**Supplementary Table 1 Alternate Allele Frequencies of the Most Significant Markers from a Series of Conditional GWAS in Sub-populations**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Step** | **Marker** | | **Gene** | | **Ref allele** | | **Alt allele** | | **African**  **(n=379)** | | **Asian**  **(n=2,017)** | **Caucasian**  **(n=4,631)** | **Native American**  **(n=189)** | **Caucasian and Native American (n=939)** | **Caucasian, African and Native American**  **(n=2,282)** | **Total**  **(n=10,542)** |
| *1* | *rs72728755* | | 8q24 | | T | | A | | 0.15 | | 0.03 | 0.23 | 0.04 | 0.06 | 0.19 | 0.16 |
| *2* | *rs7552* | | *FAM49A* | | A | | G | | 0.68 | | 0.74 | 0.34 | 0.73 | 0.63 | 0.52 | 0.50 |
| *3* | *rs2235370* | | *TRAF3IP3* | | C | | A | | - | | 0.18 | 0.04 | 0.40 | 0.35 | 0.18 | 0.13 |
| *4* | *rs16957821* | | *NTN1* | | C | | G | | 0.41 | | 0.18 | 0.19 | 0.35 | 0.37 | 0.30 | 0.24 |
| *5* | *rs12600562* | | *LRRC37A2* | | G | | T | | 0.48 | | 0.38 | 0.59 | 0.46 | 0.52 | 0.55 | 0.53 |
| *6* | *rs12543318* | |  | | C | | A | | 0.68 | | 0.44 | 0.62 | 0.49 | 0.48 | 0.49 | 0.55 |
| *7* | *rs3845903* | | *LRIG1* | | C | | T | | 0.80 | | 0.94 | - | 0.99 | 0.98 | 0.97 | 0.97 |
| *8* | *rs10778143* | | *CHPT1* | | A | | C | | 0.63 | | 0.59 | 0.25 | 0.20 | 0.21 | 0.25 | 0.33 |
| *9* | *rs6929507* | | *GMDS* | | T | | C | | 0.15 | | 0.002 | - | - | 0.007 | 0.02 | 0.01 |
| *10* | *rs138322543* | | *TRMO* | | CCACCA | | C | | 0.77 | | 0.91 | 0.66 | 0.66 | 0.67 | 0.72 | 0.73 |
|  |  |  | |  | |  | |  | |

**Supplementary Table 2 Results with suggestive evidence of association from the gene-based association study**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Gene | | Ensembl Transcript ID | Chr; Pos | Beta (S.E.) | z | p-value |
| *Whole Blood* | | | | | | |
|  | *IRGM* | ENSG00000237693.4 | 5; 150,846,523-150,900,736 | -3.1560 (0.7636) | -4.1328 | 3.58E-05 |
|  | *OSBPL11* | ENSG00000144909.7 | 3; 125,528,858-125,595,090 | -2.0234 (0.4949) | -4.0887 | 4.34E-05 |
|  | *SYCE3* | ENSG00000217442.3 | 22; 50,551,112-50,562,905 | 3.3258 (0.8238) | 4.0371 | 5.41E-05 |
|  | *ALDH5A1* | ENSG00000112294.8 | 6; 24,494,852-24,537,207 | -1.8371 (0.4635) | -3.9633 | 7.39E-05 |
|  | *PRSS45* | ENSG00000188086.8 | 3;46,742,092-46,744,755 | 2.9393 (0.7508) | 3.9150 | 9.04E-05 |
|  | | | | | | |
| *Skeletal Muscle* | | | | | | |
|  | *ATP6V1D* | ENSG00000100554.7 | 14; 67,294,371-67,360,265 | 2.4795 (0.5800) | 4.2750 | 1.91E-05 |
|  | *HSD17B12* | ENSG00000149084.7 | 11; 43,680,558-43,856,617 | -0.4123 (0.0991) | -4.1609 | 3.17E-05 |
|  | *MIF-AS1* | ENSG00000218537.1 | 22; 23,894,426-23,898,930 | 0.7923 (0.1948) | 4.0666 | 4.77E-05 |
|  | *CD151* | ENSG00000177697.13 | 11; 832,843-839,831 | -0.718 (0.1769) | -4.0581 | 4.95E-05 |
|  | *SQOR* | ENSG00000137767.9 | 15; 45,631,148-45,691,294 | -2.9416 (0.7321) | -4.0179 | 5.87E-05 |
|  | *LYSMD1* | ENSG00000163155.7 | 1; 151,159,748-151,165,948 | 1.7668 (0.4436) | 3.9829 | 6.81E-05 |
|  | *DHX30* | ENSG00000132153.10 | 3; 47,802,909-47,850,195 | 6.5430 (1.6673) | 3.9242 | 8.70E-05 |
|  | | | | | | |
| *Adipose (Subcutaneous)* | | | | | | |
|  | *ALX4* | ENSG00000052850.5 | 11; 44,260,444-44,310,166 | -0.9276 (0.2179) | -4.2564 | 2.08E-05 |
|  | *KDM1B* | ENSG00000165097.9 | 6; 18,155,329-18,223,853 | -1.4586 (0.3619) | -4.0300 | 5.58E-05 |
|  | *SFSWAP* | ENSG00000061936.5 | 12; 131,711,081-131,799,737 | -2.0699 (0.5166) | -4.0065 | 6.16E-05 |
|  | *GSTT2B* | ENSG00000133433.6 | 22; 23,957,414-23,961,186 | -1.0478 (0.2674) | -3.9185 | 8.91E-05 |
|  | | | | | | |
| *Adipose (Visceral)* | | | | | | |
|  | *MX2* | ENSG00000183486.8 | 21; 41,361,943-41,409,390 | -2.0284 (0.4610) | -4.4001 | 1.08E-05 |
|  | *GSTP1* | ENSG00000084207.11 | 11; 67,583,595-67,586,656 | 1.8047 (0.4145) | 4.3535 | 1.34E-05 |
|  | *ADAMTS13* | ENSG00000160323.14 | 9; 33,414,358-133,459,402 | -1.2160 (0.3068) | -3.9634 | 7.39E-05 |
|  | *HSD17B12* | ENSG00000149084.7 | 11; 43,680,558-43,856,617 | -0.3960 (0.1005) | -3.9410 | 8.11E-05 |
|  | *CNTNAP1* | ENSG00000108797.7 | 17; 42,682,613-42,699,814 | -1.1957 (0.3065) | -3.9012 | 9.57E-05 |
| Chr: Chromosome, Pos: Position (basepair; bp) | | | | | | |

**Supplementary Table 3 Candidate Genes in the GTEx database**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene** | **Locus** | **Phenotype** | **Study Type** | **Reference** |
| *ARHGAP29* | 1p22.1 | CL/P | GWAS | [15, 17, 19] |
| *GRHL3* | 1p36.11 | CP | GWAS, GWAS replication | [14, 18] |
| *IRF6* | 1q32.2 | CL/P | Linkage, GWAS, GWAS replication | [8, 9, 11–15, 17, 19, 23] |
| *TGFA* | 2p13 | CL/P | Linkage | [9] |
| *THADA* | 2p21 | CL/P | GWAS meta-analysis | [16] |
| *FAM49A* | 2p24 | CL/P | GWAS | [17, 19] |
| *COL8A1* | 3q12 | CL/P | GWAS, GWAS replication, GWAS meta-analysis | [14, 19, 23] |
| *TP63* | 3q27–28 | CL/P | Linkage, GWAS | [9, 19] |
| *SHROOM3* | 4q21.1 | CL/P | GWAS meta-analysis | [19] |
| *PIK3R1* | 5q13.1 | CL/P | GWAS meta-analysis | [19] |
| *NRG1* | 8p12 | CL/P | GWAS meta-analysis | [19] |
| *BAALC* | 8q22.3 | CP & multivitamins | GWAS X E | [20] |
| *SMC2* | 9q31.1 | CP & maternal alcohol | GWAS X E | [20] |
| *TBK1* | 12q14 | CP & maternal smoking | GWAS X E | [20] |
| *KRT18* | 12q13.13 | CL/P | GWAS meta-analysis | [19] |
| *PAX9* | 14q21–24 | CL/P | Linkage | [8, 9] |
| *TGFB3* |
| *TPM1* | 15q22 | CL/P | GWAS meta-analysis | [16] |
| *ARID3B* | 15q24 | CL/P | GWAS | [17, 19] |
| *CREBBP* | 16p13 | CL/P | GWAS | [27] |
| *CRISPLD2* | 16q24 | CL/P | Linkage | [9] |
| *WNT9B* | 17q21.32 | CP | GWAS meta-analysis | [19] |
| *GOSR2* |
| *TANC2* | 17q23.2 | CL/P | GWAS | [17] |
| *ZNF236* | 18q22 | CP & maternal smoking | GWAS X E | [20] |
| *RHPN2* | 19q13.11 | CL/P | GWAS | [17] |
| *MAFB* | 20q12 | CL/P | GWAS | [15, 17, 19] |

**Supplementary Table 4 Candidate Gene Study Using Predicted Expression Levels**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Gene** | **Transcript ID** | **Chr; Pos** | **Beta (SE)** | **z** | **p** |
| **Whole Blood** | | | | | | |
|  | *ARID3B* | ENSG00000179361 | 15;74,541,177-74,598,131 | -1.54 (0.59) | -2.61 | 0.0090 |
|  | *CRISPLD2* | ENSG00000103196 | 16;84,819,984-84,920,768 | 0.64 (0.51) | 1.27 | 0.2033 |
|  | *TBK1* | ENSG00000183735 | 12;64,451,880-64,502,108 | -0.48 (0.41) | -1.16 | 0.2448 |
|  | *IRF6* | ENSG00000117595 | 1;209,785,623-209,806,175 | 0.17 (0.16) | 1.07 | 0.2858 |
|  | *SMC2* | ENSG00000136824 | 9;104,094,260-104,141,417 | 0.44 (0.46) | 0.96 | 0.3348 |
|  | *BAALC* | ENSG00000164929 | 8;103,140,710-103,230,305 | 0.40 (0.43) | 0.92 | 0.3509 |
|  | *TGFB3* | ENSG00000119699 | 14;75,958,099-75,982,991 | -0.27 (0.36) | -0.73 | 0.4658 |
|  | *TGFA* | ENSG00000163235 | 2;70,447,280-70,554,193 | 0.27 (0.37) | 0.73 | 0.4662 |
|  | *KRT18* | ENSG00000111057 | 12;52,948,871-52,952,901 | -2.99(10.41) | -0.29 | 0.7743 |
|  | *TANC2* | ENSG00000170921 | 17;63,009,556-63,427,699 | 1.94 (8.53) | 0.23 | 0.8200 |
|  | *NRG1* | ENSG00000157168 | 8;31,639,386-32,767,959 | -0.02 (0.22) | -0.11 | 0.9104 |
|  | *ZNF236* | ENSG00000130856 | 18;76,822,607-76,970,727 | -0.02 (0.49) | -0.05 | 0.9578 |
| **Skeletal Muscle** | | | | | | |
|  | *RHPN2* | ENSG00000131941 | 19; 32,978,593-33,064,888 | -1.9960 (0.64) | -3.11 | 0.0019\* |
|  | *SHROOM3* | ENSG00000138771 | 4; 76,435,100-76,783,253 | 0.6720 (0.27) | 2.46 | 0.0138 |
|  | *PIK3R1* | ENSG00000145675 | 5; 68,215,720-68,301,821 | 1.2415 (0.51) | 2.45 | 0.0143 |
|  | *TBK1* | ENSG00000183735 | 12; 64,451,880-64,502,108 | -0.5811 (0.37) | -1.56 | 0.1193 |
|  | *COL8A1* | ENSG00000144810 | 3; 99,638,475-99,799,226 | 0.2524 (0.25) | 0.99 | 0.3205 |
|  | *TGFA* | ENSG00000163235 | 2; 70,447,280-70,554,193 | 0.3384 (0.37) | 0.91 | 0.3613 |
|  | *TANC2* | ENSG00000170921 | 17; 63,009,556-63,427,699 | -0.3166 (0.58) | -0.57 | 0.5701 |
|  | *ZNF236* | ENSG00000130856 | 18; 76,822,607-76,970,727 | -0.4588 (0.84) | -0.54 | 0.5866 |
|  | *GOSR2* | ENSG00000108433 | 17; 46,923,075-46,975,524 | -0.1294 (0.26) | -0.51 | 0.6119 |
|  | *SMC2* | ENSG00000136824 | 9; 104,094,260-104,141,417 | -0.4881 (1.05) | -0.46 | 0.6431 |
|  | *MAFB* | ENSG00000204103 | 20; 40,685,848-40,689,240 | 0.1451 (0.65) | 0.23 | 0.8237 |
| **Adipose (Subcutaneous)** | | | | | | |
|  | *RHPN2* | ENSG00000131941 | 19; 32,978,593-33,064,888 | -0.61 (0.19) | -3.19 | 0.0014\* |
|  | *IRF6* | ENSG00000117595 | 1; 209,785,623-209,806,175 | 0.34 (0.20) | 1.69 | 0.0910 |
|  | *TP63* | ENSG00000073282 | 3; 189,631,416-189,897,279 | -0.36 (0.39) | -0.94 | 0.3497 |
|  | *THADA* | ENSG00000115970 | 2; 43,230,836-43,596,046 | 0.32 (0.48) | 0.67 | 0.5014 |
|  | *TGFB3* | ENSG00000119699 | 14; 75,958,099-75,982,991 | -0.18 (0.42) | -0.44 | 0.6582 |
|  | *TPM1* | ENSG00000140416 | 15; 63,042,632-63,071,915 | 0.07 (0.22) | 0.34 | 0.7336 |
|  | *KRT18* | ENSG00000111057 | 12; 52,948,871-52,952,901 | -261.49 (2.18) | 3.43 | NA |
| **Adipose (Visceral)** | | | | | | |
|  | *SHROOM3* | ENSG00000138771 | 4; 76,435,100-76,783,253 | -1.28 (0.58) | -2.22 | 0.0262 |
|  | *ARHGAP29* | ENSG00000137962 | 1; 94,148,988-94,275,068 | 0.29 (0.22) | 1.34 | 0.1808 |
|  | *ZNF236* | ENSG00000130856 | 18; 76,822,607-76,970,727 | -0.45 (0.39) | -1.15 | 0.2495 |
|  | *TPM1* | ENSG00000140416 | 15; 63,042,632-63,071,915 | -0.11 (0.41) | -0.27 | 0.7847 |
|  | *THADA* | ENSG00000115970 | 2; 43,230,836-43,596,046 | -0.14 (0.51) | -0.27 | 0.7885 |
|  | *IRF6* | ENSG00000117595 | 1; 209,785,623-209,806,175 | 0.04 (0.27) | 0.16 | 0.8708 |
|  | *COL8A1* | ENSG00000144810 | 3; 99,638,475-99,799,226 | -0.0064 (0.31) | -0.02 | 0.9836 |
|  | *SHROOM3* | ENSG00000138771 | 4; 76,435,100-76,783,253 | -1.28 (0.58) | -2.22 | 0.0262 |
|  | Chr: Chromosome, Pos: Position (basepair; bp) | | | | | |