INTRODUCTION

The intestinal immune system plays a key role in maintaining the balance between immune responses and tissue injury. Pattern recognition receptors, including endosomal and membrane-bound Toll-like receptors (TLRs), are key components of the innate immune system. Upon DAMP or PAMP recognition, TLR-mediated signaling induces inflammation and chemokines such as TNF and IFN-γ. The development of chronic intestinal inflammation is believed to contribute to the development of chronic intestinal diseases like inflammatory bowel disease (IBD).

EXPERIMENTAL DESIGN AND RESULTS

**TREATMENT OF TNSB-INDUCED COLITIS IN C57BL/6 MICE WITH ORAL IMO-9200**

IMO-9200 treatment decreased inflammation and mucosal damage in colon histology.

**IMO-9200 TREATMENT REDUCED INFLAMMATORY MEDiators IN THE COLON**

IMO-9200 treatment reduced pro-inflammatory cytokine expression in the colon.

**IMO-9200 TREATMENT INCREASED COLON LENGTH AND HISTOLOGY**

IMO-9200 treatment decreased inflammation and mucosal damage in colon histology.

**IMO-9200 TREATMENT IMPROVED COlON HISTOLOGY BY DECREASING INFLAMMATORY AND MUCOSAL DAMAGE**

IMO-9200 treatment restored normal colon architecture.

**CONCLUSIONS**

- Antagonism of TLRs 7, 8, and 9 with IMO-9200 represents a novel therapeutic approach for IBD, upstream of currently available immune modulating therapies.
- IMO-9200 reduced inflammatory cytokine and chemokine expression, and restored the TGF-β/Smad3 signaling pathway.
- IMO-9200 modulated gene expression, including down-regulation of genes associated with pro-inflammatory cytokines, tissue repair and remodeling, antimicrobial peptides, and acute phase proteins and up-regulation of genes involved in maintenance of intestinal barrier integrity.
- Comparative results for IMO-9200 were also observed in a DSS-induced colitis model, including a reduction of the Colitis Disease Activity Index.
- Collectively, these data demonstrate the potential of orally administered IMO-9200 to inhibit intestinal inflammation and improve disease symptoms, supporting its further development as a treatment for patients with IBD.

**IMO-9200 TREATMENT IMPROVED COLON LENGTH AND HISTOLOGY**

IMO-9200 treatment improved colon length and histology in mouse models of colitis.

**IMO-9200 TREATMENT IMPROVED COLON HISTOLOGY BY DECREASING INFLAMMATORY AND MUCOSAL DAMAGE**

IMO-9200 treatment improved colon histology by decreasing inflammatory and mucosal damage.

**IMO-9200 TREATMENT REDUCED INFAMMATORY MEDiators IN THE COLON**

IMO-9200 treatment reduced inflammatory mediators in the colon.

**IMO-9200 TREATMENT RESTORED THE TGF-β/SMAd3 SIGNALLING PATHWAY**

IMO-9200 treatment restored the TGF-β/SMAd3 signaling pathway.

**IMO-9200 TREATMENT IMPROVED COLON HISTOLOGY**

IMO-9200 treatment improved colon histology.

**IMO-9200 TREATMENT IMPROVED COlON LENGTH AND HISTOLOGY**

IMO-9200 treatment improved colon length and histology.

**IMO-9200 TREATMENT IMPROVED COlON HISTOLOGY**

IMO-9200 treatment improved colon histology.

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