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Identification of pancreatic beta cell-related genes by representational difference analysis.

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Abstract

A knowledge of beta cell-specific gene expression provides a basis for identifying proteins potentially involved in beta cell function and pathology. To identify candidate beta cell-specific genes, we applied the PCR-based subtractive hybridization technique of representational difference analysis (RDA) to the mouse SV40-transformed endocrine cell lines, betaTC3 and alphaTC1. Following three successive subtractions of alphaTC1 complementary DNA from betaTC3 complementary DNA, difference products were cloned into pUC19 and nucleotide sequences determined. Comparison of 91 sequences against the databases identified 11 known and 8 novel genes. Known genes included previously reported beta cell-specific genes, insulin I/II and islet amyloid polypeptide, as well as other non-beta cell-specific genes such as those for insulin-like growth factor II, selenoprotein P, **neuronatin**, prohormone convertase, and type 1 protein kinase A regulatory subunit. By Northern blot hybridization, expression of the majority of known and novel genes was restricted to betaTC3 cells. Novel genes BA-12, -13, -14, and -18 were expressed not only in betaTC3 cells, but also in normal pancreatic islets and a limited number of other tissues. The deduced amino acid sequence of BA-14 showed significant homology with members of the cadherin superfamily indicating that BA-14 may encode a cadherin-like molecule potentially involved in beta cell adhesion events during islet ontogeny. In betaTC3 cells, none of the novel genes were regulated at the RNA level by high glucose. However, in parallel studies, transcription of BA-12 was significantly increased by both sodium butyrate and nicotinamide, suggesting that this gene may play a role in pancreatic beta cell growth and/or differentiation. In this study, we have demonstrated that cRDA is an effective strategy for systematically mapping differences in gene expression between two related but functionally-distinct endocrine cells. Its application to experimental animal models of islet-cell regeneration may facilitate the discovery of potential factors that mediate beta cell growth and differentiation.

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