

***Characterizing of the Bionano Interface and Mapping Extrinsic Interactions of the
Hard Corona of Nanomaterials***

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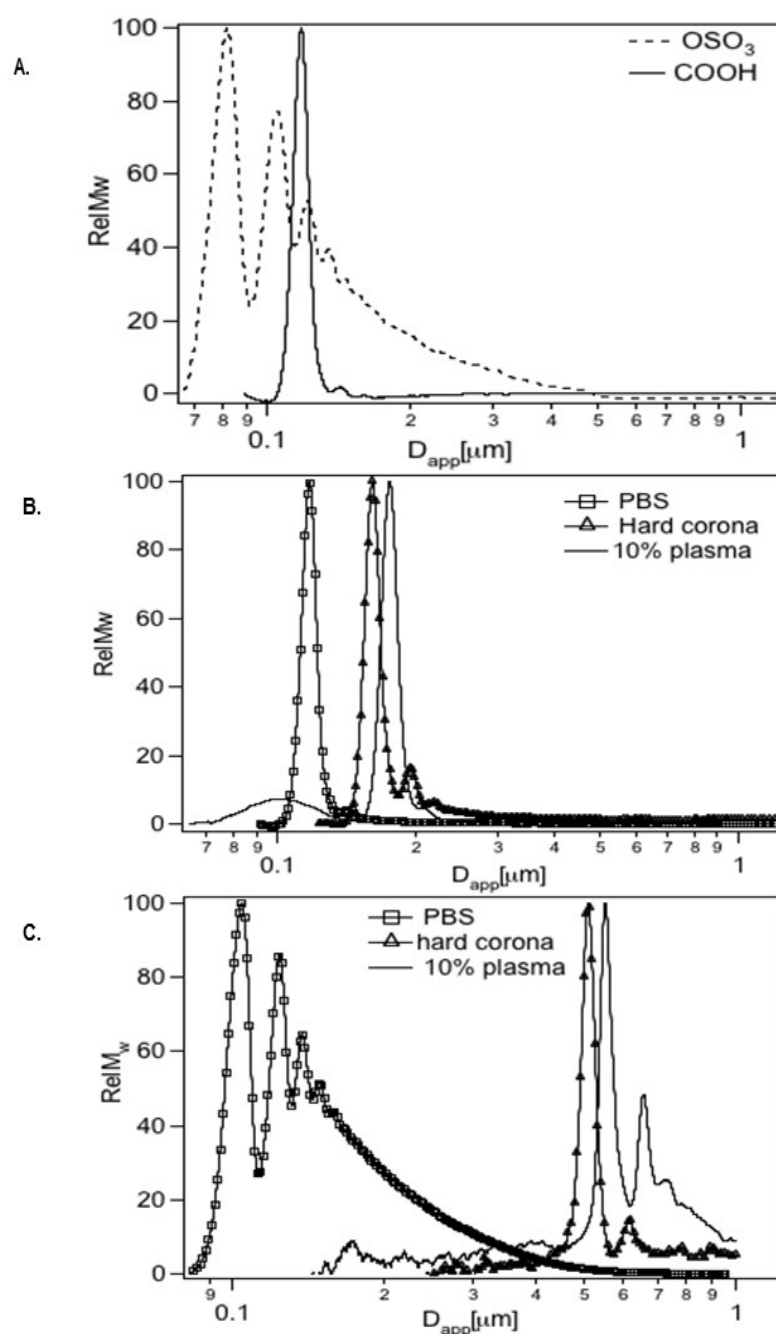


Figure S1. Comparison of 100 nm polystyrene nanoparticles in phosphate buffer and in 10% plasma using DCS. **(A)** Carboxylated and sulphonated nanoparticles in phosphate buffer **(B)** Carboxylated nanoparticles in PBS, hard corona from 10% plasma and in presence of 10% plasma **(C)** Sulphonated nanoparticles in phosphate buffer, hard corona from 10% plasma and in presence of 10% plasma.

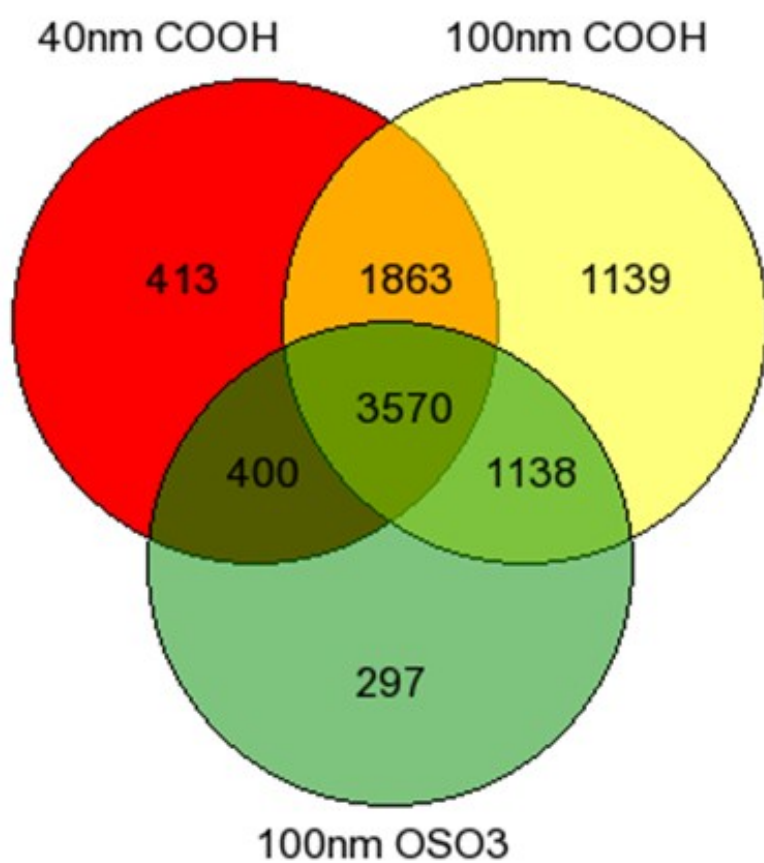


Figure S2. Comparative analysis of microarray interactomes for polystyrene nanoparticles incubated in the absence of human plasma proteins in physiological conditions.

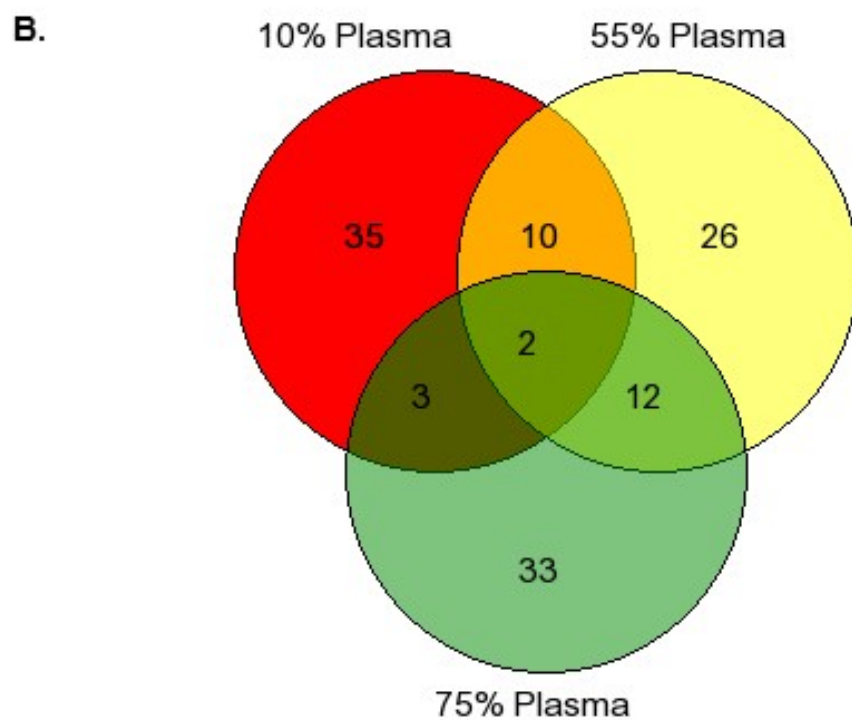
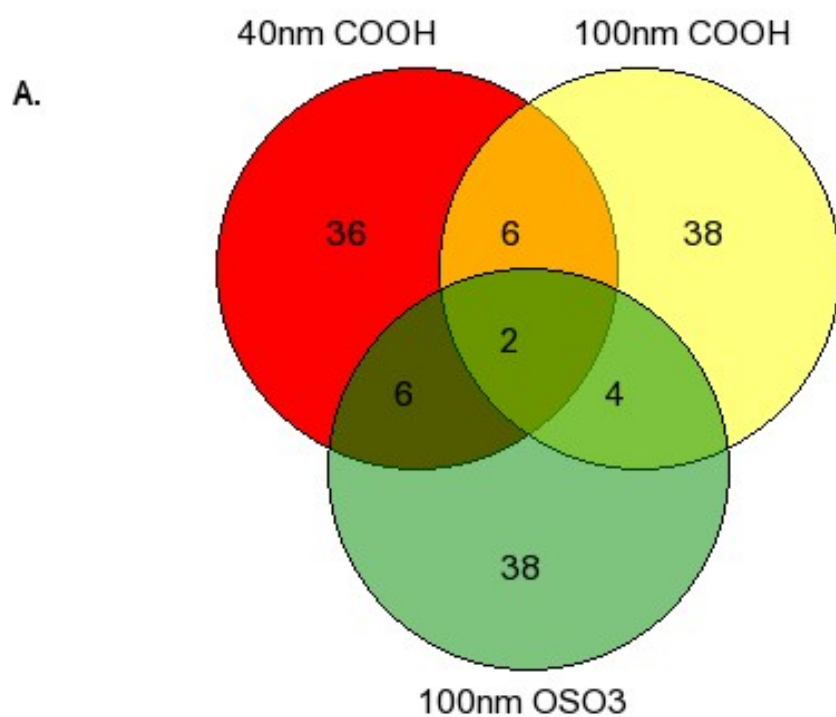


Figure S3 Comparison of the top 50 protein signals from microarray studies. **(A)** Comparison of 10% Plasma top 50 proteins from 40 nm COOH, 100 nm COOH and 100 nm OSO3 **(B)** 40 nm COOH Venn diagram of 10%, 55% and 75% plasma top 50 proteins

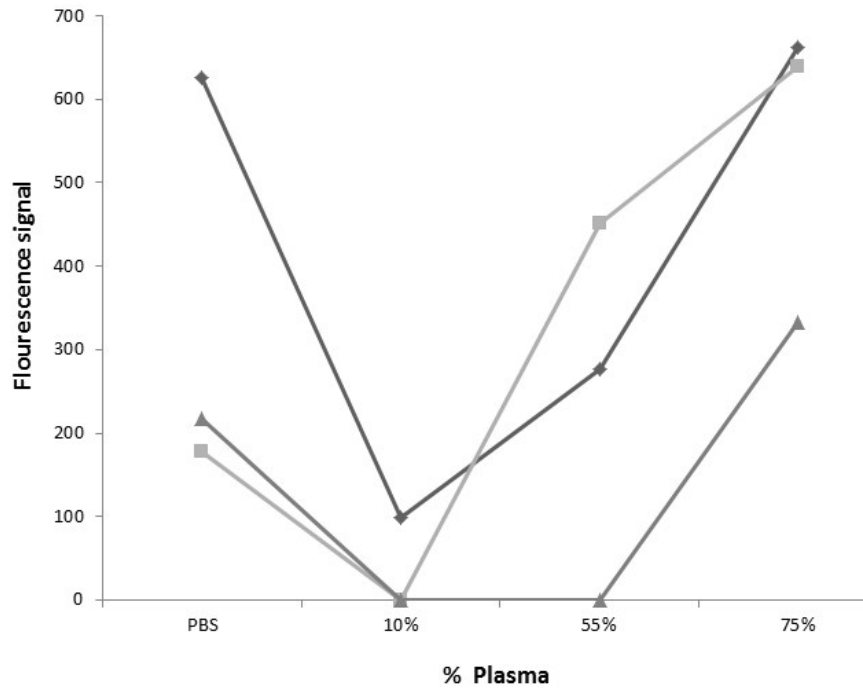


Figure S4. Fluorescence signal intensities for selected interacting arrayed proteins with 40nm PSCOOH NP in plasma free and increasing plasma conditions (x-axis). (□) phosphatidylinositol binding clathrin assembly protein (PICALM), (◇) protein tyrosine phosphatase, non-receptor type 1 (PTPN1), (△) Fibronectin type-III domain-containing protein 3A (FNDC3A).

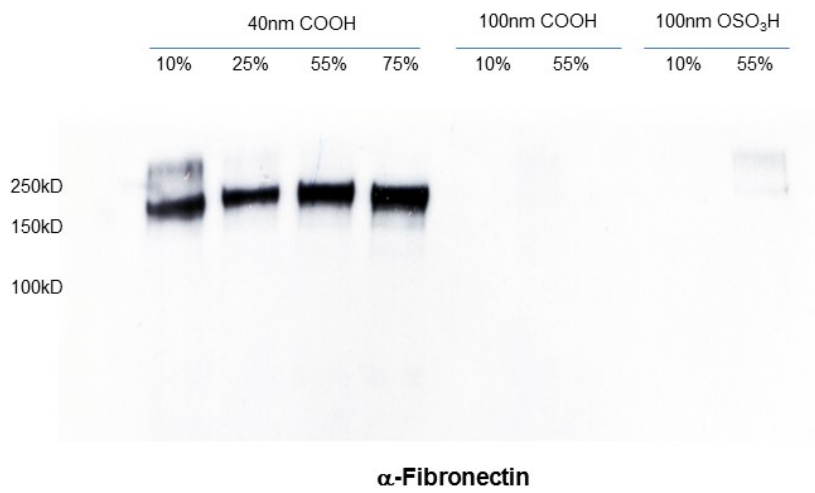


Figure S5. Anti-fibronectin Western blot of the hard corona proteins from 40 nm and 100 nm polystyrene plasma complexes as a function of human plasma concentration.

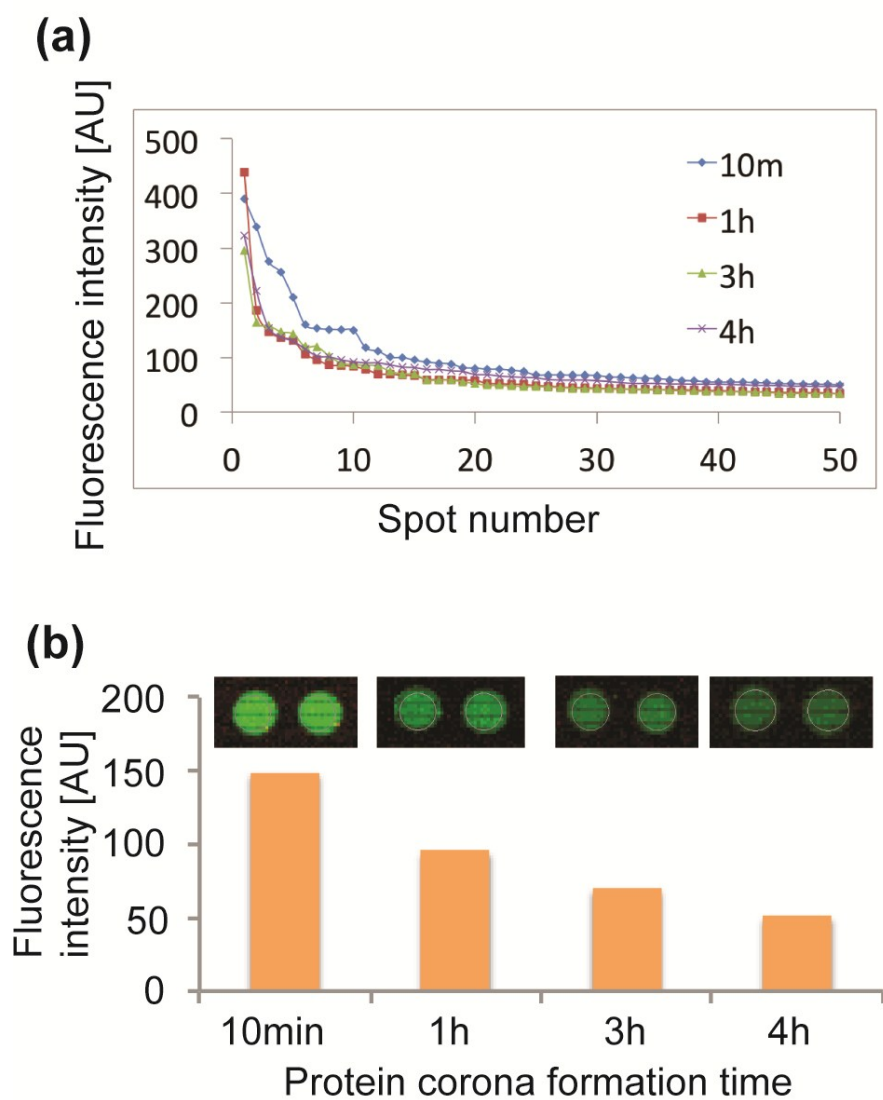


Figure S6. a) Ranked fluorescence intensities for top 50 strongest positive hits on the arrays incubated with NPs exposed for human plasma for varying times. b) Comparison of FND3C protein spots on different “timepoints” arrays, and their fluorescence intensity.

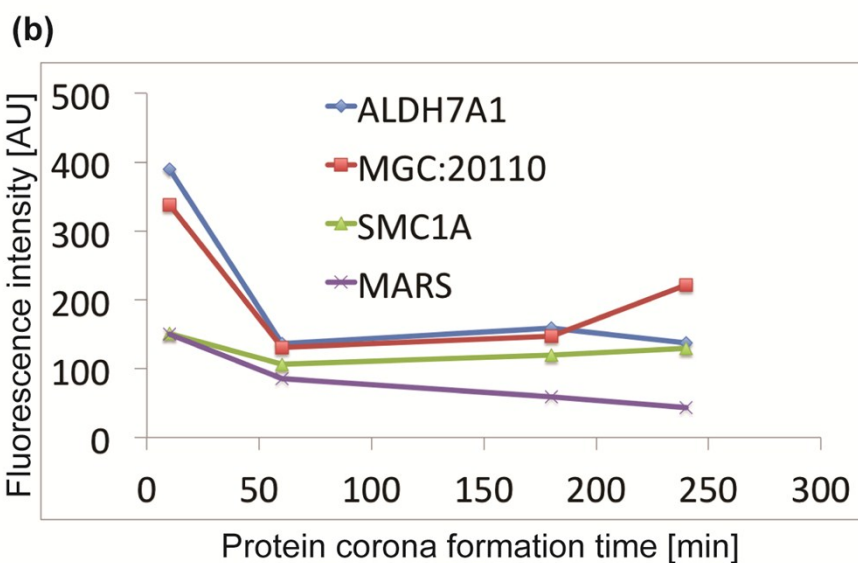
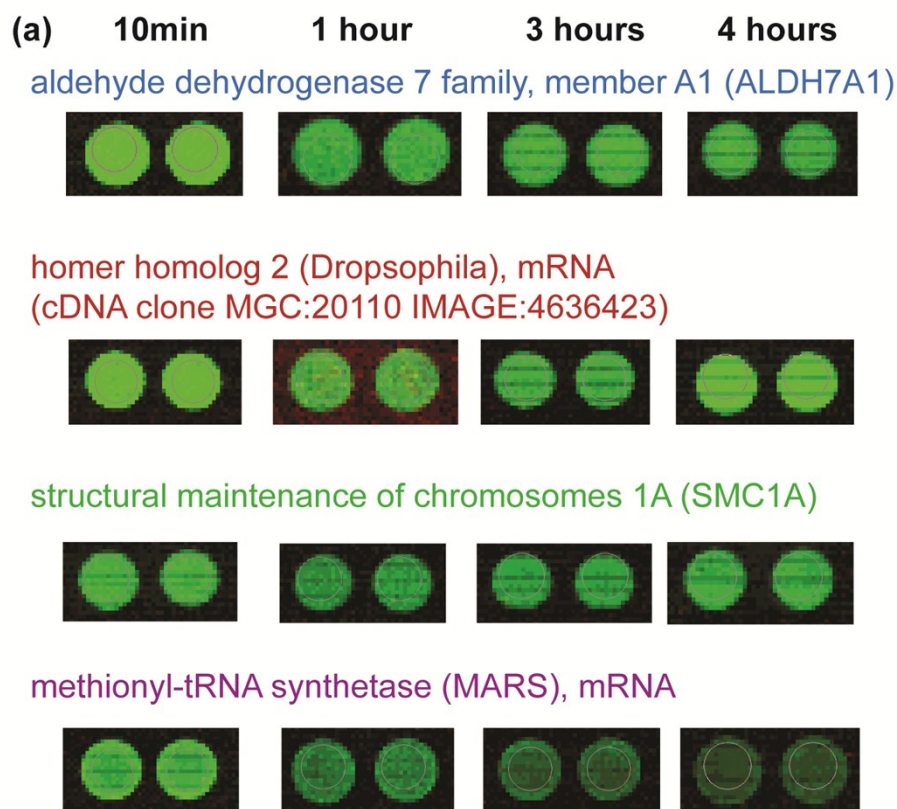


Figure S7. Examples of fluorescence intensities of positive hits for NPs array interaction, and their evolution as a function of NPs exposition time to human plasma. a) Screen shots of exemplary spots on the array corresponding belonging to strong binders of NPs. b) Comparison of NPs binding to exemplary proteins on the array as a function of NPs exposition to human plasma.

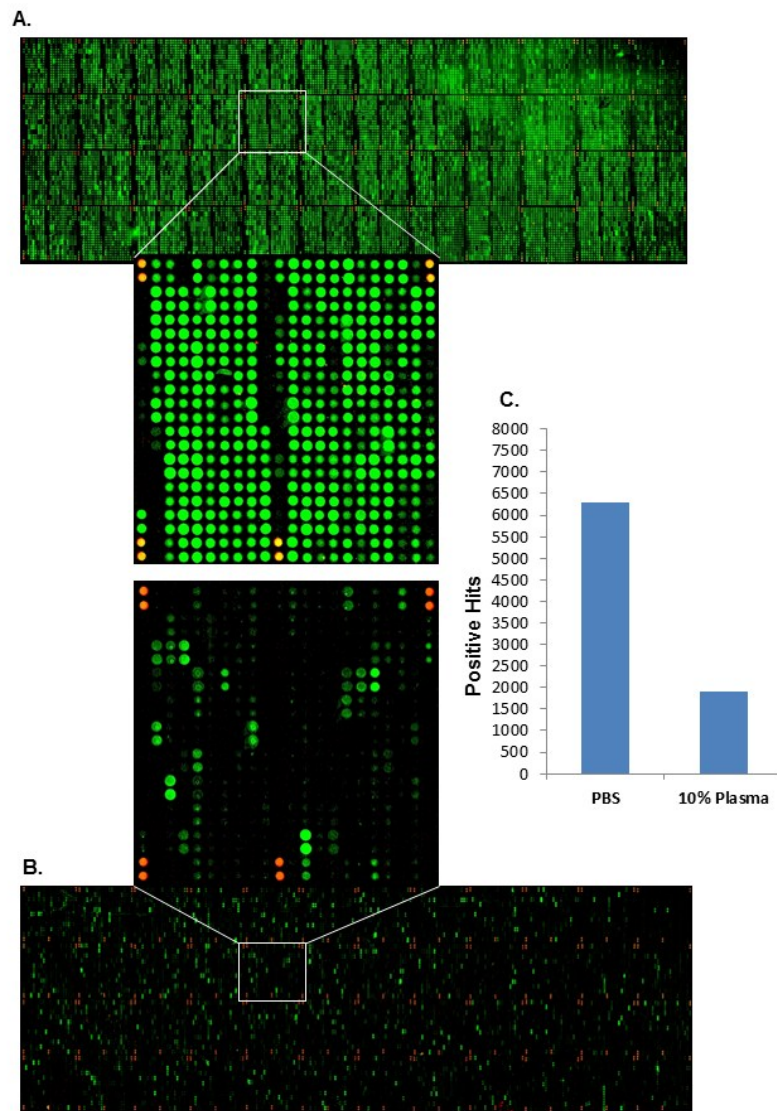


Figure S8. 40 nm PSCOOH NPs incubated on human protein microarrays. a) Image of the complete Protoarray incubated with 16 $\mu\text{g}/\text{ml}$ NPs in PBS with subarray # 19 magnified. b) Image of the complete Protoarray incubated with 16 $\mu\text{g}/\text{ml}$ NPs in 10% plasma with subarray # 19 magnified. c) Total numbers of positive signal pairs in each condition

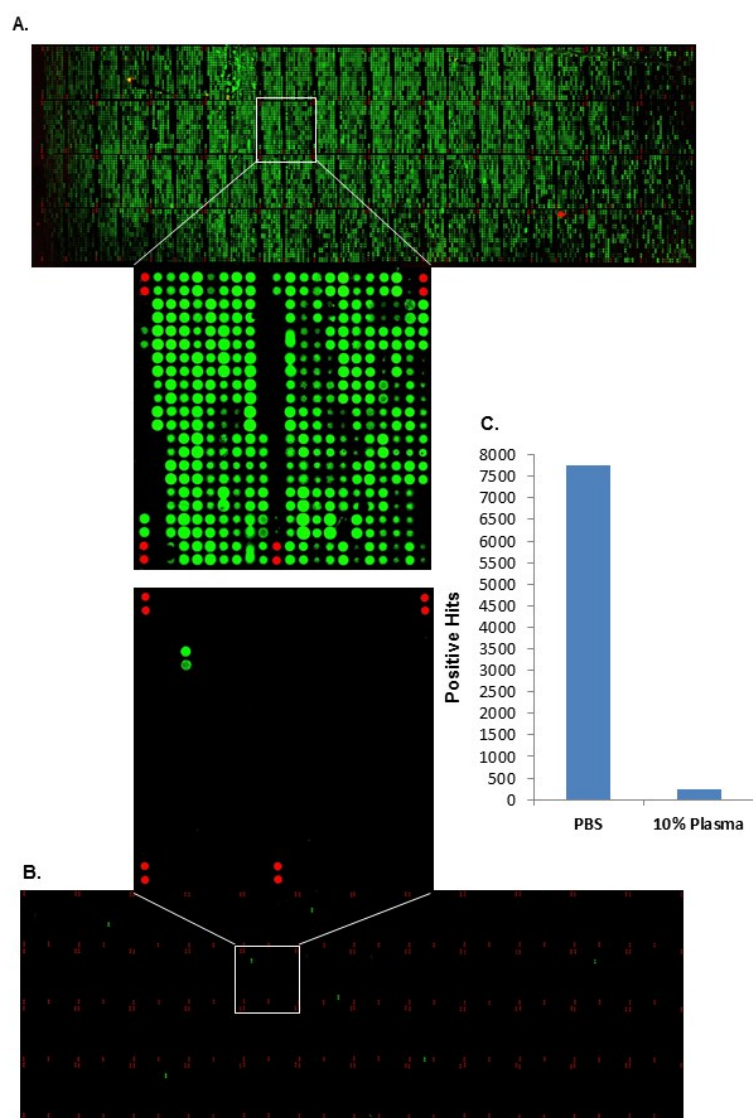


Figure S9. 100 nm PSCOOH NPs incubated on human protein microarrays. a) Image of the complete Protoarray incubated with 40 $\mu\text{g/ml}$ nanoparticles in PBS with subarray # 19 magnified. b) Image of the complete Protoarray incubated with 40 $\mu\text{g/ml}$ NPs in 10% plasma subarray # 19 magnified. c) Total numbers of positive signal pairs in each condition.

Table S1. DLS and Z-potential results of 100 nm PSCOOH, 100 nm PSOSO₃ and 40 nm PSCOOH NPs in PBS, hard corona complexes (HC) and in 10% human plasma (HP).

NPs	D _H ^a [nm]	PDI ^b	<D _H > ^c [nm]	Z-potential [mV]
PSCOOH-100nm	116.3±2.0	0.05	123.8±1.8	-53.2±1.2
PSOSO ₃ -100nm	130.0±1.7	0.09	140.1±1.7	-61.2±2.1
PSCOOH-40nm	73.7±0.9	0.06	79.9±1.5	-43.5±2.0
PSCOOH-100nm-HC	154.5±2.0	0.07	170.0±2.0	-8.2±1.2
PSOSO ₃ -100nm-HC	Agg.	n/a	n/a	n/a
PSCOOH-40nm-HC	n/a	n/a	136.5±2.0	-10.2±1.2
PSCOOH-100nm-HP	154.5±2.0	0.07	170.0±2.0	-8.2±1.2
PSOSO ₃ -100nm-HP	Agg.	n/a	n/a	n/a
PSCOOH-40nm-HP	92.9±2.0	0.27	126.5±2.0	-9.2±1.2

^a z-average hydrodynamic diameter extracted by cumulant analysis of the data. ^b Polydispersity index obtained from cumulant fitting. ^c Average hydrodynamic diameter determined from CONTIN size distribution.

Table S2. Mass spectrometry data for the top 50 hard corona proteins ranked by content from 40nm PSCOOH in 10% plasma

Rank	Accession	Name	MW	PI	Score	Coverage	Peptide (Hits)	% Area
1	P04196	Histidine-rich glycoprotein	59540.94	7.09	168.31	30.67	105 (104 1 0 0 0)	30.820
2	P01042	Kininogen-1	71912.14	6.34	170.25	21.43	50 (50 0 0 0 0)	13.340
3	P02768	Serum albumin	69321.63	5.92	170.25	31.69	53 (53 0 0 0 0)	5.310
4	Q14624	ITI heavy chain H4	103293.20	6.51	250.25	27.31	66 (66 0 0 0 0)	5.040
5	P04264	Cytokeratin-1	65998.94	8.15	180.23	26.55	104 (104 0 0 0 0)	4.480
6	P04114	Apo B-100	515283.60	6.58	770.36	21.89	136 (136 0 0 0 0)	4.450
7	P03952	Plasma kallikrein	71322.83	8.6	110.21	15.20	43 (43 0 0 0 0)	3.700
8	P04004	Vitronectin	54271.23	5.55	80.21	14.02	27 (27 0 0 0 0)	2.980
9	P05154	Protein C inhibitor	45672.76	9.3	110.27	32.51	33 (33 0 0 0 0)	2.620
10	P01871	IgM chain C	49275.57	6.35	60.22	16.37	20 (20 0 0 0 0)	2.520
11	P35908	Cytokeratin-2e	65393.19	8.07	170.23	34.27	66 (66 0 0 0 0)	2.350
12	P02649	Apolipoprotein E	36131.79	5.65	120.24	41.32	57 (57 0 0 0 0)	2.220
13	P13645	Cytokeratin-10	58791.59	5.13	170.27	30.31	67 (67 0 0 0 0)	2.210
14	P35527	Cytokeratin-9	62026.66	5.14	160.32	37.08	50 (50 0 0 0 0)	1.910
15	P03951	Coagulation factor XI	70063.57	8.53	100.25	16.96	21 (21 0 0 0 0)	1.320
16	P01024	Complement C3	187029.30	6.02	200.26	15.63	38 (38 0 0 0 0)	1.120
17	P00747	Plasminogen	90510.23	7.04	70.22	7.78	14 (14 0 0 0 0)	0.970
18	P0C0L4	Complement C4-A	192649.50	6.66	190.26	13.82	24 (24 0 0 0 0)	0.810
19	P02671	Fibrinogen alpha chain	94914.27	5.7	80.20	13.63	33 (33 0 0 0 0)	0.790
20	P02679	Fibrinogen gamma chain	51478.88	5.37	30.24	5.96	11 (11 0 0 0 0)	0.700
21	P02675	Fibrinogen beta chain	55892.23	8.54	110.24	19.76	21 (21 0 0 0 0)	0.680
22	P02647	Apolipoprotein A-I	30758.94	5.56	90.27	30.34	19 (19 0 0 0 0)	0.670
23	P02760	Protein AMBP	38973.99	5.95	50.23	17.61	12 (12 0 0 0 0)	0.660
24	P05155	C1-inhibiting factor	55119.49	6.09	100.19	14.80	16 (16 0 0 0 0)	0.590
25	P01857	IgG1 chain C	36083.16	8.46	40.19	19.39	6 (6 0 0 0 0)	0.480
26	P08603	Complement factor H	139004.40	6.21	50.19	3.90	10 (10 0 0 0 0)	0.430
27	P13647	Cytokeratin-5	62340.01	7.58	70.16	10.17	12 (12 0 0 0 0)	0.410
28	P02787	Serotransferrin	77013.67	6.81	20.17	3.72	2 (2 0 0 0 0)	0.400
29	P13646	Cytokeratin-13	49557.43	4.91	30.18	5.02	9 (9 0 0 0 0)	0.360
30	Q04756	HGF activator	70636.21	6.99	40.23	8.09	8 (8 0 0 0 0)	0.350
31	P01834	Ig kappa chain C	11601.67	5.58	40.25	65.09	6 (6 0 0 0 0)	0.340
32	P49908	Selenoprotein P	141646.70	8.08	20.16	6.04	7 (7 0 0 0 0)	0.320
33	P02746	Complement C1q subunit B	26704.49	8.83	30.23	11.07	7 (7 0 0 0 0)	0.250
34	P04003	Proline-rich protein	66989.44	7.15	30.19	7.20	7 (7 0 0 0 0)	0.240
35	P62736	Alpha-actin-2	41981.82	5.24	20.19	6.90	6 (6 0 0 0 0)	0.210
36	P0CG04	Ig lambda-1 chain C	11340.61	7.89	20.21	14.15	6 (6 0 0 0 0)	0.200
37	P14136	Glial fibrillary acidic protein	49849.71	5.42	8.16	2.55	6 (6 0 0 0 0)	0.200
38	P10909	Clusterin	52461.05	5.88	20.19	5.12	5 (5 0 0 0 0)	0.190
39	P02751	Fibronectin	262457.60	5.46	60.22	4.53	8 (8 0 0 0 0)	0.170
40	P02533	Cytokeratin-14	51529.44	5.09	30.24	7.84	8 (8 0 0 0 0)	0.170
41	P60709	Beta-actin	41709.74	5.29	20.21	10.40	3 (3 0 0 0 0)	0.160
42	P01876	Ig alpha-1 chain C	37630.65	6.08	20.15	7.65	4 (4 0 0 0 0)	0.160
43	P01859	IgG2 chain C	35877.75	7.66	20.19	5.21	3 (3 0 0 0 0)	0.150
44	P01766	Ig heavy chain V-III	13218.40	6.44	10.25	15.83	4 (4 0 0 0 0)	0.150
45	Q3SY84	Cytokeratin-71	57256.06	6.27	10.20	2.29	1 (1 0 0 0 0)	0.120
46	P06396	Gelsolin	85644.25	5.9	50.22	10.61	5 (5 0 0 0 0)	0.110
47	P18428	Lipopolysaccharide-binding protein	53350.02	6.23	50.19	9.36	7 (7 0 0 0 0)	0.100
48	P01009	Alpha-1-antitrypsin	46707.09	5.37	40.21	11.72	4 (4 0 0 0 0)	0.100
49	P01614	Ig kappa chain V-II	12668.32	5.28	10.17	11.30	3 (3 0 0 0 0)	0.100
50	P62805	Histone H4	11360.38	11.36	10.15	9.71	1 (1 0 0 0 0)	0.100

Table S3. Mass spectrometry data for the top 50 hard corona proteins ranked by content from 40nm PSCOOH in 25% plasma

Rank	Accession	Name	MW	PI	Score	Coverage	Peptide (Hits)	% Area
1	P04196	Histidine-rich glycoprotein	59540.94	7.09	230.29	34.10	145 (145 0 0 0 0)	43.400
2	P01042	Kininogen-1	71912.14	6.34	228.26	28.40	59 (58 1 0 0 0)	9.010
3	P04264	Cytokeratin-1	65998.94	8.15	300.35	43.20	126 (126 0 0 0 0)	6.230
4	P01871	IgM heavy chain	49275.57	6.35	120.31	25.70	25 (25 0 0 0 0)	6.070
5	P13645	Cytokeratin-10	58791.59	5.13	240.29	39.40	100 (100 0 0 0 0)	5.960
6	P04114	Apo B-100	515283.60	6.58	940.32	23.90	158 (158 0 0 0 0)	3.820
7	P35908	Cytokeratin-2e	65393.19	8.07	250.30	45.40	97 (97 0 0 0 0)	3.800
8	P03952	Plasma kallikrein	71322.83	8.6	160.23	28.50	35 (35 0 0 0 0)	3.380
9	P04004	Vitronectin	54271.23	5.55	60.22	18.40	19 (19 0 0 0 0)	1.470
10	P35527	Cytokeratin-9	62026.66	5.14	160.34	38.70	64 (64 0 0 0 0)	1.440
11	P02649	Apolipoprotein E	36131.79	5.65	180.25	43.50	30 (30 0 0 0 0)	1.390
12	P00747	Plasminogen	90510.23	7.04	70.27	9.90	13 (13 0 0 0 0)	1.290
13	P03951	Coagulation factor XI	70063.57	8.53	90.26	19.40	13 (13 0 0 0 0)	1.230
14	P08519	Apolipoprotein(a)	500996.40	5.58	90.19	19.00	9 (9 0 0 0 0)	1.080
15	Q14624	ITI heavy chain H4	103293.20	6.51	180.25	23.10	46 (46 0 0 0 0)	1.060
16	P05154	Protein C inhibitor	45672.76	9.3	80.27	22.90	15 (15 0 0 0 0)	0.900
17	P02768	Serum albumin	69321.63	5.92	80.23	14.60	27 (27 0 0 0 0)	0.890
18	P02679	Fibrinogen gamma chain	51478.88	5.37	110.25	33.80	21 (21 0 0 0 0)	0.760
19	P02671	Fibrinogen alpha chain	94914.27	5.7	120.25	21.20	29 (29 0 0 0 0)	0.630
20	P0C0L4	Complement C4-A	192649.50	6.66	170.25	16.70	20 (20 0 0 0 0)	0.440
21	P01876	Ig alpha-1 chain C	37630.65	6.08	40.22	15.00	6 (6 0 0 0 0)	0.440
22	P60709	Beta-actin	41709.74	5.29	60.27	21.10	9 (9 0 0 0 0)	0.420
23	P02751	Fibronectin	262457.60	5.46	150.25	10.10	20 (20 0 0 0 0)	0.410
24	P02675	Fibrinogen beta chain	55892.23	8.54	100.26	24.40	15 (15 0 0 0 0)	0.330
25	P62736	Alpha-actin-2	41981.82	5.24	30.17	11.70	5 (5 0 0 0 0)	0.300
26	P01024	Complement C3	187029.30	6.02	210.28	18.60	33 (33 0 0 0 0)	0.270
27	P08603	Complement factor H	139004.40	6.21	150.28	12.30	22 (22 0 0 0 0)	0.240
28	P01834	Ig kappa chain C	11601.67	5.58	90.28	85.80	14 (14 0 0 0 0)	0.240
29	P01614	Ig kappa chain V-II	12668.32	5.28	20.17	13.90	2 (2 0 0 0 0)	0.190
30	P02533	Cytokeratin-14	51529.44	5.09	60.20	16.90	17 (17 0 0 0 0)	0.170
31	P13647	Cytokeratin-5	62340.01	7.58	80.19	11.70	20 (20 0 0 0 0)	0.150
32	P01766	Ig heavy chain V-III	13218.40	6.44	10.24	15.80	1 (1 0 0 0 0)	0.150
33	P06312	Ig kappa chain V-IV	13371.60	5.09	10.14	7.40	2 (2 0 0 0 0)	0.150
34	P02746	Complement C1q subunit B	26704.49	8.83	60.23	13.40	8 (8 0 0 0 0)	0.140
35	P49908	Selenoprotein P	141646.70	8.08	30.15	5.50	3 (3 0 0 0 0)	0.130
36	P14136	Glial fibrillary acidic protein	49849.71	5.42	8.17	2.50	5 (5 0 0 0 0)	0.120
37	P04003	Proline-rich protein	66989.44	7.15	40.26	8.70	6 (6 0 0 0 0)	0.090
38	P01620	Ig kappa chain V-III	11767.85	8.7	20.20	31.20	3 (3 0 0 0 0)	0.090
39	P02747	Complement C1q subunit C	25757.13	8.61	10.14	4.90	1 (1 0 0 0 0)	0.090
40	P04433	Ig kappa chain V-III VG	12567.31	4.85	10.13	7.80	1 (1 0 0 0 0)	0.090
41	P05155	C1-inhibiting factor	55119.49	6.09	60.19	10.40	7 (7 0 0 0 0)	0.060
42	P02647	Apolipoprotein A-I	30758.94	5.56	40.19	16.10	11 (11 0 0 0 0)	0.060
43	P02760	Protein AMBP	38973.99	5.95	30.25	8.50	7 (7 0 0 0 0)	0.060
44	Q04756	HGF activator	70636.21	6.99	30.23	6.40	4 (4 0 0 0 0)	0.060
45	P0CG04	Ig lambda-1 chain C	11340.61	7.89	20.20	32.10	2 (2 0 0 0 0)	0.060
46	P13646	Cytokeratin-13	49557.43	4.91	20.18	5.00	5 (5 0 0 0 0)	0.060
47	P10909	Clusterin	52461.05	5.88	40.18	14.00	5 (5 0 0 0 0)	0.050
48	P01597	Ig kappa chain V-I DEE	11653.77	9.43	20.19	16.70	2 (2 0 0 0 0)	0.050
49	P01593	Ig kappa chain V-I AG	11984.88	5.67	16.19	16.70	2 (2 0 0 0 0)	0.050
50	P01606	Ig kappa chain V-I OU	11769.67	9.94	12.17	16.70	2 (2 0 0 0 0)	0.050

Table S4. Mass spectrometry data for the top 50 hard corona proteins ranked by content from 40nm PSCOOH in 55% plasma

Rank	Accession	Name	MW	PI	Score	Coverage	Peptide (Hits)	% Area
1	P04196	Histidine-rich glycoprotein	59540.94	7.09	170.28	31.80	98 (98 0 0 0 0)	33.85
2	P04114	Apo B-100	515283.60	6.58	1538.34	37.00	240 (239 1 0 0 0)	9.51
3	P04264	Cytokeratin-1	65998.94	8.15	290.34	42.20	127 (127 0 0 0 0)	7.86
4	P01042	Kininogen-1	71912.14	6.34	180.27	24.70	35 (35 0 0 0 0)	7.67
5	P01871	IgM heavy chain	49275.57	6.35	150.22	26.30	34 (34 0 0 0 0)	6.57
6	P13645	Cytokeratin-10	58791.59	5.13	250.30	42.00	97 (97 0 0 0 0)	6.16
7	P35908	Cytokeratin-2e	65393.19	8.07	260.26	48.00	99 (99 0 0 0 0)	3.68
8	P02751	Fibronectin	262457.60	5.46	280.29	18.50	40 (40 0 0 0 0)	1.84
9	P08519	Apolipoprotein(a)	500996.40	5.58	130.22	20.80	17 (17 0 0 0 0)	1.71
10	P02649	Apolipoprotein E	36131.79	5.65	150.22	33.10	23 (23 0 0 0 0)	1.63
11	P03951	Coagulation factor XI	70063.57	8.53	100.26	22.40	16 (16 0 0 0 0)	1.43
12	P03952	Plasma kallikrein	71322.83	8.60	120.21	21.30	22 (22 0 0 0 0)	1.36
13	P04004	Vitronectin	54271.23	5.55	90.20	18.40	17 (17 0 0 0 0)	1.24
14	P35527	Cytokeratin-9	62026.66	5.14	160.31	41.60	69 (69 0 0 0 0)	1.21
15	P02768	Serum albumin	69321.63	5.92	110.22	15.40	30 (30 0 0 0 0)	1.2
16	P00747	Plasminogen	90510.23	7.04	40.30	6.20	8 (8 0 0 0 0)	0.86
17	P0C0L4	Complement C4-A	192649.50	6.66	270.27	22.70	35 (35 0 0 0 0)	0.82
18	P62736	Alpha-actin-2	41981.82	5.24	30.20	11.40	5 (5 0 0 0 0)	0.67
19	P14136	Glial fibrillary acidic protein	49849.71	5.42	8.15	2.50	7 (7 0 0 0 0)	0.52
20	P01834	Ig kappa chain C	11601.67	5.58	60.25	68.90	13 (13 0 0 0 0)	0.51
21	P13647	Cytokeratin-5	62340.01	7.58	90.17	18.50	14 (14 0 0 0 0)	0.46
22	P02671	Fibrinogen alpha chain	94914.27	5.70	100.22	16.50	25 (25 0 0 0 0)	0.45
23	P01024	Complement C3	187029.30	6.02	240.28	18.80	38 (38 0 0 0 0)	0.44
24	P06312	Ig kappa chain V-IV	13371.60	5.09	20.15	19.80	2 (2 0 0 0 0)	0.38
25	P02679	Fibrinogen gamma chain	51478.88	5.37	70.24	20.10	10 (10 0 0 0 0)	0.36
26	P01620	Ig kappa chain V-III	11767.85	8.70	20.23	31.20	4 (4 0 0 0 0)	0.35
27	P02746	Complement C1q subunit B	26704.49	8.83	50.24	19.00	7 (7 0 0 0 0)	0.33
28	P05154	Protein C inhibitor	45672.76	9.30	50.24	13.30	9 (9 0 0 0 0)	0.32
29	P60709	Beta-actin	41709.74	5.29	50.26	18.40	10 (10 0 0 0 0)	0.3
30	P04003	Proline-rich protein	66989.44	7.15	50.25	8.00	10 (10 0 0 0 0)	0.3
31	P02747	Complement C1q subunit C	25757.13	8.61	20.14	12.20	3 (3 0 0 0 0)	0.29
32	P02533	Cytokeratin-14	51529.44	5.09	80.25	23.30	24 (24 0 0 0 0)	0.27
33	Q14624	ITI heavy chain H4	103293.20	6.51	90.24	11.50	15 (15 0 0 0 0)	0.24
34	P02647	Apolipoprotein A-I	30758.94	5.56	70.23	25.10	7 (7 0 0 0 0)	0.24
35	P01766	Ig heavy chain V-III	13218.40	6.44	10.20	15.80	2 (2 0 0 0 0)	0.24
36	P13646	Cytokeratin-13	49557.43	4.91	40.19	7.90	9 (9 0 0 0 0)	0.19
37	P01591	Immunoglobulin J chain	18087.0	5.09	10.13	0.00	1 (1 0 0 0 0)	0.19
38	P08603	Complement factor H	139004.40	6.21	50.18	5.50	6 (6 0 0 0 0)	0.18
39	P04433	Ig kappa chain V-III VG	12567.31	4.85	20.18	26.10	2 (2 0 0 0 0)	0.18
40	P04275	von Willebrand factor	309053.6	5.29	110.31	5.90	14 (14 0 0 0 0)	0.17
41	P02675	Fibrinogen beta chain	55892.23	8.54	90.24	28.10	9 (9 0 0 0 0)	0.16
42	P08514	Integrin alpha-IIb	113305.7	5.2	80.27	10.90	11 (11 0 0 0 0)	0.14
43	Q01546	Cytokeratin-2P	65830.1	8.38	10.21	1.90	1 (1 0 0 0 0)	0.14
44	P01781	Ig heavy chain V-III GAL	12722.2	8.7	10.15	9.50	3 (3 0 0 0 0)	0.14
45	P01625	Ig kappa chain V-IV Len	12632.2	7.92	10.20	15.80	2 (2 0 0 0 0)	0.13
46	P49908	Selenoprotein P	141646.70	8.08	10.13	2.60	2 (2 0 0 0 0)	0.13
47	P35579	Myosin-9	226390.6	5.5	170.29	13.40	20 (20 0 0 0 0)	0.12
48	P01764	Ig heavy chain V-III VH26	12574.2	8.49	10.17	9.40	2 (2 0 0 0 0)	0.12
49	P21333	Filamin-A	280561.4	5.7	160.21	9.10	18 (18 0 0 0 0)	0.11
50	P01597	Ig kappa chain V-I DEE	11653.77	9.43	20.26	16.70	2 (2 0 0 0 0)	0.1

Table S5. Mass spectrometry data for top 50 hard corona proteins ranked by content from 40nm PSCOOH in 75% plasma

Rank	Accession	Name	MW	PI	Score	Coverage	Peptide (Hits)	% Area
1	P04196	Histidine-rich glycoprotein	59540.94	7.09	170.28	31.80	98 (98 0 0 0 0)	33.85
2	P04114	Apo B-100	515283.60	6.58	1538.34	37.00	240 (239 1 0 0 0)	9.51
3	P04264	Cytokeratin-1	65998.94	8.15	290.34	42.20	127 (127 0 0 0 0)	7.86
4	P01042	Kininogen-1	71912.14	6.34	180.27	24.70	35 (35 0 0 0 0)	7.67
5	P01871	IgM heavy chain	49275.57	6.35	150.22	26.30	34 (34 0 0 0 0)	6.57
6	P13645	Cytokeratin-10	58791.59	5.13	250.30	42.00	97 (97 0 0 0 0)	6.16
7	P35908	Cytokeratin-2e	65393.19	8.07	260.26	48.00	99 (99 0 0 0 0)	3.68
8	P02751	Fibronectin	262457.60	5.46	280.29	18.50	40 (40 0 0 0 0)	1.84
9	P08519	Apolipoprotein(a)	500996.40	5.58	130.22	20.80	17 (17 0 0 0 0)	1.71
10	P02649	Apolipoprotein E	36131.79	5.65	150.22	33.10	23 (23 0 0 0 0)	1.63
11	P03951	Coagulation factor XI	70063.57	8.53	100.26	22.40	16 (16 0 0 0 0)	1.43
12	P03952	Plasma kallikrein	71322.83	8.6	120.21	21.30	22 (22 0 0 0 0)	1.36
13	P04004	Vitronectin	54271.23	5.55	90.20	18.40	17 (17 0 0 0 0)	1.24
14	P35527	Cytokeratin-9	62026.66	5.14	160.31	41.60	69 (69 0 0 0 0)	1.21
15	P02768	Serum albumin	69321.63	5.92	110.22	15.40	30 (30 0 0 0 0)	1.2
16	P00747	Plasminogen	90510.23	7.04	40.30	6.20	8 (8 0 0 0 0)	0.86
17	P0C0L4	Complement C4-A	192649.50	6.66	270.27	22.70	35 (35 0 0 0 0)	0.82
18	P62736	Alpha-actin-2	41981.82	5.24	30.20	11.40	5 (5 0 0 0 0)	0.67
19	P14136	Glial fibrillary acidic protein	49849.71	5.42	8.15	2.50	7 (7 0 0 0 0)	0.52
20	P01834	Ig kappa chain C	11601.67	5.58	60.25	68.90	13 (13 0 0 0 0)	0.51
21	P13647	Cytokeratin-5	62340.01	7.58	90.17	18.50	14 (14 0 0 0 0)	0.46
22	P02671	Fibrinogen alpha chain	94914.27	5.7	100.22	16.50	25 (25 0 0 0 0)	0.45
23	P01024	Complement C3	187029.30	6.02	240.28	18.80	38 (38 0 0 0 0)	0.44
24	P06312	Ig kappa chain V-IV	13371.60	5.09	20.15	19.80	2 (2 0 0 0 0)	0.38
25	P02679	Fibrinogen gamma chain	51478.88	5.37	70.24	20.10	10 (10 0 0 0 0)	0.36
26	P01620	Ig kappa chain V-III	11767.85	8.7	20.23	31.20	4 (4 0 0 0 0)	0.35
27	P02746	Complement C1q subunit B	26704.49	8.83	50.24	19.00	7 (7 0 0 0 0)	0.33
28	P05154	Protein C inhibitor	45672.76	9.3	50.24	13.30	9 (9 0 0 0 0)	0.32
29	P60709	Beta-actin	41709.74	5.29	50.26	18.40	10 (10 0 0 0 0)	0.3
30	P04003	Proline-rich protein	66989.44	7.15	50.25	8.00	10 (10 0 0 0 0)	0.3
31	P02747	Complement C1q subunit C	25757.13	8.61	20.14	12.20	3 (3 0 0 0 0)	0.29
32	P02533	Cytokeratin-14	51529.44	5.09	80.25	23.30	24 (24 0 0 0 0)	0.27
33	Q14624	ITI heavy chain H4	103293.20	6.51	90.24	11.50	15 (15 0 0 0 0)	0.24
34	P02647	Apolipoprotein A-I	30758.94	5.56	70.23	25.10	7 (7 0 0 0 0)	0.24
35	P01766	Ig heavy chain V-III	13218.40	6.44	10.20	15.80	2 (2 0 0 0 0)	0.24
36	P13646	Cytokeratin-13	49557.43	4.91	40.19	7.90	9 (9 0 0 0 0)	0.19
37	P01591	Immunoglobulin J chain	18087.0	5.09	10.13	0.00	1 (1 0 0 0 0)	0.19
38	P08603	Complement factor H	139004.40	6.21	50.18	5.50	6 (6 0 0 0 0)	0.18
39	P04433	Ig kappa chain V-III VG	12567.31	4.85	20.18	26.10	2 (2 0 0 0 0)	0.18
40	P04275	von Willebrand factor	309053.6	5.29	110.31	5.90	14 (14 0 0 0 0)	0.17
41	P02675	Fibrinogen beta chain	55892.23	8.54	90.24	28.10	9 (9 0 0 0 0)	0.16
42	P08514	Integrin alpha-IIb	113305.7	5.2	80.27	10.90	11 (11 0 0 0 0)	0.14
43	Q01546	Cytokeratin-2P	65830.1	8.38	10.21	1.90	1 (1 0 0 0 0)	0.14
44	P01781	Ig heavy chain V-III GAL	12722.2	8.7	10.15	9.50	3 (3 0 0 0 0)	0.14
45	P01625	Ig kappa chain V-IV Len	12632.2	7.92	10.20	15.80	2 (2 0 0 0 0)	0.13
46	P49908	Selenoprotein P	141646.70	8.08	10.13	2.60	2 (2 0 0 0 0)	0.13
47	P35579	Myosin-9	226390.6	5.5	170.29	13.40	20 (20 0 0 0 0)	0.12
48	P01764	Ig heavy chain V-III VH26	12574.2	8.49	10.17	9.40	2 (2 0 0 0 0)	0.12
49	P21333	Filamin-A	280561.4	5.7	160.21	9.10	18 (18 0 0 0 0)	0.11
50	P01597	Ig kappa chain V-I DEE	11653.77	9.43	20.26	16.70	2 (2 0 0 0 0)	0.1

Table S6. Mass spectrometry data for hard corona proteins ranked by content from 100nm PSCOOH in 10% plasma

Rank	Accession	Name	MW	PI	Score	Coverage	Peptide (Hits)	% Area
1	P04004	Vitronectin	54271.23	5.55	40.17	12.13	5 (5 0 0 0 0)	38.750
2	P04196	Histidine-rich glycoprotein	59540.94	7.09	90.21	16.40	18 (18 0 0 0 0)	17.570
3	P01042	Kininogen-1	71912.14	6.34	118.19	11.50	16 (15 1 0 0 0)	10.610
4	P03952	Plasma kallikrein	71322.83	8.6	50.18	6.74	5 (5 0 0 0 0)	9.980
5	Q14624	ITI heavy chain H4	103293.20	6.51	40.20	6.02	5 (5 0 0 0 0)	4.390
6	Q04756	HGF activator	70636.21	6.99	20.20	4.58	2 (2 0 0 0 0)	3.110
7	P02675	Fibrinogen beta chain	55892.23	8.54	50.19	15.48	7 (7 0 0 0 0)	3.000
8	P03951	Coagulation factor XI	70063.57	8.53	40.23	7.20	6 (6 0 0 0 0)	2.180
9	P62736	Alpha-actin-2	41981.82	5.24	10.18	4.24	2 (2 0 0 0 0)	1.550
10	P04264	Cytokeratin-1	65998.94	8.15	70.17	9.00	13 (13 0 0 0 0)	1.220
11	P02768	Serum albumin	69321.63	5.92	50.19	6.40	6 (6 0 0 0 0)	1.130
12	P05154	Protein C inhibitor	45672.76	9.3	20.13	6.40	3 (3 0 0 0 0)	1.120
13	P02679	Fibrinogen gamma chain	51478.88	5.37	40.18	14.57	6 (6 0 0 0 0)	0.870
14	P02671	Fibrinogen alpha chain	94914.27	5.7	40.17	5.20	6 (6 0 0 0 0)	0.820
15	P06396	Gelsolin	85644.25	5.9	50.20	10.87	5 (5 0 0 0 0)	0.690
16	P60709	Beta-actin	41709.74	5.29	20.17	10.40	2 (2 0 0 0 0)	0.620
17	P02760	Protein AMBP	38973.99	5.95	20.14	5.40	2 (2 0 0 0 0)	0.500
18	P02749	Apolipoprotein H	38272.67	8.34	10.14	4.06	1 (1 0 0 0 0)	0.350
19	P11021	GRP-78	72288.52	5.07	10.14	2.45	1 (1 0 0 0 0)	0.270
20	P02647	Apolipoprotein A-I	30758.94	5.56	10.13	5.24	1 (1 0 0 0 0)	0.250
21	P06727	Apolipoprotein A-IV	45371.52	5.68	10.16	3.54	1 (1 0 0 0 0)	0.240
22	P35908	Cytokeratin-2e	65393.19	8.07	30.15	3.76	6 (6 0 0 0 0)	0.170
23	P10909	Clusterin	52461.05	5.88	10.21	3.79	1 (1 0 0 0 0)	0.130
24	P01871	IgM chain C	49275.57	6.35	10.17	3.54	1 (1 0 0 0 0)	0.120
25	P01859	IgG2 chain C	35877.75	7.66	10.14	4.91	1 (1 0 0 0 0)	0.110
26	P13645	Cytokeratin-10	58791.59	5.13	20.16	6.16	2 (2 0 0 0 0)	0.080
27	P04114	Apolipoprotein B-100	515283.60	6.58	20.18	0.81	2 (2 0 0 0 0)	0.050
28	Q9UJZ1	Stomatin-like protein 2	38510.22	6.87	10.16	4.78	1 (1 0 0 0 0)	0.050
29	P38646	Stress-70 protein	73634.83	5.87	10.13	2.50	1 (1 0 0 0 0)	0.040
30	P00747	Plasminogen	90510.23	7.04	10.14	1.98	1 (1 0 0 0 0)	0.020
31	Q71U36	Alpha-tubulin 3	50103.65	4.94	10.13	4.43	1 (1 0 0 0 0)	0.010
32	P01857	IgG1 chain C	36083.16	8.46	10.14	4.85	1 (1 0 0 0 0)	0.000
33	P0C0L4	Complement C4-A	192649.50	6.66	10.13	0.86	1 (1 0 0 0 0)	0.000

Table S7. Mass spectrometry data for hard corona proteins ranked by content from 100nm PSOSO₃H in 10% plasma

Rank	Accession	Name	MW	PI	Score	Coverage	Peptide (Hits)	% Area
1	P02671	Fibrinogen alpha chain	94914.27	5.7	170.21	16.70	31 (31 0 0 0 0)	26.81
2	P02679	Fibrinogen gamma chain	51478.88	5.37	120.23	27.60	23 (23 0 0 0 0)	25.6
3	P02675	Fibrinogen beta chain	55892.23	8.54	230.21	26.10	45 (45 0 0 0 0)	17.46
4	P13645	Cytokeratin-10	58791.59	5.13	100.21	14.90	13 (13 0 0 0 0)	8.26
5	P02768	Serum albumin	69321.63	5.92	90.19	12.60	17 (17 0 0 0 0)	6.04
6	P04264	Cytokeratin-1	65998.94	8.15	120.20	17.90	40 (40 0 0 0 0)	6.02
7	P35908	Cytokeratin-2e	65393.19	8.07	80.17	10.80	23 (23 0 0 0 0)	3.91
8	P35527	Cytokeratin-9	62026.7	5.14	70.25	15.60	9 (9 0 0 0 0)	1.77
9	P01857	IgG1 chain C	36083.16	8.46	10.13	5.20	1 (1 0 0 0 0)	1.27
10	Q14624	ITI heavy chain H4	103293.20	6.51	20.18	3.00	2 (2 0 0 0 0)	0.76
11	P04196	Histidine-rich glycoprotein	59540.94	7.09	40.20	8.40	11 (11 0 0 0 0)	0.62
12	P10909	Clusterin	52461.05	5.88	20.19	6.50	3 (3 0 0 0 0)	0.53
13	P02647	Apolipoprotein A-I	30758.94	5.56	30.15	9.40	4 (4 0 0 0 0)	0.31
14	P04004	Vitronectin	54271.23	5.55	20.14	3.10	4 (4 0 0 0 0)	0.22
15	P01042	Kininogen-1	71912.14	6.34	10.14	2.30	1 (1 0 0 0 0)	0.12
16	P02649	Apolipoprotein E	36131.79	5.65	10.17	4.70	1 (1 0 0 0 0)	0.09
17	P13647	Cytokeratin-5	62340.01	7.58	10.14	1.70	1 (1 0 0 0 0)	0.07
18	P06727	Apolipoprotein A-IV	45371.52	5.68	20.14	6.80	2 (2 0 0 0 0)	0.04
19	P01620	Ig kappa chain V-III SIE	11767.9	8.7	10.15	16.50	1 (1 0 0 0 0)	0.04
20	P01024	Complement C3	187029.30	6.02	10.13	0.80	1 (1 0 0 0 0)	0.03
21	P04275	von Willebrand factor	309053.6	5.29	10.14	0.60	1 (1 0 0 0 0)	0.02

Table S8. ProtoArray® v4.1 content and distribution by biological function.

Class	No. on array
Protein kinases (unique)	268
Protein kinases (including domains, splice variants, and mutants)	776
Transcription factors	328
Membrane proteins	2,635
Nuclear proteins	2,252
Signal transduction	1,526
Secreted proteins	192
Cell communication	1,687
Metabolism	3,862
Cell death	505
Protease/peptidase activity	219