Reasoning of dissertation topic and competency of potential supervisor for admission into LSU biology doctoral studies with a participation of Tartu university 2023

Area of research (title and code)	Biomedical Sciences B000
Field of research (title and code)	Biology 01B
Topic of research	Aging
Institution	Lithuanian Sports University

Potential supervisor

Pedagogical and scientific degree	**Name, surname**	**Academic position**
PhD	Oron Levin	Professor

Short reasoning of proposed dissertation topic

Title
Research into the longitudinal effects of resistance training on inflammatory processes and their impact on brain and muscle health in community dwelling older adults
Short research description (including aims and objectives) (maximum 1500 characters). Systemic inflammation has long been implicated as a key factor in the development of neurodegenerative processes leading to cognitive and functional declines in the aging population. In the brain, pro-inflammatory processes trigger activation of glial cells resulting in neuro-axonal damage and neuronal loss. In the skeletal muscle, proinflammatory processes appear to contribute to inhibition of growth factor and increased oxidative stress, resulting in muscle tissue loss and declined muscle strength. These processes are expected to impact individual's intrinsic capacity (IC) which referring to the sum of physical and mental abilities that an individual can draw on at any point in time. The overarching goals of the current project are: (i) Explore mechanisms that underlie the associations between obesity and sedentary behavior to pro-inflammatory factors, neurodegenerative factors and markers of muscle wasting   (ii) Examine the contribution of these factors to development of sarcopenia and/or cognitive declines that may lead to declining IC in community dwelling older adults.   (iii) Examine whether sedentary and/or overweight older adults involved in a longitudinal 12-month strength-training program can become less susceptible to the potential damaging effects of systemic inflammation on their physical and mental abilities.   The project will require processing on neuroimaging data, blood samples and performance of batteries of cognitive and functional tests.
Relevance of the problem, its novelty at national and international level (maximum 1500 characters). The link between inflammation-related biomarkers and changes in physical and mental capacities of older individuals as they aged has been explored extensively in the past two decades[1,7,8]. However, findings have often been inconsistent, and a clearer picture about the specific effects of systemic inflammation on specific functional and cognitive domains is needed[1]. Moreover, evidence suggests that individuals with overweight and obesity may be more prone to inflammatory conditions and neuroinflammation4, which in turn could lead to accelerated cognitive and functional declines. In this project we aim to bridge this gap by examining the associations between circulating biomarkers of systemic inflammation (e.g., kynurenine, interleukin 6, and C-reactive protein – C-RP), neuroinflammation (e.g., myoinositol – a biomarker of glial cell density) and neurodegeneration (e.g., neurofilament light chain – NfL). This holistic approach where multimodal methods for researching interactions peripheral body systems and central nervous system and brain is still an emerging topic both geriatric medicine and sports medicine. Currently, our research group is one of the few group worldwide that implement this approach. Our group members are affiliated with the PhysAgeNet eCOST action (https://www.cost.eu/actions/CA20104/) and are involved in major collaboration with members of the European Group for Research into Elderly and Physical Activity

(EGREPA) (https://www.egrepa.org/) a European international scientific organization of research into healthy aging.

Research methods and possibilities for conducting these studies (maximum 1500 characters).

We will recruit 120 community dwelling older adults with normal or near-to-normal cognitive capacity. Participants will stay in the study for 1.5 years and will be randomly allocated to exercise group and active control group Participants will be tested on a battery of cognitive and motor tests to evaluate their cognitive-motor competence. Health/morbidity conditions will be assessed by physicians through medical examination and evaluation of blood biochemistry and haematology characteristics from blood tests. Structural MRI and proton magnetic resonance (MR) spectroscopy (1H-MRS) will be to assess brain tissue integrity. Intervention will consist of 2-3 weekly sessions of strength training of the lower limbs. The intensity will be kept between 70-85% of one repetition maximal (1-RM) for all exercises and the repetition range was 6-10, with initial 2-3 weeks at higher repetition range of 8-10 followed by training sessions with 6-8 repetition ranges afterwards. Participants will be trained in fitness centers next to their place and residence under supervision of qualified trainers. Findings about the associations between blood, brain, neurophysiologic biomarkers and intrinsic capacity will be analyzed with mediation analysis at baseline after 12 months of training and at follow up (18 month from baseline/only behavioral and blood biomarkers). Moderators for this model will be environmental/social factors, sedentary behavior, obesity, frailty and internal capacity at baseline.

Is the proposed topic for the doctoral thesis related to currently funded research projects? Please indicate the links between the proposed topic for the doctoral thesis and funded research projects

Founded ongoing Research projects linked to the current PhD project
1. Research Council of Lithuania (Lietuvos mokslo taryba). Title: **Resistance training and muscle - brain crosstalk**" (Grant No. Nr. S-MIP-21-37; 149,005 Euro). Period2021-2023. Awarded: M. Paasuke, O. Levin, N. Masiulis, V.J. Cesnaitiene & R. Gleizniene.
2. Research Council of Lithuania (Lietuvos mokslo taryba). Title: **Study into the long-term effects of resistance training on brain and blood biomarkers in normal cognitive aging and mild cognitive impairment** (Grant Nr P-MIP-22-217; 149,839 Euro). Period 01.07.2022 – 31.03.2025.

Is the proposed topic for the doctoral thesis related to joint research with a foreign institution? Please indicate the links between the proposed topic for the doctoral thesis and research with a foreign institution

1. Department of Imaging and Pathology, Group Biomedical Sciences, Biomedical MRI Unit, KU Leuven, Belgium. We are currently collaborating with Prof. Uwe Himmelreich who is the head of the unit on processing and interpretation of MRS data from brain/muscle tissue. This is a long lasting collaboration.
2. Institute of Sport Sciences and Physiotherapy, University of Tartu, Tartu, Estonia. Collaboration with prof. Mati Paasuke. This is a long lasting collaboration that focus on effect of exercise on structural and biochemical properties of muscle tissue.
3. Department of Rehabilitation Medicine Research School CAPHRI, Maastricht University, the Netherlands. Prof. Jeanin Verbunt and dr. Charlotte van Laake-Geelen. Join PhD project on parallel research line (Wouter Vints).
4. Gerontology Department, Vrije Universiteit Brussel (VUB), Brussels, Belgium. Prof. Ivan Bautmans. Join PhD project on parallel research line (Orgesa Qipo).
5. The Academic College at Wingate, Netanya, Israel. Prof. Yael Netz (president of EGREPA). Co-investigator on project P-MIP-22-217.

Currently I am supervisor of ___1___ doctoral students.

Supervisor _____ Oron Levin
(signature)   (Name, surname)

Date: 27/04/2023