Identifying Key Pathways/Mechanisms for the Generation of Pancreatic Beta Cells by Trans-differentiation of Acinar Cells

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Insulin is a hormone produced by the pancreatic beta cells in the human body. Individuals with diabetes either lack insulin (T1D) or have a reduced insulin secretion (T2D). Therefore, the preservation of beta cell mass is crucial for treatment. Since acinar cells are often by-products of islet transplantation, their utilization will supplement the current limited availability of viable islet cells. Transdifferentiation, reprogramming one mature cell type to another, however, requires extensive knowledge about the key regulators that control beta cell development/growth and maintain beta cell function. In order to effectively generate beta cells, critical transcription factors, a class of genes enriched for factors that determine cell fates, were utilized to identify the key underlying mechanisms/pathways for such transdifferentiation. A unique combination of transcription factors that resulted in a more efficient generation of beta cells from acinar cells was determined. Results show that when compared to basal, Rbpjl and Ptf1a knockdown in 266-6 mouse acinar cells significantly increased the overall expression of essential beta-cell genes. Additional overexpression of Ngn3, Mafb, and Nkx6.1 further increased the expression of essential beta-cell genes, including insulin. This study suggests that inhibiting Rbpjl and Ptf1a and therefore disrupting acinar cell characteristics may aid in the conversion of acinar cells to pancreatic beta cells. The findings in this innovative research would facilitate a novel alternative in mitigating the lack of islet cells for cell replacement therapies in the treatment of diabetes, and thus represent a promising advancement to the biomedical field.

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