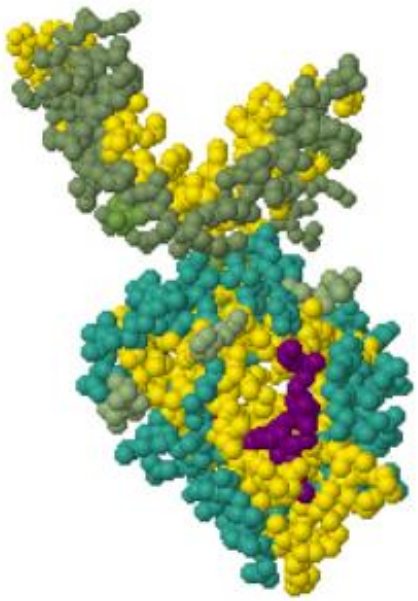
Center for BioMolecular Modeling

SMART Teams
Exploring the Molecular World

Saposin B

Jmol Model Key
Cyan and Green- polar residues on outside of Saposin B making it soluble in the lysosome
Yellow – nonpolar groove of Saposin B that can accept/bond/interact with the sulfatide
Purple- a sulfatide-like molecule trapped within the nonpolar region of Saposin B



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** Above structure was modeled by all of the different groups involved. However this actual model was Alex Bluestein's design.

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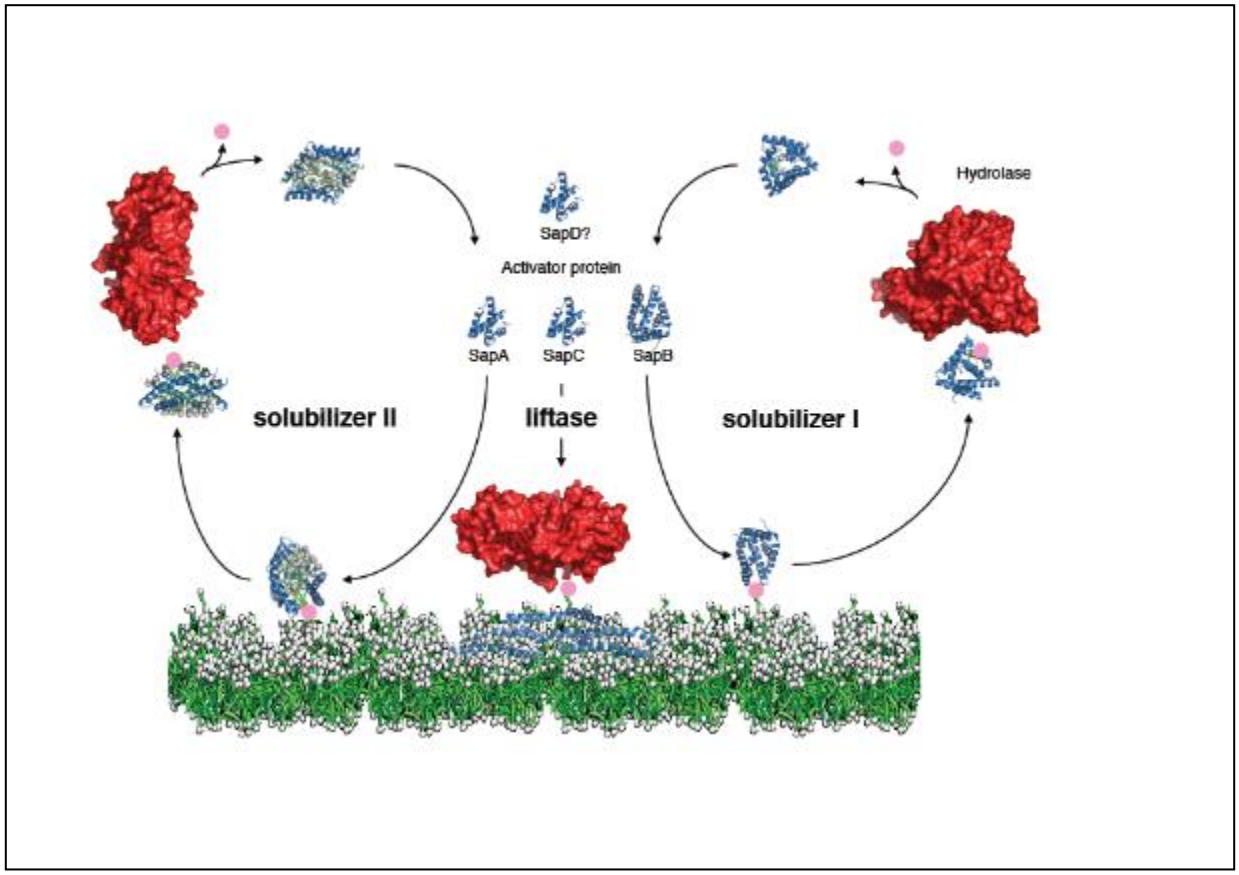
Metachromatic Leukodystrophy1 (MLD) is an inherited recessive disorder that affects myelin-producing cells of the nervous system. In affected individuals, these cells suffer an accumulation of sulfatides that, for reasons not yet known, causes the cell to stop producing the myelin that protects nerve cells and quickens nerve impulses and degradation of myelin causes damage to associated white matter. Normally, sulfatides are removed from the membrane within lysosomes, but in the case of the Metachromatic Leukodystrophy, this process may be disrupted at multiple points by various mutations in associated proteins.

One such protein is Saposin B2, which works with the enzyme arylsulfatase-A (ARSA) that cleaves the sulfate group from these sulfatides. The polar ARSA enzyme cannot remove the sulfatides from the non-polar core of the lysosomal membrane. Saposin B works as a lifter protein that encloses the hydrophobic tail of the sulfatides with its hydrophobic dimer. This dimer, created by five alpha helices, allows Saposin B to hold sulfatides while forming a water-soluble, ARSA-affinitive complex. Mutations of this protein may be detrimental, especially when occurring near the dimer. Saposin B mutations or deficiency may be involved with other lysosomal storage diseases.

Below is also pictured an image[3] describing Saposin B's role in recycling sulfatides. Notice it is clear how studying such mechanisms can provide insights as to some different ways to provide a cure/relief from the terrible consequence of MLD.



Citations

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

[2] Ahn VE, Faull KF, Whitelegge JP, Fluharty AL, Privé GG. Crystal structure of saposin B reveals a dimeric shell for lipid binding. Proc Natl Acad Sci U S A. 2003 Jan 7;100(1):38-43. Epub 2002 Dec 23.

[3] "Structural and Functional Studies of the Human Saposin Proteins" by Konstantin Popovic from the University of Toronto. https://tspace.library.utoronto.ca/bitstream/1807/31904/1/Popovic_Konstantin_201111_PhD_thesis.pdf,