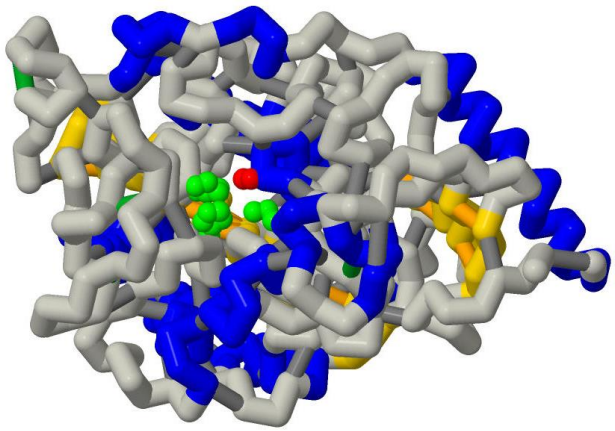
Center for BioMolecular Modeling

SMART Teams
Exploring the Molecular World

White Matters: MLD and ASA



Jmol Model Key
Blue- Alpha Helix
Gold - Beta Chains on backbone
Orange- H-bonds
Gray - Carbon Backbone
Darker Gray - Struts
Green - Disulfide Bonds
Active Site – Serine Residue 69
Lime Green – Positioning Residues

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* Primary Authors ** Above structure was modeled by all of the different groups involved.

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Primary Citation: von Bulow, R., Schmidt, B., Dierks, T., von Figura, K., Uson, 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.

PDB File: 1E1Z

Metachromatic Leukodystrophy[1] is an inherited, recessive, lysosomal storage disease that affects the cells that coat white brain matter and nerves with myelin, which protects the neurons and helps to propagate neural impulses. This disease causes an accumulation of sulfatides (fats) in these cells' membranes and may be the result of one or more mutations in the sequencing of numerous different associated proteins, one such protein being the arylsulfatase-A protein whose job is to break down these sulfatides preventing lethal accumulation.

The Arylsulfatase-A enzyme resides in the lysosomes of the cell where it breaks down sulfatides, cleansing the entire cell through a process called lysosomal recycling. The sulfatide's polar sulfate group is attracted to the polar active site of the Arylsulfatase-A. However, a mutation in this area may render the active site inaccessible to the sulfatide's sulfate group or make the active site unable to release the sulfate group it

cleaves. This slows or stops the Arylsulfatase-A's functionality resulting in a slow accumulation of sulfatides in the cell's membrane.

This is a model of the protein arylsulfatase-A (ASA). This is a modified form of ASA because the original form cannot be captured because it degrades too quickly. It is hoped that by studying the enzyme's activity, some insight into possible remediations of this terrible disease could be found.

[1] "What is MLD," *MLD Foundation*, 2014-12-21, http://mldfoundation.org/mld-101-what.html.