Tarantula venom and chili peppers target same pain sensor

November 8 2006

Venom from a West Indian tarantula has been shown to cause pain by exciting the same nerve cells in mice that sense high temperatures and the hot, spicy ingredient in chili peppers, UCSF scientists have discovered.

The findings demonstrate that some plants and animals have evolved the same molecular strategy to deter predators -- triggering pain by activating a specific receptor on sensory nerves. The research provides new tools to understand how these pain- and heat-sensing neurons work, and to help develop drugs that ease persistent pain, the scientists report. Their finding, based on studies of mice cells in culture and live mice, is published in the November 9 issue of the journal *Nature*. The senior author is David Julius, professor and chair of physiology at UCSF.

The tarantula venom targets the heat sensor on nerve cells known as the capsaicin receptor, first cloned in 1997 in the Julius laboratory. In the last 10 years, Julius and his colleagues have demonstrated that this and related receptors trigger nerves to fire pain signals when exposed to Death Valley-like heat or the fiery properties of peppery food, mustard oil and other compounds. Human pain-sensing neurons also have these receptors on their surface, and some pain treatments have been developed that target them.

The capsaicin receptor acts as a channel on the nerve surface. When certain compounds bind to it, the receptor channel opens, allowing a stream of charged sodium and calcium molecules to rush into the nerve cell. This generates an electrical signal that travels to the brain to produce pain.

The researchers examined venoms from 22 spider and scorpion species whose bites are known to cause pain. Venom from the tarantula Psalmopoeus cambridgei activated the capsaicin receptor, also called TRPV1, and the researchers identified three protein subunits or peptides in the venom that targeted the receptor to cause pain. They also showed that venom from a second spider activated TRPV1, but they did not pinpoint which peptides were responsible.

The fact that a second spider venom triggered a capsaicin receptor suggests that a variety of spider species may have evolved the ability to use such toxins to target heat- and pain-sensing neuron receptors, the scientists conclude.

"It is fascinating that plants and animals have evolved the same anti-predatory mechanism to generate noxious sensations," Julius said. "These toxins are incredibly useful for understanding how ion channels of the nervous system work. They give us clues as to how specific activators or blockers on these channels can be designed to treat

persistent pain – from arthritis, bladder infections, or other diseases."

The researchers determined the venom peptides' effect in neuron cell cultures, measuring the tell-tale rush of calcium ions when the venom peptides contacted the TRPV1 capsaicin receptor. They also showed that synthetic versions of the venom peptides activated the receptor. In studies with mice, they found that normal animals flinched when their paws were exposed to the peptides, which they call vanillotoxins. Mice genetically engineered to lack capsaicin receptors did not respond.

Source: University of California - San Francisco