Mouse study shows antibody can soothe raging, nerve-driven poison ivy itch

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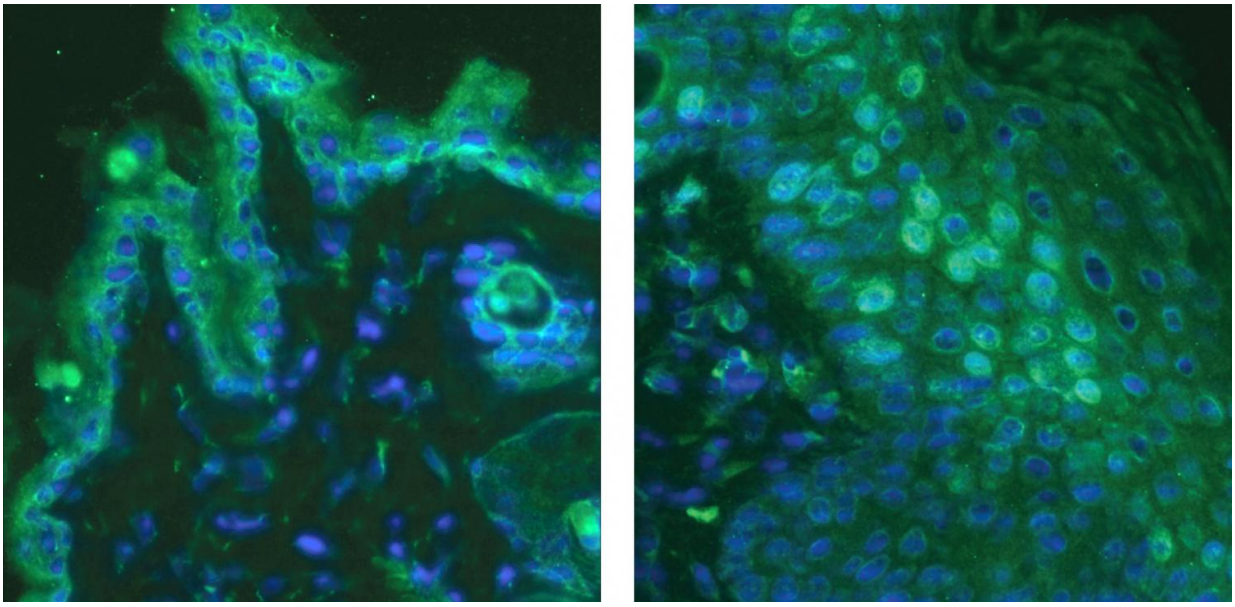

A fluorescence microscope image shows the skin of a healthy mouse (left) and skin from a mouse with a poison ivy rash (right). Interleukin-33, shown in green stain, is a protein that acts directly on the nerves, telling the brain the skin is extremely itchy. Credit: Sven-Eric Jordt/Duke Health

Scientists at Duke Health and Zhejiang Chinese Medical University have developed a strategy to stop the uncontrollable itch caused by urushiol, the oily sap common to poison ivy, poison sumac, poison oak and even mango trees.

The team found that by blocking an immune system protein in the skin with an antibody, they could halt the processes that tell the brain the skin is itchy. The research was done in mice and is described in the Nov. 7 *Proceedings of the National Academy of Sciences*. They hope their model could lead to potential treatments for people who are allergic to poison ivy—an estimated 80 percent of the population.

For most people, contact with poisonous plants is painful but not life-threatening. Still, there are significant health care costs associated with more than 10 million people in the U.S. affected each year, said senior author Sven-Eric Jordt, Ph.D., associate professor of anesthesiology at Duke.

"Poison ivy rash is the most common allergic reaction in the U.S., and studies have shown that higher levels of carbon dioxide in the atmosphere are creating a proliferation of poison ivy throughout the U.S.—even in places where it wasn't growing before," Jordt said. "When you consider doctor visits, the costs of the drugs that are prescribed and the lost time at work or at school, the societal costs are quite large."

Some symptoms of the fiery, blistering rash can be alleviated with antihistamines and steroids. But in recent years, scientists have determined that the most severe itching doesn't go away with antihistamines, because it arises from a different source, Jordt said.

Jordt and collaborators determined the itch is triggered by interleukin 33 (IL-33), a protein in the skin involved in immune response.

All people have IL-33 in their skin, but the protein is elevated in people who have eczema and psoriasis, Jordt said. The protein is known for inducing inflammation, but these new experiments show the protein also acts directly on the nerve fibers in the skin, exciting them and telling the brain that the skin is severely itchy.

The researchers used an antibody to block IL-33 and found that it not only reduced inflammation, but also cut down scratching in mice with poison ivy rashes. An antibody that counteracts human IL-33 is currently being evaluated in humans through a Phase 1 clinical trial to determine its safety and potential side effects.

In an additional approach tested in the mouse experiments, the researchers also found they could also alleviate itch by blocking a receptor for IL-33, called ST2.

"There could be translational significance here," Jordt said. "So our next step will be to look at human skin to see if we see the same activity and the same pathways. We will also look at anti-inflammatory drugs that are already approved to see if they have the potential to alleviate itch."

More information: IL-33/ST2 signaling excites sensory neurons and mediates itch response in a mouse model of poison ivy contact allergy, *Proceedings of the National Academy of Sciences*, www.pnas.org/cgi/doi/10.1073/pnas.1606608113

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