

Calbindin-D9k in Hypoxia-Induced Diabetes Mellitus like Model

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Introduction

Introduction: It has been proposed that cellular Ca²⁺ signals activate hormone secretion. In pancreatic β cells, which produce insulin, Ca²⁺ signals have been known to contribute to insulin secretion. Prior to this study, we confirmed that Calbindin-D9k (CaBP-9k) was responsible for regulation of the distribution of free calcium in the cytoplasm. We also confirmed that insulin-secreting β cells express CaBP-9k, and assumed that CaBP-9k play a role in β cell insulin synthesis or secretion. Using CaBP-9k knock out (KO) mice, we demonstrated that ablation of CaBP-9k causes type 1 diabetes by reducing insulin secretion and increasing serum glucose.

Objective: The aim of this study was to assess interactions between glucose/insulin secretion and calcium homeostasis in the pancreas of mice.

Method

Using CaBP-9k knock out (KO) mice, we demonstrated that ablation of CaBP-9k could causes insulin dependent diabetes by reducing insulin secretion and increasing serum glucose. In addition, to compare the role of CaBP-9k with hypoxic pathophysiological conditions, we exposed wild-type and CaBP-9k KO mice to hypoxic conditions for 10 days. Hypoxia induced endoplasmic reticulum (ER) stress, increasing both insulin signaling and insulin resistance.

Result

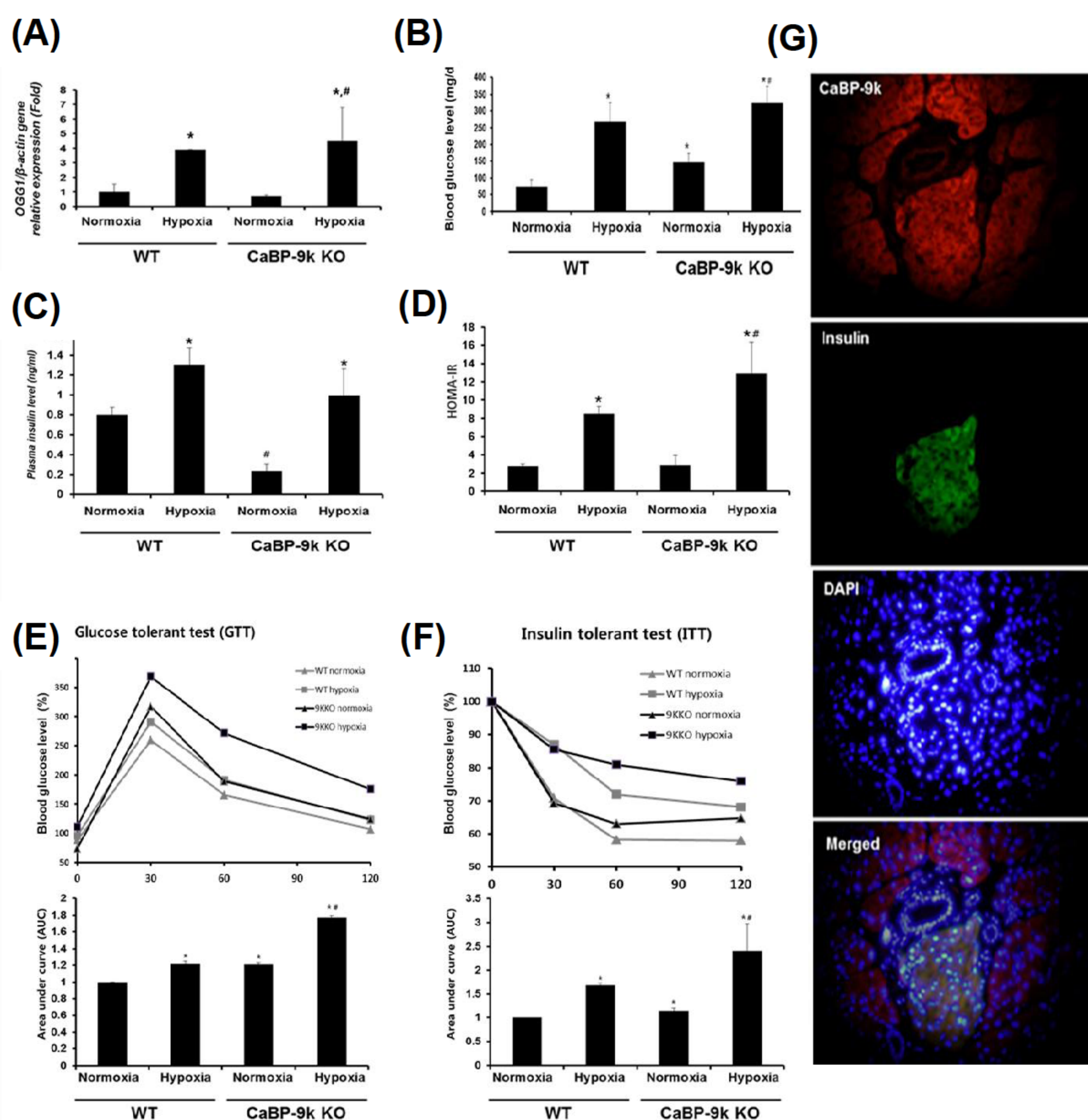


Figure 1. Regulation of glucose parameters in T2D model and CaBP-9K KO mice. (A) OGG1 expression (B) Blood glucose level. (C) Plasma insulin level. (D) Calculated insulin resistance index; HOMA-IR. (E) IPGTT and AUC (F) IPITT and AUC. (G) Immunofluorescence assay.

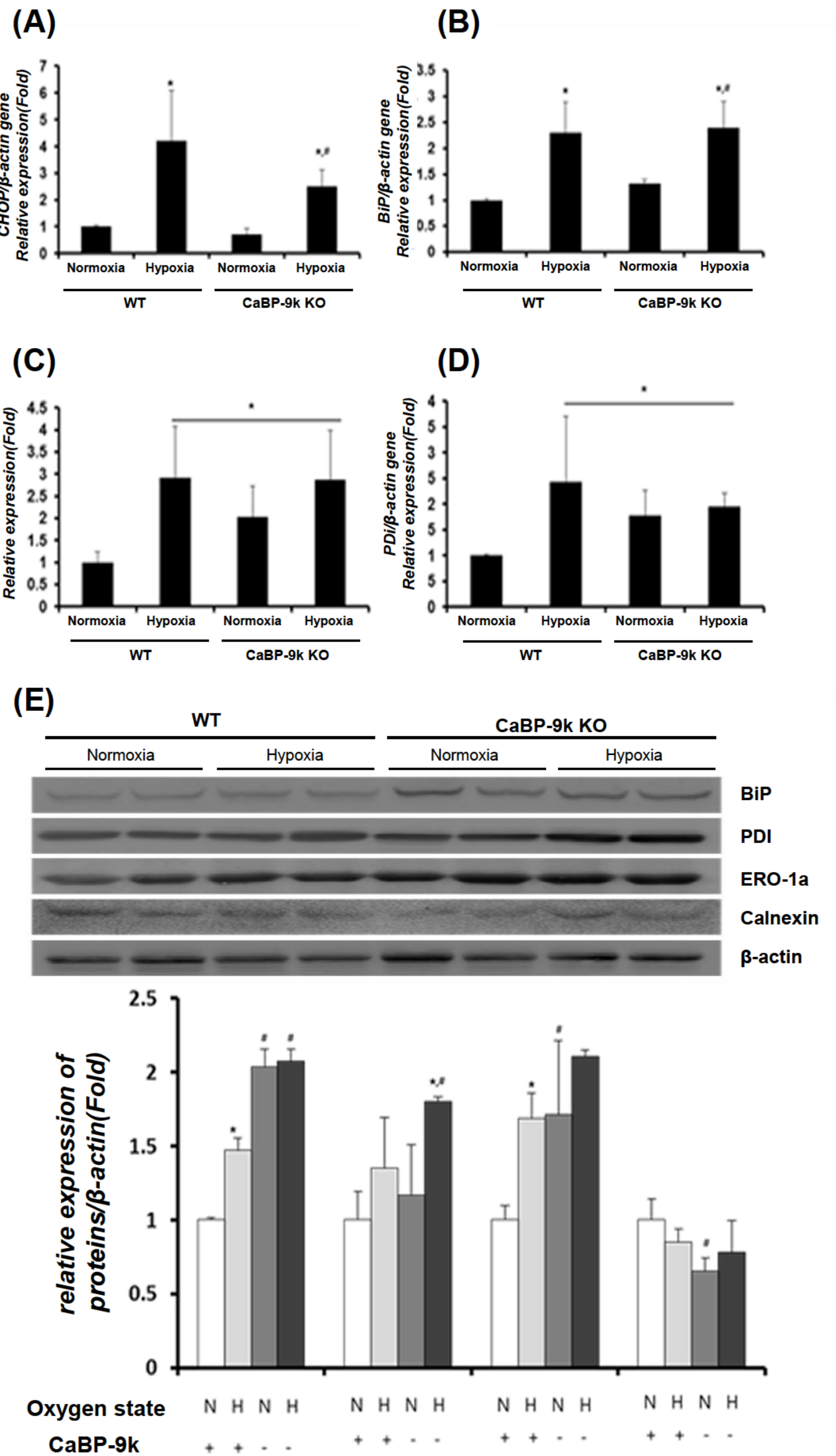


Figure 4. Expression of ER-stress maker genes in T2D model and CaBP-9K KO mice. WT and CaBP-9K KO mice were exposed to normoxic or hypoxic condition for 10 days.

Conclusion

Overall, the results of the present study demonstrated that CaBP-9k regulates synthesis of insulin and is part of the insulin-secreting calcium signaling. Therefore, impaired CaBP-9K signaling may be linked with diabetes mellitus and CaBP-9K protein is as a potential candidate for gene therapy of type 1 diabetes.

Reference

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