

**Title:**

Gene expression profile versus morphological changes in PDL pancreas: A chronobiological study on the remodeling of Beta cells in the rats' pancreas

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**Abstract:**

Pancreatic stem cells residing within the ductile epithelium have been used to generate islet-like clusters in vitro which has partially reverted diabetes Mellitus (DM) in animal models. Islet cells from pancreatic duct ligation (PDL) induced neogenesis have shown the same efficacy as foetal tissue as a model for transplantation of syngeneic tissues. However, understanding the connection between the morphological changes and the genetic induction in the lineage of endocrine pancreas will be a valuable tool in improving beta cell replacement in patients with diabetes. The aim of this study was: i) to describe the morphological changes of the pancreas during the time periods post-pancreatic duct ligation in rats; ii) to determine the expression pattern and variations of insulin, Pdx1, Ngn3, NeuroD, Pax6 and caspase3 genes across the time period post PDL; iii) to compare the temporal increase in beta cells mass to the highest expression of developmental genes across the time period post PDL. Photomicrographs, morphoimmunofluorescent evaluation of PDL pancreas, and immunohistofluorescent analysis of insulin, Pdx1, Ngn3, NeuroD, Pax6 and caspase3 gene expressions were performed using 78 Sprague-Dawley rats of PDL model. The morphological changes were characterized by the appearance of necrotic tissues at 6 hours post-PDL and the proliferations of endocrine tissue were observed at 84 hours through to 120 hours. The morphoimmunofluorescent evaluation showed the highest reactivity of caspase3 and Pdx1 at 6 hours, Ngn3 at 36 hours, pax6 and insulin at 84 hours while NeuroD expression was at 120 hours. The caspase3 expression was

earlier at 6 hours while the insulin expression appeared later at 84 hours. The immunofluorescent analysis demonstrated caspase3 expression early at 6 hours while the insulin expression appeared later at 84 hours. This study confirms the connection between morphological changes and gene expression in PDL pancreas with the same chronobiology rhythm observed during endocrine development in normal rats.