Hapten-induced Atopic Dermatitis in Mouse.

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MODEL DESCRIPTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease that is characterized by intense itching and recurrent eczematous lesions [1]. The epidermal thickness with cutaneous hypersensitivity in AD is associated with increased serum immunoglobulin E (IgE) levels and infiltration of inflammatory cells including eosinophils, mast cells and basophils [2, 3]. Chronic exposure to the allergens will cause cross-linking of the IgEs and eventual degranulation of mast cells and basophils and release of histamine and other endogenous inflammatory pruritic agents. As current treatment regimens of AD represent a therapeutic challenge, there is a growing interest in cytokine-targeted therapies that could improve the therapeutic armamentarium for AD. To understand the mechanisms of the onset and development of this disease, appropriate animal models are essential. Redoxis provides a Hapte-induced AD model based on Haptenogenic Oxazolone.

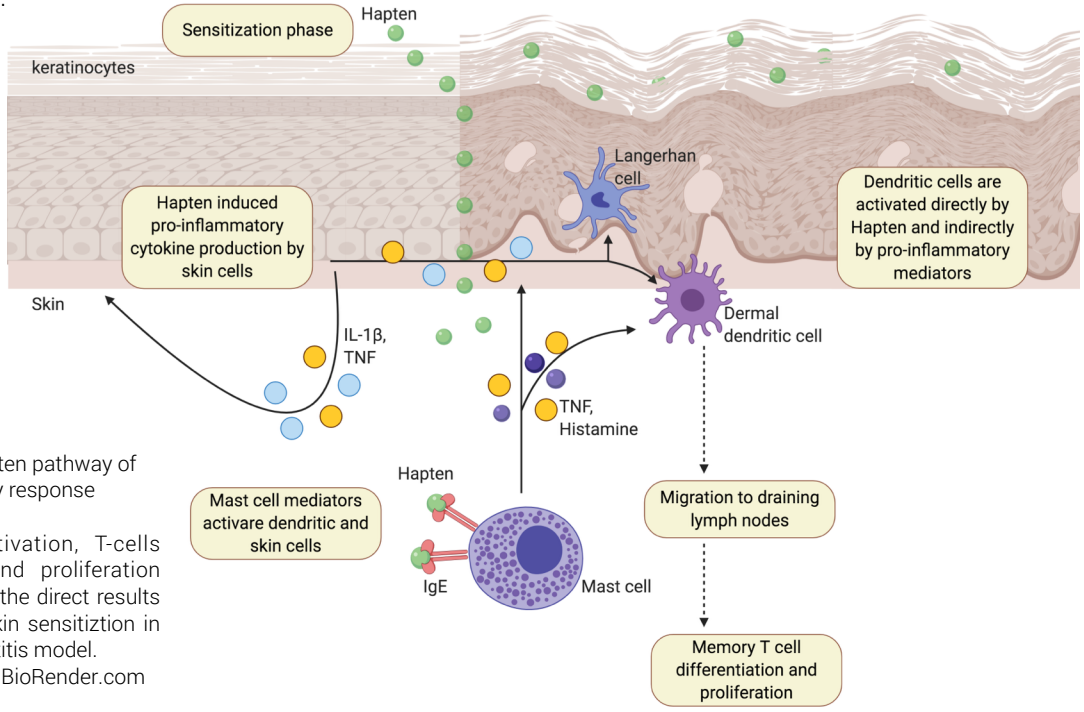

Figure 1.Hapten pathway of inflammatory response in epidermis.
Cellular activation, T-cells migration and proliferation are some of the direct results of Hapten skin sensitiztion in atopic dematitis model.
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DISEASE INDUCTION

Skin dermatitis-like disease is induced by topical administration of Hapten emulsion (4-Ethoxymethylene-2-phenyl-2-oxazolin-5-one suspended in an acetone and oil mixture). The solution is topically applied on the shaved backs and on one ear of the mice 3 times per week for a total of 3 weeks to achieve the desired sensitization response.

EVALUATION OF THE DISEASE

The mice are scored and measured 3 times per week for evaluation of inflammatory symptoms

Scoring of the ear and back:

Scaling and redness (erythems) of the ear and back skin is measured on a grade from 0 to 4, where 0 is no scaling, and 4 is the maximum scaling with also presence of scabs and blood.

Caliper measurement:

Ear and back skin thickness are also measured 3 times per week using a caliper as an evaluation of skin inflammation.

Read more:

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(1) Weidinger, S., et al., 2016. Atopic dermatitis. Lancet 387 (10023): 1109–1122. https://doi.org/10.1016/S0140- 6736(15)00149-X.
(2) Karuppagounder, V., et al., 2015. Tannic acid modulates NFkB signaling pathway and skin inflammation in NC/Nga mice through PPARγ expression. Cytokine76 (2): 206–213. 3.
(3) Liu, F.T., et al., IgE, mast cells, and eosinophils in atopic dermatitis. Clinical Reviews in Allergy & Immunology 41 (3): 298–310.

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EVALUATION OF DISEASE AND HEALTH STATUS

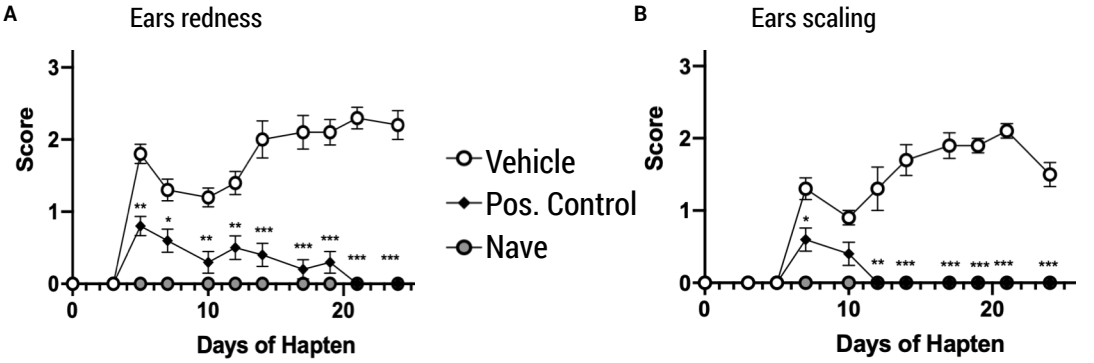
All the mice are evaluated 3 times per week for evaluation of inflammation during a period of 3 weeks, this evaluation includes caliper measurements and macroscopic observations of animals` back skin and ears.

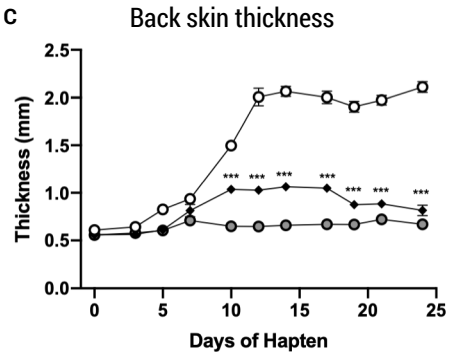
Caliper measurement

Ear and back skin thickness were measured 3 times per week using a caliper as an evaluation of skin inflammation and disease progression.

Scoring of the ears and back skin

Scaling and redness of the left ear and back skin are scored 3 times per week on a grade from 0-4 (0=not present, 1=mildly present, 2=moderately present, 3=severely present, 4=max)





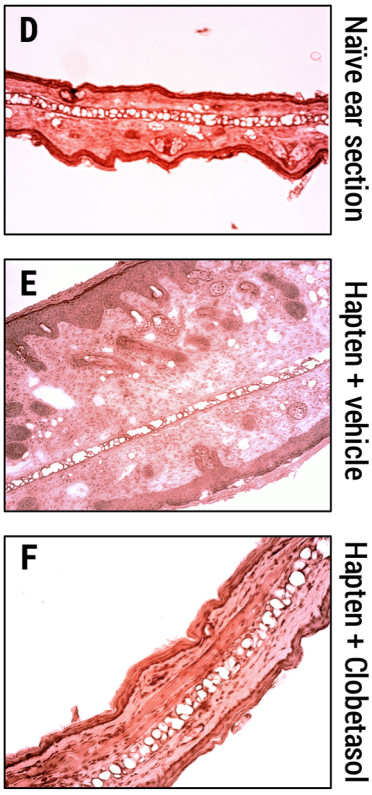


Figure 1: A) Left ear redness score. Animals treated with positive control drug had a significant reduction in ears redness vs vehicle treated mice from day 5. B) Ears scaling score. Animals treated with positive control drug had a significant reduction in skin scaling vs vehicle treated mice from treatment day 7.
C) Caliper measurements of back skin thickness. Animals treated with positive control drug had a significant reduction in skin thickness vs vehicle treated mice from treatment day 10.
Ear skin samples from D) a naïve mouse, E) a mouse daily sensitized with Hapten and treated with vehicle PBS. The tissue presents marked epidermal hyperplasia (>4-fold increase), hyperkeratosis, and apparent degenerative changes of the hypodermic adipose tissue. F) Ear skin section from a mouse daily sensitized with Hapten and topically treated three times per week with positive control drug. Pictures were acquired at 4x objective with a light microscope.

CHARACTERISTICS

Disease induction protocol:	Hapten (4-Ethoxymethylene-2-phenyl-2-oxazolin-5-one) daily treatment
Strain:	Balb/c mice (6 weeks at exp. start)
Suggested group size:	10 mice/group
Duration:	21 days
Onset:	Within 5 days
Max disease:	Around day 15
Positive controls:	Clobetasol propionate cream (Dermovat 0,05% cream)
Clinical signs:	Macroscopic scoring of scaling and redness, caliper measurements of skin thickness,
Luminex analyses on serum:	TNF-a, IL1b, IL6, IL10, IL17A, IFNg and IgE,
Histology	H&E staining, cell infiltration (on demand IHC).

Cytokines, Luminex analysis:	
	IFN- γ
	IL-1 β
	IL-6
	IL-10
	IL-17A
	TNF-α
	IgE

Figure 2: List of detectable cytokines detectable (ELISA thechnology).