

'Pain sensing' gene discovery could help in development of new methods of pain relief

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Nurse gives injection to woman, New Orleans, 1941. Credit: Wikipedia.

A gene essential to the production of pain-sensing neurons in humans has been identified by an international team of researchers co-led by the University of Cambridge. The discovery, reported today in the journal *Nature Genetics*, could have implications for the development of new

methods of pain relief.

Pain perception is an evolutionarily-conserved warning mechanism that alerts us to dangers in the environment and to potential tissue damage. However, rare individuals - around one in a million people in the UK - are born unable to feel pain. These people accumulate numerous self-inflicted injuries, often leading to reduced lifespan.

Using detailed genome mapping, two teams of researchers collaborated to analyse the genetic make-up of 11 families across Europe and Asia affected by an inherited condition known as congenital insensitivity to pain (CIP). This enabled them to pinpoint the cause of the condition to variants of the gene PRDM12. Family members affected by CIP carried two copies of the variant; however, if they had only inherited one copy from their parents, they were unaffected.

The team looked at nerve biopsies taken from the patients to see what had gone wrong and found that particular pain-sensing neurons were absent. From these clinical features of the disease, the team predicted that there would be a block to the production of pain-sensing neurons during the development of the embryo - they confirmed this using a combination of studies in mouse and frog models, and in human induced pluripotent stem cells (skin cells that had been reset to their 'master state', which enables them to develop into almost any type of cell in the body).

PRDM12 had previously been implicated in the modification of chromatin, a small molecule that attaches to our DNA and acts like a switch to turn genes on and off (an effect known as epigenetics). The researchers showed that all the genetic variants of PRDM12 in the CIP patients blocked the gene's function. As chromatin is particularly important during formation of particular specialised cell types such as neurons, this provides a possible explanation for why pain-sensing

neurons do not form properly in the CIP patients.

"The ability to sense pain is essential to our self-preservation, yet we understand far more about excessive pain than we do about lack of [pain perception](#)," says Professor Geoff Woods from the Cambridge Institute for Medical Research at the University of Cambridge, who co-led the study. "Both are equally important to the development of new pain treatments - if we know the mechanisms that underlie [pain sensation](#), we can then potentially control and reduce unnecessary pain."

PRDM12 is only the fifth gene related to lack of pain perception to have been identified to date. However, two of the previously-discovered genes have already led to the development of new pain killers that are currently being tested in clinical trials.

"We are very hopeful that this new gene could be an excellent candidate for drug development, particularly given recent successes with drugs targeting chromatin regulators in human disease," adds Dr Ya-Chun Chen from the University of Cambridge, the study's first author. "This could potentially benefit those who are at danger from lack of [pain perception](#) and help in the development of new treatments for [pain relief](#)."

More information: Chen, Y-C et al. Transcriptional regulator PRDM12 is essential for human pain perception. *Nature Genetics*; 25 May 2015. [dx.doi.org/10.1038/ng.3308](https://doi.org/10.1038/ng.3308)

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