287 STp, Protease Resistant Peptide from *Lactobacillus Plantarum*

Asset Overview

Product Type	Peptide secreted from bacteria (Lactobacillus plantarum)
Indication	Gut inflammation, Inflammatory bowel disease (IBD)
Current Stage	Preclinical
Target(MoA)	Restoring of gut immune homesotasis
Brief Description	• STp (72 residue) secreted from *L. plantarum* and present in healthy gut – lost in Ulcerative Colitis (UC) • STp resistant to degradation by gut proteases • Promotes regulatory cytokine profile in DC & T cells • Restores normal DC phenotype/function in UC *ex vivo* • May help repair of gut epithelium
Organization	Imperial College London

Differentiation

□ **Novel probiotic derived immunotherapy for IBD, suitable for oral administration**

- Current treatments for IBD include aminosalicylates, corticosteroids and immunosuppressants but many patients fail to respond
- Protease resistant and, unlike biologics, suitable for oral administration
- There is potential for development of a companion diagnostic due to absence of STp in patients with UC vs healthy individuals
- The team continues to evaluate the efficacy and PK/PD of STp in animal models vs conventional anti-TNFα

□ **Acting as an immuno modulator of Dendritic Cells, restoring gut immune homeostasis**

- STp increases IL10 and decreases IL12 production
- It restores TLR expression on UC derived DCs to 'normal' level (i.e. reduced TLR2 and TLR4)
- It restores maturation potential (CD40, CD80) and stimulatory capacity (proliferating T cells) of UC derived DCs

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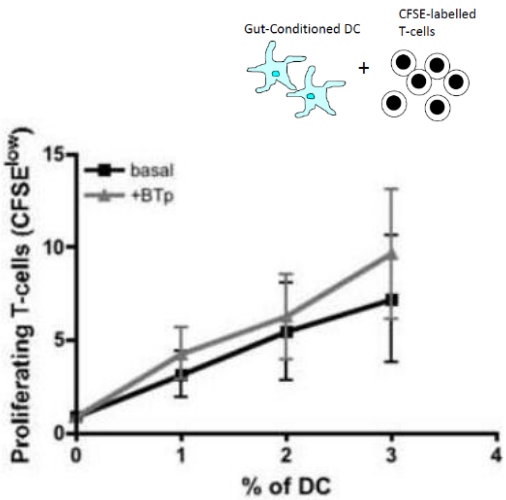
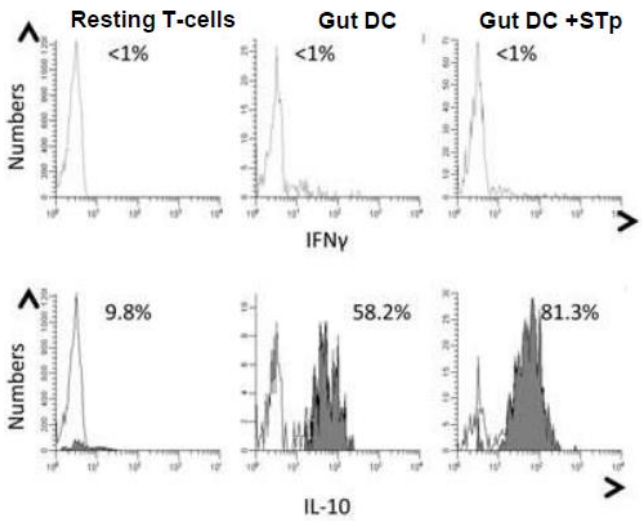
Key Data

STp-treated DCs do not promote pro-inflammatory T cells

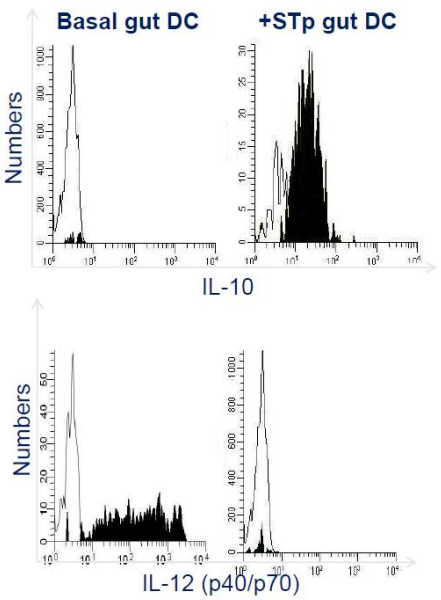
STp conditioning of intestinal DCs does not alter their T cell stimulatory capacity.

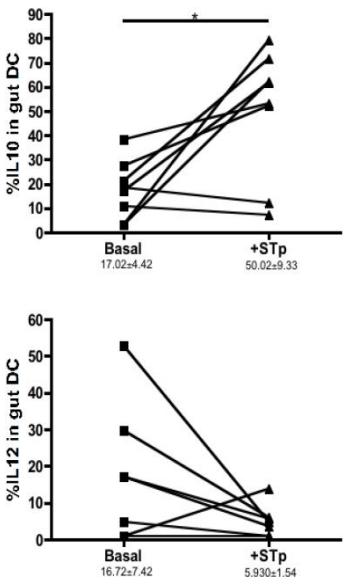


IL10 production by stimulated T cells was increased whilst IFNγ production is unchanged, suggesting STp treated DCs do not promote pro-inflammatory T cells



STp promotes "homeostatic" intestinal DC in UC





Flow cytometry diagrams representing the production of IL-10 and IL-12 in a donor whose dendritic cells of the colon mucosa displayed abnormal production of IL-12.
These dendritic cells were incubated in the presence of the ST peptide identified as SEQ ID NO: 1 (+BP). In comparison with the baseline conditions (basal) the presence of the ST peptide identified as SEQID NO: 1 **was capable of inducing the production of IL-10 and of blocking the production of IL-12.**

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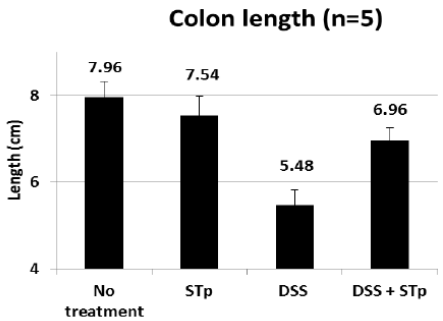
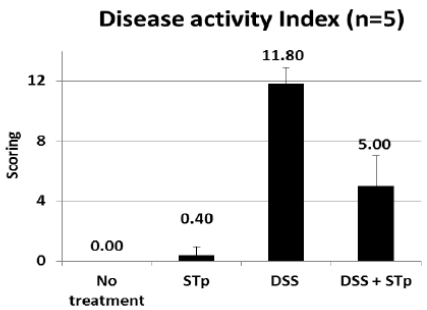
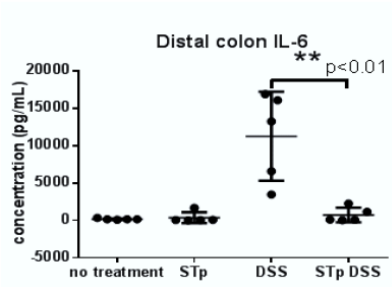
Key Data

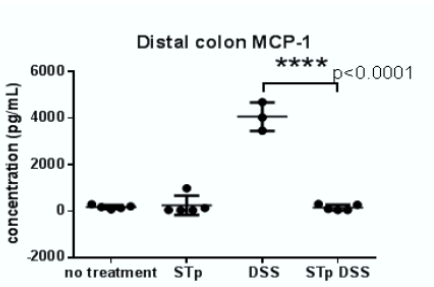
Therapeutic effects of STp in DSS mouse colitis

In vivo data showing reduced inflammation and reversal of symptoms in a model of UC









*STp given on days 1, 3, and 5 post colitis induction

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Intellectual Property

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Country	US, EP, JP, CN, AU

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