Published in final edited form as:

Semin Cell Dev Biol. 2012 August ; 23(6): . doi:10.1016/j.semcdb.2012.06.007.

Advances in pancreas development: Generation informs regeneration

Lori Sussel*

Columbia University, Department of Genetics and Development, 1150 St. Nicholas Avenue, Room 607B, New York, NY 10032, United States

The functional importance of the pancreas and its constituent cell types has been widely appreciated for over a century. While progress in pancreatic research has continued since that time, the past two decades have witnessed the accelerated emergence of novel insights and technologies to advance the field in exciting new directions. In particular, the characterization of pancreas development in several different model organisms has elucidated many of the cellular and molecular pathways underlying pancreas cell type specification. These cumulative discoveries have paved the way for the ground-breaking advances in tissue reprogramming and the directed differentiation of human pluripotent stem cells; the generation of functional beta cells from alternative cell sources has convincingly emerged as a viable option for treating diabetes.

This special issue of *Seminars in Cell and Developmental Biology* is comprised of an exciting collection of reviews that highlight many of the recent advances in our understanding of pancreas development. By integrating studies from several model organisms, this issue provides an overview of the transcriptional networks, signaling pathways and tissue interactions that are intertwined to specify each stage of pancreas development. In the first chapter, *McCracken and Wells* summarize the important developmental processes and signaling events that pattern the foregut endoderm to delineate the pancreas from the surrounding endodermally derived organs. Importantly, this chapter highlights experimental discoveries from several model organisms that have elucidated the molecular basis of endoderm regionalization, pancreas induction, and ventral and dorsal pancreatic bud specification. The second chapter by *Serup* provides a comprehensive overview of the myriad of signaling pathways that regulate pancreatic morphogenesis, growth and cell differentiation. This review describes the reiterated roles of many signaling pathways during pancreas development and emphasizes how crosstalk between the different signaling pathways can promote specific developmental events. Each subsequent chapter continually refers back to these signaling pathways, describing their respective roles in the different developmental processes. In the third chapter, *Rieck, Bankaitis and Wright* take us through the successive lineage decisions made at each stage of pancreatic development, including the steps involved in formation of multipotent precursor cells, the primary and secondary transitions, and endocrine cell type specification. The authors raise pertinent questions regarding what is known and unknown about the commitment of each pancreatic lineage, and introduce newly discovered lineage determinants that influence the differentiation process. The fourth chapter by *Cleveland et al.*, describes the molecular pathways regulating acinar and ductal cell development, and illustrates their close association with endocrine developmental pathways. This chapter also includes thought-provoking discussion of the potential origin and progenitor capacity of the centroacinar cell

population. In the fifth chapter, *Villasenor and Cleaver* discuss the influence of blood vessel endothelium on several stages of pancreatic development and emphasize how the endothelium acquires successively different roles over time. The sixth chapter by *Avrahami and Kaestner* evaluates the rapidly growing area of research related to the epigenetic mechanisms influencing pancreas development, postnatal islet cell regeneration and preservation of lineage identities. In addition, the authors summarize a number of recent studies documenting the importance of chromatin remodeling in response to changing physiological conditions and aging. Finally, in chapter seven, *Nostro and Keller* discuss the recent advances in generating pancreatic beta cells from human pluripotent stem cells. This review emphasizes how knowledge of the signaling and transcriptional pathways regulating normal pancreatic development has led to the successful *in vitro* generation of insulin-producing cells, and highlights the challenges and obstacles that remain for the production of fully functional pancreatic beta cells for therapeutic purposes.

In summary, these reviews highlight the current status of the pancreatic development field and emphasize areas of research that still need to be explored. Furthermore, they provide insights into the molecular, cellular and morphological underpinnings of pancreatic development and demonstrate the importance of studies in model organisms for understanding and treating human diseases, including diabetes and pancreatic cancer.