Research & Design Phase Model Summary

Cedarburg High School SMART Team

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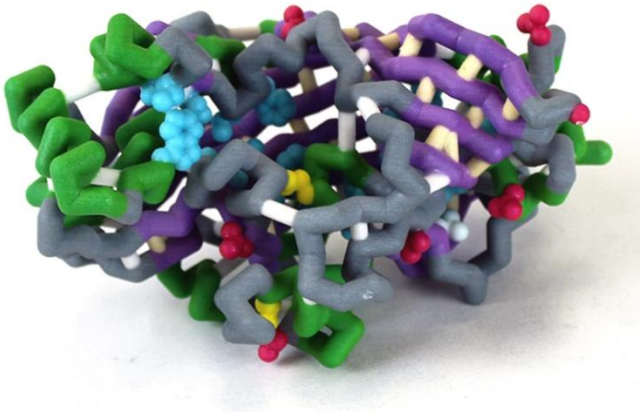
In with the Good and out with the Bad: The Role of SR-BI in Lowering Blood Cholesterol

PDB: 4F7B



Primary Citation: Neculai, D., *et al*. (2013). Structure of LIMP-2 provides functional insights with implications for SR-BI and CD36. *Nature* 504: 172-176.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:
According to the CDC, 1 in 3 adults in the US has high cholesterol, which is linked to cardiovascular disease. Cholesterol, a hydrophobic molecule, is transported in the blood by binding a lipoprotein. Scavenger receptor class B type I (SR-BI), a transmembrane protein that binds high density lipoprotein (HDL) carrying cholesterol, helps transfer cholesterol from HDL into liver cells where it can be excreted in bile. This is important for lowering blood cholesterol levels and reducing the risk of heart disease and stroke. SR-BI belongs to a larger family of scavenger receptor proteins that includes lysosome membrane protein 2 (LIMP-2), and SR-BI and LIMP-2 share structural homology. The structure of the C-terminal transmembrane domain of SR-BI, determined through NMR, is composed of three helices with a leucine zipper motif. Mutagenesis studies implicate this leucine zipper motif in dimerization of SR-BI and proper receptor function. A crystal structure of LIMP-2 revealed the existence of a large, primarily hydrophobic cavity that runs the entire length of the protein that suggests a role in the selective transfer of cholesterol into the liver cell. Using 3D printing technology, the Cedarburg SMART (Students Modeling A Research Topic) Team utilized the known structure of LIMP-2 to investigate structure-function relationships in SR-BI. Determining important HDL/SR-BI interactions will increase knowledge of how SR-BI functions in transferring cholesterol from plasma HDL to the liver for excretion and can lead to the development of medical treatments to increase cholesterol excretion by the liver and prevent heart disease and stroke.

Specific Model Information:

Amino acid side chains involved in disulfide bonds

- Cys312 and Cys318 – yellow
- Cys274 and Cys329 – yellow

Hydrophobic amino acid side chains that may line proposed tunnel through protein

- Ile41, Pro56, Leu58, Val60, Ile138, Trp146, Leu185, Ile195, Phe199, Leu201, Phe202, Phe256, Val268, Pro270, Phe273, Val277, Ala333, Ile335, Met337, Val367, Ile375, Ile376, Phe383, Ile385, Val415, Leu425 – aqua
- Leu266 – orange

Amino acid side chains that are glycosylation sites:

- Asn45, Asn68, Asn105, Asn206, Asn224, Asn249, Asn304, Asn325, Asn412 – deep pink

Highlighted protein structures:

- Alpha helix structures are colored forest green.
- Beta sheet structures are colored medium purple.
- Hydrogen bonds are colored lemon chiffon.

Supporting Features:

- Struts are colored white.