BASIC INFORMATION ON SUB-PROJECT

NAME OF PROGRAMME/FUND	Scholarship Fund - Sciex NMS^{ch}
RESEARCH FIELD AND OTHER RESEARCH FIELDS INVOLVED (if applicable)	Basic Biological Research
TITLE OF THE SUB-PROJECT	Proteolytic enzymes and inhibitors of trematode parasite Schistosoma mansoni
REGION OF THE CZECH REPUBLIC (according to the location of the home institution)	Prague
GRANT AMOUNT SPENT	60 960,03 CHF
INTERMEDIATE BODY	Swissuniversities
HOME INSTITUTION	Charles University in Prague, Faculty of Science
HOST INSTITUTION	University of Zürich, Institute of Parasitology
NAME OF THE FELLOW	Lenka Ulrychová

ABSTRACT OF THE SUB-PROJECT	Schistosomiasis denotes one of the most serious chronic parasitic diseases. According to the WHO, schistosomes infect approximately 240 million people worldwide and more than 700 million people living in endemic areas are at risk of infection, therefore presenting enormous health burden for humanity. Vaccines are not commercially available and treatment depends on a single drug, praziquantel, raising concerns of emerging drug resistance. Schistosomes survive many years in the vasculature of permissive mammalian hosts and actively interact with the host physiological processes. These immunoevasive and immunomodulatory strategies are critical for parasite survival and therefore make prime target to develop specific drug or vaccine to disrupt these mechanisms. It was shown that infection and establishment of parasitism depend on functional proteolytic pathways. However, most of the research focus to date has been given to cysteine proteases while serine proteases (SP) and cystatins (cysteine protease inhibitors) have been less well researched in Schistosoma mansoni. Work in other parasitic model organisms have elucidated SPs and cystatins as some of the key factors involved in invasion and immunomodulation processes. We aim to functionally characterize molecules expressed and secreted by invasive stages of schistosomes belonging to the families of serine proteases and cystatins. We will perform in vitro enzymatic assays on recombinant proteins and their biological role will be assessed by RNAi and immunolocalization experiments. When successful, these experiments will lead to further testing of protective potential of these molecules in vaccination trials in mouse model of the disease. A prophylactic vaccine would be the ideal method for sustained control of schistosomiasis and bioactive molecules involved in host-parasite interactions represent interesting subject for further pharmacological studies.

MAIN RESULTS	This study aimed to elucidate the biological role of trypsin-like serine protease, prolyl endpeptidase, and type 2 cystatin of a human blood fluke *S. mansoni* that seems to play an important role in the host-parasite interaction. To reach our goals we successfully established part of the parasite lifecycle, developed antibodies against desired targets and implicated standard methods for molecular biology and other powerful tools such as whole mount in situ hybridization and immunofluorescence assay. We developed constructs of recombinant proteins of all studied proteins and started with biochemical characterization while successful refolding of one studied serine protease was performed together with activity assay. During our investigation we identified the presence of gene transcripts and the protein localization mostly in the adult worms of *S. mansoni*. The distribution of various gene products support our previous data connected to expression profiling and corresponds to published work. Fellow Lenka Ulrychova became a part of prestigious scientific environment in Switzerland where she extended her knowledges in scientific field. Last but not least, we developed relationship with the host institution which paved strong way for the future collaboration and contribute to the knowledge about helminth molecules with potential for drug and/or vaccine development.
DATE OF REALISATION OF THE FELLOWSHIP	1.7.2012 - 30.6.2013
MORE INFORMATION ON THE PROGRAMME	**www.sciex.ch**