

**P066** Transdifferentiation of pancreatic ductal cells to beta cells: a model derived from the analysis of *hnf6*<sup>-/-</sup> mice  
**Eric Heinen, Frédéric Lemaigre and Patrick Jacquemin**  
*de Duve Institute and Université catholique de Louvain, 75  
Av. Hippocrate, B-1200 Brussels, Belgium*

Hepatocyte Nuclear Factor-6 (HNF-6), a transcription factor of the Onecut class, is required for pancreatic specification and endocrine differentiation. In the present work, we propose a model for transdifferentiation of ductal cells to beta cells, based on the analysis of *hnf6*<sup>-/-</sup> mice. Newborn *hnf6*<sup>-/-</sup> mice have only a few endocrine cells and no expression of Pdx-1 and many alpha and beta cells are found scattered in the ductal epithelium. The postnatal increase in beta cells does not result from increased proliferation, since beta cell proliferation is slightly reduced in *hnf6*<sup>-/-</sup> mice. Postnatal beta cell development in *hnf6*<sup>-/-</sup> pancreata is Ngn3-independent. Indeed, no Ngn3 cells are found after birth. Moreover, lineage tracing experiments show that, in adult *hnf6*<sup>-/-</sup> pancreas, some beta cells are not derived from Ngn3-expressing progenitors. Our results provide evidence for a novel mechanism of beta cell regeneration, which can be initiated in ductal cells and which is neither Ngn3-dependent nor proliferation-dependent.