Scientists uncover Achilles heel of chronic inflammatory pain

August 17 2010

Researchers have made a discovery that could lead to a brand new class of drugs to treat chronic pain caused by inflammatory conditions such as arthritis and back pain without numbing the whole body.

The team, funded by the Biotechnology and Biological Sciences Research Council (BBSRC) and working at UCL (University College London), have shown for the first time that genes involved in chronic pain are regulated by molecules inside cells called small RNAs. This mechanism is so different from what has already been discovered about the biology underpinning pain that it could be the Achilles heel of chronic inflammatory pain, which is notoriously difficult to treat. The research appears in The *Journal of Neuroscience*.

Lead researcher Professor John Wood from UCL said "When a person experiences chronic pain as a result of some sort of inflammation - as in arthritis - their pain threshold goes down very dramatically. What they can normally do without pain, such as walking or putting on clothes, becomes very painful.

"Chronic inflammatory pain can be treated with pain-killing drugs - analgesics - but these usually have an impact on the whole body and may also dull our experience of acute pain, which is actually very important as it protects us from injury. Just imagine if you didn't get a sharp pain when you accidentally touch the oven - you wouldn't be compelled to take your hand away quickly and could end up with a serious burn.

"What we would really like to be able to do is return the pain thresholds to normal in a person who has chronic inflammatory pain, rather than just numbing the whole body. This would mean that they still get the protection of acute pain. Currently, aspirin-like drugs that can do this have a number of side effects but the present discovery might make it possible to invent a class of drugs that act in a completely novel way."

The researchers studied mice that lack an enzyme called Dicer in some of their nerve cells and found that they respond normally to acute pain but don't seem to be bothered by anything that would usually cause chronic inflammatory pain. This is because Dicer makes small RNAs, which they now know are required for regulation of genes involved in chronic inflammatory pain. Without Dicer the small RNAs aren't made and without the small RNAs many of these genes are expressed at low levels. So, for example, molecules such as sodium channels that make pain nerves responsive to inflammation are produced at low levels and therefore inflammatory pain is not detected by the mouse's body.

Professor Wood concluded "Knowing that small RNAs are so important in chronic inflammatory pain provides a new avenue for developing drugs for some of the most debilitating and life-long conditions out there. We have identified small RNAs, which are possible drug targets"

Professor Douglas Kell, BBSRC Chief Executive said "It is extremely important to be able to find out as much as possible about the fundamental processes of 'normal' biology, as a vehicle for understanding what may go wrong. Because these researchers have made efforts to unpick what is happening at a molecular level in our nerves, they have been able to lay the groundwork for future drug development in the important area of chronic pain. This is an excellent example of the basic research we have to do to help ensure that our increasing lifespan does not mean that the later years of our lives are spent in ill health and discomfort."

More information: "Small RNAs Control Sodium Channel Expression, Nociceptor Excitability, and Pain Thresholds", *The Journal of Neuroscience*, 2010, 30(32):10860-10871; doi:10.1523/JNEUROSCI.1980-10.2010