Electronic Supplementary Material (ESI) for Molecular BioSystems

Binding of pyrazole-based inhibitors to *Mycobacterium tuberculosis* pantothenate synthetase: Docking and MM-GB(PB)SA analysis

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Figure S1 - Hydrogen bond mediating water molecules (W1, W2, W3 and W4) of the pantoyl adenylate reaction intermediate within the binding pocket of MTB PS (pdb code 1N2H).

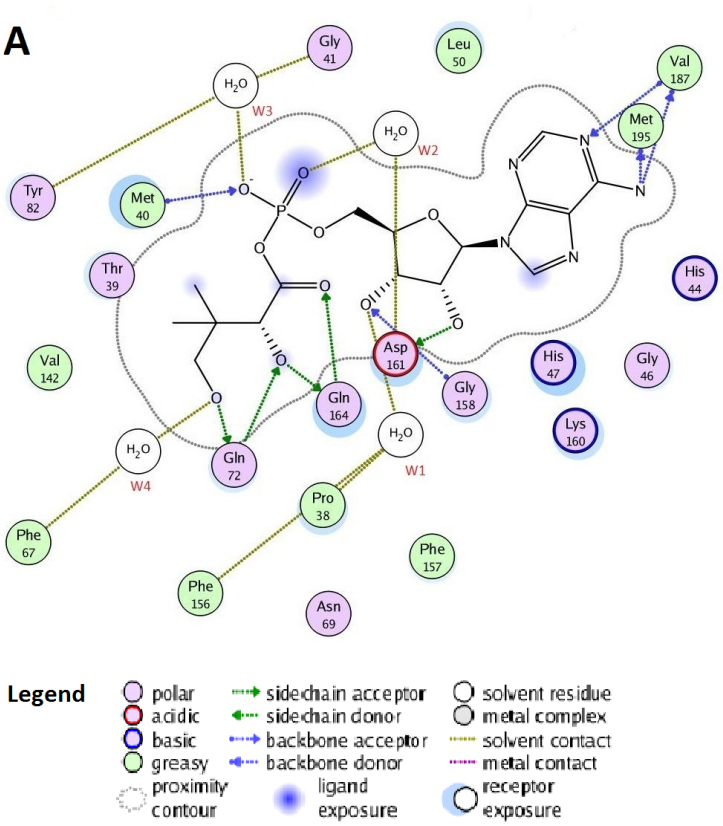
(A) H-bond network showing direct binding with active side residues as well as interactions mediated by the conserved water molecules, (B) pantoyl adenylate in ball and stick representation (with carbon atoms coloured green), protein atoms in line representation (carbon atoms in their usual colours) and hydrogen bond mediating water molecules represented as red balls. This diagram was produced using the MOE software [20].

Figure S2 - Thermodynamic cycle for absolute binding free energy calculations.

Figure S3 - (A) Superposition of docked (cyan carbon atoms) and experimental (green carbon atoms) crystal structures of the pantoyl adenylate reaction intermediate (ChemScore = 15.06, RMSD = 0.76 Å); (B) Superposition of docked (cyan carbon atoms) and experimental (pink carbon atoms) crystal structures of the native ligand 2-((benzofuran-2-carboxamido)methyl)-5-methoxy-1-*H*-indol-1,4-yl) acetic acid (GoldScore = 72.79, RMSD = 0.89 Å).

Figure S4 - (A) Solvent accessible surface of active inhibitor PS-001 in superposed binding modes I and II; (B) The van der Waals surface calculated for the same superposed ligand structures; (C) The ligand solvent accessible surface area is shown by polarity, with hydrophobic regions shown brown, while polar regions are in red; (D) The ligand solvent accessible surface area is shown by atom type, with regions occupied by donor atoms are shown in blue, acceptor atoms in red while non donor/non acceptor atoms are in grey..

All pictures were generated using LigandScout [38]



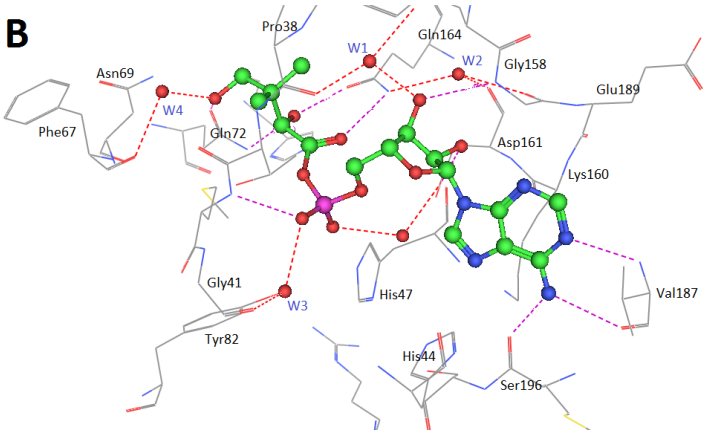


Figure S1

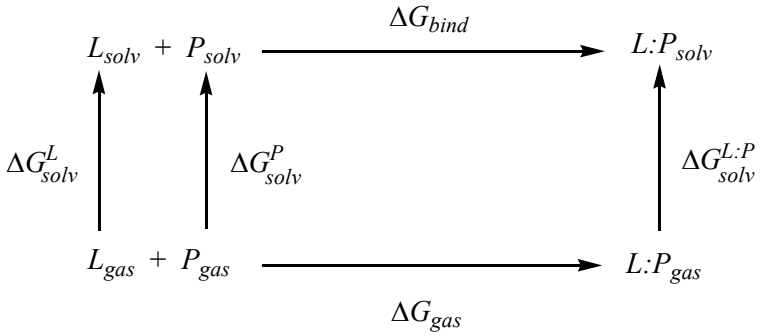


Figure S2

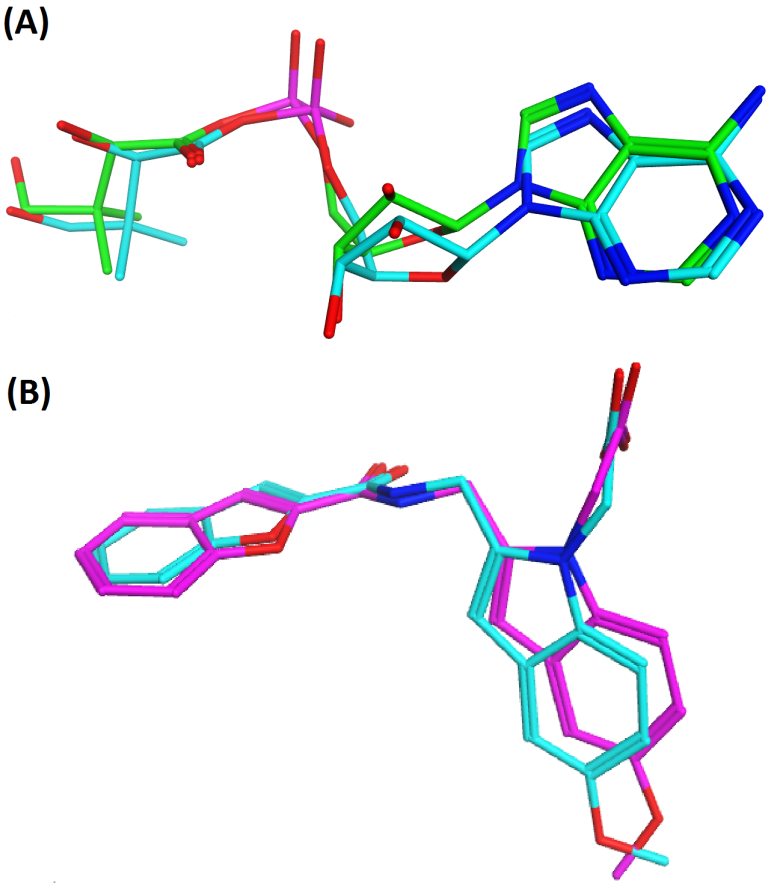


Figure S3

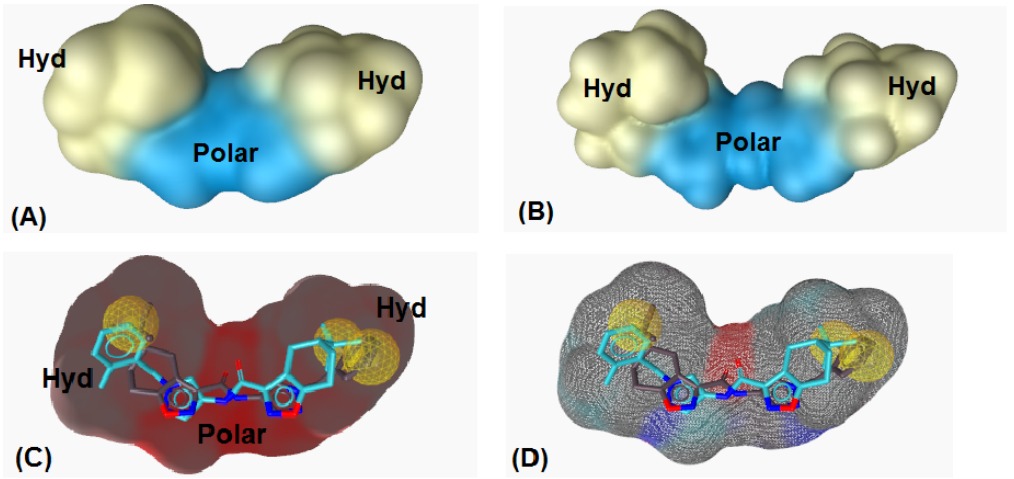


Figure S4