Two thirds of the clinically useful antibiotics are naturally produced in actinomycetes, especially in *Streptomyces* species. These antibiotics vary highly in their chemical structures, some examples being amphenicols (chloramphenicol), polyketides (tetracyclin) or aminoglycosides (*streptomycin*).

Enzymes involved in the synthesis of aminoglycoside antibiotics (AGAs) are organized in large gene clusters containing 24 or more enzymes. The AGA family can be further divided into several subfamilies; the NEO subfamily takes the common precursor paromomamine, which is further modified to AGAs such as neomycin, ribostamycin and lividomycin.[1]

Lividomycin B and neomycin B - members of the NEO subfamily - are produced by enzymes of the LIV/NEO gene cluster. The aminotransferases that catalyze the terminal transamination reaction (LivB and NeoB respectively) utilize the cofactor pyridoxal-5'-phosphate (PLP). LivB catalyzes the transamination reaction of 6''''-oxoparomomycin to the antibiotic paromycin, which is also a precursor of lividomycin B, whereas NeoB performs the transamination of 6''''-oxo-neomycin C to neomycin C.[1]

LivB and NeoB were expressed in *Streptomyces* sp., purified via Ni-affinity chromatography and crystallized. The structure of LivB could be solved using the “magic triangle compound” I3C[2] for SAD phasing, and that of NeoB by molecular replacement using the LivB structure as search model. Soaking of LivB crystals with the cofactor PLP, an amino donor and the end product paromomycin yielded crystal structures of the PLP-bound enzyme and the complex structure of LivB with an aldinine paromomycin-PLP intermediate. The latter represents a molecular snapshot of a key intermediate of the enzymatic reaction - the transamination at the 6'''' position of the lividomycin B. These structures provide a basis for analyzing substrate specificities of other carbohydrate-modifying aminotransferases.


**Keywords:** aminotransferase, aminoglycoside antibiotics, streptomycetes

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Crystal structure of hypoxanthine guanine xanthine phosphoribosyl transferase from the thermophilic archaeon *Sulfolobus solfataricus*

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Hypoxanthine guanine xanthine phosphoribosyltransferase (HGXPRTase) acts in the salvage of nucleotides by catalyzing the formation of 6-oxopurine nucleotide monophosphates IMP, GMP and XMP from D phosphoribosyl-α-1-pyrophosphate (PRPP) and the respective nucleobases. Several pathogenic parasitic protozoa are dependent on purine salvage making HGXPRTase an attractive drug target.[1]

We have determined the crystal structure of the HGXPRTase from the thermophilic archaeon *Sulfolobus solfataricus* to 1.8 Å resolution. SsHGXPRTase together with product XMP (5 mM) was crystallized by vapour diffusion using NH4SO4 at pH 5.0 and the structure was solved using molecular replacement (P3_2_1, a=b=132.2 c=103.0). SsHGXPRTase is a tetramer in the crystal having XMP and a sulfate ion bound in its active sites.

In addition synchrotron data have been recorded on crystals of SsHGXPRTase obtained in the presence of substrate PRPP diffracting to 2.3 Å resolution (P4_2_2_2, a=b=73.7 c=142.6). These structures may provide valuable insight into the function of the HGXPRTases.


**Keywords:** enzyme, nucleotide, protein

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Crystal structure of enolpyruvate transferase in *Streptococcus pneumoniae*

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Enolpyruvate transferase catalyzes the first step in the peptidoglycan synthesis pathway and it is also a fosfomycin target. We are trying to solve the three-dimensional structures of enolpyruvate transferase in different *Streptococcus pneumoniae* strains to elucidate their catalytic mechanism. We have solved the crystal structure of enolpyruvate transferase from *Streptococcus pneumoniae* strain D39. Crystal needles were obtained by a hanging drop technique with