Generation of pancreatic islet cells and progenitor cells from embryonic stem cells

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Our lab recently established an effective method for inducing the differentiation of human ES cells into insulin-producing cells using a serum-free system. The protocol is designed to mimic pancreatic islet development and includes three developmental events: definitive endoderm formation, pancreas specification and endocrinal islet maturation. We show that differentiated cells express islet specific markers such as C-peptide, pdx1, insulin, glucagon and glut2. Among the differentiated cells, we observed islet-like cluster structures and most of the cells in these clusters co-expressed C-peptide and pdx1. In the islet-like clusters, there were a few pdx1 and somatostatin co-expressing cells; however, we did not find any examples of cells that co-expressed pdx1 with either glucagon or amylase. The differentiated cells were also able to release insulin and C-peptide in response to glucose stimuli. When transplanted into renal capsules, the differentiated human ES cells maintained C-peptide expression and rescued hyperglycemia in STZ induced diabetic nude mice. Our findings offer a promising in vitro model for studying the mechanism of pancreatic islet cell and pancreatic stem/progenitor cell differentiation.

Keyword: human embryonic stem cells; directed differentiation; insulin-producing cell

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