

Supplementary Tables

Supplementary Table 1: Plasma proteins that were expressed differently between evening (E) and morning (M) samples in ten healthy participants. The morning and evening values are Label free quantitation (LFQ) intensities as obtained through utilized software (MaxQuant) and are expressed as median (min-max). The important proteins (i.e. proteins with a variable of importance (VIP) above 1.0) were identified using orthogonal partial least squares discriminant analysis (OPLS-DA). In order to facilitate the understanding of the multivariate analysis we also made Wilcoxon paired test for the variables with VIP>1.0; # indicates not significance $p > 0.05$.

UniProt	Protein name	Morning Intensity x 10 ⁶	Evening Intensity x 10 ⁶	VIP	E ver M	P- value
P05160	Coagulation factor XIII B chain	0 (0-0)	2.26 (1.58–3.11)	1.80	↑	2.87E-05
P08603	Complement factor H	103.00 (90.10-143.00)	186.50 (154.00–203.00)	1.77	↑	0.0001
P04003	C4b-binding protein alpha chain	41.40 (33.00-54.30)	72.35 (61.70-83.10)	1.71	↑	0.0001
P02774	Vitamin D-binding protein	141.00 (122.00-189.00)	234.50 (183.00-276.00)	1.65	↑	0.0001
P00734	Prothrombin	45.00 (34.10-61.20)	71.65 (61.40 (92.50)	1.64	↑	0.0001
P00747	Plasminogen	18.70 (13.90-27.00)	40.15 (23.00-58.80)	1.63	↑	0.0002
P07357	Complement component C8 alpha chain	3.83 (3.01-5.30)	5.94 (4.41-6.55)	1.62	↑	0.0002
P02753	Retinol-binding protein 4	5.72 (2.37-8.89)	11.65 (5.46-13.10)	1.60	↑	0.0009
P02760	Protein AMBP	12.70 (10.40-19.50)	19.85 (15.90-23.70)	1.58	↑	0.0004

P01008	Antithrombin-III	80.00 (71.50-87.10)	67.00(60.00-74-50)	1.56	↓	0.0002
P43652	Afamin	18.40 (10.90-24.80)	32.10 (21.20-43.20)	1.55	↑	0.0002
Q16610	Extracellular matrix protein 1	0.00 (0.00-1.83)	1.71 (1.09-2.21)	1.55	↑	0.0003
P00742	Coagulation factor X	0.00 (0.00-1.14)	1.48 (1.15-1.76)	1.55	↑	8.93E-05
P36955	Pigment epithelium-derived factor	4.31 (2.65-5.21)	2.47 (1.78-3.43)	1.55	↓	0.0004
P02787	Serotransferrin	1610.00 (1240.00-2120.00)	2450.00 (1790.00-3120.00)	1.54	↑	0.0002
P19827	Inter-alpha-trypsin inhibitor heavy chain H1	89.70 (80.60-103.00)	69.85 (58.70-86.60)	1.52	↓	0.0003
P08697	Alpha-2-antiplasmin	24.30 (19.30-28.40)	18.05 (13.60-23.40)	1.52	↓	0.0003
Q03591	Complement factor H-related protein 1	1.77 (0.00-4.77)	6.15 (2.39-9.84)	1.52	↑	0.0005
P06681	Complement C2	2.41 (2.07-2.82)	1.85 (1.45-2.25)	1.50	↓	0.0002
P19823	Inter-alpha-trypsin inhibitor heavy chain H2	183.00 (145.00-226.00)	138.50 (126.00-172.00)	1.48	↓	0.0004
P02671	Fibrinogen alpha chain	1050.00 (673.00-1270.00)	725.50 (574.00-900.00)	1.47	↓	0.002
Q14520	Hyaluronan-binding protein 2	0.00 (0.00-1.37)	1.99 (0.00-3.45)	1.46	↑	0.002
O75882	Attractin	0.88 (0.00-1.71)	2.07 (1.70-3.52)	1.44	↑	0.0001
P27918	Properdin	0.00 (0.00-0.98)	1.17 (0.78-1.46)	1.42	↑	0.0005
P06396	Gelsolin	58.10 (41.90-75.40)	45.25 (35.60-53.80)	1.38	↓	0.001
O43866	CD5 antigen-like	8.46 (3.83-21.50)	24.05 (9.31-50.20)	1.38	↑	0.002
O14791	Apolipoprotein L1	9.81 (7.23-13.60)	6.70 (4.38-9.42)	1.37	↓	0.0004

Q14624	Inter-alpha-trypsin inhibitor heavy chain H4	93.60 (68.20-119.00)	74.20 (48.30-88.00)	1.36	↓	0.002
Q96PD5	N-acetylmuramoyl-L-alanine amidase	6.91 (4.92-8.92)	8.54 (7.01-10.70)	1.35	↑	0.002
P00740	Coagulation factor IX	0.00 (0.00-0.57)	0.45 (0.00-0.58)	1.34	↑	0.005
P00751	Complement factor B	51.70 (39.10-70.00)	39.75 (26.50-49.30)	1,32	↓	0.001
P01031	Complement C5	23.90 (19.90-29.20)	20.95 (17.90-22.00)	1.32	↓	0.004
P02652	Apolipoprotein A-II	168.00 (128.00-262.00)	117.00 (70.90-158.00)	1.31	↓	0.001
Q06033	Inter-alpha-trypsin inhibitor heavy chain H3	3.93 (2.48-5.87)	3.17 (0.00-3.47)	1.28	↓	0.005
P35542	Serum amyloid A-4 protein	4.89 (0.00-6.73)	1.97 (0.00-2.81)	1.28	↓	0.003
P05452	Tetranectin	2.12 (0.00-2.89)	2.99 (2.04-4.86)	1.27	↑	0.001
P02765	Alpha-2-HS-glycoprotein	97.10 (72.50-126.00)	122.50 (102.20-157.00)	1.25	↑	0.006
P10643	Complement component C7	6.46 (4.70-7.98)	7.51 (5.72-11.10)	1.25	↑	0.006
P35858	Insulin-like growth factor-binding protein	3.56 (0.00-5.97)	1.78 (0.89-2.60)	1.25	↓	0.001
P51884	Lumican	6.13 (4.32-7.78)	4.71 (2.95-5.53)	1.23	↓	0.005
P25311	Zinc-alpha-2-glycoprotein	23.50 (12.40-30.90)	28.50 (19.30-36.20)	1.21	↑	0.024
P04217	Alpha-1B-glycoprotein	123.00 (98.40-150.00)	105.00 (93.20-111.00)	1.20	↓	0.007
P02675	Fibrinogen beta chain	1100.00 (781.00-143.00)	934.00 (709.00-1120.00)	1.19	↓	0.034

P0DOX2	Immunoglobulin alpha-2 heavy chain	14.90 (9.58-28.60)	31.90 (7.56-52.50)	1.18	↑	0.007
P02749	#Beta-2-glycoprotein 1	31.90 (21.20-49.00)	39.55 (14.80-49.70)	1.17	↑	>0.05
P20851	C4b-binding protein beta chain	0.00 (0.00-1.11)	1.18 (0.00-1.59)	1.16	↑	0.006
P0DOY3	Immunoglobulin lambda constant 3	54.50 (28.60-88.80)	36.35 (17.20-50.90)	1.15	↓	0.009
P0DOX7	Immunoglobulin kappa light chain	146.00 (66.70-254.00)	195.00 (90.50-375.00)	1.13	↑	0.024
P01019	Angiotensinogen	30.60 (22.30-35.60)	27.05 (19.80-30.60)	1.13	↓	0.007
P00450	Ceruloplasmin	312.00 (257.00-415.00)	274.00 (218.00-317.00)	1.12	↓	0.029
P00736	#Complement C1r subcomponent	14.10 (10.20-16.50)	15.95 (13.70-19.10)	1.12	↑	>0.05
P01591	Immunoglobulin J chain	13.30 (0.00-23.60)	18.60 (9.54-37.30)	1.09	↑	0.049
P05156	Complement factor I	5.75 (4.80-9.22)	4.83 (3.64-7.10)	1.08	↓	0.035
P01024	Complement C3	1240.00 (1110.00 - 1470.00)	1140.00 (1010.00-1280.00)	1.08	↓	0.041
P0C0L5	#Complement C4-B	222.00 (127.00-352.00)	165.00 (89.20-248.00)	1.07	↓	>0.05
P23142	Fibulin-1	2.03 (1.69-2.96)	2.69 (1.95-3.39)	1.07	↑	0.009
P10909	Clusterin	57.60 (47.00-73.60)	47.35 (40.40-61.50)	1.07	↓	0.017
P01619	#Immunoglobulin kappa variable 3-20	3.04 (0.00-8.15)	2.46 (1.69-6.04)	1.06	↑	>0.05
P01764	#Immunoglobulin heavy variable 3-23	4.94 (0.00-8.73)	7.08 (4.93-11.30)	1.05	↑	>0.05
P01834	Immunoglobulin kappa constant	47.90 (24.50-60.30)	31.75 (23.60-84.50)	1.05	↓	0.041

O95445	Apolipoprotein M	4.24 (2.60-5.97)	3.74 (2.44-4.50)	1.04	↓	0.017
P01871	#Immunoglobulin heavy constant mu	425.00 (258.00-950.00)	472.00 (275.00-840.00)	1.03	↑	>0.05
P06312	#Immunoglobulin kappa variable 4-1	4.84 (3.36-10.30)	4.17 (3.45-8.63)	1.03	↓	>0.05
P05543	Thyroxine-binding globulin	3.74 (2.01-5.51)	2.89 (1.47-3.77)	1.01	↓	0.041

Supplementary Table 2A: Enrichment analysis of up-regulated GO biological processes.

#Pathway ID	Pathway description	Observed gene count	Matching proteins in network
GO.0072376	protein activation cascade	12	APOH,C1R,C4BPA,C4BPB,C8A,CFH,CFHR1,CFP,F10,F2,F9,FBLN1
GO.0006956	complement activation	7	C1R,C4BPA,C4BPB,C8A,CFH,CFHR1,CFP
GO.1903034	regulation of response to wounding	11	AHSG,APOH,C4BPA,C4BPB,C8A,CFH,CFP,F2,PGLYRP2,PLG,SERPINF2
GO.0006950	response to stress	20	AHSG,APOH,ATRN,C1R,C4BPA,C4BPB,C8A,CD5L,CFH,CFP,ECM1,F10,F13B,F2,F9,FBLN1,IGJ,PGLYRP2,PLG,SERPINF2
GO.0030162	regulation of proteolysis	12	AHSG,AMBP,C4BPA,C4BPB,C8A,CFH,CFP,CLEC3B,ECM1,F2,FBLN1,SERPINF2
GO.0030449	regulation of complement activation	5	C4BPA,C4BPB,C8A,CFH,CFP
GO.0006952	defense response	14	AHSG,ATRN,C1R,C4BPA,C4BPB,C8A,CD5L,CFH,CFP,ECM1,F2,IGJ,PGLYRP2,SERPINF2
GO.0050878	regulation of body fluid levels	11	APOH,C4BPB,F10,F13B,F2,F9,FBLN1,GC,PLG,SERPINF2,TF
GO.0050727	regulation of inflammatory response	7	AHSG,C4BPA,C4BPB,C8A,CFH,CFP,PGLYRP2

GO.0002253	activation of immune response	8	C1R,C4BPA,C4BPB,C8A,CFH,CFHR1,CFP,PGLYRP2
GO.0080134	regulation of response to stress	12	AHSG,AMBP,APOH,C4BPA,C4BPB,C8A,CFH,CFP,F2,PLG,SERPINF2,TF
GO.0006958	complement activation, classical pathway	4	C1R,C4BPA,C4BPB,C8A
GO.0002455	humoral immune response mediated by circulating immunoglobulin	4	C1R,C4BPA,C4BPB,C8A
GO.0045861	negative regulation of proteolysis	7	AHSG,AMBP,C4BPA,C4BPB,ECM1,F2,SERPINF2
GO.0048585	negative regulation of response to stimulus	11	AHSG,AMBP,APOH,C4BPA,C4BPB,ECM1,F2,FBLN1,PGLYRP2,PLG,SERPINF2
GO.0050896	response to stimulus	22	AHSG,APOH,ATRN,C1R,C4BPA,C4BPB,C8A,CD5L,CFH,CFHR1,CFP,CLEC3B,F10,F13B,F2,F9,FBLN1,GC,IGJ,PGLYRP2,PLG,RBP4
GO.0006957	complement activation, alternative pathway	3	C8A,CFH,CFP
GO.0002376	immune system process	12	AZGP1,C1R,C4BPA,C4BPB,C8A,CFH,CFHR1,CFP,F2,IGJ,PGLYRP2,TF
GO.0002682	regulation of immune system process	10	AMBP,C1R,C4BPA,C4BPB,C8A,CFH,CFHR1,CFP,ECM1,RBP4
GO.0019538	protein metabolic process	16	AMBP,APOH,C1R,C4BPA,C4BPB,C8A,CFH,CFHR1,CFP,F10,F2,F9,FBLN1,HABP2,PLG,TF
GO.0050777	negative regulation of immune response	4	AMBP,C4BPA,C4BPB,PGLYRP2
GO.0045087	innate immune response	8	C1R,C4BPA,C4BPB,C8A,CFH,CFP,IGJ,PGLYRP2
GO.0051246	regulation of protein metabolic process	12	AHSG,AMBP,C4BPA,C4BPB,C8A,CFH,CFP,CLEC3B,ECM1,F2,SERPINF2,TF
GO.0006953	acute-phase response	3	AHSG,F2,SERPINF2

Supplementary Table 2B: Enrichment analysis of down-regulated GO biological processes.

#Pathway ID	Pathway description	Observed gene count	Matching proteins in network
GO.0052548	regulation of endopeptidase activity	11	AGT,C3,C5,GSN,ITIH1,ITIH2,ITIH3,ITIH4,SERPINA7,SERPINC1,SERPINF1
GO.0051248	negative regulation of protein metabolic process	12	AGT,C3,C5,CLU,FGA,ITIH1,ITIH2,ITIH3,ITIH4,SERPINA7,SERPINC1,SERPINF1
GO.0051246	regulation of protein metabolic process	15	AGT,APOA2,C7,CFI,CLU,FGA,FGB,GSN,ITIH1,ITIH2,ITIH3,ITIH4,SERPINA7,SERPINC1,SERPINF1
GO.0050727	regulation of inflammatory response	6	AGT,C5,C7,CFI,SERPINC1,SERPINF1
GO.0006954	inflammatory response	6	APOA2,C3,C5,FGA,ITIH4,SAA4
GO.0080134	regulation of response to stress	10	AGT,C5,C7,CFI,CLU,FGA,FGB,GSN,SERPINC1,SERPINF1
GO.0010001	glial cell differentiation	3	AGT,CLU,GSN
GO.0002526	acute inflammatory response	4	APOA2,FGA,ITIH4,SAA4
GO.0001819	positive regulation of cytokine production	6	AGT,APOA2,C3,C5,CLU,LUM
GO.0006950	response to stress	13	AGT,APOA2,APOL1,C5,C7,CFI,CLU,FGA,FGB,GSN,ITIH4,SAA4,SERPINC1
GO.0009605	response to external stimulus	10	AGT,APOA2,C5,CLU,FGA,FGB,GSN,SAA4,SERPINA7,SERPINC1
GO.0045765	regulation of angiogenesis	4	AGT,C3,C5,SERPINF1
GO.0050776	regulation of immune response	6	APOA2,C3,C5,C7,CFI,CLU
GO.0002682	regulation of immune system process	7	APOA2,C3,C5,C7,CFI,CLU,GSN

Supplementary Table 3: The concentrations (pg/ml) of 71 cytokines, chemokines and growth factors in plasma collected in morning and evening from ten healthy subjects.

	Morning			Evening		
	Median	Minimum	Maximum	Median	Minimum	Maximum
CTACK	1071.36	836.58	2223.15	1324.36	821.00	3145.00
ENA_78	4671.70	393.20	8476.69	5712.13	660.04	8946.85
Eotaxin	129.32	77.25	301.42	165.25	84.58	243.44
Eotaxin_2	1387.45	451.77	3661.53	1769.06	637.30	4392.54
Eotaxin_3	33.87	13.73	53.48	29.51	11.84	64.03
EPO	141.88	62.57	1174.68	183.06	80.62	1257.92
FLT3L	216.01	136.57	274.54	211.96	104.87	241.58
Fractalkine	16973.88	12586.13	20769.81	17227.13	11847.47	20265.35
G-CSF	15.17	8.47	23.50	14.48	9.97	27.82
GRO_alpha	2669.61	138.00	5310.98	3243.40	171.94	6022.01
I_309	85.43	31.94	100.90	84.20	25.65	112.18
IFN_α2a	0.39	0.12	0.95	0.35	0.03	1.12
IFN_β	27.3	2.00	57.00	37.81	6.63	58.00
IFN_γ	14.55	6.98	34.55	10.71	6.88	467.81
IL_10	0.50	0.22	1.36	0.50	0.25	1.06
IL_12_IL_23p40	208.79	123.47	441.35	213.55	116.97	444.69
IL_12p70	0.55	0.11	1.22	0.42	0.07	1.39
IL_13	6.10	1.56	8.30	6.00	1.35	12.39
IL_15	4.76	3.34	9.19	5.06	3.74	8.42
IL_16	960.83	296.46	1954.09	915.46	313.08	3041.26
IL_17A_F	1.20	0.00	3.00	1.79	0.84	5.99
IL_17B	3.28	1.82	7.63	4.41	1.75	7.89
IL_17C	7.87	2.22	25.14	7.96	3.85	16.49
IL_17D	48.55	22.95	93.28	57.72	19.20	89.63
IL_17E_IL_25	1.08	0.37	3.11	1.33	0.56	2.48
IL_17F	510.28	145.06	1167.63	570.52	261.55	1396.06
IL_18	626.32	380.92	2056.05	788.88	371.23	1998.29
IL_1RA	272.03	152.55	2431.11	355.71	225.34	874.54
IL_1α	17.04	3.25	314.87	15.41	4.72	286.42
IL_1β	0.40	0.07	0.49	0.30	0.01	0.78
IL_2	0.18	0.01	0.45	0.22	0.05	0.36
IL_21	3.18	1.79	9.32	3.90	1.89	6.90
IL_22	0.53	0.20	1.48	0.59	0.34	0.91
IL_23	3.17	1.60	9.31	4.09	2.73	7.35

IL_27	652.70	495.95	861.73	810.45	475.20	1123.87
IL_29_IFN_L1	3.74	1.55	6.05	3.17	1.60	4.29
IL_2Ra	1599.72	1062.74	4103.15	1968.45	950.77	4065.81
IL_3	49.94	4.56	123.12	67.51	8.03	132.39
IL_31	12.56	8.06	36.42	19.42	10.36	30.82
IL_33	0.29	0.03	1.59	0.59	0.05	1.91
IL_4	0.58	0.00	1.00	0.86	0.33	1.4
IL_5	0.32	0.1	1.19	0.51	0.16	1.26
IL_6	0.79	0.12	2.27	1.22	0.00	3.00
IL_7	21.10	1.53	37.66	25.63	3.61	30.38
IL_8	17.47	4.82	24.84	18.22	6.13	28.33
IL_9	0.99	0.50	1.40	1.09	0.41	1.84
IP_10	448.05	285.74	843.79	442.09	213.24	1818.76
I_TAC	132.29	28.10	369.16	149.05	28.55	1105.48
MCP_1	240.88	194.03	517.01	250.29	181.56	557.87
MCP_2	47.41	25.63	75.43	48.91	22.57	436.32
MCP_3	44.42	8.20	930.07	48.47	10.10	1171.00
MCP_4	113.93	53.07	245.07	123.44	54.17	229.52
M_CSF	19.02	14.27	23.85	20.67	11.89	29.66
MDC	1736.06	1385.26	3045.44	1884.10	1544.62	2977.12
MIF	161920.76	93364.86	180456.58	174678.48	127976.78	206584.12
MIP_1α	34.73	21.60	65.39	34.85	11.36	45.96
MIP_1β	106.08	64.90	223.71	98.16	60.17	206.40
MIP_3α	15.47	7.04	60.96	12.65	6.89	31.41
MIP_3β	291.95	215.98	396.47	286.16	198.17	437.64
MIP_5	426118.64	217771.00	22753328.00	76619.47	42236.64	619339.92
SDF_1α	2035.91	1083.92	2331.37	2257.73	1524.63	3054.54
TARC	301.58	50.84	1040.84	402.88	57.69	1161.08
TNF_α	7.41	5.57	9.27	7.29	3.97	11.22
TNF_β	0.63	0.26	13.64	0.53	0.37	1.28
TPO	752.19	335.46	1189.07	853.11	497.29	1270.73
TRAIL	356.32	274.12	456.86	342.97	213.79	771.13
TSLP	1.30	0.71	4.71	1.32	0.73	3.46
VEGF_A	141.93	43.20	364.59	149.26	71.12	331.48
YKL_40	44467.06	33997.87	52917.33	43607.80	34863.73	55586.61