Scientists discover molecular trigger for itch

Identification of distinct neural circuit distinguishes the sensation from pain.

Chris Palmer

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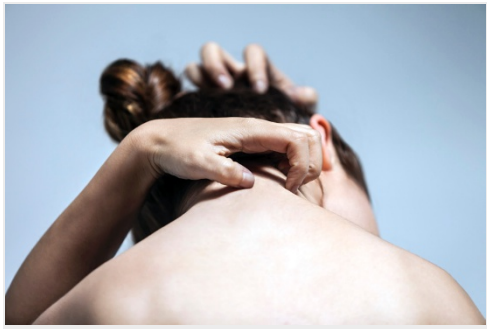
Once thought to be a low-level form of pain, itch is instead a distinct sensation with a dedicated neural circuit linking cells in the periphery of the body to the brain, a study in mice suggests.



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Researchers have discovered a protein that appears to be necessary for the itch response — at least in mice.

Neuroscientists Mark Hoon and Santosh Mishra of the National Institute of Dental and Craniofacial Research in Bethesda, Maryland, searched for the molecule that encodes the sensation of itch by screening genes in sensory neurons that are activated by touch, heat, pain and itch. They found that one particular protein, called natriuretic polypeptide b, or Nppb, was expressed in only a subset of these neurons.

Mutant mice lacking Nppb did not respond to itch-inducing compounds, but did respond normally to heat and pain. The researchers also found that when they injected Nppb in the mice's necks, it put them into a self-scratching frenzy. This occurred both in the mutants and in control mice.

“Our research reveals the primary transmitter used by itch sensory neurons and confirms that itch is detected by specialized sensory neurons,” says Hoon.

Hoon and Mishra went on to find neurons bearing receptors for Nppb in the spinal cord. Injection of a toxin made from soapwort seeds that targeted these spinal-cord neurons blocked itch responses, but not other sensory responses, suggesting that information about the itch sensation is transmitted along a distinct pathway. The researchers' results are published today in *Science*[1].

Treatment target

The result “explains problems in the literature and provides a very testable hypothesis for how itch works”, says Glenn Giesler, a neuroscientist at the University of Minnesota in Minneapolis.

Previous research suggested that gastrin-releasing peptide, or GRP, was the neurotransmitter released by sensory neurons to initiate itch-related signals[2]. But Hoon and Mishra, as well as another group of researchers[3], failed to find GRP outside the spinal cord, indicating that GRP is not the primary trigger.

However, Hoon and Mishra found that GRP is still involved in the itch response. Injecting GRP into mice lacking either Nppb or its receptor produced strong scratching responses. Also, mice in which GRP receptors were inhibited did not engage in scratching behaviour, even with spinal-cord injection of Nppb. These results place GRP-releasing neurons downstream of Nppb in the transmission of the itch sensation.

“This model fits better with what everyone else is seeing,” says Sarah Ross, a neuroscientist at the University of Pittsburgh in Pennsylvania.

The neural pathways for itch in humans are similar, though not identical, to those in mice, and it is unknown whether they involve Nppb or something similar to it, Hoon says. He adds that he plans to follow up with human studies later on.

Giesler says that itch is a common problem, being associated with more than two dozen conditions, including eczema and psoriasis. “Antihistamines work for a few forms of itch, but for the vast majority they do nothing,” he says. “This research introduces a brand new target for clinical treatment.”

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References

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3. Fleming, M. S. *et al*. *Mol. Pain* **8**, 52 (2012).