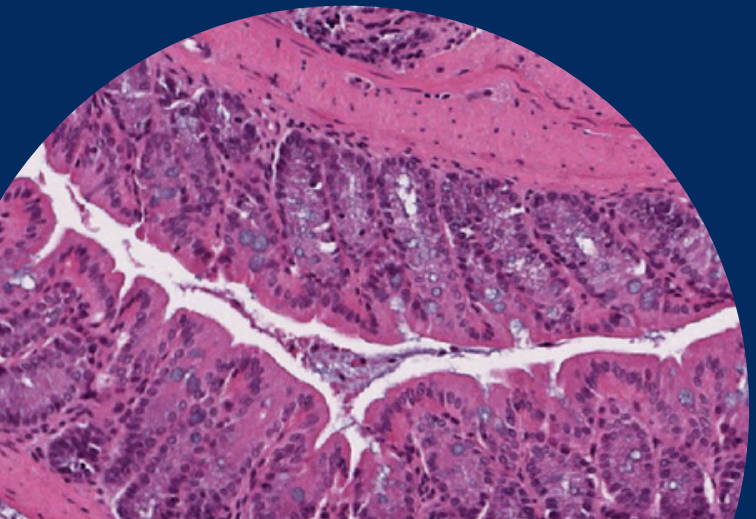
Models, Strategy, and Translational Readouts for Inflammatory Bowel Disease Research

A practical overview of preclinical support for acute and chronic colitis and Crohn's disease programs.



oncodesign services

Over 30 Years of Experience in Preclinical Research

Standard and customized research models

Available systems include chemically induced, immune-mediated, spontaneous and oncology-linked disease biology. Studies may use wild-type models, relevant custom transgenic strains, or human CD34+ reconstituted mice.

Model	Format	Research Value
DSS-induced	Colitis · Also available in BRGSF-HIS	Early-stage rapid assessment of anti-inflammatory activity and proof of concept under controlled conditions. Evaluation of durability of response, relapse, longer-term safety, and clinically relevant dosing strategies over time.
DSS + anti-CTLA4	Chronic colitis	Delayed recovery, recapitulating checkpoint inhibitor-induced chronic colitis as seen in cancer immunotherapy patients and allowing evaluation of compounds targeting recovery after crisis.
In development: **AOM-DSS-induced**	Colitis-associated cancer	Induces DNA mutations in colon epithelial cells, mimicking inflammation-driven colorectal tumorigenesis as observed in colitis-associated cancer in humans.
Anti-CD40	Immune-mediated Rag2 knockout mice	Tiggers uncontrolled activation of antigen-presenting cells (e.g., macrophages, dendritic cells) via CD40 signaling, leading to a rapid onset of innate-driven colonic inflammation.
IL-10 knockout	Spontaneous	Reflects aspects of immune-mediated chronic inflammation similar to human Crohn's disease.

***De Novo* Model Development Available for Specific Study Requirements**

Humanized mice in gastrointestinal disease research

BRGSF mice provide advantages for the in vivo study of human myeloid cell subsets which have a competitive advantage over their murine counterparts after xenotransplantation of human CD34+ hematopoietic stem cells.

BRGSF mice with a reconstituted human immune system (BRGSF-HIS) constitute a translational model for the evaluation of inflammatory disease candidate treatments, whenever the presence of human cells is critical for target engagement.

Which immune cell populations are characterized?
We routinely assess key human immune populations, including:

- CD45+ leukocytes
- T cells (CD3, CD4, CD8)
- B cells
- NK cells
- Monocytes
- Dendritic cells

Additional subsets upon request.

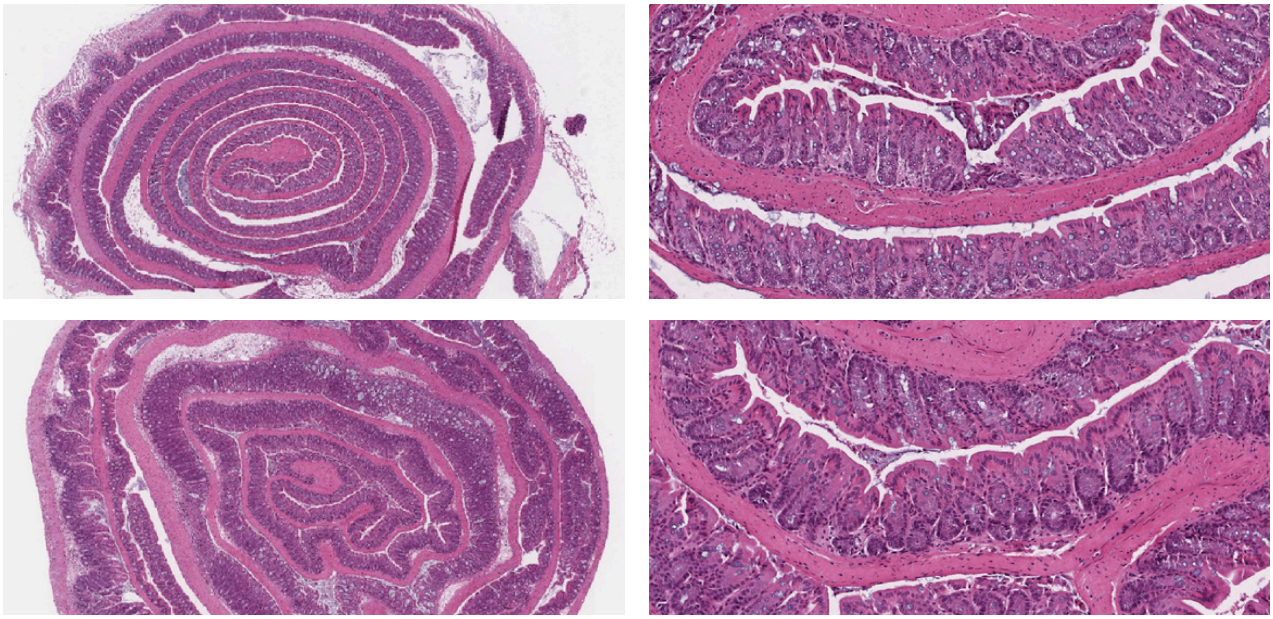
Experimental examples

Evaluation of an FK-506 immuno-suppressor

Model: DSS-induced acute colitis.

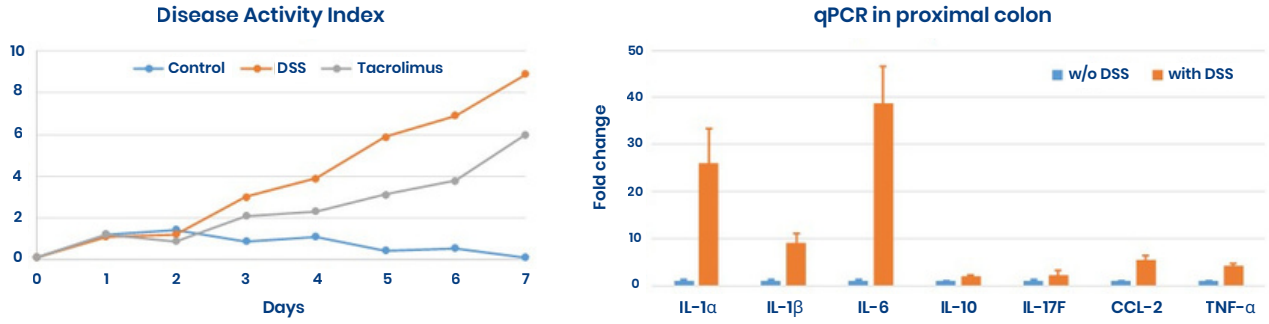
DSS is added to drinking water, over a 5-7 day treatment protocol. Tacrolimus (FK-506 immuno-suppressor) partially limits the evolution of the disease, as seen by improved DAI. Untreated animals display body weight loss, colon shortening, and increased spleen weight.

Histology examples illustrating DSS-induction in control vs challenged mice



Top row: Normal aspect histology samples of the colon - negative control group, water, no DSS, D7.
Bottom row: Histology samples of the colon following DSS challenge - 2% for 6 days, D7.

Tacrolimus limits spleen inflammatory cell accumulation. Cytokine expression can be measured by qRT-PCR, and a classic inflammatory profile is typically observed, with elevated IL-1α, IL-1β and IL-6.



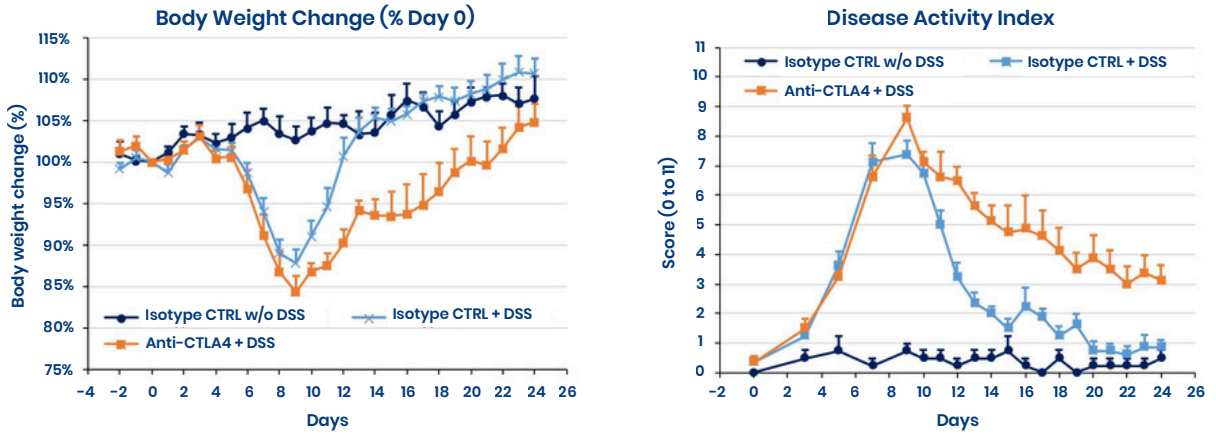
Left: Kinetics of disease activity index (DAI) in the acute DSS model. Right: qRT-PCR measurement of fold change in the expression of genes of interest in the acute DSS colitis mouse model.

DSS-induced colitis chronicized by anti-CTLA4 antibody administration

Model: DSS + anti-CTLA4.

Immuno-oncology approaches are promising new cancer treatments, but a number of unfortunate side effects need to be managed clinically. These typically result from hyper-activation of the immune system, which can affect the gut, skin, liver or endocrine glands. More than a third of patients receiving the anti-CTLA4 antibody ipilimunab report colitis symptoms.

Oncodesign Services has developed a model in which this side effect is used to create a chronic colitis model by combining the antibody with DSS as a standard colitis inducer. Mice typically recover from the DSS-induced colitis after DSS removal on D6, but anti-CTLA4 treatment delays the recovery phase, mimicking chronic colitis and allowing for the evaluation of compounds aiming to decrease recovery time after an IBD crisis.



Left: Kinetics of body weight loss (relative to D0 of the procedure) in the acute DSS model vs the chronicized DSS + anti-CTLA4 antibody model. Right: Kinetics of disease activity index (DAI) in the acute DSS model vs the chronicized DSS + anti-CTLA4 antibody model.

FAQ

Is it possible to make a decision on ex vivo analyses after reviewing DAI results?

Yes. We are flexible and can adapt the study design to help you manage timelines and budgets with scientific insight and strategy.

You may choose to wait until the disease activity index (DAI) results are available before deciding whether to proceed with ex vivo analyses. This staged approach allows you to limit upfront costs and make data-driven decisions as the study progresses. At the same time, it's important to note that ex vivo analyses such as histology and qRT-PCR can be highly informative, particularly when DAI results are not as expected. These analyses can help elucidate why a compound did not demonstrate the desired effect by providing mechanistic and biological context.

Do I need an acute or chronic model?

The choice between acute and chronic IBD models depends on the specific scientific questions you need to answer. Acute models are typically used in early-stage studies to rapidly assess anti-inflammatory activity and establish proof of concept under controlled conditions. Chronic models, by contrast, are better suited for evaluating durability of response, relapse, longer-term safety, and clinically relevant dosing strategies over time. Neither approach is inherently more realistic; each is designed to interrogate different aspects of disease biology and treatment response.

Our inflammatory disease specialists can help you align model selection with MoA, development stage, and objectives, ensuring your study generates meaningful data.

Program design

Inflammatory bowel disease is biologically and clinically heterogeneous, and so no single model reproduces the full patient condition. The strongest preclinical strategies begin with a clearly defined research objective, and then align model biology, treatment timing, and endpoints to support and test that objective.

01 Define the program objective

For example:

- Proof of anti-inflammatory activity
- Target engagement
- Durability, relapse or recovery
- Investigation of dosing

02 Model selection

Use acute models for rapid, robust proof of concept; chronic or immune-mediated systems for objectives involving sustained inflammation, recovery and longer treatment windows.

03 Dosing strategy

Establish whether the candidate can modify disease biology under informative conditions. Then refine treatment timing, exposure and maintenance schedules toward intended clinical use.

04 Endpoints and readouts

Select endpoints and readouts that are relevant to study objectives and appropriate to disease biology. Pair symptom-linked observations with histology, and molecular and cellular measures. Add PK/PD where applicable to distinguish biological limitations from exposure or study-design effects.

Confirm feasibility prior to full study initiation

To support confident model selection, histology samples from established IBD research models can be accessed ahead of full study commitment, subject to availability.

Immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH) analyses may be performed to assess target expression and tissue localization, helping confirm biological relevance before program initiation.

Subject to availability, we currently offer the following samples for inflammatory bowel disease studies:

- DSS-induced colitis (mice)
- DSS-CTLA4-induced colitis (mice)
- Anti-CD40 mouse colitis model (Rag2 -/- mice)
- Spontaneous colitis (IL-10-/- mice)

Key readouts and endpoints

Readouts and endpoints are a key component of study design. Readouts should be appropriate to the disease indication and selected models, and should reflect the research objective, covering exposure, and target biology with tissue response and observable disease benefit.

Clinical Scoring

Daily Disease Activity Index (DAI):

- Weight loss
- Stool consistency
- Blood in stool
- Colon length

Tissue Analysis

H&E and Alcian Blue-PAS-stained colon sections for assessing:

- Epithelial erosion and healing
- Crypt architecture
- Goblet cell depletion.

Molecular Profiling

- qRT-PCR/dPCR for
  - Key inflammatory mediators (TNFα, IL1β, IL6, CXCL10, etc.)
  - Relevant genes (e.g. drug target)
- Immunohistochemistry (IHC)
- Cytokine multiplex assays (e.g. IL17A/F, IFNγ)

Cellular & Biomarkers

- Flow cytometry to profile:
  - Immune infiltrates (e.g. Th1, Th17, Tregs, neutrophils, monocytes)
  - Human cell subsets in HIS mice (hCD45+, hCD4+, hCD8+)
- Serum and fecal biomarker quantification (e.g. LCN-2, calprotectin)
- PK/PD assessment when applicable

Human-specific target engagement and/or cross-reactivity
Humanized immune systems, human cell replacement and humanized target models can support compounds that do not interact appropriately with the corresponding murine target.

Immune response characterization
Available approaches include flow cytometry, immunohistochemistry, ELISA and multiplex cytokine analysis.

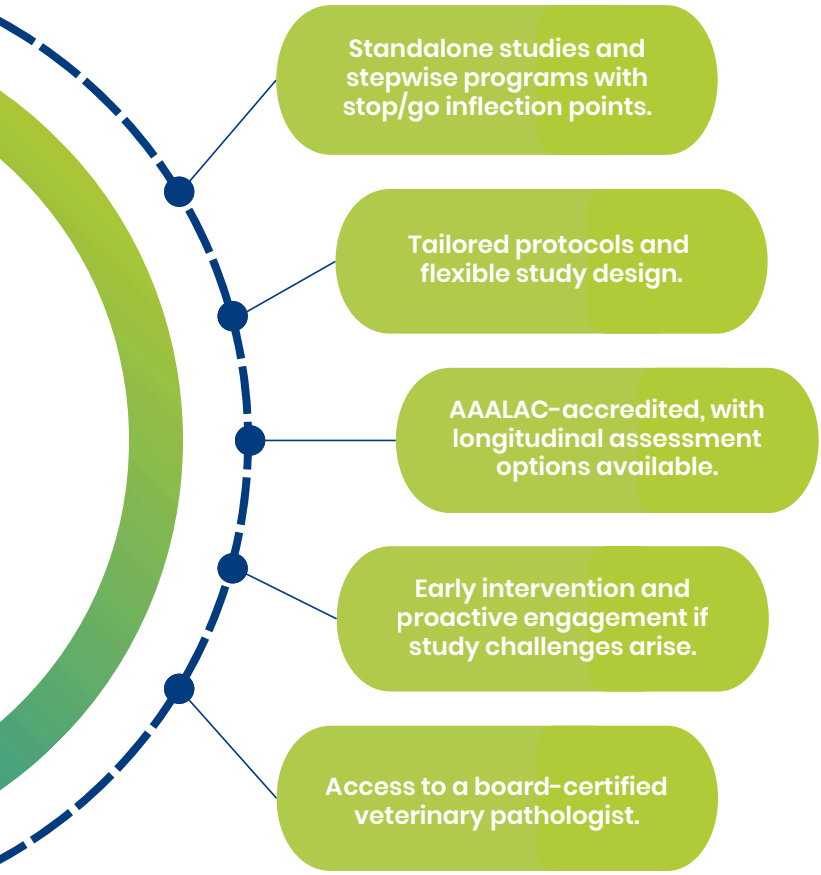
Molecular response and biomarker assessment
Gene and biomarker profiling can be performed using qRT-PCR, dPCR and complementary analytical approaches.

Tissue-level disease change evaluation
Histopathology, image analysis and review by a board-certified veterinary pathologist support assessment of tissue architecture and pathological response.

Strengthening clinical translatability
Clinically relevant biochemistry can help connect biological activity with outcomes that are meaningful in patients.

Longitudinal disease monitoring
Imaging approaches (including BLI, CT, PET/CT and MRI where appropriate) can support non-invasive monitoring, disease detection and diagnostic validation.

Working with Oncodesign Services



Oncodesign Services provides flexible support for the preclinical development of novel inflammation and autoimmunity therapeutics. We have specialized in preclinical research for more than three decades, and in inflammatory diseases for over 10 years.

Our priority is to deliver reliable, timely results that help advance your program, transparent communication, and proactive project management.

We can deliver both standalone studies and stepwise programs, with tailored or standardized protocols and flexible study design. In the unlikely event that study challenges arise, we prioritize early intervention and proactive engagement. For in vivo studies, we provide specialist surgical expertise and access to a board-certified veterinary pathologist.

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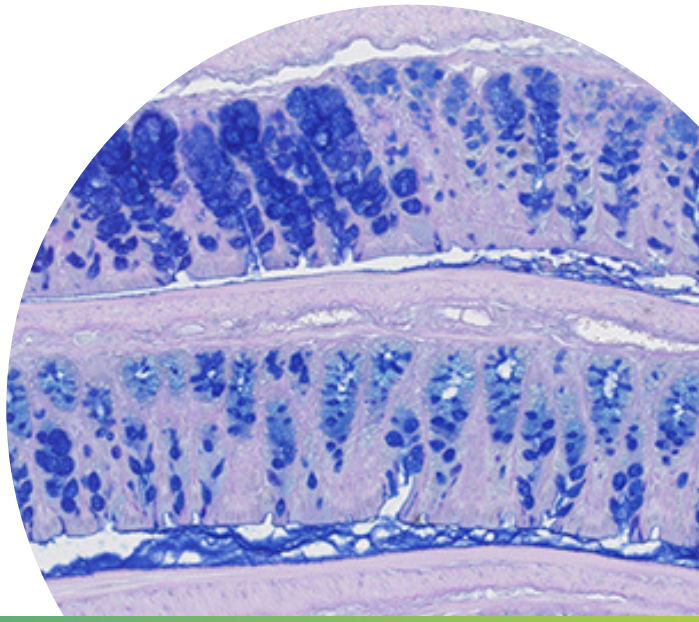
Practical next steps

If you are considering an inflammatory or autoimmune disease study with us, the first step is a discussion to understand your research objectives and requirements.

You can get in touch with us via email or by using the contact form on our website:

- contact@oncodesign-services.com
- oncodesign-services.com



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