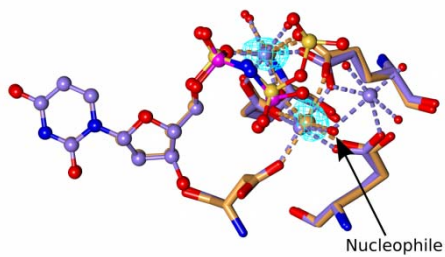


WP5. X-ray crystallography

Dimeric dUTPases from L. major, T. brucei and T. cruzi.

L. major dUTPase.

Figure 1. *L. major* dUpNp (purple) and dUpNpp (orange) complexes superimposed.



T. brucei dUTPase.

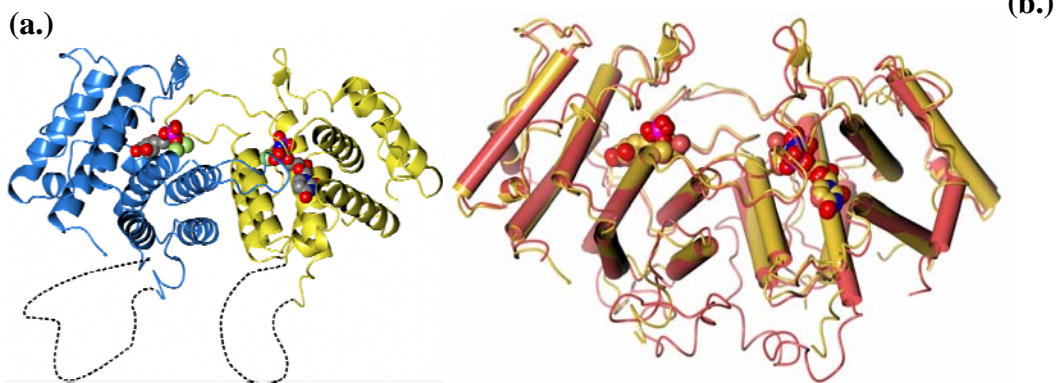


Figure 2. (a.) Closed form of *T. brucei* dUTPase. Black dotted lines indicate missing residues 90-150. (b.) Superposition of the *T. brucei* dUpNp complex (yellow) with *L. major* dUpNp complex (red).

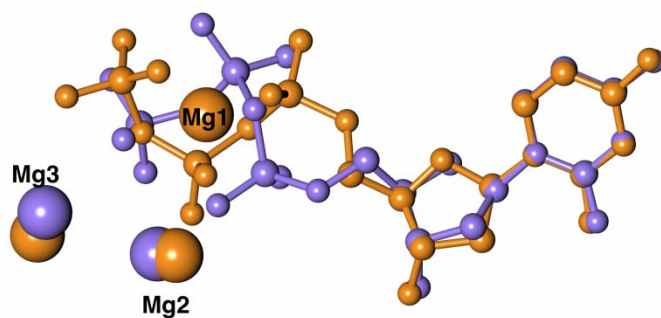


Figure 3. Superposition of chains A (purple) and B (orange) shows the difference in triphosphate conformations in the two subunits with the accompanying difference in metal binding. The conformation in chain A matches that observed in the *Leishmania* and *Campylobacter* dUTPases.

Transition State Analogue Studies

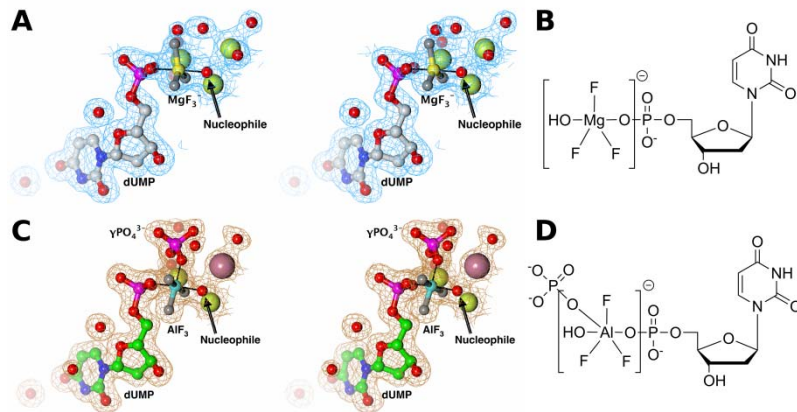


Figure 4. Stereo views of the electron density in (A) the dUMP-MgF₃⁻ and (C) the dUMP-AlF₃-OPO₃ complexes. Ligands are coloured by atom type, red spheres represent waters, and green and purple spheres show Mg²⁺ and Na⁺ respectively. (B) and (D): schematics of the respective transition state analogues.

2. Other Targets.

Adenosine Kinase (AK)

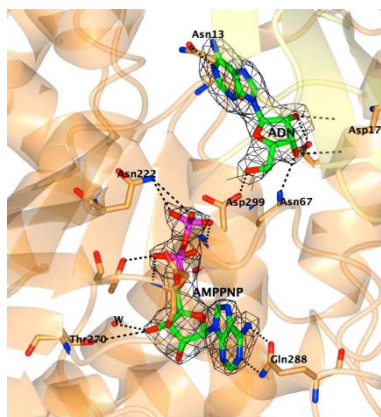


Figure 5 Active site of TbAK in complex with adenosine and AMPPNP.

Leucyl aminopeptidases

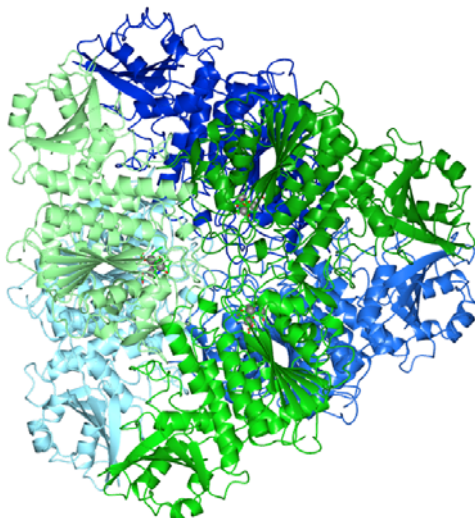


Figure 6 Structure of TbLAP in complex with the inhibitor actinonin.