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Both embryonic and adult stem cells give rise to endodermal derivatives such as cells of the pancreas and liver

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Undifferentiated cells which self-renew and produce functionally specialized cells are termed stem cells. Because of their potential in regenerative medicine, both embryonic stem cells, which are pluripotent, and adult stem cells, which are multipotent, are being utilized for cellular therapy. Embryonic stem cells differentiate spontaneously into many cell types including those of the haemopoietic system (Evans and Kaufman 1981) and the myocardium. Adult stem cells were thought to possess a very limited potential to differentiate into other cell types, but have recently been shown to differentiate into skeletal and cardiac muscle fibres, renal tubular epithelial cells and neurones. This paper will describe how both embryonic stem cells and adult stem cells are capable of giving rise to cells of the liver and pancreas.

In experiments utilizing mouse embryonic stem cells, embryoid bodies (EBs) were cultured with quail mesoderm of the dorsal pancreatic bud (Hamilton and Hamburger stage 25) to determine whether insulin- and glucagon-containing cells could be induced. Quail mesoderm was used so as to be able to identify the origin of the resulting endocrine cells. The explants were cultured for 7 days in Matrigel in the wells of a Nunclon multidish in serum-free Ham's F12.ITS culture medium at 37°C in 5% CO_2 in air. The explants were freeze dried, fixed in parabenzoquinone vapour and embedded in epon araldite resin. Insulin- and glucagon-immunoflourescence were detected in groups of cells within the EBs, indicating that EBs can generate both α- and β-cells in the presence of signalling molecules from pancreatic mesoderm.

In the second experiment*, bone marrow cells were harvested from the femurs of adult male mice (CBA) and injected into the tail vein of 6 week-old female mice (CBA), which had undergone whole-body gamma irradiation. After 11 weeks, four female mice were killed and a further six were killed 30 weeks post-transplantation. The liver and pancreata of the mice were removed, fixed in 10% buffered formalin for 24hrs, processed and embedded in paraffin wax, followed by serial sectioning at 4μm. Serial sections of tissue 16μm apart were selected for labelling. An *in situ* hybridisation method, for labeling the Y-chromosome of cells originating from male mice, was utilized. Y-chromosomes, identified by the use of the chromogen DAB, were identified in liver and pancreatic tissue. While only a few cells were found to be Y-chromosome-positive in the liver of female mice, substantially more Y-chromosome-positive cells were present in the pancreas. In addition, the tissue of mice killed 30 weeks after transplantation appeared to contain more male-derived cells than did the tissue of mice killed 11 weeks after transplantation.

The putative signaling molecules controlling the differentiation of these stem cells into functional cell types will be reviewed.

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Evans M, Kaufmann MH (1981) Establishment in culture of pluripotential cells from mouse embryos. Nature 292:154-155.

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