2016-2017 Research and Design Model

Marquette University High School SMART Team

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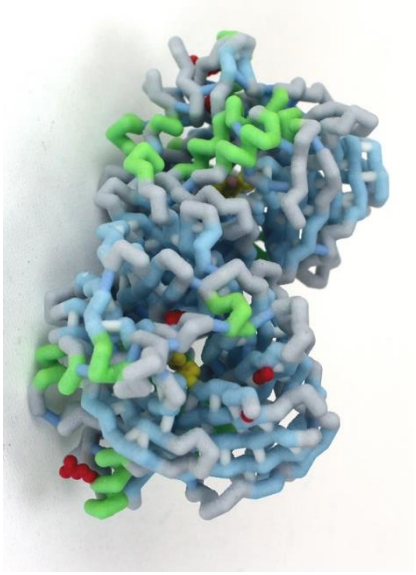
RPE65--Essential Visual Cycle Protein

PDB: 4RSC

Primary Citation: Wright, C.B., Redmond, M.T., Nickerson, J.M. (2015). A History of the Classical Visual Cycle. *Progress in Molecular Biology and Translational Science* 134: 433-448.



Format: Alpha carbon backbone

RP: Zcorp with plaster

Description: Leber congenital amaurosis (LCA) is a genetic disease associated with blindness that is caused by mutations in retinal pigment epithelium (RPE65), an enzyme involved in the visual cycle. When light hits photosensitive pigments in the retina, it conformationally changes 11-cis-retinol (a form of vitamin A) to 11-trans-retinol. This conversion allows for a series of chemical reactions and the formation of electrical signals that communicates with the brain. RPE65 is essential to the cycle because it changes 11-trans-retinol back into 11-cis-retinol--recycling the enzyme and allowing for sustained vision. The Marquette High SMART (Students Modeling A Research Topic) Team used 3D printing technology to model how mutations in LCA affect RPE65's structure and function. RPE65 has 533 amino acids folded into sheets that arrange themselves into seven propeller blades, which collectively create a mostly hydrophilic tertiary structure. One face of RPE65 is hydrophobic and is associated with the microsomal membrane. A hydrophobic, tunnel-like structure leads to an iron cofactor that facilitates its enzymatic efficiency. The iron cofactor is held in the active site by the histidine residues H180, H241, H417, and H527 in a coordinated motif. Mutations near the active site cause lowered enzymatic activity and LCA. Other residues that are commonly mutated in LCA include Gly40, Arg91, Glu102, Arg124, His182, and Val473. Ocular imaging data has shown phenotypic changes in the photoreceptors in patients with RPE65 mutations. With novel gene delivery methods and other treatment strategies, these technologies will be useful to understanding how to treat LCA and other retinal diseases.

Specific Model Information:

Amino Acids associated with the active site

- His241:yellow
- His180: yellow
- His527: yellow

Amino Acids associated with common mutations

- His182: red
- Arg91: red
- Glu102: red
- Val473: red
- Gly40: red

Iron Ligand:

Fe: pink

The Fe atom is essential to the function of the protein and is found in the active site of the protein.

Other important features:

Backbone: lightgrey
Sheets: lightblue
Helix: lightgreen
Hbonds: mintcream
Ssbonds: none
Struts: lightskyblue

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