Research & Design Phase Model Summary

The Brown Deer SMART Team

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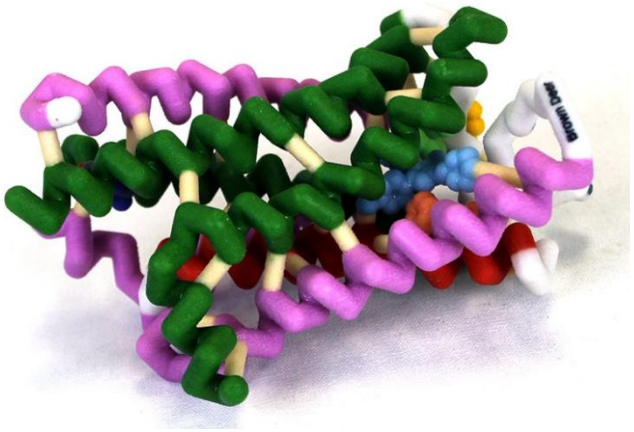
CB_1: The misunderstood marijuana receptor

PDB: 5tgz

Primary Citation: Tian Hua, et al. (2016). Crystal Structure of the Human Cannabinoid Receptor CB1. *Cell*, 167: 750-762.



Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:
As of September 2017, seven states have legalized the recreational use of marijuana, while 22 states have legalized its medical use. Regardless of attitudes toward recreational use, constituents of marijuana *(Cannabis sativa, C. indica)* known as cannabinoids are potentially useful in treating pain and inflammation, stress and anxiety disorders, and possibly seizure disorders. Diseases such as obesity and substance abuse disorders may be treated by agents that block the actions of cannabinoids. The main receptor in the brain activated by cannabinoids is the cannabinoid receptor 1 (CB_1). CB_1 is a transmembrane protein found on presynaptic neurons throughout the brain. Seven alpha helices span the cell membrane. Various ligands bind to these alpha helices throughout the protein. Agonists such as tetrahydrocannabinol (THC) and other cannabinoids bind with CB_1 in the area of alpha helices 3, 6, and 7, at Phe268 and Phe379. Antagonists such as AM6538 or rimonabant bind with CB_1 in the area of alpha helix 2 at Phe170 and Phe174. Antagonist binding brings helices 3 and 6 close together, causing an “ionic lock” to form between Arg214 and Asp338 that prevents G protein signaling. The Brown Deer SMART Team (Students Modeling a Research Topic) has designed a model of CB_1 using 3D printing technology to investigate structure-function relationships. Research on the agonists and antagonists of the CB_1 receptor is important because it is not completely understood how much therapeutic potential they possess. Perhaps when the therapeutic potential of the CB_1 receptor is developed, quality healthcare can be given to patients using cannabinoid receptor-based therapeutics.

Specific Model Information:

Amino acid side chains involved:

- Phe268 and Phe379 are colored lightgreen. These assist in agonist binding.
- Phe170 and Phe174 are colored lightsalmon. These assist in antagonist binding.
- Arg214 and Asp338 are colored cpk. These form an ionic lock.

Highlighted protein structures:

- Alpha helices that involve agonist binding are colored darkgreen
- Alpha helices that involve antagonist binding are colored red
- Alpha helices that don't involve ligand binding are colored plum
- The disulfide bond is colored gold

Ligands:

- AM6538 is colored skyblue. It is an antagonist with similar structure to rimonabant, a medicine used to help reduce obesity, but unfortunately increased stress and anxiety.

Supporting Features:

- Struts are colored papayawhip

CBM SMART Teams Website:

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