

ANTAGONISTIC EFFECTS OF INTERLEUKIN-25 ON CD14+ CELL CYTOKINE RESPONSES IN THE GUT

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Interleukin-25

- A member of the IL-17 cytokine gene family that expands Th2 cell responses and exerts both inflammatory and anti-inflammatory actions depending on the cell context analyzed
- IL-25 biological activity is mediated by a transmembrane receptor (IL-25R)

IL-25 acts preferentially on a non-B/non-T cell type expressing high levels of MHC class II and low levels of CD11c

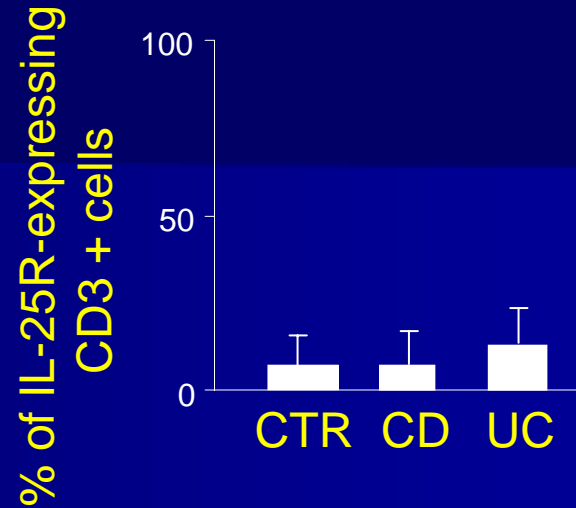
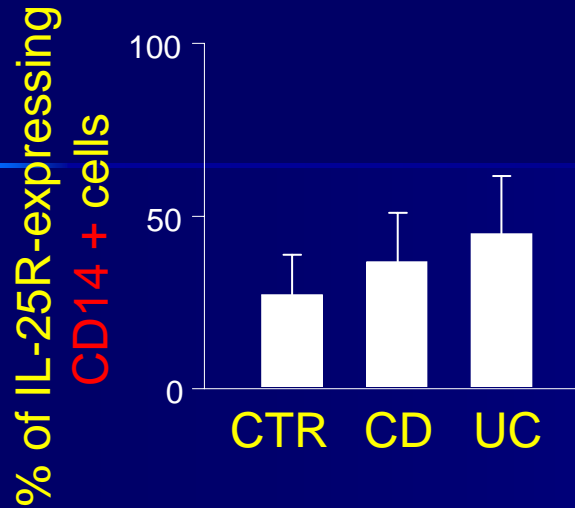
Aim of the project

To investigate the role of IL-25 in IBD

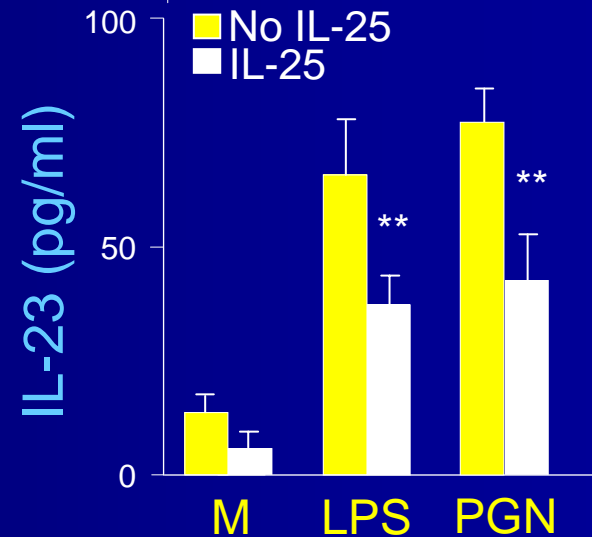
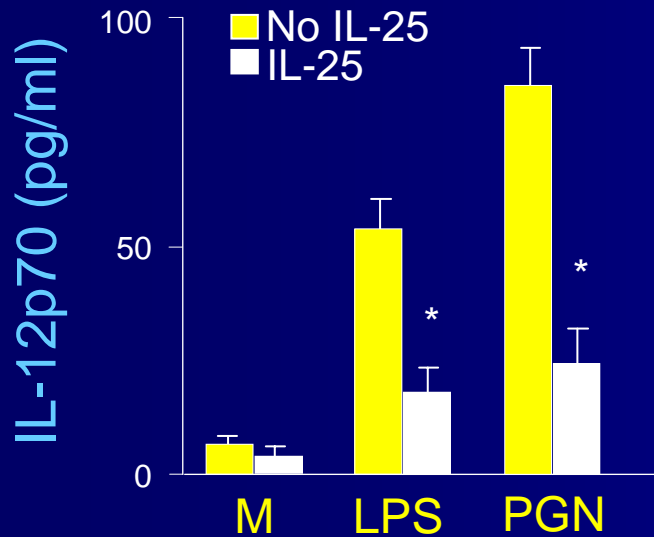
SPECIFIC AIMS:

1. To characterize IL-25R-expressing cells in the human gut
2. To examine whether IL-25 regulates the activity of intestinal mucosal cells
3. To determine whether IL-25 controls gut inflammation in murine models of IBD
4. To evaluate the expression of IL-25 in human IBD
5. To dissect mechanisms that regulate IL-25 expression in the gut

Intestinal mucosal CD14+ cells express IL-25R and respond to IL-25



CD14+ cells isolated from CD tissue



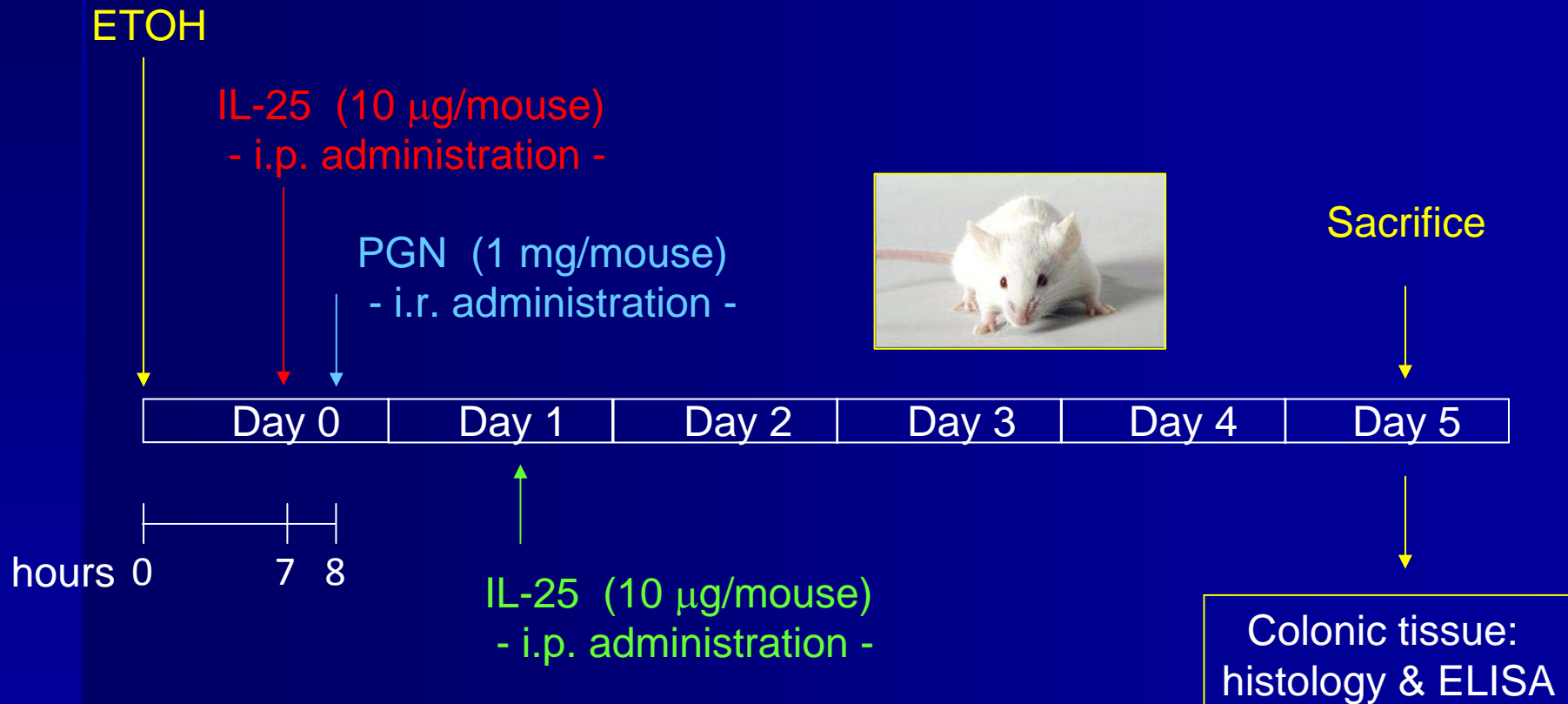
* p < 0.01
 ** p = 0.03

M= medium

Methods

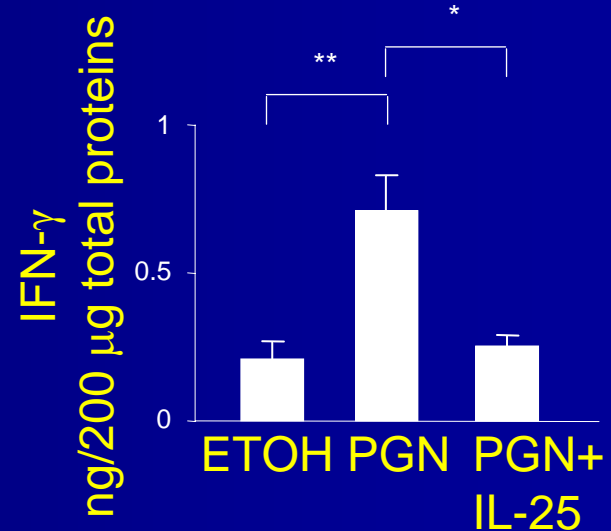
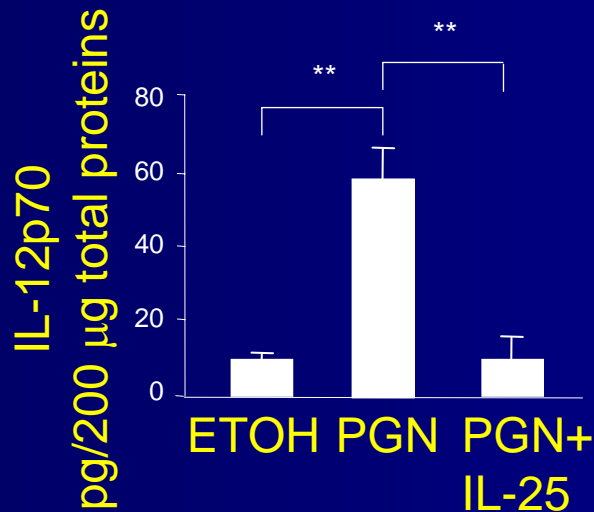
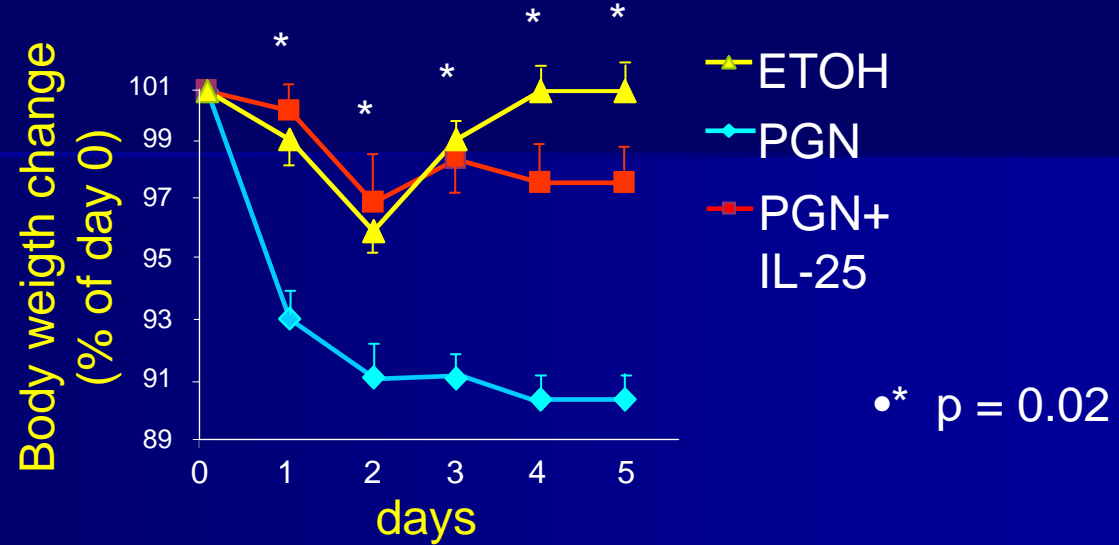
PGN-induced Colitis in Balb/c mice

Preventive & Therapeutic model

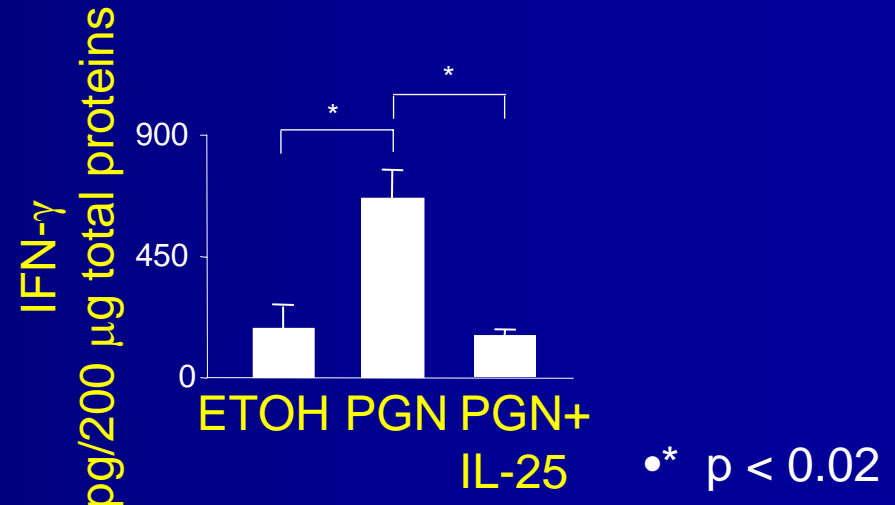
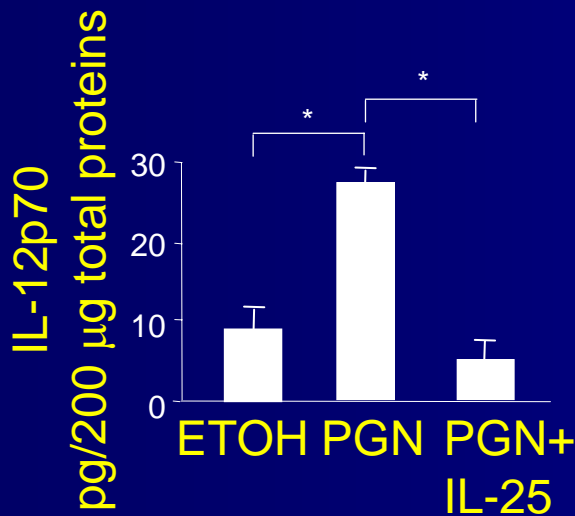
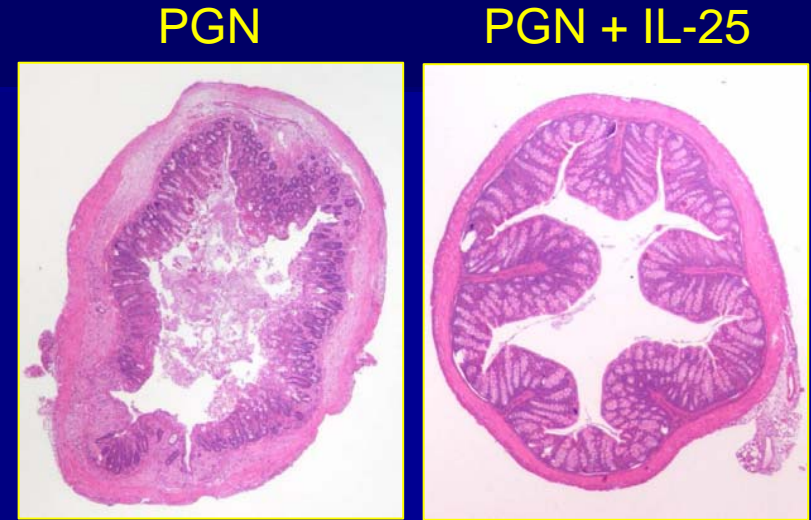
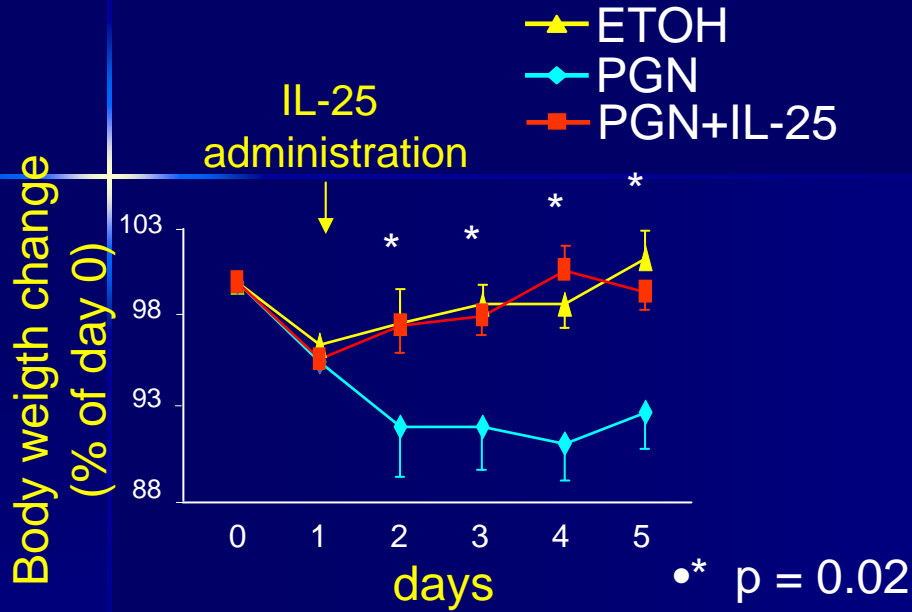


IL-25 prevents PGN-induced colitis in mice

Preventive model



Therapeutic effect of IL-25 in PGN-induced colitis



Methods

TNBS-induced Colitis

Therapeutic model

TNBS (2,5 mg/mouse)
- i.r. administration -

IL-25 (10 μ g/mouse)
- i.p. administration -



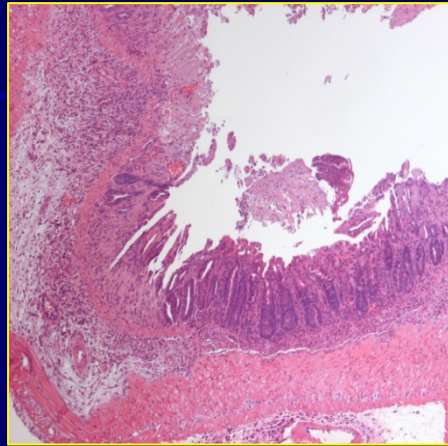
Sacrifice



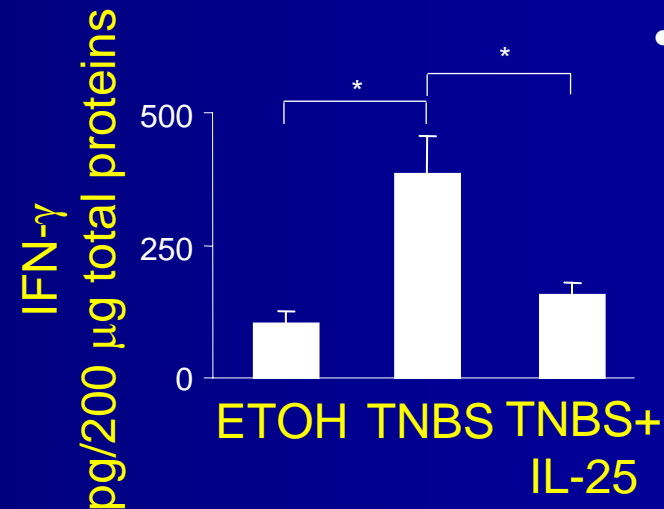
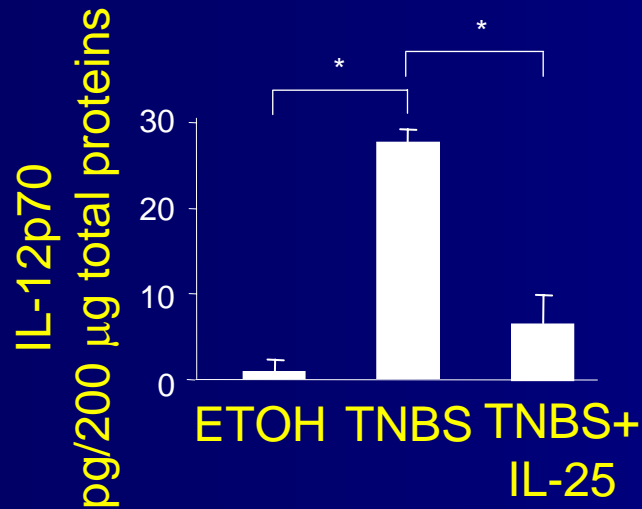
Colonic tissue:
histology & ELISA

Therapeutic effect of IL-25 in TNBS-induced colitis

TNBS

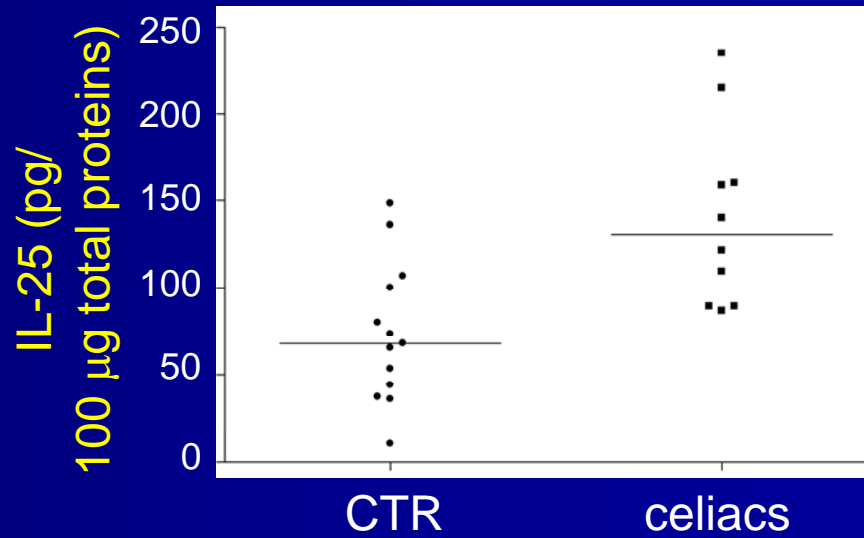
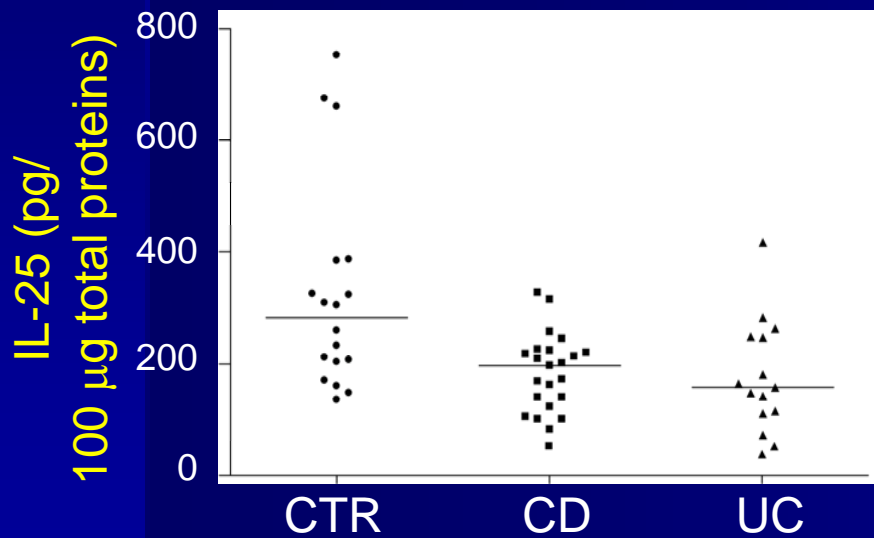
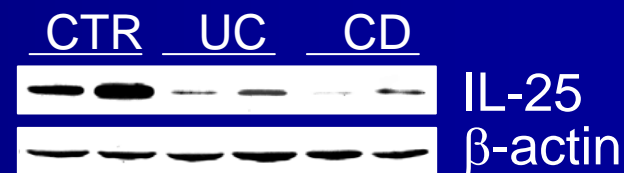
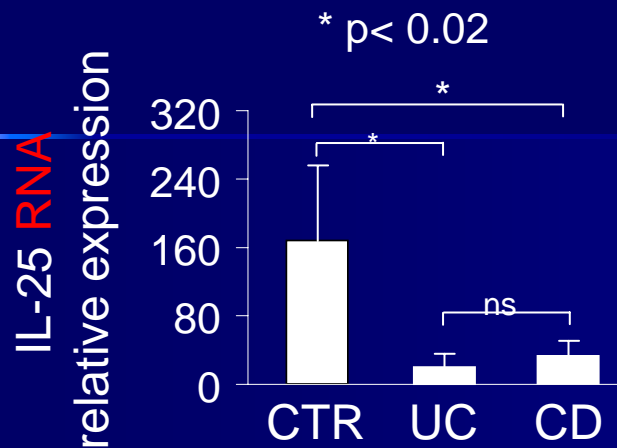


TNBS + IL-25



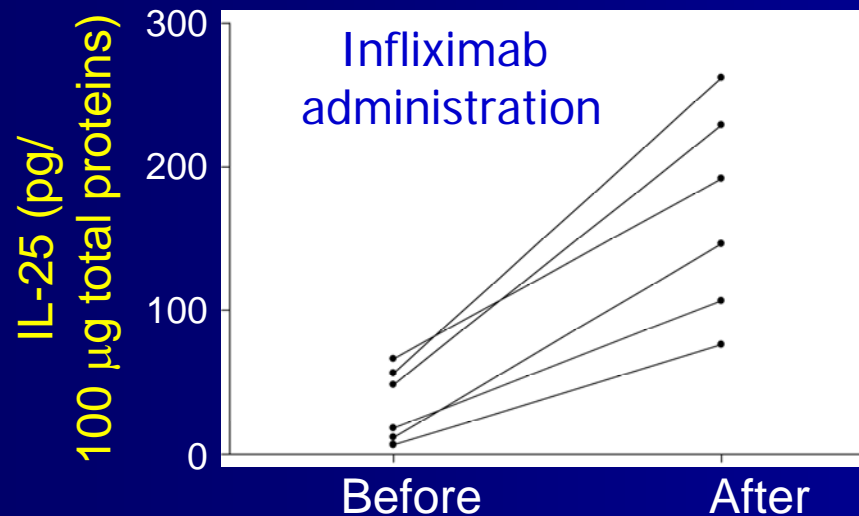
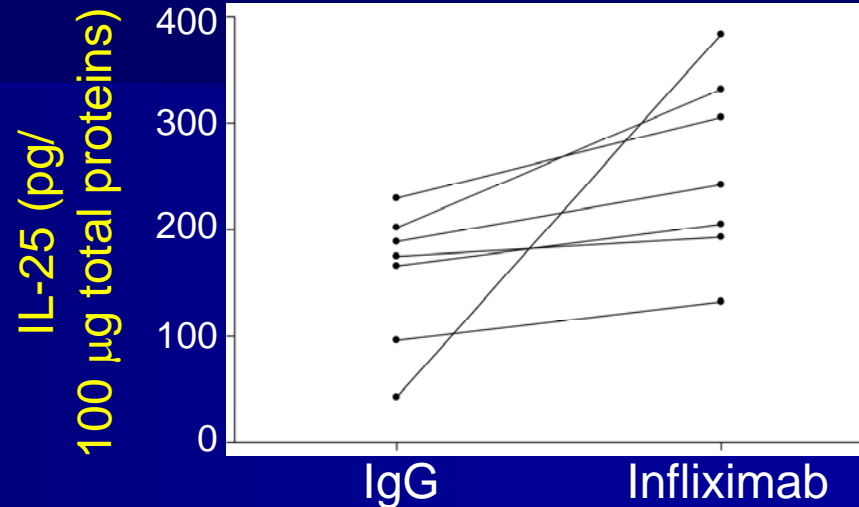
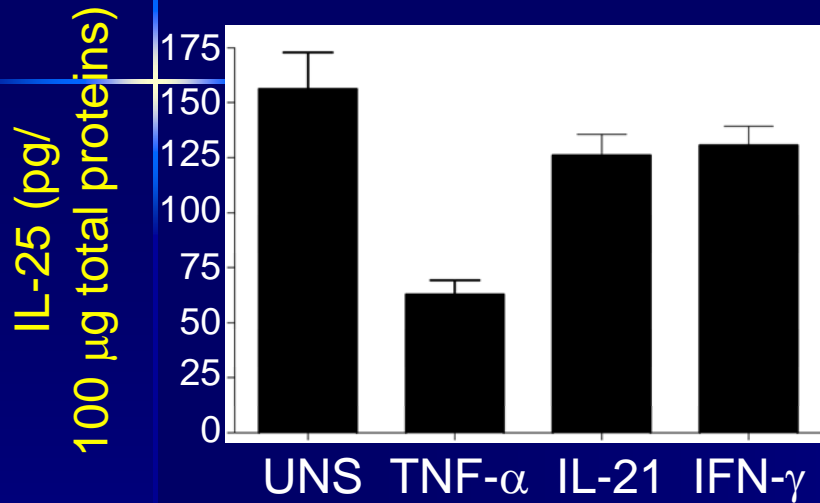
* p < 0.03

IL-25 expression is down-regulated in IBD but not celiac disease mucosa



TNF- α negatively regulates IL-25 expression in the gut

Ex vivo organ cultures of mucosal explants



Conclusions

The diminished production of IL-25 could contribute to sustain/amplify mucosal inflammation in IBD