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(54) **Title**: IN VITRO PANCREATIC DIFFERENTIATION OF PLURIPOTENT MAMMALIAN CELLS

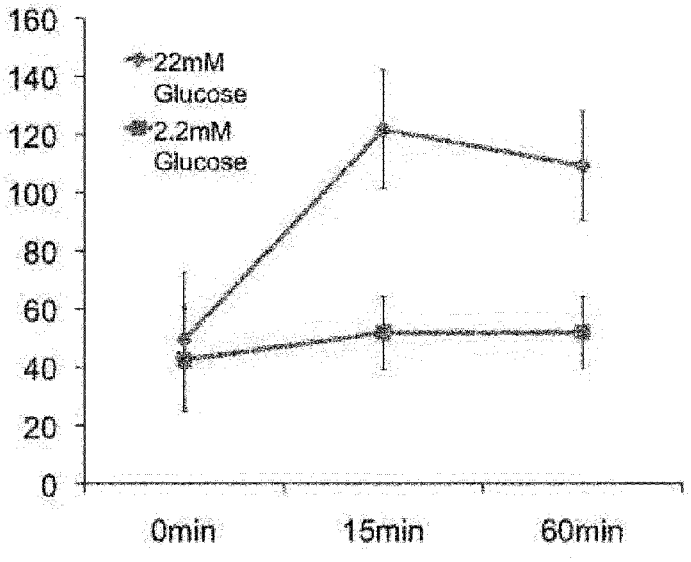


Figure 5

(57) **Abstract**: This invention relates to the in vitro differentiation of pluripotent cells into pancreatic progenitors by i) culturing pluripotent cells in a definitive endoderm (DE) medium comprising a TGFp ligand, fibroblast growth factor (FGF), bone morphogenetic protein (BMP), a PI3K inhibitor and optionally a GSK3 β inhibitor to produce a population of definitive endoderm cells, ii) culturing the definitive endoderm cells in a first pancreatic medium comprising an activin antagonist; FGF; retinoic acid; and a BMP inhibitor to produce a population of dorsal foregut cells; iii) culturing the dorsal foregut cells in a second pancreatic medium comprising FGF, retinoic acid, a BMP inhibitor, and a hedgehog signalling inhibitor, and; iv) culturing the endoderm cells in a third pancreatic medium comprising FGF. The progenitor cells thus produced may be further differentiated into pancreatic endocrine cells. These methods may be useful, for example, in producing pancreatic cells for therapy or disease modelling.

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