The IL-33/ST2 Pathway in IBD: Regional Immune Signatures across Crohn's Disease and Ulcerative Colitis

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Background and aims: The IL-33/ST2 axis is a key mediator of mucosal immune activity and epithelial barrier regulation. Yet, its expression in inflammatory bowel diseases (IBD), such as Crohn's disease (CD) and ulcerative colitis (UC), remains insufficiently defined, especially in relation to anatomical site and disease category.

Methods: A total of 31 intestinal mucosal biopsies from IBD patients (CD and UC) were analysed. Samples were obtained from multiple anatomical sites (ileum, right and left colon, rectum). Immunofluorescence staining was performed via sequential incubation with primary antibodies targeting IL-33 or ST2, followed by AlexaFluor 488-conjugated secondary antibodies. Cell nuclei were counterstained using DAPI. Imaging was performed using a Zeiss LSM 800 confocal microscope at 20x magnification. IL-33 and ST2 expression were scored visually on a 1–9 semi-quantitative scale by two independent blinded observers. Statistical analysis included Spearman correlation, Mann-Whitney U, and Kruskal-Wallis tests.

Results: IL-33 and ST2 scores were significantly correlated ($r = 0.54$, $p = 0.002$), indicating coordinated expression within the mucosa. IL-33 levels were significantly higher in CD than in UC ($p = 0.038$), while ST2 levels did not differ between diagnoses ($p = 0.558$). IL-33 expression also varied significantly with biopsy location ($p < 0.05$), with the highest scores observed in ileal samples. No significant differences were found in IL-33 or ST2 expression based on patient sex or biologic treatment exposure. These findings suggest a site- and disease-specific modulation of IL-33 expression, independent of systemic factors.

Conclusions: This study confirms a consistent mucosal co-expression of IL-33 and ST2 in IBD, with IL-33 levels significantly elevated in Crohn's disease and showing regional variation along the gut. These data support the biological relevance of the IL-33/ST2 axis in the intestinal immune landscape of IBD and provide a basis for future investigation into its mechanistic and clinical significance.

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