Supplementary Material

Genetic Variants Related to Cardiometabolic Traits Are Associated to B Cell Function, Insulin Resistance, and Diabetes among American Indians: The Strong Heart Family Study

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1   **Supplementary Tables**

1.1   **Supplementary Table 1. SNP Associations for HOMA-B, log HOMA-IR, and incident diabetes.**

rsID	Chr	Position	Alleles	MAF	Gene	Locus	Location	Log HOMA-B		Log HOMA-IR		Diabetes	
								Beta	P-value	Beta	P-value	Beta	P-value
rs2961831	5	50490690	A/C	0.40	*PARP8, LOC642366*	5q11	intergenic	0.08	0.05	0.04	0.13	-0.03	0.34
rs2962246	5	50485571	A/G	0.40	*PARP8, LOC642366*	5q11	intergenic	0.08	0.05	0.04	0.13	-0.03	0.34
rs10152552	15	23482358	A/G	0.47	*ATP10A*	15q11	intron	0.08	0.03	0.02	0.46	-0.01	0.71
rs883496	15	23481396	G/A	0.47	*ATP10A*	15q11	intron	-0.08	0.03	-0.02	0.46	0.01	0.71
rs12642615	4	36914666	G/A	0.38	*FLJ16686, KIAA1239*	4p14	intergenic	0.08	0.05	-0.01	0.95	-0.01	0.70
rs10777559	12	76822590	C/A	0.25	*NAV3*	12q21	intron	-0.09	0.04	-0.02	0.46	0.001	0.98
rs4237723	11	12594808	A/G	0.45	*PARVA, TEAD1*	11p1	intergenic	0.03	0.36	-0.02	0.4	-0.01	0.74
rs38179	7	15865240	A/G	0.45	*MEOX2, LOC729920*	7p22-p21	intergenic	0.08	0.03	0.01	0.76	0.01	0.65
rs654993	6	160488886	G/A	0.23	*SLC22A1*	6q25	intron	0.07	0.11	-0.01	0.72	-0.002	0.96
rs1252068	1	175868691	A/G	0.35	*LOC400796, SEC16B*	1q25	intergenic	0.02	0.53	0.05	0.07	-0.007	0.84
rs3732678	3	12836608	A/C	0.25	*CAND2*	3p25	coding	0.15	6.03×10^{-4}	0.08	0.01	0.002	0.97
rs16872183	8	106094163	A/G	0.26	*LRP12, ZFPM2*	8q22-q23	intergenic	-0.10	0.03	-0.05	0.14	0.02	0.55
rs10744770	12	110146961	G/A	0.21	*CUX2*	12q24	intron	-0.12	0.02	-0.03	0.39	0.02	0.62

rs4766451	12	110155065	C/A	0.22	*CUX2*	12q24	intron	-0.11	0.02	-0.02	0.51	0.02	0.54
rs6748843	2	64383898	A/G	0.47	*PELI1, LOC130773*	2p13	intergenic	0.00	0.96	0.01	0.74	0.02	0.60
rs284201	1	92012826	G/A	0.27	*TGFBR3*	1p33-p32	intron	0.03	0.44	0.02	0.55	-0.003	0.93
rs7588499	2	54581780	A/G	0.49	*SPTBN1*	2p21	intron	0.00	0.92	-0.03	0.33	0.01	0.68
rs4149270	9	106686898	G/A	0.23	*ABCA1*	9q31	intron	-0.03	0.50	-0.01	0.64	-0.001	0.98
rs997067	10	55709300	A/C	0.37	*PCDH15*	10q21	intron	-0.03	0.43	-0.05	0.09	-0.01	0.71
rs2826602	21	21198206	G/A	0.34	*PRSS7, NCAM2*	21q21	intergenic	-0.03	0.45	-0.01	0.99	0.004	0.89
rs4607517	7	44202193	G/A	0.26	*GCK, YKT6*	7p15	intergenic	-0.11	0.01	-0.05	0.12	0.003	0.94
rs131409	22	22221107	A/G	0.27	*LOC388882, IGLL1*	22q11	intergenic	0.03	0.46	-0.04	0.23	-0.005	0.86
rs1972239	1	155775425	A/G	0.18	*FCRL5*	1q21	intron	0.17	5.30×10^{-4}	0.06	0.09	0.0001	0.99
rs4139	4	163610383	A/G	0.35	*FSTL5, LOC729971*	4q32	intergenic	0.01	0.82	-0.04	0.12	-0.02	0.61
rs9528062	13	59628504	G/A	0.28	*DIAPH3*	13q21	intron	0.01	0.84	0.07	0.01	0.009	0.75
rs312726	17	65799923	T/G	0.34	*KCNJ2, LOC100133226*	17q24	intergenic	0.01	0.78	0.02	0.38	-0.002	0.89
rs420572	17	65808955	T/C	0.34	*KCNJ2, LOC100133226*	17q24	intergenic	0.01	0.76	0.03	0.34	-0.01	0.73
rs312701	17	65809179	G/C	0.34	*KCNJ2, LOC100133226*	17q24	intergenic	0.04	0.32	0.03	0.30	-0.01	0.73
rs10738708	9	25231316	A/C	0.43	*LOC100129669, TUSC1*	9p21	intergenic	0.04	0.32	0.06	0.04	-0.005	0.89
rs7386942	8	1890157	G/A	0.48	*ARHGEF10*	8p23	intron	-0.04	0.30	-0.02	0.46	-0.0004	0.99
rs4448128	6	116137499	C/G	0.25	*LOC441167, FRK*	6q21-q22	intergenic	-0.06	0.14	-0.02	0.43	0.008	0.81

Gene base position based on NCBI36/hg18 build. P-values of significant SNPs are italicized ($P < 4.13 \times 10^{-7}$). Abbreviations: Chr, chromosome; MAF, minor allele frequency.
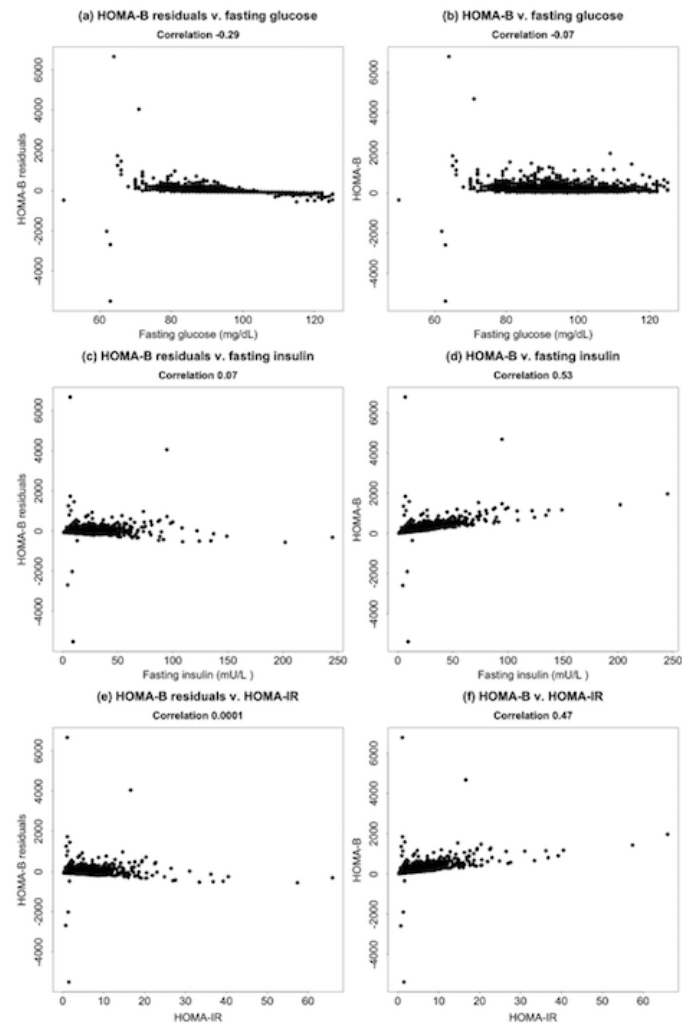
1.2 Supplementary Table 2. Candidate Diabetes Genes.

Gene	Description	Chr	Position	No. MetaboChip SNPs
PPARG	peroxisome proliferator-activated receptor gamma	3	12,368,001-12,450,855	153
IGF2BP2	insulin-like growth factor 2 mRNA binding	3	186,844,221-187,025,521	212
CDKN2A	cyclin-dependent kinase inhibitor 2A	9	21,957,751-21,965,038	26
CDKN2B	cyclin-dependent kinase inhibitor 2B	9	21,992,902-21,999,312	53
TCF7L2	transcription factor 7-like 2	10	114,699,999-114,916,060	133
KCNQ1	potassium voltage-gated channel, KQT-like	11	2,422,797-2,826,916	836

| HNF1A | transcription factor 1, hepatic | 12 | 119,900,932-119,924,697 | 33 |

List of SNPs localized to candidate diabetes genes by MetaboChip gene annotation that pass quality control. Gene base position based on NCBI36/hg18 build.
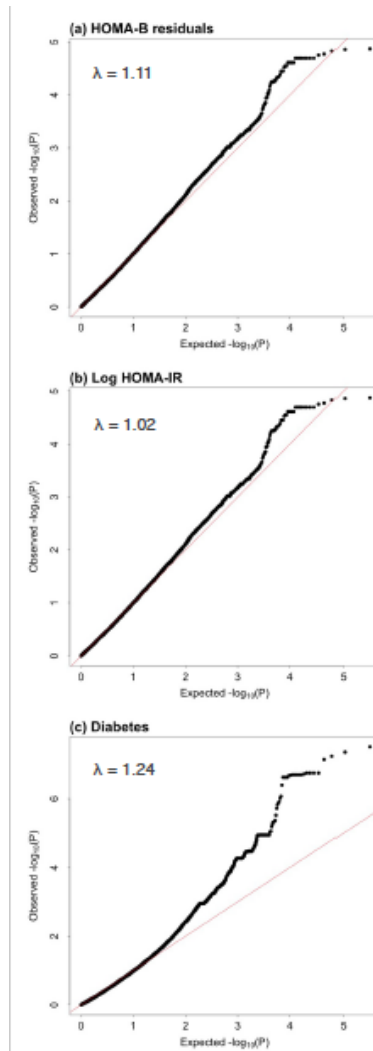
2   Supplementary Figures

2.1   Supplementary Figure 1. Correlation Plots for HOMA-B and corrected HOMA-B.

Pearson correlation calculated with fasting glucose, fasting insulin, and HOMA-IR for HOMA-B [(a), (c), (e)] and cHOMA-B [(b), (d), (f)], respectively.

2.2   Supplementary Figure 2. Quantile-Quantile Plots for HOMA-B Residuals, Log HOMA-IR, and Diabetes.

Deviation from expected p-values adjusted for genomic inflation using MetaboChip for (a) HOMA-B residuals, (b) Log HOMA-IR, and (c) Diabetes. The genomic inflation factor (λ) for cHOMA-B, HOMA-IR, and diabetes were estimated to be 1.11, 1.02, and 1.24, respectively