

Public Abstract

First Name:Min

Middle Name:

Last Name:Luo

Adviser's First Name:John

Adviser's Last Name:Tanner

Co-Adviser's First Name:

Co-Adviser's Last Name:

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Department:Chemistry

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Title:STRUCTURAL AND FUNCTIONAL STUDIES OF PROLINE CATABOLIC ENZYMES AND HUMAN ALDEHYDE DEHYDROGENASES

Proline and glutamate are two necessary amino acids in human body, and proline can get converted into glutamate in both bacteria and eukaryotes. Two enzymes get involved in this reaction, the first enzyme is called proline dehydrogenase (PRODH), the other one is pyrroline-5-carboxylate dehydrogenase (P5CDH). These two enzymes are important for human health: dysfunction of PRODH would cause type I hyperprolinemia, which is a risk factor for schizophrenia, and dysfunction of P5CDH can result in Type II hyperprolinemia, which could induce neurologic manifestations. My dissertation is mainly focused on the structural and functional studies on these two enzymes. Several important PRODH and P5CDH structures were resolved from my PhD work. Combining these structures with biochemical studies, proline recognition mechanism of PRODH was clearly determined, important information from the molecular level was gained on how these two enzymes cooperate in catalyzing proline oxidation reaction. Also, I determined the real inhibition mechanism of a widely used inhibitor for the cancer marker aldehyde dehydrogenase. These new findings largely broadened the current knowledge in amino acid oxidation, and would provide valuable information in drug discovery.