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## IMMUNOHISTOCHEMICAL LOCALISATION OF DYNORPHIN A(1-8) AND VASOACTIVE INTESTINAL POLYPEPTIDE (VIP) IN HUMAN COLONIC MUCOSA

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Gastrointestinal activity is controlled primarily by the enteric nervous system through the release of different neurotransmitters, many of which are neuropeptides. Two neuropeptides which play opposing roles in regulating intestinal secretion are dynorphin A (1-8) and vasoactive intestinal polypeptide (VIP). In addition to entric control, gut function is also regulated by neuroendocrine cells found within mucosal crypts; these cells release 5-HT and various peptides such as the enkephalins (Ahlman & Nilsson, 2001). VIP-positive nerve fibres have been shown in the lamina propria, in very close proximity to neuroendocrine cells (Anlauf *et al.*, 2003), but there is little information on either VIP or dynorphin A(1-8) in neuroendocrine cells. In this investigation, the distribution of dynorphin A(1-8) and VIP in human colonic mucosa has been determined, with particular reference to neuroendocrine-like cells.

Fresh specimens of human colon were obtained from Glasgow Royal Infirmary with informed patient consent and local ethical approval. Specimens were fixed in 10% neutral buffered formalin. Standard ABC techniques were employed and results visualised using light microscopy. Anti-dynorphin A(1-8) antibody (Bachem, UK) was used at 1:800 dilution and anti-VIP antibody (Affiniti, UK) at 1:200.

In 3 out of 5 specimens, dynorphin A(1-8)-like immunoreactivity was localised to neuroendocrine-like cells in the colonic mucosa. Staining was typically found basolateral to the nucleus, projecting away from the lumen towards the lamina propria. There were no immunoreactive nerve fibres or other immunoreactive cells in the mucosa although dynorphin A(1-8)-like immunoreactivity was clearly evident in the submucosal and myenteric nerve plexuses. In all specimens (n=7), VIP-like immunoreactivity was found in neuroendocrine-like cells, with a similar pattern to dynorphin A(1-8). There were no immunoreactive nerve fibres in the mucosa, but some cells, probably immune cells, were also VIP positive. Preliminary experiments, with chromogranin A, a neuroendorine cell marker, suggest that these are indeed neuroendocrine cells.

In conclusion, dynorphin A(1-8) and VIP are found in cells believed to be neuroendocrine cells in the human colonic mucosa. Further work is ongoing to investigate the mucosal distribution of dynorphin A(1-8) and VIP in Inflammatory Bowel Disease, where perturbations in the numbers of neuroendocrine cells have been noted (El-Salhy *et al.*, 1997).

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*Where applicable, the experiments described here conform with Physiological Society ethical requirements.*