**Supplementary Table 1.** Number of pancreatic cancer cases by cohort with available plasma leptin levels and genotyped SNPs at *LEPR*

|  |  |  |
| --- | --- | --- |
|  | **Plasma Leptin** | **Genotyped*****LEPR* SNPs** |
| Cohort | Cases | Controls | Cases | Controls |
| HPFS | 74 | 180 | 74 | 172 |
| NHS | 103 | 307 | 92 | 280 |
| PHS | 70 | 173 | 54 | 157 |
| WHI | 194 | 380 | 163 | 326 |
| WHS | 29 | 54 | 29 | 54 |
| **Total** | **470** | **1094** | **412** | **989** |

Abbreviations: SNP, single nucleotide polymorphism; HPFS, Health Professionals Follow-up Study; NHS, Nurses’ Health Study; PHS, Physicians’ Health Study; WHI, Women’s Health Initiative; WHS, Women’s Health Study

**Supplementary Table 2.** Characteristics of controls from five prospective cohorts

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Characteristic\*** | **HPFS** | **NHS** | **PHS** | **WHI** | **WHS** | **Total** |
| No. controls | 180 | 307 | 173 | 380 | 54 | 1094 |
| Male gender | 100.0 | 0.0 | 100.0 | 0.0 | 0.0 | 32.3 |
| Plasma leptin levels, ng/ml | 9.1(8.7) | 22.6(16.2) | 7.2(6.0) | 28.8(22.8) | 24.7(16.6) | 20.1(18.8) |
| No. of controls | 180 | 307 | 173 | 380 | 54 | 1094 |
| Age at blood draw, years | 65.7(7.8) | 60.2(6.8) | 55.3(8.1) | 66.6(7.2) | 57.3(7.8) | 62.4(8.5) |
| Race |  |  |  |  |  |  |
| * White
 | 95.6 | 98.7 | 87.9 | 88.4 | 96.3 | 92.8 |
| * Black
 | 0.0 | 1.0 | 0.6 | 4.5 | 0.0 | 1.9 |
| * Other
 | 4.4 | 0.3 | 11.6 | 7.1 | 3.7 | 5.3 |
| Body mass index, kg/m2  | 25.8(3.3) | 25.3(4.3) | 24.7(2.6) | 26.9(5.6) | 25.9(4.6) | 25.9(4.5) |
| Physical activity, MET-hrs/week | 41.2(45.0) | 17.1(18.0) | 13.6(12.8) | 15.0(14.9) | 16.9(22.9) | 19.8(25.4) |
| Cigarette smoking |  |  |  |  |  |  |
| * Never
 | 33.9 | 39.4 | 42.8 | 50.3 | 37.0 | 42.7 |
| * Past
 | 54.4 | 45.0 | 38.2 | 41.6 | 44.4 | 44.2 |
| * Current
 | 11.7 | 15.0 | 19.1 | 6.6 | 18.5 | 12.3 |
| * Unknown
 | 0.0 | 0.7 | 0.0 | 1.6 | 0.0 | 0.7 |
| History of diabetes mellitus | 5.0 | 3.6 | 1.2 | 3.9 | 1.9 | 3.5 |
| Regular multivitamin use | 46.7 | 44.0 | 20.8 | 43.7 | 31.5 | 40.0 |
| Plasma 25(OH)D levels, nmol/L | 71.8(24.5) | 65.1(21.3) | 71.8(25.5) | 59.8(27.5) | 59.1(21.9) | 65.1(25.3) |
| Plasma C-peptide levels, ng/ml | 2.7(2.9) | 2.0(1.3) | 2.4(1.5) | 1.8(0.8) | 2.4(1.5) | 2.1(1.6) |
| Plasma adiponectin levels, µg/ml | 6.2(4.1) | 8.5(4.7) | 5.6(2.7) | 9.6(5.6) | 7.6(3.1) | 8.0(4.9) |

\*Continuous variables are reported as mean (standard deviation) and categorical variables are reported as percent at blood collection

Abbreviations: 25(OH)D, 25-hydroxyvitamin D ; SNP, single nucleotide polymorphism; HPFS, Health Professionals Follow-up Study; NHS, Nurses’ Health Study; PHS, Physicians’ Health Study; WHI, Women’s Health Initiative; WHS, Women’s Health Study

**Supplementary Table 3**. Partial Spearman correlation coefficients between plasma leptin and covariates among controls

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Leptin | Adiponectin | C-peptide | Age | BMI | Physical activity |
| **Men** |  |  |  |  |  |  |
| Leptin | 1.0 | -0.06 | 0.26\* | 0.02 | 0.50\* | -0.19\* |
| Adiponectin |  | 1.0 | -0.23\* | 0.15\*\* | -0.17\* | 0.04 |
| C-peptide |  |  | 1.0 | 0.07 | 0.24\* | -0.05 |
| Age |  |  |  | 1.0 | -0.03 | 0.03 |
| BMI |  |  |  |  | 1.0 | -0.13\*\* |
| Physical activity |  |  |  |  |  | 1.0 |

**Women**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Leptin | 1.0 | -0.26\* | 0.51\* | -0.002 | 0.73\* | -0.21\* |
| Adiponectin |  | 1.0 | -0.28\* | 0.06 | -0.29\* | 0.04 |
| C-peptide |  |  | 1.0 | 0.05 | 0.42\* | -0.20\* |
| Age |  |  |  | 1.0 | -0.01 | 0.003 |
| BMI |  |  |  |  | 1.0 | -0.17\* |
| Physical activity |  |  |  |  |  | 1.0 |

Adjusted for age, cohort and fasting time

\* *P* < 0.001

\*\**P* < 0.05

Abbreviations: BMI, body mass index

**Supplementary Table 4**. Odds ratios (ORs) and 95% confidence intervals (CIs) for pancreatic cancer according to quintiles of plasma leptin in sensitivity analyses excluding diabetics and short time intervals from blood collection to cancer diagnosis

|  |  |  |
| --- | --- | --- |
|  | **Quintiles of plasma leptin** | ***P*trend\*** |
| **Exclusion factor** | 1 | **2** | **3** | **4** | **5** |
| ***Men*** |  |  |  |  |  |  |
| <2 years between blood collection and diagnosis | 1.0 | 1.88 (0.86-4.12) | 2.35 (1.08-5.10) | 1.92 (0.87-4.23) | 3.51 (1.43-8.60) | 0.01 |
| <4 years between blood collection and diagnosis | 1.0 | 1.90 (0.82-4.42) | 2.55 (1.09-6.00) | 2.08 (0.87-4.96) | 3.37 (1.21-9.20) | 0.03 |
| Diabetics | 1.0 | 1.68 (0.78-3.64) | 1.99 (0.93-4.29) | 1.86 (0.86-4.02) | 3.13 (1.29-7.62) | 0.02 |
| ***Women*** |  |  |  |  |  |  |
| <2 years between blood collection and diagnosis | 1.0 | 1.28 (0.83-1.98) | 0.58 (0.35-0.97) | 0.74 (0.44-1.27) | 0.89 (0.49-1.62) | 0.29 |
| <4 years between blood collection and diagnosis | 1.0 | 1.17 (0.72-1.90) | 0.50 (0.29-0.88) | 0.66 (0.37-1.19) | 0.68 (0.34-1.36) | 0.10 |
| Diabetics | 1.0 | 1.21 (0.78-1.87) | 0.55 (0.33-0.93) | 0.67 (0.40-1.15) | 0.83 (0.45-1.51) | 0.19 |

\**P*trend values were calculated by the Wald test of a score variable that contained median values of quintiles.

ORs and 95% CI were estimated by conditional logistic regression conditioned on the matching factors including year of birth, prospective cohort (HPFS, NHS, PHS, WHI, WHS), smoking status (never, past, current), fasting status (fasting, non-fasting), and month/year of blood draw, and adjusted for race (White, Black, other), history of diabetes mellitus (yes, no), current multivitamin use (yes, no), and plasma 25(OH)D (continuous), BMI (continuous), physical activity (continuous), plasma C-peptide (continuos) and plasma adiponectin (quartiles).

Abbreviations: 25(OH)D, 25-hydroxyvitamin D ; BMI, body mass index; HPFS, Health Professionals Follow-up Study; NHS, Nurses’ Health Study; PHS, Physicians’ Health Study; WHI, Women’s Health Initiative; WHS, Women’s Health Study

**Supplementary Table 5**. Multivariate-adjusted ORs (95% CI) for pancreatic cancer by plasma leptin, among subgroups\*

|  |  |  |  |
| --- | --- | --- | --- |
|  | Men |  | Women |
|  | Cases/controls | Per 5 ng/mL increase in plasma Leptin | *P*interaction |  | Cases/controls | Per 5 ng/mL increase in plasma leptin | *P*interaction |
| Overall  | 141/332 | 1.25 (1.02-1.54) |  |  | 314/676 | 0.98 (0.93-1.03) |  |
| Age at blood draw |  |  | 0.95 |  |  |  | 0.33 |
|  < median (men: 60 years; women 64 years) | 62/168 | 1.12 (0.78-1.60) |  |  | 159/370 | 0.99 (0.92-1.07) |  |
|  ≥ median | 79/164 | 1.31 (0.98-1.76) |  |  | 155/306 | 0.98 (0.90-1.05) |  |
| Time between blood collection and cancer diagnosis |  |  | 0.73 |  |  |  | 0.75 |
|  1 to < 10 years | 71/176 | 1.21 (0.90-1.63) |  |  | 242/490 | 0.99 (0.94-1.06) |  |
|  ≥ 10 years | 70/156 | 1.17 (0.85-1.61) |  |  | 72/186 | 0.99 (0.87-1.12) |  |
| Smoking status |  |  | 0.98 |  |  |  | 0.65 |
|  Never | 53/130 | 1.22 (0.83-1.81) |  |  | 136/305 | 0.98 (0.91-1.06) |  |
|  Past | 69/155 | 1.35 (0.98-1.86) |  |  | 134/288 | 0.99 (0.91-1.08) |  |
|  Current | 19/47 | 2.46 (0.94-6.45) |  |  | 41/75 | 0.90 (0.72-1.12) |  |
| BMI |  |  | 0.08 |  |  |  | 0.09 |
|  < 25 kg/m2 | 69/154 | 0.89 (0.57-1.39) |  |  | 127/315 | 0.90 (0.78-1.03) |  |
|  ≥ 25 kg/m2  | 72/178 | 1.49 (1.13-1.97) |  |  | 187/361 | 1.01 (0.95-1.07) |  |
| C-peptide levels |  |  | 0.67 |  |  |  | 0.64 |
|  < median (men: 2.0 ng/mL; women 1.7 ng/mL) | 51/161 | 1.16 (0.76-1.76) |  |  | 133/323 | 1.02 (0.93-1.14) |  |
|  ≥ median | 88/162 | 1.34 (1.00-1.78) |  |  | 180/328 | 0.98 (0.91-1.04) |  |
| Adiponectin levels |  |  | 0.16 |  |  |  | 0.11 |
|  < 4.4 µg/mL | 66/113 | 1.71 (1.14-2.55) |  |  | 69/100 | 1.03 (0.90-1.17) |  |
|  ≥ 4.4 µg/mL | 74/216 | 1.13 (0.85-1.50) |  |  | 245/568 | 0.97 (0.91-1.03) |  |
| Menopausal status | N/A |  |  |  | 0.52 |
|  Premenopausal |  |  |  |  | 24/81 | 0.96 (0.77-1.21) |  |
|  Postmenopausal |  |  |  |  | 290/595 | 1.00 (0.94-1.05) |  |
| HRT use | N/A |  |  |  | 0.86 |
|  Never |  |  |  |  | 109/207 | 0.97 (0.87-1.07) |  |
|  Ever |  |  |  |  | 181/388 | 0.99 (0.92-1.06) |  |

\* ORs and 95% CI were estimated by unconditional logistic regression adjusted for the matching factors including age (continuous), prospective cohort (HPFS, NHS, PHS, WHI, WHS), smoking status (never, past, current), fasting time (0-<4, 4-<8, 8-<12, ≥12 hours), and month/year of blood draw (2-month intervals), and other covariates, including race (White, Black, other), history of diabetes mellitus (yes, no), current multivitamin use (yes, no), plasma 25(OH)D levels (continuous), BMI (continuous), physical activity (continuous), plasma C-peptide levels (continuous), and plasma adiponectin levels (quartiles), excluding the stratifying variable. Tests for interaction were performed by the Wald test of cross-product terms, created by multiplying continuous leptin (5 ng increments) and categorical stratifying variable.

Abbreviations: 25(OH)D, 25-hydroxyvitamin D ; BMI, body mass index; CI, confidence ratio ; HPFS, Health Professionals Follow-up Study; HRT, hormone therapy use; OR, odds ratio; NHS, Nurses’ Health Study; PHS, Physicians’ Health Study; WHI, Women’s Health Initiative; WHS, Women’s Health Study

**Supplementary Table 6**. Association between SNPs at the *LEPR* gene and risk of pancreatic cancer among men

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Controls** | **Cases** | **Additive model** |
| **SNP** | **Minor allele** | **N** | **MAF (%)** | **N** | **MAF (%)** | **ORa****(95% CI)** | **Raw *P*-value** | **Corrected *P*-value** |
| rs2148683 | G | 328 | 0.43 | 127 | 0.54 | 1.50 (1.09-2.07) | 0.01 | 0.23 |
| rs12753193 | G | 328 | 0.40 | 127 | 0.34 | 0.74 (0.53-1.04) | 0.09 | 0.78 |
| rs6662904 | A | 328 | 0.45 | 127 | 0.48 | 1.28 (0.95-1.73) | 0.11 | 0.84 |
| rs1892534 | A | 328 | 0.39 | 127 | 0.34 | 0.77 (0.54-1.09) | 0.14 | 0.90 |
| rs4655537 | A | 326 | 0.34 | 126 | 0.36 | 1.18 (0.85-1.65) | 0.33 | 0.92 |
| rs4420065 | A | 328 | 0.39 | 128 | 0.35 | 0.81 (0.57-1.14) | 0.22 | 0.98 |
| rs12025906 | G | 327 | 0.17 | 127 | 0.15 | 0.78 (0.51-1.19) | 0.24 | 0.99 |
| rs6700896 | A | 326 | 0.39 | 126 | 0.35 | 0.77 (0.54-1.09) | 0.15 | 0.99 |
| rs11585329 | A | 327 | 0.15 | 127 | 0.18 | 1.28 (0.85-1.93) | 0.24 | 0.99 |
| rs9436737 | G | 325 | 0.13 | 127 | 0.17 | 1.29 (0.84-1.99) | 0.25 | 0.99 |
| rs10493380 | C | 326 | 0.17 | 127 | 0.18 | 1.19 (0.79-1.78) | 0.41 | 1.00 |
| rs3790424 | G | 328 | 0.26 | 128 | 0.24 | 0.85 (0.61-1.18) | 0.32 | 1.00 |
| rs6673324 | G | 327 | 0.49 | 127 | 0.52 | 1.16 (0.85-1.58) | 0.34 | 1.00 |
| rs2154381 | G | 326 | 0.28 | 128 | 0.25 | 0.86 (0.62-1.19) | 0.36 | 1.00 |
| rs9436746 | A | 328 | 0.38 | 127 | 0.37 | 0.86 (0.63-1.18) | 0.36 | 1.00 |
| rs9436747 | A | 327 | 0.35 | 126 | 0.35 | 0.94 (0.69-1.27) | 0.67 | 1.00 |
| rs11801408 | A | 328 | 0.21 | 127 | 0.20 | 0.90 (0.60-1.35) | 0.62 | 1.00 |
| rs41459646 | C | 326 | 0.18 | 127 | 0.15 | 0.85 (0.55-1.31) | 0.47 | 1.00 |
| rs2767485 | G | 325 | 0.20 | 127 | 0.21 | 1.05 (0.73-1.50) | 0.79 | 1.00 |
| rs9436301 | G | 325 | 0.26 | 125 | 0.26 | 0.97 (0.69-1.37) | 0.88 | 1.00 |
| rs7524834 | G | 329 | 0.46 | 127 | 0.46 | 1.08 (0.80-1.45) | 0.61 | 1.00 |
| rs9436748 | A | 327 | 0.42 | 127 | 0.42 | 1.03 (0.76-1.39) | 0.85 | 1.00 |
| rs10128072 | C | 327 | 0.16 | 128 | 0.14 | 0.82 (0.54-1.24) | 0.35 | 1.00 |
| rs7602 | A | 327 | 0.21 | 127 | 0.23 | 1.12 (0.79-1.59) | 0.51 | 1.00 |
| rs1887285 | G | 326 | 0.09 | 127 | 0.09 | 0.93 (0.55-1.57) | 0.78 | 1.00 |
| rs3828033 | A | 318 | 0.37 | 123 | 0.35 | 0.90 (0.65-1.25) | 0.53 | 1.00 |
| rs913199 | A | 327 | 0.46 | 127 | 0.51 | 1.10 (0.81-1.50) | 0.55 | 1.00 |
| rs3790431 | G | 324 | 0.24 | 127 | 0.24 | 1.04 (0.73-1.47) | 0.84 | 1.00 |
| rs3806318 | G | 325 | 0.25 | 127 | 0.25 | 0.98 (0.68-1.42) | 0.92 | 1.00 |
| rs2148682 | G | 327 | 0.33 | 127 | 0.35 | 0.95 (0.68-1.33) | 0.78 | 1.00 |
| rs3790436 | C | 327 | 0.45 | 127 | 0.47 | 1.03 (0.76-1.40) | 0.84 | 1.00 |
| rs17127601 | G | 326 | 0.14 | 126 | 0.16 | 1.29 (0.84-1.98) | 0.24 | 1.00 |

a ORs and 95% CI were estimated using conditional logistic regression, conditioning on matching factors including year of birth, prospective cohort (HPFS, NHS, PHS, WHI, WHS) which also conditions on gender, smoking status (never, past, current), fasting status (fasting, non fasting), and month/year of blood draw, and adjusted for race (White, Black, other), history of diabetes mellitus (yes, no), current multivitamin use (yes, no), plasma 25(OH)D (continuous), BMI (continuous), physical activity (continuous), plasma C-peptide (continuous) and plasma adiponectin (quartiles).

Abbreviations: 25(OH)D, 25-hydroxyvitamin D ; BMI, body mass index; CI, confidence interval; HPFS, Health Professionals Follow-up Study; MAF, minor allele frequency; NHS, Nurses’ Health Study; OR, odds ratio; PHS, Physicians’ Health Study; SNP, single nucleotide polymorphism; WHI, Women’s Health Initiative; WHS, Women’s Health Study

**Supplementary Table 7**. Genomic and functional support for rs10493380 and correlated (r2 ≥ 0.6) surrogate variants in HaploReg and Regulome DB

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Chr** | **pos (hg19)** | **LD** | **variant** | **Ref** | **Alt** | **AFR** | **AMR** | **ASN** | **EUR** | **Motifs** | **Selected eQTL** | **GENCODE** | **dbSNP** | **RegulomeDB** |
|
| **(r²)** | **(D')** | **freq** | **freq** | **freq** | **freq** | **changed** | **hits** | **genes** | **funct annot** | **score** |
| 1 | 66024233 | 0.6 | 0.93 | [rs202012285](http://www.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs202012285) | T | TG | 0.02 | 0.21 | 0.06 | 0.13 | 15 |  | LEPR | intronic | NA |
| 1 | 66036776 | 0.88 | 0.98 | [rs3790429](http://www.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs3790429) | T | A | 0.1 | 0.24 | 0.06 | 0.16 | 5 | *LEPROT*/*LEPR* in blood | LEPR | intronic | 7 |
| 1 | 66037984 | 0.85 | 0.98 | [rs70940803](http://www.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs70940803) | T | G | 0.05 | 0.23 | 0.05 | 0.16 | 14 |  | LEPR | intronic | NA |
| 1 | 66046117 | 1 | 1 | [**rs10493380**](http://www.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs10493380) | A | C | 0.07 | 0.25 | 0.06 | 0.17 | DMRT2, Ik-2 | *LEPROT*/*LEPR* in blood | LEPR | intronic | 6 |
| 1 | 66054003 | 0.96 | 1 | [rs61781283](http://www.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs61781283) | G | A | 0.09 | 0.26 | 0.06 | 0.18 | Pou2f2, RORalpha1 |  | LEPR | intronic | 6 |
| 1 | 66054038 | 0.96 | 1 | [rs61781284](http://www.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs61781284) | G | A | 0.09 | 0.26 | 0.06 | 0.18 | Maf, Pou2f2, RFX5 |   | LEPR | intronic | 7 |

No findings were noted for SiPhy cons, promoter histone marks, enhancer histone marks, DNASE hypersensitivity, bound proteins or NHGRI/EBI GWAS hits.

**Supplementary Table 8**. Association between single nucleotide polymorphisms at the *LEPR* gene and plasma leptin among controls

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  |
|  |  | **Women** | **Men** |
| **SNP** | **Minor allele** | **Count** | **Coefficient\*** | **Raw*****P*-value** | **Corrected *P*-value** | **Count** | **Coefficient\*** | **Raw*****P*-value** | **Corrected*****P*-value** |
| rs9436737 | G | 593 | -0.091 | 0.12 | 0.88 | 306 | -0.036 | 0.66 | 1.00 |
| rs11801408 | A | 600 | -0.077 | 0.15 | 0.92 | 309 | -0.026 | 0.71 | 1.00 |
| rs41459646 | C | 597 | -0.078 | 0.15 | 0.93 | 307 | -0.053 | 0.47 | 1.00 |
| rs7602 | A | 598 | -0.070 | 0.17 | 0.95 | 308 | 0.054 | 0.41 | 1.00 |
| rs7524834 | G | 602 | 0.054 | 0.18 | 0.96 | 310 | 0.000 | 1.00 | 1.00 |
| rs3790424 | G | 598 | 0.054 | 0.23 | 0.98 | 309 | -0.029 | 0.64 | 1.00 |
| rs12025906 | G | 600 | 0.062 | 0.21 | 0.98 | 308 | 0.013 | 0.85 | 1.00 |
| rs12753193 | G | 602 | -0.006 | 0.89 | 1.00 | 309 | -0.032 | 0.56 | 1.00 |
| rs4420065 | A | 594 | 0.003 | 0.94 | 1.00 | 309 | 0.004 | 0.95 | 1.00 |
| rs2767485 | G | 593 | -0.051 | 0.34 | 1.00 | 306 | 0.132 | 0.06 | 0.62 |
| rs6700896 | A | 598 | 0.001 | 0.98 | 1.00 | 308 | -0.008 | 0.89 | 1.00 |
| rs1892534 | A | 596 | -0.008 | 0.86 | 1.00 | 309 | -0.003 | 0.96 | 1.00 |
| rs2154381 | G | 597 | 0.036 | 0.41 | 1.00 | 307 | -0.029 | 0.64 | 1.00 |
| rs9436747 | A | 597 | 0.015 | 0.72 | 1.00 | 308 | -0.027 | 0.64 | 1.00 |
| rs3790431 | G | 595 | -0.045 | 0.37 | 1.00 | 305 | -0.033 | 0.61 | 1.00 |
| rs6673324 | G | 594 | -0.018 | 0.68 | 1.00 | 308 | 0.071 | 0.23 | 0.98 |
| rs2148682 | G | 598 | -0.015 | 0.72 | 1.00 | 308 | 0.055 | 0.34 | 1.00 |
| rs913199 | A | 596 | -0.003 | 0.95 | 1.00 | 308 | 0.004 | 0.94 | 1.00 |
| rs10128072 | C | 593 | -0.051 | 0.37 | 1.00 | 308 | 0.059 | 0.41 | 1.00 |
| rs6662904 | A | 591 | 0.034 | 0.41 | 1.00 | 309 | -0.008 | 0.88 | 1.00 |
| rs9436746 | A | 596 | 0.020 | 0.63 | 1.00 | 309 | -0.068 | 0.23 | 0.98 |
| rs3806318 | G | 597 | -0.004 | 0.93 | 1.00 | 306 | 0.049 | 0.44 | 1.00 |
| rs9436301 | G | 593 | -0.051 | 0.30 | 1.00 | 306 | 0.090 | 0.16 | 0.93 |
| rs3828033 | A | 592 | 0.024 | 0.56 | 1.00 | 299 | 0.010 | 0.88 | 1.00 |
| rs10493380 | C | 589 | -0.037 | 0.50 | 1.00 | 307 | -0.057 | 0.43 | 1.00 |
| rs17127601 | G | 592 | -0.032 | 0.59 | 1.00 | 307 | -0.026 | 0.74 | 1.00 |
| rs2148683 | G | 598 | 0.040 | 0.30 | 1.00 | 309 | 0.044 | 0.41 | 1.00 |
| rs11585329 | A | 598 | -0.028 | 0.62 | 1.00 | 308 | 0.046 | 0.55 | 1.00 |
| rs3790436 | C | 596 | -0.001 | 0.99 | 1.00 | 308 | 0.023 | 0.67 | 1.00 |
| rs9436748 | A | 597 | 0.023 | 0.59 | 1.00 | 308 | 0.021 | 0.71 | 1.00 |
| rs4655537 | A | 597 | 0.022 | 0.62 | 1.00 | 307 | 0.067 | 0.26 | 0.99 |
| rs1887285 | G | 600 | -0.022 | 0.75 | 1.00 | 307 | 0.108 | 0.25 | 0.99 |

\*Association of the SNP using an additive genetic model with log transformed plasma leptin in linear regression models. Adjusted for matching factors including age at blood collection (years, continuous), cohort (HPFS, NHS, PHS, WHI, WHS; also adjusts for gender), fasting status (fasting, non-fasting), smoking status (never, past, current) and month/year of blood draw.

Abbreviations: HPFS, Health Professionals Follow-up Study; NHS, Nurses’ Health Study; PHS, Physicians’ Health Study; SNP, single nucleotide polymorphism; WHI, Women’s Health Initiative; WHS, Women’s Health Study

**Supplementary Figure 1**. Association results, recombination hotspots and linkage disequilibrium for single nucleotide polymorphisms at the *LEPR* gene region among women.

**LEPR regional plot**



Top, hash marks indicate single nucleotide polymorphisms (SNPs) at the *LEPR* gene region. In the middle, association results between SNPs and risk of pancreatic cancer among women are plotted against –log10 P values (left Y axis). Each dot corresponds to one SNP; color indicates linkage disequilibrium (r2) with the statistically significant SNP (rs10493380, shown as purple diamond). Overlaid is 1000G EUR recombination rate in cM/Mb (right axis, blue line).