Gene that controls chronic pain identified

Research lays groundwork for the development of new, targeted pain medications

A gene responsible for regulating chronic pain, called HCN2, has been identified by scientists at the University of Cambridge.

The Biotechnology and Biological Sciences Research Council (BBSRC) and EU funded research, published last week (09 September) in the journal *Science*, opens up the possibility of targeting drugs to block the protein produced by the gene in order to combat chronic pain.

Approximately one person in seven in the UK suffers from chronic, or long-lasting, pain of some kind, the commonest being arthritis, back pain and headaches.

Chronic pain comes in two main varieties.

The first, inflammatory pain, occurs when a persistent injury (e.g. a burn or arthritis) results in an enhanced sensitivity of pain-sensitive nerve endings, thus increasing the sensation of pain.

More intractable is a second variety of chronic pain, neuropathic pain, in which nerve damage causes on-going pain and a hypersensitivity to stimuli.

Neuropathic pain, which is often lifelong, is a surprisingly common condition and is poorly treated by current drugs.

Neuropathic pain is seen in patients with diabetes (affecting 3.7m patients in Europe, USA and Japan) and as a painful after-effect of shingles, as well as often being a consequence of cancer chemotherapy.

Neuropathic pain is also a common component of lower back pain and other chronic painful conditions.

Professor Peter McNaughton, lead author of the study and Head of the Department of Pharmacology at the University of Cambridge, said: “Individuals suffering from neuropathic pain often have little or no respite because of the lack of effective medications.

Our research lays the groundwork for the development of new drugs to treat chronic pain by blocking HCN2.”

The HCN2 gene, which is expressed in pain-sensitive nerve endings, has been known for several years, but its role in regulating pain was not understood.

Because a related gene, HCN4, plays a critical role in controlling the frequency of electrical activity in the heart, the scientists suspected that HCN2 might in a similar way regulate the frequency of electrical activity in pain-sensitive nerves.

For the study, the researchers engineered the removal of the HCN2 gene from pain-sensitive nerves.

They then carried out studies using electrical stimuli on these nerves in cell cultures to determine how their properties were altered by the removal of HCN2.

Following promising results from the in vitro studies in cell cultures, the researchers studied genetically modified mice in which the HCN2 gene had been deleted.

By measuring the speed the mice withdrew from different types of painful stimuli, the scientists were able to determine that deleting the HCN2 gene abolished neuropathic pain.

Interestingly, they found that deleting HCN2 does not affect normal acute pain (the type of pain produced by a sudden injury– such as biting one’s tongue).

Professor McNaughton added: “Many genes play a critical role in pain sensation, but in most cases interfering with them simply abolishes all pain, or even all sensation.

What is exciting about the work on the HCN2 gene is that removing it – or blocking it pharmacologically- eliminates neuropathic pain without affecting normal acute pain.

This finding could be very valuable clinically because normal pain sensation is essential for avoiding accidental damage.”