PTU-074  ULCERATIVE COLITIS: THE ALPHAE-BETA-7 INTEGRIN IS ASSOCIATED WITH A HIGH FREQUENCY OF TH17, TH1 AND TH17/TH1 CD4 LYMPHOCYTES

CA Lamb*, 1JC Mansfield, 1GW Tew, 6AK Long, 7PM Irving, 4AK Long, 4D Gibbons, 4PM Irving, 3LD eihl, 1Chatu S

1Newcastle University, UK; 2Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK; 3Genentech, South San Francisco, USA; 4King’s College London, London, UK; 5University of Sunderland, Sunderland, UK

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Introduction T lymphocytes expressing the αβ7 integrin are highly enriched within human intestinal epithelium and lamina propria. Studies exploring pathogenic or protective functions of αβ7 expressing cells are lacking. Defining this phenotype is critical for our understanding of IBD pathogenesis and of translational importance with the development of etrolizumab, a humanised antibody specific to the β7 integrin that blocks αβ7: MAdCAM-1 and αβ7-E-cadherin interactions.

Methods Lymphocytes within colonic biopsies from a total of 43 UC and 35 non-disease control patients were studied. Multicolour FACS was optimised to determine surface and intracellular protein expression (CD45, CD3, CD4, CD8, αE, β7, CD161, IL-17A, TNFα, IFNγ and IL-10). qPCR was performed on TCRβ6+ lymphocytes, FACS sorted into CD4+αβ7+, CD4+αβ7−, CD8+αβ7+, and CD8+αβ7− prior to gene expression assay. Dual stain IHC for αE, plus CD3, CD4, CD8 and FOXP3 was performed using a Ventana Benchmark XT autostainer. Severity of UC was stratified using the Mayo endoscopic score for ulcerative colitis.

Results Ulcerative colitis was associated with a significantly increased frequency of T lymphocytes in the intestinal mucosa (p < 0.05). IHC revealed the highest expression of αE on CD4 and CD8 intraepithelial lymphocytes, although a substantial number of lamina propria lymphocytes also expressed this integrin. In UC, FACS demonstrated CD4+αβ7+ lymphocytes had a higher potential to produce the pro-inflammatory cytokines IFNγ (p < 0.01), TNFα (p < 0.001) and IL-17A (p < 0.0001) than CD4+αβ7− lymphocytes. In addition, a mean of 31.5% of the CD4+αβ7+ lymphocytes produced both IL-17A and IFNγ compared to a mean of only 7.7% in the CD4+αβ7− compartment (p < 0.001). IL-10 was not differentially expressed between CD4+αβ7+ and CD4+αβ7− lymphocytes in controls or UC, and a low frequency of αβ7+FOXP3+ cells was observed by IHC, qPCR array confirmed higher mRNA levels of IFNγ (p < 0.001), TNFα (p < 0.01) and IL-17A (p < 0.01), and lower transcription of FOXP3 (p < 0.0001) in CD4+αβ7+ compared to CD4+αβ7− cells.

Conclusion αβ7 expression was associated with an enrichment of pro-inflammatory Th17, Th1 and Th17/Th1 T lymphocytes, and not associated with a regulatory phenotype. These data suggest therapeutic interventions targeting αE expressing T cells and the αβ7 integrin itself may be viable approaches for reducing aberrant inflammatory responses in UC.

Disclosure of Interest None Declared.

PTU-075  SYSTEMATIC REVIEW AND META-ANALYSIS: SENSITIVITY AND SPECIFICITY OF TC-99M HMPAO LABELLED WHITE CELL SCINTIGRAPHY IN THE DIAGNOSIS OF ACTIVE INFLAMMATORY BOWEL DISEASE

CJM Williams*, 2AC Ford, 1A Poullis, 1Department of Gastroenterology and Hepatology, St George’s Hospital and Medical School, London, UK; 2Leeds Gastroenterology Institute, Leeds General Infirmary, Leeds, UK

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Introduction Technetium-99m hexamethylpropylene amine oxime (Tc-99m HMPAO) labelled white cell scintigraphy (WCS) is frequently used in the assessment of patients suspected of having active inflammatory bowel disease (IBD). However, no previous systematic review and meta-analysis has assessed the sensitivity, specificity, and positive and negative predictive values of this investigation in comparison with colonoscopy and histology. We therefore aim to present these data here.

Methods The MEDLINE and EMBASE databases were searched to January 2014. Prospectively and retrospectively cross-sectional studies recruiting adults suspected of a new diagnosis or flare of IBD, and comparing Tc-99m HMPAO labelled WCS with colonoscopy and histology, were eligible. True positive, false positive, true negative and false negative findings were pooled. A random effects model was used to obtain overall data for sensitivity, specificity, and positive and negative predictive values with a 95% confidence interval (CI).

Results We identified 15 eligible studies reporting data from 635 patients (174 Crohn’s disease, 136 ulcerative colitis, 36 non-IBD). In total 1300 bowel segments were examined with 698 true positives, 41 false positives, 461 true negatives and 100 false negatives. Sensitivity was 0.90 (95% CI 0.85 to 0.95), specificity was 0.91 (95% CI 0.87 to 0.94), positive predictive value was 0.95 (95% CI 0.92 to 0.97) and negative predictive value was 0.83 (0.76 to 0.89).

Conclusion Tc-99m HMPAO labelled WCS is a sensitive and specific test for the diagnosis of active inflammatory bowel disease. Physicians may therefore find this a useful test for those in whom colonoscopy and histology are impractical or contraindicated.

Disclosure of Interest None Declared.