Crystallization and preliminary X-ray crystallographic analysis of Quinolinate phosphoribosyltransferase of Helicobacter pylori

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The quinolinic acid (QA) phosphoribosyltransferase (PRTase) (EC 2.4.2.19), is a key enzyme involved in NAD\textsuperscript+ biosynthesis in prokaryotes and eukaryotes. The QAPRTase produces nicotinic acid mononucleotide (NAMN) from QA and 5-phosphoribosyl-1-pyrophosphate (PRPP). For this reaction, the QA is decarboxylated (Fig.1). Produced NAMN is used to a synthesis of nicotinate adenine dinucleotide (NAD\textsuperscript+).

The QAPRTase is a type II PRTase and only known example of that. The type II PRTase has two domains. One is N-terminal four stranded β-sandwich domain and the other is a C-terminal α/β barrel domain. The three dimensional structures of QAPRTase from Mycobacterium tuberculosis and Salmonella typhimurium have been reported in complex with their substrates (QA, NAMN) and substrate analogs (PA, PRPCP).

However, Many QAPRTases have dimeric state in Escherichia coli, Salmonella typhimurium, Mycobacterium tuberculosis, and caster bean. But some hexameric QAPRTases have been reported from other sources such as hog, rat and human. The enzyme exists as a dimer and a hexamer depending on the source. The protein sequence identity between Hp-QAPRTase and other QAPRTase is about 30%; Mycobacterium tuberculosis (34%), Salmonella typhimurium (32%), Escherichia coli (32%), Mus musculus (33%), human (29%) and so on (BLAST). Most QAPRTases have similar sequence identity with QAPRTase of Helicobacter pylori. The Hp-QAPRTase has been purified as a hexamer during size exclusion chromatography in physiological condition.

This report describes the characteristics of Hp-QAPRTase and the crystal structure of Hp-QAPRTase in complex with quinolinic acid (QA), nicotinic acid mononucleotide (NAMN) and analogue of quinolinic acid, phthalic acid (PA).