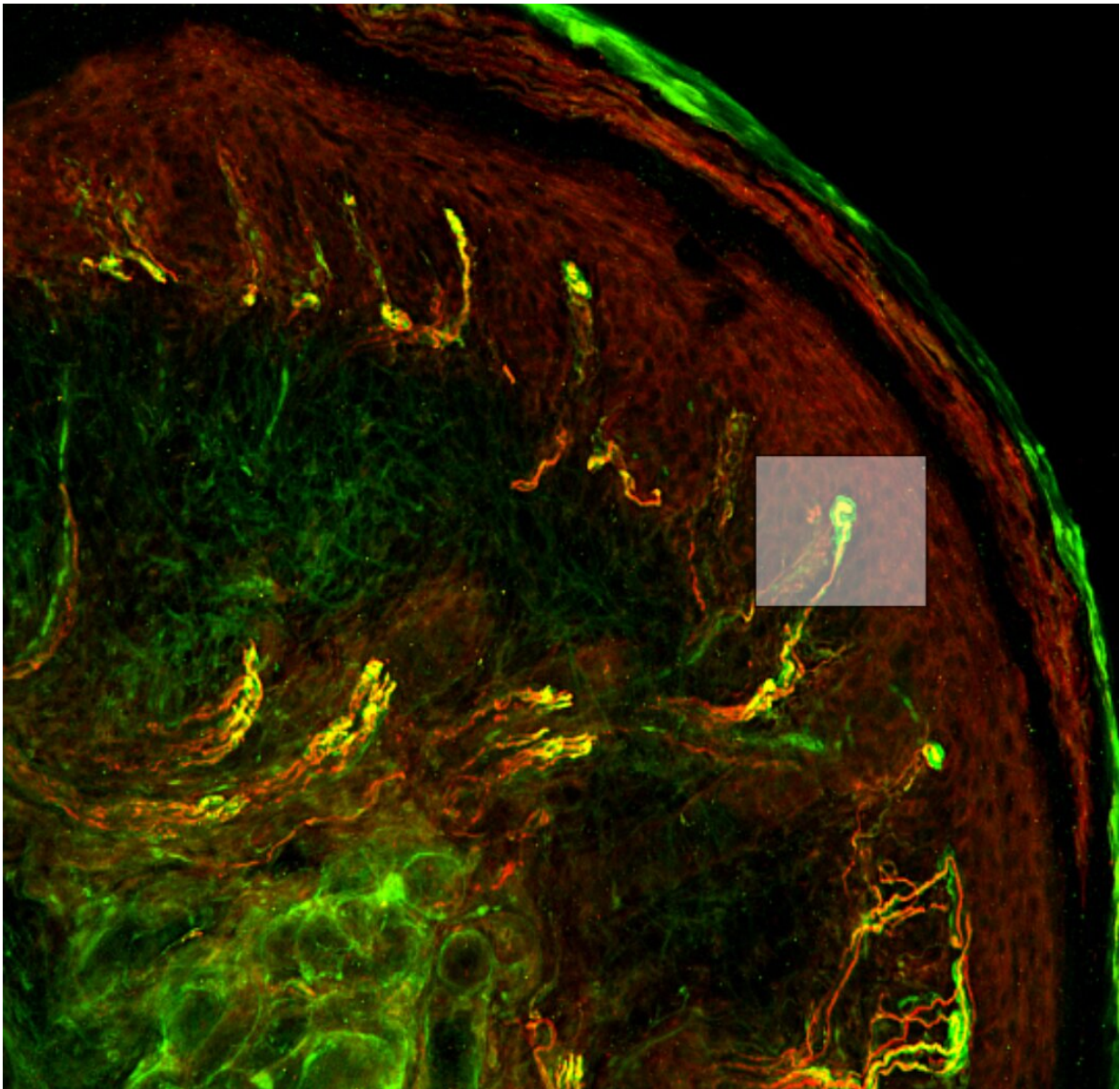


Feeling out fine differences in touch sensitivity

December 7 2020



Cross section through the skin with a number of Meissner receptors, one is highlighted in a box. Credit: Lewin Lab, MDC

A large protein produced in a unique structure in the fingertips, the Meissner corpuscle, plays a major role in touch sensitivity, new research finds. Identified in the 1850s by Georg Meissner, the Meissner corpuscle is an oval-shaped capsule found in the fingertips and lips, filled with cells intertwined with a nerve ending that sends a "touch" signal to the brain.

"For a century and a half, people have looked at the Meissner corpuscle and said "This is a beautiful structure, but we don't really know what it's there for," says Professor Gary Lewin, who heads the Molecular Physiology of Somatic Sensation Lab at the Max Delbrück Center for Molecular Medicine in the Helmholtz Association. In a new publication in the journal *Nature Neuroscience*, he and his team show that a [protein](#) made by the Meissner corpuscle is required to maintain normal touch perception.

The Usher connection

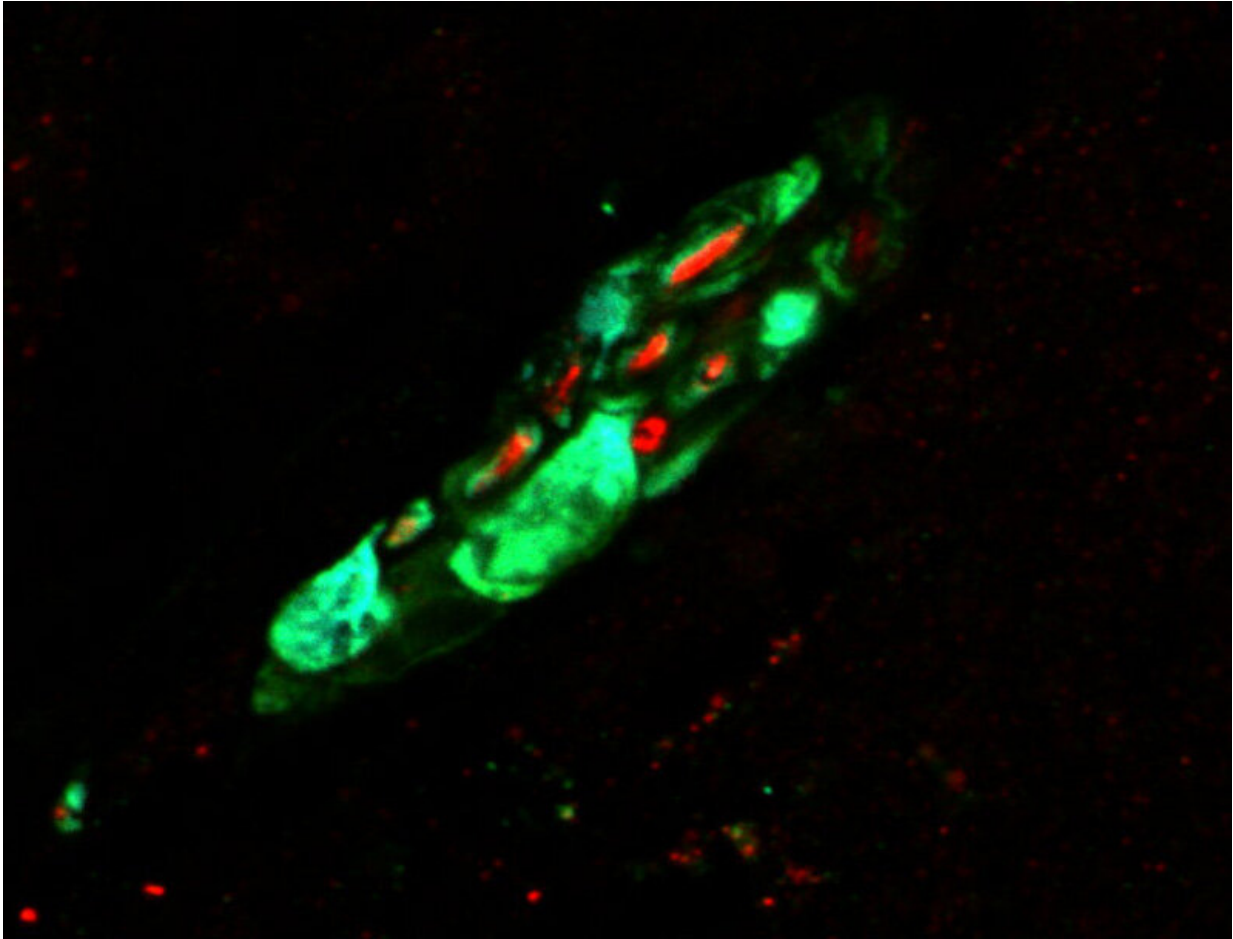
Based on previous research into the interplay between hearing and touch sensory systems, Lewin and his colleagues suspected that the protein USH2A may be involved in touch. Mutations in the gene, which codes for the USH2A protein, are common in Usher syndrome an inherited human disease, which includes hearing loss, tunnel vision and some loss of touch sensitivity.

To investigate, the researchers worked with 13 Spanish patients with Usher syndrome who have specific mutations affecting the USH2A protein. They wanted to find out what was the smallest vibration the

patients could perceive on their little finger. The researchers also tested their perceptions of temperature changes and small pin pricks. They conducted the same tests on healthy volunteers, mostly colleagues from the MDC, to compare results.

The patients with Usher syndrome could sense temperature changes and mild pain similar to the healthy controls, but had significantly reduced sensitivity to very small vibrations. Vibrations needed to be, on average, four times stronger before Usher patients could feel them.

"We are very sensitive to touch," Lewin says. "If you have a very good sense of touch, you can detect with your finger, the difference between a very fine silk and an even finer silk. But the Usher patients would not be able to tell the difference."



High resolution picture of the highlighted Meissner receptor with USH2A protein (green) and a sensory axon (red). Credit: Lewin Lab, MDC

Surprising results

While the [human studies](#) showed the USH2A protein is important for touch, it did not explain how or why. So the researchers turned to mice. First, Fred Schwaller, the lead author on the study, turned to the Neural Circuits and Behaviour Lab led by Professor James Poulet, who helped him train healthy mice and mice missing the USH2A protein to indicate when they felt very small vibrations on their forepaw. Just like the Usher

patients, mice without USH2A proteins needed a larger stimulus before feeling the vibration, but detected temperature changes and mild pain normally, suggesting the mechanism has been highly conserved through evolution.

"It's amazing to see the match between the patients and animal model. We were not expecting it to be so clear like that," says Dr. Valérie Bégay, a scientist in Lewin's lab who was involved in the study as well.

Looking more closely with the help of fluorescent biomarkers, Schwaller found the protein is produced by the cells in the Meissner corpuscle, and not in nerve cells like they had expected. "To our surprise, we could not detect the USH2A protein in sensory neurons; it wasn't there," Lewin says. This clearly demonstrated the Meissner corpuscle is essential for fine touch perception by producing the USH2A protein.

More to learn

The USH2A protein is quite large compared to other molecules in the body, and sits in the extracellular matrix of the corpuscle cells. Since [touch sensitivity](#) decreases when the protein is missing, Lewin theorizes that it serves as a physical connector, helping transmit [touch](#) vibrations from the outside of the fingertip to the nerve ending inside the corpuscle. His team is actively investigating the theory and he is interested to see what other elements the protein interacts with. "It is likely not working alone," he says.

The insight might help with research into related hearing and vision loss in Usher patients. While it is unlikely the protein works the same way in those systems, it might provide some hints about how mutations in the USH2A gene affect those senses.

The researchers were especially appreciative of their colleagues at MDC

who volunteered for the study, providing essential control data. More than 100 people over the past several years have participated. "You need good controls to increase confidence in your data, but it can be very difficult to get enough volunteers who are willing to concentrate closely for an hour or an hour and a half," says Bégay. "The support from our MDC colleagues has been invaluable."

More information: USH2A is a Meissner's corpuscle protein necessary for normal vibration sensing in mice and humans, *Nature Neuroscience* (2020). [DOI: 10.1038/s41593-020-00751-y](https://doi.org/10.1038/s41593-020-00751-y) , www.nature.com/articles/s41593-020-00751-y

Provided by Max Delbrück Center for Molecular Medicine

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