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Quantifying Pancreatic Islet Architecture: Endocrine Cell Type Distribution Effects on Hormone Secretion

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Coordination among cells within the islets of Langerhans is required to maintain blood glucose homeostasis. The major islet cell types are the insulin-secreting β cells, glucagon-secreting α cells, and somatostatin-secreting δ cells. Dysregulation of islet secretory activity can result in serious pathophysiology, notably diabetes. With the incidence of diabetes reaching epidemic proportions, investigation of the mechanisms underlying islet function is increasingly salient. Due to the clinical success of insulin therapy in the treatment of diabetes, most islet research has focused on the β cells. However, glucagon is also emerging as a critically important component of blood glucose regulation. This study takes a quantitative approach to understanding islet architecture and its implications for hormone secretion towards elucidating hypothesized modulatory effects between islet cell types. In particular, the cellular neighborhood around α cells was examined to investigate the regulation of glucagon secretion. This analysis relied on immunofluorescence imaging of islets from mouse (n = 5, 10 islets) and human (n = 2, 5 islets) populations. Islets were stained for insulin, glucagon, and somatostatin. Z-stack images were obtained using multi-channel confocal fluorescence microscopy, which enabled 3-D assessment of cell type distribution and proximity. This analysis produced data that demonstrate a clear specificity for α-α proximity and for α-δ associations, a novel finding that is significant given the known inhibitory effect of somatostatin on α cell secretion. Furthermore, we found a correlation between the number of inactive α cells in mouse islets and the number of α cells bordered by δ cells. These surprising data suggest a new hypothesis for local paracrine or juxtacrine effects from δ cells in the regulation of glucagon secretion from α cells. The results of this study support a model of proximity-mediated intercellular modulation of islet hormone secretion and introduce new hypotheses of the specific mechanisms involved in this process.