

SUPPLEMENTARY INFORMATION

QUANTITATIVE HDL PROTEOMICS IDENTIFIES PEROXIREDOXIN-6 AS A BIOMARKER OF HUMAN ABDOMINAL AORTIC ANEURYSM

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Supplementary Methods

HDL isolation

Lipoproteins were isolated from individual EDTA plasma samples by ultracentrifugation. Plasma density was adjusted to $\rho=1.063$ g/mL with KBr and the sample was overlaid with KBr saline solution ($\rho=1.063$ g/mL). Samples were ultracentrifuged at 53000 rpm for 18 h at 4°C in a TLA-100 rotor (Beckman). After centrifugation, the upper, apolipoprotein-B-containing fraction was recovered and stored. The bottom fraction, containing HDLs, was adjusted to 1.25 g/mL with KBr and overlaid with KBr saline solution ($\rho=1.22$ g/mL). The HDL-containing fraction was then ultracentrifuged at 63000 rpm for 24 h at 4°C. After this step, HDLs, in the top layer, were recovered as a single band and were extensively rinsed with saline and concentrated using a centrifugal concentrating device (cutoff 10 kDa). All HDL samples were desalted by centrifugation and 3 washes with saline.

Proteomic study

Experimental design

In each experiment, samples from 2 AAA patients and 1 control subject were compared with an internal control, prepared by pooling protein extracts from all subjects of the study. All the comparatives included independent biological preparations, making a total 14 comparatives between AAA samples vs internal control sample and 7 comparatives between control samples vs internal control sample. The use of internal control allowed comparing data from different individuals in different experiments, as described in the Methods section (FIGURE 1). Only 31 outlier proteins showed significant abundance differences

at a 1% FDR threshold in all comparisons of the 7 integration experiments. Proteins identified in at least three independent comparatives at 1% false discovery rate (FDR) were considered for the analysis. Quantitative data were analysed using the weighted spectrum, peptide, and protein (WSPP) model ¹, which allowed decomposition of the total variance into the spectral, peptide, and protein variance components. The distribution of quantitative data at the 3 levels, spectrum, peptide and protein, were in good agreement with the predictions of the statistical model, as depicted from the analysis of sigmoidal distributions obtained in all iTRAQ comparisons (Supplementary Figure S3). The variances at the spectrum and peptide levels were similar in all the pairwise comparisons (Supplementary Table S3), and were within the values expected according to results previously obtained in our laboratory ¹⁻⁵. A FDR threshold of 1% was set to detect significant protein-abundance changes from the Z values. The high inter-individual differences in protein variance observed in human HDL preparations ⁴ prompted us to use a shared all-experiment internal control as a reference for quantifications; using this approach, protein variance was consistently below 0.4, a value similar to that we obtained working with pooled human HDL samples ⁴ or human HDL samples from AAA patients ⁶ (Supplementary Figure S4).

iTRAQ labelling of peptides

The dried peptides were taken up in 15 μ L of iTRAQ solution buffer provided with the iTRAQ kit (ABSciex) and labeled by adding 35 μ L of the corresponding iTRAQ reagent in ethanol, followed by 1h incubation at room temperature in 70% ethanol in 180 mM triethylammonium bicarbonate (TEAB), pH 8.53. HDL samples from control subjects were labeled with iTRAQ tags 114, and HDL

samples from AAA patients were labeled with tags 115 and 116. In addition, a pool of all 21 samples was used as an internal control in every iTRAQ experiment and was labeled with tag 117. After quenching with 50 μ L 0.5% TFA (v/v) for 30 min, samples were fully dried to completely stop the labeling reaction. The four labeled samples were resuspended in 100 μ L 0.1% TFA (v/v), combined in one tube, and cleaned up with C18 Oasis cartridges using 50% ACN (v/v) in 0.1% TFA (v/v) as elution solvent. Samples were dried down prior to LC-MS/MS analysis.

Statistics

The \log_2 ratio of concentrations in the two samples being compared, A and B, determined by spectrum s of peptide p derived from protein q , is expressed as $X_{eqps} = \log_2(A/B)$. The \log_2 -ratio value associated with each peptide, X_{eqp} , is then calculated as a weighted average of the spectra used to quantify the peptide, and the value associated with each protein, X_{eq} , is similarly the weighted average of its peptides. In addition, a grand mean, X_e , is calculated in each experiment as a weighted average of the protein values. The global distribution of values at each level is described using a standardized variable, Z , that expresses the quantitative values in units of standard deviation and that in the null hypothesis is expected to follow a $N(0,1)$ normal distribution. Our statistical model was used to average protein quantifications from each comparison between control samples and the internal control and between AAA patient samples and the internal control^{1,5}. These averaged protein quantifications yielded integrated data for comparison of AAA patient samples with samples from control participants (FIGURE 1, green arrows), thereby increasing the statistical power to detect protein alterations¹. Again, the distribution of the

standardized variable describing the variability between different experiments within the same protein was very close to the null hypothesis (Supplementary Figure S3), demonstrating that the quantitative results from all experiments were generally reproducible and therefore can be integrated. The final distribution of averaged protein abundance ratios between AAA patients and controls was also close to that of the null hypothesis, allowing the detection of significant protein abundance changes (Supplementary Figure S3).

Systems biology analysis

Systems biology analysis were performed using the SBT model ⁵. Proteins were classified as belonging to a functional *class* or *category*, and statistical analyses were performed to determine the relative abundance of each category by integrating the quantitative values of its protein components, after eliminating protein-category outliers. Proteins were functionally annotated using the Ingenuity Knowledge Database ^{7,8}, CORUM ⁹, and DAVID ^{10,11}. Network analysis were obtained using STRINGS ¹².

References

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Supplementary Table S1.- Proteins identification in at least three iTRAQ experiments. Number of spectra and peptide for each protein identified at 1% FDR and the percent coverage in either are indicated. Accession number from Uniprot database.

Known proteins previously identified in HDL particle		iTRAQ 1			iTRAQ 2			iTRAQ 3			iTRAQ 4			iTRAQ 5			iTRAQ 6			iTRAQ 7		
Accession N°	Protein name	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage
P04114	>sp P04114 APOB_HUMAN Apolipoprotein B-100 OS=Homo sapiens GN=APOB PE=1 SV=2	726	251	56	753	247	54	642	220	50	619	214	50	588	215	50	723	245	56	833	258	58
P02768	>sp P02768 ALBU_HUMAN Serum albumin OS=Homo sapiens GN=ALB PE=1 SV=2	390	63	80	425	62	79	361	54	75	456	57	78	483	54	75	355	54	74	316	57	78
P02647	>sp P02647 APOA1_HUMAN Apolipoprotein A-I OS=Homo sapiens GN=APOA1 PE=1 SV=1	588	42	86	532	42	86	350	38	82	394	35	78	510	36	76	447	40	82	486	40	83
P01009	>sp P01009 A1AT_HUMAN Alpha-1-antitrypsin OS=Homo sapiens GN=SERPINA1 PE=1 SV=3	69	25	52	64	23	48	58	21	50	70	25	53	72	23	53	61	24	51	45	22	53
P01024	>sp P01024 CO3_HUMAN Complement C3 OS=Homo sapiens GN=C3 PE=1 SV=2	65	40	29	64	44	32	55	40	27	53	34	25	62	41	30	66	46	34	68	46	34
P05090	>sp P05090 APOD_HUMAN Apolipoprotein D OS=Homo sapiens GN=APOD PE=1 SV=1	78	13	50	61	12	52	53	10	50	58	9	34	45	11	50	50	12	57	68	11	46
P02649	>sp P02649 APOE_HUMAN Apolipoprotein E OS=Homo sapiens GN=APOE PE=1 SV=1	56	21	64	54	24	58	69	23	68	43	20	62	42	19	57	35	15	52	68	21	68
O95445	>sp O95445 APOM_HUMAN Apolipoprotein M OS=Homo sapiens GN=APOM PE=1 SV=2	48	15	70	58	17	65	45	11	61	47	11	57	50	11	59	44	12	65	53	11	65
P27169	>sp P27169 PON1_HUMAN Serum paraoxonase/arylesterase 1 OS=Homo sapiens GN=PON1 PE=1 SV=3	30	10	46	40	11	53	54	12	56	60	12	56	44	12	56	39	11	56	50	13	53
P08519	>sp P08519 APOA_HUMAN Apolipoprotein(a) OS=Homo sapiens GN=LPA PE=1 SV=1	69	40	35	60	35	35	27	20	25	38	21	26	26	19	25	34	21	33	26	14	30
P00739	>sp P00739 HPTR_HUMAN Haptoglobin-related protein OS=Homo sapiens GN=HPR PE=1 SV=2	38	13	45	35	13	41	28	13	41	42	13	41	30	13	45	52	15	47	50	17	48
P06727	>sp P06727 APOA4_HUMAN Apolipoprotein A-IV OS=Homo sapiens GN=APOA4 PE=1 SV=3	29	16	47	38	20	48	29	17	41	28	17	44	43	18	43	31	13	36	42	20	49
P02652	>sp P02652 APOA2_HUMAN Apolipoprotein A-II OS=Homo sapiens GN=APOA2 PE=1 SV=1	42	6	42	36	7	47	29	6	45	24	6	47	41	6	47	36	6	46	29	6	47
P0C0L4	>sp P0C0L4 CO4A_HUMAN Complement C4-A OS=Homo sapiens GN=C4A PE=1 SV=1	21	17	13	17	14	11	22	15	13	16	13	12	25	18	15	36	24	21	37	24	17
P0DJI8	>sp P0DJI8 SAA1_HUMAN Serum amyloid A-1 protein OS=Homo sapiens GN=SAA1 PE=1 SV=1	30	8	55	29	8	55	35	9	66	16	5	55	12	5	55	37	7	55	9	6	43
P35542	>sp P35542 SAA4_HUMAN Serum amyloid A-4 protein OS=Homo sapiens GN=SAA4 PE=1 SV=2	26	7	42	38	6	48	15	6	33	15	4	38	22	6	38	21	6	38	22	5	38
B2R5G8	>tr B2R5G8 B2R5G8_HUMAN Serum amyloid A protein OS=Homo sapiens PE=2 SV=1	15	2	42	25	3	65	4	2	33	8	2	38	26	3	56	30	3	56	25	3	56
P02656	>sp P02656 APOC3_HUMAN Apolipoprotein C-III OS=Homo sapiens GN=APOC3 PE=1 SV=1	27	6	56	20	6	59	13	3	34	15	4	54	17	6	56	16	4	54	19	4	34
O14791	>sp O14791 APOL1_HUMAN Apolipoprotein L1 OS=Homo sapiens GN=APOL1 PE=1 SV=5	20	12	36	15	11	23	20	9	17	20	9	17	17	9	27	14	7	17	19	11	32
P55058	>sp P55058 PLTP_HUMAN Phospholipid transfer protein OS=Homo sapiens GN=PLTP PE=1 SV=1	17	11	25	13	9	23	12	8	22	24	13	22	18	10	22	15	9	25	17	12	24
P10909	>sp P10909 CLUS_HUMAN Clusterin OS=Homo sapiens GN=CLU PE=1 SV=1	22	9	26	14	6	21	9	7	23	13	9	24	15	11	26	18	10	26	21	8	22
Q9UHG3	>sp Q9UHG3 PCYOX_HUMAN Prenylcysteine oxidase 1 OS=Homo sapiens GN=PCYOX1 PE=1 SV=3	15	11	25	8	7	18	15	11	25	19	13	28	16	10	27	8	6	19	16	14	36
P02766	>sp P02766 TTHY_HUMAN Transthyretin OS=Homo sapiens GN=TTR PE=1 SV=1	13	8	69	14	8	69	7	6	49	11	7	65	15	7	65	11	7	65	15	7	65
P02654	>sp P02654 APOC1_HUMAN Apolipoprotein C-I OS=Homo sapiens GN=APOC1 PE=1 SV=1	15	6	29	11	6	37	10	6	29	10	5	27	10	6	29	11	6	29	16	6	29
P02671	>sp P02671 FIBA_HUMAN Fibrinogen alpha chain OS=Homo sapiens GN=FGA PE=1 SV=2	10	7	14	11	8	14	10	6	9	6	4	6	9	6	10	14	9	13	14	6	8
P02655	>sp P02655 APOC2_HUMAN Apolipoprotein C-II OS=Homo sapiens GN=APOC2 PE=1 SV=1	10	5	50	15	6	52	9	3	32	9	3	32	15	5	50	8	4	41	5	4	41
P02765	>sp P02765 FETUA_HUMAN Alpha-2-HS-glycoprotein OS=Homo sapiens GN=AHS2 PE=1 SV=1	12	4	16	14	4	16	7	3	16	7	5	18	18	6	19	4	3	9	7	5	14
P02774	>sp P02774 VTDB_HUMAN Vitamin D-binding protein OS=Homo sapiens GN=GC PE=1 SV=1	4	3	11	8	6	17	8	7	23	12	9	31	20	9	27	11	8	29	6	6	15
P04180	>sp P04180 LCAT_HUMAN Phosphatidylcholine-sterol acyltransferase OS=Homo sapiens GN=LCAT PE=1 SV=1	8	7	18	10	6	17	9	7	22	13	7	23	10	7	18	9	5	20	9	6	19
Q15166	>sp Q15166 PON3_HUMAN Serum paraoxonase/lactonase 3 OS=Homo sapiens GN=PON3 PE=1 SV=3	8	6	23	10	7	27	6	4	16	10	6	19	11	7	30	8	6	23	11	7	23
P01834	>sp P01834 IGKC_HUMAN Ig kappa chain C region OS=Homo sapiens GN=IGKC PE=1 SV=1	5	4	65	4	3	46	15	5	80	9	3	46	12	5	80	7	4	61	6	4	65
P02753	>sp P02753 RET4_HUMAN Retinol-binding protein 4 OS=Homo sapiens GN=RBP4 PE=1 SV=3	9	5	30	7	5	30	10	6	44	9	6	41	10	6	36	6	5	36	5	4	25
P36955	>sp P36955 PEDF_HUMAN Pigment epithelium-derived factor OS=Homo sapiens GN=SERPINF1 PE=1 SV=4	6	6	18	6	6	15	7	6	20	9	7	19	12	7	18	5	5	12	9	6	15
P15144	>sp P15144 AMPN_HUMAN Aminopeptidase N OS=Homo sapiens GN=ANPEP PE=1 SV=4	1	1	1	1	1	1	21	15	19												
P02760	>sp P02760 AMB_P_HUMAN Protein AMBP OS=Homo sapiens GN=AAMP PE=1 SV=1	9	6	16	10	7	20	7	5	16	7	4	16	5	4	13	6	5	16	6	4	13
P01019	>sp P01019 ANGT_HUMAN Angiotensinogen OS=Homo sapiens GN=AGT PE=1 SV=1	7	5	13	6	5	13	6	4	11	9	6	17	4	4	12	5	4	11	7	3	11
P55056	>sp P55056 APOC4_HUMAN Apolipoprotein C-IV OS=Homo sapiens GN=APOC4 PE=1 SV=1	4	4	24	4	3	23	2	2	17	5	4	32	9	5	34	7	7	34	9	6	34
P04004	>sp P04004 VTNC_HUMAN Vitronectin OS=Homo sapiens GN=VTN PE=1 SV=1	9	4	12	4	3	9	4	3	6	5	4	12	5	4	12	5	4	12	6	3	9
P01857	>sp P01857 IGHG1_HUMAN Ig gamma-1 chain C region OS=Homo sapiens GN=IGHG1 PE=1 SV=1	3	2	9	3	3	15	8	5	22	4	3	15	6	3	22	6	3	22	8	5	25
P01876	>sp P01876 IGHA1_HUMAN Ig alpha-1 chain C region OS=Homo sapiens GN=IGHA1 PE=1 SV=2	6	4	18	5	4	22	5	4	18	5	3	12	5	4	18	5	4	18	6	4	18

Known proteins previously identified in HDL particle		iTRAQ 1			iTRAQ 2			iTRAQ 3			iTRAQ 4			iTRAQ 5			iTRAQ 6			iTRAQ 7		
Accession N ^o	Protein name	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage
P02748	>sp P02748 CO9_HUMAN Complement component C9 OS=Homo sapiens GN=C9 PE=1 SV=2	5	4	8	5	5	12	3	3	6	4	4	9	6	6	13	5	5	11	6	5	11
P02749	>sp P02749 APOH_HUMAN Beta-2-glycoprotein 1 OS=Homo sapiens GN=APOH PE=1 SV=3	5	5	25	4	3	20	2	2	13	4	3	15	8	6	33	8	5	28	2	2	13
P02775	>sp P02775 CXCL7_HUMAN Platelet basic protein OS=Homo sapiens GN=PPBP PE=1 SV=3	6	2	23	3	2	23	2	2	19	5	3	30	5	2	23	7	2	23	2	2	23
P68871	>sp P68871 HBB_HUMAN Hemoglobin subunit beta OS=Homo sapiens GN=HBB PE=1 SV=2	3	3	24	3	3	29	5	3	31	8	5	39	3	3	28	6	5	48	1	1	9
P00738	>sp P00738 HPT_HUMAN Haptoglobin OS=Homo sapiens GN=HP PE=1 SV=1	5	4	29	4	3	20	4	3	22	4	3	22	4	3	26	3	2	28	3	2	28
Q14624	>sp Q14624 ITIH4_HUMAN Inter-alpha-trypsin inhibitor heavy chain H4 OS=Homo sapiens GN=ITIH4 PE=1 SV=4	4	4	7	1	1	1	1	1	1	5	5	7	7	5	9	5	5	9	5	5	9
P62736	>sp P62736 ACTA_HUMAN Actin, aortic smooth muscle OS=Homo sapiens GN=ACTA2 PE=1 SV=1	4	4	11	6	5	15	5	5	17	4	3	6	3	3	11	1	1	2	2	2	6
P07737	>sp P07737 PROF1_HUMAN Profilin-1 OS=Homo sapiens GN=PFN1 PE=1 SV=2	1	1	10				8	5	40	5	4	30	3	2	20	1	1	10	1	1	10
P19652	>sp P19652 A1AG2_HUMAN Alpha-1-acid glycoprotein 2 OS=Homo sapiens GN=ORM2 PE=1 SV=2	3	2	18	4	2	18	4	2	18	4	3	22	2	2	18	4	2	18	1	1	18
P02679	>sp P02679 FIBG_HUMAN Fibrinogen gamma chain OS=Homo sapiens GN=FGG PE=1 SV=3	3	3	11	2	2	7	6	5	17	1	1	11	2	1	2						
P02675	>sp P02675 FIBB_HUMAN Fibrinogen beta chain OS=Homo sapiens GN=FBG PE=1 SV=2	4	4	9	4	3	10	3	3	11	1	1	3	1	1	4	4	4	14	2	2	8
P81605	>sp P81605 DCD_HUMAN Dermcidin OS=Homo sapiens GN=DCD PE=1 SV=2	2	2	23	1	1	13	6	3	25	5	2	25	2	1	25	1	1	13	2	2	25
P58335	>sp P58335 ANTR2_HUMAN Anthrax toxin receptor 2 OS=Homo sapiens GN=ANTR2 PE=1 SV=5	1	1	5	2	2	5	2	2	7	4	2	5	2	1	3	4	2	5	2	1	3
P07988	>sp P07988 PSPB_HUMAN Pulmonary surfactant-associated protein B OS=Homo sapiens GN=SPFPB PE=1 SV=3	2	2	7	4	3	10	2	2	7	3	3	12	3	3	12	2	2	8	1	1	3
P69905	>sp P69905 HBA_HUMAN Hemoglobin subunit alpha OS=Homo sapiens GN=HBA1 PE=1 SV=2	1	1	11	1	1	11	3	2	17	6	2	19	1	1	11	3	2	17	2	1	11
P02787	>sp P02787 TRFE_HUMAN Serotransferrin OS=Homo sapiens GN=TF PE=1 SV=3	4	3	7	1	1	2	2	2	4				2	2	4	2	2	4	3	3	5
Q13790	>sp Q13790 APOF_HUMAN Apolipoprotein F OS=Homo sapiens GN=APOF PE=1 SV=2	2	1	4	2	2	8	1	1	4	4	1	8	4	1	8	2	1	8	1	1	4
P60709	>sp P60709 ACTB_HUMAN Actin, cytoplasmic 1 OS=Homo sapiens GN=ACTB PE=1 SV=1	3	2	19	1	1	14	5	4	23	2	2	15	1	1	9	1	1	5	2	2	14
P01871	>sp P01871 IGHM_HUMAN Ig mu chain C region OS=Homo sapiens GN=IGHM PE=1 SV=3	1	1	4	1	1	4	3	3	8				2	2	10	3	3	8	3	3	8
P05155	>sp P05155 IC1_HUMAN Plasma protease C1 inhibitor OS=Homo sapiens GN=SERPING1 PE=1 SV=2	2	2	5	2	2	5	2	2	4	2	2	4	2	2	5	2	1	3	1	1	4
Q8TDL5	>sp Q8TDL5 BPIB1_HUMAN BPI fold-containing family B member 1 OS=Homo sapiens GN=BPIFB1 PE=2 SV=1	2	1	3	2	2	5	1	1	3	2	2	5	2	2	6	3	2	6	1	1	2
P04003	>sp P04003 C4BPA_HUMAN C4b-binding protein alpha chain OS=Homo sapiens GN=C4BPA PE=1 SV=2	2	2	7	2	2	4				2	2	4	2	2	4				1	1	3
P01023	>sp P01023 A2MG_HUMAN Alpha-2-macroglobulin OS=Homo sapiens GN=A2M PE=1 SV=3	2	1	1				1	1	1				1	1	2	3	3	3			
P07477	>sp P07477 TRY1_HUMAN Trypsin-1 OS=Homo sapiens GN=PRSS1 PE=1 SV=1	1	1	8	4	1	8	1	1	8				1	1	8						
P01034	>sp P01034 CYTC_HUMAN Cystatin-C OS=Homo sapiens GN=CST3 PE=1 SV=1	3	2	19	2	1	8	2	1	8	2	1	8	1	1	8	1	1	8	1	1	8
P01859	>sp P01859 IGHG2_HUMAN Ig gamma-2 chain C region OS=Homo sapiens GN=IGHG2 PE=1 SV=2	1	1	10				4	2	16	3	2	13	2	1	17	1	1	17	1	1	13
P10720	>sp P10720 PF4V_HUMAN Platelet factor 4 variant OS=Homo sapiens GN=PF4V1 PE=1 SV=1	1	1	14	2	1	14	1	1	14				1	1	14	4	1	14			
P15924	>sp P15924 DESP_HUMAN Desmoplakin OS=Homo sapiens GN=DSP PE=1 SV=3							1	1	1	2	2	1	2	2	1				2	2	1
P61769	>sp P61769 B2MG_HUMAN Beta-2-microglobulin OS=Homo sapiens GN=B2M PE=1 SV=1	1	1	8	2	2	27	3	2	27				1	1	8	1	1	8	1	1	8
P25311	>sp P25311 ZA2G_HUMAN Zinc-alpha-2-glycoprotein OS=Homo sapiens GN=AZGP1 PE=1 SV=2				1	1	5				2	1	5	1	1	5	2	2	10	1	1	5
P61626	>sp P61626 LYSC_HUMAN Lysozyme C OS=Homo sapiens GN=LYZ PE=1 SV=1				2	2	16	1	1	8	1	1	8	2	2	16				1	1	8
P02763	>sp P02763 A1AG1_HUMAN Alpha-1-acid glycoprotein 1 OS=Homo sapiens GN=ORM1 PE=1 SV=1	1	1	4	2	2	11	1	1	4	2	2	12	1	1	4	1	1	4			
P11597	>sp P11597 CETP_HUMAN Cholesteryl ester transfer protein OS=Homo sapiens GN=CETP PE=1 SV=2				1	1	3	2	1	3	2	1	5	1	1	5	1	1	3	1	1	3
Q9H8L6	>sp Q9H8L6 MMRN2_HUMAN Multimerin-2 OS=Homo sapiens GN=MMRN2 PE=1 SV=2										2	2	3	1	1	1	1	1	1	1	1	1
Q9UK55	>sp Q9UK55 ZPI_HUMAN Protein Z-dependent protease inhibitor OS=Homo sapiens GN=SERPINA10 PE=1 SV=1										2	2	7	1	1	2	1	1	4			
P02730	>sp P02730 B3AT_HUMAN Band 3 anion transport protein OS=Homo sapiens GN=SLC4A1 PE=1 SV=3	1	1	1	1	1	1	1	1	5	3	2	3	1	1	1	1	1	1	1	1	1
P18428	>sp P18428 LBP_HUMAN Lipopolysaccharide-binding protein OS=Homo sapiens GN=LBP PE=1 SV=3	1	1	2	1	1	2	1	1	2	2	2	5	1	1	2	2	2	5	1	1	2
P08697	>sp P08697 A2AP_HUMAN Alpha-2-antiplasmin OS=Homo sapiens GN=SERPINF2 PE=1 SV=3				1	1	3				1	1	2				1	1	3			
P49913	>sp P49913 CAMP_HUMAN Cathelicidin antimicrobial peptide OS=Homo sapiens GN=CAMP PE=1 SV=1	1	1	10	1	1	13	1	1	5	1	1	5	1	1	5	1	1	5			
Q9H6X2	>sp Q9H6X2 ANTR1_HUMAN Anthrax toxin receptor 1 OS=Homo sapiens GN=ANTR1 PE=1 SV=2	1	1	2				1	1	2				1	1	2						

Novel proteins identified in HDL particle in this study		iTRAQ 1			iTRAQ 2			iTRAQ 3			iTRAQ 4			iTRAQ 5			iTRAQ 6			iTRAQ 7		
Accession No	Protein name	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage	n spectra	n peptides	% coverage
Q96KN2	>sp Q96KN2 CNDP1_HUMAN Beta-Ala-His dipeptidase OS=Homo sapiens GN=CNDP1 PE=1 SV=4	9	8	21	8	7	20	1	1	2	9	8	22	7	6	18	9	8	21	12	9	22
Q6U2E9	>tr Q6U2E9 Q6U2E9_HUMAN C4B1 OS=Homo sapiens GN=C4B PE=4 SV=1	8	4	15	7	4	13	8	4	13	9	4	14	7	4	17	6	4	22	5	4	19
C0IYY2	>tr C0IYY2 C0IYY2_HUMAN Apolipoprotein B (Including Ag(X) antigen) OS=Homo sapiens GN=APOB PE=4 SV=1	4	2	57	3	2	55	6	2	50	4	2	51	4	2	51	4	2	57	7	2	58
D3DQX7	>tr D3DQX7 D3DQX7_HUMAN Serum amyloid A protein OS=Homo sapiens GN=SAA1 PE=3 SV=1	4	2	55	2	2	55	12	2	66	3	2	55	4	2	55	4	2	55	3	2	43
P0DJ19	>sp P0DJ19 SAA2_HUMAN Serum amyloid A-2 protein OS=Homo sapiens GN=SAA2 PE=1 SV=1	3	2	36	6	2	36	5	3	50	2	2	36	1	1	36	2	2	36	2	2	25
P12273	>sp P12273 PIP_HUMAN Prolactin-inducible protein OS=Homo sapiens GN=PIP PE=1 SV=1							1	1	5	7	4	26	1	1	8						
B9A064	>sp B9A064 IGLL5_HUMAN Immunoglobulin lambda-like polypeptide 5 OS=Homo sapiens GN=IGLL5 PE=2 SV=2	3	2	14	2	2	14				4	1	7	3	1	7	2	1	7	2	1	7
P02776	>sp P02776 PLF4_HUMAN Platelet factor 4 OS=Homo sapiens GN=PF4 PE=1 SV=2							2	1	26	2	2	27	3	2	27	3	2	27			
P62987	>sp P62987 RL40_HUMAN Ubiquitin-60S ribosomal protein L40 OS=Homo sapiens GN=UBA52 PE=1 SV=2							3	2	20	3	2	20	1	1	13	1	1	7	4	2	20
Q02413	>sp Q02413 DSG1_HUMAN Desmoglein-1 OS=Homo sapiens GN=DSG1 PE=1 SV=2				2	2	3	1	1	1	6	6	8	1	1	2	1	1	2	3	2	3
Q13093	>sp Q13093 PAFA_HUMAN Platelet-activating factor acetylhydrolase OS=Homo sapiens GN=PLA2G7 PE=1 SV=1	3	3	9	2	2	7	2	2	6	4	4	13	2	2	5	1	1	4	1	1	2
P01892	>sp P01892 IA02_HUMAN HLA class I histocompatibility antigen, A-2 alpha chain OS=Homo sapiens GN=HLA-A PE=1 SV=1							2	1					2	2	10	2	2	10			
E9PQD6	>tr E9PQD6 E9PQD6_HUMAN Serum amyloid A protein OS=Homo sapiens GN=SAA1 PE=3 SV=1	1	1	54	1	1	54	6	2	66				1	1	55	1	1	55			30
P30443	>sp P30443 IA01_HUMAN HLA class I histocompatibility antigen, A-1 alpha chain OS=Homo sapiens GN=HLA-A PE=1 SV=1	2	2	10	1	1	5	2	2	10	3	3	15	1	1	5	2	2	10	2	1	5
F6KPG5	>tr F6KPG5 F6KPG5_HUMAN Albumin (Fragment) OS=Homo sapiens PE=2 SV=1							4	1	78	1	1	82	1	1	78	1	1	77			
Q8WXW3	>sp Q8WXW3 PIBF1_HUMAN Progesterone-induced-blocking factor 1 OS=Homo sapiens GN=PIBF1 PE=2 SV=2	2	1	1	2	1	1				1	1	1									
A8K479	>tr A8K479 A8K479_HUMAN cDNA FLJ77094, highly similar to Homo sapiens apolipoprotein B (including Ag(x) antigen) (APOB)	2	1	52	2	1	51							1	1	47						
Q1HP67	>tr Q1HP67 Q1HP67_HUMAN Lipoprotein, Lp(A) OS=Homo sapiens GN=LPA PE=2 SV=1	2	1	37	1	1	36			25	1	1	29	2	1	26	2	1	31			
P05109	>sp P05109 S10A8_HUMAN Protein S100-A8 OS=Homo sapiens GN=S100A8 PE=1 SV=1							1	1	12	2	2	24	2	2	26				1	1	12
P30447	>sp P30447 IA23_HUMAN HLA class I histocompatibility antigen, A-23 alpha chain OS=Homo sapiens GN=HLA-A PE=1 SV=1	1	1	14				1	1	14				2	1	14	2	1	14			
Q98UN1	>sp Q98UN1 MENT_HUMAN Protein MENT OS=Homo sapiens GN=MENT PE=1 SV=1	2	2	4	2	2	4				1	1	4	1	1	4	1	1	4	2	2	4
A8K2W6	>tr A8K2W6 A8K2W6_HUMAN cDNA FLJ76248, highly similar to Homo sapiens phospholipase A2	2	2	12	1	1	10							2	1	9	1	1	7			2
P14151	>sp P14151 LYAM1_HUMAN L-selectin OS=Homo sapiens GN=SELL PE=1 SV=2				1	1	5				1	1	2	1	1	5	3	3	10	1	1	3
P23528	>sp P23528 COF1_HUMAN Cofilin-1 OS=Homo sapiens GN=CFL1 PE=1 SV=3							2	2	19				1	1	7	1	1	7			
P31944	>sp P31944 CASPE_HUMAN Caspase-14 OS=Homo sapiens GN=CASP14 PE=1 SV=2										2	1	6	1	1	6				1	1	6
P06702	>sp P06702 S10A9_HUMAN Protein S100-A9 OS=Homo sapiens GN=S100A9 PE=1 SV=1				1	1	13				1	1	28				1	1	13	2	2	25
Q8IV33	>sp Q8IV33 K0825_HUMAN Uncharacterized protein KIAA0825 OS=Homo sapiens GN=KIAA0825 PE=2 SV=2	2	1	1	1	1	1							1	1	1	1	1	1			
O95258	>sp O95258 UCP5_HUMAN Brain mitochondrial carrier protein 1 OS=Homo sapiens GN=SLC25A14 PE=2 SV=1	1	1	3	1	1	3							1	1	3						
P30041	>sp P30041 PRDX6_HUMAN Peroxiredoxin-6 OS=Homo sapiens GN=PRDX6 PE=1 SV=3	1	1	4				1	1	4	1	1	4									
P62834	>sp P62834 RAP1A_HUMAN Ras-related protein Rap-1A OS=Homo sapiens GN=RAP1A PE=1 SV=1				1	1	7	1	1	7	1	1	7	1	1	7	1	1	7			
Q13867	>sp Q13867 BLMH_HUMAN Bleomycin hydrolase OS=Homo sapiens GN=BLMH PE=1 SV=1										1	1	2	1	1	2	1	1	2	1	1	4
Q5D862	>sp Q5D862 FILA2_HUMAN Filaggrin-2 OS=Homo sapiens GN=FLG2 PE=1 SV=1							1	1	2	1	1	2	1	1	2	1	1	2	1	1	2
Q6P2C0	>sp Q6P2C0 WDR93_HUMAN WD repeat-containing protein 93 OS=Homo sapiens GN=WDR93 PE=2 SV=1	1	1	2	1	1	2	1	1	2	1	1	2	1	1	2	1	1	2	1	1	2
Q9BTE3	>sp Q9BTE3 MCM8BP_HUMAN Mini-chromosome maintenance complex-binding protein OS=Homo sapiens GN=MCM8BP				1	1	2	1	1	2	1	1	2	1	1	2						

Supplementary Table S2.- Protein abundance changes in HDL proteome from AAA vs control patients.

Gene name	Accession number ¹	Protein name	$Xq = \text{Log}_2(\text{AAA/control})$														Integration data					
			Individual comparatives														Xq	Zq	p-value	FDR		
			1	2	3	4	5	6	7	8	9	10	11	12	13	14						
PRDX6	P30041	PRDX6_HUMAN Peroxiredoxin-6	1.12		0.77	1.78					1.59		1.82	0.58					1.29	3.79	0.0002	0.0116
RBP4	P02753	RET4_HUMAN Retinol-binding protein 4	1.71	2.32	1.02	1.45	1.43	1.89	2.25	0.35	0.71	0.75	0.59	0.82	-0.77	-0.29			1.03	3.59	0.0003	0.0176
HLA-A	P30447	1A23_HUMAN HLA class I histocompatibility antigen, A-23 alpha chain	-1.98		-0.53		1.25	1.83		-1.65		1.34		3.61	2.74				1.13	3.51	0.0004	0.0211
PON1	P27169	PON1_HUMAN Serum paraoxonase/arylesterase 1	0.16	1.24	1.88	0.95	1.02	1.22	1.55	0.57	0.47	0.03	1.74	1.58	-0.05	1.01			0.95	3.35	0.0008	0.0309
PFN1	P07737	PROF1_HUMAN Profilin-1	1.16		0.11	1.30	2.04	1.24	-0.39	1.10		1.57	0.48	1.12	0.14	1.10			0.90	3.04	0.0024	0.0730
CST3	P01034	CYTC_HUMAN Cystatin-C	0.42	1.56	1.09	1.19	1.38	2.82	2.66	0.69	0.65	1.01	0.54	1.11	1.69	1.37			0.87	2.98	0.0029	0.0847
SAA	E9PQD6	E9PQD6_HUMAN Serum amyloid A protein	-0.31	1.82	-0.65						1.52	0.00	-0.28						0.94	2.78	0.0055	0.1454
ACTA2	P62736	ACTA_HUMAN Actin, aortic smooth muscle	0.31	0.16	-0.05	1.10	1.10	2.23	-1.03	1.25	1.31	1.87	0.82	1.47	2.28	0.93			0.77	2.69	0.0072	0.1724
PF4	P02776	PLF4_HUMAN Platelet factor 4			0.05	0.65	0.51	1.84					1.90	0.90	-0.23	0.40			0.79	2.55	0.0108	0.2370
CNDP1	Q96KN2	CNDP1_HUMAN Beta-Ala-His dipeptidase	1.41	0.99	-1.65	1.41	1.41	1.27	1.62	0.15	0.54	-0.35	0.52	-0.02	-0.53	0.48			0.72	2.52	0.0117	0.2474
LPA	Q1HP67	Q1HP67_HUMAN Lipoprotein, Lp(A)	2.95	3.39		-2.12		0.10		-0.60	0.15				-0.17			0.79	2.44	0.0148	0.2893	
SERPINF1	P36955	PEDF_HUMAN Pigment epithelium-derived factor	0.88	1.32	0.66	1.59	1.92	1.78	1.34	-0.30	0.18	0.04	0.01	0.45	-0.60	-0.16			0.64	2.28	0.0226	0.3507
GC	P02774	VTDB_HUMAN Vitamin D-binding protein	0.58	1.08	0.61	1.15	2.17	1.52	1.96	-0.16	-0.21	0.11	-0.15	0.34	0.00	-0.10			0.64	2.27	0.0235	0.3539
LOC613037	A8MRT5	K220L_HUMAN Putative NPIP-like protein LOC100132247		1.50	0.73		0.65	0.15			1.47	0.44		0.92	-1.78				0.69	2.18	0.0294	0.4082
PPBP	P02775	CXCL7_HUMAN Platelet basic protein	0.60	0.43	0.12	0.44	0.84	1.44	-0.07	1.55	0.04	1.20	0.38	-0.19	1.14	0.37			0.60	2.13	0.0331	0.4364
B2M	P61769	B2MG_HUMAN Beta-2-microglobulin	0.41	1.55	0.63	0.29	0.65	0.35	0.16	0.24	0.63	1.04	0.06	0.46	1.77	0.01			0.61	2.12	0.0339	0.4253
LCAT	P04180	LCAT_HUMAN Phphatidylcholine-sterol acyltransferase	0.51	1.05	0.55	0.73	1.15	1.58	2.23	0.13	0.46	0.02	0.46	0.95	-0.45	0.55			0.58	2.08	0.0372	0.4458
AMBP	P02760	AMBP_HUMAN Protein AMBP	0.89	1.37	0.87	0.47	1.34	1.31	1.23	-0.14	0.12	0.58	-0.25	0.31	0.41	-0.36			0.57	2.04	0.0411	0.4608
RAP1A	P62834	RAP1A_HUMAN Ras-related protein Rap-1A		-0.09	0.00	2.10	1.24	0.52			0.86	3.33	1.52	1.00	-2.12				0.65	1.98	0.0479	0.5151
LBP	P18428	LBP_HUMAN Lipopolysaccharide-binding protein	0.36	0.14	0.68	1.25	1.46	0.57	0.36	0.17	0.72	-0.11	0.42	1.46	0.28	0.32			0.55	1.94	0.0530	0.5582
N/A	B3KNA1	B3KNA1_HUMAN cDNA FLJ14021 fis, clone HEMBA1002513, highly similar to Histone deacet	0.16	-0.25					0.24	0.61	-0.28					-0.55			0.62	1.87	0.0611	0.5853
PGBD3	Q8N328	PGBD3_HUMAN PiggyBac transposable element-derived protein 3		0.66	1.22			1.22			0.27	0.02			0.10				0.59	1.78	0.0755	0.6522
ACTB	P60709	ACTB_HUMAN Actin, cytoplasmic 1	-0.08	0.24	-0.17	0.88	0.53	0.43	-0.67	0.88	0.79	1.22	0.59	0.62	0.85	0.75			0.47	1.68	0.0928	0.7193
SAA	P0DJ18	SAA1_HUMAN Serum amyloid A-1 protein	1.85	1.60	-1.97	0.23	-0.22	-0.71	-0.44	0.45	0.33	-0.58	0.17	0.40	2.24	-0.11			0.44	1.59	0.1124	0.8227
N/A	Q15994	Q15994_HUMAN Pyruvate dehydrogenase alpha subunit (Fragment)	-0.15	0.44			1.29	1.31	1.53	-0.05	0.09			0.25	0.16	0.20			0.49	1.59	0.1128	0.8145
PLA2G7	Q13093	PAFA_HUMAN Platelet-activating factor acetylhydrolase	1.63	0.95	0.97	-0.47	-0.85	-0.08	-0.62	0.23	0.37	0.74	0.47	0.48	1.24	1.07			0.43	1.54	0.1244	0.8192
PF4V1	P10720	PF4V_HUMAN Platelet factor 4 variant	-0.25	0.35	-0.09	0.10	0.38	1.62		0.47	0.33	0.60	0.18	0.46	-0.07				0.42	1.47	0.1411	0.8171
S100A9	P06702	S100A9_HUMAN Protein S100-A9		1.27		-0.04		-0.99	0.13		1.98		0.07		1.05	0.36			0.43	1.43	0.1523	0.8541
AHSG	P02765	FETUA_HUMAN Alpha-2-HS-glycoprotein	0.51	0.95	1.15	0.85	1.20	-0.25	1.37	-0.47	-0.06	-0.17	-0.07	-0.05	0.07	-0.04			0.35	1.33	0.1838	0.9139
HLA-A	P30443	1A01_HUMAN HLA class I histocompatibility antigen, A-1 alpha chain	-2.77	-0.33	0.06	1.21	1.04	1.20	0.02	-0.88	0.08	1.64	0.39	2.97	1.82	-0.19			0.33	1.21	0.2253	0.9391
UBA52	P62987	RL40_HUMAN Ubiquitin-60S ribosomal protein L40		0.37	0.20	0.16	-0.21	1.35	0.92		0.32	0.25	0.04	0.90	-0.47	0.03			0.33	1.18	0.2381	0.9578
ARHGEF17	Q96PE2	ARHGH_HUMAN Rho guanine nucleotide exchange factor 17	0.98		1.68	-0.50				0.05		0.27	-0.02						0.37	1.17	0.2409	0.9547
LYZ	P61626	LYSC_HUMAN Lysozyme C		0.80	0.24	-0.02	0.85		0.39		0.73	0.20	0.11	-0.04		0.00			0.33	1.16	0.2465	0.9623

Gene name	Accession number ¹	Protein name	$Xq = \text{Log}_2(\text{AAA}/\text{control})$														Integration data			
			Individual comparatives														Xq	Zq	<i>p</i> -value	FDR
			1	2	3	4	5	6	7	8	9	10	11	12	13	14				
ALB	P02768	ALBU_HUMAN Serum albumin	-0.08	1.25	0.51	1.74	2.05	4.75	3.86	0.02	0.18	-0.22	-0.53	0.65	-0.33	-5.91	0.28	1.08	0.2817	1.0031
SAA	D3DQX7	D3DQX7_HUMAN Serum amyloid A protein	0.36		-0.86	-0.24	0.08	-0.23	-0.55	1.15		-0.23	0.63	0.70	-0.31	0.47	0.29	1.05	0.2945	0.9825
APOA4	P06727	APOA4_HUMAN Apolipoprotein A-IV	0.50	1.11	0.73	0.59	1.00	0.74	0.21	-0.13	-0.19	0.18	-0.25	-0.04	-0.13	-0.50	0.25	1.04	0.2975	0.9804
HBA1	P69905	HBA_HUMAN Hemoglobin subunit alpha	-0.41	-0.45	0.54	-0.02	0.29	0.37	0.25	0.62	0.02	0.05	0.09	0.20	2.55	-0.05	0.25	1.00	0.3195	0.9957
CETP	P11597	CETP_HUMAN Cholesteryl ester transfer protein	0.91	1.40	0.79	0.47	0.54	1.08			0.28	-0.95	-0.31	0.61	-3.82	-1.74	0.25	0.95	0.3350	1.0031
SAA2	P0DJ19	SAA2_HUMAN Serum amyloid A-2 protein	1.44	0.55	-1.10	0.54		-1.10		0.34	-0.02	-0.59	-0.14		0.86		0.25	0.95	0.3408	1.0146
APOD	P05090	APOD_HUMAN Apolipoprotein D	-0.05	0.31	0.35	-0.09	-0.13	-0.08	-0.18	0.30	0.67	0.46	0.03	0.53	0.80	0.78	0.23	0.95	0.3438	1.0179
HPR	P00739	HPTR_HUMAN Haptoglobin-related protein	-1.34	0.41	-0.41	0.51	0.83	1.33	1.51	-1.12	0.17	-0.15	0.71	0.61	-0.56	0.62	0.22	0.89	0.3744	1.0058
PRKACG	P22612	KAPCG_HUMAN cAMP-dependent protein kinase catalytic subunit gamma	-0.13	0.68					0.73	-1.84	-0.50					0.02	0.28	0.88	0.3805	0.9975
C9	P02748	CO9_HUMAN Complement component C9	0.55	-0.09	-0.65	0.59	0.57	-0.15	-0.32	0.34	0.24	0.00	0.42	0.33	0.45	0.49	0.20	0.84	0.4024	1.0195
SREBF2	Q12772	SRBP2_HUMAN Sterol regulatory element-binding protein 2	-0.12			0.19	1.15			0.03		-0.11	0.31				0.24	0.79	0.4290	1.0004
BPIFB1	Q8TDL5	BPIB1_HUMAN BPI fold-containing family B member 1	-0.34	0.09	0.65	0.18	0.59	0.13	0.95	0.07	0.94	-0.81	0.00	0.82	-0.41	0.52	0.20	0.79	0.4314	0.9972
PIBF1	Q8WXW3	PIBF1_HUMAN Progesterone-induced-blocking factor 1	0.12	0.22		-0.13	-0.50	-0.36	-0.48	0.45	0.95		0.14	0.54	0.73	0.27	0.18	0.71	0.4775	0.9859
APOC2	P02655	APOC2_HUMAN Apolipoprotein C-II	-0.19	0.15	0.53	-0.11	0.05	-0.58	0.02	-0.51	0.48	-0.31	0.73	1.09	0.02	0.72	0.15	0.58	0.4994	1.0007
SFTPB	P07988	PSPB_HUMAN Pulmonary surfactant-associated protein B	-0.41	-0.92	0.54	-1.09	0.03	0.52	-0.56	0.55	2.31	0.17	-0.50	1.44	0.45	-0.54	0.15	0.57	0.5000	0.9981
MENT	Q9BUN1	MENT_HUMAN Protein MENT	-0.50	-0.18		0.02	0.07	-0.41	-0.17	0.15	0.43		0.45	1.30	0.37	0.77	0.17	0.57	0.5044	0.9994
FAM117A	Q9C073	F117A_HUMAN Protein FAM117A			2.25		-1.13	-0.89			0.71		0.22	0.73			0.18	0.53	0.5270	0.9813
AZGP1	P25311	ZA2G_HUMAN Zinc-alpha-2-glycoprotein		0.93		0.57	0.84	0.75	0.22		0.03		-0.44	-1.59	0.39	-0.72	0.15	0.52	0.5375	0.9570
ITIH4	Q14624	ITIH4_HUMAN Inter-alpha-trypsin inhibitor heavy chain H4	-1.14	-1.71	-0.27	2.08	1.07	2.52		-0.38	0.53	-1.53	-0.19	-0.55	-2.55		0.12	0.52	0.5012	1.0122
ORM1	P02763	A1AG1_HUMAN Alpha-1-acid glycoprotein 1	-0.71	0.42	-0.52	-1.42	1.14	1.59	0.89	-0.35	-0.07	-0.22	-1.77	0.44	-0.57	-0.09	0.12	0.52	0.5015	1.0095
HBB	P68871	HBB_HUMAN Hemoglobin subunit beta	-0.02	0.08	2.12	0.12	0.18	-0.25	0.00	1.00	-0.03	0.01	0.53	-0.49	3.29	0.93	0.11	0.50	0.5155	1.0074
APOF	Q13790	APOF_HUMAN Apolipoprotein F	0.41	-0.04	0.07	0.18	-0.25	-0.52	-0.51	0.57	0.42	0.74	-0.22	0.19	0.29	0.70	0.11	0.50	0.5197	0.9896
ORM2	P19652	A1AG2_HUMAN Alpha-1-acid glycoprotein 2	-0.49	-0.15	0.03	0.35	0.73	1.53	1.42	-0.22	-0.31	-0.22	0.32	-0.07	-0.32	-0.35	0.09	0.42	0.5745	1.0098
FAM76B	Q5HYJ3	FA76B_HUMAN Protein FAM76B	0.46	0.00	-0.05	-0.01	-0.39		0.38		-0.04	0.44	0.81	-1.15			0.09	0.40	0.5858	0.9998
HELZ2	Q9BYK8	PR285_HUMAN Peroxisomal proliferator-activated receptor A-interacting complex 285 kDa p	0.32	-0.44		0.03	-0.55		0.51	0.22		0.58	-0.05				0.09	0.40	0.5905	1.0025
S100A8	P05109	S10A8_HUMAN Protein S100-A8			-0.34	0.12	-0.42		0.46			-0.58	-0.13	1.35		0.75	0.09	0.39	0.5951	1.0035
OLR1	P78380	OLR1_HUMAN Oxidized low-density lipoprotein receptor 1				0.38	0.03	0.09	0.50			0.95	-0.28	-0.85	-0.47		0.08	0.37	0.7143	0.9985
PON3	Q15166	PON3_HUMAN Serum paraoxonase/lactonase 3	0.04	0.33	0.18	-0.07	-0.54	-0.25	-0.15	0.23	0.42	0.51	-0.09	-0.01	0.27	-0.05	0.05	0.33	0.7432	1.0017
TTR	P02766	TTHY_HUMAN Transthyretin	0.12	0.55	0.03	0.52	0.47	0.85	0.98	-0.71	-0.37	-0.30	-0.22	-0.59	-0.38	-0.34	0.04	0.29	0.7703	0.9974
C4A	P0C0L4	CO4A_HUMAN Complement C4-A	-0.85	-0.02	0.41	0.32	0.18	3.50	0.58	0.15	0.12	0.06	-0.13	-0.11	-0.19	-0.58	0.03	0.25	0.8046	1.0072
SAA	B2R5G8	B2R5G8_HUMAN Serum amyloid A protein	0.71	0.79	-0.21	-0.20	-0.82	-0.39	-0.57	0.52	-0.21	0.11	0.13	-0.46	1.05	0.01	0.03	0.24	0.8128	1.0055
APOC3	P02656	APOC3_HUMAN Apolipoprotein C-III	-0.19	0.05	0.08	-0.18	-0.52	-0.14	-0.23	-0.12	0.43	0.01	0.07	0.58	0.59	0.09	0.03	0.23	0.8142	1.0049
CASP14	P31944	CASPE_HUMAN Caspase-14				0.17	-0.58		1.08				0.23	0.10	-0.52		0.03	0.20	0.8375	1.0009

Gene name	Accession number ¹	Protein name	$Xq = \text{Log}_2(\text{AAA}/\text{control})$														Integration data			
			Individual comparatives														Xq	Zq	<i>p</i> -value	FDR
			1	2	3	4	5	6	7	8	9	10	11	12	13	14				
FGA	P02671	FIBA_HUMAN Fibrinogen alpha chain	-2.34	-1.76	-0.35	1.53	0.59	2.04	1.56	1.08	0.24	-0.73	0.00	-0.08	-0.36	-0.42	0.01	0.19	0.8516	1.0040
SAA4	P35542	SAA4_HUMAN Serum amyloid A-4 protein	0.42	0.48	-0.21	-0.32	-0.68	-0.54	-0.05	0.42	-0.85	0.24	0.09	-0.07	1.21	0.02	0.00	0.15	0.8771	1.0137
ANO9	A1A5B4	ANO9_HUMAN Anoctamin-9		0.47	-0.47				1.39		-0.19	-0.10				-0.31	0.00	0.12	0.9058	0.9977
SLC4A1	P02730	B3AT_HUMAN Band 3 anion transport protein	-0.44		0.00	0.03	-0.79	-0.94	1.15	1.36		0.76	0.52	-0.45	-1.19	-0.17	0.00	0.11	0.9106	0.9976
APOL1	O14791	APOL1_HUMAN Apolipoprotein L1	0.22	-0.05	0.39	-0.17	-0.39	-0.67	-0.20	-0.01	-0.56	0.57	-0.07	0.30	0.08	0.29	-0.02	0.08	0.9349	1.0076
HP	P00738	HPT_HUMAN Haptoglobin	-0.47	-1.65	0.31	1.04	2.35	0.86	-0.15	-0.84	-1.18	0.57	0.89	0.47	-1.58	1.26	-0.03	0.05	0.9629	1.0009
SELL	P14151	LYAM1_HUMAN L-selectin		0.11		0.58	0.04	-0.53			0.32		-0.32	-1.02	0.49		-0.04	0.01	0.9931	0.9969
CDH2	P19022	CADH2_HUMAN Cadherin-2	-0.19		1.11	0.04				-0.31		0.14	-0.57				-0.06	-0.04	0.9670	1.0012
APOE	P02649	APOE_HUMAN Apolipoprotein E	0.38	-0.44	1.28	-0.27	-0.80	-0.74	-0.90	-0.02	0.04	0.16	0.06	0.07	0.44	-0.14	-0.07	-0.10	0.9223	1.0043
C4B	Q6U2E9	Q6U2E9_HUMAN C4B1	-0.17	0.20	-0.48	0.07	-0.25	-0.08	-0.27	-0.23	0.29	0.49	0.12	0.01	0.21	-0.92	-0.08	-0.13	0.8973	1.0125
PCYOX1	Q9UHG3	PCYOX_HUMAN Prenylcysteine oxidase 1	0.18	0.23	0.45	-0.24	-0.52	-0.32	-0.13	-0.18	0.27	-0.09	0.13	0.06	-1.24	0.20	-0.08	-0.14	0.8876	1.0081
CYLD	Q9NQC7	CYLD_HUMAN Ubiquitin carboxyl-terminal hydrolase CYLD	-0.20	-0.34	-0.25					0.15	0.12	0.04					-0.09	-0.15	0.8886	1.0101
SERPINA1	P01009	A1AT_HUMAN Alpha-1-antitrypsin	-0.09	0.74	0.37	0.06	0.97	0.22		-1.51	-0.44	-0.22	-1.21	-0.38	-1.25		-0.09	-0.16	0.8717	1.0141
APOC1	P02654	APOC1_HUMAN Apolipoprotein C-I	0.15	-0.84	0.32	-0.50	-0.65	-0.38	-0.47	-0.38	-0.11	-0.15	-0.11	0.62	1.13	-0.41	-0.12	-0.26	0.7947	0.9995
MUC1	Q7Z542	Q7Z542_HUMAN Mucin short variant SV4		0.09			-0.62	-0.64			0.20			-0.33	0.47		-0.14	-0.27	0.7900	1.0008
KIAA0825	Q8IV33	K0825_HUMAN Uncharacterized protein KIAA0825	-0.17	0.01			-0.42	-1.50		-0.52	0.54			0.54	0.54		-0.13	-0.27	0.7846	0.9987
PRO2289	Q9P1D8	YP008_HUMAN Putative uncharacterized protein PRO2289		1.25	-0.31		0.63				-0.91	-0.55		-0.89			-0.15	-0.30	0.7667	1.0026
APOM	O95445	APOM_HUMAN Apolipoprotein M	0.03	-0.34	0.47	-0.34	-0.67	-0.51	-0.78	0.13	0.05	0.12	0.09	-0.34	0.31	0.10	-0.13	-0.30	0.7617	1.0035
LPA	P08519	APOA_HUMAN Apolipoprotein(a)	0.95	0.16	-1.37	0.54	1.09	0.25	-2.14	-1.87	-2.20	0.79	0.87	1.82	-0.01	0.85	-0.13	-0.32	0.7516	1.0028
AHNAK	Q09666	AHNAK_HUMAN Neuroblast differentiation-associated protein AHNAK	-0.05	-0.52			-0.57			0.43	-0.35			0.19			-0.15	-0.32	0.7486	1.0013
ANTXR1	Q9H6X2	ANTR1_HUMAN Anthrax toxin receptor 1	-0.41		-0.38	0.03				0.33		-0.40	0.04				-0.16	-0.33	0.7409	1.0037
APOC4	P55056	APOC4_HUMAN Apolipoprotein C-IV	0.01	-0.61	-0.36	-0.42	-0.53	-0.09	-0.68	-0.13	-0.17	-0.15	0.01	0.96	0.65	-0.48	-0.15	-0.36	0.7195	1.0005
PIP	P12273	PIP_HUMAN Prolactin-inducible protein			-0.05	-0.61	-0.94					-0.31	-0.08	-0.40			-0.21	-0.45	0.6505	1.0024
CASC1	Q6TDU7	CASC1_HUMAN Cancer susceptibility candidate protein 1	0.18	0.50		0.08	-0.35	0.18		-0.80	-0.70		-1.11	0.27	0.01		-0.19	-0.46	0.6467	1.0084
FLG2	Q5D862	FILA2_HUMAN Filaggrin-2			0.17	-0.27	-0.69	-0.83	-0.37			-0.38	0.35	-0.07	0.20	0.00	-0.20	-0.50	0.6158	1.0046
APOA1	P02647	APOA1_HUMAN Apolipoprotein A-I	0.17	0.97	-0.36	-0.11	1.00	-0.80	-0.76	0.20	-0.21	-0.29	0.28	-0.03	0.16	0.03	-0.19	-0.52	0.6018	1.0069
APOB	C0JY2	C0JY2_HUMAN Apolipoprotein B (Including Ag(X) antigen)	-0.07	-0.41	1.05	-0.60	0.14	-0.04	-1.08	-0.29	0.18	0.09	-0.86	-0.79	-0.07	0.03	-0.21	-0.57	0.5702	0.9724
DCD	P81605	DCD_HUMAN Dermcidin	-0.13		-0.03	0.59			0.10	-0.05		0.25	-0.07			-0.11	-0.23	-0.57	0.5653	0.9689
SERPINF2	P08697	A2AP_HUMAN Alpha-2-antiplasmin	-0.04		-0.08		-0.55			-0.04		-0.13		-0.65			-0.26	-0.62	0.5338	0.9701
VTN	P04004	VTNC_HUMAN Vitronectin	0.25	-0.05	-0.35	0.21	-0.20	-0.19	-0.04	-0.51	-0.41	-0.52	-0.29	-0.19	-0.46	-0.28	-0.23	-0.63	0.5254	0.9837
FADS1	O60427	FADS1_HUMAN Fatty acid desaturase 1	0.21	-0.62		-0.32	-0.55	-1.08	-1.02	-0.25	-0.01		-0.28	-0.11	0.26	0.45	-0.24	-0.64	0.5239	0.9826
SLC25A14	O95258	UCP5_HUMAN Brain mitochondrial carrier protein 1	-0.13	1.31		-0.11	0.64	0.05	-2.53	-0.25			-1.87	-0.96	-2.51		-0.28	-0.69	0.4874	0.9879
HABP4	Q51V50	HABP4_HUMAN Intracellular hyaluronan-binding protein 4 OS					-0.62	-0.99	-0.55				0.29	0.09	-0.05		-0.29	-0.70	0.4823	0.9851
NDEL1	Q9GZM8	NDEL1_HUMAN Nuclear distribution protein nudE-like 1	-0.40	-0.39	-0.36					-0.07	0.27	-0.49					-0.29	-0.71	0.4767	0.9891

Gene name	Accession number ¹	Protein name	$Xq = \text{Log}_2(\text{AAA}/\text{control})$														Integration data					
			Individual comparatives														Xq	Zq	p -value	FDR		
			1	2	3	4	5	6	7	8	9	10	11	12	13	14						
RANBP2	P49792	RBP2_HUMAN E3 SUMO-protein ligase RanBP2				-0.57	-0.58	-0.59							-0.02	-0.10	0.25	-0.31	-0.74	0.4510	0.9895	
ANTXR2	P58335	ANTR2_HUMAN Anthrax toxin receptor 2	-0.56	-0.19		-0.46	-0.71	-0.46	-0.92	-0.04	0.43				-0.04	-0.51	0.26	-0.08	-0.27	-0.76	0.4487	0.9853
RELL2	Q8NC24	RELL2_HUMAN RELT-like protein 2	-0.05	-1.04	1.13				-0.90		-0.25	-1.04	0.17				0.02	-0.31	-0.81	0.4199	1.0014	
P2RY12	B2RE67	B2RE67_HUMAN cDNA, FLJ94014, highly similar to Homo sapiens purinergic receptor P2Y				-0.47	-0.84	-0.18							-0.24	-0.33	0.14	-0.34	-0.82	0.4123	1.0012	
PRSS1	P07477	TRY1_HUMAN Trypsin-1	-0.57	-0.59	-0.55					-0.09	0.09	0.01						-0.32	-0.82	0.4095	1.0131	
SERPING1	P05155	IC1_HUMAN Plasma protease C1 inhibitor	0.35	-0.91	-1.30	-0.36	-1.15	1.25	-0.42	1.15	0.40	-0.51	-0.86	-0.51	-0.06	-1.06		-0.29	-0.84	0.3983	1.0140	
SERPINA10	Q9UK55	ZPI_HUMAN Protein Z-dependent protease inhibitor				-0.09	-1.11	0.70							-0.08	-1.24	-0.81	-0.34	-0.85	0.3950	1.0154	
CLU	P10909	CLUS_HUMAN Clusterin	-0.22	-0.39	0.00	-0.17	-0.27	-0.56	-0.30	-0.04	-0.08	-0.36	-0.44	-0.36	-0.33	-0.56	-0.30	-0.90	0.3666	1.0223		
IGKC	P01834	IGKC_HUMAN Ig kappa chain C region	0.06	-0.82	0.15	-0.38	-0.40	-0.94	-0.66	-0.19	-0.57	0.59	-0.31	-0.45	-0.06	-0.35	-0.31	-0.92	0.3556	1.0186		
FGG	P02679	FIBG_HUMAN Fibrinogen gamma chain	-0.31	-1.47	-0.12	-0.10			-1.21		0.04	-0.21	0.57	-0.37		-0.35	-0.33	-0.97	0.3330	1.0028		
DSP	P15924	DESP_HUMAN Desmoplakin				-0.44	0.07	-0.15	-1.08						0.04	0.15	0.09	-1.05	-0.38	-1.03	0.3050	0.9801
2 SV	A8K479	A8K479_HUMAN cDNA FLJ77094, highly similar to Homo sapiens apolipoprotein B	-0.78	-2.14							2.02	0.49			-0.24			-0.38	-1.05	0.2936	0.9856	
APOA2	P02652	APOA2_HUMAN Apolipoprotein A-II	-0.36	-0.64	0.03	-0.55	-1.15	-1.10	-0.69	0.19	-0.20	-0.17	0.23	-0.24	-0.06	-0.13	-0.35	-1.07	0.2825	0.9994		
TRANK1	O15050	TRNK1_HUMAN TPR and ankyrin repeat-containing protein 1	-0.09	-0.80	-0.31	-0.68					-0.44	-0.20	-0.43	-0.41			-0.42	-1.14	0.2551	0.9571		
AGT	P01019	ANGT_HUMAN Angiotensinogen	-1.02	0.39	-0.26	-0.45	1.24	0.87	1.37	-0.57	0.22	-0.74	-1.46	-0.95	-0.96	0.15	-0.38	-1.17	0.2433	0.9570		
PLTP	P55058	PLTP_HUMAN Phospholipid transfer protein	-0.97	-0.40	0.19	-0.42	-0.42	-1.03	-0.40	0.16	0.40	-0.46	-0.28	-0.40	-0.31	-0.95	-0.39	-1.22	0.2214	0.9411		
APOB	P04114	APOB_HUMAN Apolipoprotein B-100	-0.14	-0.48	1.16	-0.63	-0.27	-0.14	-3.34	-0.14	0.01	0.00	-0.80	-1.12	-0.32	1.28	-0.41	-1.30	0.1939	0.9126		
IGHA1	P01876	IGHA1_HUMAN Ig alpha-1 chain C region	0.08	-1.10	0.53	-0.03	-0.28	-1.44	-0.96	-0.68	0.05	0.16	-0.40	-0.50	-0.66	-0.48	-0.43	-1.33	0.1845	0.9087		
CAMP	P49913	CAMP_HUMAN Cathelicidin antimicrobial peptide	-0.27	-0.52	-0.49	-0.96	-1.64	-2.28		-0.10	-0.50	1.21	0.36	0.00	-0.67		-0.46	-1.34	0.1804	0.9144		
C6orf211	F2Z318	F2Z318_HUMAN UPF0364 protein C6orf211	-0.18	-1.02		-0.83	0.03		-1.41	0.00	0.11		-0.78	-1.22		0.15	-0.49	-1.39	0.1652	0.8881		
FGB	P02675	FIBB_HUMAN Fibrinogen beta chain	-0.55	-1.07	0.10	-0.81	-0.86	-1.32	-1.48	0.19	-0.14	0.74	-0.55	-0.28	-0.62	-0.39	-0.49	-1.50	0.1346	0.8153		
IGHG2	P01859	IGHG2_HUMAN Ig gamma-2 chain C region	-0.18			-0.59	-0.56	-1.23	-1.67	-1.31	-0.50		-0.13	0.39	-1.02	0.36	-0.04	-0.52	-1.53	0.1263	0.8018	
DSG1	Q02413	DSG1_HUMAN Desmoglein-1		1.42	-0.01	-0.32				-1.11		0.22	-0.29	0.05		-0.64	-0.54	-1.53	0.1259	0.8193		
IGHG1	P01857	IGHG1_HUMAN Ig gamma-1 chain C region	-0.49	-1.46	0.17	-0.55	-0.60	-1.55	-1.71	-0.39	-0.26	1.44	-0.51	-0.16	-0.38	-0.35	-0.49	-1.56	0.1196	0.8078		
APOH	P02749	APOH_HUMAN Beta-2-glycoprotein 1	-0.44	-0.72	0.06	-0.53	-0.78	-0.84	-0.38	0.09	0.00	1.29	-0.43	-0.71	-0.69	-1.26	-0.56	-1.75	0.0805	0.6632		
IGLL5	B9A064	IGLL5_HUMAN Immunoglobulin lambda-like polypeptide 5	-0.12	-1.42		-0.24	-0.61	-1.10	-1.49	-0.61	-0.34		0.25	-0.98	-1.04	-0.45	-0.62	-1.90	0.0572	0.5685		
MMRN2	Q9H8L6	MMRN2_HUMAN Multimerin-2 OS					-1.15	-1.05	-0.81						-0.54	-0.15	-0.34	-0.72	-1.91	0.0562	0.5698	
C3	P01024	CO3_HUMAN Complement C3	-0.80	-0.38	-0.03	-0.61	-0.35	-0.71	-0.88	-0.63	-0.54	-0.68	-0.54	-0.77	-0.72	-7.16	-0.62	-2.04	0.0412	0.4523		
C2orf15	Q8WU43	CB015_HUMAN Uncharacterized protein C2orf15	-0.01					-1.90	-2.74	-0.02					-0.17	-0.71	-0.85	-2.23	0.0259	0.3696		
IGHM	P01871	IGHM_HUMAN Ig mu chain C region	-0.18	-0.62	-0.49	-0.13	-2.16	0.20	-1.66	-0.38	-1.18	-0.04	-0.23	-2.52	-0.06	-1.02	-0.71	-2.23	0.0256	0.3752		
TF	P02787	TRFE_HUMAN Serotransferrin	-0.32	-1.04	-0.07		-1.04	-2.17	-1.84	-0.45	-1.01	-0.36		-0.99	-0.64	-0.50	-0.84	-2.66	0.0079	0.1800		
C4BPA	P04003	C4BPA_HUMAN C4b-binding protein alpha chain	-1.50	-2.03		-1.54	-2.00		-1.21	-0.95	-1.22		-0.94	-1.36		-0.49	-1.36	-4.26	0.0000	0.0018		
A2M	P01023	A2MG_HUMAN Alpha-2-macroglobulin	-0.89		0.03		-3.22	-1.86		-1.11		-0.26		-2.77	-1.33		-1.49	-4.47	0.0000	0.0008		



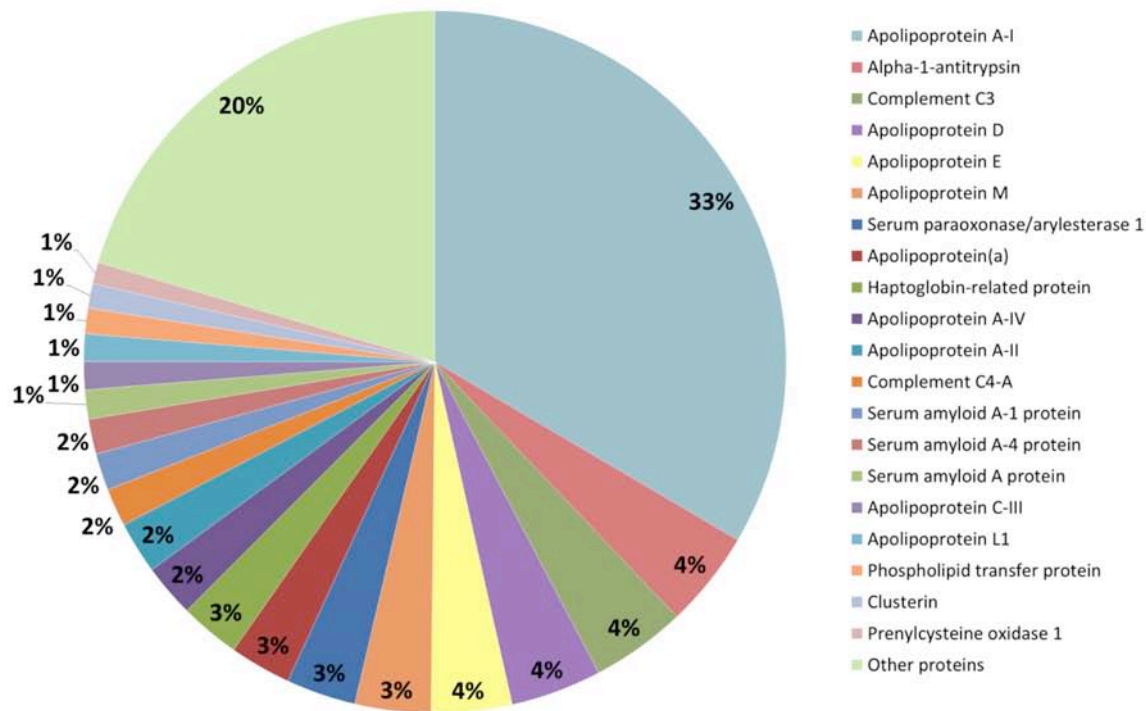
decrease in AAA

increase in AAA

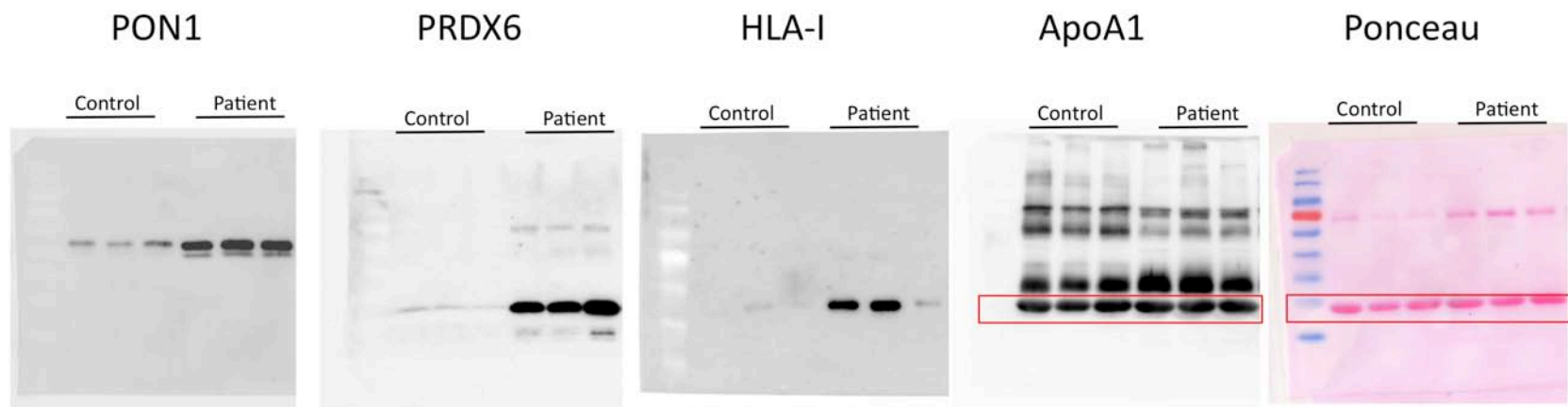
Accession number from the Uniprot database (<http://www.uniprot.org/>).

Supplementary Table S3.- Statistical parameters estimated for all the AAA/IC and C/IC comparatives from all the iTRAQ experiments

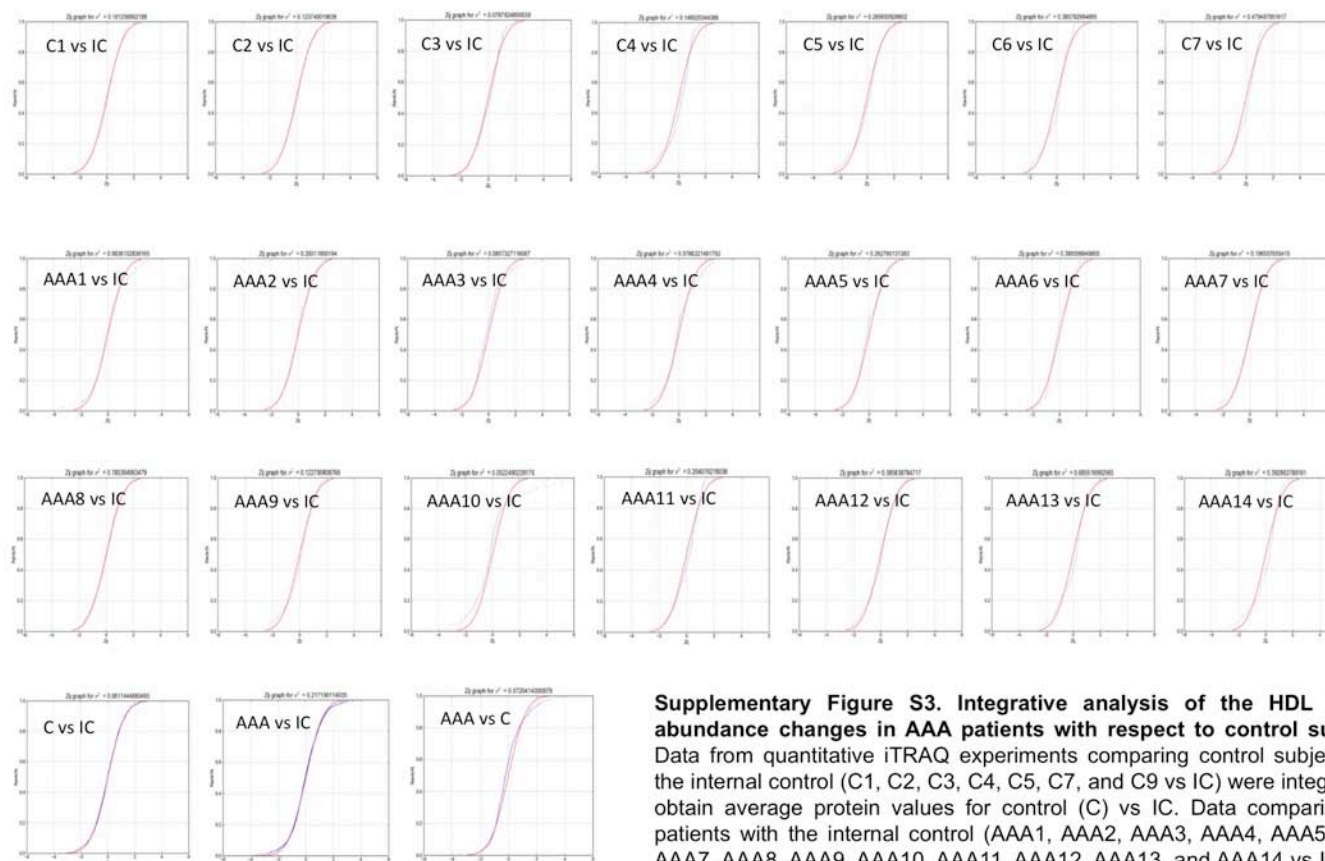
iTRAQ Experiment	Comparative	Spectrum variance (σ_s) (95% C.I.*)	Peptide variance (σ_p) (95% C.I.)	Protein variance (σ) (95% C.I.)
iTRAQ 1	116/117	0.0325 (0.029-0.036)	0.0443 (0.034-0.052)	0.1896 (0.144-0.28)
	115/117	0.0424 (0.037-0.046)	0.059 (0.047-0.078)	0.0861 (0.045-0.134)
	114/117	0.0493 (0.043-0.055)	0.0293 (0.02-0.039)	0.16 (0.079-0.199)
iTRAQ 2	116/117	0.0307 (0.029-0.035)	0.0964 (0.078-0.117)	0.1969 (0.313-0.28)
	115/117	0.045 (0.041-0.049)	0.0556 (0.043-0.069)	0.2956 (0.195-0.39)
	114/117	0.0552 (0.051-0.061)	0.0223 (0.015-0.029)	0.1193 (0.077-0.188)
iTRAQ 3	116/117	0.0392 (0.036-0.043)	0.0427 (0.033-0.056)	0.05800 (0.031-0.099)
	115/117	0.0507 (0.045-0.056)	0.0575 (0.038-0.071)	0.0855 (0.05-0.124)
	114/117	0.0777 (0.065-0.087)	0.0492 (0.015-0.063)	0.1089 (0.068-0.17)
iTRAQ 4	116/117	0.0442 (0.04-0.049)	0.03740 (0.028-0.049)	0.2132 (0.152-0.29)
	115/117	0.0507 (0.045-0.055)	0.0325 (0.025-0.044)	0.0779 (0.053-0.111)
	114/117	0.0726 (0.063-0.079)	0.0333 (0.022-0.045)	0.2295 (0.153-0.315)
iTRAQ 5	116/117	0.0768 (0.07-0.085)	0.0546 (0.039-0.07)	0.3697 (0.237-0.5)
	115/117	0.0694 (0.064-0.077)	0.0474 (0.03-0.058)	0.2343 (0.149-0.348)
	114/117	0.0816 (0.075-0.088)	0.0693 (0.054-0.088)	0.8417 (0.619-1.183)
iTRAQ 6	116/117	0.1108 (0.099-0.123)	0.1813 (0.147-0.228)	0.647 (0.424-1.007)
	115/117	0.0742 (0.068-0.081)	0.0571 (0.039-0.069)	0.3932 (0.283-0.626)
	114/117	0.0969 (0.088-0.104)	0.0365 (0.023-0.048)	0.3592 (0.249-0.524)
iTRAQ 7	116/117	0.0548 (0.051-0.06)	0.0322 (0.022-0.042)	0.4106 (0.299-0.54)
	115/117	0.0907 (0.085-0.1)	0.0638 (0.047-0.078)	0.2023 (0.126-0.313)
	114/117	0.0928 (0.084-0.102)	0.0624 (0.037-0.08)	0.4557 (0.327-0.6519)



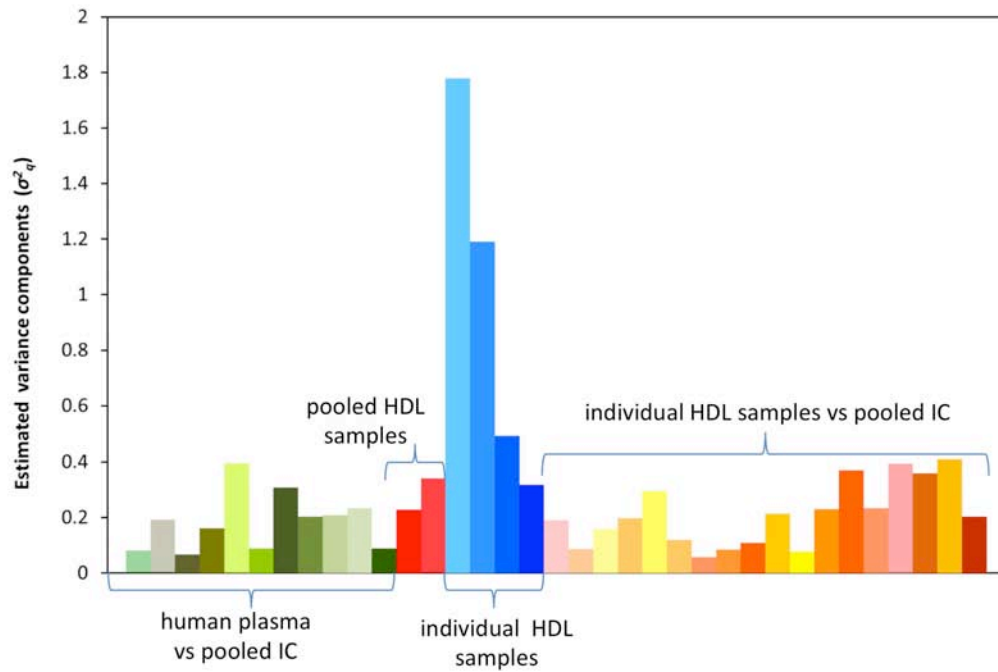
Supplementary Figure S1. Protein profile of HDL particle. Proteins were identified by LC-MS/MS in HDL samples isolated by ultracentrifugation from 7 donors and 14 AAA patients. Peptides were identified with 1% FDR and proteins identified in at least 3 experiments were counted.



Supplementary Figure S2. Western-blot of validated proteins (full-image). Representative western-blot of PON1, PRDX6, HLA-I and APOA1, and Ponceau staining of HDLs from controls and patients. Red square indicates the band of ApoA1 used for densitometric analysis (based on their molecular weight) and used as loading control (since ApoA1 is the majority protein in HDL as observed in the ponceau staining).



Supplementary Figure S3. Integrative analysis of the HDL protein abundance changes in AAA patients with respect to control subjects. Data from quantitative iTRAQ experiments comparing control subjects with the internal control (C1, C2, C3, C4, C5, C7, and C9 vs IC) were integrated to obtain average protein values for control (C) vs IC. Data comparing AAA patients with the internal control (AAA1, AAA2, AAA3, AAA4, AAA5, AAA6, AAA7, AAA8, AAA9, AAA10, AAA11, AAA12, AAA13, and AAA14 vs IC) were integrated to obtain average protein values for AAA vs IC. Finally, quantitative data for comparison of AAA vs C were obtained after integration of the comparisons of C vs IC and AAA vs IC. Plots represent the cumulative distribution of the standardized variable in logarithmic scale (\log_2 -ratios) at the different level of the integration data.



Supplementary Figure S4. Biological variability of individual and pooled samples in different experiments. Individual human plasma samples from AAA patients and control subjects were compared with a pooled internal control in different iTRAQ experiments (Burillo E, Lindholt JS, Molina-Sánchez P, et al. *Thromb Haemost.* 2015 May 26;113(6):1335-46) (green). Pooled HDL samples from CAD patients before and after angioplasty were compared in O16/O18 experiments (red). Individual HDL samples from two CAD patients before and after angioplasty were compared in different iTRAQ experiments (blue) (Jorge I, Burillo E, J. *Proteomics*, 2014). In the current iTRAQ study, individual HDL samples from AAA patients and control subjects were compared with the pooled internal control (yellow).