

Clinical Models of Pancreas Development, Developmental Disorders, and Pancreatic Disease

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INTRODUCTION

Two buds emerge from the duodenal section of the foregut, an embryonic tube that is a predecessor to the gastrointestinal system, during development to become the pancreas. It comes from the endoderm. The creation of a dorsal and ventral pancreatic bud is the first step in pancreatic development.

MODELS OF PANCREAS DEVELOPMENT

Animal models of acute and chronic pancreatitis have been created to examine mechanisms of pathogenesis, test therapeutic interventions, and study the influence of inflammation on the development of pancreatic cancer. In vitro models can be used to study early stage, short-term processes that involve acinar cell responses. Rodent models reproducibly develop mild or severe disease. One of the most commonly used pancreatitis models is created by administration of supraphysiologic concentrations of caerulein, an ortholog of cholecystokinin. Induction of chronic pancreatitis with factors thought to have a role in human disease, such as combinations of lipopolysaccharide and chronic ethanol feeding, might be relevant to human disease. Models of autoimmune chronic pancreatitis have also been developed [1]. Most models, especially chronic pancreatitis models, require more characterization to determine which aspects of human illness they contain.

PANCREAS ORGANOGENESIS

The pancreas, which includes both endocrine and exocrine functions, is a vital organ for optimal nutrient metabolism. The understanding of how the pancreas develops during embryogenesis has vastly improved over

the last two decades, thanks in great part to developmental research in model species. The molecular foundation of pancreatic lineage decisions and cell differentiation, in particular, has received a great deal of attention. The mechanisms driving the organ's three-dimensional morphogenesis are still poorly understood. The accumulation of knowledge about pancreas development has aided strategies for generating transplantable cells in vitro for diabetes treatment. In this review, we address the present state of knowledge about pancreatic lineage determination and organogenesis, as well as the implications of these discoveries for diabetes mellitus treatment via cell replacement [2].

ZEBRAFISH PANCREAS DEVELOPMENT

An accurate understanding of the molecular mechanisms that drive pancreas development could have an impact on clinical medicine for disorders including diabetes, obesity, and pancreatic cancer, which have a large public health impact. The mouse and, in some cases connected to early development, chicken and *Xenopus* were the principal animal models in which pancreas creation and differentiation could be investigated until 1996. *Danio rerio* has allowed large scale and fine multidimensional analysis of gene functions during pancreas formation and differentiation by combining functional genomics, genetics, and in vivo whole mount visualisation. This has allowed for large scale and fine multidimensional analysis of gene functions during pancreas formation and differentiation [3].

PANCREATIC MACHINE PERFUSION

Extended criteria kidney grafts are increasingly being treated with hypothermic machine perfusion (HMP). Pancreatic HMP is difficult to achieve since the pancreas is a low-flow organ prone to edoema. Preclinical HMP models were successfully developed utilizing pig pancreases as well as human pancreases that were unsuitable for clinical transplantation. Machine perfusion is feasible and successful in preclinical porcine and human pancreas models; the development of these translational models could be advantageous in enhancing pancreas

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preservation before transplantation and allowing organ viability assessment and optimization [4].

The first full atlas of human pancreas cells, which included epithelial and nonepithelial constituents, revealed three unique acinar cell types, with implications for pancreatic homeostatic and inflammatory processes. When compared to neonatal single-nucleus sequencing data, the endocrine tissue had a different cellular makeup, showing the tissue dynamics that occur during development. We discovered evidence of unique cell type neighbourhoods, dynamic topographies in the endocrine and exocrine pancreas, and principles of morphologic organisation of the organ using spatial cartography, which involved cell proximity mapping by in situ sequencing [5]. Similarly, investigations of chronic pancreatitis biopsy samples revealed the presence of acinar-REG+ cells, a reciprocal connection between macrophages and activated

stellate cells, and a new possible role for tuft cells in this condition.

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