



CBI

Murine Atopic Dermatitis Model

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Overview of Atopic Dermatitis

- Atopic Dermatitis (AD) is an inflammatory skin disease that frequently occurs in subjects with personal or family history of atopic disease.
- Mechanical injury to the skin by scratching is an important feature of AD and has been shown to induce local expression of IL-10 in patients.
- Epicutaneous sensitization with ovalbumin induction with tape stripping in mice is a useful model.
- This model displays many of the features of human AD, including scaly, inflamed skin, elevated total and specific IgE, histologic infiltration of CD3+ T cells and eosinophils in the dermis, and increased local expression of mRNA for Th2 cytokines.



Basic Study Design

- Five groups of 10 mice per group; vehicle, test article at 3 dose levels, positive control.
- Housing (46 days on study plus acclimation) in dry environment
- Weekly body weights and daily clinical observations
- Induce atopic dermatitis by albumin and tape stripping at 3 intervals to back skin. Albumin is applied to tape-stripped skin for 1 week under a Tegaderm dressing followed by a 2 week rest period. Cycle is repeated 3 times.
- Daily Draize scoring for up to 1 week during treatment phase to assess macroscopic changes.
- Treatment as per sponsor request – systemic or topical
- Necropsy and collect skin
- In-vitro assays as per sponsor request.
- Histopathology of skin – special stains and assays as per sponsor request. Perform inflammation scoring, mast cell assessments, eosinophil and mononuclear cell counts.
- Complete report.



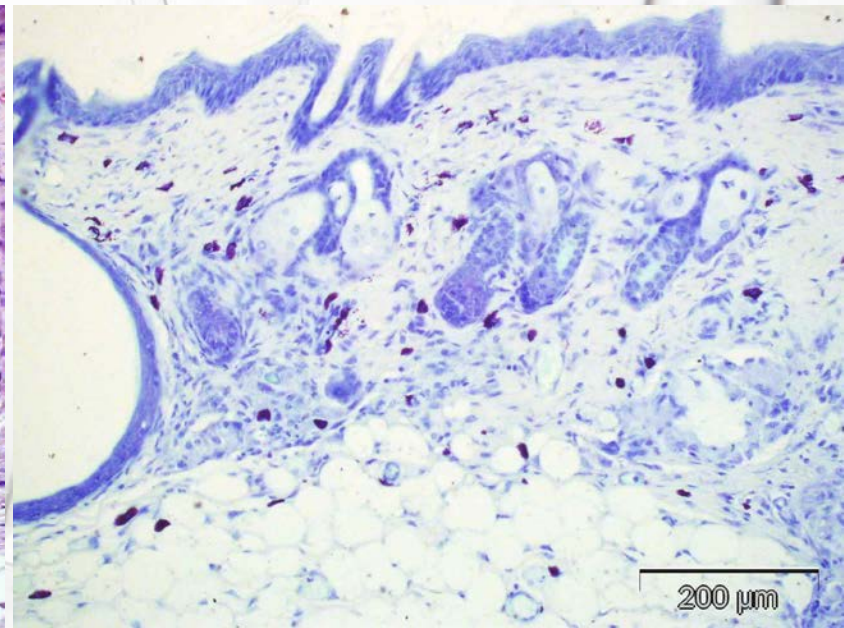
Histologic Effects

Ovalbumin sensitization and tape stripping produce

- Macroscopic: Variable scaliness, reddening, thickening, induration. In some cases, macroscopic changes are not particularly visible, although there are clear histopathologic changes
- Histology:
 - Acanthosis and hyperkeratosis of the epidermal layer.
 - Fibrosis and increased collagen in superficial dermis
 - Infiltration of dermis with eosinophils and mononuclear cells (Primarily T Cells). Chronic active multifocal to diffuse dermatitis in the tape stripped areas. Inflammation may be located peri-vascularly or around the follicles
 - Edema and reactive changes in small vessels
 - Mast cells are increased in the areas of inflammation as are eosinophils



Histopathology



The photomicrographs present the typical histopathology of this model in mice. The HE stain demonstrates the typical dermal fibrosis, multifocal inflammation and epidermal hyperplasia found in this model. The toluidine blue stain shows the increases in mast cells in the affected areas.



Histology Inflammation Scoring

- 3-5 affected areas assessed histopathologically, H&E staining
- Scored semi-quantitatively: 0=normal, 1=minimal; 2=mild; 3=moderate;4=severe
- [^]Statistically significant differences between groups

Histology Scoring	Tape Stripping and Saline Sensitization	Tape Stripping and Ovalbumin sensitization	Subcutaneous Dexamethasone
	1	3	2
	2	3	2
	3	4	3
	2	4	2
	2	4	2
	1	3	2
	2	3	3
	2	3	3
	2	3	2
	3	2	1
Average	2.0	3.2[^]	2.2
SD	0.7	0.6	0.6



Dermal Mononuclear Cell Counts

- Five high powered fields per affected area per animal counted histopathologically.
- [^]Statistically significant differences between groups

Mononuclear cell counts	Tape Stripping and Saline Sensitization	Tape Stripping and Ovalbumin sensitization	Subcutaneous Dexamethasone
	56	96	66
	45	86	56
	48	70	76
	55	65	63
	41	69	62
	62	84	75
	64	90	57
	70	84	77
	41	97	64
	39	93	64
Average	52.1	[^]83.4	66.0
SD	10.9	11.6	7.6



Summary

- CBI provides a consistent, reproducible, validated tape stripping ovalbumin sensitization model in mice as a model for atopic dermatitis
- Characterized by variable dermal thickening, scaliness and reddening macroscopically
- Dermal chronic inflammation with epidermal thickening, dermal fibrosis, increased eosinophils, mast cells and mononuclear cells, and edema histopathologically
- Dexamethasone provides amelioration of signs and histologic lesions.



Service and Quality

- ***Thoroughness in planning and execution is key to a successful study.*** All protocols are vetted and approved by multiple personnel. Our QAU has a rigorous training program. All non-GLP studies are conducted in the spirit of GLP.
- ***We believe in sound science.*** Our ratio of scientists to non-scientists is one of the highest in the industry. Every study director is a PhD-level scientist.
- ***We believe in communication.*** Timely responses to your inquiries and frequent updates on your study are mandatory.
- ***We welcome visitors.*** You are always welcome at CBI to meet the staff, tour the laboratory and discuss the progress and results of your study.

