Structure of Pteridine reductase (PTR1) from *Trypanosoma brucei*

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Anti-folate resistance in the trypanosomatid parasites is due in part to pterin reductase (PTR1) which is capable of reducing folate. This allows uptake of folate even when the primary enzyme, dihydrofolate reductase, is inhibited, and makes PTR1 an important drug target. The crystal structure of PTR1 from *Trypanosoma brucei* complexed with the cofactor NADPH and the inhibitor methotrexate has been determined to 2.2 Å. The protein structure is closely related to the previously determined *L. major* structure [1], with the cofactor and inhibitor bound in a similar fashion. The methotrexate molecule is significantly better defined in the *T. brucei* structure but there is no indication of increased MTX – protein interaction. A non-conservative Leu-Cys substition close to the active side is observed.

[1] Gourley D.G., et al., *Nature Str. Biol*., 2000, **8**, 521-525.

Keywords: enzyme inhibitor design, biological macromolecules, folate dependent enzymes