

Poster Presentation

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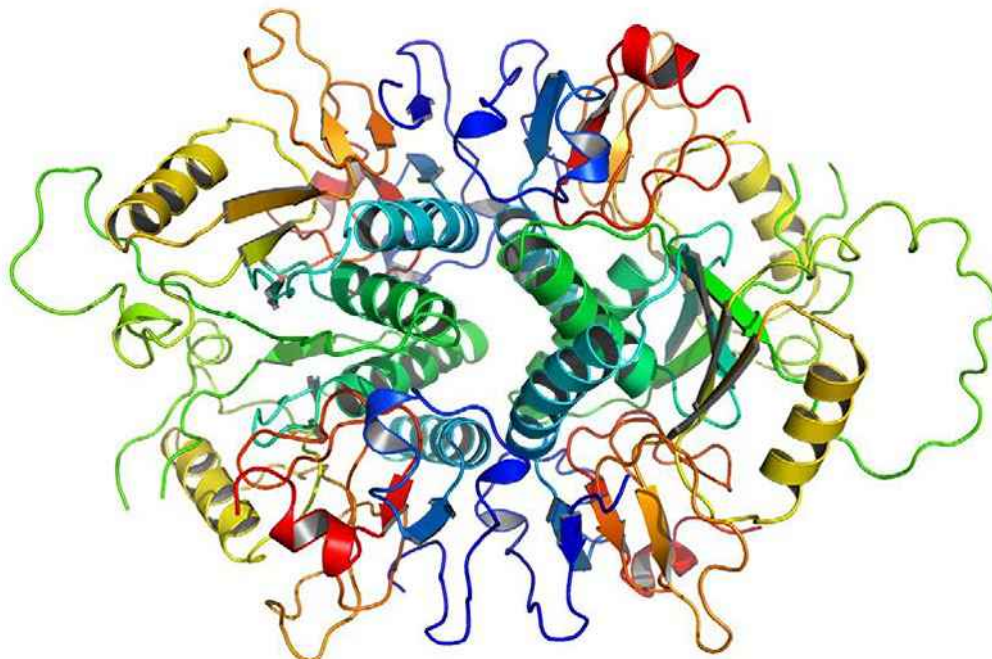
Crystal structure of Schistosoma mansoni HGPRT isoform 1

L. Romanello¹, J. de Souza¹, L. Bird³, J. Nettleship³, R. Owens³, Y. Reddivari³, J. Brandão-Neto², H. Pereira¹

¹University of São Paulo, Institute of Physics, São Carlos, Brasil, ²Diamond Light Source, Harwell Science and Innovation Campus Didcot, Oxfordshire, UK, ³Oxford Protein Production Facility UK, Didcot, Oxfordshire, UK

Schistosoma mansoni is the parasite responsible for schistosomiasis, a disease that affects about 207 million people worldwide [1], and does not have the purine “de novo” pathway, depending entirely on the purine salvage pathway to supply its demands on purines [2]. The purine salvage pathway has been reported as a potential target for developing new drugs against schistosomiasis. Hypoxanthine-guanine phosphoribosyltransferase (HGPRT) is a key enzyme in this pathway and the only validated enzyme target of the pathway [3]. HGPRT catalyzes the PRPP dependent conversion of hypoxanthine/guanine to inosine monophosphate or guanine to guanosine monophosphate. HGPRT1 gene was amplified, cloned, expressed and purified at the Oxford Protein Production Facility (OPPF-UK). Robotic crystallization trials were performed and SmHGPRT crystallized in several conditions of the Morpheus crystallization kit: A4, A8, A9, and C9. The crystals appear about a day and have about 30 μM in greatest dimension. About a hundred crystals were screened with x-rays on the macromolecular crystallography beamlines I02 and I24 at Diamond Light Source. 21 datasets was collected from 2.97 to 4.11 \AA resolution. A solution was obtained for HGPRT1 belongs space group P212121 in a dataset to 3.4 \AA resolution, with four monomer in the ASU. The structure was solved by the program Phaser using HGPRT human as a search model. The refinement is being carried out by program Phenix. The density map is acceptable for the resolution but a great manual work of interpretation is necessary for the refinement of this structure. The most important is the demonstration that it was possible to crystallize and collect data of SmHGPRT. A major effort will be undertaken to improve the size and diffraction power of HGPRT crystals as well as in the resolution of the structure of HGPRT in other space groups. This structure will increase the structural information available about the *Schistosoma mansoni* purine salvage pathway.

[1] TDR., W.H.O., *Report on Schistosomiasis. 2005: World Health Organization. 114.*, [2] Senft, A.W., et al., *Purine metabolism in Schistosoma mansoni. Int J Parasitol, 1972. 2(2): p. 249-60.*, [3] Pereira, T.C., et al., *Schistosoma mansoni: evaluation of an RNAi-based treatment targeting HGPRTase gene. Exp Parasitol, 2008. 118(4): p. 619-23.*



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