JCET Jagiellonian Centre for Experimental Therapeutics

JAGIELLONIAN UNIVERSITY IN KRAKOW

Position for the 1 position of a PhD student
in the Doctoral School of Exact and Natural Sciences
Biomedical Sciences (EN) (MCB/JCET/Solaris)
offer no 2022-221

Within the project funded by Weave-UNISONO:" **Specific pathomechanisms of aging-related endothelial dysfunction in sepsis: investigation of mechanisms and experimental therapy** "
Supervisor: prof. dr hab. Stefan Chłopicki
The Doctoral School of Exact and Natural Sciences MCB/JCET/Solaris invites applications for the position of a PhD student that will start on October2022.

Project description:

Endothelial dysfunction importantly contributes to pathophysiology of sepsis and recent studies provide key evidence that pro-inflammatory stimuli and oxidative stressors induce a significantly more severe degree of endothelial dysfunction in blood vessels of aged rats and mice, when compared to the responses in young animals [1,2]. Still, there are no studies specifically focusing on the mechanisms underlying the sepsis-associated impairment of endothelial function in aging animals. This topic represent an important challenge in medicine given the fact that as yet there are no effective pharmacological approaches for the therapy of circulatory shock and multiorgan failure of sepsis.

The central hypotheses of the project that seeks for a talented PhD student are that (1) accelerated endothelial dysfunction is a key contributor to multiple organ failure and mortality in aging animals during sepsis and (2) in aging blood vessels, unique cellular and molecular mechanisms operate that render them extremely vulnerable to the oxidative stress-associated endothelial dysfunction during sepsis. In the frame of the project we will try to identify unique pathophysiological patterns and will yield potentially targetable novel pathways that are selectively perturbed in the aged vasculature in response to sepsis. The potential target will include Nrf2 (a master regulatory factor of the antioxidant response) nuclear enzyme PARP, telomere loss age-associated down-regulation of circulating IGF1 levels, age-dependent changes in endothelial and vascular metabolism and others. This interdisciplinary project encompassing in vivo work and vascular and cellular studies, should shed light on the pharmacotherapeutic mechanisms of age-associated worsening of endothelial dysfunction in sepsis. The research is carried out in the frame of Weave-UNISONO grant and international collaboration.

[1] Joffre J, Hellman J, Ince C, & Ait-Oufella H (2020). Endothelial Responses in Sepsis. *Am J Respir Crit Care Med* **202**, 361-370.
[2] Ungvari Z, Tarantini S, Sorond F, Merkely B, & Csiszar A (2020). Mechanisms of Vascular Aging, A Geroscience Perspective: JACC Focus Seminar. *J Am Coll Cardiol* **75**, 931-941.

Required documents:
(required as part of a given education program and resulting from the specificity of the research project)

Please send your application documents to the e-mail address of the Project Manager Prof. dr hab. Stefan Chłopicki e-mail: stefan.chlopicki@jcet.eu and to the Online Application System (OAS) at: https://irk.uj.edu.pl/en-gb/

Please note that the OAS will be open on the 17th of June 2022!

For more information, please visit: Biomedical Sciences (EN) (MCB/JCET/Solaris)