

SUPPLEMENTARY DATA

Supplementary Table 1. Anti-diabetes drug target genes that lie in previously validated T2D or glycemic GWAS loci.

| Drug target gene | Anti-diabetes medication class | Associated disease / trait | GWAS Meta-Analysis (Sample size*) | Risk Allele | SNP association P-value [†] | SNP Effect [†] (95% CI or SE) | Latest Reference |
|-----------------------|--------------------------------|--|---|------------------------|--------------------------------------|---|------------------|
| <i>ABCC8</i> | Sulfonylureas, Meglitinides | T2D | DIAGRAMv3 + MetaboChip (34,840 cases, 114,981 controls) | rs5215-C | 8.5×10^{-10} | Stage 2, OR=1.07 (1.04-1.10) | (3) |
| <i>KCNJ11</i> | Sulfonylureas, Meglitinides | T2D | DIAGRAMv3 + MetaboChip (34,840 cases, 114,981 controls) | rs5215-C | 8.5×10^{-10} | Stage 2, OR=1.07 (1.04-1.10) | (3) |
| <i>GIPR</i> | DPP4 inhibitors | T2D | DIAGRAMv3 + MetaboChip (34,840 cases, 114,981 controls) | rs8108269-G | 2.1×10^{-8} | Stage 2, Female: OR=1.10 (1.06-1.15); Male: OR=1.05 (1.01-1.09) | (3) |
| | | 2 hr glucose [‡] | MAGIC (41,888 individuals) | rs10423928-A | 2.0×10^{-15} | Beta=0.09±0.01 (mmol/l) | (8) |
| | | 2 hr insulin [‡] (Adjusted for 2hr glucose & BMI) | MAGIC (32,204 individuals) | rs10423928-A | 3.7×10^{-16} | Beta=-0.044±0.006 (pmol/l) | (8) |
| | | Fasting glucose | MAGIC + MetaboChip (116,141 individuals) | rs2302593-C | 9.3×10^{-10} | Beta=0.0144±0.002 (mmol/l) | (3) |
| <i>IDE</i> | Amylin mimetics | T2D | DIAGRAMv3 + MetaboChip (34,840 cases, 114,981 controls) | rs1111875-C | 2.0×10^{-19} | Stage 2, OR=1.09 (1.06-1.12) | (3) |
| <i>IRS1</i> | Insulin | T2D | DIAGRAMv3 + MetaboChip (34,840 cases, 114,981 controls) | rs2943640-C | 2.7×10^{-14} | Stage 2, OR=1.10 (1.07-1.13) | (3) |
| | | Fasting Insulin | MAGIC + MetaboChip (99,566 individuals) | rs2972143-G | 3.2×10^{-8} | Beta=0.0142±0.003 (pmol/l) | (3) |
| | | Fasting Insulin (BMI-adjusted) | MAGIC + MetaboChip (99,023 individuals) | rs2943645-T | 2.3×10^{-19} | Beta=0.0193±0.002 (pmol/l) | (3) |
| <i>PDX1</i> | GLP-1 mimetics | Fasting glucose | MAGIC + MetaboChip (132,996 individuals) | rs11619319-G | 1.3×10^{-15} | Beta=0.0195 ±0.002 (mmol/l) | (3) |
| <i>PPARG</i> | Thiazolidinediones | T2D | DIAGRAMv3 + MetaboChip (34,840 cases, 114,981 controls) | rs1801282-C (Pro12Ala) | 1.1×10^{-12} | Stage 2, OR=1.11 (1.07-1.16) | (3) |
| <i>SLC2A2 (GLUT2)</i> | Insulin | Fasting glucose | MAGIC (119,024 individuals) | rs11920090-T | 8.1×10^{-13} | Stage 2, Beta=0.020 ±0.004 (mmol/l) | (3) |

* All samples sizes refer to Stages 1+2 (Discovery and Replication samples). The majority of studies contain individuals of European ancestry.

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[†] All SNP association *P*-values and effect sizes are reported from joint GWAS meta-analyses (Stage 1+2), unless stated otherwise. [‡] 2 hr glucose and 2 hr insulin refer to glucose or insulin plasma levels measured 2 hours after a glucose challenge during an oral glucose tolerance test (OGTT). OR: odds-ratio. CI: confidence interval. SE: Standard Error.