Structural Studies of FlaA1, a UDP-GlcNAc 4,6-dehydratase

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FlaA1 is a UDP-GlcNAc 4,6-dehydratase believed to be involved in the protein glycosylation process of *Helicobacter pylori*. The crystal structures of FlaA1 in five different ternary complexes with various substrates were determined at resolutions between 1.9 and 2.8 Å. This represents the first structure of a 4,6-dehydratase that can catalyze a UDP-saccharide. Among 4,6-dehydratases, FlaA1 possesses several unique structural features including a novel C-terminal fold and a hexameric oligomerization state in the crystal. The catalytically productive conformation observed in the FlaA1•NADPH•UDP-GlcNAc ternary complex suggests that FlaA1 employs a different mechanism for the water elimination step from that proposed for other 4,6-dehydratases. Normally, an Asp and Glu residues are the two catalytic residues that effect dehydratase activity through a concerted mechanism. In FlaA1, the corresponding residues are Asp-132 and Lys-133, precluding an analogous mechanism. Computational analysis suggests that for the water elimination step in FlaA1, Lys-133 sequentially functions as catalytic acid and base while Asp-132 closely interacts with the leaving water group.

Keywords: dehydratase, catalytic mechanism, pKa calculation