

ABSTRACT

Psoriasis is a chronic inflammatory condition of the skin affecting approximately 2% of the world population. The disease causes red scaling skin lesions, which can be painful. Patients often suffer from depression and anxiety due to the implicated disfigurement. The cause of psoriasis is unknown, but it appears to involve dysregulation of the intricate homeostatic balance between keratinocytes, T-cells and cytokines such as tumor necrosis factor- α (TNF- α). There is no cure for psoriasis; the condition is currently managed using a range of anti-inflammatory agents that have potentially serious side effects. These agents include immune response modifiers that neutralize the activity of TNF- α . Unfortunately, this strategy can lead to severe immune suppression with increased risks of infections, reactivation of latent infections such as tuberculosis and hepatitis, and lymphoma.

We have demonstrated that immediate-early inflammatory stimuli drive keratinocyte expression of a range of chemokines, suggesting that the initial activation of inflammation itself may contribute to psoriasis pathology through enhanced recruitment of T-cells into the skin. The specific targeting of these inflammatory processes may represent a promising new approach to the management of psoriasis. We will test if two novel immune response modifiers can alleviate skin inflammation through down-regulation of inflammatory gene expression and chemotaxis. Activities will be examined in human tissue cultures and a mouse model resembling psoriasis. This project will combine Dr. Jensen's extensive experience with inflammation with Dr. Herlyn's leading expertise in 3-dimensional tissue culture models and skin physiology.