

SMART Teams 2014-2015 Qualification Phase

Wauwatosa West High School SMART Team

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Metachromatic Leukodystrophy: A Pain in the ARSA

PDB: 1E1Z

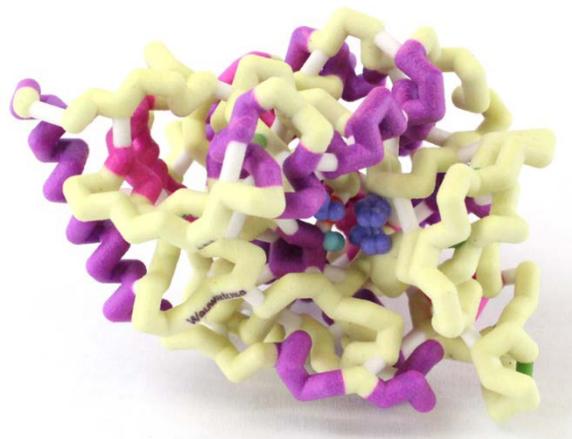
Primary Citation: von Bülow, R.; Schmidt, B; Dierks, T.; von Fogura, K.; Isón, I. (2001). Crystal Structure of an Enzyme-Substrate Complex Provides Insight into the Interaction between Human Arylsulfatase A and its Substrates During Catalysis. *J. Mol. Biol.* 305: 269-277.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Abstract: Metachromatic leukodystrophy, a recessive genetic disorder affecting the nervous system, leads to psychological regression, inability to control bodily functions, and death. Onset typically occurs during infancy, with life expectancy averaging between two and seven years. Individuals with the disease have a mutated ARSA gene, which contains the instructions for producing the enzyme arylsulfatase A.

Arylsulfatase A is located in lysosomes (which break down biomolecules) and is responsible for cleavage of sulfate ester bonds. The mutated ARSA gene produces less active arylsulfatase A. The subsequent accumulation of sulfate esters or unreleased cleaved sulfates results in the death of the myelin producing cells. Myelin, a white, fatty matter, protects and insulates nerves preventing "short circuiting" of nerve impulses. Arylsulfatase A (ASA) contains a functional residue at amino acid 69 resulting in substrate catalysis too rapid to study. Because the ASA catalyzed reaction proceeds too fast to study, C69A-ASA, a mutant of ASA, is used as a substitute for ASA with *p*-nitrocatechol sulfate, (pNCS), used as a substitute substrate. In the active site of ASA, lysine 123 and 302, serine 150, and histidine 229 make up a non-covalent bond between the enzyme and the sulfate group. The hydrolysis of sulfate esters cannot occur in the absence of a covalent bond. Scientists used the slower speed of the C69A - pNCS catalysis to provide further insight into the ASA-substrate mechanism, which would help develop a treatment for Metachromatic Leukodystrophy. The Wauwatosa West SMART (Students Modeling A Research Topic) Team modeled arylsulfatase A using 3D printing technology.



Protein Name:	Arylsulfatase A
PDB File:	1E1Z
Jpg filename:	Crystal structure of an arylsulfatase A mutant C69S
<p>Which features did you include on your model and which specific colors were used to highlight these features?</p> <p>(please be sure to indicate all colors in your mode3l, including colors selected for hydrogen bonds and struts)</p>	<p>Helices are colored purple Sheets are colored medium violet red hbonds are colored medium violet red The active site (lys123, ser150, his229, lys302) are colored royal blue Magnesium ion is colored red Ser69 is colored cyan Disulfide bridges are green Struts are colored white.</p>
<p>Which amino acids are displayed and WHY did you display them (What role do these amino acids play in the function of the protein)?</p>	<p>Ser69 is highlighted in cyan because this amino acid was replaced the wild type to allow study of the pathway of the breakdown of sulfatides, producing an intermediate product that is not released which causes cell death. The residues lys123, ser150, his229, and lys302 are displayed because they make up the active site of the enzyme. The magnesium cation is displayed because it is an electron acceptor and it helps hold the substrate in the active site.</p>

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

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