

Chronic colitis induced by trinitrobenzene sulphonic acid (TNBS)

A MODEL OF INFLAMMATORY BOWEL DISEASE (IBD) WITH CHARACTERISTIC FEATURES OF CROHN'S DISEASE

Model

Inflammatory bowel disease (IBD) includes ulcerative colitis (UC) and Crohn's disease, two chronic inflammatory disorders of the gastrointestinal tract (GIT). UC is limited to the colon and involves diffuse mucosal inflammation, while Crohn's disease may affect any part of the GIT and is characterized by patchy, transmural inflammation. Clinically, IBD is characterized by weight loss, severe diarrhea, bleeding and abdominal pain. Trinitrobenzene sulphonic acid (TNBS) renders colonic proteins immunogenic to the host immune system initiating mucosal immune response. This model captures many of the features of Crohn's disease.

Interest

- TNBS model induces transmural inflammation characterized by infiltration of the lamina propria with CD4⁺ T cells, neutrophils and macrophages.
- Disease Activity Index (DAI) can be carried out daily throughout 3 weeks allowing real-time and repeated monitoring of animal response over time.
- This model is validated by a clinically relevant compound: Remicade (anti-TNF- α antibody).
- TNBS-induced colitis is a rapid and relevant preclinical model to test therapeutic approaches for the treatment of IBD with particular interest for targeting immunologic aspects relevant to the Crohn's disease.

Specie

Rat (Wistar)

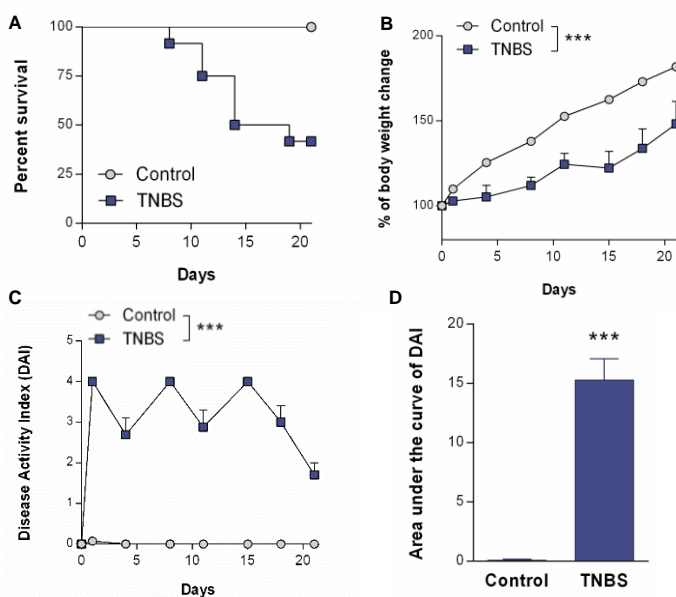
Model Description

- Rats are administered with TNBS in 50% ethanol (intracolonic) and are evaluated at least twice a week for body weight, evidence of bloody stool and diarrhea.
- On day 21, colon are dissected for macroscopic evaluation of inflammation.
- Tested compounds can be administered *via* various routes (i.v., i.p., s.c., p.o., intracolonic).

Parameters evaluated

- % body weight loss
- Area under the curve (AUC) of DAI: fecal consistency and occult blood test
- Macroscopic score in colon (clinical scoring)
- Colon weight, length and thickness
- Histological change in colon
- Mediators dosage (ELISA, multiplex assays)

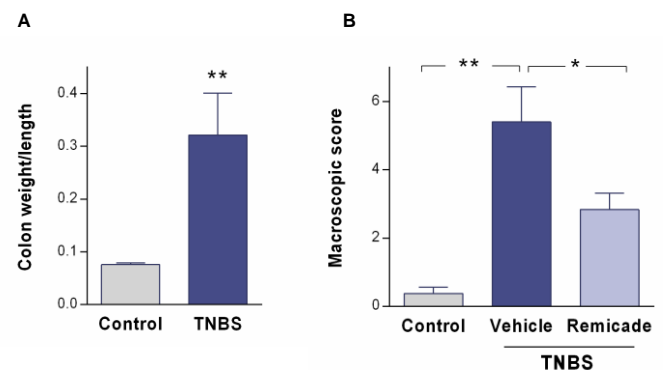
Chronic TNBS induces body weight loss and bloody diarrhea



Effects over time of TNBS (intracolonic administration) on survival (A), body weight (B), DAI (C) and corresponding AUC (D).

*** P<0.001, (n=5-8/group)

Chronic TNBS induces structural damage on the colon Remicade decreases macroscopic score in TNBS-treated rats



Effects at D21 of TNBS (intracolonic administration) on colon weight/length ratio (A) and colonic macroscopic score (B). Remicade or vehicle was administered (i.p.) at D0, D4 and D14 (B).

* P<0.05, ** P<0.01, (n=5-8/group)