



PhD position in ADP-ribosylation biology

A PhD position in liver ADP-ribosylation biology is immediately available in the group of Prof. M.O. Hottiger in the Department of Molecular Mechanisms of Disease (University of Zurich, Switzerland).

We are among the worldwide leaders in ADP-ribosylation biology. Protein ADP-ribosylation is a reversible posttranslational modification (PTM) that results from the transfer of one or several ADP-ribose (ADPr) moieties from NAD⁺ to specific amino acid residues on target proteins or to ADPr itself. The covalent attachment of ADPr to amino acids and the elongation to poly-ADPr chains is governed within cells by ADP-ribosyltransferases (ARTs, “writers”) of the ARTD protein family and can be reversed by various “eraser” enzymes. This PTM can affect the structure and, thus, the function of modified proteins likely by modulating formation and composition of protein-protein complexes. There is strong experimental evidence that ADP-ribosylation is linked to cellular stress signaling pathways including oxidative stress and those that regulate different inflammation-associated pathologies. We recently made significant advances with respect to mass spectrometry-based identification of ADP-ribose (ADPr) acceptor sites on modified proteins. These advances allow us to robustly define the ADP-ribosylomes and confidently define the sites of modification in different cellular compartments, cell types and tissues that control inflammation and inflammation-associated pathologies.

Based on the existing achievements, this PhD project will investigate the expression levels of writers and erasers involved in the shaping of the ADP-ribosylation landscape under specific stress conditions in different cell types by using targeted mass-spectrometry based technologies. These studies will be complemented with the identification of proteome-wide mono- and poly-ADP-ribosylomes under the same conditions and perturbation of the cellular system (i.e. of writers/erasers) to functionally link targets and the enzymes that modify them. To allow distinguishing between mono- and poly-ADP-ribosylation, the current MS workflow will be further developed. Finally, we also plan to characterize the kind and regulation mechanisms of ARTDs that generate specific ADP-ribosylomes in selected stress conditions. Understanding how the writers/erasers and their targets are regulated will help guide the development of therapeutics that intervene in the ADP-ribosylation stress response.

The range of technologies that you will perform include mass spectrometry-based targeted and discovery mode proteomics studies, cloning, the generation of knock-out cell lines using CRISPR/Cas, expression analyses using quantitative RT-PCR, and quantitative microscopy. For further information about the group please visit: "<http://www.dmmd.uzh.ch/en/research/hottiger.html>"



The department is integrated within the natural sciences campus of the University of Zurich, the largest University in Switzerland and one of Europe's leading research centers that offers several excellent core technology facilities such as the Functional Genomics Center, the Imaging and Flow Cytometry Center and the Animal Facilities. The department is equipped with state-of-the-art infrastructure for biochemical, molecular and cell biological investigations, offers a stimulating research environment and actively promotes dynamic interactions between scientists. The successful applicant will be expected to support the ongoing research focus of the Hottiger group.

We are thus seeking a highly-motivated individual with prior experience in mass spectrometry and if possible bioinformatics. The applicant should be an independent thinker and problem-solver who is willing to work in a team, and accept new challenges arising from working in a high-paced scientific environment. The applicant should also have good communication and writing skills and a curiosity-driven attitude, and should demonstrate enthusiasm and flexibility.

Please forward your application electronically (preferably as a single PDF file) with a detailed CV, a list of publications, a one-page summary of the scientific achievements, a statement of motivation and the names and addresses of two references to applications@dmmd.uzh.ch (informal and confidential inquiries should also be sent to this address).

There is no formal application deadline, as the position will be filled as soon as a suitable candidate has been identified. The evaluation of applications will start immediately. Job sharing is not possible.