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## HETEROGENEITY IN EXPRESSION OF ANTIMICROBIAL PROTEINS IN NORMAL AND CROHN'S DISEASE SMALL INTESTINAL PANETH CELLS

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**Introduction** Paneth cells are normally located at the base of small intestinal crypts and express a number of antimicrobial factors that are believed to be important in host protection against luminal bacteria. There is increasing interest in the role of Paneth cells in the pathogenesis of Crohn's disease. The aim of this studies was to investigate immunoreactivity for the antimicrobial proteins human defensin (HD)-5, lysozyme and secretory phospholipase A2 (sPLA2) in normal and Crohn's disease small intestinal mucosal samples.

**Methods** Sequential sections were obtained from normal small intestinal mucosal samples (n=9) and those affected by Crohn's disease (n=10) and used for immunohistochemical studies using specific antibodies. For each section, cells immunoreactive for HD-5, lysozyme and sPLA2 were counted in 10 sequential, well-orientated, crypt-villus units. To assess co-expression of antimicrobial proteins by individual cells, a suitable crypt was identified and studied in all three sequential sections from each mucosal sample. Data are expressed as mean (SEM).

**Results** Normal small intestinal crypts: compared to Paneth cells immunoreactive for HD-5 (31.1 (4.9) per 10 crypts) and lysozyme (30.0 (4.5)), there were significantly fewer sPLA2 positive cells (15.3 (2.7);  $p < 0.01$ ). Small intestinal Crohn's disease crypts: numbers of HD-5 (42.1 (7.7)) and lysozyme (43.9 (8.3)) immunoreactive cells were significantly greater than sPLA2 labelled Paneth cells (14.5 (4.0);  $p < 0.01$ ). For all the sections, sPLA2 immunoreactivity was generally weaker than for the other two antimicrobial proteins. There were no significant differences between normal and Crohn's disease crypts in the number of Paneth cells labelled for HD-5, lysozyme or sPLA2. Crypt cells immunoreactive for sPLA2 in normal and Crohn's disease samples were also positive for HD-5 (91.7% and 100% respectively) and lysozyme (91.7% and 100% respectively). Majority of HD-5 labelled cells were also positive for lysozyme (78.4% in normal and Crohn's disease). Of the lysozyme labelled Paneth cells, 85.3% and 86.6% were HD-5 immunoreactive in normal and Crohn's disease samples respectively. Crypt luminal immunoreactivity for HD-5/lysozyme/sPLA2 was seen in 4/2/1 (respectively) normal and 6/3/1 Crohn's disease samples. Outside the crypt region, HD-5/lysozyme/sPLA2 immunoreactive cells with morphological features of intermediate cells were seen in 2/1/0 (respectively) normal small intestinal and 6/4/4 Crohn's disease samples.

**Conclusion** There is heterogeneity in the expression of the antimicrobial proteins HD-5, lysozyme and sPLA2 in Paneth and non-Paneth epithelial cells in normal and Crohn's disease small intestine.