# Research & Design Phase Model Summary

## Divine Savior Holy Angels High School SMART Team

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Mentor: Dr. R. Peoples, Marquette University

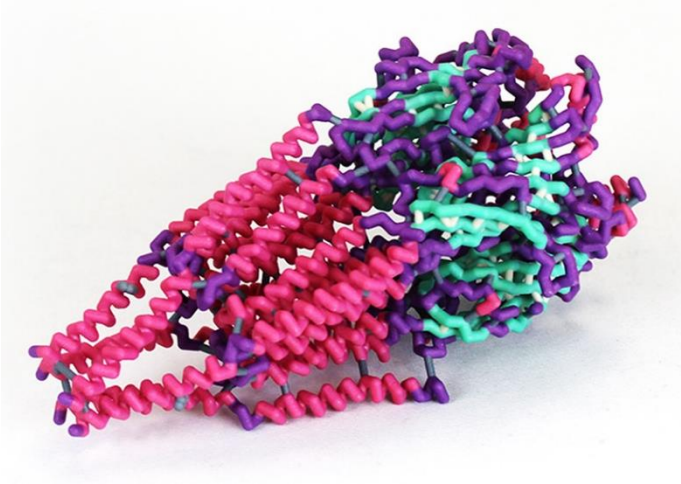
## Yo $GABA_A$ $GABA_A$:
## How the Structure of Human $GABA_A$ Receptor Affects the Action of Anesthetics

**PDB**: 2BG9 AD Chain Ser393Phe

**Primary Citation**: Unwin, N. Refined Structure of the Nicotinic Acetylcholine Receptor at 4A Resolution. (2005) *J. Mol. Biol.* 346: 967.

**Format**: Alpha carbon backbone

**RP:** Zcorp with plaster



**Description:**
Propofol, a powerful anesthetic, can be used safely in medical settings, but proves deadly when used recreationally. Propofol binds to the $GABA_A$ receptor, which consists of an integral ion channel protein embedded in the membrane of neurons in the brain that is activated by the neurotransmitter molecule gamma-aminobutyric acid, or GABA. When propofol binds to the $GABA_A$ receptor, a conformational change occurs, holding the neurotransmitter GABA in its binding site and keeping the ion channel open. This allows more chloride ions to diffuse into the cell. Resting potential becomes more negative, so even with the diffusion of $Na^+$ ions during nerve stimulation, the threshold cannot be reached and the action potential is not generated. Since the neurons cannot communicate normally, a person given propofol remains unconscious. The lower part of the $GABA_A$ receptor, located in the cytoplasm of a neuron, has an unidentified molecular structure. Phe 393 variants in the A and D chains prevent propofol from acting on the $GABA_A$ receptor. The DSHA SMART (Students Modeling A Research Topic) Team modeled the similar nicotinic receptor using 3D printing technology to better understand the structure of the $GABA_A$ receptor. A greater understanding of the structure of the $GABA_A$ receptor and the role of the Phe 393 variants in the action of propofol can lead to the development of more effective anesthetics.

**Secondary Citation:**

Moraga-Cid, G., Yevenes, G. E., Schmalzing, G., Peoples, R. W., & Aguayo, L. G. (2011). A single phenylalanine residue in the main intracellular loop of α1 γ-aminobutyric acid type A and glycine receptors influences their sensitivity to propofol.

**Specific Model Information:**

- The backbone is colored darkorchid.
- The structural supports are colored gray.
- The H-Bonds are colored floralwhite.
- The alpha helices are colored hotpink.
- The beta sheets are colored turquoise.
- The mutation site Phe393, which is a lab induced mutation on domains A and D that impedes the binding of propofol to the active site, is colored CPK.

**CBM SMART Teams Website**:
http://cbm.msoe.edu/smartTeams/smartTeamsLocal.php