

Advanced Inflammatory Bowel Disease Research

Validated Translational Disease Models for Drug Discovery

It can be difficult to choose an *in vivo* model for preclinical testing of new inflammatory bowel disease (IBD) therapeutics. The different etiology and pathology of IBD disorders significantly impacts model choice. Inotiv offers models that reflect the clinical and pathological characteristics of Crohn's disease and ulcerative colitis. Utilize our experts to help you choose the best IBD model for your preclinical studies to ensure you have accurate data for evaluating the efficacy of your novel treatment.

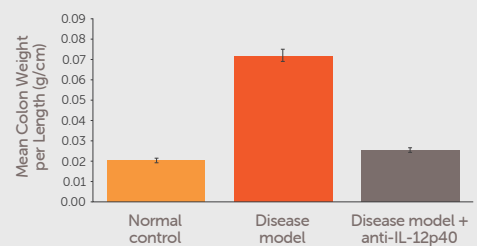
Immune Cell Driven IBD Models

Immune cells, including T cells, have been shown to be the main drivers of chronic gastrointestinal (GI) inflammation seen in IBD. Immune cell driven IBD models are excellent tools for testing new therapies targeted at regulating immunological mechanisms that induce and perpetuate IBD.

- Adoptive T Cell Transfer IBD in Mice
- Anti-CD40 Colitis in Mice

Figure 1 Colon Weight/Length in the Adoptive T Cell Transfer IBD Model

Colon weight per length measurements collected at necropsy for normal controls (n=5), Rag2 knockout (KO) mice restored with naive T cells (Disease model; n=10), and Rag2 KO disease models treated with an anti-IL-12p40 antibody (n=10) in a 7-week study.



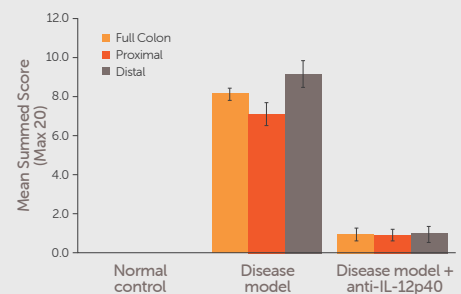
Models of Spontaneous IBD

The development of transgenic animals has uncovered new models that spontaneously develop IBD through different mechanisms such as the breakdown of the mucosal barrier or dysregulation of immune responses. These models can provide unique insights into the etiology of IBD.

- Mdr1a KO Mice
- Il10 KO Mice

Figure 2 Summed Histopathology Scores in Mdr1a KO Mice

Summed colon histopathology scores of normal controls (n=5), Mdr1a KO disease models (n=12), and Mdr1a KO disease model mice treated with an anti-IL-12p40 antibody (n=12) in a 5-week study.



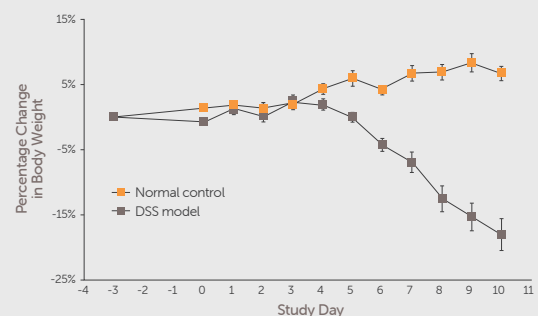
Chemically Induced IBD Models

Chemically induced models are extensively used by researchers as they are an easy to develop, reproducible model of IBD. These models are an important tool for the evaluation of ulcerations and necrosis in an IBD setting.

- Dextran Sulfate (DSS) Induced Colitis in Mice and Rats
- 2,4,6-Trinitrobenzenesulfonic acid (TNBS) Induced Colitis in Mice and Rats
- Indomethacin Induced Crohn's in Rats

Figure 3 Percent Change of Body Weight in the DSS Induced Colitis IBD Mouse Model

The percent change of weights of control animals (n=10, orange box) and DSS induced colitis mouse models (n=10, grey box) throughout a 10-day study.

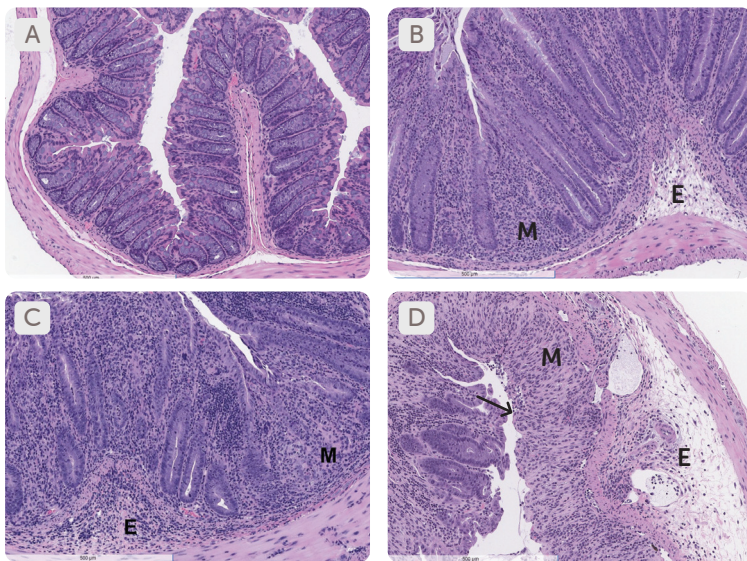


Additional Endpoints

We realize that demonstrating efficacy of novel therapeutics may require assessing endpoints beyond *in vivo* parameters. As a full-service CRO, we can provide you with the data you need to assess your therapeutic. Simply choose your desired endpoints or consult with our team of experts to customize the project to meet your research needs.

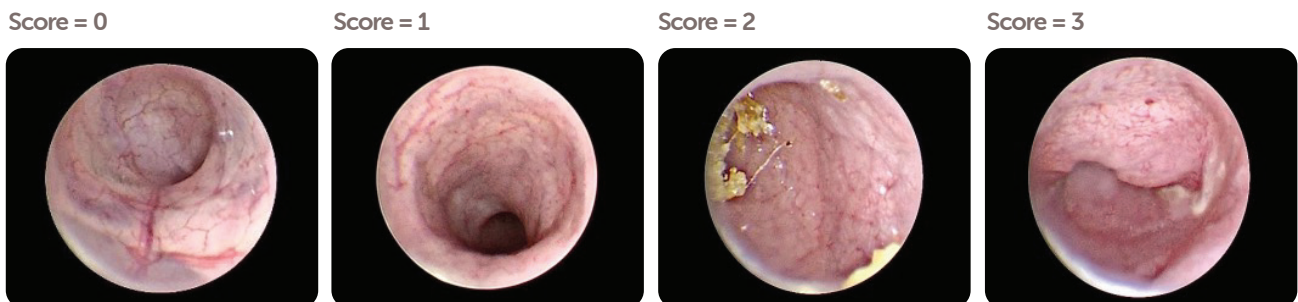
- Endoscopy
- Disease Activity Index
- Histopathological Assessment
- Cytokine and Chemokine Analysis
- FACS Analysis
- qPCR
- FITC Permeability Assay
- Immunohistochemistry and Image Analysis
- Bioanalysis and Pharmacokinetic Services

Figure 4 Histopathological Analysis of Colon Sections from IBD Models



Distal colon sections from control and IBD animal models were sectioned and stained with hematoxylin & eosin, and then evaluated by a board-certified veterinary pathologist for extent of inflammation, gland loss, erosion, and hyperplasia, as well as other disease model specific parameters. Non-diseased control animals (A) showed no lesions while colons from adoptive T cell transfer (B), Mdr1a KO (C) and DSS induced (D) models show moderate to severe inflammation with minimal to moderate gland loss. Arrow identifies area of erosion. M identifies the most severely affected area of mucosa. E identifies edema.

Figure 5 Endoscopic Evaluation of IBD Models



Photos show representative scores from the endoscopic scoring system. Score = 0 is normal tissue. Score = 1 indicates moderate loss of vascularity (small vessels can't be seen). Score = 2 indicates severe loss of vascularity, loss of transparency, and presence of contact bleeding. Score = 3 indicates the presence of mucosal erosions. Score = 4 indicates the presence of ulcerations and/or gross bleeding (image not shown).

Contact us at [inotivco.com/contact](https://www.inotivco.com/contact) to discuss how our models and services can support your IBD drug development program