Supplementary Table 1: Overview of studies focusing on gene-metformin interaction in type 2 diabetes.

Variant	Population	Study group	N	Outcome	Major findings	PMID	Author (publication year)
OCT1							
rs12208357(C>T), rs72552763(GAT>del), rs34130495(G>A), rs34059508(G>A)	Caucasians	Healthy	34	PK (AUC, Cmax, CLrenal)	No significant difference in steady state PK parameters between carriers of 0, 1 or 2 reduced function alleles.	25939711	Christensen et al (2015)
rs12208357(C>T), rs72552763(GAT>del), rs34130495(G>A), rs34059508(G>A)	Caucasians	T2D	103	PK (CL/F)	None of the SNPs showed significant association with total clearance of metformin.	23475568	Duong et al (2013)
rs12208357(C>T), rs72552763(GAT>del), rs34130495(G>A), rs34059508(G>A)	Caucasians	Healthy male	103	PK (CLrenal)	Carriers of 0, 1 and 2 reduced function variants showed increasing pattern of renal clearance (30.6, 33.1, 37.1 L/h, P = 0.04).	19536068	Tzvetkov et al (2009)
rs12208357(C>T), rs34130495(G>A), rs34059508(G>A), 420del	Caucasians	Healthy	20	PK (Cmax, AUC, V/F)	Individuals having one or more variants showed higher Cmax (P = 0.004), AUC (P = 0.01) and lower oral volume of distribution (P = 0.02).	17609683	Shu et al (2007)
rs12208357(C>T), rs72552763(GAT>del), rs34130495(G>A), rs34059508(G>A)	Caucasians	T2D	159	PK (trough steady state concentration)	Increasing number of deletions were associated with significant trend to decrease in trough steady state concentration (none, one or two: 642, 542, 397 ng/ml; P = 0.001).	21989078	Christensen et al (2011)
rs12208357(C>T), rs72552763(GAT>del), rs34130495(G>A), rs34059508(G>A)	Caucasians	T2D	159	Response (HbA1c reduction)	Individuals with zero, one and two reduced function alleles showed 0%, 0.2 % (0.2-0.6) and 1.1% (0.4-1.9) HbA1c reduction. P = 0.016,	21989078	Christensen et al (2011)
rs12208357(C>T), rs72552763(GAT>del), rs34130495(G>A), rs34059508(G>A)	Multi-ethnic	T2D	171	Response (HbA1c reduction)	None of these reduced function SNPs showed significant association with HbA1c reduction.	PMC3006596	Davis et al (2010)
rs12208357 (C>T), 420del	Caucasians	T2D	1531	Response (HbA1c reduction, achieving treatment target, the hazard of monotherapy failure)	No significant association between these loss of function variants and response.	19336679	Zhou et al (2009)
rs12208357(C>T), rs72552763(GAT>del), rs34130495(G>A**),** rs34059508(G>A)	Caucasian	PCOS women	150	Response (Insulin, total cholesterol, triglycerides)	Carriers of no reduced function allele showed significant reduction in total cholesterol (-14mg/dl, P = 0.002), and triglycerides (-17mg/dl, P = 0.008). Insulin AUC decreased in carriers of 0 or 1 reduced function OCT1 variant carriers but not in two or more.	20660041	Gambineri et al (2010)
rs622342 A>C	Caucasians	T2D	102	Response (HbA1c reduction)	Each minor C allele was associated with 0.28% (0.09-0.47, P = 0.005) less HbA1c reduction.	19381165	Becker et al (2009)
rs622342 A>C	Caucasians	T2D	148	Response (HbA1c reduction)	The minor allele was not associated with HbA1c reduction.	22882994	Tkac et al (2012)

–43T > G	Japanese	T2D	33	Response (achieving target)	The minor allele was more frequent in responders than non-responders (0.42 Vs 0.33, P < 0.05).	17111267	Shikata et al (2007)
rs628031 (Met408Val)	Japanese	T2D	33	Response (achieving target)	The Met allele was more frequent in non-responders than responders (0.28 Vs 0.19, P < 0.05).	17111267	Shikata et al (2007)
rs683369 (G>C)	Multi-ethnic	High risk	990	Response (diabetes incidence)	The major allele showed protective effect (HR = 0.69, 0.53-0.89, P =0.004).	20682687	Jablonski et al (2010)
rs12208357(C>T), rs72552763(GAT>del), rs34130495(G>A, rs34059508(G>A), rs55918055(T>C)	Caucasians	T2D	2166	Response (GI side effect)	Carriers of two or more reduced function alleles showed 2.41 (1.48-3.93, P < 0.001) times higher odds of developing GI side effects than carriers of no or one.	25510240	Dujic et al (2015)
rs12208357(C>T), rs34059508(G>A)	Caucasian	T2D	246	Response (GI side effect)	The minor alleles of these variants showed no significant association with GI side effect.	22735389	Tarasova et al (2012)
rs628031 (A>G)	Caucasian	T2D	246	Response (GI side effect)	The A allele showed significant association with GI side effect (OR = 0.389, P = 0.012).	22735389	Tarasova et al (2012)
rs36056065 (G160560908delinsGTAAGTTG)	Caucasian	T2D	246	Response (GI side effect)	8bp insertion showed significant association with GI side effect (OR = 0.405, P = 0.002)	22735389	Tarasova et al (2012)
OCT2							
OCT2_c.596C>T, OCT2_c.602C>T, OCT2_c.808G>T	*In vitro*			PK (uptake)	Carriers of the variant alleles showed significant (596C>T, 602C>T, 808G>T: 68.6, 60.1, and 39.6%) decrease in clearance than carriers of the reference alleles.	18401339	Song et al (2008)
OCT2 808G >T	*In vitro*			PK (uptake)	The minor allele showed 1.5 times higher metformin uptake than the reference allele (P < 0.01).	19483665	Chen et al (2009)
OCT2_808G >T	Chinese	T2D	18	PK (AUC, CLrenal, CLtubular)	Heterozygous GT carriers had higher AUC, CLrenal and CLtubular than wild GG genotype (P < 0.05).	25573751	Hou et al (2015)
OCT2_808G >T	Chinese	Healthy	15	PK (CLtubular)	The minor allele was associated with reduced renal tubular secretion (P = 0.037).	18551044	Wang et al (2008)
OCT2_808G >T	Caucasians	Healthy	50	PK (CLrenal, CLtubular)	The minor allele showed no effect on the PK of metformin.	23873119	Christensen et al (2013)
OCT2_808G >T	Korean	Healthy	96	PK (AUC, Cmax)	Homozygous GG carriers showed lower AUC (0.007) and lower Cmax than heterozygous GT (P = 0.012) carriers.	23417334	Yoon et al (2013)
OCT2_808G >T	Caucasian, Afro-American	Healthy	23	PK (CLrenal, CLtubular)	Subjects homozygous for the reference allele showed lower renal (0.005) and tubular clearance (0.002) than heterozygous subjects.	19483665	Chen et al (2009)
OCT2_602C>T, OCT2_c.596C>T	Korean	Healthy	26	PK (Cmax, CL/F, CLrenal, CLtubular)	Participants heterozygous for the minor allele of either of the variants showed higher Cmax and AUC & lower Cl/F, CLrenal, CLtubular.	18401339	Song et al (2008)
OCT2_808G >T	Chinese	T2D	209	Response (HbA1c reduction)	Heterozygous GT carriers showed greater HbA1c reduction than the wild type (-2.2 Vs -1.1, P < 0.05)	25573751	Hou et al (2015)
OCT2_808G >T	Caucasian	T2D	148	Response (HbA1c reduction)	The minor allele showed no significant difference in HbA1c reduction.	22882994	Tkac et al (2012)
OCT2_808G >T	Japanese	T2D	33	Response (achieving target)	No significant difference in prevalence of the minor allele between responders and non-responders.	17111267	Shikata et al (2007)
OCT2_808G >T	Caucasian	T2D	246	Response (GI side effect)	The minor allele showed no significant association with GI side effect.	22735389	Tarasova et al (2012)

OCT2_808G >T	Chinese	T2D	400	Response (lactate concentration)	Patients with the mutant genotype (TT) had higher incidence of hyperlactacidemia compared with the GG genotype (40% vs 6.9%, P = 0.05).	20139901	Li et al (2010)
OCT2_602C>T	Japanese	T2D	33	Response (achieving target)	No significant difference in prevalence of the minor allele between responders and non-responders.	17111267	Shikata et al (2007)
OCT2_602C>T	Iranian	T2D	40	Response(Insulin resistance (HOMA-IR) and beta cell function (HOMA-BCF))	The T allele was associated with significant increase in HOMA-IR (P = 0.019) but not HOMA-BCF than homozygous CC.	25662675	Kashi et al (2015)
rs662301C>T	Multi-ethnic	High risk	990	Response (diabetes incidence)	Carriers of the major allele benefit from metformin's protective effect (P = 0.02).	20682687	Jablonski et al (2010)
OCT3							
T44M_131C>T	*In vitro*			PK (uptake)	The minor allele showed 60% more uptake of metformin than the reference genotype (P < 0.001).	20859243	Chen et al (2010)
V423F_1267G>T	*In vitro*			PK (uptake)	The minor allele showed 50% less uptake of metformin than the reference genotype (P < 0.001).	20859243	Chen et al (2010)
400I_1199C>T	*In vitro*			PK (uptake)	The minor allele showed 80% less uptake of metformin than the reference genotype (P < 0.001).	20859243	Chen et al (2010)
rs3120137 G>A, rs3123634 C>T, rs12194182 A>G, rs2292334 C>T, rs2504927 G>A, rs2457576 C>G	Caucasians	Healthy male	103	PK (CLrenal)	None of the variants showed significant association with renal clearance.	19536068	Tzvetkov et al (2009)
rs2076828 C > G	Asian, Afro-American	Healthy	57	PK (AUC, CLrenal, CLtubular) Response (OGTT)	The minor allele showed no association with the PK of metformin but significantly smaller change in AUC than the wild type (P < 0.001)	25920679	Chen et al (2015)
$OCT3^{-/-}$	Knockout mice			PK	Knockout mice showed significant reduction in apparent volume of distribution, Clearance and bioavailability (P < 0.001)	25920679	Chen et al (2015)
L503F Leu>Phe	Caucasians	Healthy male	103	PK (CLrenal)	The variants showed no significant association with renal clearance	19536068	Tzvetkov et al (2009)
MATE1-metformin							
G64D and V480M	*In vitro*			PK (uptake)	These variants showed complete loss of function	19172157	Chen et al (2009)
G64D, L125F, V338I, V480M, C497S	*In vitro*			PK (uptake)	These variants showed reduced transport of metformin (P < 0.01) than the reference genotypes	19172157	Chen et al (2009)
rs2289669G>A	Chinese	T2D	30	PK (AUC, CLrenal, CLtubular)	Homozygous A allele carriers showed higher AUC and lower clearance (P <0.01) than the reference genotype.	26004431	He et al (2015)
rs2289669G>A	Japanese	T2D	48	PK (oral clearance)	Heterozygosity for the minor allele showed no significant difference in oral clearance compared with homozygous GG	20016398	Toyama et al (2010)
rs2252281T>C	Asian, Afro-American	Healthy	57	PK (Cmax, CLrenal), Response (Glucose AUC after OGTT)	No significant genotype-PK association was showed, Homozygous CC carriers had lower glucose AUC (greater response) than the reference allele.	23267855	Stocker et al (2013)
rs2289669G>A	Caucasians	T2D	148	Response (HbA1c reduction)	Homozygous A allele carriers showed higher HbA1c reduction than carriers of the G allele (1.10 ± 0.18% Vs 0.55 ± 0.09%, P = 0.02)	22882994	Tkac et al (2012)

rs2289669G>A	Multi-ethnic	T2D	171	Response (HbA1c reduction)	Carriers of the minor allele (A) had 0.45% (0.17-0.74%) smaller absolute HbA1c reduction than homozygous GG carriers	PMC3006596	Davis et al (2010)
rs2289669G>A	Caucasians	T2D	116	Response (HbA1c reduction)	Each minor allele was associated with 0.3% (-0.51 to -0.10, P < 0.005) more A1c reduction	19228809	Becker et al (2009)
rs2289669G>A	Chinese	T2D	220	Response (HbA1c reduction)	Homozygosity for the minor allele (-2.3%) showed significantly higher HbA1c reduction than GG (-1.16%) and GA (-1.07%) allele carriers (P < 0.05)	26004431	He et al (2015)
rs2289669G>A	Caucasians	T2D	246	Response (GI side effect)	The minor allele showed no significant association with GI side effect	22735389	Tarasova et al (2012)
rs2252281T>C	Caucasians, Afro-Americans	T2D	249	Response (HbA1c reduction)	After removing OCT1 variant carriers, patients homozygous for the minor allele had significantly larger relative change in HbA1c levels (i.e. greater response to metformin) than patients carrying at least one reference allele (P= 0.01).	23267855	Stocker et al (2013)
rs8065082C>T	Multi-ethnic	High risk	990	Response (diabetes incidence)	The minor allele was associated with lower incidence of T2D after metformin treatment (HR = 0.78, 0.64-0.96, P = 0.02)	20682687	Jablonski et al (2010)
MATE2-metformin							
rs12943590G>A	Multi-ethnic	T2D	171	Response (HbA1c reduction)	Homozygous AA carriers had 0.43% lower HbA1c reduction (0.43%, 0.053-0.86%) than the reference genotype	PMC3006596	Davis et al (2010)
rs12943590G>A	Caucasian, Afro-American	Healthy	57	PK (CLrenal, CLrenal), Response (Glucose AUC after OGTT)	Carriers of one or more variant allele showed higher renal and tubular clearance than homozygous GG (P < 0.05), Homozygosity for the reference allele was associated with higher glucose AUC (P < 0.05)	23267855	Stocker et al (2013)
c.485C>T, c.1177G>A	*In vitro*			PK (uptake)	Both variants showed 3-5 times lower metformin uptake than the reference (P < 0.05) allele	21956618	Choi et al (2011)
rs12943590G>A	Caucasian + Afro-American	T2D	253	Response (HbA1c reduction)	Patients homozygous for the minor allele had smaller change in HbA1c than carriers of the reference allele (−0.027 Vs −0.15, P = 0.002)	21956618	Choi et al (2011)

AUC: area under the curve; CLrenal: renal clearance; CLtubular: renal clearance by secretion; CL/F: total clearance; Cmax: maximal plasma concentration; HbA1c: glycated haemoglobin; HOMA-BCF: homeostasis model assessment of beta cell function; HOMA-IR: homeostasis model assessment of insulin resistance; OGTT: oral glucose tolerance test; PCOS: polycystic ovary syndrome; PK: pharmacokinetics; T2D: type 2 diabetes mellitus; V/F: oral volume of distribution.

Supplementary Table 2: Overview of studies focusing on gene-SU interaction in type 2 diabetes.

Gene	Variant	Population	Study group	Drug	N	Outcome	Major findings	PMID	Author (publication year)
CYPs									
CYP2C9	CYP2C9*2 and *3	Caucasians	T2D	Tolbutamide	475	Response (prescribed dose)	*3 genotype carriers were prescribed with lower dose of tolbutamide than the wild type carriers (P < 0.05). *2 carriers showed no significant difference compared to the wild type.	17597710	Becker et al (2008)
CYP2C9	CYP2C9*2 and *3	Caucasians	T2D	SUs	1073	Response (achieving target HbA1c, HbA1c	Patients with two copies of loss of function alleles were 3.4 (P = 0.0009) times more likely to achieve target HbA1c than	19794412	Zhou et al (2010)

						reduction, time to monotherapy failure)	wild type carriers or 0.5% greater HbA1c reduction, and low hazard of monotherapy failure.		
CYP2C9	CYP2C9*3	Japanese	T2D	Glimepiride	42/6	Response (HbA1c reduction), PK (AUC)	CYP2C9*1/*3 genotype was associated with significantly greater HbA1c reduction (P < 0.05).	16325295	Suzuki et al (2006)
CYP2C9	CYP2C9*2 and *3	Caucasians	T2D	SUs	207	Response (prescribed dose, time to stable dose)	No significant association but trend towards lower stable glimepiride dose was observed.	21121772	Swen et al (2010)
CYP2C9	CYP2C9*2 and *3	Caucasians	T2D	SUs	357	Response (severe hypoglycaemia)	*3/*3 and *2/*3 genotypes were more common in the hypoglycaemic group than the comparison group (10% Vs < 2%, P = 0.028).	15963101	Holstein et al (2005)
CYP2C9	CYP2C9*2 and *3	Caucasians	T2D	Glimepiride and glyclazide	176	Response (incidence of hypoglycaemia)	Patients with *1/*3 genotype had 1.69 (P = 0.011) times higher risk of hypoglycaemia.	19891554	Ragia et al (2009)
CYP2C9	CYP2C9*2 and *3	Turkish	T2D	SUs	108	Response (mild hypoglycaemia)	CYP2C9*2 and *3 were more frequent in the hypoglycaemic group than non-hypoglycaemic group (7% Vs 3%, P < 0.05)	21691805	Gokalp et al (2011)
CYP2C9	CYP2C9*2 and *3	Caucasians	T2D	SUs	203	Response (hypoglycaemia and prescribed dose)	No over representation of loss of function alleles among hypoglycaemics were observed but slower metabolizers were prescribed with lower dose (P = 0.027).	21213107	Holstein et al (2011)
CYP2C9	CYP2C9*2 and *3	South Indian	T2D	Glibenclamide	80	Response (HbA1c reduction, hypoglycaemia)	CYP2C9*1/*3 genotype showed no significant association with risk of hypoglycaemia, carriers of loss of function variants (*1/*3 and *1/*2) had better diabetic control than the wild type carriers (P < 0.001).	21336994	Surendiran et al (2011)
CYP2C9	CYP2C9*2 and *3	Caucasians	T2D	SUs	156	Response (incidence of hypoglycaemia, HbA1c reduction)	No significant association between CYP2C9 genotype and risk of hypoglycaemia or HbA1c reduction was found.	24442125	Klen et al (2014)
CYP2C9	CYP2C9*2	Caucasians	T2D	SUs	176	Response (risk of hypoglycaemia)	*2 genotype carriers that are POR*1/*1 were 3.2 (P=0.031) times more likely to encounter hypoglycaemia than the wild type carriers.	24464600	Ragia et al (2014)
CYP2C9	CYP2C9*2 and *3	Caucasians	Healthy	Glibenclamide	21	Response (Insulin and glucose concentration), PK (oral clearance)	Carriers of *3/*3 genotype had lower oral clearance (P < 0.001) and increased insulin secretion (P = 0.028) than carriers of the wild type.	11956512	Kirchheiner et al (2002)
CYP2C9	CYP2C9*3	Korean	Healthy	Tolbutamide	18	PK (AUC, Cmax, t1/2)	Carriers of *1/*3 genotype had greater AUC, Cmax, and longer t1/2 compared with the wild genotype carriers.	11875365	Shon et al (2002)
CYP2C9	CYP2C9*3	Chinese	Healthy	Glimepiride	19	PK (AUC, Cmax, t1/2, oral clearance)	Carriers of *3 genotype showed significantly greater AUC and Cmax and longer t1/2 and reduced oral clearance than the wild type carriers.	16003298	Wang et al (2005)
CYP2C9	CYP2C9*3	Chinese	Healthy male	Glibenclamide	18	PK (AUC, t1/2)	CYP2C9*1/*3 carriers showed significantly greater AUC (P < 0.05) and longer t1/2 (P < 0.05) than the wild type irrespective of their CYP2C19 genotype.	16198656	Yin et al (2005)
CYP2C9 and CYP2C19	CYP2C9*3 and CYP2C19*3	Chinese	Healthy male	Gliclazide MR	24	PK (AUC, t1/2)	Carriers of poor metabolizing CYP2C19 variants showed significantly higher AUC (P < 0.01) and prolonged t1/2 (P < 0.01) than the wild type. CYP2C9 variants showed no significant role in the PK of gliclazide MR.	17298483	Zhang et al (2007)
KCNJ11 /ABCC8									

ABCC8	S1369A (rs757110 G>T)	Caucasians	T2D	SUs	156	Response (incidence of hypoglycaemia, HbA1c reduction)	No significant association between the variant allele and risk of hypoglycaemia or HbA1c reduction was found.	24442125	Klen et al (2014)
ABCC8	S1369A (rs757110 G>T)	Chinese	T2D	Gliclazide	1268	Response (FPG, 2 hour glucose, HbA1c)	Compared to the wild type carriers, carriers of A/A genotype showed 7.7% greater reduction in FPG (P <0.001), 11.9% greater reduction in 2 hour glucose (P = 0.003) and 3.5% greater reduction in HbA1c (0.06).	18599530	Feng et al (2008)
ABCC8	E23K (rs5219A>G)	Caucasians	T2D	Glibenclamide	525	Response (risk of secondary failure)	Carriers of the K allele showed 1.69 (1.02-2.74, P = 0.04) times higher odds of secondary failure than homozygotes EE carriers.	16595597	Sesti et al (2006)
ABCC8	S1369A (rs757110 G>T	Japanese	T2D	Glibenclamide	157	Response (incidence of severe hypoglycaemia)	No significant difference in distribution of the genotype between cases and controls.	21142918	Sato et al (2010)
KCNJ11	E23K (rs5219A>G), rs5215G>A	Caucasians	T2D	SUs	156	Response (incidence of hypoglycaemia, HbA1c reduction)	No significant association between KCNJ11 variants and risk of hypoglycaemia or HbA1c reduction was found.	24442125	Klen et al (2014)
KCNJ11	E23K (rs5219A>G)	Caucasians	T2D	SUs	101	Response (HbA1c reduction)	Carriers of the K allele had greater HbA1c (P = 0.04) reduction than EE homozygotes.	22385882	Javorski et al (2012)
KCNJ11	E23K (rs5219A>G)	Caucasians	T2D	SUs	364	Response (FPG)	The minor allele showed no association with response to SUs.	11318841	Gloyn et al (2000)
KCNJ11	E23K (rs5219A>G)	Caucasians	T2D	SUs	176	Response (incidence of mild hypoglycaemia)	No difference in frequency of the variant were observed between cases and controls.	22591706	Ragia et al (2012)
KCNJ11	E23K (rs5219A>G)	Caucasians	T2D	SUs	97	Response (incidence of severe hypoglycaemia)	The K allele was associated with higher HbA1c (P = 0.04) and less frequent in hypoglycaemic groups (P = 0.04).	19214942	Holstein et al (2009)
KCNJ11	E23K (rs5219A>G)	Chinese	T2D	Gliclazide MR	108	Response (FPG, acute insulin response)	KK genotype carriers showed lower FPG (P = 0.03) and greater change in insulin (P = 0.05) than E allele carriers.	25115353	Li et al (2014)
TCF7L2									
TCF7L2	rs12255372 G>T	Caucasians	T2D	SUs	901	Response (treatment failure)	Homozygous TT genotype was associated with 1.94 (1.23-3.06) times higher odds of treatment failure than GG genotype (P = 0.005).	17519421	Pearson et al (2007)
TCF7L2	rs7903146 C>T	Caucasians	T2D	Gliclazide	101	Response (HbA1c reduction)	Homozygous C allele carriers showed 80% higher HbA1c reduction than the T allele carriers.	23509454	Javorski et al (2013)
TCF7L2	rs7903146 C>T	Caucasians	T2D	SUs	901	Response (treatment failure)	Homozygous TT genotype was associated with 1.73 (1.11–2.70) times higher odds of treatment failure than GG genotype (P = 0.015).	17519421	Pearson et al (2007)
TCF7L2	rs7903146 C>T	Caucasians	T2D	SUs	87	Response (FPG, HBA1c reduction)	Homozygous carriers of the reference allele showed significant reduction in HbA1c (P = 0.003) and FPG (P = 0.031) than carriers of the minor allele.	21114608	Schroner et al (2011)
TCF7L2	rs7903146 C>T	Caucasians	T2D	SUs	189	Response (secondary treatment failure)	Patients who failed to respond to SU treatment showed 1.57 (1.01-2.45) times higher odds of carrying the T allele (P = 0.046).	21349175	Holstein et al (2011)
Others									
ABCA1	R230C	Mexican	T2D	Glyburide	85	Response (dose to achieve target HbA1c)	Carriers of the variant allele needed significantly higher dose to achieve target than the wild type (6.3 Vs 3.3mg/day, P < 0.001).	23273975	Aguilar-Salinas et al (2013)

CDKAL 1	rs7756992A> G	Caucasians	T2D	SUs	101	Response (FPG, HbA1c reduction)	Carriers of the G allele had significantly greater FPG (P = 0.022) reduction than homozygous AA. However no significant difference in HbA1c between genotypes was observed.	22292718	Schroner et al (2012)
IRS1	rs1801278G> A	Caucasians	T2D	SUs	477	Response (secondary SU treatment failure)	Patients with the variant allele had 2 (1.38-3.86, P = 0.038) times higher odds of secondary failure than the wild type carriers.	15161794	Sesti et al (2004)
KCNQ1	rs163184T>G		T2D	SUs	87	Response (FPG reduction)	Carriers of the T allele had significantly greater FPG (1.58 Vs 1.04 mmol/L, P = 0.016) reduction than homozygous GG carriers.	21709633	Schroner et al (2011)
NOS1AP	rs10494366G >T	Caucasians	T2D	SUs	619	Response (prescribed dose)	Glibenclamide users with TG genotype were prescribed with higher dose than GG (0.38 ddd, 0.14-0.63)	18551039	Becker et al (2008)

AUC: area under the curve; Cmax: maximal plasma concentration; ddd: defined daily dose; FPG: fasting plasma glucose; HbA1c: glycated haemoglobin; MR: modified release; PK: pharmacokinetics; SUs: sulfonylureas; T2D: type 2 diabetes; t1/2: elimination half-life.

Supplementary Table 3: Overview of studies focusing on gene-glinides interaction in type 2 diabetes.

Gene	**Variant**	**Population**	**Study group**	**Drug**	**N**	**Outcome**	**Major findings**	**PMID**	**Author (publication year)**
SLCO1B1	521T>C	Caucasians	Healthy	Repaglinide	56	PK (AUC, Cmax)	Homozygous CC carriers showed higher AUC and Cmax than T allele carriers (P < 0.0001)	15961978	Niemi et al (2005)
SLCO1B1	521T>C	Caucasians	Healthy	Repaglinide	32	PK (AUC)	Participants with CC genotype showed 59 (P = 0.001) and 72% (P < 0.001) greater AUC than TC and TT carriers respectively.	18187595	Kalliokoski et al (2008)
SLCO1B1	11187G>A	Caucasians	Healthy	Repaglinide	56	Response (glucose)	Carriers of the minor allele showed 11% (P = 0.01) and 6.6% (0.056) maximum decrease in blood glucose and mean glucose change respectively, than carriers of the wild type.	15961978	Niemi et al (2005)
SLCO1B1	*1B		Healthy	Repaglinide	24	PK (AUC, Cmax)	SLCO1B1*1B/*1B carriers showed 32 and 24% of AUC (P = 0.007) and Cmax (P = 0.056) of SLCO1*1A/*1A carriers	18854776	Kalliokoski et al (2008)
SLCO1B1	*1B	Chinese	Healthy male	Repaglinide	22	PK (AUC, clearance)	Carriers of *1A/*1B or *1A/*1A showed 27.39% higher AUC than *1B/*1B (P = 0.015).	21327909	He et al (2011)
KCNJ11	E23K (rs5219A>G)	Chinese	T2D	Repaglinide	100	Response (plasma glucose reduction, HbA1c reduction)	the K allele was associated with greater reduction in HbA1c (P = 0.02) and the E/K genotype showed greater 2hr glucose reduction (P = 0.04) than homozygous E/E.	18664331	He et al (2008)
SLC30A8	rs13266634C >T	Chinese	T2D	Repaglinide	48	Response (insulin)	Patients with the T allele showed greater increase in fasting (P<0.05) and post prandial (P<0.01) insulin than homozygous CC carriers.	20809084	Huang et al (2010)
SLC30A8	rs13266634C >T	Chinese	T2D	Repaglinide	104	Response (HOMA-BCF, fasting pro insulin level)	No significant difference in insulin secretion parameters between genotypes was observed.	22424623	Feng et al (2012)
SLC30A8	rs16889462G >A	Chinese	T2D	Repaglinide	48	Response (insulin, HbA1c)	Patients heterozygous GA showed greater increase in fasting insulin (P<0.01), post prandial insulin (P<0.01) and HbA1c (P<0.05) reduction than homozygous GG individuals.	20809084	Huang et al (2010)

KCNJ11	E23K (rs5219A>G)	Chinese	T2D	Repaglinide	40	Response (FPG, 2 hour glucose and HbA1c reduction)	Patients with the A allele showed higher FPG, 2 hour glucose and HbA1c ($P < 0.05$) than GG homozygotes.	20054294	Yu et al (2009)
ABCC8	rs1799854(exon16-3T/C)	Chinese	T2D	Repaglinide	100	Response (fasting insulin)	Homozygous CC carriers showed greater change in fasting insulin than T/C ($P = 0.04$) and T/T (0.03) carriers.	18664331	He et al (2008)
CYP2C8	*3	Caucasians	Healthy	Repaglinide	28	Response (plasma glucose change), PK (AUC, Cmax)	No significant difference was found between genotypes. *1/*3 carriers showed 45% ($P < 0.005$) and 39% ($P < 0.05$) lower AUC and Cmax respectively than homozygous *1/*1 carriers.	14534525	Niemi et al (2003)
CYP2C8	*3	Caucasians	Healthy	Repaglinide	56	PK (AUC, Cmax)	Carries of *1/*3 genotype showed 48 and 44% lower AUC and Cmax respectively than *1/*1 ($P < 0.05$)	15961978	Niemi et al (2005)
CYP2C8	*3	Caucasians	Healthy	Repaglinide	29	Response (glucose, insulin), PK (AUC)	No significant differences in PK and response parameters between genotypes were showed.	21270106	Tomalik-Scharte (2011)
CYP3A4	*18	Malaysian	Healthy	Repaglinide	121	PK (elimination constant, t1/2)	CYP3A4*1/*18 carriers had 44 ($P = 0.04$) and 33.8% ($P = 0.04$) lower elimination rate constant and half-life respectively, than the wild genotype carriers.	20523106	Ruzilawati et al (2009)
IGF2BP2	rs1470579A>C	Chinese	T2D	Repaglinide	42	Response (FPG, PPG)	Compared with homozygous AA, carriers of the minor allele showed significantly less FPG ($P <0.05$) and PPG ($P <0.05$) reduction.	20523342	Huang et al (2010)
IGF2BP2	rs4402960	Chinese	T2D	Repaglinide	42	Response (insulin)	Carriers of the T allele had enhanced insulin concentration than homozygous GG carriers ($P < 0.01$)	20523342	Huang et al (2010)
KCNQ1	rs2237892C>T	Chinese	T2D	Repaglinide	91	Response (PPG)	Carriers of the TT genotype showed lower PPG and higher cumulative attainment of target PPG ($P = 0.038$) than C allele carriers.	21289621	Yu et al (2011)
KCNQ1	rs2237895A>C	Chinese	T2D	Repaglinide	91	Response (fasting insulin, HOMA-IR)	Carriers of the minor allele showed greater increment in both fasting insulin and HOMA-IR.	21289621	Yu et al (2011)
KCNQ1	rs2237892C>T	Chinese	T2D	Repaglinide	40	Response (PPG)	Carriers of the T allele showed greater reduction in PPG than homozygous CC carriers ($P < 0.05$).	22414228	Dai et al (2012)
KCNQ1	rs2237895A>C	Chinese	T2D	Repaglinide	40	Response (PPG)	Carriers of the C allele showed greater reduction in PPG than homozygous AA carriers ($P < 0.05$).	22414228	Dai et al (2012)
NOS1AP	rs10494366G>T	Chinese	T2D	Repaglinide	100	Response (HOMA-IR)	TT carriers had the least insulin resistance on HOMA-IR ($P = 0.013$)	20305679	Qin et al (2010)
NOS1AP	rs12742393A>C	Chinese	T2D	Repaglinide	84	Response (FPG, fasting insulin, HOMA-IR)	Patients with the minor C allele had reduced fasting glucose ($P < 0.01$), insulin ($P < 0.05$) and HOMA-IR ($P < 0.001$) than carriers of AA genotype.	24338736	Wang et al (2014)
PAX4	R121W	Chinese	T2D	Repaglinide	43	Response (FPG, PPG)	Patients homozygous for the reference allele showed better efficacy in terms of PPG than heterozygous RW carriers ($P < 0.05$).	22296034	Gong et al (2012)
PPARD	rs2016520T>C	Chinese	T2D	Repaglinide	84	Response (insulin)	Heterozygous TC carriers showed significantly lower increase in post prandial insulin than the wild type carriers ($P < 0.05$).	25311380	Song et al (2015)
MDR1	G2677T>A	Chinese	T2D	Repaglinide	24	PK (AUC)	Subjects with GT and TT genotype showed significantly greater AUC than GG and TA carriers ($P = 0.007$).	22398664	Xiang et al (2012)
NAMPT	3186C>T	Chinese	T2D	Repaglinide	35	Response (insulin)	Patients heterozygous CT showed significantly lower insulin elevation than homozygous CC or TT patients ($P < 0.05$)	21631570	Sheng et al (2011)

TCF7L2	rs290487C/T	Chinese	T2D	Repaglinide	40	Response (fasting insulin, triglycerides)	Homozygous TT carriers showed better efficacy in terms of fasting insulin and triglyceride levels.	20054294	Yu et al (2010)
UCP2	866G>A	Chinese	T2D	Repaglinide	41	Response (FPG, HbA1c)	Carriers of the A allele showed smaller decrease in FPG (P < 0.05), HbA1c (P < 0.05) and smaller increase in 30 min post load plasma insulin (P < 0.01) compared with GA carriers.	22393835	Wang et al (2012)
CYP2C9	CYP2C9*3	Caucasians	Healthy	Nateglinide	26	PK (CL/F), Response (Glucose, insulin, glucagon)	CYP2C9*3 carriers showed significantly reduced oral clearance than the wild type carriers (P < 0.01) but no difference in glycaemic response was observed.	15005635	Kirchheiner et al (2004)
SLCO1B1	*1B/*1B		Healthy	Nateglinide	24	PK (AUC, Cmax), Response (glucose)	Cmax occurred earlier in *1B/*1B than *1A/*1A carriers but no significant difference in other PK parameters or PD.	18854776	Kalliokoski et al (2008)
SLCO1B1	c.521T>C	Chinese	Healthy	Nateglinide	17	PK (AUC, Cmax, t1/2)	Carriers of the C allele showed significantly higher Cmax (P = 0.002) and AUC (P = 0.001) than homozygous TT carriers. Homozygous CC subjects also showed longer t1/2 than TT subjects (P = 0.036).	16796707	Zhang et al (2006)
CYP2C9 and SLCO1B1 interaction	CYP2C9*3 / c.521 T>C	Chinese	Healthy	Nateglinide	35	PK (AUC), response (glucose)	Participants with *1/*3 & 521TT (56% higher, P < 0.001), *1/*1 & 521TC/CC (34% higher, P = 0.003) and *1/*3 & 521TC (56% higher, P = 0.002) AUC, than reference carriers for both genotypes. They also showed significantly lower clearance than the reference. No significant difference in blood glucose between genotypes were showed.	22842957	Cheng et al (2012)

AUC: area under the curve; CL/F: total clearance; Cmax: maximal plasma concentration; FPG: fasting plasma glucose; HbA1c: glycated haemoglobin; HOMA-BCF: homeostasis model assessment of beta cell function; HOMA-IR: homeostasis model assessment of insulin resistance; PK: pharmacokinetics; PD: pharmacodynamics; PPG: post prandial glucose; T2D: type 2 diabetes; t1/2: elimination half-life.

Supplementary Table 4: Overview of studies focusing on gene-thiazolidinediones interaction in type 2 diabetes.

Gene	**Variant**	**Population**	**Study group**	**Drug**	**N**	**Outcome**	**Major findings**	**PMID**	**Author (publication year)**
ABCA1	R219K	Chinese	T2D	Rosiglitazone	93	Response (treatment failure, HOMA-IR)	R219K variant carriers showed greater treatment failure with per allele odds ratio of 2.04 (P < 0.05) than homozygous carriers of the variant allele. Homozygous RR carriers had significantly greater decrease in HOMA-IR (P < 0.05) than minor allele carriers.	18215356	Wang et al (2008)
ABCA1	M883I	Chinese	T2D	Rosiglitazone	93	Response (treatment failure, HOMA-IR)	No significant difference in response parameters between genotypes.	18215356	Wang et al (2008)
ABCA1	R1587K	Chinese	T2D	Rosiglitazone	93	Response (treatment failure, HOMA-IR)	No significant difference in response parameters between genotypes.	18215356	Wang et al (2008)
ADIPOQ	45T>G (rs2241766)	Japanese	T2D	Rosiglitazone	166	Response (FPG, HbA1c reduction)	GG carriers showed less reduction in both FPG (P = 0.031) and HbA1c (P = 0.013) than other genotype carriers.	15855579	Kang et al (2005)
ADIPOQ	276G>T (rs1501299)	Japanese	T2D	Rosiglitazone	166	Response (FPG, HbA1c reduction)	GG carriers showed less reduction in FPG (P = 0.001) than other genotype carriers but no significant difference in HbA1c.	15855579	Kang et al (2005)

ADRB3	Trp64Arg	Chinese	T2D	Rosiglitazone	36	Response (FPG, PPG, HbA1c, fasting and post prandial insulin)	No significant difference in response parameters between carriers of the minor allele and the wild type carriers.	19659999	Yang et al (2009)
CYP2C8	*3	Caucasians	Healthy	Rosiglitazone	31	PK (total clearance, t1/2), Response (glucose)	Subjects having *1/*1, *1/*3, *3/*3 showed 0.033, 0.038, 0.046 L/h (P = 0.02) total clearance and 4.3, 3.5, 2.9 hours elimination half-lives. No significant difference in blood glucose levels between genotypes were found.	17178266	Kirchheiner et al (2006)
CYP2C8	*3	Caucasians	Healthy	Rosiglitazone	23	PK (AUC)	No significant difference in PK parameters between genotypes.	16856883	Pederson et al (2006)
CYP2C8	*3	Caucasians	Healthy	Rosiglitazone	26	PK (AUC, Cmax, CL/F)	*1/*3 carriers showed significantly lower AUC (P = 0.006), Cmax (p = 0.02) and higher clearance (0.03) than the wild type carriers.	19129086	Aquilante et al (2008)
CYP2C8	*11	Korean	Healthy	Rosiglitazone	14	PK (AUC, Cmax)	Subjects carrying *1/*11 had 54 and 34% higher AUC (P = 0.015) and Cmax (P = 0.025), respectively than *1/*1 genotype.	21245287	Yeo et al (2011)
KCNQ1	rs2237897 C>T	Chinese	T2D	Rosiglitazone	93	Response (FPG, PPG, HbA1c reduction)	Carriers of the minor allele showed significantly greater reduction in PPG (P = 0.032) than the wild type carriers.	21289621	Yu et al (2010)
LEPTIN	G-2548A	Chinese	T2D	Rosiglitazone	42	Response (FPG, PPG, HbA1c reduction, HOMA-IR, fasting and post prandial insulin)	Homozygous AA carriers showed significantly enhanced fasting and postprandial insulin (P < 0.05) than the G allele carriers.	18438653	Liu et al (2008)
LPIN1	rs10192566 C>G	Korean	T2D	Rosiglitazone	262	Response (FPG, PPG, HbA1c reduction)	Carriers of the G allele showed greater reduction in FPG (P = 0.005), PPG (P = 0.005) and HbA1c (0.014) compared to carriers of the wild type.	18693052	Kang et al (2008)
PAX4	rs6467136A>G	Chinese	T2D	Rosiglitazone	105	Response (FPG, 2HG, HbA1c reduction)	GA and AA carriers exhibited greater decrease in 2HG (P = 0.006) and higher target attainment rate of 2HG (P = 0.009) than the wild type carriers.	24752311	Chen et al (2014)
PLIN	11482G>A	Korean	T2D	Rosiglitazone	160	Response (weight gain)	Carriers of AA, GA and GG genotypes had 0.03 ± 1.46, 0.85 ± 1.89 and 1.33 ± 1.59 KG weight gain respectively (P = 0.01).	16732015	Kang et al (2006)
PLIN	6209T>C, 13041A>G, 14995A>T	Korean	T2D	Rosiglitazone	160	Response (weight gain)	No significant difference in weight gain between genotypes.	16732015	Kang et al (2006)
PGC-1α	Thr394Thr	Chinese	T2D	Rosiglitazone	41	Response (glucose, insulin, HbA1c reduction, HOMA-IR)	Patients with the A allele had less enhanced post prandial insulin than homozygous GG carriers (7.02 ±11.8 Vs 15.37 ± 11.39, P = 0.027).	20498286	Zhang et al (2010)
PGC-1α	Gly482Ser	Chinese	T2D	Rosiglitazone	41	Response (glucose, insulin, HbA1c reduction, HOMA-IR)	Carriers of the Ser allele had significantly higher FPG, PPG and HOMA-IR (all P values < 0.05). Patients with the Ser allele also showed less attenuated fasting glucose and insulin levels (P < 0.05).	20498286	Zhang et al (2010)
PPARγ2	Pro12ala	Korean	T2D	Rosiglitazone	198	Response (response, FPG, HbA1c, Glucose, HbA1c)	Carriers of the Ala allele showed significantly greater reduction in FPG (50.6 ±27.8 mg/dL Vs 24.3 ± 41.9 mg/dL, P = 0.26), HbA1c (1.41% ± 1.47% Vs 0.57% ± 1.16%, P = 0.015) than the wild type. They also showed better response rate (86.67% Vs 43.72%, P = 0.002)	16084854	Kang et al (2005)
SLCO1B1	521 T > C	Caucasians	Healthy	Rosiglitazone	26	PK (AUC, Cmax, CL/F)	No significant difference in the PK between genotypes were found.	19129086	Aquilante et al (2008)

SLCO1B1	521 T > C	Caucasians	Healthy	Rosiglitazone	32	PK (AUC)	No significant difference in the PK between genotypes were found.	17635496	Kalliokoski et al (2008)
TNF-α	G-308A	Chinese	T2D	Rosiglitazone	42	Response (FPG, PPG, HbA1c reduction, HOMA-IR, fasting and post prandial insulin)	Carriers of the minor allele showed significantly greater attenuated fasting insulin levels ($P < 0.05$) than the wild type.	18438653	Liu et al (2008)
UCP2	866 G>A	Chinese	T2D	Rosiglitazone	36	Response (FPG, PPG, HbA1c, fasting and post prandial insulin)	Carriers of the variant allele showed smaller attenuated post prandial insulin ($P < 0.01$) and greater attenuated HbA1c ($P < 0.05$) than wild type carriers.	19659999	Yang et al (2009)
ADIPOQ	G-10068A	Chinese	T2D	Pioglitazone	113	Response (HbA1c, FPG)	No significant difference in response between genotypes was showed.	18494805	Li et al (2008)
ADIPOQ	C-11377G	Chinese	T2D	Pioglitazone	113	Response (HbA1c, FPG)	G allele carriers showed significant percentage reduction in HbA1c than CC homozygotes (-0.13 ± 0.13 Vs -0.08 ± 0.11, $P = 0.028$).	18494805	Li et al (2008)
ADIPOQ	45T>G	Iranian	T2D	Pioglitazone	101	Response (15% decrease in HbA1c)	No significant difference in response between genotypes.	22187345	Namvaran et al (2012)
ADIPOR2	795G/A	Iranian	T2D	Pioglitazone	101	Response (15% decrease in HbA1c)	No significant difference in response between genotypes.	22187345	Namvaran et al (2012)
CYP2C8	*3	Caucasians	Healthy	Pioglitazone	30	PK (AUC)	*3 carriers showed 29.7% lower AUC ($P = 0.01$) compared to homozygous *1/*1 carriers.	22625877	Aquilante et al (2012)
CYP2C8	*3	Caucasians	Healthy	Pioglitazone	16	PK (AUC)	*3/*3 and *1/*3 carriers showed 34% and 26% lower weight-adjusted AUC than the wild type ($P < 0.05$).	17913794	Torino et al (2008)
LPL	S447X	Chinese	T2D	Pioglitazone	113	Response (>10% FPG reduction or >1% reduction in HbA1c)	SS carriers had twice more odds of being a responder than carriers of the minor allele ($P < 0.05$).	17394430	Wang et al (2007)
PGC-1	Gly482Ser	Chinese	T2D	Pioglitazone	250	Response (FPG, HbA1c)	No significant difference in response between carriers of the variants were found.	20045142	Hsieh et al (2009)
PPARγ	Pro12Ala	Chinese	T2D	Pioglitazone	250	Response (FPG, HbA1c)	Carriers of the minor allele (Ala) showed 2.316 (1.100-4.874, $P = 0.027$) times higher odds of being a responder than the wild type carriers.	20045142	Hsieh et al (2009)
PPARγ	Pro12Ala	Chinese	T2D	Pioglitazone	67	Response (FPG, PPG, HbA1c)	CG carriers showed higher differential values of FPG than CC carriers (-2.24 ± 0.82 Vs -1.23 ± 1.24, $P < 0.05$).	23147557	Pei et al (2013)
PPARγ	Pro12Ala	Iranian	T2D	Pioglitazone	101	Response (> 15% HbA1c reduction)	No significant association between genotypes and response were found.	21968139	Namvaran et al (2011)
PPARγ	Pro12Ala		Obese post-menopausal women	Pioglitazone	83	(FPG, HOMA-IR, insulin)	Pro/Ala carriers showed significant reduction in FPG than the wild type carriers (-15 mg/dL Vs -7mg/dL, $P < 0.003$). However insulin and HOMA-IR were lower in carriers of the wild type ($P < 0.05$).	18551086	Ramirez-Salazar et al (2008)
PTPRD	rs17584499T>C	Chinese	T2D	Pioglitazone	67	Response (FPG, PPG, HbA1c)	Carriers of the reference allele showed significantly lower differential values of PPG than homozygous CC carriers (-0.63±3.26 Vs -3.18±3.37, $P < 0.01$).	23147557	Pei et al (2013)
RESISTIN	420C>G	Japanese	T2D	Pioglitazone	184	Response (HbA1c (β= -0.511, $P = 0.044$) reduction, FPG ($P = 0.02$), HOMA-IR (0.012))	Homozygous GG carriers showed significant reduction in HbA1c, FPG and HOMA-IR than the wild type carriers.	19738363	Makino et al (2009)

SLCO1B1	521 T > C	Caucasians	Healthy	Pioglitazone	32	PK (AUC)	No significant difference in the PK of pioglitazone between genotypes were found.	17635496	Kalliokoski et al (2008)
IGF2BP2	rs4402960G>T	Chinese	T2D	Pioglitazone	86	Response (PPG, HbA1c)	Carriers of the variant allele showed significantly lower reduction in PPG (-0.70 ± 3.92 mmol/l - -2.80 ± 3.81 mmol/l, P < 0.05) than homozygous GG carriers.	25247335	Zhang et al (2014)
IGF2BP2	rs1470579A>C	Chinese	T2D	Pioglitazone	86	Response (PPG, HbA1c)	Carriers of the variant allele showed significantly lower reduction in PPG (-1.07 ± 4.04 mmol/L Vs -2.65 ± 3.85 mmol/L, P < 0.05) than homozygous AA carriers.	25247335	Zhang et al (2014)

AUC: area under the curve; CL/F: total clearance; Cmax: maximal plasma concentration; FPG: fasting plasma glucose; HbA1c: glycated haemoglobin; HOMA-IR: homeostasis model assessment of insulin resistance; PK: pharmacokinetics; PPG: post prandial glucose; T2D: type 2 diabetes; t1/2: elimination half-life.

Supplementary Table 5: Overview of studies focusing on interaction between genes and drugs acting in the incretin pathway in type 2 diabetes.

Gene	**Variant**	**Population**	**Study group**	**Drug**	**N**	**Outcome**	**Major findings**	**PMID**	**Author (publication year)**
GLP1R	rs3765467 C > T	Chinese	T2D	Exenatide	36	Response (Glucose)	No significant association between the variant and response were found.	25785276	Lin et al (2015)
GLP1R	rs3765467C>T	Caucasians	Healthy	Exogenous GLP-1	88	Response (insulin)	Carriers of the minor allele showed greater β cell responsiveness than the wild type carriers (P < 0.05).	20805279	Sathananthan et al (2010)
GLP1R	rs761386 C>T	Chinese	T2D	Exenatide	36	Response (Glucose)	No significant association between the variant and response were found.	25785276	Lin et al (2015)
GLP1R	rs6923761G>A	Caucasians	Healthy	Exogenous GLP-1	88	Response (insulin)	Carriers of one or more copies of the minor allele showed lower β cell responsiveness than the wild type carriers (P < 0.05).	20805279	Sathananthan et al (2010)
TCF7L2	rs7903146C>T, rs12255372G>T	Caucasians	Healthy	Exogenous GLP-1	73	Response (insulin)	Carriers of the risk alleles showed significantly greater reduction in GLP-1 induced insulin secretion (P < 0.02) compared to wild type carriers.	17661009	Schafer et al (2007)
WFS1	rs10010131 G>C	Caucasians	Healthy	Exogenous GLP-1	102	Response (insulin)	Compared with the wild type, carriers of the risk allele showed 36 and 26% lower GLP-1 induced first (P = 0.007) and second (P = 0.04) phase insulin secretion respectively.	19330314	Schafer et al (2009)
TMEM114	rs7202633 A>T	Caucasians	healthy	Exogenous GLP-1	232	Response (insulin)	Homozygous carriers of the risk allele had nearly two fold increased GLP-1 induced insulin secretion than the wild type ($P = 2.0 \times 10^{-7}$).	23674605	't Hart et al (2013)
CHST3	rs4148941 A>C	Caucasians	healthy	Exogenous GLP-1	232	Response (insulin)	Carriers of the C allele had 32% ($P = 3.9 \times 10^{-8}$) lower GLP1 induced insulin secretion than the wild type carriers.	23674605	't Hart et al (2013)
CTRB1/2	rs7202877 T>G	Caucasians	Healthy	Exogenous GLP-1	232	Response (insulin)	Carriers of the G allele had 33% ($P = 1.9 \times 10^{-6}$) greater GLP1 induced insulin secretion than the wild type carriers.	23674605	't Hart et al (2013)
CTRB1/2	rs7202877 T>G	Caucasians	T2D	DPP4I	354	Response (HbA1c reduction)	G-allele carriers showed 0.51 ± 0.16% (P = 0.0015) smaller HbA1c reduction than the wild type carriers.	23674605	't Hart et al (2013)
KCNQ1	rs151290C>A, rs2237892C>T,	Caucasians	High risk	Exogenous GLP-1	102	Response (insulin)	No significant association between either of the variants and GLP-1 induced insulin secretion were found.	19366866	Mussig et al (2009)

	rs2237895A>C, rs2237897C>T								
THADA	rs7578597C>T	Caucasians	Healthy	Exogenous GLP-1	123	Response (insulin)	Homozygous carriers of the risk allele showed significantly reduced GLP-1 induced insulin secretion than CC and CT genotype carriers ($P = 1.6 \times 10^{-3}$).	19833888	Simonis-Bik et al (2010)
MTNR1B	rs10830963C>G	Caucasians	Healthy	Exogenous GLP-1	123	Response (insulin)	Carriers of the risk allele showed 30% more GLP1 stimulated insulin secretion ($P = 0.037$) compared with the wild allele carriers.	19833888	Simonis-Bik et al (2010)

DPP4I: dipeptidyl peptidase 4 inhibitor; GLP-1: glucagon like peptide-1; T2D: type 2 diabetes; HbA1c: glycated haemoglobin.