

Adoptive T-cell Transfer Colitis in Rag2 Knockout Mice

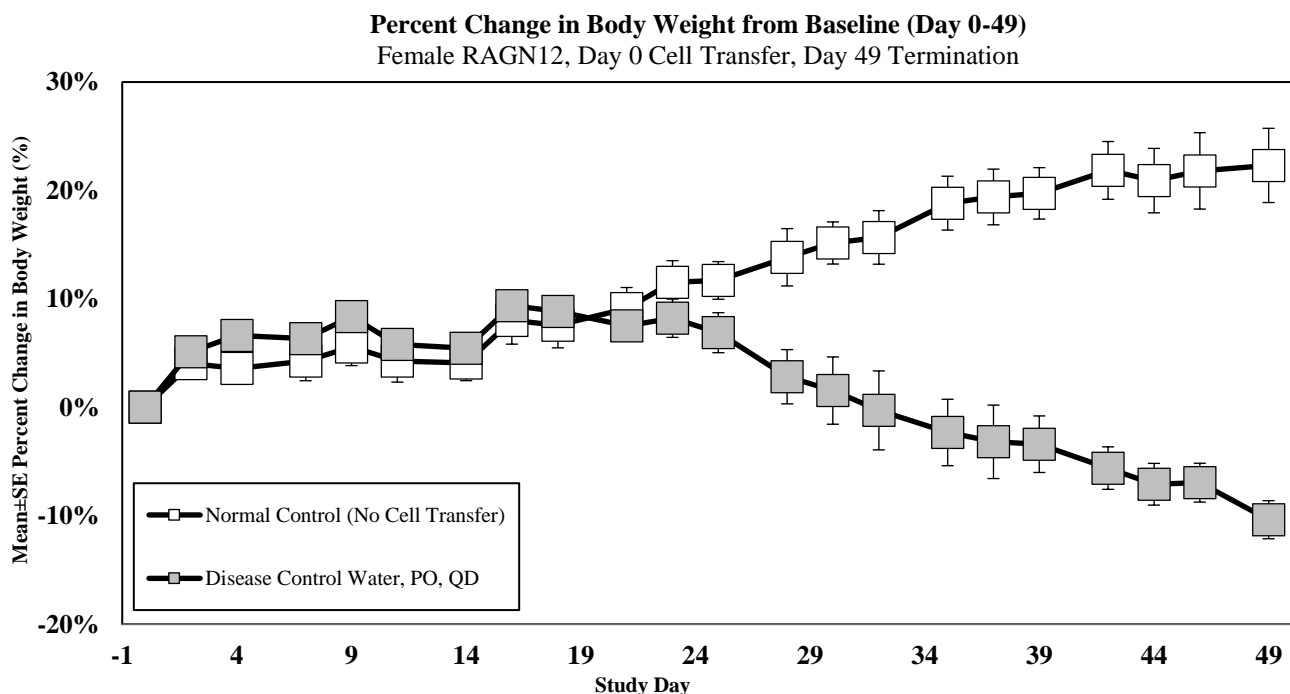
Adoptive transfer of CD4⁺ naïve T cells of normal C57BL/6 mice obtained from Taconic (Model #B6) into mutant Rag2 knockout mice obtained from Taconic (Model #RAGN12) on the same strain background has been shown to cause an acute inflammation in the colon, with gross and histopathologic changes resembling those occurring in Crohn’s disease and ulcerative colitis in humans.¹⁻⁴ RAGN12 mice restored with naïve T cells start losing weight and develop loose stools 3 to 5 weeks after inoculation. Weight loss is progressive, with mice losing up to 25% of body weight within 10 weeks of the cell transfer.

Primary model endpoints include a colon weight/length ratio collected at necropsy as well as histopathological evaluation of colons. RAGN12 mice restored with naïve T cells develop colitis with moderate to marked epithelial cell hyperplasia, significant to extensive leukocyte infiltrate in mucosa and submucosa, significant depletion of mucin-secreting goblet cells, and ulceration.⁴

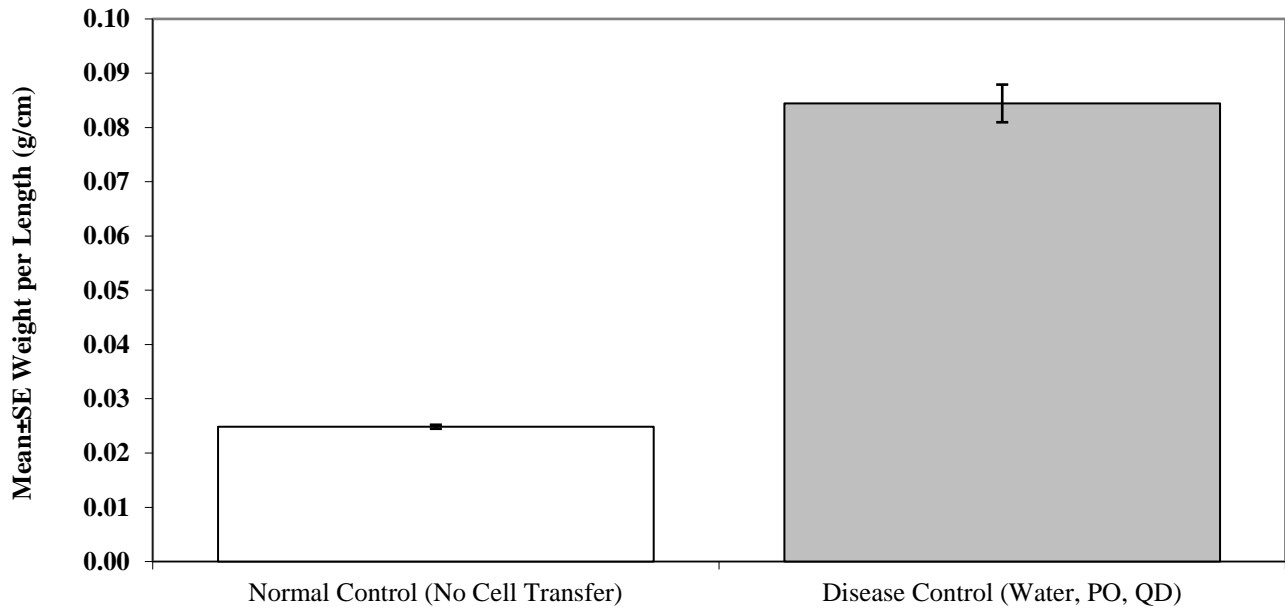
Protocol:

On study day 0, spleens for CD4⁺CD45RB^{high} naïve T cell isolation are obtained from donor B6 female mice (sourced from Taconic Biosciences, 11-12 weeks old, MPF health standard) using the “Bolder BioPATH Naive T Cell Separation Protocol.” After cells have been obtained and sorted, each female RAGN12 recipient mouse (sourced from Taconic Biosciences, 6-7 weeks old, MPF health standard) receives an intraperitoneal injection of a minimum 4×10^5 cells/mouse (200 μ L/mouse injections). Disease progresses until study termination on study day 49. Colons are measured, weighed, and collected for histopathological evaluation.

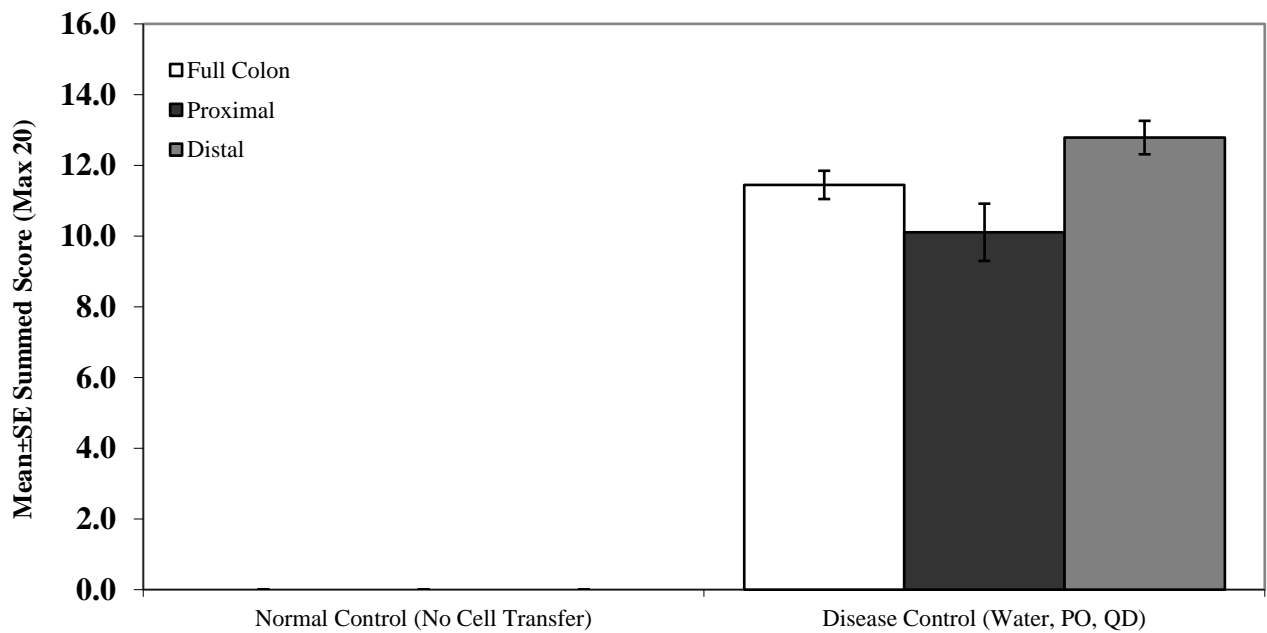
Results:



Colon Weight per Length (g/cm)
 Female RAGN12, Day 0 Cell Transfer, Day 49 Termination



Colon Histopathology Summed Score
 Female RAGN12, Day 0 Cell Transfer, Day 49 Termination



Note: Summed Score is a sum of Inflammation, Gland Loss, Erosion and Hyperplasia

References:

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2. Kobozev I, Karlsson F, Zhang S, Grisham MB. Pharmacological intervention studies using mouse models of the inflammatory bowel diseases: translating preclinical data into new drug therapies. *Inflamm Bowel Dis.* 2011 May;17(5):1229-1245.
3. Ostanin DV, Bao J, Kobozev I, Gray L, Robinson-Jackson SA, Kosloski-Davidson M, Price VH, Grisham MB. T-cell transfer model of chronic colitis: concepts, considerations, and tricks of the trade. *Am J Physiol Gastrointest Liver Physiol.* 2009 Feb;296 (2):G135-46.
4. Read S and Powrie F. Induction of inflammatory bowel disease in immunodeficient mice by depletion of regulatory T cells. *Curr Protoc Immunol.* 2001 May;Chapter 15:Unit 15.13.