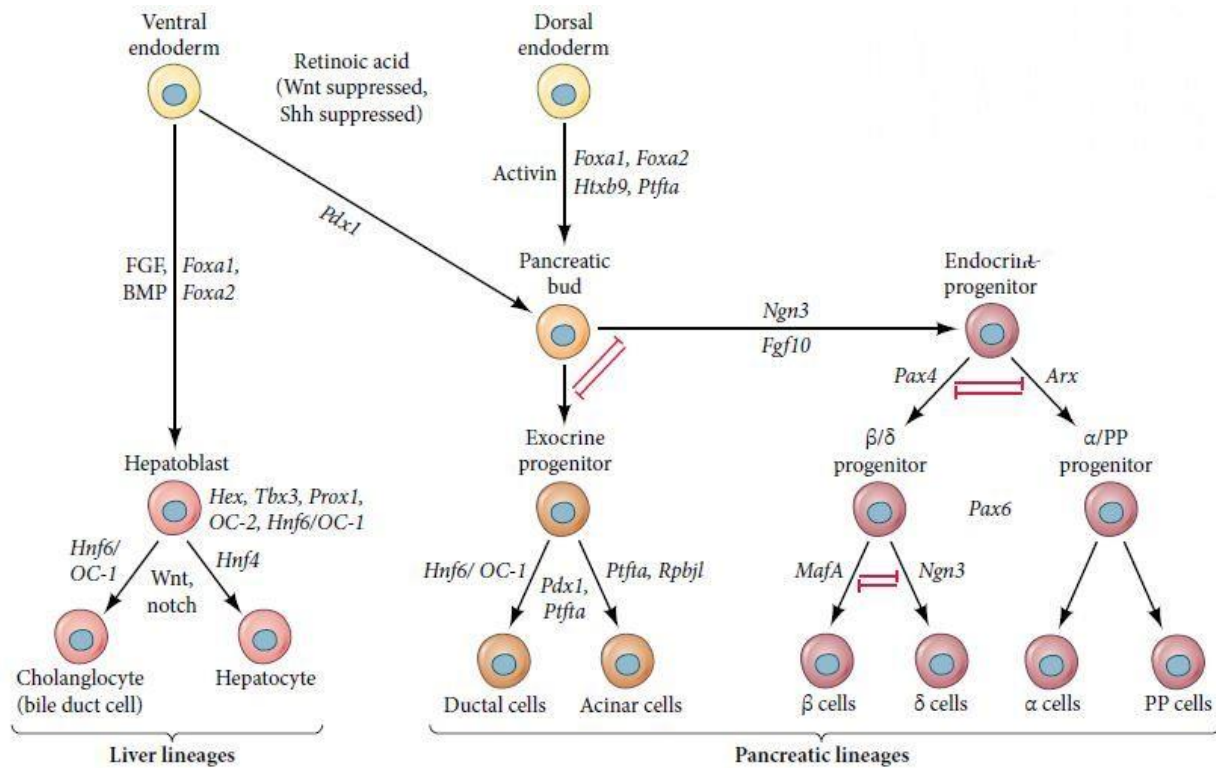


A Model for a Hierarchical Dichotomous System for Determining Cell Types

The hierarchical dichotomous system in Figure 1 resembles the scheme of blood production from a single hematopoietic stem cell (see Figure 20.24 in the text). Modeling by Zhou and colleagues (2011) suggests that the different cell types can be seen as attractor states that result from the possible interactions of a common set of transcription factors. Indeed, Dhawan and colleagues (2011) have found that when the gene for Dnmt1 methyltransferase is knocked out in insulin-producing β cells, the methylation patterns change such that the *Arx* promoter is de-repressed and the *Arx* gene activated, converting β cells into glucagon-producing δ cells. Pancreatic β cell identity is thereby maintained by the methylation-mediated repression of *Arx*.

These transcription factor networks may enable the reprogramming of one cell type into another. Horb and colleagues (2003) have shown that Pdx1 can re-specify developing liver tissue into pancreas. When *Xenopus* tadpoles were given a *pdx1* gene attached to a promoter active in liver cells, Pdx1 was made in the liver, and the liver was converted into a pancreas that contained both exocrine and endocrine cells. Thus, Pdx1 appears to be the critical factor in distinguishing the liver from the pancreatic mode of development. The expression of Ngn3, Pdx1, and MafA reprograms differentiated exocrine pancreatic cells of adult mice into functional β cells (see also Figure 1 in Further Development Online 3.11; Zhou et al. 2007).



After J. X. Zhou et al. 2011. PLoS One 6: e14752.

Figure 1 Lineage of pancreatic and liver cells. All pancreatic cells express *Pdx1*, distinguishing them from the cells that will become the liver. Within the pancreatic lineage, the *Ngn3*-expressing endocrine progenitor cells give rise to the endocrine lineages, while *Ptf1a*-expressing cells give rise to the exocrine progenitor that makes the ducts and the acinar cells (which secrete digestive enzymes). The endocrine progenitor can give rise to two lineages, one that can form β and δ cells and another that can form α and PP cells. (After Zhou et al. 2011.)

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