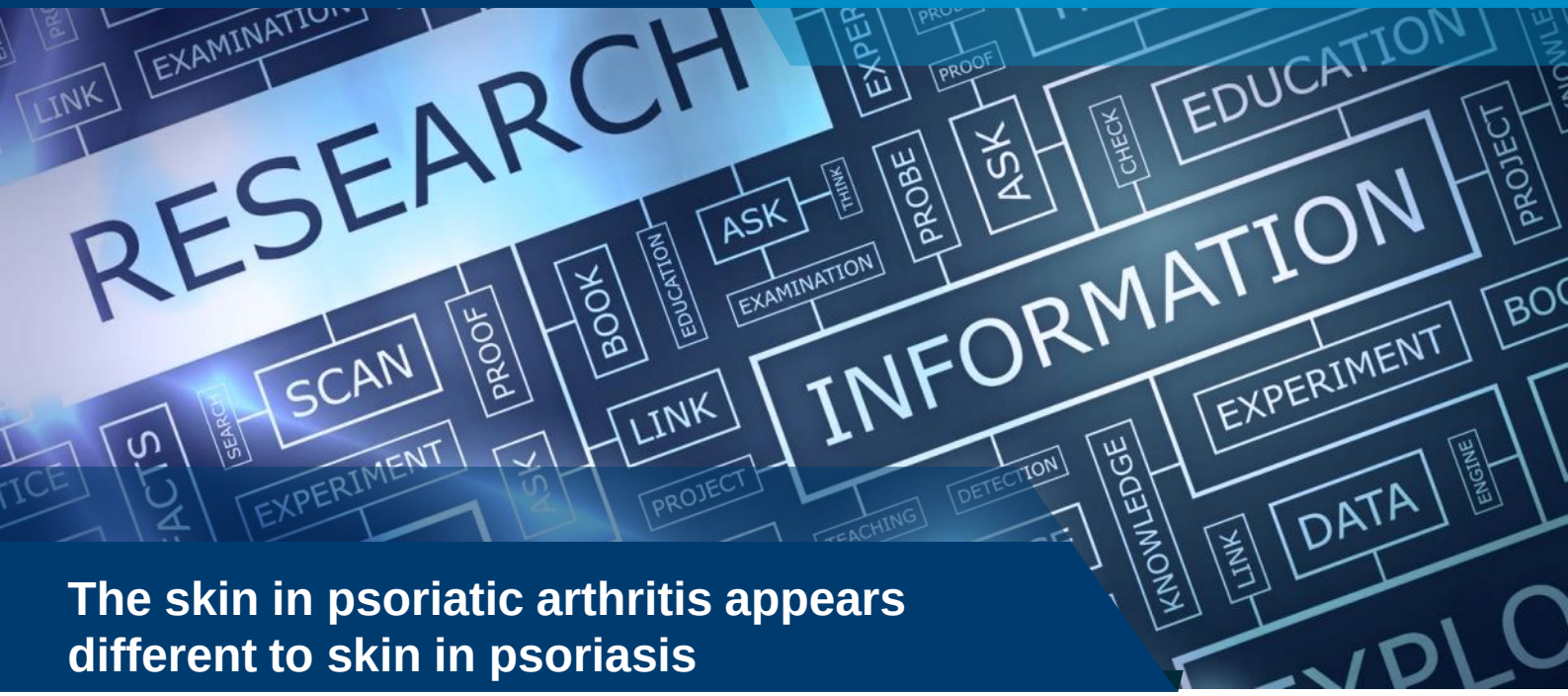
CHIEF SCIENTIST OFFICE

CODE: CAF/16/06

RESEARCH PROJECT BRIEFING



The skin in psoriatic arthritis appears different to skin in psoriasis

AIMS

Some patients with the common skin condition psoriasis also develop inflammation in their joints called psoriatic arthritis (PsA). Previous studies have shown that “normal looking” (unaffected) skin in patients with psoriasis is in fact abnormal on a molecular level. One molecule found at high levels in unaffected psoriasis skin is ACKR2 (Atypical Chemokine Receptor 2). It is thought to help prevent the rash from spreading. The skin in PsA has not been properly studied with the assumption being that it is the same as psoriasis skin. The aim of this project was to determine if unaffected skin in PsA is also abnormal, if the PsA skin rash is similar to the psoriasis skin rash and if ACKR2 may also be involved in limiting inflammation in PsA.

KEY FINDINGS

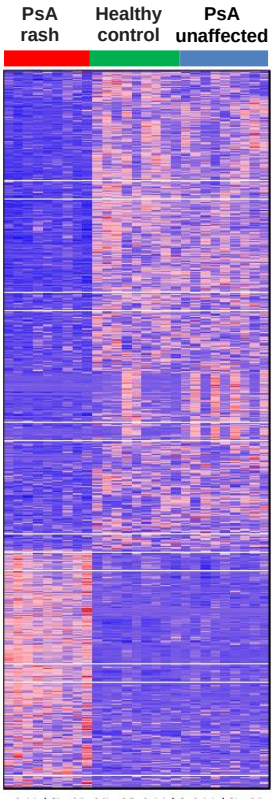
- There are fewer differences between unaffected skin in PsA and skin in healthy people than reported in other studies which compared unaffected skin in psoriasis to healthy control skin.
- However, the skin rashes in PsA and psoriasis appear similar.
- ACKR2 is high in the rash in patients with PsA, but not in unaffected PsA skin.

WHAT DID THE STUDY INVOLVE?

Skin biopsies were taken from healthy people (controls) and patients with PsA. Patients with PsA had skin biopsies taken from both unaffected skin and the skin rash. The skin biopsies were investigated for the activities of all genes which make protein (bulk RNA sequencing) and examined under the microscope (immunohistochemistry and RNAscope). The results were compared to findings in other published studies.

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

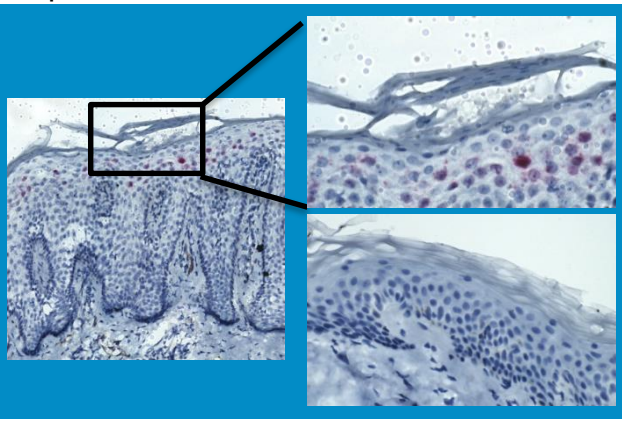
Healthy control skin and unaffected PsA skin are similar, but PsA rash is different. This picture is a heatmap which shows how active different genes are, with red being more active and blue less active. Each line is a gene and each column a sample. The nine samples in each group are next to each other, in the order of PsA rash, healthy control and PsA unaffected skin. It can be seen that samples from PsA skin rash are different to healthy control and PsA unaffected skin groups. The healthy control and PsA unaffected skin are however very similar with only 15 genes different. In contrast, other studies have found many genes to be different between unaffected psoriasis skin and healthy control skin. Many, but not all, of the genes which are different in PsA rash are also different in psoriasis skin rash.



ACKR2 is high in PsA skin rash. One of the genes which was high in the PsA skin rash but not changed in PsA unaffected skin was ACKR2. This was unexpected as an earlier study found it to be high in unaffected psoriasis skin. To investigate if there was a difference in ACKR2 between unaffected skin in PsA and psoriasis, further biopsies were taken from four patients with psoriasis. These results showed that, unlike the previous study, ACKR2 levels were high in the rash with unchanged levels in the unaffected psoriasis skin, similar to my findings in the PsA samples.

These findings have changed our understanding of ACKR2 and its potential role in preventing inflammation from spreading in the skin in psoriasis.

This picture shows PsA skin rash under the microscope. The outer top layer of the skin (the epidermis) is thickened. The top right shows part of the PsA rash at higher magnification and below it is a picture of PsA unaffected skin. The red dots are cells which make ACKR2. In the PsA skin rash there are many ACKR2 producing cells near the surface of the skin. These are not seen in unaffected skin.



WHAT IMPACT COULD THE FINDINGS HAVE?

If it is confirmed that the skin in PsA and psoriasis are different, it may help us to understand why some people with psoriasis develop PsA and to find a test for PsA. Currently, there is no reliable way of predicting who will develop PsA and the symptoms are sometimes not clear in the early stages. Diagnosing PsA early is important as patients who are treated early do better than those who are diagnosed and treated late. The differences in skin in PsA compared to psoriasis without arthritis may also help inform some of the processes involved in the joints.

HOW WILL THE OUTCOMES BE DISSEMINATED?

- Presentation at national and international scientific meetings
- Publication in peer review scientific journal

The results from this study will need to be confirmed by directly comparing samples from other patients with psoriasis and PsA. If the differences are confirmed, it will inform further studies into understanding the differences between psoriasis and PsA.

CONCLUSION

- Unaffected skin in PsA appears to be more similar to skin in healthy people in terms gene activity, than unaffected skin in psoriasis.

- The anti-inflammatory molecule ACKR2 does not seem to have a role in preventing the spread of the skin rash as previously suggested.

RESEARCH TEAM & CONTACT

Hanna Johnsson, Stefan Siebert, Iain McInnes, Gerard Graham

Hanna.Johnsson@glasgow.ac.uk

University of Glasgow, Institute of Infection, Immunity and Inflammation, 120 University Place, Glasgow G12 8TA

0141 3308379

Additional Information

CSO funded a Clinical Academic Fellowship for Dr Hanna Johnsson and research costs £149,365.98