Long-term in vitro culture of hamster pancreatic β-cells and induction of adenocarcinoma by treatment with N-nitrosobis(2-oxopropyl)amine

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OBJECTIVES
Earlier studies indicated that hamster pancreatic ductal adenocarcinoma not only derives from ductal/ductular structures but also from cells within the islet. So far unidentified cells within the islet are responsive to the carcinogenic effect of N-nitrosobis (2-oxopropyl) amine (BOP) forming poorly differentiated ductal adenocarcinoma. However, studies indicated a major role of β-cells during carcinogenesis. To find out, if β-cells are the primary target cells of BOP and if they are capable to form ductal adenocarcinoma after malignant transformation, we established a long-term culture of undifferentiated cells deriving from isolated β-cells and treated them with BOP.

METHODS
Langerhans' islets from pancreata of Syrian golden hamsters were isolated and dispersed into single cells by dispase digestion. Cells were labeled with a highly specific β-cell surface antibody (K14D10) and these K14D10+ cells were extracted from the suspension by paramagnetic Dynabeads. Cells were cultured in vitro and treated with BOP. Untreated cells served as control.

RESULTS
K14D10+ cells formed a monolayer and produced insulin over a period of 28 days in culture. However, with time in culture they became undifferentiated with a higher proliferation rate and after about 60 days in culture BOP treated cells showed anchorage independent growth. These cells autotransplanted s.c. formed a well-differentiated ductal adenocarcinoma.

CONCLUSIONS
Pancreatic β-cells are the primary target of BOP without necessarily being embedded in the compound of the Langerhans' islet. With time in culture, they give rise to undifferentiated cells and after malignant transformation they are able to form ductal adenocarcinoma.
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