Three New Gene Variants (PTPRD, SYT9, and WFS1) related to Korean MODY Children Decrease Insulin Secretion in Human Pancreatic Beta Cells.

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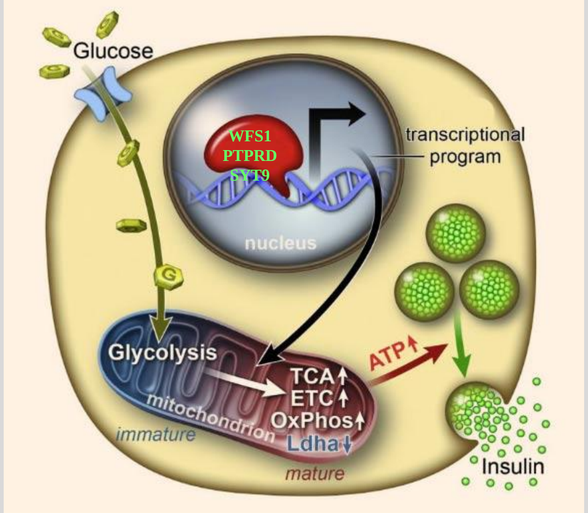
Background

Maturity-onset diabetes of the young (MODY) is a monogenic form of diabetes that is characterized by an early onset, autosomal dominant mode of inheritance and a primary defect in pancreatic β-cell function. MODY has been identified in Asian populations, however, there is a big discrepancy in the genetic locus between Asian and Caucasian patients with MODY. We previously reported that mutations in PTPRD, SYT9 and WFS1 have been identified in Korean families of MODY patients. In this study, we investigated **whether mutations (mut)** of **PTPRD, SYT9** and **WFS1 overexpression vectors effected insulin release** in human pancreatic beta cell.

Methods

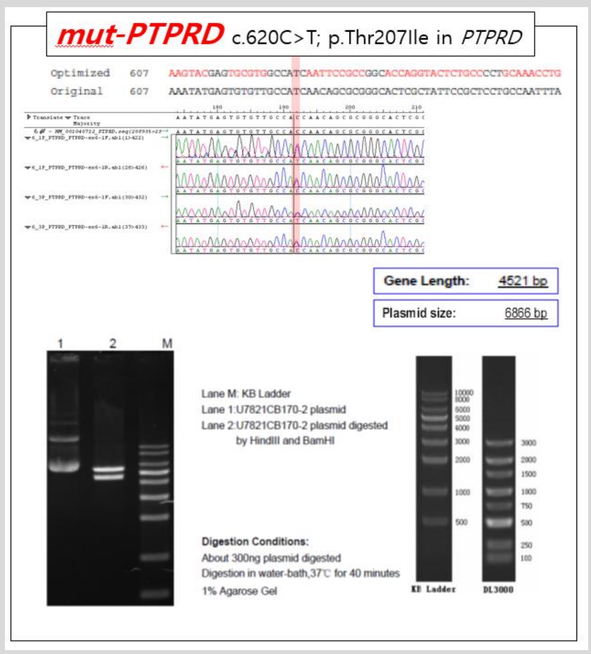


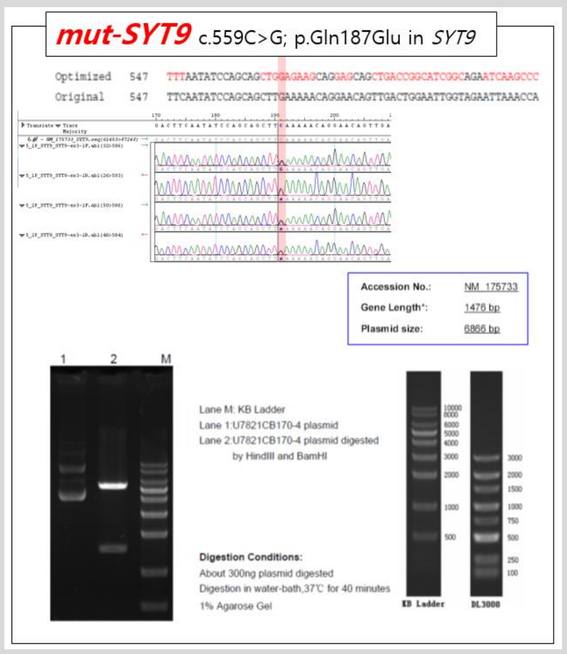
1. 1.2B4 and 1.4E7 β cell lines for **human pancreatic β cells.**

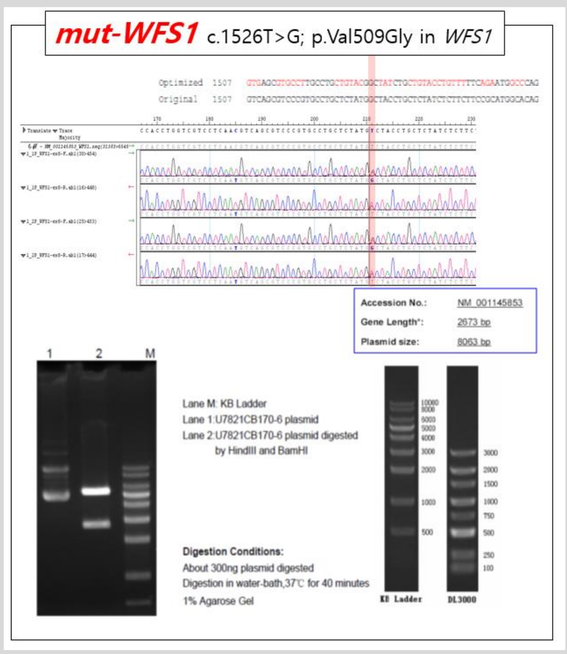
2. PTPRD, mut-PTPRD (c.620C>T:p. Thr 207 Ile), SYT9, mut-SYT9 (c.559C>G:p.Gln187Glu), WFS1 and mut-WFS1 (c.1526T>G:p.Val 509 Gly) **overexpression vectors transfected into 1.2B4 and 1.4E7 β cells.**

3. **Overexpression confirmation by RT-PCR**

4. **Analysis of glucose-induced insulin production by ELISA**







Results

Figure 1

The deficit of increased insulin release for mut-WFS1, mut-PTPRD and mut-SYT9 in 1.2B4 cells

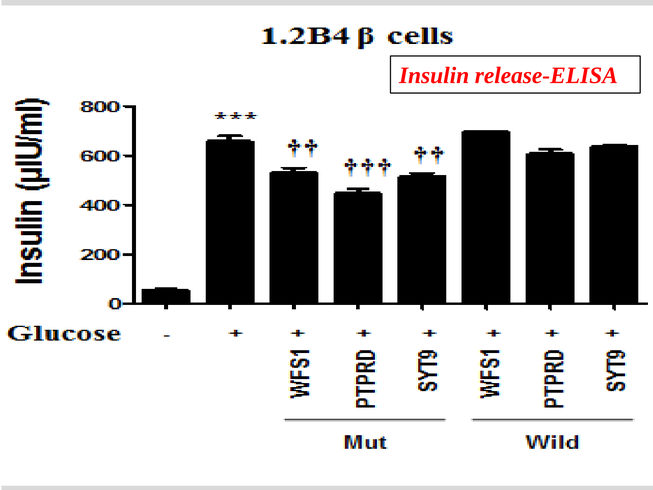
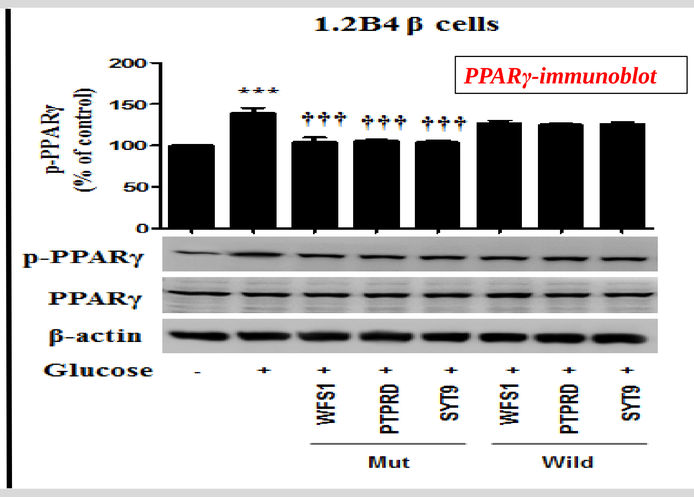


Figure 2

Decreased PPAR-γ Activation for mut-WFS1, mut-PTPRD and mut-SYT9 in 1.2B4 cells



Tukey's multiple comparison test,
*p<0.05, **p<0.001, ***p<0.0001 compared to normal control

Glucose induced insulin release in 1.2B4 and 1.4E7 β cells. There was no change in insulin release by glucose in 1.2B4 and 1.4E7 β cells transfected with PTPRD, SYT9 and WFS1 overexpression vectors.

Interestingly, **the deficit of increased insulin release** was 10-12% for mut-WFS1 and 30-35% for mut-SYT9 and mut-PTPRD, respectively in 1.2B4 and 1.4E7 β cells.

Conclusions

Based on the literatures and our findings, **PTPRD, SYT9** and **WFS1 are promising candidate genes with the potential of Korean MODY family.** In addition, further evaluation of cell signals related to insulin secretion by these genes is needed in the future.

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