Structural Studies of Quinolinate Synthase

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Nicotinamide adenine dinucleotide (NAD) is an essential cofactor in several metabolic pathways and has recently been shown to play a role in several signaling pathways [1]. Consequently, there is great interest in the biosynthesis of NAD. Quinolinate is the universal precursor in the de novo biosynthesis of NAD and can be synthesized from either tryptophan in the case of eukaryotes or aspartate in most prokaryotes [2].

The aspartate pathway begins with L-aspartate oxidase which converts aspartate to iminoaspartate. Quinolinate synthase (QS) catalyzes the condensation of iminoaspartate and dihydroxyacetone phosphate to form quinolinic acid [3]. This enzyme has been difficult to characterize due to either instability or inactivity when it is overexpressed and purified.

QS is the last enzyme in this pathway to be structurally characterized. We have determined the crystal structure of QS at 2.8 Å resolution. The crystal structure and sequence alignments provide insights into the details of the active site and the enzyme's evolution.

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