

Gastrointestinal disease

Our deep understanding of gut physiology has guided us to explore different disease models of Inflammatory Bowel Disease (IBD)

Mouse Model of Dextran Sodium Sulfate (DSS) induced colitis

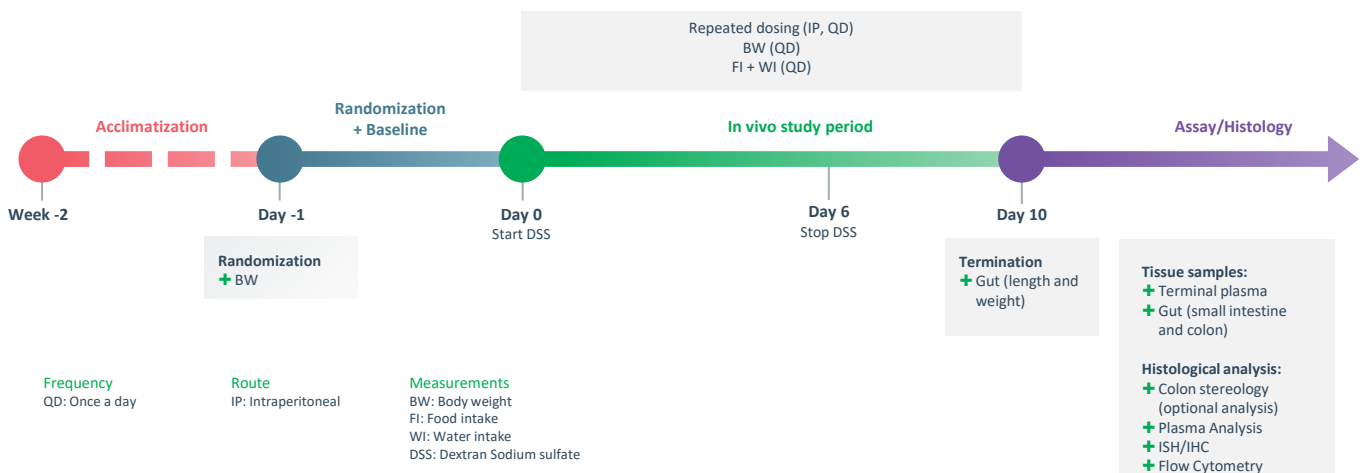
DSS induced experimental colitis is a rapid and widely used acute and chronic model of intestinal inflammation. At Gubra, we have verified increased inflammatory volume following DSS treatment and shown improvement by use of cyclosporine as positive control.

Key model traits

- Stereological assessment of total inflammatory volume.
- Multiplex cytokine measurements.
- Flow cytometry.
- Immunohistochemistry and In situ hybridizations.
- Cyclosporine as positive control.

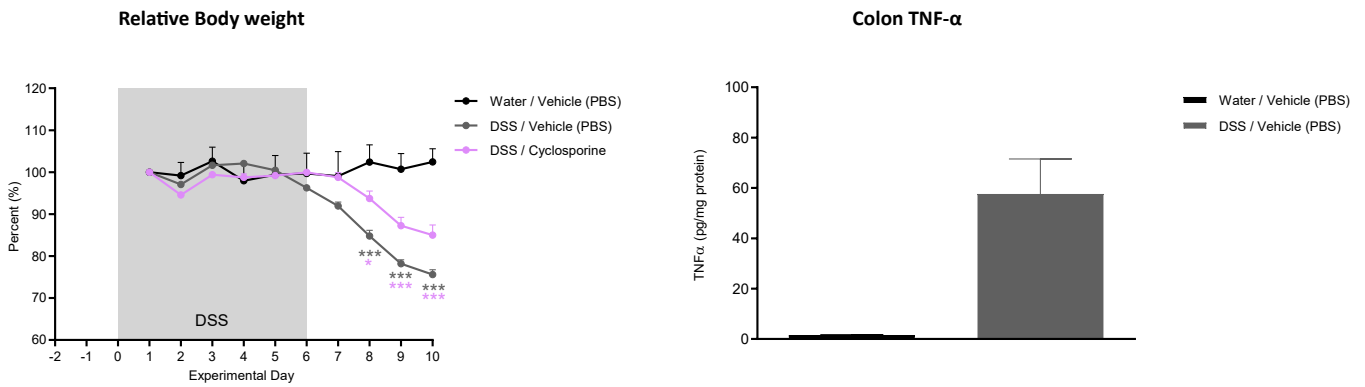
Diet	Standard chow	DSS in drinking water
Strain	C57Bl/6JRj mice	

Study outline



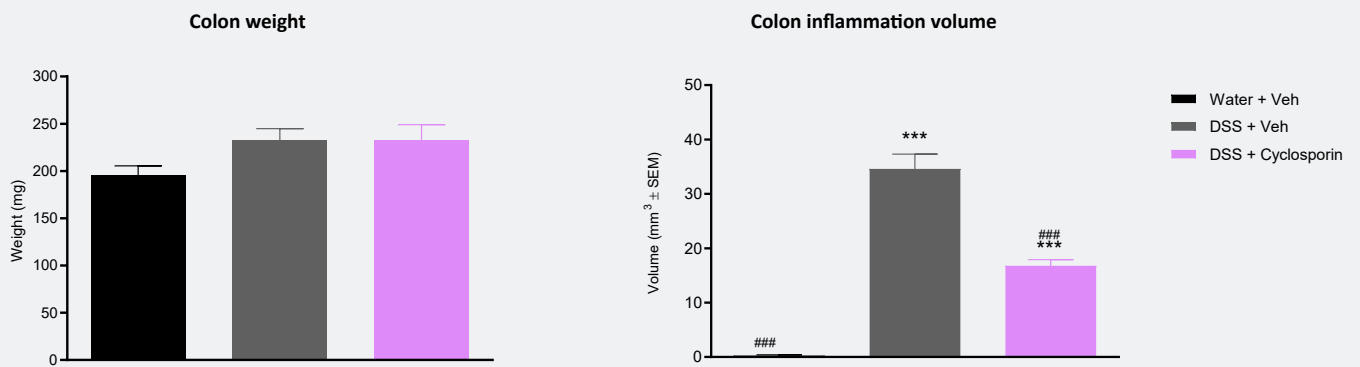
Metabolic and biochemical characteristics

DSS increases several proinflammatory markers, here shown for TNF- α . Cyclosporine delays the onset of weight loss.



Effects on gut histology

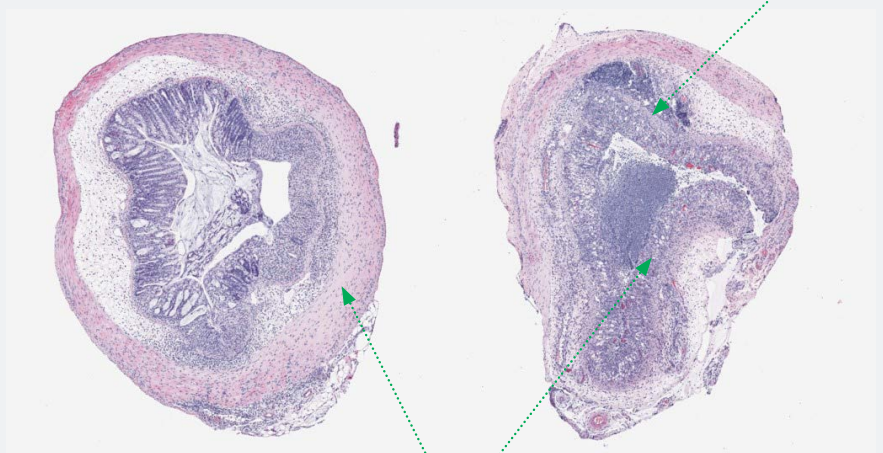
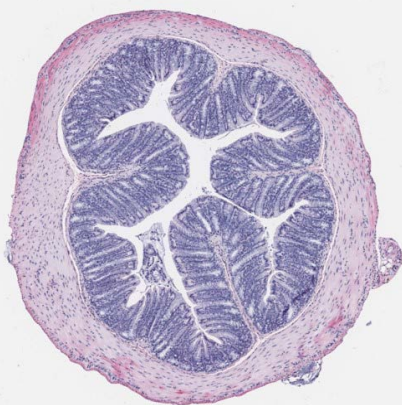
DSS lead to an increased inflammatory colon volume which was reduced following cyclosporin treatment.



Vehicle

DSS treated mice

Submucosal inflammation



500um

Group	Treatment	Survival	Inflammation severity
1	20% EtOH	100%	None to very mild
2	35% EtOH	66%	Mild
3	50% EtOH	33%	Severe
4	20% EtOH + 1.5 mg TNBS	66%	Mild to moderate
5	35% EtOH + 1.5 mg TNBS	66%	Moderate to severe
6	50% EtOH + 1.5 mg TNBS	66%	Severe
7	20% EtOH + 2.5 mg TNBS	66%	Moderate to severe
8	35% EtOH + 2.5 mg TNBS	33%	Very severe

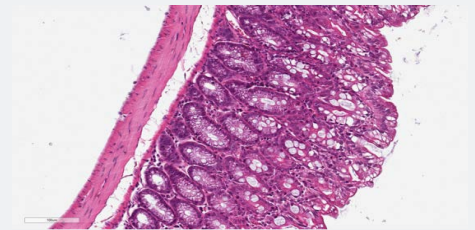
TNBS-induced colitis

TNBS induced colitis shares significant properties with human Crohn's disease. We have optimized treatment paradigms for inflammation severity while maintaining high survival.

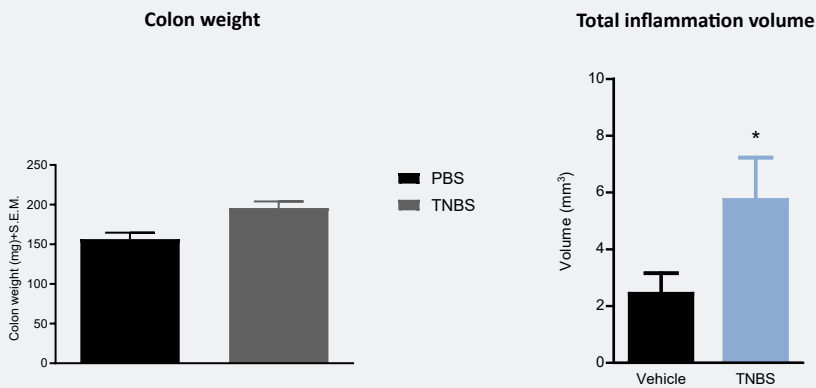
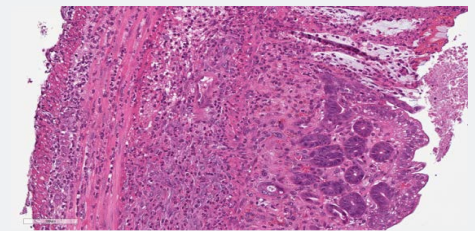
TNBS induced inflammation

TNBS treatment leads to disruption of the mucosal epithelium and crypt architecture with inflammatory cells inflammations in the submucosa and muscular layers.

Vehicle



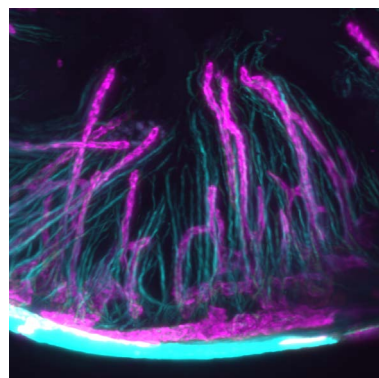
TNBS



High-end technologies

Using light-sheet microscopy it is possible to immunolabel and scan intestinal samples at single cell resolution. Allowing for quantification disease endpoints associated with pathological changes in villi morphology and structure.

Duodenum stained with antibodies against LYVE1 and aSMA. aSMA labels the smooth muscle cells while LYVE1 marks the lacteal cells responsible for taking up dietary fat in the gut.



Duodenum stained with antibodies against NG2 and aSMA for labelling of the smooth muscle cells and pericytes.

