SMART Teams 2014-2015 Research and Design Phase

Whitefish Bay High School SMART Team

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Modeling the Binding Site of α-bungarotoxin to Nicotinic Acetylcholine Receptors

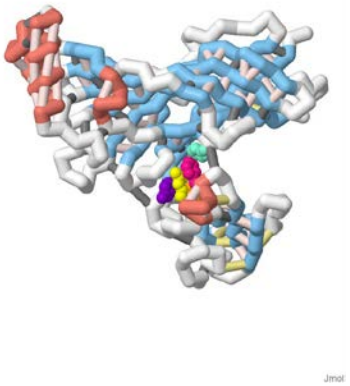
PDB: 2QC1

Primary Citation: Dellisanti, C.D., Yao, Y., Stroud, J.C., Wang, Z., Chen, L., (2007). Crystal structure of the extracellular domain of nAChR alpha 1 bound to alpha-bungarotoxin at 1.94 A resolution. *Nat.Neurosci.*10: 953-962

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:



Myasthenia gravis, a disease characterized by muscle fatigue and weakness, affects thirty million people a year. The venom of certain snakes generates a similar phenomenon in its prey, causing paralysis. In both cases, symptoms result from interference with neuromuscular transmission. In normal neuromuscular function, binding to acetylcholine creates changes in nicotinic acetylcholine receptors (nAChRs) that catalyze ion-selective transmembrane pore openings. The resultant ion flux enters the muscle cell via the neuromuscular junction, ultimately inducing movement. The Whitefish Bay High School SMART (Students Modeling A Research Topic) Team used 3D print technology to model the site where snake venom α-bungarotoxin (α-Btx) binds to nAChRs, located in a muscle's plasma membrane at neuromuscular junction. Binding primarily takes place between the tips of nAChR fingers I and II, which form a mobile region essential for proper binding; and the C-terminal loop of α-Btx, loops A, B, and C; and the carbohydrate chain in the nAchR. The α-Btx residues Y93, Y190, Y198, and R149 are inserted into the aromatic cage of the receptor by R36 and F32 in finger II of α-Btx. This binding blocks the agonists' access to the activation site. Thus, α-Btx prevents the opening of ion channels that allow the passage of electrical signals that induce movement. Further study of these ion channels and nAChRs as pharmaceutical targets could lead to medical breakthroughs in diseases such as myasthenia gravis, Parkinson's, Alzheimer's, and epilepsy.

Specific Model Information:

- Beta Sheets are highlighted light sky blue in nAChR.
- Alpha Helices are highlighted salmon in nAChR.
- Non-motif backbone sections are colored white.
- Hydrogen Bonds are colored misty rose.
- Disulfide Bonds are colored light goldenrod yellow.
- Struts are colored gray.
- Amino acids in nAChR are displayed in ball and stick and highlighted as follows:
    - Tyrosine 93 is colored aquamarine.
    - Threonine 148 is colored green.
    - Arginine 149 is colored medium blue.
    - Tyrosine 190 is colored orange.
    - Tyrosine 198 is colored medium purple.

- α-Btx backbone is colored pale green.
- Amino acids in α-Btx are displayed in ball and stick and highlighted as follows:
    - Phenylalanine 32 is colored deep pink.
    - Arginine 36 is colored yellow.

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

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