



Inflammatory Bowel Disease (IBD)

Inducible Models

- Acute 2,4 6-trinitrobenzenesulfonic acid (TNBS) hapten
- Mediated by Th1 and Th17 cells locally producing excessive proinflammatory cytokines including IFN- γ , TNF- α , IL-2, IL-12 and IL-18
- Acute dextran sulfate sodium (DSS)
- Suggested epithelial cell toxicity, increased intestinal permeability, and macrophage activation

IBD Readouts:

IBD Disease Activity Index

- Body weight
- Rectal bleeding scoring (Hemocult kit)
- Stool scoring

Additional Analyses

- Interim blood collections for PK/PD evaluation
- Histology
- collections for PK/PD evaluation

Colon Evaluation

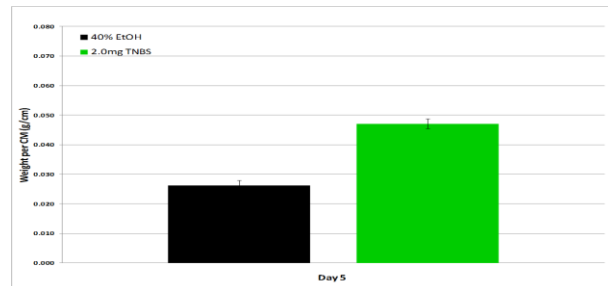
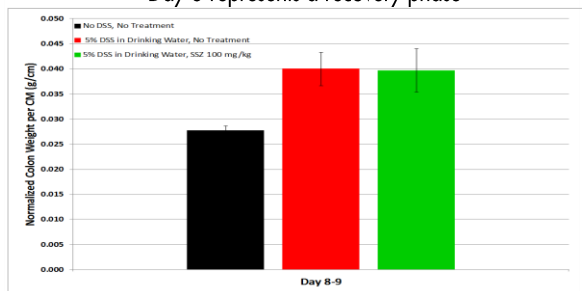
- Colon length and weight measures
- Macroscopic Colon Scoring Index
- 0 – 10 graded morphologic scoring

Microscopic Colon Scoring

- Histopathology assessment by an unbiased pathologist
- Inflammation and morphological damage

TNBS-Induced IBD in Mice

- 8 - 10 animals per group
- ~100% induction rate, low mortality
- Prophylactic or therapeutic treatment
- Intrarectal induction with TNBS hapten
- Study duration 5 to 8 days
 - ~Day 5 is the peak of disease severity
 - Day 8 represents a recovery phase



DSS Induced IBD in Mice

- 8 -10 animals per group
- Induction with 5% DSS in drinking water for 5 consecutive days
- ~100% induction rate
- Disease onset on Day 3
- Peak disease on Day 8 - 10
- Positive control is available

