Assessing the Role of 98 Established Loci for Body Mass Index in American Indians

Yunhua L. Muller, Robert L. Hanson, Paolo Piaggi, Peng Chen, Gregory Wiessner, Chidinma Okani, Graham Skelton, Sayuko Kobes, Wen-Chi Hsueh, William C. Knowler, Clifton Bogardus and Leslie J. Baier

Corresponding author:

Yunhua Muller   Ph.D.

Diabetes Molecular Genetics Section

NIDDK, NIH

445 North 5th street

Phoenix, AZ 85004, USA

Tel: (602) 440-6576   Fax: (602) 253-4140

Email: ymuller@mail.nih.gov

Table S1: The 40 lead SNPs and their respective proxies which were used for genotyping in Pima Indian.

Locus	Lead SNP		Proxy SNP		r^2
	Rs#	Allele R/N	Rs#	Allele R/N	Pima Indian
CALCR	rs9641123	C/G	rs5014937	C/A	1
ADPGK	rs7164727	T/C	rs8030477	T/C	0.98
SMG6	rs9914578	G/C	rs4061660	A/G	1
NRXN3	rs10150332	C/T	rs72690737	C/T	1
EPB41L4B	rs6477694	C/T	rs10759329	A/G	0.93
FIGN	rs1460676	C/T	rs16848820	G/C	0.97
LOC284260	rs7239883	G/A	rs183552	C/T	0.93
RASA2	rs16851483	T/G	rs77586571	T/C	0.99
ASB4	rs6465468	T/G	rs763464	C/T	0.98
MIR548X2	rs9540493	A/G	rs1333010	G/A	0.98
FOXO3	rs9400239	C/T	rs9374040	A/G	0.93
ELAVL4	rs11583200	C/T	rs12724893	G/A	0.97
MTIF3	rs4771122	G/A	rs4771127	A/C	0.97
TLR4	rs1928295	T/C	rs7038943	T/C	0.99
AGBL4	rs657452	A/G	rs666486	T/C	0.97
UBE2E3	rs1528435	T/C	rs1406257	G/A	0.91
EHBP1	rs11688816	G/A	rs2710638	G/A	0.97
PGPEP1	rs17724992	A/G	rs12459368	A/G	0.98
CLIP1	rs11057405	G/A	rs116896792	T/C	0.86
LINGO2	rs10968576	G/A	rs17770336	T/C	1
USP37	rs492400	C/T	rs642520	G/A	0.99
SCARB2	rs17001654	G/C	rs72655539	A/G	0.89
STXBP6	rs10132280	C/A	rs11624623	A/G	0.97
GBE1	rs3849570	A/C	rs11711331	A/G	1
KAT8	rs9925964	A/G	rs6565217	A/G	0.97
FHIT	rs2365389	C/T	rs4688379	G/A	0.91
TFAP2B	rs987237	G/A	rs4715207	T/C	1
ETS2	rs2836754	C/T	rs8128163	G/A	0.90
HNF4G	rs4735692	A/G	rs2596125	C/T	0.97
LOC285762	rs9374842	T/C	rs1329530	T/C	1
CBLN1	rs2080454	C/A	rs13332755	T/G	0.94
ETV5	rs9816226	T/A	rs73052033	C/T	1
MIR548A2	rs1441264	A/G	rs9544948	A/G	0.99
SEC16B	rs543874	G/A	rs589500	T/C	1
RALYL	rs2033732	C/T	rs6473525	G/A	0.95
INO80E	rs4787491	G/A	rs3814881	A/G	0.99

ZZZ3	rs17381664	C/T	rs12728967	C/T	0.97
NT5C2	rs11191560	C/T	rs77180047	A/G	1
DMXL2	rs3736485	A/G	rs12101730	C/T	1
HSD17B12	rs2176598	T/C	rs3736505	G/A	0.99

The risk allele is defined as the allele with higher risk for BMI in Europeans. r^2 was determined from whole genome sequence data of 266 full-heritage Pima Indians.

Table S2. Analysis of 98 established BMI SNPs with maximum BMI in adulthood, maximum BMI recorded from a non-diabetic exam and maximum BMI z-score in childhood in longitudinally studied full-heritage Pima Indians

Lead SNP	Locus (in/nearest)	Allele R/N	Full-heritage Pima Indians								Reported Meta-Analysis GIANT BMI Adulthood (n=339224)			Heterogeneity	
			Max-BMI Adulthood (n=3491)				Max-BMI (nondiabetic) Adulthood (n=2862)		Max-Z-score Childhood (n=1958)						
			RAF	Beta (SD)	Beta (Log$_e$)	P	Beta (Log$_e$)	P	Beta (SD)	P	RAF	Beta (SD)	P	I^2(%)	P_{het}
rs2867125	TMEM18	C/T	0.86	0.13	0.030	**3.0x10^{-4}**	0.035	**6.0x10^{-5}**	0.131	**0.005**	0.87	0.06	4.4 x10^{-52}	75.2	**0.045**
rs7903146	TCF7L2	C/T	0.92	0.16	0.039	**4.9x10^{-4}**	0.051	**2.0x10^{-5}**	0.088	0.18	0.75	0.02	1.1x10^{-12}	88.2	**0.004**
rs13041126	MRPS33P4	T/C	0.67	0.08	0.018	**0.004**	0.019	**0.006**	0.051	0.16	0.73	0.02	6.5x10^{-7}	78.6	**0.031**
rs12885454	PRKD1	C/A	0.78	0.09	0.020	**0.005**	0.016	**0.04**	0.066	0.11	0.63	0.02	9.1x10^{-11}	78.2	**0.032**
rs6091540	ZFP64	C/T	0.67	0.07	0.016	**0.01**	0.017	**0.01**	0.033	0.36	0.73	0.02	2.1x10^{-8}	70.3	0.066
rs7193144	FTO	C/T	0.14	0.10	0.022	**0.01**	0.029	**0.002**	0.14	**0.003**	0.44	0.08	6.2x10^{-142}	0.0	0.686
rs977747	TAL1	T/G	0.74	0.08	0.017	**0.02**	0.021	**0.004**	0.061	0.13	0.47	0.02	2.2x10^{-8}	75.2	**0.044**
rs9641123*	CALCR	C/G	0.09	0.11	0.023	**0.02**	0.021	**0.05**	0.059	0.32	0.39	0.01	1.8x10^{-7}	79.2	**0.028**
rs10938397	GNPDA2	G/A	0.31	0.06	0.014	**0.02**	0.014	**0.05**	0.096	**0.009**	0.43	0.03	1.4x10^{-40}	27.6	0.240
rs17203016	CREB1	G/A	0.15	0.08	0.017	**0.03**	0.016	0.06	0.073	0.12	0.20	0.02	3.4x10^{-8}	59.2	0.117
rs10733682	LMX1B	A/G	0.75	0.06	0.014	**0.04**	0.017	**0.02**	0.056	0.15	0.43	0.02	2.5x10^{-10}	41.1	0.192
rs2531995	ADCY9	T/C	0.18	0.07	0.016	**0.04**	0.010	0.21	0.082	0.06	0.59	0.02	7.6x10^{-10}	53.5	0.142
rs758747	NLRC3	T/C	0.11	0.07	0.018	**0.05**	0.014	0.14	0.074	0.15	0.27	0.02	1.5x10^{-10}	37.7	0.205
rs7164727*	ADPGK	T/C	0.40	0.05	0.011	0.06	0.016	0.01	0.039	0.25	0.78	0.01	3.9x10^{-9}	43.8	0.182
rs9914578*	SMG6	G/C	0.16	0.07	0.014	0.07	0.009	0.27	-0.019	0.68	0.17	0.02	2.1x10^{-8}	46.5	0.172
rs10150332*	NRXN3	C/T	0.36	0.03	0.011	0.08	0.008	0.24	-0.009	0.80	0.28	0.02	1.1x10^{-7}	0.0	0.606
rs4740619	C9ORF93	T/C	0.04	-0.14	-0.028	0.09	-0.033	0.06	-0.104	0.26	0.53	0.01	6.4x10^{-9}	76.4	**0.040**
rs6477694*	EPB41L4B	C/T	0.49	0.04	0.010	0.10	0.010	0.14	0.010	0.77	0.36	0.01	1.7x10^{-8}	37.3	0.207
rs1460676*	FIGN	C/T	0.07	0.08	0.018	0.11	0.018	0.16	0.143	**0.03**	0.22	0.02	5.0x10^{-8}	22.2	0.257
rs29941	KCTD15	G/A	0.32	-0.04	-0.010	0.12	-0.011	0.14	0.018	0.64	0.67	0.01	2.2x10^{-8}	70.4	0.066
rs7239883*	LOC284260	G/A	0.05	0.09	0.020	0.13	0.025	0.08	0.135	0.09	0.32	0.01	3.1x10^{-7}	41.7	0.190
rs16851483*	RASA2	T/G	0.52	-0.04	-0.009	0.14	-0.011	0.09	0.021	0.55	0.09	0.04	1.9x10^{-10}	88.6	**0.003**
rs1514175	TNNI3K	A/G	0.74	0.04	0.010	0.17	0.012	0.10	0.051	0.20	0.42	0.02	2.5x10^{-13}	0.0	0.447
rs6465468*	ASB4	T/G	0.13	0.05	0.012	0.17	0.012	0.21	0.019	0.70	0.68	0.01	2.4x10^{-6}	0.0	0.351
rs6804842	RARB	G/A	0.58	0.03	0.008	0.18	0.009	0.17	0.003	0.94	0.57	0.01	8.0x10^{-10}	0.0	0.401
rs2241423	MAP2K5	G/A	0.12	0.04	0.012	0.23	0.016	0.13	0.031	0.57	0.78	0.03	2.3x10^{-18}	0.0	0.788
rs2112347	POC5	T/G	0.82	0.04	0.010	0.23	0.015	0.08	0.011	0.81	0.62	0.02	2.0x10^{-17}	0.0	0.563
rs7243357	GRP	T/G	0.55	0.03	0.007	0.25	0.010	0.14	0.039	0.26	0.87	0.02	9.1x10^{-9}	0.0	0.789
rs2815752	NEGR1	A/G	0.91	0.05	0.012	0.25	0.009	0.45	0.047	0.44	0.65	0.03	9.3x10^{-25}	0.0	0.600
rs3817334	MTCH2	T/C	0.50	0.03	0.007	0.25	0.005	0.46	0.037	0.30	0.45	0.02	1.2x10^{-17}	0.0	0.665
rs9540493*	MIR548X2	A/G	0.58	0.03	0.007	0.25	0.003	0.60	0.018	0.61	0.45	0.01	4.0x10^{-9}	0.0	0.405
rs7503807	RPTOR	A//C	0.96	0.09	0.017	0.26	0.013	0.44	0.078	0.35	0.47	0.02	5.7x10^{-7}	2.0	0.312
rs2820292	NAV1	C/A	0.38	0.03	0.007	0.26	0.008	0.22	0.018	0.61	0.51	0.01	5.5x10^{-10}	0.0	0.540

rs9400239*	FOXO3	C/T	0.63	0.03	0.007	0.28	0.007	0.27	0.062	0.08	0.70	0.01	6.8×10^{-8}	0.0	0.528
rs713586	ADCY3	C/T	0.18	0.04	0.008	0.33	0.010	0.26	0.089	0.06	0.52	0.02	9.9×10^{-17}	0.0	0.601
rs11583200*	ELAVL4	C/T	0.55	0.02	0.006	0.34	0.007	0.30	0.000	0.99	0.38	0.01	6.0×10^{-9}	0.0	0.649
rs4771122*	MTIF3	G/A	0.08	0.05	0.010	0.35	0.009	0.42	-0.002	0.97	0.26	0.02	3.4×10^{-10}	0.0	0.558
rs1928295*	TLR4	T/C	0.66	0.03	0.006	0.35	0.008	0.20	0.044	0.21	0.57	0.01	4.3×10^{-10}	0.0	0.578
rs7359397	SH2B1	T/C	0.73	-0.03	-0.006	0.37	0.000	0.98	-0.034	0.38	0.36	0.03	1.0×10^{-23}	74.2	**0.049**
rs657452*	AGBL4	A/G	0.39	0.02	0.005	0.37	0.007	0.30	0.044	0.21	0.42	0.02	2.1×10^{-13}	0.0	0.906
rs1528435*	UBE2E3	T/C	0.84	-0.02	-0.007	0.38	-0.006	0.49	-0.004	0.94	0.58	0.01	4.8×10^{-9}	0.0	0.328
rs11688816*	EHBP1	G/A	0.58	0.02	0.005	0.38	0.005	0.44	-0.002	0.95	0.46	0.01	3.8×10^{-7}	0.0	0.678
rs206936	NUDT3	G/A	0.65	-0.02	-0.006	0.38	-0.001	0.90	-0.005	0.90	0.17	0.01	3.3×10^{-6}	22.6	0.256
rs17724992*	PGPEP1	A/G	0.63	-0.02	-0.005	0.40	-0.004	0.55	0.005	0.89	0.69	0.01	7.8×10^{-9}	41.2	0.192
rs7989336	HS6ST3	A/G	0.01	0.07	0.028	0.46	0.014	0.73	0.113	0.61	0.42	0.01	2.1×10^{-5}	0.0	0.720
rs1167827	HIP1	G/A	0.08	-0.04	-0.008	0.48	0.002	0.87	-0.044	0.49	0.54	0.02	2.0×10^{-10}	33.8	0.219
rs11057405*	CLIP1	G/A	0.93	0.03	0.007	0.49	0.005	0.64	-0.027	0.64	0.91	0.03	1.2×10^{-8}	0.0	0.983
rs1000940	RABEP1	G/A	0.27	-0.02	-0.005	0.50	-0.005	0.54	-0.026	0.52	0.23	0.01	1.8×10^{-8}	24.2	0.251
rs10767664	BDNF	A/T	0.14	0.02	0.006	0.50	0.007	0.44	0.075	0.15	0.78	0.04	8.8×10^{-25}	0.0	0.669
rs10968576*	LINGO2	G/A	0.21	0.02	0.005	0.51	0.001	0.88	-0.023	0.59	0.29	0.02	2.3×10^{-14}	0.0	0.962
rs492400*	USP37	C/T	0.31	-0.01	-0.004	0.52	-0.005	0.47	-0.034	0.36	0.32	0.01	4.9×10^{-7}	0.0	0.387
rs2245368	PMS2P11	C/T	0.61	-0.02	-0.004	0.52	-0.003	0.60	-0.004	0.90	0.24	0.02	7.0×10^{-8}	41.4	0.191
rs17001654*	SCARB2	G/C	0.16	-0.02	-0.005	0.53	-0.008	0.35	-0.007	0.89	0.16	0.03	5.0×10^{-9}	58.0	0.123
rs10132280*	STXBP6	C/A	0.67	0.01	0.003	0.57	0.000	0.96	-0.028	0.44	0.67	0.02	1.4×10^{-11}	0.0	0.846
rs3849570*	GBE1	A/C	0.46	-0.01	-0.003	0.58	0.000	0.95	0.023	0.50	0.37	0.01	3.8×10^{-8}	0.0	0.441
rs9925964*	KAT8	A/G	0.35	0.01	0.003	0.58	-0.002	0.80	-0.037	0.29	0.61	0.01	9.4×10^{-11}	0.0	0.942
rs12286929	CADM1	G/A	0.72	0.02	0.003	0.59	0.005	0.46	-0.028	0.46	0.43	0.02	5.4×10^{-13}	0.0	0.912
rs13078807	CADM2	G/A	0.01	0.10	0.022	0.59	-0.005	0.91	-0.105	0.66	0.18	0.02	3.7×10^{-13}	0.0	0.664
rs2365389*	FHIT	C/T	0.07	0.03	0.006	0.59	0.010	0.43	0.037	0.58	0.66	0.01	1.4×10^{-10}	0.0	0.720
rs987237*	TFAP2B	G/A	0.58	0.01	0.003	0.62	0.000	0.94	0.018	0.60	0.09	0.04	1.1×10^{-30}	19.9	0.264
rs2836754*	ETS2	C/T	0.13	-0.02	-0.004	0.62	-0.004	0.69	-0.051	0.31	0.65	0.01	1.6×10^{-8}	0.0	0.411
rs2890652	LRP1B	C/T	0.01	0.07	0.015	0.62	-0.006	0.87	-0.027	0.87	0.12	0.02	1.2×10^{-8}	0.0	0.698
rs13201877	IFNGR1	G/A	0.03	-0.02	-0.009	0.63	-0.009	0.62	-0.101	0.23	0.08	0.02	4.3×10^{-8}	0.0	0.572
rs4735692*	HNF4G	A/G	0.06	-0.04	-0.005	0.67	-0.013	0.31	0.056	0.42	0.56	0.02	6.1×10^{-11}	27.1	0.242
rs9374842*	LOC285762	T/C	0.86	0.02	0.003	0.68	0.011	0.23	0.139	**0.005**	0.74	0.01	7.2×10^{-9}	0.0	0.749
rs4929949	RPL27A	C/T	0.67	0.01	0.003	0.68	0.005	0.47	0.071	0.06	0.60	0.01	1.5×10^{-8}	0.0	0.933
rs2080454*	CBLN1	C/A	0.65	0.00	-0.002	0.70	0.001	0.94	0.003	0.94	0.39	0.01	8.6×10^{-9}	0.0	0.670
rs9816226*	ETV5	T/A	0.07	0.01	0.004	0.74	0.004	0.73	0.057	0.40	0.85	0.03	6.0×10^{-24}	0.0	0.745
rs1441264*	MIR548A2	A/G	0.73	0.01	0.002	0.78	0.003	0.62	0.114	**0.003**	0.55	0.01	3.0×10^{-8}	0.0	0.933
rs11126666	KCNK3	A/G	0.04	0.03	0.004	0.79	0.007	0.67	-0.066	0.46	0.31	0.02	1.3×10^{-9}	0.0	0.872
rs3810291	TMEM160	A/G	0.66	0.01	0.002	0.81	0.003	0.62	0.035	0.33	0.63	0.02	6.4×10^{-16}	0.0	0.730
rs543874*	SEC16B	G/A	0.21	0.01	0.002	0.83	0.004	0.60	0.039	0.36	0.27	0.04	2.3×10^{-40}	0.0	0.367
rs2033732*	RALYL	C/T	0.87	0.02	0.002	0.86	0.006	0.52	0.076	0.12	0.76	0.01	2.3×10^{-7}	0.0	0.844
rs4787491*	INO80E	G/A	0.16	0.00	0.001	0.86	-0.005	0.57	-0.032	0.49	0.61	0.01	2.3×10^{-6}	0.0	0.734
rs17381664*	ZZZ3	C/T	0.55	0.01	0.001	0.87	-0.002	0.76	0.008	0.83	0.43	0.02	4.6×10^{-11}	0.0	0.675
rs11191560*	NT5C2	C/T	0.25	0.00	-0.001	0.89	0.003	0.67	0.054	0.18	0.06	0.03	2.1×10^{-9}	0.3	0.317

rs3736485*	*DMXL2*	A/G	0.46	0.00	0.001	0.90	0.001	0.85	0.016	0.65	0.43	0.01	4.5×10^{-8}	0.0	0.731
rs7599312	*ERBB4*	G/A	0.93	0.00	-0.001	0.91	0.005	0.68	0.052	0.42	0.71	0.02	4.7×10^{-11}	0.0	0.623
rs17094222	*HIF1AN*	C/T	0.33	0.00	0.001	0.91	0.001	0.88	0.028	0.45	0.21	0.02	2.2×10^{-11}	0.0	0.414
rs1555543	*PTBP2*	C/A	0.54	-0.01	-0.001	0.93	-0.001	0.89	0.076	**0.03**	0.57	0.02	5.5×10^{-11}	0.0	0.336
rs2176598*	*HSD17B12*	T/C	0.52	0.00	0.000	0.99	-0.002	0.76	-0.066	0.05	0.20	0.01	3.5×10^{-8}	0.0	0.726
rs7138803	*FAIM2*	A/G	0.11	-0.01	0.000	0.99	-0.003	0.77	0.008	0.88	0.44	0.03	5.1×10^{-26}	0.0	0.358
rs12444979	*GPRC5B*	C/T	>0.99	-	-	-	-	-	-	-	0.87	0.04	1.1×10^{-18}	-	-
rs2287019	*QPCTL*	C/T	>0.99	-	-	-	-	-	-	-	0.85	0.04	1.7×10^{-18}	-	-
rs13191362	*PARK2*	A/G	>0.99	-	-	-	-	-	-	-	0.80	0.03	1.1×10^{-9}	-	-
rs11727676	*HHIP*	T/C	>0.99	-	-	-	-	-	-	-	0.92	0.04	6.2×10^{-9}	-	-
rs16907751	*ZBTB10*	C/T	>0.99	-	-	-	-	-	-	-	0.96	0.03	2.1×10^{-7}	-	-
rs7715256	*GALNT10*	G/T	>0.99	-	-	-	-	-	-	-	0.45	0.02	8.9×10^{-9}	-	-
rs13107325	*SLC39A8*	T/C	<0.01	-	-	-	-	-	-	-	0.12	0.05	1.1×10^{-12}	-	-
rs571312	*MC4R*	A/C	<0.01	-	-	-	-	-	-	-	0.28	0.05	1.1×10^{-56}	-	-
rs2650492	*SBK1*	A/G	<0.01	-	-	-	-	-	-	-	0.31	0.02	1.3×10^{-9}	-	-
rs2033529	*TDRG1*	G/A	<0.01	-	-	-	-	-	-	-	0.26	0.02	1.4×10^{-8}	-	-
rs887912	*FANCL*	T/C	mono	-	-	-	-	-	-	-	0.32	0.02	1.1×10^{-11}	-	-
rs11847697	*PRKD1*	T/C	mono	-	-	-	-	-	-	-	0.04	0.04	2.6×10^{-7}	-	-
rs17024258	*GNAT2*	T/C	mono	-	-	-	-	-	-	-	0.04	0.06	7.3×10^{-8}	-	-
rs7899106	*GRID1*	G/A	mono	-	-	-	-	-	-	-	0.05	0.04	1.3×10^{-8}	-	-
rs2176040	*LOC646736*	A/G	mono	-	-	-	-	-	-	-	0.39	0.01	1.3×10^{-6}	-	-
rs4836133	*ZNF608*	A/C	Tri-allelic	-	-	-	-	-	-	-	0.41	0.02	4.2×10^{-6}	-	-

Data are given for the analysis in full-heritage Pima Indians (n as indicated). R: risk allele; N: non-risk allele; RAF: risk allele frequency. The risk allele is defined as the allele with higher risk for BMI in Europeans. Beta and *p* value are adjusted for age, sex, birth year and the first five genetic principal components. Max-BMI is the maximum lifetime BMI (kg/m^2) recorded at age $\geq$15 years. Max-BMI (non-diabetic) is the maximum BMI recorded at a non-diabetic exam at age $\geq$15 years. The maximum BMI z-score was identified between the ages of 5 and 15 years. BMI is log$_e$-transformed before analyses to approximate a normal distribution and beta presents as log$_e$-scale. Data for meta-analysis of GIANT in Europeans are derived from the public database and beta coefficients are expressed in SD units by inverse Gaussian transformation of BMI. For inclusion in heterogeneity analyses between Pima Indians and Europeans, beta coefficients of maximum BMI in analyses of Pima Indians are also transformed to SD units as conducted in the meta-analysis of GIANT [and presented as beta (SD). I^2 represents the percentage of variance in the effect attributable to heterogeneity between Pima Indians and Europeans, and P_{het} is the *p* value for the null hypothesis that the two betas are equal. *A proxy SNP was

used for genotyping. -: SNPs with mAF<0.01 or monomorphic were omitted from data analysis. Significant p-values are reported in bold type. Bold values: $p \leq 0.05$.

Table S3: Analysis of 98 established BMI SNPs with T2D in longitudinally studied full-heritage Pima Indians
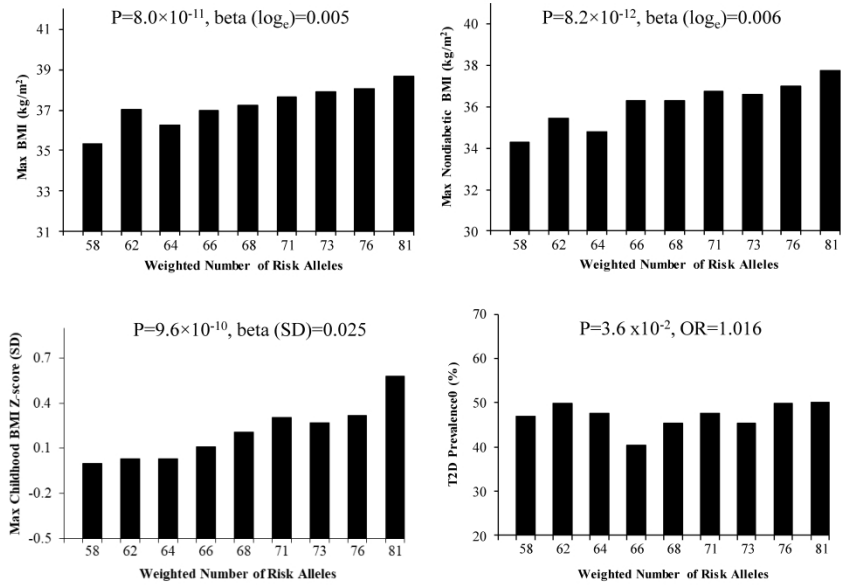
Lead SNP	Locus	Allele R/N	Full-heritage Pima Indians		
			T2D (n=3719)		
			RAF	OR (95% Cl)	*p*
rs2867125	*TMEM18*	C/T	0.86	1.02 (0.89-1.18)	0.75
rs7903146	*TCF7L2*	C/T	0.92	0.91 (0.76-1.09)	0.30
rs13041126	*MRPS33P4*	T/C	0.67	1.02 (0.91-1.14)	0.71
rs12885454	*PRKD1*	C/A	0.78	1.07 (0.95-1.22)	0.27
rs6091540	*ZFP64*	C/T	0.67	1.06 (0.95-1.18)	0.32
rs7193144	*FTO*	C/T	0.14	1.21 (1.05-1.40)	**0.008**
rs977747	*TAL1*	T/G	0.74	1.06 (0.95-1.19)	0.31
rs9641123*	*CALCR*	C//G	0.09	1.17 (0.94-1.45)	0.16
rs10938397	*GNPDA2*	G/A	0.31	1.16 (1.00-1.25)	**0.05**
rs17203016	*CREB1*	G/A	0.15	1.14 (0.96-1.35)	0.15
rs10733682	*LMX1B*	A/G	0.75	1.07 (0.92-1.24)	0.38
rs2531995	*ADCY9*	T/C	0.18	1.07 (0.91-1.27)	0.40
rs758747	*NLRC3*	T/C	0.11	1.15 (0.94-1.40)	0.18
rs7164727*	*ADPGK*	T/C	0.40	0.93 (0.82-1.04)	0.21
rs9914578*	*SMG6*	G/C	0.16	0.97 (0.82-1.13)	0.68
rs10150332*	*NRXN3*	C/T	0.36	1.09 (0.96-1.23)	0.18
rs4740619	*C9ORF93*	T/C	0.04	0.88 (0.63-1.23)	0.46
rs6477694*	*EPB41L4B*	C/T	0.49	1.07 (0.95-1.20)	0.23
rs1460676*	*FIGN*	C/T	0.07	1.22 (0.97-1.55)	0.10
rs29941	*KCTD15*	G/A	0.32	1.09 (0.95-1.25)	0.23
rs7239883*	*LOC284260*	G/A	0.05	0.82 (0.63-1.08)	0.16
rs16851483*	*RASA2*	T/G	0.52	1.07 (0.95-1.20)	0.29
rs1514175	*TNNI3K*	A/G	0.74	1.05 (0.90-1.23)	0.52
rs6465468*	*ASB4*	T/G	0.13	1.02 (0.85-1.21)	0.85
rs6804842	*RARB*	G/A	0.58	1.04 (0.92-1.17)	0.53
rs2241423	*MAP2K5*	G/A	0.12	1.01 (0.82-1.26)	0.89
rs2112347	*POC5*	T/G	0.82	1.00 (0.84-1.20)	0.98
rs7243357	*GRP*	T/G	0.55	1.05 (0.93-1.19)	0.40
rs2815752	*NEGR1*	A/G	0.91	0.94 (0.75-1.18)	0.60
rs3817334	*MTCH2*	T/C	0.50	0.98 (0.86-1.13)	0.83
rs9540493*	*MIR548X2*	A/G	0.58	0.99 (0.88-1.12)	0.92
rs7503807	*RPTOR*	A//C	0.96	1.03 (0.76-1.41)	0.83
rs2820292	*NAV1*	C/A	0.38	1.01 (0.89-1.15)	0.85
rs9400239*	*FOXO3*	C/T	0.63	0.95 (0.84-1.07)	0.41

rs713586	*ADCY3*	C/T	0.18	0.95 (0.81-1.12)	0.56
rs11583200*	*ELAVL4*	C/T	0.55	1.04 (0.92-1.17)	0.56
rs4771122*	*MTIF3*	G/A	0.08	0.94 (0.75-1.17)	0.58
rs1928295*	*TLR4*	T/C	0.66	0.97 (0.86-1.10)	0.66
rs7359397	*SH2B1*	T/C	0.73	0.88 (0.75-1.02)	0.09
rs657452*	*AGBL4*	A/G	0.39	1.06 (0.94-1.20)	0.34
rs1528435*	*UBE2E3*	T/C	0.84	1.03 (0.87-1.20)	0.76
rs11688816*	*EHBP1*	G/A	0.58	0.87 (0.77-0.99)	**0.03**
rs206936	*NUDT3*	G/A	0.65	0.96 (0.83-1.10)	0.53
rs17724992*	*PGPEP1*	A/G	0.63	1.11 (0.98-1.25)	0.10
rs7989336	*HS6ST3*	A/G	0.01	1.26 (0.47-3.36)	0.64
rs1167827	*HIP1*	G/A	0.08	0.91 (0.73-1.14)	0.43
rs11057405*	*CLIP1*	G/A	0.93	1.04 (0.85-1.28)	0.69
rs1000940	*RABEP1*	G/A	0.27	0.82 (0.71-0.95)	**0.006**
rs10767664	*BDNF*	A/T	0.14	0.99 (0.80-1.21)	0.91
rs10968576*	*LINGO2*	G/A	0.21	1.03 (0.89-1.19)	0.68
rs492400*	*USP37*	C/T	0.31	1.07 (0.94-1.22)	0.29
rs2245368	*PMS2P11*	C/T	0.61	1.06 (0.94-1.20)	0.33
rs17001654*	*SCARB2*	G/C	0.16	1.00 (0.86-1.18)	0.96
rs10132280*	*STXBP6*	C/A	0.67	1.02 (0.90-1.16)	0.71
rs3849570*	*GBE1*	A/C	0.46	0.99 (0.88-1.12)	0.89
rs9925964*	*KAT8*	A/G	0.35	0.98 (0.86-1.10)	0.70
rs12286929	*CADM1*	G/A	0.72	1.18 (1.03-1.34)	**0.02**
rs13078807	*CADM2*	G/A	0.01	1.63 (0.65-4.08)	0.29
rs2365389*	*FHIT*	C/T	0.07	1.14 (0.91-1.43)	0.25
rs987237*	*TFAP2B*	G/A	0.58	1.10 (0.97-1.24)	0.13
rs2836754*	*ETS2*	C/T	0.13	0.86 (0.72-1.03)	0.10
rs2890652	*LRP1B*	C/T	0.01	1.72 (0.85-3.48)	0.13
rs13201877	*IFNGR1*	G/A	0.03	1.03 (0.70-1.52)	0.89
rs4735692*	*HNF4G*	A/G	0.06	0.96 (0.75-1.23)	0.75
rs9374842*	*LOC285762*	T/C	0.86	0.97 (0.82-1.16)	0.77
rs4929949	*RPL27A*	C/T	0.67	1.04 (0.90-1.20)	0.62
rs2080454*	*CBLN1*	C/A	0.65	0.93 (0.82-1.05)	0.25
rs9816226*	*ETV5*	T/A	0.07	1.15 (0.91-1.45)	0.26
rs1441264*	*MIR548A2*	A/G	0.73	1.15 (1.01-1.31)	**0.04**
rs11126666	*KCNK3*	A/G	0.04	0.97 (0.68-1.38)	0.85
rs3810291	*TMEM160*	A/G	0.66	0.98 (0.86-1.10)	0.71
rs543874*	*SEC16B*	G/A	0.21	0.98 (0.84-1.13)	0.75
rs2033732*	*RALYL*	C/T	0.87	1.04 (0.87-1.23)	0.69
rs4787491*	*INO80E*	G/A	0.16	1.01 (0.85-1.18)	0.95
rs17381664*	*ZZZ3*	C/T	0.55	1.03 (0.91-1.16)	0.62
rs11191560*	*NT5C2*	C/T	0.25	0.93 (0.81-1.07)	0.32
rs3736485*	*DMXL2*	A/G	0.46	1.02 (0.90-1.14)	0.79

rs7599312	ERBB4	G/A	0.93	1.01 (0.81-1.27)	0.92
rs17094222	HIF1AN	C/T	0.33	0.90 (0.80-1.02)	0.10
rs1555543	PTBP2	C/A	0.54	0.99 (0.86-1.13)	0.86
rs2176598*	HSD17B12	T/C	0.52	0.98 (0.87-1.11)	0.74
rs7138803	FAIM2	A/G	0.11	1.14 (0.93-1.39)	0.19
rs12444979	GPRC5B	C/T	>0.99	-	-
rs2287019	QPCTL	C/T	>0.99	-	-
rs13191362	PARK2	A/G	>0.99	-	-
rs11727676	HHIP	T/C	>0.99	-	-
rs16907751	ZBTB10	C/T	>0.99	-	-
rs7715256	GALNT10	G/T	>0.99	-	-
rs13107325	SLC39A8	T/C	<0.01	-	-
rs571312	MC4R	A/C	<0.01	-	-
rs2650492	SBK1	A/G	<0.01	-	-
rs2033529	TDRG1	G/A	<0.01	-	-
rs887912	FANCL	T/C	mono	-	-
rs11847697	PRKD1	T/C	mono	-	-
rs17024258	GNAT2	T/C	mono	-	-
rs7899106	GRID1	G/A	mono	-	-
rs2176040	LOC646736	A/G	mono	-	-
rs4836133	ZNF608	A/C	Tri-allelic	-	-

Data are given for the analysis in full-heritage Pima Indians (n as indicated). R: risk allele; N: non-risk allele; RAF: risk allele frequency. The risk allele is defined as the allele with higher risk for BMI in Europeans. Odds ratios (OR) for T2D are given as per copy of this allele. *P* values for T2D were adjusted for age, sex, birth year and the first five genetic principal components. For those SNPs associated with BMI ($p<0.05$), T2D associations were additionally adjusted for maximum BMI. * A proxy SNP was used for genotyping. -: SNPs with mAF<0.01 or monomorphic were omitted for data analysis. Bold values: $p \leq 0.05$.
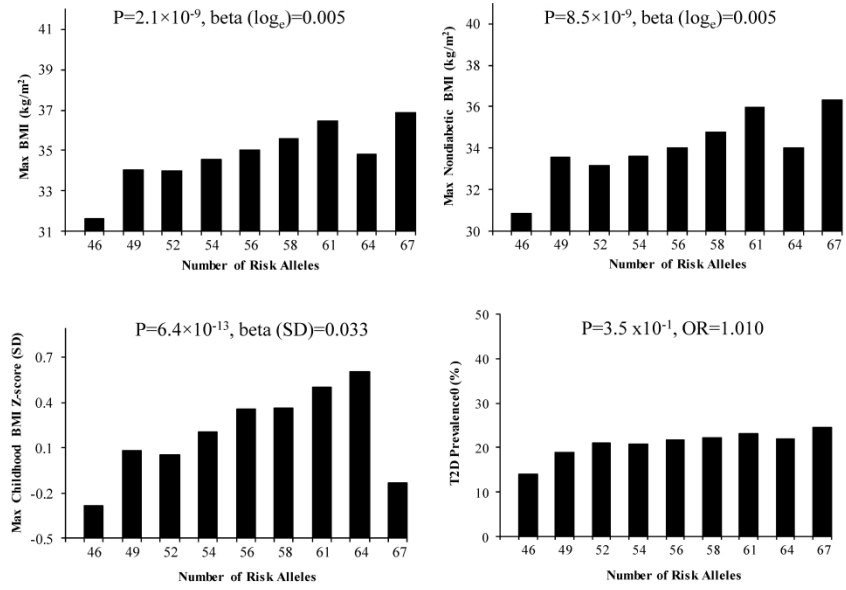
Figure S1.

The aggregate effect of 82 lead SNPs on maximum BMI in adulthood, maximum BMI recorded at a non-diabetic exam, maximum BMI z-score in childhood and T2D in full-heritage Pima Indians. The GRS was created by summing the number of the risk alleles of all 82 SNPs with a mAF ≥ 0.01, weighted by the published effect size, divided by the sum of the weights.

254x190mm (600 x 600 DPI)

Figure S2.

The aggregate effect of 82 lead SNPs on maximum BMI in adulthood, maximum BMI recorded at a non-diabetic exam, maximum BMI z-score in childhood and T2D in 3298 mixed-heritage Pima Indians.

254x190mm (600 x 600 DPI)