Discovery of why sunburn hurts could lead to new pain relief for inflammatory conditions

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CXCL5 recruits immune cells into the skin. Credit: King's College London

Researchers at King's College London have found a molecule in the body which controls sensitivity to pain from UVB irradiation, identifying it as a new target for medicines to treat pain caused by other common inflammatory conditions such as arthritis.

The molecule, called CXCL5, is part of a family of proteins called chemokines, which recruit inflammatory immune cells to the injured tissue, triggering pain and tenderness. This is the first study to reveal this molecule's role in mediating pain.

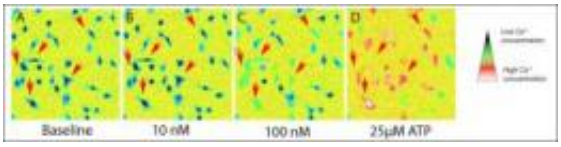
The study, funded by the Wellcome Trust (as part of the London Pain Consortium), and the UK's Biotechnology and Biological Sciences Research Council (BBSRC), is to be published in the journal *Science Translational Medicine*.

The research teams, led by Professor Stephen McMahon and Dr David

Bennett at King's College London, carried out a simple procedure in healthy human volunteers, to expose small patches of their skin to UVB irradiation, creating a small area of sunburn. The treated skin became tender over the following hours, with peak sensory change one to two days later. At this peak the researchers took small biopsies of the affected skin and analyzed the tissue for hundreds of pain mediators.

They found that several of these mediators were over-expressed, so they then examined the biology of these factors in rats to find out whether they were likely to be responsible for driving the pain in the sunburnt skin.

The mediator CXCL5 was significantly over-expressed in the human biopsies and the biology of this chemokine in rats, which suggests it is responsible for a significant amount of sensitivity in the sunburn.



CXCL5 activates cultured macrophages (immune cells). Credit: King's College London

Further tests carried out on the rats showed that a neutralising antibody targeting CXCL5 significantly reduced the sensitivity to pain caused by the UVB irradiation.

Professor Steve McMahon, from the Wolfson Centre for Age-Related Diseases at King's and head of the London Pain Consortium, said: 'These findings have shown for the first time the important role of this

particular molecule in controlling pain from exposure to UVB irradiation. But this study isn't just about sunburn – we hope that we have identified a potential target which can be utilised to understand more about pain in other inflammatory conditions like arthritis and cystitis.

'I'm excited about where these findings could take us in terms of eventually developing a new type of analgesic for people who suffer from chronic pain.'

The researchers say that not only are the findings of importance for understanding the aetiology of pain, but the approach they used by first identifying the mechanisms in humans and then looking at these in pre-clinical animal models is a novel one in the field of pain research.

Dr David Bennett, Wellcome clinical scientist at King's and honorary consultant neurologist at King's College Hospital, said: 'Traditionally scientists have first studied the biology of diseases in animal models to identify mechanisms relevant to creating that state. But this often does not translate into effective treatments in the clinic. What we have done is reverse this traditional method by identifying putative mediators in humans first, and then exploring this further in rats. This enabled us to see that the rats' response to these pain mediators closely parallel those occurring in humans and identify mechanisms of action in the preclinical studies.

'We intend to extend this approach to other types of pain and in particular to study patients suffering from chronic pain with the hope that this will speed up the process of turning science into effective treatments for patients.

'Improving healthcare by translating research more rapidly into clinical practice in this way is at the heart of our Academic Health Sciences

Centre, King's Health Partners.'

More information: UVB Irradiation–Induced Pain Is Mediated by CXCL5, *Science Translational Medicine.*

Provided by King's College London