

Crystal Structure of Nicotinic Acid Mononucleotide Adenylyltransferase from *Pseudomonas aeruginosa* in its Apo and Substrate-complexed Forms

Hye-Jin Yoon, Se Won Suh, *Department of Chemistry, Seoul National University, Korea.* E-mail: yoonhj@snu.ac.kr

The enzyme nicotinic acid mononucleotide adenylyltransferase is essential for the synthesis of nicotinamide adenine dinucleotide and is a potential target for antibiotics. It catalyzes the transfer of an adenylyl group from ATP to nicotinic acid mononucleotide to form nicotinic acid adenine dinucleotide. In order to provide missing structural information on the substrate complexes of NaMN AT and to assist structure-based design of specific inhibitors for antibacterial discovery, we have determined the crystal structures of *Pseudomonas aeruginosa* in three states, i.e., the NaMN-bound form at 1.7 Å resolution and ATP-bound form at 2.0 Å as well as its apo-form at 2.0 Å. They represent crucial structural information necessary for better understanding of the substrate recognition and the catalytic mechanism. Structural comparisons of the substrate-complexes with the apo enzyme indicate that there is little conformational change upon binding each of the substrates. Our structures indicate that a conformational change is necessary to bring the two substrates closer together for initiating the catalysis. We suggest that such a conformational change likely occurs only after both substrates are simultaneously bound in the active site.

[1] Olland, et al., *J. Biol. Chem.*, 2002, **277**, 3698-3707. [2] Zhang, et al., *Structure*, 2002, **10**, 69-79.

Keywords: nicotinic acid mononucleotide adenylyltransferase (NaMN AT), nicotinamide adenine dinucleotide (NaMN), ATP