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A Systematic Integration of Empirical and Computational Studies to Biophysically Describe Recombinant Nicotinate Mononucleotide Adenylyltransferase (NaMNAT) From *Klebsiella pneumonia*

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Nicotinate mononucleotide adenylyltransferase (NaMNAT) is an indispensable enzyme in the biosynthesis of pyridine dinucleotides. Given the vital role of NAD⁺ in controlling key cellular processes, NaMNAT represents an attractive target for the design of novel broad-spectrum antibiotics to treat nosocomial infections associated with MDR *Klebsiella pneumoniae*. This study aims to characterize the biophysical structure of NaMNAT from *K. pneumoniae* (KpNaMNAT) using a systematic combination of experimental and computational approaches. Overexpression and purification were carried out using hexa-histidine tags in *E. coli* expression system and nickel ion-immobilized metal affinity chromatography. Activity studies using NMN substrate showed KpNaMNAT to demonstrate broad pH optima of 6.5-9.5 and preference for Mg²⁺. Structural characterisation revealed KpNaMNAT as a monomer with predominate α -helices. ATP, NMN, and NAD⁺ all bind at the same site on KpNaMNAT, but do not induce any significant conformational changes, however, ATP responds to Mg²⁺ more than the other ligands and the protein response in the presence of Mg²⁺. The data and insight provided by this novel research would be useful as a molecular basis for further evaluation of the enzymes for the design of structure-based inhibitors with therapeutic potential.

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