

Some like it hot! Structure of receptor for hot chili pepper and pain revealed

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You can now not only feel the spicy kick of a jalapeno pepper, you can also see it in full 3D, thanks to researchers at Baylor College of Medicine in Houston.

Using sophisticated equipment, the research team led by Dr Theodore G. Wensel, professor of biochemistry and molecular biology at BCM, generated the first three dimensional view of the protein that allows you to sense the heat of a hot pepper. The report appears in the current issue of the *Proceedings of the National Academy of Sciences*.

“This protein, known as TRPV1, not only senses spicy foods, but also makes it possible to feel real heat and the pain and inflammation related to other medical conditions,” said Wensel, senior author on the study. “This method of viewing the protein now gives us the chance to clearly see the functional relationship between outside stimuli and the nerve cell.”

The outside stimulus used in this study was the heat of a chili pepper. It has been known for years that the burning sensation results from the action of a chemical known as capsaicin on TRPV1 found on the nerve cell membrane. TRPV1 is an ion channel, a tiny pore on the cell membrane that allows chemicals such as calcium to flux in and out.

“Any time you feel a burn or pain sensation, it is mediated by a TRPV1 channel. Different levels of heat are mediated by different TRP channels,” said Dr. Vera Moiseenkova-Bell, a postdoctoral associate in

Wensel's laboratory at BCM and first author of the study. "They are all related but each is regulated in a different manner."

Wensel said the three-dimensional image of TRPV1 revealed surprising information about its structure. It is made up of a pore domain embedded in the cell membrane, and a "hanging basket" of regulatory domains that extend into the interior of the cell.

"It's an unusual thing. There is a whole hollow 'basket' area but we don't know what's that's for," Wensel said. "Now the search is on to understand how the 'basket' area regulates the channel."

Isolating TRPV1 gives researchers an idea of how other channels are structured as well.

"Visualization of TRPV1 gives us insight on other TRP channels since they are structurally similar," said Moiseenkova-Bell. "Pharmaceutical companies target these TRP channels to make sure the drug binds properly. With this first structure we can start to build models of binding sites and hopefully in the future design more effective pharmaceuticals for a wide range of medical conditions."

Studying these channels is nothing new. In the past, scientists could measure the activity in the cells but it was unclear what each channel was responding to. Determining which proteins interacted with TRPV1, however, required Wensel's lab to create a purified model.

The protein had to be removed from cells, purified, and reconstituted in a synthetic membrane so researchers could control channel activity.

"Since calcium is involved in cell signaling, following the calcium movement confirmed the protein is active," said Wensel. "We are the first group to purify a TRPV1 channel and control what goes in and out

when the channel opens.”

Source: Baylor College of Medicine

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