Advance Your Inflammation Drug Discovery

Ideal preclinical platform to support your IBD therapeutics transition into the clinic

CrownBio provides an integrated platform for preclinical drug development and expert consultation that will enable your clear next-step decision:

- Select qualified Crohn’s disease and Ulcerative Colitis lead agents.
- Determine efficacy and response to treatment.
- Preclinical models with diverse mechanisms in each model that capture many of the key characteristic clinical and pathologic features of IBD including:
  - gut epithelial/barrier defect model
  - innate and regulatory cell mediated model.

Gut epithelia/barrier defect mouse model – DSS-induced colitis

Dextran sulfate sodium (DSS) is a sulfated polysaccharide with variable molecular weights. Administration of DSS in the drinking water causes activation of neutrophils and macrophages that result in a compromised mucosal barrier function.

- Acute DSS in the drinking water for 5-7 days, followed by several days of tap water induces a Th2 UC-like inflammation in the colon.
- Major endpoints:
  - bloody stool/diarrhea
  - weight loss
  - colon weight/length.
- Histopathological assessment:
  - Board Certified Veterinary Pathologist.

Innate and regulatory cell mediated mouse model – T cell transfer

- CD4^+CD45RB^hi cells are isolated from spleens of BALB/c mice and transferred to RAG1-/− or SCID recipients.
- Peak clinical disease observations usually occur 6–8 weeks post-transfer:
  - weight loss
  - diarrhea
  - colon weight/length.
- Histopathological assessment:
  - Board Certified Veterinary Pathologist.

DSS-Induced Colitis Mouse Model

Representative colon histology photomicrographs

Panel A represents normal non-lesional colon architecture with pertinent structures indicated as mucosa (M), muscularis mucosae (MM), and tunica muscularis externa (TME).

Panel B represents disrupted colon architecture highlighted by inflammatory cell infiltrates (I) into the mucosa (M), submucosa (SM), and tunica muscularis externa (TME), and colonic gland loss (*) and erosion (demarcated by black arrows) induced by DSS in the drinking water.

Panel C shows largely normal colon architecture with a small site of inflammation and gland loss (*) in response to cyclosporine A treatment in DSS model.

T Cell Transfer Mouse Model

Anti-IL-12 mAb treatment reduces Disease Activity Index

0.7mg Isotype IgG2b\(\kappa\) (n=13)
0.7mg Anti-IL-12 (n=13)
0.3mg Anti-IL-12 (n=13)

**p=0.0083 one way ANOVA
**p=0.0047 one way ANOVA

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