X-ray Crystallographic Study of *Helicobacter pylori* Shikimate Dehydrogenase

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TOPIC I. X-ray crystallographic study of Shikimate Dehydrogenase from *Helicobacter pylori*

Shikimate pathway is responsible for the biosynthesis of aromatic amino acids and aromatic compounds. This pathway is unique that it is conserved in bacteria, fungi, apicomplexan parasites and plants but absent in mammals. Deletion the genes of shikimate pathway in microbes will result in a reduced virulence. Glyphosate that inhibits the 5-enolpyruvylshikimate 3-pholphate synthase, the sixth enzyme in this pathway, is a worldwide-used herbicide. Thus, enzymes of shikimate pathway represent potential valid targets for new antibiotics design. Shikimate dehydrogenase (EC 1.1.1.25, SDH) that catalyzes the reduction of 3-dehydroshikimate to shikimate by NADPH is the fourth enzyme in the shikimate pathway. In this work, we expressed and purified SDH from Helicobacter pylori. The apo-form HpSDH structure has been solved to 1.57 Å using single-wavelength anomalous dispersion methods, showing an N-terminal α/β domain and a C-terminal Rossmann domain. Additionally, we have also determined two complex structures: HpSDH•shikimate complex (1.42 Å) and HpSDH•shikimate•NADPH (2.04 Å). These complex structures demonstrate that shikimate binds to the N-terminal domain, while NADPH binds to the Rossmann-fold domain.

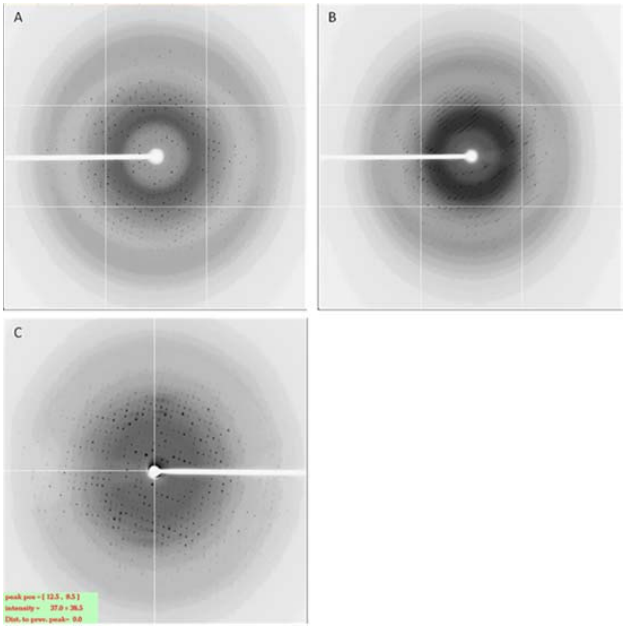

Fig. 1: A. Diffraction pattern of apo-HpSDH at 0°. B. Diffraction pattern of HpSDH•shikimate at 0°. C. Diffraction pattern of HpSDH•shikimate•NADPH at 0°.(BL13B1-75%, BL13C1-25%)

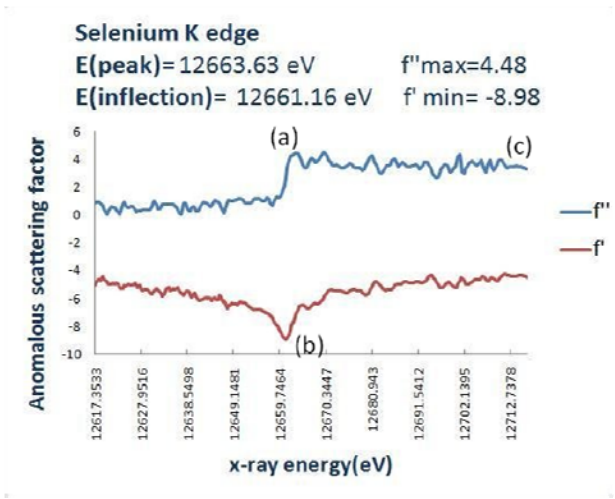

Fig. 2: Selenium absorption edge in the seleno-methionine crystal.