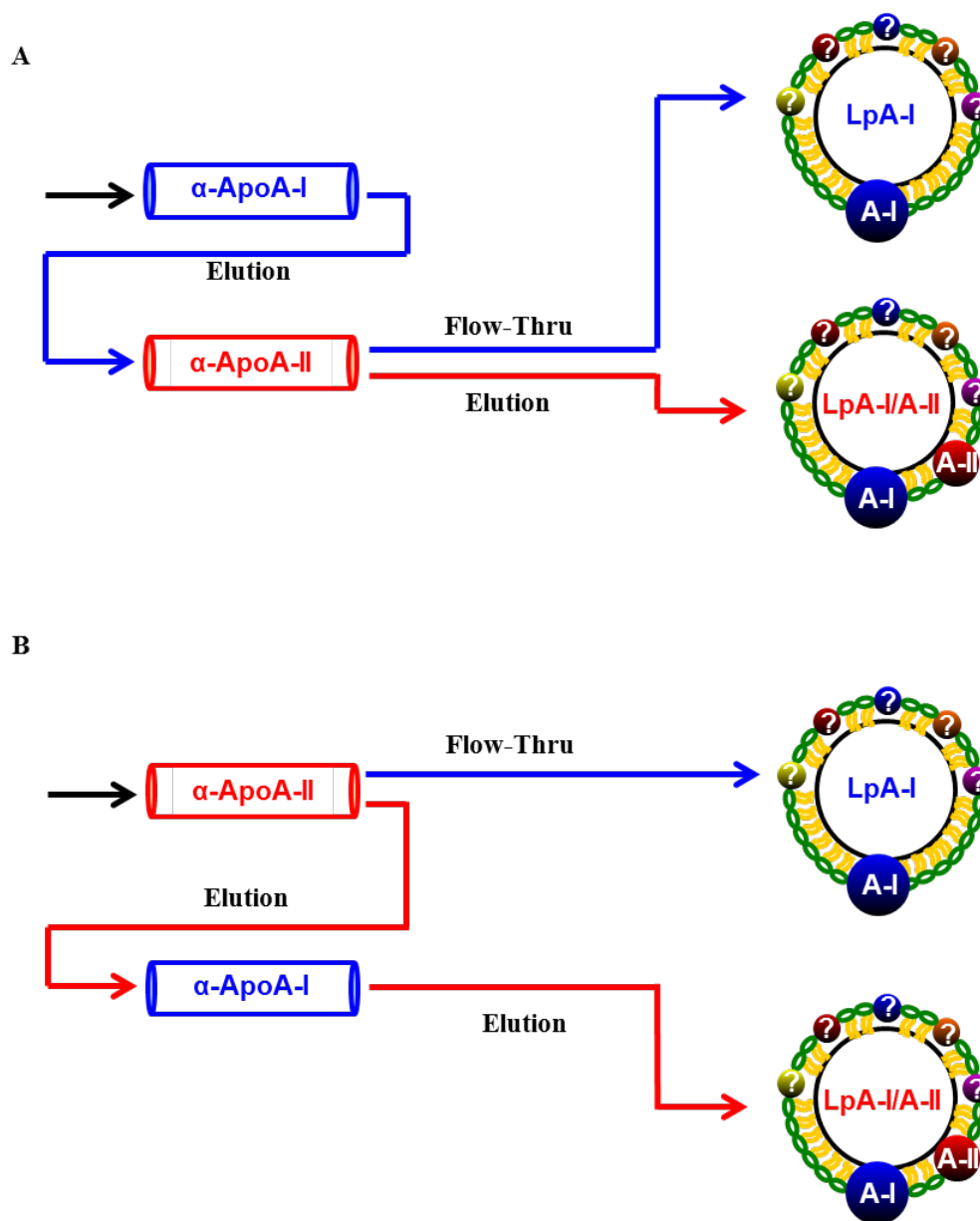


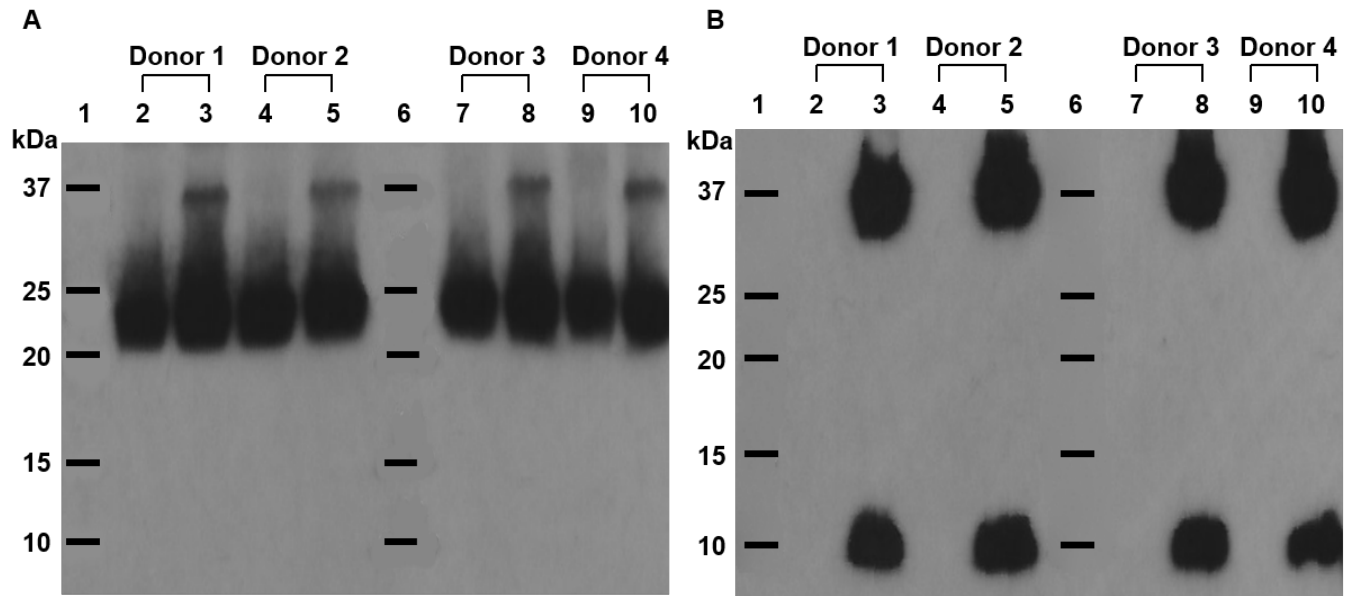
## SUPPLEMENTAL MATERIAL

### Supplemental Figure S1



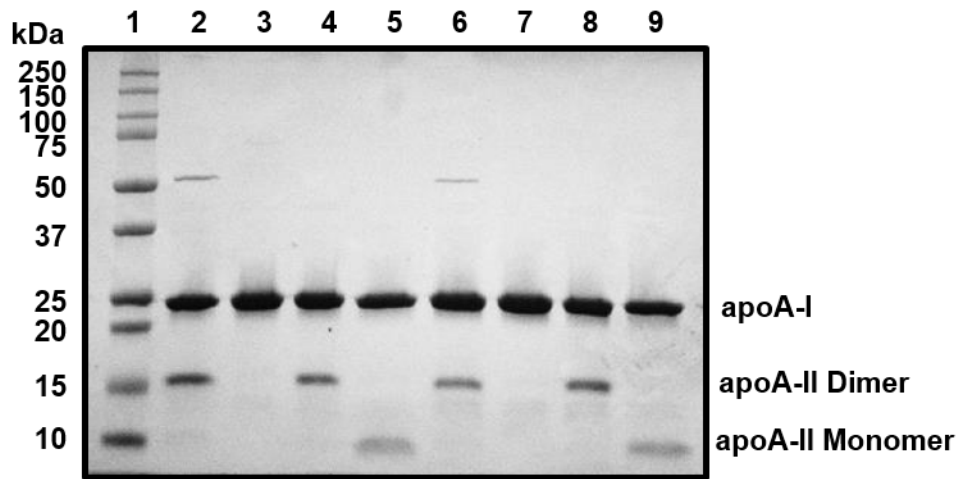
**Supplemental Figure S1: Strategy for LpA-I and LpA-I/A-II IAC isolations:** LpA-I and LpA-I/A-II particles were obtained from plasma or HDL isolated by ultracentrifugation (UC-HDL) using FPLC with columns containing resin enriched with antibodies specific for either human apoA-I or human apoA-II. The sample was applied to the column in PBS and bound material was eluted using 3M sodium thiocyanate. Elution fractions were immediately desalted using PD-10 desalting columns. Panel **(A)** shows the isolation scheme for subfractions obtained from plasma. Plasma was applied to the  $\alpha$ -apoA-I column and all bound particles containing apoA-I were eluted and desalted. ApoA-I containing particles were applied to the  $\alpha$ -apoA-II column. Unbound material contained only apoA-I with no apoA-II (LpA-I) and bound material containing both apoA-I and apoA-II (LpA-I/A-II) was desalted. Panel **(B)** shows the isolation scheme for subfractions obtained from UC-HDL. To maximize efficiency of the isolation UC-HDL was first applied to the  $\alpha$ -apoA-II column. Unbound material was collected which contained UC-HDL with only apoA-I (LpA-I). Bound material was eluted, desalted, and applied to the  $\alpha$ -apoA-I column. Bound material which contained both apoA-I and apoA-II (LpA-I/A-II) was eluted and desalted.

## Supplemental Figure S2



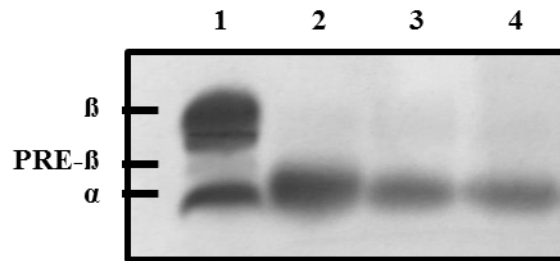
**Supplemental Figure S2: Purification of LpA-I and LpA-I/A-II particles from plasma:** Panels (A) and (B) show enlarged western blots from **Figure 1** in the main text which were probed with antibodies for apoA-I and apoA-II, respectively. 3  $\mu$ g of total protein per lane were loaded onto an Any-KD™ mini gel in sample buffer containing beta mercaptoethanol to reduce apoA-II to monomeric form. LpA-I particles are shown in lanes 2, 4, 7, and 9 and LpA-I/A-II particles are shown in lanes 3, 5, 8, and 10 with molecular weight markers in lanes 1 and 6.

### Supplemental Figure S3



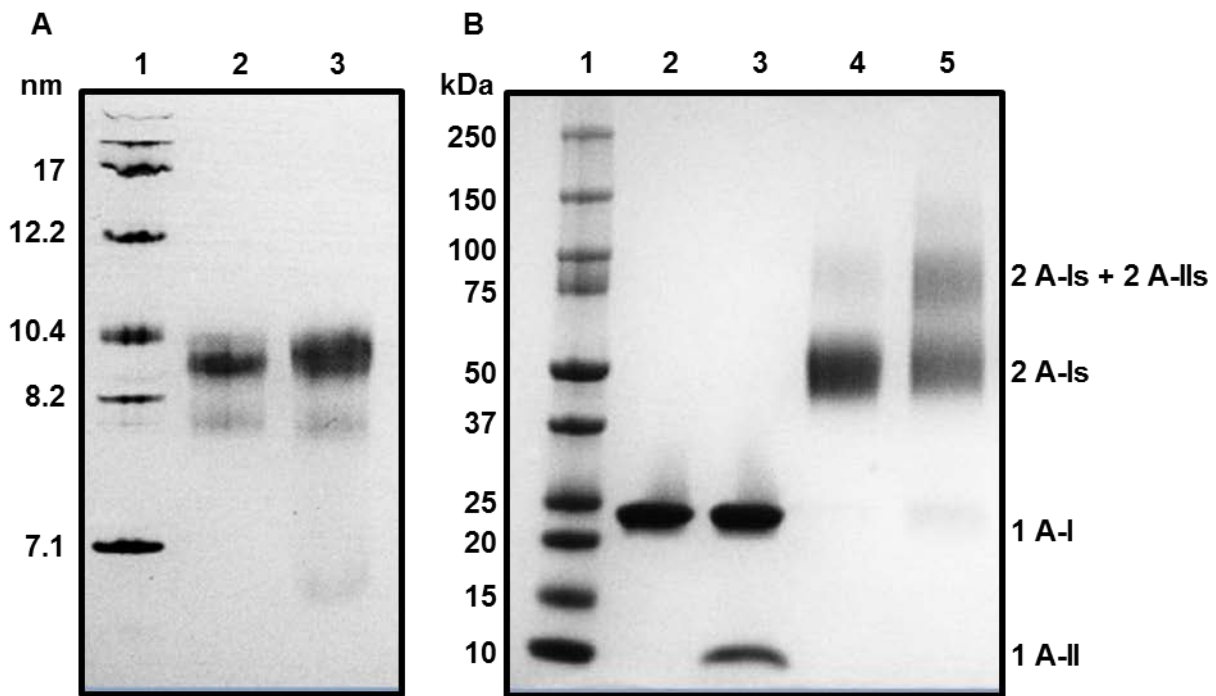
**Supplemental Figure S3: Purification of LpA-I and LpA-I/A-II particles from UC-HDL:** 4-15% SDS-PAGE analysis of LpA-I and LpA-I/A-II particles segregated from UC-HDL for two representative donors. UC-HDL starting material is shown in lanes 2 and 6 and LpA-I particles are shown in lanes 3 and 7. LpA-I/A-II particles are shown in lanes 4 and 8 in non-reducing conditions and lanes 5 and 9 in reducing conditions. Each lane contains 6  $\mu$ g of total protein.

## Supplemental Figure S4



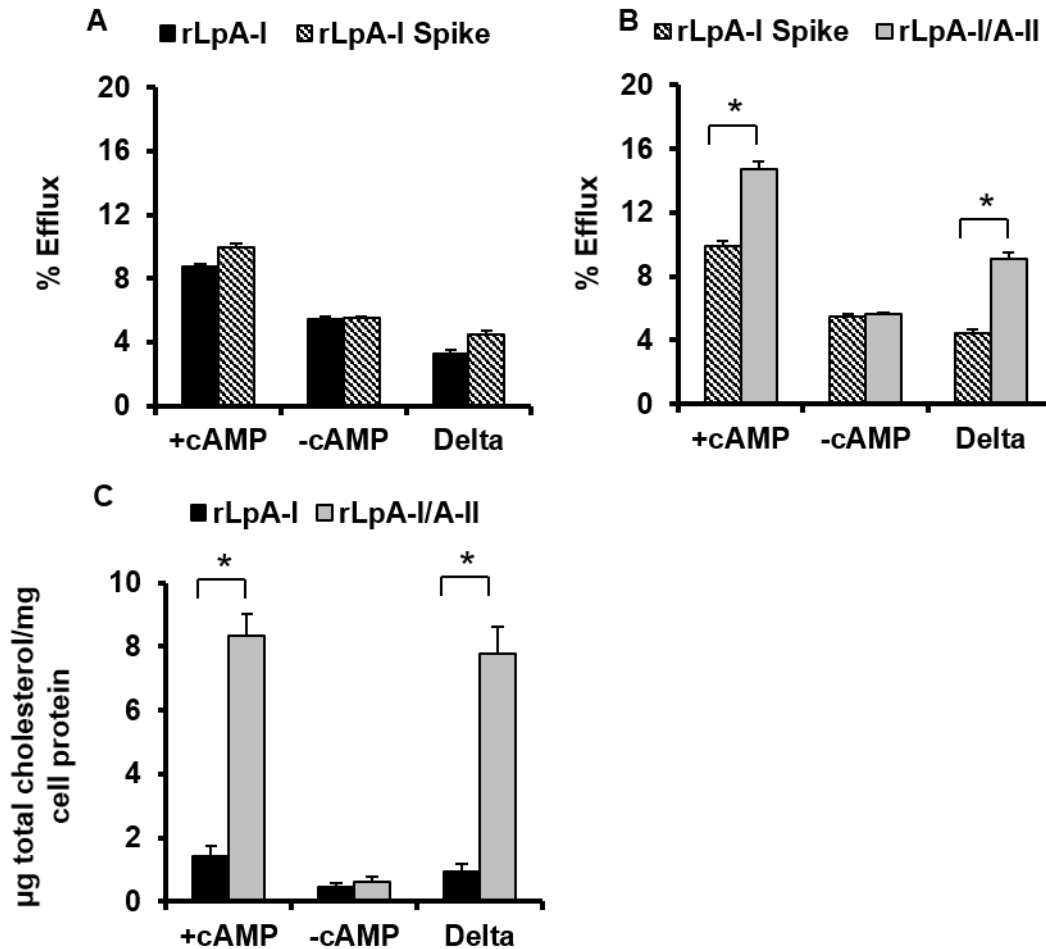
**Supplemental Figure S4: Characterization of plasma LpA-I and LpA-I/A-II particles by agarose gel electrophoresis.** Samples were analyzed by agarose gel electrophoresis using a quickgel lipoprotein electrophoresis system. Samples were loaded by volume (4  $\mu$ l each) and migration was visualized by staining with Fat Red 7B. Plasma (lane 1) and UC-HDL (lane 2) were run as controls. LpA-I particles were loaded in lane 3 and LpA-I/A-II particles were loaded in lane 4.

### Supplemental Figure S5



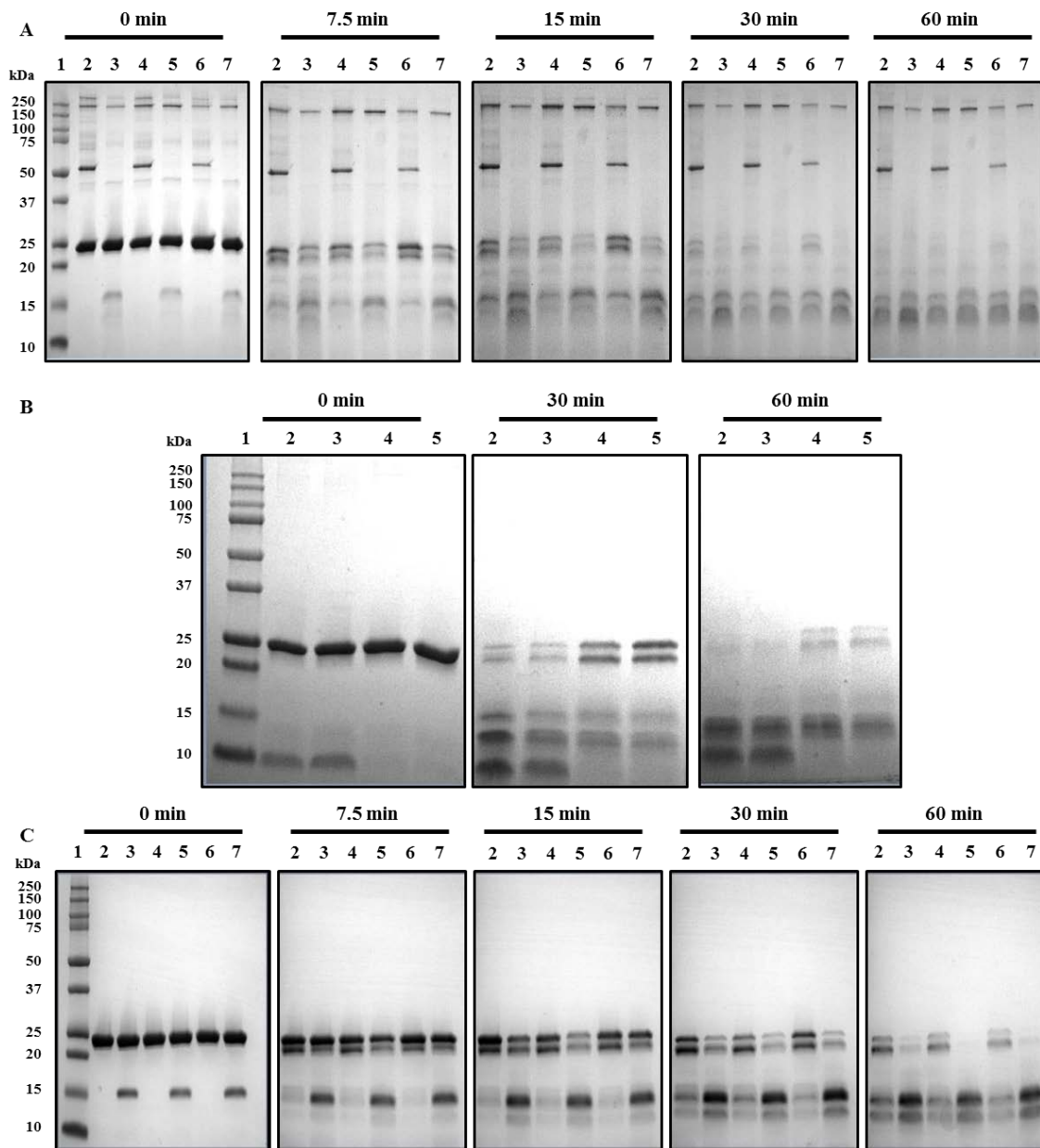
**Supplemental Figure S5: Size and cross-linking analysis of rLpA-I and rLpA-I/A-II discoidal particles generated *in vitro*.** Panel (A) shows a native gel containing a protein standards ladder (lane 1), rLpA-I discoidal particles (lane 2) and rLpA-I/A-II discoidal particles (lane 3). Panel (B) shows a 4-15% SDS Page analysis of the rLpA-I and rLpA-I/A-II particles before and after cross-linking at a molar ratio of 50:1 BS<sup>3</sup>:apoA-I. 10  $\mu$ g of total protein for each sample was loaded and visualized by staining with Coomassie Blue. rLpA-I particles before and after cross-linking are shown in lanes 2 and 4, respectively. rLpA-I/A-II particles before and after cross-linking are shown in lanes 3 and 5, respectively.

## Supplemental Figure S6



**Supplemental Figure S6. Cholesterol efflux capacity of rLpA-I particles spiked with lipid-free apoA-I and rLpA-I/A-II POPC particles.** Lipid free plasma apoA-I was spiked into rLpA-I POPC particle at equivalent masses found in rLpA-I/A-II POPC particles using densitometry analysis on gels shown in Supplemental Figure 4A. Panel **(A)**: rLpA-I POPC particles with and without addition of lipid-free plasma apoA-I were loaded by equal PC mass (20  $\mu\text{g/ml}$ ) and cholesterol efflux capacity was quantified in the presence and absence of cAMP. Panel **(B)**: rLpA-I POPC particles spiked with lipid-free apoA-I and rLpA-I/A-II POPC particles were loaded by equal PC mass (20  $\mu\text{g/ml}$ ) and cholesterol efflux capacity was quantified in the presence and absence of cAMP. Panel **(C)**: rLpA-I and rLpA-I/A-II POPC particles were loaded by equal PC mass (20  $\mu\text{g/ml}$ ) and cholesterol efflux capacity was quantified in the presence and absence of cAMP by measuring total cholesterol in the media using an Amplex Red Cholesterol assay kit. Cholesterol mass was normalized by total cell protein measured using the Markwell Lowry assay. Bars represent the average of three independent preparations ( $\pm\text{SD}$ ) and asterisks denote statistically significant differences ( $P<0.05$ ) found between the subfractions determined by a 2-tailed, paired student's t-test.

## Supplemental Figure S7



**Supplemental Figure S7: Limited proteolysis analysis of LpA-I and LpA-I/A-II particles.** LpA-I and LpA-I/A-II subfractions isolated from plasma, UC-HDL, and synthetic discoidal particles were incubated sequencing grade trypsin for the indicated time points at 37°C. Reactions were quenched by addition of SDS sample buffer and boiling samples for 10 min at 100°C. Samples were frozen at -20°C until ready for analysis by SDS-PAGE. Panel (A) shows proteolytic digestion of apoA-I from LpA-I and LpA-I/A-II fractions isolated from three plasma donors. A total of 8 µg of total protein was incubated with trypsin at a ratio of 20:1 Pro:trypsin. LpA-I particles are in lanes 2, 4 and 6. LpA-I/A-II particles are in lanes 3, 5, and 7. Panel (B) shows proteolytic digestion of apoA-I from LpA-I and LpA-I/A-II fractions isolated from UC-HDL from two donors. A total of 6 µg of total protein was incubated with trypsin at a ratio of 50:1 Pro:trypsin. LpA-I/A-II particles are in lanes 2 and 3 and LpA-I particles are in lanes 4 and 5. ApoA-II migrates as a monomer as 2-Mercaptoethanol was present in the SDS sample buffer. Panel (C) shows the proteolytic digestion of apoA-I from discoidal rLpA-I and rLpA-I/A-II particles from three independent preps. A total of 4 µg of total protein was incubated with trypsin at a ratio of 40:1 Pro:trypsin. LpA-I particles are in lanes 2, 4 and 6 and rLpA-I/A-II particles are in lanes 3, 5 and 7.

### Supplemental Table S1

*Total peptide spectral counts for non-specifically bound proteins*

Accession Number	LpA-I					LpA-I/A-II				
	Control <sup>a</sup>	1 <sup>b</sup>	2 <sup>b</sup>	3 <sup>b</sup>	4 <sup>b</sup>	Control <sup>a</sup>	1 <sup>b</sup>	2 <sup>b</sup>	3 <sup>b</sup>	4 <sup>b</sup>
ALBU	73	383	197	270	333	--	29	18	12	14
IGHM	12	165	116	142	71	--	43	95	88	69
IGKC	5	96	48	70	85	--	56	67	100	54
IGHG1	5	65	35	52	67	1	27	18	39	49
K2C1	30	9	6	10	1	1	10	7	10	8
HPTR	1	46	29	30	15	--	11	18	9	8
TRFE	7	60	49	49	46	--	--	--	--	--
K1C10	14	10	7	7	3	1	8	5	5	6
IGHG4	4	54	29	26	52	--	27	24	25	34
K1C9	8	3	3	8	--	--	2	4	7	6
A2MG	1	20	9	11	27	--	--	--	--	--
K22E	9	4	4	3	2	--	3	3	4	2
A1AG1	5	10	6	8	10	--	2	2	1	2
HPT	2	31	22	21	23	--	--	--	--	5
K1C14	1	--	--	--	--	--	--	--	--	--

<sup>a</sup> Peptide counts for proteins in a control sample isolated from plasma applied to a dummy column containing resin and no antibodies followed by application to the  $\alpha$ -apoA-II column.

<sup>b</sup> Peptide counts for non-specifically bound proteins identified in individual donors.



## Supplemental Table S2

### Total peptide spectral counts for proteins identified in UC-HDL and AI-LPs

Protein	Accession Number	UC-HDL				AI-LPs			
		1 <sup>a</sup>	2 <sup>a</sup>	3 <sup>a</sup>	4 <sup>a</sup>	1 <sup>a</sup>	2 <sup>a</sup>	3 <sup>a</sup>	4 <sup>a</sup>
Apolipoprotein A-I	APOA1	520.4	596.5	579.3	539.0	--	1097.4	--	1126.0
Apolipoprotein A-II	APOA2	155.9	149.4	177.0	175.0	--	225.4	--	204.0
Fibronectin	FINC	--	--	--	--	--	126.5	--	97.0
Apolipoprotein B-100	APOB	64.2	2.6	5.6	40.0	--	70.4	--	99.0
Apolipoprotein A-IV	APOA4	9.2	7.7	15.7	16.0	--	29.6	--	35.0
Clusterin	CLUS	3.4	2.6	1.1	--	--	63.2	--	70.0
Apolipoprotein D	APOD	37.8	30.7	43.7	21.0	--	17.3	--	19.0
Apolipoprotein C-III	APOC3	29.8	47.3	24.7	32.0	--	23.5	--	26.0
Serum paraoxonase/arylesterase 1	PON1	3.4	21.7	12.3	2.0	--	24.5	--	21.0
Apolipoprotein C-I	APOC1	26.4	35.8	26.9	28.0	--	8.2	--	6.0
Apolipoprotein E	APOE	18.3	8.9	28.0	50.0	--	10.2	--	14.0
Apolipoprotein M	APOM	26.4	26.8	22.4	26.0	--	8.2	--	9.0
Apolipoprotein C-II	APOC2	29.8	35.8	21.3	30.0	--	4.1	--	3.0
Alpha-1-antitrypsin	A1AT	33.2	10.2	9.0	7.0	--	16.3	--	17.0
IgGFc-binding protein	FCGBP	--	--	--	--	--	19.4	--	19.0
Ig lambda-2 chain C regions	LAC2	--	--	--	--	--	19.4	--	15.0
Fibrinogen gamma chain	FIBG	--	--	--	--	--	10.2	--	12.0
Ig alpha-1 chain C region	IGHA1	--	--	--	--	--	12.2	--	9.0
Phosphatidylinositol-glycan-specific phospholipase D	PHLD	--	--	--	--	--	13.3	--	14.0
Fibrinogen beta chain	FIBB	--	--	--	--	--	12.2	--	17.0
Apolipoprotein L1	APOL1	5.7	3.8	6.7	6.0	--	9.2	--	10.0
Serum amyloid A-4 protein	SAA4	2.3	5.1	9.0	13.0	--	--	--	--
Fibrinogen alpha chain	FIBA	1.1	--	--	--	--	2.0	--	4.0
Ig gamma-2 chain C region	IGHG2	--	--	--	--	--	17.3	--	18.0
Complement C3	CO3	1.1	--	--	--	--	11.2	--	12.0
Coagulation factor V	FA5	--	--	--	--	--	7.1	--	13.0
Phospholipid transfer protein	PLTP	2.3	2.6	3.4	1.0	--	4.1	--	4.0
Complement C1q subcomponent subunit B	C1QB	--	--	--	--	--	16.3	--	12.0
Apolipoprotein F	APOF	12.6	7.7	5.6	6.0	--	2.0	--	2.0
Vitronectin	VTNC	--	--	--	--	--	7.1	--	8.0
CD5 antigen-like	CD5L	--	--	--	--	--	8.2	--	--
Kininogen-1	KNG1	--	--	--	--	--	10.2	--	9.0
Ig kappa chain V-III region HAH	KV312	--	--	--	--	--	7.1	--	5.0
Immunoglobulin J chain	IGJ	--	--	--	--	--	3.1	--	--
Complement C1q subcomponent subunit C	C1QC	--	--	--	--	--	10.2	--	11.0
Serum amyloid A-1 protein	SAA1	3.4	--	2.2	2.0	--	2.0	--	10.0
Complement C4-A	CO4A	1.1	--	1.1	--	--	2.0	--	5.0
Complement C1r subcomponent	C1R	--	--	--	--	--	2.0	--	3.0
Inter-alpha-trypsin inhibitor heavy chain H4	ITIH4	--	--	--	--	--	3.1	--	2.0
Transthyretin	TTHY	6.9	--	--	1.0	--	1.0	--	3.0
Hemopexin	HEMO	--	--	--	--	--	5.1	--	3.0
Alpha-1-acid glycoprotein 2	A1AG2	--	--	--	--	--	5.1	--	4.0
Plasminogen	PLMN	--	--	--	--	--	5.1	--	5.0
Beta-2-glycoprotein 1	APOH	--	--	--	--	--	7.1	--	7.0
Coagulation factor XI	FA11	--	--	--	--	--	1.0	--	1.0
Ig gamma-3 chain C region	IGHG3	--	--	--	--	--	9.2	--	--
C4b-binding protein alpha chain	C4BPA	--	--	--	--	--	2.0	--	3.0
Vitamin D-binding protein	VTDB	--	--	--	--	--	1.0	--	2.0
Cholesteryl ester transfer protein	CETP	--	--	--	--	--	3.1	--	5.0
Ig alpha-2 chain C region	IGHA2	--	--	--	--	--	8.2	--	--
Alpha-2-HS-glycoprotein	FETUA	--	--	--	--	--	1.0	--	--
Prothrombin	THRB	--	--	--	--	--	2.0	--	--
Alpha-1B-glycoprotein	A1BG	--	--	--	--	--	1.0	--	--
Phosphatidylcholine-sterol acyltransferase	LCAT	--	--	--	--	--	--	--	1.0
Angiotensinogen	ANGT	--	--	--	--	--	4.1	--	--
Alpha-1-antichymotrypsin	AACT	--	--	--	--	--	1.0	--	--
Ceruloplasmin	CERU	--	--	--	--	--	2.0	--	--
Ficolin-2	FCN2	--	--	--	--	--	1.0	--	1.0
Histidine-rich glycoprotein	HRG	--	--	--	--	--	--	--	1.0

<sup>a</sup> Total peptide spectral counts for proteins identified in individual donors. Spectral counts were normalized to the total spectral count summed across all proteins for the subfraction in the donor with the maximal total spectral count within each method; i.e. spectral counts for UC-HDL were normalized to max total spectral counts with the UC-HDL donors and spectral counts for AI-LPs were normalized to the max total spectral counts with the AI-LPs donors.

### Supplemental Table S3

Total peptide spectral counts for proteins identified in the LpA-I and LpA-I/A-II subfractions isolated from plasma

Protein	Accession Number	LpA-I				LpA-I/A-II			
		1 <sup>a</sup>	2 <sup>a</sup>	3 <sup>a</sup>	4 <sup>a</sup>	1 <sup>a</sup>	2 <sup>a</sup>	3 <sup>a</sup>	4 <sup>a</sup>
Apolipoprotein A-I	APOA1	740.8	1061.2	938.0	749.8	1063.0	1177.9	1098.6	1022.3
Apolipoprotein A-II	APOA2	2.2	2.4	1.0	2.2	188.0	171.5	151.4	181.3
Fibronectin	FINC	191.1	197.6	244.0	276.4	108.8	112.2	106.8	112.7
Apolipoprotein B-100	APOB	118.8	80.2	97.0	126.5	70.9	51.7	72.0	95.0
Apolipoprotein A-IV	APOA4	92.9	95.8	86.0	75.0	114.7	108.5	134.1	142.6
Clusterin	CLUS	137.1	73.1	87.0	79.5	75.7	61.8	70.8	72.9
Apolipoprotein D	APOD	27.0	37.1	32.0	24.6	62.7	73.1	57.1	49.7
Apolipoprotein C-III	APOC3	8.6	16.8	10.0	9.0	39.0	56.7	34.8	34.3
Serum paraoxonase/arylesterase 1	PON1	79.9	59.9	55.0	60.4	44.9	40.4	37.2	38.7
Apolipoprotein C-I	APOC1	8.6	20.4	10.0	9.0	23.6	32.8	33.5	27.6
Apolipoprotein E	APOE	16.2	27.5	22.0	24.6	31.9	37.8	53.4	63.0
Apolipoprotein M	APOM	11.9	10.8	13.0	9.0	15.4	17.7	16.1	18.8
Apolipoprotein C-II	APOC2	13.0	31.1	16.0	20.1	24.8	36.6	22.3	24.3
Alpha-1-antitrypsin	A1AT	37.8	15.6	25.0	26.9	11.8	3.8	11.2	19.9
IgGfC-binding protein	FCGBP	42.1	12.0	37.0	31.3	43.7	20.2	14.9	17.7
Ig lambda-2 chain C regions	LAC2	36.7	32.3	24.0	25.7	39.0	21.4	18.6	29.8
Fibrinogen gamma chain	FIBG	36.7	38.3	48.0	69.4	7.1	6.3	8.7	8.8
Ig alpha-1 chain C region	IGHA1	43.2	27.5	32.0	38.1	17.7	16.4	42.2	18.8
Phosphatidylinositol-glycan-specific phospholipase D	PLHD	41.0	10.8	35.0	49.2	16.6	3.8	11.2	19.9
Fibrinogen beta chain	FIBB	35.6	35.9	34.0	49.2	7.1	6.3	3.7	9.9
Apolipoprotein L1	APOL1	8.6	7.2	9.0	14.5	11.8	3.8	5.0	17.7
Serum amyloid A-4 protein	SAA4	2.2	4.8	5.0	5.6	3.5	5.0	7.4	8.8
Fibrinogen alpha chain	FIBA	29.2	27.5	34.0	41.4	1.2	2.5	1.2	4.4
Ig gamma-2 chain C region	IGHG2	50.8	34.7	33.0	44.8	46.1	40.4	60.8	42.0
Complement C3	CO3	34.6	9.6	18.0	33.6	8.3	--	--	5.5
Coagulation factor V	FA5	36.7	20.4	13.0	16.8	2.4	--	1.2	1.1
Phospholipid transfer protein	PLTP	13.0	6.0	11.0	11.2	16.6	13.9	8.7	13.3
Complement C1q subcomponent subunit B	C1QB	7.6	15.6	11.0	15.7	5.9	5.0	5.0	7.7
Apolipoprotein F	APOF	6.5	7.2	4.0	2.2	8.3	8.8	7.4	11.1
Vitronectin	VTNC	18.4	12.0	9.0	13.4	9.5	6.3	5.0	8.8
CD5 antigen-like	CD5L	14.0	20.4	13.0	4.5	3.5	16.4	7.4	3.3
Kininogen-1	KNG1	18.4	15.6	15.0	15.7	--	--	--	--
Ig kappa chain V-III region HAH	KV312	11.9	4.8	10.0	12.3	5.9	8.8	14.9	6.6
Immunoglobulin J chain	IGJ	11.9	16.8	11.0	7.8	4.7	12.6	11.2	3.3
Complement C1q subcomponent subunit C	C1QC	7.6	14.4	7.0	11.2	3.5	6.3	5.0	7.7
Serum amyloid A-1 protein	SAA1	2.2	2.4	2.0	3.4	8.3	2.5	6.2	6.6
Complement C4-A	CO4A	9.7	8.4	2.0	7.8	9.5	6.3	2.5	2.2
Complement C1r subcomponent	C1R	14.0	7.2	9.0	10.1	1.2	1.3	1.2	2.2
Platelet factor 4	PLF4	6.5	2.4	17.0	25.7	--	--	--	1.1
Inter-alpha-trypsin inhibitor heavy chain H4	ITIH4	9.7	2.4	11.0	12.3	--	--	--	--
Transferrin	TTHY	7.6	4.8	9.0	7.8	2.4	1.3	--	1.1
Hemopexin	HEMO	10.8	4.8	10.0	7.8	--	--	--	--
Alpha-1-acid glycoprotein 2	A1AG2	8.6	6.0	8.0	9.0	5.9	5.0	2.5	4.4
Plasminogen	PLMN	3.2	2.4	5.0	3.4	--	1.3	--	--
Beta-2-glycoprotein 1	APOH	--	4.8	7.0	10.1	--	--	--	--
Coagulation factor XI	FA11	5.4	4.8	5.0	11.2	--	--	--	--
Ig gamma-3 chain C region	IGHG3	50.8	25.2	35.0	50.4	26.0	--	34.8	37.6
C4b-binding protein alpha chain	C4BPA	7.6	3.6	3.0	3.4	--	--	--	1.1
Vitamin D-binding protein	VTDB	6.5	1.2	7.0	6.7	--	--	--	--
Protein AMBP	AMBP	7.6	4.8	3.0	3.4	--	1.3	--	--
Cholesteryl ester transfer protein	CETP	1.1	--	1.0	--	7.1	--	3.7	5.5
Ig alpha-2 chain C region	IGHA2	25.9	13.2	19.0	--	14.2	11.3	26.1	--
Alpha-2-HS-glycoprotein	FETUA	5.4	2.4	4.0	4.5	--	--	--	--
Prothrombin	THRB	2.2	3.6	1.0	3.4	--	--	--	--
Alpha-1B-glycoprotein	A1BG	5.4	--	2.0	4.5	--	--	--	--
Complement factor H	CFAH	7.6	--	1.0	4.5	--	--	--	--
Phosphatidylcholine-sterol acyltransferase	LCAT	1.1	--	--	--	3.5	--	1.2	5.5
Angiotensinogen	ANGT	3.2	3.6	--	--	1.2	--	--	--
Alpha-1-antichymotrypsin	AACT	4.3	3.6	2.0	2.2	--	--	--	--
Ceruloplasmin	CERU	4.3	1.2	2.0	4.5	--	--	--	--
Ficolin-2	FCN2	3.2	--	1.0	2.2	--	--	--	--
Complement C1s subcomponent	C1S	6.5	1.2	--	2.2	--	--	--	--
Inter-alpha-trypsin inhibitor heavy chain H2	ITIH2	4.3	--	1.0	1.1	--	--	--	--
Platelet basic protein	CXCL7	--	--	1.0	3.4	--	--	--	--

<sup>a</sup> Total peptide spectral counts for proteins identified in individual donors. Spectral counts were normalized to the total spectral count summed across all proteins for the subfraction in the donor with the maximal total spectral count.

### Supplemental Table S4

Total peptide spectral counts for proteins identified in the LpA-I and LpA-I/A-II subfractions isolated from UC-HDL

Protein	Accession Number	LpA-I				LpA-I/A-II			
		1 <sup>a</sup>	2 <sup>a</sup>	3 <sup>a</sup>	4 <sup>a</sup>	1 <sup>a</sup>	2 <sup>a</sup>	3 <sup>a</sup>	4 <sup>a</sup>
Apolipoprotein A-I	APOA1	776.6	762.2	837.7	787.4	632.3	646.6	591.0	605.8
Apolipoprotein A-II	APOA2	29.9	52.8	42.3	56.3	171.3	161.3	174.0	177.5
Apolipoprotein B-100	APOB	12.6	3.7	--	35.3	1.3	--	--	3.6
Apolipoprotein A-IV	APOA4	4.7	13.5	2.6	2.2	7.6	17.8	26.0	18.0
Clusterin	CLUS	6.3	--	1.3	--	--	--	1.0	--
Apolipoprotein D	APOD	9.4	23.3	17.9	5.5	40.3	34.0	48.0	20.4
Apolipoprotein C-III	APOC3	31.4	38.0	28.2	28.7	46.6	51.8	40.0	55.2
Serum paraoxonase/arylesterase 1	PON1	4.7	20.9	14.1	5.5	3.8	10.4	13.0	1.2
Apolipoprotein C-I	APOC1	22.0	23.3	16.7	25.4	29.0	44.4	28.0	42.0
Apolipoprotein E	APOE	3.1	7.4	1.3	15.5	22.7	11.8	37.0	49.2
Apolipoprotein M	APOM	33.0	36.8	33.3	23.2	31.5	20.7	36.0	19.2
Apolipoprotein C-II	APOC2	40.9	49.1	28.2	37.5	34.0	41.4	20.0	36.0
Alpha-1-antitrypsin	A1AT	50.3	8.6	11.5	6.6	13.9	3.0	6.0	6.0
Apolipoprotein L1	APOL1	12.6	1.2	2.6	8.8	7.6	--	7.0	6.0
Serum amyloid A-4 protein	SAA4	6.3	8.6	9.0	12.1	2.5	5.9	14.0	7.2
Phospholipid transfer protein	PLTP	6.3	2.5	5.1	2.2	1.3	3.0	2.0	1.2
Apolipoprotein F	APOF	6.3	4.9	5.1	2.2	8.8	4.4	11.0	6.0
Serum amyloid A-1 protein	SAA1	1.6	1.2	1.3	3.3	2.5	--	3.0	3.6

<sup>a</sup> Total peptide spectral counts for proteins identified in individual donors. Spectral counts were normalized to the total spectral count summed across all proteins for the subfraction in the donor with the maximal total spectral count.

### Supplemental Table S5

#### Spectral count distribution for proteins across LpA-I and LpA-I/A-II subfractions isolated from plasma

Accession Number	LpA-I				LpA-I/A-II				LpA-I	LpA-I/A-II	LpA-I	LpA-I/A-II	P-Value <sup>b</sup>
	1 <sup>a</sup>	2 <sup>a</sup>	3 <sup>a</sup>	4 <sup>a</sup>	1 <sup>a</sup>	2 <sup>a</sup>	3 <sup>a</sup>	4 <sup>a</sup>	Avg	Avg	SD	SD	
APOA1	41.1%	47.4%	46.1%	42.3%	58.9%	52.6%	53.9%	57.7%	44.2%	55.8%	3.0%	3.0%	0.031
APOA2	1.1%	1.4%	0.7%	1.2%	98.9%	98.6%	99.3%	98.8%	1.1%	98.9%	0.3%	0.3%	0.000
FINC	63.7%	63.8%	69.6%	71.0%	36.3%	36.2%	30.4%	29.0%	67.0%	33.0%	3.8%	3.8%	0.003
APOB	62.6%	60.8%	57.4%	57.1%	37.4%	39.2%	42.6%	42.9%	59.5%	40.5%	2.7%	2.7%	0.006
APOA4	44.7%	46.9%	39.1%	34.5%	55.3%	53.1%	60.9%	65.5%	41.3%	58.7%	5.6%	5.6%	0.054
CLUS	64.4%	54.2%	55.1%	52.1%	35.6%	45.8%	44.9%	47.9%	56.5%	43.5%	5.5%	5.5%	0.098
APOD	30.1%	33.7%	35.9%	33.1%	69.9%	66.3%	64.1%	66.9%	33.2%	66.8%	2.4%	2.4%	0.001
APOC3	18.1%	22.8%	22.3%	20.7%	81.9%	77.2%	77.7%	79.3%	21.0%	79.0%	2.1%	2.1%	0.000
PON1	64.0%	59.7%	59.6%	61.0%	36.0%	40.3%	40.4%	39.0%	61.1%	38.9%	2.0%	2.0%	0.002
APOC1	26.8%	38.3%	23.0%	24.5%	73.2%	61.7%	77.0%	75.5%	28.1%	71.9%	7.0%	7.0%	0.008
APOE	33.7%	42.1%	29.2%	28.1%	66.3%	57.9%	70.8%	71.9%	33.3%	66.7%	6.4%	6.4%	0.014
APOM	43.6%	37.9%	44.6%	32.3%	56.4%	62.1%	55.4%	67.7%	39.6%	60.4%	5.7%	5.7%	0.036
APOC2	34.3%	46.0%	41.7%	45.3%	65.7%	54.0%	58.3%	54.7%	41.8%	58.2%	5.4%	5.4%	0.056
A1AT	76.2%	80.5%	69.1%	57.4%	23.8%	19.5%	30.9%	42.6%	70.8%	29.2%	10.1%	10.1%	0.026
FCGBP	49.0%	37.2%	71.3%	63.9%	51.0%	62.8%	28.7%	36.1%	55.4%	44.6%	15.2%	15.2%	0.531
LAC2	48.5%	60.1%	56.3%	46.3%	51.5%	39.9%	43.7%	53.7%	52.8%	47.2%	6.5%	6.5%	0.451
FIBG	83.8%	85.9%	84.7%	88.7%	16.2%	14.1%	15.3%	11.3%	85.8%	14.2%	2.1%	2.1%	0.000
IGHA1	70.9%	62.7%	43.1%	66.9%	29.1%	37.3%	56.9%	33.1%	60.9%	39.1%	12.3%	12.3%	0.175
PHLD	71.3%	74.0%	75.8%	71.2%	28.7%	26.0%	24.2%	28.8%	73.1%	26.9%	2.2%	2.2%	0.000
FIBB	83.4%	85.1%	90.1%	83.2%	16.6%	14.9%	9.9%	16.8%	85.4%	14.6%	3.2%	3.2%	0.000
APOL1	42.2%	65.5%	64.4%	45.1%	57.8%	34.5%	35.6%	54.9%	54.3%	45.7%	12.4%	12.4%	0.534
SAA4	37.8%	48.7%	40.2%	38.8%	62.2%	51.3%	59.8%	61.2%	41.4%	58.6%	5.0%	5.0%	0.041
FIBA	96.1%	91.6%	96.5%	90.4%	3.9%	8.4%	3.5%	9.6%	93.6%	6.4%	3.1%	3.1%	0.000
IGHG2	52.4%	46.3%	35.2%	51.6%	47.6%	53.7%	64.8%	48.4%	46.4%	53.6%	7.9%	7.9%	0.426
CO3	80.7%	100.0%	100.0%	85.9%	19.3%	--	--	14.1%	91.6%	8.4%	9.9%	9.9%	0.004
FA5	93.9%	100.0%	91.3%	93.8%	6.1%	--	8.7%	6.2%	94.8%	5.2%	3.7%	3.7%	0.000
PLTP	43.9%	30.2%	55.9%	45.8%	56.1%	69.8%	44.1%	54.2%	43.9%	56.1%	10.6%	10.6%	0.334
C1QB	56.1%	75.5%	68.9%	66.9%	43.9%	24.5%	31.1%	33.1%	66.9%	33.1%	8.1%	8.1%	0.025
APOF	43.9%	44.9%	34.9%	16.8%	56.1%	55.1%	65.1%	83.2%	35.1%	64.9%	13.0%	13.0%	0.106
VTNC	66.0%	65.5%	64.4%	60.3%	34.0%	34.5%	35.6%	39.7%	64.1%	35.9%	2.6%	2.6%	0.002
CD5L	79.8%	55.4%	63.6%	57.4%	20.2%	44.6%	36.4%	42.6%	64.1%	35.9%	11.1%	11.1%	0.085
KNG1	100.0%	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
KV312	66.8%	35.2%	40.2%	65.0%	33.2%	64.8%	59.8%	35.0%	51.8%	48.2%	16.4%	16.4%	0.843
IGJ	71.5%	57.1%	49.6%	70.3%	28.5%	42.9%	50.4%	29.7%	62.1%	37.9%	10.6%	10.6%	0.106
C1QC	68.1%	69.5%	58.5%	59.1%	31.9%	30.5%	41.5%	40.9%	63.8%	36.2%	5.8%	5.8%	0.018
SAA1	20.7%	48.7%	24.4%	33.6%	79.3%	51.3%	75.6%	66.4%	31.8%	68.2%	12.5%	12.5%	0.062
CO4A	50.7%	57.1%	44.6%	78.0%	49.3%	42.9%	55.4%	22.0%	57.6%	42.4%	14.5%	14.5%	0.373
C1R	92.2%	85.1%	87.9%	82.0%	7.8%	14.9%	12.1%	18.0%	86.8%	13.2%	4.3%	4.3%	0.000
PLF4	100.0%	100.0%	100.0%	95.9%	--	--	--	4.1%	99.0%	1.0%	2.1%	2.1%	0.000
ITIH4	100.0%	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
TTHY	76.2%	79.2%	100.0%	87.6%	23.8%	20.8%	--	12.4%	85.7%	14.3%	10.7%	10.7%	0.007
HEMO	100.0%	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
A1AG2	59.4%	54.3%	76.3%	66.9%	40.6%	45.7%	23.7%	33.1%	64.2%	35.8%	9.6%	9.6%	0.059
PLMN	100.0%	65.5%	100.0%	100.0%	--	34.5%	--	--	91.4%	8.6%	17.2%	17.2%	0.017
APOH	--	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
FA11	100.0%	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
IGHG3	66.1%	100.0%	50.2%	57.3%	33.9%	--	49.8%	42.7%	68.4%	31.6%	22.1%	22.1%	0.194
C4BPA	100.0%	100.0%	100.0%	75.2%	--	--	--	24.8%	93.8%	6.2%	12.4%	12.4%	0.006
VTDB	100.0%	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
AMBP	100.0%	79.2%	100.0%	100.0%	--	20.8%	--	--	94.8%	5.2%	10.4%	10.4%	0.003
CETP	13.2%	--	21.2%	--	86.8%	--	78.8%	100.0%	11.5%	88.5%	10.7%	10.7%	0.025
IGHA2	64.6%	53.7%	42.2%	--	35.4%	46.3%	57.8%	--	53.5%	46.5%	11.2%	11.2%	0.643
FETUA	100.0%	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
THRB	100.0%	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
A1BG	100.0%	--	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
CFAH	100.0%	--	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
LCAT	23.3%	--	--	--	76.7%	--	100.0%	100.0%	7.8%	92.2%	13.5%	13.5%	0.032
ANGT	73.3%	100.0%	--	--	26.7%	--	--	--	86.6%	13.4%	18.9%	18.9%	0.223
AACT	100.0%	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
CERU	100.0%	100.0%	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
FCN2	100.0%	--	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
C1S	100.0%	100.0%	--	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
ITIH2	100.0%	--	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	
CXCL7	--	--	100.0%	100.0%	--	--	--	--	100.0%	0.0%	0.0%	0.0%	

<sup>a</sup> Distribution of peptide spectral counts between LpA-I and LpA-I/A-II subfractions isolated from plasma. Total spectral counts for a given protein were summed across LpA-I and LpA-I/A-II subfractions for individual donors. Spectral counts for each individual are expressed as a percentage of that total.

<sup>b</sup> Statistically significant differences (P<0.05) are highlighted in red as calculated by a 2-tailed student's t-test between LpA-I and LpA-I/A-II subfractions.

