

Supplementary Table 1. Distribution of plasma sOB-R levels and other characteristics among the study population

Characteristics	N	Value ^a
Age (yr)	1,504	56.2 (6.9)
BMI (kg/m ²)	1,504	28.0 (5.6)
WHR	1,022	0.80 (0.07)
Physical activity (MET-hr/week)	1,487	15.8 (17.8)
Alcohol (g/day)	1,488	5.4 (8.7)
Smoking status (%)	1,504	
Never smoked		719 (47.8)
Past smoker		618 (41.9)
Current smoker		167 (11.1)
Menopausal status (%) ^b	1,504	
Pre-menopause		335 (22.3)
Post-menopause, never used hormone		467 (31.5)
Post-menopause, hormone past user		196 (13.0)
Post-menopause, hormone current user		506 (33.6)
Family history of diabetes (%)	1,504	477 (31.7)
Type 2 diabetes (%)	1,504	684 (45.5)
Fasting status (%)	1,504	968 (64.4)
Total energy (kcal/day)	1,488	1800 (518)
Glycemic load	1,488	96.1 (15.8)
Cereal fiber (g/day)	1,488	4.0 (1.7)
Polyunsaturated to saturated fat ratio	1,488	0.51 (0.13)
Trans fat (g/day)	1,488	1.9 (0.5)
sOB-R (ng/mL)	1,504	31.4 (10.5)
Leptin (ng/mL)	1,504	25.0 (14.3)

^aMean (SD) for continuous variables; n (%) for categorical variables. ^bHormone refers to hormone replacement therapy.

Supplementary Table 2. Top genotyped and imputed SNPs ($P < 5 \times 10^{-8}$) for plasma sOB-R^a

SNP	Position (bp) ^b	Gene	Gene region	Alleles (+/-)	MAF ^c	r ²	Beta ^d	s.e.	P ^d
rs2767485	65751505	LEPR	Intron	T/C	0.17	0.9986	0.098	0.012	5.77E-15
rs12079231	65743743	LEPR	Intron	C/G	0.17	0.9999	0.097	0.012	6.88E-15
rs11208656	65743375	LEPR	Intron	A/G	0.17	1	0.097	0.012	7.11E-15
rs12062820	65743083	LEPR	Intron	T/C	0.17	1	0.097	0.012	7.11E-15
rs1782755	65759392	LEPR	Intron	C/A	0.17	1	0.097	0.012	8.66E-15
rs1627238	65758667	LEPR	Intron	G/A	0.17	0.9999	0.096	0.012	8.88E-15
rs1171275	65755221	LEPR	Intron	C/T	0.17	0.9995	0.096	0.012	1.13E-14
rs1180445	65755507	LEPR	Intron	T/C	0.17	0.9995	0.096	0.012	1.13E-14
rs1171278	65760734	LEPR	Intron	C/T	0.17	0.9786	0.096	0.012	2.42E-14
rs1171276	65760037	LEPR	Intron	A/G	0.19	0.9348	0.095	0.012	5.43E-14
rs1751492	65765213	LEPR	Intron	T/C	0.30	1	-0.076	0.010	4.00E-13
rs1186403	65773121	LEPR	Intron	T/C	0.30	1	-0.076	0.010	4.40E-13
rs2154381	65768289	LEPR	Intron	A/G	0.30	1	-0.076	0.010	4.61E-13
rs1171266	65776412	LEPR	Intron	C/T	0.30	0.9925	-0.075	0.010	1.35E-12
rs1171274	65753426	LEPR	Intron	T/C	0.27	0.9984	-0.076	0.011	3.62E-12
rs7516840	65745183	LEPR	Intron	G/C	0.27	0.9992	-0.076	0.011	3.68E-12
rs10889556	65742140	LEPR	Intron	A/G	0.27	1	-0.076	0.011	3.74E-12
rs10889558	65749554	LEPR	Intron	G/A	0.27	0.9984	-0.076	0.011	3.79E-12
rs1327116	65748639	LEPR	Intron	C/A	0.27	0.9985	-0.076	0.011	3.80E-12
rs7533108	65750432	LEPR	Intron	G/C	0.27	0.9983	-0.076	0.011	3.83E-12
rs12068561	65746541	LEPR	Intron	C/T	0.27	0.9988	-0.076	0.011	3.84E-12
rs10889557	65743292	LEPR	Intron	G/A	0.28	0.9587	-0.076	0.011	3.94E-12
rs4655680	65814057	LEPR	Intron	G/T	0.29	0.9884	-0.074	0.011	4.03E-12
rs6697315	65766144	LEPR	Intron	T/C	0.36	1	-0.070	0.010	5.30E-12
rs3828039	65826144	LEPR	Intron	A/G	0.28	0.9764	-0.074	0.011	5.57E-12
rs11208674	65811905	LEPR	Intron	T/C	0.29	1	-0.073	0.010	5.66E-12
rs12033452	65811023	LEPR	Intron	C/A	0.29	1	-0.073	0.010	5.66E-12
rs4655518	65812446	LEPR	Intron	T/G	0.29	1	-0.073	0.010	5.66E-12
rs6657632	65811254	LEPR	Intron	A/G	0.29	1	-0.073	0.010	5.66E-12
rs2104564	65742018	LEPR	Intron	T/C	0.27	1	-0.076	0.011	5.87E-12
rs12042884	65825780	LEPR	Intron	C/G	0.28	0.9771	-0.074	0.011	5.89E-12
rs1782754	65765936	LEPR	Intron	A/G	0.27	0.9992	-0.075	0.011	6.71E-12
rs12042877	65825736	LEPR	Intron	C/T	0.28	0.9784	-0.074	0.011	6.76E-12
rs12028951	65825669	LEPR	Intron	G/A	0.28	0.9788	-0.073	0.011	7.08E-12
rs4370791	65824816	LEPR	Intron	A/G	0.28	0.9807	-0.073	0.011	7.29E-12
rs1475398	65755845	LEPR	Intron	G/C	0.27	1	-0.075	0.011	8.01E-12
rs11208657	65745941	LEPR	Intron	A/G	0.28	0.9610	-0.075	0.011	8.09E-12

rs1171270	65770429	LEPR	Intron	A/G	0.27	0.9995	-0.075	0.011	8.12E-12
rs1171269	65769390	LEPR	Intron	C/T	0.27	0.9996	-0.075	0.011	8.18E-12
rs1171271	65771378	LEPR	Intron	T/C	0.27	0.9995	-0.075	0.011	8.19E-12
rs1177681	65771707	LEPR	Intron	A/G	0.27	0.9996	-0.075	0.011	8.19E-12
rs1022981	65772622	LEPR	Intron	A/G	0.27	0.9997	-0.075	0.011	8.20E-12
rs1171272	65772399	LEPR	Intron	T/G	0.27	0.9996	-0.075	0.011	8.20E-12
rs6676495	65824705	LEPR	Intron	G/A	0.28	0.9845	-0.073	0.011	8.88E-12
rs1171262	65774334	LEPR	Intron	T/A	0.27	0.9984	-0.075	0.011	9.86E-12
rs1171263	65774521	LEPR	Intron	C/T	0.27	0.9968	-0.075	0.011	1.09E-11
rs1171264	65775602	LEPR	Intron	G/C	0.27	0.9945	-0.074	0.011	1.48E-11
rs1171267	65776442	LEPR	Intron	G/T	0.36	0.9857	-0.069	0.010	1.59E-11
rs12038998	65821716	LEPR	Intron	C/A	0.28	0.9946	-0.072	0.011	1.59E-11
rs4655528	65822077	LEPR	Intron	A/G	0.28	0.9946	-0.072	0.011	1.62E-11
rs11208676	65820711	LEPR	Intron	A/G	0.28	0.9945	-0.072	0.011	1.69E-11
rs11208677	65821005	LEPR	Intron	A/G	0.28	0.9944	-0.072	0.011	1.72E-11
rs10493379	65818515	LEPR	Intron	G/A	0.28	1	-0.072	0.011	1.83E-11
rs11208679	65822326	LEPR	Intron	G/A	0.28	0.9998	-0.072	0.011	1.83E-11
rs6691346	65818985	LEPR	Intron	G/A	0.28	0.9999	-0.072	0.011	1.83E-11
rs11208675	65818012	LEPR	Intron	T/G	0.28	0.9999	-0.072	0.011	1.83E-11
rs1343981	65817916	LEPR	Intron	A/G	0.28	0.9999	-0.072	0.011	1.83E-11
rs1343982	65817839	LEPR	Intron	C/T	0.28	0.9999	-0.072	0.011	1.83E-11
rs3790424	65816601	LEPR	Intron	A/G	0.28	0.9999	-0.072	0.011	1.83E-11
rs1938487	65819855	LEPR	Intron	T/C	0.28	0.9998	-0.072	0.011	1.84E-11
rs3790425	65815700	LEPR	Intron	A/G	0.28	1	-0.071	0.011	1.92E-11
rs1171261	65773990	LEPR	Intron	C/T	0.27	1	-0.074	0.011	2.08E-11
rs6696954	65827583	LEPR	Intron	G/T	0.37	0.8718	0.072	0.011	2.30E-11
rs1409802	65793939	LEPR	Intron	G/A	0.27	0.9861	-0.074	0.011	3.01E-11
rs1171265	65775840	LEPR	Intron	G/A	0.37	0.8990	-0.070	0.010	3.70E-11
rs6676419	65824797	LEPR	Intron	C/T	0.50	0.9662	-0.063	0.010	4.48E-11
rs6673324	65803651	LEPR	Intron	A/G	0.50	0.9932	0.063	0.009	4.55E-11
rs7519977	65806084	LEPR	Intron	G/A	0.27	0.9975	-0.072	0.011	6.97E-11
rs4655517	65812013	LEPR	Intron	T/C	0.50	0.9987	0.062	0.009	7.13E-11
rs10158279	65806284	LEPR	Intron	G/T	0.50	1	0.062	0.009	7.46E-11
rs10789184	65809550	LEPR	Intron	G/A	0.27	1	-0.072	0.011	9.24E-11
rs1137100	65809029	LEPR	Missense (Lys109Arg)	A/G	0.27	1	-0.072	0.011	9.24E-11
rs3790427	65815338	LEPR	Intron	T/C	0.27	0.9982	-0.071	0.011	1.02E-10
rs10789186	65823065	LEPR	Intron	G/A	0.50	0.9779	-0.062	0.009	1.06E-10
rs10889563	65821755	LEPR	Intron	A/G	0.49	0.9795	-0.061	0.009	1.11E-10

rs6673591	65820977	LEPR	Intron	A/G	0.49	0.9827	-0.061	0.009	1.18E-10
rs10789185	65818452	LEPR	Intron	G/C	0.49	0.9907	-0.061	0.009	1.49E-10
rs10889568	65832033	LEPR	Intron	T/C	0.26	0.9970	-0.070	0.011	1.56E-10
rs12405556	65835705	LEPR	Intron	G/T	0.26	1	-0.070	0.011	1.58E-10
rs4655539	65832251	LEPR	Intron	A/T	0.44	0.9692	-0.061	0.010	1.77E-10
rs10732836	65832048	LEPR	Intron	C/T	0.44	0.9705	-0.061	0.010	1.78E-10
rs6669117	65833660	LEPR	Intron	T/C	0.44	0.9684	-0.061	0.010	1.78E-10
rs4655537	65831389	LEPR	Intron	G/A	0.39	0.9086	0.066	0.010	1.85E-10
rs1137101	65831101	LEPR	Missense (Gln223Arg)	A/G	0.44	0.9752	-0.061	0.010	1.91E-10
rs2154380	65830029	LEPR	Intron	T/C	0.44	0.9777	-0.061	0.010	2.04E-10
rs11208682	65829184	LEPR	Intron	G/A	0.44	0.9766	-0.061	0.010	2.06E-10
rs10736402	65830588	LEPR	Intron	C/T	0.44	0.9759	-0.061	0.010	2.06E-10
rs10449758	65829705	LEPR	Intron	A/G	0.44	0.9786	-0.061	0.010	2.08E-10
rs12564626	65829130	LEPR	Intron	G/A	0.44	0.9740	-0.061	0.010	2.13E-10
rs10749754	65827228	LEPR	Intron	G/A	0.44	0.9660	-0.061	0.010	2.34E-10
rs1475397	65755746	LEPR	Intron	C/T	0.26	1	0.069	0.011	2.92E-10
rs10889567	65829638	LEPR	Intron	T/C	0.45	1	-0.059	0.009	3.10E-10
rs10157275	65739091	LEPR	Intron	C/T	0.13	0.9917	0.087	0.014	5.09E-10
rs1782763	65780488	LEPR	Intron	T/C	0.33	0.9858	-0.065	0.010	5.77E-10
rs10158579	65722644	LEPR	Intron	T/C	0.13	0.9996	0.086	0.014	5.95E-10
rs11808888	65725369	LEPR	Intron	G/A	0.13	0.9988	0.086	0.014	6.17E-10
rs9436302	65669149	LEPR	Intron	G/A	0.20	0.8588	0.080	0.013	6.75E-10
rs17127673	65728313	LEPR	Intron	A/G	0.14	1	0.085	0.014	6.80E-10
rs10128072	65729684	LEPR	Intron	A/C	0.13	1	0.086	0.014	7.64E-10
rs7602	65670539	LEPR	Intron	G/A	0.20	0.9984	0.072	0.012	8.57E-10
rs17127677	65730862	LEPR	Intron	G/T	0.13	0.9989	0.085	0.014	8.59E-10
rs11800275	65736292	LEPR	Intron	T/A	0.13	0.9979	0.085	0.014	9.49E-10
rs6694528	65735604	LEPR	Intron	C/T	0.13	0.9979	0.085	0.014	9.49E-10
rs17127690	65735537	LEPR	Intron	A/G	0.13	0.9980	0.085	0.014	9.52E-10
rs9436303	65669262	LEPR	Intron	A/G	0.24	0.8981	0.070	0.012	2.53E-09
rs1171279	65761081	LEPR	Intron	C/T	0.26	0.9859	0.065	0.011	2.96E-09
rs6690625	65850178	LEPR	Intron	T/G	0.19	0.9591	-0.073	0.013	5.98E-09
rs12040007	65852748	LEPR	Intron	G/A	0.19	0.9589	-0.073	0.013	6.78E-09
rs4655556	65853151	LEPR	Intron	G/A	0.19	0.9591	-0.073	0.013	8.0E-09
rs1938484	65853870	LEPR	Intron	C/A	0.19	0.9590	-0.073	0.013	8.0E-09
rs9436300	65667852	LEPR	Intron	G/A	0.33	0.7046	-0.069	0.012	1.5E-08
rs7534511	65667718	LEPR	Intron	G/A	0.34	0.6901	-0.070	0.012	1.6E-08
rs12567606	65914472	NA	NA	A/G	0.22	0.9645	-0.067	0.012	1.7E-08

rs1046011	65671584	<i>LEPR</i>	Intron	C/T	0.30	0.9014	-0.062	0.011	2.0E-08
rs4655555	65852857	<i>LEPR</i>	Intron	T/A	0.22	0.8930	-0.069	0.012	2.3E-08
rs6667615	65935218	NA	NA	G/A	0.21	0.8965	-0.070	0.013	2.6E-08
rs6588156	65933021	NA	NA	G/A	0.21	0.9100	-0.069	0.012	2.6E-08
rs6667616	65935219	NA	NA	C/A	0.21	0.8877	-0.070	0.013	2.7E-08
rs4655583	65927995	NA	NA	C/A	0.22	0.9463	-0.067	0.012	2.7E-08
rs6664534	65932663	NA	NA	A/T	0.21	0.9192	-0.069	0.012	3.0E-08
rs9436301	65668515	<i>LEPR</i>	Intron	T/C	0.24	0.8046	0.069	0.012	3.0E-08
rs4655795	65931956	NA	NA	G/T	0.21	0.9222	-0.069	0.012	3.2E-08
rs4394621	65938424	NA	NA	A/G	0.21	0.8792	-0.070	0.013	3.4E-08
rs4655792	65931852	NA	NA	T/G	0.20	0.9456	-0.068	0.012	3.6E-08
rs12130476	65897438	NA	NA	G/C	0.20	0.9761	-0.068	0.012	3.7E-08
rs2186245	65890652	NA	NA	C/T	0.19	0.9787	-0.068	0.012	3.8E-08
rs4655793	65931866	NA	NA	C/A	0.21	0.9378	-0.068	0.012	3.9E-08
rs7518632	65875938	NA	NA	C/A	0.19	0.9894	-0.068	0.012	4.1E-08
rs3762274	65836701	<i>LEPR</i>	Intron	T/C	0.37	0.9232	-0.055	0.010	4.4E-08
rs1892535	65869769	<i>LEPR</i>	Intron	G/A	0.19	0.9936	-0.068	0.012	4.5E-08
rs12145237	65897470	NA	NA	C/T	0.20	0.9762	-0.067	0.012	4.6E-08
rs12043772	65907622	NA	NA	T/A	0.20	0.9860	-0.066	0.012	4.8E-08

^an = 1,504; sOB-R levels were transformed on a natural logarithm scale. ^bPosition based on NCBI build 36.3. ^cMinor allele frequency among study participants. ^dRegression coefficients and *P* values for every one copy of minor allele were estimated from linear regression models adjusted for age at blood draw, diabetes case-control status, fasting status, body mass index, menopausal status, and postmenopausal hormone use..

Supplementary Table 3. Top genotyped and imputed SNPs ($P < 1 \times 10^{-6}$) for plasma sOB-R^a among controls

SNP	Position (bp) ^b	Gene	Gene region	Alleles (+/-)	MAF ^c	Beta ^d	s.e.	P ^d
rs2767485	65751505	LEPR	Intron	T/C	0.17	0.104	0.017	5.97E-10
rs12079231	65743743	LEPR	Intron	C/G	0.17	0.104	0.017	6.13E-10
rs11208656	65743375	LEPR	Intron	A/G	0.17	0.104	0.017	6.17E-10
rs12062820	65743083	LEPR	Intron	T/C	0.17	0.104	0.017	6.17E-10
rs1171275	65755221	LEPR	Intron	C/T	0.17	0.101	0.017	1.20E-09
rs1180445	65755507	LEPR	Intron	T/C	0.17	0.101	0.017	1.20E-09
rs1627238	65758667	LEPR	Intron	G/A	0.17	0.101	0.016	1.20E-09
rs1782755	65759392	LEPR	Intron	C/A	0.17	0.101	0.016	1.20E-09
rs1171278	65760734	LEPR	Intron	C/T	0.17	0.100	0.017	2.45E-09
rs1171276	65760037	LEPR	Intron	A/G	0.19	0.100	0.017	2.75E-09
rs2104564	65742018	LEPR	Intron	T/C	0.27	-0.091	0.016	8.69E-09
rs7516840	65745183	LEPR	Intron	G/C	0.27	-0.090	0.016	1.11E-08
rs10889556	65742140	LEPR	Intron	A/G	0.27	-0.090	0.016	1.13E-08
rs1171274	65753426	LEPR	Intron	T/C	0.27	-0.090	0.016	1.13E-08
rs10889558	65749554	LEPR	Intron	G/A	0.27	-0.090	0.016	1.14E-08
rs7533108	65750432	LEPR	Intron	G/C	0.27	-0.090	0.016	1.14E-08
rs1327116	65748639	LEPR	Intron	C/A	0.27	-0.090	0.016	1.14E-08
rs12068561	65746541	LEPR	Intron	C/T	0.27	-0.090	0.016	1.14E-08
rs1475398	65755845	LEPR	Intron	G/C	0.27	-0.089	0.016	1.80E-08
rs6697315	65766144	LEPR	Intron	T/C	0.36	-0.081	0.014	1.81E-08
rs1751492	65765213	LEPR	Intron	T/C	0.30	-0.084	0.015	1.85E-08
rs11208657	65745941	LEPR	Intron	A/G	0.28	-0.088	0.016	2.07E-08
rs10889557	65743292	LEPR	Intron	G/A	0.28	-0.088	0.016	2.52E-08
rs1186403	65773121	LEPR	Intron	T/C	0.30	-0.083	0.015	2.80E-08
rs2154381	65768289	LEPR	Intron	A/G	0.30	-0.083	0.015	2.80E-08
rs1171265	65775840	LEPR	Intron	G/A	0.37	-0.082	0.015	3.89E-08
rs1171267	65776442	LEPR	Intron	G/T	0.36	-0.079	0.014	4.92E-08
rs1171266	65776412	LEPR	Intron	C/T	0.30	-0.082	0.015	5.36E-08
rs1782754	65765936	LEPR	Intron	A/G	0.27	-0.086	0.016	5.76E-08
rs1171270	65770429	LEPR	Intron	A/G	0.27	-0.085	0.016	7.82E-08
rs1171269	65769390	LEPR	Intron	C/T	0.27	-0.085	0.016	7.84E-08
rs1171271	65771378	LEPR	Intron	T/C	0.27	-0.085	0.016	7.88E-08
rs1177681	65771707	LEPR	Intron	A/G	0.27	-0.085	0.016	7.88E-08
rs1022981	65772622	LEPR	Intron	A/G	0.27	-0.085	0.016	7.89E-08
rs1171272	65772399	LEPR	Intron	T/G	0.27	-0.085	0.016	7.89E-08
rs1171262	65774334	LEPR	Intron	T/A	0.27	-0.085	0.016	8.21E-08
rs1171263	65774521	LEPR	Intron	C/T	0.27	-0.085	0.016	8.59E-08

rs4655680	65814057	<i>LEPR</i>	Intron	G/T	0.29	-0.081	0.015	1.04E-07
rs1171264	65775602	<i>LEPR</i>	Intron	G/C	0.27	-0.084	0.016	1.05E-07
rs11208674	65811905	<i>LEPR</i>	Intron	T/C	0.29	-0.080	0.015	1.07E-07
rs12033452	65811023	<i>LEPR</i>	Intron	C/A	0.29	-0.080	0.015	1.07E-07
rs4655518	65812446	<i>LEPR</i>	Intron	T/G	0.29	-0.080	0.015	1.07E-07
rs6657632	65811254	<i>LEPR</i>	Intron	A/G	0.29	-0.080	0.015	1.07E-07
rs1171261	65773990	<i>LEPR</i>	Intron	C/T	0.27	-0.084	0.016	1.27E-07
rs3828039	65826144	<i>LEPR</i>	Intron	A/G	0.28	-0.080	0.015	2.00E-07
rs12042884	65825780	<i>LEPR</i>	Intron	C/G	0.28	-0.080	0.015	2.10E-07
rs1782763	65780488	<i>LEPR</i>	Intron	T/C	0.33	-0.078	0.015	2.27E-07
rs1409802	65793939	<i>LEPR</i>	Intron	G/A	0.27	-0.082	0.016	2.38E-07
rs12042877	65825736	<i>LEPR</i>	Intron	C/T	0.28	-0.079	0.015	2.39E-07
rs12028951	65825669	<i>LEPR</i>	Intron	G/A	0.28	-0.079	0.015	2.44E-07
rs4370791	65824816	<i>LEPR</i>	Intron	A/G	0.28	-0.079	0.015	2.46E-07
rs7519977	65806084	<i>LEPR</i>	Intron	G/A	0.27	-0.081	0.016	2.75E-07
rs6676495	65824705	<i>LEPR</i>	Intron	G/A	0.28	-0.079	0.015	2.78E-07
rs12405556	65835705	<i>LEPR</i>	Intron	G/T	0.26	-0.081	0.016	2.81E-07
rs10789184	65809550	<i>LEPR</i>	Intron	G/A	0.27	-0.081	0.016	2.98E-07
rs1137100	65809029	<i>LEPR</i>	Missense (Lys109Arg)	A/G	0.27	-0.081	0.016	2.98E-07
rs3790427	65815338	<i>LEPR</i>	Intron	T/C	0.27	-0.081	0.016	3.23E-07
rs10889568	65832033	<i>LEPR</i>	Intron	T/C	0.26	-0.080	0.016	3.25E-07
rs10493379	65818515	<i>LEPR</i>	Intron	G/A	0.28	-0.076	0.015	5.12E-07
rs11208675	65818012	<i>LEPR</i>	Intron	T/G	0.28	-0.076	0.015	5.12E-07
rs11208679	65822326	<i>LEPR</i>	Intron	G/A	0.28	-0.076	0.015	5.12E-07
rs1343981	65817916	<i>LEPR</i>	Intron	A/G	0.28	-0.076	0.015	5.12E-07
rs1343982	65817839	<i>LEPR</i>	Intron	C/T	0.28	-0.076	0.015	5.12E-07
rs1938487	65819855	<i>LEPR</i>	Intron	T/C	0.28	-0.076	0.015	5.12E-07
rs3790424	65816601	<i>LEPR</i>	Intron	A/G	0.28	-0.076	0.015	5.12E-07
rs3790425	65815700	<i>LEPR</i>	Intron	A/G	0.28	-0.076	0.015	5.12E-07
rs6691346	65818985	<i>LEPR</i>	Intron	G/A	0.28	-0.076	0.015	5.12E-07
rs12038998	65821716	<i>LEPR</i>	Intron	C/A	0.28	-0.077	0.015	5.28E-07
rs4655528	65822077	<i>LEPR</i>	Intron	A/G	0.28	-0.077	0.015	5.28E-07
rs11208676	65820711	<i>LEPR</i>	Intron	A/G	0.28	-0.076	0.015	5.39E-07
rs11208677	65821005	<i>LEPR</i>	Intron	A/G	0.28	-0.076	0.015	5.44E-07
rs17127673	65728313	<i>LEPR</i>	Intron	A/G	0.14	0.091	0.018	7.94E-07
rs7602	65670539	<i>LEPR</i>	Intron	G/A	0.20	0.079	0.016	8.80E-07
rs10157275	65739091	<i>LEPR</i>	Intron	C/T	0.13	0.091	0.018	9.50E-07

^asOB-R levels were log-transformed. n = 820. ^bPosition based on NCBI build 36.3. ^cMinor allele frequency among study participants. ^dRegression coefficients and *P* values for every one copy of minor allele were estimated from linear regression models adjusted for age at blood draw, fasting status, body mass index, menopausal status, and postmenopausal hormone use.

Supplementary Table 4. Top genotyped and imputed SNPs (combined $P < 5 \times 10^{-8}$) for plasma sOB-R^a in a meta-analysis pooling results of cases and controls.

SNP	Gene	Gene region	Left Gene	Right Gene	Alleles (+/-)	z score ^b	P ^c	Direction ^d
rs2767485	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	7.883	3.19E-15	++
rs12079231	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/G	7.861	3.83E-15	++
rs12062820	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	7.856	3.98E-15	++
rs11208656	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	A/G	7.856	3.98E-15	++
rs1782755	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/A	7.838	4.56E-15	++
rs1627238	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	G/A	7.835	4.68E-15	++
rs1171275	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/T	7.800	6.20E-15	++
rs1180445	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	7.800	6.20E-15	++
rs1171278	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/T	7.708	1.27E-14	++
rs1171276	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	A/G	7.574	3.61E-14	++
rs1751492	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	-7.524	5.30E-14	--
rs2154381	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	A/G	-7.483	7.27E-14	--
rs1186403	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	-7.480	7.45E-14	--
rs1171266	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/T	-7.323	2.42E-13	--
rs6697315	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	-7.274	3.50E-13	--
rs7516840	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	G/C	-7.202	5.93E-13	--
rs10889556	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	A/G	-7.200	6.02E-13	--
rs1171274	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	-7.199	6.07E-13	--
rs12068561	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/T	-7.196	6.21E-13	--
rs10889558	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	G/A	-7.194	6.29E-13	--
rs1327116	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/A	-7.194	6.30E-13	--
rs7533108	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	G/C	-7.192	6.38E-13	--
rs10889557	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	G/A	-7.167	7.67E-13	--
rs4655680	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	G/T	-7.165	7.76E-13	--
rs1782754	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	A/G	-7.135	9.66E-13	--
rs2104564	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	-7.132	9.87E-13	--
rs12033452	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/A	-7.110	1.16E-12	--
rs4655518	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/G	-7.110	1.16E-12	--
rs6657632	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	A/G	-7.110	1.16E-12	--
rs11208674	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	-7.110	1.16E-12	--
rs1171269	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	A/G	-7.097	1.28E-12	--
rs1171270	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/T	-7.096	1.28E-12	--
rs1022981	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/C	-7.096	1.29E-12	--
rs1171271	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	A/G	-7.096	1.29E-12	--
rs1171272	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	A/G	-7.095	1.29E-12	--
rs1177681	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	T/G	-7.095	1.29E-12	--

rs3828039	LEPR	Intron	LOC100128633	PDE4B	A/G	-7.094	1.31E-12	--
rs12042884	LEPR	Intron	LEPROT	LOC100128633	C/G	-7.089	1.35E-12	--
rs11208657	LEPR	Intron	LOC100128633	PDE4B	A/G	-7.09	1.35E-12	--
rs1475398	LEPR	Intron	LEPROT	LOC100128633	G/C	-7.083	1.41E-12	--
rs1171267	LEPR	Intron	LEPROT	LOC100128633	G/T	-7.082	1.43E-12	--
rs1171262	LEPR	Intron	LEPROT	LOC100128633	T/A	-7.068	1.57E-12	--
rs12042877	LEPR	Intron	LOC100128633	PDE4B	C/T	-7.067	1.58E-12	--
rs12028951	LEPR	Intron	LOC100128633	PDE4B	G/A	-7.062	1.65E-12	--
rs4370791	LEPR	Intron	LOC100128633	PDE4B	A/G	-7.059	1.68E-12	--
rs1171263	LEPR	Intron	LEPROT	LOC100128633	C/T	-7.053	1.75E-12	--
rs6676495	LEPR	Intron	LOC100128633	PDE4B	G/A	-7.035	1.99E-12	--
rs1171264	LEPR	Intron	LEPROT	LOC100128633	G/C	-7.008	2.41E-12	--
rs6696954	LEPR	Intron	LOC100128633	PDE4B	G/T	-6.987	2.81E-12	--
rs12038998	LEPR	Intron	LOC100128633	PDE4B	C/A	-6.965	3.27E-12	--
rs4655528	LEPR	Intron	LOC100128633	PDE4B	A/G	-6.964	3.31E-12	--
rs11208676	LEPR	Intron	LOC100128633	PDE4B	A/G	-6.957	3.48E-12	--
rs11208677	LEPR	Intron	LOC100128633	PDE4B	A/G	-6.955	3.52E-12	--
rs1171265	LEPR	Intron	LEPROT	LOC100128633	G/A	-6.954	3.54E-12	--
rs1171261	LEPR	Intron	LEPROT	LOC100128633	C/T	-6.945	3.79E-12	--
rs10493379	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.936	4.02E-12	--
rs11208679	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.936	4.02E-12	--
rs6691346	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.936	4.02E-12	--
rs11208675	LEPR	Intron	LOC100128633	PDE4B	T/G	-6.936	4.03E-12	--
rs1343981	LEPR	Intron	LOC100128633	PDE4B	T/C	-6.936	4.03E-12	--
rs1343982	LEPR	Intron	LOC100128633	PDE4B	A/G	-6.936	4.03E-12	--
rs1938487	LEPR	Intron	LEPROT	PDE4B	C/T	-6.936	4.03E-12	--
rs3790424	LEPR	Intron	LOC100128633	PDE4B	A/G	-6.936	4.03E-12	--
rs3790425	LEPR	Intron	LEPROT	PDE4B	A/G	-6.927	4.30E-12	--
rs1409802	LEPR	Intron	LEPROT	LOC100128633	G/A	-6.898	5.29E-12	--
rs6673324	LEPR	Intron	LEPROT	LOC100128633	A/G	6.861	6.85E-12	++
rs6676419	LEPR	Intron	LOC100128633	PDE4B	C/T	-6.819	9.15E-12	--
rs4655517	LEPR	Intron	LEPROT	LOC100128633	T/C	6.787	1.14E-11	++
rs10158279	LEPR	Intron	LEPROT	LOC100128633	G/T	6.783	1.18E-11	++
rs7519977	LEPR	Intron	LEPROT	LOC100128633	G/A	-6.760	1.38E-11	--
rs10789184	LEPR	Intron	LEPROT	LOC100128633	A/G	-6.716	1.87E-11	--
rs1137100	LEPR	Missense (Lys109Arg)	LEPROT	LOC100128633	G/A	-6.716	1.87E-11	--
rs3790427	LEPR	Intron	LEPROT	PDE4B	T/C	-6.713	1.91E-11	--
rs10889563	LEPR	Intron	LOC100128633	PDE4B	A/G	-6.711	1.93E-11	--

rs10789186	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.701	2.07E-11	--
rs6673591	LEPR	Intron	LOC100128633	PDE4B	A/G	-6.699	2.10E-11	--
rs10789185	LEPR	Intron	LOC100128633	PDE4B	G/C	-6.653	2.87E-11	--
rs12405556	LEPR	Intron	LOC100128633	PDE4B	G/T	-6.648	2.96E-11	--
rs10889568	LEPR	Intron	LOC100128633	PDE4B	T/C	-6.648	2.98E-11	--
rs4655537	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.645	3.04E-11	++
rs4655539	LEPR	Intron	LOC100128633	PDE4B	A/T	-6.596	4.23E-11	--
rs6669117	LEPR	Intron	LOC100128633	PDE4B	T/C	-6.595	4.25E-11	--
rs10732836	LEPR	Intron	LOC100128633	PDE4B	C/T	-6.594	4.29E-11	--
rs1137101	LEPR	Missense (Gln223Arg)	LOC100128633	PDE4B	A/G	-6.588	4.45E-11	--
rs2154380	LEPR	Intron	LOC100128633	PDE4B	T/C	-6.576	4.83E-11	--
rs10736402	LEPR	Intron	LOC100128633	PDE4B	C/T	-6.575	4.86E-11	--
rs10449758	LEPR	Intron	LOC100128633	PDE4B	A/G	-6.575	4.88E-11	--
rs11208682	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.574	4.91E-11	--
rs12564626	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.571	5.00E-11	--
rs1782763	LEPR	Intron	LEPROT	LOC100128633	T/C	-6.553	5.62E-11	--
rs10749754	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.553	5.65E-11	--
rs10889567	LEPR	Intron	LOC100128633	PDE4B	T/C	-6.511	7.49E-11	--
rs10157275	LEPR	Intron	LEPROT	LOC100128633	C/T	6.334	2.39E-10	++
rs10158579	LEPR	Intron	LEPROT	LOC100128633	T/C	6.309	2.81E-10	++
rs11808888	LEPR	Intron	LEPROT	LOC100128633	G/A	6.306	2.86E-10	++
rs10128072	LEPR	Intron	LEPROT	LOC100128633	A/C	6.276	3.48E-10	++
rs1475397	LEPR	Intron	LEPROT	LOC100128633	C/T	6.264	3.76E-10	++
rs17127677	LEPR	Intron	LEPROT	LOC100128633	G/T	6.258	3.90E-10	++
rs17127673	LEPR	Intron	LEPROT	LOC100128633	A/G	6.256	3.94E-10	++
rs11800275	LEPR	Intron	LEPROT	LOC100128633	T/A	6.243	4.31E-10	++
rs6694528	LEPR	Intron	LEPROT	LOC100128633	C/T	6.243	4.31E-10	++
rs17127690	LEPR	Intron	LEPROT	LOC100128633	A/G	6.242	4.33E-10	++
rs9436302	LEPR	Intron	DNAJC6	LOC100128633	G/A	6.239	4.40E-10	++
rs7602	LEPR	Intron	DNAJC6	LOC100128633	G/A	6.189	6.04E-10	++
rs6690625	LEPR	Intron	LOC100128633	PDE4B	T/G	-6.118	9.49E-10	++
rs12040007	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.098	1.08E-09	--
rs9436303	LEPR	Intron	DNAJC6	LOC100128633	A/G	6.082	1.19E-09	++
rs4655556	LEPR	Intron	LOC100128633	PDE4B	G/A	-6.078	1.22E-09	--
rs1938484	LEPR	Intron	LOC100128633	PDE4B	C/A	-6.073	1.26E-09	--
rs12567606	NA	NA	LEPR	PDE4B	A/G	-6.068	1.30E-09	--
rs6667616	NA	NA	LEPR	PDE4B	C/A	-5.930	3.03E-09	--
rs6667615	NA	NA	LEPR	PDE4B	G/A	-5.928	3.07E-09	--

rs6588156	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	G/A	-5.924	3.13E-09	--
rs4655583	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/A	-5.911	3.40E-09	--
rs6664534	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	A/T	-5.893	3.80E-09	--
rs4394621	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	A/G	-5.891	3.84E-09	--
rs4655795	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	G/T	-5.883	4.02E-09	--
rs1171279	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/T	5.881	4.09E-09	++
rs12130476	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	G/C	-5.862	4.57E-09	--
rs4655792	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	T/G	-5.857	4.70E-09	--
rs2186245	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/T	-5.856	4.74E-09	--
rs4655555	<i>LEPR</i>	Intron	<i>LOC100128633</i>	<i>PDE4B</i>	T/A	-5.855	4.76E-09	--
rs7518632	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/A	-5.846	5.03E-09	--
rs4655793	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/A	-5.845	5.07E-09	--
rs4425959	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	A/G	-5.820	5.88E-09	--
rs12043772	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/T	-5.816	6.03E-09	--
rs12145237	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	T/A	-5.816	6.03E-09	--
rs1892535	<i>LEPR</i>	Intron	<i>LOC100128633</i>	<i>PDE4B</i>	G/A	-5.810	6.24E-09	--
rs9436300	<i>LEPR</i>	Intron	<i>DNAJC6</i>	<i>LOC100128633</i>	G/A	-5.797	6.74E-09	--
rs12025906	<i>LEPR</i>	Intron	<i>LOC100128633</i>	<i>PDE4B</i>	T/C	-5.793	6.90E-09	--
rs11208720	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	A/G	-5.789	7.08E-09	--
rs7534511	<i>LEPR</i>	Intron	<i>DNAJC6</i>	<i>LOC100128633</i>	G/A	-5.785	7.23E-09	--
rs11208707	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/T	-5.785	7.24E-09	--
rs10889576	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/T	-5.785	7.26E-09	--
rs10736403	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	A/G	-5.784	7.30E-09	--
rs11208710	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	A/G	-5.783	7.32E-09	--
rs1046011	<i>LEPR</i>	Intron	<i>LEPROT</i>	<i>LOC100128633</i>	C/T	-5.783	7.34E-09	--
rs10749756	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/T	-5.778	7.58E-09	--
rs12117858	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/T	-5.777	7.61E-09	--
rs12026918	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/G	-5.777	7.62E-09	--
rs4655779	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	A/G	-5.775	7.69E-09	--
rs4655782	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	A/G	-5.774	7.76E-09	--
rs4655780	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	C/A	-5.772	7.84E-09	--
rs11208709	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	G/A	-5.772	7.85E-09	--
rs4655778	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	G/A	-5.771	7.87E-09	--
rs12042379	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	G/T	-5.764	8.21E-09	--
rs3828033	<i>LEPR</i>	Intron	<i>LOC100128633</i>	<i>PDE4B</i>	C/T	-5.690	1.27E-08	--
rs3762274	<i>LEPR</i>	Intron	<i>LOC100128633</i>	<i>PDE4B</i>	T/C	-5.689	1.28E-08	--
rs9436301	<i>LEPR</i>	Intron	<i>DNAJC6</i>	<i>LOC100128633</i>	T/C	5.669	1.44E-08	++
rs10158937	NA	NA	<i>LEPR</i>	<i>PDE4B</i>	A/C	-5.668	1.45E-08	--

^asOB-R levels were log-transformed. ^bAverage of z statistics corresponding to the P value of association for each single SNP in cases and controls, with weights proportional to the square root of the number of individuals in cases and controls, respectively. The z statistics were derived from a fixed-effects linear regression model. ^c P value for each SNP was based on the average z statistics. ^dDirection of association in cases or controls. “++” indicated that each copy of the reference allele was associated with increased sOB-R levels in both cases and controls; “--” indicated that each copy of the reference allele was associated with decreased sOB-R levels in both cases and controls; “+-” or “-+” indicated that the direction of associations was opposite for cases and controls.

Supplementary Table 5. Associations between selected SNPs and diabetes risk factors, as well as type 2 diabetes risk in the Nurses' Health Study

	N	SNPs									
		rs1137100 ^a		rs1137101 ^b		rs2767485 ^b		rs1751492 ^a		rs4655555 ^b	
		Beta±s.e.	<i>P</i>	Beta±s.e.	<i>P</i>	Beta±s.e.	<i>P</i>	Beta±s.e.	<i>P</i>	Beta±s.e.	<i>P</i>
BMI (kg/m ²)	3279	0.04±0.15	0.80	0.04±0.13	0.77	-0.22±0.17	0.20	-0.04±0.14	0.78	-0.18±0.16	0.28
WHR	2236	-0.01±0.004	0.17	-0.002±0.003	0.46	-0.006±0.004	0.18	-0.005±0.004	0.17	0.003±0.004	0.54
Leptin (ng/mL)	1508	-0.01±0.02	0.64	-0.006±0.02	0.74	0.03±0.02	0.21	0.01±0.02	0.59	-0.003±0.02	0.89
HMW adiponectin (µg/mL)	1506	-0.02±0.03	0.42	-0.02±0.03	0.33	0.02±0.03	0.49	-0.01±0.03	0.83	0.02±0.03	0.45
CRP (mg/dL)	830	-0.07±0.06	0.18	-0.05±0.05	0.34	-0.03±0.06	0.61	-0.10±0.05	0.07	0.17±0.06	0.005
TNF-αR2 (pg/mL)	843	-0.03±0.021	0.15	0.001±0.02	0.96	-0.06±0.02	0.02	-0.0±0.02	0.08	0.05±0.02	0.02
IL-6 (ng/mL)	815	-0.09±0.04	0.02	-0.07±0.03	0.04	-0.07±0.04	0.10	-0.07±0.04	0.05	0.08±0.04	0.06
IL-18 (pg/mL)	1505	-0.02±0.02	0.23	-0.01±0.02	0.50	0.02±0.02	0.39	0.001±0.02	0.97	0.04±0.02	0.02
Insulin (µU/mL)	604	0.04±0.05	0.45	0.05±0.04	0.25	-0.14±0.05	0.008	-0.01±0.04	0.75	-0.08±0.05	0.12
Type 2 diabetes ^c	3279	0.07±0.06	0.23	0.007±0.05	0.90	0.02±0.07	0.76	0.08±0.06	0.18	-0.07±0.07	0.30

^aGenotyped SNPs. ^bImputed SNPs. ^cBoth incident and prevalent cases were included. To convert beta ± s.e. to odds ratio (95% CI), exponentiate beta ± 1.96×s.e.

Supplementary Table 6. Genotyped SNPs that only reached nominal significance level ($P < 1 \times 10^{-5}$) for plasma sOB-R levels in the Nurses' Health Study^a

SNP	Chr	Position (bp) ^b	Gene	Alleles (+/-)	MAF ^c	Geometric LS mean (95% CI), ng/mL ^d			Beta ^d	s.e.	P value ^d
						0	1	2			
rs12025906	5	65873972	<i>LEPR</i>	T/C	0.19	30.7 (30.2 -31.2)	28.7 (28.0 -29.3)	27.0 (25.0 -29.0)	-0.066	0.12	1.15E-7
rs4655754	5	65887335	NA	T/C	0.19	30.6 (30.1 -31.2)	28.7 (28.1 -29.4)	27.0 (25.0 -29.0)	-0.065	0.12	1.48E-7
rs10158937	5	65917464	NA	C/A	0.20	30.6 (30.1 -31.2)	28.9 (28.2 -29.5)	26.9 (25.1 -28.7)	-0.062	0.12	2.91E-7
rs1567214	5	69299270	NA	G/C	0.40	31.0 (30.3 -31.7)	29.7 (29.1 -30.2)	28.2 (27.3 -29.1)	-0.047	0.10	1.55E-6
rs6669354 ^e	5	65697937	<i>LEPR</i>	T/G	0.13	29.0 (23.6 -35.6)	31.0 (26.4 -37.9)	34.2 (27.8 -42.4)	0.069	0.14	1.97E-6
rs10997637 ^e	5	68863607	<i>CTNNA3</i>	T/C	0.14	29.3 (24.0 -36.1)	32.8 (26.9 -40.0)	31.1 (28.7 -70.0)	0.116	0.25	2.92E-6
rs6527988	5	20300789	NA	N/A	0.26	29.2 (28.7	30.8 (30.1	32.0 (30.5	0.051	0.11	4.51E-6

	6						-29.7)	-31.5)	-33.7)			
rs100		287198	<i>ACCN</i>	G	0		29.6	32.7	31.1	0.	0	4.5
7033	5	87	<i>I</i>	/A	.0		(29.2	(31.3	(25.3	093	.0	2E-6
	0				6		-30.0)	-34.2)	-38.8)		20	
	3											
rs112		657381	<i>LEPR</i>	T	0		30.9	29.2	28.5	-	0	4.7
08654	5	54		/C	.3		(30.3	(28.7	(27.3	0.0	.0	1E-6
	0				3		-31.5)	-29.8)	-29.8)	47	10	
	3											
rs943		656841	<i>LEPR</i>	T	0		31.1	29.4	28.6	-	0	4.7
6747	5	95		/C	.3		(30.4	(28.8	(27.5	0.0	.0	8E-6
	0				8		-31.8)	-29.9)	-29.7)	46	10	
	4											
rs311		135280	<i>ADAM</i>	T	0		31.3	29.6	28.8	-	0	5.2
8667	4	884	<i>TS13</i>	/C	.4		(30.6	(29.1	(28.0	0.0	.0	6E-6
	4				7		-32.1)	-30.2)	-29.6)	44	10	
	9											
rs595		203033	NA	N	0		29.2	30.8	32.1	0.	0	6.5
0304	5	16		A	.2		(28.7	(30.1	(30.5	050	.0	6E-6
	0				6		-29.7)	-31.5)	-33.7)		11	
	4											
rs671		196040	NA	T	0		31.0	29.7	28.3	-	0	8.0
7199	5	109		/G	.4		(30.3	(29.2	(27.4	0.0	.0	5E-6
	0				0		-31.8)	-30.3)	-29.2)	45	10	
	3											
rs202		657187	<i>LEPR</i>	T	0		30.9	29.2	28.6	-	0	8.3
5804	5	09		/C	.3		(30.3	(28.7	(27.4	0.0	.0	3E-6
	0				3		-31.5)	-29.8)	-29.8)	46	10	
	2											
rs171		196083	NA	T	0		30.9	29.8	28.2	-	0	8.9
77643	5	765		/C	.3		(30.2	(29.2	(27.3	0.0	.0	1E-6
	0				9		-31.6)	-30.3)	-29.1)	45	10	
	5											
rs109		689446	<i>CTNN</i>	G	0		29.3	32.5	70.0	0.	0	9.3
	5				.0						.0	

97688 ^c	0	0	82	A3	/A	4	(24.0	(26.3	(70.0	108	24	6E-6
	3						-36.0)	-39.0)	-70.0)			

^asOB-R levels were log-transformed. ^bPosition based on NCBI build 36.3. ^cMinor allele frequency among study participants. ^dAdjusted for age at blood draw, diabetes case-control status, fasting status, body mass index, menopausal status, and postmenopausal hormone use. ^eLeast square means could not be obtained due to rare homozygous minor alleles (1.7% for rs6669354, 0.2% for rs10997637, and 0.1% for rs10997688). Median (interquartile range) was provided instead.

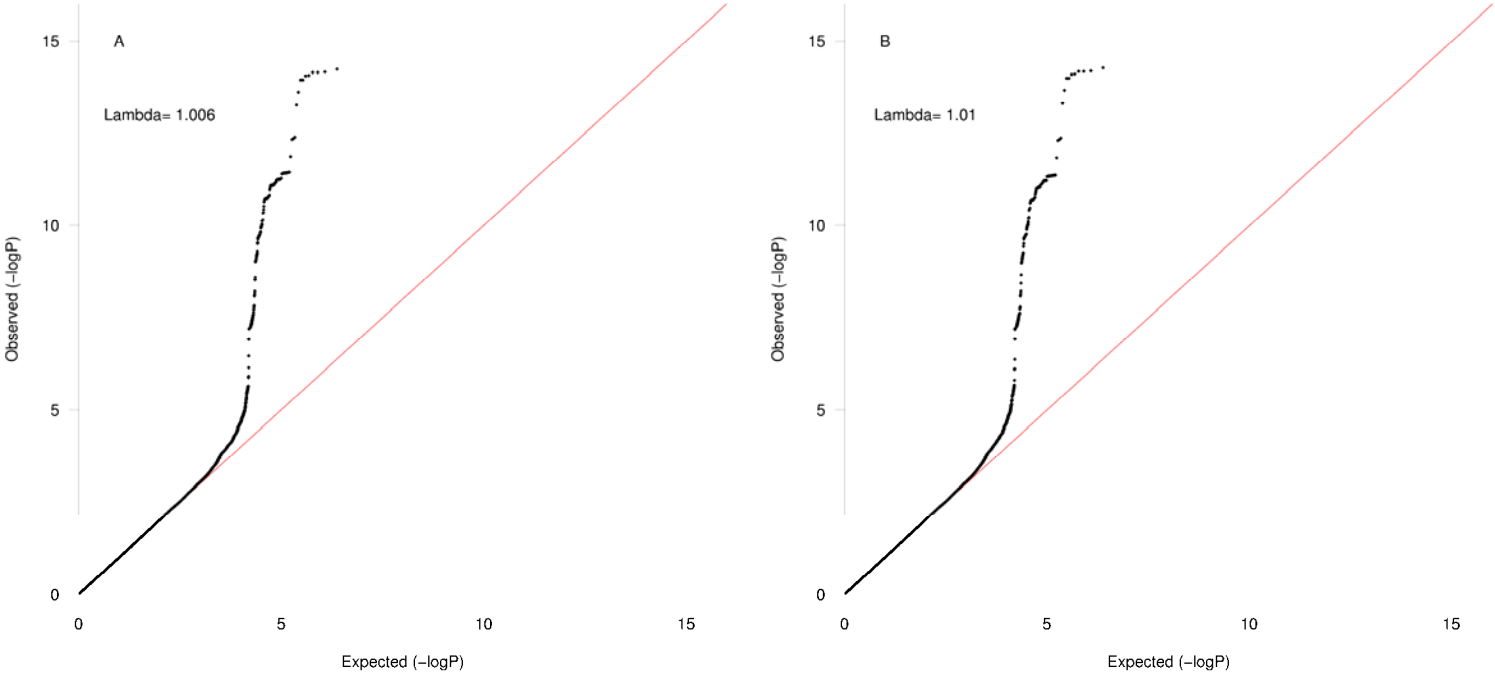
Supplementary Table 7. Genotyped and imputed SNPs that only reached nominal significance level ($P < 1 \times 10^{-5}$) for plasma sOB-R levels^a

SNP	Chr.	Position (bp) ^b	Gene	Gene region	Alleles (+/-)	MAF ^c	r ²	Beta ^d	s.e.	P ^d
rs11208720	1	65931643	NA	NA	A/G	0.20	0.9603	-0.067	0.012	5.0E-08
rs4425959	1	65940407	NA	NA	A/G	0.21	0.8548	-0.070	0.013	5.2E-08
rs3828033	1	65837298	<i>LEPR</i>	Intron	C/T	0.37	0.9137	-0.056	0.010	5.2E-08
rs12025906	1	65873972	<i>LEPR</i>	Intron	T/C	0.19	1	-0.067	0.012	5.3E-08
rs11208707	1	65912101	NA	NA	C/T	0.20	0.9960	-0.065	0.012	5.7E-08
rs11208710	1	65918627	NA	NA	A/G	0.20	0.9968	-0.065	0.012	5.8E-08
rs10736403	1	65912984	NA	NA	A/G	0.20	0.9961	-0.065	0.012	5.8E-08
rs12042379	1	65931052	NA	NA	G/T	0.20	0.9833	-0.066	0.012	5.8E-08
rs10749756	1	65913099	NA	NA	C/T	0.20	0.9962	-0.065	0.012	6.0E-08
rs12026918	1	65918834	NA	NA	C/G	0.20	0.9969	-0.065	0.012	6.0E-08
rs12117858	1	65914682	NA	NA	C/T	0.20	0.9962	-0.065	0.012	6.0E-08
rs4655779	1	65915118	NA	NA	A/G	0.20	0.9963	-0.065	0.012	6.1E-08
rs4655782	1	65915560	NA	NA	A/G	0.20	0.9965	-0.065	0.012	6.1E-08
rs11208709	1	65918605	NA	NA	G/A	0.20	0.9971	-0.065	0.012	6.1E-08
rs4655780	1	65915365	NA	NA	C/A	0.20	0.9966	-0.065	0.012	6.2E-08
rs4655778	1	65914924	NA	NA	G/A	0.20	0.9961	-0.065	0.012	6.2E-08
rs10889576	1	65941154	NA	NA	C/T	0.21	0.8306	-0.070	0.013	6.3E-08
rs10158937	1	65917464	NA	NA	A/C	0.20	0.9999	-0.064	0.012	1.2E-07
rs4655811	1	65695745	<i>LEPR</i>	Intron	G/C	0.32	0.9870	-0.053	0.010	3.4E-07
rs11800909	1	65734368	<i>LEPR</i>	Intron	A/G	0.08	0.9778	0.088	0.018	7.1E-07
rs1567214	1	69299270	NA	NA	G/C	0.40	1	-0.048	0.010	1.2E-06
rs12131840	1	66004359	NA	NA	C/T	0.15	0.9466	-0.070	0.015	1.3E-06
rs11208700	1	65906031	NA	NA	T/A	0.46	0.9013	0.048	0.010	2.2E-06
rs970468	1	65679078	<i>LEPR</i>	Intron	A/C	0.37	0.9350	-0.049	0.010	2.3E-06
rs6657868	1	65686295	<i>LEPR</i>	Intron	G/A	0.37	0.9956	-0.048	0.010	2.3E-06
rs4655783	1	65915632	NA	NA	C/T	0.46	0.9012	0.048	0.010	2.4E-06
rs11804091	1	65676467	<i>LEPR</i>	Intron	A/G	0.15	0.9893	0.063	0.013	2.4E-06
rs9436747	1	65684195	<i>LEPR</i>	Intron	C/T	0.37	1	-0.047	0.010	2.6E-06
rs12022410	1	65926521	NA	NA	G/A	0.46	0.9017	0.047	0.010	2.6E-06
rs6669354	1	65697937	<i>LEPR</i>	Intron	T/G	0.13	1	0.067	0.014	2.8E-06
rs1007033	17	28719887	<i>ACCN1</i>	Intron	C/T	0.06	0.9994	0.095	0.020	3.0E-06
rs1327121	1	65729925	<i>LEPR</i>	Intron	A/G	0.33	0.9997	-0.048	0.010	3.1E-06
rs11208654	1	65738154	<i>LEPR</i>	Intron	T/C	0.33	1	-0.048	0.010	3.1E-06
rs2025804	1	65718709	<i>LEPR</i>	Intron	A/G	0.33	1	-0.048	0.010	3.1E-06
rs10997637	10	68863607	<i>CTNNA3</i>	Intron	C/T	0.04	0.9995	0.115	0.025	3.3E-06
rs3790433	1	65666930	<i>LEPR</i>	Intron	C/T	0.24	0.7239	0.060	0.013	3.4E-06
rs13438451	7	14581455	<i>DGKB</i>	Intron	C/T	0.09	0.7836	0.083	0.018	3.5E-06

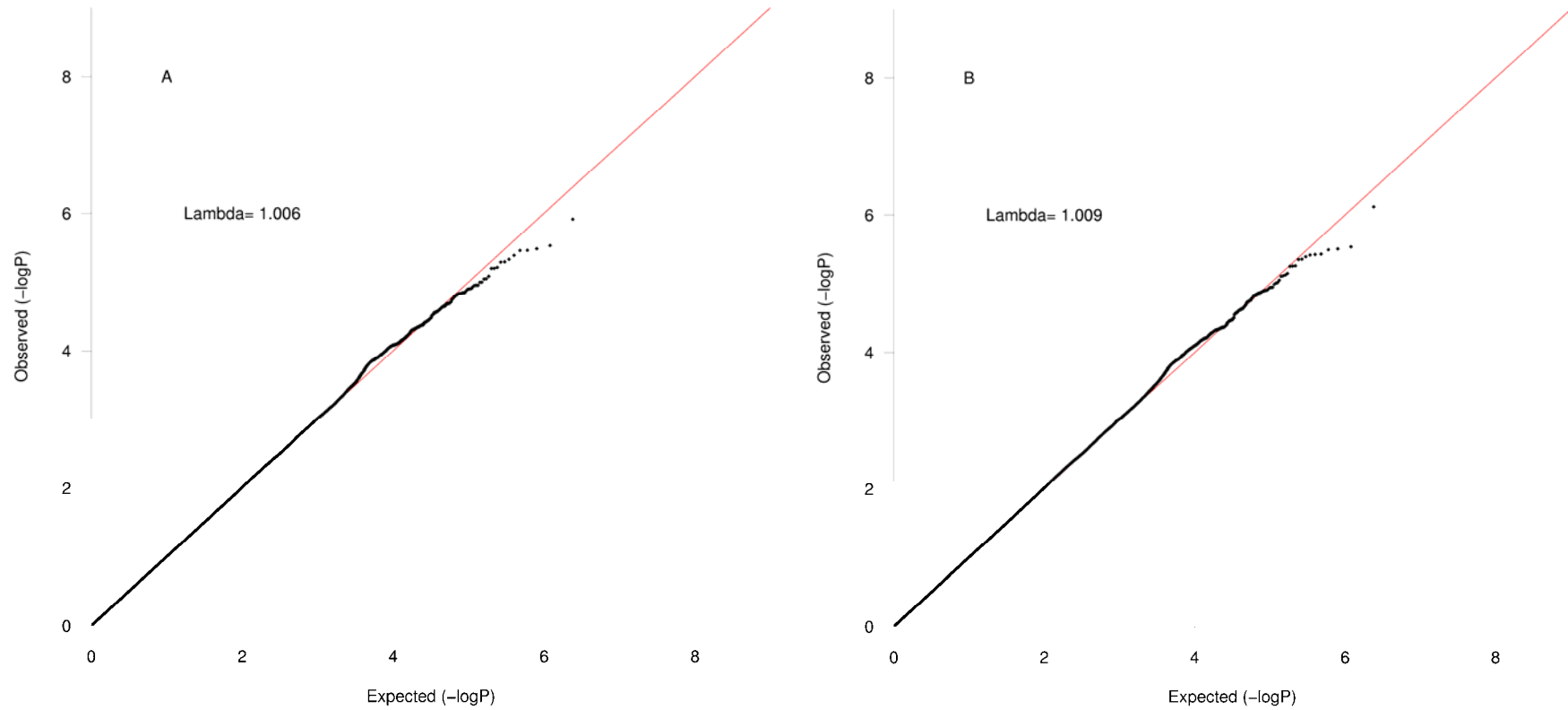
rs17557153	17	35890351	<i>TNS4</i>	Intron	C/A	0.48	0.9171	-0.046	0.010	3.5E-06
rs4655794	1	65931889	NA	NA	C/T	0.47	0.8791	0.047	0.010	3.6E-06
rs10019936	4	161650948	NA	NA	T/C	0.25	0.8978	-0.053	0.012	4.1E-06
rs7907340	10	68864243	<i>CTNNA3</i>	Intron	C/G	0.04	0.9933	0.116	0.025	4.7E-06
rs7524581	1	65939087	NA	NA	C/T	0.36	0.8656	-0.049	0.011	5.1E-06
rs7907588	10	68864374	<i>CTNNA3</i>	Intron	C/G	0.04	0.9888	0.115	0.025	5.1E-06
rs7915595	10	68866036	<i>CTNNA3</i>	Intron	T/A	0.04	0.9845	0.115	0.025	5.2E-06
rs12753193	1	65942267	NA	NA	A/G	0.36	0.8366	-0.050	0.011	5.5E-06
rs12131089	1	69301953	NA	NA	C/A	0.39	0.9919	-0.045	0.010	6.1E-06
rs7900877	10	68874863	<i>CTNNA3</i>	Intron	T/G	0.04	0.9763	0.114	0.025	6.3E-06
rs7900696	10	68875017	<i>CTNNA3</i>	Intron	C/A	0.04	0.9757	0.114	0.025	6.4E-06
rs7541434	1	65941087	NA	NA	C/A	0.36	0.8427	-0.049	0.011	6.5E-06
rs1327115	1	65739427	<i>LEPR</i>	Intron	G/T	0.38	0.9732	-0.046	0.010	6.8E-06
rs6678033	1	65850212	<i>LEPR</i>	Intron	G/A	0.36	0.9718	-0.046	0.010	7.7E-06
rs743516	22	20851498	NA	NA	G/A	0.38	0.9334	-0.046	0.010	8.3E-06
rs4655557	1	65853375	<i>LEPR</i>	Intron	T/C	0.36	0.9720	-0.046	0.010	8.7E-06
rs10997688	10	68944682	<i>CTNNA3</i>	Intron	G/A	0.04	1	0.109	0.024	9.0E-06
rs1507860	1	69293184	NA	NA	G/A	0.39	1	-0.043	0.010	9.0E-06

^an = 1,504; sOB-R levels were transformed on a natural logarithm scale. ^bPosition based on NCBI build 36.3. ^cMinor allele frequency among study participants. ^dRegression coefficients and *P* values for every one copy of minor allele were estimated from linear regression models adjusted for age at blood draw, diabetes case-control status, fasting status, body mass index, menopausal status, and postmenopausal hormone use.

Supplementary Figure 1. Log Quantile-Quantile (QQ) P value plot for genome-wide scan for log-transformed plasma sOB-R levels. (A) Age at blood draw, fasting and diabetes case-control status, body mass index, menopausal status, and postmenopausal hormone use were adjusted for. (B) Top three eigenvectors for European ancestry were further adjusted for.



Supplementary Figure 2. Log Quantile-Quantile (QQ) P value plot for genome-wide scan for log-transformed plasma sOB-R levels after excluding SNPs in and adjacent to *LEPR* region on chromosome 1 (65000 kb and 67000 kb on chromosome 1). (A) Age at blood draw, fasting and diabetes case-control status, body mass index, menopausal status, and postmenopausal hormone use were adjusted for. (B) Top three eigenvectors for European ancestry were further adjusted for.



Supplementary Figure 3. Eigenvectors 1 and 2 from the principal components analysis of all unduplicated NHS samples (n = 3,369) and all unduplicated and unrelated HapMap controls (n = 209: 59 CEU, 60 YRI, 45 JPT, 45 CHB). Color- and symbol-coding is by self-identified ethnic group.

