

Milwaukee Academy of Science SMART Team

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Who demyelinated my oligodendrocytes?: Arylsulfatase A and Its Role in Myelin Regulation

PDB File: 1E1Z

Primary Citation: von Bulow, Rixa, Schmidt, Bernhard, Dierks, Thomas, von Figura, Kurt, Uson, Isabel (2001). Crystal Structure of an Enzyme-Substrate Complex Provides Insight into the Interaction between Human Arylsulfatase A and its Substrates During Catalysis. *J. Mol. Biol.* 305, 269-277.

Format: Alpha Carbon Backbone

RP: Zcorp with plaster

Abstract: Visualize that you are in the social prime of your adolescence: parties, friends, sports, et cetera, only to be cut short by the need to treat a degenerative neurological disorder. This disorder is called metachromatic leukodystrophy (MLD). MLD causes the deterioration of myelin sheaths, which insulate nerve axons that facilitate electrical impulses. In result of this myelin loss, nerves can't communicate, leading to the gradual loss of bodily functions. These problems arise from the accumulation of sulfatides, a group of lipids required for the construction of myelin sheaths. Sulfatides are found in the lysosomes of oligodendrocytes, a nerve cell that produces myelin, and buildup when the sulfatases (enzymes that break down sulfatides) are mutated, causing a harmful accumulation of sulfatides. At the root of the disorder is a mutation in the protein arylsulfatase A. The Milwaukee Academy of Science SMART (Students Modeling A Research Topic) Team modeled the arylsulfatase A protein using 3D modeling technology. Arylsulfatase A is a 489 amino acid enzyme responsible for preventing the harmful accumulation of sulfatides within the oligodendrocytes. The active site of arylsulfatase A consists of the serine 69 amino acid which is responsible for sulfate binding. However, it's proposed that the histidine 229 protonates (adds a hydrogen atom) the alcoholate produced via hydrolysis so the products can no longer rejoin to form sulfatase. Arylsulfatase A of those affected by MLD have a mutation to serine 69. Further studies of the structure and function of arylsulfatase A could lead to the development of treatments for this devastating disease.



Model Description: serine 150 and serine 69 (cyan), lysine 123 (lime green), lysine 302 (purple), histidine 229 (magenta), hydrogen bonds (blue), disulfide bonds(orange), struts(green), α -helices(red), β -sheets(yellow)

The colored side chains are colored because they are parts of the active site.

Reference to the CBM Website: <http://cbm.msoe.edu/smartTeams/>

Funding Statement: The SMART Team Program is supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant Number 8UL1TR000055. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.