

MS001.P07

H. pylori purine nucleoside phosphorylase: catalytic features and 3D-structure

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Antibiotics have been developed for more than 80 years and since then, the number of drug-resistant bacteria, "superbugs", became so large that this has grown into a serious public health concern. How big this problem really is, is shown by the fact that in September 2016, the United Nations General Assembly held a meeting focussing on antimicrobial resistance.

Helicobacter pylori was discovered at the beginnings of the 1980s [1]. Nowadays one-half of the worldwide population is infected by *H. pylori* [2]. Chronic gastritis, peptic ulcer disease, gastric cancer and MALT lymphoma are all linked with the presence of this bacterium [3].

Genetic analysis indicated that *H. pylori* is missing several genes from the de novo purine nucleoside biosynthesis pathway and consequently *H. pylori* cannot synthesize purine rings de novo. Thus, *H. pylori* has to produce purines required for RNA and DNA synthesis relying on the salvage pathway. Purine nucleoside phosphorylase is one of the key enzymes of this pathway.

Recently, we have investigated the basic biochemical and structural characterization of recombinant PNP from the *H. pylori* clinical isolate (unpublished data). Structural and biophysical characterization of *H. pylori* PNP from the referent strain 26695 is under way. In order to find a good inhibitor of *H. pylori* PNP (which could then inhibit a *H. pylori* growth, as well), we have tested several potential PNP inhibitors and prepared their complexes with the enzyme from referent strain. For potential inhibitor, a noncleavable analog of the nucleoside substrate, MIC values were determined. Protein-ligand complexes were crystallized and their 3D-structures solved. Insight into active sites and detailed analysis of the ligand-protein interactions with possible implications on the PNP enzymatic mechanism will be discussed.

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Keywords: [enzyme](#), [catalysis](#), [purine nucleoside phosphorylase](#)