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RESEARCH NEWS

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Researchers Discover Molecule That Detects Touch

Researchers have identified a protein that may play an important role in sensing delicate touch. According to the scientists, their finding may offer new avenues for investigating the molecular basis of touch.

In an article published in the October 26, 2000, issue of the journal *Nature,* a research team that included Howard Hughes Medical Institute investigator Michael J. Welsh reported that knocking out the gene *BNC1* in mice greatly reduces the ability to sense light touch. Deleting the gene impairs the function of receptors that surround the hair follicles on the animal's skin. When a hair is touched, receptors near the hair fire, triggering a nerve impulse that signals that the hair has been moved.

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— Michael J. Welsh

"Although there has been excellent anatomical and physiological work on the sense of touch, the molecules that actually detect touch have remained elusive," said Welsh, who is at the University of Iowa School of Medicine. According to Welsh, the sense of touch is not as well understood at the molecular level as the senses of vision and smell primarily because it is difficult to study the tiny nerve endings that sense touch.

Nevertheless, scientists had long suspected that mechanical touch stimuli are translated into nerve impulses when ion channels are opened in response to touch. The opening of these channels, which are pores in the membranes of nerve cells, allows sodium to flood in, launching a nerve impulse. "The hypothesis that an ion channel is involved was based on the fact that a touch response is much faster than could be attributed to the types of slower chemical receptors that underlie vision or smell," said Welsh.

The scientists concentrated their studies on the sodium ion channel protein BNC1 because it was a mammalian member of a sodium channel family that had been implicated in touch sensing in the roundworm, *C. elegans.* BNC1's similarity to the worm channel led the scientists to test its involvement in touch. They found that BNC1 contributed to one form of touch, called rapidly-adapting light touch.

"Light touch allows you to detect, for example, a mosquito landing on your arm," said Welsh. "However, while this touch sense is sensitive, it does not persist. In the case of the mosquito, if you look away and the mosquito does not move or bite, you can no longer feel it." By contrast, said Welsh, mammals have other nerves that can detect heavier and more persistent touch sensation.

To investigate BNC1's function in mice, Welsh and his colleagues knocked out the gene for BNC1 and tested whether the skin of the mice showed normal detection of light touch. Gary R. Lewin and colleagues at the Max-Delbrück-Center for Molecular Medicine in Germany used a small computer-controlled probe to touch a patch of skin on the knockout mouse. This experimental approach enabled Lewin and his colleagues to record the level of electrical nerve impulse triggered by various levels of hair deflection. Lewin and Margaret P. Price of Welsh's laboratory were co-lead authors of the *Nature* article.

Tests of skin patches from normal and knockout mice revealed that the knockout mice had greatly reduced touch sensitivity when compared to normal mice. Touch sensation in the knockout mice was diminished, but it did not disappear entirely. "We postulate that the BNC1 channel may be one component of a larger receptor complex," he said. "In the absence of BNC1, other components of the channel may retain sufficient function for some residual sense of light touch."

Welsh and his colleagues also showed that BNC1 protein surrounds hair follicles, as would be expected for a protein involved in sensing touch. "We found the protein located in fibers that surround the hair shaft like a picket fence," said Welsh. "So, when a shaft of hair bends in any direction, these fibers are deflected."

BNC1 may also be involved in detecting pain, so the scientists explored whether neurons involved in pain-sensing functioned normally in the *BNC1* -knockout mice. "Those nerve cells seemed normal," said Welsh. "And although it's difficult to exclude the possibility that BNC1 is involved in pain perception, we could find no evidence for that involvement." Welsh emphasized that the discovery of BNC1's role opens a promising research pathway for understanding touch.

"I think this is an important first step toward understanding this elusive sense of touch," he said. "Now, we need to look at other members of this family of ion channel proteins, as well as the proteins that associate with these channels," Welsh said. Studies of BNC1 and related proteins may also aid in understanding the stretch-sensing mechanisms in blood vessels and the heart that signal the brain to control blood pressure, Welsh noted.