Poster Presentation

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The Structural Basis for BVMO Substrate Profile and Stereospecificity

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The Baeyer-Villiger monooxygenases (BVMOs) are a group of bacterial enzymes that are able to catalyze the synthetically useful Baeyer-Villiger oxidation reaction. As such, these enzymes have attracted considerable attention as potential industrial biocatalysts. The interest in these enzymes has led to a desire to be able to rationally design them for tailored biocatalytic applications. While recent years have seen the publication of a number of crystal structures (1-3), we have been lacking a structure of a BVMO that has its native substrate or product bound in a conformation that will allow the determination of substrate specificity and stereospecificity. Without such a structure, progress towards tailored BVMOs has been hampered. We have been able to solve two crystal structures of cyclohexanone monooxygenase (CHMO) with its lactone product, ε-caprolactone, bound. These structures place the lactone in an ideal position for the determination of its substrate specificity and stereospecificity. These structures have provided us with a better understanding of the structural basis for substrate binding, paving the way for the rational design of tailored BVMOs. At the same time, we have pursued small-angle X-ray scattering (SAXS) and nuclear magnetic resonance (NMR) studies to better understand the dynamic nature of the enzyme. These studies have allowed us to explain the relationship between the various crystallized states of BVMOs and their complex, fourteen step enzyme mechanism.

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