

Supplemental Table S1 Association of 39 SNPs related to beta-cell dysfunction with GDM

SNP	Chr	Position	Nearest gene	MAF	risk allele	Model 1 (non-adjustment)		Model 2 (adjustment)	
						OR	P	OR	P
rs340874	1	214159256	PROX1	0.398	C	0.94 (0.71-1.24)	0.669	0.96 (0.68-1.34)	0.800
rs6780171	3	185503456	IGF2BP2	0.266	A	0.97 (0.72-1.31)	0.840	1.14 (0.78-1.66)	0.500
rs4481184	3	185505787	IGF2BP2	0.268	T	0.95 (0.70-1.28)	0.722	1.09 (0.75-1.59)	0.648
rs11717959	3	185541213	IGF2BP2	0.201	G	1.01 (0.73-1.42)	0.931	0.88 (0.58-1.33)	0.536
rs1801212	4	6302519	WFS1	0.011	A	1.02 (0.29-3.58)	0.972	0.57 (0.12-2.70)	0.481
rs4457053	5	76424949	ZBED3	0.055	G	0.90(0.51-1.58)	0.714	0.98 (0.49-2.00)	0.966
rs9379084	6	7231843	RREB1	0.126	G	2.41 (1.57-3.70)	1×10 ⁻⁴	1.99 (1.19-3.33)	0.009
rs9505097	6	7255650	RREB1	0.059	C	1.54 (0.87-2.72)	0.135	2.11 (1.02-4.33)	0.043
rs7756992	6	20679709	CDKAL1	0.476	G	1.42 (1.08-1.85)	0.011	1.40 (1.01-1.95)	0.046
rs10228066	7	15063569	DGKB	0.365	T	0.89 (0.68-1.17)	0.392	0.86 (0.61-1.20)	0.364
rs1708302	7	28198677	JAZF1	0.016	C	1.56 (0.54-4.44)	0.409	1.68 (0.53-5.34)	0.379
rs878521	7	44255643	GCK	0.419	A	1.23 (0.94-1.60)	0.126	1.30 (0.95-1.79)	0.106
rs791595	7	127862802	LEP	0.097	A	0.98 (0.64-1.50)	0.917	1.03 (0.62-1.70)	0.911
rs13262861	8	41508577	ANK1	0.131	C	0.89 (0.60-1.32)	0.565	1.17 (0.72-1.89)	0.523
rs4736819	8	41509915	ANK1	0.395	T	0.99 (0.76-1.29)	0.950	0.99 (0.72-1.36)	0.955
rs3802177	8	118185025	SLC30A8	0.407	G	1.08 (0.83-1.40)	0.589	1.19 (0.87-1.63)	0.286
rs10974438	9	4291928	GLIS3	0.357	C	1.07 (0.82-1.41)	0.609	1.08 (0.77-1.49)	0.665
rs10811660	9	22134068	CDKN2A/B	0.486	G	1.06 (0.82-1.37)	0.656	1.05 (0.76-1.44)	0.771
rs10757283	9	22134172	CDKN2A/B	0.355	T	0.90 (0.69-1.18)	0.432	0.91 (0.66-1.27)	0.584
rs505922	9	136149229	ABO	0.469	C	1.00 (0.76-1.32)	0.983	0.94 (0.67-1.31)	0.705
rs12378717	9	139286060	GPSM1	0.029	G	1.21 (0.54-2.67)	0.645	1.40 (0.53-3.66)	0.497
rs11257655	10	12307894	CDC123/CAMK1D	0.435	T	0.76 (0.59-0.98)	0.032	0.81 (0.59-1.10)	0.180

rs10882101	10	94462427	HHEX/IDE	0.286	T	1.11 (0.83-1.48)	0.497	0.98 (0.68-1.40)	0.893
rs1112718	10	94479107	HHEX/IDE	0.177	A	1.21 (0.87-1.70)	0.261	1.22 (0.82-1.83)	0.332
rs7903146	10	114758349	TCF7L2	0.048	T	0.98 (0.52-1.82)	0.939	1.22 (0.56-2.64)	0.612
rs34855922	10	114871594	TCF7L2	0.012	A	0.85 (0.26-2.82)	0.789	0.52 (0.09-2.94)	0.463
rs234853	11	2850828	KCNQ1	0.353	G	0.80 (0.61-1.06)	0.118	0.83 (0.59-1.16)	0.274
rs2237895	11	2857194	KCNQ1	0.352	C	1.27 (0.96-1.66)	0.091	1.15 (0.82-1.61)	0.414
rs2237897	11	2858546	KCNQ1	0.311	C	1.28 (0.97-1.70)	0.085	1.40 (0.98-1.99)	0.062
rs445084	11	2908754	KCNQ1	0.114	G	1.02 (0.68-1.53)	0.930	0.89 (0.54-1.46)	0.636
rs102275	11	61557803	TMEM258	0.302	T	1.02 (0.77-1.36)	0.882	0.99 (0.70-1.40)	0.964
rs77464186	11	72460398	CENTD2/ARAP1	0.087	A	0.83 (0.52-1.35)	0.455	0.69 (0.37-1.27)	0.234
rs10830963	11	92708710	MTNR1B	0.452	G	1.44 (1.12-1.86)	0.005	1.72 (1.26-2.34)	0.001
rs57235767	11	93013531	MTNR1B	0.218	C	1.08 (0.79-1.48)	0.621	1.30 (0.88-1.91)	0.185
rs10842994	12	27965150	KLHDC5	0.167	C	0.94 (0.66-1.32)	0.703	0.88 (0.57-1.34)	0.545
rs1359790	13	80717156	SPRY2	0.274	G	1.12 (0.83-1.50)	0.462	1.05 (0.72-1.52)	0.812
rs8038040	15	62394264	C2CD4A/B	0.392	G	1.17 (0.89-1.52)	0.255	0.95 (0.68-1.33)	0.775
rs1005752	15	77818128	HMG20A	0.354	A	0.89 (0.68-1.18)	0.422	0.92 (0.66-1.28)	0.617
rs12910825	15	91511260	PRC1	0.018	G	1.74 (0.62-4.86)	0.293	1.73 (0.50-6.02)	0.391

Model 2 was adjusted for factors age, gestational weeks, baseline BMI, family history of diabetes, drinking history, smoking history, education attainment, ethnicity group, weight gain during pregnancy, ALT, SBP, DBP and parity.

Supplemental Table S2 Association of 23 SNPs related to insulin resistance with GDM

SNP	Chr	Position	Nearest gene	MAF	risk allele	Model 1 (non-adjustment)		Model 2 (adjustment)	
						OR	P	OR	P
rs3768321	1	40035928	MACF1	0.121	T	1.02 (0.68-1.53)	0.934	1.30 (0.78-2.16)	0.319
rs1260326	2	27730940	GCKR	0.459	C	1.24 (0.95-1.62)	0.114	1.26 (0.92-1.74)	0.154
rs2249105	2	65287896	CEP68	0.354	A	1.25 (0.95-1.64)	0.107	1.28 (0.92-1.78)	0.142
rs2052261	2	65355270	CEP68	0.359	G	0.87 (0.67-1.14)	0.319	0.88 (0.63-1.21)	0.428
rs10195252	2	165513091	GRB14/COBLL1	0.119	T	0.98 (0.65-1.48)	0.933	1.00 (0.60-1.66)	0.992
rs2972144	2	227101411	IRS1	0.081	G	1.46 (0.90-2.37)	0.122	1.21 (0.66-2.23)	0.531
rs11709077	3	12336507	PPARG	0.041	G	1.87 (0.95-3.66)	0.070	1.77 (0.82-3.79)	0.143
rs11926707	3	46925539	KIF9	0.318	C	0.96 (0.73-1.27)	0.784	0.77 (0.54-1.10)	0.158
rs9860730	3	64701146	ADAMTS9	0.257	A	1.17 (0.87-1.59)	0.303	1.23 (0.86-1.77)	0.260
rs28819812	4	157652753	PDGFC	0.318	C	0.96 (0.72-1.28)	0.779	1.01 (0.71-1.43)	0.962
rs702634	5	53271420	ARL15	0.123	A	1.11 (0.75-1.62)	0.609	1.15 (0.73-1.82)	0.553
rs465002	5	55808475	ANKRD55	0.446	T	1.21 (0.94-1.57)	0.141	1.47 (1.07-2.01)	0.017
rs9687832	5	55861595	ANKRD55	0.107	A	1.15 (0.75-1.75)	0.523	1.01 (0.62-1.67)	0.957
rs2280141	10	124193181	PLEKHA1	0.373	T	0.94 (0.73-1.22)	0.655	1.09 (0.80-1.49)	0.574
rs4148856	12	123450765	MPHOSPH9	0.153	C	1.04 (0.73-1.50)	0.815	1.11 (0.72-1.69)	0.638
rs2738809	16	75516534	BCAR1	0.467	G	0.85 (0.66-1.09)	0.203	0.72 (0.52-0.99)	0.042
rs2925979	16	81534790	CMIP	0.373	T	1.11 (0.85-1.44)	0.450	1.28 (0.93-1.76)	0.134
rs12454712	18	60845884	BCL2A	0.474	T	1.05 (0.81-1.37)	0.702	1.04 (0.75-1.44)	0.821
rs8107974	19	19388500	TM6SF2	0.075	T	0.92 (0.56-1.50)	0.731	1.40 (0.75-2.61)	0.293
rs889138	19	33890838	PEPD	0.467	C	1.05 (0.81-1.36)	0.711	0.96 (0.70-1.33)	0.820
rs10406431	19	46157019	GIPR	0.295	A	0.89 (0.67-1.18)	0.421	0.89 (0.63-1.26)	0.500
rs2238689	19	46178661	GIPR	0.302	C	1.04 (0.79-1.39)	0.771	1.13 (0.80-1.59)	0.491

rs112915006	22	50604696	PIM3	0.152	G	1.15 (0.81-1.64)	0.443	1.43 (0.92-2.23)	0.112
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Model 2 was adjusted for factors: age, gestational weeks, baseline BMI, family history of diabetes, drinking history, smoking history, education attainment, ethnicity group, weight gain during pregnancy, ALT, SBP, DBP and parity.

Supplemental Table S3 Distribution of other bile acid species measured in the cohort

	Bile acid (nmol/mL)			Missing
	Non-GDM group	GDM group	Total	
THDCA	0.009 (0.008,0.010)	NA	0.009 (0.008,0.010)	351 (78.5%)
TUDCA	0.009 (0.006,0.013)	NA	0.009 (0.006,0.013)	337 (75.4%)
LCA	0.049 (0.039,0.062)	NA	0.050 (0.040,0.060)	311 (69.6%)
GLCA	0.011 (0.007,0.023)	NA	0.010 (0.010,0.020)	278 (62.2%)
TLCA	0.002 (0.001,0.005)	0.003 (0.002,0.004)	0.002 (0.001,0.005)	270 (60.4%)
DHCA	0.350 (0.250,0.480)	0.170 (0.140,0.220)	0.250 (0.160,0.400)	142 (31.8%)
UDCA	0.024 (0.014,0.037)	0.025 (0.019,0.038)	0.024 (0.016,0.038)	104 (23.3%)

Non-GDM group were matched on age ± 1 year of the GDM group. Values are described as median (Q1, Q3) or n, n (%).

Abbreviations: THDCA, taurohyodeoxycholic acid; TUDCA, tauroursodeoxycholic acid; LCA, lithocholic acid; GLCA, glycolithocholic acid; TLCA, tauroolithocholic acid; DHCA, dehydrocholic acid; UDCA, ursodeoxycholic acid.

Supplemental Table S4 Associations of GRS and bile acids in Chinese women

	BC-GRS (#SNP=39)				IR-GRS (#SNP=23)			
	Model 1 (non-adjustment)		Model 2 (adjustment)		Model 1 (non-adjustment)		Model 2 (adjustment)	
	Beta (SE)	p-value	Beta (SE)	p-value	Beta (SE)	p-value	Beta (SE)	p-value
TDCA	-0.130(0.044)	0.003	-0.177(0.048)	2.66×10⁻⁴	0.001(0.044)	0.984	0.036(0.050)	0.465
GDCA	-0.110(0.048)	0.024	-0.141(0.053)	0.009	-0.043(0.049)	0.376	0.008(0.055)	0.890
TCDCA	-0.100(0.041)	0.014	-0.108(0.046)	0.020	0.035(0.041)	0.390	0.078(0.048)	0.103
GCA	-0.104(0.044)	0.019	-0.113(0.052)	0.029	0.042(0.045)	0.349	0.082(0.053)	0.122
TCA	-0.073(0.029)	0.014	-0.072(0.035)	0.039	0.054(0.030)	0.070	0.072(0.036)	0.044
GCDCA	-0.106(0.045)	0.018	-0.099(0.051)	0.051	0.032(0.045)	0.481	0.045(0.052)	0.388
DCA	-0.045(0.037)	0.229	-0.081(0.043)	0.060	-0.060(0.037)	0.104	-0.040(0.044)	0.363
CA	-0.017(0.027)	0.522	-0.042(0.033)	0.211	-0.046(0.027)	0.089	-0.060(0.034)	0.076
CDCA	-0.033(0.045)	0.460	-0.056(0.052)	0.289	-0.021(0.045)	0.648	-0.045(0.053)	0.404
HDCA	-0.015(0.034)	0.654	-0.037(0.040)	0.350	-0.020(0.033)	0.546	-0.022(0.039)	0.577
GUDCA	-0.034(0.049)	0.489	-0.019(0.058)	0.751	0.004(0.049)	0.930	-0.005(0.058)	0.935

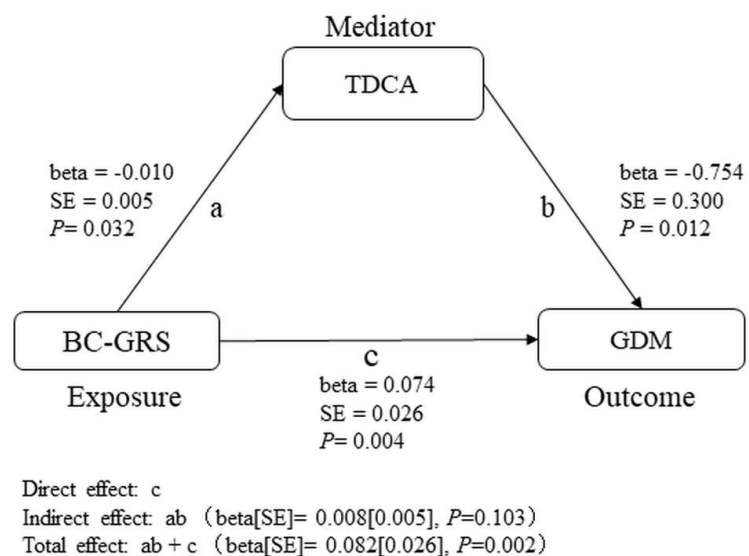
Abbreviations: BC, beta cell; IR, insulin resistance; TDCA, taurodeoxycholic acid; GDCA, glycodeoxycholic acid; TCDCA, taurochenodeoxycholic acid; GCA, glycocholic acid; TCA, taurocholic acid; GCDCA, glycochenodeoxycholic acid; DCA, deoxycholic acid; CA, cholic acid; CDCA, chenodeoxycholic acid; HDCA, hyodeoxycholic acid; GUDCA, glyoursodeoxycholic acid.

Model 2 was adjusted for conventional risk factors including age, gestational weeks, baseline BMI, family history of diabetes, drinking history, smoking history, education attainment, ethnicity group, weight gain during pregnancy, ALT, SBP, DBP and parity.

Supplemental Table S5 Interaction between IR-GRS and TCDCA

Concentration	OR (95% CI)			<i>P</i> for trend
	Tertile 1	Tertile 2	Tertile 3	
High (> 0.2 nmol/L)	1	4.51 (0.41,49.26)	6.92 (0.68,70.77)	0.025
Low (\leq 0.2 nmol/L)	10.95 (1.21,99.51)	11.70 (1.29,106.44)	14.39 (1.59,130.16)	0.366

ORs were adjusted for conventional risk factors including age, gestational weeks, baseline BMI, family history of diabetes, drinking history, smoking history, education attainment, ethnicity group, weight gain during pregnancy, ALT, SBP, DBP and parity. Abbreviations: IR, insulin resistance. TCDCA, taurochenodeoxycholic acid.



Supplemental Figure 1 Mediation analysis of the role of TDCA in mediating the relationship between BC-GRS and GDM.

a, the association between BC-GRS and TDCA; b, the association between TDCA and GDM; c, the direct association between BC-GRS and GDM after adjustment for TDCA; ab, the indirect effect (or mediation effect) of BC-GRS on GDM through TDCA; ab + c, the total effect of BC-GRS on GDM. All associations were adjusted for age, gestational weeks, baseline BMI, family history of diabetes, drinking history, smoking history, education attainment, ethnicity group, weight gain during pregnancy, ALT, SBP, DBP, and parity.