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**Perspectives of Pancreas Stem Cells: Expansion and Differentiation of Adult Pancreas Stem Cells *in vivo* and *in vitro***

Kun-Ho Yoon

*Department of Endocrinology & Metabolism, Kangnam St. Mary's hospital, The Catholic University of Korea, Seoul 137-701*

Recent reports showed a linear relation of body mass and  $\beta$ -cell mass in rodents and type 2 diabetic patients in Korea. These results suggest that non-obese type 2 diabetic patients also will be good candidates for the islet transplantation. The current success with islet allograft transplantation is reviewed however the shortage of human islet tissue means that only a small fraction of people with diabetes would be able to benefit. For these reasons there is considerable interest in alternative source for transplantation. Neonatal porcine tissue has several attractive features. From 3-day-old newborn pigs, cellular aggregates are called porcine neonatal pancreatic cell clusters (NPCCs) were obtained. Transplantation of 2000 NPCCs into diabetic nude mice typically normalized glucose values in 10-20 weeks. The starting NPCCs consisted of 17% insulin-staining cells, but the grafts of mice with reversed diabetes consisted of 94% beta cells. The mass of insulin producing cells rose from  $0.22 \pm 0.08$  mg 1 week after transplantation to  $4.34 \pm 0.27$  mg in mice sacrificed at 27-35 weeks. In summary, NPCCs contain mostly islet precursor cells, which when transplanted into nude mice undergo striking differentiation and beta cell expansion. To learn more, the development of these cells when cultured as monolayers was evaluated. Using Ki-67 immunostaining, the fraction of beta cells in the cell cycle was shown to decrease from 20% at day 3 to 10% at day 8, and for duct cells from 36 to 19%. Insulin secretion increased 2.4-fold upon glucose stimulation, showing the responsiveness of the neonatal beta cells. Reaggregated monolayers consisted mostly of duct cells, but 4 weeks after transplantation, grafts contained predominantly endocrine cells. Approximately 60% of duct cells but less than 5% of beta cells expressed the transgene delivered by a Moloney Murine Leukemia Virus-based vector, indicating that precursor duct cells are better targets for transgene expression. Our results clearly showed that adult pancreas stem cells isolated from neonatal pig could be one of the alternative sources for islet transplantation. We hope these results will be able to reproduce with human adult pancreas cells.