The *Schistosoma mansoni* Pyri-purinome Project

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Schistosoma mansoni lacks the "de novo" purine pathway and depends on it's host for purine requirements. The opposite situation is observed in the case of pyrimidine pathways where the parasite has both "de novo" and the salvage pathways. These pathways have been used in the past as targets for chemotherapeutic intervention.

The current project aims to solve crystallographic structure of all the enzymes involved in the purine salvage pathway and some specifically selected from the pyrimidine salvage and "de novo" pathways as well as the determination of their kinetic constants. The following enzymes were selected for this project: Adenine phosphorybosyltransferase (APRT), Purine nucleoside phosphorylase isoform 2 (SmPNP2), Adenosine Kinase (AK), Adenosine deaminase (ADA1 and ADA2), Hypoxanthine-guanine phosphorybosyltransferase (HGPRT), Thymidilate synthase (TS), uridine phosphorylase (UNP), nucleoside diphosphate kinase (NDPK), Dihydrofolate reductase (DHFR), cytidine deaminase (CytADA), methyltioadenosine phosphorylase (MTAP) and uracil phosphorybosyltransferase (UPRT). The cDNA of these enzymes was obtained by RT-PCR from adult total mRNA and was amplified by PCR. The amplified products were cloned in pGEM vector and, after digestion, were inserted in pET28a expression vector. The gene products were confirmed by DNA sequencing. Only two genes did not amplify due to incorrect gene sequences in the *S. mansoni* genome project database. The first enzyme in our pipeline, adenosine kinase, was successful produced, robotically crystallized and has been solved by X-ray at 2.3Å resolution in complex with AMP and 2.8Å resolution using Synchrotron radiation at LNLS MX2 beamline, the structures are currently under refinement.

We expect that the increase in the number of solved drug targets together with their kinetic constants will help the development of selective compounds against schistosomiasis.

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