

SMART Teams 2014-2015

Research and Design Phase

West Bend High School SMART Team

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MscL: The Magic Behind the Touch

PDB: 2OAR

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Format: Alpha carbon backbone

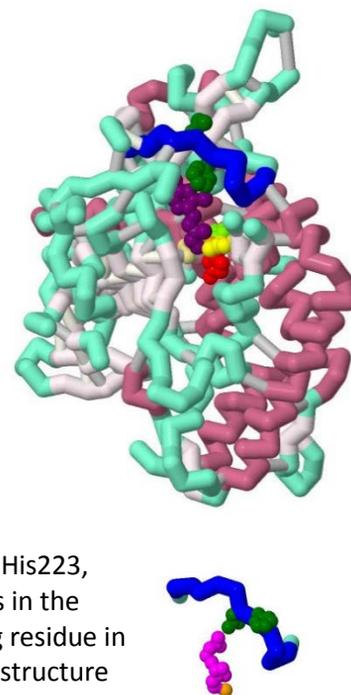
RP: Zcorp with plaster

Description:

USATODAY reports that the most toxic biological compound is used by 5.6 million people annually. The bacterium, *Clostridium botulinum* makes a toxin called botulinum neurotoxin (BoNT) (or BotoxA). Signs say BoNT may remedy ailments, but excess Botox can cause nerve damage and death. It is key to create a drug that can block BoNT's effects if misused. BoNT enters motor neurons and interrupts nerve impulses, causing paralysis. The toxin consists of a heavy chain that is the targeting infiltration system, and a light chain is the warhead.

When the light chain enters a motor neuron, it cleaves SNAP-25 at a Gln-Arg peptide bond, ending the nerve's ability to release neurotransmitters. Vital for the toxin's catalysis, key amino acids include His223, His227, and Glu262, which bind the Zn(II) ion. The Glu224 side chain joins in the BoNT catalytic machinery. Asp370 is essential for interacting with the Arg residue in the substrate's scissile peptide bond. The BoNT/A active site can alter its structure to bind to unlike molecules: arginine and a hydrophobic cinnamic acid derivative.

The West Bend SMART (Students Modeling A Research Topic) Team made a model showing how BoNT houses polar and hydrophobic molecules using 3D printing.



Specific Model Information:

2IMA with GB4:

- The 370 loop (which includes residues 365-375) is colored blue .
- Amino acids Phe369 and Asp370 are colored green. They are involved in inhibitor binding.
- The amino acid His223, which is included in the zinc binding site is colored chartreuse.
- The amino acid Glu224, colored khaki, is also involved in the zinc binding site.
- Amino acid, His227, is included in the zinc binding site, and is colored red.
- The amino acid Glu262 is colored yellow, and is included in the zinc binding site.
- Zn500 is colored orange, and is located in the zinc binding site.
- The inhibitor, 2,4-dichlorocinnamic hydroxamate (GB4 600) is colored purple.
- Hydrogen bonds are ivory.
- The non-motif alpha carbon backbone is colored aquamarine.
- The sheets are colored lavender blush.
- The helices are colored pale violet red.
- The struts are light grey.

2IMB with AHL:

- The 370 loop (which includes residues 365-375) is colored blue .
- Amino acids Phe369 and Asp370 are colored green. They are involved in inhibitor binding.
- Zn500 is colored orange, and is located in the zinc binding site.
- The inhibitor L-arginine hydroxamate (AHL) is colored fuchsia.

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

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