

Table S1 Table summarizing the currently known association with HDLc, LDLc, TC and TG. Only the single top signal per locus is shown plus statistically significant independently associated SNPs as identified by conditional analysis.

| Locus    | Chr | Lead SNP   | Lead trait | Other traits | MAF   | P                  |
|----------|-----|------------|------------|--------------|-------|--------------------|
| ANGPTL3  | 1   | rs2131925  | TG         | TC, LDL      | 0.329 | $\times 10^{-43}$  |
| EVI5     | 1   | rs7515577  | TC         |              | 0.213 | $\times 10^{-8}$   |
| FCGR2A   | 1   | rs1801274  | TC         |              | 0.504 | $\times 10^{-8}$   |
| GALNT2   | 1   | rs4846914  | HDL        | TG           | 0.404 | $\times 10^{-21}$  |
| IRF2BP2  | 1   | rs514230   | TC         | LDL          | 0.485 | $\times 10^{-14}$  |
| LDLRAP1  | 1   | rs12027135 | TC         | LDL          | 0.454 | $\times 10^{-11}$  |
| MOSC1    | 1   | rs2642442  | TC         | LDL          | 0.326 | $\times 10^{-13}$  |
| PABPC4   | 1   | rs4660293  | HDL        |              | 0.234 | $\times 10^{-10}$  |
| PCSK9    | 1   | rs2479409  | LDL        | TC           | 0.302 | $\times 10^{-28}$  |
| SORT1    | 1   | rs629301   | LDL        | TC           | 0.221 | $\times 10^{-170}$ |
| ZNF648   | 1   | rs1689800  | HDL        |              | 0.353 | $\times 10^{-10}$  |
| ABCG5/8  | 2   | rs4299376  | LDL        | TC           | 0.302 | $\times 10^{-47}$  |
| APOB     | 2   | rs1367117  | LDL        | TC           | 0.304 | $\times 10^{-114}$ |
| APOB     | 2   | rs1042034  | TG         | HDL          | 0.221 | $\times 10^{-45}$  |
| COBLL1   | 2   | rs10195252 | TG         |              | 0.402 | $\times 10^{-10}$  |
| COBLL1   | 2   | rs12328675 | HDL        |              | 0.133 | $\times 10^{-10}$  |
| GCKR     | 2   | rs1260326  | TG         | TC           | 0.416 | $\times 10^{-133}$ |
| INSIG2   | 2   | rs12464355 | TC         |              | 0.931 | $\times 10^{-8}$   |
| IRS1     | 2   | rs2972146  | HDL        | TG           | 0.373 | $\times 10^{-9}$   |
| RAB3GAP1 | 2   | rs7570971  | TC         |              | 0.342 | $\times 10^{-8}$   |
| UGT1A1   | 2   | rs11563251 | TC         |              | 0.093 | $\times 10^{-9}$   |
| MSL2L1   | 3   | rs645040   | TG         |              | 0.223 | $\times 10^{-8}$   |
| PPARG    | 3   | rs12631819 | HDL        |              | 0.038 | $\times 10^{-6}$   |
| RAF1     | 3   | rs2290159  | TC         |              | 0.224 | $\times 10^{-9}$   |
| KLHL8    | 4   | rs442177   | TG         |              | 0.419 | $\times 10^{-12}$  |
| SLC39A8  | 4   | rs13107325 | HDL        |              | 0.077 | $\times 10^{-11}$  |
| ARL15    | 5   | rs6450176  | HDL        |              | 0.265 | $\times 10^{-8}$   |
| HMGCR    | 5   | rs12916    | TC         | LDL          | 0.399 | $\times 10^{-47}$  |
| MAP3K1   | 5   | rs9686661  | TG         |              | 0.201 | $\times 10^{-10}$  |
| TIMD4    | 5   | rs6882076  | TC         | LDL, TG      | 0.357 | $\times 10^{-28}$  |
| C4B      | 6   | rs389883   | TG         |              | 0.631 | $\times 10^{-18}$  |
| C6orf106 | 6   | rs2814944  | HDL        |              | 0.164 | $\times 10^{-9}$   |
| C6orf106 | 6   | rs2814982  | TC         |              | 0.115 | $\times 10^{-11}$  |
| CITED2   | 6   | rs605066   | HDL        |              | 0.423 | $\times 10^{-8}$   |
| FRK      | 6   | rs9488822  | TC         | LDL          | 0.352 | $\times 10^{-10}$  |
| HFE      | 6   | rs1800562  | LDL        | TC           | 0.066 | $\times 10^{-10}$  |
| HLA      | 6   | rs3177928  | TC         | LDL          | 0.164 | $\times 10^{-19}$  |
| HLA      | 6   | rs2247056  | TG         |              | 0.252 | $\times 10^{-15}$  |
| LPA      | 6   | rs1564348  | LDL        | TC           | 0.172 | $\times 10^{-17}$  |
| LPA      | 6   | rs1084651  | HDL        |              | 0.163 | $\times 10^{-8}$   |
| LPAL2    | 6   | rs3123629  | TG         |              | 0.344 | $\times 10^{-8}$   |
| MYLIP    | 6   | rs3757354  | LDL        | TC           | 0.221 | $\times 10^{-11}$  |
| DNAH11   | 7   | rs12670798 | TC         | LDL          | 0.239 | $\times 10^{-10}$  |
| GCK      | 7   | rs2070971  | TG         |              | 0.132 | $\times 10^{-7}$   |
| KLF14    | 7   | rs4731702  | HDL        |              | 0.481 | $\times 10^{-15}$  |
| MLXIPL   | 7   | rs17145738 | TG         | HDL          | 0.126 | $\times 10^{-58}$  |
| NPC1L1   | 7   | rs2072183  | TC         | LDL          | 0.253 | $\times 10^{-11}$  |
| TYW1B    | 7   | rs13238203 | TG         |              | 0.041 | $\times 10^{-9}$   |
| CYP7A1   | 8   | rs2081687  | TC         | LDL          | 0.352 | $\times 10^{-12}$  |
| GATA4    | 8   | rs6983129  | TG         |              | 0.493 | $\times 10^{-8}$   |
| GPIHBP1  | 8   | rs7388248  | HDL        |              | 0.293 | $\times 10^{-9}$   |
| LPL      | 8   | rs12678919 | TG         | HDL          | 0.122 | $\times 10^{-115}$ |
| NAT2     | 8   | rs1495741  | TG         | TC           | 0.225 | $\times 10^{-14}$  |
| PINX1    | 8   | rs11776767 | TG         |              | 0.371 | $\times 10^{-8}$   |
| PLEC1    | 8   | rs11136341 | LDL        | TC           | 0.404 | $\times 10^{-13}$  |
| PPP1R3B  | 8   | rs9987289  | HDL        | TC, LDL      | 0.096 | $\times 10^{-25}$  |
| TRIB1    | 8   | rs2954029  | TG         | TC, LDL, HDL | 0.473 | $\times 10^{-55}$  |
| TRPS1    | 8   | rs2293889  | HDL        |              | 0.416 | $\times 10^{-11}$  |
| TRPS1    | 8   | rs2737229  | TC         |              | 0.302 | $\times 10^{-8}$   |
| ABCA1    | 9   | rs1883025  | HDL        | TC           | 0.252 | $\times 10^{-33}$  |
| ABO      | 9   | rs9411489  | LDL        | TC           | 0.206 | $\times 10^{-13}$  |
| TTC39B   | 9   | rs581080   | HDL        | TC           | 0.183 | $\times 10^{-12}$  |
| VLDLR    | 9   | rs7024888  | LDL        |              | 0.958 | $\times 10^{-8}$   |
| CHUK     | 10  | rs11597086 | TC         |              | 0.593 | $\times 10^{-9}$   |

|           |              |     |              |                          |
|-----------|--------------|-----|--------------|--------------------------|
| CYP26A1   | 10rs2068888  | TG  |              | $0.462 \times 10^{-8}$   |
| GPAM      | 10rs2255141  | TC  | LDL          | $0.302 \times 10^{-10}$  |
| JMJD1C    | 10rs10761731 | TG  |              | $0.433 \times 10^{-12}$  |
| AMPD3     | 11rs2923084  | HDL |              | $0.175 \times 10^{-8}$   |
| APOA1     | 11rs964184   | TG  | TC, HDL, LDL | $0.137 \times 10^{-240}$ |
| DGAT2     | 11rs11236530 | HDL |              | $0.421 \times 10^{-9}$   |
| FADS1-2-3 | 11rs174546   | TG  | HDL, TC, LDL | $0.345 \times 10^{-24}$  |
| LRP4      | 11rs3136441  | HDL |              | $0.153 \times 10^{-18}$  |
| SPTY2D1   | 11rs10128711 | TC  |              | $0.283 \times 10^{-8}$   |
| SPTY2D1   | 11rs11024739 | LDL |              | $0.556 \times 10^{-10}$  |
| ST3GAL4   | 11rs11220462 | LDL | TC           | $0.141 \times 10^{-15}$  |
| UBASH3B   | 11rs7941030  | TC  | HDL          | $0.382 \times 10^{-10}$  |
| BRAP      | 12rs11065987 | TC  | LDL          | $0.427 \times 10^{-12}$  |
| HCAR2     | 12rs4759361  | HDL |              | $0.162 \times 10^{-12}$  |
| HNF1A     | 12rs1169288  | TC  | LDL          | $0.331 \times 10^{-14}$  |
| LRP1      | 12rs11613352 | TG  | HDL          | $0.234 \times 10^{-10}$  |
| MVK       | 12rs7134594  | HDL |              | $0.477 \times 10^{-15}$  |
| PDE3A     | 12rs7134375  | HDL |              | $0.424 \times 10^{-8}$   |
| SBNO1     | 12rs4759375  | HDL |              | $0.067 \times 10^{-9}$   |
| SCARB1    | 12rs838880   | HDL |              | $0.313 \times 10^{-14}$  |
| UBE3B     | 12rs7298565  | TC  |              | $0.532 \times 10^{-6}$   |
| ZNF664    | 12rs4765127  | HDL | TG           | $0.343 \times 10^{-10}$  |
| BRCA2     | 13rs9534275  | LDL | TC           | $0.516 \times 10^{-9}$   |
| NYNRIN    | 14rs8017377  | LDL |              | $0.475 \times 10^{-11}$  |
| CAPN3     | 15rs2412710  | TG  |              | $0.022 \times 10^{-8}$   |
| FRMD5     | 15rs2929282  | TG  |              | $0.052 \times 10^{-11}$  |
| LACTB     | 15rs2652834  | HDL |              | $0.209 \times 10^{-9}$   |
| LIPC      | 15rs1532085  | HDL | TC, TG       | $0.393 \times 10^{-96}$  |
| CETP      | 16rs3764261  | HDL | TC, LDL, TG  | $0.327 \times 10^{-380}$ |
| CMIP      | 16rs2925979  | HDL |              | $0.302 \times 10^{-11}$  |
| CTF1      | 16rs11649653 | TG  |              | $0.403 \times 10^{-8}$   |
| FTO       | 16rs1421085  | HDL |              | $0.612 \times 10^{-8}$   |
| HPR       | 16rs2000999  | TC  | LDL          | $0.203 \times 10^{-24}$  |
| LCAT      | 16rs16942887 | HDL |              | $0.128 \times 10^{-33}$  |
| ABCA8     | 17rs4148008  | HDL |              | $0.322 \times 10^{-10}$  |
| APOH      | 17rs1801689  | LDL |              | $0.969 \times 10^{-14}$  |
| OSBPL7    | 17rs7206971  | LDL | TC           | $0.492 \times 10^{-8}$   |
| PGS1      | 17rs4129767  | HDL |              | $0.498 \times 10^{-9}$   |
| SERPINF2  | 17rs2070863  | TG  |              | $0.212 \times 10^{-5}$   |
| SOCS3     | 17rs4082919  | TC  | LDL          | $0.529 \times 10^{-7}$   |
| STARD3    | 17rs11869286 | HDL |              | $0.341 \times 10^{-13}$  |
| LIPG      | 18rs7241918  | HDL | TC           | $0.173 \times 10^{-49}$  |
| MC4R      | 18rs12967135 | HDL |              | $0.237 \times 10^{-9}$   |
| ANGPTL4   | 19rs7255436  | HDL |              | $0.473 \times 10^{-8}$   |
| APOE      | 19rs4420638  | LDL | TC, HDL      | $0.179 \times 10^{-147}$ |
| APOE      | 19rs439401   | TG  |              | $0.361 \times 10^{-30}$  |
| CILP2     | 19rs10401969 | TC  | TG, LDL      | $0.073 \times 10^{-38}$  |
| FLJ36070  | 19rs492602   | TC  |              | $0.492 \times 10^{-10}$  |
| INSR      | 19rs8112883  | TG  |              | $0.335 \times 10^{-6}$   |
| LDLR      | 19rs6511720  | LDL | TC           | $0.114 \times 10^{-117}$ |
| LILRA3    | 19rs386000   | HDL |              | $0.204 \times 10^{-16}$  |
| LOC55908  | 19rs737337   | HDL |              | $0.083 \times 10^{-9}$   |
| ERGIC3    | 20rs2277862  | TC  |              | $0.154 \times 10^{-10}$  |
| HNF4A     | 20rs1800961  | HDL | TC           | $0.031 \times 10^{-15}$  |
| MAFB      | 20rs2902940  | TC  | LDL          | $0.296 \times 10^{-11}$  |
| PLTP      | 20rs6065906  | HDL | TG           | $0.182 \times 10^{-22}$  |
| TOP1      | 20rs6029526  | LDL | TC           | $0.474 \times 10^{-19}$  |
| PLA2G6    | 22rs5756931  | TG  |              | $0.404 \times 10^{-8}$   |
| UBE2L3    | 22rs181362   | HDL |              | $0.201 \times 10^{-8}$   |

Table S2 Biological process VLAD results, triglyceride trait associated genes

| GO Term   | P-value  | k  | M     | Genes  |
|---|----------|----|-------|--|
| <a href="#">GO:0008150: biological process</a>                        | 1.00E+00 | 29 | 29612 | ANGPTL3, APOA1, APOB, APOE, CAPN3, CETP, CTF1, CYP26A1, FADS1, FADS2, FADS3, *FRMD5, GALNT2, GCKR, IRS1, JMJD1C, LIPC, LPL, LRP1, MAP3K1, MLXIPL, MSL2, NAT2, PINX1, PLA2G6, PLTP, TRIB1, TYW1B, *ZNF664 |
| <a href="#">GO:0044710: single-organism metabolic process</a>         | 4.68E-06 | 26 | 14505 | ANGPTL3, APOA1, APOB, APOE, CAPN3, CETP, CYP26A1, FADS1, FADS2, FADS3, GALNT2, GCKR, IRS1, JMJD1C, LIPC, LPL, LRP1, MAP3K1, MLXIPL, MSL2, NAT2, PINX1, PLA2G6, PLTP, TYW1B, ZNF664                       |
| <a href="#">GO:0008152: metabolic process</a>                         | 7.68E-06 | 26 | 14817 | ANGPTL3, APOA1, APOB, APOE, CAPN3, CETP, *CYP26A1, FADS1, FADS2, FADS3, GALNT2, GCKR, IRS1, JMJD1C, LIPC, LPL, LRP1, MAP3K1, MLXIPL, MSL2, NAT2, PINX1, PLA2G6, PLTP, TYW1B, ZNF664                      |
| <a href="#">GO:0044238: primary metabolic process</a>                 | 9.13E-06 | 25 | 13667 | ANGPTL3, APOA1, APOB, APOE, CAPN3, CETP, CYP26A1, FADS1, FADS2, FADS3, GALNT2, GCKR, IRS1, JMJD1C, LIPC, LPL, LRP1, MAP3K1, MLXIPL, MSL2, PINX1, PLA2G6, PLTP, TYW1B, ZNF664                             |
| <a href="#">GO:0071704: organic substance metabolic process</a>       | 2.09E-05 | 25 | 14197 | ANGPTL3, APOA1, APOB, APOE, CAPN3, CETP, CYP26A1, FADS1, FADS2, FADS3, GALNT2, GCKR, IRS1, JMJD1C, LIPC, LPL, LRP1, MAP3K1, MLXIPL, MSL2, PINX1, PLA2G6, PLTP, TYW1B, ZNF664                             |
| <a href="#">GO:0044237: cellular metabolic process</a>                | 9.92E-06 | 24 | 12556 | ANGPTL3, APOA1, APOB, APOE, CETP, CYP26A1, FADS1, FADS2, FADS3, GALNT2, GCKR, JMJD1C, LIPC, LPL, LRP1, MAP3K1, MLXIPL, MSL2, NAT2, PINX1, PLA2G6, PLTP, TYW1B, ZNF664                                    |
| <a href="#">GO:0044281: small molecule metabolic process</a>          | 1.72E-09 | 17 | 3455  | ANGPTL3, *APOA1, *APOB, *APOE, *CETP, *CYP26A1, *FADS1, *FADS2, FADS3, *GCKR, LIPC, *LPL, LRP1, *MLXIPL, *NAT2, *PLA2G6, PLTP  |
| <a href="#">GO:0065008: regulation of biological quality</a>          | 1.50E-07 | 15 | 3451  | ANGPTL3, APOA1, APOB, APOE, CAPN3, CETP, CYP26A1, GCKR, IRS1, JMJD1C, LIPC, LPL, MAP3K1, MLXIPL, PINX1   |
| <a href="#">GO:0009058: biosynthetic process</a>                      | 2.16E-04 | 15 | 6142  | APOA1, APOB, APOE, FADS1, FADS2, FADS3, GALNT2, JMJD1C, LIPC, LPL, MLXIPL, PINX1, PLA2G6, PLTP, ZNF664   |
| <a href="#">GO:0006629: lipid metabolic process</a>                   | 1.37E-11 | 15 | 1762  | ANGPTL3, *APOA1, *APOB, *APOE, *CETP, CYP26A1, FADS1, FADS2, FADS3, IRS1, LIPC, *LPL, LRP1, PLA2G6, *PLTP  |
| <a href="#">GO:0044249: cellular biosynthetic process</a>             | 1.12E-04 | 15 | 5811  | APOA1, APOB, APOE, FADS1, FADS2, FADS3, GALNT2, JMJD1C, LIPC, LPL, MLXIPL, PINX1, PLA2G6, PLTP, ZNF664   |
| <a href="#">GO:1901576: organic substance biosynthetic process</a>    | 1.54E-04 | 15 | 5967  | APOA1, APOB, APOE, FADS1, FADS2, FADS3, GALNT2, JMJD1C, LIPC, LPL, MLXIPL, PINX1, PLA2G6, PLTP, ZNF664   |
| <a href="#">GO:0042221: response to chemical stimulus</a>             | 6.65E-06 | 14 | 3988  | ANGPTL3, APOB, APOE, CAPN3, CYP26A1, FADS1, GCKR, IRS1, LPL, MAP3K1, MLXIPL, NAT2, PLA2G6, TRIB1   |
| <a href="#">GO:0048518: positive regulation of biological process</a> | 5.35E-04 | 13 | 5136  | ANGPTL3, APOA1, APOB, APOE, CAPN3, CTF1, GCKR, IRS1, LPL, LRP1, MAP3K1, MLXIPL, TRIB1  |
| <a href="#">GO:0032879: regulation of localization</a>                | 5.79E-08 | 12 | 1830  | ANGPTL3, APOA1, APOB, APOE, CAPN3, CETP, GCKR, IRS1, LPL, LRP1, MAP3K1, TRIB1  |
| <a href="#">GO:0042592: homeostatic process</a>                       | 2.56E-08 | 12 | 1700  | ANGPTL3, APOA1, APOB, APOE, CAPN3, CETP, GCKR, IRS1, LIPC, LPL, MLXIPL, PINX1  |
| <a href="#">GO:0044255: cellular lipid metabolic process</a>          | 1.00E-09 | 12 | 1274  | ANGPTL3, *APOA1, APOB, APOE, CETP, CYP26A1, *FADS1, FADS2, FADS3, LIPC, LPL, PLA2G6  |
| <a href="#">GO:0033036: macromolecule localization</a>                | 1.54E-05 | 11 | 2555  | ANGPTL3, APOA1, APOB, APOE, CAPN3, CETP, GCKR, IRS1, LIPC, LRP1, PLTP  |
| <a href="#">GO:0048878: chemical homeostasis</a>                      | 8.04E-08 | 10 | 1156  | ANGPTL3, APOA1, APOB, APOE, CETP, GCKR, IRS1, LIPC, LPL, MLXIPL  |

|   |          |    |      |  |
|---|----------|----|------|--|
| <a href="#">GO:0010033: response to organic substance</a>               | 1.80E-04 | 10 | 2751 | ANGPTL3, APOB, APOE, CYP26A1, FADS1, GCKR, IRS1, MAP3K1, MLXIPL, TRIB1 |
| <a href="#">GO:0065009: regulation of molecular function</a>            | 2.66E-04 | 9  | 2329 | ANGPTL3, APOA1, APOE, CAPN3, GCKR, IRS1, LRP1, PINX1, TRIB1            |
| <a href="#">GO:0009893: positive regulation of metabolic process</a>    | 9.89E-04 | 9  | 2783 | ANGPTL3, APOA1, APOE, CAPN3, GCKR, IRS1, MAP3K1, MLXIPL, TRIB1         |
| <a href="#">GO:0055088: lipid homeostasis</a>                           | 1.37E-15 | 9  | 115  | *ANGPTL3, APOA1, APOB, APOE, *CETP, GCKR, LIPC, LPL, MLXIPL            |
| <a href="#">GO:0050790: regulation of catalytic activity</a>            | 4.35E-05 | 9  | 1840 | ANGPTL3, APOA1, APOE, *CAPN3, GCKR, IRS1, LRP1, PINX1, TRIB1           |
| <a href="#">GO:0009056: catabolic process</a>                           | 3.97E-04 | 9  | 2457 | ANGPTL3, APOB, APOE, CYP26A1, IRS1, LIPC, LPL, MAP3K1, PLA2G6          |
| <a href="#">GO:0043933: macromolecular complex subunit organization</a> | 5.29E-06 | 9  | 1414 | APOA1, APOB, APOE, CAPN3, CETP, IRS1, LIPC, LPL, MAP3K1                |
| <a href="#">GO:1901575: organic substance catabolic process</a>         | 2.08E-04 | 9  | 2254 | ANGPTL3, APOB, APOE, CYP26A1, IRS1, LIPC, LPL, MAP3K1, PLA2G6          |
| <a href="#">GO:1901615: organic hydroxy compound metabolic process</a>  | 1.24E-08 | 8  | 471  | ANGPTL3, APOA1, APOB, APOE, CETP, LIPC, LRP1, PLA2G6                   |
| <a href="#">GO:0016042: lipid catabolic process</a>                     | 4.33E-10 | 8  | 307  | ANGPTL3, APOB, APOE, CYP26A1, *IRS1, LIPC, LPL, *PLA2G6                |
| <a href="#">GO:0070887: cellular response to chemical stimulus</a>      | 7.99E-04 | 8  | 2141 | APOB, APOE, CAPN3, CYP26A1, IRS1, MAP3K1, MLXIPL, NAT2                 |
| <a href="#">GO:0006066: alcohol metabolic process</a>                   | 2.05E-09 | 8  | 374  | ANGPTL3, APOA1, APOB, APOE, CETP, LIPC, LRP1, PLA2G6                   |
| <a href="#">GO:0006082: organic acid metabolic process</a>              | 1.28E-04 | 8  | 1635 | ANGPTL3, CYP26A1, FADS1, FADS2, FADS3, GCKR, LIPC, LPL                 |
| <a href="#">GO:0044711: single-organism biosynthetic process</a>        | 4.05E-06 | 7  | 702  | APOA1, FADS1, FADS2, FADS3, LIPC, LPL, PLTP                            |
| <a href="#">GO:0051049: regulation of transport</a>                     | 2.27E-04 | 7  | 1321 | APOA1, APOE, CAPN3, CETP, GCKR, IRS1, LRP1                             |
| <a href="#">GO:0019637: organophosphate metabolic process</a>           | 4.86E-04 | 7  | 1497 | ANGPTL3, APOA1, CETP, FADS1, LIPC, LPL, PLA2G6                         |
| <a href="#">GO:0032787: monocarboxylic acid metabolic process</a>       | 1.80E-06 | 7  | 621  | ANGPTL3, CYP26A1, FADS1, FADS2, FADS3, LIPC, LPL                       |
| <a href="#">GO:0070328: triglyceride homeostasis</a>                    | 1.02E-15 | 7  | 31   | *ANGPTL3, *APOA1, *CETP, *GCKR, *LIPC, *LPL, *MLXIPL                   |
| <a href="#">GO:0055090: acylglycerol homeostasis</a>                    | 1.31E-15 | 7  | 32   | *ANGPTL3, APOA1, CETP, GCKR, LIPC, LPL, MLXIPL                         |
| <a href="#">GO:0008203: cholesterol metabolic process</a>               | 3.08E-11 | 7  | 126  | *ANGPTL3, *APOA1, *APOB, *APOE, *CETP, *LIPC, *LRP1                    |
| <a href="#">GO:0016125: sterol metabolic process</a>                    | 6.83E-11 | 7  | 141  | ANGPTL3, APOA1, APOB, APOE, CETP, LIPC, LRP1                           |
| <a href="#">GO:0008202: steroid metabolic process</a>                   | 2.14E-08 | 7  | 322  | ANGPTL3, APOA1, APOB, APOE, CETP, LIPC, LRP1                           |
| <a href="#">GO:0046486: glycerolipid metabolic process</a>              | 2.22E-07 | 7  | 454  | APOA1, APOB, APOE, CETP, LIPC, LPL, PLA2G6                             |
| <a href="#">GO:0006644: phospholipid metabolic process</a>              | 5.96E-07 | 7  | 526  | *ANGPTL3, APOA1, CETP, FADS1, LIPC, *LPL, *PLA2G6                      |
| <a href="#">GO:0008610: lipid biosynthetic process</a>                  | 8.76E-06 | 7  | 790  | APOA1, FADS1, FADS2, FADS3, LIPC, LPL, PLA2G6                          |
| <a href="#">GO:0010876: lipid localization</a>                          | 6.71E-09 | 7  | 272  | ANGPTL3, APOA1, APOB, APOE, CETP, LIPC, PLTP                           |
| <a href="#">GO:0044283: small molecule biosynthetic process</a>         | 3.28E-06 | 7  | 680  | APOA1, FADS1, FADS2, FADS3, LIPC, LPL, PLTP                            |
| <a href="#">GO:0019752: carboxylic acid metabolic process</a>           | 4.63E-04 | 7  | 1485 | ANGPTL3, CYP26A1, FADS1, FADS2, FADS3, LIPC, LPL                       |
| <a href="#">GO:0043436: oxoacid metabolic process</a>                   | 7.71E-04 | 7  | 1617 | ANGPTL3, CYP26A1, FADS1, FADS2, FADS3, LIPC, LPL                       |
| <a href="#">GO:0030334: regulation of cell migration</a>                | 1.51E-05 | 6  | 563  | ANGPTL3, APOE, IRS1, LRP1, *MAP3K1, TRIB1                              |
| <a href="#">GO:2000145: regulation of cell motility</a>                 | 1.92E-05 | 6  | 588  | ANGPTL3, APOE, IRS1, LRP1, MAP3K1, TRIB1                               |
| <a href="#">GO:0044092: negative regulation of molecular function</a>   | 1.05E-04 | 6  | 798  | ANGPTL3, APOA1, APOE, GCKR, PINX1, TRIB1                               |
| <a href="#">GO:0055092: sterol homeostasis</a>                          | 1.69E-10 | 6  | 82   | ANGPTL3, APOA1, APOB, APOE, CETP, LIPC                                 |
| <a href="#">GO:0042632: cholesterol homeostasis</a>                     | 1.69E-10 | 6  | 82   | *ANGPTL3, *APOA1, *APOB, *APOE, *CETP, *LIPC                           |
| <a href="#">GO:0006631: fatty acid metabolic process</a>                | 3.42E-06 | 6  | 434  | *ANGPTL3, FADS1, FADS2, FADS3, LIPC, LPL                               |
| <a href="#">GO:0006869: lipid transport</a>                             | 1.28E-07 | 6  | 247  | APOA1, APOB, APOE, *CETP, LIPC, *PLTP                                  |
| <a href="#">GO:0042157: lipoprotein metabolic process</a>               | 1.50E-08 | 6  | 172  | *APOA1, *APOB, *APOE, *CETP, *LPL, *LRP1                               |
| <a href="#">GO:0034369: plasma lipoprotein particle remodeling</a>      | 1.48E-13 | 6  | 27   | APOA1, APOB, APOE, CETP, LIPC, LPL                                     |
| <a href="#">GO:0034368: protein-lipid complex remodeling</a>            | 1.48E-13 | 6  | 27   | APOA1, APOB, APOE, CETP, LIPC, LPL                                     |

|  |          |   |      |  |
|--|----------|---|------|--|
| <u>GO:0034367: macromolecular complex remodeling</u>                 | 1.48E-13 | 6 | 27   | APOA1, APOB, APOE, CETP, LIPC, LPL       |
| <u>GO:0071825: protein-lipid complex subunit organization</u>        | 5.52E-13 | 6 | 33   | APOA1, APOB, APOE, CETP, LIPC, LPL       |
| <u>GO:0071827: plasma lipoprotein particle organization</u>          | 5.52E-13 | 6 | 33   | APOA1, APOB, APOE, CETP, LIPC, LPL       |
| <u>GO:0019216: regulation of lipid metabolic process</u>             | 2.79E-07 | 6 | 282  | ANGPTL3, APOA1, APOB, APOE, IRS1, MLXIPL |
| <u>GO:0043086: negative regulation of catalytic activity</u>         | 2.30E-05 | 6 | 607  | ANGPTL3, APOA1, APOE, GCKR, PINX1, TRIB1 |
| <u>GO:0051338: regulation of transferase activity</u>                | 1.43E-04 | 6 | 844  | APOA1, APOE, GCKR, IRS1, PINX1, TRIB1    |
| <u>GO:0097006: regulation of plasma lipoprotein particle levels</u>  | 2.45E-11 | 6 | 60   | APOA1, APOB, APOE, CETP, LIPC, LPL       |
| <u>GO:0048585: negative regulation of response to stimulus</u>       | 7.40E-04 | 6 | 1148 | APOA1, APOE, CYP26A1, IRS1, LRP1, TRIB1  |
| <u>GO:0040012: regulation of locomotion</u>                          | 2.88E-05 | 6 | 632  | ANGPTL3, APOE, IRS1, LRP1, MAP3K1, TRIB1 |
| <u>GO:0051270: regulation of cellular component movement</u>         | 2.96E-05 | 6 | 635  | ANGPTL3, APOE, IRS1, LRP1, MAP3K1, TRIB1 |
| <u>GO:0042325: regulation of phosphorylation</u>                     | 7.19E-04 | 6 | 1142 | APOA1, APOE, GCKR, IRS1, MLXIPL, TRIB1   |
| <u>GO:0015850: organic hydroxy compound transport</u>                | 1.83E-08 | 5 | 84   | APOA1, APOB, APOE, CETP, LIPC            |
| <u>GO:0009896: positive regulation of catabolic process</u>          | 9.48E-07 | 5 | 185  | ANGPTL3, APOE, IRS1, MLXIPL, TRIB1       |
| <u>GO:0055114: oxidation-reduction process</u>                       | 4.92E-04 | 5 | 686  | APOA1, FADS1, FADS2, FADS3, MLXIPL       |
| <u>GO:0009894: regulation of catabolic process</u>                   | 6.33E-04 | 5 | 725  | ANGPTL3, APOE, IRS1, MLXIPL, TRIB1       |
| <u>GO:0006641: triglyceride metabolic process</u>                    | 6.21E-08 | 5 | 107  | APOB, *APOE, *CETP, LIPC, *LPL           |
| <u>GO:0006639: acylglycerol metabolic process</u>                    | 8.54E-08 | 5 | 114  | APOB, APOE, CETP, LIPC, LPL              |
| <u>GO:0006638: neutral lipid metabolic process</u>                   | 9.32E-08 | 5 | 116  | APOB, APOE, CETP, LIPC, LPL              |
| <u>GO:0044242: cellular lipid catabolic process</u>                  | 9.23E-07 | 5 | 184  | ANGPTL3, APOB, CYP26A1, LIPC, LPL        |
| <u>GO:0006633: fatty acid biosynthetic process</u>                   | 1.29E-06 | 5 | 197  | FADS1, FADS2, FADS3, *LIPC, *LPL         |
| <u>GO:0030301: cholesterol transport</u>                             | 2.77E-09 | 5 | 58   | *APOA1, *APOB, APOE, *CETP, LIPC         |
| <u>GO:0015918: sterol transport</u>                                  | 2.77E-09 | 5 | 58   | APOA1, APOB, APOE, CETP, LIPC            |
| <u>GO:0045834: positive regulation of lipid metabolic process</u>    | 1.25E-07 | 5 | 123  | ANGPTL3, APOA1, APOE, IRS1, MLXIPL       |
| <u>GO:0072330: monocarboxylic acid biosynthetic process</u>          | 5.82E-06 | 5 | 268  | FADS1, FADS2, FADS3, LIPC, LPL           |
| <u>GO:0016053: organic acid biosynthetic process</u>                 | 9.81E-05 | 5 | 484  | FADS1, FADS2, FADS3, LIPC, LPL           |
| <u>GO:0046394: carboxylic acid biosynthetic process</u>              | 9.81E-05 | 5 | 484  | FADS1, FADS2, FADS3, LIPC, LPL           |
| <u>GO:0048844: artery morphogenesis</u>                              | 3.25E-07 | 4 | 59   | *ANGPTL3, *APOB, *APOE, LRP1             |
| <u>GO:0060840: artery development</u>                                | 6.89E-07 | 4 | 71   | ANGPTL3, APOB, APOE, LRP1                |
| <u>GO:0006898: receptor-mediated endocytosis</u>                     | 6.62E-06 | 4 | 125  | *APOB, *APOE, *CETP, *LRP1               |
| <u>GO:0006897: endocytosis</u>                                       | 6.25E-04 | 4 | 405  | APOB, APOE, CETP, LRP1                   |
| <u>GO:0046470: phosphatidylcholine metabolic process</u>             | 4.82E-07 | 4 | 65   | APOA1, *CETP, LIPC, PLA2G6               |
| <u>GO:0006650: glycerophospholipid metabolic process</u>             | 4.23E-04 | 4 | 365  | APOA1, CETP, LIPC, PLA2G6                |
| <u>GO:0043691: reverse cholesterol transport</u>                     | 2.85E-09 | 4 | 19   | *APOA1, *APOE, *CETP, *LIPC              |
| <u>GO:0034381: plasma lipoprotein particle clearance</u>             | 5.35E-08 | 4 | 38   | APOA1, APOB, APOE, LIPC                  |
| <u>GO:0034372: very-low-density lipoprotein particle remodeling</u>  | 2.59E-11 | 4 | 7    | *APOE, *CETP, *LIPC, *LPL                |
| <u>GO:0034370: triglyceride-rich lipoprotein particle remodeling</u> | 1.55E-10 | 4 | 10   | APOE, CETP, LIPC, LPL                    |
| <u>GO:0034374: low-density lipoprotein particle remodeling</u>       | 5.27E-10 | 4 | 13   | *APOB, *APOE, *CETP, *LIPC               |

|  |          |   |     |                             |
|--|----------|---|-----|-----------------------------|
| GO:0034375: high-density lipoprotein particle remodeling               | 1.00E-09 | 4 | 15  | *APOA1, *APOE, *CETP, *LIPC |
| GO:0032374: regulation of cholesterol transport                        | 2.62E-08 | 4 | 32  | APOA1, APOE, CETP, *LRP1    |
| GO:0032371: regulation of sterol transport                             | 2.62E-08 | 4 | 32  | APOA1, APOE, CETP, LRP1     |
| GO:0032368: regulation of lipid transport                              | 8.14E-07 | 4 | 74  | APOA1, APOE, CETP, LRP1     |
| GO:0051348: negative regulation of transferase activity                | 6.99E-05 | 4 | 228 | APOE, GCKR, PINX1, TRIB1    |
| GO:0009743: response to carbohydrate stimulus                          | 9.38E-05 | 4 | 246 | *APOB, FADS1, GCKR, MLXIPL  |
| GO:0042439: ethanolamine-containing compound metabolic process         | 2.13E-06 | 4 | 94  | APOA1, CETP, LIPC, PLA2G6   |
| GO:0031331: positive regulation of cellular catabolic process          | 8.22E-06 | 4 | 132 | APOE, IRS1, MLXIPL, TRIB1   |
| GO:0044106: cellular amine metabolic process                           | 1.63E-05 | 4 | 157 | APOA1, CETP, LIPC, PLA2G6   |
| GO:0006576: cellular biogenic amine metabolic process                  | 1.63E-05 | 4 | 157 | APOA1, CETP, LIPC, PLA2G6   |
| GO:0009308: amine metabolic process                                    | 4.12E-05 | 4 | 199 | APOA1, CETP, LIPC, PLA2G6   |
| GO:0031400: negative regulation of protein modification process        | 6.19E-04 | 4 | 404 | APOE, CAPN3, MLXIPL, TRIB1  |
| GO:0033500: carbohydrate homeostasis                                   | 4.23E-04 | 3 | 150 | GCKR, IRS1, MLXIPL          |
| GO:0042593: glucose homeostasis  | 4.23E-04 | 3 | 150 | GCKR, *IRS1, *MLXIPL        |
| GO:0030336: negative regulation of cell migration                      | 5.58E-04 | 3 | 165 | APOE, LRP1, TRIB1           |
| GO:2000146: negative regulation of cell motility                       | 5.78E-04 | 3 | 167 | APOE, LRP1, TRIB1           |
| GO:0010743: regulation of macrophage derived foam cell differentiation | 9.45E-06 | 3 | 42  | APOB, CETP, LPL             |
| GO:0015748: organophosphate ester transport                            | 3.71E-05 | 3 | 66  | APOA1, APOE, CETP           |
| GO:0055091: phospholipid homeostasis                                   | 7.07E-08 | 3 | 9   | *ANGPTL3, *APOA1, *CETP     |
| GO:0019433: triglyceride catabolic process                             | 1.48E-06 | 3 | 23  | *APOB, *LIPC, *LPL          |
| GO:0046464: acylglycerol catabolic process                             | 2.16E-06 | 3 | 26  | APOB, LIPC, LPL             |
| GO:0046461: neutral lipid catabolic process                            | 2.16E-06 | 3 | 26  | APOB, LIPC, LPL             |
| GO:0046503: glycerolipid catabolic process                             | 4.11E-06 | 3 | 32  | APOB, LIPC, LPL             |
| GO:0006636: unsaturated fatty acid biosynthetic process                | 4.05E-05 | 3 | 68  | *FADS1, *FADS2, *FADS3      |
| GO:0042158: lipoprotein biosynthetic process                           | 1.61E-04 | 3 | 108 | *APOA1, *APOB, *APOE        |
| GO:0033559: unsaturated fatty acid metabolic process                   | 1.70E-04 | 3 | 110 | *FADS1, *FADS2, FADS3       |
| GO:0015914: phospholipid transport                                     | 8.78E-06 | 3 | 41  | APOA1, APOE, *CETP          |
| GO:0065005: protein-lipid complex assembly                             | 3.81E-07 | 3 | 15  | APOA1, APOB, APOE           |
| GO:0034377: plasma lipoprotein particle assembly                       | 3.81E-07 | 3 | 15  | APOA1, APOB, APOE           |
| GO:0010906: regulation of glucose metabolic process                    | 1.44E-04 | 3 | 104 | GCKR, IRS1, MLXIPL          |
| GO:0010675: regulation of cellular carbohydrate metabolic process      | 2.59E-04 | 3 | 127 | GCKR, IRS1, MLXIPL          |
| GO:0006109: regulation of carbohydrate metabolic process               | 2.91E-04 | 3 | 132 | GCKR, IRS1, MLXIPL          |
| GO:0019218: regulation of steroid metabolic process                    | 1.24E-04 | 3 | 99  | APOA1, APOB, APOE           |
| GO:0046890: regulation of lipid biosynthetic process                   | 2.97E-04 | 3 | 133 | APOB, APOE, MLXIPL          |
| GO:0010874: regulation of cholesterol efflux                           | 5.69E-07 | 3 | 17  | APOE, *CETP, LRP1           |
| GO:0051271: negative regulation of cellular component movement         | 6.40E-04 | 3 | 173 | APOE, LRP1, TRIB1           |

|  |          |   |     |                        |
|--|----------|---|-----|------------------------|
| <u>GO:0040013: negative regulation of locomotion</u>                                   | 8.66E-04 | 3 | 192 | APOE, LRP1, TRIB1      |
| <u>GO:0022900: electron transport chain</u>  | 8.66E-04 | 3 | 192 | *FADS1, *FADS2, *FADS3 |
| <u>GO:0045862: positive regulation of proteolysis</u>                                  | 7.90E-05 | 3 | 85  | APOE, *CAPN3, TRIB1    |
| <u>GO:0030317: sperm motility</u>  | 6.37E-04 | 2 | 38  | *APOB, *PLTP           |
| <u>GO:0014912: negative regulation of smooth muscle cell migration</u>                 | 4.15E-05 | 2 | 10  | *LRP1, *TRIB1          |
| <u>GO:0043651: linoleic acid metabolic process</u>                                     | 2.58E-05 | 2 | 8   | *FADS1, *FADS2         |
| <u>GO:0042159: lipoprotein catabolic process</u>                                       | 5.07E-05 | 2 | 11  | *APOB, *APOE           |
| <u>GO:0009395: phospholipid catabolic process</u>                                      | 5.71E-04 | 2 | 36  | *ANGPTL3, LPC          |
| <u>GO:0033700: phospholipid efflux</u>   | 6.07E-05 | 2 | 12  | *APOA1, *APOE          |
| <u>GO:0033344: cholesterol efflux</u>  | 2.97E-04 | 2 | 26  | *APOA1, *APOE          |
| <u>GO:0034384: high-density lipoprotein particle clearance</u>                         | 1.94E-05 | 2 | 7   | *APOA1, *APOE          |
| <u>GO:0034382: chylomicron remnant clearance</u>                                       | 3.32E-05 | 2 | 9   | *APOE, *LIPC           |
| <u>GO:0071830: triglyceride-rich lipoprotein particle clearance</u>                    | 3.32E-05 | 2 | 9   | APOE, LIPC             |
| <u>GO:0042953: lipoprotein transport</u>   | 7.18E-05 | 2 | 13  | *APOB, *LRP1           |
| <u>GO:0034380: high-density lipoprotein particle assembly</u>                          | 1.39E-05 | 2 | 6   | *APOA1, *APOE          |
| <u>GO:0010907: positive regulation of glucose metabolic process</u>                    | 4.51E-04 | 2 | 32  | *IRS1, MLXIPL          |
| <u>GO:0010676: positive regulation of cellular carbohydrate metabolic process</u>      | 7.78E-04 | 2 | 42  | IRS1, MLXIPL           |
| <u>GO:0010873: positive regulation of cholesterol esterification</u>                   | 1.94E-05 | 2 | 7   | *APOA1, *APOE          |
| <u>GO:0010872: regulation of cholesterol esterification</u>                            | 3.32E-05 | 2 | 9   | APOA1, APOE            |
| <u>GO:0045540: regulation of cholesterol biosynthetic process</u>                      | 2.11E-04 | 2 | 22  | *APOB, APOE            |
| <u>GO:0045940: positive regulation of steroid metabolic process</u>                    | 3.45E-04 | 2 | 28  | APOA1, APOE            |
| <u>GO:0090181: regulation of cholesterol metabolic process</u>                         | 4.80E-04 | 2 | 33  | APOB, APOE             |
| <u>GO:0045923: positive regulation of fatty acid metabolic process</u>                 | 5.71E-04 | 2 | 36  | IRS1, MLXIPL           |
| <u>GO:0050996: positive regulation of lipid catabolic process</u>                      | 2.97E-04 | 2 | 26  | *ANGPTL3, IRS1         |
| <u>GO:0010875: positive regulation of cholesterol efflux</u>                           | 5.07E-05 | 2 | 11  | *APOE, *LRP1           |
| <u>GO:0032373: positive regulation of sterol transport</u>                             | 7.18E-05 | 2 | 13  | APOE, LRP1             |
| <u>GO:0032376: positive regulation of cholesterol transport</u>                        | 7.18E-05 | 2 | 13  | APOE, LRP1             |
| <u>GO:0032370: positive regulation of lipid transport</u>                              | 6.04E-04 | 2 | 37  | APOE, *LRP1            |
| <u>GO:0010886: positive regulation of cholesterol storage</u>                          | 1.57E-04 | 2 | 19  | *APOB, *LPL            |
| <u>GO:0010885: regulation of cholesterol storage</u>                                   | 2.74E-04 | 2 | 25  | APOB, LPL              |
| <u>GO:0010884: positive regulation of lipid storage</u>                                | 3.20E-04 | 2 | 27  | *APOB, LPL             |
| <u>GO:0032489: regulation of Cdc42 protein signal transduction</u>                     | 1.92E-04 | 2 | 21  | *APOA1, *APOE          |
| <u>GO:0036109: alpha-linolenic acid metabolic process</u>                              | 5.07E-05 | 2 | 11  | *FADS1, *FADS2         |
| <u>GO:0010744: positive regulation of macrophage derived foam cell differentiation</u> | 3.70E-04 | 2 | 29  | *APOB, *LPL            |
| <u>GO:0019915: lipid storage</u>   | 4.51E-04 | 2 | 32  | *ANGPTL3, *APOA1       |
| <u>GO:0014910: regulation of smooth muscle cell migration</u>                          | 5.40E-04 | 2 | 35  | LRP1, TRIB1            |
| <u>GO:0006775: fat-soluble vitamin metabolic process</u>                               | 3.45E-04 | 2 | 28  | CYP26A1, PLTP          |

k is the number of genes in the query set annotated to that node, and M is the number of genes in the database annotated to that node.  
 \*next to the gene symbol indicates that the gene is annotated to the node, and not any of the child terms.  
 Based on annotation dataset 12<sup>th</sup> November 2012 and GO ontology from 27<sup>th</sup> November 2012.

Table S3 Biological process VLAD results, total cholesterol trait associated genes

| GO Term   | P-value  | k  | M     | Genes  |
|---|----------|----|-------|--|
| <a href="#">GO:0008150: biological process</a>                    | 1.00E+00 | 49 | 29612 | ABCA1, ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, BRAP, *C6orf106, CETP, CYP7A1, DNAH11, ERGIC3, EVI5, FADS1, FADS2, FADS3, FRK, GCKR, GPAM, HFE, HMGCR, HNF1A, HNF4A, IRF2BP2, LDLR, LDLRAP1, LIPC, LIPG, LPA, MAFB, MAMSTR, MARC1, MYLIP, NAT2, NPC1L1, OSBPL7, PCSK9, PLEC, PPP1R3B, RAB3GAP1, RAF1, SORT1, *SPTY2D1, ST3GAL4, TOP1, TRIB1, TRPS1 |
| <a href="#">GO:0008152: metabolic process</a>                     | 2.37E-04 | 37 | 14817 | ABCA1, ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, FADS1, FADS2, FADS3, FRK, GCKR, GPAM, HFE, HMGCR, HNF1A, HNF4A, IRF2BP2, LDLR, LDLRAP1, LIPC, LIPG, LPA, MAFB, MARC1, MYLIP, NAT2, NPC1L1, PCSK9, PPP1R3B, RAF1, ST3GAL4, TOP1, TRPS1  |
| <a href="#">GO:0044237: cellular metabolic process</a>            | 1.02E-05 | 36 | 12556 | ABCA1, ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, FADS1, FADS2, FADS3, FRK, GCKR, GPAM, HMGCR, HNF1A, HNF4A, IRF2BP2, LDLR, LDLRAP1, LIPC, LIPG, LPA, MAFB, MARC1, MYLIP, NAT2, NPC1L1, PCSK9, PPP1R3B, RAF1, ST3GAL4, TOP1, TRPS1   |
| <a href="#">GO:0044710: single-organism metabolic process</a>     | 4.23E-04 | 36 | 14505 | ABCA1, ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, FADS1, FADS2, FADS3, FRK, GCKR, GPAM, HMGCR, HNF1A, HNF4A, IRF2BP2, LDLR, LDLRAP1, LIPC, LIPG, LPA, MAFB, MARC1, MYLIP, NAT2, NPC1L1, PCSK9, PPP1R3B, RAF1, ST3GAL4, TOP1, TRPS1   |
| <a href="#">GO:0044238: primary metabolic process</a>             | 8.54E-04 | 34 | 13667 | ABCA1, ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, FADS1, FADS2, FADS3, FRK, GCKR, GPAM, HMGCR, HNF1A, HNF4A, IRF2BP2, LDLR, LDLRAP1, LIPC, LIPG, LPA, MAFB, MYLIP, NPC1L1, PCSK9, PPP1R3B, RAF1, ST3GAL4, TOP1, TRPS1  |
| <a href="#">GO:0044707: single-multicellular organism process</a> | 9.16E-06 | 28 | 8030  | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, EVI5, GPAM, HFE, HMGCR, HNF1A, HNF4A, LDLR, LDLRAP1, LIPC, LIPG, LPA, MAFB, MYLIP, NPC1L1, PCSK9, RAB3GAP1, RAF1, SORT1, TOP1, TRPS1  |
| <a href="#">GO:0032501: multicellular organismal process</a>      | 1.01E-05 | 28 | 8067  | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, EVI5, GPAM, HFE, HMGCR, HNF1A, HNF4A, LDLR, LDLRAP1, LIPC, LIPG, LPA, MAFB, MYLIP, NPC1L1, PCSK9, RAB3GAP1, RAF1, SORT1, TOP1, TRPS1  |
| <a href="#">GO:0019222: regulation of metabolic process</a>       | 1.31E-05 | 26 | 7178  | ABCA1, ANGPTL3, APOA1, APOB, APOE, CYP7A1, FADS1, GCKR, GPAM, HMGCR, HNF1A, HNF4A, IRF2BP2, LDLR, LDLRAP1, LIPG, LPA, MAFB, MAMSTR, MYLIP, PCSK9, RAB3GAP1, RAF1, SORT1, TRIB1, TRPS1  |
| <a href="#">GO:0044281: small molecule metabolic process</a>      | 1.96E-12 | 26 | 3455  | *ABCA1, *ABCG5, *ABCG8, ANGPTL3, *APOA1, *APOB, *APOE, *CETP, *CYP7A1, *FADS1, *FADS2, FADS3, *GCKR, *GPAM, *HMGCR, HNF1A, HNF4A, *LDLR, LDLRAP1, LIPC, *LPA, MARC1, *NAT2, *NPC1L1, PCSK9, *ST3GAL4   |

|   |          |    |      |   |
|---|----------|----|------|---|
| <a href="#">GO:0080090: regulation of primary metabolic process</a>   | 2.44E-05 | 24 | 6458 | ABCA1, ANGPTL3, APOA1, APOB, APOE, CYP7A1, FADS1, GCKR, GPAM, HMGCR, HNF1A, HNF4A, IRF2BP2, LDLR, LDLRAP1, LIPG, MAFB, MAMSTR, MYLIP, PCSK9, RAB3GAP1, RAF1, TRIB1, TRPS1 |
| <a href="#">GO:0006629: lipid metabolic process</a>                   | 7.37E-16 | 23 | 1762 | *ABCA1, *ABCG5, *ABCG8, ANGPTL3, *APOA1, *APOB, *APOE, *CETP, CYP7A1, FADS1, FADS2, FADS3, GPAM, HMGCR, HNF1A, *HNF4A, *LDLR, LDLRAP1, LIPC, *LIPG, *LPA, *NPC1L1, PCSK9  |
| <a href="#">GO:0051179: localization</a>                              | 2.41E-05 | 23 | 5992 | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, ERGIC3, GCKR, GPAM, HFE, HNF1A, LDLR, LDLRAP1, LIPC, LIPG, LPA, NPC1L1, OSBPL7, PCSK9, SORT1, TRPS1                |
| <a href="#">GO:0065008: regulation of biological quality</a>          | 5.75E-09 | 22 | 3451 | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, GCKR, GPAM, HFE, HNF1A, HNF4A, LDLR, LDLRAP1, LIPC, LIPG, MYLIP, NPC1L1, PCSK9, RAF1                       |
| <a href="#">GO:0006810: transport</a>                                 | 1.96E-06 | 22 | 4771 | ABCA1, ABCG5, ABCG8, APOA1, APOB, APOE, CETP, ERGIC3, GCKR, GPAM, HFE, HNF1A, LDLR, *LDLRAP1, LIPC, LIPG, LPA, NPC1L1, OSBPL7, PCSK9, SORT1, TRPS1                        |
| <a href="#">GO:0051234: establishment of localization</a>             | 2.83E-06 | 22 | 4875 | ABCA1, ABCG5, ABCG8, APOA1, APOB, APOE, CETP, ERGIC3, GCKR, GPAM, HFE, HNF1A, LDLR, LDLRAP1, LIPC, LIPG, LPA, NPC1L1, OSBPL7, PCSK9, SORT1, TRPS1                         |
| <a href="#">GO:1901360: organic cyclic compound metabolic process</a> | 4.34E-04 | 22 | 6677 | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, GCKR, HMGCR, HNF1A, HNF4A, IRF2BP2, LDLR, LDLRAP1, LIPC, MAFB, NPC1L1, PCSK9, TOP1, TRPS1                  |
| <a href="#">GO:0048878: chemical homeostasis</a>                      | 3.04E-17 | 21 | 1156 | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, GCKR, GPAM, HFE, HNF1A, HNF4A, LDLR, LDLRAP1, LIPC, LIPG, MYLIP, NPC1L1, PCSK9                             |
| <a href="#">GO:0009058: biosynthetic process</a>                      | 3.82E-04 | 21 | 6142 | ABCA1, ABO, APOA1, APOB, APOE, CYP7A1, FADS1, FADS2, FADS3, GPAM, HFE, HMGCR, HNF1A, HNF4A, IRF2BP2, LIPC, MAFB, NPC1L1, ST3GAL4, TOP1, TRPS1                             |
| <a href="#">GO:0042592: homeostatic process</a>                       | 6.36E-14 | 21 | 1700 | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, GCKR, GPAM, HFE, HNF1A, HNF4A, LDLR, LDLRAP1, LIPC, LIPG, MYLIP, NPC1L1, PCSK9                             |
| <a href="#">GO:0042221: response to chemical stimulus</a>             | 4.26E-07 | 21 | 3988 | ABCA1, ABCG5, ANGPTL3, APOB, APOE, CYP7A1, FADS1, GCKR, GPAM, HMGCR, HNF1A, HNF4A, LDLR, LIPG, MARC1, NAT2, PCSK9, RAF1, SORT1, TOP1, TRIB1                               |
| <a href="#">GO:0031323: regulation of cellular metabolic process</a>  | 8.66E-04 | 21 | 6511 | ABCA1, APOA1, APOE, CYP7A1, FADS1, GCKR, GPAM, HMGCR, HNF1A, HNF4A, IRF2BP2, LDLR, LIPG, MAFB, MAMSTR, MYLIP, PCSK9, RAB3GAP1, RAF1, TRIB1, TRPS1                         |
| <a href="#">GO:1901576: organic substance biosynthetic process</a>    | 7.52E-04 | 20 | 5967 | ABCA1, ABO, APOA1, APOB, APOE, CYP7A1, FADS1, FADS2, FADS3, GPAM, HMGCR, HNF1A, HNF4A, IRF2BP2, LIPC, MAFB, NPC1L1, ST3GAL4, TOP1, TRPS1                                  |
| <a href="#">GO:0071702: organic substance transport</a>               | 3.71E-09 | 19 | 2430 | ABCA1, ABCG5, ABCG8, APOA1, APOB, APOE, CETP, GCKR, GPAM, HNF1A, LDLR, LDLRAP1, LIPC, LIPG, LPA, NPC1L1, OSBPL7, SORT1, TRPS1   |
| <a href="#">GO:0033036: macromolecule localization</a>                | 8.48E-09 | 19 | 2555 | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, GCKR, GPAM, HNF1A, LDLR, LDLRAP1, LIPC, LIPG, LPA, NPC1L1, OSBPL7, TRPS1   |
| <a href="#">GO:0048519: negative regulation of biological process</a> | 5.19E-05 | 19 | 4507 | ABCA1, ABCG5, ABCG8, APOA1, APOE, BRAP, CETP, FRK, GPAM, HMGCR, HNF1A, HNF4A, MAFB, MYLIP, PCSK9, RAF1, SORT1, TRIB1, TRPS1   |
| <a href="#">GO:0048518: positive regulation of biological process</a> | 3.09E-04 | 19 | 5136 | ABCA1, ANGPTL3, APOA1, APOB, APOE, GCKR, GPAM, HMGCR, HNF1A, HNF4A, LDLR, LDLRAP1, LIPG, MAFB, MAMSTR, MYLIP, PCSK9, RAF1, TRIB1  |
| <a href="#">GO:0055088: lipid homeostasis</a>                         | 5.62E-34 | 19 | 115  | ABCA1, ABCG5, ABCG8, *ANGPTL3, APOA1, APOB, APOE, *CETP, CYP7A1, GCKR, GPAM, *HNF4A, LDLR, LDLRAP1, LIPC, LIPG, MYLIP, NPC1L1, PCSK9                                      |

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| <a href="#">GO:0032879: regulation of localization</a>                        | 2.53E-09 | 17 | 1830 | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, GCKR, GPAM, HNF1A, HNF4A, LDLRAP1, LIPG, PCSK9, RAF1, TRIB1             |
| <a href="#">GO:0048523: negative regulation of cellular process</a>           | 6.20E-04 | 16 | 4093 | ABCA1, APOA1, APOE, BRAP, CETP, FRK, GPAM, HMGCR, HNF1A, HNF4A, MAFB, PCSK9, RAF1, SORT1, TRIB1, TRPS1                         |
| <a href="#">GO:0009893: positive regulation of metabolic process</a>          | 5.81E-06 | 16 | 2783 | ABCA1, ANGPTL3, APOA1, APOE, GCKR, GPAM, HNF1A, HNF4A, LDLR, LDLRAP1, MAFB, MAMSTR, MYLIP, PCSK9, RAF1, TRIB1                  |
| <a href="#">GO:0055092: sterol homeostasis</a>                                | 7.84E-30 | 16 | 82   | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, LDLR, LDLRAP1, LIPC, LIPG, MYLIP, NPC1L1, PCSK9                 |
| <a href="#">GO:0042632: cholesterol homeostasis</a>                           | 7.84E-30 | 16 | 82   | *ABCA1, *ABCG5, *ABCG8, *ANGPTL3, *APOA1, *APOB, *APOE, *CETP, *CYP7A1, *LDLR, *LDLRAP1, *LIPC, *LIPG, *MYLIP, *NPC1L1, *PCSK9 |
| <a href="#">GO:0044255: cellular lipid metabolic process</a>                  | 1.10E-10 | 16 | 1274 | *ABCA1, ANGPTL3, *APOA1, APOB, APOE, CETP, *CYP7A1, *FADS1, FADS2, FADS3, *GPAM, *HMGCR, HNF1A, LIPC, LIPG, PCSK9              |
| <a href="#">GO:0010876: lipid localization</a>                                | 4.20E-21 | 16 | 272  | ABCA1, ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, HNF1A, LDLR, LDLRAP1, LIPC, LIPG, LPA, NPC1L1, OSBPL7                   |
| <a href="#">GO:0006793: phosphorus metabolic process</a>                      | 2.06E-05 | 15 | 2720 | ABCG5, ABCG8, ANGPTL3, APOA1, CETP, FADS1, FRK, GPAM, HMGCR, HNF4A, LIPC, LIPG, PCSK9, RAF1, TOP1                              |
| <a href="#">GO:0006869: lipid transport</a>                                   | 5.25E-20 | 15 | 247  | ABCA1, ABCG5, ABCG8, APOA1, APOB, APOE, *CETP, HNF1A, LDLR, LDLRAP1, LIPC, LIPG, *LPA, NPC1L1, *OSBPL7                         |
| <a href="#">GO:0010033: response to organic substance</a>                     | 2.36E-05 | 15 | 2751 | ABCA1, ANGPTL3, APOB, APOE, CYP7A1, FADS1, GCKR, GPAM, HNF1A, HNF4A, LDLR, PCSK9, RAF1, SORT1, TRIB1                           |
| <a href="#">GO:1901615: organic hydroxy compound metabolic process</a>        | 2.22E-14 | 14 | 471  | ABCA1, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, HMGCR, HNF1A, LDLR, LDLRAP1, LIPC, NPC1L1, PCSK9                              |
| <a href="#">GO:0051239: regulation of multicellular organismal process</a>    | 1.18E-04 | 14 | 2790 | ABCG5, ABCG8, ANGPTL3, APOA1, APOE, GPAM, HMGCR, HNF4A, LIPG, MAFB, MAMSTR, MYLIP, PCSK9, TRPS1                                |
| <a href="#">GO:0008203: cholesterol metabolic process</a>                     | 1.80E-22 | 14 | 126  | *ABCA1, *ANGPTL3, *APOA1, *APOB, *APOE, *CETP, CYP7A1, HMGCR, *HNF1A, *LDLR, *LDLRAP1, *LIPC, NPC1L1, *PCSK9                   |
| <a href="#">GO:0016125: sterol metabolic process</a>                          | 9.30E-22 | 14 | 141  | ABCA1, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, HMGCR, HNF1A, LDLR, LDLRAP1, LIPC, NPC1L1, PCSK9                              |
| <a href="#">GO:0008202: steroid metabolic process</a>                         | 1.17E-16 | 14 | 322  | ABCA1, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, HMGCR, HNF1A, LDLR, LDLRAP1, LIPC, NPC1L1, PCSK9                              |
| <a href="#">GO:0006066: alcohol metabolic process</a>                         | 9.33E-16 | 14 | 374  | ABCA1, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, HMGCR, HNF1A, LDLR, LDLRAP1, LIPC, NPC1L1, PCSK9                              |
| <a href="#">GO:0006796: phosphate-containing compound metabolic process</a>   | 5.75E-05 | 14 | 2610 | ABCG5, ABCG8, ANGPTL3, APOA1, CETP, FADS1, FRK, GPAM, HMGCR, LIPC, LIPG, PCSK9, RAF1, TOP1                                     |
| <a href="#">GO:0015850: organic hydroxy compound transport</a>                | 7.03E-23 | 13 | 84   | ABCA1, ABCG5, ABCG8, APOA1, APOB, APOE, CETP, HNF1A, LDLR, LDLRAP1, LIPC, LIPG, NPC1L1   |
| <a href="#">GO:0051049: regulation of transport</a>                           | 1.53E-07 | 13 | 1321 | ABCA1, ABCG5, ABCG8, APOA1, APOE, CETP, GCKR, GPAM, HNF1A, HNF4A, LDLRAP1, LIPG, PCSK9   |
| <a href="#">GO:0065009: regulation of molecular function</a>                  | 7.58E-05 | 13 | 2329 | ANGPTL3, APOA1, APOE, GCKR, HMGCR, HNF4A, LDLRAP1, LPA, PCSK9, RAB3GAP1, RAF1, SORT1, TRIB1                                    |
| <a href="#">GO:0030301: cholesterol transport</a>                             | 3.65E-25 | 13 | 58   | ABCA1, ABCG5, ABCG8, *APOA1, *APOB, APOE, *CETP, HNF1A, *LDLR, LDLRAP1, LIPC, LIPG, *NPC1L1                                    |
| <a href="#">GO:0015918: sterol transport</a>                                  | 3.65E-25 | 13 | 58   | ABCA1, *ABCG5, *ABCG8, APOA1, APOB, APOE, CETP, HNF1A, LDLR, LDLRAP1, LIPC, LIPG, *NPC1L1                                      |
| <a href="#">GO:0050793: regulation of developmental process</a>               | 4.96E-05 | 13 | 2235 | ABCA1, ANGPTL3, APOA1, APOB, APOE, CETP, FADS1, HMGCR, HNF4A, MAFB, MAMSTR, RAF1, TRPS1  |
| <a href="#">GO:0031325: positive regulation of cellular metabolic process</a> | 9.49E-04 | 12 | 2626 | ABCA1, APOA1, APOE, GPAM, HNF1A, HNF4A, LDLR, MAFB, MAMSTR, PCSK9, RAF1, TRIB1   |

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| <a href="#">GO:0006082: organic acid metabolic process</a>                   | 1.05E-05 | 12 | 1635 | ANGPTL3, CYP7A1, FADS1, FADS2, FADS3, GCKR, GPAM, HNF1A, HNF4A, LPC, MARC1, ST3GAL4 |
| <a href="#">GO:0016192: vesicle-mediated transport</a>                       | 7.00E-06 | 11 | 1300 | ABCA1, APOA1, APOB, APOE, CETP, *ERGIC3, HFE, LDLR, LDLRAP1, LPA, SORT1             |
| <a href="#">GO:0044092: negative regulation of molecular function</a>        | 5.82E-08 | 11 | 798  | ANGPTL3, APOA1, APOE, GCKR, HMGCR, HNF4A, LPA, PCSK9, RAF1, SORT1, TRIB1            |
| <a href="#">GO:0019637: organophosphate metabolic process</a>                | 2.62E-05 | 11 | 1497 | ABCG5, ABCG8, ANGPTL3, APOA1, CETP, FADS1, GPAM, HMGCR, LPC, LIPG, PCSK9            |
| <a href="#">GO:0050790: regulation of catalytic activity</a>                 | 1.68E-04 | 11 | 1840 | ANGPTL3, APOA1, APOE, GCKR, HMGCR, LPA, PCSK9, RAB3GAP1, RAF1, SORT1, TRIB1         |
| <a href="#">GO:0043436: oxoacid metabolic process</a>                        | 5.30E-05 | 11 | 1617 | ANGPTL3, CYP7A1, FADS1, FADS2, FADS3, GPAM, HNF1A, HNF4A, LPC, MARC1, ST3GAL4       |
| <a href="#">GO:1901575: organic substance catabolic process</a>              | 9.45E-04 | 11 | 2254 | ABCG5, ABCG8, ANGPTL3, APOB, APOE, CYP7A1, LDLR, LPC, LIPG, MYLIP, PCSK9            |
| <a href="#">GO:0008610: lipid biosynthetic process</a>                       | 5.53E-07 | 10 | 790  | APOA1, CYP7A1, FADS1, FADS2, FADS3, GPAM, HMGCR, HNF1A, LPC, NPC1L1                 |
| <a href="#">GO:0043086: negative regulation of catalytic activity</a>        | 4.87E-08 | 10 | 607  | ANGPTL3, APOA1, APOE, GCKR, HMGCR, LPA, *PCSK9, RAF1, SORT1, TRIB1                  |
| <a href="#">GO:0009719: response to endogenous stimulus</a>                  | 3.13E-04 | 10 | 1650 | ABCA1, ANGPTL3, APOB, FADS1, GPAM, HNF4A, LDLR, PCSK9, RAF1, SORT1                  |
| <a href="#">GO:0019220: regulation of phosphate metabolic process</a>        | 2.63E-04 | 10 | 1614 | ABCA1, APOA1, APOE, GCKR, HMGCR, HNF4A, LDLR, RAB3GAP1, RAF1, TRIB1                 |
| <a href="#">GO:0051174: regulation of phosphorus metabolic process</a>       | 2.79E-04 | 10 | 1626 | ABCA1, APOA1, APOE, GCKR, HMGCR, HNF4A, LDLR, RAB3GAP1, RAF1, TRIB1                 |
| <a href="#">GO:0006897: endocytosis</a>                                      | 1.94E-08 | 9  | 405  | ABCA1, APOB, APOE, CETP, HFE, *LDLR, LDLRAP1, LPA, *SORT1                           |
| <a href="#">GO:0044711: single-organism biosynthetic process</a>             | 1.98E-06 | 9  | 702  | APOA1, CYP7A1, FADS1, FADS2, FADS3, HMGCR, HNF1A, LPC, NPC1L1                       |
| <a href="#">GO:0042157: lipoprotein metabolic process</a>                    | 1.03E-11 | 9  | 172  | *ABCA1, *APOA1, *APOB, *APOE, *CETP, *LDLR, *LPA, *NPC1L1, *PCSK9                   |
| <a href="#">GO:0019216: regulation of lipid metabolic process</a>            | 8.35E-10 | 9  | 282  | ANGPTL3, APOA1, APOB, APOE, CYP7A1, GPAM, *HNF4A, LDLR, LDLRAP1                     |
| <a href="#">GO:0097006: regulation of plasma lipoprotein particle levels</a> | 5.92E-16 | 9  | 60   | ABCA1, APOA1, APOB, APOE, CETP, LDLR, LDLRAP1, LPC, LIPG                            |
| <a href="#">GO:0045595: regulation of cell differentiation</a>               | 9.98E-04 | 9  | 1576 | ABCA1, APOB, APOE, CETP, *FADS1, MAFB, MAMSTR, *RAF1, TRPS1                         |
| <a href="#">GO:0044283: small molecule biosynthetic process</a>              | 1.52E-06 | 9  | 680  | APOA1, CYP7A1, FADS1, FADS2, FADS3, HMGCR, HNF1A, LPC, NPC1L1                       |
| <a href="#">GO:0019752: carboxylic acid metabolic process</a>                | 6.53E-04 | 9  | 1485 | ANGPTL3, CYP7A1, FADS1, FADS2, FADS3, GPAM, HNF1A, HNF4A, LPC                       |
| <a href="#">GO:0043933: macromolecular complex subunit organization</a>      | 4.59E-04 | 9  | 1414 | ABCA1, APOA1, APOB, APOE, CETP, HFE, HMGCR, LPC, LIPG                               |
| <a href="#">GO:0032787: monocarboxylic acid metabolic process</a>            | 7.56E-06 | 8  | 621  | ANGPTL3, CYP7A1, FADS1, FADS2, FADS3, GPAM, HNF1A, LPC                              |
| <a href="#">GO:0006644: phospholipid metabolic process</a>                   | 2.24E-06 | 8  | 526  | *ANGPTL3, APOA1, CETP, FADS1, *GPAM, LPC, LIPG, *PCSK9                              |
| <a href="#">GO:0009725: response to hormone stimulus</a>                     | 5.75E-04 | 8  | 1157 | *ANGPTL3, APOB, FADS1, GPAM, LDLR, PCSK9, RAF1, SORT1                               |
| <a href="#">GO:0006898: receptor-mediated endocytosis</a>                    | 1.49E-09 | 7  | 125  | *APOB, *APOE, *CETP, *HFE, *LDLR, *LDLRAP1, *LPA                                    |
| <a href="#">GO:0009894: regulation of catabolic process</a>                  | 1.80E-04 | 7  | 725  | ANGPTL3, APOE, LDLR, MYLIP, PCSK9, RAB3GAP1, TRIB1                                  |
| <a href="#">GO:0055091: phospholipid homeostasis</a>                         | 7.79E-19 | 7  | 9    | *ABCA1, *ANGPTL3, *APOA1, *CETP, *GPAM, *HNF4A, *LIPG                               |
| <a href="#">GO:0006631: fatty acid metabolic process</a>                     | 6.99E-06 | 7  | 434  | *ANGPTL3, FADS1, FADS2, FADS3, *GPAM, HNF1A, LPC                                    |
| <a href="#">GO:0046486: glycerolipid metabolic process</a>                   | 9.37E-06 | 7  | 454  | APOA1, APOB, APOE, CETP, GPAM, LPC, PCSK9   |
| <a href="#">GO:0043691: reverse cholesterol transport</a>                    | 1.08E-15 | 7  | 19   | *ABCA1, *APOA1, *APOE, *CETP, *HNF1A, *LIPC, *LIPG                                  |
| <a href="#">GO:0071827: plasma lipoprotein particle organization</a>         | 8.98E-14 | 7  | 33   | ABCA1, APOA1, APOB, APOE, CETP, LPC, LIPG   |
| <a href="#">GO:0071825: protein-lipid complex subunit organization</a>       | 8.98E-14 | 7  | 33   | ABCA1, APOA1, APOB, APOE, CETP, LPC, LIPG   |
| <a href="#">GO:0045834: positive regulation of lipid metabolic process</a>   | 1.33E-09 | 7  | 123  | ANGPTL3, APOA1, APOE, GPAM, HNF4A, LDLR, LDLRAP1                                    |

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| <a href="#">GO:0032374: regulation of cholesterol transport</a>                     | 7.08E-14 | 7 | 32  | ABCA1, ABCG5, ABCG8, APOA1, APOE, CETP, LIPG   |
| <a href="#">GO:0032371: regulation of sterol transport</a>                          | 7.08E-14 | 7 | 32  | ABCA1, ABCG5, ABCG8, APOA1, APOE, CETP, LIPG   |
| <a href="#">GO:0032368: regulation of lipid transport</a>                           | 3.59E-11 | 7 | 74  | ABCA1, ABCG5, ABCG8, APOA1, APOE, CETP, LIPG   |
| <a href="#">GO:0009743: response to carbohydrate stimulus</a>                       | 1.60E-07 | 7 | 246 | *APOB, CYP7A1, FADS1, GCKR, GPAM, HNF1A, HNF4A |
| <a href="#">GO:0031667: response to nutrient levels</a>                             | 1.22E-05 | 7 | 473 | ABCG5, FADS1, *GPAM, HFE, HMGCR, LIPG, PCSK9   |
| <a href="#">GO:0010243: response to organic nitrogen</a>                            | 9.30E-04 | 7 | 954 | FADS1, GPAM, HNF4A, LDLR, PCSK9, RAF1, SORT1   |
| <a href="#">GO:0009991: response to extracellular stimulus</a>                      | 2.22E-05 | 7 | 519 | ABCG5, FADS1, GPAM, HFE, HMGCR, LIPG, PCSK9    |
| <a href="#">GO:0015748: organophosphate ester transport</a>                         | 1.26E-09 | 6 | 66  | ABCA1, ABCG8, APOA1, APOE, CETP, LDLR          |
| <a href="#">GO:0055114: oxidation-reduction process</a>                             | 9.07E-04 | 6 | 686 | APOA1, FADS1, FADS2, FADS3, *MARC1, PPP1R3B    |
| <a href="#">GO:0051241: negative regulation of multicellular organismal process</a> | 1.68E-04 | 6 | 499 | ABCG5, ABCG8, APOA1, APOE, MYLIP, PCSK9        |
| <a href="#">GO:0070328: triglyceride homeostasis</a>                                | 1.07E-11 | 6 | 31  | *ANGPTL3, *APOA1, *CETP, *GCKR, *HNF4A, *LIPC  |
| <a href="#">GO:0055090: acylglycerol homeostasis</a>                                | 1.31E-11 | 6 | 32  | *ANGPTL3, APOA1, CETP, GCKR, HNF4A, LIPC       |
| <a href="#">GO:0006641: triglyceride metabolic process</a>                          | 2.38E-08 | 6 | 107 | APOB, *APOE, *CETP, GPAM, LIPC, *PCSK9         |
| <a href="#">GO:0006639: acylglycerol metabolic process</a>                          | 3.48E-08 | 6 | 114 | APOB, APOE, CETP, GPAM, LIPC, PCSK9            |
| <a href="#">GO:0006638: neutral lipid metabolic process</a>                         | 3.87E-08 | 6 | 116 | APOB, APOE, CETP, GPAM, LIPC, PCSK9            |
| <a href="#">GO:0016042: lipid catabolic process</a>                                 | 1.14E-05 | 6 | 307 | ANGPTL3, APOB, APOE, CYP7A1, LIPC, LIPG        |
| <a href="#">GO:0015914: phospholipid transport</a>                                  | 6.43E-11 | 6 | 41  | ABCA1, *ABCG8, APOA1, APOE, *CETP, *LDLR       |
| <a href="#">GO:0034381: plasma lipoprotein particle clearance</a>                   | 3.96E-11 | 6 | 38  | APOA1, APOB, APOE, LDLR, LDLRAP1, LIPC         |
| <a href="#">GO:0034369: plasma lipoprotein particle remodeling</a>                  | 4.31E-12 | 6 | 27  | APOA1, APOB, APOE, CETP, LIPC, LIPG            |
| <a href="#">GO:0034368: protein-lipid complex remodeling</a>                        | 4.31E-12 | 6 | 27  | APOA1, APOB, APOE, CETP, LIPC, LIPG            |
| <a href="#">GO:0034367: macromolecular complex remodeling</a>                       | 4.31E-12 | 6 | 27  | APOA1, APOB, APOE, CETP, LIPC, LIPG            |
| <a href="#">GO:0046890: regulation of lipid biosynthetic process</a>                | 8.74E-08 | 6 | 133 | APOB, APOE, CYP7A1, GPAM, HNF4A, LDLR          |
| <a href="#">GO:0043434: response to peptide hormone stimulus</a>                    | 4.79E-04 | 6 | 607 | FADS1, GPAM, LDLR, PCSK9, RAF1, SORT1          |
| <a href="#">GO:1901652: response to peptide</a>                                     | 5.40E-04 | 6 | 621 | FADS1, GPAM, LDLR, PCSK9, RAF1, SORT1          |
| <a href="#">GO:0072330: monocarboxylic acid biosynthetic process</a>                | 5.24E-06 | 6 | 268 | CYP7A1, FADS1, FADS2, FADS3, HNF1A, LIPC       |
| <a href="#">GO:0016053: organic acid biosynthetic process</a>                       | 1.43E-04 | 6 | 484 | CYP7A1, FADS1, FADS2, FADS3, HNF1A, LIPC       |
| <a href="#">GO:0046394: carboxylic acid biosynthetic process</a>                    | 1.43E-04 | 6 | 484 | CYP7A1, FADS1, FADS2, FADS3, HNF1A, LIPC       |
| <a href="#">GO:0031329: regulation of cellular catabolic process</a>                | 4.50E-04 | 6 | 600 | APOE, LDLR, MYLIP, PCSK9, RAB3GAP1, TRIB1      |
| <a href="#">GO:0006694: steroid biosynthetic process</a>                            | 4.81E-06 | 5 | 149 | APOA1, CYP7A1, HMGCR, HNF1A, NPC1L1            |
| <a href="#">GO:0006633: fatty acid biosynthetic process</a>                         | 1.86E-05 | 5 | 197 | FADS1, FADS2, FADS3, *HNF1A, *LIPC             |
| <a href="#">GO:0033344: cholesterol efflux</a>                                      | 6.44E-10 | 5 | 26  | *ABCA1, *ABCG5, *ABCG8, *APOA1, *APOE          |
| <a href="#">GO:0034375: high-density lipoprotein particle remodeling</a>            | 2.98E-11 | 5 | 15  | *APOA1, *APOE, *CETP, *LIPC, *LIPG             |
| <a href="#">GO:0019218: regulation of steroid metabolic process</a>                 | 6.40E-07 | 5 | 99  | APOA1, APOB, APOE, CYP7A1, LDLRAP1             |
| <a href="#">GO:0051346: negative regulation of hydrolase activity</a>               | 8.79E-05 | 5 | 273 | ANGPTL3, *APOA1, LPA, RAF1, SORT1              |
| <a href="#">GO:0009746: response to hexose stimulus</a>                             | 9.95E-06 | 5 | 173 | CYP7A1, GCKR, GPAM, HNF1A, HNF4A               |
| <a href="#">GO:0034284: response to monosaccharide stimulus</a>                     | 1.82E-05 | 5 | 196 | CYP7A1, GCKR, GPAM, HNF1A, HNF4A               |

|   |          |   |     |                                   |
|---|----------|---|-----|-----------------------------------|
| <a href="#">GO:0032868: response to insulin stimulus</a>  | 4.42E-04 | 5 | 387 | *FADS1, GPAM, PCSK9, RAF1, *SORT1 |
| <a href="#">GO:0046434: organophosphate catabolic process</a>   | 2.72E-04 | 5 | 348 | ABCG5, ABCG8, ANGPTL3, LIPC, LIPG |
| <a href="#">GO:0033500: carbohydrate homeostasis</a>  | 1.12E-04 | 4 | 150 | CYP7A1, GCKR, HNF1A, HNF4A        |
| <a href="#">GO:0042593: glucose homeostasis</a>   | 1.12E-04 | 4 | 150 | CYP7A1, GCKR, *HNF1A, *HNF4A      |
| <a href="#">GO:0044241: lipid digestion</a>   | 6.54E-09 | 4 | 14  | ABCG5, ABCG8, LDLR, NPC1L1        |
| <a href="#">GO:0050892: intestinal absorption</a>   | 1.32E-07 | 4 | 28  | ABCG5, ABCG8, LDLR, NPC1L1        |
| <a href="#">GO:0022600: digestive system process</a>  | 1.44E-06 | 4 | 50  | ABCG5, ABCG8, LDLR, NPC1L1        |
| <a href="#">GO:0007586: digestion</a>   | 4.57E-05 | 4 | 119 | ABCG5, ABCG8, LDLR, NPC1L1        |
| <a href="#">GO:0009896: positive regulation of catabolic process</a>                                  | 2.51E-04 | 4 | 185 | ANGPTL3, APOE, MYLIP, TRIB1       |
| <a href="#">GO:0042176: regulation of protein catabolic process</a>                                   | 7.46E-04 | 4 | 247 | APOE, MYLIP, PCSK9, TRIB1         |
| <a href="#">GO:0042158: lipoprotein biosynthetic process</a>  | 3.12E-05 | 4 | 108 | ABCA1, *APOA1, *APOB, *APOE       |
| <a href="#">GO:0044242: cellular lipid catabolic process</a>  | 2.46E-04 | 4 | 184 | ANGPTL3, APOB, LIPC, LIPG         |
| <a href="#">GO:0030299: intestinal cholesterol absorption</a>   | 4.61E-10 | 4 | 8   | *ABCG5, *ABCG8, *LDLR, *NPC1L1    |
| <a href="#">GO:0034374: low-density lipoprotein particle remodeling</a>                               | 4.68E-09 | 4 | 13  | *APOB, *APOE, *CETP, *LIPC        |
| <a href="#">GO:0034377: plasma lipoprotein particle assembly</a>                                      | 8.91E-09 | 4 | 15  | ABCA1, APOA1, APOB, APOE          |
| <a href="#">GO:0065005: protein-lipid complex assembly</a>  | 8.91E-09 | 4 | 15  | ABCA1, APOA1, APOB, APOE          |
| <a href="#">GO:0033673: negative regulation of kinase activity</a>                                    | 4.13E-04 | 4 | 211 | APOE, GCKR, HMGCR, TRIB1          |
| <a href="#">GO:0051348: negative regulation of transferase activity</a>                               | 5.53E-04 | 4 | 228 | APOE, GCKR, HMGCR, TRIB1          |
| <a href="#">GO:0009749: response to glucose stimulus</a>  | 1.51E-04 | 4 | 162 | CYP7A1, *GPAM, *HNF1A, *HNF4A     |
| <a href="#">GO:0048844: artery morphogenesis</a>  | 1.30E-04 | 3 | 59  | *ANGPTL3, *APOB, *APOE            |
| <a href="#">GO:0060840: artery development</a>  | 2.25E-04 | 3 | 71  | ANGPTL3, APOB, APOE               |
| <a href="#">GO:0015758: glucose transport</a>   | 1.89E-04 | 3 | 67  | *GCKR, HNF1A, SORT1               |
| <a href="#">GO:0008645: hexose transport</a>  | 1.98E-04 | 3 | 68  | *GCKR, HNF1A, SORT1               |
| <a href="#">GO:0015749: monosaccharide transport</a>  | 2.16E-04 | 3 | 70  | GCKR, HNF1A, SORT1                |
| <a href="#">GO:0030300: regulation of intestinal cholesterol absorption</a>                           | 8.49E-08 | 3 | 6   | ABCG5, ABCG8, *APOA1              |
| <a href="#">GO:0044058: regulation of digestive system process</a>                                    | 1.68E-05 | 3 | 30  | ABCG5, ABCG8, APOA1               |
| <a href="#">GO:0032803: regulation of low-density lipoprotein particle receptor catabolic process</a> | 4.25E-08 | 3 | 5   | APOE, *MYLIP, *PCSK9              |
| <a href="#">GO:2000644: regulation of receptor catabolic process</a>                                  | 8.49E-08 | 3 | 6   | APOE, MYLIP, PCSK9                |
| <a href="#">GO:0010743: regulation of macrophage derived foam cell differentiation</a>                | 4.67E-05 | 3 | 42  | ABCA1, APOB, CETP                 |
| <a href="#">GO:0045732: positive regulation of protein catabolic process</a>                          | 9.23E-04 | 3 | 115 | APOE, *MYLIP, TRIB1               |
| <a href="#">GO:0042159: lipoprotein catabolic process</a>   | 6.96E-07 | 3 | 11  | *APOB, *APOE, *LDLR               |
| <a href="#">GO:0009395: phospholipid catabolic process</a>  | 2.93E-05 | 3 | 36  | *ANGPTL3, LIPC, *LIPG             |
| <a href="#">GO:0006695: cholesterol biosynthetic process</a>  | 4.34E-05 | 3 | 41  | *APOA1, *HMGCR, *NPC1L1           |
| <a href="#">GO:0016126: sterol biosynthetic process</a>   | 8.89E-05 | 3 | 52  | APOA1, HMGCR, NPC1L1              |
| <a href="#">GO:0046470: phosphatidylcholine metabolic process</a>                                     | 1.73E-04 | 3 | 65  | APOA1, *CETP, LIPC                |
| <a href="#">GO:0006636: unsaturated fatty acid biosynthetic process</a>                               | 1.98E-04 | 3 | 68  | *FADS1, *FADS2, *FADS3            |
| <a href="#">GO:0033559: unsaturated fatty acid metabolic process</a>                                  | 8.11E-04 | 3 | 110 | *FADS1, *FADS2, FADS3             |
| <a href="#">GO:0033700: phospholipid efflux</a>   | 9.27E-07 | 3 | 12  | *ABCA1, *APOA1, *APOE             |
| <a href="#">GO:0010984: regulation of lipoprotein particle clearance</a>                              | 1.20E-06 | 3 | 13  | LIPG, MYLIP, PCSK9                |

|   |          |   |     |                       |
|---|----------|---|-----|-----------------------|
| <a href="#">GO:0034383: low-density lipoprotein particle clearance</a>                          | 1.91E-06 | 3 | 15  | *APOB, *LDLR, LDLRAP1 |
| <a href="#">GO:0034380: high-density lipoprotein particle assembly</a>                          | 8.49E-08 | 3 | 6   | *ABCA1, *APOA1, *APOE |
| <a href="#">GO:0034372: very-low-density lipoprotein particle remodeling</a>                    | 1.48E-07 | 3 | 7   | *APOE, *CETP, *LIPC   |
| <a href="#">GO:0034370: triglyceride-rich lipoprotein particle remodeling</a>                   | 5.07E-07 | 3 | 10  | APOE, CETP, LIPC      |
| <a href="#">GO:0045940: positive regulation of steroid metabolic process</a>                    | 1.35E-05 | 3 | 28  | APOA1, APOE, LDLRAP1  |
| <a href="#">GO:0090181: regulation of cholesterol metabolic process</a>                         | 2.24E-05 | 3 | 33  | APOB, APOE, LDLRAP1   |
| <a href="#">GO:0050810: regulation of steroid biosynthetic process</a>                          | 2.44E-04 | 3 | 73  | APOB, APOE, CYP7A1    |
| <a href="#">GO:0046889: positive regulation of lipid biosynthetic process</a>                   | 1.05E-04 | 3 | 55  | GPAM, HNF4A, LDLR     |
| <a href="#">GO:0032376: positive regulation of cholesterol transport</a>                        | 1.20E-06 | 3 | 13  | ABCA1, APOE, *LIPG    |
| <a href="#">GO:0032373: positive regulation of sterol transport</a>                             | 1.20E-06 | 3 | 13  | ABCA1, APOE, LIPG     |
| <a href="#">GO:0010874: regulation of cholesterol efflux</a>                                    | 2.85E-06 | 3 | 17  | ABCA1, APOE, *CETP    |
| <a href="#">GO:0032370: positive regulation of lipid transport</a>                              | 3.18E-05 | 3 | 37  | ABCA1, APOE, LIPG     |
| <a href="#">GO:0009267: cellular response to starvation</a>                                     | 6.70E-04 | 3 | 103 | *FADS1, HFE, *PCSK9   |
| <a href="#">GO:0032489: regulation of Cdc42 protein signal transduction</a>                     | 5.55E-06 | 3 | 21  | *ABCA1, *APOA1, *APOE |
| <a href="#">GO:0046164: alcohol catabolic process</a>   | 1.89E-04 | 3 | 67  | APOE, CYP7A1, LIPC    |
| <a href="#">GO:0042439: ethanolamine-containing compound metabolic process</a>                  | 5.13E-04 | 3 | 94  | APOA1, CETP, LIPC     |
| <a href="#">GO:0008643: carbohydrate transport</a>  | 6.33E-04 | 3 | 101 | GCKR, HNF1A, SORT1    |
| <a href="#">GO:0030802: regulation of cyclic nucleotide biosynthetic process</a>                | 7.49E-04 | 3 | 107 | ABCA1, APOE, RAF1     |
| <a href="#">GO:0030808: regulation of nucleotide biosynthetic process</a>                       | 7.69E-04 | 3 | 108 | ABCA1, APOE, RAF1     |
| <a href="#">GO:1900371: regulation of purine nucleotide biosynthetic process</a>                | 7.69E-04 | 3 | 108 | ABCA1, APOE, RAF1     |
| <a href="#">GO:0030799: regulation of cyclic nucleotide metabolic process</a>                   | 9.70E-04 | 3 | 117 | ABCA1, APOE, RAF1     |
| <a href="#">GO:0030804: positive regulation of cyclic nucleotide biosynthetic process</a>       | 2.44E-04 | 3 | 73  | ABCA1, APOE, RAF1     |
| <a href="#">GO:1900373: positive regulation of purine nucleotide biosynthetic process</a>       | 2.54E-04 | 3 | 74  | ABCA1, APOE, RAF1     |
| <a href="#">GO:0030810: positive regulation of nucleotide biosynthetic process</a>              | 2.54E-04 | 3 | 74  | ABCA1, APOE, RAF1     |
| <a href="#">GO:0030801: positive regulation of cyclic nucleotide metabolic process</a>          | 2.64E-04 | 3 | 75  | ABCA1, APOE, RAF1     |
| <a href="#">GO:1901616: organic hydroxy compound catabolic process</a>                          | 2.75E-04 | 3 | 76  | APOE, CYP7A1, LIPC    |
| <a href="#">GO:1900544: positive regulation of purine nucleotide metabolic process</a>          | 2.86E-04 | 3 | 77  | ABCA1, APOE, RAF1     |
| <a href="#">GO:0045981: positive regulation of nucleotide metabolic process</a>                 | 2.86E-04 | 3 | 77  | ABCA1, APOE, RAF1     |
| <a href="#">GO:0046323: glucose import</a>  | 1.61E-05 | 2 | 4   | *HNF1A, *SORT1        |
| <a href="#">GO:0010949: negative regulation of intestinal phytosterol absorption</a>            | 2.68E-06 | 2 | 2   | *ABCG5, *ABCG8        |
| <a href="#">GO:0045796: negative regulation of intestinal cholesterol absorption</a>            | 2.68E-06 | 2 | 2   | *ABCG5, *ABCG8        |
| <a href="#">GO:0060457: negative regulation of digestive system process</a>                     | 4.04E-04 | 2 | 18  | ABCG5, ABCG8          |
| <a href="#">GO:0010745: negative regulation of macrophage derived foam cell differentiation</a> | 2.07E-04 | 2 | 13  | *ABCA1, *CETP         |
| <a href="#">GO:0043651: linoleic acid metabolic process</a>                                     | 7.46E-05 | 2 | 8   | *FADS1, *FADS2        |

|   |          |   |    |                  |
|---|----------|---|----|------------------|
| <a href="#">GO:0006707: cholesterol catabolic process</a>                                     | 2.07E-04 | 2 | 13 | *APOE, *CYP7A1   |
| <a href="#">GO:0016127: sterol catabolic process</a>  | 2.07E-04 | 2 | 13 | APOE, CYP7A1     |
| <a href="#">GO:0006699: bile acid biosynthetic process</a>                                    | 6.64E-04 | 2 | 23 | *CYP7A1, *HNF1A  |
| <a href="#">GO:0019433: triglyceride catabolic process</a>                                    | 6.64E-04 | 2 | 23 | *APOB, *LIPC     |
| <a href="#">GO:0046464: acylglycerol catabolic process</a>                                    | 8.50E-04 | 2 | 26 | APOB, LIPC       |
| <a href="#">GO:0046461: neutral lipid catabolic process</a>                                   | 8.50E-04 | 2 | 26 | APOB, LIPC       |
| <a href="#">GO:0035376: sterol import</a>   | 8.04E-06 | 2 | 3  | APOA1, LDLR      |
| <a href="#">GO:0070508: cholesterol import</a>  | 8.04E-06 | 2 | 3  | *APOA1, *LDLR    |
| <a href="#">GO:0035382: sterol transmembrane transport</a>                                    | 8.04E-06 | 2 | 3  | APOA1, LDLR      |
| <a href="#">GO:0032367: intracellular cholesterol transport</a>                               | 7.46E-05 | 2 | 8  | *ABCA1, LDLRAP1  |
| <a href="#">GO:0032366: intracellular sterol transport</a>                                    | 7.46E-05 | 2 | 8  | ABCA1, LDLRAP1   |
| <a href="#">GO:0032365: intracellular lipid transport</a>                                     | 4.04E-04 | 2 | 18 | ABCA1, LDLRAP1   |
| <a href="#">GO:0034384: high-density lipoprotein particle clearance</a>                       | 5.60E-05 | 2 | 7  | *APOA1, *APOE    |
| <a href="#">GO:0034382: chylomicron remnant clearance</a>                                     | 9.59E-05 | 2 | 9  | *APOE, *LIPC     |
| <a href="#">GO:0071830: triglyceride-rich lipoprotein particle clearance</a>                  | 9.59E-05 | 2 | 9  | APOE, LIPC       |
| <a href="#">GO:0010873: positive regulation of cholesterol esterification</a>                 | 5.60E-05 | 2 | 7  | *APOA1, *APOE    |
| <a href="#">GO:0010872: regulation of cholesterol esterification</a>                          | 9.59E-05 | 2 | 9  | APOA1, APOE      |
| <a href="#">GO:0045540: regulation of cholesterol biosynthetic process</a>                    | 6.07E-04 | 2 | 22 | *APOB, APOE      |
| <a href="#">GO:0010867: positive regulation of triglyceride biosynthetic process</a>          | 1.46E-04 | 2 | 11 | *GPAM, *LDLR     |
| <a href="#">GO:0010866: regulation of triglyceride biosynthetic process</a>                   | 3.17E-04 | 2 | 16 | GPAM, LDLR       |
| <a href="#">GO:0090208: positive regulation of triglyceride metabolic process</a>             | 3.59E-04 | 2 | 17 | GPAM, LDLR       |
| <a href="#">GO:0032375: negative regulation of cholesterol transport</a>                      | 1.46E-04 | 2 | 11 | ABCG5, ABCG8     |
| <a href="#">GO:0010875: positive regulation of cholesterol efflux</a>                         | 1.46E-04 | 2 | 11 | *ABCA1, *APOE    |
| <a href="#">GO:0032372: negative regulation of sterol transport</a>                           | 1.46E-04 | 2 | 11 | ABCG5, ABCG8     |
| <a href="#">GO:0010989: negative regulation of low-density lipoprotein particle clearance</a> | 1.61E-05 | 2 | 4  | *MYLIP, *PCSK9   |
| <a href="#">GO:0010988: regulation of low-density lipoprotein particle clearance</a>          | 5.60E-05 | 2 | 7  | MYLIP, PCSK9     |
| <a href="#">GO:0010985: negative regulation of lipoprotein particle clearance</a>             | 5.60E-05 | 2 | 7  | MYLIP, PCSK9     |
| <a href="#">GO:0051005: negative regulation of lipoprotein lipase activity</a>                | 4.01E-05 | 2 | 6  | *ANGPTL3, *SORT1 |
| <a href="#">GO:0060192: negative regulation of lipase activity</a>                            | 2.07E-04 | 2 | 13 | ANGPTL3, SORT1   |
| <a href="#">GO:0010885: regulation of cholesterol storage</a>                                 | 7.85E-04 | 2 | 25 | ABCA1, APOB      |
| <a href="#">GO:0009750: response to fructose stimulus</a>                                     | 2.07E-04 | 2 | 13 | *GCKR, *GPAM     |
| <a href="#">GO:0036109: alpha-linolenic acid metabolic process</a>                            | 1.46E-04 | 2 | 11 | *FADS1, *FADS2   |
| <a href="#">GO:0060395: SMAD protein signal transduction</a>                                  | 6.64E-04 | 2 | 23 | *HNF1A, *HNF4A   |
| <a href="#">GO:0006706: steroid catabolic process</a>   | 8.50E-04 | 2 | 26 | APOE, CYP7A1     |
| <a href="#">GO:0090207: regulation of triglyceride metabolic process</a>                      | 9.17E-04 | 2 | 27 | GPAM, LDLR       |
| <a href="#">GO:0050663: cytokine secretion</a>  | 9.17E-04 | 2 | 27 | ABCA1, GPAM      |

|  |          |   |    |              |
|--|----------|---|----|--------------|
| GO:0032369: negative regulation of lipid transport | 9.17E-04 | 2 | 27 | ABCG5, ABCG8 |
|--|----------|---|----|--------------|

k is the number of genes in the query set annotated to that node, and M is the number of genes in the database annotated to that node.  
 \*next to the gene symbol indicates that the gene is annotated to the node, and not any of the child terms.  
 Based on annotation dataset 12<sup>th</sup> November 2012 and GO ontology from 27<sup>th</sup> November 2012.

Table S4 Biological process VLAD results, LDL cholesterol trait associated genes

| GO Term   | P-value  | k  | M     | Genes   |
|---|----------|----|-------|---|
| <a href="#">GO:0008150: biological process</a>                    | 1.00E+00 | 38 | 29612 | ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, BRAP, CETP, CYP7A1, DNAH11, FADS1, FADS2, FADS3, FRK, GPAM, HFE, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, LPA, MAFB, MARC1, MYLIP, NPC1L1, *NYNRIN, OSBPL7, PCSK9, PLEC, PPP1R3B, PRKCA, SFN, SORT1, ST3GAL4, TOP1, TRIB1 |
| <a href="#">GO:0009987: cellular process</a>                      | 8.23E-04 | 37 | 23018 | ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, BRAP, CETP, CYP7A1, DNAH11, FADS1, FADS2, FADS3, FRK, GPAM, HFE, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, LPA, MAFB, MARC1, MYLIP, NPC1L1, NYNRIN, PCSK9, PLEC, PPP1R3B, PRKCA, SFN, SORT1, ST3GAL4, TOP1, TRIB1          |
| <a href="#">GO:0008152: metabolic process</a>                     | 5.86E-05 | 31 | 14817 | ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, FADS1, FADS2, FADS3, FRK, GPAM, HFE, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, LPA, MAFB, MARC1, MYLIP, NPC1L1, NYNRIN, PCSK9, PPP1R3B, PRKCA, ST3GAL4, TOP1   |
| <a href="#">GO:0044237: cellular metabolic process</a>            | 4.75E-06 | 30 | 12556 | ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, FADS1, FADS2, FADS3, FRK, GPAM, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, LPA, MAFB, MARC1, MYLIP, NPC1L1, NYNRIN, PCSK9, PPP1R3B, PRKCA, ST3GAL4, TOP1  |
| <a href="#">GO:0044710: single-organism metabolic process</a>     | 1.47E-04 | 30 | 14505 | ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, FADS1, FADS2, FADS3, FRK, GPAM, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, LPA, MAFB, MARC1, MYLIP, NPC1L1, NYNRIN, PCSK9, PPP1R3B, PRKCA, ST3GAL4, TOP1  |
| <a href="#">GO:0044238: primary metabolic process</a>             | 1.49E-04 | 29 | 13667 | ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, FADS1, FADS2, FADS3, FRK, GPAM, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, LPA, MAFB, MYLIP, NPC1L1, NYNRIN, PCSK9, PPP1R3B, PRKCA, ST3GAL4, TOP1   |
| <a href="#">GO:0071704: organic substance metabolic process</a>   | 3.40E-04 | 29 | 14197 | ABCG5, ABCG8, ABO, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, FADS1, FADS2, FADS3, FRK, GPAM, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, LPA, MAFB, MYLIP, NPC1L1, NYNRIN, PCSK9, PPP1R3B, PRKCA, ST3GAL4, TOP1   |
| <a href="#">GO:0044707: single-multicellular organism process</a> | 6.32E-05 | 22 | 8030  | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, GPAM, HFE, HMGCR, HNF1A, LDLR, LDLRAP1, LPA, MAFB, MYLIP, NPC1L1, PCSK9, PRKCA, SFN, SORT1, TOP1  |
| <a href="#">GO:0032501: multicellular organismal process</a>      | 6.82E-05 | 22 | 8067  | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, GPAM, HFE, HMGCR, HNF1A, LDLR, LDLRAP1, LPA, MAFB, MYLIP, NPC1L1, PCSK9, PRKCA, SFN, SORT1, TOP1  |

|   |          |    |      |   |
|---|----------|----|------|---|
| <a href="#">GO:0044281: small molecule metabolic process</a>          | 9.53E-12 | 22 | 3455 | *ABCG5, *ABCG8, ANGPTL3, *APOA1, *APOB, *APOE, *CETP, *CYP7A1, *FADS1, *FADS2, FADS3, *GPAM, *HMGCR, HNF1A, *LDLR, LDLRAP1, *LPA, MARC1, *NPC1L1, PCSK9, *PRKCA, *ST3GAL4 |
| <a href="#">GO:0019222: regulation of metabolic process</a>           | 1.50E-04 | 20 | 7178 | ANGPTL3, APOA1, APOB, APOE, CYP7A1, FADS1, GPAM, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, LPA, MAFB, MYLIP, PCSK9, PRKCA, SFN, SORT1, TRIB1                                  |
| <a href="#">GO:0006629: lipid metabolic process</a>                   | 5.63E-14 | 19 | 1762 | *ABCG5, *ABCG8, ANGPTL3, *APOA1, *APOB, *APOE, *CETP, CYP7A1, FADS1, FADS2, FADS3, GPAM, HMGCR, HNF1A, *LDLR, LDLRAP1, *LPA, *NPC1L1, PCSK9                               |
| <a href="#">GO:1901360: organic cyclic compound metabolic process</a> | 1.90E-04 | 19 | 6677 | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, MAFB, NPC1L1, NYNRIN, PCSK9, PRKCA, TOP1                                    |
| <a href="#">GO:0080090: regulation of primary metabolic process</a>   | 4.22E-04 | 18 | 6458 | ANGPTL3, APOA1, APOB, APOE, CYP7A1, FADS1, GPAM, HMGCR, HNF1A, IRF2BP2, LDLR, LDLRAP1, MAFB, MYLIP, PCSK9, PRKCA, SFN, TRIB1  |
| <a href="#">GO:0051179: localization</a>                              | 1.58E-04 | 18 | 5992 | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, GPAM, HFE, HNF1A, LDLR, LDLRAP1, LPA, NPC1L1, OSBPL7, PCSK9, PRKCA, SORT1   |
| <a href="#">GO:0048878: chemical homeostasis</a>                      | 1.34E-14 | 17 | 1156 | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, GPAM, HFE, HNF1A, LDLR, LDLRAP1, MYLIP, NPC1L1, PCSK9, PRKCA  |
| <a href="#">GO:0065008: regulation of biological quality</a>          | 3.31E-07 | 17 | 3451 | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, GPAM, HFE, HNF1A, LDLR, LDLRAP1, MYLIP, NPC1L1, PCSK9, PRKCA  |
| <a href="#">GO:0048519: negative regulation of biological process</a> | 1.40E-05 | 17 | 4507 | ABCG5, ABCG8, APOA1, APOE, BRAP, CETP, FRK, GPAM, HMGCR, HNF1A, MAFB, MYLIP, PCSK9, PRKCA, SFN, SORT1, TRIB1  |
| <a href="#">GO:0009058: biosynthetic process</a>                      | 7.46E-04 | 17 | 6142 | ABO, APOA1, APOB, APOE, CYP7A1, FADS1, FADS2, FADS3, GPAM, HFE, HMGCR, HNF1A, IRF2BP2, MAFB, NPC1L1, ST3GAL4, TOP1  |
| <a href="#">GO:0042592: homeostatic process</a>                       | 6.70E-12 | 17 | 1700 | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, GPAM, HFE, HNF1A, LDLR, LDLRAP1, MYLIP, NPC1L1, PCSK9, PRKCA  |
| <a href="#">GO:0006810: transport</a>                                 | 1.25E-04 | 16 | 4771 | ABCG5, ABCG8, APOA1, APOB, APOE, CETP, GPAM, HFE, HNF1A, LDLR, *LDLRAP1, LPA, NPC1L1, OSBPL7, PCSK9, SORT1  |
| <a href="#">GO:0051234: establishment of localization</a>             | 1.63E-04 | 16 | 4875 | ABCG5, ABCG8, APOA1, APOB, APOE, CETP, GPAM, HFE, HNF1A, LDLR, LDLRAP1, LPA, NPC1L1, OSBPL7, PCSK9, SORT1   |
| <a href="#">GO:0042221: response to chemical stimulus</a>             | 1.32E-05 | 16 | 3988 | ABCG5, ANGPTL3, APOB, APOE, CYP7A1, FADS1, GPAM, HMGCR, HNF1A, LDLR, MARC1, PCSK9, PRKCA, SORT1, TOP1, TRIB1  |
| <a href="#">GO:0032879: regulation of localization</a>                | 2.67E-08 | 14 | 1830 | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, GPAM, HNF1A, LDLRAP1, PCSK9, PRKCA, SFN, TRIB1  |
| <a href="#">GO:0071702: organic substance transport</a>               | 8.83E-07 | 14 | 2430 | ABCG5, ABCG8, APOA1, APOB, APOE, CETP, GPAM, HNF1A, LDLR, LDLRAP1, LPA, NPC1L1, OSBPL7, SORT1   |
| <a href="#">GO:0033036: macromolecule localization</a>                | 1.61E-06 | 14 | 2555 | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, GPAM, HNF1A, LDLR, LDLRAP1, LPA, NPC1L1, OSBPL7   |
| <a href="#">GO:0048523: negative regulation of cellular process</a>   | 3.33E-04 | 14 | 4093 | APOA1, APOE, BRAP, CETP, FRK, GPAM, HMGCR, HNF1A, MAFB, PCSK9, PRKCA, SFN, SORT1, TRIB1   |

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|---|----------|----|------|--|
| <a href="#">GO:0055088: lipid homeostasis</a>                               | 6.99E-25 | 14 | 115  | ABCG5, ABCG8, *ANGPTL3, APOA1, APOB, APOE, *CETP, CYP7A1, GPAM, LDLR, LDLRAP1, MYLIP, NPC1L1, PCSK9      |
| <a href="#">GO:0055092: sterol homeostasis</a>                              | 1.06E-24 | 13 | 82   | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, LDLR, LDLRAP1, MYLIP, NPC1L1, PCSK9              |
| <a href="#">GO:0042632: cholesterol homeostasis</a>                         | 1.06E-24 | 13 | 82   | *ABCG5, *ABCG8, *ANGPTL3, *APOA1, *APOB, *APOE, *CETP, *CYP7A1, *LDLR, *LDLRAP1, *MYLIP, *NPC1L1, *PCSK9 |
| <a href="#">GO:0044255: cellular lipid metabolic process</a>                | 3.23E-09 | 13 | 1274 | ANGPTL3, *APOA1, APOB, APOE, CETP, *CYP7A1, *FADS1, FADS2, FADS3, *GPAM, *HMGCR, HNF1A, PCSK9            |
| <a href="#">GO:0010876: lipid localization</a>                              | 1.10E-17 | 13 | 272  | ABCG5, ABCG8, ANGPTL3, APOA1, APOB, APOE, CETP, HNF1A, LDLR, LDLRAP1, LPA, NPC1L1, OSBPL7                |
| <a href="#">GO:1901615: organic hydroxy compound metabolic process</a>      | 4.25E-13 | 12 | 471  | ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, HMGCR, HNF1A, LDLR, LDLRAP1, NPC1L1, PCSK9                     |
| <a href="#">GO:0006793: phosphorus metabolic process</a>                    | 9.80E-05 | 12 | 2720 | ABCG5, ABCG8, ANGPTL3, APOA1, CETP, FADS1, FRK, GPAM, HMGCR, PCSK9, PRKCA, TOP1                          |
| <a href="#">GO:0009893: positive regulation of metabolic process</a>        | 1.22E-04 | 12 | 2783 | ANGPTL3, APOA1, APOE, GPAM, HNF1A, LDLR, LDLRAP1, MAFB, MYLIP, PCSK9, PRKCA, TRIB1                       |
| <a href="#">GO:0008203: cholesterol metabolic process</a>                   | 5.07E-20 | 12 | 126  | *ANGPTL3, *APOA1, *APOB, *APOE, *CETP, CYP7A1, HMGCR, *HNF1A, *LDLR, *LDLRAP1, NPC1L1, *PCSK9            |
| <a href="#">GO:0016125: sterol metabolic process</a>                        | 2.05E-19 | 12 | 141  | ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, HMGCR, HNF1A, LDLR, LDLRAP1, NPC1L1, PCSK9                     |
| <a href="#">GO:0008202: steroid metabolic process</a>                       | 4.68E-15 | 12 | 322  | ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, HMGCR, HNF1A, LDLR, LDLRAP1, NPC1L1, PCSK9                     |
| <a href="#">GO:0006869: lipid transport</a>                                 | 1.94E-16 | 12 | 247  | ABCG5, ABCG8, APOA1, APOB, APOE, *CETP, HNF1A, LDLR, LDLRAP1, *LPA, NPC1L1, *OSBPL7                      |
| <a href="#">GO:0010033: response to organic substance</a>                   | 1.09E-04 | 12 | 2751 | ANGPTL3, APOB, APOE, CYP7A1, FADS1, GPAM, HNF1A, LDLR, PCSK9, PRKCA, SORT1, TRIB1                        |
| <a href="#">GO:0006066: alcohol metabolic process</a>                       | 2.78E-14 | 12 | 374  | ANGPTL3, APOA1, APOB, APOE, CETP, CYP7A1, HMGCR, HNF1A, LDLR, LDLRAP1, NPC1L1, PCSK9                     |
| <a href="#">GO:0006796: phosphate-containing compound metabolic process</a> | 6.57E-05 | 12 | 2610 | ABCG5, ABCG8, ANGPTL3, APOA1, CETP, FADS1, FRK, GPAM, HMGCR, PCSK9, PRKCA, TOP1                          |
| <a href="#">GO:0051049: regulation of transport</a>                         | 5.28E-07 | 11 | 1321 | ABCG5, ABCG8, APOA1, APOE, CETP, GPAM, HNF1A, LDLRAP1, PCSK9, PRKCA, SFN                                 |
| <a href="#">GO:0065009: regulation of molecular function</a>                | 1.14E-04 | 11 | 2329 | ANGPTL3, APOA1, APOE, HMGCR, LDLRAP1, LPA, PCSK9, PRKCA, SFN, SORT1, TRIB1                               |
| <a href="#">GO:0051239: regulation of multicellular organismal process</a>  | 5.53E-04 | 11 | 2790 | ABCG5, ABCG8, ANGPTL3, APOA1, APOE, GPAM, HMGCR, MAFB, MYLIP, PCSK9, PRKCA                               |
| <a href="#">GO:0015850: organic hydroxy compound transport</a>              | 8.59E-18 | 10 | 84   | ABCG5, ABCG8, APOA1, APOB, APOE, CETP, HNF1A, LDLR, LDLRAP1, NPC1L1                                      |
| <a href="#">GO:0044092: negative regulation of molecular function</a>       | 4.56E-08 | 10 | 798  | ANGPTL3, APOA1, APOE, HMGCR, LPA, PCSK9, PRKCA, SFN, SORT1, TRIB1  |
| <a href="#">GO:0030301: cholesterol transport</a>                           | 1.66E-19 | 10 | 58   | ABCG5, ABCG8, *APOA1, *APOB, APOE, *CETP, HNF1A, *LDLR, LDLRAP1, *NPC1L1                                 |
| <a href="#">GO:0015918: sterol transport</a>                                | 1.66E-19 | 10 | 58   | *ABCG5, *ABCG8, APOA1, APOB, APOE, CETP, HNF1A, LDLR, LDLRAP1, *NPC1L1                                   |
| <a href="#">GO:0043086: negative regulation of catalytic activity</a>       | 3.43E-09 | 10 | 607  | ANGPTL3, APOA1, APOE, HMGCR, LPA, *PCSK9, PRKCA, SFN, SORT1, TRIB1                                       |
| <a href="#">GO:0050790: regulation of catalytic activity</a>                | 7.94E-05 | 10 | 1840 | ANGPTL3, APOA1, APOE, HMGCR, LPA, PCSK9, PRKCA, SFN, SORT1, TRIB1  |
| <a href="#">GO:0016192: vesicle-mediated transport</a>                      | 3.03E-05 | 9  | 1300 | APOA1, APOB, APOE, CETP, HFE, LDLR, LDLRAP1, LPA, SORT1  |

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|---|----------|---|------|---|
| <a href="#">GO:0019637: organophosphate metabolic process</a>                       | 9.06E-05 | 9 | 1497 | ABCG5, ABCG8, ANGPTL3, APOA1, CETP, FADS1, GPAM, HMGCR, PCSK9     |
| <a href="#">GO:0008610: lipid biosynthetic process</a>                              | 5.33E-07 | 9 | 790  | APOA1, CYP7A1, FADS1, FADS2, FADS3, GPAM, HMGCR, HNF1A, NPC1L1    |
| <a href="#">GO:0043436: oxoacid metabolic process</a>                               | 1.63E-04 | 9 | 1617 | ANGPTL3, CYP7A1, FADS1, FADS2, FADS3, GPAM, HNF1A, MARC1, ST3GAL4 |
| <a href="#">GO:0006082: organic acid metabolic process</a>                          | 1.77E-04 | 9 | 1635 | ANGPTL3, CYP7A1, FADS1, FADS2, FADS3, GPAM, HNF1A, MARC1, ST3GAL4 |
| <a href="#">GO:0006897: endocytosis</a>   | 3.90E-08 | 8 | 405  | APOB, APOE, CETP, HFE, *LDLR, LDLRAP1, LPA, *SORT1                |
| <a href="#">GO:0044711: single-organism biosynthetic process</a>                    | 2.50E-06 | 8 | 702  | APOA1, CYP7A1, FADS1, FADS2, FADS3, HMGCR, HNF1A, NPC1L1          |
| <a href="#">GO:0042157: lipoprotein metabolic process</a>                           | 4.64E-11 | 8 | 172  | *APOA1, *APOB, *APOE, *CETP, *LDLR, *LPA, *NPC1L1, *PCSK9         |
| <a href="#">GO:0019216: regulation of lipid metabolic process</a>                   | 2.34E-09 | 8 | 282  | ANGPTL3, APOA1, APOB, APOE, CYP7A1, GPAM, LDLR, LDLRAP1           |
| <a href="#">GO:0009725: response to hormone stimulus</a>                            | 9.11E-05 | 8 | 1157 | *ANGPTL3, APOB, FADS1, GPAM, LDLR, PCSK9, PRKCA, SORT1            |
| <a href="#">GO:0009719: response to endogenous stimulus</a>                         | 9.96E-04 | 8 | 1650 | ANGPTL3, APOB, FADS1, GPAM, LDLR, PCSK9, PRKCA, SORT1             |
| <a href="#">GO:0044283: small molecule biosynthetic process</a>                     | 1.97E-06 | 8 | 680  | APOA1, CYP7A1, FADS1, FADS2, FADS3, HMGCR, HNF1A, NPC1L1          |
| <a href="#">GO:0006898: receptor-mediated endocytosis</a>                           | 2.28E-10 | 7 | 125  | *APOB, *APOE, *CETP, *HFE, *LDLR, *LDLRAP1, *LPA                  |
| <a href="#">GO:0055114: oxidation-reduction process</a>                             | 2.35E-05 | 7 | 686  | APOA1, FADS1, FADS2, FADS3, *MARC1, PPP1R3B, PRKCA                |
| <a href="#">GO:0051241: negative regulation of multicellular organismal process</a> | 2.97E-06 | 7 | 499  | ABCG5, ABCG8, APOA1, APOE, MYLIP, PCSK9, PRKCA                    |
| <a href="#">GO:0032787: monocarboxylic acid metabolic process</a>                   | 1.24E-05 | 7 | 621  | ANGPTL3, CYP7A1, FADS1, FADS2, FADS3, GPAM, HNF1A                 |
| <a href="#">GO:0009894: regulation of catabolic process</a>                         | 2.99E-04 | 6 | 725  | ANGPTL3, APOE, LDLR, MYLIP, PCSK9, TRIB1                          |
| <a href="#">GO:0006631: fatty acid metabolic process</a>                            | 1.78E-05 | 6 | 434  | *ANGPTL3, FADS1, FADS2, FADS3, *GPAM, HNF1A                       |
| <a href="#">GO:0046486: glycerolipid metabolic process</a>                          | 2.29E-05 | 6 | 454  | APOA1, APOB, APOE, CETP, GPAM, PCSK9                              |
| <a href="#">GO:0006644: phospholipid metabolic process</a>                          | 5.20E-05 | 6 | 526  | *ANGPTL3, APOA1, CETP, FADS1, *GPAM, *PCSK9                       |
| <a href="#">GO:0045834: positive regulation of lipid metabolic process</a>          | 1.12E-08 | 6 | 123  | ANGPTL3, APOA1, APOE, GPAM, LDLR, LDLRAP1                         |
| <a href="#">GO:0051338: regulation of transferase activity</a>                      | 6.67E-04 | 6 | 844  | APOA1, APOE, HMGCR, PRKCA, SFN, TRIB1                             |
| <a href="#">GO:0097006: regulation of plasma lipoprotein particle levels</a>        | 1.40E-10 | 6 | 60   | APOA1, APOB, APOE, CETP, LDLR, LDLRAP1                            |
| <a href="#">GO:0009743: response to carbohydrate stimulus</a>                       | 6.83E-07 | 6 | 246  | *APOB, CYP7A1, FADS1, GPAM, HNF1A, PRKCA                          |
| <a href="#">GO:0031667: response to nutrient levels</a>                             | 2.88E-05 | 6 | 473  | ABCG5, FADS1, *GPAM, HFE, HMGCR, PCSK9                            |
| <a href="#">GO:0043434: response to peptide hormone stimulus</a>                    | 1.14E-04 | 6 | 607  | FADS1, GPAM, LDLR, PCSK9, *PRKCA, SORT1                           |
| <a href="#">GO:1901652: response to peptide</a>                                     | 1.29E-04 | 6 | 621  | FADS1, GPAM, LDLR, PCSK9, PRKCA, SORT1                            |
| <a href="#">GO:0009991: response to extracellular stimulus</a>                      | 4.83E-05 | 6 | 519  | ABCG5, FADS1, GPAM, HFE, HMGCR, PCSK9                             |
| <a href="#">GO:0060341: regulation of cellular localization</a>                     | 6.35E-04 | 6 | 836  | APOA1, GPAM, HNF1A, LDLRAP1, PRKCA, SFN                           |
| <a href="#">GO:0007568: aging</a>   | 1.20E-04 | 5 | 380  | *APOE, *FADS1, *HMGCR, *LDLR, *PRKCA                              |
| <a href="#">GO:0015748: organophosphate ester transport</a>                         | 2.23E-08 | 5 | 66   | ABCG8, APOA1, APOE, CETP, LDLR                                    |
| <a href="#">GO:0001933: negative regulation of protein phosphorylation</a>          | 2.47E-05 | 5 | 272  | APOE, HMGCR, PRKCA, SFN, TRIB1                                    |
| <a href="#">GO:0006641: triglyceride metabolic process</a>                          | 2.56E-07 | 5 | 107  | APOB, *APOE, *CETP, GPAM, *PCSK9                                  |
| <a href="#">GO:0006639: acylglycerol metabolic process</a>                          | 3.51E-07 | 5 | 114  | APOB, APOE, CETP, GPAM, PCSK9                                     |
| <a href="#">GO:0006638: neutral lipid metabolic process</a>                         | 3.83E-07 | 5 | 116  | APOB, APOE, CETP, GPAM, PCSK9                                     |
| <a href="#">GO:0006694: steroid biosynthetic process</a>                            | 1.32E-06 | 5 | 149  | APOA1, CYP7A1, HMGCR, HNF1A, NPC1L1                               |

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|---|----------|---|-----|------------------------------------|
| GO:0015914: phospholipid transport                                    | 1.92E-09 | 5 | 41  | *ABCG8, APOA1, APOE, *CETP, *LDLR  |
| GO:0034381: plasma lipoprotein particle clearance                     | 1.29E-09 | 5 | 38  | APOA1, APOB, APOE, LDLR, LDLRAP1   |
| GO:0019218: regulation of steroid metabolic process                   | 1.73E-07 | 5 | 99  | APOA1, APOB, APOE, CYP7A1, LDLRAP1 |
| GO:0046890: regulation of lipid biosynthetic process                  | 7.55E-07 | 5 | 133 | APOB, APOE, CYP7A1, GPAM, LDLR     |
| GO:0032374: regulation of cholesterol transport                       | 5.20E-10 | 5 | 32  | ABCG5, ABCG8, APOA1, APOE, CETP    |
| GO:0032371: regulation of sterol transport                            | 5.20E-10 | 5 | 32  | ABCG5, ABCG8, APOA1, APOE, CETP    |
| GO:0032368: regulation of lipid transport                             | 4.00E-08 | 5 | 74  | ABCG5, ABCG8, APOA1, APOE, CETP    |
| GO:0006469: negative regulation of protein kinase activity            | 5.60E-06 | 5 | 200 | APOE, HMGCR, PRKCA, *SFN, *TRIB1   |
| GO:0033673: negative regulation of kinase activity                    | 7.26E-06 | 5 | 211 | APOE, HMGCR, PRKCA, SFN, TRIB1     |
| GO:0051348: negative regulation of transferase activity               | 1.06E-05 | 5 | 228 | APOE, HMGCR, PRKCA, SFN, TRIB1     |
| GO:0051346: negative regulation of hydrolase activity                 | 2.51E-05 | 5 | 273 | ANGPTL3, *APOA1, LPA, SFN, SORT1   |
| GO:0042326: negative regulation of phosphorylation                    | 3.19E-05 | 5 | 287 | APOE, HMGCR, PRKCA, SFN, TRIB1     |
| GO:0071900: regulation of protein serine/threonine kinase activity    | 4.34E-04 | 5 | 502 | APOE, HMGCR, PRKCA, SFN, TRIB1     |
| GO:0072330: monocarboxylic acid biosynthetic process                  | 2.30E-05 | 5 | 268 | CYP7A1, FADS1, FADS2, FADS3, HNF1A |
| GO:0016053: organic acid biosynthetic process                         | 3.68E-04 | 5 | 484 | CYP7A1, FADS1, FADS2, FADS3, HNF1A |
| GO:0046394: carboxylic acid biosynthetic process                      | 3.68E-04 | 5 | 484 | CYP7A1, FADS1, FADS2, FADS3, HNF1A |
| GO:0031329: regulation of cellular catabolic process                  | 9.70E-04 | 5 | 600 | APOE, LDLR, MYLIP, PCSK9, TRIB1    |
| GO:0010563: negative regulation of phosphorus metabolic process       | 7.43E-05 | 5 | 343 | APOE, HMGCR, PRKCA, SFN, TRIB1     |
| GO:0045936: negative regulation of phosphate metabolic process        | 7.43E-05 | 5 | 343 | APOE, HMGCR, PRKCA, SFN, TRIB1     |
| GO:0031400: negative regulation of protein modification process       | 1.60E-04 | 5 | 404 | APOE, HMGCR, PRKCA, SFN, TRIB1     |
| GO:0032269: negative regulation of cellular protein metabolic process | 5.99E-04 | 5 | 539 | APOE, HMGCR, PRKCA, SFN, TRIB1     |
| GO:0044241: lipid digestion   | 2.29E-09 | 4 | 14  | ABCG5, ABCG8, LDLR, NPC1L1         |
| GO:0050892: intestinal absorption                                     | 4.62E-08 | 4 | 28  | ABCG5, ABCG8, LDLR, NPC1L1         |
| GO:0022600: digestive system process                                  | 5.09E-07 | 4 | 50  | ABCG5, ABCG8, LDLR, NPC1L1         |
| GO:0007586: digestion   | 1.65E-05 | 4 | 119 | ABCG5, ABCG8, LDLR, NPC1L1         |
| GO:0009896: positive regulation of catabolic process                  | 9.22E-05 | 4 | 185 | ANGPTL3, APOE, MYLIP, TRIB1        |
| GO:0042176: regulation of protein catabolic process                   | 2.79E-04 | 4 | 247 | APOE, MYLIP, PCSK9, TRIB1          |
| GO:0055091: phospholipid homeostasis                                  | 2.89E-10 | 4 | 9   | *ANGPTL3, *APOA1, *CETP, *GPAM     |
| GO:0006633: fatty acid biosynthetic process                           | 1.17E-04 | 4 | 197 | FADS1, FADS2, FADS3, *HNF1A        |
| GO:0016042: lipid catabolic process                                   | 6.33E-04 | 4 | 307 | ANGPTL3, APOB, APOE, CYP7A1        |
| GO:0030299: intestinal cholesterol absorption                         | 1.61E-10 | 4 | 8   | *ABCG5, *ABCG8, *LDLR, *NPC1L1     |
| GO:0043691: reverse cholesterol transport                             | 8.81E-09 | 4 | 19  | *APOA1, *APOE, *CETP, *HNF1A       |
| GO:0033344: cholesterol efflux  | 3.38E-08 | 4 | 26  | *ABCG5, *ABCG8, *APOA1, *APOE      |
| GO:0034369: plasma lipoprotein particle remodeling                    | 3.96E-08 | 4 | 27  | APOA1, APOB, APOE, CETP            |
| GO:0034368: protein-lipid complex remodeling                          | 3.96E-08 | 4 | 27  | APOA1, APOB, APOE, CETP            |
| GO:0034367: macromolecular complex remodeling                         | 3.96E-08 | 4 | 27  | APOA1, APOB, APOE, CETP            |
| GO:0071827: plasma lipoprotein particle organization                  | 9.18E-08 | 4 | 33  | APOA1, APOB, APOE, CETP            |

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|---|----------|---|-----|----------------------------|
| <a href="#">GO:0071825: protein-lipid complex subunit organization</a>                                | 9.18E-08 | 4 | 33  | APOA1, APOB, APOE, CETP    |
| <a href="#">GO:0043405: regulation of MAP kinase activity</a>   | 8.67E-04 | 4 | 334 | APOE, HMGCR, PRKCA, *TRIB1 |
| <a href="#">GO:0048844: artery morphogenesis</a>  | 6.03E-05 | 3 | 59  | *ANGPTL3, *APOB, *APOE     |
| <a href="#">GO:0060840: artery development</a>  | 1.05E-04 | 3 | 71  | ANGPTL3, APOB, APOE        |
| <a href="#">GO:0030300: regulation of intestinal cholesterol absorption</a>                           | 3.89E-08 | 3 | 6   | ABCG5, ABCG8, *APOA1       |
| <a href="#">GO:0044058: regulation of digestive system process</a>                                    | 7.73E-06 | 3 | 30  | ABCG5, ABCG8, APOA1        |
| <a href="#">GO:0048259: regulation of receptor-mediated endocytosis</a>                               | 3.89E-05 | 3 | 51  | LDLRAP1, PCSK9, *PRKCA     |
| <a href="#">GO:0032803: regulation of low-density lipoprotein particle receptor catabolic process</a> | 1.95E-08 | 3 | 5   | APOE, *MYLIP, *PCSK9       |
| <a href="#">GO:2000644: regulation of receptor catabolic process</a>                                  | 3.89E-08 | 3 | 6   | APOE, MYLIP, PCSK9         |
| <a href="#">GO:0045732: positive regulation of protein catabolic process</a>                          | 4.36E-04 | 3 | 115 | APOE, *MYLIP, TRIB1        |
| <a href="#">GO:0046165: alcohol biosynthetic process</a>  | 5.82E-04 | 3 | 127 | APOA1, HMGCR, NPC1L1       |
| <a href="#">GO:0070328: triglyceride homeostasis</a>  | 8.55E-06 | 3 | 31  | *ANGPTL3, *APOA1, *CETP    |
| <a href="#">GO:0055090: acylglycerol homeostasis</a>  | 9.42E-06 | 3 | 32  | *ANGPTL3, APOA1, CETP      |
| <a href="#">GO:0042159: lipoprotein catabolic process</a>   | 3.19E-07 | 3 | 11  | *APOB, *APOE, *LDLR        |
| <a href="#">GO:0006695: cholesterol biosynthetic process</a>  | 2.01E-05 | 3 | 41  | *APOA1, *HMGCR, *NPC1L1    |
| <a href="#">GO:0016126: sterol biosynthetic process</a>   | 4.13E-05 | 3 | 52  | APOA1, HMGCR, NPC1L1       |
| <a href="#">GO:0006636: unsaturated fatty acid biosynthetic process</a>                               | 9.22E-05 | 3 | 68  | *FADS1, *FADS2, *FADS3     |
| <a href="#">GO:0042158: lipoprotein biosynthetic process</a>  | 3.63E-04 | 3 | 108 | *APOA1, *APOB, *APOE       |
| <a href="#">GO:0033559: unsaturated fatty acid metabolic process</a>                                  | 3.83E-04 | 3 | 110 | *FADS1, *FADS2, FADS3      |
| <a href="#">GO:0034383: low-density lipoprotein particle clearance</a>                                | 8.78E-07 | 3 | 15  | *APOB, *LDLR, LDLRAP1      |
| <a href="#">GO:0034374: low-density lipoprotein particle remodeling</a>                               | 5.53E-07 | 3 | 13  | *APOB, *APOE, *CETP        |
| <a href="#">GO:0034377: plasma lipoprotein particle assembly</a>                                      | 8.78E-07 | 3 | 15  | APOA1, APOB, APOE          |
| <a href="#">GO:0065005: protein-lipid complex assembly</a>  | 8.78E-07 | 3 | 15  | APOA1, APOB, APOE          |
| <a href="#">GO:0034375: high-density lipoprotein particle remodeling</a>                              | 8.78E-07 | 3 | 15  | *APOA1, *APOE, *CETP       |
| <a href="#">GO:0045940: positive regulation of steroid metabolic process</a>                          | 6.25E-06 | 3 | 28  | APOA1, APOE, LDLRAP1       |
| <a href="#">GO:0090181: regulation of cholesterol metabolic process</a>                               | 1.04E-05 | 3 | 33  | APOB, APOE, LDLRAP1        |
| <a href="#">GO:0050810: regulation of steroid biosynthetic process</a>                                | 1.14E-04 | 3 | 73  | APOB, APOE, CYP7A1         |
| <a href="#">GO:0060191: regulation of lipase activity</a>   | 6.09E-04 | 3 | 129 | ANGPTL3, PRKCA, SORT1      |
| <a href="#">GO:0009267: cellular response to starvation</a>   | 3.16E-04 | 3 | 103 | *FADS1, HFE, *PCSK9        |
| <a href="#">GO:0031669: cellular response to nutrient levels</a>                                      | 8.05E-04 | 3 | 142 | FADS1, HFE, PCSK9          |
| <a href="#">GO:0042594: response to starvation</a>  | 9.26E-04 | 3 | 149 | FADS1, HFE, PCSK9          |
| <a href="#">GO:0043407: negative regulation of MAP kinase activity</a>                                | 1.85E-04 | 3 | 86  | *APOE, *HMGCR, PRKCA       |
| <a href="#">GO:0071901: negative regulation of protein serine/threonine kinase activity</a>           | 4.82E-04 | 3 | 119 | APOE, HMGCR, PRKCA         |
| <a href="#">GO:0046323: glucose import</a>  | 9.61E-06 | 2 | 4   | *HNF1A, *SORT1             |
| <a href="#">GO:0010949: negative regulation of intestinal phytosterol absorption</a>                  | 1.60E-06 | 2 | 2   | *ABCG5, *ABCG8             |

|  |          |   |    |                  |
|--|----------|---|----|------------------|
| <u>GO:0045796: negative regulation of intestinal cholesterol absorption</u>          | 1.60E-06 | 2 | 2  | *ABCG5, *ABCG8   |
| <u>GO:0060457: negative regulation of digestive system process</u>                   | 2.42E-04 | 2 | 18 | ABCG5, ABCG8     |
| <u>GO:0043651: linoleic acid metabolic process</u>                                   | 4.47E-05 | 2 | 8  | *FADS1, *FADS2   |
| <u>GO:0006707: cholesterol catabolic process</u>                                     | 1.24E-04 | 2 | 13 | *APOE, *CYP7A1   |
| <u>GO:0016127: sterol catabolic process</u>  | 1.24E-04 | 2 | 13 | APOE, CYP7A1     |
| <u>GO:0006699: bile acid biosynthetic process</u>                                    | 3.99E-04 | 2 | 23 | *CYP7A1, *HNF1A  |
| <u>GO:0035376: sterol import</u>   | 4.81E-06 | 2 | 3  | APOA1, LDLR      |
| <u>GO:0070508: cholesterol import</u>  | 4.81E-06 | 2 | 3  | *APOA1, *LDLR    |
| <u>GO:0035382: sterol transmembrane transport</u>                                    | 4.81E-06 | 2 | 3  | APOA1, LDLR      |
| <u>GO:0033700: phospholipid efflux</u>   | 1.05E-04 | 2 | 12 | *APOA1, *APOE    |
| <u>GO:0034384: high-density lipoprotein particle clearance</u>                       | 3.35E-05 | 2 | 7  | *APOA1, *APOE    |
| <u>GO:0010984: regulation of lipoprotein particle clearance</u>                      | 1.24E-04 | 2 | 13 | MYLIP, PCSK9     |
| <u>GO:0034380: high-density lipoprotein particle assembly</u>                        | 2.40E-05 | 2 | 6  | *APOA1, *APOE    |
| <u>GO:0034372: very-low-density lipoprotein particle remodeling</u>                  | 3.35E-05 | 2 | 7  | *APOE, *CETP     |
| <u>GO:0034370: triglyceride-rich lipoprotein particle remodeling</u>                 | 7.17E-05 | 2 | 10 | APOE, CETP       |
| <u>GO:0010873: positive regulation of cholesterol esterification</u>                 | 3.35E-05 | 2 | 7  | *APOA1, *APOE    |
| <u>GO:0010872: regulation of cholesterol esterification</u>                          | 5.74E-05 | 2 | 9  | APOA1, APOE      |
| <u>GO:0045540: regulation of cholesterol biosynthetic process</u>                    | 3.64E-04 | 2 | 22 | *APOB, APOE      |
| <u>GO:0010867: positive regulation of triglyceride biosynthetic process</u>          | 8.76E-05 | 2 | 11 | *GPAM, *LDLR     |
| <u>GO:0010866: regulation of triglyceride biosynthetic process</u>                   | 1.90E-04 | 2 | 16 | GPAM, LDLR       |
| <u>GO:0090208: positive regulation of triglyceride metabolic process</u>             | 2.15E-04 | 2 | 17 | GPAM, LDLR       |
| <u>GO:0032375: negative regulation of cholesterol transport</u>                      | 8.76E-05 | 2 | 11 | ABCG5, ABCG8     |
| <u>GO:0032372: negative regulation of sterol transport</u>                           | 8.76E-05 | 2 | 11 | ABCG5, ABCG8     |
| <u>GO:0010874: regulation of cholesterol efflux</u>                                  | 2.15E-04 | 2 | 17 | APOE, *CETP      |
| <u>GO:0010989: negative regulation of low-density lipoprotein particle clearance</u> | 9.61E-06 | 2 | 4  | *MYLIP, *PCSK9   |
| <u>GO:0010988: regulation of low-density lipoprotein particle clearance</u>          | 3.35E-05 | 2 | 7  | MYLIP, PCSK9     |
| <u>GO:0010985: negative regulation of lipoprotein particle clearance</u>             | 3.35E-05 | 2 | 7  | MYLIP, PCSK9     |
| <u>GO:0051005: negative regulation of lipoprotein lipase activity</u>                | 2.40E-05 | 2 | 6  | *ANGPTL3, *SORT1 |
| <u>GO:0060192: negative regulation of lipase activity</u>                            | 1.24E-04 | 2 | 13 | ANGPTL3, SORT1   |
| <u>GO:0031664: regulation of lipopolysaccharide-mediated signaling pathway</u>       | 1.24E-04 | 2 | 13 | PRKCA, TRIB1     |
| <u>GO:0032489: regulation of Cdc42 protein signal transduction</u>                   | 3.32E-04 | 2 | 21 | *APOA1, *APOE    |
| <u>GO:0036109: alpha-linolenic acid metabolic process</u>                            | 8.76E-05 | 2 | 11 | *FADS1, *FADS2   |
| <u>GO:0006706: steroid catabolic process</u>   | 5.11E-04 | 2 | 26 | APOE, CYP7A1     |
| <u>GO:0090207: regulation of triglyceride metabolic process</u>                      | 5.52E-04 | 2 | 27 | GPAM, LDLR       |
| <u>GO:0032369: negative regulation of lipid transport</u>                            | 5.52E-04 | 2 | 27 | ABCG5, ABCG8     |
| <u>GO:0010543: regulation of platelet activation</u>                                 | 7.28E-04 | 2 | 31 | APOE, PRKCA      |

|  |          |   |    |                  |
|--|----------|---|----|------------------|
| GO:0048260: positive regulation of receptor-mediated endocytosis | 7.76E-04 | 2 | 32 | *LDLRAP1, PCSK9  |
| GO:0019915: lipid storage  | 7.76E-04 | 2 | 32 | *ANGPTL3, *APOA1 |

k is the number of genes in the query set annotated to that node, and M is the number of genes in the database annotated to that node.  
\*next to the gene symbol indicates that the gene is annotated to the node, and not any of the child terms.  
Based on annotation dataset 12<sup>th</sup> November 2012 and GO ontology from 27<sup>th</sup> November 2012.

Table S5 Biological process VLAD results, HDL cholesterol trait associated genes

| Term  | P-value  | k  | M     | Genes   |
|---|----------|----|-------|---|
| GO:0008150: biological process                        | 1.00E+00 | 34 | 29612 | ABCA1, ABCA8, ANGPTL4, APOA1, APOB, APOE, ARL15, *C6orf106, CETP, CITED2, FADS1, GALNT2, HNF4A, IRS1, KLF14, LCAT, LILRA3, LPC, LPA, LRP4, MC4R, MLXIPL, PDE3A, PGS1, PLTP, PPP1R3B, *SBNO1, SLC39A8, STARD3, TRIB1, TRPS1, UBE2L3, ZNF648, *ZNF664 |
| GO:0065007: biological regulation                     | 3.92E-04 | 27 | 14777 | ABCA1, ANGPTL4, APOA1, APOB, APOE, ARL15, CETP, CITED2, FADS1, HNF4A, IRS1, KLF14, LCAT, LILRA3, LPC, LPA, LRP4, MC4R, MLXIPL, PDE3A, SBNO1, STARD3, TRIB1, TRPS1, UBE2L3, ZNF648, ZNF664   |
| GO:0050789: regulation of biological process          | 4.85E-04 | 26 | 13977 | ABCA1, ANGPTL4, APOA1, APOB, APOE, ARL15, CETP, CITED2, FADS1, HNF4A, IRS1, KLF14, LCAT, LILRA3, LPC, LPA, LRP4, MC4R, MLXIPL, PDE3A, SBNO1, TRIB1, TRPS1, UBE2L3, ZNF648, ZNF664   |
| GO:0044237: cellular metabolic process                | 8.30E-04 | 24 | 12556 | ABCA1, ANGPTL4, APOA1, APOB, APOE, CETP, FADS1, GALNT2, HNF4A, KLF14, LCAT, LPC, LPA, MC4R, MLXIPL, PDE3A, PGS1, PLTP, PPP1R3B, STARD3, TRPS1, UBE2L3, ZNF648, ZNF664   |
| GO:0019222: regulation of metabolic process           | 1.75E-05 | 20 | 7178  | ABCA1, ANGPTL4, APOA1, APOB, APOE, CITED2, FADS1, HNF4A, IRS1, KLF14, LPA, LRP4, MC4R, MLXIPL, SBNO1, TRIB1, TRPS1, UBE2L3, ZNF648, ZNF664  |
| GO:0009058: biosynthetic process                      | 3.39E-05 | 18 | 6142  | ABCA1, APOA1, APOB, APOE, FADS1, GALNT2, HNF4A, KLF14, LCAT, LPC, MLXIPL, PGS1, PLTP, STARD3, TRPS1, UBE2L3, ZNF648, ZNF664   |
| GO:0080090: regulation of primary metabolic process   | 6.87E-05 | 18 | 6458  | ABCA1, APOA1, APOB, APOE, CITED2, FADS1, HNF4A, IRS1, KLF14, LRP4, MC4R, MLXIPL, SBNO1, TRIB1, TRPS1, UBE2L3, ZNF648, ZNF664  |
| GO:0044249: cellular biosynthetic process             | 1.54E-05 | 18 | 5811  | ABCA1, APOA1, APOB, APOE, FADS1, GALNT2, HNF4A, KLF14, LCAT, LPC, MLXIPL, PGS1, PLTP, STARD3, TRPS1, UBE2L3, ZNF648, ZNF664   |
| GO:1901576: organic substance biosynthetic process    | 2.25E-05 | 18 | 5967  | ABCA1, APOA1, APOB, APOE, FADS1, GALNT2, HNF4A, KLF14, LCAT, LPC, MLXIPL, PGS1, PLTP, STARD3, TRPS1, UBE2L3, ZNF648, ZNF664   |
| GO:1901360: organic cyclic compound metabolic process | 4.12E-04 | 17 | 6677  | ABCA1, APOA1, APOB, APOE, CETP, HNF4A, KLF14, LCAT, LPC, MLXIPL, PDE3A, PLTP, STARD3, TRPS1, UBE2L3, ZNF648, ZNF664   |
| GO:0031323: regulation of cellular metabolic process  | 3.00E-04 | 17 | 6511  | ABCA1, APOA1, APOE, CITED2, FADS1, HNF4A, IRS1, KLF14, LRP4, MC4R, MLXIPL, SBNO1, TRIB1, TRPS1, UBE2L3, ZNF648, ZNF664  |
| GO:0006629: lipid metabolic process                   | 1.83E-11 | 16 | 1762  | *ABCA1, ANGPTL4, *APOA1, *APOB, *APOE, *CETP, FADS1, *HNF4A, IRS1, *LCAT, LPC, *LPA, *PDE3A, PGS1, *PLTP, *STARD3   |
| GO:0051179: localization                              | 3.98E-04 | 16 | 5992  | ABCA1, ABCA8, APOA1, APOB, APOE, CETP, IRS1, LCAT, LPC, LPA, LRP4, MC4R, PLTP, SLC39A8, STARD3, TRPS1   |

|   |          |    |      |  |
|---|----------|----|------|--|
| <u>GO:0044281: small molecule metabolic process</u>               | 3.16E-07 | 16 | 3455 | *ABCA1, *ANGPTL4, *APOA1, *APOB, *APOE, *CETP, *FADS1, HNF4A, *LCAT, LIPC, *LPA, *MLXIPL, PDE3A, *PGS1, PLTP, STARD3 |
| <u>GO:0009889: regulation of biosynthetic process</u>             | 5.78E-05 | 16 | 5118 | ABCA1, APOB, APOE, CITED2, FADS1, HNF4A, IRS1, KLF14, MC4R, MLXIPL, SBNO1, TRIB1, TRPS1, UBE2L3, ZNF648, ZNF664      |
| <u>GO:0065008: regulation of biological quality</u>               | 2.03E-06 | 15 | 3451 | ABCA1, ANGPTL4, APOA1, APOB, APOE, CETP, CITED2, HNF4A, IRS1, LCAT, LIPC, MC4R, MLXIPL, PDE3A, STARD3                |
| <u>GO:0006810: transport</u>                                      | 1.07E-04 | 15 | 4771 | ABCA1, *ABCA8, APOA1, APOB, APOE, CETP, LCAT, LIPC, LPA, LRP4, MC4R, PLTP, SLC39A8, STARD3, TRPS1                    |
| <u>GO:0051234: establishment of localization</u>                  | 1.38E-04 | 15 | 4875 | ABCA1, ABCA8, APOA1, APOB, APOE, CETP, LCAT, LIPC, LPA, LRP4, MC4R, PLTP, SLC39A8, STARD3, TRPS1                     |
| <u>GO:0031326: regulation of cellular biosynthetic process</u>    | 2.20E-04 | 15 | 5077 | ABCA1, APOE, CITED2, FADS1, HNF4A, IRS1, KLF14, MC4R, MLXIPL, SBNO1, TRIB1, TRPS1, UBE2L3, ZNF648, ZNF664            |
| <u>GO:0048523: negative regulation of cellular process</u>        | 3.54E-04 | 13 | 4093 | ABCA1, ANGPTL4, APOA1, APOE, CETP, CITED2, HNF4A, IRS1, LRP4, MLXIPL, PDE3A, TRIB1, TRPS1                            |
| <u>GO:0048519: negative regulation of biological process</u>      | 9.13E-04 | 13 | 4507 | ABCA1, ANGPTL4, APOA1, APOE, CETP, CITED2, HNF4A, IRS1, LRP4, MLXIPL, PDE3A, TRIB1, TRPS1                            |
| <u>GO:0010033: response to organic substance</u>                  | 5.32E-06 | 13 | 2751 | ABCA1, APOB, APOE, CITED2, FADS1, HNF4A, IRS1, LCAT, MC4R, MLXIPL, PDE3A, TRIB1, UBE2L3                              |
| <u>GO:0042221: response to chemical stimulus</u>                  | 2.73E-04 | 13 | 3988 | ABCA1, APOB, APOE, CITED2, FADS1, HNF4A, IRS1, LCAT, MC4R, MLXIPL, PDE3A, TRIB1, UBE2L3                              |
| <u>GO:0034645: cellular macromolecule biosynthetic process</u>    | 6.13E-04 | 13 | 4326 | ABCA1, APOA1, APOB, APOE, GALNT2, HNF4A, KLF14, LCAT, MLXIPL, TRPS1, UBE2L3, ZNF648, ZNF664                          |
| <u>GO:0009059: macromolecule biosynthetic process</u>             | 7.19E-04 | 13 | 4397 | ABCA1, APOA1, APOB, APOE, GALNT2, HNF4A, KLF14, LCAT, MLXIPL, TRPS1, UBE2L3, ZNF648, ZNF664                          |
| <u>GO:0033036: macromolecule localization</u>                     | 1.50E-05 | 12 | 2555 | ABCA1, APOA1, APOB, APOE, CETP, IRS1, LCAT, LIPC, LPA, LRP4, PLTP, TRPS1   |
| <u>GO:0042592: homeostatic process</u>                            | 2.07E-07 | 12 | 1700 | ABCA1, ANGPTL4, APOA1, APOB, APOE, CETP, CITED2, HNF4A, IRS1, LCAT, LIPC, MLXIPL                                     |
| <u>GO:0048878: chemical homeostasis</u>                           | 3.83E-08 | 11 | 1156 | ABCA1, ANGPTL4, APOA1, APOB, APOE, CETP, HNF4A, IRS1, LCAT, LIPC, MLXIPL   |
| <u>GO:0071702: organic substance transport</u>                    | 5.38E-05 | 11 | 2430 | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC, LPA, MC4R, PLTP, TRPS1   |
| <u>GO:0051239: regulation of multicellular organismal process</u> | 1.87E-04 | 11 | 2790 | ANGPTL4, APOA1, APOE, CITED2, HNF4A, LCAT, LRP4, MC4R, MLXIPL, PDE3A, TRPS1  |
| <u>GO:0050793: regulation of developmental process</u>            | 2.48E-05 | 11 | 2235 | ABCA1, ANGPTL4, APOA1, APOB, APOE, CETP, CITED2, FADS1, HNF4A, PDE3A, TRPS1  |
| <u>GO:0055088: lipid homeostasis</u>                              | 6.34E-17 | 10 | 115  | ABCA1, ANGPTL4, APOA1, APOB, APOE, *CETP, *HNF4A, LCAT, LIPC, MLXIPL   |
| <u>GO:0044255: cellular lipid metabolic process</u>               | 1.07E-06 | 10 | 1274 | *ABCA1, *ANGPTL4, *APOA1, APOB, APOE, CETP, *FADS1, LCAT, LIPC, PGS1   |
| <u>GO:0009719: response to endogenous stimulus</u>                | 1.07E-05 | 10 | 1650 | ABCA1, APOB, CITED2, FADS1, HNF4A, IRS1, LCAT, MC4R, PDE3A, UBE2L3   |
| <u>GO:0032879: regulation of localization</u>                     | 1.65E-04 | 9  | 1830 | ABCA1, APOA1, APOB, APOE, CETP, CITED2, HNF4A, IRS1, TRIB1   |
| <u>GO:0006869: lipid transport</u>                                | 7.39E-12 | 9  | 247  | ABCA1, APOA1, APOB, APOE, *CETP, LCAT, LIPC, *LPA, *PLTP   |
| <u>GO:0010876: lipid localization</u>                             | 1.75E-11 | 9  | 272  | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC, LPA, PLTP  |
| <u>GO:0070887: cellular response to chemical stimulus</u>         | 5.30E-04 | 9  | 2141 | ABCA1, APOB, APOE, CITED2, HNF4A, IRS1, MLXIPL, PDE3A, UBE2L3  |

|   |          |   |      |  |
|---|----------|---|------|--|
| <u>GO:0019220: regulation of phosphate metabolic process</u>        | 6.29E-05 | 9 | 1614 | ABCA1, APOA1, APOE, HNF4A, IRS1, LRP4, MC4R, MLXIPL, TRIB1 |
| <u>GO:0051174: regulation of phosphorus metabolic process</u>       | 6.66E-05 | 9 | 1626 | ABCA1, APOA1, APOE, HNF4A, IRS1, LRP4, MC4R, MLXIPL, TRIB1 |
| <u>GO:0043933: macromolecular complex subunit organization</u>      | 2.23E-05 | 9 | 1414 | ABCA1, ANGPTL4, APOA1, APOB, APOE, CETP, IRS1, LCAT, LIPC  |
| <u>GO:1901615: organic hydroxy compound metabolic process</u>       | 4.88E-08 | 8 | 471  | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC, STARD3         |
| <u>GO:0008203: cholesterol metabolic process</u>                    | 1.42E-12 | 8 | 126  | *ABCA1, *APOA1, *APOB, *APOE, *CETP, *LCAT, *LIPC, *STARD3 |
| <u>GO:0016125: sterol metabolic process</u>                         | 3.54E-12 | 8 | 141  | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC, STARD3         |
| <u>GO:0008202: steroid metabolic process</u>                        | 2.54E-09 | 8 | 322  | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC, *STARD3        |
| <u>GO:0071310: cellular response to organic substance</u>           | 5.33E-04 | 8 | 1692 | ABCA1, APOB, APOE, CITED2, IRS1, MLXIPL, PDE3A, UBE2L3     |
| <u>GO:0006066: alcohol metabolic process</u>                        | 8.19E-09 | 8 | 374  | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC, STARD3         |
| <u>GO:0016192: vesicle-mediated transport</u>                       | 5.87E-04 | 7 | 1300 | ABCA1, APOA1, APOB, APOE, CETP, LPA, LRP4                  |
| <u>GO:0015850: organic hydroxy compound transport</u>               | 5.79E-12 | 7 | 84   | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC                 |
| <u>GO:0055092: sterol homeostasis</u>                               | 4.87E-12 | 7 | 82   | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC                 |
| <u>GO:0042632: cholesterol homeostasis</u>                          | 4.87E-12 | 7 | 82   | *ABCA1, *APOA1, *APOB, *APOE, *CETP, *LCAT, *LIPC          |
| <u>GO:0046486: glycerolipid metabolic process</u>                   | 7.15E-07 | 7 | 454  | APOA1, APOB, APOE, CETP, LCAT, LIPC, PGS1                  |
| <u>GO:0030301: cholesterol transport</u>                            | 3.92E-13 | 7 | 58   | ABCA1, *APOA1, *APOB, APOE, *CETP, *LCAT, LIPC             |
| <u>GO:0015918: sterol transport</u>                                 | 3.92E-13 | 7 | 58   | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC                 |
| <u>GO:0042157: lipoprotein metabolic process</u>                    | 9.30E-10 | 7 | 172  | *ABCA1, *APOA1, *APOB, *APOE, *CETP, *LCAT, *LPA           |
| <u>GO:0071825: protein-lipid complex subunit organization</u>       | 5.69E-15 | 7 | 33   | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC                 |
| <u>GO:0071827: plasma lipoprotein particle organization</u>         | 5.69E-15 | 7 | 33   | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC                 |
| <u>GO:0097006: regulation of plasma lipoprotein particle levels</u> | 5.03E-13 | 7 | 60   | ABCA1, APOA1, APOB, APOE, CETP, LCAT, LIPC                 |
| <u>GO:0033993: response to lipid</u>                                | 8.57E-05 | 7 | 949  | ABCA1, APOB, CITED2, FADS1, LCAT, TRIB1, UBE2L3            |
| <u>GO:0009725: response to hormone stimulus</u>                     | 2.91E-04 | 7 | 1157 | APOB, CITED2, FADS1, IRS1, LCAT, MC4R, UBE2L3              |
| <u>GO:0042325: regulation of phosphorylation</u>                    | 2.69E-04 | 7 | 1142 | APOA1, APOE, HNF4A, IRS1, LRP4, MLXIPL, TRIB1              |
| <u>GO:0006897: endocytosis</u>                                      | 6.13E-06 | 6 | 405  | ABCA1, APOB, APOE, CETP, LPA, *LRP4                        |
| <u>GO:0044711: single-organism biosynthetic process</u>             | 1.33E-04 | 6 | 702  | APOA1, FADS1, LCAT, LIPC, PLTP, STARD3                     |
| <u>GO:0044092: negative regulation of molecular function</u>        | 2.65E-04 | 6 | 798  | ANGPTL4, APOA1, APOE, HNF4A, LPA, TRIB1                    |
| <u>GO:0070328: triglyceride homeostasis</u>                         | 1.04E-12 | 6 | 31   | *ANGPTL4, *APOA1, *CETP, *HNF4A, *LIPC, *MLXIPL            |
| <u>GO:0055090: acylglycerol homeostasis</u>                         | 1.27E-12 | 6 | 32   | ANGPTL4, APOA1, CETP, HNF4A, LIPC, MLXIPL                  |
| <u>GO:0006644: phospholipid metabolic process</u>                   | 2.69E-05 | 6 | 526  | APOA1, CETP, FADS1, *LCAT, LIPC, *PGS1                     |
| <u>GO:0008610: lipid biosynthetic process</u>                       | 2.51E-04 | 6 | 790  | APOA1, FADS1, LCAT, LIPC, PGS1, STARD3                     |
| <u>GO:0043691: reverse cholesterol transport</u>                    | 3.86E-14 | 6 | 19   | *ABCA1, *APOA1, *APOE, *CETP, *LCAT, *LIPC                 |
| <u>GO:0034369: plasma lipoprotein particle remodeling</u>           | 4.18E-13 | 6 | 27   | APOA1, APOB, APOE, CETP, LCAT, LIPC                        |
| <u>GO:0034368: protein-lipid complex remodeling</u>                 | 4.18E-13 | 6 | 27   | APOA1, APOB, APOE, CETP, LCAT, LIPC                        |
| <u>GO:0034367: macromolecular complex remodeling</u>                | 4.18E-13 | 6 | 27   | APOA1, APOB, APOE, CETP, LCAT, LIPC                        |
| <u>GO:0019216: regulation of lipid metabolic process</u>            | 7.60E-07 | 6 | 282  | APOA1, APOB, APOE, *HNF4A, IRS1, MLXIPL                    |
| <u>GO:0044283: small molecule biosynthetic process</u>              | 1.11E-04 | 6 | 680  | APOA1, FADS1, LCAT, LIPC, PLTP, STARD3                     |

|   |          |   |      |  |
|---|----------|---|------|--|
| <u>GO:0014070: response to organic cyclic compound</u>                | 9.25E-04 | 6 | 1011 | CITED2, *FADS1, HNF4A, LCAT, PDE3A, UBE2L3 |
| <u>GO:0042158: lipoprotein biosynthetic process</u>                   | 1.50E-07 | 5 | 108  | ABCA1, *APOA1, *APOB, *APOE, *LCAT         |
| <u>GO:0006639: acylglycerol metabolic process</u>                     | 1.97E-07 | 5 | 114  | APOB, APOE, CETP, LIPC, PGS1               |
| <u>GO:0006638: neutral lipid metabolic process</u>                    | 2.15E-07 | 5 | 116  | APOB, APOE, CETP, LIPC, PGS1               |
| <u>GO:0006650: glycerophospholipid metabolic process</u>              | 5.74E-05 | 5 | 365  | APOA1, CETP, LCAT, LIPC, PGS1              |
| <u>GO:0034375: high-density lipoprotein particle remodeling</u>       | 4.37E-12 | 5 | 15   | *APOA1, *APOE, *CETP, *LCAT, *LIPC         |
| <u>GO:0045834: positive regulation of lipid metabolic process</u>     | 2.88E-07 | 5 | 123  | APOA1, APOE, HNF4A, IRS1, MLXIPL           |
| <u>GO:0043086: negative regulation of catalytic activity</u>          | 6.06E-04 | 5 | 607  | ANGPTL4, APOA1, APOE, LPA, TRIB1           |
| <u>GO:0006898: receptor-mediated endocytosis</u>                      | 1.27E-05 | 4 | 125  | *APOB, *APOE, *CETP, *LPA                  |
| <u>GO:0015748: organophosphate ester transport</u>                    | 9.92E-07 | 4 | 66   | ABCA1, APOA1, APOE, CETP                   |
| <u>GO:0009896: positive regulation of catabolic process</u>           | 5.91E-05 | 4 | 185  | APOE, IRS1, MLXIPL, TRIB1                  |
| <u>GO:0001933: negative regulation of protein phosphorylation</u>     | 2.60E-04 | 4 | 272  | APOE, HNF4A, MLXIPL, TRIB1                 |
| <u>GO:0055091: phospholipid homeostasis</u>                           | 1.82E-10 | 4 | 9    | *ABCA1, *APOA1, *CETP, *HNF4A              |
| <u>GO:0046470: phosphatidylcholine metabolic process</u>              | 9.33E-07 | 4 | 65   | APOA1, *CETP, LCAT, LIPC                   |
| <u>GO:0006641: triglyceride metabolic process</u>                     | 6.87E-06 | 4 | 107  | APOB, *APOE, *CETP, LIPC                   |
| <u>GO:0008654: phospholipid biosynthetic process</u>                  | 3.86E-04 | 4 | 302  | APOA1, *FADS1, LCAT, PGS1                  |
| <u>GO:0016042: lipid catabolic process</u>                            | 4.11E-04 | 4 | 307  | APOB, APOE, *IRS1, LIPC                    |
| <u>GO:0015914: phospholipid transport</u>                             | 1.42E-07 | 4 | 41   | ABCA1, APOA1, APOE, *CETP                  |
| <u>GO:0034381: plasma lipoprotein particle clearance</u>              | 1.04E-07 | 4 | 38   | APOA1, APOB, APOE, LIPC                    |
| <u>GO:0034372: very-low-density lipoprotein particle remodeling</u>   | 5.06E-11 | 4 | 7    | *APOE, *CETP, *LCAT, *LIPC                 |
| <u>GO:0034370: triglyceride-rich lipoprotein particle remodeling</u>  | 3.03E-10 | 4 | 10   | APOE, CETP, LCAT, LIPC                     |
| <u>GO:0034374: low-density lipoprotein particle remodeling</u>        | 1.03E-09 | 4 | 13   | *APOB, *APOE, *CETP, *LIPC                 |
| <u>GO:0065005: protein-lipid complex assembly</u>                     | 1.96E-09 | 4 | 15   | ABCA1, APOA1, APOB, APOE                   |
| <u>GO:0034377: plasma lipoprotein particle assembly</u>               | 1.96E-09 | 4 | 15   | ABCA1, APOA1, APOB, APOE                   |
| <u>GO:0046890: regulation of lipid biosynthetic process</u>           | 1.62E-05 | 4 | 133  | APOB, APOE, HNF4A, MLXIPL                  |
| <u>GO:0032374: regulation of cholesterol transport</u>                | 5.09E-08 | 4 | 32   | ABCA1, APOA1, APOE, CETP                   |
| <u>GO:0032371: regulation of sterol transport</u>                     | 5.09E-08 | 4 | 32   | ABCA1, APOA1, APOE, CETP                   |
| <u>GO:0032368: regulation of lipid transport</u>                      | 1.57E-06 | 4 | 74   | ABCA1, APOA1, APOE, CETP                   |
| <u>GO:0009743: response to carbohydrate stimulus</u>                  | 1.77E-04 | 4 | 246  | *APOB, FADS1, HNF4A, MLXIPL                |
| <u>GO:0042326: negative regulation of phosphorylation</u>             | 3.19E-04 | 4 | 287  | APOE, HNF4A, MLXIPL, TRIB1                 |
| <u>GO:0042439: ethanolamine-containing compound metabolic process</u> | 4.10E-06 | 4 | 94   | APOA1, CETP, LCAT, LIPC                    |
| <u>GO:0031331: positive regulation of cellular catabolic process</u>  | 1.58E-05 | 4 | 132  | APOE, IRS1, MLXIPL, TRIB1                  |
| <u>GO:0044106: cellular amine metabolic process</u>                   | 3.12E-05 | 4 | 157  | APOA1, CETP, LCAT, LIPC                    |
| <u>GO:0006576: cellular biogenic amine metabolic process</u>          | 3.12E-05 | 4 | 157  | APOA1, CETP, LCAT, LIPC                    |

|  |          |   |     |                            |
|--|----------|---|-----|----------------------------|
| GO:0009308: amine metabolic process  | 7.84E-05 | 4 | 199 | APOA1, CETP, LCAT, LIPC    |
| GO:0045936: negative regulation of phosphate metabolic process             | 6.23E-04 | 4 | 343 | APOE, HNF4A, MLXIPL, TRIB1 |
| GO:0010563: negative regulation of phosphorus metabolic process            | 6.23E-04 | 4 | 343 | APOE, HNF4A, MLXIPL, TRIB1 |
| GO:0048844: artery morphogenesis   | 4.30E-05 | 3 | 59  | *APOB, *APOE, CITED2       |
| GO:0060840: artery development   | 7.49E-05 | 3 | 71  | APOB, APOE, CITED2         |
| GO:0033500: carbohydrate homeostasis                                       | 6.79E-04 | 3 | 150 | HNF4A, IRS1, MLXIPL        |
| GO:0042593: glucose homeostasis  | 6.79E-04 | 3 | 150 | *HNF4A, *IRS1, *MLXIPL     |
| GO:0030336: negative regulation of cell migration                          | 8.95E-04 | 3 | 165 | APOE, *CITED2, TRIB1       |
| GO:2000146: negative regulation of cell motility                           | 9.27E-04 | 3 | 167 | APOE, CITED2, TRIB1        |
| GO:0010743: regulation of macrophage derived foam cell differentiation     | 1.54E-05 | 3 | 42  | ABCA1, APOB, CETP          |
| GO:0033700: phospholipid efflux  | 3.02E-07 | 3 | 12  | *ABCA1, *APOA1, *APOE      |
| GO:0033344: cholesterol efflux   | 3.53E-06 | 3 | 26  | *ABCA1, *APOA1, *APOE      |
| GO:0034380: high-density lipoprotein particle assembly                     | 2.76E-08 | 3 | 6   | *ABCA1, *APOA1, *APOE      |
| GO:0010907: positive regulation of glucose metabolic process               | 6.70E-06 | 3 | 32  | HNF4A, *IRS1, MLXIPL       |
| GO:0010676: positive regulation of cellular carbohydrate metabolic process | 1.54E-05 | 3 | 42  | HNF4A, IRS1, MLXIPL        |
| GO:0045913: positive regulation of carbohydrate metabolic process          | 2.46E-05 | 3 | 49  | HNF4A, IRS1, MLXIPL        |
| GO:0010906: regulation of glucose metabolic process                        | 2.33E-04 | 3 | 104 | HNF4A, IRS1, MLXIPL        |
| GO:0010675: regulation of cellular carbohydrate metabolic process          | 4.18E-04 | 3 | 127 | HNF4A, IRS1, MLXIPL        |
| GO:0006109: regulation of carbohydrate metabolic process                   | 4.68E-04 | 3 | 132 | HNF4A, IRS1, MLXIPL        |
| GO:0019218: regulation of steroid metabolic process                        | 2.01E-04 | 3 | 99  | APOA1, APOB, APOE          |
| GO:0045923: positive regulation of fatty acid metabolic process            | 9.62E-06 | 3 | 36  | HNF4A, IRS1, MLXIPL        |
| GO:0019217: regulation of fatty acid metabolic process                     | 2.26E-04 | 3 | 103 | HNF4A, IRS1, MLXIPL        |
| GO:0010874: regulation of cholesterol efflux                               | 9.30E-07 | 3 | 17  | ABCA1, APOE, *CETP         |
| GO:0032489: regulation of Cdc42 protein signal transduction                | 1.81E-06 | 3 | 21  | *ABCA1, *APOA1, *APOE      |
| GO:0030802: regulation of cyclic nucleotide biosynthetic process           | 2.53E-04 | 3 | 107 | ABCA1, APOE, MC4R          |
| GO:0030808: regulation of nucleotide biosynthetic process                  | 2.60E-04 | 3 | 108 | ABCA1, APOE, MC4R          |
| GO:1900371: regulation of purine nucleotide biosynthetic process           | 2.60E-04 | 3 | 108 | ABCA1, APOE, MC4R          |
| GO:0030799: regulation of cyclic nucleotide metabolic process              | 3.29E-04 | 3 | 117 | ABCA1, APOE, MC4R          |
| GO:0030804: positive regulation of cyclic nucleotide biosynthetic process  | 8.14E-05 | 3 | 73  | ABCA1, APOE, MC4R          |
| GO:1900373: positive regulation of purine nucleotide biosynthetic process  | 8.48E-05 | 3 | 74  | ABCA1, APOE, MC4R          |
| GO:0030810: positive regulation of nucleotide biosynthetic process         | 8.48E-05 | 3 | 74  | ABCA1, APOE, MC4R          |
| GO:0030801: positive regulation of cyclic nucleotide metabolic process     | 8.82E-05 | 3 | 75  | ABCA1, APOE, MC4R          |

|   |          |   |    |                   |
|---|----------|---|----|-------------------|
| GO:1900544: positive regulation of purine nucleotide metabolic process          | 9.55E-05 | 3 | 77 | ABCA1, APOE, MC4R |
| GO:0045981: positive regulation of nucleotide metabolic process                 | 9.55E-05 | 3 | 77 | ABCA1, APOE, MC4R |
| GO:0030317: sperm motility  | 8.77E-04 | 2 | 38 | *APOB, *PLTP      |
| GO:0010470: regulation of gastrulation  | 6.21E-04 | 2 | 32 | APOA1, *HNF4A     |
| GO:0010745: negative regulation of macrophage derived foam cell differentiation | 9.90E-05 | 2 | 13 | *ABCA1, *CETP     |
| GO:0042159: lipoprotein catabolic process                                       | 6.99E-05 | 2 | 11 | *APOB, *APOE      |
| GO:0019433: triglyceride catabolic process                                      | 3.19E-04 | 2 | 23 | *APOB, *LIPC      |
| GO:0046464: acylglycerol catabolic process                                      | 4.09E-04 | 2 | 26 | APOB, LIPC        |
| GO:0046461: neutral lipid catabolic process                                     | 4.09E-04 | 2 | 26 | APOB, LIPC        |
| GO:0046503: glycerolipid catabolic process                                      | 6.21E-04 | 2 | 32 | APOB, LIPC        |
| GO:0034384: high-density lipoprotein particle clearance                         | 2.68E-05 | 2 | 7  | *APOA1, *APOE     |
| GO:0034382: chylomicron remnant clearance                                       | 4.58E-05 | 2 | 9  | *APOE, *LIPC      |
| GO:0071830: triglyceride-rich lipoprotein particle clearance                    | 4.58E-05 | 2 | 9  | APOE, LIPC        |
| GO:0010873: positive regulation of cholesterol esterification                   | 2.68E-05 | 2 | 7  | *APOA1, *APOE     |
| GO:0010872: regulation of cholesterol esterification                            | 4.58E-05 | 2 | 9  | APOA1, APOE       |
| GO:0045540: regulation of cholesterol biosynthetic process                      | 2.91E-04 | 2 | 22 | *APOB, APOE       |
| GO:0045940: positive regulation of steroid metabolic process                    | 4.75E-04 | 2 | 28 | APOA1, APOE       |
| GO:0090181: regulation of cholesterol metabolic process                         | 6.61E-04 | 2 | 33 | APOB, APOE        |
| GO:0045723: positive regulation of fatty acid biosynthetic process              | 1.33E-04 | 2 | 15 | *HNF4A, *MLXIPL   |
| GO:0010875: positive regulation of cholesterol efflux                           | 6.99E-05 | 2 | 11 | *ABCA1, *APOE     |
| GO:0032373: positive regulation of sterol transport                             | 9.90E-05 | 2 | 13 | ABCA1, APOE       |
| GO:0032376: positive regulation of cholesterol transport                        | 9.90E-05 | 2 | 13 | ABCA1, APOE       |
| GO:0032370: positive regulation of lipid transport                              | 8.31E-04 | 2 | 37 | ABCA1, APOE       |
| GO:0010885: regulation of cholesterol storage                                   | 3.78E-04 | 2 | 25 | ABCA1, APOB       |
| GO:0034405: response to fluid shear stress                                      | 6.21E-04 | 2 | 32 | ABCA1, *CITED2    |
| GO:0019934: cGMP-mediated signaling   | 1.28E-05 | 2 | 5  | *APOE, *PDE3A     |
| GO:0002021: response to dietary excess  | 1.72E-04 | 2 | 17 | *APOE, MC4R       |
| GO:0006656: phosphatidylcholine biosynthetic process                            | 4.41E-04 | 2 | 27 | *APOA1, *LCAT     |
| GO:0019935: cyclic-nucleotide-mediated signaling                                | 5.10E-04 | 2 | 29 | APOE, PDE3A       |
| GO:0042304: regulation of fatty acid biosynthetic process                       | 7.87E-04 | 2 | 36 | HNF4A, *MLXIPL    |

k is the number of genes in the query set annotated to that node, and M is the number of genes in the database annotated to that node. \*next to the gene symbol indicates that the gene is annotated to the node, and not any of the child terms. Based on annotation dataset 12<sup>th</sup> November 2012 and GO ontology from 27<sup>th</sup> November 2012.

Table S7 Combined biological process VLAD summary results, triglyceride, total cholesterol, LDL cholesterol and HDL cholesterol trait associated genes

| <b>GO term grouping</b> | <b>Gene Ontology term</b>                        | <b>M</b> | <b>TG k</b> | <b>TC k</b> | <b>LDLc k</b> | <b>HDLc k</b> |
|-------------------------|--|----------|-------------|-------------|---------------|---------------|
| coagulation             | blood coagulation                                | 533      | -           | -           | -             | -             |
| development             | aging  | 380      | -           | -           | 5             | -             |
| development             | circulatory system development                   | 1053     | -           | -           | -             | -             |
| development             | regulation of cell differentiation               | 1576     | -           | 9           | -             | -             |
| development             | homeostatic process                              | 1700     | 12          | 21          | 17            | 12            |
| metabolism              | cellular carbohydrate metabolic process          | 246      | -           | -           | -             | -             |
| metabolism              | digestion  | 119      | -           | 4           | 4             | -             |
| metabolism              | lipid metabolic process                          | 1762     | 15          | 23          | 19            | 16            |
| metabolism              | lipoprotein metabolic process                    | 172      | 6           | 9           | 8             | 7             |
| metabolism              | plasma lipoprotein particle clearance            | 38       | 4           | 6           | 5             | 4             |
| metabolism              | regulation of glucose metabolic process          | 104      | 3           | -           | -             | 3             |
| metabolism              | regulation of lipid metabolic process            | 282      | 6           | 9           | 8             | 6             |
| metabolism              | small molecule metabolic process                 | 3455     | 17          | 26          | 22            | 16            |
| metabolism              | regulation of enzyme activity                    |          |             |             |               |               |
| signalling              | cell communication                               | 6835     | -           | -           | -             | -             |
| signalling              | response to chemical stimulus                    | 3988     | 14          | 21          | 16            | 13            |
| signalling              | response to nutrient levels                      | 473      | -           | 7           | 6             | -             |
| signalling              | response to stress                               |          |             |             |               |               |
| transport               | vesicle-mediated transport                       | 1300     | -           | 11          | 9             | 7             |
| transport               | plasma lipoprotein particle organization         | 33       | 6           | 7           | 4             | 7             |
| transport               | regulation of lipid transport                    | 74       | 4           | 7           | 5             | 4             |
| transport               | regulation of plasma lipoprotein particle levels | 60       | 6           | 9           | 6             | 7             |
| transport               | establishment and maintenance of position        |          |             |             |               |               |

k is the number of genes in the query set annotated to that node, and M is the number of genes in the database annotated to that node. Based on annotation dataset 12<sup>th</sup> November 2012 and GO ontology from 27<sup>th</sup> November 2012.

Individual lipid trait SNP datasets associated with each of the listed GO terms. HDL-C: HDL cholesterol trait, LDL-C: LDL cholesterol trait, TC: total cholesterol, TG: triglyceride.