# Enzymes of the purine salvage pathway from *Schistosoma mansoni: a high-throughput approach.*

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The parasite *Schistosoma mansoni* is one of the etiological agents of Schistosomiasis, lacks the “de novo” purine pathway and depends on it’s host for purine requirements. The parasite uses the purine salvage pathway to supply their purine requirements. This branched pathway is composed by 13 enzymes, some with different isoforms totaling 17 enzymes. We started a systematic approach to obtain all enzymes of the purine pathway aiming to solve the crystallographic structures of these enzymes and the determination of their kinetic constants. Three rounds of cloning and expression were performed, in the first one the genes were amplified from enriched cDNA library and were cloned and expressed using standard procedures at IFSC-USP in Brazil. In other two, synthetic genes were cloned in multiples vectors and a parallel expression was performed using OPPF-UK facilities. Using these approaches all 18 purine salvage genes were cloned and soluble expression were obtained for 14 enzymes. Crystals were obtained for 9 enzymes, hundreds crystals were cooled for data collection in Diamond Light Source-UK, where approximately 140 datasets were obtained. Crystal structure was solved for 8 different enzymes and dozens of complexes were obtained. All kinases involved in the purine metabolism were solved (Adenosine kinase, Adenylate kinase and Nucleoside diphosphate kinase) and the structures of three different nucleoside phosphorylases (methythionucleoside phosphorylase and the two isoforms for purine nucleoside phosphorylase). Structures of Adenylosuccinate lyase and Hypoxanthine-guanine phosphorybosiltransferase were also solved. Some interesting features discovered will be discussed: the structural basis for preference of Adenosine Kinase for adenosine analogues and the presence of an adenosine phosphorylase in *S. mansoni*. The structural data together with kinetic data will be invaluable to the understanding of the purine metabolism for this important human parasite.

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