

The imiquimod mouse model of psoriasis

Psoriasis is a complex, chronic, immuno-inflammatory skin disease characterized by thickening and scaling of the skin. Although it is generally accepted that type 1 helper T-cells, and mediators released by them, play a central role in the development of psoriasis, it is likely that other cell types (e.g. dendritic and natural killer cells) are also involved.

The daily topical application of Imiquimod to mouse skin results in a dermal inflammation characterized by parakeratosis, epidermal thickening, acanthosis, and cellular infiltration. These are characteristics of psoriasis. Importantly, as in psoriasis, IL-23 and IL-17 play an essential role in the mechanism of psoriasis (See Reference).

Possible mechanisms by which imiquimod induces a skin lesion in mice

- TLR7 dependent activation of MyD88 pathway in immune cells.
- NALP3 activation of the inflammasome.
- Antagonism of adenosine receptor signalling resulting in reduced levels of cyclic AMP.
- Direct cytotoxic effect of Imiquimod leading to the release of preformed IL-1 α .

Protocol

- Day 1. The backs of BALBc mice, 8-11 weeks old, are shaved.
- Day 2-6. Mice are treated 1 x day topically with 62.5 mg of commercially available 5% imiquimod cream (Aldara; 3M Pharmaceuticals)
- Day 6. Mice are sacrificed and samples of the back skin treated for histological examination (paraffin or frozen sections).

End points

- Skin thickness, scaling and redness are measured/evaluated daily.
- Other parameters (characterisation of infiltrating cells, cytokine expression, gene expression etc) can be measured after consultation with the client.

Advantages of the model

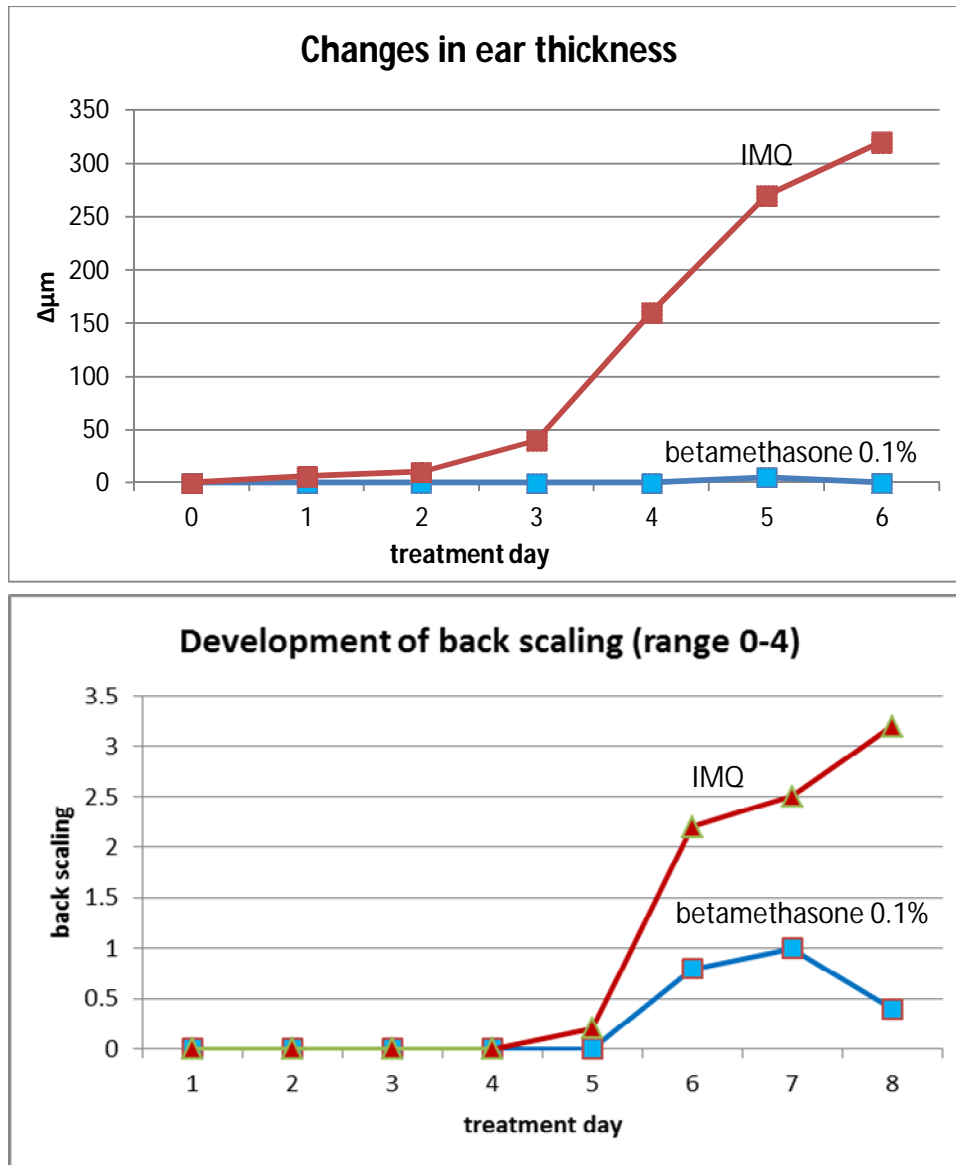
- Compounds can be tested quickly
- Compounds can be administered by all routes used to treat patients
- Combination of this model with the acute lesional psoriasis skin explant and the chronic transplant model of psoriasis will allow a routine development and screening of compounds in vitro and then in vivo at one centre, saving time and money

Time lines

- Animal ethical committee approval: 2 months
- Order mice and allow to acclimatize: 3 weeks
- Experimental phase: 6 days (mice can be pre-treated before we apply Imiquimod).
- Basic Histological/IHC analysis: Usually less than 3 weeks (depends on agreed parameters).
- Other parameters (qPCR, ELISA, blotting etc.): Depends on what is agreed with client.
- Preparation of initial report: 2 weeks.

Note: In addition to the preclinical services, Derphartox can also support you with the development, preparation and submission of the essential documents for early phase clinical trials when the decision is made to proceed to the proof of concept in humans.

Data imiquimod mouse model of psoriasis



Associated (disease) models

- Normal and diseased human skin explant culture
- The human skin transplant model of psoriasis
- Mouse oxazolone-induced delayed type hypersensitivity model (also for pruritus)
- Wound healing (in vitro and mouse and humanized mouse models)

Contact persons and details

Graham Elliott, PhD & Clifton Meije, PhD
 E: info@derphartox.com
 W: www.derphartox.com
 M: +31 (0)614716584/+31 (0)636579694

Reference

Van der Fits, et al., J. Immunol. 2009. 182:p5836–45.