Serotonin receptor is involved in eczema and other itch conditions

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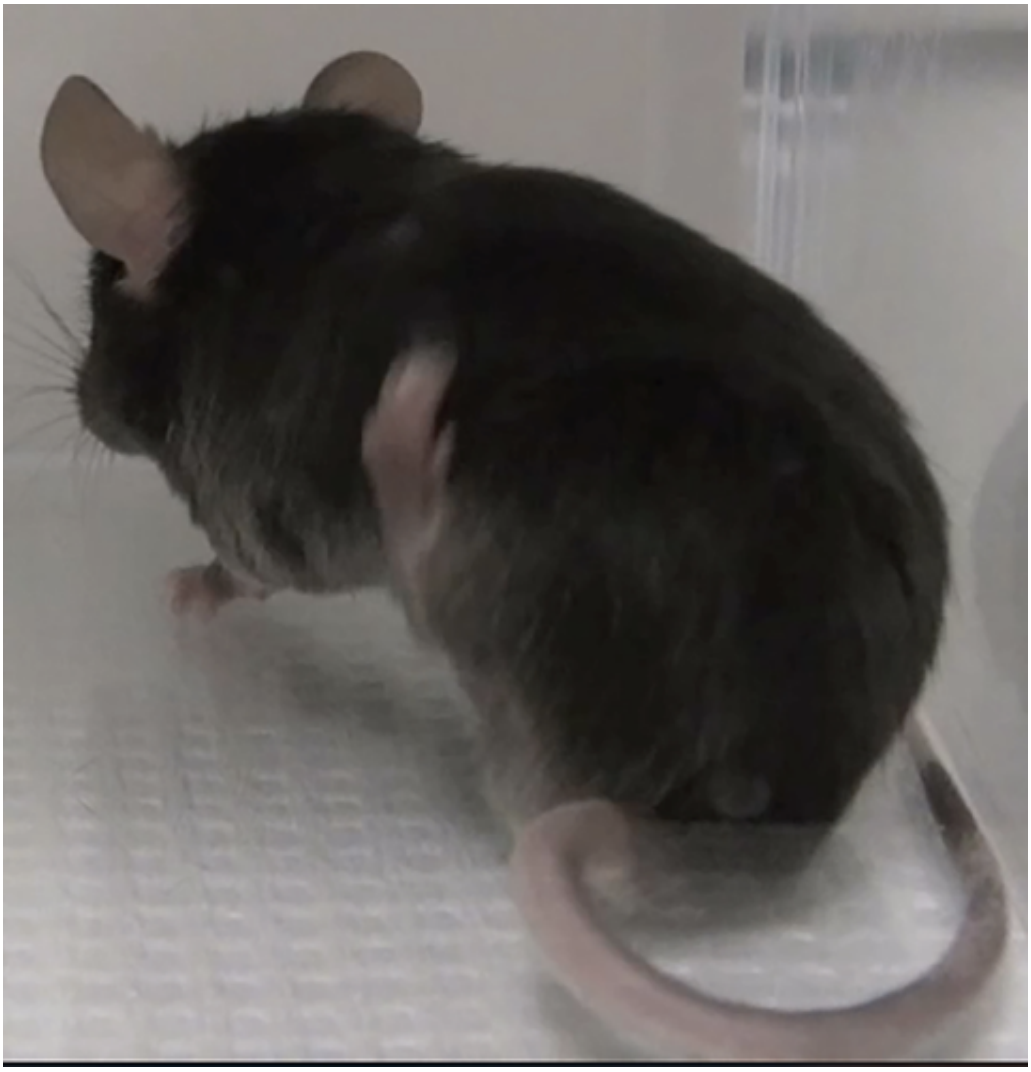

This mouse was involved in the study which identified serotonin receptor HTR7 as a key mediator of chronic itch. Credit: Courtesy of Diana Bautista, UC Berkeley

Dermatologists have long known that available treatments for chronic itch, including eczema, are simply not up to scratch. But scientists have now discovered a new gene that promotes itch, suggesting a way forward for powerful new therapies. In a paper published June 11 in the early-online edition of *Neuron*, researchers at the Buck Institute for Research on Aging and the University of California, Berkeley have identified a serotonin receptor, HTR7, as a key mediator of eczema and other forms of itch. Eczema is a debilitating condition that affects up to 10 percent of the worldwide population. Its symptoms include intense itch sensations, dry flaky skin, and a flaming red rash. Eczema can erode quality of life as dramatically as chronic pain does, and is incurable, and treatments to manage eczema are often not effective. But now, the Buck/Berkeley team has identified a new gene that may accelerate development of chronic itch therapies.

The work involved a collaboration between UC Berkeley neuroscientist Diana Bautista, Ph.D., who runs a lab focused on the molecular basis of the sensations of itch, touch and pain, and Buck Associate Professor Rachel Brem, Ph.D., a geneticist who studies how and why traits differ between individuals. Bautista, Brem, and collaborators sought out genes whose expression was correlated with itch behavior across genetically distinct mouse strains. The serotonin receptor, HTR7, caught the scientists' attention because the itchiest mice expressed the most HTR7 in the neurons that innervate the skin, and because abnormal serotonin signaling has long been linked to a variety of human chronic itch disorders, including eczema.

A battery of follow-up experiments then validated the role of HTR7 in chronic itch. In a mouse model of eczema, loss of the HTR7 gene in mice led to significantly less scratching and less severe skin lesions. 'We are really excited about these results. The dramatic decrease in itching suggests that HTR7 may represent a new drug target for chronic itch,' said Bautista, who is an associate professor in the Department of

Molecular and Cell Biology and a member of the Helen Wills Neuroscience Institute at UC Berkeley.

Brem says that, in addition to eczema, altered serotonin signaling in the skin is found in other forms of itch, including psoriasis and allergic itch. Therefore, the new findings hold promise for treatment of many itch disorders. In fact, in humans, itching and scratching can be side effects of taking antidepressants, which can elevate levels of serotonin in the skin. In the Buck/UC Berkeley study, this side effect was observed in mice, too—the drug Zoloft caused intense scratching, which vanished when HTR7 was ablated. Given that in humans HTR7 is also expressed in the neurons that innervate the skin, this new gene may well be responsible for itch in human patients taking antidepressants.

'An estimated 10 to 20 percent of the population will suffer from chronic itch at some point in their lifetime,' said Brem. 'In addition to eczema, chronic itch can stem from systemic conditions including kidney failure, cirrhosis and some cancers. Understanding the molecular basis of chronic itch is of significant clinical interest, and now there is a new target available to explore.'

More information: HTR7 mediates serotonergic acute and chronic itch, *Neuron*, 2015.

Provided by Buck Institute for Age Research