Department of
Molecular Mechanisms of Disease

Master Thesis Project
Master of Science in Biology

Identification of the AML and CHD1L (oncogene)-specific cellular ADP-ribosylome

Intracellular ADP-ribosylation (ADPr) is a phylogenetically ancient, covalent, and reversible post-translational protein modification (PTM) catalyzed by ADP-ribosyltransferases that are structurally similar to diphtheria toxin (ARTDs, formerly PARPs), and requires nicotinamide adenine dinucleotide (NAD^+) as a substrate. Protein modifications can either be mono- or poly- ADPr and have been implicated in cancer, as inhibition of these enzymes by so-called PARP inhibitors is anti-tumorigenic in both experimental and clinical studies. The identity of the ADP-ribosylated proteins modified by ARTDs has been extensively debated, and different amino acids have been put forward as ADPr acceptors. This knowledge is important for the development of more specific ADPr inhibitors.

Our research over the past few years has led to the establishment of mass-spectrometry based screening platform for the identification of ADP-ribosylated peptides.

In this project, we aim to identify in a comprehensive way 1) all proteins ADP-ribosylated in the Kazumi cell line (acute myeloid leukemia), whose proliferation is dependent on ADPr and 2) particularly the modified proteins interacting with the macrodomain of the oncogene *CHD1L* (chromodomain helicase/ATPase DNA binding protein 1-like gene). These findings should help to obtain further insights for a possible treatment of tumors with PARP inhibitors.

Supervisor: Prof. Dr. Dr. Michael O. Hottiger
Institute: Department of Molecular Mechanisms of Disease (DMMD)
E-mail: michael.hottiger@dmmd.uzh.ch Phone: 044 645 5474
Conditions: Start immediately
Links: http://www.dmmd.uzh.ch/en/research/hottiger.html