Cudahy High School SMART Team

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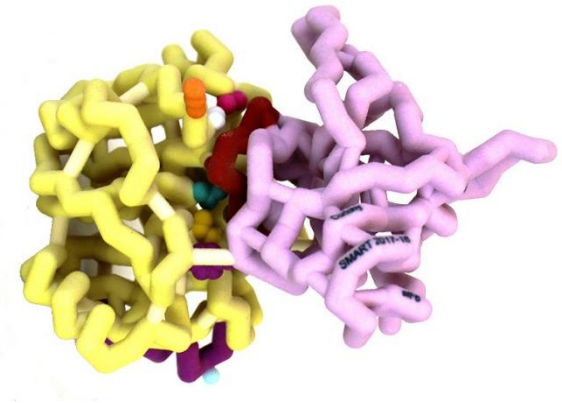
eIF We Could Cure Cancer: eIF6 and the Connection to Cancer

PDB: 4v8p

Primary Citation: Klinge, S., Voigts-Hoffmann, F., Leiundbundgut, M., Arpagaus,S., Ban, N. (2011) *Science* 334: 941. Crystal Structure of the Eukaryotic 60S Ribosomal Subunit in Complex with Initiation Factor 6.



Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

The World Health Organization (2017) lists cancer as a leading cause of death. Eukaryotic Initiation Factor 6 (eIF6) is critical for cancer cell growth/survival. Understanding its mechanism of action will help to develop new drug targets that can slow the cancer epidemic. One of the hallmarks of cancer is increased rate of protein synthesis, supporting the rapid growth and reproduction of cancer cells. eIF6 is crucial to maintaining these enhanced levels of protein production. Data show eIF6 is upregulated in human cancer cells, but its mode of regulation is unknown. eIF6 is essential for the synthesis of the 60S ribosomal subunit and for mediating interactions between the 60S and 40S ribosomal subunits. eIF6 binds to 60S using residues Y151, T150, N106, S102, K100, T75, and D12 to interact with 60S ribosomal protein L23 (RPL23) residues K132, N136, A137, G138, S139, V140, and V141. eIF6 was modeled by the Cudahy SMART (Students Modeling A Research Topic) Team using 3D printing technology to investigate structure and function relationships. eIF6 interactions with 60S must be regulated as the release of eIF6 from the 60S allows the 60S and 40S subunits to bind and initiate protein synthesis. C-terminus sites could functionally regulate eIF6 interaction. One model suggests that when the C-terminal tail is phosphorylated, eIF6 is released from 60S, initiating protein synthesis. Previous research suggests by reducing levels of eIF6 or by preventing its release from the 60S subunit, protein synthesis is attenuated and tumor growth is inhibited. Therefore, determining the exact mechanism of binding between eIF6 and the 60S ribosomal protein-RPL23 in cancer cells is important and could aid in the development of new treatments for cancer patients.

Specific Model Information:

Amino acid side chains

Many amino acids are individually colored to show their importance - these specific residues are where eIF6 interacts with the Rpl23, found on the ribosome. When bound together, eIF6 inhibits the ribosome from performing protein synthesis.

eIF6

- Y151 is colored dark magenta
- T150 is colored gold
- N106 is colored teal
- S102 is colored alice blue
- K100 is colored dark orange
- T75 is colored fuchsia
- D12 is colored dark slate gray

Rpl23

- K123, N136, A137, G138, S139, V140, V141 is colored maroon

C-Terminus is colored purple with the residue 212 colored pale turquoise - it is the area of known regulation for protein function

Highlighted protein structures:

Backbone

- eIF6 is colored khaki
- RPL23 is colored thistle

Hydrogen bonds

- Thistle to match the protein portion they are a part of

Supporting Features:

- Struts are colored lemon chiffon

Secondary Citation: Muluzio, A., Beugnet, A., Grosso, S., Brina, D., Mancino, M., Campaner, S., Amati, B., de Marco, A., Biffo, S. (2011). Impairment of Cytoplasmic eIF6 Activity Restricts Lymphomagenesis and Tumor Progression without Affecting Normal Growth. *Cancer Cell* (19): 765-775.