A New Scientific Breakthrough for Treating Chronic Pain

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The genetic study of a boy who is unable to feel pain has identified a protein that could be used to develop a new generation of analgesics for chronic pain.

From a physiological perspective, pain can be considered an alarm signal intended to preserve the body's integrity. For example, if your hand encounters a hot object, the sensory nerves present in this region will generate a nerve impulse that will first be routed to the spinal cord, then transmitted to the brain regions specialized in processing this information. Alerted by this message, the brain in turn sends a nerve impulse that travels back along the spinal cord, reaching the muscles controlling hand movements to move it away from the source of pain. This entire process is completed in a fraction of a second, making it possible to quickly put an end to a situation that could lead to serious injury if it persisted.

ABSENCE OF PAIN

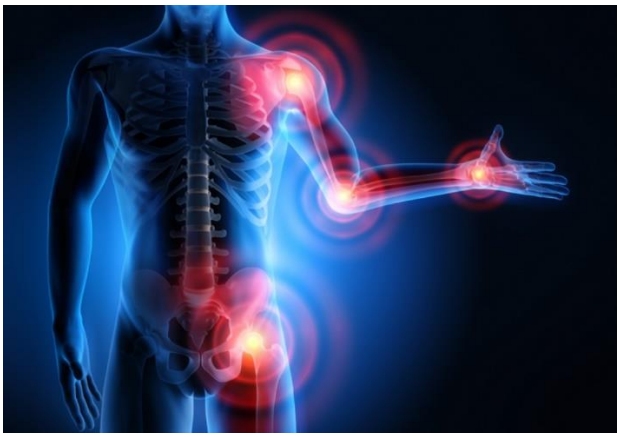
This protective system, essential for survival, is, however, defective in certain neurological disorders such as congenital insensitivity to pain. As its name suggests, individuals affected by this very rare genetic disease (about one in a million) can correctly perceive all physical sensations (touch, pressure), but are nevertheless, from birth, completely insensitive to painful stimuli. In the absence of this protective signal, these individuals are therefore constantly at risk of injuries (bites, burns, fractures) which, if left untreated, can cause disabilities or even serious, life-threatening infections. The molecular mechanisms involved remain poorly understood, but mutations in several genes essential for the sensation of pain have been identified, the best characterized being the one that prevents the production of a protein (called Nav1.7) in sensory nerves, thereby blocking the transmission of pain nerve impulses.

NEW GENE

According to new results obtained by a team of brilliant researchers at the University of Calgary, another protein, called USP5, could also play an important role in transmitting pain signals (1). In this study, the researchers analyzed in detail the entire genome of a child who died suddenly at the age of 16 and who had been completely insensitive to pain since birth.

This analysis revealed a unique mutation in a gene encoding the protein USP5, an enzyme (deubiquitinase) known to control the activity of an ion channel (Cav3.2) that transports calcium into sensory neurons and is involved in nerve impulses associated with pain. Since this channel is 99% identical to the one found in mice, they created an equivalent mutation in these animals using the CRISPR editing tool, a revolutionary technology (winner of the 2020 Nobel Prize in Chemistry) that allows for very precise modification of the sequence of any DNA.

They then observed that mice with a mutated USP5 protein were less efficient at detecting acute pain than normal mice and that they had also developed resistance to inflammatory and chronic pain.



CHRONIC PAIN

These results suggest that the USP5 protein could be an interesting target for the development of a new type of analgesic. This is particularly important in the context of chronic pain: it should be remembered that approximately 20% of the Canadian population is affected by persistent pain that disrupts daily activities and significantly reduces quality of life. This is a serious problem because these pains are often resistant to currently available analgesics, while those with a stronger pain-relieving effect, such as opiates, can create addiction problems. Another important step in pain research has thus been taken.

(1) Antunes FTT et al. A pathological missense mutation in the deubiquitinase USP5 leads to insensitivity to pain. J. Exp. Med. 2025; 222: e20241877.