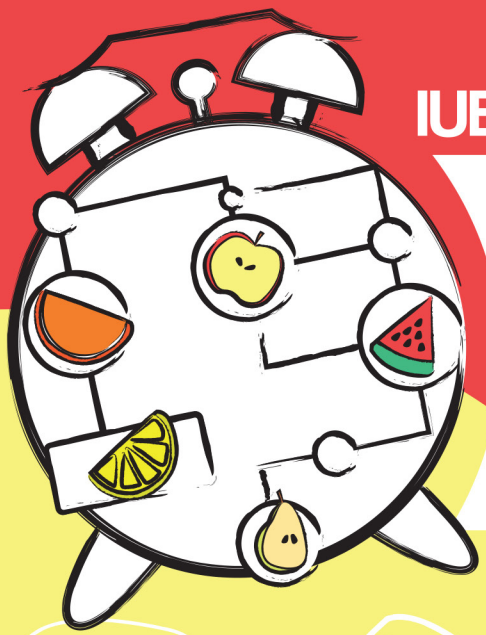

IUBMB ADVANCED SCHOOL

NUTRITION, METABOLISM AND AGING

PROGRAM & BOOK OF ABSTRACTS

Institute for
Biological Research
"Siniša Stanković"
University of Belgrade

BELGRADE, 2018

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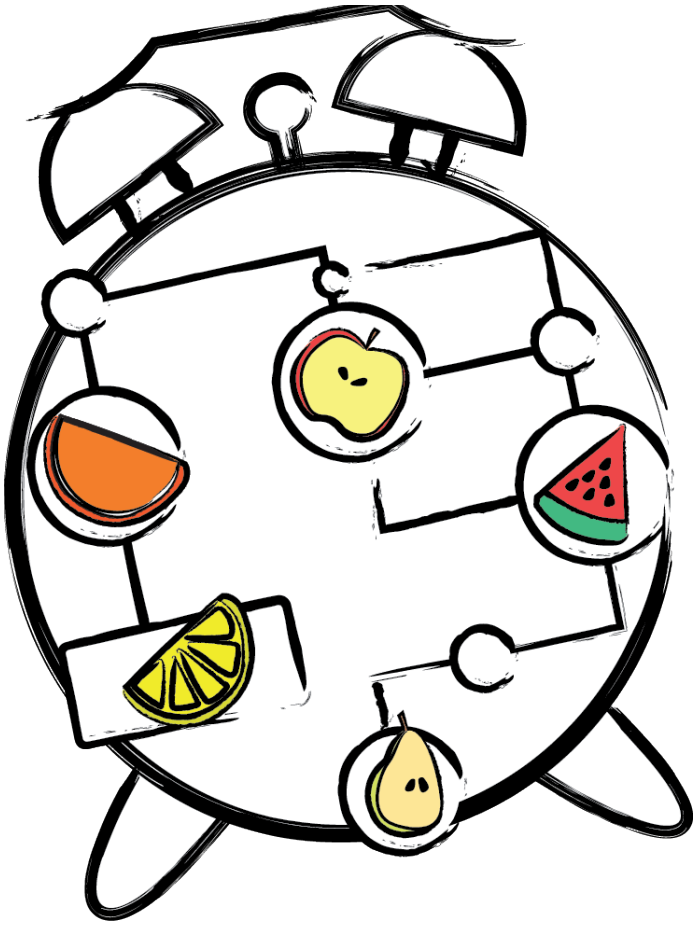

PROGRAM & BOOK OF ABSTRACTS

IUBMB ADVANCED SCHOOL 2018

PETNICA, SERBIA

WELCOME ADDRESS

The Serbian Society for Molecular Biology (MolBioS) welcomes you to the IUBMB Advanced School on Nutrition, Metabolism and Aging. It is our pleasure to invite you to Petnica Science Center, situated in the untouched nature of western Serbia, and representing a great venue for the School with its well equipped laboratories, teaching center, computer classroom, restaurant, library and hotel-type accommodation.

The program covers a wide spectrum of contemporary topics in nutrition, metabolism and aging in the context of diabetes, metabolic syndrome, obesity, healthy aging and neurodegenerative diseases. Distinguished speakers from all over the world have been invited to present their up-to date findings on molecular mechanisms underlying obesity-related metabolic disorders, metabolic effects of dietary fructose, association of gut microbiota dysbiosis with various diseases, as well as on cell senescence and dysfunction related to aging. The inevitable part of modern science are current techniques that provide deep insight in biological phenomena. The participants will have the opportunity to attend workshops on microbiota profiling and bioinformatic analysis of microbiome, bisulfite sequencing and confocal microscopy of aging brain. We are confident that the cutting-edge topics from our invited speakers will contribute to fulfilling our aim of creating an opportunity for young scientists to exchange ideas and get inspired by state-of-the-art lectures of eminent scientists and acknowledged experts.

The main goal of IUBMB Advanced School on Nutrition, Metabolism and Aging is to foster curiosity, communication and collaboration, especially among young researchers. It will provide them with comprehensive insight in the current state of knowledge and research in the field of molecular biology of nutrition, metabolism and aging through direct contact with the renowned scientists and through sharing experiences among themselves. We believe that the training and experience gained at Petnica IUBMB Advanced School will help the young researchers to create new ideas, research concepts and international collaborations.

On behalf of the Organizing and Scientific Committees we welcome you to the IUBMB Advanced School “Nutrition, Metabolism and Aging”!

Professor Gordana Matić
Faculty of Biology,
University of Belgrade
President of the Scientific Committee

Dr. Ana Đorđević
Institute for Biological Research
“Siniša Stanković”, University of Belgrade
President of the Organizing Committee

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Ljiljana Stojković
Miloš Brkušanin

PROGRAM

Monday, October 15, 2018

10:00 - 15:00	**Registration** (*Conference room, Central building*)
14:00 - 15:00	**Lunch** (*Restaurant*)
15:00 - 15:30	**Welcome speeches** (**Andrew H.-J. Wang,** President-elect of IUBMB and **Gordana Matić,** President of MolBioS) (*Conference room, Central building*)
15:30 - 16:15	**Plenary lecture 1** (*Conference room, Central building*) **Joan J. Guinovart, Institute for Research in Biomedicine (IRB Barcelona) and CIBERDEM, Barcelona, Spain** Corpora Amylacea, Brain Glycogen and Aging
16:15 - 16:30	**Discussion**
16:30 - 17:15	**Plenary lecture 2** (*Conference room, Central building*) **Efstathios Gonos, National Helenic Research Foundation, Athens, Greece** Aging and Proteasome
17:15 - 17:30	**Discussion**
18:00 - 19:30	**Welcome party: Participants introduction and music program** (*Conference room, Central building*)
20:00	**Dinner** (*Restaurant*)

Tuesday, October 16, 2018 NUTRITION

9:00 - 10:00	**Breakfast** (*Restaurant*)
10:00 - 11:00	**Lecture** (*Conference room, Central building*)) **Luc Tappy, Department of Physiology, University of Lausanne, Switzerland** Nutritional Quality of Sugars?
11:00 - 11:15	**Coffee break**

11:15 - 12:15	**Lecture** (*Conference room, Central building*) **Juan Carlos Laguna, Department of Pharmacology, Toxicology and Therapeutic Chemistry, School of Pharmacy and Food Sciences IBUB, CIBERObn, Barcelona, Spain** Fructose and cardiovascular risk: From Epidemiology to Translational Research
12:30 - 14:00	**Round table** (*Biological laboratory*) **Renata Jurkowska, BioMedX, Heidelberg, Germany** Young scientists' career opportunities
14:00 - 15:00	**Lunch** (*Restaurant*)
15:00 - 16:00	**Field trip** (*Petnica cave*)
16:00 - 17:00	**Lecture** (*Conference room, Central building*) **Ilaria Bellantuono, Academic Unit of Bone Biology, University of Sheffield, UK** Geroprotectors to Improve Healthspan
17:00 - 17:15	**Coffee break**
18:00 - 20:00	**Workshop** (*Computer laboratory*) Hot topic: Bioinformatics **Ivan Vujković-Cvijin, National Institute of Allergy and Infectious Disease, NIH, Bethesda, USA** Current Methods for Microbiota Profiling and Analysis
20:00	**Dinner** (*Restaurant*)

Wednesday, October 17, 2018 METABOLISM

9:00 - 10:00	**Breakfast** (*Restaurant*)
10:00 - 11:00	**Lecture** (*Conference room, Central building)*) **Edwin R. Sanchez, Department of Physiology and Pharmacology, University of Toledo, Ohio, USA** Nuclear Receptors and the Functioning Adipocyte
11:00 - 11:15	**Coffee break**
11:15 - 12:15	**Lecture** (*Conference room, Central building*) **Tomasz Jurkowski, Institute of Biochemistry and Technical Biochemistry, University of Stuttgart** Targeted DNA Methylation as an Epigenetic Tool for Cellular Reprograming
12:30 - 14:00	**Workshop** (*Biological laboratory*) **Melita Vidaković and Nevena Grdović, Department of Molecular Biology, Institute for Biological Research „Siniša Stanković", University of Belgrade, Serbia** High Throughput Total Nucleic Acid Isolation Using SPRI Magnetic Beads
14:00 - 15:00	**Lunch** (*Restaurant*)
15:00 - 17:00	**Field trip** (*Valjevo*)
17:00 - 18:00	**Lecture** (*Conference room, Central building*) **Marija Herholz, CECAD Research Center, University of Cologne, Koeln, Germany** Mitochondrial Dysfunction, Regulation of Metabolism and Aging
18:15 - 19:00	**Poster session 1** (*Hall, Central building*)
19:00 - 20:00	**Young scientist hour: flash presentations** (*Conference room, Central building*)
20:00	**Dinner** (*Restaurant*)

Thursday, October 18, 2018 AGING

9:00 - 10:00	**Breakfast** (*Restaurant*)
10:00 - 11:00	**Lecture** (*Conference room, Central building)*) **Susan Howlett, Department of Pharmacology, Dalhousie University, Nova Scotia, Canada** Aging and Frailty in Animal Models: Clinical Relevance and Applications for Basic Research
11:00 - 11:15	**Coffee break**
11:15 - 12:15	**Lecture** (*Conference room, Central building*) **Aleksandra Mladenović Đorđević, Department of Neurobiology, Institute for Biological Research „Siniša Stanković“, University of Belgrade, Serbia** Frailty Index vs Frailty Score in 5xFAD Mice: the Influence of Age and Gender
12:30 - 14:00	**Workshop** (*Biological laboratory*) Confocal microscopy **Marija Švirtlih, Institute for Molecular Genetics and Genetic Engineering, University of Belgrade, Serbia**
14:00 - 15:00	**Lunch** (*Restaurant*)
15:00 - 17:00	**Sport activities (swimming, basketball, volleyball, badminton, yoga...)**
17:00 - 18:00	**Lecture** (*Conference room, Central building*) **Ewa Sikora, Nencki Institute of Experimental Biology, Warsaw, Poland** Cell Senescence in Aging and Cancer
18:15 - 19:00	**Poster session 2** (*Hall, Central building*)
19:00 - 20:00	**Young scientist hour: flash presentations** (*Conference room, Central building*)
20:00	**Farewell dinner with party** (*Restaurant*)

Friday, October 19, 2018

9:00 - 10:00	**Breakfast** (*Restaurant*)
10:00 - 10:45	**Plenary lecture 3** (*Conference room, Central building*) **Angelo Azzi, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, Massachusetts, USA** Aging and Dietary Antioxidants
11:45 - 11:00	**Discussion**
11:15 - 12:30	**Workshop** (*Computer laboratory*) Hot topic: Bioinformatics **Aleksandra Stanković and Ivan Jovanovic, Vinča Institute for Nuclear Sciences, University of Belgrade, Serbia** Bioinformatic Analysis of Transcriptome: The Interpretation of Aging Gene Expression Signatures
12:30 - 13:30	**Round table: „Take Home Messages“** (*Conference room, Central building*)
13:30 - 13:45	**Assignment of certificates, awards and acknowledgements** (*Conference room, Central building*)
13:45 - 14:00	**Photo session** (*Open field*)
14:00	**Lunch** (*Restaurant*)

LECTURERS BIOGRAPHIES

Joan J. Guinovart,

Institute for Research in Biomedicine (IRB Barcelona) and CIBERDEM, Barcelona, Spain

Prof. Joan J. Guinovart is Group Leader at the Institute for Research in Biomedicine (IRB Barcelona) and CIBERDEM, and Emeritus Professor at University of Barcelona (Spain). He is Past-President of the International Union of Biochemistry and Molecular Biology (IUBMB) and member of the Editorial board of IUBMB Life. Prof. Guinovart is full member of the Royal Spanish Academy, the Catalan Academy of Arts and Science and the Academia Europaea. Prof. Guinovart's entire research career is focused on glycogen metabolism with special attention to the study of the alternations in carbohydrate metabolism in diabetes and neurodegenerative disorders, such as Lafora disease. He has published more than 170original articles and review papers that had been cited over 6600 times.

Efstathios Gonos,

National Helenic Research Foundation, Athens, Greece

Dr Efstathios Gonos graduated from the Department of Pharmacy, University of Athens, Greece, obtained his Ph.D. at the Department of Biochemistry, University of Glasgow, Britain and a Docent in Biomedicine at the Orebro University, Medical School, Sweden. He worked at the Ludwig Institute for Cancer Research in London, Britain and since 2002 is Director of Research at the National Hellenic Research Foundation/IBMCB. His research focuses on the genetic and environmental factors that are linked to human aging and longevity. He has published more than 120 research articles, is author of 14 monographs and patents holder that have resulted in the development of novel anti-aging products. Dr. Gonos has been a ''senior expert'' of E.U. in ''Human development and the aging process'' and Deputy National Representative of Greece in E.U. in ''Genomics and Biotechnology for Health''. He is past member of the Executive Committee of International Union of Biochemistry and Molecular Biology (IUBMB), the Advanced Course Committee of Federation of European Biochemical Societies (FEBS) and the Board of Directors of the ''Society of Free Radicals Research-Europe''. He is Editor-in-Chief of ''Mechanisms of Aging & Development'' and Editorial Board member of "Experimental Gerontology", ''Free Radicals Research", "IUBMB Life", "Redox Biology", "Ageing Research Reviews", "Aging Cell'' (-2007), ''Biogerontology'' (-2009) and ''Molecular Aspects of Medicine'' (-2016).

Luc Tappy,

Department of Physiology, University of Lausanne, Switzerland

Dr. Luc Tappy is Full Professor of physiology at Department of Physiology, Faculty of Biology and Medicine University of Lausanne and Associate Physician at the Division of Endocrinology and Metabolism at the Le Centre hospitalier universitaire vaudois (CHUV). He is member of the Swiss Federal Committee for Nutrition and of the French Scientific Counsel for Nutrition at the French Agency for Health, Food and Safety at Work (ANSES). He is one of the directors of newly constituted European Society of Preventive Medicine. Prof. Tappy`s studies are focused on nutrition, physical exercise and metabolism in healthy individuals as well as in various clinical conditions, such as diabetes, obesity, organ transplant patients and critically ill patients. Main focus of his research is to evaluate the role of dietary sugars in the development of obesity and insulin resistance, as well as assessing the effects and efficiency of novel treatment for metabolic diseases (drugs, functional nutrients) and implementing novel approaches for the prevention of chronic diseases through physical activity. Prof. Tappy has published more than 200 original articles and reviews papers in international scientific journals, that have been cited over 15000 times, with h-index 64 and i-10 209.

Juan Carlos Laguna Egea,

Department of Pharmacology, Toxicology and Therapeutic Chemistry, School of Pharmacy and Food Sciences, IBUB, and CIBERObn, Barcelona, Spain

Prof. Juan Carlos Laguna is the Director of the Department of Pharmacology, Toxicology and Therapeutic Chemistry University of Barcelona (Spain). He is well known for his work on nuclear receptors, energy metabolism and therapy of metabolic diseases. Prof. Laguna`s initial research was on molecular mechanism of action of hypolipidemic drugs, then his interest was expanded to the study of RXR heterodimeric (PPAR, FXR, LXR) receptors and other nuclear receptors that participate in the control of energy metabolism in liver, adipose tissue, skeletal muscle and macrophages. Focus of his research team is on atherosclerosis-related pathologies (metabolic syndrome, diabetes, dyslipidemia and fatty liver), and their control by drugs which act directly or indirectly on nuclear receptors (fibrates, statins, thiazolidinediones). Further, his research has been also focused in the study of dietary factors, such a simple sugars in beverages, as a key factors in the development of metabolic syndrome.

Ilaria Bellantuono,

Academic Unit of Bone Biology, University of Sheffield, UK

Dr. Ilaria Bellantuono is professor in Musculoskeletal Ageing at University of Sheffield (UK). She is also co-investigator in the MRC-Arthritis Research UK Centre for Integrated research into Musculoskeletal Ageing (CIMA) and Chair of the COST Action MouseAge. This is a European network that includes over 200 scientists from 25 European countries trying to develop a unified research roadmap to speed up the translation of geroprotectors to clinical use. Prof. Ballantuono's research focus is on ways to reduce the onset of multiple age-related diseases by preventing or reversing the ageing of stem cells using medicinal drugs. Her primary interest is in the disease of the musculoskeletal system such as osteoporosis and osteoarthritis. Prof. Bellantuono has published more than 50 original articles and reviews papers in scientific journals, which have been cited 4600 times.

Renata Jurkowska,

BioMed X Innovation Center, Heidelberg, Germany

Dr. Renata Jurkowska is the group leader of Epigenetics and COPD (EAC) research team at BioMed X Innovation Center in Heidelberg (Germany) that promotes new collaboration model at the interface between academia and industry. Her team is exploring the role of epigenetic regulation in the development and progression of chronic obstructive pulmonary disease (COPD). Dr. Jurkowska`s group employs high-throughput epigenomic assays, such as whole-genome bisulfite sequencing (WGBS), ChIP-seq and RNA-seq in combination with cutting-edge epigenetic and molecular biology tools, to advance the biological understanding of the disease, identify epigenetic biomarkers for diagnosis and devise novel therapeutic strategies. Dr. Jurkowska finished her PhD studies at the Institute of Biochemistry, Jacobs University in Bremen (Germany). After receiving her PhD she went to two postdocs, at the Institute of Biochemistry, Jacobs University Bremen (Germany) and at the Institute of Biochemistry, University of Stuttgart (Germany). During 2014 and 2015 she was a group leader at the Institute of Biochemistry, University of Stuttgart. Dr. Jurkowska published over 40 original articles and review papers in scientific journals, which have been cited 4000 times.

Edwin R. Sanchez,

Department of Physiology and Pharmacology, University of Toledo, Ohio, USA

Dr. Edwin R. Sanchez is Professor of Physiology at Department of Physiology and Pharmacology in University of Toledo College of Medicine, and Assistant Director of the Center for Diabetes and Endocrine Research (CeDER) at University of Toledo College of Medicine, Health Science Campus in Ohio (USA). Prof. Sanchez is well-known for his research in the field of steroid receptor physiology and their control by molecular chaperones. His recent research emphasis is on the tetratricopeptide repeat (TPR) proteins that act as molecular chaperones to the receptors. The most recent findings of Prof. Sanchez suggest that the TPR chaperones act as tissue-selective modulators of steroid receptor physiology and that they could be used as novel and potentially important targets for drug development against male and female infertility, prostate cancer, and metabolic disorders, such as diabetes and obesity. Prof. Sanchez has authored more than 80 research and review articles in the scientific journals.

Tomasz Jurkowski,

Institute of Biochemistry and Technical Biochemistry, University of Stuttgart

Dr. Jurkowski is a Junior Professor of Biochemistry and Molecular Epigenetics in the Institute of Biochemistry at the University of Stuttgart, Germany. In his research he and his team are aiming to elucidate the molecular principles of epigenetic regulation by using CRISPR-Cas9-based epigenetic editing as well as biochemical approaches. He further employs the gained knowledge to epigenetically program cell's differentiation state and function (synthetic epigenetics).

Marija Herholz,

CECAD Research Center, University of Cologne, Koeln, Germany

Marija Herholz's is a Postdoc researcher in the Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD) in the lab leaded by Prof. Aleksandra Trifunovic. The lab's main research aim is elucidating mitochondrial stress responses and cell's corresponding adaptive reactions. By using C. elegans as a model system, the team aims to decipher the signaling pathways that underlie longevity induced by mitochondrial dysfunction. Marija graduated from Biology Faculty in Belgrade in 2005 in the department for Molecular Biology and Physiology. In 2009 she received PhD degree in Neurosciences in the International Max Planck Research School for Neurosciences in Goettingen, Germany. During her PhD studies she got interested into the molecular mechanisms that underlie aging, when she joined the lab of Prof. Trifunovic in 2010.

Susan Howlett,

Department of Pharmacology, Dalhousie University, Nova Scotia, Canada

Susan Howlett is Professor of Pharmacology and Medicine (Geriatric Medicine) at Dalhousie University. Professor Howlett is best known for her work on cardiac excitation-contraction coupling. She has discovered profound sex differences in how heart cells function, how this changes with age and how sex hormones regulate these processes. She pioneered the measurement of frailty in animals with a novel "frailty index" tool and showed that maladaptive cardiac remodeling in aging is better graded by frailty than chronological age. She has also shown that the frailty index tool is responsive to known longevity interventions and that it can be used to identify new biomarkers of frailty, such as inflammatory cytokines. The ability to quantify frailty in animals is a major advance that promises to accelerate the effort to translate basic mechanisms of cellular dysfunction in aging into meaningful clinical interventions.

Ewa Sikora,

Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Prof. Ewa Sikora is the Head of Laboratory of the Molecular Bases of Ageing at the Nencki Institute. During her career Prof. Sikora received a visiting professorship at the Cross Cancer Institute in Edmonton (Canada), a UNESCO and FEBS stipend for training at the University of Modena School of Medicine (Italy) and a postdoctoral fellowship of the National Union Against Cancer at the Institute of Cancer Research in Sutton (England). She was an organizer of the Polish Centenarian Project and a coordinator of the SSA FP6 Seneca Project. Prof. Sikora participated in several European grants, e.g. the IP FP6 GEHA (Genetic of Healthy Ageing), the IP FP7 MarkAge (Markers of Ageing) and organized many international conferences on ageing and cancer in Poland. Her research is focused on the molecular mechanisms of senescence and autophagy of normal proliferating and post-mitotic cells as well as cancer cells. She is also recognized for her work on cell response to treatment with curcumin, a natural polyphenol. In 2007 she received the award and in 2017 the distinction of the Polish Academy of Sciences for a series of papers concerning the mechanisms of cell senescence.

Aleksandra Mladenović Djordjević,

Institute for Biological Research "Sinisa Stankovic", Belgrade, Serbia

Aleksandra Mladenovic Djordjevic is Associate Professor at the Institute for Biological Research "Sinisa Stankovic" in Belgrade (IBISS). She received her B.Sc. and Ph.D. degrees from the University of Belgrade, Serbia. Her post-doctoral training was at the laboratory for molecular neurobiology at the Institute for Biological Research "Sinisa Stankovic". In 2003 she received a permanent position at the IBISS, where she is working presently on several research projects on neurodegenerative disease, brain ageing, frailty and environmental interventions to postpone ageing.

Angelo Azzi,

Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, Massachusetts, USA

Prof. Angelo Azzi was Professor at University of Padua (Italy), Professor and Head of Department at Medical Chemistry Institute and Director of the Institute for Biochemistry and Molecular Biology at University of Bern (Switzerland) and Senior Scientist of the Human Nutrition Center at Tufts University (Boston, USA). He is Past-President of the International Union of Biochemistry and Molecular Biology (IUBMB), Editor-in-Chief of IUBMB Life, BioFactors and Molecular Aspects of Medicine and past-member of the international scientific advisory board of UNESCO. Prof. Azzi research is well-known for discovery of the aspartate/glutamate carrier in mitochondria and for the mechanism of action of vitamin E. He holds patents for Vitamin E plus lycopene in the prevention of prostate cancer. Prof. Azzi published over 600 articles that were cited more than 20800 times, with h-index 76 and i-10 260.

WORKSHOP COORDINATORS

Marija Švirtlih,

Laboratory for human molecular genetics, Institute of molecular genetics and genetic engineering (IMGGE), University of Belgrade, Serbia

EDUCATION: 2009 - PhD in Medical Sciences, Semmelweiss University, Budapest, Hungary. In 2012, nostrificated as PhD in Biological Sciences, Faculty of Biology (FB), UB (Molecular components and functionality of the GABA signaling during development: a study on two model systems); 1998 - B.Sc. in Molecular Biology and Physiology, FB, University of Belgrade; CAREER HISTORY: 2012 – Senior Research Associate, Laboratory for human molecular genetics Institute of molecular genetics and genetic engineering (IMGGE) University of Belgrade; 2001 - 2010 - Research Fellow, Laboratory of Molecular Biology and Genetics, Institute of Experimental Medicine Hungarian Academy of Sciences, Budapest, Hungary; 1998 - 2001 - Research Trainee, Department of Neurobiology, Institute for Biological Research "Sinisa Stankovic", Belgrade, Serbia; RESEARCH INTEREST: The main research field of interest is developmental neurobiology. Mechanisms involved in the regulation of SOXB1(SOX1, SOX2, SOX3) and SOXB2 (SOX14 and SOX21) genes expression during embryonic and adult neurogenesis. Furthermore, molecular mechanisms involved in the trophic role of gamma-Aminobutyric acid (GABA) in the regulation of numerous developmental processes in the brain.

Ivan Vujković-Cvijin,

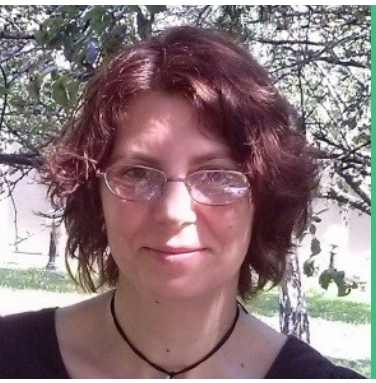
National Institute of Allergy and Infectious Disease, NIH, Bethesda, USA

Dr. Ivan Vujkovic-Cvijin is a Postdoctoral Fellow at Cancer Research Institute Irvington in the Mucosal Immunology Section at the National Institute of Allergy and Infectious Disease in Bethesda (Maryland, USA). His current research is focused on mechanisms of commensal microbe-mediated control of inflammation. Ivan Cvijin received his PhD in Immunology from the Biomedical Sciences Program of the University of California San Francisco (UCSF) in 2015, where he was among the first to describe HIV-associated shifts in the gut microbiome and their potential link to HIV disease progression. His work is broadly centered on dissecting relationships between host-associated microbes and the human immune system, with a focus on developing tools and methodologies to identify immunostimulatory and immunoregulatory microbiome constituents that impact human disease.

Melita Vidaković,

Department of Molecular Biology, Institute for Biological Research „Siniša Stanković", University of Belgrade, Serbia

Dr. Vidakovic received postdoctoral fellowship from Alexander von Humboldt Foundation and spent 2 years in Epigenetic regulation Department, Helmholtz Center for Infections Research, Braunschweig, Germany. She has a wide interest and partial expertise in : Molecular Biology and biochemistry: DNA repair and cell death; Gene expression; Chromatin modulation; Nuclear architecture; S/MAR DNA structure. Major interest for the present moment is field of Epigenetics, mostly DNA methylation and demethylation in regard of oxidative stress and Diabetes mellitus. Her lab is focused into the molecular control mechanisms in pancreatic b-cells and the molecular patho physiology of diabetes that has laid the foundation for the paradigm for diabetes prevention which envisages the application of strategies that support the maintenance of appropriate b-cell numbers. Current emphasis is on epigenetic mechanisms, i.e. on revealing basic principles of DNA and histone methylation/demethylation and its involvement in diabetes development. At present, working on transdifferentiation of pancreatic alpha to beta cells via targeted epigenome editing using Epi-CRISPRs directed DNA methylation and starting to explore active DNA demethylation via TET family of enzymes. Dr. Vidaković teaching duties involve Molecular Biology of the Cell (DS-MB-02) and Epigenetics (DN-MB-l9). She supervised two defended PhD theses and current is mentoring four PhD projects. She has more than 60 research papers published in international scientific journals and 3 book chapters. Citations: > 500; h-index: 14. At present she holds two international projects and has several collaborators in Germany, Japan, Croatia, France and Holland.



Nevena Grdović,

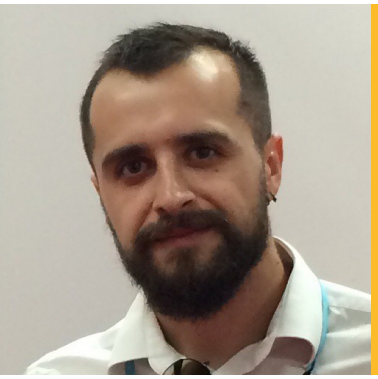
Department of Molecular Biology, Institute for Biological Research „Siniša Stanković", University of Belgrade, Serbia

Dr. Nevena Grdovic is a Senior Research Associate employed at Department of Molecular Biology, Institute for Biological Research „Siniša Stanković" (IBISS), University of Begrade, Serbia. Currently engaged in national project "Signaling molecules in diabetes: search for potential targets in intrinsic pathways for prediction and intervention in diabetes" and two international projects. Also, Dr Nevena Grdovic is engaged as a lecturer in (i) Cell biology and(ii) Epigenetics courses at PhD studies, Molecular Biology course, Faculty of Biology, University of Belgrade. Current research interest includes (i) Epigenetic regulation of expression of genes involved in beta-cell survival in diabetes and (ii) DNA methylation as epigenetic mechanism potentially involved in regulation of Epithelial to Mesenchymal Transition (EMT).

Aleksandra Stanković,

Laboratory for Radiobiology and Molecular Genetics
Vinča Institute of Nuclear Sciences,
University of Belgrade, Serbia

Participation in Scientific Projects: 2011- ongoing. Project leader "Genetic basis of vascular and inflammatory human diseases" funded by Republic Ministry of Science and Technology, Serbia (Project OI 175085); 2011- ongoing. Principal Investigator "An integral study to identify the regional genetic and environmental risk factors for the common non-communicable diseases in the human population of Serbia" funded by Republic Ministry of Science and Technology, Serbia (Project III 41028); 2014-2019. "Strengthening of the MagBioVin Research and Innovation Team for Development of Novel Approaches for Tumour Therapy based on Nanostructured Materials", First "ERAChairs" FP7th IP/14/125 Grant agreement No. 621375, Group leader: "Group for biological response to applications of MNPs in therapy". Research: Research Design: The candidate gene approach: The SNP analysis and association of SNPs with gene expression; The haplotype analysis; The association of haplotypes with gene expression Micro RNA analysis. The whole genome analysis on microarray scanner: Whole genome expression analysis; GWAS for SNPs, whole genome methylation analysis; The case-control and case-case design for human studies and experimental design in animal models. The exposed cell culture design. Strong collaboration with clinicians. Research Topics: Primarily genomics, but also combining with epigenetics and proteomics. Current research: Genetic basis of human inflammatory and vascular disease; Common and rare allele variants in association with susceptibility/outcome of the disease. The gene expression and protein expression of cytokines, chemokines, growth factors and other important molecules in inflammatory pathways in human target tissues (atherosclerotic plaque and blood, MS blood and CSF, CKD blood, urine, kidney and urinary tract tissue) and experimental animal (rat) tissues. Global methylation analysis of the DNA.



Ivan Jovanović,

Laboratory for Radiobiology and Molecular Genetics
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Ivan Jovanović defended his PhD thesis titled: "Analysis of whole genome expression in order to identify the key genes and microRNAs for the occurrence of congenital anomalies of the kidney and urinary tract in humans" at Faculty of Biology, University of Belgrade in 2016. He previously defended his Master of Science thesis titled: "Effects of Roxithromycin on wound healing" at the same Faculty in 2011. He is currently employed as Assistant Research Professor in the Laboratory for Radiobiology and Molecular Genetics, Institute of Nuclear Sciences „Vinča", University of Belgrade. From August to November 2009 he did the practical work at the Laboratory for Molecular Biology of the ORL Clinic, University of Greifswald, Germany. Dr. Jovanović currently coordinates the project "Implementation of the new platform for genetic testing with multidisciplinary potential for scientific and commercial purposes, VINseq" funded by the Vinča Institute of Nuclear Sciences, University of Belgrade, through the Vinča Horizon program. He also participates in following projects: "Genetic basis of vascular and inflammatory human diseases" funded by Serbian Ministry of Education, Science and Technological development, (Project OI175085), Institute of Nuclear Sciences "Vinča", University of Belgrade, Belgrade, Serbia and "Noninvasive and invasive diagnostics and percutaneous treatment of vascular bifurcation constrictions" funded by Serbian Ministry of Education, Science and Technological development, (Project OI175082), Medical Faculty, University of Belgrade, Belgrade, Serbia. Scholarships and professional training: „Introduction to the statistical analysis of genome-wide association studies", 4-8th July, Imperial College, London, UK (2016.); „State of the Art, Novel Concepts, and Clinical Applications of Pharmacogenomics and Personalised Therapy", 20-25th August, Belgrade, Serbia (2016); „Clinical genomics and NGS", 30th April – 5th May 2017., University of Bologna, Bertinoro, Italy (2017). Awards: Goran Ljubijankić Foundation Award for the best doctoral dissertation in the field of molecular biology, defended in 2016, January 30, 2017, Institute of Molecular Genetics and Genetic Engineering IMGGI, University of Belgrade

Session 1

WINE, CHOCOLATE AND COFFEE – DELICIOUS TREATS WITH HEALTHY BENEFITS

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Introduction: Among all beverages consumed worldwide, wine, chocolate and coffee are considered as favorite treats of many. Besides just providing pleasure, numerous reports declare they have beneficial effect on health due to their antioxidant properties associated with high amounts of polyphenols, mostly in the form of catechin and epicatechin. Since oxidative stress is implicated in various diseases, such as cardiovascular and neurodegenerative diseases, cancer, inflammation and ageing, consuming foods rich in antioxidants is very important.
The aim: This study was conducted to compare the antioxidant and neuroprotective properties of wine (Cabernet Sauvignon), cocoa powder, dark chocolate (70% cocoa content) and coffee (roasted ground blend of Arabica and Robusta coffee) commercially available in Serbian markets.
Methods: Biological activities of the products were assessed through the antioxidant potential (scavenging of DPPH•, inhibition of lipid peroxidation and reducing power) and by evaluating the neuroprotective properties through the inhibition of acetylcholinesterase. Total phenolic, flavonoid and tannin contents were determined spectrophotometrically.
Results: Coffee gave by far the best results in all applied assays, followed by wine, cocoa and lastly, chocolate. Only coffee and wine showed neuroprotective properties. Biological activity was in good correlation with total phenolic and tannin content.
Conclusion: Comparing four products that are consumed and liked by many, coffee and wine stood out as most promising samples with good antioxidant and neuroprotective activities. Thus, moderate consumption of the tested products could have a positive impact on human health.

Acknowledgements: This study was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia (Grant No. 172058).

DIETARY ANTHOCYANINS AND THEIR METABOLITES DECREASE MONOCYTE ADHESION AND MIGRATION ACROSS ACTIVATED ENDOTHELIAL CELLS THROUGH MECHANISMS THAT REGULATE ENDOTHELIAL PERMEABILITY

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Introduction: Cardioprotective effects of dietary anthocyanins are partly ascribed to their ability to improve endothelial function. Still, the underlying mechanisms are not completely understood. This study aimed to examine the effect of anthocyanins and their gut metabolites on endothelial cell function and decipher underlying molecular mechanisms using integrated omics approaches.

Methods: Primary endothelial cells were exposed to a mixture of cyanidin-3-glucoside, cyanidin-3-arabinoside, cyanidin-3-galactoside, delphinidin-3-glucoside, peonidin-3-glucoside and degradation product 4-hydroxybenzaldehyde or a mixture of ferulic, protocatechuic, hippuric and vanillic acid, at physiologically relevant concentrations. Inflammation was induced and monocytes added to investigate adhesion and transmigration. Gene and miRNA expression, cell-signalling protein phosphorylation and *in silico* docking analyses were performed.

Results: Anthocyanins and their metabolites significantly reduced monocyte adhesion and transendothelial migration. Gene expression analysis showed that these compounds modulated the expression of genes involved in the regulation of cell-cell adhesion, cytoskeleton organisation or focal adhesion. Bioinformatics analyses of gene expression data identified potential transcription factors involved in the observed nutrigenomic effects and signalling proteins regulating their activity. Molecular docking revealed cell-signalling proteins to which these bioactives may bind to and potentially affect their activity and activation of downstream signalling proteins and transcription factors, the effects in agreement with the results of Western blot analyses. Tested compounds also modulated the expression of microRNAs, especially those involved in regulation of endothelial permeability, contributing to the observed changes in endothelial function.

Conclusion: Integration of these results revealed endothelial-protective properties of anthocyanins and their metabolites and deciphered new underlying multi-target and multi-layered mode of action.

GLUCOCORTICOID-MEDIATED EFFECTS OF *Mif* DEFICIENCY AND FRUCTOSE - ENRICHED DIET ON ENERGY METABOLISM IN THE MOUSE LIVER

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Introduction: The macrophage migration inhibitory factor (MIF) is a proinflammatory cytokine involved in the regulation of energy metabolism and glucocorticoid action in the liver. Genetic deletion of *Mif* may contribute to the development of systemic insulin resistance, especially in the setting of fructose overload that can be associated with pertubed hepatic metabolism.
The Aim: The aim of the present study was to elucidate the impact of combined effects of *Mif* deficiency and dietary sugar on energy metabolism and insulin sensitivity in the liver of male mice.
Methods: Wild type (WT) and *Mif* deficient ($MIF^{-/-}$) C57Bl/6J mice were used to analyze the effects of 9-week 20% fructose-enriched diet on energy intake, and indicators of insulin sensitivity and glucocorticoid receptor (GR) signaling. Deregulation of Akt signaling pathway was used as a hallmark of hepatic insulin resistance. Changes in energy metabolism were estimated by AMP-activated protein kinase (AMPK) and SIRT1 protein levels.
Results: All fructose-fed animals had increased energy intake, while elevated APMK and SIRT1 protein levels compared to the WT ones. Although enhanced glucocorticoid prereceptor metabolism was observed in all fructose-fed mice, GR protein level was increased only in $MIF^{-/-}$ animals. *Mif* deficient animals exibited impaired systemic insulin sensitivity. However, the impaired hepatic insulin signaling, revealed by decreased pAkt/total Akt ratio, was observed only in fructose-fed $MIF^{-/-}$ animals.
Conclusion: The results showed that *Mif* deficiency under the conditions of dietary fructose overload leads to systemic insulin resistance, and impaired hepatic insulin signaling and energy metabolism, possibly through enhanced glucocorticoid signaling.

Acknowledgements: This study was supported by the grant No. III41009 from the Ministry of Education, Science and Technological Development, Republic of Serbia

DE NOVO LIPOGENESIS AND GLUCONEOGENESIS IN THE LIVER OF MALE FRUCTOSE-FED RATS EXPOSED TO CHRONIC STRESS

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The Aim: High fructose diet and chronic stress were both linked with metabolic disturbances. Thus, we analyzed their separate and combined effects on metabolic homeostasis, with particular focus on hepatic lipogenesis and gluconeogenesis.
Methods: Male Wistar rats were subjected to 9-week 20% fructose diet and/or 4-week chronic unpredictable stress. The following morphological and biochemical parameters of lipid and glucose metabolism were measured: body and liver mass, energy intake, blood glucose and plasma insulin levels, free fatty acids (FFA), lactate, triglycerides (TG) and VLDL-TG, as well as hepatic VLDL production rate, total hepatic TG and palmitate and stearate percentage shares. Furthermore, the expression of transcriptional regulators and enzymes of hepatic *de novo* lipogenesis (DNL), lipoprotein export and gluconeogenesis were analyzed.
Results: Although energy intake was increased after fructose diet, body and liver mass remained unaltered. Plasma TG were elevated in both fructose-fed groups, whereas FFA were increased in the non-stressed fructose-fed group. Parameters of hepatic TG and VLDL production and export were unaffected, except for the hepatic palmitate production which was increased after combined treatment. The increments of fractional DNL and palmitate production accompanied the upregulation of lipogenic enzymes, fatty acid sythase and acetyl-CoA carboxylase, which was, interestingly, not preceeded by the increase of their transcriptional regulators. In both fructose-fed groups blood glucose level was increased, although hepatic gluconeogenesis was unaffected.
Conclusion: Combined stress/fructose treatment is more aggravating than separate treatments, since it leads to an increase in hepatic *de novo* lipogenesis and total hepatic TG palmitate, without concomitant changes in VLDL production and export.

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IMPACT OF COCOA POWDER SUPPLEMENTATION ON EMOTIONAL REACTIVITY IN HEALTHY MICE

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Introduction: Specific polyphenols in the presence of methylxanthines allow various physiological effects of cocoa powder that exceed the nutritional role of this food. It is often classified into popular group of "functional foods".
The aim: The experimental goal was the examination role of cocoa powder or methylxanthines supplementation on emotional reactivity in healthy C57BL/6 mice.
Methods: Behaviour battery (step down test, basket test, novel object test and open field test) was used after short-term (one month) and long-term supplementation (six months) with dietary relevant quantities of cocoa powder (3% of standard diet) and an equivalent amount of methylxanthines (theobromine (0.075%) and caffeine (0,012%)). Study was conducted on control (n=11), and two experimental groups: cocoa (n=11) and methyxanthines group (n=12).
Results: There were not differences between groups in regard to body weight, food and water intake as well as to performances in step down and basket test ($p>0.05$). In open field test, it was observed that mice short-term exposed to cocoa powder have spent prolonged time in the central zone ($t11=2.411$, $p=0,035$), but this effect has disappeared after long-term supplementation. Considering novel object test, it is noticed that mice from cocoa group have maintained exploratory time after short-term supplementation ($t11=1.498$, $p=0.162$), contrary to control ($t11=2.699$, $p=0.021$) and methylxanthines mice, in which it has significantly decreased ($t11=2.575$, $p=0.026$).
Conclusion: Obtained results indicate that short-term cocoa powder supplementation could have modulating effect on mice affective domain of brain functions. In addition, this finding confirms that different bioactive compounds and their interaction contribute to functionality of cocoa powder.

Session 2

EVALUATION OF CHANGES IN HISTONE MODIFICATIONS AND PROTEIN HP1α LEVELS IN REPLICATIVE AND PREMATURE SENESCENT VASCULAR SMOOTH MUSCLE CELLS

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Aim of the study: During senescence the decrease of histone H3 methylation (H3K9me3) and HP1α protein is usually observed. It results in reduction of heterochromatin in favour of euchromatin. Our preliminary results suggested that chromatin modification in different types of senescence can vary, thus the aim of the project is to analyse the compaction of chromatin structure during replicative (RS) and stress induced premature senescence (PS) in vascular smooth muscle cells (VSMC).
Methods: VSMC subjected to RS and PS induced by doxorubicin (DNA-damage dependent) and curcumin (DNA-damage independent), were stained against different histone modifications to visualize changes in chromatin compaction. The regions of compaction were analysed by ChIP-seq. The change in protein levels was detected by Western blotting and the microarray was used for the analysis of the gene expression level. The structure of chromatin was analysed by AFM.
Results: In RS level of heterochromatin marks, especially H3K9me3, decrease along with HP1α as compared to the young cells. In contrast, premature senescent cells do not display significant loss of neither H3K9me3 nor HP1α. The microarray analysis revealed vast changes in gene expression between RS and PS.
Conclusions: Alterations affecting chromatin seems to differ depending on the type of senescence. Since both types of senescence might occur simultaneously, further analysis of changes in histone modifications might serve as a diagnostic tool recognizing source of senescence and therefore help in reducing the risk of, e.g. cardiovascular disease.

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ANALYSIS OF EXCITATION AND INHIBITION IN CONTEXT OF ENRICHED ENVIRONMENT IN THE HIPPOCAMPUS AND RETROSPLENIAL CORTEX OF MICE DEFICIENT FOR MATRIX METALOPROTEINASE 9

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Introduction: Matrix metaloproteinase-9 (MMP-9) is a component of the extracellular matrix that is involved in the regulation of brain plasticity. Our previous study has shown that enriched environment (EE) can influence brain structural plasticity by changing the activity of MMP-9 (Stamenković et al, 2017).

Aim: Here, we investigated the role of MMP-9 in synaptic coverage by following expression levels of vesicular glutamate and GABA transporters (VGlut-1, VGlut-2 and VGAT) in the hippocampus and retrosplenial cortex of MMP-9 deficient (MMP-$9^{-/-}$) and wild-type (MMP-$9^{+/+}$) mice.

Methods: Animals were housed in EE (vs. standard conditions - SC) for 8 weeks starting from P21. Immunohistochemistry was utilized to fluorescently stain brain sections. Images were acquired and analyzed on a confocal laser scanning microscope.

Results: We showed that housing in EE markedly increased VGlut and VGAT staining intensity in the dentate gyrus and CA1 region of the hippocampus of MMP-$9^{+/+}$ mice, while similar changes were not detected in MMP-$9^{-/-}$ mice. Interestingly, in the CA2 and CA3 hippocampal regions we found a reduction in VGlut-1 signal intensity in both genotypes after EE, while VGAT signal intensity was increased only in MMP-$9^{+/+}$ mice. Contrary to the hippocampus, EE induced more pronounced changes in the expression levels of all investigated vesicular transporters in the retrosplenial cortex of MMP-$9^{-/-}$ mice compared to MMP-$9^{+/+}$ mice.

Conclusion: This study reveals a region-specific contribution of MMP-9 in the modulation of the balance between excitation and inhibition.

AGING OF THE EYE: CHOLESTEROL AND FATTY ACID RELATED GENE EXPERSSION

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Introduction: Although the etiology of age-related macular degeneration (AMD) is not known, aging is considered the major risk factor for the development of this progressive and degenerative disease, that is the main cause of blindness among the elderly. Recent findings revealed that in both the AMD and Alzheimer's disease (AD), the amyloid beta (Aβ) has a pivotal role in the formation of the pathological extracellular deposits – drusen in AMD and plaques in AD. Changes in the cholesterol and fatty acid membrane composition have been implicated in the regulation of the (Aβ) production.
Aim: The analyses of the expression of the cholesterol and unsaturated fatty acids (DHA) related genes, APP and Aβ in retina and retinal pigmented epithelium (RPE) in the eye during physiological (wild type, WT) and pathological (5xFAD transgenic AD mouse model) aging.
Methods: Real-time PCR (qPCR) was used to quantify the expression levels of 1. cholesterol-related genes (*hmgcr*, *lxrβ*, *srebp-2*, *abca1*, *apoE*, *cyp27*, and *cyp46*), and 2. genes regulating fatty acid uptake (*adipoR1* and *mfsd2a*) in wild type (WT) and 5xFAD mice during aging. Immunohistochemistry was used to analyze the distribution of the App and Aβ expression in the aging WT and 5xAFD eyes.
Results: The expression levels of above-mentioned genes are severely altered in retina and RPE during physiological and pathological aging.
Conclusions: The severe alterations in cholesterol and unsaturated fatty acids related gene expression in the aging eye in WT and 5xFAD implicate the possible target genes/pathways in therapies for the prevention and treatment of AMD.

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SIRNA ATG5- EVOKED DYSFUNCTION OF AUTOPHAGY INITIATION ATTENUATES C10-INDUCED SENESCENCE IN MCF-7 CELLS

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Introduction: Autophagy is an evolutionally conserved cytoplasmic degradation system of intracellular components. It was demonstrated that autophagy is whirled with senescence and both processes play an important role in cancer initiation and progression. Thus, their regulation became new target in anticancer therapy. Presently, more attention is paid to autophagy or senescence regulators that are able to enhance efficacy of anticancer therapy. Recently, we have demonstrated that tacrine-melatonin heterodimer (C10) has anticancer properties due to simultaneous induction and blockade of autophagy. Moreover, we have found that 24-hour treatment with cytostatic IC_{50} dose of C10 followed by culture in drug free medium for few days led to cellular senescence of 20% of cells.

Aim: To verify whether there is interconnection between autophagy and senescence evoked by C10 in MCF-7 cells.

Methods: We inhibited autophagy genetically at initiation stage, using siRNA against ATG5. Cell viability was analyzed using MTT assay. Several markers of autophagy and senescence were analyzed by western blotting, immunostaining or flow cytometry.

Results: After treatment with C10 MCF-7 cells transfected with siRNA ATG5 preserved enhanced proliferation capacity in comparison with the control cells. Moreover, cells with decreased level of ATG5 secreted lower amount of IL-6 and IL-8, both characteristic for senescence-associated secretory phenotype (SASP). Surprisingly no significant changes in SA-β-gal activity was observed.

Conclusion: C10-evoked autophagy disorder is essential for strength of senescence phenotype that appears after drug removal. However, cells with faulty autophagy initiation (transfected with siRNA ATG5) are not able to develop full set of senescence features.

OBESITY AND AGING AFFECTS SKELETAL MUSCLE RENIN ANGIOTENSIN SYSTEM AND MYOSIN HEAVY CHAIN PROPORTIONS IN PREDIABETIC ZUCKER RATS

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Local renin-angiotensin system (RAS) in skeletal muscle affects insulin-stimulated glucose uptake and might contribute to the systemic RAS. There is a gap in the knowledge regarding regulation of muscle RAS during development of obesity in vivo. This study evaluates the age- and obesity-related changes in the expression of RAS components. Male Zucker fatty rats and their lean controls were killed at the age of 3 and 8 months. Expression of the RAS components was determined in musculus quadriceps using qPCR and/or Western blot analysis. The enzymatic activity of aminopeptidase A (APA) was determined flourometrically. We detected a discrepancy of renin expression on mRNA and protein levels. The renin receptor (ReR)/promyelocytic leukemia zinc finger ultrashort loop negative feedback mechanism was activated in obesity. The expression of angiotensinogen and AT1 receptor was downregulated, while the expression of neutral endopeptidase (NEP) and AT2 receptor was upregulated in obese rats with aging. Skeletal muscle APA activity was decreased in obesity, which negatively correlated with the increased plasma APA activity and plasma cholesterol. The expression of angiotensin-converting enzyme (ACE) positively correlated with myosin heavy chain (MyHC) mRNAs characteristic for fast-twitch muscle fibres. The age- and obesity- related alterations in the expression of both classical and alternative RAS components suggest an onset of a new equilibrium of the two opposing pathways on a lower level shifted toward increased renin/ReR/PLZF pathway activation. Increased APA release from the skeletal muscle in obesity might contribute to increased plasma APA activity. There is a link between reduced ACE expression and altered muscle MyHC composition by obesity and aging.

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POSTER PRESENTATIONS

	Poster No.	Presenting Author	Poster Title
SESSION 1	N1	Ana Magdalena Velázquez	Eleven months of liquid fructose and glucose supplementation induce metabolic alterations in a hepatocarcinogenesis model in female, but not in male rats
	N2	Ana Pantović	How does a simulation of a half marathon race, with or without aronia juice consumption, affect the plasma free fatty acid profile in trained men?
	N3	Diandra Pintać	Wine, chocolate and coffee – delicious treats with healthy benefits
	N4	Ibitade Jawonisi	Physicochemical characterisation of *Annona muricata* and *Telfairia occidentalis* seed oils
	N5	Irena Krga	Dietary anthocyanins and their metabolites decrease monocyte adhesion and migration across activated endothelial cells through mechanisms that regulate endothelial permeability
	N6	Ivana Kolić	Polyphenol-rich *Aronia melanocarpa* juice modulates transcriptome profile of peripheral blood mononuclear cells in adults at mild cardiovascular risk
	M1	Ljupka Gligorovska	Glucocorticoid-mediated effects of *Mif* deficiency and fructose-enriched diet on energy metabolism in the mouse liver
	M2	Marina Nikolić	*De novo* lipogenesis and gluconeogenesis in the liver of male fructose-fed rats exposed to chronic stress
	N7	Mohd Shamoon Asmat	A bioconjugate of lipase with novel fabricated nanocellulose fused polypyrrole/graphene oxide nanocomposite as promising nanobiocatalyst: characterization and application to flavour synthesis
	M3	Sanja Kovačević	Effects of fructose-enriched diet on inflammation and insulin signaling in the hypothalamus and visceral adipose tissue of female rats
	N8	Vanja Todorović	Impact of cocoa powder supplementation on emotional reactivity in healthy mice
SESSION 2	A1	Agnieszka Gadecka	Evaluation of changes in histone modifications and protein HP1α levels in replicative and premature senescent vascular smooth muscle cells
	M4	Ana Jakovljević	Analysis of excitation and inhibition in context of enriched environment in the hippocampus and retrosplenial cortex of mice deficient for matrix metaloproteinase 9
	M5	Ana Teofilović	Modulation of glucocorticoid and insulin signaling in the rat liver after high fructose diet and chronic stress
	A2	Irena Jovanović Macura	Aging of the eye: cholesterol and fatty acid related gene experssion
	A3	Kamil Ziaja	siRNA ATG5-evoked dysfunction of autophagy initiation attenuates C10-induced senescence in MCF-7 cells
	M6	Maja Bošković	Estradiol ammeliorates antioxidant axis SIRT1/FOXO3a/MnSOD in the heart of fructose-fed ovariectomized rats
	A4	Michaela Vaškovičová	Double-strand DNA breaks response in Huntington´s disease
	A5	Miloš Mandić	Phorbol 12-myristate 13-acetate induces senescence of HL-60 leukemic cells
	M7	Tamara Dakić	Effect of short term fasting on hypothalamic insulin expression and signaling
	A6	Viktória Lóry	Obesity and aging affects skeletal muscle renin angiotensin system and myosin heavy chain proportions in prediabetic Zucker rats

Abstract is chosen for Flash presentation

Session 1

ELEVEN MONTHS OF LIQUID FRUCTOSE AND GLUCOSE SUPPLEMENTATION INDUCE METABOLIC ALTERATIONS IN AN HEPATOCARCINOGENESIS MODEL IN FEMALE, BUT NOT IN MALE RATS

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The aim: High simple sugar consumption is related to obesity, fatty liver and insulin resistance, which are risk factors for the development of hepatocellular carcinoma. Our aim was to investigate the effects of long term liquid fructose and glucose supplementation in an hepatocarcinogenesis model induced by diethylnitrosamine (DEN) in rats.
Methods: 15-day-old male and female Sprague-Dawley rats were injected with 5 mg/kg DEN, and after weaning were distributed in 3 groups (n= 9 each): control (C), supplemented with fructose 10% w/v in drinking water (F) and supplemented with glucose 10% w/v in drinking water (G)for 11 months. Organ weight and plasma analytes were determined.
Results: Treatments did not result in the appearance of macroscopically observable liver tumors, but induced several metabolic alterations. In female, but not in male rats, both sugars increased body and adipose tissue weight and induced hyperleptinemia and hyperinsulinemia. The insulin sensitivity index was reduced by both sugars only in female rats. On the other hand, only fructose induced hypertrigliceridemia in female rats.
Conclusion: Our results show that female rats were more susceptible to metabolic alterations induced by chronic sugar supplementation than males. Although no hepàtic tumors were observed, these metabolic alterations could lead to precancerous lesions in this tissue. For example, it has been reported that sustained hyperinsulinemia promotes the activation of the mTORC1 system, favoring cellular proliferation. To examine this possibility, we will determine the expression of proteins related to insulin and leptin signalling in the livers of male and female rats, including p-Akt, p-mTOR and SOCS-3.

HOW DOES A SIMULATION OF A HALF MARATHON RACE, WITH OR WITHOUT ARONIA JUICE CONSUMPTION, AFFECT THE PLASMA FREE FATTY ACID PROFILE IN TRAINED MEN?

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Introduction and aim: Plasma free fatty acids are an important fuel supply during physical activity, which induces changes in their profile. We aimed to observe the change in plasma free saturated fatty acids profile after a half-marathon race with or without Aronia juice consumption.

Materials and methods: Ten recreational male runners (30.8±2.3 y old) were involved in a single-blinded, randomized, placebo-controlled, crossover study with one week of wash-out period between two study visits. The intervention consisted of 200 ml Aronia or polyphenol-free placebo juice which was consumed after calorically identical breakfast. We assessed plasma free fatty acid profile at 4 time-points: baseline (before intervention), 15 minutes, 1 hour and 24 hours after the half-marathon race, by solid-phase extraction and gas chromatography.

Results: Two-way repeated measures ANOVA showed no significant differences between the two experimental groups. However, the fatty acid profile significantly changed over time. There was a statistically significant increase in the levels of myristic and palmitic acid as well as in total saturated fats 15 minutes after the race. Their levels gradually decreased over time, but without reaching significance. However, 24 hours after the race (the muscle recovery period), only the levels of total saturated fatty acids significantly decreased by 17%, compared with the baseline.

Conclusion: Aronia juice consumption prior to half-marathon race did not affect the turnover rate of saturated fatty acids in trained men. The profile, however, did significantly change over time, presenting an increase at first, followed by a gradual decrease over time.

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PHYSICOCHEMICAL CHARACTERISATION OF *Annona muricata* AND *Telfairia occidentalis* SEED OILS

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Introduction: *Annona muricata* and *Telfairia occidentalis* are commonly found in southern part of Nigeria. They are often cultivated in home gardens.
Aim: This study sought to assess the quality of oils extracted from *Annona muricata* and *Telfairia occidentalis* seeds.
Methods: Extraction of both seed oils was done using petroleum ether (60-800C) via soxhlet extractor. Physicochemical parameters were analysed using standard methods. The lipid composition of both oils were determined by methylation of the fatty acids in the oils. The fatty acid methyl esters were subjected to gas chromatography coupled with mass spectrometer.
Results: The percentage yield of *Annona muricata* and *Telfairia occidentalis* seed oils were 21.44% and 35.89% respectively.The physicochemical parameters for *Annona muricata* were specific gravity; 0.98, refractive index; 1.4739, acid value; 2.24, iodine value; 5.08 mg/g, peroxide value; 24.8 meq/kg, saponification value; 42.01 mgKOH/g, unsaponifiable matter; 1.1g. Fatty acid composition of oil from *Annona muricata* seed revealed presence of lauric acid; 12.27%, oleic acid; 21.82%, palmitic acid; 9.83% and stearic acid; 3.93%. The physicochemical parameters for *Telfairia occidentalis* were specific gravity; 1.04, refractive index, 1.5267, acid value; 8.42, iodine value; 5.08 mg/g, peroxide value; 41.4 meq/kg, saponification value; 53.30 mgKOH/g, unsaponifiable matter; 1.5g. Fatty acid composition of oil from *Telfairia occidentalis* seed revealed presence of linolenic acid; 7.92%, oleic acid;18.02%, palmitic acid; 7.05% and stearic acid; 14.79%.
Conclusion: The results obtained shows that both oils contain substantial amount of monounsaturated omega-9 fatty acid; oleic acid hence both oils can be considered for food and industrial uses.

POLYPHENOL-RICH *ARONIA MELANOCARPA* JUICE MODULATES TRANSCRIPTOME PROFILE OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN ADULTS AT MILD CARDIOVASCULAR RISK

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Introduction: *Aronia melanocarpa* fruit consumption has many beneficial effects on human health. Polyphenols are the main bioactive constituents of aronia fruit.
The aim: This study aimed to explore the effects of aronia juice total polyphenols on the transcriptome profile of peripheral blood mononuclear cells (PBMCs) in subjects at mild cardiovascular risk.
Methods: The study included 10 individuals (age=40.6±3.8 years, BMI=26.6±3.8 kg/m2, serum LDL=3.4±0.5 mmol/L) who were allocated to two different four-week treatments: 6 subjects consumed 100 mL of aronia juice daily, containing 1.17 g of total polyphenols, and 4 subjects consumed placebo with the same nutrient composition as aronia juice but lacking polyphenols. The PBMCs of all participants were sampled before and after the treatment period. Transcriptome was obtained by employing Illumina iScan microarray technology. Differentially expressed genes (DEGs) were identified using R/Bioconductor *limma* package. Gene Set Enrichment Analysis was used to detect concordant differences in *a priori* defined Hallmark gene set collection, after vs before treatment. NetworkAnalyst.ca was used to generate minimal protein interaction network based on DEGs.
Results: 458 DEGs were identified after the polyphenol-containing treatment. Ten gene sets were significantly enriched in DEGs: TNFα signaling, apoptosis, inflammatory response, IFNα response, IFNγ response, p53 pathway, hypoxia, UV response, IL6/JAK/STAT3 signaling and KRas signaling. These gene sets contained the highly interconnected nodes from the interaction network.
Conclusion: Aronia total polyphenols affect interconnected biological processes, involving immune response and regulation of cell proliferation and death, in subjects at mild cardiovascular risk. The key mechanisms of this response should be elucidated.

Acknowledgement: This work was funded by Serbian Ministry of Education, Science and Technological development Grants OI175085, III41028 and III41030.

A BIOCONJUGATE OF LIPASE WITH NOVEL FABRICATED NANOCELLULOSE FUSED POLYPYRROLE/GRAPHENE OXIDE NANOCOMPOSITE AS PROMISING NANOBIOCATALYST: CHARACTERIZATION AND APPLICATION TO FLAVOUR SYNTHESIS

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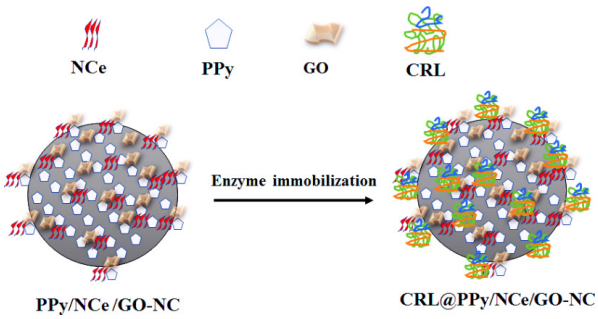

Enzymatic biocatalysis has a vast reputation on an industrial scale especially lipases which perform hydrolysis, esterification and aminolysis under mild conditions. Free enzyme faces major hindrance of low stability and difficulties in recovery and reuse, hindering their potential. Immobilization of enzymes is a promising technology that can overcome these limitations. Further, to sustain the cost-effectiveness from nutritional point of view, employment of nanomaterial immobilized lipase for enzymatic flavour synthesis holds vital potential. This work was performed to describe the facile procedure of a novel nanobiocatalyst, nano cellulose fused polypyrrole/graphene oxide nanocomposite for the efficacious immobilization of lipase, a versatile hydrolytic enzyme having potential applications in industries. The fabricated nanocomposite was characterized using Fourier transform infrared spectroscopy, differential thermal analysis, thermogravimetric analysis, X-ray diffraction, scanning electron microscopy, atomic force microscopy, transmission electron microscopy, and *Candida rugosa* lipase was immobilized onto nanocomposite through physical adsorption. The catalytic efficiency and operational stabilities of immobilized lipase were improved significantly compared to the free lipase. The reusability profile outcomes showed that the immobilized formulation was an outstanding nanobiocatalyst as it retained 85% of its original catalytic activity after 10 repetitive cycles. The nanobiocatalyst was employed for the synthesis of the fruit flavour compound, ethyl acetoacetate. The immobilized lipase successfully synthesised flavour compound in solvent free media and n-hexane having 27.5% and 75.5% ester yields respectively. Moreover, these outcomes demonstrating graphene oxide modified carrier induced stabilization, amended solvent tolerance and operational stability of immobilized enzyme, will have quintessential influence on practical scale up of biotechnological industries.

EFFECTS OF FRUCTOSE-ENRICHED DIET ON INFLAMMATION AND INSULIN SIGNALING IN THE HYPOTHALAMUS AND VISCERAL ADIPOSE TISSUE OF FEMALE RATS

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Introduction: Increased fructose consumption, mainly through sweetened beverages, coincides with growing rate of obesity, women being more prone than men. Chronic low-grade inflammation has been implicated in the pathogenesis of obesity-related disorders including metabolic syndrome and insulin resistance.
The aim: We investigated whether fructose overconsumption causes inflammation in the visceral adipose tissue (VAT) and hypothalamus of female rats contributing to development of obesity and insulin resistance.
Methods: Using qPCR and Western blot, we examined the effects of 9-week fructose-enriched diet on inflammatory status, insulin and leptin signaling in the VAT and hypothalamus, as well as on the expression of orexigenic and anorexigenic neuropeptides in the hypothalamus.
Results: Fructose-fed rats had increased nuclear accumulation of nuclear factor κB (NF-κB) and elevated expression of pro-inflammatory cytokines (IL-1β, IL6, and TNFα), as well as increased protein level of macrophage-specific marker F4/80 in the VAT. In the same tissue, fructose overconsumption reduced protein content and stimulatory phosphorylation of Akt kinase, while increasing inhibitory phosphorylation of insulin receptor substrate-1 (IRS-1). There were no changes in VAT mass, nor in inflammatory markers, insulin and leptin signaling (leptin receptor and SOCS3 expression) and appetite regulation (NPY, AgRP, POMC and CART) in the hypothalamus.
Conclusions: The results suggest that fructose overconsumption causes alterations in pro-inflammatory markers and reduces insulin signaling in the VAT of female rats. These alterations could be one of the first consequences of fructose overconsumption, since they were detected in the absence of obesity, and hypothalamic inflammation and insulin and leptin resistance.

Acknowledgement: This work was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia, [Grant III41009] and Swiss National Science Foundation, [Grant SCOPES JRP IZ73Z0_152331].

Session 2

MODULATION OF GLUCOCORTICOID AND INSULIN SIGNALING IN THE RAT LIVER AFTER HIGH FRUCTOSE DIET AND CHRONIC STRESS

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Introduction: Overconsumption of fructose enriched drinks and everyday stress cause various metabolic disturbances. Balanced action of two counterregulated hormones, glucocorticoids and insulin, is the most important factor that regulate hepatic glucose metabolism. Our aim was to investigate possible link between these hormonal pathways in the rat liver and glucose homeostasis disturbed by fructose rich diet and/or exposure to chronic stress.
Methods: We analyzed the effects of 9-week 20% fructose solution and 4 week chronic unpredictable stress on glucocorticoid prereceptor metabolism, corticosterone level and glucocorticoid receptor subcellular redistribution in the liver of male Wistar rats. Hepatic insulin signaling was examined by stimulatory phosphorylation of insulin receptor supstrate 1 and expression of Akt kinase, Forkhead box protein O1 and main gluoneogenic enzymes, while systemic insulin sensitivity was assessed by intraperitoneal glucose tolerance test.
Results: High-fructose diet, alone and in combination with stress, led to hyperinsulinemia and hypoglycemia, while fructose treatment alone resulted in glucose intolerance. These metabolic disturbances were not accompanied with altered hepatic insulin signaling, but rather with decreased expression of gluconeogenic enzymes. Fructose diet led to an enhancement of hepatic glucocorticoid prereceptor metabolism irrespectively of stress, but without affecting downstream glucocorticoid signaling. Stress treatment alone did not influence hepatic glucocorticoid or insulin signaling, nor it induced perturbation of glucose metabolism.
Conclusion: The results demonstrate that dietary fructose-related decrease of gluconeogenic enzymes in the liver results in systemic hypoglycemia. However, fructose-induced glucose intolerance is not a result of altered insulin or glucocorticoid signaling in the liver.

Acknowledgement: This study was supported by grants III41009 from the Ministry of Education, Science and Technological Development, Republic of Serbia and SCOPES IZ73Z0_152331 from the Swiss National Science Foundation.

ESTRADIOL AMMELIORATES ANTIOXIDANT AXIS SIRT1/FOXO3a/MnSOD IN THE HEART OF FRUCTOSE-FED OVARIECTOMIZED RATS

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Introduction: Fructose-rich diet (FRD) promotes oxidative stress in heart, while estradiol has a protective effect. NADPH oxidase 4 (Nox4) is a major source of ROS in the vasculature, the effect that could be attributed to the reduction of Sirtuin 1 (SIRT1) level. SIRT1 deacetylates forkhead box O3a (FoxO3a), allowing its dephosphorylation and activation. FoxO3a upregulates the main antioxidant enzymes such as manganese superoxide dismutase (MnSOD).
Aim: We investigated the effect of FRD and estradiol on Nox4 and MnSOD mRNA level, FoxO3a phosphorylation as well as on SIRT1 and MnSOD protein level in the heart of ovariectomized rats.
Methods: Control and fructose-fed ovariectomized females with or without 17β-estradiol treatment (C-OVX, F-OVX, F-OVX+E2) were subjected to FRD for 9 weeks. Protein and mRNA levels were assessed by Western blot and Real-time PCR.
Results: FRD did not affect while estradiol treatment decreased Nox4 and MnSOD mRNA level in fructose-fed ovariectomized rats compared to both, F-OVX group ($p<0.0001$ and $p<0.01$, respectively) and C-OVX group ($p<0.001$ and $p<0.01$, respectively). FRD elevated phosphorylation of FoxO3a ($p<0.01$), thereby decreasing its activity, while estradiol treatment reverted this change (Fru-Ovx vs. Fru-Ovx+E, $p<0.05$). FRD decreased SIRT1 and MnSOD protein level ($p<0.05$ and $p<0.05$, respectively), while estradiol treatment increased SIRT1 protein level (Fru-Ovx vs. Fru-Ovx+E, $p<0.05$) and showed a trend toward increasing MnSOD protein level (Fru-Ovx vs. Fru-Ovx+E, $p=0.05$).
Conclusion: FRD induces oxidative stress in heart, which could be mediated through Nox4-SIRT1-FoxO3a-MnSOD axis, while estradiol acts protectively by upregulating expression/activation of molecules involved in the antioxidative signaling pathway.

The acknowledgement: This work was supported by The Ministry of Education, Science and Technological Development of the Republic of Serbia (grant numbers: OI175085, III 41009).

DOUBLE-STRAND DNA BREAKS RESPONSE IN HUNTINGTON´S DISEASE

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Introduction: Huntington's disease (HD) is neurodegenerative disease caused by the mutation in the huntingtin gene, which gives rise to mutated form of huntingtin protein (mHtt). Recent findings suggest that mHtt may also affect double-strand DNA breaks (DSBs) response. However, it is not clear whether mHtt compromises detection of new DSBs or repair mechanism itself.
Aim: The main aim is to characterize DSBs response in primary fibroblasts isolated from transgenic minipig HD model during aging.
Methods: To study DSBs response, we monitored kinetics of γH2AX and 53BP1, and activatory phosphorylation of p53 protein and ATM kinase by immunofluorescence in primary fibroblasts isolated from wild-type (WT) and HD transgenic (TgHD) minipigs of age 8, 24, 36 and 60 months. New double-strand breaks were induced by radiomimetic drug neocarzinostatin (NCS). The quantitative analysis of confocal images was done by FindFoci algorithm in ImageJ.
Results: We found that 60 months TgHD fibroblasts exhibit decreased number of γH2AX foci after NCS treatment in comparison to WT fibroblasts. Moreover, after NCS treatment, 60 months TgHD fibroblasts exhibit higher phosphorylation of nuclear ATM and also p53 compared to WT fibroblasts. Surprisingly, 60 months WT fibroblasts show generally reduced ability to recognize new DSBs compared to 8 months WT fibroblasts.
Conclusion: We found that TgHD fibroblasts exhibit compromised ability to recognize new DSBs and changes in dynamics of repair factor 53BP1 are present. Interestingly, we found that ability to respond on newly formed DSBs in WT and also in TgHD fibroblasts is strongly age dependent.

Acknowledgement: This study was supported by CHDI foundation (A-5378) and by National Sustainability Programme, project number LO1609 (Czech Ministry of Education, Youth and Sports). The research leading to these results has received funding from the Norwegian Financial Mechanism 2009-2014 and the Ministry of Education, Youth and Sports under Project Contract no. MSMT-28477/2014 (project ID 7F14308)

PHORBOL 12-MYRISTATE 13-ACETATE INDUCES SENESCENCE OF HL-60 LEUKEMIC CELLS

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Introduction: Phorbol myristate acetate (PMA) is in clinical investigation for treatment of acute myeloid leukemia due to its differentiating ability. Cell differentiation could be accompanied by senescence, a state of irreversible cell cycle arrest.
Our aim was to investigate the ability of PMA to initiate senescence in HL60 human leukemia cells.
Methods: Cell morphology was analyzed using phase contrast microscopy. Cell cycle arrest was assessed by flow cytometric analysis of propidium iodide stained cells and BrdU colorimetric assay. Activity of senescence-associated beta-galactosidase (SA-βgal) was assessed by cytochemical staining and flow cytometric analysis of fluorescein di-β-D-galactopyranoside (FDG) stained cells. Senescence-associated gene expression of: cell cycle inhibitor p21, interleukin-8 (IL-8), lamin B1 were quantified by RT-PCR, while activation of NF-κB, main regulator of senescence associated secretory phenotype, was examined by immunoblotting.
Results: After the PMA treatment HL60 were enlarged and flattened with cytoplasmic vacuoles resembling morphology of senescent cells. Block in leukemia cell proliferation in G1 phase was accompanied with increase in expression of cell cycle inhibitor p21 in PMA treated cells. Finally, PMA stimulated SA-βgal activity, expression of genes responsible for senescence associated secretory phenotype, NF-κB and IL-8, while downregulating Lamin B1 expression.
Conclusion: Our results suggest that in addition to PMA-induced cellular differentiation, senescence participates in its previously shown cytostatic effect, further supporting its investigation as a potential antileukemic drug.

Acknowledgements: This study was supported by the Ministry of Education, Science and Technological Development, Republic of Serbia (Grant No. 41025 and 173053)

EFFECT OF SHORT TERM FASTING ON HYPOTHALAMIC INSULIN EXPRESSION AND SIGNALING

Tamara Dakic, Milica Vranic, Tanja Jevdjovic, Iva Lakic, Jelena Djordjevic and Predrag Vujovic

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The aim: Considering ambiguous data on insulin expression in the brain, the aim of this study was to examine effects of six-hour fasting on insulin expression and signaling in the rat hypothalamus.

Methods: Food was removed at 6 pm and male Wistar rats were sacrificed at midnight. Controls which had free access to food were simultaneously sacrificed. Insulin mRNA expression was assessed by qPCR. Immunoblotting was used to determine the levels of insulin, insulin receptor (IR), insulin receptor substrate (IRS) 1 and 2, mTOR1 Ser/Thr kinase and extracellular signal–regulated kinases ERK1/2 and their phosphorylated forms (pIR^{Tyr1361}, pIRS1^{Tyr612}, pIRS2^{Ser731}, pmTOR^{Ser2448}, pERK1/2$^{Thr202/Tyr204}$). Hypothalamic distribution of insulin and p-IR^{Tyr1361} was determined by immunofluorescence.

Results: Fasting increased both insulin mRNA expression and its content in the hypothalamus. Insulin immunopositivity was detected in the NeuN-positive cells of periventricular nucleus (PeV) and in the ependymal cells surrounding the third ventricle. Phospho-IR^{Tyr1361} immunoreactivity was detected at the roof of the third ventricle in the region of PeV. The levels of IR and phospho-IR^{Tyr1361} were increased, while those of IRS1 and 2 were not altered. However, pIRS1^{Tyr612} content was decreased under the same circumstances. The amount of ERK1/2 was lower in fasting rats, unlike that of pERK1/2$^{Thr202/Tyr204}$ which was increased. Lastly, the levels of both mTOR and pmTOR^{Ser2448} were unchanged.

Conclusion: Results showed that short-term fasting promoted insulin production in the hypothalamus. The fact that we simultaneously detected increased amount of activated ERK1/2 indicates that locally produced insulin may potentially be involved in regulation of gene expression.

Acknowledgements: This study was supported by Ministry of Education, Science and Technological Development, Republic of Serbia (173023).

SOCIAL ACTIVITIES

Monday, October 15, 2018

18:00 - 19:30	**Welcome party: Participants introduction and music program** (*Conference room*)

Tuesday, October 16, 2018

15:00 - 16:00	**Field trip** (*Petnica cave*)

Wednesday, October 17, 2018

15:00 - 17:00	**Field trip** (*Valjevo*)

Thursday, October 18, 2018

15:00 - 17:00	**Sport activities (swimming, basketball, volleyball, badminton, yoga...)**
20:00 - 24:00	**Farewell dinner with party** (*Restaurant*)

Friday, October 19, 2018

13:45 - 14:00	**Photo session** (*Open field*)

CIP

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