

Table 2. Summary of GWAS Meta-analysis Stage 1 Results (includes all signals with $p < 5 \times 10^{-7}$)

| Locus | | | Association Signal | | | | Corroborating Signals ($p < 10^{-6}$) | | Nearby Genes | |
|------------------------------------|-----|---------------|--------------------|----------|----------------|---|---|---------------------------|--|--|
| SNP | Chr | Position (Mb) | Allele (+/-) | Freq (+) | Effect (mg/dl) | P-value | SNPs | LD Groups ($r^2 < 0.2$) | (Relative Position) (-upstream, +downstream) | |
| HDL Cholesterol (N = 8,656) | | | | | | | | | | |
| rs3764261 | 16 | 55.6 | A/C | .29 | 2.42 | 2.8×10^{-19} | 14 | 2 | <i>CETP</i> (-2.4kb) | |
| rs12678919 | 8 | 19.9 | G/A | .12 | 2.44 | 1.3×10^{-11} | 84 | 2 | <i>LPL</i> (+19.5kb) | |
| rs10468017 | 15 | 56.5 | T/C | .32 | 1.76 | 8.6×10^{-11} | 18 | 2 | <i>LIPC</i> (-45.7kb) | |
| rs1323432 | 9 | 101.4 | A/G | .87 | 1.93 | 2.5×10^{-8} | 4 | 1 | <i>GRIN3A</i> (Intron 6); <i>PPP3R2</i> (-5.7kb) | |
| rs4149274 | 9 | 104.7 | G/A | .69 | 1.51 | 7.4×10^{-8} | 20 | 1 | <i>ABCA1</i> (Intron 5) | |
| rs4939883 | 18 | 45.4 | C/T | .86 | 1.87 | 1.4×10^{-7} | 2 | 1 | <i>LIPG</i> (+47.9kb) | |
| rs4846914 | 1 | 226.6 | A/G | .62 | 1.15 | 2.9×10^{-7} | 4 | 1 | <i>GALNT2</i> (Intron 1) | |
| LDL Cholesterol (N = 8,589) | | | | | | | | | | |
| rs4420638 | 19 | 50.1 | G/A | .16 | 8.02 | 3.2×10^{-21} | 2 | 1 | <i>APOE/APOC</i> cluster | |
| rs515135 | 2 | 21.2 | C/T | .83 | 6.08 | 3.1×10^{-14} | 116 | 3 | <i>APOB</i> (-19.1kb) | |
| rs602633 | 1 | 109.5 | G/T | .80 | 6.09 | 4.8×10^{-14} | 8 | 1 | <i>CELSR2</i> (+3.1kb); <i>PSRC1</i> (+668bp); <i>SORT1</i> (-30kb) | |
| rs6511720 | 19 | 11.1 | G/T | .91 | 8.03 | 6.8×10^{-10} | 1 | 1 | <i>LDLR</i> (Intron 1) | |
| rs2228603 | 19 | 19.2 | C/T | .93 | 6.46 | 1.8×10^{-7} | 3 | 1 | <i>NCAN</i> (Pro92Ser) | |
| Triglycerides (N = 8,684) | | | | | | | | | | |
| rs964184 | 11 | 116.2 | G/C | .12 | 18.12 | 1.5×10^{-16} | 29 | 2 | <i>APOA5</i> (+11.2kb) | |
| rs1260326 | 2 | 27.6 | T/C | .40 | 10.25 | 1.5×10^{-15} | 52 | 2 | <i>GCKR</i> (Leu446Pro) | |
| rs6993414 | 8 | 19.9 | A/G | .88 | 14.20 | 1.4×10^{-13} | 85 | 2 | <i>LPL</i> (+78.1kb) | |
| rs2954029 | 8 | 126.6 | A/T | .56 | 6.42 | 2.8×10^{-8} | 15 | 1 | <i>TRIB1</i> (+40.3kb) | |
| rs10401969 | 19 | 19.3 | T/C | .92 | 12.28 | 2.3×10^{-7} | 5 | 1 | <i>NCAN</i> (+44.7 kb); <i>SF4</i> (Intron 8) | |

The table summarizes association signals observed in the analysis of lipid levels in three GWAS scans. Chromosome assignments, position, and gene annotations all refer to the March 2006 Genome Build (UCSC). Alleles are ordered such that the first allele (+) is associated with increased lipid levels. Effect sizes are measured as additive effects, which correspond to the average change in phenotype when one (-) allele is replaced with one (+) allele. Summaries of LD information around the strongest hit in each locus (number of LD groups, $r^2 < 0.20$, among nearby SNPs with $p < 10^{-6}$) are based on the HapMap CEU sample. Corroborating signals refers to the number of additional SNPs within 1 Mb with $p < 10^{-6}$. P-values in **bold** exceed a threshold of 5×10^{-8} , which corresponds to false positive rate of 0.05 after adjustment for 1 million independent tests, comparable to the number of independent common SNPs in the Phase II CEU HapMap. For each locus, the most strongly associated SNP is indicated together with its position relative to nearby genes, with a focus on genes previously implicated in lipid metabolism. In the nearby gene column, positions are relative to the transcription start for the nearest gene.

Table 3. Summary of Most Significant Stage 1+2 Results.

| SNP | Chr | Pos (Mb) | Alleles (+/-) | Freq (+) | Effect (mg/dl) | Association p-values | | | Sample sizes | | | Nearby Genes |
|--------------------------------------|-----|-------------|------------------|-------------|-------------------|------------------------|------------------------|-------------------------|--------------|---------|--------------------|--------------|
| | | | | | | Stage 1 (two-sided) | Stage 2 (one-sided) | Combined (two-sided) | Stage 1 | Stage 2 | | |
| SNPs Associated with HDL Cholesterol | | | | | | | | | | | | |
| rs3764261 | 16 | 55.6 | A/C | .31 | 3.47 | 2.8x10 ⁻¹⁹ | 6.4x10 ⁻⁴³ | 2.3x10 ⁻⁵⁷ | 8,656 | 8,072 | CETP | |
| rs1864163 | 16 | 55.6 | G/A | .80 | 4.12 | 3.0x10 ⁻¹⁷ | 4.3x10 ⁻²⁸ | 6.9x10 ⁻³⁹ | 8,656 | 3,684 | CETP | |
| rs9989419 | 16 | 55.5 | G/A | .65 | 1.72 | 8.0x10 ⁻¹⁶ | 1.8x10 ⁻¹⁷ | 3.2x10 ⁻³¹ | 8,656 | 6,981 | CETP | |
| rs12596776 | 16 | 55.5 | G/C | .13 | 1.26 | 3.7x10 ⁻⁵ | 1.0x10 ⁻⁴ | 2.8x10 ⁻⁸ | 8,656 | 7,030 | CETP | |
| rs1566439 | 16 | 55.6 | C/T | .45 | 0.96 | 2.0x10 ⁻⁵ | 2.1x10 ⁻⁴ | 3.3x10 ⁻⁸ | 8,656 | 4,881 | CETP | |
| rs4775041 | 15 | 56.5 | C/G | .33 | 1.38 | 2.8x10 ⁻⁹ | 9.6x10 ⁻¹³ | 3.2x10 ⁻²⁰ | 8,656 | 11,426 | LIPC | |
| rs261332 | 15 | 56.5 | A/G | .19 | 1.41 | 1.7x10 ⁻⁹ | 1.3x10 ⁻⁷ | 2.3x10 ⁻¹⁵ | 8,656 | 6,956 | LIPC | |
| rs10503669 | 8 | 19.9 | A/C | .10 | 2.09 | 3.2x10 ⁻¹⁰ | 9.4x10 ⁻¹¹ | 4.1x10 ⁻¹⁹ | 8,656 | 11,431 | LPL | |
| rs2197089 | 8 | 19.9 | A/G | .58 | 1.38 | 3.4x10 ⁻⁸ | 3.2x10 ⁻⁵ | 1.0x10 ⁻¹¹ | 8,656 | 3,644 | LPL | |
| rs6586891 | 8 | 20 | A/C | .66 | 1.00 | 3.5x10 ⁻⁵ | 9.7x10 ⁻⁶ | 2.9x10 ⁻⁹ | 8,656 | 7,017 | LPL | |
| rs2144300 | 1 | 226.6 | T/C | .60 | 1.11 | 6.6x10 ⁻⁷ | 4.0x10 ⁻⁹ | 2.6x10 ⁻¹⁴ | 8,656 | 11,406 | GALNT2 | |
| rs2156552 | 18 | 45.4 | T/A | .84 | 1.20 | 8.4x10 ⁻⁷ | 7.1x10 ⁻⁷ | 6.4x10 ⁻¹² | 8,656 | 11,437 | LIPG | |
| rs4149268 | 9 | 104.7 | C/T | .64 | 0.82 | 3.3x10 ⁻⁷ | 2.2x10 ⁻⁵ | 1.2x10 ⁻¹⁰ | 8,656 | 11,327 | ABCA1 | |
| rs2338104 | 12 | 108.4 | G/C | .45 | 0.48 | 1.9x10 ⁻⁶ | 7.6x10 ⁻⁴ | 3.4x10 ⁻⁸ | 8,656 | 11,399 | MVK/MMAB | |
| rs255052 | 16 | 66.6 | A/G | .17 | 0.74 | 1.5x10 ⁻⁶ | .0087 | 1.2x10 ⁻⁷ | 8,656 | 4,534 | LCAT | |
| rs1323432 | 9 | 101.4 | A/G | .88 | -0.03 | 2.5x10 ⁻⁸ | .82 | 7.7x10 ⁻⁴ | 8,656 | 8,176 | GRIN3A | |
| SNPs Associated with LDL Cholesterol | | | | | | | | | | | | |
| rs4420638 | 19 | 50.1 | G/A | .18 | 6.61 | 3.2x10 ⁻²¹ | 4.9x10 ⁻²⁴ | 3.0x10 ⁻⁴³ | 8,589 | 10,806 | APOE/C1/C4 | |
| rs10402271 | 19 | 50 | G/T | .33 | 2.62 | 9.8x10 ⁻⁶ | 1.5x10 ⁻⁵ | 1.2x10 ⁻⁹ | 8,589 | 6,519 | APOE/C1/C4 | |
| rs599839 | 1 | 109.5 | A/G | .77 | 5.48 | 1.2x10 ⁻¹³ | 2.7x10 ⁻²¹ | 6.1x10 ⁻³³ | 8,589 | 10,783 | CELSR2/PSRC1/SORT1 | |
| rs6511720 | 19 | 11.1 | G/T | .90 | 9.17 | 6.8x10 ⁻¹⁰ | 3.3x10 ⁻¹⁹ | 4.2x10 ⁻²⁶ | 8,589 | 7,442 | LDLR | |
| rs562338 | 2 | 21.2 | G/A | .82 | 4.89 | 1.2x10 ⁻¹¹ | 3.6x10 ⁻¹² | 5.6x10 ⁻²² | 8,589 | 10,849 | APOB | |
| rs754523 | 2 | 21.2 | G/A | .28 | 2.78 | 7.0x10 ⁻⁷ | 1.3x10 ⁻⁶ | 8.3x10 ⁻¹² | 8,589 | 6,542 | APOB | |
| rs693 | 2 | 21.1 | A/G | .42 | 2.44 | 1.2x10 ⁻⁷ | .0034 | 3.1x10 ⁻⁹ | 8,589 | 3,222 | APOB | |
| rs11206510 | 1 | 55.2 | T/C | .81 | 3.04 | 7.5x10 ⁻⁶ | 5.4x10 ⁻⁷ | 3.5x10 ⁻¹¹ | 8,589 | 10,805 | PCSK9 | |
| rs16996148 | 19 | 19.5 | G/T | .89 | 3.32 | 2.4x10 ⁻⁶ | 8.3x10 ⁻⁵ | 2.7x10 ⁻⁹ | 8,589 | 10,841 | NCAN/CILP2 | |
| rs2254287 | 6 | 33.3 | G/C | .38 | 1.91 | 2.9x10 ⁻⁶ | .0015 | 5.1x10 ⁻⁸ | 8,589 | 7,440 | B3GALT4 | |
| rs12695382 | 3 | 120.4 | A/G | .90 | 2.23 | 4.9x10 ⁻⁶ | .0067 | 1.0x10 ⁻⁶ | 8,589 | 10,802 | B4GALT4 | |

| SNP | Chr | Pos (Mb) | Alleles (+/-) | Freq (+) | Effect (mg/dl) | Association p-values | | | Sample sizes | | | Nearby Genes |
|---|-----|-------------|------------------|-------------|-------------------|-----------------------------|-----------------------------|-----------------------------|--------------|--------------|-----------------------|--------------|
| | | | | | | Stage 1 (two-sided) | Stage 2 (one-sided) | Combined (two-sided) | Stage 1 | Stage 2 | | |
| SNPs Associated with Triglycerides | | | | | | | | | | | | |
| rs780094 | 2 | 27.7 | T/C | .39 | 8.59 | 1.7x10⁻¹⁴ | 2.0x10⁻¹⁹ | 6.1x10⁻³² | 8,684 | 9,723 | GCKR | |
| rs11127129 | 2 | 28.0 | C/G | .79 | 3.77 | 2.0x10 ⁻⁴ | 3.2x10 ⁻⁴ | 4.7x10 ⁻⁷ | 8,684 | 9,700 | RBKS/GCKR | |
| rs12286037 | 11 | 116.2 | T/C | .06 | 25.82 | 1.1x10⁻⁷ | 1.6x10⁻²² | 1.0x10⁻²⁶ | 8,684 | 9,738 | APOA5/A4/C3/A1 | |
| rs662799 | 11 | 116.2 | G/A | .05 | 16.88 | 4.3x10⁻⁸ | 2.7x10⁻¹⁰ | 2.4x10⁻¹⁵ | 8,684 | 3,248 | APOA5/A4/C3/A1 | |
| rs2000571 | 11 | 116.1 | A/G | .17 | 6.93 | 4.7x10 ⁻⁵ | 8.7x10 ⁻⁵ | 5.7x10 ⁻⁸ | 8,684 | 3,209 | APOA5/A4/C3/A1 | |
| rs486394 | 11 | 116.0 | C/A | .28 | 1.50 | 1.7x10 ⁻⁴ | .0073 | 7.4x10 ⁻⁶ | 8,684 | 3,597 | APOA5/A4/C3/A1 | |
| rs10503669 | 8 | 19.9 | C/A | .90 | 11.57 | 1.4x10⁻⁹ | 1.6x10⁻¹⁴ | 3.9x10⁻²² | 8,684 | 9,711 | LPL | |
| rs2197089 | 8 | 19.9 | G/A | .42 | 3.38 | 3.1x10⁻¹¹ | .0029 | 1.1x10⁻¹² | 8,684 | 3,202 | LPL | |
| rs6586891 | 8 | 20.0 | C/A | .34 | 4.60 | 2.4x10 ⁻⁴ | 5.0x10 ⁻⁴ | 1.1x10 ⁻⁶ | 8,684 | 3,622 | LPL | |
| rs17321515 | 8 | 126.6 | A/G | .56 | 6.42 | 6.8x10⁻⁸ | 1.0x10⁻⁶ | 7.0x10⁻¹³ | 8,684 | 5,312 | TRIB1 | |
| rs17145738 | 7 | 72.4 | C/T | .84 | 8.21 | 4.1x10⁻⁶ | 5.0x10⁻⁸ | 2.0x10⁻¹² | 8,684 | 9,741 | MLXIPL | |
| rs1748195 | 1 | 62.8 | C/G | .70 | 7.12 | 2.3x10⁻⁴ | 5.4x10⁻⁸ | 1.7x10⁻¹⁰ | 8,684 | 9,559 | ANGPTL3 | |
| rs16996148 | 19 | 19.5 | G/T | .92 | 6.10 | 6.3x10⁻⁷ | 2.4x10⁻⁴ | 2.5x10⁻⁹ | 8,684 | 9,707 | NCAN/CILP2 | |
| rs4775041 | 15 | 56.5 | C/G | .33 | 3.62 | 7.3x10⁻⁵ | 2.9x10⁻⁵ | 1.6x10⁻⁸ | 8,684 | 8,462 | LIPC | |
| rs2144300 | 1 | 226.6 | C/T | .40 | 4.25 | 4.9x10 ⁻⁴ | 2.4x10 ⁻⁴ | 7.9x10 ⁻⁷ | 8,684 | 8,473 | GALNT2 | |

The table summarizes association signals after follow-up of the promising SNPs in Stage 2 samples. Column headings are as described for Table 2, with the addition of one-sided p-values for the Stage 2 samples, in which we tested for the same direction of effect as Stage 1 – consistent with current best practice for replication of GWAS findings. The effect sizes shown were estimated from Stage 2 samples only. SNPs with a Combined (Stage 1 + 2) p-value $< 10^{-5}$ were included, although we also show GRIN3A for completeness because it was significant in the initial scan. SNPs in this table may not match those in Table 2, which only displays the strongest signal in each locus. The discrepancy also reflects our bias towards genotyped Affymetrix 500K SNPs in the Stage 2 follow-up. Association p-values for each of the six Stage 2 samples are shown in Supplemental Table 4.