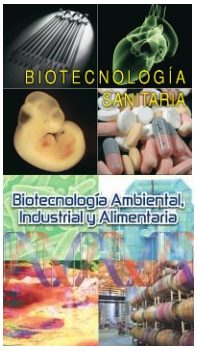
Poster

Role of pyruvate carboxilase on β cell function



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ABSTRACT

Type 2 Diabetes is the most common metabolic disorder in the world. It is characterized by insulin resistance and dysfunction of β cells that results in high blood glucose levels. A critical process in blood glucose homeostasis is glucose-stimulated insulin secretion (GSIS) from pancreatic beta cells. This process is regulated by a multitud of cofactors, enzymes and metabolic intermediates.

Pyruvate carboxylase (PC) is an enzyme involved in several metabolic pathways, including oxidative glucose metabolism. Previous studies have revealed high PC activity in mature pancreatic beta cells, which decreases under diabetic conditions, suggesting a link between PC activity and insulin secretion. Previous work from the receptor group indicate that the inactivation of the Pcx gene has a detrimental effect on pancreatic β cells function.

In this line of research, a conditional PC knocout mouse model will be used to study its role in insulin secretion. To validate the model, PC expression in beta cells will be analyzed by TaqMan mRNA expression assays and Western Blot. The PC knockdown mouse model will also be evaluated in vivo by glucose tolerance (GTT) and insulin tolerance (ITT) tests to determine the impact of reduced PC activity on glucose homeostasis. In addition, immunofluorescence and immunohistochemistry assays will be performed on the pancreas of this mouse model in order to identify specific markers of beta cells. Finally, RNA microarray will be analyzed to elucidate the underlying molecular mechanisms.

This study will provide a deeper understanding of the role of PC in insulin secretion and β cell function, which could lead to the development of new therapeutic strategies for treating diabetes type 2.

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