

Valders High School SMART Team

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Heterotrimeric G-Protein

PDB: 1GOT

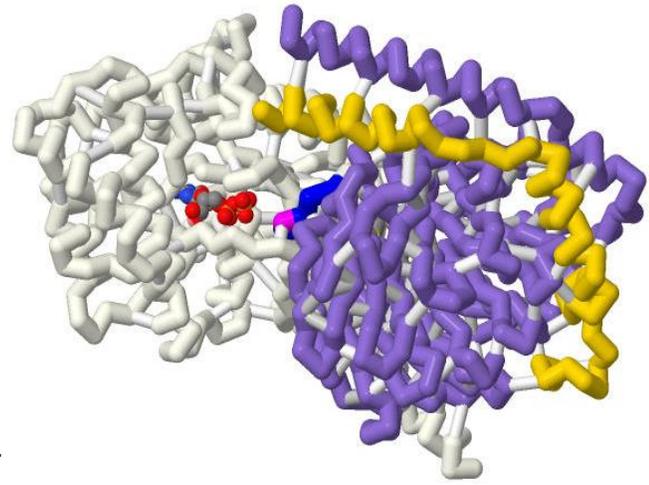
Primary Citation: Lambright, D., Sondek, J., Bohm, A., Skiba, N., Hamm, H., Sigler, P. (1996). The 2.0 Å Crystal Structure of a Heterotrimeric G Protein. *Nature*, vol 379, 25 January 1996.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

Neonatal stress may permanently alter hypothalamic-pituitary-gonadal function and accelerate the onset of puberty in female rats. Heterotrimeric G proteins, found coupled to membrane-bound receptors on the inside of cell membranes, form a central link in cell signaling. Inactive G proteins bind guanosine diphosphate (GDP). When a signaling molecule, such as gonadotropin releasing hormone (GnRH), binds to membrane receptors of cells in the anterior pituitary gland, GDP is displaced by GTP (guanosine triphosphate), and the alpha subunit separates from the beta and gamma subunits. The alpha-GTP subunit then triggers a cell signaling cascade. In pituitary gonadotroph cells, this cascade results in the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH). These hormones will cause female gonads (ovaries) to release estrogen and progesterone and, if hypothalamic-pituitary-gonadal function is altered, may trigger early onset of puberty in female rats. The Valders SMART Team modeled a G Protein using 3D printing technology to study structure-function relationships in cell signaling. Hydrophobic amino acids form the switch interface between the alpha subunit and the beta-gamma subunits stabilizing the heterotrimeric G protein. When the alpha subunit binds GTP, Gly199 interacts with the terminal (gamma) phosphate of GTP, and the activated alpha subunit separates from the beta-gamma subunits resulting in cell signal propagation. Understanding how the hypothalamic-pituitary-gonadal axis is influenced by neonatal stress in rats may help scientists to better understand puberty onset in humans.



Specific Model Information:

- The A subunit (chain) in alpha carbon backbone is colored ivory.
- The B subunit (chain) in alpha carbon backbone is colored medium purple.
- The G subunit (chain) in alpha carbon backbone is colored gold.
- Amino acids (Ile180, Phe195, Trp201, His209, Cys210, and Phe211) on the A subunit are displayed in ball and stick and colored cpk. Amino acids (Tyr59, Trp99, Met101, and Leu117) on the B subunit are displayed in ball and stick and colored cpk. These hydrophobic amino acids form the switch interface between the A subunit and the B subunit.
- Amino acids (Gly198, Gln200, Arg201, and Ser202) are displayed in alpha carbon backbone and colored medium orchid. Amino acid Gly199 is colored yellow and interacts with the terminal (gamma) phosphate of GTP. This interaction triggers conformational changes in the switch interface and causes the A subunit to separate from the B/G subunit. All these amino acids together, on the A subunit form a flexible loop that interacts the A with the B subunit, stabilizing the switch interface, holding the A subunit to the B/G subunit.
- GDP, bound by the A subunit is displayed in ball and stick and colored cpk. GDP keeps the heterotrimer stable. When GDP is replaced by GTP, and GTP's terminal (gamma) phosphate interacts with Gly199 conformational changes occur which destabilize the switch region, and the A subunit separates from the B/G subunits.
- Hydrogen bonds are colored light gray.
- Structural supports in the model are colored white.

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

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