JOB OFFER – *Post-Doc*

A postdoctoral research position is available to participate in a research that has been designed to elucidate the role of the Nox2-ROS-Nlrp3 inflammasome axis in migration, homing, and engraftment of HSPCs

Project Title:

Role of Nox2-ROS-Nlrp3 inflammasome axis in homing ang engraftment of hematopoietic stem/progenitor cells

Project Background:

Delayed engraftment of hematopoietic stem/progenitor cells (HSPCs), or even failure to engraft, is still a significant clinical problem, mainly if the number of HSPCs is limited. The mechanisms that direct homing and engraftment of HSPCs after transplantation to BM are still not well understood. We propose that these processes could be enhanced by employing some safe, innovative, and efficient approaches. We will shed more light on these processes and propose new innovative strategies by i) improving the responsiveness of infused HSPCs so that they can better migrate toward a gradient of the main BM chemoattractant, stromal-derived factor 1 (SDF-1), and the two supporting BM chemoattractants, sphingosine-1-phosphate (S1P) and extracellular adenosine triphosphate (eATP), and ii) we will manipulate in BM microenvironment of transplant recipient a state of "sterile inflammation" induced by myeloablative condition for transplantation, to promote better homing and engraftment. Our pioneering data indicate that receptors for HSPCs chemoattractants, including CXCR4 for SDF-1, S1P1R for S1P, and P2X7 for eATP, have to be included in membrane lipid rafts (MLRs) for optimal migration and BM homing. These MLRs are assembled on the cell surface in response to NADPH oxidase 2 (Nox2) that generates reactive oxygen species (ROS) to trigger activation of Nlrp3 inflammasome. Thus, we propose that the Nox2-ROS-Nlrp3 inflammasome axis regulates the migration of HSPCs and their homing properties. Similarly, our data indicate that the same axis facilitates the homing response of the BM microenvironment after myeloablative conditioning before transplantation.Therefore, based on our intriguing published and preliminary evidence, we propose three interrelated specific aims. Specific Aim 1. To enhance the Nox2–ROS–Nlrp3 inflammasome-mediated MLRs formation to increase migration of HSPCs to BM chemoattractants. We will test strategies to improve the responsiveness of transplanted HSPCs to BM chemoattractants by increasing the formation of MLRs on HSPCs in Nox2–ROS–Nlrp3 inflammasome-dependent manner. Specific Aim 2. To enhance homing of HSPCs by modulating Nox2-ROS-Nlrp3 inflammasome mediated sterile inflammation in the recipient BM microenvironment after myeloablative conditioning for transplantation. Since myeloablative conditioning for transplantation fuels a state of "sterile inflammation" in the BM microenvironment that directs the homing of transplanted HSPCs, we will manipulate the state of sterile inflammation in the BM microenvironment to promote better homing and engraftment. Specific Aim 3. To explain at the cellular and

molecular level, the role of the Nox2-ROS-Nlrp3 inflammasome axis in migration, homing, and engraftment of HSPCs. We will employ state of the art strategies to analyze cellular and molecular effects that regulate i) optimal MLRs-dependent migration of HSPCs and ii) sterile inflammation induced BM microenvironment that facilitates homing and expansion of transplanted HSPCs.

We are looking for a highly motivated person to participate as a post-doctoral fellow within scientific project at the Warsaw Medical University at the Department of Regenerative Medicine

Supervisors: Mariusz Ratajczak, MD, PhD,
Type of employment relationship: Contact of mandate
Employing entity: Warsaw Medical University
Application deadline: July 31st, 2022
Expected start date: September 2022
Duration: 36-month position
Salary: 10 000 PLN gross gross (tax included)

Eligibility:
A suitable applicant should have the following qualifications:

1. PhD degree in Biology or Biotechnology
2. Basic previous experience in the following biology techniques: RNA seq, Mass Spectrometry, flow cytometry
3. Academic background in cell biology, molecular biology, and/or genetics.
4. Scientific research experience (full-text international publications, full-text articles published in Polish journals, international abstracts, active participation in (inter)national meetings, and scientific courses)
5. Ability to work independently
6. The candidate is required to have knowledge of stem cell biology
7. Good knowledge of English
8. Strong interest in science

How to apply:
Please send:

1. Letter of interest
2. CV
3. Publication list
4. Photo
5. Contact details of 1-2 potential referees with **recommendation letter**

to: ***mzrata01@louisville.edu*.**
mariusz.ratajczak@wum.edu.pl
medycyna.regeneracyjna@wum.edu.pl

All documents should be sent as PDF files.
The e-mail heading should be: „**Post-doc – OPUS grant”.**

Please provide also the statement that you grant us a permission to process your personal details for the recruitment process:
"I hereby give consent for my personal data included in the job offer to be processed for the purposes of recruitment conducted by the Medical University of Warsaw located in Warsaw".

The rules for the protection of personal data used by the Medical University of Warsaw:

1. The administrator of personal data is the Medical University of Warsaw located in Warsaw, Żwirki i Wigury 61, 02-091 Warszawa,
2. Contact to the Data Protection Officer - email address: iod@wum.edu.pl.
3. Personal data will be processed in order to implement the recruitment process pursuant to art. 22^1 of the Labor Code, and in the case of providing a broader scope of data pursuant to art. 6 § 1a GDPR - consent expressed by the candidate.
4. Access to personal data within the University's organizational structure shall only have employees authorized by the Administrator in the necessary scope.
5. Personal data will not be disclosed to other entities, except for entities authorized by law.
6. Personal data will be stored for the period necessary to carry out the recruitment process, up to 12 months from the settlement of the recruitment process. After this period, they will be removed.
7. You have the right to access your data, the right to rectify, delete, limit processing, the right to transfer data, the right to object to the processing, the right to withdraw consent.
8. You have the right to withdraw consent to the processing of your personal data at any time, which will not affect the lawfulness of the processing that was carried out on the basis of consent before its withdrawal.
9. You have the right to lodge a complaint with the Office for Personal Data Protection when it is justified that his personal data are processed by the Administrator in breach of the general regulation on the protection of personal data of April 27, 2016.
10. Providing personal data is voluntary, but necessary to participate in the recruitment process to the extent specified in art. 22^1 § 1 of the Labor Code, voluntary in the remaining scope.
11. Decisions will not be taken in an automated manner and personal data will not be subject to profiling.

Project "*Role of Nox2-ROS-Nlrp3 inflammasome axis in homing ang engraftment of hematopoietic stem/progenitor cells"* is funded
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