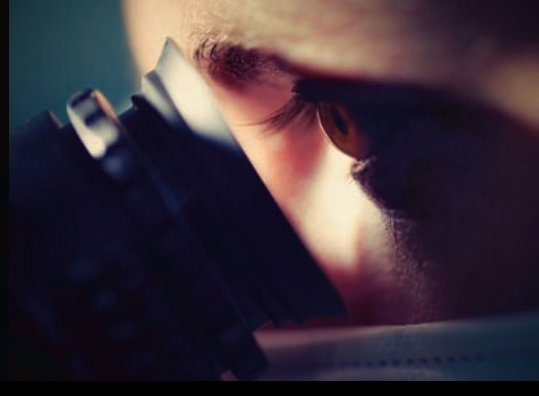

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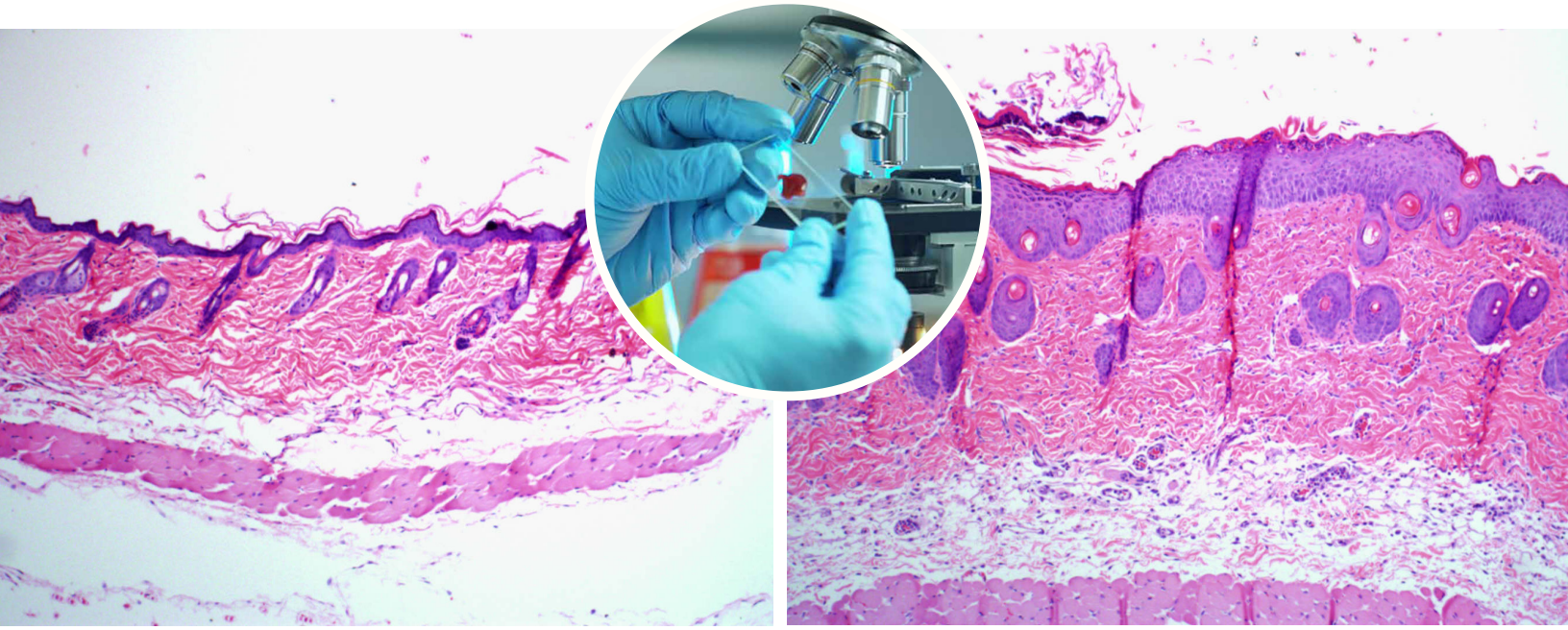
A TRANSLATIONAL APPROACH TO PRECLINICAL RESEARCH

Technical Bulletin:
IMIQUIMOD-INDUCED DERMATITIS IN MICE



A Model of Psoriasis

Psoriasis is a chronic skin condition associated with multiple contributing factors including autoimmune disease. The imiquimod-induced Psoriasis model is particularly translational into the clinic as it has many of the significant markers of human disease, including histopathology of lesions and strong activation of the immune system. CBI's extensive immunology expertise allows our scientists to implement these translational models to mimic human disease, and our experienced pathologists can analyze the pathology associated with the Psoriasis disease model.

In our studies we present various in vivo dermal models that mimic these clinical conditions.

Imiquimodis - Induced Dermatitis In Mice:

- Lesions similar to man
- Erythema, swelling and scaling
- Histologically similar to man
- Responds to similar human therapies

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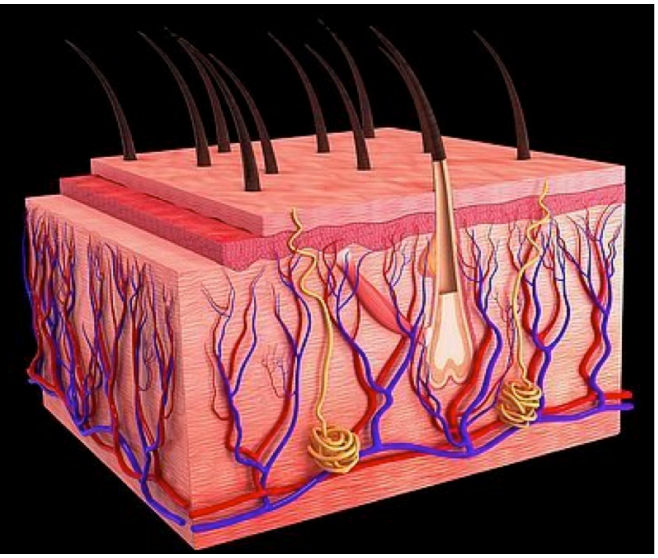

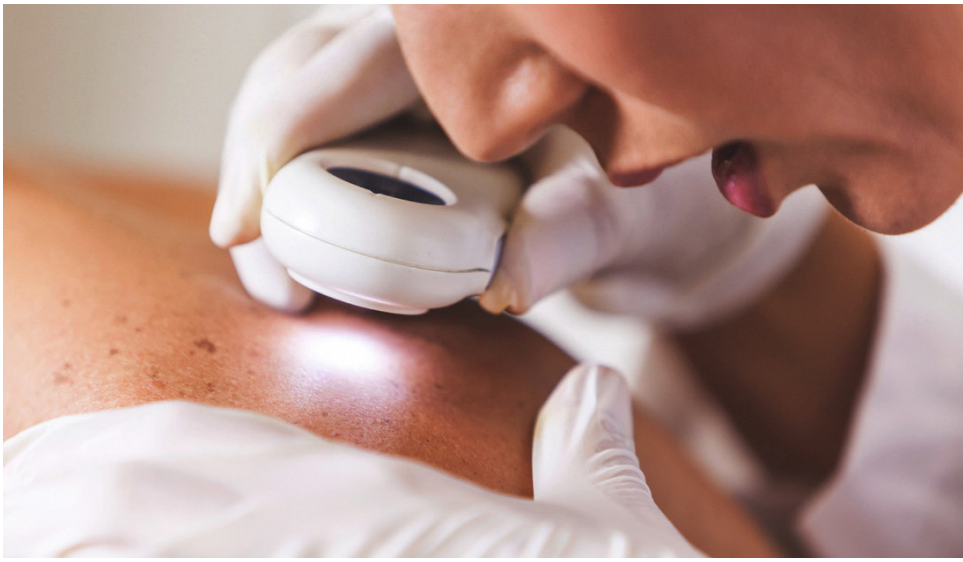

IMQ-Induced Psoriasis Mouse Model / Overview

Imiquimod (IMQ) produces a cutaneous phenotype in mice frequently studied as an acute model of human psoriasis.
IMQ is a Toll-like Receptor (TLR7) agonist that can be applied to mouse skin to elicit erythema, scaling, epidermis hyperplasia, hyperkeratosis, parakeratosis and dermis inflammation. IMQ induces also IL-17/ IL-23 axis cytokines.
At CBI, Imiquimod-Induced Psoriasis Mouse Model is a **convenient, easy-to-use and affordable mouse model of acute inflammatory response,** which is widely used in mechanistic pharmacology of pathology and as a pre-clinical animal model for drug screening and testing before clinical testing on volunteers psoriatic patients.

INTRODUCTION:
Psoriasis is a chronic inflammatory skin disease affecting up to 2–3% of the world's population. Psoriasis is characterized by the presence of scaly skin plaques that display histological features including a thickened stratum corneum (hyperkeratosis), retention of nuclei within corneocytes (parakeratosis), and infiltration of inflammatory cells. The term psoriasis is derived from the Greek word "psora," meaning "itching condition." Pruritus has been reported in 60–90% of psoriasis patients. One of the aggravating factors of psoriatic itch is contact with clothes. This phenomenon, known as alloknesis, results from the sensitization of itch signaling pathways and is an important aspect of chronic itch. As chronic itch is extremely difficult to treat, there is no universal treatment for psoriatic itch.

The pathogenesis of psoriasis has been investigated through the study of human as well as animal models. Repeated topical application of the drug imiquimod on the skin induces psoriasis-like inflammation in mice as well as humans and is considered a valid model for psoriasis. The pathogenesis of itch in psoriasis is unclear. A recent study found that there is no correlation between the severity of the disease and the intensity of pruritus in patients with psoriasis.

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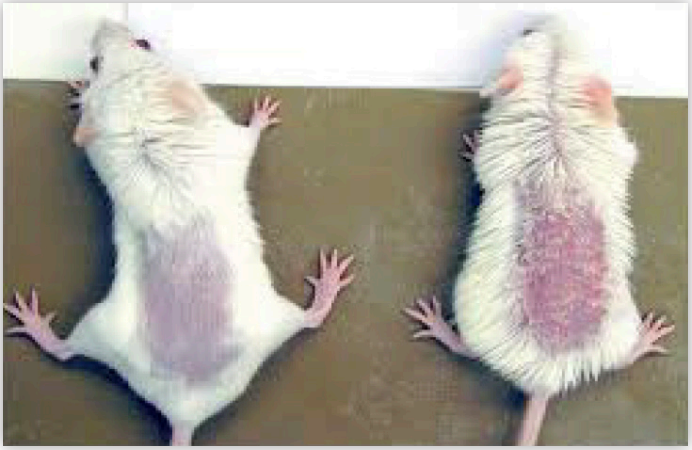
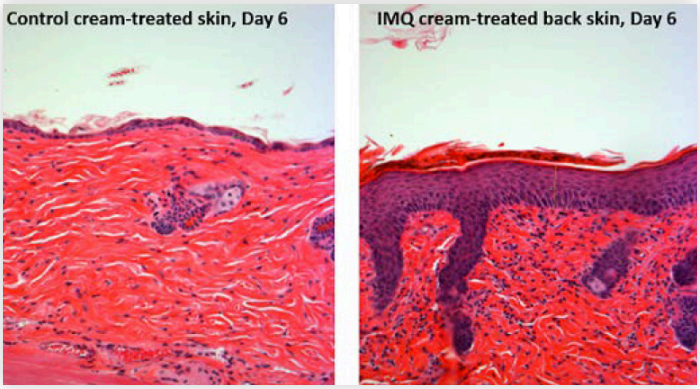




Imiquimod-Induced Dermatitis: Pathology

GROSS PATHOLOGY

. Left: Normal Mouse

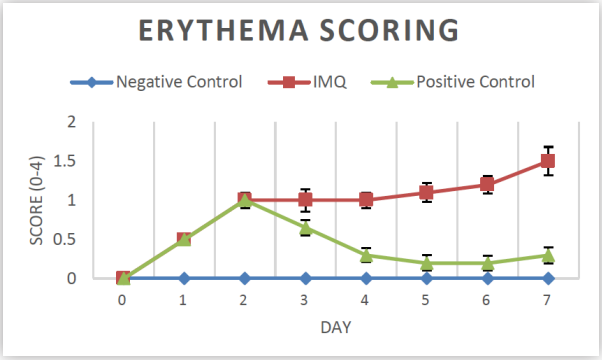
. Right: Imiquimod-Treated Mouse

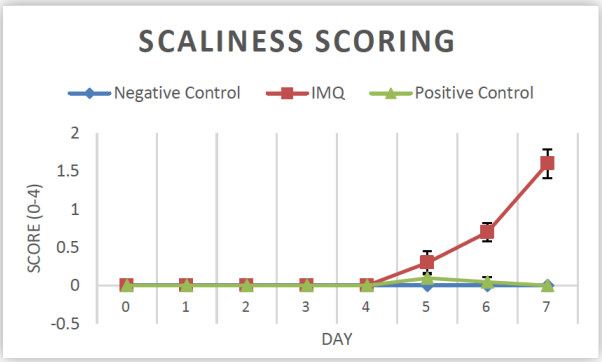
MICROSCOPIC PATHOLOGY

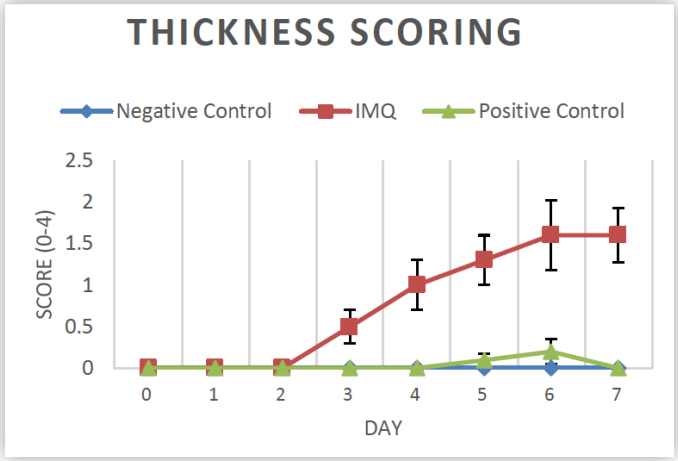
. Left: Normal Skin

. Right: Imiquimod-Treated Mouse with Increased Epithelial Thickness and Dermal Inflammation

Imiquimod-Induced Dermatitis in Mice: Dermal Clinical Assessments







Imiquimod produces increases in dermal thickness, erythema and scaliness. The positive control (clobetasol) reduces the clinical signs.

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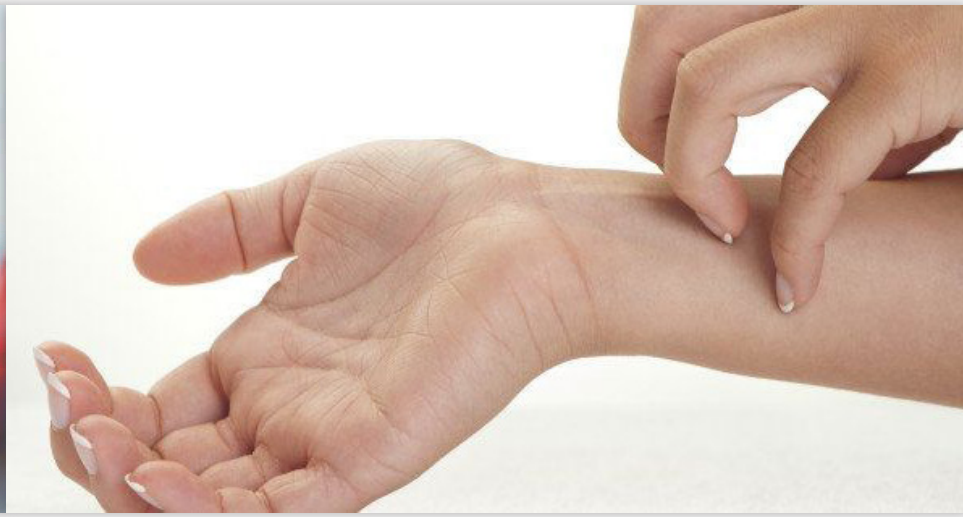

SUMMARY:
IMQ-Induced Psoriasis Mouse Model

• CBI offers a robust and validated murine model of psoriasis induced by dermal application of imiquimod, an emmune modifying toll-like receptor agonst.

• Topical application to susceptible BALB/c mice rapidly induces apsoriatic skin inflammation that responds to standard treatment with clobetasol.

• Lesions similar to man and characterized by application site increases in erythem, dermal thickness and scaling that is similar to psoriasis in patients.

CONSULTATION, STUDY AND REFERRAL GUIDELINES CITING THE EVIDENCE:
HOW THE ALLERGIST / IMMUNOLOGIST CAN HELP.

The statistics are clear. Lack of appropriate management of allergies and asthma results in a tremendous financial burden and impacts the quality of life for millions of people with allergic disease. For many of our clients, working with an allergist / immunologist can be beneficial in managing their disease studies.

HOW CAN CBI IMMUNOLOGISTS SUPPORT YOUR PROGRAM?

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