New target for psoriasis treatment discovered

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Researchers at King's College London have identified a new gene (PIM1), which could be an effective target for innovative treatments and therapies for the human autoimmune disease, psoriasis.

Psoriasis affects around 2 per cent of people in the UK and causes dry, red lesions on the skin which can become sore or itchy and can have significant impact on the sufferer's quality of life.

It is thought that psoriasis is caused by a problem with the body's immune system in which new skin cells are created too rapidly, causing a build up of flaky patches on the skin's surface. It is not known exactly why this problem occurs but it is thought that certain genes may play a role.

The study, published today in *Science Translational Medicine* highlights for the first time the role of PIM1 and the IL-22 cytokine – a protein that sends messages between cells – in skin inflammation such as that seen in psoriasis patients.

Scientists, led by Professor Frank Nestle from the St John's Institute of Dermatology at Guy's and St Thomas' NHS Foundation Trust and King's College London, injected IL-22 into models of normal human skin in mice.

The changes that subsequently occurred in the skin were reminiscent of psoriasis. Injecting an antibody to block the IL-22 cytokine caused these changes to reverse.

They were then able to perform computer analysis, comparing the data from these human skin models with existing gene datasets, in order to identify the gene PIM1 as one of the genes 'switched on' by the presence of IL-22. They further showed that a small molecule drug blocking PIM1 was effective in models of psoriasis. The link between the IL-22 cytokine, which causes inflammation, and subsequent changes in the PIM1 gene suggests a direct link between PIM1 and psoriasis.

It is the first time that this gene has been identified as having a specific link to the condition. The combined use of computer analysis of complex gene data sets and disease relevant human skin models, also called integrative biology, is innovative and means that research can be more easily translated to further clinical studies for patient benefit. This new type of approach will likely generate more insights into disease mechanisms but also new drugs for the treatment of psoriasis, thereby reducing the gap between discovery and the clinic

Professor Nestle said: 'We have been able to confirm that the protein IL-22 causes inflammatory changes in human skin contributing to psoriasis.

The most exciting part of the study was that detailed analysis of genes induced by IL-22 in skin allowed us to uncover a novel treatment target for this disease. We are hopeful that our research will lead to the development of new approaches for the treatment for this common and irritating skin condition.'

The authors say that whilst this is a significant development providing proof of principle in pre-clinical models of disease, further research, in the form of clinical trials, is necessary in order to test potential new treatments for effectiveness in humans. However, as the findings are easily transferable to clinical studies, the discovery of this new gene target has promise for the development of new drug therapies.

More information: Integrative Biology Approach Identifies Cytokine Targeting Strategies for Psoriasis," by G.K. Perera et al. *Science Translational Medicine*, 2014.

Provided by King's College London