

PTH-046

# **TH1/TH17 PROFILES IN CROHN'S DISEASE: A CROSS SECTIONAL SINGLE CENTRE STUDY IN POSTOPERATIVE CROHN'S DISEASE**

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**Introduction** Th1 and Th17 pathways are implicated in Crohn's disease (CD). In operative resection samples healthy ileum shows high TGFβ levels in patients who develop recurrence, with TGFβ being a known activator of the Th17 response. Other studies in CD show a dominant Th1 cytokine profile, with high levels of IFNγ, which reduce Th17 response and augment Th1 response. The relationship of Th1/Th17 cytokine profiles in postoperative CD has not been examined. The authors aimed to study tissue Th1/Th17 cytokine secretion after in vitro biopsy culture in postoperative CD.

**Methods** Colonoscopy was undertaken in postoperative CD patients. Recurrence graded as no/minimal inflammation (Rutgeert Score (RS) ≤1) or progressive inflammation (RS≥2). Ileal biopsies were cultured overnight and cell free supernatants obtained. Supernatant cytokines (IL-2, IL-4, IL-10, IL-17 TNFα, INFγ and IL-6) were assessed by flow cytometry using cytometric bead array (Becton Dickinson). Statistical analysis was via unpaired t tests.

**Results** Consecutive patients attending endoscopy (n=24, 9M/15F) were identified. Mean age 45.0 years and time from I to C resection was 5.8 years; 5 patients were smokers. Drugs

**Table 1** PTH-046

Cytokine	Mean cytokine level±SEM (pg/ml)	
	Rutgeert score ≤1	Rutgeert score ≥2
IL-2	2.4±0.1	2.3±0.1
IL-4	0.3±0.2	0.5±0.3
IL-6	2469.1±969.2	5485.7±2020
IL-10	7.3±4.8	4.6±0.8
TNFα	1.6±0.1	2.7±1.5
IFNγ	1.3±0.2	6.6±2.1
IL-17a	0.5±0.4	2.5±0.7

were thiopurines 13, Infliximab 1 and nil 10. Endoscopic severity was i0 n=5, i1 n=6, i2 n=5, i3 n=3, i4 n=5. Mean cytokine concentrations from supernatants are shown in the table 1. Comparison between RS≤1 and ≥2 showed that pro-inflammatory cytokines IL-17a (p<0.02) and IFNγ (p<0.03) were significantly higher in RS i2-i4 neo terminal ileum as compared with those with RS i0-i1. The regulatory cytokine IL-10 was significantly higher in patients with RS≤1 (p<0.038).

**Conclusion** Cytokine profiles in those with RS≥2, show higher levels of IL-17a and IFNγ and reduced IL-10 compared to RS≤1. This profile supports a Th17 and Th1 mediated response as one of the early instigators of endoscopic progression in postoperative CD. The authors' observation is consistent with recent findings of a T cell subset able to produce cytokines involved in both Th1 and Th17 responses. Previous therapies directed at Th1 pathway, for example, anti-IL-12p40 antibody ustekinumab and anti-IFNγ Fontolizumab failed to show significant clinical benefit in CD. Given our findings targeting the Th17 response, for example, with anti-IL-23 antibodies and anti-IL-17 may deliver improved therapeutic outcome.

**Competing interests** None.

**Keywords** cytokines, postoperative Crohn's disease, TH1/TH17.