Enteroendocrine cell signalling: implications in the GI tract and beyond

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Enteroendocrine cells collectively constitute the largest endocrine tissue in the body. These cells are scattered amongst the gastrointestinal (GI) epithelium and make-up about 1% of all cells lining the GI tract. They consist of an array of different cell types, each containing specific hormone markers that they actively secrete in response to various physiological stimuli including nutrients and gut distension. It is unsurprising that these endocrine cells serve a multitude of physiological functions but are difficult to study in isolation. We have focused our recent studies on the largest population of these cells, the serotonin (5-HT) containing enterochromaffin (EC) cells. EC cells produce ~95% of the body's 5-HT and this circulating 5-HT is vital for a multitude of bodily functions including enteric motility, bone mass, liver regeneration and glucose homeostasis. We have identified several roles for EC cells associated with the control of gut motility and peristalsis and measured 5-HT release in real-time from intact tissue. Understanding how 5-HT is released from EC cells and the mechanisms that control this release is therefore important in terms of both health and disease. Despite the importance of EC cells no studies have investigated the physiological function of single primary EC cells. We have developed a method of rapid primary culture of guinea pig, mouse and human EC cells, allowing analysis of single EC cell function using electrophysiology, electrochemistry, Ca^{2+} imaging, immunocytochemistry and 3D modelling. We find that EC cells release 5-HT from single vesicles in response to an array of stimuli, secretion involves Ca^{2+} entry via plasma membrane Ca^{2+} channels and that EC cells release 60-100 times less 5-HT per fusion event compared to other endocrine cells. We also observe alterations in 5-HT release under various culturing conditions and in different disease settings. Our findings indicate that the mechanisms controlling 5-HT release from EC cells as well as 5-HT synthesis has direct relevance to GI tract function and glucose homeostasis pathways.