SMART Teams 2014-2015 Qualification Phase

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Messmer SMART Team

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Arylsulfatase A and Myelin Production

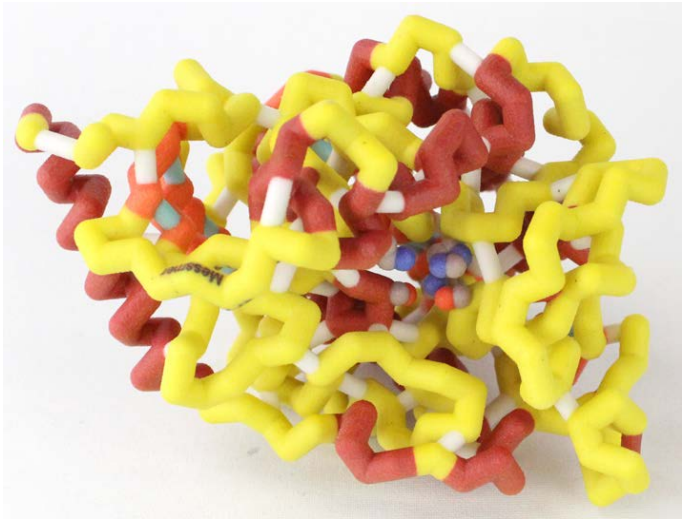
PDB: 1E1Z

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

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:



One in 40,000 people are carriers of metachromatic leukodystrophy (MLD), a rare genetic disorder. People diagnosed with MLD have a choice to undergo a risky and potentially fatal bone marrow transplant that could possibly rid them of this potentially fatal disorder. The enzyme behind the disorder is arylsulfatase A (ARSA). ARSA is found in lysosomes, the cell's recycling center where it breaks down sulfatides into cerebrosides and sulfates. Sulfatides, a type of fat, accumulate in myelin producing cells in the nervous system. Myelin surrounds the neurons throughout the body and helps to conduct nerve impulses. For individuals with MLD, the breakdown of sulfatides does not occur. A buildup of sulfatides causes the myelin producing cells to die. Furthermore, through research, we know that the key amino residues vital to the function of ARSA are lysine 123 and 302, serine 150 and 69, and histidine 229. Without the normal breakdown of sulfatides taking place and subsequent loss of myelin producing cells, myelin, a key substance in the formation of white matter goes left unsynthesized. White matter protects nerves from damage and insulates nervous signals from corruption while being transmitted throughout the body. The result for people with MLD is the loss of control over body functions and motor skills, and mental impairment as the disease progresses. The Messmer SMART (Students Modeling A Research Topic) Team developed a 3D model of ARSA to help understand its function and role in MLD.

Specific Model Information:

The key amino residues vital to the function of ARSA are lysine 123 and 302, serine 150 and 69, and histidine 229. Without this active region, ARSA would not be able to break down sulfatides into cerebrosides and sulfates. These residues are highlighted in our model through cpk coloring. The other areas that are highlighted are as follows:

Alpha helixes are colored maroon.
Hbonds are colored light blue.
Struts are colored white.
Beta sheets are colored orange.
Non-motif portions are colored light yellow.

http://cbm.msoe.edu/smartTeams/index.php

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