Proteomic Approach to Search for Proteins Differentially Expressed Between Human Pancreatic Islets and Human Insulinomas

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Transplantation of isolated pancreatic islets from cadaveric organ donors is a promising alternative for treatment of type 1 Diabetes, however, this approach is severely limited by the shortage of organ donors. *Ex-vivo* islet cell culture prior to transplantation appears as an attractive alternative, however, maintenance of human islets in culture has been a difficult task. Therefore, stimulation of islet cell proliferation and differentiation *in vitro* constitutes a major scientific and clinical challenge. The *in vitro* culture of insulinomas, which are rare pancreatic tumors arising from beta-cells, provides an important tool to study cell proliferation and insulin synthesis and secretion. Interestingly, only a few human beta-cell lines have been described, with long-term passage resulting in loss of insulin secretion. We have developed three human beta cell lines which maintain the antigenic characteristics and insulin secretion profiles of the original tumors. In order to better characterize these beta cell lines, we set out to identify proteins displaying altered expression levels between normal and neoplastic beta cells, using 2-dimensional gel electrophoresis (2D-DIGE: Differential in gel Electrophoresis) and mass spectrometry (MS). An average of 1,800 different protein spots were obtained, with a mean of 60% match between the gels, with 11 of these proteins being differentially expressed (cut-off = 2 Standard Deviation). Currently, we are identifying the spots by peptide-mass-fingerprinting. Our study may provide important proteomic information towards understanding the molecular mechanisms involved in the neoplastic transformation of insulinomas. In addition, the new approach presented here may be useful to reveal relevant molecular mechanisms involved in islet cell function and proliferation.

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