Structural studies on a unique glucosamine kinase unveil a novel enzyme family

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The discovery of novel enzymes from antibiotic production pathways is nowadays a topic of utmost importance due to worldwide concerns with the increased resistance of pathogenic bacteria to antibiotics. In this work, we used a combination of X-ray crystallography, SAXS, and biochemical studies to identify the molecular fingerprints for a novel glucosamine kinase (GlcNK) family potentially implicated in antibiotic biosynthesis in *Actinobacteria*. We determined the high-resolution structure of a bacterial GlcNK in apo form and in complex with its biological substrates, providing unparalleled structural evidence of a transition state of the phosphoryl-transfer mechanism in this unique family of enzymes (PDB IDs 6HWJ, 6HWK and 6HWL; Fig. 1a-c). Conservation of glucosamine-contacting residues across a large number of uncharacterized proteins unveiled a specific glucosamine binding sequence motif. As result, a new UniProt annotation rule was created (MF_02218; Fig. 1d). The structural characterization of this enzyme provides new insights into the role of these unique GlcNKs as the missing link for the incorporation of environmental glucosamine to the metabolism of important intermediates in antibiotic production [1].

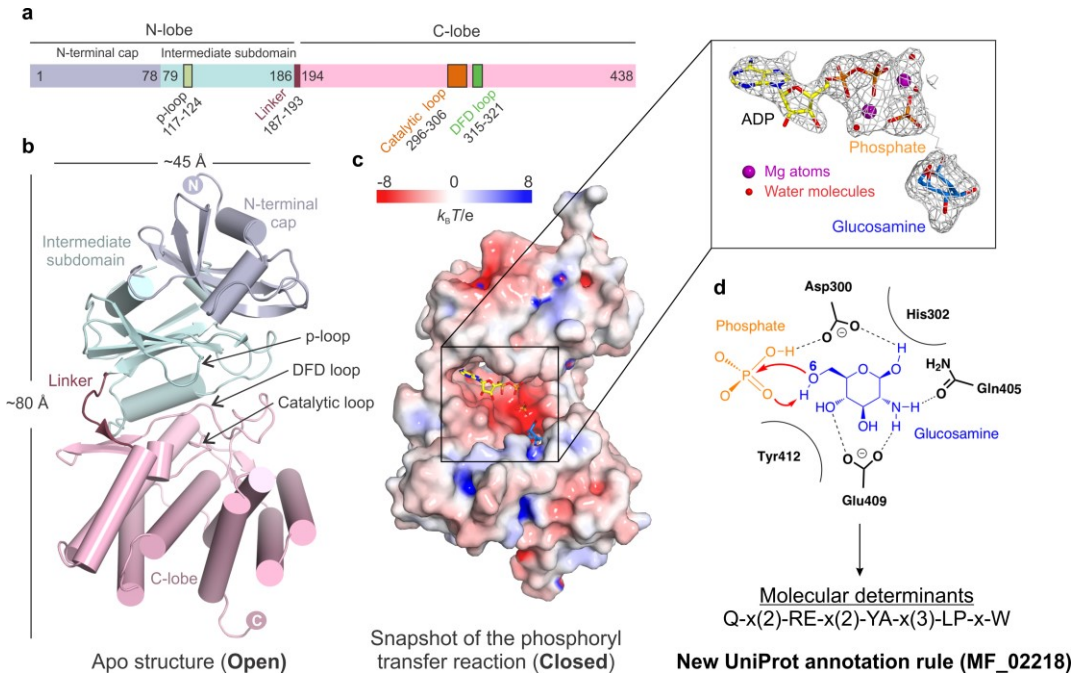

Figure 1. Molecular fingerprints for a novel GlcNK family in *Actinobacteria*. **a)** Structural organization of GlcNK. **b-c)** Cartoon and solid surface representations of the 3D structure of GlcNK in its apo form and in complex with its biological substrates (electron density map (2*mF*o-*DF*c contoured at 1.0 σ) represented as a grey mesh). **d)** Scheme of the glucosamine-protein interactions.

[1] Manso, J. A., Nunes-Costa, D., Macedo-Ribeiro, S., Empadinhas, N., Pereira, P. J. B. (2019). *mBio*. **10**, e00239-19.

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