GENERATION AND CHARACTERIZATION OF HUMAN INSULINOMAS CELL LINES.

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Insulinomas are rare pancreatic tumors arising from ß-cells. Their *in vitro* culture provides a desirable tool to study tumor progression and insulin synthesis and secretion. Therefore, we set out to establish and characterize human insulinoma cell cultures.*Ex-vivo* primary cultures (APM, VGA and CPR) obtained from independent human insulinoma tumors, were cultured up to passage number 15, presenting a similar doubling time (40h). We observed that these cell lines produce and secrete human insulin, but none of them present glucose-induced insulin secretion. Immunofluorescence assays confirmed the neuroendocrine ß-cell origin of these cultures.APM cells were more sensitive to apoptosis induced by serum starvation and only CPR cells were sensitive to Doxorubicin. All lines survived in an anchorage independent culture, while only APM proliferated under these conditions. VGA cells presented the highest motility. However, none of them were able to invade an extracellular matrix substrate. Therefore, we have developed three human insulinoma cell lines that maintain the antigenic and insulin secretion profile of the original tumors. Until very recently, islet-derived cell lines have represented sub-optimal surrogates for primary ß cells due to their undifferentiated or unstable phenotypic features, however, the results presented here provide a powerful research model to study tumor biology and insulin secretion disorders.

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