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\(^\text{high}\) 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 Naïve 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 µL/mouse injections). Disease progresses until study termination on study day 49. Colons are measured, weighed, and collected for histopathological evaluation.

Results:

![Graph showing percent change in body weight from baseline (Day 0-49).](../images/figure1.png)
Note: Summed Score is a sum of Inflammation, Gland Loss, Erosion and Hyperplasia
References:


