvascular functions. The activity of the antioxidant enzymes CAT (catalase), GPx (glutathione peroxidase) and SOD (superoxide dismutase), changes in biomarkers of oxidative stress and antioxidant capacity, levels of pro- and anti-inflammatory cytokines, lipid profile and protein expression of the enzymes eNOS, iNOS, and nNOS were assessed, which are important in the mechanisms of microvascular reactivity in patients with ACS.

Results: Consumption of Nutri4 eggs significantly decreased serum cholesterol and n6/n3 PUFA ratio and had a positive effect on microvascular reactivity, as shown by significantly PORH and AChID. The dietary protocol did not significantly affect on antioxidative capacity. Also, it did not significantly affect the levels of pro- and anti-inflammatory cytokines level. However, Nutri4 eggs consumption led to a decrease in the levels of nNOS and iNOS, while the levels of eNOS increased, although not significantly.

Conclusion: In patients with ACS, consuming Nutri 4 eggs enriched with n-3 PUFA, lutein, vitamin E, and selenium as part of their dietary protocol had a positive impact on microvascular function while not causing any negative effects on oxidative stress.

The rationale for introducing low salt diet for the management of Th17-mediated skin disorders

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Psoriasis is a chronic immune-mediated inflammatory disorder of the skin with a dominant Th17 inflammatory pattern. Due to its chronic course and resulting systemic low-grade inflammation, psoriasis has been appointed as a risk factor for the development of cardiovascular, liver, psychiatric, and many other diseases. A turning point in the treatment of psoriasis patients was the introduction of biologics, which allowed us to block the underlying processes at very specific signaling levels (i.e. anti-TNFalpha, IL-17, IL-12/23). In the clinical setting that meant achievement of PASI 100 (clear or almost clear skin) in a great number of patients. It is yet to be established how this will impact previously described late and chronic side effects and comorbidities of psoriasis, although very positive results are objectively expected.

Nevertheless, there is a great proportion of psoriatic patients with only mild psoriasis who are not candidates for the system treatment. Their skin changes are successfully treated with local therapy, but relapses are frequent, and ultimately lead to very low patient adherence to the treatment. These patients are left with foci of chronic inflammation which, according to recent studies, leads to subclinical vascular and hepatic inflammation in mild psoriasis.

Since the discovery that the salt-sensitive kinases (i.e. serum- and glucocorticoid-induced kinase 1, SGK1) can be found in immune cells, namely the CD4 T-helper lymphocytes and Treg cells, a number of studies have investigated the effects of changing NaCl concentration in the vicinity of T cells, including the effects of reducing dietary salt intake on the balance of Treg and Th17 lymphocytes. Based on these results, it has been proposed that the Th17-mediated inflammation could be sustained by reducing dietary intake of kitchen salt. Indeed, this has been demonstrated in patients with rheumatoid arthritis and systemic lupus erythematosus, who presented with reduced Th17 and increased frequencies of Treg lymphocytes following dietary intervention.

Currently available *in vitro* and clinical data suggest that dietary intervention aiming to reduce daily salt intake could be beneficial for the psoriasis patient in terms of reducing long-term complications.

The influence of intensive physical activity on perforin and granulysin expression

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Introduction: Physical activities represent a planned, structured and purposeful movement of the body to maintain physical fitness and overall wellness. Physical activity may be a sort of natural protector against different chronic inflammatory diseases which is accompanied with increasing secretion of anti-inflammatory cytokines in the circulation. Intensive physical activity has to be good planned with adequate sufficient recovery period to improve athletic performance and therefore has anti-inflammatory influence. On the other hand, intensive physical activity may have the opposite effect and initiates a series of inflammatory cascades that depend on exercise intensity and duration. Intensive physical activity requires more energy in comparison with regular physical activity and may stimulate release of pro-inflammatory cytokines and free radicals from activated leukocytes, which may lead to muscle damage and tissue injury. A stress-recovery imbalance may lead to negative states of overtraining. Granulysin represents a cytotoxic granule protein which is specific for cytotoxic T-lymphocytes and natural killer cells. During intensive physical activity, granulysin expression may be elevated. Activated T lymphocytes may produce a big amount of granulysin in the cell. Perforin is also stored in the cytoplasmic granules of the cytotoxic cells. We hypothesized that secretion of cytolytic molecules granulysin and perforin are elevated in different lymphocyte subpopulation in peripheral blood of subjects with intensive physical activity in comparison with subjects without physical activity (sedentary way of life) or recreative subjects.

Methods: Venous blood samples were taken from all subjects and peripheral blood mononuclear cells (PBMC) were isolated. Phenotype of lymphocytes and expression of granulysin and perforin were analyzed using intracellular and surface immunofluorescence (flow cytometry on FACSCalibur). Statistical analysis was done in computer program Statistica per Windows.

Results: Our preliminary data showed that the granulysin and perforin expression are increased in professional athletes in comparison with healthy controls and noncompetitive athletes, indicated that intensive physical activity may contribute to cytolytic potential of athletes.

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The maternal tolerance development during pregnancy: role of natural autoantibodies

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Introduction: In autoimmune diseases, the regulatory role of natural autoantibodies (nAAb) in tolerance induction is well known, but their effect on the development of fetal tolerance during pregnancy is not yet clear. The aim of the present study was to identify 3 families of nAAbs, IgM and IgG against mitochondrial citrate synthase (CS), heat shock proteins (Hsp60 and Hsp70) and IgG nAAbs against cytokines important during pregnancy.

Methods: Serum samples from normal and Hashimoto's thyroiditis (HT) pregnant women in the first and third trimesters were compared with samples from healthy control and HT women. Measurements were performed using in-house developed ELISA kits and MILLIPLEX anti-cytokine autoantibody kit.

Results: Our results show that IgM nAAb against CS are elevated, while against Hsp60 and Hsp70 are lower in healthy pregnant women than in HC. Anti-Hsp60 and Hsp70 IgG nAAb levels are elevated in HT patients compared to HC, but diminished during their pregnancy. A regulatory, scavenging role of IgM nAAbs against Hsp60 and Hsp70 is hypothesized in pregnancies. The opposite changes in the levels of natural IgG autoantibodies against Th1 and inflammatory cytokines and BAFF, responsible for B-cell activation during pregnancy also support a regulatory role of these autoantibodies on cytokine availability and activity.

Conclusion: We hypothesize that upon a prompt immunological trigger like pregnancy, the physiological nAAbs exhibit a moderate plasticity and inducibility to recent antigenic triggers to regulate immunological mechanisms like cytokine levels.

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Bone marrow stromal cells decrease differentiation of acute myeloid leukemia cells induced by low-dose cytarabine

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Introduction: Low-dose cytarabine (LDAC) is a therapy approach for patients suffering from acute myeloid leukemia (AML) who are unfit for intensive chemotherapy. Cytotoxic doses of cytarabine on AML cells induce apoptosis, but LDAC triggered AML remissions without cytotoxicity and induced differentiation of leukemic cells *in vitro*. However, such differentiation is rarely observed *in vivo*. We hypothesize that this discrepancy may be due to the effect of bone marrow (BM) stromal cells on AML cells. BM stroma is known to protect AML cells from toxic doses of cytarabine, but the effect of LDAC-induced differentiation has not been investigated. This study aims to investigate the effects of BM stroma on AML differentiation induced by LDAC.

Methods: Human AML cell lines U937 or MOLM-13 were seeded on BM stromal cell line MS-5, with or without transwell inserts. The effects of increasing doses of AraC on viability, cell cycle, apoptosis, reactive oxygen species (ROS), and differentiation were determined by flow cytometry analysis. Morphology was analyzed by microscopy, the cytokines levels by LEGENDplex™, and the protein expression by western blot. RNA Sequencing and bioinformatical analysis were performed by Novogene Company Limited.

Results: Our results show that the presence of MS-5 cells decreased LDAC-induced cell cycle arrest, DNA damage signaling, and differentiation of U937 and MOLM-13 cells. Although transcriptomic analysis revealed that the stroma reduces the expression of genes involved in cytokine signaling and oxidative stress, experiments with pharmacological inhibitors and neutralizing antibodies did not support the role of CXCL12, TGF- β 1, or ROS. Stromal cells reduce LDAC-induced differentiation in primary samples from AML-M4 and myelodysplastic syndrome/AML patients.

Conclusion: The presence of stromal cells inhibits LDAC-induced differentiation, which suggests that the impact of the BM microenvironment on AML may be one of the reasons for the modest and/or rare differentiation effects observed in patients.

Changes in the concentration of matrix metalloproteinases 2 and 9 in residents near waste disposal centers

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Introduction: The growth of the world population is accompanied by an increase in produced waste. Waste management is a huge problem of the world's major metropolises, and it is at the center of attention of the world's leading experts in ecology and environmental health. The huge amount of waste materials created by human activity, as well as the potentially harmful effects on the environment and public health, led to the need to introduce modern scientific methods for safe waste disposal. Local residents near waste management centers may be exposed to harmful effects in and outside the workplace. Matrix metalloproteinases (MMPs) are a family of extracellular zinc-dependent endopeptidases that have the ability to break down almost every component of the extracellular matrix (ECM). Tissue inhibitors of matrix metalloproteinases TIMPs inhibit the proteolytic activity of MMPs. A disruption in the balance between MMPs and TIMPs is involved in the pathophysiology and progression of many diseases. The study aimed to examine the influence of vicinity of waste management centers on changes in the expression of MMP and TIMP.

Methods: in this research we included respondents who have lived in the vicinity of waste management centers for more than five years and do not suffer from acute inflammatory diseases, chronic and malignant diseases. The healthy control group will consist of subjects of appropriate age and gender from the group of voluntary blood donors who do not live in an industrial area with the same exclusion criteria.

Results and conclusion: our preliminary results showed a significant increase in the enzymes MMP-2 and 9 in the urine of subjects living near waste management centers in comparison with healthy volunteers, indicated that this very sensitive method may be a way for good monitoring of early changes in enzyme profiles.

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Effects of dietary salt intake on vascular endothelial function in healthy pregnant women during third trimester of uncomplicated pregnancy

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Introduction: This study aimed to investigate the impact of dietary salt intake during third trimester of normal pregnancy on maternal micro- and macrovascular endothelial function and oxidative stress level.

Methods: This was a cross-sectional study involving 65 women with singleton pregnancies between 37 and 40 weeks of gestation. Based on estimated daily salt intake from 24-hour urinary excretion 33 subjects comprised normal daily salt intake group (NS; average salt intake 5.9 g salt/day), and 32 subjects comprised high daily salt intake group (HS; average salt intake 10.5 g salt/day). Laser Doppler flowmetry was used to measure microvascular reactivity in response to vascular occlusion (PORH), iontophoresis of acetylcholine (AChID) and sodium nitroprusside (SNPID), and local heating (LTH), while for macrovascular endothelium-dependent vasodilation was assessed by flow mediated dilation (FMD) of brachial artery. Serum nitric oxide (NO) and endocan concentration, as well as 8-iso prostaglandin F₂ α (8-iso-PGF₂ α), thiobarbituric acid reactive substances (TBARS) and ferric reducing ability of plasma assay (FRAP) were measured as biomarkers of endothelial function/activation and oxidative stress, respectively.

Results: Brachial artery FMD, as well as microvascular AChID and LTH were significantly decreased in HS compared to NS group of pregnant women, while PORH and SNPID did not significantly differ between groups. There was no difference in serum NO and endocan concentration between groups. 8-iso-PGF₂ α and TBARS were significantly increased in HS compared to the NS group, while FRAP did not significantly differ between groups. Daily salt intake moderately positively correlated with TBARS. There was moderate negative correlation between TBARS and LTH, and moderate positive correlation between FRAP and AChID.

Conclusions: High dietary salt intake has been associated with decreased endothelial-dependent vascular reactivity in both the peripheral micro- and the macrocirculation of healthy pregnant women during the third trimester of uncomplicated pregnancy. In addition, this attenuated endothelial vasodilator capacity could be associated with higher oxidative stress level in pregnant women who had high dietary salt intake compared to those with a normal one.

Thyroid function and short- and middle-term outcomes of SARS-CoV patients

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Introduction: the interaction between thyroid and sars cov-2 is complex and not yet fully understood. the aim of this study was to identify a possible association of the previous thyroid disease and serum tsh level on the short-term and middle-term outcomes of patients hospitalised for covid-19.

Methods: we retrospectively analysed the data of 1423 patients aged 18 years or older, with known previous thyroid status who were admitted for covid-19 to clinical hospital dubrava, zagreb, croatia, between march 2020 and june 2021. for 614 patients whose serum tsh was determined during hospitalisation we examined short-term outcomes, including the required level of oxygen supplementation, admission to the icu and death. the msct image of the chest and tsh was recorded in the post-covid outpatient clinic six to eight weeks after the discharge from the hospital and was used to estimate the middle-term covid-19 complications. patients were divided into three groups according to measured tsh levels during the hospitalization.

Results: those with lower/suppressed tsh (<0.4 miu/l) had worse short-term outcomes and were more frequently admitted to the icu (p=0.011), needed mechanical ventilation (p=0.001) or died (p=0.03). in the post-covid period, there was an overall increase in the tsh levels when compared to tsh during hospitalisation. the greatest increase was detected among the patients with suppressed/lowered tsh level during hospitalisation, and it correlated significantly with msct finding of higher pulmonary involvement (p=0.001).

Conclusion: changes in the serum tsh level may be an important indicator for the course of covid-19 and its middle-term outcomes.

Keywords: sars cov-2, covid-19, thyroid, tsh, outcomes

Lipid indices in abdominal fat and ovaries in *Podarcis siculus* and *Podarcis melisellensis*

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Introduction: Lipids in reptiles, stored subcutaneously or as abdominal depoes, are utilized for growth, energy production and reproduction. The aim of the study was to evaluate the calculated lipid indices from fat body weight and total body weight, ovaries weight and total body weight, fat body weight and total extracted lipids and ovaries weight and total extracted lipids from ovaries in two species of lizards.

Methods: Samples were collected from *Podarcis siculus* (Italian wall lizard; Rafinesque-Schmaltz, 1810; N=10) and *P. melisellensis* (Dalmatian wall lizard; Braun, 1877; N=10). Total lipids were extracted in a chloroform-methanol mixture and evaporated.

Results: Taking into account body weight and abdominal lipid depoes, a higher correlation was detected in *P. siculus* compared to *P. melisellensis* (0.80 vs. 0.56). Also, correlation coefficient from body weight and ovaries wight was higher for *P. siculus* compared with *P. melisellensis* (0.79 v. 0.39). *P. siculus* deposited $63.68 \pm 6.25\%$ and *P. melisellensis* $75.75 \pm 14.82\%$ of total lipids in the abdominal depoes. The total lipid content in *P. siculus ovaries* was $12.13 \pm 8.27\%$ and for *P. melisellensis* $35.16 \pm 23.62\%$.

Conclusion: As *P. siculus* is an invasive species in this region, it can be concluded that it is more effective in hunting and consequently deposits more fat in its lipid reserves. Differences in ratio of abdominal depoes and body weight and higher percentage of lipids in ovaries can indicate that *P. melisellensis* reproduce earlier than *P. siculus*.

Keywords: Lipid indices, abdominal fat, ovaries, *Podarcis siculus*, *P. melisellensis*

Nutritional lipid quality indices in goat's milk regarding lactation period

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Introduction: Colostrum and milk are important sources of energy, carbohydrates, and fat for the newborn kid, while milk components provide valuable nutrients in the human diet. The aim of the study was to evaluate the nutritional lipid quality indices in goat's milk during lactation. **Methods:** Milk samples were taken from clinically healthy Saanen goats (N=70) during first 24 hours after parturition, and after 30, 60 and 150 days of lactation. Total lipids from colostrum and milk were extracted, and gas chromatography (GC) was used for the analysis of methyl esters of fatty acids. Indices of concern were: polyunsaturated fatty acid/ the saturated fatty acid index (PUFA/SFA), the n-6/n-3, the hypocholesterolemic/hypercholesterolemic index ($h/H = [(C\ 18:1+PUFA)/(C14:0+C16:0)]$), the atherogenicity index ($AI=(C12:0+4*C14:0+C16:0)/UFA$), the thrombogenicity index ($TI=C14:0+C16:0+C18:0)/[(0.5*MUFA)+(0.5*n-6)+(3*n-3)+(n-3/n-6)]$), and the peroxidation index ($PI=(\text{monoenoic acid}*0.025)+(\text{dienoic acid}*1)+(\text{trienoic acid}* 2)+(\text{tetraenoic acid}*4)+(\text{pentaenoic acid}*6)+(\text{hexaenoic acid}*8)$).

Results: The PUFA/SFA and PI indexes were similar in all lactation periods. The highest n-6/n-3 and h/H indices were determined in milk after 30 days of lactation, which were significantly higher compared to indices after 60 and 150 days of lactation. The AI and TI indices were the lowest after 150 days of lactation. Lower concentration of C12:0, C14:0, and C16:0 can decrease cholesterol concentration and prevent blood vessels wall lipid adhesion, which in turn leads to a lower risk of atherosclerosis and thrombosis. Fatty acids originated from diet and synthesised in the mammary gland reflect nutritional lipid quality indices, which in turn influence goat's milk quality.

Conclusion: Based on results, it can be concluded that goat's milk fatty acid composition changes during lactation and that goat's milk quality varies during lactation.

Key words: goat's milk, lipid nutritional quality indices, fatty acids

Plasma cytokine profiling in patients with chronic graft-versus-host disease

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Introduction: Chronic graft-versus-host disease (cGVHD) is a significant allo- and autoimmune complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT), affecting multiple organ systems. Monocytes, cells of innate immunity, exhibit diverse subpopulations characterized by their functions, ranging from phagocytic to inflammatory, anti-inflammatory, or variable roles. Their roles in cGVHD are unclear, with studies showing differences in activation markers and chemokine receptors but inconsistent cytokine secretion. Unlike certain chemokines as cGVHD biomarkers, the role of monocyte-related cytokines remains unexplored. Our primary objective was to assess the relationship between monocyte-associated cytokines and cGVHD, differentiating between de novo and established cases. We also aimed to compare these cohorts with allo-HSCT patients without cGVHD.

Methods: We enrolled 62 adult cGVHD patients (de novo=31, established=31) and 31 control allo-HSCT patients at University Hospital Centre Zagreb from 2017 to 2023. Plasma samples were analysed using microsphere bead array technology to quantify 12 cytokines (IL-4, IL-2, CXCL10, IL-1 β , TNF- α , MCP-1, IL-17A, IL-6, IL-10, IL- γ , IL-12p70, IL-8). Age and sex distributions were evaluated among groups.

Results: Age and sex did not significantly differ between groups. CXCL10 levels were significantly elevated in de novo cGVHD patients compared to controls ($p < 0.001$). Moreover, both CXCL10 ($p < 0.001$) and immunosuppressive IL-10 ($p = 0.049$) were higher in de novo cGVHD patients than those with established cGVHD. IL-6 demonstrated a positive correlation with the global NIH cGVHD score ($\rho = 0.448$, $p < 0.001$) and a negative correlation with the Karnofsky score ($\rho = -0.524$, $p < 0.001$) across all cGVHD patients, indicating its association with disease severity.

Conclusion: This study provides preliminary evidence supporting CXCL10 as a potential biomarker for cGVHD, with marked elevation in de novo cases. Additionally, our findings highlight a link between elevated IL-6 levels and increased cGVHD severity. These results underscore the clinical relevance of these cytokines in understanding and managing cGVHD, warranting further validation in larger cohorts.

The effects of bradykinin type 2 receptor deficiency on microglia activation and survival after cerebral ischemia in mice

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Introduction: Previous studies suggest a possible involvement of the bradykinin signaling pathway in microglial activation during post-ischemic inflammation in the brain. This research aimed to evaluate the changes in population size and morphology of microglial cells in different areas of the brain to determine the influence of bradykinin type 2 receptor (B2R) deficiency on microglial response in the acute phase of ischemic stroke in mice.

Methods: Male C57BL/6J/Bdkrb2^{tm1Jfh/SmiJ} mice aged 3 to 4 months (B2R-KO, n=9) and their wild-type controls (WT, n=9) underwent 30-minute intraluminal middle cerebral artery occlusion (MCAO) to cause cerebral ischemic injury. On the first and third day following MCAO, the brain was imaged using a 7T BioSpec 70/20 US magnetic resonance system. An automatic analysis of immunohistologically stained microglia cell number and 3D morphology in the lesion, perilesional and contralateral areas of the cortex and striatum was conducted using an adapted version of a previously published MATLAB-based script.

Results: Ischemic injury in the acute phase caused extensive loss of microglial cells in both hemispheres which was diminished by B2R deficiency, especially in the perilesional cortex (p=0,0024) and contralateral areas (p<0,01) compared to WT mice. On the 1st day after MCAO, a significant decrease in the ramification index indicated a high activation state of microglial cells in the lesion areas of both groups. However, B2R-KO mice showed a stronger initial response in the perilesional (p<0,001) and contralateral (p<0,0001) areas compared to controls. By the 3rd day, the activation state of microglial cells was the same in both groups, despite the significantly lower number of microglial cells in WT mice.

Conclusion: B2R deficiency leads to better survival and pronounced morphological changes of microglial cells in the acute phase of ischemic stroke supporting the suggested role of B2R in microglial activation during post-ischemic inflammation.

Keywords: brain ischemia, bradykinin type 2 receptor, microglia

Acknowledgment: The study is supported by the Croatian Science Foundation project BRADISCHEMIA (UIP2017-05-8082). Multimodal imaging was done at Laboratory for Regenerative Neuroscience - GlowLab, University of Zagreb School of Medicine.

Sex-related differences in zinc, metallothionein I/II, and estrogen receptor-alpha interaction in iron-overloaded EAE rats

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Introduction: Recent discoveries show that disturbance of mechanisms that prevent the deleterious effect of iron (Fe)-induced oxidative stress may contribute to demyelination during multiple sclerosis (MS). Although iron is essential for the normal function of the human body, it is also the source of oxidative stress which can be involved in demyelination in multiple sclerosis. Various protective mechanisms prevent the effects of oxidative stress. One of them could be the interaction between zinc (Zn), metallothionein I/II (MT-I/II), and estrogen receptor-alpha (ER- α). Therefore, we analyzed Zn, MT-I/II, and ER- α status in spinal cord tissue of iron-overloaded (FeO) male and female *Dark Agouti* (DA) rats during the experimental autoimmune encephalomyelitis (EAE), an animal model for MS.

Methods: Male and female DA rats were treated with Fe-sucrose or with saline solution for two weeks before immunization. Spinal cord (SC) tissue was sampled on day 13 post-immunization and from untreated non-immunized control rats. Fe and Zn content in the tissue was determined by ICP spectrometry and the expression of Zn, MT-I/II, and ER- α by immunohistochemistry and immunofluorescence. Immunohistochemical staining quantification was performed using Cell F v3.1 software.

Results: The results showed that female EAE rats reacted to FeO by greater content of Zn and MT-I/II in the SC tissue, especially in the SC neurons. Also, female EAE rats showed a greater interaction between ER- α and Zn in the SC neurons. Besides, in all immunized rats, the SC MT-I/II expression was greater than in untreated male and female rats.

Conclusions: The data point to sexual dimorphism in mechanisms that regulate Fe homeostasis and imply that during an autoimmune attack, the harmful consequences of Fe-induced oxidative stress might be restrained by the MT/Zn/ER network.

Correlation of explosive muscle strength and body composition in young adults: difference between athletes and non-athletes

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Introduction: Explosive strength is a valuable measure of musculoskeletal fitness. The aim of this study was to test the explosive strength of college students and to examine relationship of explosive strength with body mass and body composition.

Methods: A total of fifty-five participants (40 women and 15 men) aged 20-22 years were included in this cross-sectional study: 25 athletes and 30 non-athletes. They were measured for explosive strength using counter movement jump (CMJ) measurements by MyJump App. Body composition was assessed by bioelectric impedance analysis.

Results: Statistically significant differences were found between athletes and non-athletes both in the body mass composition and in the explosive strength of the legs. Athletes have less fat and more muscle tissue compared to non-athletes. Also, athletes have higher explosive leg strength than non-athletes, regardless of muscle content. Explosive strength of the legs correlates negatively with fat content and positively with muscle tissue content in the entire sample and among non-athletes, while among athletes only fat content is negatively correlated to explosive strength, but there is no correlation between explosive strength and muscle content.

Conclusion: Regression analysis revealed that body fat content, as well as % of fat in the legs are a predictors of explosive leg strength in the whole sample. Additional predictor of explosive strength among non-athletes is a body muscle content, while in athletes there was no predictor of explosive strength among the body composition variables.

Key words: explosive strength, body composition, athletes, non-athletes

Impact of Personalized Kinesitherapy on Lymphedema Management in Women with Breast Cancer After Surgical Treatment and Adjuvant Radiotherapy – A Retrospective Reanalysis

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Introduction: Lymphedema is a prevalent concern among women with breast cancer, with estimates indicating that between 20% and 60% of patients experience symptoms. This condition is characterized by the accumulation of fluid in interstitial tissues, primarily affecting arm, shoulder, neck, or trunk. It is often attributed to damage incurred by lymph nodes during breast cancer treatments, including radiation therapy and axillary node dissection. The progression and severity can vary. This retrospective reanalysis investigates the influence of personalized kinesitherapy on lymphedema management in women who have undergone surgical treatment and adjuvant radiotherapy aiming to improve their quality of life and treatment outcomes.

Methods: In this retrospective reanalysis, we included 729 patients diagnosed with breast cancer, with an average age of 58.17 years (± 10.44). These patients underwent physical therapy at the Clinical Unit for the Rehabilitation of Oncological Patients at KBC Sestre milosrdnice between 1.1.2015. and 31.12.2019. Patients received adjuvant radiotherapy alongside individually planned kinesitherapy. To assess the impact of kinesitherapy, we categorized the patients into four groups based on the duration of their sessions (16, 20, 25, or 30 days). The program included exercises for shoulder mobility and scapula stabilization, hand drainage techniques, lymphedema prevention, and skin care. We analysed medical records, categorizing data into demographic, clinical, and kinesiological parameters.

Results: Out of 729 patients, 415 (56.93%) received chemotherapy, and 314 (43.07%) did not. On average, patients underwent 23.25 (± 5.09) kinesitherapy sessions. The initial hand index measured 2.79 (± 3.15 cm) and decreased to 2.27 (± 2.85 cm) after kinesitherapy, with an average lymphedema reduction of -0.51 (± 1.65 cm). At the beginning, 679 patients (93.14%) had lymphedema, and after kinesitherapy, 643 (88.0%) retained it, while 36 patients (4.94%) reduced lymphedema.

Conclusion: Personalized kinesitherapy significantly reduced lymphedema in breast cancer patients after surgery and adjuvant radiotherapy. This highlights the importance of multimodal rehabilitation strategies in enhancing the care of this patient population, offering promising prospects for improved outcomes and quality of life for breast cancer survivors.

Hyperventilation and orthostasis-provoked response of heart rate variability and baroreceptor sensitivity in young, healthy individuals after a short-term high-salt diet

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Introduction: The purpose of the study was to investigate if it is possible to apply a short-term high-salt diet to influence heart rate variability (HRV) and baroreceptor sensitivity (BRS) in young healthy subjects, in response to selected physiological research stimuli: hypocapnia induced by the hyperventilation and orthostasis. The study was designed as a controlled intervention study in which all subjects were subjected to the same protocol.

Methods: In total, 27 people participated in the research (female: 21, male: 6, age range 19-24). Participants were on a 7-day low-salt diet (LS; <2.3 g table salt/day), followed by a 7-day high-salt diet (HS; >11.2 g table salt/day). After both dietary protocols, blood and urine analyzes and anthropometric measurements were performed. For the parameters of HRV (low frequency/high frequency; LF/HF) and BRS, the data were obtained by continuous and simultaneous measurement and recording by The Task Force® Monitor, before and after the mentioned stimuli.

Results: The subjects remained normotensive during both weeks of measurement. After hypocapnia provoked by hyperventilation test, the LF/HF after the HS diet measurements and BRS after both LS and HS diet become lower. There is shown that salt intake did not cause a significant impact on HRV and BRS. On the other hand, orthostasis lead to significant increase of LF/HF and decrease of BRS after only LS, while HS blunted the answers of autonomic system.

Conclusion: The results suggest that salt intake, even after one week of short-term HS diet, affects the autonomic parameters such as HRV and BRS in young, healthy individuals tested by physiology stimuli.

Key words: orthostasis, hyperventilation, cerebral circulation

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The role of adenosine A1 and A2a receptor in cerebral blood vessels of Sprague-Dawley rats exposed to hyperbaric oxygen

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Introduction: Hyperbaric oxygenation (HBO₂) modulates signaling pathways and affects vascular function, which is of great importance in physiopathological processes. Adenosine receptors (AR) can play an important role in the mechanism of action of oxygen as a signaling molecules and vasoactive substances. The aim of this study was to determine the role of adenosine A1 (A1R) and A2a receptor (A2aR) in isolated middle cerebral artery (MCA) of Sprague-Dawley (SD) rats after exposure to acute and intermittent HBO₂.

Methods: Male and female healthy SD rats aged 8-10 weeks were divided into 3 groups: CTRL (control non HBO₂), A-HBO₂ (animals exposed to a single HBO₂ session at a pressure of 2 bars for 2 hours) and 4D-HBO₂ (animals exposed to HBO₂ once daily for 4 days, with vascular experiments conducted on the fifth day). The MCA's were isolated, cannulated and pressurized for 60' at 80 mmHg to assess basal diameter using pressure myograph Danish Myo Technology. A1R or A2aR selective agonist and antagonist (final concentrations 10⁻⁶ M) were added to the vessel chamber, and blood vessel diameter was measured 10 minutes after drug incubation. Statistical analyses were performed with Two-way ANOVA test; p<0.05 was considered significant. All experimental procedures conformed to the European Guidelines for the Care and Use of Laboratory Animals (directive 86/609) and were approved by the local and national Ethical Committee (#2158-61-07-21-88; EP-348/2021).

Results: The vascular response of MCA's to flow-induced dilation (FID) was reduced in rats exposed to A-HBO₂ compared to CTRLs and compared to rats exposed to 4D-HBO₂. Application of agonists and antagonists of A1Rs does not lead to a significant change in vascular reactivity of MCA's of SD rats exposed to A-HBO₂ and 4D-HBO₂. Vasorelaxation in response to A2a agonist stimulation in MCA's of SD rats exposed to 4D-HBO₂ was significantly reduced compared to control and A1 agonist. Application of agonists and antagonists of A1Rs and A2aRs does not lead to a significant change in vascular reactivity of MCA's exposed to hypoxia in SD rats previously exposed to acute and intermittent HBO₂.

Conclusion: The cerebral arteries of rats exposed to A-HBO₂ have significantly reduced vascular response to FID. FID in response to A2a agonist stimulation was significantly reduced in MCA's of SD rats exposed to intermittent HBO₂.

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Key words: hyperbaric oxygenation, adenosine receptors, cerebral blood vessels, protein expression, Sprague-Dawley rats

Reliability of a Low-Cost, High-Speed Camera-Based Method for Assessing Selected Kinematic Variables in the Unilateral Countermovement Jump

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Introduction: The assessment of the unilateral countermovement jump (UCMJ) is essential in sports science, biomechanics, and physical therapy. It provides insights into an individual's lower body explosive power and strength, reveals imbalances or asymmetries and helps track rehabilitation progress. UCMJ assessment can also be used for talent identification, training program design, motivation of athletes, and injury prevention. While many different measurement options are available, such as force plates, inertial measurement units (IMUs), marker-based motion capture systems, and jump mats, low-cost, high-speed cameras are often preferable due to their cost-effectiveness and practicability. Kinovea is a free and open-source video annotation tool for sports analysis, including unilateral countermovement jumps. It allows capturing, slowing down, comparing, annotating, and measuring video motion. With its features, Kinovea is an ideal tool for athletes, coaches, and medical professionals who want to analyze unilateral countermovement jumps. This study explores the reliability of selected kinematic variables of the unilateral countermovement jump.

Methods: Sixteen professional female handball players ($M_{\text{age}} = 20.98 \pm 2.91$ years) performed three UCMJ on dominant and non-dominant side. Each repetition was separated by a 15s rest period to avoid the influence of fatigue. Subsequently, video analysis was conducted using Kinovea (0.9.5) software to obtain vertical jump height and knee flexion angle during transition between eccentric and concentric phase. Reliability was analyzed using intraclass correlation coefficient (ICC 3,1) and repeated measures ANOVA.

Results: The results show good to excellent reliability ($\text{ICC} = 0.896 - 0.984$, $p < 0.05$) and no significant differences between repetitions ($F = 0.564 - 2.832$, $p > 0.05$) for all measured variables of the unilateral countermovement jump.

Conclusions: These findings suggest that proposed method of video analysis using Kinovea could serve as a simple and reliable tool for assessing selected unilateral countermovement jump metrics; furthermore, this can facilitate coaches in regular and low-cost assessment of athletes in a field-based setting.

Pphysical and psychosocial limitations short before and short after COVID-19 pandemic in individuals with multiple sclerosis

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Introduction: The COVID-19 pandemic had an impact on the physical and mental health of many people, particularly those with multiple sclerosis (MS). The aim of this study was to investigate whether there are differences in physical and mental limitations in performing activities of daily living in persons with MS before and after the COVID -19 pandemic.

Methods: An online survey was conducted using the same questions for the period before 4 weeks and for the period before COVID-19. The survey included questions about limitation in performing usual daily activities because of physical health, psychosocial health and pain. Respondents voluntarily gave consent to participate in the survey.

Results: A total of 23 individuals with EDSS scores ranging from 0 to 6.5 participated in the survey. There was a significant difference in achieving less than desired daily output due to physical health ($p=0.049$), i.e. people with MS were able to do more before the COVID-19. There was a difference in physical and emotional limitations and a difference in less than desired performance due to emotional problems, i.e., those with MS were able to do less after the COVID-19 pandemic, but without statistical significance. No difference was found in work limitation due to pain before and after the COVID-19 pandemic. The lack of statistically significant differences is due to the small number of respondents and the usual difficulty in obtaining consent from MS individuals to participate in research.

Conclusion: Pandemic COVID-19 negatively affected the physical and psychosocial abilities of people with MS, probably due to isolation and inability to perform timely physical rehabilitation and maintain continuity of exercise in organized centers, swimming pools and fitness clubs, as social distance had to be maintained during pandemic COVID-19.

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The diagnostic accuracy of calprotectin in patients with suspected sepsis

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New biomarkers are necessary to diagnose sepsis quickly and accurately, as it is a life-threatening condition with an increasing frequency and high mortality worldwide. Awareness for early recognition and treatment of sepsis arose from the results of numerous studies that showed that the use of an appropriate antimicrobial drug within the first hour is associated with a survival rate of approximately 80%. The process of recognizing sepsis and/or the risk of developing sepsis during the patient's first examination is often not straightforward. Therefore, biomarkers can play a vital role in diagnosing and managing sepsis in a timely manner. The definition of sepsis is determined by the pathobiology and pathophysiology of the host's response to infection, which involves the release of numerous endogenous mediators of inflammation into the bloodstream. Calprotectin is one of the acute phase proteins that was originally found in the cytosol of neutrophil granulocytes and is released upon their activation. As a member of the S100 protein family, it has been identified to be involved in innate immunity as an inflammatory mediator triggering neutrophil recruitment and release of cytokine - crucial mechanisms in inflammatory responses and immunodefence. According to recent literature, calprotectin is a sensitive indicator of the inflammatory process, and it is believed that it could be a valuable indicator during the early stages of sepsis. Significantly increased serum calprotectin level was found in spontaneous bacterial peritonitis, sepsis-associated encephalopathy and sepsis-induced acute kidney injury, as well as in the amniotic fluid as a potent predictor of neonatal sepsis. Furthermore, calprotectin outperformed conventional biomarkers in predicting the need for intensive care unit admission and provided a more accurate prediction of mortality. Therefore, calprotectin could be used as a promising tool to aid the selection of traditional biomarkers used for early recognition and treatment of sepsis.

Physiological role of systemic uroguanylin in mouse salivary glands

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Introduction: Guanylin peptides are considered only internal regulators of salivary gland function. Their physiological role in regulation of saliva secretion remains unknown. The aim of this study is to determine the effects of systemic uroguanylin (UGN) on saliva flow rate and its ionic composition, and whether these effects include the activation of guanylate cyclase C (GC-C).

Methods: This study was performed on 7 months old C57Bl6Ncr1 (wild type, WT), GC-C knockout (KO) mice and their GC-C WT littermates. After pilocarpine stimulation, effects of i.p. applied UGN (30 µg/animal) on salivary flow rate and ion composition were determined. The expression of AQPs, NHEs, NBCn1, Slc26a3/a6 and CFTR were determined by qPCR in submandibular salivary glands, duodenum and kidney cortex.

Results: When UGN is administered i.p. there is a decrease in the flow rate of saliva stimulated by pilocarpine and increase the concentration of Na⁺, H⁺ and Cl⁻. In GC-C KO mice, UGN has no effect on salivary flow rate, while Na⁺, H⁺ and Cl⁻ concentrations are the when compared to GC-C WT mice. UGN (i.p.) increased the expression of Slc26a6. The similar results were obtained in salivary glands of GC-C KO mice suggesting the involvement of a GC-C independent signalling pathway for UGN. The difference in expression of Slc26a6 in GC-C KO mice when compared to GC.C WT mice is not unique to the salivary glands. This difference was found in duodenum and renal cortex as well.

Conclusion: In our study, UGN, when applied i.p., decreased salivary flow rate, pH, changed composition of other ions and by GC-C independent signalling pathway, increase expression of Slc26a6. Therefore, postprandial increase in UGN plasma concentration could have a role in regulation of physiological processes of salivary glands.

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Role and potential mechanisms of walnut consumption-induced improvement of endothelial function in cardiovascular diseases

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Introduction: Cardiovascular diseases (CVD) are one of the leading causes of death worldwide. Previous studies have provided ample evidence that healthy diet has an important role in delaying the development of many modifiable risk factors. In this review we are focusing on the protective role of walnuts on endothelial dysfunction, in hypertension, abdominal obesity and dyslipidemia.

Methods and Results: Previous studies have shown that higher consumption of walnuts has a positive impact on both primary and secondary prevention of CVD (GBD 2015 Risk Factors Collaborators, 2016). Due to their high lipid profile and bioactive compounds (such as phenolic acids, polyphenols, K and E vitamins and phytosterols) regular daily intake of walnuts is recommended. Epidemiological studies indicate that there is a dose-effect relationship between the daily intake of nuts and CVD risk reduction, walnuts showing the strongest association (Lui X., 2020). In 11 cohort comparisons (including 376,228 participants) high consumption of nuts was associated with lower risk of CVD mortality however, it was also found that the optimal intake might be 15-20 g/day and above that the benefits are limited (up to 28g/day) (Glenn A. et al., 2023). Other studies investigated the potential effects of walnut consumption on vascular function and suggested that it is due to their high polyunsaturated fatty acid (PUFA) contents (walnuts being the highest among nuts), which reduces low-density lipoprotein cholesterol (LDL-C) and triglycerides levels in the plasma thereby contributing to the improvements of the vasomotor of function of the endothelium (Drenjančević I. et al, 2022). In a randomized crossover trial, it was found that four weeks after following a Mediterranean diet - where walnuts replaced approximately 32% of the energy from monounsaturated fat - significantly improved endothelium-dependent vasodilation, reduced cell adhesion and total cholesterol (Ros E. et al., 2004).

Conclusion: In summary, nuts, especially walnuts - a non-pharmacological, dietary interventions - have a great potential to improve the vasomotor function of the endothelium, however further studies are needed to elucidate the optimal dose of walnuts supplementation in various cardiovascular diseases.

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Dual role of bradykinin receptor type 2 in mouse retinal ischemia

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Introduction: Bradykinin (BK) is one of the first inflammatory mediators released at the onset of ischemia. The aim of this study was to investigate the role of bradykinin type 2 receptor (B2R) in the acute and chronic stages of retinal ischemia in mice.

Methods: Retinal ischemia was induced in 5-month-old male B2R-deficient C57BL/6J/Bdkrb2^{tm1Jfh/SmiJ} (B2R-KO; n = 28) and control C57BL/6J (WT; n = 28) mice by 30-minute middle cerebral artery occlusion (MCAO). Seven days prior and 2, 9, and 35 days after MCAO, the animals were subjected to fundus photography, fluorescein angiography, and magnetic resonance (MR) imaging. On days 2 and 9, an evaluation of vascular permeability was performed using Evans Blue (EB) and Sodium Fluorescein (NAF). On days 2 and 35, eyes were processed for histological analysis.

Results: MR assessment showed that B2R-KO mice exhibited exacerbated thickening of the retina caused by vasogenic edema formation and extended period of edema retention in the subacute phase (day 9, p<0,05) after MCAO, along with a higher incidence of pathological signs of ischemia on fundus photographs compared to controls. Additional analysis of vascular permeability showed a significant increase in EB and NAF extravasation in the absence of B2R (p<0,05) suggesting a subacute deterioration of blood-retina barrier integrity. In the chronic phase, histological analysis showed significant changes in morphology, thinning of the retinal layers, and cell loss that reflect long-term degenerative changes in the retina after ischemic injury in both groups. In contrast to the acute phase, in the chronic phase, B2R deficiency had a protective effect on ischemic injury which was demonstrated by reduced loss of retinal ganglion cells (p<0,01) compared to controls.

Conclusion: B2R deficiency has a dual effect on retinal ischemic injury by increasing subacute vascular permeability and reducing ischemic damage in the chronic phase.

Acknowledgement: The study is supported by the Croatian Science Foundation project BRADISCHEMIA (UIP2017-05-8082). Multimodal imaging was done at Laboratory for Regenerative Neuroscience - GlowLab, University of Zagreb School of Medicine.

Intraoperative neurophysiological parameters in patients with radiculopathy and myelopathy

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Introduction: Degenerative disease of cervical spine are increased. Clinical signs can be in the form of radiculopathy, myelopathy or both. During anterior cervical discectomy and fusion (ACDF) we used intraoperative neurophysiological monitoring (IONM) that provide us insight in function of somatosensory and motor system.

Methods: This study included 30 patients who underwent ACDF. Patients were divided in two groups, 15 patients with clinical signs of radiculopathy and 15 with clinical signs of myelopathy. During surgery Somatosensory (SSEP) and Motor evoked potentials (MEP) were registered.

Results: There were statistically significant difference ($p < 0,05$) in latencies and amplitudes of SSEP of right and left median nerve. Difference is also found in amplitudes ($p < 0,05$) but not between latencies ($p > 0,05$) of SSEP of left and right tibial nerve ($p < 0,05$). In four patients with clinical signs of myelopathy SSEP of tibial nerve could not be registered. Statistically significant difference ($p < 0,05$) in threshold MEP were found.

Conclusion: Patients with clinical signs of myelopathy had longer latencies and lower amplitudes of SSEP in comparison with patients with radiculopathy. Also in these patients threshold to elicit MEP was significantly higher. These results were consistent with clinical severity and time to recover after surgery. IONM can provide us not only with useful insights on functional status of long tracts in spinal cord, but also with important information regarding prognosis.

Essential arterial hypertension attenuated endothelium-dependent microvascular response in pediatric patients

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Introduction: Hypertension has become a global medical and public health problem worldwide that affects endothelium vascular function. It is well known that hypertension has an adverse effect on endothelial microvascular function in adults, but there is a lack of data related to juvenile hypertension. The present study aimed to investigate the impact of essential arterial hypertension on microvascular reactivity in children and adolescents with essential arterial hypertension.

Methods: In this cross-sectional study, a total of 52 participants were divided into two groups: NT group (healthy normotensive children, N=26) and HT group (children with diagnosed essential arterial hypertension, N=26), both sexes, 9-17 years old. In addition to anthropometric and blood pressure measurements, forearm skin microvascular endothelium-dependent responses to vascular occlusion (post-occlusive reactive hyperemia, PORH), local heating (local thermal hyperemia, LTH), iontophoresis of acetylcholine (ACh) and sodium nitroprusside (SNP) was assessed by laser Doppler flowmetry (LDF).

Results: Forearm skin microvascular responses to PORH, ACh and LTH were significantly decreased in hypertensive compared to normotensive children and adolescents, while the endothelium-independent response to SNP was similar in both groups.

Conclusion: Even in childhood, essential arterial hypertension has a significant impact on endothelial function and attenuated the endothelium-dependent microvascular responses to various physiological stimuli.

Funding: This study was supported by institutional grants from the Faculty of Medicine Osijek IP9-2021-MEFOS grant (PI Ivana Jukić) and IP17-2022-MEFOS grant (PI Ivana Jukić).

Association of spinal curvatures with BMI, body composition and muscular endurance of trunk muscles in college students

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Introduction: Introduction: Physical inactivity and sedentary behavior in college students negatively affect body composition and musculoskeletal health leading to poor posture.

Aim: The aim of this study is to investigate the relationship between physiological spinal curvatures (lordosis and kyphosis) with body composition (body fat and muscle mass) and endurance of trunk flexors and extensors in college students aged 18 to 25 years.

Participants and Methods: Study included 82 college students (42% male, 59% female) aged 18 to 25 years. Outcome measures included: body mass index (BMI), assessment of the angles of thoracic kyphosis and lumbar lordosis in the neutral standing position using the Spinal Mouse® device; body composition using the Tanita RD -545 analyzer; testing of trunk muscle endurance using standardized trunk flexor and extensor endurance tests. Correlations were analyzed using the Pearson correlation coefficient.

Results: The mean value of thoracic kyphosis angle was $46.5^\circ \pm 8.7$ and $-32.8^\circ \pm 9.2$ for lumbar lordosis angle. No correlation was found between kyphosis and any of these variables. However, an increased percentage of hyperkyphotic students (59%) was noted, and most students had neutral lordosis (73%). There was found a positive correlation of lumbar lordosis with body fat ($r = 0.277$, $p = 0.038$), trunk extensor endurance test ($r = 0.264$, $p = 0.049$), and trunk extensor/flexor trunk test ratio ($r = 0.323$, $p = 0.015$), and a negative correlation with muscle mass ($r = -0.284$, $p = 0.034$). However, no correlation was found between lumbar lordosis and BMI.

Keywords: college students, kyphosis, lordosis, trunk muscle endurance, body composition

Funding: This study has been supported by the University of Rijeka (numbers: uniri-biomed-18-41 and uniri-biomed-18-283).

The role of bradykinin receptor type 2 in murine cerebral glucose metabolism

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Introduction: Bradykinin (BK) is a vasoactive peptide with a prospective role in glucose metabolism. By binding to the constitutively expressed bradykinin receptor type 2 (B2R), BK modulates glucose transporter expression and activity enhancing glucose uptake in different organs and tissues. However, as its action in cerebral glucose metabolism remains unexplored, the aim of this study was to determine whether B2R deficiency affects cerebral glucose uptake and the expression of glucose transporters and insulin receptor in the mouse brain.

Methods: Five months old male C57BL/6J (WT, n=8) and C57BL/6J/Bdkrb2^{tm1J^{fh}/SmiJ} (B2R-KO, n=8) mice were subjected to blood glucose concentration and HbA1c measurements followed by intraperitoneal glucose and insulin tolerance tests. First cohort of animals (n=4 per group) were subjected to optical *in vivo* monitoring of cerebral uptake of fluorescently labeled glucose administered i.v. and *ex vivo* brain imaging using the IVIS Spectrum system. From the second cohort (n=4 per group), glucose transporters and insulin receptor expression was determined with qPCR.

Results: Our preliminary results show that B2R deficiency leads to higher basal (p=0.003) and fasting (p=0.008) blood glucose levels in B2R-KO mice compared to controls but has no effect on intraperitoneal tolerance of glucose and insulin. *In vivo* fluorescence imaging showed that B2R deficiency significantly increases cerebral glucose uptake in the first 10 minutes after injection in B2R-KO mice compared to controls (p=0.03). However, *ex vivo* imaging showed no significant difference between groups. B2R-KO mice had higher expression of *glut3* (p=0.02) and *irs-1* (p=0.01), while *glut1*, *glut4*, *glut8*, and *insr* showed no difference compared to WT mice.

Conclusion: Our initial findings indicate that B2R influences the early kinetics of cerebral glucose uptake without altering total brain glucose uptake. Additionally, B2R-deficient mice exhibited elevated expression of *glut3*, implying its potential role in cerebral glucose metabolism.

Acknowledgement: The study is supported by the Croatian Science Foundation project BRADISCHEMIA (UIP-2017-05-8082). The work of doctoral student Marta Pongrac has been fully supported by the “Young researchers' career development project – training of doctoral students” of the Croatian Science Foundation. Research was done at Laboratory for Regenerative Neuroscience - GlowLab, University of Zagreb School of Medicine.

Karnozin EXTRA[®] inhibits growth, survival, and migration of human glioblastoma cells through inducing mitochondrial dysfunction

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Introduction: Previous studies documented that L-carnosine affects the regulation of tumor growth and metabolism. *Karnozin EXTRA[®]* capsule is a unique patented formula of L-carnosine combined with vitamin E, coenzyme Q10, L-carnitine, grape seed extract and northern bilberry extract. Up to now, no effects of L-carnosine in the form of *Karnozin EXTRA[®]* on human glioblastoma cells have been reported. In the present study, we investigated whether different concentrations of L-carnosine from *Karnozin EXTRA[®]* capsule effectively suppressed the proliferation, migration, and activity of mitochondrial respiratory complexes in U87 tumor cells.

Methods: Using standard hematoxylin and eosin staining, we analyzed the morphology of U87 tumor cells before and after treatment. To look more closely at the effects on cell morphology, phase contrast was used. Proliferation inhibition was measured by the MTT assay. Cell migration was determined using the scratch assay. Oxygen uptake rates were recorded using the Clarke electrode (*Oxygraph, Hansatech Instruments, England*).

Results: *Karnozin EXTRA[®]* altered the morphological features of human glioblastoma cells. All concentrations of L-carnosine (2 mM, 5 mM, and 10 mM) inhibited proliferation, and the inhibitory effect increased in a dose-dependent manner. It was also found that *Karnozin EXTRA[®]* capsule exhibited inhibitory potential for cell migration. These effects were mediated by mitochondrial dysfunction. A significant reduction in basal cellular respiration was observed in all treated groups. Moreover, the activities of complexes I, II and IV of the mitochondrial respiratory chain were decreased.

Conclusions: Our study highlights the fundamental changes in bioenergetic potential, survival and migration following exposure of glioblastoma cells to *Karnozin EXTRA[®]* and suggests that it is a potentially effective new alternative therapy for human glioblastoma.

Keywords: glioblastoma, carnosine, cell respiration, cell migration, cancer therapy

The effect of endurance exercise on arterial blood pressure in trained type 1 diabetic patients compared to healthy controls

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Introduction: Exercise is one of the most effective non-pharmacological regulators of cardiovascular health and is therefore recommended in treatment guidelines for type 1 diabetes (T1D). The aim of this study was to compare the effect of endurance exercise (EE) on arterial blood pressure response in trained T1D participants and age-, VO₂max-, and sex-matched healthy controls immediately after and 24 hours after completion of EE.

Methods: Mean arterial blood pressure (MAP) was measured in 9 T1D (age 31.3 ± 13.3, BMI 24.3 ± 2.5) and 9 healthy runners (age 30.5 ± 13.9, BMI 22.7 ± 1.6) before (baseline) and at two consecutive time points after EE in the form of 2h of cycling below the anaerobic threshold. A two-way repeated measurements ANOVA with Bonferroni post hoc test was used to examine changes between groups. Time was a within-participant factor, while control and T1D were two between-group factors.

Results: A significant time effect showed that MAP decreased 24 hours after completion of EE compared to baseline (94.51 ± 11.06 and 102.13 ± 11.03 mmHg, $p = 0.015$, $\epsilon = 0.429$) and no differences between baseline and immediately after completion of EE ($p = 0.107$) or between immediately after and 24 hours after completion of EE ($p = 0.99$). No main effect of group was found ($p = 0.236$, $\epsilon = 0.086$) and there was no significant interaction between group and time on MAP ($p = 0.467$, $\epsilon = 0.042$).

Conclusion: Our results show that the pattern of change in MAP to EE is well maintained in trained T1D participants. Postexercise recovery lasted at least 24 hours after cessation of EE.

Key words: type 1 diabetes, endurance exercise, mean arterial pressure, postexercise hypotension

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Guanylate cyclase C expression in the human brain

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Introduction: Guanylate cyclase C (GC-C) is widely expressed in the rodent brain, specifically in neurons of the cerebral cortex, amygdala, midbrain, hypothalamus and cerebellum. GC-C expression in the human brain is less known, and its presence has only been reported in the prefrontal cortex and hypothalamic arcuate nucleus. The aim of this study was to further explore GC-C expression in the human brain.

Methods: GC-C protein expression was determined by ELISA (Shanghai Korain Biotech Co., E5383Hu) in brain samples of 21 male and 13 female subjects with a *postmortem* delay under 24h. Examined were four Brodmann areas (BA9, 10, 11, 32), hypothalamic arcuate nucleus and the cerebellar cortex, with *substantia nigra* as positive control.

Results: GC-C expression was confirmed in all investigated brain areas. In hypothalamus, higher GC-C expression was found in male subjects. As shown for rodents, gender differences in hypothalamic GC-C expression exist only when the stomach content at autopsy was higher than 100 mL, but not at fasting conditions. In males, GC-C expression in the cerebellum positively correlates to the hypothalamic GC-C expression ($r=0.67$, $p=0.0012$). In females that correlation is negative ($r=-0.76$, $p=0.01$). Of all tested BAs, only BA9 showed a significantly higher expression of GC-C in female subjects, particularly in the left hemisphere.

Conclusion: GC-C is expressed in several human brain regions. Expression levels are gender-dependent. Lower GC-C expression in female hypothalamus may suggest a reduced satiety effect. In prefrontal cortex, differential GC-C expression in BA9 could exacerbate excitatory responses mediated by glutamate and acetylcholine receptors previously observed in rodent midbrain. This may be related to observed gender differences in BA9 function involving verbal fluency, empathy or ability to infer the intention of others.

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Oxidative Stability of Muscle Tissue in a Free-Living Lizard *Podarcis siculus* from two different locations – a Pilot Study

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Introduction: Oxidative stress is a major challenge for the survival of animals living on carst due to high temperatures in the summer, frequent lack of water and food and everyday more pronounced environmental changes; however, lifelong exposure to a harsh environment could generate certain adaptabilities which make them more tolerant to these environments. Increasing interest in the role of oxidative stress (OS) as a tool for quantifying the impact of environmental changes on all animals has highlighted the need to develop reliable methods to quantify it. The aim of the present study was, for the first time, to test and compare the antioxidant status-biological antioxidant potential (BAP) and glutathione peroxidase (GPx) and reactive oxygen metabolites (ROM), from muscles between two carst populations of *Podarcis siculus*.

Methods and Results: We compared oxidative stability and ROM between two free-living groups of 8 adult males, one group was from the island Pag and the other was from the coast region (town Knin) from Croatia. The results of this pilot study showed that there is no statistically significant difference in the antioxidative status determined between these two populations of *P. siculus*. **Conclusion:** These findings can serve as a base for future studies with a larger sample size, different locations, sex or between different species of the same location.

Keywords: antioxidant status, lizard, muscle, *P. siculus*

Retrospective analysis of breathing exercise intervention in patients with type 2 diabetes scheduled for abdominal cancer surgery and how it affects patients' outcomes

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Introduction: Type 2 diabetes mellitus (T2DM) confers a greater risk for the development of colorectal cancer (CRC) and might alter patients' short and long-term outcomes after surgery. Prehabilitation of CRC patients is important but programs are diverse and still not standardized. **Methods:** We retrospectively analyzed the impact of additional preoperative breathing exercises for opera singers on curative open surgery CRC patients with T2DM vs control cohort without diabetes, along with analysis of postoperative complications.

Results: Included were 291 consecutive patients treated in a single institution. Patients' mean age was 66 years. Thirty nine of them (13.4%) had T2DM. Overall 31 patients completed the breathing protocol, of whom 3 with T2DM. Of diabetic patients included, 74.4% were males, 51.9% had NRS-2002 score 4 and 44.4% had BMI >30 kg/m². In this cohort, T2DM *per se* was not a significant predictor of prolonged stay in the surgical ward (OR=0.949, p=0.889, 95% CI:0.453-1.988) nor in the ICU (OR=1.162, p=0.674, 95%CI:0.577-2.342). However, older age (above 68 years) and higher glucose levels before admission negatively influenced duration of ICU stay (p=0.01 and p=0.021, respectively). Moreover, there was a tendency for prolonged surgical ward stay (≥7 days) in cases >67.68 years and higher at-admission glucose levels (p=0.071 and p=0.084, respectively). Presence of diabetes did not influence complications within 30 days (OR=1.227, p=0.585, 95%CI:0.588-2.560) or a year post-surgery (OR=1.100, p=0.784, 95%CI:0.557-2.172), nor patients' ability to complete chemotherapy (OR=0.952, p=0.953, 95%CI:0.188-4.834).

Conclusion: The addition of breathing exercises to usual prehabilitation protocol provided additional benefit to whole cohort in terms of shortening the ICU stay.

Key words: prehabilitation; type 2 diabetes mellitus; colorectal cancer; outcomes; prognosis

Health benefit of the consumption of functionally enriched eggs in healthy young subjects

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Introduction: Functional foods offer both nutritional benefits and targeted effects on body functions, enhancing overall health and reducing risk for diseases. Previous research demonstrated that consuming functional foods rich in n-3 polyunsaturated fatty acids (n-3 PUFAs) improves microvascular reactivity, though the underlying mechanisms are unclear. This study aims to assess the impact of hen eggs enriched with four nutrients on microvascular reactivity in young, healthy individuals, as well as the role of cyclooxygenase (COX-1 and COX-2) enzymes.

Methods: The randomized, double-blind, placebo-controlled study involved a control group (N=14) consuming regular eggs and a Nutri4 group (N=20) consuming n-3 PUFA-enriched eggs with selenium, vitamin E, and lutein. Over three weeks, participants consumed three boiled eggs daily. Microvascular reactivity was assessed using laser Doppler flowmetry, measuring responses to sodium nitroprusside (SNP), acetylcholine (ACh), and reactive hyperemia (PORH) in forearm skin microcirculation. Measurements were taken before and after the dietary protocol, and in a separate group before and after oral administration of 100 mg indomethacin (a non-selective COX inhibitor) on two occasions. Serum levels of free fatty acids, vitamin E, lutein, and selenium were also measured.

Results: After consuming Nutri4 eggs, serum concentrations of n-3 PUFAs, vitamin E, and lutein significantly increased compared to controls. Nutri4 group participants exhibited improved ACh-induced dilation and PORH after the dietary protocol, while controls showed no change. SNP-induced dilation remained unchanged in both groups. In a separate group, Nutri4 participants demonstrated significantly enhanced microvascular blood flow during PORH after the dietary protocol, which was attenuated by indomethacin administration.

Conclusion: Incorporating eggs enriched with n-3 PUFAs, selenium, lutein, and vitamin E enhances microvascular reactivity in young, healthy individuals. Additionally, the results suggest the involvement of n-3 PUFA metabolites through cyclooxygenase pathways in response to reactive hyperemia.

Keywords: cyclooxygenase; endothelial function; fatty acids, n-3 PUFAs; lutein; selenium; vitamin E; vascular reactivity

Acknowledgement: The study was funded by European Structural and Investment Funds to Scientific Centre of Excellence for Personalized Health Care, the Josip Juraj Strossmayer University of Osijek, Scientific Unit for Research, Production and Medical Testing of Functional Food, # KK.01.1.1.01.0010.

Ongoing study: Effect of consumption of chicken meat enriched with carnosine on microvascular function and immune system in patients with chronic coronary artery disease

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Introduction: There are a large number of factors that promote the development of endothelial dysfunction underlying cardiovascular diseases such as hyperlipidemia, arterial hypertension, diabetes mellitus, oxidative stress, and secretion of pro-inflammatory cytokines. Due to its anti-inflammatory and antioxidant role in body, carnosine may be useful in treating cardiovascular diseases. Since increased level of oxidative stress and endothelial activation underlies the development of endothelial dysfunction in cardiovascular diseases, food enrichment with carnosine could contribute to the improvement of vascular reactivity in the microcirculation. The aim of this study is to investigate the effects of consumption of functionally enriched chicken meat with carnosine on microvascular function, oxidative stress and inflammation response in patients with chronic coronary artery disease.

Methods: The study will include at least 20 adult subjects of both sexes with chronic coronary artery disease. Subjects will be divided into two groups, the experimental group, which will eat enriched chicken meat and a control group which will eat regular chicken meat for three weeks. Before and after the dietary protocol, changes in the values of post-occlusive reactive hyperemia (PORH), acetylcholine-induced dilation (Ach ID) and sodium nitroprusside-induced dilation (SNP ID) will be determined using the laser doppler blood flow measurement method in the skin microcirculation. The markers of endothelial dysfunction and oxidative stress (CRP, pro-inflammatory and anti-inflammatory cytokines, TBARS, FRAP) will be measured in serum before and after the dietary protocol.

Expected scientific contribution: The expected scientific contribution of this research is to investigate the mechanisms, effects and possible benefits of the consumption of chicken meat enriched with carnosine as a functional food in improving the cardiovascular health of patients with chronic coronary artery disease.

Can measuring pulse wave velocity alert us to the need for early treatment of prediabetes and metabolic syndrome?

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Introduction: Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality in developed and transition countries. The metabolic syndrome (MetS) and prediabetes (PreD) predispose CVD development as acquired factors that have an underlying inflammatory process. There are more non-classical factors influencing pulse wave velocity (PWv). The PWv is an important tool for detecting arterial stiffness caused mostly by subclinical atherosclerosis predicting CV incidents. Women after menopause represent a vulnerable group in terms of CV risk. We investigated the interdependence of PWv and markers of metabolic syndrome (blood pressure, serum HDL and triglyceride level, glucose levels and waist circumference) as well as age, HbA1c, waist/hip ratio, central and peripheral blood pressure, serum levels of uric acid, creatinine, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) in postmenopausal women.

Methods: All women included in the study (226) signed informed consent, underwent clinical examination including antropometry, central and peripheral arterial blood pressure and pulse wave velocity (PWv). Peripheral blood was sampled for routine laboratory tests, as mentioned above using Dimension RXL analyzer (Siemens Healthcare Diagnostics, New York, SAD). Arterial stiffness was measured using a medical device Agedio® B900 osillometric device (IEM, Stolberg, Germany) .

Results: PWv statistically significantly correlates with systolic blood pressure, glucose, HbA1c, waist circumference and serum HDL, triglyceride and uric acid levels, ESR, central and systolic arterial pressures, and age in postmenopausal women. PWv also correlates positively with SCORE 2/SCORE 2-OP risk prediction algorithms. PWv did not correlate with hip circumference, body mass index, CRP and inversely correlated with creatinine in postmenopausal women.

Conclusion: PWv measurement is a simple, cheap, available, fast and noninvasive method for detecting arterial stiffness, and it can be of great importance for the assessment of classical and non-classical CV risk factors in postmenopausal women particularly in primary care.

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