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Institute for Biological Research "Siniša Stanković" (IBISS)

Department for Neurobiology

During the last 20 years our team has investigated the plastic capacity of the brain to adapt to constant requirements of the environment. This capability of the brain decreases with age and in various pathological conditions, like neurodegenerative disorders. To determine the extent to which we can influence this plastic potential by various environmental manipulations (nutrition, brain trauma, social isolation, dexamethasone treatment..) we have used an *in vitro* approach and various animal models. We have experience in establishing and handling animal models of Alzheimer's and Parkinson's disease (transgenic and non-transgenic), and dietary and anaesthesia exposures as challenging environmental treatments/interventions during physiological and pathological ageing. We perform comprehensive behavioural and molecular characterization of the effects of various environmental interventions in vivo. We offer expertise in the measurements and analysis of rodent behaviour related to general motor activity, anxiety, sociability, anhedonia/depression and learning/memory, and frailty status. Using different molecular approaches we examine aging and age-disease-related brain pathology and synaptic plasticity, and how the brain manages to preserve neuronal survival and to improve functionality.

Methodology: IBISS possesses animal behavioural facilities and our group has expertise in a wide range of behavioural techniques (motor performances, anxiety testing, cognitive testing, learning and memory, frailty testing...). We perform in vitro and in vivo experiments; isolation of primary cell cultures, propagation of commercial cell lines, wild type and transgenic animal models, various molecular techniques for RNA, DNA and protein examination (RT-PCR, western blot, immunochemistry, light and confocal microscopy...)

Our group has collaborations with the most important scientific institutions in Serbia, including the Medical Faculty, Biology Faculty, and Institute for Public Health "Milan Jovanović Batut", Agency for Environmental Protection, Institute of Social Sciences, Ministry of Health, and Regional Office of the World Health Organization (dr Marjan Ivanuša). We also collaborate with several groups from Europe (Croatia, Greece, Italy, Germany, Slovenia), UK and USA.

Group references (in the last 5 years):

Mladenovic Djordjevic A, Loncarevic-Vasiljkovic N, Gonos ES (2020). Dietary restriction and oxidative stress: friends or enemies? Antioxid Redox Signal;10.1089/ars.2019.7959. doi:10.1089/ars.2019.7959 (IF 5.8)

Lazic D, Tesic V, Jovanovic M, Brkic M, Milanovic D, Zlokovic B, Kanazir S, Perovic M.(2020). Everyother-day feeding exacerbates inflammation and neuronal deficits in 5XFAD mouse model of Alzheimer's disease. Neurobiol Dis;136:104745. doi:10.1016/j.nbd.2020.104745 (IF 5.2)

Todorovic S, Loncarevic-Vasiljkovic N, Jovic M, Sokanovic S, Kanazir S, Mladenovic Djordjevic A (2020). Frailty index and phenotype frailty score: Sex- and age-related differences in 5XFAD transgenic mouse model of Alzheimer's disease. Mech Ageing Dev.;185:111195. doi:10.1016/j.mad.2019.111195 (IF 3.6)

Pavkovic Z, Potrebic M, Kanazir S, Pesic V (2020). Motivation, risk-taking and sensation seeking behavior in propofol anesthesia exposed peripubertal rats. Prog Neuropsychopharmacol Biol Psychiatry. 96:109733. (IF 4.3)

Milanovic D, Petrovic S, Brkic M, Avramovic V, Perovic M, Ivkovic S, Glibetic M, Kanazir S. (2018) Short-term fish oil treatment changes the composition of phospholipids while not affecting the expression of Mfsd2a omega-3 transporter in the brain and liver of the 5xFAD mouse model of Alzheimer's disease. Nutrients; 10(9):1250. doi:10.3390/nu10091250 (IF 4.2)

Jovic M, Loncarevic-Vasiljkovic N, Ivkovic S, Dinic J, Milanovic D, Zlokovic B, Kanazir S. (2019). Short-term fish oil supplementation applied in presymptomatic stage of Alzheimer's disease enhances microglial/macrophage barrier and prevents neuritic dystrophy in parietal cortex of 5xFAD mouse model. PLoS One.;14(5):e0216726. doi:10.1371/journal.pone.0216726 (IF 2.8)

Todorovic ST, Smiljanic KR, Ruzdijic SD, Djordjevic ANM*, Kanazir SD* (2018). Effects of different dietary protocols on general activity and frailty of male Wistar rats during aging. J Gerontol A Biol Sci Med Sci;73(8):1036-1044. doi:10.1093/gerona/gly015 (IF 4.7) (* equal contribution)

Smiljanic K, Todorovic S, Mladenovic Djordjevic A, Vanmierlo T, Lütjohann D, Ivkovic S, Kanazir S (2018). Limited daily feeding and intermittent feeding have different effects on regional brain energy homeostasis during aging. Biogerontology;19(2):121-132. doi:10.1007/s10522-018-9743-y (IF 3.8)

Pavkovic Z, Milanovic D, Ruzdijic S, Kanazir S, Pesic V (2018). The influence of propofol anesthesia exposure on nonaversive memory retrieval and expression of molecules involved in memory process in the dorsal hippocampus in peripubertal rats. Paediatr Anaesth. 28(6):537-546. (IF 1.8)

Pavkovic Z, Smiljanic K, Kanazir S, Milanovic D, Pesic V, Ruzdijiz S (2017). Brain molecular changes and behavioral alterations induced by propofol anesthesia exposure in peripubertal rats. Paediatr Anaesth. 27(9):962-972. (1.8)

Milanovic D, Pesic V, Loncarevic-Vasiljkovic N, Avramovic V, Tesic V, Jevtovic-Todorovic V, Kanazir S, Ruzdijic S (2017). Neonatal Propofol anesthesia changes expression of synaptic plasticity proteins and increases stereotypic and anxyolitic behavior in adult rats. Neurotox Res. 32(2):247-263. (IF 3.5)

Milanovic D, Pesic V, Loncarevic-Vasiljkovic N, Pavkovic Z, Popic J, Kanazir S, Jevtovic-Todorovic V, Ruzdijic S. (2016). The Fas ligand/Fas death receptor pathways contribute to Propofol-induced apoptosis and neuroinflammation in the brain of neonatal rats. Neurotox Res. Oct;30(3):434-52. doi: 10.1007/s12640-016-9629-1. (IF 3.5)

International projects of the group related to lifespan, including ageing:

- 2004-2005 Greek Serbian bilateral collaboration »Gene expression and protein interactions of Presinilin-1: Implication in development of Alzheimer's disease« (Greek recepient: Dr S. Efthimiopoulos, University of Athens, Greece).
- 2006-2007 Slovenian Serbian bilateral collaboration »The effect of Dietary Restriction on Synaptic Plasticity in the Aging Brain« (Slovenian recipient dr Marko Živin, Institute of Pathophysiology, Medical Faculty, University of Ljubljana)
- 2007-2010 NIH Fogarty International Research Collaboration Award (GC11479-128322) »The role of neurotrophins in anesthesia-induced developmental neuroapopotosis« (USA PI: Vesna Jevtovic-Todorovic, PhD, School of Medicine, University of Colorado, Aurora, CO, USA)
- 2011-2012 German Serbian bilateral collaboration (DAAD and Serbian Ministry of Science) »Influence of dietary restriction on the plasticity of the aging central and enteric nervous system« (DAAD recipient: prof. Schafer KH, University of Applied Sciences, Kaiserslautern, Germany)
- 2014-2016 Joint Research Projects, Swiss National Science Foundation, International Co-operation (SCOPES) »The molecular links between cholesterol homeostasis, membrane trafficking and Alzheimer's disease« (dr Silva Katušić Hećimović, IRB, Zagreb, Croatia; dr Lawrence Rajendran, Universität Zürich ZH, Switzerland)
- 2013-2017 NIH Fogarty International Research Collaboration Award (R03AG046216) «Caloric restriction and Alzheimer's Abeta clearance pathway« (USA PI: Berislav Zlokovic, PhD; University of Southern California, Los Angeles, CA, USA)
- 2018-2019 Croatia-Serbia bilateral project (Croatian and Serbian Ministry of Science) »Elucidating BACE1-substrate processing and distribution in a transgenic mouse model of Alzheimer's disease and their potential role in the disease pathogenesis« (dr Silva Katušić Hećimović, IRB, Zagreb, Croatia)
- 2019. QR GCRF Pump Priming Award »Meeting the challenge of multimorbidity in post-conflict Serbia« funded by UK Global Challenge Research Fund (UK PI Ilaria Bellantuono, HELSI Institute, University of Sheffield, UK)
- 2020. QR GCRF grant »A Multidisciplinary approach to prevention of multimirbidity in post-conflict Serbia« (UK PI Prof. Elizabeth Goyder, Professor of Public Health, ScHARR, University of Sheffield, UK)

 https://www.ibiss.bg.ac.rs/index.php/en/present/international/item/1531-a-multidisciplinary-approach-to-prevention-of-multimorbidity-in-post-conflict-serbia-2020

Resources:

We currently have a group of 10 researchers: 4 senior scientists:



Dr. Aleksandra Mladenovic Djordjevic, anamikos@ibiss.bg.ac.rs, orcid.org/0000-0001-9011-5634



Dr. Vesna Pesic, vesnav@ibiss.bg.ac.rs, orcid.org/0000-0002-1415-5834



Dr. Desa Milanovic, desan@ibiss.bg.ac.rs, orcid.org/0000-0001-9799-0335

Dr Selma Kanazir, selkan@ibiss.bg.ac.rs

<u>3 Postdocs</u> (Zeljko Pavkovic, Smilja Todorovic, Maja Pavkovic), and <u>3 PhD students</u> (Milica Potrebic, Milica Prvulovic, Milena Jovic).

We closely collaborate with several Serbian research groups, including the group of Dr. Nataša Milić who is Head of the Department of Biostatistics, at Belgrade University Medical Faculty. Dr. Milić has expertise in ageing research and biostatistics and she would act as part of our group in the current application (link: http://statistika.mfub.bg.ac.rs/o-katedri, dr Milić: sillystat@gmail.com). Dr. Milic leads a group of five scientists. Their references are listed below.

Weissgerber TL, Winham SJ, Heinzen EP, Milin-Lazovic JS, Garcia-Valencia O, Bukumiric Z, Savic MD, Garovic VD, Milic NM. (2019) Reveal, Don't Conceal: Transforming Data Visualization to Improve Transparency. Circulation. 140(18):1506-1518. doi: 10.1161/CIRCULATIONAHA.118.037777. (IF 23.05)

Weissgerber TL, Garovic VD, Savic M, Winham SJ, Milic NM. (2016) From Static to Interactive: Transforming Data Visualization to Improve Transparency. PLoS Biol.;14(6):e1002484. doi: 10.1371/journal.pbio.1002484. (IF 8.3)

Weissgerber TL, Garovic VD, Milin-Lazovic JS, Winham SJ, Obradovic Z, Trzeciakowski JP, Milic (2016). Reinventing Biostatistics Education for Basic Scientists.

NM.PLoS Biol. 8;14(4):e1002430. doi: 10.1371/journal.pbio.1002430. (IF 8.3)

Group achievements

Dr Aleksandra Mladenović Đorđević is the <u>Editor for Reviews and Special issues of Mechanisms of Ageing and Development</u>, the Serbian representative in European Society of Preventive, Regenerative and Anti-Aging Medicine (website under construction) and an organizer of the <u>FEBS- and IUBMB-supported Advanced Lecture Course</u>.

Gallery: https://www.ibiss.bg.ac.rs/index.php/en/gallery



Web: https://www.ibiss.bg.ac.rs/index.php/en/events/item/1577-the-beginning-of-the-project