

FOCUS ON RESEARCH

INDIVIDUALITY IN CUTANEOUS GENE EXPRESSION AS A POTENTIAL MARKER OF RESPONSE TO THERAPY IN PATIENTS WITH PSORIASIS – FURTHER VALIDATION OF THE EXPERIMENTAL MODEL

Researchers

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Aims

How much variation in the enzymes which metabolise drugs and protect us from ultraviolet light is there in skin of patients with psoriasis at:

1. Different body sites?
2. Different sites within a single plaque of psoriasis?

Project Outline/Methodology

Ten patients with untreated chronic plaque psoriasis were recruited. Skin biopsies were taken from psoriatic plaque and adjacent uninvolved control skin at trunk and limb sites in five patients, and from separate sites within a single plaque of psoriasis and adjacent control skin in the other five patients. We used sensitive laboratory methods to compare DME and CP gene expression in control skin and in psoriasis plaque at different body sites and at different sites within a single plaque of psoriasis.

Key Results

In previous CSO-funded work, we showed that many DMEs and CP genes are expressed in healthy human skin and that gene expression is altered in plaque psoriasis, suggesting that inter-individual differences in gene expression may influence treatment response in psoriasis patients. In this study, we confirmed individuality in the expression of a variety of enzymes. We found significant differences in gene expression in non-lesional control skin of psoriasis patients at different body sites. However, there were no significant differences in gene expression in psoriatic plaques at different body sites or in separate sites within a single plaque of psoriasis.

Conclusions

This study has allowed us to confirm that different patients have different enzyme expression in skin, and has shown that intra-plaque variation in gene expression in a single subject is not significantly altered at different body sites or within a single plaque of psoriasis. These data validate the use of this experimental approach to study gene expression and regulation in human skin and will allow us to continue our studies relating individuality in gene

expression in skin with treatment responses in psoriasis patients.

What does this study add to the field?

This study has allowed us to confirm marked inter-subject variability in enzyme expression and validates the use of this *in vivo* model for the study of individuality in response to existing and novel therapies for psoriasis. These results enable us to extend our analyses to identify enzymes which may influence treatment response and to develop tests which may allow us to predict which patients will best respond to existing and novel anti-psoriatic treatments.

Implications for Practice or Policy

Psoriasis affects 2-3% of the population and is a cause of considerable morbidity, time off work and psychological disturbance. Treatments for psoriasis are often only partially effective and difficult to use, and we are currently unable to predict treatment response in individual patients. There is therefore a clinical need to develop new therapies for psoriasis with improved outcomes, and to identify predictive markers of treatment response. The findings of this study are important as they justify further analysis of these genes as predictive markers of treatment response, which may lead to the development and optimisation of new therapies for psoriasis. These approaches could ultimately lead to the possibility of cost effective personalised treatments for psoriasis and other common skin diseases.

Where to next?

We intend to extend the findings of this study to larger patient groups to further examine the mechanisms of action, therapeutic and adverse effects of a range of anti-psoriatic therapies, with a view to the identification of new therapeutic targets and possible predictive markers of outcome.

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