**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 |

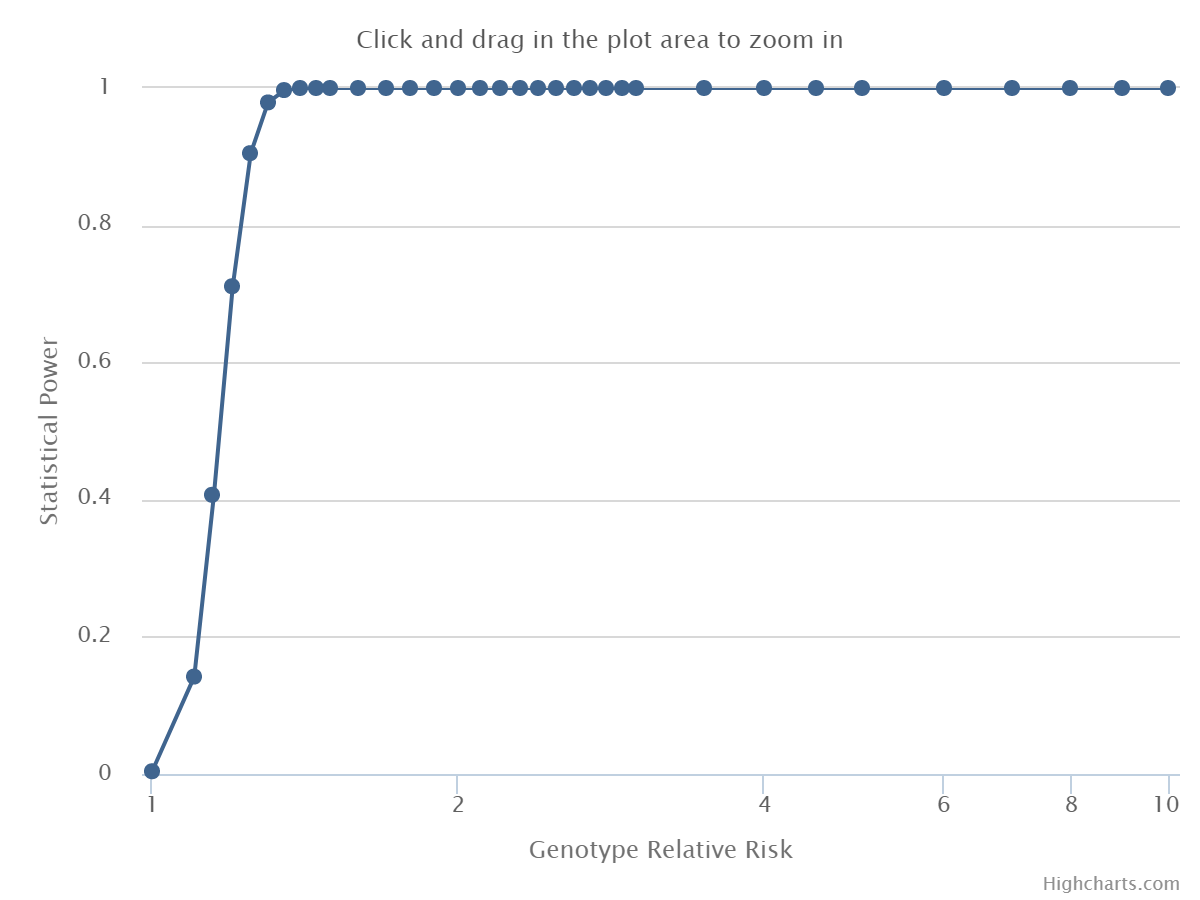
NES: normalized effect size. Threshold of P values was 0.05/48≈0.001.

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 |

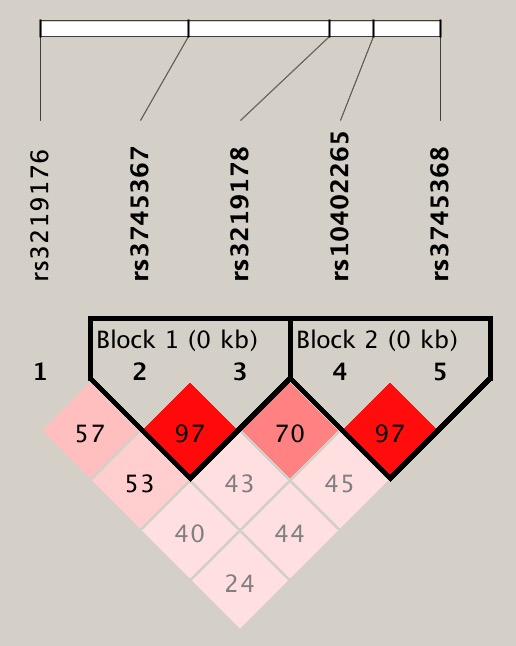
NES: normalized effect size. Threshold of P values was 0.05/48≈0.001.

**Supplemental Figures.**

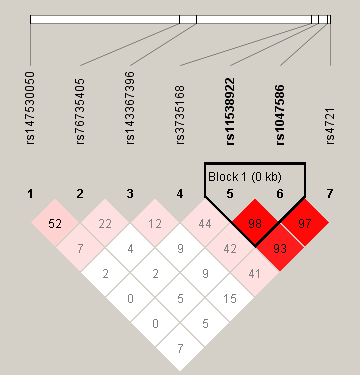
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**Power=90.5%, RR=1.25**

**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.