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Scientists develop new method that uses light to manage neuropathic pain in mice

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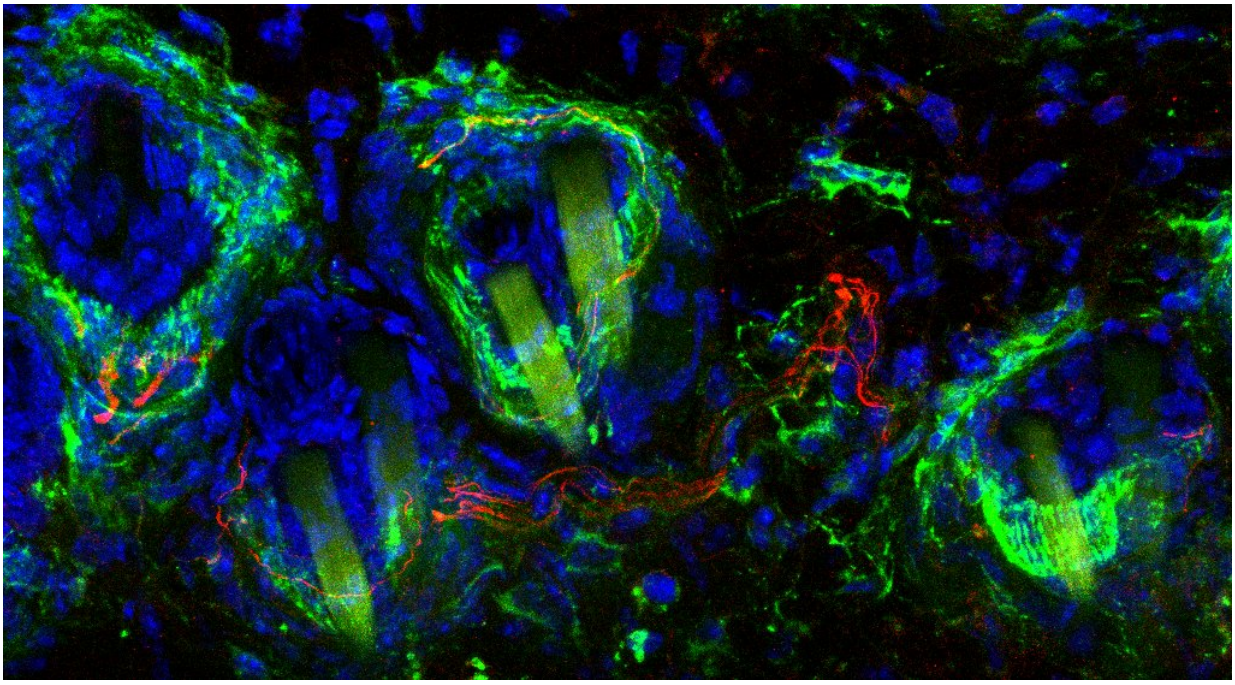

Hairy skin of a mouse, with the nerve cells that are responsible for sensitivity to gentle touch in green. The neurons are located around the hair follicles (in light green). Credit: Dhandapani et al., *Nature Communications*.

For patients with neuropathic pain, a chronic condition affecting 7 to 8 percent of the European population, extreme pain and sensitivity are a daily reality. There is currently no effective treatment. Scientists from EMBL Rome have now identified a special population of nerve cells in

the skin that are responsible for sensitivity to gentle touch. These are the cells that cause severe pain in patients with neuropathic pain. The research team, led by EMBL group leader Paul Heppenstall, developed a light-sensitive chemical that selectively binds to this type of nerve cell. By first injecting the affected skin area with the chemical and then illuminating it with near-infrared light, the targeted nerve cells retract from the skin's surface, leading to pain relief. *Nature Communications* publishes the results on 24 April 2018.

Strong curry

By clipping off the nerve endings with light, the gentle touch that can cause severe pain in neuropathic patients is suppressed. "It's like eating a strong curry, which burns the nerve endings in your mouth and desensitizes them for some time," says Heppenstall. "The nice thing about our technique is that we can specifically target the small subgroup of neurons causing neuropathic pain."

There are many types of nerve cells in skin, which cause specific sensations like vibration, cold, heat, or normal pain. These cells are not affected by the light treatment. The skin is only desensitized to the gentlest touch, like a breeze, tickling, or an insect crawling across the skin.

Illumination vs. drugs

Previous attempts to develop drugs to treat neuropathic pain have mostly focused on targeting single molecules. "We think, however, that there's not one single molecule responsible, there are many," Heppenstall explains. "You might be able to succeed in blocking one or a couple, but others would take over the same function eventually. With our new illumination method, we avoid this problem altogether."

Touch and pain were assessed by measuring reflexes in mice affected by neuropathic pain in their limbs. Affected mice will quickly withdraw their paw when it is gently touched. After the light therapy, however, they exhibited normal reflexes upon gentle touch. The effect of the therapy lasts for a few weeks, after which the nerve endings grow back and gentle touch again causes pain.

The team also investigated human skin tissue. The overall makeup of the tissue and the specifics of the neurons of interest appear to be similar, indicating that the method might be effective in managing neuropathic pain in humans. "In the end, our aim is to solve the problem of pain in both humans and animals," says Heppenstall. "Of course, a lot of work needs to be done before we can do a similar study in people with neuropathic pain. That's why we're now actively looking for partners and are open for new collaborations to develop this method further, with the hope of one day using it in the clinic."

More information: Rahul Dhandapani et al, Control of mechanical pain hypersensitivity in mice through ligand-targeted photoablation of TrkB-positive sensory neurons, *Nature Communications* (2018). DOI: 10.1038/s41467-018-04049-3

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