



2014  
2015 | SMART  
Teams

# SMART Teams 2014-2015 Research and Design Phase

## Divine Savior Holy Angels High School SMART Team

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## Modeling TRPV1, a Detector of Thermal and Chemical Stimuli, Producing Pain: No Capsaicin Sensation

**PDB:** 3J5R

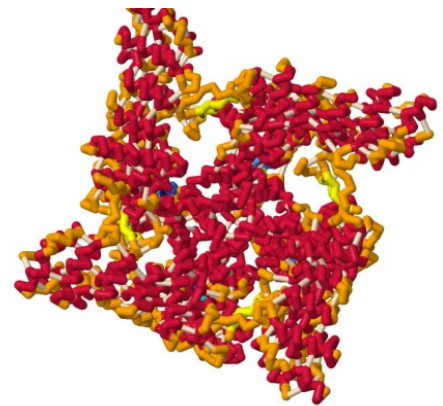
**Primary Citation:** Cao Erhu, Maofu Liao, Yifan Cheng, and David Julius.  
"TRPV1 Structures in Distinct Conformations Reveal Activation  
Mechanisms." *Nature* 504.7478 (2013): 113-18

**Format:** Alpha carbon backbone

**RP:** Zcorp with plaster

### Description:

According to the Institute of Medicine, 100 million Americans suffer from chronic pain every year and the US spends over \$500 billion trying to treat them. Pain begins as a stimulus that is detected by nociceptors, which are nerve fibers responsible for the detection of noxious mechanical, thermal, or chemical stimuli that give rise to pain sensations. These nociceptors transmit pain signals from the periphery to neurons in the spinal cord and brain. The Transient Receptor Potential Vanilloid 1 (TRPV1) is a nociceptive ion channel activated by capsaicin (the spicy component of hot peppers), heat, and endogenous pain molecules. Therefore, creating an inhibitor that partially blocks TRPV1 could treat chronic pain. The amino acids in the active site of TRPV1 are Y511, S512, M547, and T550. In addition, E600 controls the selectivity filter at the top gate of the channel and the hydrophobic seal mediated through I679 controls the lower gate. When capsaicin binds to the channel, a conformational change occurs that pulls the I679s on each subunit away from each other, opening up the lower gate. Understanding how activation of TRPV1 occurs may lead to the discovery of novel inhibitors of TRPV1 to help treat those suffering from chronic pain and reduce healthcare spending. The Divine Savior Holy Angels SMART (Students Modeling A Research Topic) Team modeled TRPV1 in a partially activated state using 3D printing technology. Program supported by a grant from NIH-CTSA.



Jmol

### Specific Model Information:

- The struts are colored bisque
- The hydrogen bonds are colored indianred
- The backbone is colored orange
- The helix is colored crimson
- The sheet is colored yellow
- The amino acids are located in the active site of TRPV1. This is where capsaicin binds to TRPV1, in a hydrophobic pocket that is within the S3-S4 helices and the S4-5 linker.
  - Serine 512 is colored aqua
  - Tyrosine 511 is colored royalblue
  - Methionine 547 is colored midnightblue
  - Threonine 550 is colored cornflowerblue
- E600 is also displayed because it is a residue at the selectivity filter at the top of the ion channel that acts as a partial gate to allow ions through. E600 can be “protonated” – a proton is added to it – which causes the selectivity filter to be more open. When muscles hurt, it may be that lactic acid is donating a proton (protonating) E600 of TRPV1 to open up the selectivity pore and make it easier for ions to move through TRPV1.
  - E600 is colored chartreuse.
  - I679 is colored gold. I679 is displayed because it controls the lower gate of the channel

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

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