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Characterization of Enzyme Structure-Function Relationship of Adenylosuccinate Lyase STEPHEN RAY, University of Denver (DU), DAVID PATTERSON, Eleanor Roosevelt Institute (ERI), KINGSHUK GHOSH, DU, TERRY WILKINSON, ERI, SEAN SHAHEEN, DU — Adenylosuccinate lyase (ADSL) is an enzyme involved in de novo purine biosynthesis required for several important biological functions. Occasionally disturbances within the enzyme occur, causing a disorder known as ADSL deficiency. It is likely these mutations affect the formation of the tetramer structure by protein misfolding or aggregation. We are beginning to study fundamental properties of the enzyme structure-function relationship of Wild-Type ADSL compared to mutants associated with ADSL Deficiency with two major studies: i) Stability and formation of multimeric complexes in a heterogeneous pool of other structures, ii) Enzymatic activity and reaction kinetics studies by measuring reaction rates of the conversion of substrate into products and enzyme substrate complex formation equilibrium. Our group has successfully expressed Wild-Type (WT) and the mutants R426H and A291V in a protein expression vector and have measured their respective enzyme activity after purification. Modelling approaches for molecular interactions of monomer subunits show the trimer structure could be problematic. We have also carried out our preliminary analysis of the structure-function relationship using microscopic model for the A291V mutant compared to the WT protein.

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