Supplemental Material

Expanded Materials & Methods

HDL analyses: <u>Cholesterol efflux assays:</u> Serum was reconstituted from freshly thawed plasma by addition of 2.5 M calcium chloride and incubated for 1 h. Polyethylene glycol (20% PEG8000, 2:5 v/v) was then added to precipitate apoB-containing lipoproteins. Cells were incubated in Dulbecco's modified Eagle medium supplemented with 0.1% (wt/vol) fatty acid-free albumin (Dulbecco's modified Eagle medium+fatty acid-free albumin), [3H]-cholesterol (0.5 μ Ci/mL), and an ACAT inhibitor (34.4 μ mol/L; Sandoz) for 24 hours at 37°C in a 5% CO2 atmosphere with or without presence of 8CPTcAMP (0.3 mM). After 1 wash with PBS, the cells were incubated in Dulbecco's modified Eagle medium+fatty acid-free albumin supplemented with 8CPTcAMP (0.3 mM; Sigma) for 24 h. Cells were washed again with PBS and then incubated with serum HDL (1.6% v/v) for 4 h.

<u>HDL particle concentration</u>: Lipoproteins were rapidly isolated from plasma at density 1.21 g/ml, dialyzed into 20 mM ammonium acetate, pH 7 and analyzed on a electrospray differential ion mobility analyzed (TSI Inc., Shoreview, MN). HDL subspecies were fitted to the DMA profiles by an unsupervised, iterative curve-fitting.³⁵ Areas under the curve fitted for each subspecies were directly converted to HDL particle concentration using a glucose oxidase calibration curve. For total HDL particle concentration, intra-day and inter-day coefficients of variation were <10%. The %CVs were <10% for HDL subpopulations.

HDL proteomics: 10µg HDL protein was solubilized with 0.5% sodium deoxycholate (SDC) (Sigma-Aldrich, St Louis, MO) in 200 mM NH₄HCO₃, spiked with 0.5 µg of [¹⁵N]APOA1 as internal standard³⁷, reduced with dithiothreitol, alkylated with iodoacetamide, and digested with two additions of trypsin (1:20, w/w HDL protein; sequencing grade; Promega, Fitchburg, WI) for 4 hours, and overnight. After precipitation of SDC with formic acid (1% final concentration), samples were frozen and stored at -20° C until analysis (less than a week). For the LC/MS analysis an equivalent of 200 ng of HDL protein was injected.³⁸ The DIA analysis was performed as follows: After desalting on a C18 trapping column (Reprosil-Pur 120 C18-AQ, 5 µm, 0.1 x 40 mm, Dr. Maisch HPLC GmbH, Germany) (flow rate 4 µL/min), the digested peptides were separated on an analytical column (Reprosil-Pur 120 C18-AQ, 5 µm, 250x0.075 mm, Dr. Maisch HPLC GmbH). Following multi-step linear gradient was used: 1-5%B in 2 min, 5-25% in 50 min, 25-35% in 10 min. At the end of the gradient column was washed with a ramp to 80%B and reequilibrated (A - 0.1% formic acid in water, B - acetonitrile, 0.1% formic acid, flow rate of 0.4 μ L/min). An LC-MSMS consisting of a nanoAquity UPLC (Waters, MA), and a Thermo Fusion Lumos (Thermo Fisher, San Jose, CA) tribrid mass spectrometer with electrospray ionization were used for the analysis. DIA parameters were: MS1 scan (395-1005 Da, resolution 120,000, maximum injection time 50 ms) followed with 60 MS/MS scans across 400-1000 Da range with 10 Da mass selection window each (resolution 15,000, maximum injection time 22 ms, loop time 3 sec). Fragmentation was induced by HCD activation at normalized collision energy 30%. Further data processing was accomplished using Skyline³⁹ to extract fragment ion chromatograms of the MS2 scans with 10 ppm accuracy windows. Chromatograms were integrated and chromatographic peak areas were exported for further analysis. Protein abundance was quantified after normalization of the representative peptides to 15N-APOA1 peptide VQPYLDDFQK. To quantify each protein, a response of at least 2 peptides specific to each protein was averaged. Peptide and protein abundance are therefore expressed in arbitrary units [a.u.].



Supplemental Figure I

(A) Representative pictures of the aortic arch in the donor mouse (*left*), during aortic transplantation (*middle*) and after two weeks of atherosclerosis regression (*right*). Arrows indicate atherosclerotic lesions (B) Body weight in baseline and regression groups before and after the 2 weeks atherosclerosis regression period. N= 5-24/group; data represented as mean \pm SEM,*** P < 0.0001, 2-way ANOVA with Tukey's multiple comparison test



Supplemental Figure II

Correlation of plasma TG levels with (A) lesion size and (B) %CD68



Supplemental Figure III

iLpL^{-/-} with LpL expressing macrophages do not impair atherosclerosis regression.

(A) Study setup (B) Genotyping using blood DNA confirming BMT (C) body weight in baseline and regression groups before and after the 2 weeks atherosclerosis regression period (D) Plasma Cholesterol (E) Plasma TG. Cholesterol (F) and triglyceride levels (G) of isolated lipoproteins (H) CD68 staining (I) CD68 area of lesion size (%). N= 4-14/group; data represented as mean \pm SEM, *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001, 1-way ANOVA with Tukey's multiple comparison test (C,I), Kruskal-Wallis Test (D,E), students unpaired t-test (F-G).



● LpL^{fl/fl}Tie2LPL (Baseline) ● iLpl^{-/-}Tie2LPL (Baseline) ■ LpL^{fl/fl}Tie2LPL (Regression) ■ iLpl^{-/-}Tie2LPL (Regression)

Supplemental Figure IV. Hypertriglyceridemia and enhanced endothelial LPL expression does not alter atherosclerosis regression in a non-invasive model of regression. Atherosclerosis was created in $Lpl^{n/n}$ Tie2LPL and $iLpl^{r/r}$ Tie2LPL mice with LDLR antisense oligonucleotides (ASO) and western diet feeding for 16 weeks. One set of mice were analyzed at 16 weeks as the baseline group and the rest of the mice were treated with SO to induce regression and were analyzed after 3 weeks. The mice in regression group were also treated with tamoxifen at Week 13 to induce hypertriglyceridemia in $iLpl^{r/r}$ Tie2LPL mice. Plasma (A) total cholesterol (TC) and (B) triglyceride (TG) levels in baseline and regression groups. (C) Total plaque area, (D) % of macrophages (CD68+) within aortic root lesions, (E) total plaque area, (F) % of macrophage (Mac2+) in plaques within the BCA in the baseline and regression groups. N= Baseline $Lpl^{n/n}$ Tie2LPL 4, Regression $Lpl^{n/n}$ Tie2LPL 4 and Regression $iLpl^{r/r}$ Tie2LPL 3. Results expressed as mean \pm SEM. *P < 0.05, **P < 0.01 using 1-way ANOVA with Tukey's multiple comparison test.



Supplemental Figure V. Circulating ApoA-I levels are reduced with HyperTG. (A) Plasma ApoA-I levels (uM) measured by mass spectrometry. (B) Comparison of HDL-C and ApoA-I reduction in HyperTG plasma +/- hCETP (%, relative to $Lpl^{fl/fl}$ (+LacZ)). N= Lpl^{fl/fl} 5, Lpl^{-/-} 4, Lpl^{fl/fl} +hCETP 5, Lpl^{-/-} + hCETP 4. * P < 0.05, ** P < 0.01, Kruskal-Wallis Test with Dunn's multiple comparison test.



Figure VI. HyperTG does not change the ratio of circulating Ly6C^{hi}/Ly6C^{low} monocytes. (A) Ly6C^{hi} and (B) Ly6C^{low} monocytes assessed by flow cytometry and corrected by total white blood cell count (10³/ul). N= (A) Lp1^{fl/fl} 14, Lp1^{-/-} 12, Lp1^{fl/fl} +hCETP 7, Lp1^{-/-} + hCETP 7; WT BM Lp1^{fl/fl} 5, Lp1^{-/-} 2 (B) Lp1^{fl/fl} 12, Lp1^{-/-} 13, Lp1^{fl/fl} +hCETP 7, Lp1^{-/-} + hCETP 7; WT BM Lp1^{fl/fl} 5, Lp1^{-/-} 2. Data shown as mean ± SEM.

Supplemental Table I

qPCR Primer

Gene	Forward (5' - 3')	Reverse (5' - 3')
Cetp	GATGGGAGACGAGTTCAAGG	CTGGGCGTGGAAAGAGGA
LacZ	TATCCGAACCATCCGCTGT	CTCCGCCGCCTTCATACT
Lpl	AGGTGGACATCGGAGAACTG	TCCCTAGCACAGAAGATGACC
Plin2	TCTGCGGCCATGACAAGTG	GCAGGCATAGGTATTGGCAAC
Cpt1a	TGCACTACGGAGTCCTGCAA	GGACAACCTCCATGGCTCAG
Glut1	TCGTAACGAGGAGAACCG	GGCCGTGTTGACGATA
Fasn	TCTTTCTAACAACCACCCTCTGG	CTTCACGACTCCATCACGAATG
Cd36	CCTTAAAGGAATCCCCGTGT	TGCATTTGCCAATGTCTAGC
Tnf	TGGAACTGGCAGAAGAGG	AGACAGAAGAGCGTGGTG
Mcp1	CCCAATGAGTAGGCTGGAGA	TCTGGACCCATTCCTTCTTG
Nos2	CAGCTGGGCTGTACAAACCTT	CATTGGAAGTGAAGCGTTTCG
Fizz l	CCAATCCAGCTAACTATCCCTCC	AAGCCACAAGCACACCCAGT
Mrc1	TGATTACGAGCAGTGGAAGC	GTTCACCGTA-AGCCCAATTT
1110	CTGGACAACATACTGCTAACCG	GGGCATCACTTCTACCAGGTAA

Supplemental Table II Overview of detected Proteins

Protein.Gene	Protein.Name	Protein.Accession	Protein.Description
Acth	spl P607101ACTB_MOUSE	P60710	Acting opposing 1 OS-Mus musculus GN-Acth PE-1 SV-1
Δσt	splP11859LANGT_MOUSE	P11859	Angiotensingen OS=Mus musculus GN=Agt PE=1 SV=1
Aben		P20600	Alpha-2-HS-diveopratain OS-Mus musculus GN-Absa PE-1 SV-1
Alb	spin 20000 relok_MOUSE	P07724	Sarum albumin OS-Mus musculus GN-Alb PE-1 SV-3
Alb		000182	Assistantial control of the state of the sta
Angpus Antur2	SPIQ9R182 ANGLS_MOUSE	Q9R182	Angiopoletin-related protein 5 OS=Wus musculus GN=Angpti5 PE=1 SV=1
Antxr2	spiQ6DFX2/ANTR2_MOUSE	Q6DFX2	Anthrax toxin receptor 2 US=Mus musculus GN=Antxr2 PE=1 SV=1
Apoaz	spip09813 APOA2_MOUSE	P09813	Apolipoprotein A-II OS=Mus musculus GN=Apol2 PE=1 SV=2
Apoa4	spipu6728 APOA4_MOUSE	P06728	Apolipoprotein A-IV US=Mus musculus GN=Apoa4 PE=1 SV=3
Apob	sp[E9Q414]APOB_MOUSE	E9Q414	Apolipoprotein B-100 OS=Mus musculus GN=Apob PE=1 SV=1
Apoc1	sp P34928 APOC1_MOUSE	P34928	Apolipoprotein C-I OS=Mus musculus GN=Apoc1 PE=1 SV=1
Apoc2	sp Q05020 APOC2_MOUSE	Q05020	Apolipoprotein C-II OS=Mus musculus GN=Apoc2 PE=2 SV=1
Apoc3	sp P33622 APOC3_MOUSE	P33622	Apolipoprotein C-III OS=Mus musculus GN=Apoc3 PE=1 SV=2
Apod	sp P51910 APOD_MOUSE	P51910	Apolipoprotein D OS=Mus musculus GN=Apod PE=1 SV=1
Apoe	sp P08226 APOE_MOUSE	P08226	Apolipoprotein E OS=Mus musculus GN=Apoe PE=1 SV=2
Apon	tr G3X9D6 G3X9D6_MOUSE	G3X9D6	Apolipoprotein N OS=Mus musculus GN=Apon PE=1 SV=1
Arhgdia	GDIR1_MOUSE	sp Q99PT1 GDIR1_MOUSE	Rho GDP-dissociation inhibitor 1 OS=Mus musculus GN=Arhgdia PE=1 SV=3
B2m	sp P01887 B2MG_MOUSE	P01887	Beta-2-microglobulin OS=Mus musculus GN=B2m PE=1 SV=2
Blvrb	sp Q923D2 BLVRB_MOUSE	Q923D2	Flavin reductase (NADPH) OS=Mus musculus GN=Blvrb PE=1 SV=3
Bpifa2	spIP07743 BPIA2_MOUSE	P07743	BPI fold-containing family A member 2 OS=Mus musculus GN=Bpifa2 PE=1 SV=1
C3	splP01027LCO3_MOUSE	P01027	Complement C3 OS=Mus musculus GN=C3 PE=1 SV=3
C4b	splP01029LCO4B_MOUSE	P01029	Complement C4-B OS=Mus musculus GN=C4b PE=1 SV=3
Ca1	splR13634LCAH1_MOUSE	P13634	Carbonic anhydrase 1 OS-Mus musculus GN-Ca1 DE-1 SV-4
Ca2			Carbonic annyurase 2 OS-Mas musculus GN=Ca2 DE-1 SV=4
Cd2		SP[F00520]CAH2_WO03E	Children Contraction Contracti
C097		Q9201016	Cost and gen user where the Children and
CTIL	spip18760[COF1_MOUSE	P18760	Continent OSEMUS musculus GNECTI PEET SVE3
Clu	sp[Q06890]CLUS_MOUSE	Q06890	Clusterin OS=Mus musculus GN=Clu PE=1 SV=1
Ср	CERU_MOUSE	sp Q61147 CERU_MOUSE	Ceruloplasmin OS=Mus musculus GN=Cp PE=1 SV=2
Ctsd	sp P18242 CATD_MOUSE	P18242	Cathepsin D OS=Mus musculus GN=Ctsd PE=1 SV=1
Dbi	sp P31786 ACBP_MOUSE	P31786	Acyl-CoA-binding protein OS=Mus musculus GN=Dbi PE=1 SV=2
Dmkn	sp Q6P253 DMKN_MOUSE	Q6P253	Dermokine OS=Mus musculus GN=Dmkn PE=2 SV=2
Dsc3	sp P55850 DSC3_MOUSE	P55850	Desmocollin-3 OS=Mus musculus GN=Dsc3 PE=1 SV=3
Dsp	DESP_MOUSE	sp E9Q557 DESP_MOUSE	Desmoplakin OS=Mus musculus GN=Dsp PE=1 SV=1
Fabp4	sp P04117 FABP4_MOUSE	P04117	Fatty acid-binding protein, adipocyte OS=Mus musculus GN=Fabp4 PE=1 SV=3
Fga	splE9PV24LFIBA_MOUSE	E9PV24	Fibringen alpha chain OS=Mus musculus GN=Fga PE=1 SV=1
Egh	spl08K0E8LEIBB_MOUSE	O8K0E8	Fibringen beta chain OS=Mus musculus GN=Egb PE=1 SV=1
Ge	col D21614 LVTDR_MOUSE	D21614	Vitamia D bioding actorin OS=Mus musculus GN=GS DE1 SV=2
GC Cm20425	sp[F21014]VIDB_W003E	F21014	Vitamin D'olinang protein 03-1/was masculus GN-Ct PL-1 3/2
GI120425		630055	Uncharacterized protein US=Mus musculus GN=Gm20425 PE=4 SV=1
GIII8909	II I GSUKEA GSUKEA MOUSE	GSUXES	Outralacterized brotein O2=inits information of the Gill Solar Sector 201
Gpld1	sp 070362 PHLD_MOUSE	070362	Phosphatidylinositol-glycan-specific phospholipase D OS=Mus musculus GN=Gpld1 PE=1 SV=1
Gpx3	sp P46412 GPX3_MOUSE	P46412	Glutathione peroxidase 3 OS=Mus musculus GN=Gpx3 PE=1 SV=2
Gpx5	GPX5_MOUSE	sp P21765 GPX5_MOUSE	Epididymal secretory glutathione peroxidase OS=Mus musculus GN=Gpx5 PE=2 SV=3
H2-L	sp P01897 HA1L_MOUSE	P01897	H-2 class I histocompatibility antigen, L-D alpha chain OS=Mus musculus GN=H2-L PE=1 SV=2
H2-Q10	sp P01898 HA10_MOUSE	P01898	H-2 class I histocompatibility antigen, Q10 alpha chain OS=Mus musculus GN=H2-Q10 PE=1 SV=3
H2-Q4	tr Q8HWB2 Q8HWB2_MOUSE	Q8HWB2	Histocompatibility 2, Q region locus 4 OS=Mus musculus GN=H2-Q4 PE=1 SV=1
H2-Q7	sp P14429 HA17_MOUSE	P14429	H-2 class I histocompatibility antigen, Q7 alpha chain OS=Mus musculus GN=H2-Q7 PE=1 SV=1
Hba	sp P01942 HBA_MOUSE	P01942	Hemoglobin subunit alpha OS=Mus musculus GN=Hba PE=1 SV=2
Hbbt1	tr A8DUK4 A8DUK4 MOUSE	A8DUK4	Reta-globin OS=Mus musculus GN=Hbbt1 PE=1 SV=1
Icam1	snIP13597UCAM1_MOUSE	P13597	Intercellular adhesion molecule 1 OSEMus musculus GNEIcam1 PE=1 SV=1
Infals	splP70389LALS_MOUSE	P70389	Insulia-like growth factor-binding protein complex acid labile subunit OS-Mus musculus GN-lafals DE-1 SV-1
Ighm	sp[170305]AES_MOUSE	D01973	In much growth ratio bining process complex and statistic solutions musculas diverginals FE-1 SV-1
Ignin			Ig the chain of egotion of white moscillas diverginin FE-1 3V-2
IGRC		spipo1837 ligkc_woose	Ing kappa chain c region OS=Wids musculus PE=1 SV=1
lgkv14-126	tr A0A075B5K0 A0A075B5K0_MOUSE	A0A075B5K0	Uncharacterized protein (Fragment) OS=Mus musculus GN=lgkv14-126 PE=4 SV=7
ltih4	sp A6X935 ITIH4_MOUSE	A6X935	Inter alpha-trypsin inhibitor, heavy chain 4 OS=Mus musculus GN=ltih4 PE=1 SV=2
K1C10_HUMAN	sp K1C10_HUMAN	K1C10_HUMAN	#N/A
K22E_HUMAN	sp K22E_HUMAN	K22E_HUMAN	#N/A
Kng1	sp 008677 KNG1_MOUSE	008677	Kininogen-1 OS=Mus musculus GN=Kng1 PE=1 SV=1
Krt1	sp P04104 K2C1_MOUSE	P04104	Keratin, type II cytoskeletal 1 OS=Mus musculus GN=Krt1 PE=1 SV=4
Krt10	sp P02535 K1C10_MOUSE	P02535	Keratin, type I cytoskeletal 10 OS=Mus musculus GN=Krt10 PE=1 SV=3
Krt13	sp P08730 K1C13_MOUSE	P08730	Keratin, type I cytoskeletal 13 OS=Mus musculus GN=Krt13 PE=1 SV=2
Krt14	sp Q61781 K1C14_MOUSE	Q61781	Keratin, type cytoskeletal 14 OS=Mus musculus GN=Krt14 PE=1 SV=2
Krt5	sp10922U21K2C5_MOUSE	0922U2	Keratin, type II cytoskeletal 5 QS=Mus musculus GN=Krt5 PE=1 SV=1
Krt72	K2C72 MOUSE	spl O6IME91K2C72_MOUSE	Keratin type II cytoskeletal 72 OS=Miis misculus GN=Krt72 PE=3 SV=1
KRT9	splK1C9 HUMAN	P35527	Keratin, type II cytoskeletal 9 (Cytokeratin-9) (CK-9) (Keratin-9) (K9)
KH15	501701701700170 MOUSE	500170	Kendin (ipe reviowership) (choleradio 5) (cendin 5) (co)
Loot		D16201	Decembratid debaling starsh and transference OS-Mus museulus CM-List 25, 4, 51, 2
LCOL	spir 10301 LLCAI_MOUSE	F 10301	Phospharogylunome-steroi acyltransierase OS=ivius musculus GN=LCat PE=1 SV=2
IVID Mum1	spiro4247 INITO_MOUSE	FU4247	nivyogrouni op-ivids musculus GN=IVID PE=1 SV=3
IVIUG 1		F 20000	Invit mogrobulth - 1 US=IVIUS ITIUSCUIUS GIV=MUBI PE=1 SV=3
Mup18	sp1A2BIM81MUP18_MOUSE	AZRIMS	Major urinary protein 18 US=Mus musculus GN=Mup18 PE=3 SV=1
Mup20	spiusEw601M0P20_MOUSE	U2FW60	Major urinary protein 20 US=Mus musculus GN=Mup20 PE=1 SV=1
Napsa	sp10090431NAPSA_MOUSE	009043	Napsin-A US=Mus musculus GN=Napsa PE=1 SV=1
Pcyox1	sp1u9CQF91PCYOX_MOUSE	Q9CQF9	Prenylcysteine oxidase OS=Mus musculus GN=Pcyox1 PE=1 SV=1
Pfn1	sp P62962 PROF1_MOUSE	P62962	Protilin-1 OS=Mus musculus GN=Pfn1 PE=1 SV=2
Pla2g7	sp Q60963 PAFA_MOUSE	Q60963	Platelet-activating factor acetylhydrolase OS=Mus musculus GN=Pla2g7 PE=2 SV=2
Pltp	sp P55065 PLTP_MOUSE	P55065	Phospholipid transfer protein OS=Mus musculus GN=Pltp PE=1 SV=1
Pm20d1	sp Q8C165 P20D1_MOUSE	Q8C165	N-fatty-acyl-amino acid synthase/hydrolase PM20D1 OS=Mus musculus GN=Pm20d1 PE=1 SV=1
Pon1	sp P52430 PON1_MOUSE	P52430	Serum paraoxonase/arylesterase 1 OS=Mus musculus GN=Pon1 PE=1 SV=2
Ppia	PPIA_MOUSE	sp P17742 PPIA_MOUSE	Peptidyl-prolyl cis-trans isomerase A OS=Mus musculus GN=Ppia PE=1 SV=2
Ppic	sp P30412 PPIC_MOUSE	P30412	Peptidyl-prolyl cis-trans isomerase C OS=Mus musculus GN=Ppic PE=1 SV=1
Prdx2	sp Q61171 PRDX2_MOUSE	Q61171	Peroxiredoxin-2 OS=Mus musculus GN=Prdx2 PE=1 SV=3
Psap	sp Q61207 SAP_MOUSE	Q61207	Prosaposin OS=Mus musculus GN=Psap PE=1 SV=2
Pzp	sp Q61838 PZP_MOUSE	Q61838	Pregnancy zone protein OS=Mus musculus GN=Pzp PE=1 SV=3
Osox1	splQ8BND5/QSOX1_MOUSE	Q8BND5	Sulfhydryl oxidase 1 OS=Mus musculus GN=Osox1 PE=1 SV=1
Rbp4	spl0007241RET4_MOUSE	000724	Retinol-binding protein 4 OS=Mus musculus GN=Rho4 PF=1 SV=2
Saa1	sn[P05366[SAA1_MOUSE	P05366	Serum amyloid A-1 protein OS=Mus musculus GN=Saa1 PE-1 SV-2
\$337	cn[005367[\$4A2_MOUL5	P05367	Serum amyloid A-2 protein OS-Mus musculus CN=Soo2 DE=1 CV=1
Sadd2	sp[r0307]SAA2_WUUSE	FUJ30/ 021522	Serum amyrolu A-2 protein OS=Mus musculus ON=Sad2 PE=1 SV=1
5884	spir31532[SAA4_MOUSE	P31532	perum amyolo A-4 protein US=Mus musculus GN=Saa4 PE=1 SV=2
Sell	spip1833/jlyAM1_MOUSE	P1833/	L-selectin US=INIUS MUSCUlus GN=Sell PE=1 SV=1
Serpina1a	sp P07758 A1AT1_MOUSE	PU/758	Alpha-1-antitrypsin 1-1 OS=Mus musculus GN=Serpina1a PE=1 SV=4
Serpina1b	sp P22599 A1AT2_MOUSE	P22599	Alpha-1-antitrypsin 1-2 OS=Mus musculus GN=Serpina1b PE=1 SV=2
Serpina1e	sp Q00898 A1AT5_MOUSE	Q00898	Alpha-1-antitrypsin 1-5 OS=Mus musculus GN=Serpina1e PE=1 SV=1
Serpina3k	sp P07759 SPA3K_MOUSE	P07759	Serine protease inhibitor A3K OS=Mus musculus GN=Serpina3k PE=1 SV=2
Serpinf2	A2AP_MOUSE	sp Q61247 A2AP_MOUSE	Alpha-2-antiplasmin OS=Mus musculus GN=Serpinf2 PE=1 SV=1
Tfrc	sp Q62351 TFR1_MOUSE	Q62351	Transferrin receptor protein 1 OS=Mus musculus GN=Tfrc PE=1 SV=1
Thbs1	sp P35441 TSP1_MOUSE	P35441	Thrombospondin-1 OS=Mus musculus GN=Thbs1 PE=1 SV=1
Ttr	sp P07309 TTHY_MOUSE	P07309	Transthyretin OS=Mus musculus GN=Ttr PE=1 SV=1
Vcam1	sp P29533 VCAM1 MOUSE	P29533	Vascular cell adhesion protein 1 OS=Mus musculus GN=Vcam1 PE=1 SV=1
Vtn	snIP29788IVTNC_MOUSE	P29788	Vitronectin OS=Mus musculus GN=Vtn PF=1 SV=2

Supplemental Table III

Detected Proteins in iLpl^{-/-} versus Lpl^{fl/fl}



Protein	Fold Change	P value
Dmkn Apoc3	0.299	<0,001 <0.001
Apoc2 Apoc4	0.176	< 0.001
Rbp4	1.588	0.001
Camp Hpx	0.281 4.842	0.001
Apoc1	0.125	0.001
Ctsd	1677	0.001
Apoe F6Y6L6	0.362	0.001
Lrg1	2.055	0.001
Psap	3.343	0.002
Cst6	0.221	0.002
Clec3b	4.941	0.002
Apoa5 Apod	3.663	0.002
Grn	1.771	0.003
Agt Blvrb	3.109	0.003
Tmsb4x Pnic	3.142	0.004
Apoa1	0.797	0.004
Ttr Apom	0.703	0.004
Fabp5	3.580	0.007
Serpina1b	1.694	0.008
Pitp Servina1a	0.771	0.009
Cfl1	2.214	0.011
Ca1 Iefals	3.043	0.012
Vnn1	2.693	0.013
Gm20425	4.585	0.015
Itih4 Semina ¹ 4	1.963	0.017
Snca	3.082	0.018
Cd97 Prdx2	1.791 2.318	0.019
Thbs1	2.974	0.021
Antxr2	4.959	0.025
Ahsg	1.359	0.029
Pcyox1	0.825	0.031
Angptl3 Pla2#7	0.383	0.035
Kng1	1.775	0.040
H2-Q1 H2-Q10	0.809	0.049
G	1.533	0.055
Saai Krt10	2.176	0.061
Pzp	2.033	0.064
Ambp	1.506	0.066
Fga Tfpi	1.917 0.833	0.067
Krt13	2.159	0.078
HZ-L B2m	0.822	0.082
K22E	2.505	0.089
Apcs	1.751	0.094
Saa3 Hbbt1	0.513 4.038	0.094
Napsa	0.802	0.104
Bpifa2	1.390	0.114
hHBA Gm8909	3.786	0.130
Dbi	2.087	0.140
Scgb1a1 K1C10	1.767	0.147
Gpx3	1.757	0.151
Actb Igkv14-126	4.334 0.333	0.171 0.175
Fabp4	2.193	0.179
Fgb	1.135	0.182
Dsc3 Saa4	1.521	0.222
H2-K1	0.852	0.241
Mup15 Fgg	1.592 1.474	0.258
Gpld1 Osov1	1.226	0.297
H2-Q7	0.877	0.302
Mb	1.566	0.348
Mup18	1.551	0.392
Apoa4 KRT9	1.128 0.320	0.447
Serpina3k	1.229	0.480
namp Krt2	1.817	0.535
Tfrc C4h	1.144	0.545
Vcam1	0.869	0.562
Mup17 H2-Q4	1.560 0.946	0.592
Mup3	1.222	0.596
wupz K2C1	0.582	0.604
P01837	1.185	0.625
Krt90	0.647	0.659
CSN1S1 Arsg	1.047 0.902	0.665
Pon1	1.036	0.710
icam1 Krt78	1.113 0.743	0.728
Enpp7	1.040	0.776
Anxa2	1.129	0.800
Krt1 Serninala	0.813	0.809
Apoh	1.043	0.840
Emc9 Vtn	0.964	0.846
Krt5	1.125	0.860
rabp3 Mup20	1.092 0.909	0.867
TRY1	0.987	0.901
Mug1	1.013	0.926
Sell	0.993	0.961

Supplemental Table IV

Detected Proteins in iLpl^{-/-}+hCETP versus Lpl^{fl/fl}+hCETP



Protein	Fold Change	P value
Pfn1	2.096	0.009
Dbi	1.926	0.010
Arhgdia	2.725	0.013
Fga	1.908	0.020
Hbbt1	3 166	0.024
Kng1	3.343	0.025
Blvrb	2.449	0.032
Serpinf2	2.864	0.032
Prdx2	2.220	0.032
Fabp4	2.209	0.033
Ca1 Pzn	2.462	0.040
Apoa2	0.819	0.044
Itih4	2.670	0.045
Thbs1	3.245	0.056
Ppic	1.415	0.061
Ctl1	2.862	0.065
Serpina3k Serpina1b	1.588	0.077
IGKC	2.200	0.082
Hba	2.408	0.088
Apoa4	1.383	0.095
Gpld1	0.584	0.104
Apoa1	0.706	0.107
Pnia	2 500	0.110
Ttr	1.405	0.120
Tfrc	0.177	0.122
Qsox1	0.173	0.122
Igfals	0.125	0.129
Pla2g7	0.288	0.130
rgb Gm20425	1.617	0.134
Vcam1	0.272	0.134
Serpina1a	1.469	0.152
Ca2	2.596	0.159
Cd97	0.168	0.187
Pon1	0.658	0.192
Gpx5	1.632	0.197
Mb	1.561	0.201
Cp	2.750	0.235
C4b	0.554	0.237
Apoc2	0.670	0.243
Pm20d1	2.010	0.253
Gc	1.460	0.257
Antxr2	0.494	0.310
B2m	1.214	0.329
Mup18	1.697	0.339
Saa2	1.635	0.346
Mup20	1.813	0.362
Ighm	1.564	0.370
Apocs Saal	1.439	0.375
Agt	1.205	0.393
Lcat	0.793	0.409
Dmkn	0.713	0.427
H2-Q7	1.388	0.430
KRT9	1.307	0.438
Dsn	0.000	0.447
C3	0.805	0.459
lcam1	0.477	0.474
Krt14	0.310	0.479
Serpina1e	1.253	0.504
Clu	0.775	0.513
H2-I	0.224	0.520
Pltp	1.544	0.587
Apon	1.284	0.590
Ahsg	1.193	0.592
H2-Q4	0.900	0.604
Igkv14-126	1.357	0.605
Anod	0.840	0.620
Krt13	0.644	0.637
Apoc1	1.110	0.640
Pcyox1	0.908	0.641
Krt72	0.650	0.650
Krt5	0.603	0.651
H2-010	1.226	0.730
K1C10 HUMAN	0.771	0.753
Krt90	0.822	0.766
Krt1	0.830	0.781
Psap	0.759	0.804
TRYPS	1.012	0.821
Krt10	0.827	0.822
Rhn4	1.150	0.620
Saa4	1.054	0.876
K22E_HUMAN	0.922	0.887
Vtn	0.939	0.932
Sell	0.953	0.936
Ctsd	1.025	0.947

Supplemental Table V

Overlapping Proteins Supplemental Table III and IV



Total of 85 proteins were detected in both proteomic data sets. 9 of them were significantly downregulated, 52 upregulated. They were associated with lipoprotein remodeling. Red bars: $iLpl^{-/-}$ versus $Lpl^{fl/fl}$; Grey bars: $iLpl^{-/-}$ + hCETP versus $Lpl^{fl/fl}$ +hCETP. $Lpl^{fl/fl}$ n=8, $iLpl^{-/-}$ n=8, $Lpl^{fl/fl}$ + hCETP n=17, $iLpl^{-/-}$ + hCETP n=10

	Cre vs Flox	Cre vs flox hCETP	
Protein	Fold Change	Fold Change	P value
Qsox1	1.304	0.172	0.001
Cd97	1.791	0.168	0.002
Apoc1	0.125	1.110	0.019
Thbs1	2.974	3.245	0.032
Ppic	0.717	1.414	0.047
Apoc3	0.206	0.806	0.058
	0.821	0.176	0.064
Sernina3k	1 228	2 132	0.066
Anon	1.225	1 284	0.121
Pltn	0.771	1.204	0.143
Serpina1a	1.466	1.468	0.183
Actb	4.334	0.223	0.188
Dmkn	0.298	0.713	0.195
Fgb	1.581	1.616	0.197
H2-Q10	0.810	1.102	0.198
H2-Q4	0.946	0.899	0.200
Gm8909	0.847	1.164	0.210
Apoc2	0.176	0.669	0.211
Rbp4	1.587	1.128	0.214
Ahsg	1.358	1.192	0.215
Sell	0.992	0,952	0.223
Apod	0.744	0.849	0.238
Krt5	1.124	0.602	0.238
GC	1.693	1.459	0.252
5882	0.446	1.634	0.253
rviup20	0.909	1.812	0.256
CIII Daife 2	2.214	2.861	0.274
opiid2 Dhi	2.369	1 075	0.260
Anoa4	1 128	1.925	0.295
Krt10	2 175	0.826	0.303
Saa1	0.503	1.438	0.304
Mb	1.566	1.692	0.305
Pfn1	2.352	2.095	0.305
Apoe	0.362	1.352	0.326
B2m	0.827	1.214	0.328
Ca1	3.042	2.462	0.328
KRT9	0.320	1.306	0.330
Mug1	1.012	1.226	0.334
H2-Q7	0.876	1.388	0.338
Serpina1e	0.887	1.253	0.352
Vtn	1.043	0.939	0.359
Napsa	0.801	0.859	0.368
Pzp	2.033	4.668	0.383
Krt1	0.813	0.829	0.397
USC3	1.521	2.094	0.401
Faa	4.005	2.407	0.405
Sernina1h	1.510	1.507	0.415
Gold1	1.007	0.583	0.420
Psan	1 392	0.759	0.437
Krt90	0.646	0.822	0.449
Agt	2.336	1.204	0.454
Antxr2	0.684	0.494	0.456
Blvrb	3.108	2.448	0.463
C3	1.533	0.805	0.466
Igfals	1.626	0.124	0.469
Ctsd	1.677	1.025	0.472
Gm20425	4.584	2.947	0.486
Kng1	1.774	3.343	0.488
Krt13	2.158	0.644	0.504
Pm20d1	0.372	2.010	0.507
Vcam1	0.869	0.271	0.508
Pcyox1	0.824	0.908	0.508
Fabp4	2.192	2.208	0.515
C4b	1.140	0.554	0.526
Apoa2	0.700	0.818	0.553
Jdd4	1.062	1.054	0.5/1
Angnt12	1.303	2.009	0.587
Icam1	1 117	0.476	0.642
Ttr	1 681	1 404	0.673
Mup18	1 551	1 697	0 716
Clu	1.060	0.775	0.716
Lcat	0.974	0.792	0.752
Gpx3	1.756	1.580	0.783
Prdx2	2,318	2,220	0,802
Hbbt1	4,038	3,166	0,820
lgkv14-126	0,333	1,357	0.854
Pon1	1.036	0.658	0.900
Apoa1	0.797	0.705	0.914
Pla2g7	0.643	0.288	0.925
lghm	0.574	1.564	0.989

Supplemental Table VI

Patient characteristics

Patient	Diagnosis	LpL deficient
	1 HyperTG, Pancreatitis	
	2 LCAT Deficient	
	3 HyperTG	
	4 HyperTG	Х
	5 Hyperlipidemia	Х
	6 HyperTG, Pancreatitis, T1D, Ketoacidosis	
	7 No Pancreatitis, Good TGs, On Meds	Х
	8 HyperTG	
	9 Recurring Pancreatitis, DM	

Supplemental Table VII

HyperTG versus Control

90 detected proteins in human samples, 6 being significantly

downregulated, 14 upregulated with HyperTG.



Protein	Fold change	P-value
AN IXR2 ORM1	0.336	<0.001
GC	4.023	0.003
FGG	3.300	0.004
FGB	3.164	0.004
SERPINA1	3.128	0.007
APOA1	2 509	0.007
FGA	3.798	0.009
MENT	0.476	0.010
CD44	0.519	0.010
PLTP	0.494	0.011
SERPINE1	4.354	0.013
APOH	1.718	0.019
AHSG	3.104	0.021
AZGP1	2.171	0.023
ALB AROC3	4.670	0.039
PPBP	2.769	0.046
LPA	0.065	0.048
APOA2	0.669	0.063
C1R	4.764	0.064
	2 399	0.075
IGHA1	1.696	0.080
TTR	1.927	0.083
IGHG1	4.492	0.084
	3.779	0.091
\$100A8	2.797	0.095
CST3	3.877	0.116
APOE	2.382	0.134
RBP4	3.897	0.143
APOD	0.638	0.147
VTN	0.761	0.162
APOM	0.798	0.164
CA1	74.468	0.166
CLU	0.745	0.171
KRT10	2.324	0.172
APOA5	7.754	0.173
C4BPA	13.435	0.173
SAA4	0.707	0.174
APOL1	1.436	0.175
CA2	34.141	0.204
A2M	6.285	0.211
KRT2	2.327	0.224
SAA1	41.561	0.234
	6 197	0.249
KRT5	1.876	0.254
KRT1	2.102	0.256
IGHM	8.624	0.257
B2M	7.417	0.262
KRT14	1.901	0.267
APOC1	1.288	0.288
TF	9.556	0.294
PCYOX1	0.847	0.301
MADCAM1	0.769	0.306
\$100A7	1.533	0.318
SHH	0.566	0.327
PSAP	0.697	0.335
PONS	0.827	0.335
IGHG2	2.638	0.374
KRT9	1.953	0.384
HBA1	175.992	0.415
нвв	365.166	0.417
PON1	0.832	0.420
HBZ	58.339	0.422
ANXA2P2	1.663	0.423
KRT75	1.534	0.428
KRT6A	1.532	0.456
HLA-A	2.551	0.473
DCD	1.321	0.486
KRT16	1.724	0.510
L4A	1.251	0.528
LTF	0.806	0.643
SFTPB	0.768	0.657
POTEF	0.934	0.818
KRT17	0.936	0.916
C3orf85	1.011	0.986
	0.000	0.000

Supplemental Table VIII

	Figure	Comparison	P-value
Figure 1B	Total Cholesterol	Baseline versus Regression (Average)	1.1x10 ⁻⁵
Figure 1C	Total Triglycerides -Before aortic transplant	$Lpl^{n/l}$ versus $Lpl^{-/-}$	1.6x10 ⁻⁶
	•	$Lpl^{l/l} + hCETP$ versus $Lpl^{-/-} + hCETP$	6.6x10 ⁻⁷
	Total Triglycerides -After aortic transplant	$Lpl^{n/l}$ versus Lpl^{-1}	2.7x10 ⁻⁶
	•	Lpl fl/fl + hCETP versus Lpl -/- + hCETP	1.3x10 ⁻⁶
Figure 1D	CETP activity	Lpl fl/fl versus Lpl -/-	0.0021
		Lpl fl/fl + hCETP versus Lpl -/- + hCETP	0.0010
Figure 1E	VLDL Cholesterol	Baseline versus Regression (Average)	1×10^{-15}
		$Lpl^{n/n}$ versus $Lpl^{-/-}$	0.0455
	LDL Cholesterol	Baseline versus Regression	2.4×10^{-13}
		$Lpl^{l/l}$ versus Lpl^{-}	0.0012
		$Lpl^{l/l}$ versus $Lpl^{-} + hCETP$	0.0490
	HDL Cholesterol	Baseline versus Regression (Average)	0.0143
		$Lpl^{l/l}$ versus $Lpl^{-/-}$	0.0038
		$Lpl^{l/l}$ versus $Lpl^{l/l}$ +hCETP	0.0005
		$Lpl^{l/l}$ versus $Lpl^{-/-}$ + hCETP	2.8x10 ⁻⁵
		$Lpl^{-/-}$ versus $Lpl^{-/-}$ + hCETP	0.0198
Figure 1F	VLDL Triglyceride	$Lpl^{n/l}$ versus $Lpl^{-/-}$	1.2×10^{-5}
		$Lpl^{l/l}$ +hCETP versus $Lpl^{-/-}$ + hCETP	0.0497
	HDL Triglyceride	$Lpl^{l/fl}$ versus $Lpl^{l/fl}$ +hCETP	0.0306
Figure 2C	%CD68+ area (Aortic Arch)	Baseline versus Regression (Average)	1.1x10 ⁻⁵
Figure 3B	Total Cholesterol	Baseline versus <i>Lpl</i> ^{fl/fl} Regression	1×10^{-15}
		Baseline vs i <i>Lpl</i> ^{-/-} Regression	1×10^{-15}
Figure 3C	Triglycerides	<i>Lpl</i> ^{fl/fl} Regression versus <i>iLpl</i> ^{-/-} Regression	1×10^{-15}
Figure 3D	%CD68+ area (Root)	Baseline versus <i>Lpl</i> ^{tl/fl} Regression	1×10^{-15}
		Baseline vs i <i>Lpl</i> ^{-/-} Regression	0.0466
Figure 3F	%Mac+ area (BCA)	Baseline versus <i>Lpt</i> ^{tivil} Regression	0.0018
		Baseline vs i <i>Lpl</i> ^{-/-} Regression	0.0121
Figure 2E	Fibrous Cap	Baseline	0.0444
		thin versus thick fibrous cap	a 10 ⁸
Figure 5A	Total HDL-P	Lpl^{μ} versus Lpl^{-}	2x10-*
		Lpl^{μ} versus Lpl^{μ} +hCETP	0.0003
		Lpl^{μ} versus Lpl^{-} + hCETP	0.00042
	Small HDL-P	$Lpl^{n/n}$ versus $Lpl^{n/n}$	6.4x10 ⁻⁶
		Lpl^{μ} versus Lpl^{μ} +hCETP	0.0032
		Lpl'''' versus Lpl'' + hCETP	0.0066
	Medium HDL-P	Lpl''' versus Lpl'	0.0003
		Lpt'''' versus Lpt'''' + hCETP	0.0012
		$Lpt^{r,r} \text{ Versus } Lpt^{r} + \text{hCETP}$	0.0105
Figure 5B	I otal Efflux	Lpl''' versus Lpl'	0.0002
Einer 50	I OTAL ETTIUX	$Lpl \text{versus } Lpl^{n} + \text{nCETP}$	0.0296
Figure 5C	I OTAL ETTILIX	Lpt''' Versus Lpt''' + hCETP	0.0181
	ABCAI-mediated efflux	Lpt^{n} versus Lpt^{n} +hCETP	0.0139

	ABCA1-mediated efflux	Lpl^{-} versus $Lpl^{l/l}$ +hCETP	0.0432
Figure 6B	Total HDL-P	Ctrl versus HyperTG	3x10 ⁻⁶
	Medium HDL-P	Ctrl versus HyperTG	4.7×10^{-5}
	Large HDL-P	Ctrl versus HyperTG	0.0007
Figure 6C	ABCA1-mediated Efflux	Ctrl versus HyperTG	0.0074
Figure 6D	Total Efflux	Ctrl versus HyperTG	0.0044
	ABCA1-mediated Efflux	Ctrl versus HyperTG	0.0077
Supplemental Figure I	Body weight	Baseline versus Regression (Average)	0.0040
Supplemental Figure III C	Body weight -Before aortic transplant	Baseline versus <i>Lpt</i> ^{<i>n</i>/<i>n</i>}	0.0046
		Baseline versus <i>Lpl</i> ^{-/-}	0.0263
	Body weight - After aortic transplant	Baseline versus <i>Lpt</i> ^{<i>n</i>/<i>n</i>}	0.0187
		Baseline versus <i>Lpl</i> ^{-/-}	0.0380
Supplemental Figure III D	Total Cholesterol	Baseline versus $Lpl^{n/n}$	4.7x10 ⁻⁶
		Baseline versus <i>Lpt</i> ^{-/-}	0.0316
Supplemental Figure III E	Total Triglycerides	Baseline versus <i>Lpt</i> ^{<i>n</i>/<i>n</i>}	0.0003
		$Lpl^{l/l}$ versus $Lpl^{-/-}$	0.0006
Supplemental Figure III F	VLDL Cholesterol	$Lpl^{n/p}$ versus $Lpl^{-/-}$	0.0117
	LDL Cholesterol	$Lpl^{l/l}$ versus $Lpl^{-/-}$	0.0078
Supplemental Figure III G	VLDL-TG	$Lpl^{n/l}$ versus Lpl^{-l}	0.0029
Supplemental Figure III I	%CD68+ area (Aortic Arch)	Baseline versus Regression (Average)	0.0006
Supplemental Figure IV A	Total Cholesterol	Baseline <i>Lpl</i> ^{fl/fl} Tie2LPL versus Regression <i>Lpl</i> ^{fl/fl} Tie2LPL	0.0019
		Baseline <i>iLpl</i> ^{-/-} Tie2LPL versus Regression <i>iLpl</i> ^{-/-} Tie2LPL	0.0076
Supplemental Figure IV F	%Mac+ area (BCA)	Baseline <i>iLpl^{-/-}</i> Tie2LPL versus Regression <i>iLpl^{-/-}</i> Tie2LPL	0.0358
Supplemental Figure V A	ApoA-I	$Lpl^{n/l}$ versus $Lpl^{-/-}$	0.0052
		$Lpl^{l/l}$ +hCETP versus $Lpl^{-/-}$ + hCETP	0.0167