Abstract

Schistosomiasis is a serious parasitic disease, caused by blood flukes of the genus *Schistosoma*. It remains a global health problem in the 21st century, with more than 250 million people infected in 78 countries. Current therapy relies on the drugs praziquantel and oxamniquine, for which there are concerns of emerging drug resistance. Proteases of schistosomes are involved in critical steps of host-parasite interactions and are promising targets for the development of new therapeutic strategies against schistosomiasis. This work focuses on the characterization of *Schistosoma mansoni* serine proteases (SmSPs) and the determination of their role in the interaction with the human host using a variety of genomic, bioinformatic, RNA- and protein-based techniques. First, the major types of proteolytic activities secreted by the blood-dwelling developmental stages of *S. mansoni* were classified using functional proteomics. The analysis revealed the complexity of proteolytic activities secreted by the schistosome life stages parasitizing the human host. All stages secreted significant serine protease activities, and consequently their genes were retrieved from the genome database and annotated. Localization in adult worms determined by fluorescence *in situ* RNA hybridization revealed complex expression patterns of individual SmSPs in different tissues. Two SmSPs, serine protease 2 (SmSP2) and prolyl oligopeptidase (SmPOP), were biochemically and functionally characterized using recombinant proteins, and their biological roles in modulating host hemostasis were proposed. The work provides important new information on *S. mansoni* serine proteases and their potential roles in host-parasite interactions by modulating host physiology, which is relevant for the development of novel anti-schistosomal interventions.