

Table S1. Characteristics of non-diabetic subjects genotyped in Sample 1 (subset for whole exome sequencing, $n=177$).

	Males	Females
N	325 (103)	230 (74)
Age range (yrs)	18–46 (18–35)	18–42 (18–36)
Mean Age (yrs) \pm SD	26.7 \pm 6.3 (23.3 \pm 4.5)	26.9 \pm 5.9 (25.3 \pm 4.9)
Mean BMI (kg/m^2) \pm SD	32.8 \pm 7.6 (32.0 \pm 7.4)	34.3 \pm 7.3 (25.3 \pm 4.9)
Mean PFAT (%) \pm SD	28.1 \pm 7.4 (27.4 \pm 8.1)	38.2 \pm 6.4 (39.7 \pm 5.0)
Mean \log_{10} of glucose disposal rates during insulin infusions ($\text{mg}\cdot\text{kg EMBS}^{*-1}\cdot\text{min}^{-1}$) \pm SD	0.56 \pm 0.14 (0.46 \pm 0.16)	0.54 \pm 0.10 (0.37 \pm 0.08)
Mean \log_{10} acute insulin response [†] ($\mu\text{U}/\text{ml}$) \pm SD	2.32 \pm 0.28 (2.37 \pm 0.27)	2.32 \pm 0.28 (2.37 \pm 0.22)
Mean 2-hour plasma glucose concentrations (mg/dl) \pm SD	114.9 \pm 28.4 (111.0 \pm 29.5)	132.4 \pm 29.9 (132.4 \pm 29.3)
Disposition index [†] ($\text{mg}\cdot\text{kg}\cdot\mu\text{U EMBS}^{*-1}\cdot\text{min}^{-1}\text{ml}^{-1}$) \pm SD	906.4 \pm 517.1 (1018.5 \pm 550.8)	882.6 \pm 566.6 (957.1 \pm 540.0)

*EMBS= estimated metabolic body size; † only full-heritage Pima Indians with normal glucose tolerance (N=297) were analyzed for AIR and disposition index.

Table S2. Characteristics of full-heritage Pima Indians genotyped in Sample 2.

Analysis	N	Diabetes status	Mean age (years) \pm SD	Mean max BMI (kg/m^2) \pm SD
Type 2 Diabetes	3604	46% Diabetic (37% male)	49.1 \pm 14.1	38.7 \pm 8.6
		54% Nondiabetic (48% male)	32.1 \pm 14.6	36.1 \pm 8.5
Maximum recorded BMI	2842	100% Nondiabetic (42% male)	32.1 \pm 11.8	36.3 \pm 8.2
Maximum childhood z-score*	2276	100% Nondiabetic (45% male)	13.9 \pm 4.0	0.3 \pm 1.1

* Childhood z-score is the highest age and sex adjusted z-score from an exam at age <20yrs. For Presentation, the Z-scores were sex and age (female, 12yr) standardized to a BMI scale.

Table S3. Characteristics of mixed-heritage American Indians genotyped in Sample 3

Analysis	N	Diabetes status	Mean age (yrs) \pm SD at max BMI	Mean max BMI (kg/m^2) \pm SD
Type 2 Diabetes	4063	21% Diabetic (41% male)	41.1 \pm 14.2	38.7 \pm 8.7
		79% Nondiabetic (47% male)	24.9 \pm 11.9	33.5 \pm 8.4
Maximum recorded BMI	3038	100% Nondiabetic (45% male)	27.3 \pm 10.5	34.0 \pm 8.4
Maximum childhood z-score*	3040	100% Nondiabetic (46% male)	13.7 \pm 3.8	0.3 \pm 1.2

* Childhood z-score is the highest age and sex adjusted z-score from an exam at age <20yrs. For Presentation, the Z-scores were sex and age (female, 12yr) standardized to a BMI scale.

Table S4. Summary of variants identified in 177 Pima Indian exomes (~38Mb capture).

Variant Frequency	Variant counts (% novel)	Coding		5' UTR	3' UTR	Splicing sites	Intron	ncRNA	Intergenic
		Nonsynonymous coding	Synonymous coding						
0.01 - 0.05	34,191 (31.7%)	4,607	3,386	311	932	55	18,863	1,925	4,112
0.05 - 0.1	22,434 (8.9%)	2,437	2,254	223	636	26	12,700	1,367	2,791
0.1 - 0.5	91,991 (4.0%)	8,755	10,002	832	2,564	70	53,099	5,217	11,452
Total	148,616 (11.1%)	15,799	15,642	1,366	4,132	151	84,662	8,509	18,355

Figure S1. Genotyping strategy.

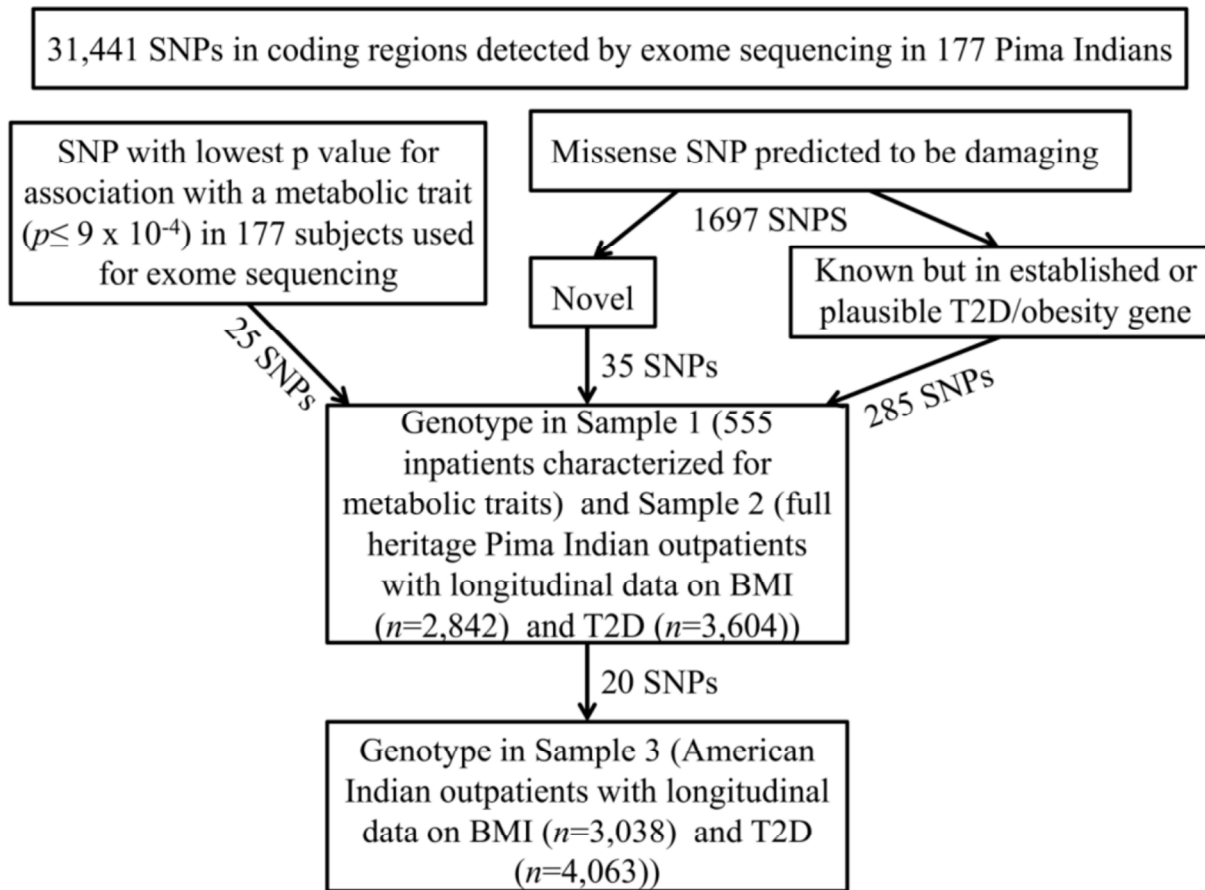


Table S5: Association data for coding SNPs with PFAT, Log₁₀M, 2-hr glucose, Log₁₀AIR, disposition index, maximum childhood z-score, maximum recorded BMI and T2D in full heritage Pima Indians. Only SNPs with $p \leq 0.05$ for any trait are shown.

chr:SNP	Gene	R/NR allele	fR	Sample 1										Sample 2					
				PFAT (N=555)		Log ₁₀ M (N=555)		2-hr glucose (N=555)		Log ₁₀ AIR (N=297)		Log ₁₀ Disposition index (N=297)		Maximum Childhood z-score [§] (N=2,276)		Maximum Recorded BMI [§] (N=2,842)		T2D (N=3,604)	
				beta	P*	beta	p [†]	beta	p [†]	beta	p [‡]	beta	p [‡]	beta	p [§]	beta	p [§]	OR	p [§]
1:rs2890565	<i>UTS2</i>	C/T	0.55	-0.418	0.38	-0.012	0.05	6.698	7.0E-05	-0.009	0.67	-0.014	0.54	0.038	0.23	-0.007	0.26	0.96	0.54
1:rs6688832	<i>H6PD</i>	T/C	0.43	0.177	0.69	-0.007	0.33	4.207	0.02	-0.050	0.06	-0.052	0.06	0.034	0.30	0.006	0.32	1.01	0.83
1:rs4845898	<i>VPS13D</i>	A/T	0.77	0.592	0.28	0.001	0.86	-1.061	0.56	0.050	0.04	-0.051	0.06	0.006	0.85	0.009	0.21	0.89	0.10
1:rs6429757	<i>AGMAT</i>	G/C	0.68	0.534	0.26	-0.007	0.32	3.619	0.04	-0.071	4.2E-03	0.076	0.004	0.014	0.68	0.003	0.65	0.94	0.40
1:rs848210	<i>SPEN</i>	A/G	0.15	1.696	1.5E-03	-0.007	0.39	3.609	0.13	0.009	0.74	-0.001	0.99	-0.003	0.95	-0.009	0.30	0.86	0.06
1:rs1057746	<i>SSX2IP</i>	T/C	0.49	1.163	2.8E-03	-0.010	0.11	1.759	0.31	0.027	0.20	0.021	0.34	0.069	0.03	0.008	0.20	0.99	0.89
1:rs3768235	<i>BCL10</i>	G/A	0.93	-1.289	0.07	0.005	0.63	-1.468	0.56	-0.087	2.1E-03	0.093	1.4E-03	-0.049	0.40	-0.017	0.15	1.02	0.83
1:rs41274114	<i>SYT6</i>	A/G	0.18	0.384	0.50	0.002	0.81	4.690	0.07	-0.030	0.45	-0.030	0.47	-0.049	0.23	-0.014	0.08	0.93	0.40
1:rs509749	<i>LY9</i>	A/G	0.09	-0.388	0.59	-0.016	0.14	6.571	0.01	-0.032	0.42	-0.051	0.20	-0.026	0.62	-0.010	0.35	1.07	0.49
1:rs913257	<i>GORAB</i>	A/G	0.87	1.537	0.02	-0.019	0.05	-1.120	0.68	-0.005	0.89	-0.017	0.64	0.068	0.14	0.017	0.07	1.12	0.23
1:rs3176443	<i>FAM5B</i>	C/G	0.07	-1.668	0.04	-0.007	0.61	0.406	0.90	-0.140	5.0E-04	-0.141	5.0E-04	-0.046	0.48	-0.008	0.53	0.90	0.45
1:rs4252716	<i>MDM4</i>	A/G	0.94	2.561	0.01	-0.035	0.01	7.508	0.05	-0.006	0.86	-0.021	0.56	0.033	0.63	0.015	0.27	1.11	0.45
1:rs1136410	<i>PARP1</i>	C/T	0.67	1.463	1.6E-03	-0.005	0.41	0.074	0.97	0.026	0.32	0.016	0.55	0.017	0.61	0.012	0.06	0.96	0.55
1:rs2274067	<i>C1orf131</i>	C/G	0.62	1.029	0.02	-0.005	0.46	-0.776	0.69	-0.017	0.47	0.022	0.36	0.039	0.27	0.009	0.18	0.88	0.04
2:rs1801699	<i>APOB</i>	T/C	0.86	1.329	0.03	-0.013	0.21	2.728	0.26	0.029	0.49	0.021	0.62	0.058	0.19	0.008	0.36	0.89	0.16
2:rs188718007	<i>MFSD2B</i>	C/G	0.10	-0.203	0.76	-0.017	0.07	5.372	0.05	-0.051	0.24	-0.060	0.18	-0.048	0.35	-0.001	0.94	1.09	0.38
2:rs1052161	<i>ALMS1</i>	T/C	0.82	0.471	0.42	-0.011	0.16	2.207	0.29	-0.048	0.07	-0.057	0.05	0.027	0.50	0.015	0.05	0.95	0.48
2:rs6715329	<i>FAM178B</i>	C/T	0.08	-1.696	0.06	-0.010	0.46	7.394	0.04	-0.100	0.04	0.093	0.05	0.058	0.37	0.006	0.63	1.02	0.90
2:rs6746030	<i>SCN9A</i>	A/G	0.11	2.380	2.1E-04	-0.013	0.22	4.423	0.13	-0.014	0.73	-0.033	0.40	0.044	0.36	0.017	0.09	1.06	0.54
2:169830328	<i>ABCB11</i>	G/A	0.31	-0.295	0.54	-0.007	0.31	3.951	0.03	-0.023	0.34	0.024	0.33	0.049	0.15	0.000	1.00	0.92	0.21
2:rs6433818	<i>CWC22</i>	A/T	0.18	0.789	0.18	-0.014	0.05	-0.355	0.87	0.003	0.93	0.006	0.86	-0.062	0.14	0.007	0.33	0.98	0.79
2:rs10804166	<i>C2orf80</i>	A/G	0.15	0.610	0.28	-0.027	8.9E-04	2.255	0.31	-0.025	0.43	-0.047	0.14	0.025	0.58	0.016	0.06	1.00	0.97
2:rs3770214	<i>ZNF142</i>	C/T	0.69	-0.034	0.94	-0.024	1.0E-03	0.574	0.78	0.010	0.72	0.010	0.71	0.042	0.22	0.006	0.38	0.90	0.13

chr:SNP	Gene	R/NR allele	fR	Sample 1										Sample 2					
				PFAT (N=555)		Log ₁₀ M (N=555)		2-hr glucose (N=555)		Log ₁₀ AIR (N=297)		Log ₁₀ Disposition index (N=297)		Maximum Childhood z-score [§] (N=2,276)		Maximum Recorded BMI [§] (N=2,842)		T2D (N=3,604)	
				beta	P*	beta	p [†]	beta	p [†]	beta	p [‡]	beta	p [‡]	beta	p [§]	beta	p [§]	OR	p [§]
2:rs4674941	<i>DOCK10</i>	C/G	0.93	-0.011	0.99	0.011	0.29	-0.116	0.97	-0.144	2.8E-04	0.156	4.5E-04	0.031	0.61	0.005	0.67	1.15	0.24
2:rs12465491	<i>OR6B3</i>	G/A	0.88	-0.371	0.55	-0.004	0.75	-2.011	0.49	-0.113	6.2E-03	0.096	0.02	0.111	0.03	0.011	0.26	1.20	0.05
3:rs4857302	<i>CRYBG3</i>	A/C	0.33	-0.515	0.29	0.002	0.77	0.355	0.85	0.031	0.23	0.037	0.17	0.031	0.36	-0.006	0.38	1.09	0.20
3:rs6804162	<i>GUCA1C</i>	C/T	0.07	1.539	0.07	-0.020	0.07	7.963	0.02	0.031	0.53	-0.018	0.70	-0.011	0.86	0.023	0.08	1.17	0.16
3:rs7614116	<i>COL6A6</i>	G/A	0.84	0.384	0.46	0.003	0.69	1.455	0.54	0.060	0.05	-0.068	0.04	0.070	0.10	0.009	0.32	1.04	0.60
4:rs2301788	<i>MAN2B2</i>	C/T	0.4	1.280	2.4E-03	-0.007	0.24	3.823	0.03	0.031	0.14	-0.029	0.18	-0.023	0.48	0.005	0.38	0.94	0.33
4:rs9654132	<i>FLJ16686</i>	G/A	0.9	1.546	0.05	-0.004	0.69	-5.668	0.02	0.014	0.71	-0.014	0.73	-0.012	0.80	-0.001	0.96	1.03	0.75
4:rs35597368	<i>PDGFRA</i>	G/A	0.54	0.237	0.61	-0.018	2.9E-03	3.091	0.07	0.028	0.25	-0.020	0.42	0.007	0.84	0.001	0.87	1.07	0.28
4:rs7699006	<i>HERC5</i>	G/A	0.89	0.359	0.64	0.016	0.08	-5.915	0.04	-0.032	0.44	0.022	0.62	0.006	0.92	-0.002	0.82	1.02	0.83
4:rs3762891	<i>LOC91431</i>	C/G	0.91	1.582	0.02	0.012	0.24	2.098	0.49	-0.002	0.95	-0.008	0.80	0.008	0.87	0.011	0.25	0.90	0.31
4:rs25754	<i>ADAMTS12</i>	A/G	0.82	-0.484	0.48	-0.025	2.1E-03	3.190	0.13	0.004	0.88	-0.009	0.74	0.007	0.87	-0.004	0.65	1.05	0.52
5:rs638333	<i>TMEM171</i>	G/A	0.49	-0.051	0.90	0.005	0.45	2.633	0.10	-0.047	0.04	0.042	0.08	0.012	0.69	-0.004	0.47	1.06	0.32
5:rs636926	<i>TMEM171</i>	C/A	0.65	0.592	0.20	0.006	0.36	1.878	0.31	-0.053	0.03	0.048	0.05	0.005	0.88	0.006	0.32	0.94	0.32
5:rs1878878	<i>GPR98</i>	G/A	0.08	0.672	0.41	-0.031	0.03	3.283	0.33	-0.104	0.02	0.130	5.0E-03	0.091	0.14	0.006	0.66	0.91	0.37
5:rs62624460	<i>PCDHA8</i>	G/C	0.92	2.662	2.3E-04	-0.006	0.61	-0.314	0.90	-0.030	0.44	-0.034	0.40	0.098	0.12	0.008	0.51	1.24	0.06
5:rs10044879	<i>FAT2</i>	T/C	0.16	1.203	0.02	-0.006	0.49	8.530	1.4E-03	-0.033	0.24	-0.029	0.31	-0.064	0.11	-0.005	0.59	1.00	0.98
5:rs1432862	<i>FAT2</i>	A/G	0.27	0.733	0.11	-0.010	0.15	6.851	9.5E-04	-0.014	0.58	-0.020	0.43	-0.062	0.08	-0.008	0.27	0.92	0.23
5:rs13360277	<i>UIMC1</i>	C/T	0.1	-0.680	0.32	0.001	0.93	-1.873	0.41	-0.086	2.8E-03	0.097	2.0E-03	-0.002	0.97	0.016	0.11	1.09	0.39
6:rs2294689	<i>TTRAP</i>	C/G	0.8	1.793	4.2E-03	-0.004	0.63	-1.630	0.48	-0.020	0.47	-0.020	0.49	0.055	0.20	0.007	0.40	0.95	0.48
6:rs1801270	<i>CDKN1A</i>	A/C	0.52	0.217	0.63	-0.003	0.66	5.407	2.9E-03	0.024	0.36	0.029	0.28	0.037	0.25	0.011	0.08	0.98	0.73
6:rs3747742	<i>TREML2</i>	T/C	0.4	-0.111	0.78	-0.013	0.04	0.521	0.79	0.021	0.36	0.011	0.65	-0.043	0.21	-0.006	0.35	1.11	0.08
6:43968814	<i>C6orf223</i>	G/A	0.16	1.218	0.01	-0.003	0.68	-1.403	0.47	0.058	0.03	-0.061	0.03	0.005	0.91	0.010	0.23	0.84	0.04
6:rs2297019	<i>MEP1A</i>	A/G	0.71	1.339	2.3E-03	0.000	1.00	4.475	0.01	0.040	0.08	0.040	0.08	-0.021	0.54	-0.001	0.89	0.92	0.19
6:rs2747701	<i>FAM135A</i>	T/C	0.9	1.914	0.02	0.010	0.37	-3.901	0.19	-0.008	0.84	0.001	0.99	-0.035	0.55	0.008	0.46	0.95	0.59
6:rs2295837	<i>FIG4</i>	T/A	0.19	-0.294	0.58	-0.020	4.2E-03	-0.099	0.96	0.040	0.15	0.017	0.55	-0.050	0.22	-0.006	0.47	1.10	0.18

chr:SNP	Gene	R/NR allele	fR	Sample 1										Sample 2					
				PFAT (N=555)		Log ₁₀ M (N=555)		2-hr glucose (N=555)		Log ₁₀ AIR (N=297)		Log ₁₀ Disposition index (N=297)		Maximum childhood z-score [§] (N=2,276)		Maximum Recorded BMI [§] (N=2,842)		T2D (N=3,604)	
				beta	P [*]	beta	p [†]	beta	p [†]	beta	p [‡]	beta	p [‡]	beta	p [§]	beta	p [§]	OR	p [§]
6:rs2244008	LAMA2	C/T	0.2	1.135	0.02	0.001	0.92	-1.053	0.64	-0.015	0.67	0.019	0.60	0.047	0.26	0.000	0.97	1.02	0.84
7:rs2070607	OGDH	G/A	0.92	-1.475	0.02	-0.008	0.46	1.190	0.60	-0.093	3.1E-04	0.100	2.0E-04	-0.014	0.81	-0.021	0.06	1.01	0.92
7:rs1830035	ZNF679	G/A	0.23	0.609	0.20	-0.019	0.01	1.840	0.37	0.008	0.76	0.011	0.69	0.054	0.15	0.010	0.14	0.97	0.64
7:86978458	CROT	G/A	0.24	0.727	0.16	0.001	0.91	0.215	0.92	-0.017	0.54	0.020	0.48	0.018	0.63	0.002	0.83	1.14	0.07
7:rs542137	ZAN	G/C	0.81	0.507	0.40	-0.006	0.43	-0.684	0.74	-0.059	0.01	-0.068	0.01	-0.078	0.06	-0.007	0.41	1.05	0.51
7:rs74343948	FAM71F2	G/C	0.93	0.668	0.42	-0.042	1.0E-03	3.846	0.24	-0.019	0.63	-0.043	0.31	0.040	0.41	-0.009	0.45	1.11	0.37
7:rs9088	TMEM176A	A/G	0.45	0.530	0.23	0.000	0.99	-2.109	0.28	0.017	0.47	0.012	0.63	-0.042	0.19	-0.003	0.65	1.02	0.76
9:rs6475273	FAM154A	C/T	0.36	0.082	0.85	0.001	0.84	1.829	0.33	-0.067	3.0E-03	0.057	0.02	0.008	0.80	-0.003	0.61	0.94	0.31
9:rs17062264	PCSK5	C/G	0.68	0.045	0.93	-0.015	0.03	1.389	0.45	-0.023	0.37	0.041	0.11	0.063	0.07	0.009	0.17	1.11	0.09
10:rs7918793	ACBD5	T/C	0.45	0.486	0.28	-0.003	0.68	2.882	0.08	-0.050	0.02	-0.057	0.01	0.042	0.17	0.006	0.33	1.12	0.06
10:rs2291428	MARCH 8	G/C	0.33	1.166	0.03	-0.008	0.16	0.374	0.85	-0.033	0.16	0.039	0.11	0.057	0.09	0.004	0.60	0.98	0.76
10:rs1062465	KIF20B	T/A	0.14	-1.337	0.01	-0.016	0.08	6.215	8.1E-03	-0.027	0.45	-0.035	0.35	0.048	0.33	-0.005	0.59	1.18	0.07
11:rs2499953	MMP26	C/T	0.43	0.924	0.04	-0.015	0.02	-0.419	0.82	0.026	0.23	-0.019	0.39	0.020	0.55	0.005	0.43	1.02	0.75
11:rs2512219	OR8D2	C/T	0.87	1.290	0.02	0.006	0.46	-3.014	0.21	-0.012	0.67	0.006	0.82	0.043	0.36	0.010	0.26	0.88	0.17
11:rs138907505	HIPK3	C/G	0.93	-0.954	0.17	0.012	0.26	-1.552	0.59	-0.106	8.6E-03	-0.097	0.02	-0.052	0.36	-0.007	0.55	1.03	0.78
11:rs1064608	MTCH2	G/C	0.5	1.453	3.1E-04	0.007	0.29	-4.496	0.01	0.035	0.13	-0.039	0.09	0.044	0.18	0.005	0.43	0.98	0.72
11:rs7947780	C11orf82	T/G	0.59	-0.258	0.61	-0.019	5.9E-03	1.751	0.33	-0.051	0.04	-0.063	0.02	0.018	0.57	0.015	0.02	1.01	0.88
11:rs7130899	C11orf82	T/C	0.73	-0.350	0.51	-0.020	4.8E-03	1.743	0.33	-0.032	0.21	-0.051	0.04	0.038	0.28	0.011	0.11	1.04	0.51
11:118244312	UBE4A	G/A	0.96	-0.314	0.79	-0.034	0.06	17.154	2.7E-04	0.026	0.79	-0.025	0.79	0.019	0.82	-0.016	0.30	1.03	0.82
12:rs4980895	CCDC77	C/A	0.26	-0.153	0.78	-0.012	0.07	4.435	0.03	0.001	0.98	-0.003	0.91	-0.005	0.90	-0.009	0.18	1.11	0.14
12:rs17788563	ANO2	C/T	0.92	-0.949	0.17	0.016	0.10	-0.659	0.80	-0.102	0.01	0.097	0.02	0.095	0.09	0.020	0.08	1.01	0.95
12:rs1056320	DENND5B	G/T	0.93	1.184	0.10	-0.007	0.59	0.958	0.74	0.118	0.02	-0.108	0.05	0.065	0.25	0.005	0.65	0.98	0.87
15:rs17677991	MGA	G/C	0.55	0.735	0.06	0.001	0.90	-3.739	0.02	0.006	0.82	-0.004	0.87	0.047	0.14	0.013	0.04	1.06	0.36
15:rs35875311	FANCI	A/T	0.16	-0.079	0.90	0.000	1.00	0.817	0.74	-0.057	0.03	-0.058	0.03	0.022	0.62	0.001	0.88	0.87	0.09
15:rs140893433	LYSM4	G/A	0.18	-0.789	0.19	-0.004	0.64	5.011	0.04	-0.045	0.19	0.043	0.24	0.021	0.62	-0.002	0.85	1.03	0.68

chr:SNP	Gene	R/NR allele	fR	Sample 1										Sample 2					
				PFAT (N=555)		Log ₁₀ M (N=555)		2-hr glucose (N=555)		Log ₁₀ AIR (N=297)		Log ₁₀ Disposition index (N=297)		Maximum Childhood z-score [§] (N=2,276)		Maximum Recorded BMI [§] (N=2,842)		T2D (N=3,604)	
				beta	P*	beta	p [†]	beta	p [†]	beta	p [‡]	beta	p [‡]	beta	p [§]	beta	p [§]	OR	p [§]
17:rs9902398	<i>SMYD4</i>	C/T	0.87	-0.787	0.19	0.015	0.09	-0.650	0.77	-0.014	0.58	-0.006	0.82	-0.032	0.48	-0.017	0.05	0.97	0.68
17:rs1133295	<i>STX8</i>	G/T	0.93	1.640	0.03	-0.004	0.73	-1.479	0.58	-0.016	0.69	0.034	0.39	0.019	0.75	0.001	0.91	1.12	0.35
18:rs2282632	<i>ASXL3</i>	A/G	0.12	-0.044	0.94	-0.036	2.0E-05	2.103	0.47	-0.026	0.51	-0.039	0.34	-0.010	0.85	-0.017	0.09	1.05	0.60
19:rs16978738	<i>ZNF225</i>	T/A	0.61	0.558	0.23	-0.014	0.05	7.053	3.2E-04	-0.029	0.21	-0.034	0.17	0.026	0.43	0.016	0.01	1.02	0.79
19:rs3745833	<i>GALP</i>	C/G	0.71	-0.506	0.28	0.006	0.39	2.049	0.33	-0.053	0.04	-0.045	0.10	-0.030	0.42	0.004	0.55	1.11	0.14
20:rs450739	<i>RAD21L1</i>	A/G	0.8	-0.829	0.13	-0.016	0.05	4.024	0.07	0.057	0.04	0.041	0.17	0.051	0.21	-0.001	0.92	1.17	0.04
20:rs72620874	<i>SIRPA</i>	C/G	0.6	0.197	0.67	0.003	0.64	4.058	0.03	-0.005	0.85	-0.007	0.77	0.004	0.92	-0.001	0.82	1.13	0.08
20:rs6079391	<i>FLRT3</i>	T/G	0.45	-0.342	0.42	0.006	0.37	-1.656	0.35	-0.059	8.3E-03	-0.055	0.02	-0.022	0.49	-0.009	0.17	1.10	0.14
20:rs707555	<i>PCK1</i>	C/G	0.75	-0.613	0.27	-0.018	0.03	4.568	0.02	0.007	0.80	0.008	0.78	0.025	0.51	-0.006	0.44	1.03	0.66
20:rs2295357	<i>CTSZ</i>	C/A	0.87	1.246	0.05	-0.001	0.95	3.267	0.26	0.001	0.97	0.005	0.91	0.038	0.42	0.013	0.17	1.01	0.95
20:rs1883847	<i>DIDO1</i>	A/G	0.47	0.435	0.34	-0.013	0.03	2.985	0.11	0.025	0.31	0.029	0.24	-0.050	0.15	0.000	0.96	1.01	0.92
20:rs1883848	<i>DIDO1</i>	G/A	0.59	0.993	0.02	-0.015	0.01	1.306	0.44	0.002	0.92	0.002	0.94	-0.044	0.19	0.003	0.70	0.98	0.71
22:rs7575	<i>MRPL40</i>	T/C	0.12	0.404	0.52	0.004	0.71	-2.672	0.28	-0.079	0.03	-0.077	0.05	0.020	0.68	0.004	0.63	1.03	0.72
22:rs1018448	<i>ARFGAP3</i>	C/A	0.9	0.218	0.76	-0.012	0.24	5.507	0.05	-0.067	0.07	0.077	0.04	0.021	0.69	0.005	0.64	1.11	0.31

R: risk allele based on the trait with the best *p* value, NR: non-risk allele, fR: frequency of risk allele, PFAT: percent body fat, Log₁₀ M: logarithmic value of glucose disposal rate during insulin infusion, 2-hr glucose: 2-hour plasma glucose concentrations in response to a 75g OGTT, Log₁₀ AIR: logarithmic value of acute insulin response to a 25g intravenous glucose bolus, § Maximum recorded BMI is defined as the highest BMI measured at a longitudinal exam at which the subject was non-diabetic and >15 years of age, § Childhood z-score is the highest age and sex adjusted Z score from an exam at age<20 yr.

* *p* values were adjusted for age, sex and nuclear family membership; † *p* values were adjusted for age, sex, PFAT and nuclear family membership; ‡ analysis is restricted to full-heritage Pima Indians who are normal glucose tolerant and *p* values were adjusted for age, sex, PFAT, nuclear family membership and Log₁₀ M (for AIR only). § *p* values were adjusted for age, sex, birth year, nuclear family membership. *p*≤0.05 was highlighted in bold. SNPs shown in Table 1 are highlighted in bold, novel SNPs are underlined with dashed lines.

Table S6 SNPs genotyped in all Samples 1-3 and their association with pre-diabetic traits (PFAT, Log₁₀M, 2-hr glucose, Log₁₀AIR, disposition index, maximum childhood z-score and maximum recorded BMI) and T2D.

chr:SNP	Gene	R/NR	fR	Sample 1					Sample 2			Sample 3			Sample 2+3 combined		
				PFAT (N=555)	Log ₁₀ M (N=555)	2-hr glucose (N=555)	Log ₁₀ AIR (N=297)	Log ₁₀ Dispo sition index (N=297)	Maximum Childhood z- score § (N=2,276)	Maximum Recorded BMI§ (N=2,842)	T2D (N=3,604)	Maximum Childhood z-score§ (N=3,040)	Maximum Recorded BMI§ (N=3,038)	T2D (N=4,063)	Maximum Childhood z-score§ (N=5,316)	Maximum Recorded BMI§ (N=5,880)	T2D (N=7,667)
				beta/p*	beta/p†	beta/p†	beta/p‡	beta/p‡	beta/p‡	beta/p‡	OR/p‡	beta/p [§]	beta/p [§]	OR/p [§]	beta/p [§]	beta/p [§]	OR/p [§]
12:rs2075260	<i>ACACB</i>	T/C	0.96	0.09/0.94	0.01/0.65	3.21/0.49	0.004/0.93	0.034/0.51	0.15/0.08	0.02/0.25	1.39/0.03	0.10/0.03	0.02/0.16	1.31/0.04	0.12/5.3E-3	0.01/0.1	1.35/3.8E-3
4:rs309370	<i>BBS12</i>	T/C	0.55	0.37/0.36	-0.01/0.04	1.24/0.45	-0.04/0.15	-0.045/0.08	0.06/0.07	-0.00/0.98	1.19/2.7E-3	-0.03/0.29	-0.01/0.48	1.06/0.37	0.01/0.79	-0.002/0.63	1.13/4.3E-3
19:rs2360543	<i>ZNF530</i>	T/A	0.48	0.48/0.32	-0.01/0.03	2.89/0.13	0.008/0.74	0.009/0.71	-0.009/0.77	-0.01/0.40	1.17/7.6E-3	-0.009/0.77	-0.01/0.32	1.09/0.19	-0.01/0.74	-0.006/0.21	1.13/5.5E-3
6:44081587	<i>MRPL14</i>	G/T	0.03	2.74/1.2E-3	0.003/0.86	-3.70/0.35	-0.002/0.96	-0.012/0.82	-0.13/0.12	0.01/0.47	0.62/7.0E-3	0.11/0.37	0.04/0.10	0.77/0.34	-0.02/0.82	0.02/0.12	0.66/5.8E-3
12:120990399	<i>RNF10</i>	C/T	0.97	1.36/0.26	0.003/0.86	-1.95/0.69	-0.03/0.46	-0.004/0.93	0.37/1.3E-7	0.05/6.8E-4	1.82/2.0E-3	0.18/0.03	0.03/0.20	1.03/0.89	0.27/8.5E-7	0.04/7.2E-4	1.49/9.5E-3
18:rs7238987	<i>CYB5A</i>	T/C	0.32	2.03/7.0E-6	-0.008/0.31	0.83/0.69	0.04/0.19	-0.037/0.22	0.05/0.17	0.02/2.0E-4	1.10/0.13	0.11/1.2E-3	0.02/1.2E-3	1.18/0.03	0.08/5.9E-4	0.02/6.2E-7	1.13/1.0E-2
6:rs9358856	<i>LRRC16A</i>	C/T	0.82	1.38/0.02	-0.01/0.10	4.11/0.08	-0.07/0.03	0.081/0.01	0.14/3.1E-4	0.02/0.01	1.15/0.07	-0.012/0.67	0.010/0.41	1.16/0.09	0.05/0.08	0.01/2.2E-2	1.15/1.3E-2
1:rs3795523	<i>CENPF</i>	C/G	0.42	1.38/1.7E-3	-0.006/0.41	0.95/0.59	0.010/0.67	0.011/0.67	0.06/0.04	0.02/1.1E-4	1.11/0.07	-0.01/0.72	0.004/0.58	0.92/0.25	0.02/0.30	0.02/1.3E-3	1.03/0.49
7:rs854524	<i>PPP1R9A</i>	A/G	0.81	1.18/0.03	-0.006/0.45	0.98/0.68	0.03/0.29	0.029/0.33	0.03/0.41	0.02/7.0E-3	1.11/0.17	0.02/0.62	0.02/0.05	1.06/0.47	0.03/0.35	0.17/1.5E-3	1.09/0.13
3:rs2270781	<i>WDR52</i>	C/T	0.84	1.48/7.4E-3	0.006/0.47	0.49/0.85	0.03/0.40	-0.026/0.42	0.06/0.15	0.02/0.03	1.07/0.37	0.05/0.25	0.02/0.04	1.02/0.85	0.06/0.06	0.02/2.8E-3	1.04/0.44
1:rs5368	<i>SELE</i>	T/C	0.72	1.01/0.05	0.002/0.76	3.58/0.07	0.02/0.59	0.021/0.48	0.10/5.6E-3	0.02/7.3E-3	1.00/0.99	0.002/0.96	0.01/0.18	0.99/0.94	0.04/0.09	0.01/5.0E-3	1.0/0.97
10:rs156697	<i>GSTO2</i>	T/C	0.95	2.15/0.01	0.002/0.90	-2.92/0.47	0.01/0.85	0.018/0.76	0.15/0.02	0.04/7.4E-3	1.10/0.50	0.07/0.11	0.01/0.23	1.01/0.92	0.09/0.02	0.02/2.9E-2	1.04/0.68
1:rs2235541	<i>TCEB3</i>	C/T	0.97	4.14/1.7E-3	0.009/0.58	-4.27/0.28	0.05/0.45	-0.045/0.43	0.22/0.02	0.05/0.01	1.32/0.16	-0.02/0.82	0.01/0.37	0.96/0.81	0.06/0.29	0.02/3.5E-2	1.08/0.55
2:rs11677877	<i>COL4A3</i>	A/G	0.75	1.17/0.03	0.003/0.70	-1.66/0.41	-0.02/0.46	-0.018/0.47	0.05/0.13	0.01/0.05	0.93/0.29	0.07/0.05	0.01/0.30	0.92/0.27	0.06/0.02	0.01/0.06	0.92/0.12
2:rs12463674	<i>TTN</i>	C/T	0.11	1.16/0.05	-0.02/0.007	2.80/0.27	-0.02/0.70	0.024/0.60	0.11/0.02	0.02/6.7E-3	1.02/0.84	-0.06/0.18	-0.01/0.37	1.03/0.77	0.02/0.58	0.01/0.24	1.02/0.78
17:rs12453124	<i>KRT27</i>	C/T	0.43	0.51/0.29	-0.01/0.08	5.14/3.8E-3	-0.07/6.4E-4	0.074/1.1E-3	0.06/0.04	0.001/0.86	1.09/0.14	0.01/0.86	-0.003/0.58	0.96/0.58	0.033/0.13	-0.002/0.73	1.04/0.43
9:rs35929428	<i>PTPRD</i>	G/A	0.82	1.25/0.02	-0.001/0.93	-2.38/0.31	-0.020/0.51	0.009/0.79	0.03/0.50	0.02/0.05	0.97/0.68	-0.03/0.47	-0.01/0.16	0.93/0.42	-0.01/0.83	0.002/0.76	0.96/0.45
19:rs366793	<i>ZNF701</i>	T/A	0.61	-0.73/0.09	-0.004/0.51	3.56/0.03	-0.04/0.07	-0.043/0.08	-0.08/0.01	-0.01/0.02	0.97/0.63	0.06/0.08	0.01/0.06	1.10/0.16	-0.00/0.98	-0.00/0.96	1.03/0.52
1:rs3806339	<i>GBP5</i>	A/G	0.10	1.05/0.10	0.000/0.97	-2.19/0.44	0.02/0.68	0.019/0.61	0.11/0.03	0.02/0.01	1.32/0.16	0.01/0.91	0.004/0.76	0.81/0.12	0.06/0.12	0.01/0.07	0.86/0.07
11:rs11227599	<i>OR5T2</i>	T/C	0.13	-1.44/0.02	0.01/0.27	-3.30/0.18	-0.08/7.0E-3	-0.073/0.01	0.000/1.00	-0.01/0.16	1.27/6.0E-3	-0.01/0.87	-0.002/0.82	0.77/0.02	-0.001/0.99	-0.01/0.36	1.02/0.76

R: risk allele based on the trait with the best *p* value, NR: non-risk allele, fR: frequency of risk allele, § Maximum recorded BMI is defined as the highest BMI measured at a longitudinal exam at which the subject was non-diabetic and >15 years of age, § Maximum childhood z-score is the highest age and sex adjusted z score from an exam at age <20 yr. * *p* values were adjusted for age, sex, birth year, nuclear family membership and the estimate of admixture. † *p* values were adjusted for age, sex, birth year,

nuclear family membership. [†] *p* values were adjusted for age, sex, birth year, nuclear family membership and estimated admixture. $p \leq 0.05$ was highlighted in bold. SNPs shown in Table 1 are highlighted in bold.