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Gene Expression and Profiling of Human Islet Cell Subtypes

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GENE EXPRESSION AND PROFILING OF HUMAN ISLET CELL SUBTYPES

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Abstract

The endocrine pancreas contains multiple cell types co-localized into clusters called the islets of Langerhans. The predominant cell types include alpha and beta cells, which produce glucagon and insulin, respectively. The regulated release of these hormones maintains whole body glucose homeostasis, essential to prevent complications from diabetes (e.g. blindness, kidney failure, and cardiovascular disease). In type 1 diabetes, an autoimmune reaction destroys the beta cells and patients must monitor their blood sugar levels and inject insulin in order to maintain euglycemia. In type 2 diabetes, the beta cells fail to produce sufficient insulin to overcome the individual's decreased insulin sensitivity. Most studies to date have focused on whole islets, which are very heterogeneous. Recent focus has shifted to studying the individual islet cell subsets (i.e. alpha, beta, delta, PP, and other cell types). Unlike immunological cells, surface molecule reagents do not yet exist to specifically distinguish beta from alpha cells. We have successfully isolated pure populations of insulin producing beta cells and glucagon producing alpha cells by using intracellular hormone staining and fluorescence activated cell sorting. We present data that describe the ratio of beta cells to alpha cells across gender, age, and BMI. Further, we have characterized the miRNA profiles of alpha and beta cells and have begun to investigate the unique gene expression patterns of the two cell types. By developing the ability to profile multiple characteristics of alpha and beta cells, we hope to determine how gene, miRNA, and protein profiles change under environmental conditions that lead to beta cell failure, and others that may promote beta cell health or stimulate beta cell growth and proliferation.