MicroRNA-21 promotes pancreatic β cell function through modulating glucose uptake

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1. 簡述論文的概要以及重大發現

糖尿病是由於人體胰臟的 β-cell 無法產生胰島素，導致沒辦法調節血糖，所以造成糖尿病。β-cell 的功能缺失或下降是第一型和第二型糖尿病的主要原因，所以了解 β-cell 分泌胰島素功能缺失的原因，才能加以預防或治療糖尿病的發生。此研究藉由 Knock down 胰島 β 細胞的 miR-21（miR-21β KO）的小鼠實驗，確認了胰島 β 細胞中的 miR-21 通過調控葡萄糖代謝從而促進胰島素分泌，並進一步證實 miR-21 經由 miR-21-Pdcd4-AP-1-Glut2 路徑促進胰島素分泌的機轉。藉由這個發現，通過體外實驗證實在小鼠和人的胰島 overexpression miR-21 可以顯著增加胰島素分泌，並再透過動物實驗證明將 miR-21 導入第 2 型糖尿病小鼠的胰腺中可顯著降低血糖值，使我們更了解 miR-21 在調節胰腺 β 細胞功能，為第 2 型糖尿病的預防和治療提供了新的思考策略。

2. 對論文內容的提問

Glut5 是在小腸中的腸細胞的頂端邊界上表達的果糖轉運蛋白，Fig5 圖 a 結果顯示 miR-21βKO 小鼠的 Glut5 表現多於野生小鼠，雖然無顯著差異但 miR-21βKO 是否也可以藉由 Glut5 來代謝部分葡萄糖呢？

3. 論文的缺點與評論

作者於本篇 paper 中，在小鼠實驗中用了不同基因品系以及小鼠，驗證 miR-21 對於糖尿病患者有特異性，也在整體實驗中藉由不同的檢驗方法和實驗，大大了增加這篇 paper 的可信度。

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MicroRNA-21 promotes pancreatic β cell function through modulating glucose uptake

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Pancreatic β cell dysfunction contributes to the pathogenesis of type 2 diabetes. MiR-21 has been shown to be induced in the islets of glucose intolerant patients and type 2 diabetic mice. However, the role of miR-21 in the regulation of pancreatic β cell function remains largely elusive. In the current study, we identify the pathway by which miR-21 regulates glucose-stimulated insulin secretion utilizing mice lacking miR-21 in their β cells (*miR-21β*KO). We find that *miR-21β*KO mice develop glucose intolerance due to impaired glucose-stimulated insulin secretion. Mechanistic studies reveal that miR-21 enhances glucose uptake and subsequently promotes insulin secretion by up-regulating Glut2 expression in a miR-21-Pdcd4-AP-1 dependent pathway. Over-expression of Glut2 in knockout islets results in rescue of the impaired glucose-stimulated insulin secretion. Furthermore, we demonstrate that delivery of miR-21 into the pancreas of type 2 diabetic *db/db* male mice is able to promote Glut2 expression and reduce blood glucose level. Taking together, our results reveal that miR-21 in islet β cell promotes insulin secretion and support a role for miR-21 in the regulation of pancreatic β cell function in type 2 diabetes.

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