SMART Teams 2013-2014
Research and Design Phase

Westosha Central High School SMART Team

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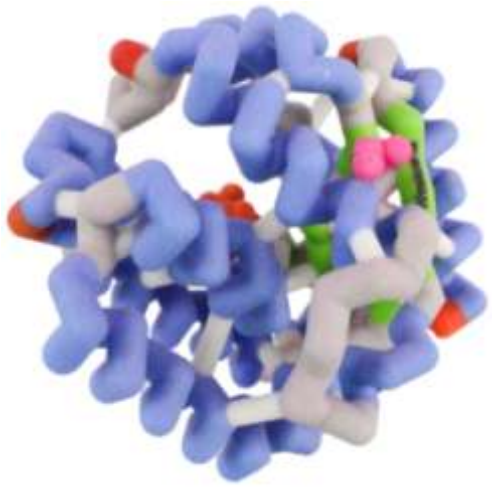
Deleterious Deoxyguanosine Kinase (dGK) Double Destruction

PDB: 2OCP

Primary Citation: Eriksson, S. (2003). Mitochondrial deoxyguanosine kinase mutations and mitochondrial DNA depletion syndrome. *FEBS Letters*, *554*(3), 319-322.



Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

Mitochondrial Deficiency Syndrome (MDS) is characterized by a deficient amount of mitochondrial DNA (mtDNA). Without sufficient copies of mtDNA, the mitochondria cannot manufacture an adequate amount of ATP, leading to failure of energy expensive tissues such as the brain, skeletal muscle, and liver, ultimately causing death in early infancy. Deoxyguanosine kinase (dGK), an enzymatic protein, plays a role in regulating the replication of mtDNA by attaching a phosphate to a sugar/nitrogen-base nucleoside at the active site, amino acids Glu70 and Arg142. Once phosphorylated, the assembly of mtDNA proceeds. Mutations in dGK prevent the phosphorylation of mtDNA and lead to a decrease in mitochondrial function. Two point mutations have been shown to have a deleterious impact on dGK: the R142K mutation is 0.2% active when compared to the wild type, and the E227K mutation is 5.5% active when compared to the wild type. The 3D model designed by the Westosha Central SMART (Students Modeling A Research Topic) Team displays the active site, two specific mutations and additional mutations reported in MDS patients. Screening for MDS is difficult because the condition can be caused by a wide variety of dysfunctional proteins. One such protein is dGK, therefore identifying its structure can hasten an accurate diagnosis.

Specific Model Information:

- The alpha carbon backbone is colored silver.
- Alpha helices are highlighted in dodger blue.
- Beta sheets are highlighted in lime green.
- Glu227, displayed in ball and stick and colored deep pink, is highlighted because a point mutation to lysine (interchangeable with glu227 , displayed in ball and stick and colored gold) causes decreased protein function.
- Truncation mutations are highlighted in red.
- Amino acids in the active site (Glu70 and Arg142) are displayed in ball and stick and colored tomato.
- The N terminus in each chain is highlighted in dark blue.
- The C terminus in each chain is highlighted in firebrick.
- Hydrogen bonds are colored thistle.
- Structural supports are colored white.

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

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