

## Impact of Disease-Linked Mutations on the Structure and Activity of Aldehyde Dehydrogenase 7A1 (ALDH7A1)

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Aldehyde dehydrogenase 7A1 (ALDH7A1) is involved in lysine catabolism, catalyzing the oxidation of  $\alpha$ -aminoadipate semialdehyde to  $\alpha$ -aminoadipate. Certain mutations in the *ALDH7A1* gene, which are presumed to reduce catalytic activity, cause an autosomal recessive seizure disorder known as pyridoxine-dependent epilepsy (PDE). The mutational spectrum of PDE is large - over 60 different mutations within the 18 exons of the *ALDH7A1* gene have been reported, including splice-site mutations, insertions, deletions, nonsense mutations, and over two dozen missense mutations. Although the genetic association between ALDH7A1 and PDE is well established, little is known about the impact of PDE-mutations on the structure and catalytic properties of the enzyme. Herein, I will describe structural and biophysical studies of several disease-linked variants of ALDH7A1.