**Supplemental Tables**

Supplemental Table S1. Genetic information of the genotyped SNPs.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| CHR | POS | SNP | A1 | A2 | FUNC | LOCI | MAF | HWE |
| 7 | 150329343 | rs147530050 | T | C | near-gene-5 | *RARRES2* | 0.05  | 0.34  |
| 7 | 150333889 | rs76735405 | G | A | near-gene-5 | *RARRES2* | 0.13  | 1.00  |
| 7 | 150334397 | rs143367396 | A | G | near-gene-5 | *RARRES2* | 0.05  | 0.69  |
| 7 | 150337862 | rs3735168 | A | G | near-gene-5 | *RARRES2* | 0.10  | 0.66  |
| 7 | 150338094 | rs11538922 | T | C | near-gene-5 | *RARRES2* | 0.25  | 0.92  |
| 7 | 150338370 | rs1047586 | G | T | intron | *RARRES2* | 0.25  | 1.00  |
| 7 | 150338437 | rs4721 | G | T | intron | *RARRES2* | 0.42  | 0.65  |
| 19 | 7669160 | rs3219176 | T | C | intron | *RETN* | 0.07  | 1.00  |
| 19 | 7669625 | rs3745367 | A | G | intron | *RETN* | 0.35  | 1.00  |
| 19 | 7670065 | rs3219178 | G | C | intron | *RETN* | 0.25  | 0.71  |
| 19 | 7670203 | rs10402265 | G | C | intron | *RETN* | 0.35  | 0.79  |
| 19 | 7670411 | rs3745368 | A | G | untranslated-3 | *RETN* | 0.18  | 0.94  |

CHR: chromosome; POS:position; A1: minor allele; A2: major allele; FUNC: function; MAF: minor allele frequency; HWE: Hardy-Weinberg Equilibrium.

Supplemental Table S2. Parameters setting for power analysis

|  |  |  |
| --- | --- | --- |
| Parameters | Values | Note |
| No. of cases | 1,180 | No. of cases in this study |
| No. of controls | 2,560 | No. of controls in this study |
| Significance level | 0.004 | 0.05/12 |
| Prevalence | 0.16 | Global pooled prevalence of OA  |
| Disease allele frequency | 0.2 | Average minor allele frequency |

Supplemental Table S3. Full results of single marker based association analyses.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| CHR | SNP | A1 | A2 | TEST | AFF | UNAFF | χ2 | DF | *P* Values |
| 7 | rs1047586 | G | T | GENO | 68/439/673 | 159/957/1444 | 0.33  | 2 | 0.8477  |
| 7 | rs1047586 | G | T | ALLELIC | 575/1785 | 1275/3845 | 0.25  | 1 | 0.6163  |
| 7 | rs1047586 | G | T | DOM | 507/673 | 1116/1444 | 0.13  | 1 | 0.7189  |
| 7 | rs1047586 | G | T | REC | 68/1112 | 159/2401 | 0.28  | 1 | 0.5937  |
| 7 | rs11538922 | T | C | GENO | 78/448/654 | 161/968/1431 | 0.17  | 2 | 0.9194  |
| 7 | rs11538922 | T | C | ALLELIC | 604/1756 | 1290/3830 | 0.14  | 1 | 0.7130  |
| 7 | rs11538922 | T | C | DOM | 526/654 | 1129/1431 | 0.07  | 1 | 0.7859  |
| 7 | rs11538922 | T | C | REC | 78/1102 | 161/2399 | 0.14  | 1 | 0.7091  |
| 7 | rs143367396 | A | G | GENO | 5/120/1055 | 8/251/2301 | 0.42  | 2 | 0.8121  |
| 7 | rs143367396 | A | G | ALLELIC | 130/2230 | 267/4853 | 0.28  | 1 | 0.5986  |
| 7 | rs143367396 | A | G | DOM | 125/1055 | 259/2301 | 0.20  | 1 | 0.6558  |
| 7 | rs143367396 | A | G | REC | 5/1175 | 8/2552 | 0.29  | 1 | 0.5912  |
| 7 | rs147530050 | T | C | GENO | 4/118/1058 | 10/261/2289 | NA | NA | NA |
| 7 | rs147530050 | T | C | ALLELIC | 126/2234 | 281/4839 | 0.07  | 1 | 0.7914  |
| 7 | rs147530050 | T | C | DOM | 122/1058 | 271/2289 | NA | NA | NA |
| 7 | rs147530050 | T | C | REC | 4/1176 | 10/2550 | NA | NA | NA |
| 7 | rs3735168 | A | G | GENO | 16/219/945 | 28/461/2071 | 0.67  | 2 | 0.7141  |
| 7 | rs3735168 | A | G | ALLELIC | 251/2109 | 517/4603 | 0.51  | 1 | 0.4763  |
| 7 | rs3735168 | A | G | DOM | 235/945 | 489/2071 | 0.34  | 1 | 0.5584  |
| 7 | rs3735168 | A | G | REC | 16/1164 | 28/2532 | 0.48  | 1 | 0.4895  |
| 7 | rs4721 | G | T | GENO | 254/573/353 | 412/1244/904 | 20.38  | 2 | 3.75E-05 |
| 7 | rs4721 | G | T | ALLELIC | 1081/1279 | 2068/3052 | 19.43  | 1 | 1.05E-05 |
| 7 | rs4721 | G | T | DOM | 827/353 | 1656/904 | 10.54  | 1 | 0.0012  |
| 7 | rs4721 | G | T | REC | 254/926 | 412/2148 | 16.28  | 1 | 5.46E-05 |
| 7 | rs76735405 | G | A | GENO | 16/260/904 | 41/568/1951 | 0.35  | 2 | 0.8415  |
| 7 | rs76735405 | G | A | ALLELIC | 292/2068 | 650/4470 | 0.15  | 1 | 0.6961  |
| 7 | rs76735405 | G | A | DOM | 276/904 | 609/1951 | 0.07  | 1 | 0.7895  |
| 7 | rs76735405 | G | A | REC | 16/1164 | 41/2519 | 0.32  | 1 | 0.5688  |
| 19 | rs10402265 | G | C | GENO | 144/540/496 | 305/1167/1088 | 0.10  | 2 | 0.9497  |
| 19 | rs10402265 | G | C | ALLELIC | 828/1532 | 1777/3343 | 0.10  | 1 | 0.7500  |
| 19 | rs10402265 | G | C | DOM | 684/496 | 1472/1088 | 0.07  | 1 | 0.7886  |
| 19 | rs10402265 | G | C | REC | 144/1036 | 305/2255 | 0.06  | 1 | 0.8003  |
| 19 | rs3219176 | T | C | GENO | 8/156/1016 | 12/328/2220 | 0.80  | 2 | 0.6702  |
| 19 | rs3219176 | T | C | ALLELIC | 172/2188 | 352/4768 | 0.42  | 1 | 0.5153  |
| 19 | rs3219176 | T | C | DOM | 164/1016 | 340/2220 | 0.26  | 1 | 0.6076  |
| 19 | rs3219176 | T | C | REC | 8/1172 | 12/2548 | 0.66  | 1 | 0.4149  |
| 19 | rs3219178 | G | C | GENO | 67/446/667 | 156/968/1436 | 0.26  | 2 | 0.8777  |
| 19 | rs3219178 | G | C | ALLELIC | 580/1780 | 1280/3840 | 0.16  | 1 | 0.6936  |
| 19 | rs3219178 | G | C | DOM | 513/667 | 1124/1436 | 0.06  | 1 | 0.8047  |
| 19 | rs3219178 | G | C | REC | 67/1113 | 156/2404 | 0.25  | 1 | 0.6178  |
| 19 | rs3745367 | A | G | GENO | 144/543/493 | 323/1172/1065 | 0.13  | 2 | 0.9386  |
| 19 | rs3745367 | A | G | ALLELIC | 831/1529 | 1818/3302 | 0.06  | 1 | 0.8036  |
| 19 | rs3745367 | A | G | DOM | 687/493 | 1495/1065 | 0.01  | 1 | 0.9182  |
| 19 | rs3745367 | A | G | REC | 144/1036 | 323/2237 | 0.13  | 1 | 0.7220  |
| 19 | rs3745368 | A | G | GENO | 58/387/735 | 72/722/1766 | 21.44  | 2 | 2.21E-05 |
| 19 | rs3745368 | A | G | ALLELIC | 503/1857 | 866/4254 | 20.91  | 1 | 4.81E-06 |
| 19 | rs3745368 | A | G | DOM | 445/735 | 794/1766 | 16.35  | 1 | 5.27E-05 |
| 19 | rs3745368 | A | G | REC | 58/1122 | 72/2488 | 10.64  | 1 | 0.0011  |

CHR: chromosome; GENO: genotyic analyses; A1:minor allele; A2: major allele; AFF: cases; UNAFF: controls; ALLELIC: allelic analyses; DOM: dominant mode; REC: recessive mode; DF: degree of freedom.

Supplemental Table S4. eQTL signals of SNP rs4721 on gene *RARRES2* in multiple types of human tissues.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Gene Symbol | SNP | *P* Value | NES | T-statistic | Tissue |
| *RARRES2* | rs4721 | 1.10E-13 | 0.23  | 7.60  | Adipose - Subcutaneous |
| *RARRES2* | rs4721 | 1.10E-04 | 0.11  | 3.90  | Adipose - Visceral (Omentum) |
| *RARRES2* | rs4721 | 0.04  | 0.10  | 2.10  | Adrenal Gland |
| *RARRES2* | rs4721 | 1.30E-08 | 0.24  | 5.80  | Artery - Aorta |
| *RARRES2* | rs4721 | 0.04  | 0.13  | 2.10  | Artery - Coronary |
| *RARRES2* | rs4721 | 4.40E-10 | 0.15  | 6.40  | Artery - Tibial |
| *RARRES2* | rs4721 | 0.14  | -0.07  | -1.50  | Brain - Amygdala |
| *RARRES2* | rs4721 | 0.22  | -0.06  | -1.20  | Brain - Anterior cingulate cortex (BA24) |
| *RARRES2* | rs4721 | 0.70  | 0.01  | 0.38  | Brain - Caudate (basal ganglia) |
| *RARRES2* | rs4721 | 0.42  | 0.04  | 0.80  | Brain - Cerebellar Hemisphere |
| *RARRES2* | rs4721 | 0.78  | 0.01  | 0.28  | Brain - Cerebellum |
| *RARRES2* | rs4721 | 0.67  | -0.02  | -0.42  | Brain - Cortex |
| *RARRES2* | rs4721 | 0.37  | -0.04  | -0.90  | Brain - Frontal Cortex (BA9) |
| *RARRES2* | rs4721 | 0.42  | -0.04  | -0.80  | Brain - Hippocampus |
| *RARRES2* | rs4721 | 0.98  | 0.00  | -0.02  | Brain - Hypothalamus |
| *RARRES2* | rs4721 | 0.85  | 0.01  | 0.18  | Brain - Nucleus accumbens (basal ganglia) |
| *RARRES2* | rs4721 | 0.92  | 0.00  | 0.10  | Brain - Putamen (basal ganglia) |
| *RARRES2* | rs4721 | 0.02  | -0.17  | -2.50  | Brain - Spinal cord (cervical c-1) |
| *RARRES2* | rs4721 | 0.91  | 0.01  | 0.12  | Brain - Substantia nigra |
| *RARRES2* | rs4721 | 8.40E-07 | 0.15  | 5.00  | Breast - Mammary Tissue |
| *RARRES2* | rs4721 | 2.00E-22 | 0.32  | 10.00  | Cells - Cultured fibroblasts |
| *RARRES2* | rs4721 | 0.05  | -0.19  | -2.00  | Cells - EBV-transformed lymphocytes |
| *RARRES2* | rs4721 | 0.02  | 0.09  | 2.30  | Colon - Sigmoid |
| *RARRES2* | rs4721 | 7.70E-03 | -0.07  | -2.70  | Colon - Transverse |
| *RARRES2* | rs4721 | 0.21  | 0.03  | 1.20  | Esophagus - Mucosa |
| *RARRES2* | rs4721 | 1.00E-05 | 0.11  | 4.50  | Esophagus - Muscularis |
| *RARRES2* | rs4721 | 0.93  | 0.00  | 0.08  | Heart - Atrial Appendage |
| *RARRES2* | rs4721 | 5.60E-04 | 0.13  | 3.50  | Heart - Left Ventricle |
| *RARRES2* | rs4721 | - | - | - | Kidney - Medulla |
| *RARRES2* | rs4721 | 0.76  | 0.02  | 0.30  | Liver |
| *RARRES2* | rs4721 | 0.15  | -0.03  | -1.40  | Lung |
| *RARRES2* | rs4721 | 0.18  | 0.09  | 1.30  | Minor Salivary Gland |
| *RARRES2* | rs4721 | 1.10E-17 | 0.21  | 8.80  | Muscle - Skeletal |
| *RARRES2* | rs4721 | 1.10E-17 | 0.16  | 8.90  | Nerve - Tibial |
| *RARRES2* | rs4721 | 0.13  | -0.08  | -1.50  | Ovary |
| *RARRES2* | rs4721 | 5.60E-09 | -0.22  | -6.00  | Pancreas |
| *RARRES2* | rs4721 | 0.01  | -0.10  | -2.50  | Pituitary |
| *RARRES2* | rs4721 | 0.03  | -0.06  | -2.10  | Prostate |
| *RARRES2* | rs4721 | 1.40E-03 | 0.09  | 3.20  | Skin - Not Sun Exposed (Suprapubic) |
| *RARRES2* | rs4721 | 1.80E-05 | 0.10  | 4.30  | Skin - Sun Exposed (Lower leg) |
| *RARRES2* | rs4721 | 0.68  | -0.01  | -0.41  | Small Intestine - Terminal Ileum |
| *RARRES2* | rs4721 | 0.90  | 0.00  | -0.13  | Spleen |
| *RARRES2* | rs4721 | 0.01  | -0.07  | -2.50  | Stomach |
| *RARRES2* | rs4721 | 0.10  | 0.04  | 1.60  | Testis |
| *RARRES2* | rs4721 | 0.29  | 0.03  | 1.10  | Thyroid |
| *RARRES2* | rs4721 | 0.67  | -0.03  | -0.43  | Uterus |
| *RARRES2* | rs4721 | 0.18  | -0.05  | -1.40  | Vagina |
| *RARRES2* | rs4721 | 0.92  | 2.90E-03 | 0.10  | Whole Blood |

NES: normalized effect size. Threshold of P values was 0.05/48≈0.001.

Supplemental Table S5. eQTL signals of SNP rs3745368 on gene *RETN* in multiple types of human tissues.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Gene | SNP | *P* Value | NES | T-statistic | Tissue |
| *RETN* | rs3745368 | 0.26  | -0.11  | -1.10  | Adipose - Subcutaneous |
| *RETN* | rs3745368 | 0.16  | -0.14  | -1.40  | Adipose - Visceral (Omentum) |
| *RETN* | rs3745368 | 0.42  | 0.15  | 0.81  | Adrenal Gland |
| *RETN* | rs3745368 | 0.03  | -0.30  | -2.20  | Artery - Aorta |
| *RETN* | rs3745368 | 0.58  | 0.09  | 0.56  | Artery - Coronary |
| *RETN* | rs3745368 | 0.08  | -0.20  | -1.80  | Artery - Tibial |
| *RETN* | rs3745368 | 0.09  | 0.46  | 1.70  | Brain - Amygdala |
| *RETN* | rs3745368 | 0.35  | -0.23  | -0.95  | Brain - Anterior cingulate cortex (BA24) |
| *RETN* | rs3745368 | 0.60  | -0.12  | -0.52  | Brain - Caudate (basal ganglia) |
| *RETN* | rs3745368 | 0.52  | -0.12  | -0.64  | Brain - Cortex |
| *RETN* | rs3745368 | 0.52  | 0.12  | 0.65  | Brain - Frontal Cortex (BA9) |
| *RETN* | rs3745368 | 0.92  | -0.02  | -0.10  | Brain - Hypothalamus |
| *RETN* | rs3745368 | 0.05  | -0.40  | -2.00  | Brain - Nucleus accumbens (basal ganglia) |
| *RETN* | rs3745368 | 0.85  | -0.04  | -0.18  | Brain - Putamen (basal ganglia) |
| *RETN* | rs3745368 | 0.37  | 0.26  | 0.89  | Brain - Spinal cord (cervical c-1) |
| *RETN* | rs3745368 | 0.88  | 0.05  | 0.15  | Brain - Substantia nigra |
| *RETN* | rs3745368 | 0.97  | 0.01  | 0.04  | Breast - Mammary Tissue |
| *RETN* | rs3745368 | 0.50  | -0.10  | -0.68  | Colon - Sigmoid |
| *RETN* | rs3745368 | 0.06  | -0.25  | -1.90  | Colon - Transverse |
| *RETN* | rs3745368 | 0.16  | -0.14  | -1.40  | Esophagus - Mucosa |
| *RETN* | rs3745368 | 0.01  | -0.29  | -2.50  | Esophagus - Muscularis |
| *RETN* | rs3745368 | 0.23  | -0.15  | -1.20  | Heart - Atrial Appendage |
| *RETN* | rs3745368 | 0.51  | -0.08  | -0.66  | Heart - Left Ventricle |
| *RETN* | rs3745368 | - | - | - | Kidney - Medulla |
| *RETN* | rs3745368 | 0.46  | 0.12  | 0.73  | Liver |
| *RETN* | rs3745368 | 0.02  | -0.20  | -2.30  | Lung |
| *RETN* | rs3745368 | 0.63  | 0.08  | 0.49  | Minor Salivary Gland |
| *RETN* | rs3745368 | 0.53  | -0.06  | -0.62  | Muscle - Skeletal |
| *RETN* | rs3745368 | 0.04  | -0.22  | -2.00  | Nerve - Tibial |
| *RETN* | rs3745368 | 0.84  | 0.05  | 0.21  | Ovary |
| *RETN* | rs3745368 | 0.59  | 0.08  | 0.54  | Pancreas |
| *RETN* | rs3745368 | 0.88  | -0.03  | -0.15  | Pituitary |
| *RETN* | rs3745368 | 0.16  | -0.23  | -1.40  | Prostate |
| *RETN* | rs3745368 | 0.89  | 0.02  | 0.14  | Skin - Not Sun Exposed (Suprapubic) |
| *RETN* | rs3745368 | 0.10  | -0.17  | -1.60  | Skin - Sun Exposed (Lower leg) |
| *RETN* | rs3745368 | 0.03  | -0.53  | -2.10  | Small Intestine - Terminal Ileum |
| *RETN* | rs3745368 | 0.10  | -0.25  | -1.70  | Spleen |
| *RETN* | rs3745368 | 0.74  | -0.05  | -0.33  | Stomach |
| *RETN* | rs3745368 | 0.38  | 0.15  | 0.88  | Testis |
| *RETN* | rs3745368 | 0.53  | -0.06  | -0.62  | Thyroid |
| *RETN* | rs3745368 | 0.19  | -0.44  | -1.30  | Uterus |
| *RETN* | rs3745368 | 0.62  | -0.14  | -0.50  | Vagina |
| *RETN* | rs3745368 | 1.30E-06 | -0.27  | -4.90  | Whole Blood |

NES: normalized effect size. Threshold of P values was 0.05/48≈0.001.

**Supplemental Figures.**

****

**Power=90.5%, RR=1.25**

**Supplemental Figure S1.** Results of power analysis.



**Supplemental Figure S2.** Linkage disequilibrium structure for genotyped SNPs in gene *RTEN*. Values of D’ were indicated in each cell.



**Supplemental Figure S3.** Linkage disequilibrium structure for genotyped SNPs in gene *RARRES2*. Values of D’ were indicated in each cell.