Table footnotes and figure legends

Supplementary Table 1

Association results for the variants genotyped in the full-heritage Pima Indian population sample (n = 2842). M, major allele; m, minor allele. mAF, minor allele frequency. *P*-values were adjusted for age, sex, birth date, family membership, and Pima heritage.

Supplementary Figure 1

The larger plot shows the linkage disequilibrium pattern for the 80 variants genotyped in the population-based sample of full-heritage Pima Indians. Colors indicate *D*' and numbers indicate r^2. The 4 variants shown in Table 1 are denoted by the open rectangles. The smaller plot shows the LD pattern for the 4 variants genotyped in the mixed-heritage Native American sample.

Table 1

Association analyses for the 4 tag variants ($D' < 0.99$, $r^2 < 0.85$) with BMI, body weight, and height. Allele frequency is given for the designated risk allele. The risk alleles were consistent between the full-heritage and mixed-heritage samples; however, for some variants the risk allele was the major allele in the full-heritage sample but the minor allele in the mixed-heritage sample. For each variant, the mean BMI by genotype is shown in the 1st row, the mean body weight by genotype is shown in the 2nd row, and the mean height by genotype is shown in the 3rd row. [a]*P*-values were adjusted for age, sex, birth year, and family membership, and in the mixed-heritage sample the *P*-values were additionally adjusted for Indian heritage

Table 2

The allele frequencies for the HapMap populations were obtained from the HapMap SNPs track, UCSC Genome Browser, build 37.1.

Figure 1

Energy expenditure over 24hrs adjusted for age, sex, fat mass, fat free mass, and activity based on genotypes for rs2025804. Twenty four hour energy expenditure was measured by indirect calorimetry in a metabolic chamber. Oxygen consumption and carbon dioxide production were measured and energy expenditure calculated over 15 minute intervals. Arrows indicate when meals were given. Red line, homozygous G/G (n = 167); blue line, heterozygous G/A (n = 110); green line, homozygous A/A (n = 26).

Supplementary Figure 2

Schematic showing the predicted regulatory elements (ENCODE Regulation Tracks, UCSC Genome Browser, build 37.1) in the 5' region of the short *LEPR* isoforms. Black horizontal bar indicates the location of the rs2025804 LD block. Variants in LD (r^2 = 1.0) with rs2025804 are shown below the black bar. The novel C/T variant and rs2025804 are highlighted by red boxes. Variants denoted by (*) have been genotyped in the full-heritage Pima Indian population set (supplementary Table 1).

Supplementary Table 1.

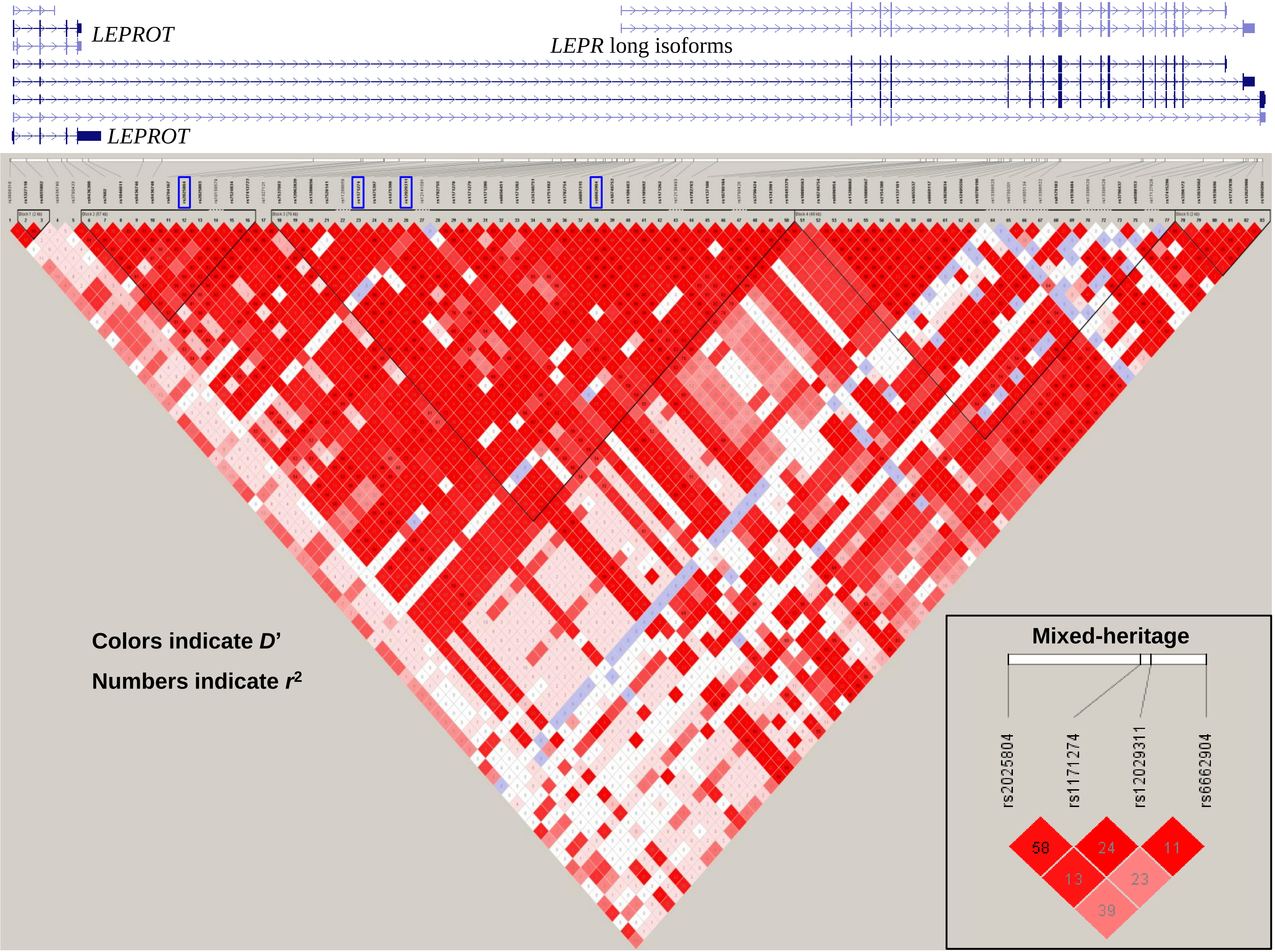
Associations between *LEPR/LEPROT* variants and BMI in the full-heritage Pima Indian population sample (*n* = 2842)

			Mean BMI (kg/m^2)			
Variant	M/m	mAF	M/M	M/m	m/m	*P*
rs3806318	A/G	0.04	36.4 ± 8.2	37.2 ± 8.8	34.4 ± 12.1	0.44
rs1327118	G/C	0.30	36.4 ± 8.1	36.4 ± 8.3	35.9 ± 8.5	0.83
rs4655802	G/A	0.30	36.5 ± 8.2	36.4 ± 8.3	35.9 ± 8.6	0.62
rs9436740	A/T	0.25	36.6 ± 8.3	36.4 ± 8.1	36.8 ± 8.6	0.57
rs3790433	G/A	0.09	36.4 ± 8.2	36.9 ± 8.6	39.3 ± 9.7	0.20
rs9436300	A/G	0.34	36.5 ± 8.1	36.4 ± 8.1	36.1 ± 8.9	0.24
rs7602	G/A	0.10	36.3 ± 8.2	37.4 ± 8.5	38.3 ± 9.2	0.04
rs1046011	A/G	0.34	36.4 ± 8.1	36.4 ± 8.2	35.8 ± 8.9	0.15
rs9436746	A/C	0.38	36.5 ± 8.2	36.5 ± 8.2	35.8 ± 8.6	0.07
rs9436748	G/T	0.24	36.8 ± 8.2	35.9 ± 7.9	36.6 ± 9.4	0.03
rs6704167	A/T	0.23	36.8 ± 8.2	36.1 ± 8.0	36.7 ± 9.3	0.04
novel[a]	C/T	0.24	36.8 ± 8.3	35.8 ± 7.9	36.2 ± 9.1	0.003
rs2025804	G/A	0.27	36.7 ± 8.2	35.6 ± 8.1	35.7 ± 8.9	0.004
rs2025803	T/C	0.26	36.8 ± 8.2	35.9 ± 8.0	36.1 ± 9.3	0.005
rs10158579	T/C	0.02	36.5 ± 8.3	36.8 ± 8.3	—	0.57
rs7524834	T/C	0.25	36.8 ± 8.3	35.8 ± 8.0	36.2 ± 9.1	0.005
rs17412723	A/G	0.25	36.7 ± 8.2	35.8 ± 8.1	36.0 ± 9.1	0.005
rs1327121	G/A	0.27	36.9 ± 8.3	35.9 ± 8.0	36.3 ± 8.9	0.01
rs7537093	T/C	0.25	36.9 ± 8.3	35.9 ± 8.0	36.2 ± 9.0	0.004
rs12062820	T/C	0.13	36.2 ± 8.1	36.8 ± 8.4	37.4 ± 8.9	0.23
rs11208656	A/G	0.13	36.2 ± 8.1	36.8 ± 8.4	37.3 ± 8.9	0.19
rs7526141	C/T	0.25	36.9 ± 8.3	35.9 ± 8.0	36.2 ± 9.0	0.005
rs11208659	T/C	0.02	36.4 ± 8.2	35.3 ± 8.2	—	0.82
rs1171274	C/T	0.40	36.6 ± 8.2	36.3 ± 8.2	35.8 ± 8.7	0.05
rs1475397	C/T	0.15	36.3 ± 8.2	36.6 ± 8.4	36.6 ± 8.8	0.46
rs1475398	C/G	0.40	36.5 ± 8.2	36.2 ± 8.2	35.8 ± 8.7	0.05
rs12029311	G/A	0.25	35.9 ± 8.2	36.3 ± 8.0	38.6 ± 9.3	0.006
rs12141591	C/G	0.01	36.6 ± 8.3	37.6 ± 9.1	—	0.13
rs1782755	G/T	0.13	36.2 ± 8.1	36.8 ± 8.4	37.1 ± 8.9	0.21
rs1171278	C/T	0.13	36.2 ± 8.1	36.9 ± 8.5	37.0 ± 8.8	0.18
rs1171279	C/T	0.15	36.3 ± 8.1	36.8 ± 8.5	36.6 ± 8.7	0.28
rs1171280	C/T	0.41	36.8 ± 8.0	36.5 ± 8.2	35.9 ± 8.7	0.04
rs6656451	C/T	0.26	36.8 ± 8.2	35.7 ± 8.0	35.9 ± 9.1	0.003
rs1171282	C/T	0.13	36.3 ± 8.0	36.7 ± 8.2	37.3 ± 9.1	0.29
rs34340751	–/GG	0.16	36.3 ± 8.2	36.6 ± 8.0	37.0 ± 9.9	0.33
rs1751492	G/A	0.47	36.6 ± 8.4	36.6 ± 8.1	36.1 ± 8.4	0.15
rs1782754	C/T	0.48	36.6 ± 8.4	36.4 ± 8.1	36.0 ± 8.4	0.09
rs6697315	C/T	0.46	36.6 ± 8.4	36.6 ± 8.1	36.1 ± 8.4	0.10
rs6662904	G/A	0.30	36.7 ± 8.4	35.8 ± 7.8	36.1 ± 8.8	0.008
rs10749753	G/A	0.30	36.9 ± 8.4	35.8 ± 7.8	36.3 ± 8.8	0.007
rs1186403	C/T	0.47	36.5 ± 8.3	36.4 ± 8.0	36.1 ± 8.4	0.20
rs1185692	C/G	0.48	36.6 ± 8.3	36.4 ± 8.1	36.1 ± 8.4	0.11
rs1171262	A/T	0.48	36.7 ± 8.3	36.5 ± 8.1	36.0 ± 8.4	0.06
rs12138493	A/T	0.009	36.5 ± 8.2	36.1 ± 8.9	—	0.47
rs1782763	C/T	0.47	36.6 ± 8.4	36.6 ± 8.1	36.1 ± 8.4	0.10

rs1137100 (Arg109Lys)	A/G	0.50	36.2 ± 8.6	36.4 ± 8.2	36.8 ± 8.4	0.10
rs10789184	G/A	0.49	36.1 ± 8.4	36.4 ± 8.1	36.8 ± 8.3	0.10
rs3790426	G/T	0.01	36.4 ± 8.2	35.8 ± 8.4	—	0.49
rs3790424	T/C	0.49	36.7 ± 8.3	36.4 ± 8.1	36.1 ± 8.4	0.12
rs1343981	T/C	0.50	36.2 ± 8.4	36.4 ± 8.1	36.7 ± 8.3	0.16
rs10493379	G/A	0.50	36.1 ± 8.4	36.3 ± 8.1	36.7 ± 8.3	0.12
rs10889563	G/A	0.48	36.6 ± 8.4	36.5 ± 8.2	35.7 ± 8.4	0.02
rs10749754	A/G	0.30	36.3 ± 8.3	36.7 ± 8.2	36.7 ± 8.3	0.35
rs6696954	G/T	0.20	36.3 ± 8.3	36.3 ± 8.0	37.1 ± 9.4	0.64
rs11208682	A/G	0.30	36.3 ± 8.2	36.6 ± 8.2	36.4 ± 8.3	0.46
rs10889567	C/T	0.30	36.2 ± 8.3	36.6 ± 8.2	36.4 ± 8.3	0.42
rs2154380	G/A	0.30	36.1 ± 8.3	36.7 ± 8.2	36.4 ± 8.4	0.20
rs1137101 (Gln223Arg)	G/A	0.30	36.3 ± 8.3	36.7 ± 8.2	36.4 ± 8.3	0.39
rs4655537	G/A	0.20	36.4 ± 8.3	36.4 ± 7.9	37.5 ± 9.6	0.41
rs6669117	C/T	0.30	36.2 ± 8.3	36.7 ± 8.2	36.3 ± 8.1	0.30
rs3828034	T/C	0.01	36.5 ± 8.3	37.1 ± 8.2	35.6 ± 6.8	0.28
rs12405556	T/G	0.31	36.4 ± 8.3	36.8 ± 8.2	36.4 ± 8.3	0.46
rs10789190	A/G	0.30	36.2 ± 8.3	36.6 ± 8.2	36.5 ± 8.2	0.34
rs13306525	G/T	0.001	36.6 ± 8.2	31.7 ± 5.8	—	0.09
rs6700201	C/T	0.007	36.4 ± 8.3	35.3 ± 8.4	—	0.23
rs1805134 (Ser343Ser)	T/C	0.02	36.3 ± 8.2	35.3 ± 8.0	—	0.94
rs13306522	G/A	0.008	36.4 ± 8.3	34.2 ± 6.6	28.4 ± 0.0	0.13
rs8179183 (Asn656Lys)	G/C	0.09	36.4 ± 8.3	36.5 ± 7.9	35.6 ± 6.6	0.65
rs1938484	A/C	0.31	36.4 ± 8.3	36.7 ± 8.2	36.2 ± 8.2	0.59
rs13306520	A/G	0.008	36.4 ± 8.2	37.0 ± 8.6	—	0.18
rs13306528	A/C	0.001	36.6 ± 8.2	37.2 ± 10.2	—	0.72
rs3790437	A/G	0.09	36.4 ± 8.2	36.9 ± 8.2	35.6 ± 6.5	0.45
rs6588153	A/T	0.21	36.6 ± 8.3	36.5 ± 8.0	36.9 ± 9.2	0.94
rs17127828	A/G	0.01	36.4 ± 8.2	35.8 ± 8.5	—	0.57
rs17415296	C/A	0.09	36.4 ± 8.3	36.7 ± 8.0	35.6 ± 6.5	0.53
rs3206172	C/G	0.10	36.4 ± 8.3	36.6 ± 8.0	35.3 ± 6.6	0.58
rs12034502	T/C	0.21	36.3 ± 8.2	36.5 ± 8.1	37.1 ± 9.6	0.36
rs1938496	A/G	0.31	36.1 ± 8.2	36.7 ± 8.2	36.3 ± 8.3	0.22
rs17127838	G/T	0.10	36.3 ± 8.3	36.8 ± 8.2	35.8 ± 6.6	0.30
rs12025906	C/T	0.31	36.2 ± 8.2	36.6 ± 8.3	36.4 ± 8.2	0.23
rs1805096 (Pro1019Pro)	T/C	0.20	36.3 ± 8.2	36.5 ± 8.1	38.0 ± 10.3	0.20

[a] Novel variant identified by whole genome squencing. Chr1:65945750, build 37, GCCTGTCAATCTACC[C/T]TTCAGTTCTAGATT.

Supplementary figure 1



Supplementary figure 2