



Position: **Ph.D. position in the project:** „Interplay of posttranslational redox cysteine modifications and metal ion binding as key to conformational and functional plasticity of innate immunity and cancer biomarkers - S100A8 and S100A9 proteins,,

Number of positions: 1

Institution: Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw

Maximum period of position agreement: 29 months

Position starts on November 2017

Salary (scholarship) amount: **3 000** PLN/ month

We are looking for a highly motivated Ph.D. student who will work on detailed analysis of the role of metallation and posttranslational modifications in regulation of human proteins.

Candidate should be strongly motivated to use modern experimental techniques, including mass spectrometry methods, to study interactions of proteins and their cofactors. The research project will be run in Warsaw and Wrocław and assembles a cross-disciplinary team of experienced researchers drawn from IBB PAS in Warsaw and University of Wrocław - experts in protein chemistry, mass spectrometry, modern methods of protein structural studies and protein/metal ions interactions.

The Ph.D. Scholarship will be funded within a 3-year research project „Interplay of posttranslational redox cysteine modifications and metal ion binding as key to conformational and functional plasticity of innate immunity and cancer biomarkers - S100A8 and S100A9 proteins „(OPUS grant, Polish National Science Centre).

The project:

The research program aims at a better understanding of the regulatory factors leading to the versatile functions of human S100A8 and S100A9 proteins in human physiology and pathology. S100A8 and S100A9 consist 30-60% of the protein fraction of human neutrophils. Inflammatory mediators or oxidative stress may induce very high expression of S100A8 and S100A9 in every human cell type. The proteins are diagnostic markers for rheumatoid arthritis, ulcerative colitis, Crohn's disease and established biomarkers of many types of human cancers including breast, prostate, pancreatic, liver or skin cancer. S100A8 and S100A9 play important roles in innate immunity as antibacterial and antifungal molecules produced by the human host.

Mechanisms used by cells to provide the functional diversity of S100A8 and S100A9 are not entirely understood. Their activity relies in part on the binding of metal ions like Ca^{2+} , but also Zn^{2+} , Cu^{2+} , and Ni^{2+} , Mn^{2+} or Fe^{2+} . Overexpression of S100A8 and S100A9 often occurs in states with highly disturbed cellular redox homeostasis, i.e., under hypoxic conditions in cancer, at sites of increased production of reactive oxygen (ROS) and nitrogen (RNS) species, and even in the presence of high hypochlorous acid concentration in phagocytes. Redox posttranslational modifications of S100A8 and S100A9 influence the proteins activities in inflammatory processes *in vivo*. Recent work from our laboratory has shown that an interplay of metal ion binding and redox modifications modulates the conformation of some S100 proteins. In this project, we address a hypothesis that conformational and functional diversity of S100A8 and S100A9 proteins relies on a synergy between redox and metal-ion based regulation. To carry out the project we will use a large variety of methods including modern, nonclassical mass spectrometry-based protein structure elucidation techniques to study differently metallated S100A8 and S100A9 proteins in their native sequence and with redox modified residues. Additionally, we will investigate the interaction sites of S100A8/S100A9 which provide specificity to the endogenous post-translational S-nitrosylation of important protein substrates.



The proposed basic research is relevant to gain better insight into the factors that underly regulation of a very potent molecule with important roles in human physiology and pathology. Understanding these factors is important for people's health needs, especially in the design of new ways of combating two critical diseases: inflammatory disease and cancer.

Candidates profile:

- Master's degree (or equivalent) in Life Sciences
- Motivation, scientific curiosity, and independent thinking
- high capability in managing and designing experimental procedures
- willingness to collaborate with other scientists and laboratories
- good written and verbal English
- knowledge of protein expression and purification, organic chemistry, analysis of protein-protein interaction or mass spectrometry mass spectrometry would be a strong asset

Required documents:

1. Cover letter (explaining background and motivation) addressed to the Director of the Institute of Biochemistry and Biophysics, PAS.
2. CV
3. A copy of the Master's degree certificate (or equivalent).

Please send the application in English to Dr. Aleksandra Wyślouch-Cieszyńska <olawyslouch@gmail.com>. Include the required documentation and a contact of at least one reference familiar with your work.

Important: All applications must contain the following statement to allow us process your data: "I hereby give consent for my personal data included in the job offer to be processed for the purposed of recruitment under the Data Protection Act 1997 (Dz. U. 2002 no. 101, item 926 with subs. changes)."

Principal Investigator: Dr Aleksandra Wyślouch-Cieszyńska

Address for applications: olawyslouch@gmail.com The granting institution may seek to contact the best candidates only

Closing date: 26.10.2017