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Day 1

Thursday, 18th May 2023

FEBS Education Session "Innovative teaching as a basis for Excellent Research in BioSciences"

Chairs: Adlija Čaušević, Ferhan Sagin, Tamer Bego

08:00 – 09:00	***Registration***
09:00 – 09:15	Introduction and presentation of FEBS activities *Miguel de la Rosa (University of Sevilla, Spain) & Jerka Dumić (University of Zagreb Faculty of Pharmacy and Biochemistry, Zagreb, Croatia)*
09:15 – 10:00	**Plenary Lecture** Why and how should you develop and improve your educator skills?: Tips for both junior & senior scientists *Plenary Speaker: Ferhan Sagin (Ege University Faculty of Medicine, Izmir, Turkey)*
10:00 – 10:25	Transferable skills and biochemistry education for the needs of industry *Invited Speaker: Jerka Dumić (University of Zagreb Faculty of Pharmacy and Biochemistry, Zagreb, Croatia)*
10:25 – 10:50	Raising the innovation potential through teaching programs in molecular biology *Invited Speaker: Lejla Kapur Pojskić (University of Sarajevo-Institute for Genetic Engineering and Biotechnology, Sarajevo, Bosnia and Herzegovina)*
10:25 – 11:00	***Coffee Break***
11:00 – 11:25	Innovative Teaching I - Integrative online tools for learning and teaching biochemistry face to face *Invited Speaker: Nino Sinčić (University of Zagreb, School of Medicine, Zagreb, Croatia)*
11:25 – 11:50	Innovative Teaching II - Integration of virtual laboratories in learning of biochemistry

Invited Speaker: Angel Herraez (University of Alcalá, Department of Systems Biology, Biochemistry and Molecular Biology Unit, Spain)

11:50 – 12:30 Expert Talk

Be a scientist, not a worker in science

Invited Speaker: Miguel de la Rosa (University of Sevilla, Spain)

12:30 – 14:00 ***Lunch Break***

14:00 – 15:30 Workshop

How to keep a good lab book?

Invited Speaker: Jason Perret (Universite Libre de Bruxelles (ULB), Faculty of Medicine-Campus Erasme, LBPN-Biochemistry Department, Laboratory of Pathophysiological and Nutritional Biochemistry, Belgium)

17:00 – 18:00 ***Registration***

18:00 – 18:40 ***Opening Ceremony***

18:40 – 19:30 **Opening Plenary Lecture**

FEBS National Lecturer

From Bench to Bedside: Translating Science from the Lab to Clinical Practice

Plenary Speaker: Dragan Primorac (University of Split, School of Medicine, Croatia; St Catherine Specialty Hospital, Zagreb, Croatia)

19:30-19:50 Sponsored Symposium - Diamedic: BD Totalys - Total Solution for Cervical Cancer Screening

Danijel Sumpor (BD, Zagreb, Croatia)

Day 2

Friday, 19th May 2023

08:00 – 09:00 **Registration**

09:00 – 09:30 **Honorary Lecture**
The Matter of Life and its Corrosion in the Course of Aging and Diseases

Plenary Speaker: Miroslav Radman, online (Mediterranean Institute for Life Sciences, Split, Croatia)The Matter of Life and its Corrosion in the Course of Aging and Diseases

Session I - Basic and applied biochemistry

Chairs: Emina Kiseljaković, Jerka Dumić, Edhem Hasković

09:30 - 10:10 **Plenary Lecture**
Functional Diversity of Cytochrome c in its Journey from Mitochondria to Nucleus

Plenary Speaker: Miguel de la Rosa (University of Sevilla, Spain)

10:10 - 10:30 Galectin-3 in pathogenesis, diagnosis and outcome prediction of Covid-19

Invited Speaker: Jerka Dumić (University of Zagreb, Faculty of Pharmacy and Biochemistry, Zagreb, Croatia)

10:30-10:50 The Aquaporins water channels and pleotropically beyond – an overview

Invited Speaker: Jason Perret (Universite Libre de Bruxelles (ULB), Faculty of Medicine-Campus Erasme, LBPN-Biochemistry Department, Laboratory of Pathophysiological and Nutritional Biochemistry, Belgium)

10:50 - 11:05 Sponsored Symposium - Labunica: Trends in molecular diagnosis of respiratory virus infections

Irena Tabain (Croatian Institute of Public Health, Zagreb, Croatia)

11:05 - 11:25	High-content screening and multi-omics as advanced tools in toxicology of nanoparticles *Invited Speaker: Andi Alijagić, online (Örebro University, Sweden)*
11:25 - 11:40	Sponsored Symposium - Farmavita
11:40 - 11:55	Sponsored Symposium - Medichem: Noninvasive procedures in liver fibrosis diagnostics *Filip Filipić (Medichem d.o.o, Sarajevo, Bosnia and Herzegovina)*
11:55 - 12:10	*Discussion*
12:10 - 12:30	***Coffee Break***
12:30 - 12:40	Determination of the mechanism and cause of death in heat stroke: Focus on the correlation of troponin I and 70 kDa heat shock protein *Short Talk: Dervišević Emina (University of Sarajevo, Faculty of Medicine, Department of Forensic Medicine, Sarajevo, Bosnia and Herzegovina)*
12:40 - 12:50	The C-Reactive Protein/Albumin Ratio and Glasgow Prognostic Score as Indicators of Disease Activity in Patients with Inflammatory Bowel Disease *Short Talk: Mlaćo Lamija (University of Sarajevo, Medical Faculty, Department of Human Physiology, Sarajevo, Bosnia and Herzegovina)*
12:50 - 13:00	Evaluation of Serum Pentraxin 3 Levels in Patients with Migraine *Short Talk: Kösem Arzu; Evaluation of Serum Pentraxin 3 Levels in Patients with Migraine (Ministry of Health Ankara Etlik City Hospital, Department of Biochemistry, Ankara, Turkey)*
13:00 - 14:30	***Lunch and Poster Session (Sessions I, II and V)***

Parallel Sessions	*Session II - Molecular genetics*	*Session V - Interactions between organisms and the environment*	
	Chairs: Kasim Bajrović, Lejla Kapur Pojskić	Chairs: Dalibor Ballian, Erna Karalija	
14:30 – 15:15	**Plenary Lecture** Microbiome in post-genomic era *Plenary Speaker: Maria Gazouli*	14:30 – 15:10	**Plenary Lecture** Molecular based selection methods and genetic diversity in forestry

	(National and Kapodistrian University of Athens, Faculty of Medicine of the NKUA, Laboratory of Biology, Greece)		*Plenary Speaker: Gaye Eren Kandemir (Ministry of Agriculture and Forestry, Forest Tree Seeds and Tree Breeding Research Institute Directorate, Ankara, Turkey)*
15:15 – 15:45	Genome Editing in Plants: Advances and Applications in Agriculture (Invited lecture) *Invited Speaker: Mehmet Cengiz Baloglu, online (Kastamonu University, Turkey)*	15:10 – 15:30	Application of DNA barcoding for identification of different organisms within forest ecosystems *Invited Speaker: Nevenka Ćelepirović (Laboratory of molecular-genetic testing, Division of genetics, forest tree breeding and seed science, Croatian Forest Research Institute, Jastrebarsko, Croatia)*
15:45 – 16:05	Some molecular, biochemical and nutritional aspects of human obesity - Case study from N. Macedonia (Invited lecture) *Invited Speaker: Zoran Popovski (Ss. Cyril and Methodius University, Faculty of Agriculture and Food Sciences, Department for biochemistry and genetic engineering, North Macedonia)*	15:30 – 15:50	Raising the progeny to fight back: from seed priming to transgenerational memory *Invited Speaker: Erna Karalija (University of Sarajevo, Faculty of Science, Sarajevo, Bosnia and Herzegovina)*
16:05 – 16:25	Liquid biopsies in cancer diagnosis monitoring and prognosis *Invited Speaker: Ines Stevic, online (Sysmex Inostics, Hamburg, Germany)*	15:50 - 16:10	Interaction of Douglas fir provenances in Bosnia and Herzegovina with the environment *Invited Speaker: Mirzeta Memišević Hodžić (University of Sarajevo, Faculty of Forestry, Sarajevo, Bosnia and Herzegovina)*
16:25 – 16:45	Discussion/ Coffee Break	16:10- 16.45	Discussion/ coffee break

16:45-17:00	Genetics of thermal stress tolerance in breeding animals *Short Talk: Husein Ohran (University of Sarajevo - Veterinary Faculty, Department of Physiology, Bosnia and Herzegovina)*	16:45 - 16:55	Identification of vitamin biosynthesis pathway in thermophilic Leptolyngbya sp. and effects of macronutrients manipulation on its growth *Short Talk: Mohd Noh Nur Izzati (Universiti Teknologi Malaysia, Faculty of Science, Department of Biosciences, Malaysia)*
17:00 - 17:15	Influence of the ACE2 gene polymorphism (rs2285666) on complete blood count *Short Talk: Neven Meseldzic (University of Sarajevo - Faculty of Pharmacy, Bosnia and Herzegovina)*	16:55 - 17:05	Terpene compounds and their pharmacological potential *Short Talk: Carev Ivana (Mediterranean Institute for Life Sciences, Split, Croatia)*
17:15 - 17:30	***Discussion***	17:05-17.15	***Discussion***

Day 3

Saturday, 30th May 2023

Parallel Sessions	*Session III - Molecular and precision medicine* Chairs: Adlija Čaušević, Tanja Dujić, Daria Ler	*Session IV - Molecular Biotechnology* Chairs: Lada Lukić Bilela, Jasmina Čakar, Filipe Natalio
09:00 – 09:45	**Plenary Lecture** Genomics as a basis for precision medicine *Plenary Speaker: Sonja Pavlović (Institute of Molecular Genetics and Genetic Engineering (IMGGE), University of Belgrade, Belgrade, Serbia)*	**Plenary Lecture** Lum[AI]: Neutrophil chemiluminescent fingerprint kinetics for etiological agent phylum triage in an emergency room setting *Plenary Speaker: Robert S. Marks (Ben-Gurion University of the Negev, Be'er Sheva, Israel)*
09:45 – 10:10	Precision medicine in type 2 diabetes *Invited Speaker: Sabina Semiz (College of Medicine and Health Sciences, Khalifa University, Abu Dhabi, United Arab Emirates)*	From a vision to new research established in the field of marine biotechnology *Invited Speaker: Ana Rotter (Marine Biology Station Piran, National Institute of Biology, Piran, Slovenia)*
10:10 – 10:35	Pharmacogenomics and pharmacotranscriptomics of acute leukemia in children: a path to personalized medicine *Invited Speaker: Branka Zukić (Institute of Molecular Genetics and Genetic Engineering (IMGGE), University of Belgrade, Belgrade, Serbia)*	Harnessing the power of enzymes: Innovative approaches for designing new materials *Invited Speaker: Filipe Natalio (Weizmann Institute of Science, Department of Plants and Environmental Science, Rehovot, Israel)*
10:35– 10:45	***Short Break***	***Short Break***
10:45 – 11:10	Pharmacogenomics of hematopoietic stem cell transplantation *Invited Speaker: Vid Mlakar*	Molecular basis of stress tolerance of wheat cultivars - How complex it might be?

	(CANSEARCH Research platform for pediatric oncology and hematology, University of Geneva, Geneva, Switzerland)	*Invited Speaker: Ariola Bacu, online (University of Tirana, Faculty of Natural Sciences, Department for Biotechnology, Tirana, Albania)*
11:10 – 11.35	Multiomics approaches uncovering epigenetic regulation of non-coding-loci Invited Speaker: Tijana Mitić, online (Center for Cardiovascular Science, The Queen's Medical Research Institute, Edinburgh BioQuarter, Edinburgh, Scotland)	Discovery of biocatalysts and the paths for their identification Invited Speaker: Inga Matijošyté, online (Sector of Applied Biocatalysis, Institute of Biotechnology, Life Sciences Center of Vilnius University, Lithuania)
11:35 – 12:00	Sponsored Symposium - Roche: Comprehensive genomic profiling: Taking precision medicine from vision to reality *Inga Marijanović (Department of Oncology, University Clinical Hospital of Mostar; School of Medicine, University of Mostar, Mostar, Bosnia and Herzegovina)*	***Discussion***
12:00 – 13:30	***Light Lunch and Poster Session (Sessions III and IV)***	***Light Lunch and Poster Session (Sessions III and IV)***
13:30 – 13:40	Overview of parallel clinical exome sequencing in diagnostics of rare diseases from a 2-year period *Short Talk: Rijad Konjhodžić (ALEA Genetic Center, Sarajevo, Bosnia and Herzegovina)*	Initial experiences with home-developed mitochondrial DNA software “Mitowizz” for clinical and forensic application *Short Talk: Nejira Handžić (ALEA Genetic Center, Sarajevo, Bosna and Hercegovina)*
13:40 – 13:50	*CDKAL1* variants and response to metformin in patients with type 2 diabetes *Short Talk: Selma Imamović Kadrić (University of Sarajevo-Faculty of Pharmacy, Sarajevo, Bosnia and Herzegovina)*	Effects of lyophilized leech saliva extract on in vitro cell migration and apoptotic/ necrotic cell death on the human breast cancer cell line (MDA-MB-231) *Short Talk: Ünal Kübranur (University of Gazi, Faculty of Medicine, Department of Medical Biochemistry, Ankara, Türkiye)*

13:50 – 14:00	Evaluation of gene expressions of ER stress markers ATF6, IRE1 and PERK in neutrophils during multiple sclerosis attack therapy *Short Talk: Canan Akçin (TOBB University of Economics and Technology, Department of Biomedical Engineering, Ankara, Turkey)*	Diagnostic testing for SARS-CoV-2 by Real Time RT-PCR *ShortTalk: Danijela Blagojević (Hospital Sveti Vračevi, Bijeljina, Bosnia and Herzegovina)*
14:00 – 14:10	Apoptotic pathway of human colorectal carcinoma can be regulated via scorpion venom *Short Talk: Serdar Karakurt (Selcuk University, Faculty of Science, Department of Biochemistry, Konya, Turkey)*	
14:10 – 14:40	**Closing Lecture** Molecular anthropology - How to predict past? Invited Speaker: Damir Marjanović (International Burch University, Sarajevo, Bosnia and Herzegovina; Laboratory for Molecular Anthropology, Center for Applied Bioanthropology, Institute for Anthropological Research, Zagreb, Croatia)	
14:40 – 15:00	**FEBS Open Bio Poster Prize/ Closing Ceremony**	


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Plenary lectures
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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Plenary lecture

FROM BENCH TO BEDSIDE: TRANSLATING SCIENCE FROM THE LAB TO CLINICAL PRACTICE

Primorac Dragan[1,2,3,4,5,6,7,8,9,10]

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Translational medicine, where research results from the laboratory will be directly used to develop new ways to diagnose and treat patients will change the medicine we practice today. On the other hand, personalized medicine is an emerging practice that uses an individual's multi-OMICS profile to provide disease prevention and tailor-made treatment. Pharmacogenomics (PGx) is one of the core elements of personalized medicine. PGx information reduces the likelihood of adverse drug reactions and optimizes therapeutic efficacy. At St. Catherine Hospital, panel-based testing for single nucleotide polymorphisms (SNPs) was implemented for 27 genes (111 polymorphisms) known to influence the pharmacologic properties of over 300 drugs. Recently, with our partners, we introduced a comprehensive whole genome sequencing (WGS) approach that provides a comprehensive view of a person's entire genome, allowing for the detection of genetic variations, including single nucleotide polymorphisms (SNPs), insertions and deletions (InDels), copy number variations (CNVs), and structural variants. By introducing WGS in routine clinical practice, we aim to determine the risk in the general population of developing hereditary forms of cancer, obesity, endocrinological, cardiovascular, and other diseases. Simultaneously, in collaboration with Croatian Football Federation, St. Catherine Hospital launched the "Croatian model of preventing sudden cardiac death in athletes by analyzing targeted genes and associated mutations associated with conditions that can lead to sudden cardiac death in athletes. Currently, using our NGS panel, it is possible to determine gene variants in 294 genes associated with sudden cardiac death. Such multi-gene testing is the only way to detect individuals at risk for sudden cardiac death in asymptomatic patients. Yet, our group was among the first to apply micro-fragmented autologous adipose tissue containing mesenchymal stromal cells (AdMSCs) into the joints of osteoarthritis patients or in the joints of patients with damaged cartilage. The results of our studies indicate that the use of autologous and micro-fragmented adipose tissue in patients with knee OA (measured by dGEMRIC MRI) increased glycosaminoglycan (GAG) content in hyaline cartilage, which is in line with observed clinical improvements. However, MSC, with its immunomodulatory, antiapoptotic, angiogenic, anti-bacterial, and anti-apoptotic effects, can be a valuable therapeutic agent for other diseases. During my lecture, I will discuss the potential of MSCs in treating severe pneumonia

since, during the COVID-19 pandemic, we have shown that compassionate MSC allogenic treatment was not associated with any side effects, was well tolerated, and affected ARDS regression.

Keywords: Translational medicine, Personalized medicine, Pharmacogenomics, Whole Genome Sequencing, Mesenchymal Stromal Cells

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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Honorary lecture

THE MATTER OF LIFE AND ITS CORROSION IN THE COURSE OF AGING AND DISEASES

Radman Miroslav[1,2]

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[2] *University R. Descartes – Paris5 Medical School, 75014 Paris, France*

A general overview will be presented on the construction and maintenance of key biological macromolecules: (i) proteins, which carry out all biological functions (either directly or by synthesizing themselves and all other macromolecules and small metabolites) and (ii) DNA (genes) as biological information containing the construction plans for the synthesis of proteins and of RNA molecules that link biological information to function. Proteins and nucleic acids (DNA and RNA) are susceptible to diverse kinds of corrosion and damage that introduce noise in the biological systems as the root cause of aging and diseases. Oxidative phosphorylation and glycolysis provide energy for biological functions, but produce the leakage of uncoupled electrons that generate oxygen free radicals (ROS). ROS cause the corrosion of biological materials, but life has evolved a plethora of mechanisms to fight entropy and prevent, repair and finally eliminate unrepaired biomolecules. These protective mechanisms are also carried out by proteins and when they fail - because of protein damage - then aging and diseases ensue. A review of research in MedILS on chemistry and biology of aging and diseases will be presented.

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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Plenary lecture

WHY AND HOW SHOULD YOU DEVELOP AND IMPROVE YOUR EDUCATOR SKILLS?: TIPS FOR BOTH JUNIOR & SENIOR SCIENTISTS

Sağın Ferhan

Ege University Medical School, Izmir, Türkiye

As an educator, you have the power to inspire and shape the minds of the next generation of scientists. But to be truly effective, you must continually develop and improve your skills. Effective teaching requires more than just knowledge of the subject matter; it requires the ability to communicate that knowledge to others in a way that is engaging, informative, and memorable. For junior scientists, developing your educator skills can help you to effectively communicate your research findings to a wider audience, whether it be through classroom instruction, conference presentations, or public outreach. We will discuss ways to build confidence in your ability to teach, develop effective teaching experiences in different settings, and readjust mind-sets for shaping one's career also as an educator. For senior scientists, improving your educator skills can help you to stay current with the latest teaching techniques and technologies, and enable you to mentor the next generation of scientists. We will discuss strategies on how to stay updated in the fast changing teaching and learning world, how to create a positive learning environment, promoting diversity and inclusion, and how to use your experience and expertise to guide the next generation of scientists. This talk is aimed to raise some awareness in young researchers and also in senior educators about the latest scientific research in teaching & learning with the hope that participants will continue to follow this interesting area besides their research field. Whether you're just starting out or have years of experience under your belt, investing in your educator skills is a powerful way to make a lasting impact on the future of science. So join us for this exciting and inspiring talk on how to develop and improve your educator skills!

Keywords: education, PhD training, teaching skills, learning and teaching, effective communication

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Session 1 – Plenary lecture

FUNCTIONAL DIVERSITY OF CYTOCHROME C IN ITS JOURNEY FROM MITOCHONDRIA TO NUCLEUS

De la Rosa Miguel A.

Institute for Chemical Research, cicCartuja, University of Seville-CSIC, Seville, Spain

It was once assumed that the biological function of cytochrome c (Cc) was confined to mitochondria and restricted to its ability to connect complexes III and IV in the respiratory electron transport chain. Such a canonical function of the hemeprotein was however questioned with the discovery that Cc is released from mitochondria to cytoplasm upon treatment of cells with apoptotic agents. In the cytoplasm, Cc interacts with the apoptosis-activating factor 1 (Apaf-1), triggering i) apoptosome assembly, ii) subsequent activation of caspases, and iii) controlled cell dismantlement. Beyond cytosolic Cc being a key element in apoptosis, several findings have led in the last few years to the emergence of Cc as a pleiotropic mitochondrial factor that migrates to the cell nucleus upon DNA damage both in mammals and plants. Mitochondrial Cc in the nucleus targets histone chaperones that might share common structural—and probably functional—features. In this lecture, an overview of the molecular basis for Cc signaling in the mitochondria, cytoplasm and nucleus will be addressed, with emphasis on the structure-to-function relationships of nucleolar targets, namely nucleophosmin (NPM) and SET/template-activating factor (TAF)-Iβ. The NPM-Cc nucleolar interaction, in particular, will be extended to a general mechanism for DNA damage in which the lysine-rich regions of Cc—rather than the canonical, arginine-rich stretches of membrane-less organelle components—control the trafficking and availability of nucleolar proteins.

Keywords: cytochrome c, DNA damage, liquid-liquid phase separation, mitochondria, nucleolus, nucleus

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Session 2 – Plenary lecture

MICROBIOME IN POST-GENOMIC ERA

Gazouli Maria

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The human genome has been referred to as the blueprint of human biology. However, an essential but largely unnoticed overlay to that blueprint is the human microbiome, which is composed of those micro-organisms that live in and on our bodies. The human microbiome is a basic source of genetic diversity, a modifier of disease, an important component of immunity, and a key entity that influences metabolism and modulates drug function. New genome technologies enable both sequencing of the human genome and sequence-based cataloging of microbial communities inhabiting human organs (ie gut, skin etc). The study of them has revealed bidirectional relationships between the microbiome and the genome. Thus the recent studies are suggesting a new important role of the microbiome in human health and disease.

Keywords: microbiome, genetics

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Session 3 – Plenary lecture

GENOMICS AS A BASIS FOR PRECISION MEDICINE

Pavlović Sonja

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Although medicine always aimed to be personalized, true implementation of personalized medicine in health care practice has started recently. Fascinating progress of molecular genetics has strongly contributed to this great achievement of modern medicine. Personalized medicine, also known as genome-based medicine and precision medicine, uses the knowledge of molecular basis of the disease in order to individualize treatment for each patient. Development of novel powerful high-throughput technologies has enabled better insight into "oms" landscape of many diseases, resulting in application of precision medicine approaches in their treatment. There are four cornerstones of modern precision medicine: "omics"-based diagnostics, pharmacogenomics, specific molecular targeted, gene and cellular therapy and predictive genetics. One of the most important successes of precision medicine is a discovery of novel diagnostic molecular markers. Furthermore, numerous newly discovered molecular markers have contributed to more precise classification of patients in distinct prognostic groups, leading to specific, more successful treatment protocols. Development of pharmacogenomics platforms and application of molecular–targeted therapy have led to the individualization of therapy, tailored to genetic profile of a disease in each patient. The development of gene therapies which can cure or prevent a disease by targeting disease-causing molecular defect has confirmed that the precision medicine has responded successfully to a great challenge. Additionally, cellular and tissue therapies have opened new possibilities for personalized treatment of many patients. Growing knowledge in predictive genetics leads to the preventive medicine, the most important goal of modern medicine. There is no doubt that we are getting closer to full implementation of precision medicine in every day clinical practice.

Keywords: genomics, gene therapy, molecular diagnosis, molecular targeted therapy, precision medicine, pharmacogenomics, stem cell therapy

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Session 3 – Plenary lecture

Molecular Anthropology – How to Predict the Past!?

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Molecular anthropology represents one of the most innovative, dynamic and scientifically promising branches of anthropology. Molecular anthropologist deals with the reconstruction of the history of the human species, the process of expansion and settlement of certain continents, regions, but also the entire Planet, the analysis of ancient human DNA from found skeletal remains and the discovery of the role of genetic diversity in the process of speciation of the anatomically modern human species. Lineage markers (Y chromosome and mtDNA) are still mostly in the main focus of these studies. The paternally inherited non-recombining portion of the Y chromosome (NRY) is the material of choice when it comes to tracing the paternal lineage of populations. The potential applications of the NRY in human population studies are numerous and it is, therefore, extensively used in the studies of human origin, population history, sex-biased admixture, male-female differences in migration, and medical and clinical studies. The two most important classes of Y-chromosomal markers deployed in such studies are short tandem repeats (Y-STRs) and single nucleotide polymorphisms (Y-SNPs), and as these markers are transmitted directly by paternal lineage without recombination, they are highly sensitive to genetic drift and allow for a very informative haplotype construction. A single Y haplogroup represents a group or a family of Y chromosomes related by descent or ancestry, and each such haplogroup is determined by a specific set of Y-SNPs, which makes them extremely important when it comes to better understanding of past migrations and demographic processes that shaped modern populations). The main aim of this presentation is to update the information about regional Y-chromosome diversity by using additional Y-chromosomal markers and to provide updated genetic scenario for the populating of this part of Europe.

Keywords: Y chromosome, SNP, STR, genetic diversity

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Session 4 – Plenary lecture

LUM^{AI}, NEUTROPHIL CHEMILUMINESCENT FINGERPRINT KINETICS FOR ETIOLOGICAL AGENT PHYLUM TRIAGE IN AN EMERGENCY ROOM SETTING

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The major obstacle in prescribing a timely and appropriate antimicrobial treatment is not knowing whether the patient has an infection, where its focus is, and which are its etiological agents. The treating clinician is faced with a potential overtreatment or prospect of failing to identify potentially life-threatening bacteremia. Stakeholders have expressed a need for a rapid and simple point-of-care triage diagnostics system to rapidly determine whether the patient's infection is caused by a bacterium, virus, fungus, protozoan, or a helminth. The premise of our invention is based on the hypothesis that when phagocytes meet their new invading pathogen enemy, they will recognize their basic external chemical structure and will prepare themselves to swallow the offending etiological agent to destroy it. In so doing they prepare a tailored set of reactive oxygen species (ROS) to destroy the engulfed pathogen most efficiently. While communicating with their fellow peers in the bloodstream via chemical messages they can send an 'accurate' message of the type of pathogen they are about to encounter which make them 'primed'. Our test uses, our bodies' first line of defense, living host pathogen-primed phagocytes (mainly neutrophils) that circulate in the bloodstream as biomarkers of the nature of the invasive etiological agent. When these primed cells are triggered to phagocytose by our immunoassay, they will reveal their diagnostic information that we will 'visualize' by the intermediary of a luminescence 'fingerprint' specific to either microbial phyla or etiological agents! The release of ROS molecules is associated with the emission of light, generated from reactive species, which can be amplified and detected as luminol-dependent chemiluminescence resulting in measurable light emission kinetics. So far, from our research findings the answer is yes! We have reached a 91% accuracy to differentiate between bacterial and viral infections.

Keywords: infectious diseases, neutrophils, triage, chemiluminescence

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Session 5 – Plenary lecture

MOLECULAR BASED SELECTION METHODS AND GENETIC DIVERSITY IN FORESTRY

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It is called "plant breeding" to obtain new plants with desired characteristics through heredity by making use of the variations in the genetic structure and natural distribution of plants. In recent years, significant developments in advanced techniques in biotechnology and genetic engineering have brought a different dimension to selection methods targeting plant breeding, apart from classical crosses. Contrary to agricultural plants with hundreds of years or even a thousand years of breeding history, the breeding history of forest trees is very new. The difficulty in meeting the demand for wood raw materials for the increasing need for construction materials, paper and fuel, and the destruction and decrease in natural forests have necessitated the domestication of forest trees. The breeding of forest trees and shrubs is quite difficult compared to agricultural plants. The main reason for this is their long-life cycle. Long juvenile period, that is, late flowering and late start of seed production, physical size, need for large areas for trials and long-term observations make forest tree breeding difficult. The long period of forest tree breeding needs to be shortened with various applications. In this case, molecular methods come to the fore and offer some ways to shorten this long breeding period. With the selection made with the help of molecular methods, besides time, space and labor force are also saved. Molecular techniques are also used as a reliable way to identify and protect gene sources more accurately. In the development of molecular methods ne inventions genomics, proteomics etc. are very important steps on the development of the molecular breeding. In recent years, many plant species have been included among the organisms whose genomes have been completed. Some forest trees are among them. Parallel to this, knowledge of molecular markers has also increased and their use in some forest tree breeding is expected to become more widespread.

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Session I -
Basic and applied biochemistry
Genetics & Applications

Session 1 – Oral presentation *S1-01*

GALECTIN-3 IN PATHOGENESIS, DIAGNOSIS AND OUTCOME PREDICTION OF COVID-19

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One of the crucial events in Covid-19 disease is SARS-CoV-2 infection of lung-resident macrophages, which consequently activate inflammasomes, release pro-inflammatory cytokines, and undergo pyroptosis, thus significantly contributing hyperinflammation in the lungs. M1 macrophages are the main source of galectin-3 (Gal-3), a ß-galactoside binding lectin involved in numerous pro-inflammatory processes. It is known to promote activation of innate immune cells, e.g. neutrophil infiltration and the release of pro-inflammatory cytokines, which in case of SARS-CoV-2 infection may result in acute respiratory distress syndrome (ARDS), multi-organ failure and death. In addition, M2 macrophages secrete a substantial quantity of Gal-3, which has been also recognised as a powerful pro-fibrogenic molecule, thus in parallel promoting pulmonary fibrosis. Given to known the Gal-3 role in inflammation and fibrosis, key events that lead to the development of severe COVID-19 and its long-term consequences, we aimed to estimate the value of serum Gal-3 levels in SARS-CoV-2 positive individuals for prediction of a severe COVID-19 outcomes (invasive mechanical ventilation and/or death). For that purpose, serum samples were collected from SARS-CoV-2 positive patients (i) with mild symptoms who were discharged immediately after examination (N=122), and (ii) who were hospitalized (N=130). Gal-3 levels discriminated well between these two groups ($P<0.001$) and correlated with classical markers of COVID-19 severity (CRP, leukocyte and neutrophils count, neutrophil to lymphocyte ratio (NLR)). The Gal-3 concentration of 7.59 ng/mL was identified as a cut-off value for predicting hospitalization (sensitivity of 73.1%; specificity of 69.9%) whereas for death it was 10,19 ng/mL (sensitivity of 63,0% and specificity of 60,0%), suggesting its usefulness in the Covid-19 outcome prediction. Furthermore, combination of Gal-3 and aforementioned markers had significant high ability to predict severe outcomes [AUC 0.896 (95% CI: 0.852-0.931)] as well as death [AUC 0.746 (95% CI: 0.661-0.819)] of SARS-CoV-2 infection.

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Session 1 – Oral presentation *S1-02*

THE AQUAPORINS WATER CHANNELS AND PLEIOTROPICALLY BEYOND – AN OVERVIEW

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Cell homeostasis relies on both the integrity and permeability of plasma membrane to water and electrolytes. Because of its amphipathic nature, additional mechanisms to simple diffusion are required in order for water and solutes to pass through the cell membrane. This is ensured by Aquaporins (AQPs) ubiquitous transmembrane water proteins that allow the transport of water but also some small solutes across cell membranes down a concentration gradient. Aquaporins are expressed in all kingdoms. In mammals, there are 13 AQPs, at least one of which is found in every organ system, having characteristic distribution across different cell types, which is species-specific. Aquaporins are subdivided according to their permeability into: Classical AQPs (AQP0, AQP1, AQP2, AQP4, AQP5, AQP6 and AQP8) permeable to water; Aquaglyceroporins (AQP3, AQP7,AQP9 and AQP10) permeable to small solutes, such glycerol, urea, ammonia in addition to water; and Unorthodox AQPs (AQP11 and AQP12) localized in the membranes of intracellular organelles presenting sequence variations to the other groups of AQPs. Structurally, the functional AQPs channels are formed of homotetramers within the plasma membrane. Each homotetramer consists of four water channels. Each water channel is functionally independent. The AQP monomers are comprised of six membrane-spanning helices. The amino- and carboxy-termini of APQs are both intracellular. Two opposing, shorter helices do not span the entire membrane forming the pore itself. These half helices contain the family's signature i.e. a triplet amino acid NPA (Asn-Pro-Ala) motif. Many functions for AQPs have been reported in health and disease. AQP expression is linked to numerous pathologies including tumor metastasis, obesity, wound healing, fluid dysregulation, metabolic dysregulation and autoimmune syndromes.

Keywords: aquaporins, water channel, transmembrane protein

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Session 1 – Oral presentation *S1-03*

HIGH-CONTENT SCREENING AND MULTI-OMICS AS ADVANCED TOOLS IN TOXICOLOGY OF NANOPARTICLES

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In (nano)particle safety assessment, cell-based assays offer the possibility to provide valuable insights into the cellular responses to exposure. Induced cellular responses can be cell-specific as well as organelle-specific and very often involve complex biological mechanisms of action (MoAs). Cell Painting is high-content phenotypic profiling assay that reveals impact of perturbation(s) on eight broadly relevant cell compartments, including nucleus (DNA), actin/Golgi apparatus/plasma membrane (AGP), mitochondria (Mito), endoplasmic reticulum (ER), and RNA/nucleoli (RNA). To gain knowledge about the cell compartments/organelles and putative biological pathways affected by prototypical nanoparticles (AuNPs) and nanoparticles found in the occupational setting (emissions in 3D printing industry), we have applied Cell Painting assay and exposed human osteosarcoma U2-OS and lung epithelial A549 cells to different nanoparticle concentrations. Afterwards, cells were stained, fixed, and imaged on a high-throughput imaging platform. The image feature extraction workflow for Cell Painting was performed by a CellProfiler image-processing software, that yields in extraction of ~3200 cellular phenotypic features/descriptors for each cell. Obtained results disclosed strong impact of exposure on the cell cytoskeleton (AGP), indicative of nanoparticle internalization and the rearrangement of the cytoskeletal protein actin. In addition, nanoparticles affected every observed cell compartment to different extent, especially texture and intensity-related phenotypic features. Importantly, cell phenotypic alterations were more pronounced by decreasing the nanoparticle size. To the best of our knowledge, this is the first application of Cell Painting in the field of nanoparticle toxicology. Integrating high-content screening to study structure-specific profiles at single-cell resolution, supported with multi-omics (metabolomics/lipidomics, transcriptomics) and machine learning tools, offers great opportunities in the field of New Approach Methodologies (NAMs) to improve current nanosafety assessment practices.

Keywords: heat stroke, experimental, biomarkers, cTnI, hsp70

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Session 1 – Oral presentation *S1-04*

DETERMINATION OF THE MECHANISM AND CAUSE OF DEATH IN HEAT STROKE: FOCUS ON THE CORRELATION OF TROPONIN I AND 70 KDA HEAT SHOCK PROTEIN

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There is intensive research related to the forensic importance of biomarkers that would be the gold standard for postmortem damage to cardiomyocytes and the mechanism of the resulting damage. The aim of the research was to determine the forensic-medical significance of serum levels of biomarkers as detectors of terminal hyperthermic damage to the myocardium. The rats were divided into groups: control group (KG) exposed to 37°C water temperature, group 41-A (antemortem) group exposed to 41°C water temperature in duration of exposure with 20 minutes, G41-P (postmortem) group exposed to 41°C water temperature until death, G44-A (antemortem) group exposed to 44°C water temperature in duration of exposure with 20 minutes, G44-P (postmortem) group exposed to 44°C water temperature with exposure time until death. A probe was used to measure the core temperature of rats, and the core temperature was read on a thermometer.The concentration of cardiac TnI and Hsp70 was determined in serum by immunochemical enzyme-labeled immunoabsorption method. A positive correlation was found between the temperature measured at the time of death and the serum values of cardiac troponin I ($p=0.02$), in G41, and Hsp70 values did not significantly correlate with the body temperature of rats in this group, $p>0.005$. A positive correlation was significant between the concentration of Hsp 70 and the body temperature of rats in the group of rats with a fatal outcome was determined, $p=0.03$. hanges in the concentration of cTnI and Hsp70 in rat serum may indicate hyperthermic damage to the myocardium in the Wistar rat model of heat stroke.

Keywords: heat stroke, experimental, biomarkers, cTnI, hsp70

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Session 1 – Oral presentation *S1-05*

THE C-REACTIVE PROTEIN/ALBUMIN RATIO AND GLASGOW PROGNOSTIC SCORE AS INDICATORS OF DISEASE ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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The aim of this study was to evaluate the C-reactive protein/albumin ratio (CAR) and Glasgow prognostic score (GPS) as indicators of disease activity in patients with inflammatory bowel disease (IBD). In the present cross-sectional study, 119 IBD patients were included, of which 66 with ulcerative colitis (UC) and 53 with Crohn's disease (CD). Diagnosis of IBD was previously established by anamnestic data, laboratory tests, endoscopic examination with histopathological findings and radiological examinations. Based on the disease activity index, UC and CD patients were divided into two subgroups: active and inactive phase of the disease. The serum C-reactive protein (CRP) and albumin (ALB) were determined by standard laboratory methods. We calculated inflammatory indices comprising the CAR and GPS. In differentiation between active and inactive UC and CD patients, receiver operating characteristic (ROC) curves and their corresponding areas under the curve (AUC) were used. The values of serum CRP level, CAR and GPS were significantly higher ($p=0.001$), while serum albumin level was significantly lower ($p=0.001$) in active than in inactive UC and CD patients. In differentiation between active and inactive UC patients, AUC was for GPS 0.819, for CAR 0.811, for CRP 0.794 and for albumin 0.790. For discriminating active from inactive CD patients AUC for albumin was 0.850, for CAR 0.809, GPS 0.794 and for CRP 0.776. GPS and CAR were the most accurate indicators in differentiation of patients with active from patients with inactive UC. For differentiation between patients with active and inactive CD, CAR had good overall diagnostic accuracy while GPS had fair overall diagnostic accuracy.

Keywords: C-reactive protein/albumin ratio, Glasgow prognostic score, inflammatory bowel disease, ulcerative colitis, Crohn's disease

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Session 1 – Oral presentation *S1-06*

EFFECTS OF LYOPHILIZED LEECH SALIVA EXTRACT ON *IN VITRO* CELL MIGRATION AND APOPTOTIC/ NECROTIC CELL DEATH ON THE HUMAN BREAST CANCER CELL LINE (MDA-MB-231)

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Medical leech therapy/ Hirudotherapy, which is in high demand in many countries, especially in Turkiye, China, India and Iran, is a traditional and complementary treatment method with a centuries-old history. Medical leech therapy contributes to the treatment of diseases by showing anti-inflammatory, antimicrobial, analgesic, vasodilator and/or anesthetic effects. The benefits obtained from the leech therapy are mainly due to the various bioactive substances found in their saliva, which secreted into the host's blood stream during blood sucking. In this study, the effects of lyophilized leech saliva extract on the cell viability, cell migration, apoptosis, necrosis and possible mRNA expression responsible for these effects were evaluated under *in vitro* conditions. Leech saliva was obtained from sterile medicinal leeches of *Hirudo verbana* genus and then this saliva was lyophilized. The total protein concentration from this saliva was determined and then the dose amounts (800 µg/ml, 400 µg/ml, 200 µg/ml and 100 µg/ml) were adjusted by serial dilution. In this study, the Human Breast Cancer cell line (MDA-MB-231) and Human Umbilical Cord Vein Endothelial Cell (HUVEC-CRL-1730) line were used. An MTT assay, cell migration assay, PCR and flow cytometry analysis were performed. The results indicated that lyophilized leech saliva extract can reduce cell viability, cell migration and induce necrosis along with apoptosis in this cancer cell line. In this study, it was found that the lyophilized leech saliva extract applied at different doses had significant effects on the MDA-MB-231. This study investigated for the first time that lyophilized leech saliva extract has the potential effect in the MDA-MB-231. LLSE applied at different doses had significant and different effects on the MDA-MB-231 cancerous-cell line and HUVEC healthy-cell line. The results indicated that LLSE dose-dependently decreases cell proliferation and migration in the MDA-MB-231 cell line.

Keywords: apoptosis, cell migration, human breast cancer cell line (MDA-MB-231), leech saliva, necrosis

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Session 1 – Oral presentation *S1-07*

EVALUATION OF SERUM PENTRAXIN-3 LEVELS IN PATIENTS WITH MIGRAINE

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Systemic inflammation is thought to influence neurogenic inflammation in many neurological diseases. Neurogenic inflammation is one of the most important components of migraine pathophysiology. Pentraxin-3 is a novel acute-phase protein recognized as an inflammatory response of the body. In this study, it was aimed to investigate the levels of pentraxin-3 in patients with migraine. 45 patients with migraine and 39 healthy controls were included in the study. Peripheric blood samples were taken from patients and control group. After the samples were centrifuged and the levels of pentraxin-3 were measured from the acquired serums by enzyme-linked immunosorbent assay (ELISA). Statistical Package for the Social Sciences (SPSS, version 18.0, Chicago, IL, USA) statistics program was used for evaluating the data. Mann-Whitney U test was performed on non-normally distributed data and was reflected as median (minimum value-maximum value). $p \leq 0.05$ was accepted as statistically significant between groups. 26 patients were male and 19 patients were female. Patient's average of age was 49.36±11.92 years. In healthy control group, 21 person male and 18 person were female. The average age of healthy control was 53.3±9.93 years. In the comparison between migraine patients and the control group, serum Pentraxin-3 levels were found to be statistically significantly higher in migraine patients (11.10(2.09-15.95)) ng/mL) than in the control group (9.65 (0.97-12.34)) ng/mL). Pentraxin-3 plays an important role in activation of innate immunity and in the regulation of inflammatory reactions. Results from this study suggest that Pentraxin-3 level may be a novel biochemical marker for migraine. Further studies are needed to confirm the pathophysiological role of pentraxin-3 in migraine.

Keywords: migraine, pentraxin-3, inflamation

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Session 1 – Oral presentation *S1-08*

TERPENE COMPOUNDS AND THEIR PHARMACOLOGICAL POTENTIAL

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The *Centaurea* genus, which belongs to the Asteraceae family, is commonly known as the knapweed and includes over 700 species. Terpenes are large group of chemical compounds, identified in various *Centaurea* species, and are known to have several biological activities. The mechanism of action of terpenes varies depending on the specific compound and its target in the body. However, terpenes are known to have diverse biological activities due to their ability to interact with various molecular targets. They can inhibit the expression of pro-inflammatory mediators such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) through various pathways, including inhibition of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling. Terpenes have also been shown to have antifungal and antimicrobial properties by disrupting the cell membrane of microorganisms, inhibiting their growth and replication. Some terpenes have been shown to have anti-tumor effects by interacting with the cannabinoid receptors CB2 and reducing the growth of cancer cells. Terpenes exert their biological effects through various mechanisms depending on the specific compound and its target. Their ability to interact with different molecular targets makes them promising therapeutic candidates for a variety of diseases. These compounds have been studied for their potential pharmacological properties, including anti-inflammatory, analgesic, and antitumor effects.

Keywords: *Centaurea*, terpenes, pharmacology

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Session 1 – Poster presentation *S1-09*

PROGNOSTIC VALUES OF BIOCHEMICAL AND HEMATOLOGICAL PARAMETRES IN PATIENTS WHO DIED OF THE CORONAVIRUS DISEASE

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Consequences of the SARS-Cov-2 virus infection are still in focus of many studies worldwide including causes of lethal outcomes. Until August 2022 the Federation of Bosnia and Herzegovina registered 9056 death cases, while the number of recovered patients was 248742. The aim of the study was to analyse values of basic biochemical and haematological parameters in SARS-Cov-2 patients with lethal outcome. Examined parameters were correlated with age and sex of the SARS-Cov-2 patients with the lethal outcome. The lethal outcome was found more frequently in the female population. Out of the examined parameters in women, haemoglobin, MCV and MCH were significantly lower when compared with men. Data from the literature show that the severity of the disease in patients with the lethal outcome correlates with age, which was confirmed by our research too. The average age of the examined patients was 74 years. A negative correlation of thrombocytes was noted, whose value decreased with older age. Urea and creatinine show a high connection and correlation in the same way as the AST, ALT and LDH, and can be used as prognostic biomarkers in COVID-19 patients.

Keywords: COVID-19, biochemical parameters, hematological parameters, age, death outcome

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Session 1 - Poster presentation *S1-10*

SERUM FIBRINOGEN-TO-ALBUMIN RATIO INDEX IN EVALUATION OF INFLAMMATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Rheumatoid arthritis (RA) is a chronic, inflammatory disease, associated with elevation in acute-phase response mediators. Fibrinogen-to-Albumin-Ratio Index (FARI) is novel, easily measurable inflammatory index whose role in evaluating the inflammation status in RA patients is still unknown. The aim of this study was to assess value of FARI in patients with RA and analyze its association with parameters of inflammation. The study included 96 patients with RA and 34 apparently healthy volunteers (control group). RA patients were assigned into two groups based on the C-reactive protein (CRP) concentration: RA patients with CRP < 5.0 mg/L (n=36) and RA patients with CRP ≥ 5.0 mg/L (n=60). All RA patients fulfilled the American College of Rheumatology criteria for RA. FARI was calculated by the equation: Fibrinogen/Albumin. All laboratory parameters were determined by standard laboratory methods. The differences between the groups were analyzed by the Mann-Whitney U test and Kruskal-Wallis test. Coefficients of correlation were determined by Spearman's test. A significant difference ($p<0.001$) in FARI was found between RA patients and healthy controls. FARI value in the CRP ≥ 5.0 mg/L group was significantly higher compared to the CRP < 5.0 mg/L group ($p<0.001$) and the control group ($p<0.001$). Significant difference in FARI was observed between the CRP < 5.0 mg/L group and controls ($p=0.005$). Statistically significant positive correlations were obtained between FARI: and CRP (rho=0.538, $p<0.001$), and erythrocyte sedimentation rate (ESR) (rho=0.516; $p<0.001$) in RA patients. FARI values were significantly associated with ESR (rho=0.416; $p=0.012$) in the CRP < 5.0 mg/L group, and with ESR (rho=0.393; $p=0.003$) and CRP (rho=0.223; $p=0.03$) in CRP ≥ 5.0 mg/L group. The obtained results suggest that the FARI closely interconnect with inflammatory biomarkers and probably may serve as indicator in the assessment of inflammation in RA. Larger prospective multicenter studies are required.

Keywords: rheumatoid arthritis, fibrinogen, fibrinogen-to-albumin ratio index, inflammation

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Session 1 – Poster presentation *S1-11*

OXIME BLOT: A NOVEL METHOD FOR RELIABLE AND SENSITIVE DETECTION OF CARBONYLATED PROTEINS IN DIVERSE BIOLOGICAL SYSTEMS

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Oxidative stress and the ensuing oxidative protein damage occur in various biological processes and diseases. The carbonyl group on amino acid side chains is the most widely used protein oxidation biomarker. Carbonyl groups are commonly detected indirectly, through their reaction with 2,4-dinitrophenylhydrazine (DNPH) under low pH conditions and further labeling with an anti-DNP antibody. However, the DNPH immunoblotting method lacks protocol standardization, exhibits technical bias, and has low reliability. To overcome these shortcomings, we have developed a new blotting method in which the carbonyl group reacts with the biotin-aminooxy probe to form a chemically stable oxime bond. The reaction speed and the extent of the carbonyl group derivatization are increased by a p-phenylenediamine (pPDA) catalyst under neutral pH conditions. This protocol improvement is crucial because it ensures that the carbonyl derivatization step reaches a reaction plateau and increases the sensitivity and robustness of protein carbonyl detection. Furthermore, derivatization under pH-neutral conditions ensures a good SDS-PAGE protein migration pattern and minimizes protein loss while being compatible with protein immunoprecipitation. This work describes the new Oxime blot method and demonstrates its use in the detection of protein carbonylation in complex matrices from diverse biological samples.

Keywords: oxidative stress, carbonylated proteins, Western blot, 2,4 dinitrophenylhydrazine (DNPH), age-related diseases, alpha-synuclein, biotin-aminooxy

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Session 1 – Poster presentation *S1-12*

BIOLOGICAL THERAPY IN TREATMENT INFLAMMATORY BOWEL DISEASE

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When we speak of inflammatory bowel diseases we usually refer to patients who either have Crohn's disease or ulcerative colitis. Both these conditions can cause inflammation of the colon and rectum with similar symptoms. Crohn's disease is a chronic inflammation of the intestinal wall. Ulcerative colitis is a long-term condition where the colon and rectum become inflamed, small ulcers can develop on the colon's lining, causing high temperatures and stomach cramps. Medical drugs used for Crohn's disease and ulcerative colitis are adalimumab and infliximab which stabile concentration is reached 14. weeks after therapy start. During treatment, some patients can develop antibodies against adalimumab/infliximab. Subjects included in the study were patients who were treated in UCH Mostar or were referred to DLD from the Health Centers, with the signed informed consent. The study included 48 respondents. For the quantitative determination of adalimumab/ infliximab and anti-adalimumab/anti-infliximab concentration, we used enzyme linked immunoassay (ELISA). For the normality of data distribution, the Kolmogorov-Smirnov test was used. Due to the abnormal distribution of data, the Mann Whitney statistical test determined the median concentration of drugs in patients suffering from Crohn's disease, 5.6 (0.2-15.0) µg/L, and in patients with ulcerative colitis, the median was 5.3770 (0.8000-12.9440) µg/L and P=0,884. Reference range for antibodies of adulimumab/infliximab is <2.5 ng/L. In our study 4/24 patients with Crohn's disease and 5/24 patients with ulcerative colitis developed drug antibodies. There was no significant statistical difference in drug concentration between patients with Crohn's disease and ulcerative colitis. In our study, 9/48 patients developed antibodies. In future, it is necessary to include a larger number of respondents and maybe do the pharmacogenetic profile for patients who developed antibodies.

Keywords: Crohn's disease, ulcerative colitis, adalimumab, infliximab, antibodies

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Session 1 – Poster presentation *S1-13*

MORPHOLOGICAL CHANGES ON LUNG AND BRAIN CAUSED BY HYPERTHERMIA - PILOT STUDY OF WISTAR RAT

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Studies on biopsy material show dilatation of glomerular capillaries, bleeding into the interstitium and vascular path, in small and large vessels. The aim of the pilot study was to observe the appearance and occurrence of morphological characteristics on lung and brain that were exposed to long-term effects of hyperthermia. A sample of 7 rats was exposed to a water temperature of 41 °C, which is defined in the literature as "heat stroke temperature", both sexes, weighing 250 to 300 g were used. Tissue samples, obtained by dissection of rats, were fixed in 10% buffered neutral formalin, at room temperature, then incorporated into paraffin blocks, cut at 4-5 microns, mounted and stained with standard hematoxylin-eosin (HE) method. In order to prove/exclude lipid and glycogen accumulation in hepatocytes we did additional histochemical staining, using Sudan black and Periodic Acid Shiff (PAS) method, respectively. We obtained samples from lung and brain. Analyzing tissue samples of different organs obtained from seven Wistar rats, we gained insight into morphological changes caused by induced hyperthermia. All sampled organs showed congestion and some degree of oedema. The most prominent changes were observed in liver and lung samples. Tissue samples of the lung of all seven rats showed signs of acute bronchitis and bronchiolitis, together with signs of initial bronchopneumonia. We also noticed signs of focal acute emphysema as well as focal accumulations of foamy macrophages. Our study suggests that changes in the vascular bed occur soon after hyperthermia and while some organs are more tolerant to heat stroke than others, most organs show similar changes consisting of capillary dilation, vascular pathway and extravasation, observed after 30 minutes at a temperature of 40.5 ° C, with the most significant changes were observed in lung samples.

Keywords: pilot, experimental, heat, lung, brain

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Session 1 – Poster presentation *S1-14*

FREQUENCY OF INSULIN RESISTANCE ASSESSMENT OF HOMA/IR

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Insulin resistance is the inability of insulin to produce its normal biological effects in concentrations that are effective in healthy individuals. It can be related to all aspects of insulin action. Insulin resistance should be suspected in patients with a history of diabetes mellitus among the closest relatives; patients with gestational diabetes or polycystic ovary syndrome; patients with impaired glucose tolerance, arterial hypertension, dyslipidemia and elevated liver enzymes, as well as obese patients, especially those with abdominal obesity. As insulin resistance often occurs before the development or diagnosis of various clinical conditions, its recognition and treatment in the general population has a certain preventive significance. Several methods are used to determine the presence and degree of insulin resistance, and the homeostasis model (HOMA) was used in this paper. In the assessment of the frequency of insulin resistance, 100 patients with problems with obesity and polycystic ovaries were included.

Keywords: insulin resistance, HOMA-IR

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Session 1 - Poster presentation *S1-15*

NO ASSOCIATION BETWEEN SERUM OXIDIZED LOW-DENSITY LIPOPROTEIN CHOLESTEROL LEVELS AND CHRONIC KIDNEY DISEASE COMPLICATIONS

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Lipid disturbances are common in patients with verified chronic kidney disease (CKD), and atherogenic dyslipidemia is known as the main risk factor for the development of cardiovascular complications. Oxidized LDL (oxLDL) is a product of enzymatic and non-enzymatic oxidative stress pathways. The aim of this study was to investigate the impact of eGFR decline and atherosclerotic complications in predialysis CKD patients on oxLDL levels in serum. The observational, case-control study enrolled 87 patients of both sexes, 35–66 years old. They attended the Nephrology Counseling Center of the University Clinical Center Sarajevo during the period December 2016–August 2018. Glomerular filtration rate (eGFR) was estimated using the MDRD formula. According to eGFR, patients were divided into two groups: group 1-eGFR 15–59 mL/min/1.73 m2 and group 2-eGFR 60 mL/min/1.73 m2. Lipid parameter analysis was done using standard methods. Tests significance was set at p 0.05. Patients in group 1 were significantly older as compared to those in group 2 ($p = 0.001$), with a significant difference in illness duration ($p = 0.001$). The mean values of total cholesterol, LDLc, and HDLc were lower in the patients in Group 1 compared to the patients in the Second Group. Among the tested parameters, HDLc and LDLc showed statistical significance ($p = 0.002$ and $p = 0,026$, respectively). The mean values of triglycerides, VLDLc, and oxLDL were higher in patients in group 1 as compared to the patients in the second group ($p > 0.05$). After a year of follow-up with patients regarding the development of atherosclerotic complications, 13 of them have developed atherosclerotic complications. Glomerular filtration rate has influenced blood levels of LDLc and HDLc. The decline of the eGFR below 60 mL/min/1.73 m2 and atherosclerotic complications were not significantly associated with oxLDL blood levels.

Keywords: CKD, oxLDL, eGFR, atherosclerotic complications

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Session 1 – Poster presentation *S1-16*

EFFECT OF BOROXINE ON OXIDOREDUCTASE ACTIVITY BY SPECTROPHOTOMETRIC METHOD

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Enzymes control and regulate all physiological processes and are considered necessary for any metabolic processes in the cell. They act in small amounts, do not change during the reaction and can act for a very long time in the cell. Enzymes that work inside the cells are the best indicators of the health of the organism. Considering that the use of alternative methods of therapy (eg. radiation) destroys healthy and diseased cells, today more and more work is being done on the formation of drugs that will have a targeted effect only on diseased cells. The action of potential drugs is based on the inhibition/activation of oxidoreductases. In this work, the influence of the selected boronic acid derivative dipotassium trioxohydroxytetrafluorotriborate (K2[B3O3F4OH]), as a targeted therapeutic, on the activity of the enzyme catalase, isolated from beef liver, was examined. Relying on recently published research in which the inhibitory effect of K2[B3O3F4OH] on other enzymes, as well as its antitumor activity, has already been demonstrated, this work was carried out in order to prove the inhibitory effect of the mentioned substance on the enzyme catalase. A spectrophotometric method with ammonium molybdate was used to monitor catalase enzyme activity. Kinetic parameters without and with the presence of a potential inhibitor and the mechanism of action of catalase were determined. It has been proven that boroxine competitively binds to the enzyme catalase.

Keywords: enzyme, boroxine, spectrophotometric method

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Session 1 – Poster presentation *S1-17*

THE EFFECT OF SODIUM FLUORIDE ON CERTAIN HEMATOLOGICAL AND BIOCHEMICAL PARAMETERS IN RATS Rattus norvegicus (BERKENHOUT, 1769)

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Fluoride is necessary for bone and tooth health in small doses in humans and mammals. It is widely used as a cofactor in medicine, it is present in food and water in different concentrations. Sodium fluoride (NaF) induces oxidative stress and immunotoxicity in rats. Chronic exposure to high amounts is associated with inflammatory bowel disease, mucosal tissue disruption, and damage to the gastrointestinal tract. In this work, the effect of sodium fluoride on certain hematological and biochemical parameters in 15 individuals was examined. Five individuals made up the control group, and 10 individuals were divided into two experimental groups to which different concentrations of NaF were administered intraperitoneally. The first group of 5 individuals was administered intraperitoneal sodium fluoride in a concentration of 5.78 mg/170 g of body weight, while the second group of 5 individuals was administered intraperitoneal sodium fluoride in a concentration of 6.98 mg/170 g of body weight. The obtained results show that the intraperitoneal administration of NaF influenced a significant change in the examined biochemical parameters. After the application of NaF, there was a statistically significant decrease in the concentration of calcium in the second experimental group compared to the control group. Also, the applied NaF influenced a statistically significant decrease in the concentration of albumin and total proteins in both experimental groups compared to the control group of rats. While the application of NaF did not significantly affect the concentration of magnesium in the test groups. By applying a higher dose of NaF, there was a decrease in the concentration of Hb, the number of erythrocytes and hematocrit values, a decrease in the total number of leukocytes and a decrease in neutrophil granulocytes, as well as a decrease in MCV and MCH, and an increase in MCHC.

Keywords: sodium fluoride, hematological and biochemical parameters, in vivo study

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Session 1 – Poster presentation *S1-18*

THE INFLUENCE OF LONG-TERM BLOOD STORAGE ON THE OSMOTIC FRAGILITY OF ERYTHROCYTES

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Erythrocyte fragility has been expressed in different ways by different authors. MCF (mean cell fragility) a saline concentration in which 50% haemolysis occured is most common. In this research we aimed to compare the efficiency of new parameter for determination of osmotic properties; slope of the steepest part of haemolysis curve and MCF to asses the stability of erythrocytes in blood sample during prolonged storage. Ten venous blood samples from healty donors were used. Osmotic fragility test was performed at day of venipuncture (day 0) and day 1, 2, 4, 7, 9, 11 and 14 after venipuncture. The test was performed using 12 hypotonic NaCl solutions ranging from 0.1 % to 0.85%. Haemolysis curves were plotted using mean haemolysis percentage values. The steepest parts of haemolysis curves were estimated to be linear so it was possible to create a line that overlaps that part of the curves. The slope of the line was calculated and mean values are shown. Significant increase in MCF value was observed, starting from day of venipuncture. Average MCF values were compared for each day of analysis. First significant difference in MCF values was observed on day 4 compared to day of venipucture ($p=0.006$), 0.53±0.030 % and 0.41±0.014% respectively. Meanwhile difference in slope values was observed on day 2, compared to day of venipuncture ($p=0,046$), -966.23±233.07 and -588.01±222.85 respectively. Prolonged storage of blood causes increase in osmotic fragility eg. it is shifted toward higher NaCl concentration, as well as change in the shape of haemolysis curve, indicating that delay in osmotic fragility test could result in diagnostic inaccuracy. This results point that slope is a more sensitive parameter which indicates changes in erythrocyte stability during storage, compared to MCF value. It gives better description of osmotic properties of erythrocytes as well as shape of haemolysis curve.

Keywords: erythrocyte fragility, mean cell fragility, slope of haemolysis curve

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Session 1 – Poster presentation *S1-19*

FALSELY ELEVATED VITAMIN B12 LEVEL DUE TO MACRO VITAMIN B12 INTERFERENCE

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Current recommendations for interpreting elevated B12 level do not consider the possibility of Macro B12 interference. Since we received several questions from clinicians, who were not able to explain elevated B12 level, we decide to examine the existence and frequency of such interference, which cause falsely elevated results of laboratory analysis, as well as to propose an algorithm for treatment with such samples. Since macro B12 complex can be precipitated using Polyethylene glycol 6000 (PEG), aim of this research was to define the reference range value after performing such procedure (post -PEG RI), and to report it as recovery (%) and concentration value (pmol/L). Obtained values are used for evaluation of Macro B12 incidence in population of Bosnia and Herzegovina. Macro B12 was measured in serum samples of 81 healthy volunteers using Roche Cobas Electrochemiluminescence immunoassay pre- and post-PEG precipitation. Recovery was calculated, and reference range for post-PEG vitamin B12 was established using robust method recommended by CLSI EP28A3 document. Routine patients' samples (n = 121) with elevated vitamin B12 level (>569 pmol/L) were screened for Macro B12 presence. The Reference range for serum post-PEG vitamin B12 were 125,19 - 494,81 (CI: 106,21 to 144,48 and 462,88 to 527,45) pmol/L. Mean Post-PEG recovery was 91,56%, ranged from 66,83%-109.17% (CI: 61,58 to 71,98 and 105,64 to 112,48). Of 121 patients screened for Macro B12 16 (13,22%) had Macro vitamin B12 interference according to recovery calculation. According to post-PEG RI 22 (18,18%) patients have Macro B12 interference. 6 (4,9%) patients had interference according both criteria used. Considering the prevalence in our population we recommend to perform PEG precipitation procedure in case when other causes for elevated B12 levels are excluded. Even taught it is simple and effective method for removing Macro B12 interference it should be compared with size-exclusion chromatography (reference method).

Keywords: vitamin B12, macro B12, polyethylene glycol, electrochemiluminescence immunoassay

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Session 1 – Poster presentation *S1-20*

ASSOCIATION OF PLASMA FREE FATTY ACIDS AND HEPATIC ENZYMES IN PREDIABETES PATIENTS

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Prediabetes is condition characterized impaired fasting plasma glucose and insulin resistance followed by alteration of fat and protein metabolism. Increased flow of free fatty acids (FFAs) into the blood that is coming from the adipocytes as well as an elevated flux of FFAs from *de novo* lipid synthesis in the liver contribute to these metabolic disturbances. Previous studies suggested a strong association of the hepatic activity of certain enzymes, such as aspartate and alanine transferase (AST, ALT), gamma glutamyl transpeptidase (GGT), and alkaline phosphatase (ALP) with the progression of T2D. A total of 85 participants of which 45 prediabetes patients and 40 controls were recruited in this study. Biochemical analyses include measurements and fasting plasma samples for the quantification of hepatic enzymes (ALT, AST, GGT, and ALP), glucose, glycated Hemoglobin, and lipid profile were performed using standard IFCC methods. The plasma concentrations of individual FFAs were determined by gas chromatography analysis. The results demonstrated significant differences in glucose, HbA1c, triglycerides, age and AST levels ($P<0.001$) between prediabetes patients and control individuals. Also, showed a positive association between ALT activity with C16:0 and TG levels ($P<0.05$) while the activity of GGT was significantly associated with C18:0 and TG levels ($P<0.05$). In control group, a positive correlation was found between C16:1 with ALT activity ($P<0.05$), and a negative correlation of C18:2 levels with ALP activity ($P<0.05$) was observed. In prediabetes group, no association was found between the measured FFAs and ALT, AST, and ALP activities ($P>0.05$) while a significant association between C16:0, C18:0, and C18:1 acids with GGT was shown ($P<0.05$). These data suggest that elevated concentrations of different types of FFAs, particularly C16:0, C16:1, C18:0, and C18:1 as main fatty acid in *de novo* lipogenesis appear to be associated with enzyme activities in the liver of prediabetes patients.

Keywords: free fatty acids, hepatic enzymes, Prediabetes

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Session 1 – Poster presentation *S1-21*

COMPARISON CYSTATIN C ASSAYS ON ALINITY CI AND BN II NEPHELOMETER ANALYZERS

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The main objective of this study was to compare two different methods for Cystatin c (Cys c) BN II Siemens and Alinity ci analyzers. The research was conducted in the Department of Laboratory Diagnostics (DLD) of the University Clinical Hospital Mostar (UCH Mostar) in Bosnia and Herzegovina. The specific objectives of the paper were to investigate the comparability of analytical methods, and to determine the constant and proportional deviations between individual methods. Subjects included in the study were patients older than 18 years who were treated in UCH Mostar or were referred to DLD from the Health Centers, with the signed informed consent. The study included 45 respondents. The methods used to analyze Cys c concentration were commercially available assays; BN II Nephelometry and particle-enhanced turbidimetric-inhibition immunoassay (PETINIA) on Alinity ci. The reference range for Cys c; on the BN II analyzer is 0,62-1,11 mg/L, and on Alinity is 0,40-0,99 mg/L. Bland-Altman analysis and Passing Bablok regression in MedCalc software were used for statistical data processing. For Bland-Altman analysis mean difference (MD) between two measurements was 14,0785% (11,9721-16,1849) with limits of agreement D ±1,96. The results according to Bland-Altman analysis showed statistically significant constant deviation. Passing Bablok regression equation y=0,03390 (-0,01615-0,09000) + 1,1039 (1,0571-1,1538)x showed statistically proportional deviation, but doesn't significant constant deviation. According to the results, it is concluded that the methods are not comparable. Bland-Altman analysis showed that the limits of the confidence interval are different from zero, which confirmed the null hypothesis about the difference and incomparability of the methods. Regression equations, obtained by Passing Bablok analysis, also confirmed that there is a statistically significant difference between these methods and analyzers. Also, the differences in measurement by the above methods are greater than the usual analytical variability, and thus may affect the clinical outcome.

Keywords: Cystatin c, comparison method, Alinity ci, BN II Siemens

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Session 1 – Poster presentation *S1-22*

THO2 MOONLIGHTS IN THE MRNP QUALITY CONTROL

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The eukaryotic THO complex coordinates the assembly of so-called messenger-ribonucleoprotein particles (mRNPs), a process that involves co-transcriptional coating of nascent RNAs with proteins. Once formed, mRNPs undergo a quality control step that marks them for either active transport to the cytoplasm or Rrp6/RNA exosome-mediated degradation in the nucleus. However, the mechanism behind the quality control of nascent mRNPs is still unclear. We investigated the co-transcriptional quality control of mRNPs in budding yeast by expressing the bacterial Rho helicase, which globally perturbs yeast mRNP formation. We examined the genome-wide binding profiles of the THO complex subunits Tho2, Thp2, Hpr1, and Mft1 upon perturbation of the mRNP biogenesis, and found that Tho2 plays two roles. In addition to its function as a subunit of the THO complex, free Tho2 targets Rrp6 to chromatin via its C-terminal domain. This finding raises the possibility that Tho2 is involved in co-transcriptional mRNP quality control independently of other THO subunits. Considering that both the THO complex and the RNA exosome are evolutionarily highly conserved, our findings are likely relevant for mRNP surveillance in mammals.

Keywords: Rrp6, Tho2, THO complex, mRNP quality control, ChIP-Seq

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Session 1 – Poster presentation *S1-23*

OXIDATION MODULATES AGGREGATION AND MEMBRANE INTERACTION PROPERTIES OF SUPEROXIDE DISMUTASE 1

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Amyotrophic lateral sclerosis (ALS) is an age-related neurodegenerative disease characterized by the progressive loss of motor neurons that control voluntary movement. Genetic studies revealed the involvement of superoxide dismutase 1 enzyme (SOD1) in the pathophysiology of the disease. Both wild-type and mutant forms of SOD1 can gain toxic function which is reflected in their increased aggregation and cytotoxicity in ALS patients. However, it remains unclear how aging contributes to this toxic gain-of-function in SOD1. Since oxidative damage to proteins accumulates with age, in this study we tested the hypothesis that age-related oxidation contributes to SOD1 toxicity by modulating its biochemical characteristics. Thus, we analysed the impact of oxidation on SOD1 aggregation properties and cellular behaviour, with the focus on its interactions with the lipid membranes. We found that oxidized SOD1 displayed slower aggregation kinetics, yielding smaller aggregates with less beta-sheets and more amyloid oligomers in comparison with the non-oxidized SOD1. Moreover, externally applied oxidized SOD1 aggregates were more toxic in NSC34 motor neuron-like cell line and more efficient in permeabilizing artificial lipid vesicles. This was accompanied with stronger interactions of oxidized SOD1 aggregates with the lipid membranes *in vitro*. In conclusion, oxidation modulates SOD1 aggregation, thus leading to its increased interactions with the membranes and acquisition of cellular toxicity. These data may explain the role of age-related oxidative damage to proteins in the onset of ALS.

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Session 1 – Poster presentation *S1-24*

NOVEL AGRICULTURAL TECHNOLOGY: COLD PLASMA-INDUCED STIMULATION OF NATURAL SWEETENER BIOSYNTHESIS IN Stevia rebaudiana IN THE AEROPONIC SYSTEM

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Stevia rebaudiana Bertoni is an economically valuable plant due to its secondary metabolites steviol glycosides (SGs) which are responsible for the sweetness of stevia and are widely used as natural sweeteners. Stevioside (Stev) and rebaudioside A (RebA) are the most abundant SGs in stevia. We have recently demonstrated the potential of pre-sowing stevia seed treatment with cold plasma (CP) in SGs synthesis stimulation when plants are cultivated in soil. This study aimed to substantiate the basis for a novel agricultural technology for the stimulation of natural sweetener biosynthesis based on the combination of plasma used for the short treatment (5 min) of stevia seeds and aeroponic cultivation. The CP-treated group had significantly higher concentrations of total phenolic compounds (by 43%) and flavonoids (by 19%) compared to the control. CP increased antioxidant activity measured by DPPH radical scavenging method by 45% compared to the control. These concentrations were decreased or unchanged in stevia grown in soil. The CP-treated group contained significantly lower amounts of chlorophyll a (by 24%) and chlorophyll b (by 27%). The amount of carotenoids wasn't influenced by CP. CP group plants had higher dry matter amount, containing 58% and 20% more of RebA and RebA+Stev, respectively, compared to the control. The concentrations of RebA, Stev and RebA+Stev in fresh leaf material exceeded the control by 128%, 49% and 73%, respectively. Although CP treatment stimulated biosynthesis/accumulation of SGs per unit of dry or fresh leaf material, biomass growth was inhibited, plants were smaller, and SGs yield per plant or area unit was 35% lower. We have demonstrated for the first time that short (5 min) pre-sowing stevia seed treatment with CP can substantially enrich plant material with valuable secondary metabolites when stevia is grown in an aeroponic system.

Keywords: *Stevia rebaudiana* Bertoni, cold plasma, steviol glycosides, aeroponic

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Session 1 – Poster presentation *S1-25*

EVALUATION OF INFLAMMATORY STATUS AND ASSOCIATION WITH THE DISEASE SEVERITY IN COVID-19 PATIENTS

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Inflammation is a natural response of the body's immune system to protect against infections and injuries. In COVID-19, the virus triggers an inflammatory response in the body, which can lead to acute respiratory distress syndrome and multiple organ failure. The aim of our study was to evaluate the inflammatory status in COVID-19 patients using the most important biomarkers such as ESR (Erythrocyte Sedimentation Rate), CRP (C-Reactive Protein) and WBC (leukocytes count). The study included 750 COVID-19 patients with different disease severity (mild, moderate-severe, exitus letalis - EL). Patients were recruited at the time of admission to the General Hospital Tešanj, Bosnia and Herzegovina. Inflammatory biomarkers (ESR, CRP, WBC) were analyzed using standard IFCC procedures. Statistical analysis showed that ESR values were highest in the EL group of patients, while the lowest values were in the group of patients with mild disease severity. The results showed a statistically significant difference in ESR values between the mild and moderate-severe ($p<0.001$) and between the mild and EL group of patients ($p<0.001$). Also, statistical analysis showed that CRP values were highest in EL group of patients, while the lowest values were in the group of patients with mild disease severity. Our results show a statistically significant difference in CRP values between the mild and moderate-severe ($p<0.001$), mild and EL group of patients ($p<0.001$) as well as moderate-severe and EL group of patients ($p=0.008$). Also, results demonstrated that WBC count was the highest in EL group of patients while the lowest count was in patients with mild disease severity. The results did not show a statistically significant difference in WBC count between groups. Inflammation may play a role in the development of severe COVID-19. It is crucial to follow preventive measures and get vaccinated to reduce the risk of severe illness and death from COVID-19.

Keywords: COVID-19, inflammation, disease severity, CRP, ESR, WBC

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Session 1 – Poster presentation *S1-26*

DISCREPANCY OF SEROLOGICAL AND MOLECULAR TESTING IN THE SCREENING ALGORITHM OF VOLUNTARY BLOOD DONORS

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Safe blood and blood products require the implementation of good practice standards in the work of blood transfusion services. Serological testing is performed on automatic analyzers that meet European standards for testing blood. All laboratory tests are validated before application, and each donation must undergo testing, in accordance with European Directives 2002/98/EC (Directive 2005/62/EC Appendix 6.3.2), and according to the testing algorithm in WHO recommendations. In the Institute for Transfusion Medicine FBIH, serological screening is performed on the Architect i2000sr platform, and since 2016, molecular screening with NAT testing on the Cobas s201 platform, which has been replaced by the Cobas 5800 since November 2022. In testing on Cobas s201, testing was done in a pool of 6 samples, in the case of a positive pool, repeated testing is done 1 test - 1 sample. Only serologically and molecularly negative results can be released for processing. The results of the tested samples in the period from 2016 to 20223 on the existing platforms were analyzed for the research. During the testing, a deviation was noticed in the results of the molecular testing, a certain number of tested pools showed positive results for HBV, and after the individual testing, the results of the molecular test were negative. Testing of samples for anti HBc, anti HBe, anti HBs showed positive results for some samples from the pool. Additional testing of samples with positive RT PCR results did not confirm the presence of HBV. By switching to the new platform Cobas 5800 and individual testing, invalid results were observed. Testing of samples for anti HBc, anti HBe, anti HBs showed positive results for individual samples for anti HBc and Anti HBs. The discrepancy between serological and molecular testing points to a review of the testing algorithm, as well as the determination of possible interferences and potential inhibitors in the sample. It is necessary to consider the introduction of new analyzes that would save the donor and increase blood safety.

Keywords: blood donors, screening, discrepancy

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Session 1 – Poster presentation *S1-27*

RELATIONSHIP BETWEEN URINARY COPPER EXCRETION BETWEEN PATIENTS WITH WILSON DISEASE, BEFORE AND AFTER THE TREATMENT

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Wilson's disease (WD) is an autosomal recessive inherited disease, caused by a mutation in the *ATP7B* gene, located on chromosome 13, which is responsible for synthesizing enzymes needed to transport copper from the liver to the bile. The disease is characterized by a pathological accumulation of copper, first in the liver and then in the brain, kidneys, bones, and cornea. The biochemical characteristics of WD include decreased serum ceruloplasmin and copper concentrations and increased urinary copper excretion. Determination of copper in the urine by atomic absorption spectrometry is a rapid method for determining excess copper in the body which helps to remove the excess copper in the body through the urine. The aim of this study task is to point out the importance of biomonitoring of urinary copper excretion, using atomic absorption spectrometry, in patients with WD, before and after chelating agent therapy or treatment. The laboratory examination of the copper content in 24hour urine was performed at the PHI University Institute of Clinical Biochemistry in Skopje, at the Clinical Center "Mother Teresa" using atomic absorption with a PinAAcle 900F spectrometer. The relationships between urinary copper excretion in 24h urine between patients with WD, before and after treatment observe high concentration (μg) of copper in 24h urine (108,92±35,44) in patients without chelating agent therapy compare with concentrations of copper in 24h urine (24,49±13,95) with chelating agent therapy. Minimum values of copper in 24-hour urine in patients with and without chelating agent therapy are 91,39 and 4,44 respectively. Maximum values of copper in these two group of patients are 172,88 and 42,94 respectively. Determining the concentration of copper in various biological media is becoming increasingly important, but in WD it has been shown that determining 24-hour urinary copper excretion is important for diagnostic purposes and monitoring.

Keywords: Wilson's disease, copper, urinary copper excretion, monitoring treatment

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Session 1 – Poster presentation *S1-28*

THIOPURINE S-METHYLTRANSFERASE VARIANTS IN ÇUKUROVA REGION; FIRST OBSERVATION OF TPMT*47 (C323G) IN SOUTHERN TURKEY

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Thiopurine S-Methyltransferase is a cytoplasmic enzyme that catalyzes the S-methylation of aromatic and heterocyclic sulfhydryl compounds. TPMT enzyme activity varies considerably from one individual to another and this variation is genetically determined. About 89% of people have relatively high TPMT activity. The remaining ~11% have partial or complete TPMT deficiency. TPMT deficient individuals can not tolerate thiopurine drugs such as 6-mercaptopurine or azathioprine, resulting in haematopoeitic toxicity or sometimes death. Several studies among different populations have demonstrated a concordance (>98%) between TPMT enzyme activity and genotype. Three point mutations in the TPMT gene are responsible for low TPMT activity. The wild-type allele is named as TPMT*1 and the common mutant alleles include TPMT*2 (G238C), TPMT*3A (G460A and A719G), TPMT*3B (G460A) and TPMT*3C (A719G). In this study, DNA was isolated from white blood cell. TPMT*2, TPMT*3B and TPMT*3C point mutations were analyzed by Real Time PCR. A sequencing was used for verification of G460A and A719G mutations. A total of 200 person were analyzed and three different genotypes were identifed. One of the cases had two mutations (TPMT*3B and TPMT*3C) on the same chromosome (TPMT*3A), the other was heterozygote for TPMT*3B. Another case was identified by DNA sequencing as TPMT*47 (C323G) variants. We conclude that RT-PCR can be easly integrated into genetic testing of the TPMT variants. But DNA sequencing is necessary for identification and verification of new variants as TPMT*47.

Keywords: Thiopurine S-methyltransferase, TPMT*3A, TPMT*3B, TPMT*47 (C323G)

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Session 1 – Poster presentation *S1-29*

UTERINE LEIOMYOMA: PATHOGENESIS, PREDISPOSING FATORS AND GENETICS

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Uterine leiomyoma (UL) is a type of gynecologic disorder representing the most common tumors in women worldwide. There is strong evidence that hormonal, biochemical, genetic and cytogenetic alterations play an important role in the etiology and pathogenesis of uterine leiomyoma. Here, we demonstrate the significance of the predisposing variables in UL, including the various pathogenetic elements including genetics, hormones, growth factors, cytokines, chemokines, and extracellular matrix components that have been linked to the initiation and progression of leiomyoma. Smad protein, phosphatidylinositol-3-kinase and the mammalian target of rapamycin – PI3K/AKT/mTOR pathway, mitogen-activated protein kinases/extracellular signal-regulated kinases – MAPK/ERK pathway, wingless-type (Wnt)/β-catenin and retinoic acid pathways are involved in UL growth and proliferation indicating that they could serve as targets for possible therapies. Apart from biochemical changes chromosomal abnormalities in fibroids are nonrandom and tumor-specific. Translocations, rearrangements involving 6p21, 10q, trisomy 12, and deletions of 1p3q are the common alterations in leiomyomas. The most common genes associated with fibroids are TP53 and ESR1. As a result of a better understanding of the pathogenomics of leiomyomas, new strategies for preventing, diagnosing, and treating the disease become possible. Here, we focus to share up to date the literature about etiology and pathogenesis of uterine fibroids which can be used for the treatment and shed light on future works.

Keywords: uterine leiomyomas, leiomyomas, signalling pathways, pathogenesis, pathogenetic factors

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Session 1 - Poster presentation *S1-30*

INVESTIGATION OF ORGANIC ACID LEVELS AS A PROGNOSTIC INDICATOR IN COVID-19 POSITIVE PATIENTS

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The aim of this study is to evaluate the organic acids detected in the urine due to the metabolic processes affected by hypoxia in COVID-19 patients who develop clinically mild, moderate and severe pneumonia, to determine their relationship with the disease severity and to compare the results with the control group. A total of 120 patients with the clinical spectrum of SARS-CoV-2 infection as mild, moderate and severe according to the WHO COVID-19 disease severity classification were included in the present study. First morning urine samples taken inpatient setting were aliquoted and frozen immediately until the analysis day. Urine organic acid levels were measured using Gas chromatography-mass spectrometry. Among 104 organic acids, pyruvic acid, lactic acid, 2-hydroxybutyric acid levels were significantly higher in the severe disease group ($p=0.006$, $p<0.001$, $p<0.001$, respectively), citric acid and homovanilic acid (HVA) levels were significantly lower in all disease groups ($p<0.001$), α-ketoglutaric acid, vanillylmandelic acid and succinic acid levels were significantly lower in the severe and moderate disease group ($p<0.001$), β-hydroxybutyric acid was significantly higher in the severe and moderate disease group p(<0.001), oxalic acid was significantly higher in the moderate disease group compared to the control group ($p=0.041$). The binary logistic regression model included, α-ketoglutaric acid, succinic acid, and HVA. It was statistically significant with $\chi 2 = 98.680$; $p < 0.001$. α-ketoglutaric acid, succinic acid and HVA were independent predictors of the disease severity, measurement of these spesific metabolites might facilitate the developments of novel therapies and may improve responses to currently available therapies with the ease of prognosis prediction of COVID-19.

Keywords: COVID-19, severity, organic acids, urine, GC-MS

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Session 1 – Poster presentation *S1-31*

THE EFFECTS OF L-ASCORBIC ACID ON ISONIAZID-INDUCED PROTEIN OXIDATION AND HEPATOTOXICITY IN RATS

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Isoniazid (INH) is hepatotoxic drug. Oxidative stress has been reported as one of the mechanisms of INH induced hepatotoxicity. In the current study, our aim was to evaluate the redox status of plasma and liver proteins as well as the protective role and dose of ascorbic acid (AA) in INH-induced hepatotoxicity in rats. Protein oxidation parameters such as protein carbonyl (PCO), total thiol (T-SH) levels and paraoxonase-1 (PON-1) activity was determined in the liver and the plasma of rats. Rats under study were randomly divided into four groups: (1) control; (2) INH (50mg/kg/day); (3) INH (50mg/kg/day) + AA (100 mg/kg/day); and (4) INH + AA (1000 mg/kg/day). INH administration resulted in abnormal elevation of plasma and hepatic PCO levels. On the other hand, the levels of the plasma and hepatic T-SH and PON1 activity significantly decreased. Supplementation of AA (100 mg/kg/day) dose partially reverted these abnormalities in the redox status of the proteins and activities of PON1 after the administration of INH. Changes in oxidative stress are likely involved in the pathogenesis of INH-induced hepatoxicity in rats.

Keywords: ascorbic acid, isoniazid, paraoxonase, protein carbonyl, total thiol, protein oxidation

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Session 1 – Poster presentation *S1-32*

REDUCED AND OXIDIZED GLUTATHIONE AFFECTS SMOOTH MUSCLE CONTRACTILITY AND ANTI-OXIDANT ENZYMES ACTIVITY IN ISOLATED ILEUM OF MALE RAT

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Normal redox status of the cell is maintained by a number of enzymes, such as superoxide dismutase, catalase, glutathione peroxidase and low molecular weight antioxidants, such as ascorbate, tocopherols and gluathione. Maintaining high levels of reduced glutathione enhances antioxidant defense and preserves cellular homeostasis. The aim of this study was to examine whether, to what extent and in what way changes in physiological processes occurred in conditions when cellular redox homeostasis is in imbalance. The experiments were performed on isolated ileum of male Wistar rats, electrically stimulated and treated with cumulative doses of reduced or oxidized glutathione. The activity of antioxidant enzymes (catalase, glutathione reductase, glutathione peroxidase, copper–zinc superoxide dismutase and manganese superoxide dismutase) was determined in treated ileum. Glutathione in both forms decreased amplitude of ileum contractions. Cumulative doses of oxidized glutathione led to higher glutathione reductase activity while the addition of reduced glutathione increased activity of glutathione peroxidase. The results showed that maintenance of cellular redox homeostasis have influence to physiological processes.

Keywords: redox homeostasis, oxidative stress, antioxidant enzymes, ileum, rat

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Session 1 – Poster presentation *S1-33*

EVALUATION OF ARGININE METABOLITES IN BLUNT THORACIC TRAUMA

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Blunt thoracic trauma (BTT) causes high morbidity and mortality and Acute lung injury (ALI) is seen in 50-60% of patients. It is thought that arginine metabolites (ADMA, arginine etc.) play a role in the pathophysiology of many diseases and may be biomarkers in predicting mortality and damage. Considering the pathophysiology of trauma, there is increased proteolysis and decreased elimination, and this situation increases arginine metabolites. The aim of this study is to measure serum arginine metabolites levels in experimentally created BTT model in rabbits and to investigate the potential clinical values of them. The study was conducted on 27 New Zealand rabbits which were 1-2 years old, and trauma was created by applying different energy levels with the help of the apparatus. Four groups were studied as control (C) and low (G1), medium (G2) and high (G3) energy trauma groups. Blood samples were taken at 1st, 12th and 24th hour of trauma, and analyzed by LC-MS/MS device. According to the results of analysis, a statistically significant difference was found for arginine, L-NMMA, ornithine and homoarginine at 1st hour ($p<0.05$). Ornithine levels increased relative with trauma and the highest homoarginine level was seen in the G1. A statistically significant difference was found for arginine, ADMA and L-NMMA according to the 12th hour data ($p<0.05$). ADMA levels increased relative with trauma and the highest L-NMMA level was seen in the G3. At the 24th hour, only arginine was significant (relative with trauma). In ALI caused by blunt thoracic trauma, it was observed that the levels of arginine metabolites changed in relation to time, between groups and trauma severity. According to our study we think that the levels of arginine metabolites may contribute to the evaluation of the prognosis of trauma and predict mortality.

Keywords: thoracic trauma, lung injury, arginine metabolites

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Session 1 - Poster presentation *S1-34*

EVALUATION OF D VITAMIN AND INFLAMMATORY MARKERS IN OBESE PAEDIATRIC POPULATION IN BOSNIA AND HERZEGOVINA

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Excessive body weight, obesity and vitamin D deficiency represent serious health concerns among paediatric population. Childhood obesity is accompanied by vitamin D deficiency and low-grade systemic inflammation, contributing to the development of insulin resistance and cardiovascular complications later in life. The aim of this study was to analyse the association between inflammatory markers and vitamin D levels in obese pubertal children and compare it to their healthy peers.The research was conducted at the Clinical Center of the University of Sarajevo on 80 obese children and 40 non-obese healthy peers, aged 12-18 years, with no other underlying conditions. The values of vitamin D, CRP, fibrinogen, alongside neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) and systemic immuno-inflammatory index (SII) were determined for all study subjects according to standard laboratory procedures. Nonparametric tests were used in analysis and $p=0.05$ was considered statistically significant. The groups were age and gender matched. Median (IQR) BMI values in group of obese children was 31.0 (29.4-33.5) compared to 21.4 (19.2-23.3) kg/m2 in non-obese controls. Median (IQR) values of all inflammatory indices (fibrinogen, CRP, NLR, PLR, SII) were significantly higher in obese children compared to group of children with normal body weight, $p<0.001$ for all. Median (IQR) values of vitamin D were significantly lower in obese children compared to non-obese group, with $p=0.016$. Furthermore, we found significant positive correlations between BMI and: fibrinogen ($p=0.002$), CRP ($p=0.004$), NLR ($p<0.001$), PLR ($p=0.001$) and SII ($p<0.001$). BMI showed significant negative corelation with vitamin D, $p=0.018$. Inflammatory markers are higher and vitamin D levels lower in obese paediatric population compared to non-obese peers. Existence of low-grade systemic inflammation and vitamin D deficiency underlines the need for the correction of vitamin D levels in overweight and obese children as it has potent anti-inflammatory properties.

Keywords: vitamin D, childhood obesity, inflammation

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Session 1 – Poster presentation *S1-35*

ELUCIDATION OF PHA BIOSYNTHESIS THROUGH FATTY ACIDS COMPOSITION IN *CHROOCOCCUS SP.*

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Thermophilic cyanobacteria are photoautotrophic organisms capable of converting climate-damaging carbon dioxide (CO_2) into biomass using light as an energy source, allowing them to thrive in high-temperature environments. These properties make them promising candidates for the production of valuable chemicals in cell factories. In this study, *Chroococcus sp*. isolated from a hot spring in Malaysia was cultivated under nitrogen-deprived and high-carbon conditions to enhance the production of polyhydroxyalkanoates (PHA). PHA is composed of hydroxy fatty acids that accumulate in the cytosol in the presence of excessive carbon sources, while growth is inhibited due to low nutrient availability. Total lipids were extracted using sonication, and the composition of fatty acids and PHA was determined using gas chromatography mass spectrometry (GC-MS). Additionally, the structure of PHA was visualized using scanning electron microscopy (SEM). The detected fatty acids included heptadecanoic acid (C17:0), octadecanoic acid (C18:0), heneicosanoic acid (C21:0), and docosanoic acid (C22:0), which are long-chain fatty acids that can be utilized for various industrial chemical productions, particularly in the production of bioplastics.

Keywords: polyhydroxyalkanoates, fatty acids, thermophilic cyanobacteria

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Session 1 - Poster presentation *S1-36*

KIDNEY FUNCTION EVALUATION IN THE PEDIATRIC POPULATION WITH TYPE 1 DIABETES MELLITUS

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Impaired kidney function is one of the most common complications of diabetes. Patients with type 2 diabetes will eventually develop diabetic nephropathy, but data on diabetes effects on kidney function in the pediatric population with type 1 diabetes (T1DM) are lacking. The aim of our study was to evaluate kidney function in diabetic children, using the estimated Glomerular filtration rate (eGFR), and to compare it to their healthy peers. The research was conducted at the Clinical Center of the University of Sarajevo on a total of 140 children, 70 diagnosed with T1DM and 70 healthy peers aged 5-15 years. The values of urea, creatinine, HbA1c and eGFR (Schwartz formula) were determined for all study subjects according to standard laboratory procedures. Results are presented as median(IQR-interquartile range) and p=0.05 was considered statistically significant. The groups were age and gender matched. T1DM patients had higher urea values, median of 4.8 (IQR 4.0-5.6) vs 4.0 (IQR 3.2-4.6) in healthy peers, p<0.001. There was no difference in median (IQR) creatinine values between patients with T1DM and healthy peers, median 46.0 (IQR 41.0-58.0) vs 51.0 (IQR 46.0-56.5), respectively, p=0.06. Patients with T1DM had higher eGFR values, a median of 152.0 (IQR 130.5-173.0) vs 140.0 (IQR 130.0-156.5) in healthy peers, p=0.005. The values of all parameters, regardless of the established differences, were within the reference values for both groups. In children with T1DM, HbA1c values didn't show a significant correlation with eGFR, Spearman rho -0.113, p=0.269. According to our results, there are no clinically significant differences in the renal function of children with T1DM and healthy peers. eGFR didn't show a significant correlation with HbA1c. More extensive future studies including the effects of Diabetes duration are necessary.

Keywords: type 1 diabetes mellitus, pediatric population, kidney function, estimated glomerular filtration rate

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Session 1 – Poster presentation *S1-37*

EVALUATION OF LIPID PROFILE IN CHILDREN WITH TYPE 1 DIABETES MELLITUS IN COMPARISON TO HEALTHY PEERS

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The complications of type 1 diabetes mellitus (T1DM) are numerous, and one of the significant ones is the accelerated development of atherosclerosis caused by dyslipidemia, which increases the risk of developing cardiovascular diseases later in life. The aim of our study was to evaluate the lipid profile in prepubertal school children with T1DM compared to their healthy peers. The research was conducted at the Clinical center of the University of Sarajevo on 50 children with T1DM, and 50 healthy controls, with no other underlying conditions, aged 6-12 years. The values of HbA1C, total cholesterol, HDL-cholesterol (HDL-C), LDL-cholesterol (LDL-C) and triglycerides were analyzed according to standard laboratory procedures. Statistical analysis was performed using the Mann-Whitney test and Spearman's correlation coefficient. Results are presented as median (IQR-interquartile range), and p=0.05 was considered statistically significant. Study groups were age and gender matched. Median for HbA1C, T1DM group is 7.9 (IQR 7.1-8.5) compared to control group 5.1 (IQR 5.0-5.2), p<0.0001. There was no significant difference in median values of HDL-C and LDL-C between children with T1DM and healthy peers. A significant difference in the median values of total cholesterol and triglycerides were observed in children with T1DM compared to the control group. Median for total cholesterol in T1DM group was 4.4 (IQR 4.0-4.9) compared to 4.05 (IQR 3.7-4.5) in control group, p=0.0039. Median for triglycerides in T1DM group was 1.01 (IQR 0.68-1.5) compared to the 0.71 (IQR 0.53-0.84) in control group, p<0.0001. HbA1C showed a positive correlation with total cholesterol (rho=0.38, p=0.0001) and triglycerides (rho=0.356, p=0.0003). Levels of total cholesterol and triglycerides were higher in prepubertal school children with T1DM compared to nondiabetic healthy peers. Further studies to address the impact of these changes on the atherosclerosis development and cardiovascular risk in patients with T1DM are needed.

Keywords: jouvenile diabetes, lipid profile, atherosclerosis, cardiovascular risk

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Session 1 – Poster presentation *S1-38*

SELECTED INFLAMMATION BIOMARKERS IN YOUTH WITH TYPE 1 DIABETES COMPARED TO HEALTHY PEERS

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Emerging role of inflammation in both type 1 (T1D) and type 2 diabetes (T2D) is arousing scientific interest, as managing inflammation could help the prevention and control of the disease. Various hypotheses have been developed to describe inflammation mechanisms involved in the propagation of diabetes, mainly focusing on T2D. The predominant theory in T1D is that the beta cell islets are inflamed, through the course of T1D. Individuals with T1D show higher expression of proinflammatory cytokines, a possible critical factor in both inflammatory and autoimmune-mediated pancreatic cell death. We aimed to analyze low-grade inflammation in children with T1D and compare it to healthy peers using inexpensive, easily obtainable markers. The research was conducted at the Clinical Center of the University of Sarajevo on 70 children with T1D and 40 healthy peers, aged 12-18 years, with no other underlying conditions. The values of HbA1c, CRP, fibrinogen, MPV, alongside neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) and systemic immuno-inflammatory index (SII) were determined for all study subjects according to standard laboratory procedures. Nonparametric analysis, with $p=0.05$ considered statistically significant, was conducted. The groups were age and gender matched. Median (IQR) HbA1c values in group of children with T1D was 8.0 (7.2-9.3) compared to 5.1 (4.9-5.3) % in healthy controls. Median (IQR) values of MPV and all inflammatory indexes were significantly higher in children with T1D compared to healthy peers, MPV and PLR ($p<0.001$), NLR ($p=0.001$) and SII ($p=0.003$). Fibrinogen and CRP didn't differ significantly between the groups. Furthermore, we found significant positive correlations between HbA1c and: MPV ($p=0.002$), NLR ($p=0.001$), PLR ($p<0.001$) and SII ($p=0.001$). Inflammation markers are higher in pediatric population with T1D compared to healthy peers. HbA1c is positively associated with inflammation. MPV, NLR, PLR and SII are commonly available and inexpensive inflammation indicators easily utilizable in management of juvenile diabetes.

Keywords: jouvenile diabetes, inflammatory markers, pediatric population, hemoglobin A1c

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Session 1 - Poster presentation *S1-39*

BLOOD HEMOGLOBIN LEVELS IN ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS

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An association between diabetes and anemia in adults is well known. However, evidence for this association in children with Type 1 diabetes mellitus is lacking. The aim of this study was to determine hemoglobin status in teenage children diagnosed with Type 1 diabetes, and to assess the frequency of anemia compared to their healthy peers. 30 children with diabetes and 30 healthy controls, aged 13-18 (M=15.10, SD=1.78), were included in this research. Hemoglobin concentration was determined in all children, following standard laboratory procedures. The possible presence of anemia was defined as a hemoglobin level two standard deviations below the mean value for a certain age (<130 g/l for males and <120 g/l for females). Study groups were age and gender matched. The results were processed using the IBM SPSS Statistics program, version 23. A statistically significant difference (p=0.041) was found between hemoglobin levels in adolescents with Type 1 diabetes (MT1DM=143.9 g/l, SD=11.75) and healthy controls (MCTRL=149.2 g/l, SD=7.46). Neither of the study groups showed hemoglobin values below predefined values for the diagnosis of anemia. Patients with Type 1 diabetes had a higher frequency of hemoglobin concentrations below the mean value (within two standard deviations) (50.0%) compared to the healthy controls (3.33%). These hemoglobin values could represent pre-anemic state. Frequency of hemoglobin concentrations below the mean value in patients with type 1 diabetes did not show gender differences (p=0.804). Blood hemoglobin levels, although within reference values, are significantly lower in adolescents with Type 1 diabetes compared to healthy peers. This could be indicative of an anemia development. Periodic monitoring of blood hemoglobin could help avoid this complication. In future studies, it may be necessary to include more parameters, primarily RBC and MPV, serum iron and ferritin.

Keywords: type 1 diabetes, adolescents, hemoglobin, anemia

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Session 1 - Poster presentation *S1-40*

IMPORTANCE OF MINERAL DETERMINATION AND THEIR CORRELATION WITH HBA1C IN CHILDREN WITH TYPE 1 DIABETES MELLITUS

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Type 1 diabetes mellitus (T1DM) is caused by insulin deficiency resulting from the destruction of pancreatic β cells. Patients with T1DM often develop a hypoglycemia, hyperglycemia and diabetic ketoacidosis and number of electrolyte disorders. The main focus of this study is to determine whether there is a statistically significant difference in mineral status in correlation with HbA1c in children with diagnosed T1DM compared to healthy children. 50 children diagnosed with T1DM for more than 6 months and 50 healthy controls, aged 1-10 years, without other underlyng conditions were included in the research. Mineral concentrations were determined using indirect potentiometric method with ion-selective membrane electrodes. Total calcium concentrations were determined using the spectrophotometric method with ortho-cresol phthalein. HbA1c was determined by the immunoturbidimetric method. The results were edited with the program IBM SPSS Statistics, ver.23. The results of our studies showed statistically lower values of sodium ($p<0.001$), chloride ($p=0.002$) and calcium ($p=0.035$) in patients with T1DM compared to healthy subjects. Also, the correlation results indicated a significant positive correlation of HbA1c with chloride values ($p=0.002$; $r=0.423$) in the group of healthy patients, while in patients with T1D the results indicated a negative significant correlation of HbA1c with chloride values ($p=0,018$; $r= -0.334$). Our results indicate significant lower values of sodium, chloride and calcium in T1DM patients compared to healthy subjects of the same age, as well as correlation of chloride and HbA1c, which indicates the importance of monitoring this marker in relation to good control of T1DM in children aged 1-10 years.

Keywords: type 1 diabetes, mineral status, HbA1c

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Session 1 – Poster presentation *S1-41*

STRENGTHENING THE POTENTIAL OF R-PHYCOCYANIN FROM *PORPHYRA SP*. FOR SUSTAINABLE COLORATION IN THE FOOD INDUSTRIES

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Porphyra sp. (Nori), red algae, is a highly nutritious superfood due to its abundance of vitamins, minerals, antioxidants, and proteins, including R-phycocyanin (R-PC), a purple-coloured phycobiliprotein. However, the limited stability of R-PC poses a challenge to its application in the food industry. This study aimed to purify, characterize, and stabilize R-PC for use as a natural colourant in the food, cosmetic, and pharmaceutical industries. Highly pure R-PC was obtained from Nori flakes, and its trimeric ((αβ)3) structure was determined using SAXS measurements. Far-UV CD spectroscopy revealed the dominant secondary structure to be α-helix, and R-PC was stable in the pH range of 4 to 8. However, thermal treatment at 60 °C had detrimental and irreversible effects on the R-PC's colour and antioxidant capacity (22% residual capacity). Encapsulation within the calcium alginate beads preserved its purple colour and retained its antioxidant capacity (78% residual capacity). Our findings demonstrate the potential of R-PC as a replacement for toxic synthetic dyes and highlight the importance of stabilizing R-PC through encapsulation for its bioactivity and colour preservation.

Keywords: R-phycocyanin, purification, stability, SAXS, CD spectroscopy, calcium-alginate, antioxidant capacity

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Session 1 – Poster presentation *S1-42*

BINDING DETERMINATION OF HUMAN ALBUMIN SERUM WITH SELECTED 4-METHYLCOUMARINS

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Human serum albumin (HSA) is the most abundant plasma protein characterized by its outstanding ligand binding ability. In this study, the interaction of HSA with three derivatives of 4-methylcoumarin was monitored. Selected coumarins were: 7-methoxy-4-methylnaphthalen-2(1H)-one (7K), 7-hydroxy-4-methylnaphthalen-2(1H)-one (8K) and 4,5-dimethyl-7-oxo-7,8-dihydronaphthalen-2-yl acetate (11K). The interaction was followed by spectrofluorimetric titration at three different temperatures (295 K, 303 K and 310 K) and pH was 7,4. The binding activity was determined through the determination of the Stern-Volmer quenching constant (KSV), bimolecular quenching constant (kq), the binding constant (Kb) and the number of binding places. Synchronous spectroscopy and three-dimensional fluorescent spectroscopy were used to monitor conformational changes in the microenvironment near chromophores. A FRET analysis was also conducted with the aim of determining the efficiency of energy transfer (E) and critical distance during protein-ligand interaction. Fluorescence quenching occurred with increasing concentration of coumarins, and the quenching constant of 4-methylcoumarin derivatives with HSA was found to be ~ 1012 M-1s-1. The binding affinity was strongest for 8K and ranked in the order 8K > 11K > 7K. Based on the thermodynamic parameters, the interactions of selected 4-methylcoumarins with HSA are spontaneous and the binding to HAS is mainly via hydrogen bonding and van der Waals forces. Moreover, the selected 4-methylcoumarins slightly changes the microenvironment around the tryptophan and tyrosine residues of HSA. The FRET analysis was used to calculate the distance (r) between HSA and 4-methylcoumarins. The results showed that there is energy transfer from HSA to 4-methylcoumarins and that all distances between 4-methylcoumarins and HSA are less than 4 nm.

Keywords: human serum albumin, binding constant, 4-methylcoumarins, spectrofluorimetric titration

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Session 1 – Poster presentation *S1-43*

EFFECT OF SYNTHESIZED 4-METHYLCOUMARIN BENZOATES ON BINDING TO BOVINE SERUM ALBUMIN

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The interaction of four synthesized 4-methylcoumarin benzoates with bovine serum albumin (BSA) at physiological pH and three temperatures using the fluorescence spectroscopic technique has been investigated in this study. Selected derivatives of 4-methylcoumarin are: 4,8-dimethyl-2-oxo-2H-chromen-7-yl benzoate (14K), 4-methyl-2-oxo-2H-chromen-7,8-diyl benzoate (15K), 4-methyl-2-oxo-2H-chromen-7-yl benzoate (16K) and 4,5-dimethyl-2-oxo-2H-chromen-7-yl benzoate (17K). From the obtained data, the following were calculated: the Stern-Volmer constant (Ksv), bimolecular quenching constant (Kq), binding constants (Kb) and the number of binding sites (n). Analysis of the fluorescence quenching data showed a possible binding is a static process (except for BSA-17K) and the strongest static binding occurs with HAS-14K interaction at a temperature of 310 K (Kq=89,1x1012). According to studied thermodynamic parameters, interaction between selected 4-methylcoumarins and BSA indicates spontaneous process (except for BSA-17K) and involvement of hydrophobic forces. Secondary structure perturbation (caused by the π-$\pi*$ transition of the carbonyl group) in HAS was observed upon selected coumarins binding, as revealed by synchronous and three-dimensional fluorescence spectra results. The distance (r) between the donor (HSA) and the acceptor (substituted 4-methylcoumarin benzoates) was also calculated using FRET analysis and indicates the occurrence of energy transfer. In all cases, the distance of HAS from the 4-methylcoumarins is less than 8 nm.

Keywords: bovine serum albumin, binding constant, 4-methylcoumarin benzoates, spectrofluorimetric titration

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Session 1 – Poster presentation *S1-44*

DETERMINATION OF ANTIOXIDANT AND ANTI-INFLAMMATORY ACTIVITIES OF *ACHILLEA* PLANT EXTRACTS

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The aim of this study was to determine and compare the antioxidant (AA%) and anti-inflammatory activity (AIA%) of two species of the genus Achilles. The first species is the widespread and very well researched Achillea millefolium (M), and the second one is a rare species, that grows in the Balkan Peninsula, *Achillea lingulata* (L). Antioxidant activity was determined by four different methods: DMPD method, determination of reducing power, phosphomolybdenum assay, and H2O2 scavenging assay. While AIA% was determined by protein denaturation assay. Samples were prepared by Soxhlet extraction with 70% ethanol for all the above analyzes and by cold (C.E.) and hot water (H.E.) extraction were used for AIA%. The results of AA% are expressed as equivalents of gallic acid, ascorbic acid, curcumin, and Trolox. The results of AA% obtained by the DMPD method showed higher AA% of *A. lingulata* (82.79±5.42 mg(EAA)/gextract) than *A. millefolium* (43.79±4.42 mg(EAA)/gextract); method of reducing power showed lower IC50 value of the *A. lingulata* (1073.22 µg/mL) than the *A. millefolium* (2817.55 µg/mL), which means that *A. lingulata* shows higher AA%. The results obtained by the phosphomolybdenum assay expressed via Trolox and gallic acid equivalents, show similar AA% of both samples. The H2O2 scavenging assay showed that *A. lingulata* (95.28±2.72%) has a higher AA% than *A. millefolium* (69.01±0.73%). Analysis of AIA% in both samples for the concentration (10 mg/mL) prepared by hot extraction (M.-H.E. 72.80% and L.-H.E. 39.07%) show higher AIA% than the samples obtained by cold extraction (M.-C.E 41.61% and L.-C.E. 32.76%). Also, for the same concentration, the *A. millefolium* (M.-H.E. 72,80% and M.-H.E. 41.61%) showed higher AIA% than the *A. lingulata* sample in the case of hot (39.07%) and also in the case of cold (32.76%) extraction. When analyzing the Soxhlet extracts, the *A. millefolium* (19.83%) showed better AIA% for the concentration of 0.1.

Keywords: antioxidant activity, anti-inmmflamatory activity, *Achillea millefolium*, *Achillea lingulata*, protein denaturation assay, DMPD

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Session 1 – Poster presentation *S1-45*

ANTIOXIDANT AND ANTI-INFLAMMATORY ACTIVITIES OF *MELISSA OFFICINALIS* L. PLANT EXTRACTS

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The use of medicinal plants and herbal medicines is a centuries-old tradition, recent advances in modern therapy have encouraged the use of natural products worldwide against various diseases. The World Health Organization estimates that about 3.5 to 4 billion of the world's population rely on plant resources for medicines. The aim of this work was to investigate and compare the antioxidant and anti-inflammatory activity of *Mellisa officinalis* L. plant extracts obtained by different extraction methods. The antioxidant activity (AA%) was done with three different methods: DMPD method, methods of reduction of Fe(III) and Mo(VI) ion. Anti-inflammatory activity (AIA%) was determined spectrophotometrically, by protein denaturation test. Extracts were prepared by Soxhlet and ultrasonic extraction, with 70% ethanol. The results of AA% are expressed through IC50 values and equivalents of: ascorbic acid, gallic acid, Trolox and curcumin. The results of DMPD method showed that the ultrasonic extract of the *M. officinalis* showed twice as good AA% (IC50 = 1402.43 µg/mL) than the extract of *M. officinalis* obtained by Soxhlet extraction (IC50= 3154.4 µg /mL).The results obtained by the reduction of Fe(III) ion showed that the ultrasonic extract has better AA% (IC50= 1205.65 µg/mL) than Soxhlet extract (IC50 = 2166.52 µg/mL). The results of the Mo(VI) ion reduction method, expressed through the equivalents of the Trolox standard and gallic acid, show that the ultrasonic extract (1131.52±0.06 µg(ET)/gextract; 1065.97±0.04 µg(EGA)/g extract ; 933.43±0.03 µg(EAA)/g extract ; 1183.37±0.15 µg(EK)/g extract) shows slightly higher AA% compared to the Soxhlet extract (578.93±0.09 µg(ET)/g extract; 914.87±0.06 µg(EGA)/g extract; 933.43±0.04 µg(EAA)/g extract; 1015.63±0.01 µg(EC)/g extract). The sample obtained by Soxhlet extraction (36.14%) shows better AIA% compared to the sample obtained by ultrasonic extraction (21.75%).

Keywords: Antioxidant activity, anti-inflammatory activity, Melissa officinalis, protein denaturation assay, DMPD

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Session 1 – Poster presentation *S1-46*

POTENTIALLY NEPHROPROTECTIVE PROPERTIES OF CURCUMIN IN AN ANIMAL STUDY OF ADENINE-INDUCED CHRONIC KIDNEY DISEASE

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Curcumin is a natural polyphenol which is extracted from turmeric powder, the dried rhizome of the *Curcuma longa* L. The aim of this work was to evaluate the effects of curcumin on catalase activity and the inhibition of oxidative damage in an animal model of adenine- induced chronic kidney disease (CKD). In this study 36 male Wistar rats were randomly divided into six groups. The 1st group (control group) was on a standard diet, the 2nd group was the adenine control group, the 3rd group received 5 mg rosuvastatin, the 4th group received 1.25 mg rosuvastatin, the 5th group received 100 mg/kg curcumin and the 6th group received a combination of the reduced rosuvastatin dose and curcumin. Groups 2-6 were on an adenine rich diet (0.75% w/w in feed). The treatment lasted 25 days. Renal catalase activity was measured spectrophotometrically by following the decomposition of hydrogen peroxide. The obtained results showed that the adenine treatment caused a significant decrease of catalase activity (12.05 IU/mg protein) in comparison to the control group (21.41 IU/mg protein). Rosuvastatin, alone or in combination with curcumin did not counteract the processes of oxidative stress. A valuable finding was that there was no significant difference in CAT activity between the control group and the curcumin group (17.7 IU/mg protein) suggesting nephroprotective properties of this bioactive substance. Curcumin may therefore be a promising candidate in prevention or reducing the progression of CKD.

Keywords: curcumin, adenine, catalase, chronic kidney disease

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Session 1 - Poster presentation *S1-47*

MONOCYTE DISTRIBUTION WIDTH (MDW) AS AN EARLY MARKER OF SEPSIS WITH LOW MONOCYTE COUNT - CASE REPORT

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The coefficient of variation of monocyte size - MDW is a hematological parameter which describes changes in the size of circulating monocytes during the sepsis development. This marker of monocyte activation is effective in the early diagnosis of sepsis combined with procalcitonin (PCT). MDW is available on the Beckman Coulter DxH 900 analyzer as part of the complete and differential blood count. A 29-year old female patient was admitted to the Infectious Disease Clinic with suspected sepsis. Different laboratory findings were performed (complete and differential blood count included) according to standard laboratory procedures. An increased white blood cells count (WBC) of 22.90x109/L was observed with increase in the neutrophils percentage of 92.6% (21.2x109/L) and severe thrombocytopenia (platelet number (PLT)- 38x109/L). Although the concentration of monocytes was extremely low, 0.8% (0.2x109/L), the results showed changes in the size distribution of monocytes (MDW=42.51, reference value <20). This was also confirmed by the optical examination of the blood. An increased percentage of unsegmented neutrophils (39% of WBC) was founded. The results of serum protein analysis showed hypoproteinemia (total proteins=46 g/L) with hypoalbuminemia (Albumin=28.7 g/L). After 24 hours clinician asked for serum PCT (PCT=25.19 ng/mL), which also correlated with a suspected sepsis diagnose. Existing biomarkers of sepsis such as PCT are usually performed only if the clinician has a high index of sepsis suspicion. MDW is analyzed within the blood count very fast, at the patient's admission, without any additional costs. We concluded that MDW as an early marker of sepsis has a good correlation with other markers, such as WBC, neutrophils, serum proteins and especially PCT, even when the monocytes count is significantly reduced.

Keywords: sepsis, monocyte distribution width, MDW

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Session 1 – Poster presentation *S1-48*

INVESTIGATION OF RE1-SILENCING TRANSCRIPTION FACTOR AS TRANSCRIPTIONAL REGULATOR IN NEURODEGENERATIVE DISEASE BY MOLECULAR MODELING

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Neurodegenerative diseases (NDs) may cause serious or life-threatening consequences, depending on their types. While the majority of them are untreatable, available treatments mostly help relieve symptoms. There is no known prevention or early treatment which delay the progression of NDs. Repressor element-1 silencing transcription factor (REST) is a transcriptional repressor that regulates the expression of neuronal genes in neural cells and non-neuronal cells. REST has been identified as a crucial transcriptional regulator whose aberrant expression may lead to NDs. Therefore, understanding the mechanism of REST may help improve current treatments for NDs. This study aimed to examine the interactions between proteins associated with neurological disorders and possible isoform structures of REST using molecular modeling techniques. Protein Data Bank (PDB) and AlphaFold databases were used to screen structure isoforms of REST. The molecular docking was performed using AutoDock Vina 1.2.2. The Molecular Dynamics (MD) simulations was calculated using AMBER20 and data analysis was performed with the xmgrace and VMD 1.9 programs. Our findings are expected to support the identification of potential target regions for therapeutic agents in the treatment of NDs.

Keywords: repressor element-1 silencing transcription factor, molecular dynamics, neurodegenerative diseases

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Session 1 – Poster presentation *S1-49*

THIOPURINE S-METHYLTRANSFERASE IN SOUTHEAST ANATOLIA, TURKEY; IDENTIFICATION OF A NOVEL MUTATION (323C>G) IN EXON V

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The *TPMT* gene located on chromosome 6 (6p22.3) is 34 kb long and consists of 10 exons, eight of which encode Thiopurine S-Methyltransferase. It is a cytosolic enzyme which catalyzes the S-methylation of aromatic or heterocyclic sulfhydryl compounds, especially exogenous substances such as 6-tioguanin or 6-MP. The activity of TPMT in humans is extremely variable from one individual to another and divides the population into three categories: A majority group of subjects for whom the TPMT activity is high, a group of individuals for whom the activity is known to be intermediate, and a small group of subjects for whom the TPMT activity is undetectable. Thus, genotyping may become increasingly important in clinical practice because it provides clear benefits to the patient and allows the adaptation of pre-therapeutic doses for patients carrying the mutation. Until now, 46 variants of the *TPMT* gene with low enzymatic activity have been described with three major alleles: TPMT*2 (c.238G > C), *3A (c.460 G > A, c.719A > G), and *3C (c.719A > G), accounting for 80% to 95% of inherited TPMT deficiency in different populations in the world. The aim of the study was to screen a rapid and sensitive method of analysis for all exons of the *TPMT* gene and to determine the spectrum and prevalence of the TPMT variations in the Southeast Anatolia population. Real Time Polymerase Chain Reaction (RT-PCR) melting curve (MCA) analysis was used for screening of *TPMT* exons. In total, 210 alleles were analyzed and 2 different variants (2 cases; TPMT*3A and one unknown) were detected. Unknown case was charecterized a novel mutations in Exon V as *TPMT**47 by DNA sequencing. This newly observed variant is caused by a single nucleotide polymorphism resulting in nonsense mutation (c.323C>G; Ser108Stop) and the partial loss of amino acids in the TPMT.

Keywords: thiopurine S-methyltransferase, 6-methylthioguanine, *TPMT**47

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Session 1 – Poster presentation *S1-50*

VERBASCUM SINUATUM EXTRACT INDUCES CELL DEATH IN K7M2 OSTEOSARCOMA CELLS BY ITS IMMUNOMODULATORY EFFECT ON LPS-STIMULATED RAW 264.7 CELLS

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Osteosarcoma (OS), is the most common primary bone tumor in children and adolescents, has high malignancy and mostly metastasizes to the lungs and other bones. Despite advances in chemotherapy regimens, little progress has been made in osteosarcoma survival. In our study, we aimed to investigate the anti-tumoral effects of *Verbascum sinuatum* extract (VE) on K7M2 osteosarcoma cells and the immunomodulatory effect on LPS-stimulated RAW 264.7 cells. *V. sinuatum* was harvested in the spring and dried at 37°C. The extract was prepared by mixing the whole plant with 80% methanol (v/v) for 24 hours. The total antioxidant capacity (TAC), total phenolic content (TPC), and total flavonoid content (TFC) were measured. For the MTT cell viability assay, different concentrations (50-1000µg/ml) were applied to K7M2 cells. Besides, Raw 264.7 macrophage cells were stimulated with LPS and the VE was applied to analyze the immunomodulatory effect. Then, K7M2 cells were treated with supernatants of macrophage cells. Acridine orange/ethidium bromide and caspase-3 immunofluorescent staining were performed and examined using the fluorescent microscope. According to the results, TPC was 275 mg Eq Gallic acid/g; TFC was 35 mg Eq Quercetin/g, and TAC was 822 mM Eq Ascorbic acid/g. MTT data showed that in 48 hours VE was cytotoxic to the K7M2 cells at 500 and 1000 µg/ml concentrations but not to the Raw 264.7 macrophage cells. In osteosarcoma cells treated with macrophage supernatant, VE must have increased the activity of macrophage cells, since we detected more death of cancer cells on fluorescent images. In conclusion, VE has cytotoxic and apoptotic effects on K7M2 osteosarcoma cells as well as immunomodulatory effects on macrophage cells. However, further studies are required to prove that it could be a potential treatment option.

Keywords: *Verbascum*, osteosarcoma, apoptosis, macrophages, immunomodulation

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Session 1 - Poster presentation *S1-51*

THE IMPORTANCE OF DETERMINING URIC ACID IN THE EARLY DIAGNOSIS OF COVID-19 INFECTION AND THE ASSOCIATION WITH DISEASE SEVERITY

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The disease of COVID-19 is characterized by predominantly respiratory symptoms, although increasing evidence indicates the involvement of multiple organs. Elevated levels of uric acid in serum or hyperuricemia correlate with respiratory diseases and in patients with severe COVID-19 can contribute to acute kidney injury and poor outcomes. The main aim of this study is to determine whether uric acid could serve as a biomarker that would indicate the severity of the outcome in COVID-19 patients. Data needed for this study was obtained from 750 patients that were admitted to General Hospital in Tešanj, Bosnia and Herzegovina. All of the patients in the study were positive for SARS-CoV-2 confirmed by PCR testing. Uric acid was measured on a BT 3500 Biotecnica Instruments in accordance with the IFCC standard protocols. Results showed that for samples of patients with mild, moderate, severe, and lethal cases of COVID-19 levels of uric acid were increased respectively. Values of uric acid were as following: mild cases 251.50 (202.00-337.00), moderate cases 280.00 (208.75-372.50), severe cases 277.50 (219.75-394.50), and lethal cases 349.00 (249.50-489.00). By comparing groups, the statistically significant difference in uric acid levels was found between mild and moderate ($p=0.013$), mild and severe ($p=0.012$), mild and lethal ($p<0.001$), moderate and lethal ($p=0.001$), and severe and lethal cases ($p=0.011$), but not when comparing samples of moderate and severe cases ($p=0.623$). This study shows that it is common for patients hospitalized due to COVID-19 to have disturbed levels of uric acid in their serum, which seems to be associated with both the severity of the disease and the likelihood of progressing to respiratory failure..

Keywords: COVID-19 disease, SARS-CoV-2, biomarkers, uric acid

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Session 1 – Poster presentation *S1-52*

ANTIOXIDATIVE EFFECTS OF MAGNESIUM SULPHATE CONTRIBUTE TO RELAXATION OF HUMAN UMBILICAL VEIN

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Maintaining umbilical circulation is of vital importance for the fetus and a big challenge for therapy. Because of preassumed safety, $MgSO_4$ has very widespread use in obstetrics. Even though the mechanism of its action on the umbilical circulation is not completely understood. This study aimed to check if $MgSO_4$ influences on antioxidative defense system and to determine the correlation of its antioxidative and relaxant effects on isolated human umbilical veins. Isolated segments of the umbilical vein were suspended in isolated organ baths containing Krebs-Ringer solution. The level of antioxidative enzymes (SOD, CAT, GPx, GR) were measured before and after treatment with $MgSO_4$. The effect of increasing concentrations of $MgSO_4$ (0,1-30 mM) in the absence and the presence of potential antagonists (glibenclamide 10 μM, 4-aminopyridine 1 mM, tetraethylammonium-chloride 1mM, $BaCl_2$ 10 μM) was examined on umbilical vessels precontracted with 5-hydroxytryptamine (10μM). $MgSO_4$ induced concentration-dependent relaxation of isolated human umbilical veins precontracted with 5-hydroxytryptamine (ANOVA, $MgSO_4$ concentration effect: $F=10.5$; $p<0.001$). Pretreatment with 4-aminopyridine inhibited the relaxant effect of ($MgSO_4$ ANOVA, pretreatment effect: $F=6.6$; $p<0.01$). Pretreatments with glibenclamide, tetraethylammonium-chloride, and $BaCl_2$ did not change the MgSO4 effect. Treatment of isolated umbilical veins by $MgSO_4$ increased the activity of CAT, which was even more emphasized in HUV pre-treated with 4-aminopyridine, a selective blocker of Kv channels. Treatment with $MgSO_4$ induced decreasing of GPx and GR in the human umbilical vein. SOD activity was not changed after treatment with $MgSO_4$. Pretreatment with 4-aminopyridine antagonized the relaxant effect of $MgSO_4$ on the human umbilical veins and increased the activity of CAT. It indicates the overlapping of receptor and metabolic influence of MgSO4 at the Kv signal pathway. 4-aminopyridine-induced reversion of the MgSO4 relaxant effect is followed by increasing H_2O_2 and suppression of the glutathione-dependent antioxidative enzymes GPx and GR.

Keywords: antioxidative effect, antioxidative enzyme, magnesium sulphate, human umbilical vein, Kv channels

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Session 1 – Poster presentation *S1-53*

CHARACTERIZING IGG GLYCOSYLATION PATTERNS IN MS PATIENTS: A PURIFICATION APPROACH

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MS is a chronic inflammatory disease that causes demyelination throughout the central nervous system. The detection of oligoclonal bands (OCBs) in cerebrospinal fluid (CSF) using isoelectric focusing (IEF) is the gold standard method for MS diagnosis. However, its limited sensitivity necessitates the identification of accurate biomarkers, with IgG protein glycosylation motifs showing potential as such markers. The aim of this preliminary study was to isolate IgG proteins from serum and cerebrospinal fluid (CSF) samples using an IgG affinity matrix for subsequent glycomics analysis in MS patients. In this study, IgG proteins from MS patients and controls serum and CSF samples were isolated and typed for OCBs using the IEF technique. IgG's were purified with the IgG affinity matrix and quantified with A280 measurement on a Nanodrop One. The IgG's heavy and light chains were separated with TCEP and analyzed for presence, structure, and purity using SDS-PAGE and MALDI-TOF analysis. IgG proteins were isolated and purified from serum and CSF using an IgG affinity matrix and typed for OCBs with IEF analysis. The purified IgG's heavy and light chains were separated and analyzed using SDS-PAGE and MALDI-TOF analysis. The light chains were found to have a size of 25 kDa, while the heavy chains had a size of 55 kDa in SDS-PAGE. The presence of lambda and kappa chains for both heavy and light chains was confirmed in the 11400-11800 m/z range using MALDI-TOF analysis. $[M+2H]^{+2}$ -$[M+5H]^{+5}$ forms of IgG were also detected in the 10000-26000 m/z range. In conclusion, the IgG affinity matrix shows promise for glycomics analysis in MS patients, with the potential to identify measurable biomarkers for early diagnosis and treatment. Further large-scale studies are needed to validate the use of IgG protein glycosylation motifs as MS diagnostic biomarkers.

Keywords: multiple sclerosis, immnuglobulin G, IgG purification, MALDI-TOF

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Session 1 – Poster presentation *S1-54*

THE IMPORTANCE OF DETERMINING TOTAL PROTEINS AND ALBUMIN IN THE EARLY DIAGNOSIS OF COVID-19 INFECTION AND THE ASSOCIATION WITH THE DESEASE SEVERITY

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Proteins represent the major building blocks of body tissues, and they regulate signaling involved in most cellular activities. Coronavirus disease 2019 (COVID-19) infection has been connected with high fatality. The main cause of death is pulmonary tissue damage and multiple organ failure. Previous studies have shown that serum total proteins and albumin levels were abnormally low in COVID-19 patients and might be used as a prognosis biomarker. The disease is associated with a hypercatabolic state that entails excessive protein loss. In our study, we were included 750 patients recruited at the General Hospital Tešanj, Bosnia and Herzegovina. Total proteins and albumins were measured on a BT 3500 Biotecnica Instruments in accordance with the IFCC standard protocols. All subjects included in this study were positive for SARS-CoV-2, which was confirmed by RT-PCR test. Patients involved in our study were divided into four groups according to the severity of the clinical picture: mild, moderate, severe and fatal outcome. The results showed that the levels of total proteins and albumin decreased with increasing severity of the clinical picture. The results of our study indicate significantly lower levels of total proteins between patients with a fatal outcome and patients with a moderate ($p=0.002$) and mild clinical picture ($p<0.001$) retrospectively. Albumin levels were also significantly lower in patients with a fatal outcome compared to patients with a mild clinical picture ($p<0.001$), as well as significantly lower values between patients with a severe clinical picture and patient with mild clinical picture ($p<0.001$), and lower albumin levels between patients with moderate and patients with mild clinical picture ($p<0.001$). These findings suggest that low levels of total protein and albumin may be useful indicators of the severity and prognosis of COVID-19 infection.

Keywords: COVID-19, total proteins, albumin, prognosis, early diagnosis

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Session 1 – Poster presentation *S1-55*

END STAGE RENAL DISEASE, HEMODIALYSIS AND THEIR EFFECTS ON HEMOGRAM PARAMETERS

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End-Stage Renal Disease (ESRD) is diagnosed when the kidneys are no longer able to function adequately, resulting in the need for kidney transplantation or hemodialysis (HD) or Peritoneal Dialysis. The word dialysis is the combination of two Greek words dia and lysis, meaning "through," and "splitting.", respectively. The first attempt on humans was in 1924, and by that time, its saving lives for a century. It affects nearly 3.500.000 people in the United States and 70.000 in Turkiye. In patients with ESRD and hemodialysis, chronic volume overload is unfortunately common. Sodium goes to retention in body space, and this process goes to volume load and hypertension. Ultrafiltration is a method for hemodialysis patients for overcoming volume overload, but this situation goes with normal sodium levels, most of the time. The Volume, Conductivity and Scatter (VCS) technology of Coulter LH780 hematological analyzer (Beckman Coulter, CA) can analyze data of WBC and by this “analyzed” data, we can obtain the changes in the volume of the neutrophils (MNV), lymphocytes (MLV), eosinophils (MEV) and basophils (MBV). This was a retrospective study conducted at Selcuk University Medical Faculty, between January 2023 and May 2023. All patients had ESRD and were having dialysis in the clinic of nephrology. The control group was healthy subjects, who were applied to the family medicine outpatient clinic for a general examination. Hematological parameters were performed in Coulter LH780. A total of 25 patients and 25 controls enrolled in the study; the mean age was 58 for the control group and 56,44 for patients. Urea, Creatinine, ALT, Phosphor, Potassium, Ferritin and MLV levels were found to be higher in the patient group ($p<0,05$). With further investigations by higher participant numbers, MLV values could be used to determine the volume load in ESRD patients with normal sodium values.

Keywords: end-stage renal disease, hemogram parameters, hemodialysis, hypertension, volume load

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Session 1 – Poster presentation *S1-56*

CLINICAL SIGNIFICANCE OF SERUM SOLUBLE LECTIN-LIKE OXIDIZED LOW-DENSITY LIPOPROTEIN-1 AND CAROTID INTIMA-MEDIA THICKNESS IN THE EVALUATION OF ENDOTHELIAL DYSFUNCTION IN TYPE 2 DIABETES MELLITUS

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Lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) is regarded as a central element in the initiation of endothelial dysfunction (ED). LOX-1 has been implicated as a key causative of a number of cardiovascular diseases. LOX-1 is viewed as a biomarker of ED. Measurement of soluble LOX-1 (sLOX-1) may provide a novel diagnostic tool for the prediction of ED. Since endothelial dysfunction is a very early step in atherogenesis, we investigated whether sLOX-1 could be a novel diagnostic tool for the prediction of ED in patients with type 2 diabetes mellitus (DM) without cardiovascular disease. We evaluated relationship of serum sLOX-1 with carotid intima-media thickness (CIMT). The three groups; DM with cardiovascular diseases (Group I), DM without cardiovascular diseases (Group II) and control were comprised. CIMT were measured on ultrasonography images. Serum oxidized low density lipoprotein (oxLDL), sLOX-1 levels and paraoxonase-1 (PON-1) activity were measured from collected blood samples. All statistical comparisons were performed using the analysis of variance was used to compare multiple-group means. OxLDL, sLOX-1 levels were significantly higher in the Group I and Group II than in the control ($p<0.001$). sLOX-1 levels were significantly higher in the Group I compared with the Group II ($p<0.01$). PON-1 activity were significantly lower in the Group I and Group II groups than in the control ($p<0.001$). There were no significant differences between the Group I and Group II. CIMT were significantly higher in the Group I and Group II than in the control ($p<0.001$) but were significantly higher in the Group I compared with the Group II ($p<0.01$). There was a significant positive correlation between sLOX-1 and CIMT in Group I and Group II. Conclusion: sLOX-1 levels could be strong biomarker for determining early endothelial damage in DM patients without cardiovascular diseases.

Keywords: carotid intima-media thickness, endothelial dysfunction, lectin-like oxidized low-density lipoprotein receptor-1, type 2 diabetes mellitus

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Session 1 – Poster presentation *S1-57*

TRANSFER OF METAL IMPURITIES DURING THE MECHANOCHEMICAL SYNTHESIS OF PRAZIQUANTEL COCRYSTALS, POLYMERIC DISPERSION AND CYCLODEXTRIN COMPLEX

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Mechanochemical synthesis by grinding is a versatile, environmentally friendly chemical approach able to address the problems of limited drug solubility and associated low oral bioavailability through the preparation of amorphous drug forms or their cocrystals, polymeric dispersions and cyclodextrin complexes. However, wearing of the grinding apparatus during the mechanochemical synthesis may introduce metal impurities into the products obtained. The presence of metal impurities in pharmaceutical products is of great concern, as may lead to significant toxicity upon administration and/or negatively affect the chemical stability and shelf life of the product by catalysing the degradation of the drug and/or excipients used in the formulation, thus their content must be monitored. In this work, praziquantel (PZQ) was co-ground with malic acid, poloxamer F-127, and hydroxypropyl-β-cyclodextrin to obtain cocrystals, dispersions and inclusion complexes able to improve the low oral bioavailability of the commercially available anhydrous Form A of the drug. Grinding was performed in stainless steel and agate jars with a ball of the same material at different processing times (30 and 90 minutes) to systematically study the transfer of potential impurities from the grinding apparatus to the final products. The metal impurities present in the obtained products were quantified by inductively coupled plasma mass spectrometry. The results obtained show that products obtained in an agate-based setup contain a smaller amount of metallic impurities than those prepared using stainless steel-based apparatus under the same grinding time. It should be noted that only one sample, produced using stainless steel apparatus, showed an increase in the content of elemental impurities (Cr and Fe) due to an increase in the reaction time. For all other samples, the elemental contents are generally similar regardless the grinding time applied and was mostly introduced into the products through the reactants.

Keywords: metal impurities, mechanochemical synthesis, cocrystals, polymeric dispersions, cyclodextrin complexes

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Session 1 – Poster presentation *S1-58*

IL-1B SERUM CONCENTRATIONS IN COVID-19 PATIENTS AND ASSOCIATION WITH THE DISEASE SEVERITY

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COVID-19, caused by the SARS-CoV-2 virus, has been associated with cytokine storm, a state described as intense production of cytokines in infectious processes responsible for triggering immunological and pathological reactions. The aim of our study was to evaluate serum concentrations of an important cytokine, interleukin-1β (IL-1β), as one of a key mediator, and therefore biochemical marker, of the inflammatory response, and its correlation with disease severity. The study included 174 positive COVID-19 patients with different disease severity ("mild", "moderate" and "severe and ex letalis patients"). Patients were recruited at the time of admission to the General Hospital Tešanj, Bosnia and Herzegovina. Interleukin-1β (IL-1β) levels in serum samples were analyzed using ELISA assay kit by DRG Instruments GmbH, Germany. In our study, statistical analysis showed that IL-1β levels were highest in the group of patients with severe disease severity and ex letalis paitents (10.48 ± 2.93), while the lowest values were in the group of patients with the mild disease severity (4.49 ± 0.69). Our results showed that IL-1β levels were 9.77 ± 3.22 in group of patients with moderate disease severity. IL-1β levels did not show statistically significant difference between these groups of patients ($p > 0.05$). COVID-19 patients have an abnormal levels of various cytokine, among them interleukin-1β, as indicated by the results of biochemistry markers. Our results showed that the serum levels of IL-1β have no statistical significance between COVID-19 patients with different disease severity but also showed that patients with mild clinical outcome had lowest values. Further studies are needed to investigate the underlying mechanisms of cytokine storms and its effect on clinical outcomes in COVID-19 patients.

Keywords: COVID-19, SARS-CoV-2, Interleukin-1β, ELISA assay

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Session II -
Molecular genetics
Genetics & Applications

Session 2 – Oral presentation *S2-01*

GENOME EDITING IN PLANTS: ADVANCES AND APPLICATIONS IN AGRICULTURE

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As a result of the development of genome editing techniques, a real revolution has taken place in biotechnology and genetic engineering. Targeted editing of live organisms' genomes enables research into the fundamental principles underlying biological systems as well as the pursuit of a wide variety of objectives aimed at enhancing crop production and quality. Zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and clustered regularly interspaced short palindromic repeats/Cas9 (CRISPR/Cas9) are a few of the innovative genome editing technologies that have been created in recent years. Among them, CRISPR/Cas9 gene-editing technology has matured and has been widely used for crop improvement. The CRISPR/Cas9 gene-editing system has been a critical step in influencing the effectiveness of plant molecular breeding, with recent research focusing on improving gene-editing efficiency. Through its two-component system, CRISPR/Cas is capable of performing a wide range of genetic operations in plants, including targeted gene insertions, deletions, and substitutions. Among the CRISPR/Cas technologies used for genome editing, Cas9, Cas12, and Cas13 systems are widely utilized in biology and agriculture. In addition to the Cas systems, the new high-precision genome editing tools, base editors, and prime editors that can alter a genome in living cells without generating double-stranded breaks in DNA and without relying on a donor have been improved. The CRISPR/Cas technology is becoming an important tool in improving certain traits of crops, such as yield, plant architecture, nutrient composition, disease resistance, and adaptation to different stresses. CRISPR/Cas technology has undoubtedly become a breakthrough tool for plant research and has definitely revolutionized both agriculture and plant biotechnology, and will continue to do so.Grant References: Science Fund of the Republic of Serbia, PROMIS, grant number 6060866, ROLERS.

Keywords: Gene editing technologies; CRISPR/Cas9, Plant molecular breeding, Crop improvement

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Session 2 – Oral presentation *S2-02*

Biopsies in cancer diagnosis monitoring and prognosis

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Liquid biopsy with circulating tumor DNA (ctDNA) profiling by next-generation sequencing holds great promise for clinical oncology. Analysis of ctDNA in plasma reduces the risk of missing clinically-actionable mutations in cancer patients due to tumor heterogeneity. Moreover, as blood draws for liquid biopsy are minimally invasive, there is little potential for either inadequate material for analysis or complications arising from obtaining the needed sample.Profiling ctDNA by NGS technologies is becoming more and more popular since it can be applied in the whole process of cancer diagnosis and management. NGS-based Plasma-Safe-SeqS (PSS) cell-free DNA (cfDNA) detection platform delivers unparalleled dynamic range enabling high resolution of treatment response providing deeper insights into efficacy of new therapies. Flexibility and utility of PSS facilitates treatment selection at diagnosis and early detection of resistance to therapy. Next-generation sequencing (NGS) offers the sensitivity and specificity that researchers need to detect low levels of ctDNA in the bloodstream. In addition to targeting a single gene or a subset of genes, NGS can also identify genome-wide tumor-derived alterations in ctDNA.

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Session 2 – Oral presentation *S2-03*

SOME MOLECULAR, BIOCHEMICAL AND NUTRITIONAL ASPECTS OF HUMAN OBESITY – CASE STUDY FROM N.MACEDONIA

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Pandemic surge of obesity is becoming a concern for the civilization. The number of overweight and obese people is growing dramatically. The analysis of WHO data for North Macedonia shows an increasing trend in BMI among young people and an increasing percentage of young people who fall in the overweight and obese categories. Obesity is a result of multiple factors including nutritional, genetic, environmental and behavioral. Genetic factors play an important role in obesity. More than 300 genes and chromosomal regions have been found to be associated with various human obesity phenotypes. In our study we included four so-called obesity genes. One of the first identified candidate genes related to obesity is the fat mass and obesity gene (FTO). PPARγ gene encodes a peroxisome proliferator-activated nuclear gamma receptor. Polymorphism in FABP2 (fatty acid binding protein) is also causative factor of obesity. Beta3-adrenergic receptor gene (*ADRB3*) has been associated with body weight disorder and obesity, whose protein is located mainly in adipose tissue.. This receptor has an important role in the regulation of lipolysis and thermogenesis and causes a difference in energy consumption. The relationship between the ADRB3 polymorphism and BMI has been controversial. In our study, we have analyzed the association between the Trp64Arg polymorphism in the *ADRB3* gene and anthropometric and biochemical parameters. The sample consisted of 110 youngsters from North Macedonia. Obesity was measured using the body mass index (BMI) and weight groups were determined according to the World Health Organization (WHO) guidelines. Other anthropometric measurements were recorded and waist/hip ratio was calculated. The biochemical analysis of glucose, total cholesterol and triglycerides were also part of the study. Genotyping for the *ADRB3* polymorphism was performed by the PCR-RFLP method. Tukey's Honest Significant Difference test was used to test each pair of groups for the genotypes where ANOVA showed statistically significant differences among groups. ADRB3 polymorphism is a potential risk factor for body weight disorder.

Keywords: *ADRB3* gene, polymorphism, anthropometry, biochemistry

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Session 2 – Oral presentation *S2-04*

MOLECULAR MECHANISMS OF ALZHEIMER'S AND NIEMANN-PICK TYPE C DISEASES: SIMILARITIES AND DIFFERENCES

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Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder, and the major cause of dementia worldwide, which develops in the elderly population, usually after the age of 65. This is the so-called late-onset AD. In contrast, an early-onset AD develops in individuals who harbour a mutation in one of these three genes - APP, PS1 or PS2 - sometimes at 25 years of age. The most prominent clinical characteristic of AD is a progressive cognitive decline, which is first manifested as a loss of ability to form new memories. Therefore, an area of the human brain which first develops AD-type neuropathology is hippocampus, the brain region that plays a key role in learning and memory. The first disease-modifying treatment for AD called lecanemab was approved in January 2023. However, as lecanemab only slows-down the progression of the disorder, it may be considered that AD is still an incurable disorder. Niemann-Pick type C (NPC) disease is a rare, neurodegenerative disorder, which develops mostly during childhood in individuals who have a mutation in the *NPC1* gene. One of the most prominent early clinical characteristic of NPC disease is ataxia. Therefore, an area of the brain which is firstly affected by the NPC-type neuropathology is the cerebellum. NPC disease is an incurable disease, despite cyclodextrin use for the treatment of the disease in cat and mouse models of it. Although different at first glance, both AD and NPC disease share a common neuropathological pathway: both are characterised by accumulations of amyloid plaques, formed by amyloid-beta (A-beta) peptides, and neurofibrillary tangles, formed by hyperphosphorylated microtubule associated protein tau (MAPT). This presentation will provide an overview of both AD and NPC disease, and describe in vitro and in vivo experiments used for understanding of their molecular mechanisms.

Keywords: Alzheimer's disease, Niemann-Pick type C disease

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Session 2 – Oral presentation *S2-05*

GENETICS OF THERMAL STRESS TOLERANCE IN BREEDING ANIMALS

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Climate change is one of the biggest global concerns regarding livestock production. The negative impacts of climate change on the welfare and production of breeding animals are numerous. It leads to losses of pastures and reduction of water resources, outbreaks of diseases and infectious agents, all of which negatively influence the quantity and quality of animal products and cause financial burdens. Climate affects livestock growth rates, reproduction, milk and egg products, morbidity, and mortality. When the ambient temperature exceeds the upper or lower critical values of the internal temperature of animals, a special form of stress called thermal stress occurs. It is accompanied by damage to intracellular structures, i.e. essential macromolecules such as proteins and lipoproteins, DNA and RNA, as well as changes in gene expression patterns. The detection of genomic regions, whose activation is mediated by climate, is one of the central research topics in evolutionary biology, with the potential to illuminate the genetic basis of adaptation and tolerance to climate change. The identification of such genetic markers is necessary for the selection of superior breeds that can survive in different agroecological zones. There are over 400 genes that are associated with the response to temperature change. This paper aims to review the potential biomarkers responsible for adaptability traits, which can be further used for the selection of animals tolerant to thermal stress in the changing climate scenario.

Keywords: Thermal Stress, Climate Change, Genetic markers, Animals

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Session 2 – Oral presentation *S2-06*

INFLUENCE OF THE ACE2 GENE POLYMORPHISM (RS2285666) ON COMPLETE BLOOD COUNT

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COVID-19 can cause a wide range of symptoms, from mild to severe, and can be fatal in some cases. The ACE2 (angiotensin-converting enzyme 2) gene is a human gene that encodes the ACE2 protein, which is a receptor found on the surface of human cells that plays a crucial role in regulating blood pressure and cardiovascular function. The aim of the study was to investigate the influence of the *ACE2* gene polymorphism (rs2285666) on complete blood count (CBC), especially on red blood cell (RBC) count (RBC) and hemoglobin (Hb) levels. The study included 750 positive COVID-19 patients recruited at General Hospital Tešanj. Patients were divided into 3 groups (mild, moderate, and severe). DNA was extracted from whole blood and stored at -20°C. Genotyping was performed using Applied Biosystems QuantStudio5 RT-PCR System. Our results showed that in the group of patients with a mild clinical picture carriers of the CC genotype (136.54±1.41) showed an association with significantly higher Hb levels (p=0.015) compared to carriers of the CT genotype (128.03±3.65). In the group of patients with the moderate clinical picture, carriers of the CC genotype (4.32±0.04; 132.44±1.32) showed an association with significantly higher values of RBC count (p=0.002) and Hb levels (p=0.001) compared to carriers of the CT genotype (4.08±0.08; 124.11±2.39). In the group of patients with the severe clinical picture, carriers of the TT genotype (4.61±0.13) showed an association with significantly higher values of RBC count (p=0.005) compared to carriers of the CT genotype (4.14±0.10). In the same group of patients, carriers of the CC genotype (133.52±1.50) showed an association with significantly higher Hb levels (p=0.002) compared to carriers of the CT genotype (123.70±3.10). The rs2285666 polymorphism was associated with RBC count and Hb levels in COVID-19 patients.

Keywords: COVID-19, SARS-CoV-2, complete blood count, red blood cell, hemoglobin

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Session 2 – Poster presentation *S2-07*

BOSNIAN UNEXPLAINED ABORTIONS (BUNA) AND PGR GENE POLYMORPHISM OF RS1042838

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It is estimated that infertility affects 50 to 80 million couples worldwide. At Caucasian population 10-14% of the clinically diagnosed pregnancies ends with spontaneous abortion (SA). Approximately 50% of SA remains unexplained, which creates problems in therapy and is a challenge for public health. As a possible cause of SA autoimmune, metabolic and abnormal karyotype are suggested. Among the explored factors the selected gene variants were examined. The progesterone receptor (PGR) encoded by the PGR gene is expressed the most in the endometrium and plays an important role in many reproductive pathways, including: oocyte maturation, preparation of the uterine lining for egg implantation, and maintenance of pregnancy at an early stage. Due to inconsistent results of PGR variants in the survival of pregnancy we investigated the potential association of PGR rs1042838 (known as: 1978G>T, c.3432G>T or Val660Leu) with SA in Bosnian women. We enrolled 308 women: 154 with SA, mean age 33 (±5.4) yr. and 154 mothers, mean age 31.4 (±6.7) yr., with at least one live-born child, as a control group. The PGR rs1042838 was genotyped using TaqMan SNP assay. The prevalence of genotypes GG, GT, TT in the group with and without SA were: 72.8%, 22.7%, 4.5% and 61.0%, 34.4%, 4.6%, respectively. The distribution of rs1042838 variants was not significantly linked to the number of SA, ($\chi 2$=1.848; p=0.933). Due to the different prevalence of genetic variants between populations, PGR variants might be a marker of SA only in selected populations. The confirmation of rs1042838 PGR as a genetic marker of SA requires further studies involving larger groups, due to the fact that in many populations the studied variant is rare.

Keywords: pregnancy loss, PGR, rs1042838, single nucleotide polymorphism

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Session 2 – Poster presentation *S2-08*

LGALS3 RS4644 GENE POLYMORPHISM IS ASSOCIATED WITH OBESITY RELATED METABOLIC TRAITS IN SERBIAN ADOLESCENT POPULATION

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Among many genes which have been analyzed to understand obesity and related metabolic traits among children and adolescents, not many studies are conducted on *LGALS3* gene, especially in the population of children. Previous researchers have found a positive correlation between circulating galectin 3 serum levels in the general population with impaired blood glucose, and high blood pressure as well as with higher values of serum lipids and obesity Also, galectins promote preadipocytes maturation into the lipid-loaded adipocyte, which might contribute to central obesity. One of the single nucleotide polymorphisms (SNP) within the *LGALS3* gene that affects the function of galectin 3 as a transcriptional co/regulator is rs4644 (c.191C>A, p.Pro64His). The aim was to investigate an association of rs4644 with BMI, glycaemia, and lipid profile in Serbian adolescents. The study included 76 boys and 83 girls, 14-15 years of age. Among boys 51 (67.1%) had normal values of BMI, 11 (14.5%) were overweight, and 14 (18.4%) were obese. Among girls, 53 (63.9%) had normal BMI, 16 (19.3%) were overweight, and 14 (16.9%) were obese. Diabetes type 1 or 2, genetic syndromes, generalized inflammation, cardiovascular and malignant diseases were criteria for exclusion. Genotyping was performed by real-time PCR. The frequency of CC genotype was 91 (57.2%), CA 51 (32.1%), and AA 17 (10.7%). Girls carriers of CC genotype had statistically higher mean values of BMI, and triglycerides in comparison to the girls carriers of CA+AA genotypes, p=0.028, and p=0.036, respectively. A higher frequency of obesity was found among group of girls who were carriers of CC genotype, p=0.039. No statistically significant association was observed among other analyzed parameters in either examined group. Our research indicates that there is an association between the CC genotype of rs4644 polymorphism with obesity and higher triglyceride levels in the group of female adolescents.

Keywords: LGALS3, rs4644, lipid profile, BMI

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Session 2 – Poster presentation *S2-09*

SWOT ANALYSIS IN MOLECULAR DIAGNOSTICS: STUDY CASE BASED ON COVID-19 PANDEMIC

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Currently, the healthcare sector and ultimately laboratory organizations are using clearly defined business management concepts. Many managers utilize SWOT analysis as a foundation for company growth, but it's sometimes questioned what it should look like in emergency scenarios such as a pandemic. Through this research, we intend to demonstrate the best methods for handling crisis circumstances while also determining the most applicable reagents to use in the diagnosis of SARS-CoV-2 pathogen (COVID-19). A SWOT analysis was employed as a method to determine the organization's strengths, weaknesses, opportunities, and threats from an economic and health perspective, respectively. With this unique analysis, we obtained an objective evaluation of the entire engagement and activity in laboratories for molecular diagnostics in crisis situations, which pointed out the biggest threat - the selection of adequate detection kits. Due to that, a comparison of three SARS-CoV-2 detection kits was conducted on 30 randomly selected positive samples. After the Real-time PCR analyzes were conducted, and the Ct-values were obtained, the coefficient of variation (CV) was calculated for each sample. The results showed a CV of slightly above 10% for all three analyzed kits and showed a high degree of similarity in the sensitivity for SARS-CoV-2 detection, which indicates that the diagnostic accuracy of the three assays is comparable. Additionally, in the conditions of a pandemic, when the correct qualitative detection was of the highest priority, the three different SARS-CoV-2 tested kits successfully detected the targeted gene sequences of SARS-CoV-2.

Keywords: Strengths-Weaknesses-Opportunities-Threats analysis (SWOT analysis), COVID-19, molecular diagnostics, laboratory management, Real-time PCR

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Session 2 – Poster presentation *S2-10*

MUTATION RATES OF 22 AUTOSOMAL STR LOCI IN A EUROPEAN POPULATION FROM CENTRAL BALKAN, REPUBLIC OF SERBIA

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Analysis of short tandem repeats (STRs) is a tool for human DNA identification, including paternity and criminal investigations. Locus-specific STR mutation rates are critical for interpretation of DNA identification in practice. Accumulating evidence suggests that STR mutation rates are population-specific. However, STR mutation rates based on trios have not been analyzed in European population yet. In this study, mutation rates of 20 CODIS and two additional autosomal STR loci (Penta E and Penta D) were determined from 1279 cases of paternity testing in the Serbian population, and the relationships between STR mutation rates and sex, allele length, and heterozygosity were investigated. A total of 63 mutations were observed at 18 loci in a total of 28278 allele transmissions, including 62 (98.4%) single-step and 1 (1.6%) two-step mutations. The average mutation rate was 1.7×10-3 (95% CI: 1.3-2.3×10-3), whereas locus-specific mutation rates ranged from 5.6×10-3 (D12S391) to 0.6×10-3 (D2S1338, D5S818, and D21S11). No mutation was observed at the TPOX, TH01, D16S539, and D22S1045 loci. The mutation rate of paternal origin (2.4×10-3) was eight times higher than that of maternal origin (0.3×10-3), and long alleles mutated more frequently than short and medium alleles ($\chi2$=4.436 and $\chi2$=4.646, respectively, $p<0.05$). No differences were found when analyzing overall expansion versus contraction ($\chi2$=0.999, p=0.317). Among short alleles two expansions and no contraction were detected, while among long ones three expansions and nine contractions were observed. Furthermore, we found no correlation between locus-specific mutation rates and corresponding heterozygosity (rs=-0.188, p=0.559). Comparisons between populations revealed statistically significant differences in locus-specific mutation rates of 13 CODIS STRs between Serbian population and Chinese or Brazilian. Our results show that STR mutation rates depend on sex, allele size and population, and provide useful data on STR mutation rate based on trios for human DNA identification in European populations.

Keywords: short tandem repeat (STR), mutation rate, paternity testing, DNA identification, population data

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Session 2 – Poster presentation *S2-11*

THE COMMON SEXUALLY TRANSMITTED DISEASES QUALITATIVELY DETECTED BY MULTIPLEX REAL TIME PCR REACTION IN THE FEMALE POPULATION OF BOSNIA AND HERZEGOVINA

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Sexually transmitted diseases (STDs) or sexually transmitted infections (STIs), have been recognized as a public-health problem in expansion. More than 30 bacterial, viral, and parasitic agents have been identified that can be transmitted by sexual contact and cause one of the infectious diseases. The aim of this study is the presentation of the prevalence of STDs in the female population of Bosnia and Herzegovina analyzing 200 biological samples from February 2019 to February 2023. Multiplex real time PCR was used as an instrumental method for STD detection. Molecular testing leads to detection and treatment of symptomatic and asymptomatic patients more effectively, which also interrupts the epidemiological transmission chain without delay. Cervical swabs were tested for the presence of Neisseria gonorrhoeae, Chlamydia trachomatis, Trichomonas vaginalis, Ureaplasma urealyiticum, Ureaplasma parvum, Mycoplasma genitalium, and Mycoplasma hominis in a single reaction. Our results show the highest prevalence of Ureaplasma urealyiticum bacteria in the female population of Bosnia and Herzegovina. The conclusion of this study is that real time PCR is highly sensitive, specific and cost-effective instrumental analysis for the detection of certain STDs. Also, this study shows that massive testing could raise awareness of the population about the importance of early detection and even STD prevention.

Keywords: Sexually transmitted diseases, STDs, STIs, Multiplex Real time PCR, Molecular testing, Screening

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Session 2 – Poster presentation *S2-12*

ANALYSIS OF GENOME COPY NUMBER VARIATIONS IN CHILDREN WITH DEVELOPMENTAL SPEECH AND LANGUAGE DISORDERS

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Accomplishment of an adequate function of speech and language represents one of the key aspects of human developmental milestones. However, in the last few years, there has been an increasing trend in the rate of delays and disorders in speech and language development. It is considered that more than 7% of preschool children have some sort of delayed and unformed speech. The presence of copy number variations represents a special entity and its identification plays an important role in the clarification of complex etiopathogenesis of developmental dysphasia. Our aim was to evaluate the diagnostic contribution of molecular karyotipisation in children with developmental disorders of speech and language and to analyze the phenotype of children with confirmed clinically significant copy number variations. Children who were referred for genetic testing in 2020. to 2023. predominantly due to delayed speech/language development, the insufficient effect of speech therapy or speech or language regression were included in our study. Data about the presence of facial dysmorphism, delay in motor development, autistic spectrum disorder phenotype and the presence of developmental delay of speech or language in the family were recorded. Molecular karyotyping was performed by array CGH method on 8x60k slides. Our study included 119 children (95 boys and 24 girls) with a mean age of 5.11±2.4. The detection rate of clinically significant copy number variations was 10.9%. We also observed that children with positive results were statistically more likely to have facial dysmorphism (p=0.002) or delayed motor development (p=0.014). Considering the results obtained, speech and language developmental delay should be an indication of molecular karyotipisation. Additionally, it is necessary to increase the awareness of doctors and parents of the patients about the importance of genetic testing in discovering the etiology of this disorder.

Keywords: copy number variations, molecular karyotipisation, developmental delay of speech and language

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Session 2 – Poster presentation *S2-13*

ALTERED PDZD3, P2RY4, GUCA2B AND TNFSF15 GENE EXPRESSION IN TISSUE OF PATIENTS WITH THE IRRITABLE BOWEL SYNDROME

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Previous research have shown that inflammation and immunological changes may be relevant in etiopathogenesis of Irritable Bowel Syndrome (IBS). In this study an expression analysis was performed for four genes: *TNFSF15, P2RY4, GUCA2B* and *PDZD3.* Altered expressions of these genes were found in colon biopsy in patients and were linked to the occurrence of IBS. The aim of this study was to determine is there a difference in the expression of *TNFSF15, P2RY4, GUCA2B* and *PDZD3* genes between different types of biological samples (blood and biopsy) in the group of patients with IBS and in the control group. Total RNA was isolated from blood (20 patients and 9 healthy volunteers) and tissue (9 patients and 7 healthy volunteers), and used for relative gene expression by real-time PCR. The relative expression between these two groups have been calculated with statistical iteration using REST. Increased gene expression in biopsies compared to the blood samples in the patient group was confirmed at a significant level for all four genes: *PDZD3* (P=0.021), *P2RY4* (P=0.043), *GUCA2B* (P=0.002) and *TNFSF15* (P=0.001). Comparing the difference in gene expression between blood and tissue in the control group, increased expression of *TNFSF15* (P=0.001) and *GUCA2B* (P=0.001) genes could be observed. Changed expression of *P2RY4* and *PDZD3* genes was found only in the tissues of patients, and not found in the control group. This leads to the conclusion that the up-regulation of *P2RY4* and *PDZD3* is associated with the occurrence of IBS. The up-regulation of *GUCA2B* and *TNFSF15* is not necessarily related to IBS and the protein products are regularly expressed in tissues in large amounts.

Keywords: gene, gene expression, Irritable Bowel Syndrome

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Session 2 – Poster presentation *S2-14*

CELLULAR PARABIOSIS: IMPACT OF THE CELLULAR ENVIRONMENT ON PHENOTYPE EXPRESSION

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Aging is a complex physiological process characterized by a progressive loss in physiological function and the emergence of age-related diseases. Much of the contemporary aging research focuses on cell-autonomous processes such as oxidative stress and impaired proteostasis, which are thought to be responsible for age-related diseases. However, non-cell autonomous processes may also play a role in the development of age-related phenotypes. We named such an impact of the cellular environment on the expression of aberrant phenotypes "cellular parabiosis". While the bystander effect – spreading of aberrant phenotypes from damaged cells to the surrounding intact cells – has been well described, it remains unknown how the healthy cells may influence the damaged, dying cells in their vicinity. In this study, we investigated how cells that are damaged by UV radiation behave in the presence of healthy cells compared to the damaged cells in monocultures. We found that the survival of damaged cells is significantly decreased when they are co-cultured with healthy cells and that this effect mostly depends on the unknown factors secreted by the healthy cells. The underlying mechanism of this phenomenon might be linked with the arrested transcriptomic response to UV radiation that we identified in the UV-treated cells grown in co-culture with intact cells. Such accelerated dismissal of damaged cells due to the surrounding healthy cells might be a natural mechanism for cleaning the tissues from dying cells which can act as sources of toxicity.

Keywords: cellular parabiosis, aging, UV radiation, cellular communication

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Session 2 – Poster presentation *S2-15*

CHARACTERIZATION OF SMALL SUPERNUMERARY MARKER CHROMOSOMES BY MOLECULAR KARYOTYPING

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A small supernumerary marker chromosome (sSMC) is an additional structurally abnormal chromosome fragment that could be of different sizes and structures and originate from any of the 24 human chromosomes. Molecular karyotyping (Array- Comparative Genome Hybridisation, aCGH) has made it possible to determine the origin and gene content of sSMC in a single test, which is not possible with classical cytogenetic techniques. That is crucial for predicting clinical manifestations of aberration, especially in prenatal settings. The aim of this study was to analyze aCGH results in patients in whom an sSMC of unknown origin was detected cytogenetically. From the total sample of patients analyzed by aCGH between 2018 and 2023 at the Institute of Human Genetics, Faculty of Medicine, University of Belgrade, those with a detected or suspected sSMC were selected from the database. Agilent 8x60K oligonucleotide platforms were applied. Patient data were taken from accompanying medical records. In 8/9 cases (88.9%) aCGH had positive, while in one prenatal case (11.1%) had negative findings. In patients with one sSMC (47, XX,+mar or 47, XY,+mar) the excess genetic material originated from chromosomes 12q (2 cases), 15q11.2 – q13.3 (2 cases), 22q11.1-q11.21, 18p, and Y. One patient had a mosaic karyotype with multiple cell lines ranging from one to four sSMC originating from chromosomes 8, 9, and 11. One patient had 45, X,+mar karyotype, and the marker originated from the pericentromeric regions of the other X chromosome. Fetus with negative findings most probably had sSMC of heterochromatin or acrocentric p arms origin. Molecular karyotyping showed high success in determining the origin, breakpoints, and gene content of sSMC chromosomes of euchromatin origin.

Keywords: sSMC, molecular karyotyping, aCGH

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Session 2 – Poster presentation *S2-16*

ASSOCIATION OF GSTP1 POLYMORPHISMS RS1695 AND RS113827 WITH SUSCEPTIBILITY TO BALKAN ENDEMIC NEPHROPATHY

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Balkan endemic nephropathy (BEN) is recognized as an endemic chronic tubulointerstitial disease in rural areas of Bosnia, Serbia, Croatia, Bulgaria, and Romania. Despite extensive research, its aetiology is still unclear. Current data suggest aristolochic acid (AA) exposure as a putative cause of BEN. The cellular metabolism of AA includes complex metabolic activation, associated with the production of reactive oxygen species, resulting in oxidative distress. The cytosolic family of glutathione S-transferases (GSTs) is involved in the detoxification various toxic compounds and antioxidant protection. Organs with intense metabolic activity, like kidneys, are known to have high expression of cytosolic GSTs, especially the pi (GSTP) izoenzymes. In the case of *GSTP1* gene polymorphisms, two most commonly occurring single nucleotide polymorphisms (SNPs) are rs1695 and rs113827. We hypothesized that GST polymorphisms with a consequent absent or lower enzyme activities may modify individual susceptibility to BEN. Therefore, we evaluated the effect of these SNPs, as well as GSTP1ABCD haplotypes on the risk for BEN development. The case-control study comprised 209 BEN patients and 140 healthy individuals, residents of endemic settlements. The *GSTP1* genotypes were determined by qPCR using Applied Biosystem Taqman Drug Metabolism Genotyping assays. There was no statistically significant association between distinct GSTP1 genotypes and BEN risk ($p > 0.05$). The haplotype composed of wild-type A and C alleles was the most frequent among BEN patients (68%) and controls (70%). The haplotype consisting of variant alleles for both polymorphisms G and T was associated with 1.6-fold increased risk (OR=1.64; 95%CI=0.75-3.58; p=0.21). The results showed that there was no individual impact of this polymorphism on the susceptibility toward BEN development. Although haplotype analysis revealed higher risk of BEN in carriers of both variant alleles, the observed effect did not reach statistical significance. More extensive research in this field in BEN patients are needed.

Keywords: Balkan endemic nephropathy, AA, oxidative stress, Glutathione S-transferases
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Session 2 – Poster presentation *S2-17*

RECURRENT MICRODELETIONS AND MICRODUPLICATIONS OF THE 16P11.2 REGION

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Recurrent copy number variations (CNVs) in the 16p11.2 region have a wide range of clinical manifestations, most commonly developmental delay/intellectual disability (DD/ID), epilepsy, and autism spectrum disorders (ASD). Some other somatic reciprocal phenotypic characteristics were observed among carriers of deletion and duplication, like differences in body mass index (BMI) and head circumference (HC). Aim of this work is to estimate the frequency of recurrent pathogenic 16p11.2 CNVs in the population of patients with neurodevelopmental disorders (NDDs) who were analyzed by the molecular karyotyping at the Institute of human genetics in Belgrade, and analysis of genotype-phenotype correlation. From a total sample of 850 patients with NDDs in whom a molecular karyotype was performed (using Agilent 6x80K oligonucleotide microarrays), all patients with CNVs in the 16p11.2 region were singled out. Detailed phenotypic characteristics were collected from the accompanying medical records. The frequency of examined CNVs in our cohort was 0.82%. A typical proximal 16p11.2 microduplication (BP4-BP5, includes TBX6) was detected in 4/7, while the microdeletion was detected in 3/7 patients, proximal in one and distal type (BP2-BP3, includes SH2B1) in two. All patients had a certain level of DD/ID, but in patients with duplications, we observed epilepsy (2/4), behavioral problems (3/4), and tremor (2/4). Conversely, 2/3 of patients with the deletion had significant hypotonia and hyporeflexia and only 1/3 had behavioral problems. Also, patients with duplication had HC and BMI values below average, while deletion patients had the same parameters above the average of their peers. The frequency of recurrent CNVs in the 16p11.2 region in our NDD cohort was 0.82%. A genotypic-phenotypic correlation was observed in neurological and somatic findings that fit the descriptions of mirror phenotype found in the literature.

Keywords: 16p11., molecular karyotyping, copy number variations

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Session 2 – Poster presentation *S2-18*

CHROMOSOMAL ABBERATIONS IN FEMALES WITH REPRODUCTIVE PROBLEMS

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Chromosomal abnormalities and genetic defects can cause reproduction failures, and for this reason genetic analysis can play an important role in reproductive problems research. The aim of this study was to determine the type and frequency of chromosomal aberrations in the female population sample, as well as to determine if the difference between groups with and without chromosomal aberrations was statistically significant. 100 women aged 15-46 were included in the study, all having different reproductive disorder diagnoses and requiring karyotype analysis in the Sarajevo Medical Faculty Genetic Center in 2015-2017 period. Cytogenetic analysis was performed on the peripheral blood. Karyotype analysis was done using Olympus BX 53 fluorescent microscope and Cytovision karyotyping software. The results were analyzed using SPSS 20 for Windows OS. Out of 100 women included in the study, an abnormal karyotype was found in 16% of women (16/100), suggesting a statistical significance ($p < 0.05$). Out of these 16 observed abnormal karyotypes, eight had aberrations of autosomal chromosomes, seven had aberrations of sex chromosomes and one had both autosomal and sex aberrations. Nine karyotypes had structural aberrations, five had numerical aberrations, and one karyotype had both structural and numerical aberrations. For autosomal chromosomes, one reciprocal translocation and one chromosome derivative was found, as well as four Robertsonian translocations and four chromosome 9 inversions. In all cases of sex chromosome aberrations, Turner syndrome was found in combination with either mosaicism, testicular feminization or X chromosome inversion. A unique karyotype which included mosaicism, Turner and Down syndrome was also observed. The difference between the frequency of genetic and non-genetic causes in women with reproductive problems identified in this study was found to be statistically significant. Results of the study emphasize the importance of obtaining a karyogram and performing its analysis for women with reproductive problems.

Keywords: reproductive problems, genetic causes, karyotype, chromosomal aberrations

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Session 2 – Poster presentation *S2-19*

A RELIABLE POLYDIMETHYLSILOXANE (PDMS) MEMBRANE DESIGN FOR IN-VITRO APPLICATIONS ON HUMAN SKELETAL MUSCLE CELLS

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Creating innovative techniques for tissue engineering in skeletal muscle is crucial for rebuilding muscle that has been lost or damaged due to traumatic injuries or neuromuscular conditions like muscular dystrophies. Sell stretching is one of the fundamental test to investigate the behaviour of the cells under stresses. The reliability of the tests are of paramount importance, which largely dependes on the membrane geometry and type of loading. In this study we have designed and fabricate a membrane form polydimethylsiloxane (PDMS) which reveales a more uniform strain distribution and durability compare to the available commercial membranes. A shape optimization based on finite element analysis is used along with tailoring material properties to achieve the desired performance of the mebranes. The biocompatibility properties of the fabricated PDMS membranes and the effects of synthesis conditions on cell response were assessed. The results showed the suitability of the membranes for in-vitro applications on human myoblast cell lines. The adhesion, proliferation, and differentiation rates of cells were not significantly different from the control group. The study will aid in creating innovative biomaterials that can be used to cultivate skeletal muscle cells.

Keywords: PDMS, Finite element, Skeletal muscle cell

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Session 2 – Poster presentation *S2-20*

CHALLENGES AND CASE REPORTS IN NON-INVASIVE PRENATAL TESTING: REVIEW OF CURRENT STATUS AND FUTURE PERSPECTIVES

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Non-invasive prenatal testing (NIPT) is a relatively new screening method that analyzes fragments of fetal DNA that are present in the mother's blood (cffDNA). The use of NIPT has been growing rapidly around the world, with increasing numbers of pregnant women choosing this screening method over traditional invasive methods. By identifying the specific chromosomes that are responsible for certain genetic conditions, such as Down syndrome, Edwards syndrome, and Patau syndrome, NIPT can accurately detect these conditions with a high degree of sensitivity and specificity. This can provide expectant parents with important information about the health of their unborn child and can help them make informed decisions about their pregnancy. This paper presents several case reports and challenges in non-invasive prenatal testing from our laboratory over the past year. These case reports underscore the need for collaboration between molecular biologists and healthcare providers, as well as ongoing education and training to ensure the highest quality of non-invasive prenatal testing. They serve as a reminder of the critical role played by the genetic laboratory in modern healthcare and highlight the ongoing efforts of our laboratory to provide the best possible care for our patients. Our study suggests that NIPT is a promising tool for prenatal screening and diagnosis and has the potential to reduce the need for invasive testing methods.

Keywords: Non-invasive prenatal testing, prenatal screening, fetal aneuploidy, cell-free fetal DNA, fetal fraction

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Session 2 – Poster presentation *S2-21*

PROGESTERONE RECEPTOR GENE ALU INSERTION VARIANT ASSOCIATES WITH DISEASE FEATURES IN BRAIN TUMORS

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Pregnancy, progesterone-containing hormone replacement therapy, and oral contraceptives influence brain tumor growth. Low doses of progesterone stimulate glial tumor growth, while higher doses act as antiproliferative. Despite higher expression of Progesterone Receptor (PR) associated with increased proliferation in meningiomas; PR levels decrease in higher-grade meningeal tumors. Sex steroids stimulate tumor growth, yet they induce tumors with higher cell differentiation and lesser aggressiveness. PR-encoding gene (PGR) locates at chromosome 11q22 where protumorigenic genes IAP and YAP1 also reside. The biological influence of PGR Alu insertion polymorphism is unknown. It may cause abnormal gene transcription, leading to the receptor's hormone inability to cohere progesterone as well as become activated, leading to a decline in the progesterone-mediated task. The impaired PGR gene may affect oncogenesis. It examined whether PGR Alu insertion polymorphism was associated with pathological characteristics of glial brain tumors. 83 brain tumor patients and 45 healthy controls were studied for Alu insertion by PCR.The genotype distributions of Alu insertion variation were similar between groups ($p>0.05$). High-grade tumors were encountered more frequently among Alu insertion allele carrier (T2T2\T1T2) male ($p=0.076$,OR:2.84,CI 95%:0.88–9.147). The Alu insertion carrier females frequency was lesser among those with high-grade tumors ($p=0.061$,OR:0.31,CI 95%:0.109–1.069). The cut-off value of the proliferation index Ki67 was calculated as 10.50%($p<0.001$). High-grade brain tumor patients had a higher frequency of Ki67>10.5 levels than low-grade tumors ($p<0.001$;OR:18.0,CI95%:2.95-1.965). In glial tumors, Alu insertion (T2) allele carrier females accumulated among the group with lesser proliferation index (Ki67<10.50) ($p=0.049$; OR:0.308,CI95%:0.094-1.011). In high-grade brain tumors, Alu insertion carrier males (75%) had a higher frequency of p53wild type ($p=0.043$;OR:0.067;CI 95%:0.005-0.823). We suggested that PGR gene Alu insertion variation may have a decreasing effect on pathological parameters such as p53 and Ki67 being cell proliferation markers. This is the first study showing the importance of PGR gene polymorphism in brain tumors. Further studies in more homogenous groups may illuminate novel and important factors in the molecular biogenesis of these neoplasias.

Keywords: Alu insertion, Progesterone receptor gene, Glial brain tumors, Ki67
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Session 2 – Poster presentation *S2-22*

ASSOCIATION BETWEEN IL10RA RS3135932 POLYMORPHISM AND RHEUMATOID ARTHRITIS SUSCEPTIBILITY

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Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by chronic autoimmune synovitis which leads to synovial joint impairment. Interleukin 10 receptor (IL10) is a heterotetrameric receptor containing two A subunits (IL10RA) and two B subunits (IL10RB). This receptor is a part of the interleukin 10 immunoregulatory pathway. Polymorphisms in genes coding IL10R subunits could affect their interaction with each other as well as their interaction with IL10. In RA, the balance between proinflammatory and antiinflammatory mediators is disturbed, and this unbalance could initiate the development of autoimmunity in RA patients. We aimed to analyse associations between IL10RA rs3135932 polymorphisms and RA susceptibility. The study included 132 RA patients diagnosed and treated at the Institute of Rheumatology in Belgrade and 128 controls without autoimmune diseases. All RA patients are diagnosed according to the 2010 ACR/EULAR Classification Criteria for RA. Genotypisation for IL10RA rs3135932 polymorphism was performed using TaqMan assays. Among our patients 84 (63.6%) had AA genotype, 41 (31.1%) carried AG and 7 (5.3%) had GG genotype, while in controls 99 (77.3%) participants had AA genotype and 29 carried (22.7%) AG genotype. G allele carriers significantly more often had RA than participants with AA genotype (62.3% vs 45.9%, p=0,016; OR=1.95, 95%CI: 1,131-3,364). The findings of this study suggest that IL10RA rs3135932 polymorphism could be associated with RA susceptibility. Further studies in larger populations are needed for a definitive conclusion.

Grant References: Science Fund of the Republic of Serbia, PROMIS, grant number 6060866, ROLERS.

Keywords: rheumatoid arthritis, susceptibility, polymorphism, IL10RA

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Session 2 – Poster presentation *S2-23*

ANALYSIS OF THE ASSOCIATION BETWEEN INDUCIBLE NITRIC OXIDE SYNTHASES (INOS) 2087G/A POLYMORPHISM AND THROMBOLYTIC THERAPY SIDE EFFECTS IN ACUTE ISCHEMIC STROKE PATIENTS

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Recombinant tissue plasminogen activator (rtPA) besides its known benefits may cause serious side effects (SE) and deteriorations after acute ischemic stroke (AIS) patients' treatment. There have been indications that after AIS, certain inflammatory processes are activated, additionally contributing to ischemic brain damage. Nitrogen oxide (NO), mediator involved in inflammatory processes, is synthesized by nitric oxide synthases (NOS), whereas inducible NOS (iNOS) represent NOS isoform. Nevertheless, following ischemia, NO is produced by neuronal NOS (nNOS), afterward, by iNOS, which leads to further progression of the brain damage. Polymorphism 2087G/A (rs2297518) within the INOS gene affects iNOS gene expression and could influence rtPA-induced SE. The aim was to investigate the association between genotypes of the iNOS 2087G/A polymorphism and the occurrence of the rtPA-induced SE in the AIS patients. For two years, 164 subsequent patients with AIS treated with rtPA were included in the study. During the hospitalization, the following rtPA-induced SE were monitored: intracranial hemorrhage (ICH)- extended from ischemic hemorrhage, hemorrhagic transformation (HT) and symptomatic intracranial hemorrhage (sICH). Patients underwent a control CT scan 24 hours after rtPA. In case of a sudden deterioration of the neurological condition, a CT scan was urgently performed. Genotypisation was done using the Real-Time PCR method. The GG genotype was the most frequent among our patients (62.8%), whereas seven (4.3%) patients had an AA genotype. Patients with AA genotype more frequently had ICH after rtPA than G-allele carriers (p=0.029; OR=12.16; CI95%:1.88–78.59). Additionally, A-allele carriers significantly more often developed HT after rtPA than patients with GG genotype (p=0.009; OR=3.96; CI95%:1.40–11.18). The findings of our study suggest that iNOS 2087G/A polymorphism could be associated with rtPA-induced hemorrhagic complications in patients with AIS.

Grant References: Ministry of Education, Science and Technological Development of the Republic of Serbia [grant numbers 175087 and 175091].

Keywords: acute ischemic stroke, thrombolytic therapy, rtPA, hemorrhagic transformation, iNOS 2087G/A polymorphism

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Session III -
Molecular and precision medicine
Genetics & Applications

Session 3 – Oral presentation *S3-01*

PRECISION MEDICINE IN TYPE 2 DIABETES

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Type 2 diabetes mellitus (T2D) is a multifactorial, metabolic disease characterized by hyperglycemia. Genetic association studies have identified more than 600 genetic loci of T2D, implicating many genes in disease pathogenesis, although environmental factors, age, sex, and disease subtypes also have a significant effect. Recent evidence emphasized an emerging diabetes subclassification with more refined subgroups, involving phenotypic and genetic patient characteristics, in line with the precision medicine' major goal to tailor disease treatment to an individual patient. Here we summarize findings of the recent studies, with particular focus on optimization of the diagnosis, prediction, prevention or treatment of diabetes while considering individual differences. Integration of the multiomics data, in particular proteomics and metabolomics together with genomics, has been emerging as the new powerful approach in identifying patients at high-risk for T2D and in implementing intensive preventative measures, all leading to precision medicine. It is expected that more efficient transfer of precision medicine approach in predicting, diagnosing, and treating T2D will be reinforced by investigating further the use of the polygenic risk scores, multiomics and clinical data in diverse ethnic population. The artificial intelligence technologies, such as machine learning, most likely will be soon employed in analyzing these complex data and interactions. Thus, precision medicine is facing the diverse challenges and its future direction depends how they are dealt with in order to be successfully incorporated into the clinical setting and management of Type 2 diabetes.

Keywords: type 2 diabetes, genomics, pharmacogenomics, metabolomics, stratified medicine

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Session 3 – Oral presentation *S3-02*

PHARMACOGENOMICS AND PHARMACOTRANSCRIPTOMICS OF ACUTE LEUKEMIA IN CHILDREN: A PATH TO PERSONALIZED MEDICINE

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Personalized medicine is focused on research disciplines which contribute to the individualization of therapy, like pharmacogenomics and pharmacotranscriptomics. Acute lymphoblastic leukemia (ALL) is the most common malignancy of childhood. It is one of the pediatric malignancies with the highest cure rate, but still a lethal outcome due to therapy accounts for 1- 3% of deaths. Further improvement of treatment protocols is needed through implementation of pharmacogenomics and pharmacotranscriptomics. Emerging high-throughput technologies, microarrays and next-generation sequencing, have provided an enormous amount of molecular data with potential to be implemented in childhood ALL treatment protocols. In the current review, we summarized the contribution of these novel technologies to pharmacogenomics and pharmacotranscriptomics of childhood ALL. We have presented data on molecular markers responsible for efficacy, side effects and toxicity of the drugs commonly used for childhood ALL treatment, i.e., glucocorticoid drugs, vincristine, asparaginase, anthracyclines, thiopurines and methotrexate. Big data was generated using high-throughput technologies, but their implementation in clinical practice is poor. Research efforts have to be focused on data analysis and designing prediction model using machine learning algorithms. Bioinformatics tools and implementation of artificial intelligence are expected to open the door wide for personalized medicine in clinical practice of childhood ALL.

Keywords: pharmacogenomics, pharmacotranscriptomics, high-throughput analysis, childhood acute lymphoblastic leukemia

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Session 3 – Oral presentation *S3-03*

PHARMACOGENOMICS OF HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Busulfan (Bu) is an alkylating agent that is used in the conditioning regiment before hematopoietic stem cell transplantation (HSCT) in children. GSTA1 and GSTM1 encode enzymes that add glutathione (GSH) to target electrophiles such as carcinogens, environmental toxins, and drugs including Bu. In this study, we demonstrated that several SNPs in the promoter region of GSTA1 modulate gene expression and affect the pharmacokinetics of Bu. In addition, we investigated the effect of the knockout of GSTA1 on the functioning and sensitivity of hepatic cells to Bu and Treosulfan (Treo).CellTiter2.0 and pGl4.10 with luciferase reporter assay (LRA) were used to measure cell viability after treatment with Bu and SNPs' impact on the promoter region's activity, respectively. The allelic frequencies of different promoter haplotypes in various human populations were obtained from the 1000 genomes project data. CRISPR/Cas9 was used to generate GSTA1 knockout (KO) HepaRG cell lines. The expression of proteins was assessed by western blot. We used 1-chloro-2,4-dinitrobenzene and GSH-GloTM Glutathione Assay to measure GST activity and GSH concentration, respectively. CellTiter2.0 was used to measure cell viability after treatment with selected drugs used in HSCT. RNAseq and Proteome profiler Kinase assays were used to evaluate gene expression profiles and kinase phosphorylation profiles of GSTA1 KO HepaRG cells, respectively.LRA demonstrated that various SNPs in the GSTA1 promoter region have a strong impact on GSTA1 expression. The distributions of GSTA1 promoter haplotypes and diplotypes were significantly different between various human populations. The knockout of GSTA1 has a strong effect on cell viability after Bu or but borderline in Treo treatment. Our results demonstrate that the resistance to alkylating agents is correlated with the absence of GSTM1 and the regulation of the GCLC/GCLM expression, which results in a 1.5-fold increase in intracellular GSH concentrations. The comparison of wild-type and knockout cell lines showed that cells with downregulated GSTM1 expression also present altered expression profiles of genes involved in the regulation of transcription, translation, cell migration, and cell cycle. Further deletion of GSTA1 has only a minor effect on the global transcription profile except for the regulation of transcription by RNA polymerase II. The kinase phosphorylation profiles showed changes in the phosphorylation of ERK1/2, p53, and RSK1/2/3 in GSTM1 downregulated cells. Using LRA we developed a new GSTA1 metabolic grouping and a new model of cis-elements interaction. Newly created cell models confirm previous evidence, which showed that GSTA1 is involved in the cellular response to Bu but less in Treo. Cell resistance to Bu and Treo is also largely dependent on cellular levels of GSH, which suggests that Bu and Treo undergo detoxification by spontaneous glutathionylation. GSTM1 regulates levels of

GSH through regulation of GCLC expression. The analysis of the gene expression profiles reveal that GST enzymes could also have an impact on important pharmacogenes such as CYP3A4, CYP3A5, CYP2E1 and AHR transcription factor.

Keywords: GSTA1, GSTM1, busulfan, glutathione, liver, metabolism

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Session 3 – Oral presentation *S3-04*

MULTIOMICS APPROACHES UNCOVERING EPIGENETIC REGULATION OF NON-CODING-LOCI

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Long non-coding RNAs (lncRNAs) have emerged as essential epigenetic regulators and with specific actions in primary endothelial cells (ECs) of relevance to cardiovascular diseases (CVD). Advances in medical imaging and endovascular surgical technologies, as well as identification of genetic factors through genome-wide association studies (GWAS), have improved diagnosis of CVD. Despite the identification of numerous CVD-associated genetic loci, the specific mechanisms of regulation by lncRNAs are only starting to get linked to specific CVD pathology. Multidisciplinary approach and omics technologies have helped generate molecular and functional characteristics of lncRNAs. Further, integration of omics data with GWAS has enable us to develop multi-omics pipeline and identify specific protein:RNA interactions. This work describes context specific role for maternally expressed gene (MEG3) to guide transcriptional repression in endothelial cells.

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Session 3 – Oral presentation *S3-05*

EXPRESSION LEVELS OF BCL2, BAX AND MDR1 AS PHARMACOTRANSCRIPTOMIC AND PROGNOSTIC MARKERS OF PROGNOSIS IN ACUTE MYELOID LEUKEMIA

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Acute myeloid leukemia (AML) is a malignancy of hematopoetic tissue which occurs due to a halt in differentiation, loss of proliferation control and dysregulated apoptosis of myeloid progenitor cells. In many cancers, as well as AML, dysregulation of apoptosis constitutes the basis of pathogenesis and this phenomenon is important for chemotherapy success. Pharmacotranscriptomic markers of AML prognosis could be targets of specific therapy. The anti-apoptotic gene BCL2 (B-cell lymphoma protein 2), the pro-apoptotic BAX (BCL2-associated X) and genes involved in drug resistance, like MDR1 could have a significant impact on AML prognosis and therapy response. Bone-marrow samples at diagnosis were collected from 51 adult patients with AML-NK. Expressions of BCL2, BAX and MDR1 were analysed using the real-time polymerase chain reaction method. Statistical evaluation was performed. The presence of chemoresistance was found to be associated with overexpression of BCL2 (BCL2+) ($p=0.018$), while underexpression of BAX in patients has shown a greater affinity towards relapse ($p=0.034$). Evaluating the expressions of BCL2 and BAX in a combined effect has shown that 87% of patients with BAX/BCL2low status were resistant to therapy ($p=0.024$). BCL2+ status was associated with high expression of MDR1 ($p<0.001$). Likewise, high expression of MDR1 was associated with the absence of NPM1 and FLT3-ITD mutations ($p=0.048$ and $p=0.010$, respectively). This is the first study that focused only on AML-NK patients, when it comes to analysis of BCL2, BAX and MDR1 gene expression profiles. The results of this preliminary study have shown that high BCL2 expression would likely lead to resistance from chemotherapy, making anti-BCL2 treatment a viable option in patients with this expression profile. A study on a larger group of patients could clarify the prognostic importance of the studied genes in adult AML-NK patients and improve the precision medicine approach in the field of hematology.

Keywords: AML, BCL2, BAX, MDR1, prognosis

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Session 3 – Oral presentation *S3-06*

OVERVIEW OF PARALLEL CLINICAL EXOME SEQUENCING IN DIAGNOSTICS OF RARE DISEASES FROM A 2 YEAR PERIOD

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Clinical exome sequencing has revolutionized diagnostics of rare diseases, especially in pediatric cases. It comprises over 4800 genes previously associated with known genetic disorders. Current practices in diagnostics of rare diseases are based on the clinical findings, which can often be missleading and non definitive, especially when it comes to pediatric cases. Aim of this study is to determine an impact of clinical exome sequencing on diagnostic procedures of rare diseases which in practice took years, and often led to misdiagnosis and wrong therapeutic choices. Similar to this, clinical exome sequencing could identify individuals who are at risk of developing the disease. Materials and methods include DNA extraction, DNA quantification, library preparation using TruSight One sequencing panel from Illumina, sequencing on MiSeq Illumina platform and comprehensive bioinformatic data analysis using variety of tools and data bases. As the final filtration of genetic variants, Varsome clinical software was used. Since it is a comprehensive approach of rare disease diagnostics, results will be displayed as patients case reports with clearly defined pathogenic, likely pathogenic and variants of uncertain significance that could be associated with rare genetic disorders. To conclude, understanding the complexity of genetic variants provides insights into the human disease for diagnostic applications and therapeutic managment of the disease. Future prospective is to clearly define protocols for parallel clinical exome sequencing and establish patient indiciations for its use in diagnostics.

Keywords: clinical exome sequencing, diagnostics, rare diseases, next generation sequencing

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Session 3 – Oral presentation *S3-07*

CDKAL1 VARIANTS AND RESPONSE TO METFORMIN IN PATIENTS WITH TYPE 2 DIABETES

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CDKAL1 gene has been consistently associated with type 2 diabetes (T2D). A few studies have shown that common variants in CDKAL1 affect response to sulfonylureas and DPP-IV inhibitors in T2D. In this study we investigated the association of CDKAL1 variants with response to metformin in T2D. The study included 79 newly diagnosed patients with T2D who had been prescribed metformin as their initial T2D therapy. Genotyping of the variants was performed by the Sequenom MassARRAY© iPLEX© platform. Biochemical and anthropometric parameters were measured at baseline, and 6 and 12 months after metformin treatment. After 6 months of metformin treatment, homozygous carriers of diabetes risk rs7756992 G allele had significantly higher HbA1c (p=0.040) and triglyceride levels (p=0.032), adjusted for baseline values, compared to the A allele carriers. After 12 months of treatment, GG carriers had also significantly higher fasting glucose (p=0.026), triglyceride (p=0.016) and HOMA-IR levels (p=0.022), after adjusting for baseline values. Likewise, homozygous carriers of the risk rs7754840 C allele had significantly higher HbA1c levels after 6 months of metformin therapy (p=0.016) and higher fasting glucose levels (p=0.029) after 12 months of treatment, adjusted for baseline values, compared to the rs7754840 G allele carriers. Our results suggest that CDKAL1 variants are associated with poorer glycemic response to metformin in newly diagnosed patients with T2D.

Keywords: pharmacogenetics, metformin, type 2 diabetes, glycemic response

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Session 3 – Oral presentation *S3-08*

EVALUATION OF GENE EXPRESSIONS OF ER STRESS MARKERS ATF6, IRE1 AND PERK IN NEUTROPHILS DURING MULTIPLE SCLEROSIS ATTACK THERAPY

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Multiple sclerosis (MS) is a chronic neurodegenerative disease of central nervous system associated with uncontrolled inflammation and autoimmunity, caused by the attack of autoreactive T cells to myelin. Most common type is relapsing remitting MS (RRMS) with periods of recovery and recurrence. Corticosteroids are administered to relapsed patients for treatment. Recent research showed that neutrophils have an important role in MS. Endoplasmic reticulum (ER) stress is a condition that occurs when misfolded proteins accumulate in the ER lumen. The cell survives when it can be relieved by the unfolded protein response (UPR) and undergoes apoptosis when stress cannot be reduced. UPR is initiated by IRE1, PERK, and ATF6 proteins. Biopsy samples of MS patients showed increased ER stress markers but ER stress in neutrophils has never been studied before in MS. The aim of this study was to investigate the IRE1, PERK and ATF6 gene expressions in neutrophils during and after relapse (attack). For this purpose, whole blood samples were collected from healthy controls (n=52), and RRMS patients during an MS attack before treatment (BT) (n=10), after treatment (AT) (n=10), and 1 month after the treatment (1M) (n=10) in Ankara City Hospital, Neurology Clinic. Neutrophils used to obtain RNA were isolated from blood and gene expressions were determined using qRT-PCR. As a result of this study, the relative expression levels of PERK and IRE1 were significantly lower in BT group compared to the controls (P=0.042 for PERK, P=0.017 for IRE1), but any significant difference was not determined in either AT or 1M groups. Also, no significant difference was observed between any groups for ATF6. To conclude, ER stress can be induced during an MS attack, but this does not persist after treatment. Further studies should be done to fully understand the mechanism.

Keywords: multiple sclerosis, treatment response, apoptosis, neutrophil, attack

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Session 3 – Oral presentation *S3-09*

TARGETING BRPF PROTEINS AS A POTENTIAL THERAPEUTIC STRATEGY FOR TAXANE-RESISTANT PROSTATE CANCER

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To treat initial prostate cancer (PCa), androgen suppression or surgery is typically the preferred approach. However, patients may eventually advance to the castration-resistant (CR) stage, at which point therapeutic options are limited and taxanes (such as docetaxel and cabazitaxel) are often used as the first line of treatment. Despite the use of these chemotherapeutic drugs, some patients develop resistance, which further restricts the available treatment options. Epigenetic reprogramming is one of the ways that cancer cells develop drug resistance. Targeting specific epigenetic modifications can potentially reverse this resistance and allow for reuse of available drugs in treatment. The notion led us to conduct epidrug inhibitor screens and CRISPR dropout screens, which revealed the critical role of BRPF proteins that have become indispensable for the resistant phenotype. The inhibition of BRPF proteins via small molecules restored the sensitivity of taxane-resistant CR-PCa cell. Interestingly, although BRPF1 and BRPF2 gene silencing sensitized cells to both taxanes, they only mildly affected resistance. RNA-seq analysis data showed that reversing taxane resistance involved differential expression of multiple genes in both docetaxel- and cabazitaxel-resistant cells. Inhibition of BRPFs in resistant cells induced transcriptional changes, and silencing or knocking out BRPFs resulted in downregulation of ABCB1, which may explain the restored sensitivity of cells to taxane therapy. The direct binding of BRPF1 to the ABCB1 promoter appears to be the cause of suppression, as revealed by ChIP-qPCR studies. By conducting ChIP-sequencing, we are currently identifying other molecular actors responsible for BRPF-mediated drug resistance. Inhibition of BRPF proteins could be a potential therapeutic strategy for anticancer therapy in taxane-resistant CRPCa, likely through the inhibition of drug efflux. Our current research involves overexpressing BRPF proteins to observe the effects on taxane-sensitive cells. By doing so, we hope to demonstrate BRPFs binding to the ABCB1 promoter and also its inhibition.

Keywords: BRPF , taxane , castration-resistant prostate cancer , chemotherapeutic drug resistance , epigenetics

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Session 3 – Oral presentation *S3-10*

M1 POLARIZED TUMOR ASSOCIATED MACROPHAGES FAVOR TUMOR PROGRESSION AND DRIVE ANTI-ANDROGEN RESISTANCE IN HORMONE SENSITIVE PROSTATE CANCER CELLS

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In this study, it was aimed to explore the effects of M1 polarized macrophage mediated inflammatory stress on the antiandrogen therapeutic efficacy, tumorigenesis and cancer progression in hormone-sensitive prostate cancer in LNCaP cell line. The data obtained from this study shown that inflammatory environmental stress stimulus, which originated from M1 polarized TAMs, increased LNCaP cell viability and proliferation, besides decreased cellular cytotoxicity. Furthermore, UPR, integrated stress response and antioxidant defense mechanisms with concominant cellular signaling pathways, which play a salient role in tumor cell survival and support carcinogenesis, were found to be activated at the highest level in experimental group modeling of inlammatory stress. On the other hand, reactive oxygen species mediated oxidative DNA damage and DNA damage repair responses were found to be increased, compatible with the data which demonstrated activation of caspase-3-mediated apoptosis. Experimental data obtained from molecular analysis shows that inflammatory environmental stress mediated cellular alterations caused loss of anti-proliferative and cytotoxic effects of apalutamide on hormone-sensitive prostate cancer cells. Notwithstanding the finding, apalutamide remained to exhibit suppressive effects on the adaptive cellular signaling pathways regarding inflammatory stress mediated changes which comprised of stimulation of AR signaling, induction of angiogenesiss, EMT, stemness, and carcinogenesis in LNCaP tumor biology, which associated with tumor progression. Research findings of this study shows that M1 polarized TAMs mediated inflammatory environmental stress facilitate tumor progression and drive anti-androgen resistance through the activation of carcinogenic signaling pathways and adaptive cellular integrated stress response in LNCaP tumor cells.

Keywords: prostate cancer, tumor-associated macrophage, tumor progression, antiandrogen, apalutamide, drug resistance

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Session 3 – Oral presentation *S3-11*

APOPTOTIC PATHWAY OF HUMAN COLORECTAL CARCINOMA CAN BE REGULATED VIA SCORPION VENOM

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Colorectal carcinoma (CRC) is the leading cause of cancer death worldwide. Due to the inadequacy of treatment methods such as chemotherapy, radiotherapy, gene therapy and immunotherapy in the treatment of colon cancer and the severe side effects of these methods, research has focused on natural drug sources. Among potential drug candidates, scorpion venoms have received great attention as therapeutic agents. The study aims to reveal whether scorpion venoms of Iurus kinzelbachi and Scorpio fuscus species have a potential role in the alteration of apoptotic genes and proteins in human DLD-1 colon cancer cells. For this purpose, two different scorpion species were collected and their venoms were obtained and their cytotoxic effects on DLD-1, human colon cancer cell line, and CCD-18Co, human healthy colon cell line, were determined. Subsequently, cell death mechanisms were determined by flow cytometry. The changes in gene and protein expressions in the apoptotic pathway were determined by qRT-PCR and western methods, respectively. According to our results; Iurus kinzelbachi and *Scorpio fuscus* species scorpion venoms showed dose-dependent toxic effects on DLD-1 cells with the IC50 values of 20.86 µg/mL and 14.80 µg/mL, respectively, while they did not show any toxicity in CCD-18Co (IC50: >250 µg/mL) cells. The genes/proteins in apoptotic pathways including Bax, BcL-2, Caspase-3, Caspase-9, Caspase-12 were significantly ($p<0.0001$) altered following the venom treatment. Especially, *S. fuscus* venom increased BcL-2 (3.0-fold) and Caspase-3 (8.0-fold) mRNA and protein expressions. In conclusion, scorpion venom shows promise for obtaining alternative and new agents in the treatment of CRC, which is a serious public health problem.

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Session 3 – Poster presentation *S3-12*

IMPROVING THE DIAGNOSTICS OF RARE LUNG DISORDERS USING A UNIQUELY DESIGNED PIPELINE FOR ANALYSIS OF NGS DATA

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Rare lung diseases (RLDs) are a group of diseases that individually affect one in 2,000 people, with an estimate that about 80% of RLDs have a genetic origin. Despite the variations among RLDs in clinical characteristics and manifestations, most of these diseases similarly damage the lungs, making diagnosis difficult. The utility of NGS technology in RLDs for diagnostic purposes allows a better understanding of the genetic background, however, the identification and classification of disease-causing variants are challenging. Further, numerous VUS (variants of uncertain significance) that cannot be precisely defined and classified are produced. The main goal of this study was to create a unique guideline that will enable the standardization of the assessment of novel genetic variants in RLDs causative genes. The designed pipeline consists of three main steps: (1) sequencing, detection, and identification of genes/variants, (2) classification of variants, and (3) characterization of variants using in silico structural and functional analysis. The pipeline validation was performed through the analysis of variants detected in a disease-causing and candidate genes of one of the RLDSs, and detected VUS variants have gained diagnostic significance. The application of this pipeline resulted in the identification and classification of novel variants, through analysis at the transcriptional, translational, and posttranslational levels, and led to accurate diagnosis.

Keywords: pipeline, rare lung diseases (RLDs), classification of variants, characterization of variants, sequencing, detection, identification of genes/variants

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Session 3 -Poster presentation *S3-13*

DIAGNOSTIC RELIABILITY OF THE METHYLATION STATUS OF MGMT IN FRESH-FROZEN AND FORMALIN-FIXED PARAFFIN-EMBEDDED DIFFUSE GLIOMAS

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Diffuse gliomas are a heterogeneous group of diffusely infiltrating primary brain tumors which are considered to be incurable with standard surgical and combined chemoradio - treatments. The methylation of the promoter of the O6-methylguanine-DNA methyltransferase (MGMT) gene is known prognostic and predictive epigenetic biomarker of diffuse gliomas. The aim of our study was to compare diagnostic reliability of the conventional methylation-specific PCR (MSP) for MGMT promoter methylation status assessment with the Real Time MSP (qMSP) method in 20 paired fresh-frozen (FF) and formalin-fixed paraffin-embedded (FFPE) glioma samples. Unmethylate (U) and methylated (M) MGMT amplicons from the MSP and qMSP were separated on agarose gel, submitted to the ImageJ software analysis and methylation status defined for paired gliomas samples. The level of coincidence of MSP in FFPE samples was reasonably high in comparison with both MSP (ICC (95% CI) = 0.868 (0.666-0.948)) and qMSP (ICC (95% CI) = 0.737 (0.348 – 0.895) in paired FF samples. These preliminary findings suggest reliability of MGMT testing in FFPE glioma samples when FF samples are not available. For more accurate evaluation, further evaluation of MGMT promoter methylation status on larger sample study is planned.

Keywords: diffuse gliomas, MGMT, FF glioma, FFPE glioma, MSP, qMSP

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Session 3 – Poster presentation *S3-14*

CYP7A1 POLYMORPHISM IS A POTENTIAL GENETIC MARKER OF ATORVASTATIN EFFICACY IN DYSLIPIDEMIA THERAPY

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Statins are the drugs of choice in the prevention of cardiovascular diseases, which remain the leading cause of death worldwide. However, substantial interindividual differences in response to therapy have been observed, thus identifying variations in genes involved in cholesterol or statin metabolism may help predict drug response. Single nucleotide polymorphism rs3808607 (g.58500365G > T) in the cytochrome P450 family 7 subfamily A member 1 (CYP7A1) gene was shown to be associated with inadequate statin efficacy. Our aim was to test this hypothesis in patients with dyslipidemia from Montenegro. A retrospective cross-sectional study was conducted at the Faculty of Medicine, University of Montenegro, from May 2021-April 2022. Patients with dyslipidemia on atorvastatin therapy for at least one month participated in the study. Excluding criteria were use of concomitant medications and poor compliance. Demographic and clinical data, information on dose, duration of therapy, and baseline lipid status from the time atorvastatin was introduced into therapy were obtained. Lipid status was re-evaluated at the time of recruitment, and genotyping of CYP7A1 was performed. A total of 110 subjects participated in the study, of whom 25.45% were carriers of the variant (GG) genotype, while the rest were heterozygous (GT). Homozygous carriers were found to have significantly higher basal levels of total cholesterol and LDL (p=0.0143, p=0.0269, respectively) with respect to heterozygous carriers. However, efficiency of atorvastatin therapy on triglyceride levels was higher in homozygous than in heterozygous carriers, odds ratio 2.625 (1.046-6.539, 95%CI, p=0.0483). Our results evidenced that the GG genotype of CYP7A1 is correlated with high basal levels of total cholesterol and LDL, but also with higher efficiency of atorvastatin at the level of triglycerides. This suggests that CYP7A1 polymorphism analysis could enable timely detection of patients likely to respond well to atorvastatin therapy.

Keywords: pharmacogenetics, CYP7A1 polymorphism, atorvastatin

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Session 3 – Poster presentation *S3-15*

HIGH-RISK POPULATION SCREENING FOR FABRY DISEASE IN PATIENTS WITH CHRONIC RENAL FAILURE OF UNKNOWN ETIOLOGY

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Fabry disease (FD) is a rare X-linked disorder caused by variants in the GLA gene leading to the deficiency of lysosomal α-galactosidase-A and progressive accumulation of globotriaosylceramide affecting the heart, nervous system, and kidneys. FD has overlapping phenotypes and often remains undiagnosed. Therefore, a precise molecular-genetic diagnosis and the earliest possible treatment are essential to avoid significant disease progression. The study aimed to determine the strategy for establishing routine molecular genetic diagnostics of FD in Serbia to provide an early application of appropriate therapy and genetic advice to families with a high risk for the birth of a child with FD. We analyzed 95 (34 female and 61 male) hemodialysis patients with clinical suspicion of FD using Sanger sequencing of all coding exons (7) and flanking intron regions of the GLA gene and measured the relative expression of the GLA gene in available samples. The genetic analysis revealed 3 patients with a missense variant (p.Asp313Tyr), and 10 patients with combinations of non-coding variants, described as complex intronic haplotypes (CIHs). CIH1 (c.-10C>T, c.370-81_370-77delCAGCC, c.640-16A>G, c.1000-22C>T), the most frequent haplotype, was detected in 7 (7.4%) patients. Lyso-Gb3 biomarker levels were within the normal range in each tested patient. However, RT-qPCR analysis revealed decreased relative expression of the GLA gene in PBMC of 2 female patients with CIH1 and one female patient carrying only c.-10C>T variant by 9,1%, 7,4%, 46,3%, respectively, pointing out that further analyses are needed to confirm/exclude FD in these patients. Because the effects of CIHs are not yet fully understood, our work highlights the importance of analyzing intronic regions of the GLA gene as genetic modifiers and the need to include expression analysis in the diagnostic algorithm.

Keywords: Fabry disease, precise molecular-genetic diagnosis, high-risk population screening

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Session 3 - Poster presentation *S3-16*

A POTENTIAL ROLE OF GSTP1, GSTO1 AND GSTO2 POLYMORPHISMS IN DIABETES MELLITUS DEVELOPMENT

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Genetic and environmental factors play important roles in the development of type 2 diabetes mellitus (T2DM). It has been shown that polymorphism in antioxidant enzymes genes is associated with susceptibility to T2DM and its complications in various populations. The present study was designed to investigate the possible modifying effect of glutathione transferase polymorphisms (GSTP1 rs1138272/rs1695, GSTO1 rs4925 and GSTO2 rs156697) in the susceptibility to T2DM. Because of the great significance of advanced glycation end products (AGEs) in oxidative stress-related diabetes complications, it was important to analyze the relationship of GST polymorphisms with the plasma AGEs in patients with T2DM. GSTO1, GSTO2, and GSTP1 polymorphisms were determined by the real-time PCR in 160 T2DM patients and 248 age- and gender-matched controls. Plasma AGEs were measured by ELISA. A significant association between the GST genotypes and susceptibility for development of diabetes mellitus was found for the GSTP1 (rs1138272) and GSTO1 (rs4925) polymorphisms. Diabetic patients, carriers of the variant GSTO1*AA genotype, had significantly increased levels of AGEs in comparison with carriers of the referent GSTO1*CC genotype ($p = 0.004$).Namely, carriers of the heterozygous GSTP1*CT rs1138272 genotype were in 3.4-fold higher odds compared to the carriers of the GSTP1*CC genotype to develop diabetes (OR = 3.43, 95%CI = 1.53–7.70, $p = 0.003$). On the contrary, individuals with the GSTO1*CA genotype had significantly lower odds of symptomatic diabetes development compared to the carriers of the wild-type GSTO1*CC genotype (OR = 0.28, 95%CI = 0.15–0.51, $p < 0.001$).Patients who were carriers of the variant GSTO1*AA genotype had significantly increased levels of AGEs in comparison with carriers of the referent GSTO1*CC genotype ($p = 0.004$). Despite the certain limitations, this study supports the hypothesis that GST modulates the risk of diabetes development and influences the AGEs concentration.

Keywords: GST polymorphisms, T2DM development, AGE

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Session 3 – Poster presentation *S3-17*

THE PHARMACOGENOMICS OF VINCRISTINE-INDUCED PERIPHERAL NEUROPATHY IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS IN SERBIA

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Vincristine (VCR) is one of the key drugs in current treatment protocols for pediatric acute lymphoblastic leukemia (ALL). By destabilization of microtubules, VCR arrests cells in metaphase, inducing apoptosis of malignant cells. VCR also causes axonal degradation and impairment of axonal transport, which leads to vincristine-induced peripheral neuropathy (VIPN). The aim of this study was to determine if the selected genetic variants are associated with the development of VIPN in ALL children treated with VCR in Serbia. This study also aimed to discover candidate pharmacogenomic markers of VIPN in Serbian population. PCR and sequencing-based methodology was used to detect variants in following genes: CYP3A5 (rs776746), CEP72 (rs924607), ACTG1 (rs1135989), MIR3117 (rs12402181) and MIR4481 (rs7896283). Statistical analyses were performed for investigation of their association with VIPN in 56 pediatric ALL patients. Population VCR pharmacogenomics analysis of 17 pharmacogenes from in-house next-generation sequencing data was also done. Data on allele frequency distribution for European population were extracted from public databases. During the treatment, 17.86% of patients developed VIPN. Association analyses have shown that none of the investigated genetic variants contributed to the occurrence of VIPN in our study group. Population pharmacogenomics study didn't reveal valid candidate pharmacovariants for the occurrence of VIPN. Our results suggested that pre-emptive pharmacogenetic testing for VCR is not applicable. More comprehensive approaches are needed to identify panel of genes that could explain the VIPN development after VCR administration in ALL patients. Utilizing better designed GWAS studies and more robust artificial intelligence-based tools would provide a panel of pharmacogenes for pre-emptive tests of VIPN to individualize therapy for ALL in children.

Keywords: vincristine, vincristine-induced peripheral neuropathy, pediatric acute lymphoblastic leukemia, pharmacogenetics, CYP3A5, CEP72, ACTG1, MIR3117, MIR4481

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Session 3 – Poster presentation *S3-18*

FUNCTIONAL CHARACTERIZATION OF NOVEL VARIANTS IN THE DNAI1 GENE IN A PATIENT WITH PRIMARY CILIARY DYSKINESIA

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Primary ciliary dyskinesia (PCD) is a rare motor ciliopathy, which predominantly affects the lungs and reproductive organs. PCD has a heterogeneous genetic basis, and it is necessary to analyze more than 40 causative genes in order to establish a precise diagnosis, which is essential for optimal treatment and adequate genetic counseling. Five patients suspected of PCD were analyzed using next-generation sequencing (NGS). The pathogenicity of the genetic variants was tested by in silico, qRT-PCR and Western blot methods. Two newly discovered variants p.N450Lfs*6 and p.D562N in the DNAI1 gene were detected in one patient suspected of PCD. The results of in silico prediction showed that the p.N450Lfs*6 variant affects the structure of the 3D model of the protein, abolishes ligand binding sites and post-translational modifications, thereby disrupting protein-protein interactions (PPI). The p.D562N variant has no effect on the 3D structure of the protein, but affects the ligand binding site and is located in the WD-40 domain, which most likely disrupts PPI. The results of the qRT-PCR method showed a decreased expression level of DNAI1 mRNA by about 50% in the patient compared to the control group, while Western blot analysis showed the presence of two protein products (699 ak and 455 ak). By analyzing the obtained results, it was concluded that the changes p.N450Lfs*6 and p.D562N affect the length and quantity of the DNAI1 protein, leading to the loss of protein function and are responsible for the occurrence of primary ciliary dyskinesia in the analyzed patient.

Keywords: PCD, DNAI1, NGS, qRT-PCR, Western Blot

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Session 3 - Poster presentation *S3-19*

EFFECTS OF OPRK1 RS997917, RS12548098, RS6473797 AND RS963549 POLYMORPHISMS ON PLASMA BUPRENORPHINE LEVELS IN OPIOID USERS

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Buprenorphine (BUP), a thebaine derivative, is used for the long-term treatment of opioid use disorder (OUD) by reducing withdrawal symptoms. Its pharmacological properties are different from other opioids such as methadone. It is a partial mu-opioid receptor agonist, delta- and kappa-opioid receptor (KOR) antagonist. It has been suggested that buprenorphine is more effective in the treatment of OUD as compared to methadone by improving negative mood and dysphoric states that could increase drug seeking behavior due to its KOR antagonist activity. Although its high efficacy, the rate of treatment failure is high among opioid users, which is attributed in part to genetic variations. Thus, the study aimed to examine the genetic contribution to BUP treatment in individuals with OUD, with a specific focus on OPRK1 gene in a sample of 122 individuals with OUD who have been receiving BUP/naloxone combination. OPRK1 rs997917, rs12548098, rs6473797 and rs963549 polymorphisms were analyzed by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) method. Plasma BUP and norbuprenorphine levels were detected by Liquid Chromatography Tandem Mass Spectrometry (LC–MS/MS). The genotype frequencies of the OPRK1 polymorphisms in all samples were consistent with Hardy–Weinberg equilibrium ($p>0.05$). The median plasma concentrations of BUP and norbuprenorphine were 0.061 ng/mL (IQR:0.04-0.11 ng/mL) and 1.54 ng/mL (IQR:0.93-2.82 ng/mL). There were not statistically significant differences between the genotypes of OPRK1 polymorphisms analyzed in the current study in view of plasma BUP and norbuprenorphine levels ($p>0.05$). This study indicated that OPRK1 rs997917, rs12548098, rs6473797 and rs963549 polymorphisms did not influence the inter-individual variability in human responses to buprenorphine in Turkish population.

Keywords: pharmacogenomics, buprenorphine, kappa-opioid receptor, OPRK1

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Session 3 - Poster presentation *S3-20*

EVALUATION OF THE EFFECTIVENESS OF CORONAVIRUS DISEASE (COVID-19) THERAPEUTIC PROTOCOLS USING COAGULATION MARKERS

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Impaired coagulation markers are associated with poor prognosis in COVID-19 (Coronavirus Disease) patients and affect the choice of an anticoagulant. This paper aims to examine coagulation markers in COVID-19 patients, and then analyze the impact of the severity of clinical presentation and the type of used anticoagulant on these markers. A total of 200 patients with mild, moderate or severe illness were included in this study. Coagulation markers [PT (Prothrombin Time), INR (International Normalized Ratio), aPTT (Activated Partial Thromboplastin Time) and D-dimer] were examined on three occasions: twice during hospitalization and once after discharge. Anticoagulants used intrahospital were fraxiparine, rivaroxaban or unfractionated heparin. Posthospital, patients were taking either rivaroxaban or did not use any anticoagulants. In regard to the severity of clinical presentation, the second intrahospital measurement of PT, INR and aPTT showed a significant difference (p=0,002, p=0,002, p=0,041, respectively), while D-dimer significantly differed on all three occasions (p=0,000). Three anticoagulants used intrahospital showed a significant impact on all coagulation markers (p=0,000), but the effect size (ES) was the biggest with fraxiparine, then rivaroxaban, and lastly unfractionated heparin. All three anticoagulants showed medium ES on PT and INR, but on aPTT and D-dimer, rivaroxaban and unfractionated heparin showed medium ES, while fraxiparine – large. Posthospital, rivaroxaban showed a significant impact on all coagulation markers [PV (p=0,003), INR (p=0,003), aPTT (p=0,005), D-dimer (p=0,000)]. However, in patients who did not take any anticoagulants, there was a significant difference in aPTT and D-dimer (p=0,004, p=0,000, respectively, with medium ES), but none in PV and INR. The progress of COVID-19 patients regarding coagulation markers was the most notable in patients with severe clinical presentation. Fraxiparine was proven to be the most effective anticoagulant in hospitalized patients. Rivaroxaban was shown to be a good option for improving coagulation markers posthospital.

Keywords: COVID-19, coagulation markers, anticoagulants

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Session 3 – Poster presentation *S3-21*

ASSOCIATION OF APOB AND GALNT2 GENETIC VARIANTS WITH ANTROPOMETRIC AND BIOCHEMICAL PARAMETERS IN THE POPULATION FROM BOSNIA AND HERZEGOVINA

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Genome Wide Association (GWA) studies have demonstrated the association between two single nucleotide polymorphysms (SNPs) - SNPs rs693 in ApoB gene and rs4846914 in GALNT2 gene with certain metabolic parameters. The aim of this study was to investigate the association of these single nucleotide polymorphisms (SNPs) and antropometric and biochemical parameters in the population of Bosnia and Herzegovina (BH). Our study involved 352 patients with T2D and 156 healthy subjects. Biochemical and anthropometric parameters were measured in all participants. DNA was extracted from the peripheral blood for the purpose of genetic testing. Polymorphism in ApoB (rs693) and GALNT2 (rs4846914) gene were analyzed with the use of Sequenom IPLEX platform.In the group of diabetic patients, results showed a significant association of rs693 in ApoB gene with BMI ($p = 0.025$), systolic blood pressure ($p = 0.027$), fasting insulin ($p = 0.037$) and HOMA-IR ($p = 0.023$) levels. Significant associations were also observed for rs4846914 in GALNT2 gene with HbA1C ($p = 0.013$) and triglyeride ($p = 0.043$) levels. In the group of healthy subjects, significant associations were observed for rs4846914 in GALNT2 with HOMA_IR ($p = 0.054$). In conclusion, this is the first study that examined the impact of variations of candidate genes on a wide range of metabolic parameters in BH population. Our results suggest an association of variations of ApoB and GALNT2 genes with specific antropometric and biochemical parameters. Further studies would be needed in order to confirm these genetic effects in other ethnic groups as well.

Keywords: ApoB, GALNT2, rs693, rs4846914, SNPs

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Session 3 – Poster presentation *S3-22*

COVID-19 DISEASE SEVERITY ASSOCIATED WITH VITAMIN D RELATED GENETIC VARIANTS

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COVID-19 pandemic has proved to be an unrelenting health threat for more than a year now. The emerging amount of data indicates that vitamin D could be important for clinical presentation of COVID-19. Here, we investigated association of genetic variants related to the altered level and bioavailability of vitamin D with clinical severity of COVID-19. We analyzed variants in genes significant for the status of vitamin D (DHCR7/NADSYN1 rs12785878, GC rs2282679, and CYP2R1 rs10741657), and vitamin D effect (VDR rs2228570) in 120 Serbian adult and pediatric COVID-19 patients using allelic discrimination. Furthermore, we carried out comparative population genetic analysis among European and other worldwide populations to investigate variation in allelic frequencies of selected variants. The results showed that DHCR7/NADSYN rs12785878 and CYP2R1 rs10741657 variants were associated with severe COVID-19 in adults ($p = 0.03$, $p = 0.017$, respectively); carriers of DHCR7/NADSYN TG+GG and CYP2R1 GG genotypes had 0.21 and 5.9 the odds for developing severe disease, OR 0.21 (0.05–0.9) and OR 5.9 (1.4–25.2), respectively. There were no associations between selected genetic variants and disease severity in pediatric patients. Comparative population genetic analysis revealed that Serbian population had the lowest frequency of CYP2R1 rs10741657 G allele compared to other non-Finish Europeans (0.58 compared to 0.69 and 0.66 in Spanish and Italian population, respectively), suggesting that other populations should also investigate the relationship of CYP2R1 variant and the COVID-19 disease course. The results of the study indicated that vitamin D related genetic variants were implicated in severe COVID-19 in adults. This could direct prevention strategies based on population specific nutrigenetic profiles.

Keywords: COVID-19, vitamin D, nutrigenetics

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Session 3 – Poster presentation *S3-23*

THE EFFECTS OF TRICETIN AND 5-FLUOROURACIL COMBINATION ON HCT-116 COLORECTAL CANCER CELL LINES

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Colorectal cancer (CRC) is the third most common cancer worldwide with still no effective treatment as of today. There are new strategies against colorectal cancer that needs to be developed. Novel studies suggests that natural products combined with conventional therapeutics as a new strategy against cancer progression. One of those natural products is Tricetin, a flavonoid with anticancer properties. In this study, we have investigated the anticancer activity of tricetin on colorectal adenocarcinoma cell line HCT-116 cells. We examined the effects of tricetin either individually or in combination with the conventional chemotherapeutic 5-fluorouracil (5-FU) on viability of cells by Sulforhodamin-B assay, on cell death by Hoechst 33342 / PI method, and on apoptotic pathway-related protein expression by Western blotting. Here, we described the first experimental evidence of benefit from combination of tricetin and 5-FU in the in vitro model of HCT-116 cells. The aim of this study was to reveal if this combination could be used in translational sense of oncological medicine. When compared to their individual use, 5-FU and tricetin further reduced the viability of HCT-116 colorectal cancer cells when used in combination. The IC30 of tricetin (40 μM) and the IC50 of 5-FU (20 μM) were used for the experimental settings. Western blot analysis of PARP, caspase-3, and caspase-8 proteins in the apoptosis pathway was performed. PARP is a nuclear poly (ADP-ribose) polymerase which is involved in DNA repair in response to environmental stress. During apoptotic signaling, PARP is cleaved by caspase-3 inactivating its DNA repair ability. Detection of cleaved PARP is a recognized marker of apoptotic signaling. Thus, according to our results, PARP cleavage by caspase-3 suggested that 5-FU and tricetin combination has an apoptotic activity on HCT-116 cells through these proteins, and can be of therapeutic aid and create an advantage when used in the clinic.

Keywords: colorectal cancer, apoptosis, flavonoid, tricetin, combination therapy

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Session 3 - Poster presentation *S3-24*

EVALUATION OF PLASMA HSA-MIR-181D-3P RELATIVE EXPRESSION LEVEL AS A BIOMARKER IN RELAPSING-REMITTING MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is a chronic, autoimmune disorder that affects the central nervous system, characterized by neuroinflammation and demyelination of nerve fibers, resulting in disrupted neural transmission and a range of clinical manifestations, including muscle weakness, visual disturbances, and cognitive dysfunction. The most common type is relapsing-remitting MS (RRMS) with acute attacks. Immunomodulatory treatments such as glatiramer acetate (GA) slow down the prognosis of the disease. MicroRNAs (miRNAs) play important roles in the regulation of gene expression and disease activity. This study aimed to evaluate the biomarker potential of hsa-miR-181d-3p, involved in the regulation of inflammatory responses. Blood samples from 25 naïve, 25 RRMS patients treated with GA, and 25 healthy individuals were collected in Ankara City Hospital Neurology Clinic. After the separation of plasma from blood samples, total RNA was isolated from plasma, and the relative expression levels of hsa-miR-181d-3p in plasma were determined by the qRT-PCR method. The mean plasma hsa-miR-181d-3p relative expression level was 4.07 ± 3.13 in the GA group, 6.18 ± 5.36 in the naïve group, and 2.00 ± 2.52 in the controls (P= .002). The mean plasma miR-181d-3p relative expression levels of the naïve and GA groups were significantly higher than the controls (GA vs. control: P= .05, naïve vs. control: P=.002). There was no significant difference between the GA and naïve groups. The diagnostic performance of the mean relative expression level of plasma miR-181d-3p between the GA and control groups was "moderate" (Cut-off point: 2.32, AUC=0.717, P= .05); between the naïve and control groups was "moderate" (Cut-off point: 3.06, AUC=0.759, P=.002) according to ROC analysis. The plasma miR-181d-3p relative expression level has the potential to be developed as a blood biomarker for RRMS; new diagnostic tests aiming to measure this parameter can be developed.

Keywords: multiple sclerosis, RRMS, microRNA, miR-181d-3p, biomarker

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Session 3 - Poster presentation *S3-25*

LONGITUDINAL STUDY OF NEUTROPHIL GENE EXPRESSIONS OF APOPTOSIS MARKERS BAX, BCL2, AND CASP3 DURING DIMETHYL FUMARATE THERAPY IN PATIENTS WITH MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is a demyelinating auto-immune central nervous system disease. Relapsing-remitting MS (RRMS) presents with periods of relapses and without progression between attacks. Immune-modulating treatments such as dimethyl fumarate (DMF) aim to slow disease progression. Neutrophils are associated with the pathogenesis of MS, and endoplasmic reticulum (ER) stress is also associated with neurodegenerative diseases. In the ER, which is involved in the maturation of proteins, a balance is established between protein folding and protein load, which is called ER homeostasis. The increase in the number of unfolded proteins stresses the ER and the unfolded protein response (UPR) develops. Apoptosis occurs if homeostasis is not achieved by attempts to slow down translation along the UPR. In this study, which aimed to examine the relationship between DMF treatment and apoptosis pathways in neutrophils in RRMS patients, the changes in the relative expression levels (REL) of BAX, BCL2 and CASP3 in neutrophils were investigated. For this aim, blood samples were obtained from controls (n=52) and naïve RRMS patients (0M; n=30), 3 months (3M; n=20) and 6 months (6M; n=14) after they started using DMF at Ankara City Hospital Neurology Clinic. RNA to be used in qRT-PCR was isolated from neutrophils separated from the blood. According REL analysis, BCL2 and CASP3 was higher in 6M (P=0.001 and P=0.002) compared to the controls. In addition, BAX (P=0.030) was decreased in 6M compared to 0M, while BCL2 (P=0.048) and CASP3 (P=0.035) were increased in 6M group than 0M group. No significant difference was observed in the comparison of 3M vs 0M and 6M vs 3M. In conclusion, differences in BAX, BCL2, and CASP3 REL may be related to the apoptosis process in neutrophils in MS pathogenesis and DMF therapeutic mechanism. These are the preliminary results of an ongoing study.

Keywords: multiple sclerosis, neutrophils, apoptosis, dimethyl fumarate

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Session 3 – Poster presentation *S3-26*

INVESTIGATION OF THE EFFECT OF CORTICOSTEROID TREATMENT ON THE NEUTROPHIL NUCLEAR LOBE INDEX (ARNETH INDEX) IN RELAPSING- REMITTING MULTIPLE SCLEROSIS PATIENTS DURING ATTACK

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Multiple Sclerosis (MS) is a chronic, autoimmune, neurodegenerative central nervous system disease. The most common clinical type is relapsing-remitting MS (RRMS), which continues with recovery after attacks. Expanded Disability Status Scale (EDSS) is used clinical scale to measure the degree of disability due to MS, ranging from 0 to 10. Corticosteroids are the therapy method used in the treatment of attacks due to their anti-inflammatory and immunosuppressive effects. Neutrophils have been associated with the pathogenesis of MS. Neutrophils may have a nucleus with multiple lobes. Older neutrophils have more lobes than younger neutrophils. With the Arneth Count, neutrophils can be classified according to their nuclear lobe number. The ratio of the total lobe count of neutrophils to the total neutrophil count gives the nuclear lobe index (Arneth Index). In this study, effect of corticosteroid treatment on the neutrophil nuclear lobe index was investigated. Blood samples and EDSS status information were collected from 10 RRMS patients before treatment (BT), after treatment (AT) and 1 month after relapse treatment (1M) at Ankara City Hospital Neurology Clinic. Whole blood smear was performed on the slide and stained with Giemsa, then nuclear lobes of neutrophils were counted under microscope with immersion oil. There was a significant difference between the groups in terms of Arneth Index (BT vs. AT, P=001; BT vs. 1M, P=.037; AT vs. 1M, P=.003) and EDSS (BT vs. AT, P=.015; BT vs. 1M, P=.038). However, there was no significant difference between AT and 1M groups in terms of EDSS. Also, there was no correlation between EDSS and Arneth Index changes. According to these results, which are the first findings of an ongoing large-scale study, there is a relationship between attack treatment, Arneth index, and EDSS, while there is no relationship between EDSS and Arneth Index.

Keywords: multiple sclerosis, RRMS, EDSS, corticosteroids, Arneth

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Session 3 – Poster presentation *S3-27*

CHRYSIN MODULATES APOPTOTIC EFFECTS OF LPS-INDUCED RAW 264.7 MACROPHAGE IN MCF-7 BREAST CANCER CELLS

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Breast cancer is a global public health problem which is seen in more than 2 million women in the world. Due to the limited effectiveness and side effects of available treatments, search for alternative methods continues in breast cancer therapy. In particular, modulating the anti-cancer effects of immune system elements with natural agents has been frequently studied in recent years. This study aimed to investigate the anti-tumoral effects of a phytochemical flavone; Chrysin (5,7-dihydroxyflavone) on MCF-7 breast cancer cells and to determine whether this effect is mediated by immunomodulation of LPS-induced RAW 264.7 cells. For the MTT cell viability assay, different concentration of chrysin (12.5-200 µM) were applied to RAW 264.7 and MCF-7 cells in order to determine non-toxic dose to macrophages and IC50 dose on MCF-7 cells. Raw 264.7 cells were induced by 1 µg/ml LPS and chrysin for 24 hr. After induction, supernatants of only LPS induced and LPS + chrysin induced macrophage cells were harvested to analyze the immunomodulatory effect of chrysin. Then MCF-7 cells were also treated with those supernatants. In order to show how chrysin modulates apoptotic effects of macrophage cells on MCF-7 cells; acridine orange/ethidium bromide and caspase-3 immunofluorescent staining were performed with fluorescence microscope. According to the results, IC50 dose of chrysin was found 140 uM which is not cytotoxic to the Raw 264.7 macrophage cells. In breast cancer cells treated with different supernatants, the apoptotic activity of chrysin and LPS induced macrophages was found higher than only LPS induced group due to the more apoptosis detection in fluorescent images. In conclusion, chrysin has cytotoxic and apoptotic effect on MCF-7 cells as well as modulation activity on cytotoxic and apoptotic effects of RAW 264.7 macrophage. However, further studies are required to reveal specific signaling pathways involved in anti-cancer effect of macrophage cells.

Keywords: chrysin, breast cancer, macrophages, apoptosis, immunomodulation

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Session 3 – Poster presentation *S3-28*

PREDICTION OF ESOMEPRAZOLE PHARMACOKINETICS IN RELATION TO CYP2C19 PHENOTYPE

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Proton pump inhibitors (PPIs) are widely used in the treatment of conditions related to gastric acid secretion. They are metabolised primarily by polymorphic CYP2C19 enzyme and CYP2C19 phenotypes have been associated with PPI exposure and treatment efficacy. Physiologically based pharmacokinetic (PBPK) modelling is a powerful tool for prediction of drug exposure in different populations, including drug-metabolising phenotypes. In this study we assessed the PBPK model for esomeprazole in Simcyp Simulator using clinical pharmacokinetic data from the literature, including studies in different populations (Caucasians, Chinese and Japanese) and CYP2C19 phenotype groups. A total of 16 studies were simulated including 6 pharmacokinetic studies with different phenotypes (40 datasets overall). The performance of the model was assessed by visual inspection of the plasma concentration-time profiles and by comparison of the predicted PK parameters to the clinically observed areas under the concentration-time curve (AUC) and maximum concentrations (Cmax). The simulated data were within 2-fold of the observed data for 78% AUC values and 85% Cmax values. The predicted AUC ratios between intermediate and normal metabolisers as well as poor and normal metabolisers were within acceptance criteria for four out of five studies. Our results show that Simcyp model captured fairly well pharmacokinetics of esomeprazole in different CYP2C19 phenotype groups.

Keywords: esomeprazole, PBPK modelling, CYP2C19 phenotypes

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Session 3 – Poster presentation *S3-29*

BIOELECTRICITY AS AN INDICATOR OF CELLULAR METABOLISM AND COMMUNICATION FLOW

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Oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) tend to change when the cell is exposed to metabolic activators or extreme stressor conditions suggesting biological effects on the intensity of mitochondrial respiration and glycolysis. The Seahorse XF24 (Agilent) measures concentration of oxygen ions and exchange of protons in the cell supernatant over time following exposure to substances of known (positive control) and unknown effect. In our experiment, we collected raw data following treatment of BC cells (bladder carcinoma cell) following treatment with test substance X (investigated synthetic compound). Relative OCR and ECAR rates have been measured and calculated following treatment in regular time slots. These measurements results are converted in OCR and ECAR values and enabled direct quantification of biological effect of testing substance. Our experiment revealed distinct dependence of mitochondrial respiration and glycolysis on the concentration of test substance and length of the exposure.

Keywords: ECAR, OCR, test substance X

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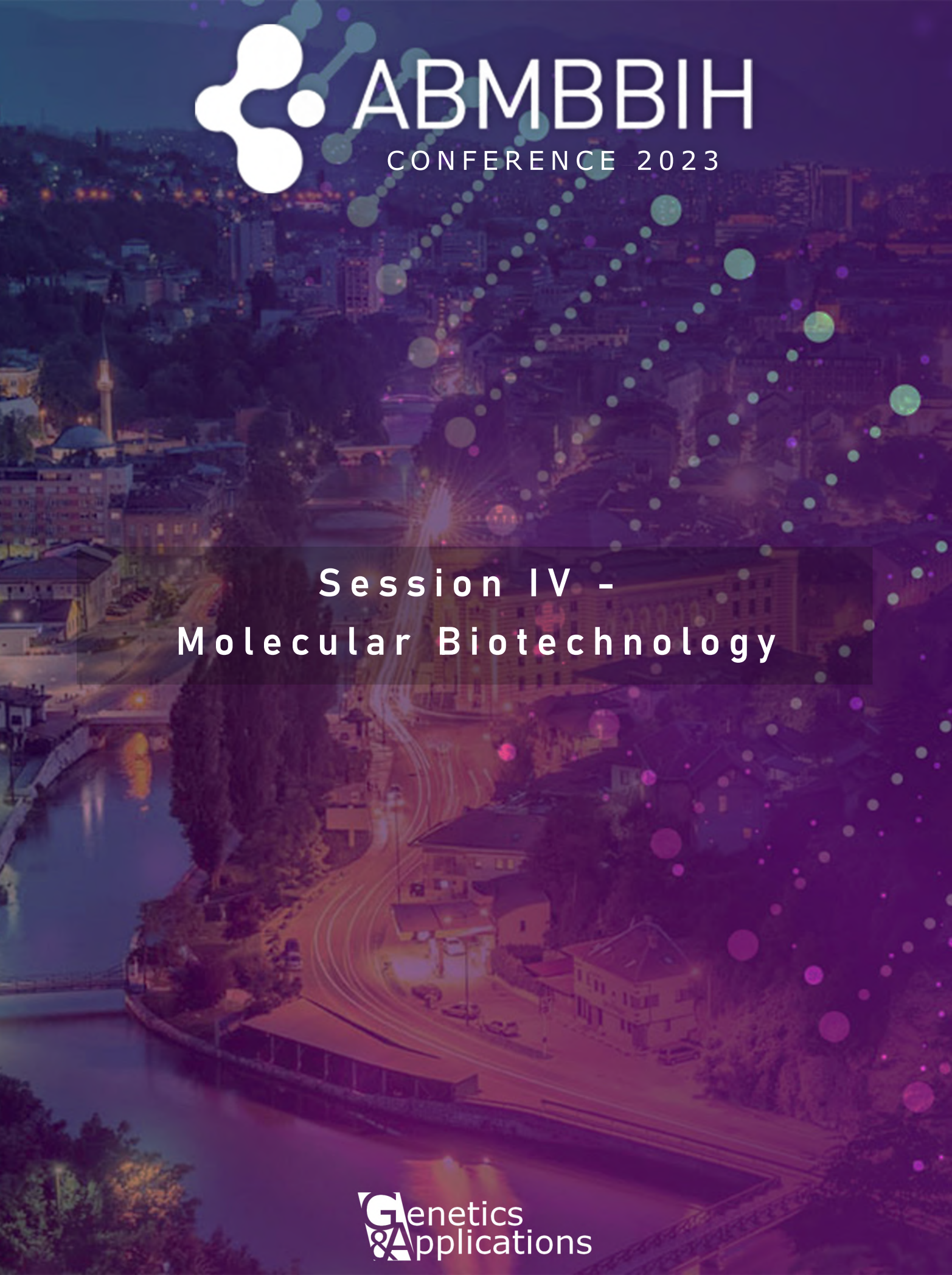
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Session IV -
Molecular Biotechnology
Genetics
Applications

Session 4 – Oral presentation *S4-01*

FROM A VISION TO NEW RESEARCH ESTABLISHED IN THE FIELD OF MARINE BIOTECHNOLOGY

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What are the scientific options out there? How does one navigate through established collaborations, former networks, glass ceilings, closed doors, on one hand, but also an immense wealth of opportunities on the other? I will explain my professional path so far, full of unexpected turns and challenges. They were relevant to organize the process of: identification of needs (professional and societal), opportunities (collaborative and financial), obstacles and personal affinity. Through this process, I identified marine biotechnology as an underexplored and underexploited scientific field. What was the process, why marine biotechnology? Where did we start and where are we now? Through the 4 billion years of evolution in the oceans, marine organisms evolved to produce a plethora of bioactive molecules – secondary metabolites that are produced in response to environmental stimuli and play important biological roles like helping in defensive mechanisms against stress and facilitating effective reproductive processes. Not only these organisms survive in sometimes extreme marine and associated conditions, they strive in them. For the society, the compounds they produce can be of interest in various industries - food, feed, cosmetics, medicine and other industries. This is what essentially marine biotechnology does, i.e., sustainably valorize marine resources to address societal challenges, such as increasing need for alternative food and feed resources, new industrial products and processes, circular economy implementation, longer and healthier lives. Understanding that this field is of immense potential is one thing, but establishing new collaborations and a research field is another big challenge that demands dedication, structure, planning, thick skin and committment to the now-accepted rule of thumb that it takes 10.000 hours to achieve expertise."

Keywords: marine biotechnology, collaboration, valorization

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Session 4 – Oral presentation *S4-02*

MOLECULAR BASIS OF STRESS TOLERANCE OF WHEAT CULTIVARS - HOW COMPLEX IT MIGHT BE?

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Soft wheat (*Triticum aestivum* L.) continues to be in the top list of crops worldwide considering surface occupied, production and usage for human needs. However, compared to its wild pre-ancestors well adapted to extreme environmental conditions, it still suffers the impact of biotic and abiotic stresses. The response is prone to several genes/quantitative trait loci (QTLs), mainly expressed in a cultivar specific manner. Here we discuss results of the research conducted on local Albanian wheat cultivars under stress conditions on GSH (γ-glutamyl cysteinyl glycine) metabolization, which serves in plant growth, development, management of food resources and resistance toward stresses; GSTs (Glutathione S-transferases), which play an important role among effective defense mechanisms against stress-induced oxidative damages; Rubisco genes (*rbcL/S*), which impact the photosynthetic rate through the amount of Rubiscos produced; Rubisco activase genes, which code for enzymes responsible for modifying the catalytic efficiency of Rubisco. Morphological parameters and photosynthetic pigments were also used to understand the impact of treatments on photosynthesis. In conclusion, genetic and epigenetic mechanisms are at the basis of the adaptive responses of wheat, thus a better understanding of the process could serve the selection of local tolerant cultivars, which can be further used in breeding programs for the development of genotypes adapted in different pedo-climatic regions of the world.

Keywords: glutathione, glutathione transferases, gene expression, pigment synthesis, redox homeostasis, epigenetics

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Session 4 – Oral presentation *S4-03*

DISCOVERY OF BIOCATALYSTS AND THE PATHS FOR THEIR IDENTIFICATION

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Understanding enzymatic catalysis and enzymatic activity is central to biochemistry and critical for biotechnology and biocatalysis, particularly for developing rapid and low-cost screening methods for identifying potentially relevant enzymes for industrial applications, such as screening metagenomic libraries or impurity-containing environmental samples. It is common that enzyme assays are standardized experimental protocols established to measure enzyme activity or concentration. Some of these function detection systems became conventional over the years. However, not all of these activity assays fulfill the needs for discovering biocatalysts: easy to handle, stability over incubation time, no interference with impurities, etc. During the presentation, we will share the experience of discovering biocatalysts such as cellulase urethanase, lipase, laccase and lipoxygenase in environmental samples. The developed indigogenic assay method will be presented based on the esterase activity of carbonic anhydrases (CA). Using indoxyl acetate as a substrate for CA has shown promising results in gaining simplicity, repeatability, and applicability to implement high-throughput screening methods. Also, we researched and developed a new amine substrate (Ferbamine), ideal for functional analysis and calorimetric agar-plate-based high-throughput screening for discovering enzymes with laccase activity. Investigation of Ferbamine properties, pH and thermal stability showed that its long-term stability in an aqueous medium is superior to that of commercially available conventional but very unstable substrates. Ferbamine displayed validating performance in detecting laccase activity on agar plates in typical laccase products and in the collection of extracts from terrestrial fungi (42 species, 65 extracts).

Keywords: biocatalyst, enzyme activity assay, environmental samples

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Session 4 – Oral presentation *S4-04*

HARNESSING THE POWER OF ENZYMES: INNOVATIVE APPROACHES FOR DESIGNING NEW MATERIALS

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Enzymes are essential building blocks for various regulatory biological processes including the fabrication of biological materials with relevant socio-industrial interests. In this presentation, I will talk about exploring the interface between biochemistry and material sciences and how to harness the power of the enzymes - be it catalytic or their ability to self-assemble - to design future sustainable materials with emergent properties that surpass their natural/unmodified counterparts. Finally, I will present advances in harnessing the cellulose biosynthetic pathway in cotton to create cotton fibers with tailored properties in a process called material farming.

Keywords: enzymes, biological fabrication, material farming

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Session 4 – Oral presentation *S4-05*

INITIAL EXPERIENCES WITH HOME-DEVELOPED MITOCHONDRIAL DNA SOFTWARE "MITOWIZZ" FOR CLINICAL AND FORENSIC APPLICATION

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Geneticists face a constant challenge in genetic research, regardless of purpose in discovering new methods for analyzing genomic polymorphisms. Following the evolution, the mitochondrial genome (mtDNA) remained a very conserved molecule, however, it does harbor possible polymorphisms with relevance in both clinical and forensic applications. Detection of the mutations in mtDNA genome is essential for the diagnostics of certain medical conditions, as well as a potential target for research, especially in tumorous tissues. More commonly, mtDNA has a standing role in forensic practice, especially in cases where an STR genomic profile cannot be obtained or it's not informative enough. Furthermore, as an added benefit, mtDNA has its proven role in genealogy, as we are able to trace maternal ancestry. In this research, we show the rapid and successful examination of mtDNA sequences obtained by Sanger sequencing and analyzed using Mitowizz software, in comparison with existing methods. The described approach showed excellent results in mitigating the possibility of human error, increasing the accuracy of determination of mutational's positions, and shortening the time for mtDNA typing. Mapping polymorphic locations in mtDNA, can immensely contribute to the formation of both clinical and forensic databases for the population of Bosnia and Herzegovina. This research was based on an experimental sample of 100 unrelated individuals living in Bosnia and Herzegovina. In order to protect personal data, the identity of the participants in the study will remain anonymous and will be distinguished based on a unique identification number.

Keywords: mtDNA, Mitowizz software, polymorphisms, mtDNA typing

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Session 4 – Oral presentation *S4-06*

DIAGNOSTIC TESTING FOR SARS-COV-2 BY REAL TIME RT-PCR

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Geneticists face a constant challenge in genetic research, regardless of purpose in discovering new methods for analyzing genomic polymorphisms. Following the evolution, the mitochondrial genome (mtDNA) remained a very conserved molecule, however, it does harbor possible polymorphisms with relevance in both clinical and forensic applications. Detection of the mutations in mtDNA genome is essential for the diagnostics of certain medical conditions, as well as a potential target for research, especially in tumorous tissues. More commonly, mtDNA has a standing role in forensic practice, especially in cases where an STR genomic profile cannot be obtained or it's not informative enough. Furthermore, as an added benefit, mtDNA has its proven role in genealogy, as we are able to trace maternal ancestry. In this research, we show the rapid and successful examination of mtDNA sequences obtained by Sanger sequencing and analyzed using Mitowizz software, in comparison with existing methods. The described approach showed excellent results in mitigating the possibility of human error,increasing the accuracy of determination of mutational's positions, and shortening the time for mtDNA typing. Mapping polymorphic locations in mtDNA, can immensely contribute to the formation of both clinical and forensic databases for the population of Bosnia and Herzegovina. This research was based on an experimental sample of 100 unrelated individuals living in Bosnia and Herzegovina. In order to protect personal data, the identity of the participants in the study will remain anonymous and will be distinguished based on a unique identification number.

Keywords: SARS-CoV-2

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Session 4 – Poster presentation *S4-07*

APPLICATION OF *HELICHRYSUM ARENARIUM* EXTRACTION OIL IN BIOTECHNOLOGY OBTAINED BY SOXHLET AND UTRASOUND ASSISTED EXTRACTION

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The raw material *Helichrysum* is used in medicine mainly due to its bioactive properties, for the treatment of tropical infections, respiratory diseases, reduce inflammation, cardiovascular diseases, rheumatism, as a detoxifying herbal medicine and as well in food and nutritional supplements. It is reported that this plant has biological activities: antimalarial, antioxidant, antidiabetic, antiviral, anti-tuberculosis, anti-inflammatory, antifungal and antibacterial properties. The chemical nature of this plant is complex and is composed of various organic compounds such as flavonoids, chalcones, phloroglucinol derivatives, essential oils, fatty acids, α-pyrone derivatives and diterpenes. The essential oil from the flowers of *Helichysum arenarium* obtained by hydrodestillation was analyzed by gas chromatography-mass spectrometry. The analysis identified 25 compounds that represent 100% of the total composition of the essential oil. Sesquiterpenes (54%) and monoterpenes (24%) were identified in the composition of the obtained essential oil. The major compounds in sesquiterpenes are: italicenes (4.4%), β-caryophyll (4.5%), γ-curcumin (16.2%) and β-selinene (6.3%). The most common compounds in monoterpenes are limonene (4.3%) and α-pinene (16.4%), while in smaller quantities there are monoterpene oxides, alcohols and esters. The main non-terpene compound is isoamyl angelate (1.4%).Qualitative composition of *Helichrysum* extract obtained by Soxhlet extraction when 55%, 70% and 96% ethanol is used as solvent contains α-longingine and humulin. The chemical composition of the *Helichrysum* extract obtained by ultrasonic extraction is identical to that of the identified compounds of the extract obtained by Soxhlet extraction, the difference being that ultrasonic extraction produces a larger amount of components.

Keywords: essential oil, sesquiterpenes, hydrodistillation, monoterpenes, GC-MS

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Session 4 – Poster presentation *S4-08*

B-GLUCOSIDASE B FROM *MICROBACTERIUM SP.* BG28 AS A BIOFILM CONTROL AGENT IN FOOD PROCESSING ENVIRONMENT

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About one in ten people contract a foodborne illness within a year. Children under the age of five are the most affected, with 125,000 deaths each year. Many of the foodborne illness outbreaks can be linked to the presence of biofilms in the food industry, and *Salmonella enteritidis* is an extremely important foodborne pathogen that thrives in these conditions. It has been shown that biofilms can be resistant to physical and chemical treatments used in cleaning and disinfection procedures in food processing. The problem with using more aggressive disinfectants is that they often violate food safety regulations. The use of enzymes which degrade biofilm matrix structural components should facilitate current disinfection procedures and not compromise food safety. In this study, the anti-biofilm activity of recombinantly expressed β-glucosidase B and its potential use as a protective agent to control *Salmonella* biofilm formation is investigated. The putative target of this enzyme is cellulose, the structural component of the *Salmonella* biofilm matrix. β-Glucosidase B deriving from the environmental strain *Microbacterium sp*. BG28 was heterologously expressed in *Escherichia coli* and successfully purified by affinity chromatography. The anti-biofilm activity of the enzyme was evaluated in in vitro assays using various clinical isolates of *S. enteritidis*. The toxicity of the enzyme was studied in *Caenorhabditis elegans*. β-glucosidase B effectively inhibited the formation of *Salmonella* biofilms grown in a temperature range of 8°C to 37°C, achieving 50% inhibition at concentrations of 100μg/ml. Biochemical characterization showed that the optimal pH activity of the enzyme is between 6 and 7, with the highest activity observed at temperatures between 37°C and 47°C. The absence of toxicity and other presented results indicate that beta-glucosidase B can be used in biofilm control in the food industry.

Keywords: *Salmonella*, biofilm, beta glucosidase, enzyme

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Session 4 – Poster presentation *S4-09*

STUDENTS' KNOWLEDGE AND ATTITUDES TOWARDS BIOTECHNOLOGY AND ITS APPLICATION

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Today biotechnology has a wide range of activities in numerous fields such as healthcare, agriculture, and diagnostics. The application of biotechnology has led to the rapid and efficient development of new products and improved the business of numerous industries. In the case of Bosnia and Herzegovina, the development of biotechnology faces limitations related to the system of public financing and the lack of industrial capacity. There is no adequate biotechnology program in our country, but it is part of programs of natural sciences. Therefore, the aim of this study is to gain insight into the knowledge and attitudes of health studies students about biotechnology and its application. Cross-sectional, quantitative, and descriptive study was conducted at the University of Sarajevo - Faculty of Health Studies over the period of two months. The questionnaire included the following two parts: 12 questions about knowledge of biotechnology and its application and 19 questions about attitudes of biotechnology and its applications. The study included 100 undergraduate students of study programs Laboratory technologies (N=63) and Sanitary engineering (N=37). Higher knowledge scores about biotechnology were demonstrated by the students of Laboratory Technologies compared to the students of Sanitary Engineering. The mean value of correct answers between two study programs was 29.48%. Students of both study programs answered the question about the manipulation of the DNA molecule correctly to the greatest extent. Students showed negative attitudes related to purchasing (SGMP) and consumption of GMO products (CGMP). Participants' attitudes on public awareness of GMOs (PAGMO) and environmental impacts of genetic engineering (EIGE) were significantly related to their biotechnology knowledge ($p<0.05$). This is the first study regarding this topic in Bosnia and Herzegovina. Results from this study provide baseline data that may be used to conduct future research.

Keywords: biotechnology, students, knowledge, attitude

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Session 4 – Poster presentation *S4-10*

POTENTIAL REPURPOSING OF VIRAL INHIBITORS AGAINST GLYCOPROTEIN N OF RIFT VALLEY FEVER VIRUS (RVFV)

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Rift Valley fever virus (RVFV) is an arbovirus that belongs to the *Bunyaviridae* family and *Phlebovirus* genus. First outbreak of this virus was discovered in 1930, when happened a sudden increase of deaths and abortions among sheep in the greater Rift Valley of Kenya. This is a zoonotic virus that affects both humans and livestock, causing Rift Valley hemorrhagic fever or in some cases encephalitis. RVFV genome is segmented into three parts marked by their lengths, small (S), medium (M) and large (L). Two structural proteins encoded by M segment are glycoproteins Gc and Gn, which participate in the structure of the envelope and have a role as receptors. Because of limitation of ativiral agents against this virus and no licensed vaccine for human use, there is urgent need to find potential drug. Molecular docking is the most commonly used tool for drug repurposing. Using this method, we analysed the binding affinity of hexachloropene, arbidol, calyxin J and rhodanine derivate LJ-001 to the Gn glycoprotein of RVFV (PDB ID: 6F8P), via AutoDock Vina 1.1.2.. Favipiravir and benzavir-2 were used as positive controls of binding affinity as they have shown antiviral effect against RVFV. The highest affinities for binding to Gn glycoprotein of RVFV were observed for positive control benzavir-2 (-8.2 kcal/mol), then for arbidol (-7.4 kcal/mol), LJ-001 (-7.1 kcal/mol), hexachloropene (-6.5 kcal/mol), calyxin J (-5.7 kcal/mol) and favipiravir (-5.7 kcal/mol). The antiviral potential of these compounds is also reflected in the fact that most of these ligands created polar hydrogen bonds with the Gn glycoprotein. This findings could be helpful for scientist in selection of potential antiviral agents against RVFV for further studies such as in vitro, in vivo and clinical studies. This knowledge is valuable for planning for epidemiological preparedness in post-COVID-19 era.

Keywords: Rift Valley fever virus, molecular docking, arbidol, drug repurposing

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Session 4 – Poster presentation *S4-11*

IDENTIFICATION OF *CANDIDA* SPECIES IN ORAL RINSE SOLUTION BY REAL TIME PCR

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Oral candidiasis is one of the most common fungal infections affecting the oral mucosa. These lesions are caused by Candida species. There are nearly five *Candida* species that are seen in the oral cavity (*Candida albicans*, *Candida tropicalis*, *Candida krusei*, *Candida parapsilosis* and *Candida dubliniensi*s). Correct identification of *Candida* species is important for targeted antifungal therapy and for epidemiological purposes. This study aims to develop a simple method for the detection and identification of medically important *Candida* species by Real Time Polymerase Chain Reaction (RT-PCR). A total of 100 adults at Çukurova University between the ages of 18 and 56 participated in this study. Each volunteer gargled 15 ml sterile distilled water, and the samples were centrifuged at 3,000 rpm for 10 min. The pellets were suspended in 200 µL sterile distilled water and inoculated into a plate of CHROMagar Candida. Genomic DNA was purified by Quick DNA Fungal/Bacterial Miniprep kit. Two specific primers were used for gene amplification. We evaluated RT-PCR assays for the detection of seven reference *Candida* species, namely, *Candida albicans*, *Candida dubliniensis*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis*, *Candida tropicalis* and *Candida inconspicua*. The detection and identification of *Candida* species by conventional phenotypic methods take a few days. Real-time PCR followed by melting curve analysis (MCA) is a simple, rapid and inexpensive tool to identify *Candida* species in a day. In this study, a methodology employing RT PCR with melting curve analysis procedures was optimized for the detection of medically important *Candida* species. This project was supported by Çukurova University Research Grant (FYL-2021-13346).

Keywords: oral candidiasis, Candida species, Real Time PCR

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Session 4 – Poster presentation *S4-12*

COULD CAVES BE OUR NEW HOPE FOR THE DISCOVERY OF PROMISING ANTIMICROBIAL BIOACTIVE COMPOUNDS?

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The search for bioactive metabolites, including new antibiotic compounds from microbial sources for potential use in agricultural, pharmaceutical and industrial applications, has become important due to the development of antibiotic resistance in most pathogenic microorganisms. The intensive explore for new, effective broad-spectrum antimicrobial compounds is primarily focused on extreme environment such as subterranean, ancient lake and deep-sea habitats. During the speleological expedition ""Ponor Kovači-Izvor Ričine"" in August 2022, various samples of underground microbial biofilm were collected, including samples from bedrock, water, sediments and calcite moonmilk. The samples were kept cold all the time (up to +8 ºC) until processing in the laboratories (LAM and LAMB) of the Faculty of Science of the University of Sarajevo. Here, we have presented preliminary results on the cultivable bacterial diversity of calcite moonmilk from selected caves of the Dinaric arc. Primary screening to assess the antimicrobial potential of isolates was performed using the cross-line method. The antimicrobial properties of the following reference strains of bacteria were tested: *Enterococcus faecalis* ATCC 19433, *Staphylococcus aureus* ATCC 6538, *Staphylococcus epidermidis* ATCC 12228, *Bacillus subtilis* subsp. *spizizenii* ATCC 6633, *Escherichia coli* ATCC 8739, *Pseudomonas aeruginosa* ATCC 9027, *Methicillin resistant Staphylococcus aureus* ATCC 33591 (MRSA) and the fungus *Candida albicans* ATCC 10231. Most of the tested cave isolates showed better antagonistic activity against Gram-positive bacteria than against the tested Gram-negative bacteria. The most promising isolates belong to the genera *Pseudomonas* and *Bacillus*, which was confirmed by PCR amplification and Sanger sequencing of bacterial 16S-rRNA genes using universal primers, after which molecular characterization of the new strains is forthcoming.

Keywords: bioactive compounds, antibiotics, subterranean habitats, *Pseudomonas*, *Bacillus*

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Session 4 – Poster presentation *S4-13*

COMPARATIVE ANALYSIS OF HIGH AND LOW NEURAL INVASION GENE EXPRESSION DIFFERENTIAL USING BIOINFORMATICS TOOLS

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Pancreatic cancer is a highly aggressive malignancy with a poor prognosis. Neural invasion, the infiltration of tumor cells into the surrounding neural tissue, is a known histopathological feature of pancreatic cancer and is associated with increased tumor aggressiveness and poor patient outcomes.In this study, we aimed to compare gene expression profiles in pancreatic cancer patients with high and low neural invasion scores using bioinformatics tools to gain insight into the molecular mechanisms underlying neural invasion in pancreatic cancer. We used 13 tissue samples from pancreatic cancer patients undergoing surgical resection and divided them into two groups based on histopathological examination: high neural invasion score (NIS) and low NIS. RNA sequencing was performed from tissue samples. Obtained RNA sequencing data were used to identify differentially expressed genes (DEGs) and for pathway enrichment analysis. Results were analyzed using bioinformatics tools to identify signaling pathways between the high NIS and low NIS groups. As a result of bioinformatic analysis, it was determined that there was a difference in the expression of 1117 genes between the high NIS and low NIS groups. Among them, there are genes that may have a role in cancer metastasis and neural invasion, such as *CDKN2A, TP53I11, MMP8, MMP11, MMP19, SEMA3B, SEMA3D, CXCR5, CCL2*, and *CCL3*. The differentially expressed genes and enriched pathways identified may play important roles in the molecular mechanisms underlying neural invasion and tumor aggressiveness in pancreatic cancer. The findings of this study contribute to a better understanding of the complex molecular landscape of pancreatic cancer. Further functional validation of these differentially expressed genes and pathways could lead to the development of new therapeutic targets for pancreatic cancer patients with high neural invasion scores.

Keywords: pancreatic cancer, neural invasion, differentially expressed genes

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Session V -
Interactions between organisms
and the environment
Genetics
Applications

Session 5 – Oral presentation *S5-01*

INTERACTION OF DOUGLAS FIR PROVENANCES WITH ENVIRONMENTAL CONDITIONS IN TWO PROVENANCE TESTS IN BOSNIA AND HERZEGOVINA

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Douglas fir (Pseudotsuga menziesii (Mirbel) Franco) is the most important and most productive species in Europe, outside its natural range. This study aimed to examine the interaction between the effects of the genetic structure of provenances and two localities of provenance tests in Bosnia and Herzegovina. The results will be used for the selection of best provenances for further use in wood production. Two provenance tests of Douglas fir (Batalovo Brdo and Rosulje), with different environmental conditions, were established in 1966. by seedlings 2+2 years old, in three blocks, with 250 plants per provenance and block. Four provenances were represented in both tests (11-0.5 Yoyce Washington; 25-1.0 Wishkah Washington; 65-1.0 Darrington Washington; 83-3.0 Palmer Oregon), and both tests had one additional provenance. Diameters at breast height and heights of all survived trees were measured in 2022 (60 year-old trees), and basal area and tree volume were calculated. The variances of traits caused by provenance tests (environments), provenances, and interaction of provenance tests and provenances were examined using multivariate analysis. Test of Between-Subjects Effests showed statistically significant differences in diameters at breast height caused by provenance tests, provenances and interaction between provenance tests and provenances. Test of Between-Subjects Effests showed statistically significant differences in heights caused by provenances and by interaction of provenance tests x provenances but not caused by provenance tests. All provenances except 83-3.0 showed better growth in height in Batalovo Brdo provenance test. All provenances except 65-1.0 showed better growth in breast height diameter in Rosulje provenance test. Basal area and volume acts like breast height diameter. The obtained results can be used for the selection of the best provenances for afforestation at predefined habitats that correspond to the conditions of the experimental plots, as well as for raising clone plantations or seed plantations of the species.

Keywords: Douglas fir, environmental contidions, genetic structure, interaction

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Session 5 – Oral presentation *S5-02*

APPLICATION OF DNA BARCODING FOR IDENTIFICATION OF DIFFERENT ORGANISMS WITHIN FOREST ECOSYSTEMS

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DNA barcoding is used to identify a number of different organisms (viruses, bacteria, fungi, insects and plants) in the forest ecosystem. This method identifies a species by analyzing short, standardized DNA sequences from a particular region of the genome. The aim of implementing DNA barcoding as a diagnostic method in the Laboratory of Molecular Genetic Testing (LMGT) of the Croatian Forest Research Institute (CFRI) was to establish faster and more accurate diagnostic tools for forest pests and other forest organisms of interest for professional and scientific purposes. The professional application refers to the participation of the CFRI in the monitoring and control programme for the presence of quarantine forests pests in Croatia. The main advantage of the survey programme is the early detection of quarantine pests and the knowledge gained about their prevalence, spread and patterns of movement within the European Union. Since 2011, the LMGT has carried out DNA analyses and species confirmations for 15 quarantine pests (13 insects and two fungi). The protocols for the DNA analysis were issued by the European and Mediterranean Plant Protection Organization (EPPO). On average, about 250 samples were examined annually. So far analysed quarantine species have not been detected in Croatian forests. Furthermore, DNA barcoding is very applicable in scientific research. The LMGT has been participated in a scientific project with a special task "DNA barcoding of the mycoflora of forest tree species in continental and Mediterranean areas" with the aim of determining the biodiversity of fungi-caused diseases in forest trees. The samples were collected in the forests of the management units of the East-Psunj and Papuk Natural Park and the Učka Natural Park in Croatia. Molecular identification of fungi was carried out using primary (internal transcribed nuclear ribosome spacer (ITS)) and secondary (translation prolongation factor 1α, TEF1α) regions of fungal DNA barcode. After determining the reference sample in the GenBank (NCBI), all sequences were registered in the GeneBank under a unique access number. As a result, 47 fungi belonging to Ascomycota and Basidiomycota were identified, including two unknown fungal endophytes. For species identification in forest ecosystems, DNA barcoding is widely accepted and is constantly being improved.

Keywords: DNA barcoding, Forests, Quarantine pests, ITS, Fungi, Insects

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Session 5 – Oral presentation *S5-03*

RAISING THE PROGENY TO FIGHT BACK: FROM PRIMING TO TRANSGENERATIONAL MEMORY

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Environmental stressors can pose a limiting factor to plant development and being sessile organisms and not able to flee, plants have been forced to develop mechanisms to fight. In perennial plants activation of defence mechanisms can result in transgenerational memory of experienced stress in subsequent generations of the progeny. In the context of climate change drought stress has been one of the most impactful stressors affecting crop growth and yield, especially in arid areas such as the Mediterranean area. Different methods have been tested for improvement of drought stress tolerance in crops and seed priming has been demonstrating good results. Seed priming in chickpeas can increase tolerance to drought even in sensitive genotypes and research demonstrates that this is possible due to changes in the expression of drought tolerance-related genes. Exposure to adverse factors of the environment such as heavy metals can "prime" parent plants inducing primed memory to be embedded into produced seeds enhancing tolerance in progeny. Exposure of tomatoes to Ni stress induces metabolic changes in tomato plants resulting in the inhibition of seed dormancy and induction of vivipary. The effects of Ni exposure can be seen in F1 generation as well even in optimal conditions with no Ni exposure. Such memory as a result of priming (by seed or plant priming) increases the survival chances of progeny in adverse environmental conditions.

Keywords: plant stress, plant memory, priming, climate change

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Session 5 – Oral presentation *S5-04*

IDENTIFICATION OF VITAMIN BIOSYNTHESIS PATHWAY IN THERMOPHILIC *LEPTOLYNGBYA* SP. AND EFFECTS OF MACRONUTRIENTS MANIPULATION ON ITS GROWTH

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Leptolynbya is one of the most common cyanobacterial genera in soils and in periphyton and metaphyton in freshwater and marine. This taxonomically difficult genus has an indistinct morphological characteristics resulting in difficulties for identification of species. In this study, we examined the genome sequence of thermophilic *Leptolyngbya* sp. isolated from Malaysia hotspring to identify the vitamin biosynthesis pathway. The putative pathways of Vitamin B and K of this thermophilic *Leptolyngbya* sp were predicted by comparing the gene sequence of enzymes involved in vitamin biosynthesis pathway of other cyanobacterial strains with the genome of this thermophilic *Leptolyngbya* sp. In addition, this study identified effects of rich-nitrate (NO_3^-) and -carbonate (CO_3^{2-}) conditions as well as flue gas wastewater influenced the growth of thermophilic *Leptolyngbya* sp. isolated from two different hot springs, SKS and SKW from Sg. Kling hot spring (sediment and water, respectively) and aa from Lubuk Timah hot spring (water). The growth of SKS was high in rich-nitrate and -carbon media, while the growth of aa was high only in rich-carbon media. However, the growth of both wild type and mutant aa was inhibited in media with flue gas wastewater. On the other hand, SKW showed higher growth in media with flue gas wastewater compared to SKS. Thus, suggests that SKW could be a suitable strain for biorefinery of flue gas water.

Keywords: vitamin biosynthesis, genome, Thermophilic cyanobacteria, flue gas biorefinery

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Session 5 – Oral presentation *S5-05*

INTEGRATIVE ONLINE TOOLS FOR LEARNING AND TEACHING BIOCHEMISTRY FACE TO FACE

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Face to face teaching and learning is the oldest and surely most exploited education environment. It is indeed recognized as gold standard, usually compared to new, alternative or experimental approaches, defining standard well known coordinate system of education. Still, face to face education is far from rigid strictly defined system deprived of implementing new tools, technology, approaches....new ideas. Face to face education is not in contrast to online times we live in, but rather in line. It selectively integrates online tools when and were beneficial for both educators and students. Let's take a journey together through the vivid field of online tools that can be integrated in face to face teaching and learning. Let's discuss these tools as valuable "spices" providing new flavour to a face to face education environment.

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Session 5 – Poster presentation *S5-06*

PER- AND POLYFLUOROALKYL SUBSTANCES AS A FACTOR MODULATING COVID-19: PRELIMINARY DATA

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Per- and polyfluoroalkyl substances (PFAS) are a large chemical group which are biopersistent and bioaccumulative. They have been shown to alter metabolism, thyroid function, and immune system. Exposure mainly occurs through drinking water and foods of animal origin. Only a few studies have investigated correlations between exposure to different PFAS and COVID-19 indicating a potential relationship between high PFAS exposure and COVID-19 susceptibility. This study aimed to investigate the causality and correlation between the PFAS serum concentration and the immunological response in the general non-occupationally exposed population that has been infected with SARS-CoV-2. Serum samples with PCR-confirmed SARS-CoV-2 infection were obtained from General Hospital Tešanj, Bosnia and Herzegovina. Samples were aliquoted and analyzed for specific biomarkers, in order to assess the stage of infection and the immune response of patients. Samples were classified into four groups according to the patient's clinical presentation of the disease (mild to asymptomatic, moderate, severe, and ex-letalis). Additional serum aliquots were stored at -20°C, for retesting for immune response analysis and analysis on PFAS. A subset of 16 samples (8 females aged 67.12±3.53 and 8 males aged 63.37±3.56 years, divided into 4 categories) were analyzed for several PFAS using liquid chromatography tandem mass spectrometry. The mean concentrations of PFOS, PFOA, PFHxS, PFNA, PFDA, PFHpS, PFUnDA, PFHpA, and PFPeS were 2.59±1.07, 0.57±0.26, 0.52±0.41, 0.37±0.18, 0.20±0.08; 0.11±0.08, 0.06±0.03, 0.02±0.01, and 0.006±0.006 ng/mL, respectively. No significant differences in PFAS levels found among patient groups with varying clinical symptoms. Due to the limited sample size, the results could only be interpreted as preliminary and further research is needed to additionally validate these results. High PFAS exposure may be linked to an altered immunresponse to the infection of SARS-CoV-2 and possibly other viruses. It is crucial to understand the mechanism behind this, with regards to further pandemics or vaccination reponse.

Keywords: COVID-19, PFAS, immunresponse

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Session 5 – Poster presentation *S5-07*

FOLIAR APPLICATION OF METHYL JASMONATE AFFECTED GROWTH, LEAF PHYSIOLOGY PARAMETERS AND AQUAPORIN GENES EXPRESSION IN DROUGHT-STRESSED IMPATIENS WALLERIANA

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This research evaluated the effects of foliarly applied elicitor methyl jasmonate (MeJA) on the potential improvement of drought tolerance in Impatiens walleriana. Growth and leaf physiology parameters (Stomatal conductance, Chlorophyll, Flavonoid, Anthocyanin, and Nitrogen Balance Index - NBI), as well the expression of four aquaporin genes (*IwPIP1;4, IwPIP2;2, IwPIP2;7* and *IwTIP4;1*), were evaluated. These parameters could serve as indicators of drought tolerance in I. walleriana, a worldwide popular horticultural plant, very sensitive to drought. The experiment included four treatments: control plants, drought-stressed plants foliarly sprayed with distilled water, drought-stressed plants foliarly sprayed with 5 µM MeJA, and drought-stressed plants foliarly sprayed with 50 µM MeJA. Foliar spraying was performed seven days before drought induction, and on the day of drought stress induction. The stressed plant groups were non-irrigated to reach 15 and 5% soil water content (SWC), while control plants were well-watered (35-37% SWC) during the entire experiment. Drought reduced fresh and dry shoot weight, as well total leaf area but dry matter content was not affected. Foliarly applied MeJA improveda growth parameters, depending on the elicitor concentration and drought intensity. Stomatal conductance was slightly reduced at 5% SWC in plants foliarly sprayed with MeJA regardless of the used concentration. Similarly, the flavonoid index was reduced at 15 and 5% SWC when 50 µM MeJA was foliarly applied, while there were no observed changes in the anthocyanin index in any treatment. The foliar application of 50 µM MeJA increased I. walleriana chlorophyll index and NBI at 5% SWC, indicating an elicitor contribution to plant drought tolerance at physiological level. Among the four analyzed aquaporin genes, expression of *IwPIP1;4* and *IwPIP2;7* was strongly induced in drought-stressed plants foliarly pre-treated with 50 µM MeJA, indicating an improvement of water flow through cells to maintain homeostasis.

Keywords: Impatiens walleriana, methyl jasmonate, drought, leaf physiology, aquaporins

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Session 5 – Poster presentation *S5-08*

DIFFERENTIAL BLOOD PICTURE OF CHUB (*SQUALIUS CEPHALUS*, LINNAEUS, 1758) FROM THE WATER COURSES OF NORTHEAST BOSNIA

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Biochemical and hematological parameters of fish are often used to assess their physiological status. They are suitable biomarkers of fish health, which are also used as bioindicators in monitoring the quality of the aquatic environment. In this research, the differential blood count of 200 individuals of chub (*Squalius cephalus*, Linnaeus, 1758) caught from ten streams of northeastern Bosnia: Spreča, Gostelja, Turija, Suha, Tinja, Jala, Sapna, Oskova, Brka and Bosna was analyzed. Blood was sampled by puncture of the chub's heart, and native blood without the addition of anticoagulants was used for analysis. The research determined that the average percentage of lymphocytes in chub is from 83.15% in the locality Brka to 93.85% in the localities of Turija and Tinja; neutrophils from 4.05% in the river Turija to 10.65% in the river Brka; eosinophils from 0.05% in the river Tinja to 1.20% in the river Gostelja; basophils from 0.00% in the river Bosna to 4.85% in the river Brka; monocytes from 0.90% in the rivers Spreča and Brka to 5.60% in the river Gostelja. The post-hoc Tukey test was determined statistically significant differences in percentage of neutrophils between the localities of Brka and the localities of Spreča, Gostelja, Turija, and Tinja and Jala; eosinophils between the Gostelja locality and the Spreča, Suha, Tinja, Jala, and Sapna localities; basophils between the Gostelja locality and Turija, Tinja, Jala and Bosna localities; lymphocytes between the localities of Gostelja and the localities of Spreča, Turija, Tinja, Jala and Sapna, and monocytes between individuals of chub from the river Gostelja and individuals of chub caught from all other investigated rivers. The highest average number of neutrophils, basophils, and the lowest percentage of lymphocytes was found in chub caught from the Brka River, which is characterized by a significant number of wild dumps in the coastal area.

Keywords: Squalius cephalus, differential blood count, north-eastern Bosnia

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Session 5 – Poster presentation *S5-09*

SEED PRIMING ENHANCES TOLERANCE AND ACCUMULATION OF HEAVY METALS IN CD HYPERACCUMULATOR *SILENE SENDTNERI* THROUGH CHANGES IN GENE EXPRESSION

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To improve our understanding of the molecular mechanisms underlying seed priming, RNA transcriptome analysis was performed using primed and non-primed seeds of *Silene sendtneri*. Seed priming was performed by submerging the seeds in different priming agents for 24h at 4°C, followed by rinsing with sterilized water and desiccation to the original moisture content. Silene sendtneri is a species with no sequenced genome and annotation of de novo assembly of the transcriptome was done using different species for the reference genome. Gene ontology (GO) analysis indicated that genes related to heavy metal transporters and heat shock proteins are differentially expressed after priming in relation to the used priming agent. Within these gene categories, genes such as heavy metal-associated isoprenylated plant protein 26-like (log2fold -8.79) were downregulated, while others such as heavy metal ATPase 5 (log2fold 6.46), heat shock factor protein HSF30-like isoform X1 (log2fold 5,98) were upregulated. Some gene categories are commonly highly expressed after seed priming regardless of the used agent, but some specific gene categories have been recorded to be expressed in relation to the used agent.

Keywords: Cd hyperaccumulator, heavy metal tolerance, seed priming, primed memory

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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Oral presentation *SEDU-01*

TRANSFERABLE SKILLS AND BIOCHEMISTRY EDUCATION FOR THE NEEDS OF INDUSTRY

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"Knowledge or skills, that is the question?", which every employer considers as a difficult one. However, in the end, most of them would choose the skills as an answer because most of the potential employees usually have knowledge or its level could be at least easily tested, but assessing the skills is challenging. Yet, today's academic education still focuses on equipping students with a higher level of knowledge, whereas skills "will be picked up along the way" (or won't). Reflecting the European Skills, Competences and Occupations (ESCO) classification that identifies and categorises skills, competencies, qualifications, and occupations relevant to the EU labour market and education, it is unquestionable that skills development should be a crucial part of education and deeply incorporated in academic curricula. It is crucial for students to be equipped with transversal skills that enable them to be interoperable between different sectors, such as public institutions, academia, industry, and business. Being equipped with a wide spectrum of skills enables future professionals access to an enlarged number of opportunities for career development and for the labour market, which is in constant need of highly skilled talents. But how to develop self-discipline, adaptability, or problem-solving, some of the most in-demand soft skills globally in our students? Are we, university teachers, aware of students' need for these skills? Even if we are, are we equipped with the skills required for this task or do we need assistance of experts in the HECI (Humanity, Ethics, Creativity, Imagination) field? These and some other relevant questions will be discussed in order to shed light on the challenges but also the opportunities we are already facing.

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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Oral presentation *SEDU-02*

RAISING THE INNOVATION POTENTIAL THROUGH TEACHING PROGRAMS IN MOLECULAR BIOLOGY

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Economical development level is a direct result of well developed relationships between science and innovation capacities (academia) and industry. Investment in innovation and scientific capacities have multiple effects and societal development, being a driver for industrial expansion. Global societal challenge of COVID-19 has proven that knowledgeable societies were the most resilient ones in fighting pandemic. Meeting Sustainable Development Goals requires in-depth transformation of industrial concepts that include supporting science and innovation capacities with potential for translation of knowledge and technology to industrial sector regardless of the geographic boundaries or socioeconomic origin. Molecular biology is the most propulsive innovation field and polygon for future game changing discoveries especially in the field of biodiversity and environment, secure and functional food production and medicine. Academic resources integrate higher education and science and innovation stakeholders. Quality education and skills building through university programs is the fastest and the most resourceful way of societal developmental breakthroughs. Consequently, enhanced industry will drive the adaptation of university programs and serve as source of skills development. The empowerment of future professionals should involve research and innovation skills with societal impact dimension. What methodologies are applicable will also be discussed here.

Keywords: science, innovation, university education, molecular biology, sustainable development goals

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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Oral presentation *SEDU-03*

INTEGRATION OF VIRTUAL LABORATORIES IN LEARNING OF BIOCHEMISTRY

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The recent Covid-19 pandemic brought more awareness and a greater need for something that already existed: the possibility of using computer-based simulation of real laboratory experiments. Indeed, the demand and use of such virtual laboratories increased enormously during the forced lock-up period worldwide. It is the time now to consider this as something that may be retained as a way to enrich the students' learning experience. However, it is not just a question of picking informatic tools and resources and sending the students to visit them, but rather to reflect on what is the most profitable way of using these resources to improve the training of our students. Specifically, we are dealing with gaining laboratory work competences, which are not trivial outside the hands-on physical laboratory. The idea is not to replace the wet lab, but to complement and enhance the experience. We propose that instructors should thoughtfully design activities which demand an active role of the student, e.g. make decisions, observe, extract information, to test a hypothesis or answer a question and hence obtain a conclusion. It is paramount that the virtual experiment is not just some procedure to be followed, but instead that we force reflection and analysis about the development of the experiment. Some tips will be presented about building activities as well as design of the simulation and virtual laboratories themselves. For instance, it should be set as a realistic experience, akin to a physical laboratory, not so much because of an attractive look, but because there is variability, flexibility in the choice of parameters and the course of action, obtaining consequently different results, even negative ones. Some available free resources will be offered.

Keywords: simulations, virtual labs, learning, practicals, techniques

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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Oral presentation *SEDU-04*

BE A SCIENTIST, NOT A WORKER IN SCIENCE

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"When running experiments at the bench in a research lab, when discussing data and conclusions with your supervisor, when writing manuscripts at the office, when travelling to attend any congress or workshop… do you feel like a scientist, or like a worker in science? The answer you choose is crucial for you to greatly enjoy every second of your time as a scientific researcher, for you to whole-heartedly celebrate your findings as a discoverer "…seeing what everybody else has seen, and thinking what nobody else has thought (Albert Szent-Gyorgyi)". But what is a scientist? The term 'scientist' was coined by the English philosopher and historian William Whewell in the nineteenth century, in 1835, when he announced that a scientist is like an 'artist', using their imagination and mind to create unique masterpieces. A worker in science, in contrast, is like any worker in any other economic sector or field, namely car industry, tourism, construction, etc. In this session, we will try to carefully reflect on what the attitude of a scientist should be, and what thinking skills a young researcher should develop in their professional career to become an independent team leader.

Further reading:

- https://doi.org/10.1515/tjb-2020-0503"**Keywords:** simulations, virtual labs, learning, practicals, techniques

Keywords: early-career researcher, team leader, thinking skills, young scientist

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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Oral presentation *SEDU-05*

HOW TO KEEP A GOOD LAB NOTEBOOK

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Keeping a good Lab Notebook is one of the most overlooked skills during university studies, be it undergraduate, graduate or postgraduate studies, be you a lab scientist, architect, engineer, medical doctor, nurse, etc. However, astonishingly, all academics and professionals will agree that this is an essential skill at all levels. Failure to write, keep and "upgraded" a good Lab Notebook may lead to damageable (scientifically and even legally) and sad situations. Furthermore, in many settings, namely industry, it is mandatory to provide a "Lab Notebook" responding to defined criteria. We will share and try to make you apprehend the importance, not to say utmost importance, of your Lab Notebook. We will also address the emergence of the digital Lab Notebooks and discuss the issues surrounding this evolution. It is essential to understand that a Lab Notebook IS NOT "YOUR PRESS BOOK", that "sells you"! A Lab Notebook is your "LOGBOOK", it should reflect what you plan to do, what you did (and all changes to the plan), what happened while you were doing it, the observations made all along, the outcome(s), remarks and finally the interpretation with "what next". When all is going smoothly then there is no problem. However, when the going gets rough and things do not look so good … then those details in your lab notebook will allow you to evaluate where the problems could be and thereby propose solutions, and most likely save you precious time an efforts. It is also your tool of communication with your PI and colleagues. It allow you (and others) to reproduce or change the way of doing the next experiments, blueprints or care for your patients.These are just some of the requisites behind the art of consigning the "good science" being done at the bench.

Keywords: Lab Book, workshop

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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Poster presentation *SEDU-06*

USING SARS-COV-2 TO MOTIVATE LEARNING OF IMMUNOASSAYS AND PCR DIAGNOSIS

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The recent pandemic caused by corona virus attracted worldwide attention and made society aware of the importance of basic and applied science for human welfare. This societal awareness may be profited to engage our students into learning the fundamentals of the laboratory techniques involved in detection and diagnosis. A couple of learning resources were developed in this context and made available for free as web pages. The first one focuses on the first "rapid tests" developed for detection of antibodies against the SARS-CoV-2, It is an interactive illustration of the design and mechanism at the molecular level, as well as display of results obtained under different situations (i.e. patient with or without IgG or IgM antibodies, and also failure of the test). The second resource involves running a virtual PCR experiment on some samples, which may be infected by either SARS-CoV-2, influenza A H1N1 virus, or nothing. This is run on the Cybertory virtual molecular biology platform, where the student must acquire samples and reagents, make appropriate reaction mixtures using a micropipette, run the PCR and analyse amplified DNA fragments on agarose gel eletrophoresis.

Keywords: SARS-CoV-2, virtual labs, learning, immunoassays, PCR

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FEBS session „Innovative teaching as a basis of Excellent Research in BioSciences"
Poster presentation *SEDU-07*

IQPHARM EE-PLATFORM FOR EXPERIENTIAL EDUCATION MANAGEMENT

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The Innovating Quality Assessment Tools for Pharmacy Studies in Bosnia and Herzegovina (IQPharm) project is an ongoing Erasmus+ initiative aimed at enhancing the capacity building, digitization, and modernization of pharmacy studies in Bosnia and Herzegovina (BiH). The project focuses on introducing new quality improvement tools, including the Knowledge Retention Evaluation Framework and Objective Structured Clinical Examination, and novel EE-platform for management and monitoring of experiential education (EE). The main goal of the project is to raise and harmonize the quality standards of pharmaceutical studies in compliance with European Union standards and regulations for regulated professions, thus improving the quality of the pharmaceutical profession and healthcare. The EE-platform is the most innovative component of the project and aims to simplify bureaucratic procedures at higher education institutions (HEIs) and community pharmacies, matching of students and mentors in pharmacies, and improving the monitoring of experiential education processes. The platform was developed and will be maintained by BiH HEIs. Its is fully implemented in spring semester of 2023. So far, it has very positive impacts not only in the ease of access, simplification and modernization of administrative processes but also in the positive attitude changes towards the experiential education by all beneficiaries. The use of the EE-platform could have a significant impact on the quality of the teaching process, increased student competencies, and stakeholder/future employers' satisfaction. Moreover, the EE-platform will be sustainable after the end of the project and can be modified for use in other study programs with EE, especially in biomedical studies, but in other fields as well. In general, the project has the potential to enhance the quality of pharmacy education and healthcare in BiH, and serve as a model for other countries in the region.

Keywords: IQPharm, experiential education, EE-platform

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