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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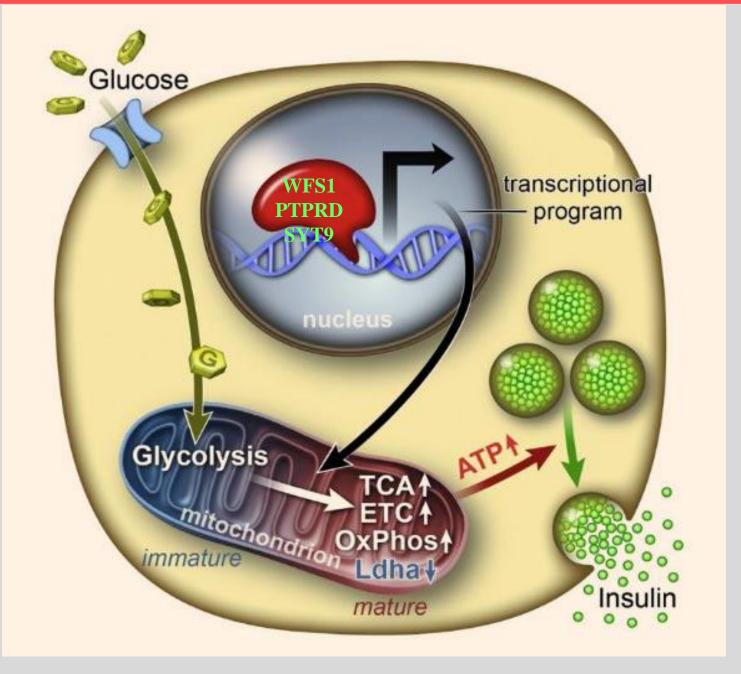


Background

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 ß cells.

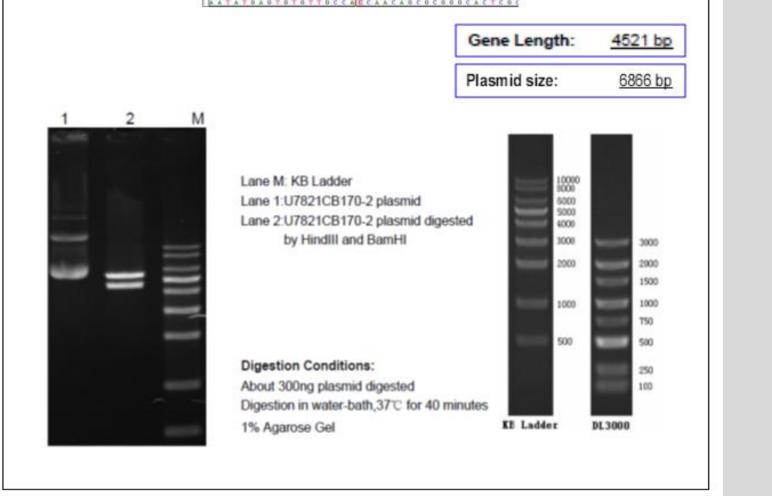
3. Overexpression confirmation by RT-PCR

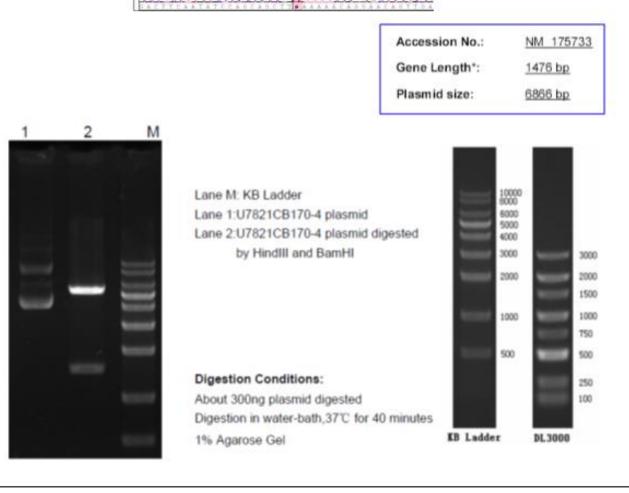
4. Analysis of glucose-induced insulin production by ELISA

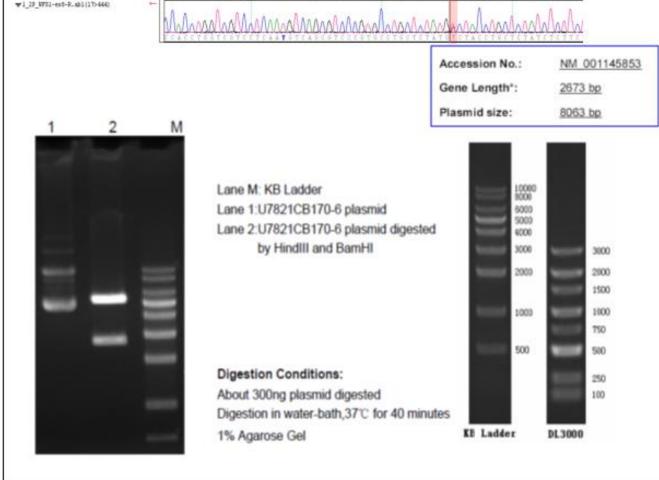
Optimized	607	AAGTACGAGTGCGTGGCCATCAATTCCGCCGGCACCAGGTACTCTGCCCCTGCAAACC
Original	607	AAATATGAGTGTGTGTGCCATCAACAGCGCGGGGCACTCGCTATTCCGCTCCTGCCAATT
		, 190 , 290 , 210
Translate * Trace Hajority		A A T A T G A G T G T G T G C C A A C A G C G G G G G G G C A C T C G C
6.# - NM_002040722_FIFAD.se ★ 6_1F_FIFAD_FIF6D-ex6-1F.eb1(- Manana Mana
▼6_1F_FTFRD_FTFRD-ex6-18.mb1(28>426)	- hannannannannannannannannan

mut-	SYT9 c.559C>G; p.Gln187Glu in <i>SYT9</i>
Optimized	547 TTTAATATCCAGCAGCTGGAGAAGCAGGAGCAGCTGACCGGCATCGGCAGAATCAAGCC
Original	547 TTCAATATCCAGCAGCTTGAAAAAACAGGAACAGTTGACTGGAATTGGTAGAATTAAACC
6 # - NM_175731_SYT9.seg(61463> • 5_1P_3YT9_3YT9-ex3-1F.eb1(32>586)	7248) - OASTTCAATATCCAOCAOCTT
▼ 5_1 P_31179_3119-ex:)-18.ab1(26)59)	- management
▼ 5_2F_3YT9_3YT9-ex3-1F.eb1(500586)	
▼5_2P_3YT9_3YT9-ex3-1P.sb1(46>504)	- management

mut-	WFS1 c.1526T>G; p.Val509Gly in WFS1
	Optimized 1507 GTGAGCGTGCCTTGCCTGCTGTACGGCTATCTGCTGTACCTGTTTTCAGAATGGCCC
	Original 1507 GTCAGCGTCCCGTGCCTGCTCTATGGCTACCTGCTCTATCTCTTCCCGCATGGCAC
P Translate - Trace	178 180 190 200 218 228 229 CCACCTGGTCGTCGTCGACGTCGGCCGGCCTGCTCTATCTCCTCCC
Re)stity 5 ∰ - 300 00144361 9051.seg(31361> ▼1_17_9711-set-7.sb1(310464)	- CONCENTRATESTORIA CONCENTRATESTORIA CONTRACTION CONTRACTORIA CONTRAC
▼1_12_9781-ex8-9, sb1(16)448)	Mushmannananananananananananananana
♥1_17_W31-cc9-F.@1(25)453)	mannahannahannahannahannah
₩1_12_W751-ext0-P.sb1(175444)	CCACCTOOTCETCETCAAT OTCASCETCCCOTECTCTATC





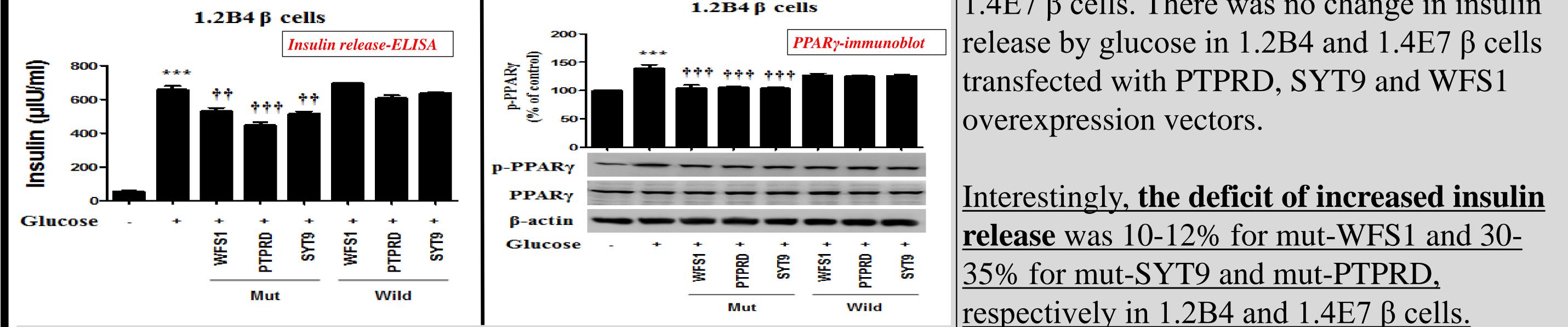


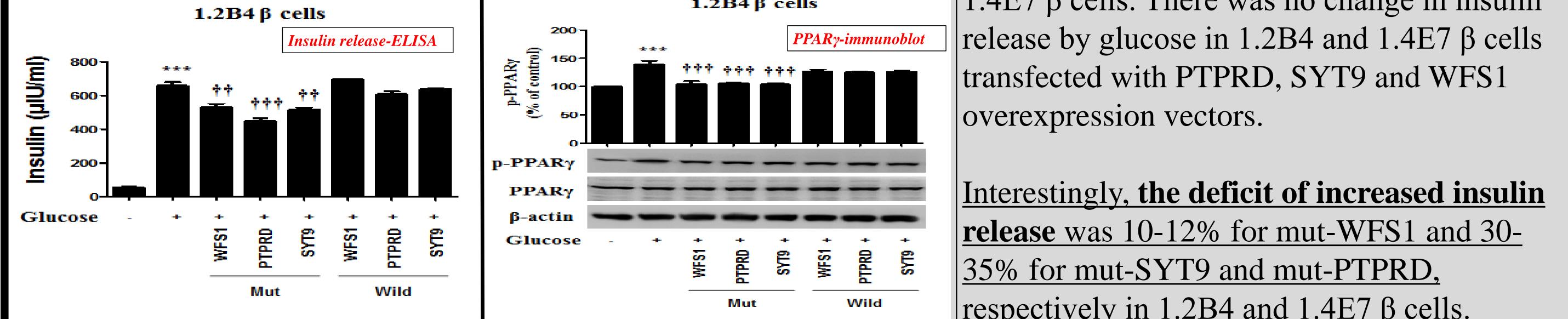
Results





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





Glucose induced insulin release in 1.2B4 and 1.4E7 β cells. There was no change in insulin

Tukey's multiple comparison test,

*p<0.05, **p<0.001, ***p<0.0001 compared to normal control

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.

