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Structures of Wild Type *E. coli* Adenylosuccinate Lyase and a Mutant-substrate Complex Provide New Insights Into the Enzymatic Mechanism. M. Tsai^{1,2}, P. Yip¹, J. Koo^{1,2}, M.L. Segall³, R.F. Colman³, P.L. Howell^{1,2}, ¹Hospital for Sick Children, ²Univ. of Toronto, Toronto, Ontario, Canada; ³Univ. of Delaware, Newark, DE, USA.

Adenylosuccinate lyase (ADL) participates in the *de novo* purine biosynthetic pathway where it catalyzes the breakdown of adenylosuccinate (ADS) to AMP and fumarate. ADL is a member of the class II fumarase superfamily, which includes argininosuccinate lyase(ASL)/ δ 2-crystallin, fumarase C, L-aspartase, and 3-carboxy-*cis-cis*-muconate lactonizing enzyme. To gain further insight into the ADL enzymatic mechanism, and those of the other superfamily members, we have determined the crystal structures of wild type *E. coli* ADL and an H171A mutant with bound substrate to 2.0 and 1.85Å resolution, respectively. The H171A-ADS complex has enabled us to precisely identify for the first time the residues involved in substrate binding, as well as the putative catalytic residues for this enzyme. Furthermore, structural comparisons suggest conformational changes occur in ADL upon substrate binding and catalysis, similar to those observed previously in ASL/ δ 2-crystallin. Details regarding the catalytic mechanism of ADL and those of other superfamily members have been re-examined in light of the current results.