

Modeling Inflammatory Bowel Disease and Psoriasis in Mice Through T Cell Adoptive Transfer

Epidemiologic analysis has revealed the association of psoriasis with inflammatory bowel disease (IBD) in humans^{1,2}. In mice, transfer of CD45RB^{hi} CD4⁺ naive T cells into immunodeficient animals induces colitis and psoriasis-like phenotypes^{3,4}. This sample study describes the utility of such an adoptive transfer model to evaluate novel compounds for the treatment of IBD and psoriasis.

CD45 adoptive transfer methods

Isolate CD45RB^{high} cells from spleen and mesenteric lymph nodes of BALB/cByJ mice (Stock Number 001026)

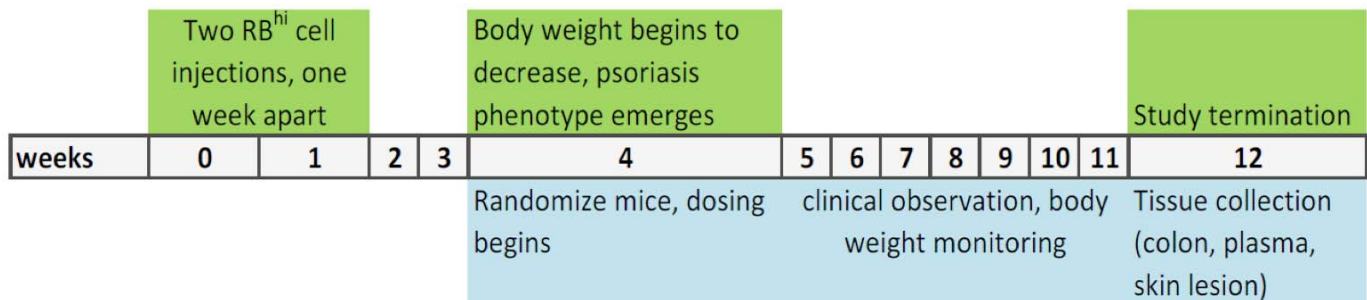
↓
IV inject 2–4 x 10⁵ cells into BALB/c *scid* mice (Stock Number 001803)

↓
Formulate groups based on body weight loss

↓
Begin dosing & scoring; monitor body weight

↓
Sacrifice for histology

Experimental timeline



Disease phenotypes of interest

IBD-like Phenotype

Body weight
Colon length
Colon weight
Colon weight/length ratio
Histopathology

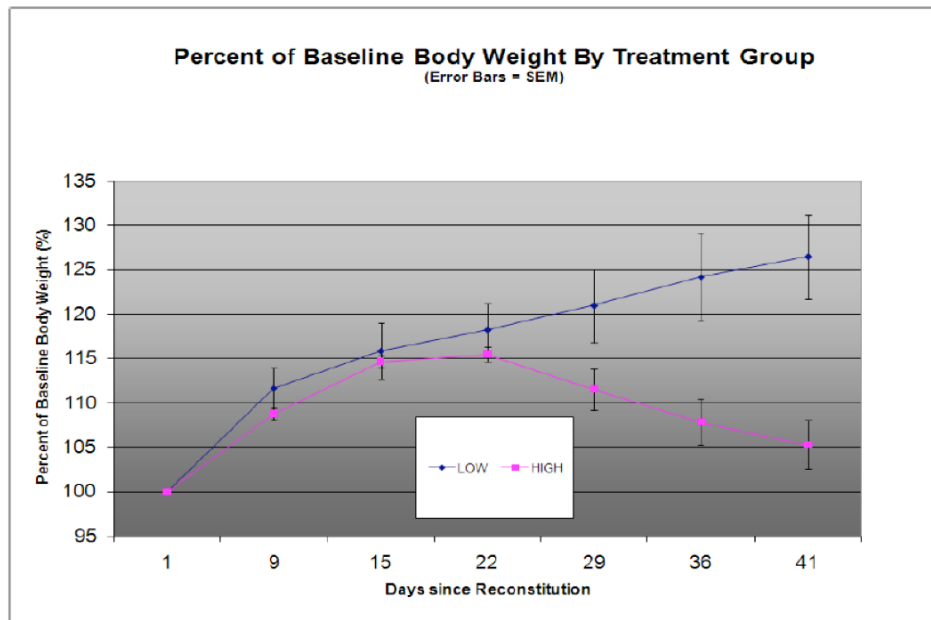
Psoriasis-like Phenotype

Skin lesions (erythema and scaling)
Hair loss
Histopathology

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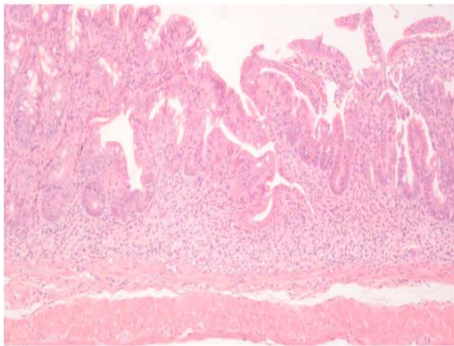
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Body weight decrease 3~4 weeks post cell transfer

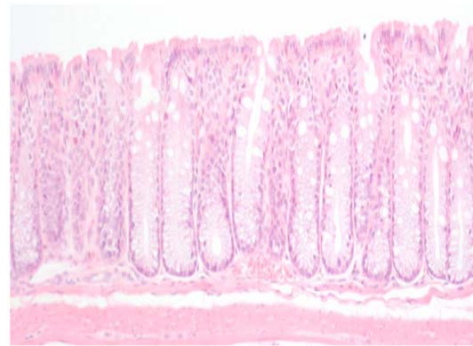


Transfer of CD45RB^{high} cells results in body weight loss whereas mice received CD45RB^{low} cells gain weight as the study progresses.

Histological changes in the colon



Focal mucosal ulcer induced by adoptive transfer



Normal colon

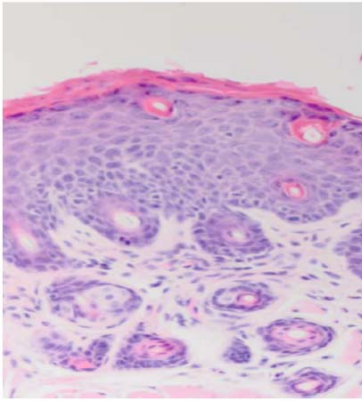
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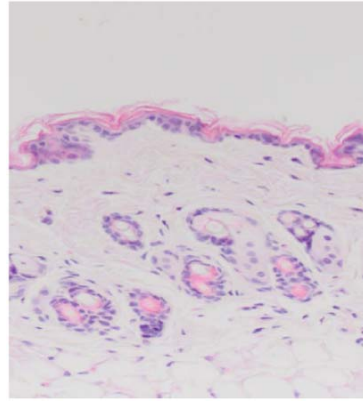
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Histological changes in the skin



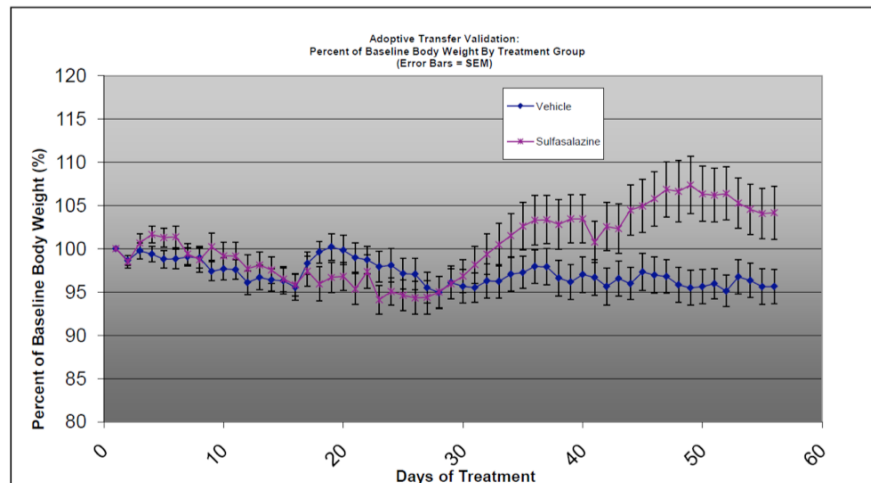
Acanthosis, hyperkeratosis and dermal infiltrates induced by adoptive transfer



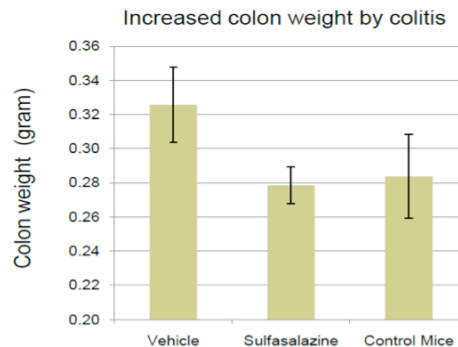
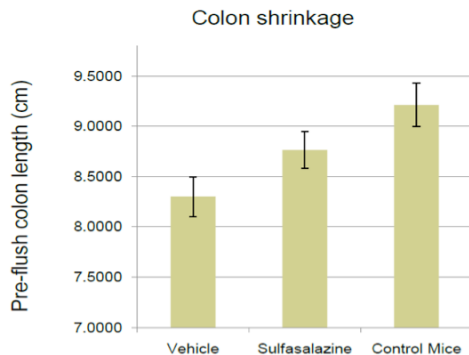
Normal skin

Skin samples collected from the “mask” region, area surrounding the nose and the eyes

Improvement of body weight by Sulfasalazine



Modification of the colitis phenotype by Sulfasalazine



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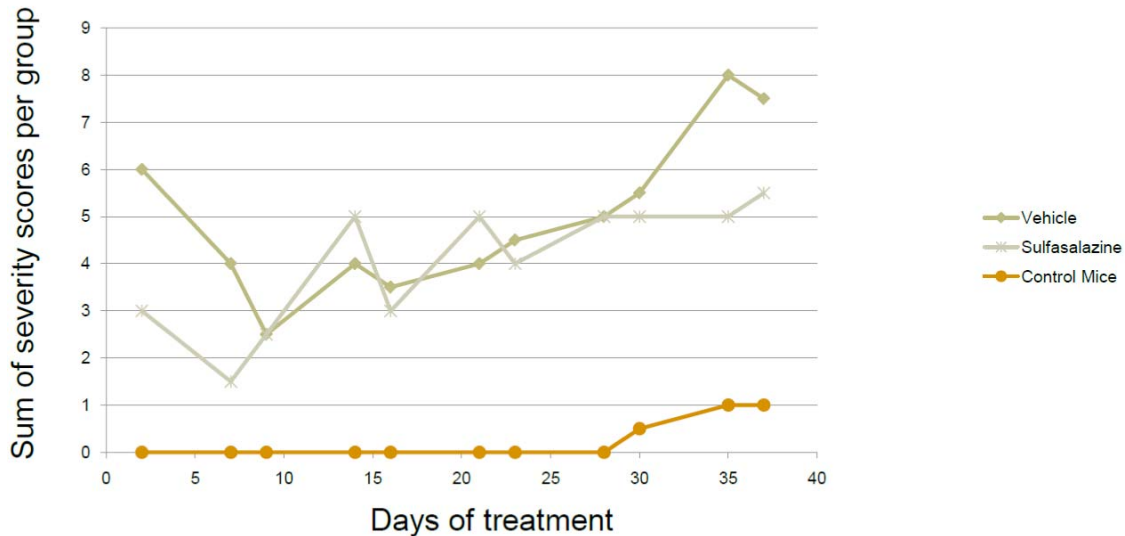
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Clinical evaluation of psoriasis

- 0 no skin or ear abnormalities
- 0.5 slight erythema on either the ears or eyelids
- 1 mild to moderate erythema on the ears or eyelids
- 2 moderate to severe erythema and mild scaling on 2–10% of the body surface
- 3 severe erythema and scaling on 10-20% of the body surface
- 4 severe erythema and extensive scaling on 20–40% of the body surface
- 5 severe erythema and extensive scaling on 40-60% of the body surface
- 6 severe erythema and extensive scaling on >60% of the body surface

Modification of the psoriasis clinical score by Sulfasalazine



Conclusion

1. Adoptive transfer of CD45RB^{high} cells leads to colitis and psoriasis in the same cohort of animals.
2. Sulfasalazine as a reference compound appears to moderate both the colitis and the psoriasis phenotypes.
3. An economical way of testing experimental therapies in two disease areas at the same time.

References

1. Bernstein CN, *et al.* 2005. The clustering of other chronic inflammatory diseases in inflammatory bowel disease: a population-based study. *Gastroenterology* 129: 827-836.
2. Najarian DJ and Gottlieb AB. 2003. Connections between psoriasis and Crohn's disease. *J Am Acad Dermatol* 48:805-821.
3. Davenport CM, *et al.* 2002. Inhibition of proinflammatory cytokine generation by CTLA4-Ig in the skin and colon of mice adoptively transplanted with CD45RB^{hi}CD4⁺ T cells correlates with suppression of psoriasis and colitis. *Int Immunopharmacol* 2: 653-672.
4. Leon F, *et al.* 2006. Antibodies to complement receptor 3 treat established inflammation in murine models of colitis and a novel model of psoriasisform dermatitis. *J Immunol* 177: 6974-6982.

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