

VISUAL EXPERIMENT

## Imiquimod-induced psoriasis-like skin inflammation in mouse model

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### ABSTRACT

Psoriasis is a skin disorder characterized by skin inflammation and plaques. Induction of psoriasis in animal model include following steps: a) Selection of animal model, b) Hair removing from the back or ear, c) treatment of skin with Aldara, a cream containing 5% imiquimod and d) Observation. Imiquimod-induced skin inflammation in animal model resembles with psoriasis.

### INTRODUCTION

Psoriasis is chronic inflammatory skin disease. The disease is characterized by skin inflammation, plaques and increased vascularity in dermis. Approximately 125 million people are affected with this disease worldwide. The disease onset is generally between 15-25 years of age. However, it may affect people of all ages. The excessive growth of epithelial cells results in plaques; therefore, alters the structure of skin phenotypically. Like ulcerative colitis, the etiology of psoriasis is not completely known; however, it is considered to be a complex autoimmune inflammatory disorder.

In recent years, models of psoriasis have been studied for pre-clinical studies on monkey (Lowe et al., 1981; Zanolli et al., 1989) and mouse (Gudjonsson et al., 2007). Knockout, multiple transgenic and reconstituted models of psoriasis have been developed. However, not all models resemble with human psoriasis. Imiquimod-induced psoriasis-like skin inflammation in mice model is considered to have same resemblance with human psoriasis. The treatment of skin with Aldara (a cream containing 5% imiquimod) on the ears and hair-free back of mice results in skin inflammation (psoriasis-like lesions), redness and skin thickening within 5 days of application (van der Fits et al., 2009). Drugs like corticosteroids and cyclosporine A are found effective at treating psoriasis. In this visual experiment, we demonstrated the induction of imiquimod-induced psoriasis-like skin inflammation in mice.

### MATERIALS AND EQUIPMENTS

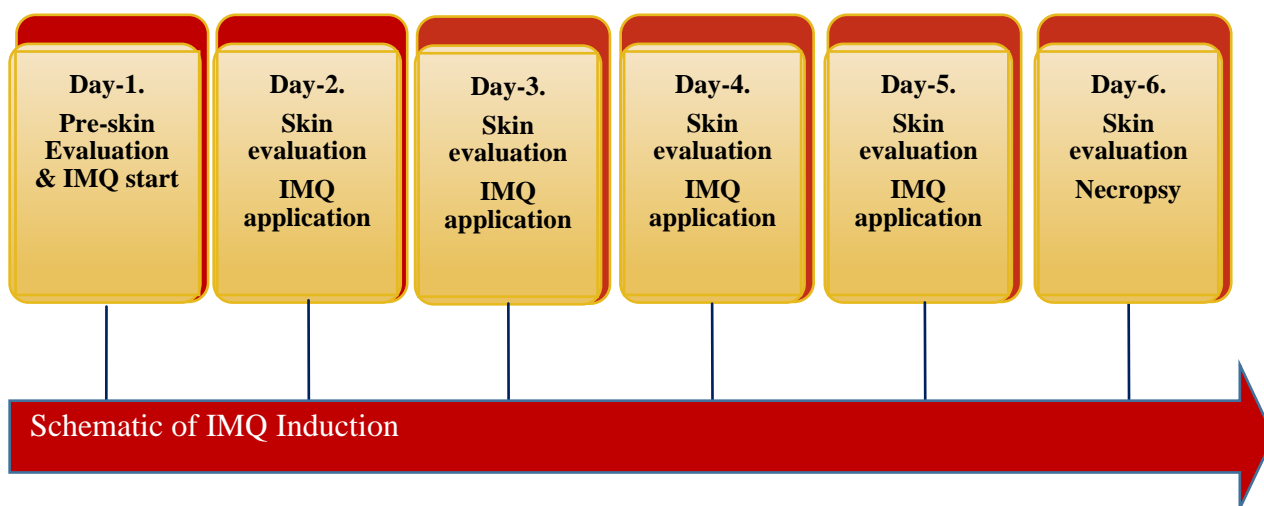
1. Mice
2. Mini electric hair clippers
3. Hair removing cream
4. Aldara containing 5% IMQ
5. Sterilized plastic spatula
6. Sterilized cotton buds or apply brushes
7. Gloves

8. Mask
9. Micrometer or caliper to measure skin and ear thickness

### PROTOCOL

1. Shave mouse on back using hair removing cream (anesthetize lightly if you are not comfortable; however, try to avoid anesthetizing mice).
2. Apply Aldara cream containing 5% imiquimod using plastic spatula or cotton bud or apply brush on shaved skin on back and on ear.
3. Cage each mouse individually.
4. Continue the same procedure for 5-7 consecutive days, depending on the results you will see after 5 days of application of Aldara.
5. Measure skin thickness and ear. The skin thickness may increase after day 2 and ear from day 4. So, it is recommended to measure skin thickness from day 2.
6. Check the parameters like erythema (skin-redness), increase in scales, and skin thickening.
7. Once the signs of psoriasis are achieved, sacrifice the mice and analysis based on your requirements.

Other parameters such as spleen weight, mRNA expression levels such as IL-17, IL-23, and TNF- $\alpha$  can be evaluated from spleen and skin.



Please note that one sachet of Aldara cream contains 250 mg, divide it into four equal parts on a non-sticky butter paper using sensitive balance and use one sachet for 4 mice (i.e. 62.5 mg per mouse).

### Scoring severity of skin inflammation

The scoring system should be developed based on the clinical Psoriasis Area and Severity Index (PASI). To make it easy, score erythema (redness), scaling, and skin thickness on a scale of 0-4. Follow the scoring scale as below:

Value	0	1	2	3	4
Result	None	Slight	Moderate	Marked	Very marked

The erythema that skin redness is evaluating visually; therefore, it may lead to inconsistent results. To avoid such variations, please follow scoring tips as below:

Lesion color	Value
No lesion	0
Slightly pink	1
Pink	2
Red	3
Dark red or purple	4

## VIDEO CLIPS

Part 1: 9 min 10 sec

## DISCUSSION

Psoriasis is a chronic skin disease that causes skin cell to build up rapidly results in thick, scaly and itchy skin. At present, there are number of treatments for psoriasis, and treatments are chosen based on the servility of psoriasis. Nevertheless, there is no permanent cure for psoriasis, the primary goal of every treatment is to inhibit the skin cells from growing rapidly. In this study, drug-induced psoriasis is developed. Psoriasis can also be developed transplanting the psoriatic skin (xenograft model) onto immunodeficient mice. This model is claimed to be the only model that is close to incorporate the immunogenic, genetic and phenotypic changes of psoriasis (Gudjonsson et al., 2007). Xenotransplant model has several limitations. They are technically difficult as they require large keratome sheets or multiple punch biopsies from patients. The grafting needs to be done quickly to minimize graft ischemia (Gudjonsson et al., 2007).

Imiquimod is also used to induce psoriasis to measure the skin penetration of some anti-psoriatic drugs (Lin et al., 2015).

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## PRECAUTION

It is possible that if imiquimod treatment is more than 5-6 days, few mice may die out of 10-12 due to prolonged exposure and dehydration.