

Supplemental Table 2. Convergence of human genes identified by GWAS to be associated with lipid risk factors and ApoA-I modulation by siRNA targeting the gene. The table includes the gene symbol, a brief description of the known function of the gene, the leading and other lipid traits identified with SNP associations in *Nature* 466, 707-713, the mean fold change in secreted ApoA-I that resulted from siRNA knockdown. Genes are listed according to magnitude of secreted ApoA-I change in the siRNA knock-down study and either HDL or triglycerides as the leading trait. HDL= high density lipoprotein, TG = triglycerides, TC= total cholesterol

Gene Symbol	Description	Lead Trait	Other Traits	Fold Δ ApoA-I
PLTP	Phospholipid transfer protein; a phosphatidylcholine transporter; controls cholesterol; triglyceride; and Vit-E levels; upregulation correlates with acute-phase reaction; arteriosclerosis; Alzheimer disease; alcoholism; type I and II diabetes mellitus	HDL	TG	1.86
MC4R	Melanocortin 4 receptor; a GPCR that acts in regulation of food intake and body size; involved in bone resorption; copulation; and synaptic transmission; regulates fatty acid oxidation and blood pressure; gene mutation causes obesity	HDL	--	1.82
GALNT2	UDP N acetyl alpha D galactosamine polypeptide N acetylgalactosaminyltransferase 2; acts in protein amino acid O-linked glycosylation; increased expression in nonkeratinized conjunctival epithelium correlates with ocular cicatricial pemphigoid	HDL	TG	1.45
LPA	Lipoprotein; a lipid transporter that regulates TGF-beta1 production; endothelial cell proliferation; and angiogenesis; acts in blood circulation; upregulated in rheumatoid arthritis; arteriosclerosis; stroke; ischemia; and Turner syndrome	HDL	--	1.42
AMPD3	Adenosine monophosphate deaminase; plays a role in AMP catabolic process and purine nucleotide metabolic process; upregulated in lung adenocarcinoma	HDL	--	1.37
PGS1	Phosphatidylglycerophosphate synthase 1; a likely phosphatidylglycerophosphate synthase that functions in mitochondrial phosphatidylglycerol metabolism; may play a role in apoptosis	HDL	--	1.36
ANGPTL4	Angiopoietin-like 4; a secreted glycoprotein that inhibits lipoprotein lipase activity; triglyceride catabolism; endothelial cell apoptosis; and stress fiber assembly; acts in oxidative stress response; mRNA is upregulated in renal and breast carcinomas	HDL	--	1.33

Gene Symbol	Description	Lead Trait	Other Traits	Fold Δ ApoA-I
TRPS1	Trichorhinophalangeal syndrome I; a transcription regulator that acts in Wnt signaling; cell proliferation; and skeletal system development; upregulated in breast cancer; gene mutation correlates with Langer-Giedion syndrome and osteochondrodysplasias	HDL	--	1.30
LCAT	Lecithin cholesterol acyltransferase; acts in cholesterol and lipoprotein metabolic process; aberrant expression correlates with diabetes mellitus and kidney diseases; gene mutation causes Tangier disease associated with hyperlipoproteinemia type II	HDL	--	1.29
COBLL1	COBL-like 1; negatively regulates apoptosis; altered mRNA expression may correlate with survival probability associated with malignant pleural mesothelioma	HDL	--	1.22
SCARB1	Scavenger receptor class B member I; a lipid transporter that acts in cholesterol metabolism; upregulated in arteriosclerosis; gene polymorphism is associated with hyperlipoproteinemia type II; downregulated in adrenal cortex neoplasms and carcinoma	HDL	--	1.19
ABCA8	ATP binding cassette subfamily A member 8; an ATPase that directly drives the active transport of a substance across a membrane; plays a role in transporting xenobiotics; decreased mRNA expression is associated with psoriasis	HDL	--	1.18
LRP4	Low density lipoprotein receptor-related protein 4; binds to LDL receptor; regulates canonical Wnt; BMP; and smoothed signaling and bone mineralization; acts in kidney and limb development; gene mutation causes Cenani-Lenz syndrome and sclerosteosis	HDL	--	1.17
PDE3A	Phosphodiesterase 3A cGMP-inhibited; a phosphoric diester hydrolase that plays a role in activation of protein kinase activity; oocyte maturation; regulates apoptosis; cAMP catabolism; and protein localization; downregulated in heart failure	HDL	--	1.12
C6orf106	Protein of unknown function; has a region of low similarity to C. elegans C36E6.2; which is involved in growth rate regulation; larval development; locomotory behavior; and egg-laying	HDL	--	1.02
SLC39A8	Solute carrier family 39 member 8; a putative metallopeptidase that mediates zinc ion transport; may play a role in cytokine and chemokine mediated signaling pathway	HDL	--	1.02
PABPC4	Poly(A)-binding protein cytoplasmic 4 (inducible form); binds to poly(A); poly(U) and AU-rich regions of mRNA; positively regulates interleukin-2 (IL2) mRNA translation; may play a role in blood coagulation and RNA catabolism	HDL	--	0.89

Gene Symbol	Description	Lead Trait	Other Traits	Fold Δ ApoA-I
PPP1R3B	Protein phosphatase 1 regulatory subunit 3B; an enzyme activator that acts in glucose transport; premeiotic DNA synthesis; and skeletal muscle tissue development; involved in insulin receptor signaling pathway and regulation of glycogen biosynthesis	HDL	TC,LDL	0.83
CETP	Cholesteryl ester transfer protein plasma; a cholesterol transporter that acts in cholesterol metabolism and homeostasis; upregulated in arteriosclerosis; coronary artery disease; type 1 diabetes mellitus; hypercholesterolemia; and xanthomatosis	HDL	TC,LDL,TG	0.81
LILRA3	Leukocyte immunoglobulin-like receptor; a putative receptor that may play a role in defense response and signal transduction; gene deletion is associated with multiple sclerosis and Sjogren syndrome	HDL	--	0.69
ABCA1	ATP-binding cassette subfamily A member 1; a cholesterol transporter that acts in lipid metabolism; insulin secretion; and phagocytosis; gene polymorphism correlates with coronary artery disease; familial form of hypolipoproteinemias; and Tangier disease	HDL	TC	0.66
LACTB	Lactamase beta; a putative beta-lactamase and a structural constituent of ribosome that forms polymers into ordered filaments inside mitochondria	HDL	--	0.64
UBE2L3	Ubiquitin-conjugating enzyme E2L 3; a transcriptional coactivator that is involved in ubiquitin-dependent protein catabolism; steroid hormone receptor signaling; and in utero embryonic development; genetic polymorphisms are associated with Crohn disease	HDL	--	0.63
CITED2	Cbp-p300 interacting transactivator with Glu-Asp rich carboxy terminal domain 2; a transcriptional coactivator that mediates angiogenesis; hemopoiesis; neural tube formation; and organ development; gene mutations correlate with congenital heart defects	HDL	--	0.53
LIPC	Lipase C; involved in lipid metabolism; fatty acid transport; and glucose metabolic process; aberrant protein activity correlates with type I diabetes mellitus and type II diabetes mellitus; mRNA expression is downregulated in coronary artery disease	HDL	TC,TG	0.50
KLF14	Kruppel-like factor 14; a TGFbeta (TGFB1)-inducible protein that silences the TGFbeta receptor II (TGFB2) promoter via a corepressor complex containing mSin3A and HDAC2; may regulate expression of genes associated with adiposity and metabolism	HDL	--	0.49

Gene Symbol	Description	Lead Trait	Other Traits	Fold Δ ApoA-I
MVK	Mevalonate kinase; acts in isoprenoid and cholesterol synthesis; downregulated in rhizomelic chondrodysplasia unctata; inborn metabolic errors; hypergammaglobulinemia; and Zellweger syndromes; gene mutation correlates with hepatocellular carcinoma	HDL	--	0.49
IRS1	Insulin receptor substrate 1; an signal transducer; activates MAPK activity; aberrant expression is associated with arteriosclerosis; diabetes mellitus; insulin resistance; gestational diabetes; obesity; and prostatic and several other neoplasms	HDL	TG	0.43
STARD3	StAR-related lipid transfer domain containing 3; acts in cholesterol transport; bile acid metabolism; and multivesicular body sorting pathway; aberrantly expressed in psoriasis; atopic dermatitis; and breast cancer; mRNA is upregulated in prostate cancer	HDL	--	0.38
SBNO1	Protein with very strong similarity to strawberry notch homolog 1 (mouse Sbn1); which exhibits induced expression in the developing nervous system by Reelin (mouse Rln); member of the helicase conserved C-terminal domain containing family	HDL	--	0.35
LIPG	Lipase endothelial; a triglyceride lipase that plays a role in high-density lipoprotein particle remodeling and cholesterol homeostasis; upregulated in arteriosclerosis; aberrant expression correlates with type 1 diabetes and fetal growth retardation	HDL	TC	0.26
CMIP	c-Maf-inducing protein; a proximal signaling protein regulating T cell activation; Src phosphorylation; cytoskeleton reorganization; and distribution of cytoskeleton-associated L-plastin; may act in short term memory associated with language impairment	HDL	--	0.20
HNF4A	Hepatocyte nuclear factor 4 alpha; a transcriptional coactivator that acts in hepatocyte differentiation and glucose metabolism; downregulated in Crohn disease; mRNA is overexpressed in hepatocellular carcinoma and SNP correlates with type 2 diabetes	HDL	TC	0.20
ARL15	ADP-ribosylation factor-like 15; may play a role in determining circulating levels of adiponectin; gene SNP is associated with increased risk of coronary heart disease; gene duplication may be associated with childhood obesity	HDL	--	--
C19orf80	Chromosome 19 open reading frame 80; gene hypermethylation is associated with hepatocellular carcinoma	HDL	--	--
TTC39B	Tetratricopeptide repeat domain 39B; gene polymorphism may correlate with blood levels of high density lipoprotein cholesterol	HDL	TC	--

Gene Symbol	Description	Lead Trait	Other Traits	Fold Δ ApoA-I
ZNF648	Protein containing ten zinc finger C2H2 type repeats; which bind nucleic acids; has a region of high similarity to a region of mouse Zfp2; which is a putative Kruppel-type zinc-finger transcription factor that may be required for neuronal development	HDL	--	--
UBASH3B	Cbl-interacting protein Sts-1; a CBL binding protein that regulates receptor mediated endocytosis	TC	HDL	--
KLHL8	Kelch-like 8; component of an E3 ubiquitin ligase complex that regulates ubiquitination and stability of rapsyn (RAPSN)	TG	--	1.88
PLA2G6	Phospholipase A2 group VI; a transferase that plays a role in cellular lipid metabolic process; calcium ion homeostasis; and mitochondrion organization; regulates cell cycle and cell migration; gene mutations are associated with neurodegenerative diseases	TG	--	1.64
GCKR	Glucokinase (hexokinase 4) regulator; a kinase inhibitor that regulates glucokinase translocation; functions in glucose metabolism; corresponding gene maps to a chromosomal region associated with obesity; polymorphism correlates with type II diabetes	TG	TC	1.47
ANGPTL3	Angiopoietin-like 3; a phospholipase inhibitor that plays a role in cholesterol homeostasis and lipid storage; induces endothelial cell adhesion and migration; angiogenesis; and proteolysis; heterozygous mutation correlates with hypolipidemia	TG	TC,LDL	1.35
LRP1	Low density lipoprotein-related protein 1; a receptor that acts in cell migration and lipoprotein metabolism; upregulated in malignancies; rheumatoid arthritis; and atherosclerosis; gene polymorphisms correlates with Alzheimer disease	TG	HDL	1.28
TRIB1	Tribbles homolog 1; a transcription cofactor that regulates RAR signaling; MAPK activation; and SMC proliferation; mRNA is upregulated in ischemic heart disease and downregulated in myeloid leukemia; gene mutation correlates with hypertriglyceridemia	TG	TC,LDL,HDL	1.27
COBLL1	COBL-like 1; negatively regulates apoptosis; altered mRNA expression may correlate with survival probability associated with malignant pleural mesothelioma	TG	--	1.22
NAT2	N-acetyltransferase 2 (arylamine N-acetyltransferase); catalyzes the reaction of acetyl-CoA and arylamine to CoA and N-acetylarylamine; gene polymorphisms are associated with arthritis; cataract; endometriosis; Parkinson disease; and several neoplasms	TG	TC	1.07

Gene Symbol	Description	Lead Trait	Other Traits	Fold Δ ApoA-I
LPL	Lipoprotein lipase; an hydrolase that acts in lipoprotein catabolism and blood circulation; gene polymorphism causes type 2 diabetes mellitus; hyperlipidemia; Alzheimer disease; hypertension; prostatic neoplasm; arteriosclerosis; and hypertriglyceridemia	TG	HDL	1.07
HLA-DRA	Histocompatibility antigen HLA-DR alpha, acts in immune response and T cell differentiation, aberrantly expressed in autoimmune diseases and muscular dystrophy; gene polymorphism is associated with multiple sclerosis and IgA glomerulon	TG	--	1.02
CTF1	Cardiotrophin 1; a LIFR ligand that acts in MAPKK activation; cardiac muscle hypertrophy; cell death; and nervous system development; upregulated in heart and kidney failure; angina pectoris; metabolic syndrome X; and blood pressure	TG	--	0.86
PINX1	PIN2-TERF1 interacting telomerase inhibitor 1; a putative tumor suppressor that binds to and inhibits TERT telomerase; regulates mitotic chromosome congression and stability; decreased mRNA expression correlates with stomach neoplasms	TG	--	0.83
MAP3K1	Mitogen-activated protein kinase kinase kinase 1; a transcription coactivator that acts in keratinocyte differentiation; JNK cascade; and apoptosis; decreased processing correlates with ovarian neoplasms; gene polymorphism correlates with breast neoplasms	TG	--	0.69
APOE	Apolipoprotein E; a lipid transporter that plays a role in cholesterol metabolism; cell proliferation; and musculoskeletal movement; gene polymorphism correlates with Alzheimer disease; carotid artery diseases; diabetic angiopathies; and amnesia	TG	--	0.67
FADS1	Fatty acid desaturase 1; a C-5 sterol desaturase that is involved in unsaturated fatty acid biosynthesis; may play a role in cell differentiation; upregulated in obesity; decreased mRNA expression correlates with psoriasis	TG	HDL,TC,LDL	0.65
CYP26A1	Cytochrome P450 family 26 subfamily A polypeptide 1; a retinoic acid 4-hydroxylase that acts in neuron differentiation; anteroposterior patterning; and brain development; upregulated in ovarian cancer; mouse Cyp26a1 is associated with caudal agenesis	TG	--	0.64
JMJD1C	Jumonji domain containing 1C; a transcriptional coactivator that interacts with androgen and glucocorticoid receptors; mRNA is downregulated in breast cancer; gene disruption correlates with autism	TG	--	0.63

Gene Symbol	Description	Lead Trait	Other Traits	Fold Δ ApoA-I
APOB	Apolipoprotein B; acts in cholesterol metabolism and absorption; aberrantly expressed in Alzheimer disease; AIDS; arthritis; diabetes; cardiac and pulmonary diseases; hypercholesterolemia; and hepatitis; mutation correlates with hypobetalipoproteinemia	TG	HDL	0.42
MSL2	Male-specific lethal 2 homolog; a component of a multisubunit histone acetyltransferase complex that mediates the majority of histone H4 acetylation at lysine 16; an MOF complex component and E3 ubiquitin ligase for H2B K34	TG	--	0.38
CAPN3	Calpain 3; a calcium-dependent cysteine-type endopeptidase that plays a role in skeletal muscle development; muscle contraction; visual perception; NF-kappaB cascade and cytolysis; gene mutations correlates with muscular dystrophy type 2A	TG	--	0.32
APOA1	Apolipoprotein A-I; a cholesterol transporter that acts in cAMP biosynthesis and blood circulation; upregulated in Alzheimer disease; arthritis; arteriosclerosis; diabetes; and breast neoplasms; gene mutations cause amyloidosis and hypolipoproteinemia	TG	TC,HDL,LDL	0.14
FRMD5	FERM domain containing 5; gene expression in glioblastoma cells is regulated by a TP53 R273H mutant; indicating a role in oncogenesis	TG	--	--