Międzynarodowe Centrum Badań nad Szczepionkami Przeciwnowotworowymi
(International Centre for Cancer Vaccine Science)
Uniwersytet Gdański
ul. Kładki 24, 80-822 Gdańsk
Kontakt: tel. 0048-58-523 3460
iccvs@ug.edu.pl | www.iccvs.ug.edu.pl

Job offer - postdoctoral researcher at the International Centre for Cancer Vaccine Science, University of Gdańsk

Project: Characteristics of the function and regulation of isoform 2 of the Nrf2 transcription factor, NCN SONATA, UMO-2021/43/D/NZ1/02059

About the project:

This project aims to characterise an alternative isoform of Nrf2 transcription factor that we have identified: dN-Nrf2.

Nrf2 pathway arose to overcome the metabolic toxicity that results from the use of highly reactive molecular oxygen and is dated back to the Great Oxidative Event that took place on earth at 2.45–1.85 billion years (Ga) ago when cyanobacteria and their evolutionary ancestors began utilizing photosynthesis to produce molecular oxygen (O2).

As its name suggests, Nuclear factor erythroid 2-Related Factor 2 (Nrf2) was discovered for its roles in erythropoiesis. It was identified as one of the transcription factors occupying the enhancer region of the haemoglobin subunit – β-globin. Interestingly, first generated Nrf2 knockout (KO) mice did not show any specific phenotype, neither expressed altered haematological markers. What they did show though, was a markedly reduced expression of class II detoxification enzymes in response to oxidative stress in comparison to the Nrf2 wild type (wt) and heterozygous mice. This discovery directed Nrf2 studies towards toxicology and chemoprevention, marginalizing the research on Nrf2 in erythropoiesis. Since Nrf2 paved its way as a key regulator of responses to oxidative, xenobiotic and electrophilic stressors, its pathway has been studied from the perspective of stress-activation. This is how Keap1 was identified as its main negative regulator, which anchors Nrf2 to the Cullin3-RING ubiquitin ligase complex (CLR3), mediating its constitutive degradation under no stress. Later on it Nrf2 was shown to be involved in basic metabolic processes essential for cell homeostasis. Interestingly, another generated Nrf2 KO mice showed sign of anaemia, progressing with ageing. Therefore it became obvious that basal Nrf2 activity is essential for cell physiology. This function of Nrf2 had to originate early in evolution, be conserved and strictly regulated.

We have identified the Nrf2 form that seems to be resistant to Keap1-Cul3 degradation, is exceptionally stable and in the SDS-PAGE migrates below the stress-activated form. We have traced its origin and found that it is produced from an alternative mRNA variant - transcript 2, which utilizes another AUG for translation initiation, resulting in the Nrf2 form that lacks first 16 amino acids (ΔN-Nrf2 or dN-Nrf2). Modelling studies showed that this N-terminal deletion disrupts binding with Keap1 via an evolutionary conserved DLG motif and in consequence, impairs dN-Nrf2 ubiquitination and degradation. Interestingly, under no-stress conditions this form is the most abundant Nrf2 form in cancer cell lines, primary lung cancer cells and in normal lung fibroblasts. This proposal aims at comprehensive characterisation of this form in terms of regulation and function. We will perform isoform-specific knockdowns/knockouts to look at the role of the dN-Nrf2 in cells. We will look into the interactome of dN-Nrf2 as well as at its translational regulation in comparison to the canonical full-length Nrf2.

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About the Candidate

Interested in studying cellular responses to environmental stimuli on DNA, RNA and protein levels and integrating the information obtained from these analyses.

Interested in studying how an environmental stimulus is translated into cellular responses.

With motivation to pursue impactful questions with adequate and precise cellular models.

- Confident in eukaryotic cell culture, cloning, transfections of human cells (overexpression and knockdowns), molecular biology work with DNA, RNA and proteins such as Real-Time PCR, western blot etc.
- Familiar with confocal microscopy, immune fluorescence and proximity ligation assays.
- Familiar with or eager to learn polysome isolation and studying regulation of mRNA .translation.
- Fluent English in communication and writing. Experienced in writing scientific manuscripts.

Requirements:

1) PhD degree in biotechnology/biology or similar discipline where the Candidate gained skills stated above
2) PhD degree obtained maximum 7 years before the year of employment in the project. It can be extended beyond 7 years for the following properly documented circumstances:

Maternity - 18 months extension for each child born before or after the date of the successful defense of their PhD degree. If the applicant can document a longer total maternity leave, the eligibility period will be extended by the documented amount of actual leave(s) for all children taken

Paternity extension by the documented time of paternity leave taken for each child

Long-term illness (>90 days): extension by the documented amount of leave

3) PhD degree obtained in an entity other than University of Gdansk or the Candidate has completed a continuous and documented postdoctoral training of at least 10 months at an institution abroad.
4) PhD degree in biotechnology/biology or similar discipline where the Candidate gained skills stated above
5) PhD degree obtained maximum 7 years before the year of employment in the project. It can be extended beyond 7 years for the following properly documented circumstances:

Maternity - 18 months extension for each child born before or after the date of the successful defense of their PhD degree. If the applicant can document a longer total maternity leave, the eligibility period will be extended by the documented amount of actual leave(s) for all children taken

Paternity extension by the documented time of paternity leave taken for each child

Long-term illness (>90 days): extension by the documented amount of leave

6) PhD degree obtained in an entity other than University of Gdansk or the Candidate has completed a continuous and documented postdoctoral training of at least 10 months at an institution abroad.

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Working conditions

- Employment contract for maximum 24 month (full time, “adjunct” position). Salary before tax & social insurance deductions approx. 7.600 PLN (gross). Additional yearly remuneration (so-called “13th salary”) if eligible and according to binding provisions at the University.
- Starting date to be discussed, not later than 1 January 2024.
- Friendly and inspiring working atmosphere.
- Presentation of work at international and national conferences.
- While employed in this project, the candidate shall not receive renumeration coming from direct costs of other NCN research projects as well as from another employment contract, including an employer from outside Poland.
- In case of questions you are encouraged to contact dr Alicja Sznarkowska alicja.sznarkowska@ug.edu.pl before submitting the application.

Application documents

Application documents shall be prepared **as one single PDF** and include:

- a full CV of the Candidate including a list of publications and achievements;
- copy of the PhD diploma;
- a letter of motivation explaining your general interest for this position;
- name, affiliation, email, and phone number of at least two referees to contact for recommendation;
- declaration of the applicant that his work is not financed by other projects of the National Science Center.

Please include the signed statement on the GDPR information clause for this recruitment downloaded from: https://iccvs.ug.edu.pl/work-with-us/open-positions/

Application in English shall be sent to: alicja.sznarkowska@ug.edu.pl with “Nrf2 postdoc” in the email’s title **until November 24th, 2023**, 23:59.

Selected candidates will be invited to an (online) interview. The candidates will be selected by a competition committee appointed by the Rector of University of Gdansk.