Supporting Information

Visualization of the Protein Corona: towards a biomolecular understanding of nanoparticle-cell-interactions

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Contents

Physicochemical properties of nanoparticles 3
Visualizing protein nanoparticle interactions by electron microscopy 3
Monitoring the protein corona with dynamic light scattering 5
Quantification of adsorbed proteins and remaining content of proteins in the supernatant 8
Classification of corona proteins 9
Cellular interactions of protein corona coated nanoparticles 12
Methods ..... **Fehler! Textmarke nicht definiert.**
Nanoparticle Synthesis ..... **Fehler! Textmarke nicht definiert.**
LC MS Analysis 15
Literature 29

Physicochemical properties of nanoparticles

Table 1: Physicochemical properties as hydrodynamic radius and ζ-potential of polystyrene nanoparticles determined by multi angle dynamic light scattering in aqueous solution and PBS. The fluorescence intensity of the BODIPY labeled nanoparticles (525/535 nm) was determined by Tecan Microplate Reader and normalized to the value for un-functionalized polystyrene nanoparticles.

	R_h (H_2O)	R_h (PBS)	ζ-Potential	Fluorescence Intensity Factor
PS	73 ± 7.3 nm	75 ± 7.5 nm	- 3.70 mV	1
PS- COOH	70 ± 7.0 nm	72 ± 7.0 nm	- 7.21 mV	1.16
PS- NH_2	74 ± 4.3 nm	79 ± 7.9 nm	+ 7.58 mV	1.05

Visualizing protein nanoparticle interactions by electron microscopy

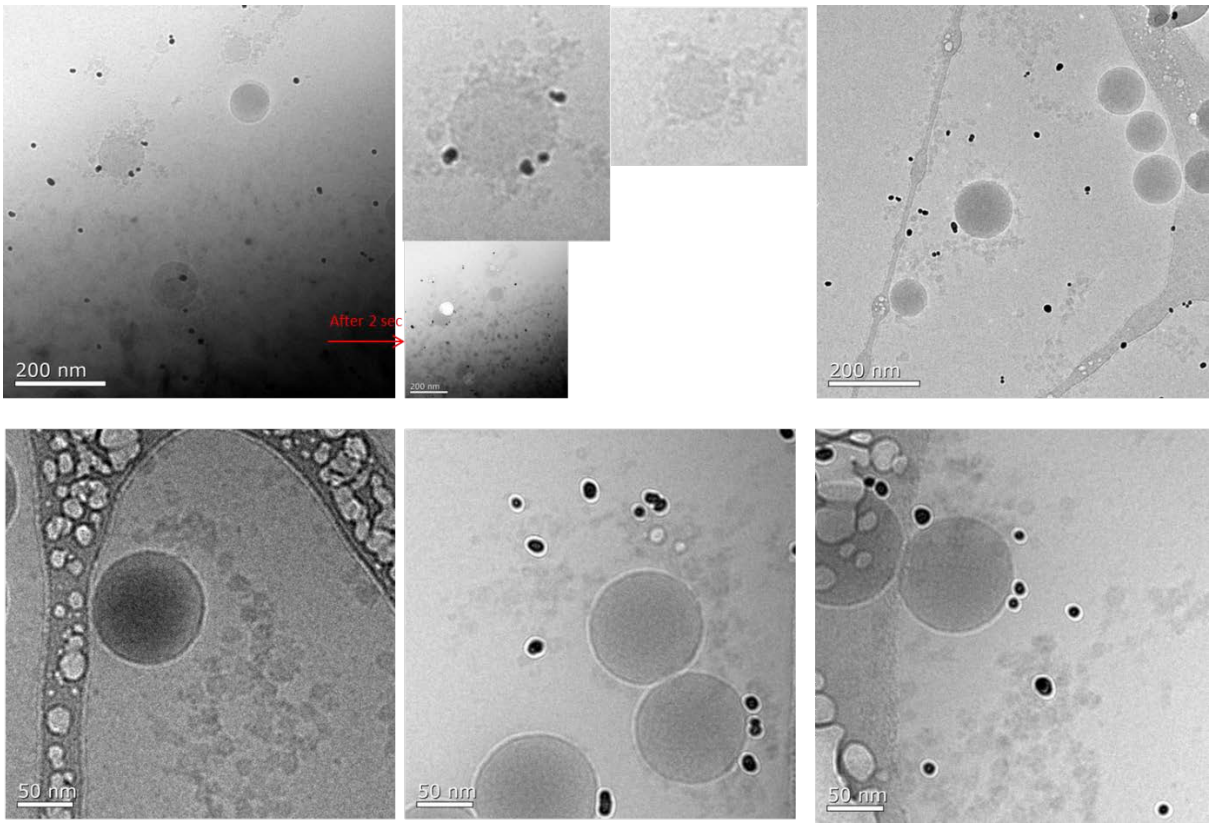

Figure 1: Cryo-TEM micrographs of un-functionalized PS nanoparticles incubated with gold-labelled bovine serum albumin visualize the structure of the protein corona. Nanoparticles (0.05 m^2) were incubated with 100 µg of protein for 1h at 37°C before measurements were performed.

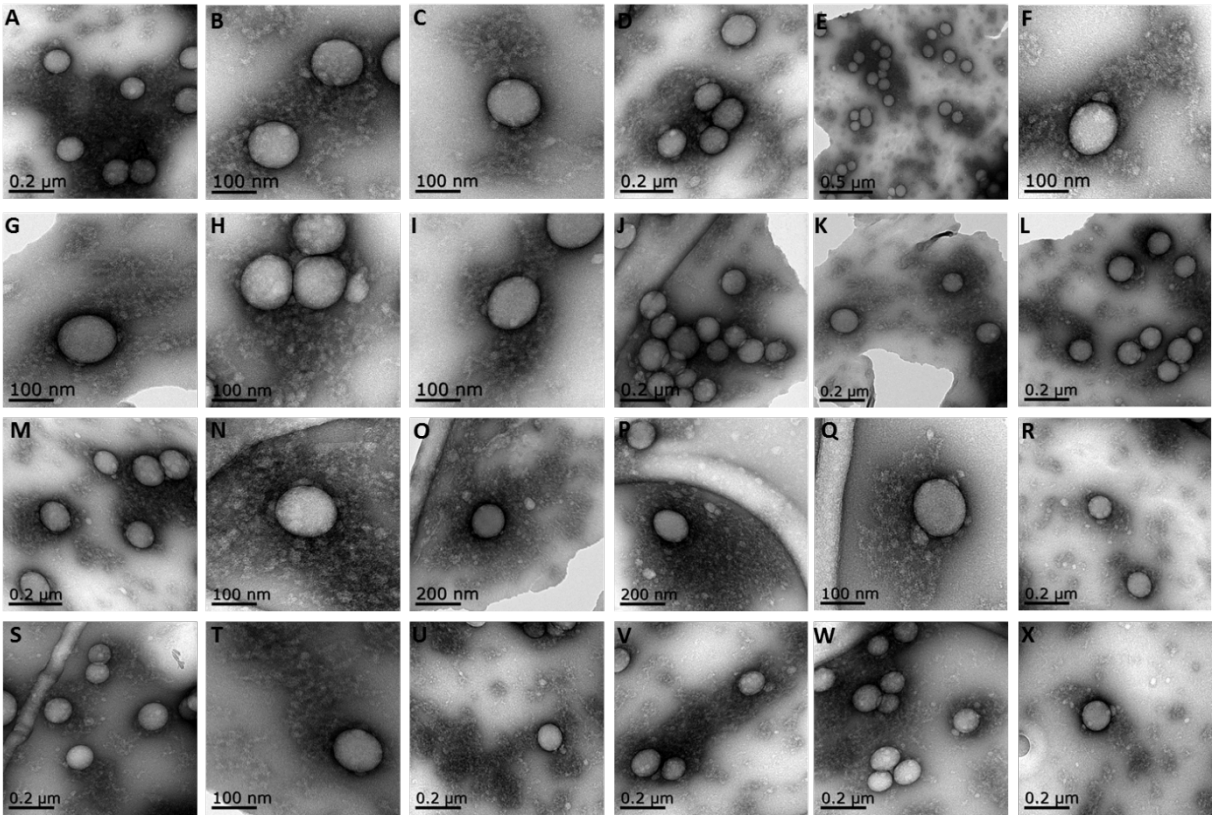

Figure 2: TEM micrographs of un-functionalized PS nanoparticles incubated with human serum and centrifuged once (A). Nanoparticles are surrounded by a huge protein cloud.

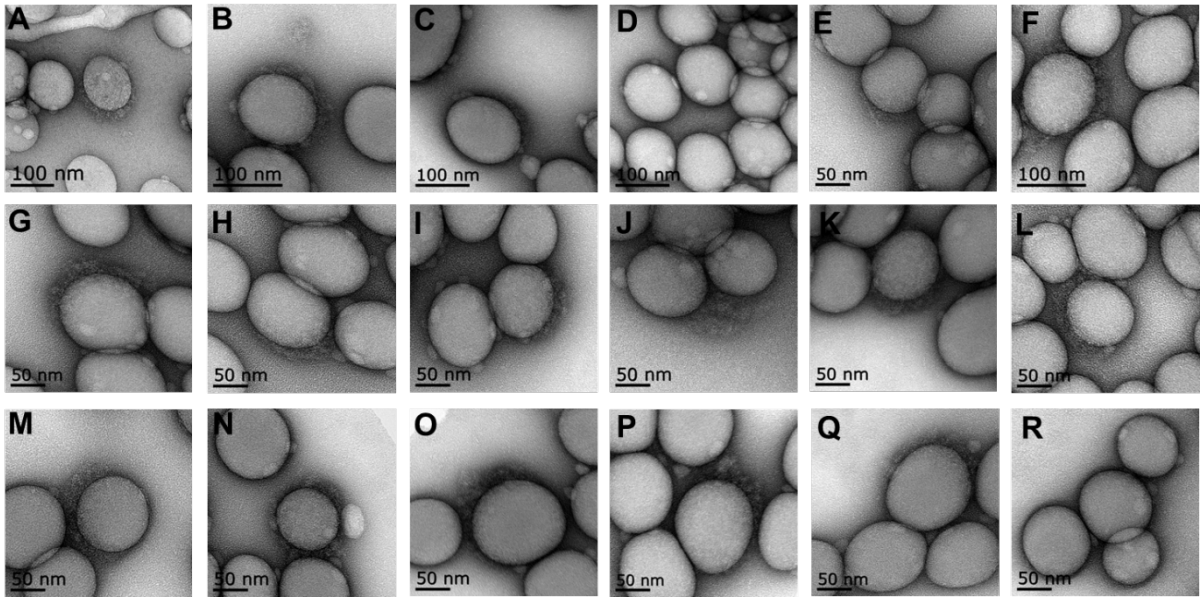

Figure 3: TEM micrographs of un-functionalized PS nanoparticles incubated with human serum centrifuged and washed three times (D). The hard protein corona surrounding nanoparticles is visualized.

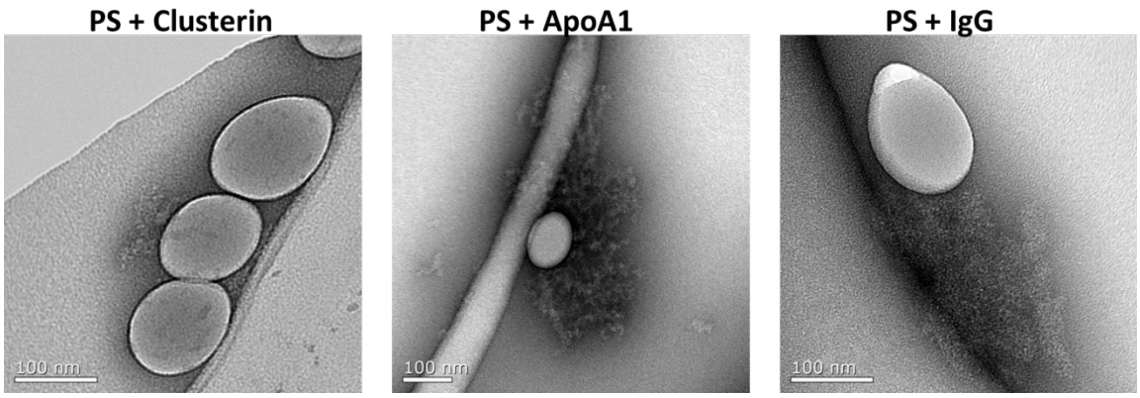

Figure 4: TEM micrographs of un-functionalized PS incubated with identified hard corona proteins. Nanoparticles (0.05 m^2) were incubated with 100 µg of protein for 1h at 37°C before measurements were performed.

Monitoring the protein corona with dynamic light scattering

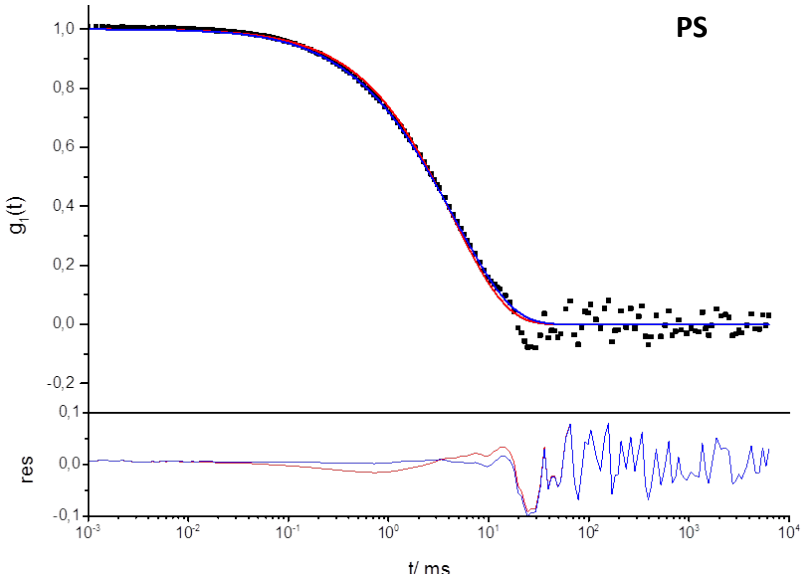

Figure 5: Autocorrelation function of un-functionalized PS nanoparticles incubated with human serum exemplary shown for a scattering angle of 30°. *Upper graph:* The blue line (–) represents the forced fit composed of the sum of the individual components whereas the red line (–) represents the fit with an additional aggregation function. *Lower graph:* Corresponding residuals resulting from the difference between the data and the two fits. The overlay of the red and blue fit indicates that there is no significant aggregation of un-functionalized PS nanoparticles incubated with human serum. Strong aggregation formation of nanoparticles in human serum would result in a great shift between the addition aggregation function (red) and the forced fit (blue).

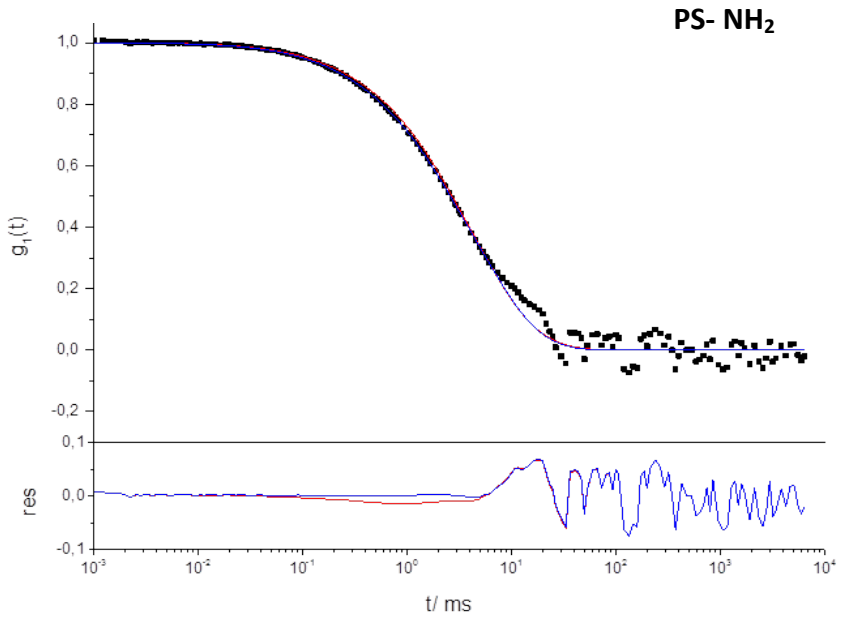

Figure 6: Autocorrelation function of PS -NH_2 nanoparticles incubated with human serum exemplary shown for a scattering angle of 30°. *Upper graph:* The blue line (–) represents the forced fit composed of the sum of the individual components whereas the red line (–) represents the fit with an additional aggregation function. *Lower graph:* Corresponding residuals resulting from the difference between the data and the two fits. The overlay of the red and blue fit indicates that there is no significant aggregation of PS- NH_2 nanoparticles incubated with human serum.

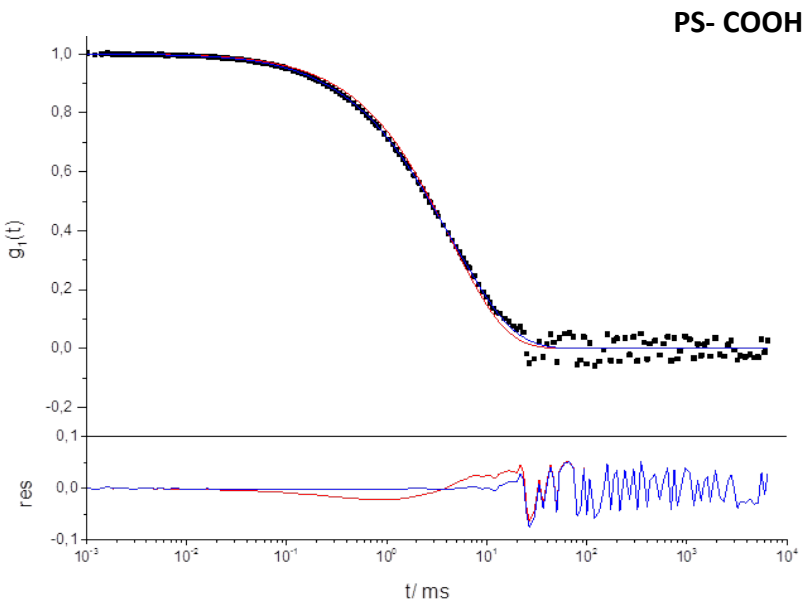

Figure 7: Autocorrelation function of PS- COOH nanoparticles incubated with human serum exemplary shown for a scattering angle of 30°. *Upper graph:* The blue line (–) represents the forced fit composed of the sum of the individual components whereas the red line (–) represents the fit with an additional aggregation function. *Lower graph:* Corresponding residuals resulting from the difference between the data and the two fits. The overlay of the red and blue fit indicates that there is no significant aggregation of PS- COOH nanoparticles incubated with human serum.

Table 2: *Soft* corona hydrodynamic radii of polystyrene nanoparticles incubated within human serum measured by multi angle dynamic light scattering. The size of the nanoparticles was measured directly within human serum. Nanoparticles are surrounded by a huge protein causing a size increase. Values are exemplary given for a scattering angle at 30° as the system has the greatest sensitivity towards detection of aggregation formation. [1]

	Hydrodynamic radius (NP with *soft* corona) (Scattering angle **30°**)	**Intensity (I%)**
PS	140 ± 14 nm	22
PS- COOH	178 ± 18 nm	21
PS- NH_2	188 ± 19 nm	18

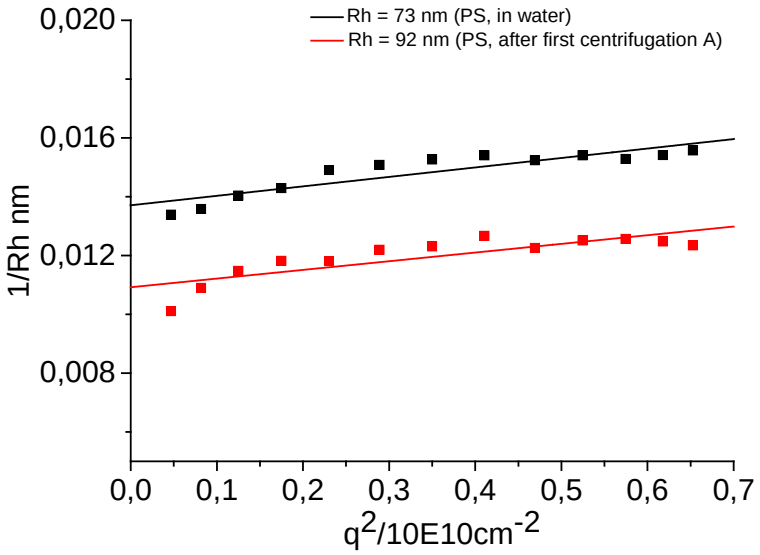

Figure 8: Incubation of un-functionalized PS with human serum and further centrifugation to isolate NPs with hard protein corona (PS; A) in comparison to PS in water. There is a size increase of 19 ± 2 nm monitored by multi angle dynamic light scattering attributed to the hard protein corona around nanoparticles. The angular dependency of the inverse hydrodynamic radii of un-functionalized PS is demonstrated.

Table 3: *Hard* corona hydrodynamic radii of polystyrene nanoparticles incubated within human serum and centrifuged was measured by multi angle dynamic light scattering.

	Hydrodynamic radius (NP with *hard* corona) R_h (H_2O)
PS	92 ± 9.2 nm
PS- COOH	80 ± 8.0 nm
PS- NH_2	88 ± 8.8 nm

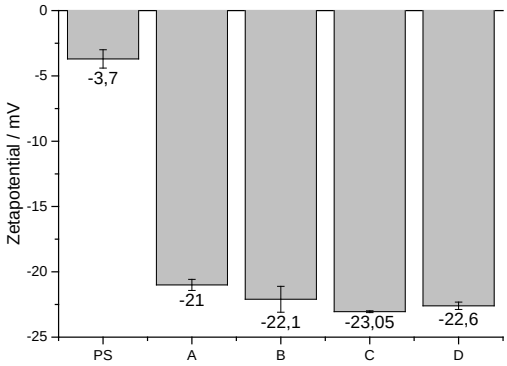

Figure 9: Zeta-potential after incubation, centrifugation and washing of un-functionalized PS nanoparticles incubated with human serum. Due to protein adsorption the zeta-potential is strongly decreased.

Quantification of adsorbed proteins and remaining content of proteins in the supernatant

Table 4: Amount of adsorbed protein in µg per 0.05 m^2 NP determined after each purification step (A = First centrifugation, B = 1. Wash, C = 2. Wash, D = Third wash)

Preparation PS	Amount of adsorbed protein per 0.05 m2 NP
A	781.9 ± 38.6 µg
B	87.22 ± 2.42 µg
C	50.51 ± 2.28 µg
D	49.18 ± 3.00 µg

Preparation PS- COOH	Amount of adsorbed protein per 0.05 m2 NP
A	1208.22 ± 101.38 µg
D	137.35 ± 1.38 µg

Preparation PS- NH_2	Amount of adsorbed protein per 0.05 m2 NP
A	1055.97 ± 18.78 µg
D	66.70 ± 4.93 µg

Table 5: Protein concentration in the remaining supernatant after centrifugation and washing. After the third wash the protein concentration is below the detectable range of the Pierce assay.

Supernatant	Concentration (mg/mL)

A	47.97 ± 1.71 mg/mL
B	1.43 ± 0.03 mg/mL
C	0.07 ± 0.02 mg/mL
D	* (below 0.05 mg/mL)

Table 6: Amount of recovered nanoparticle after the first centrifugation and last washing steps for all nanoparticles measured via fluorescence intensity of nanoparticles at the initial concentration.

Preparation	PS	PS- COOH	PS- NH2
A	71.7 ± 4.8 %	83.6 ± 3.2 %	86.8 ± 5.9 %
D	68.3 ± 3.4 %	72.7 ± 3.4 %	66.8 ± 1.2 %

Classification of corona proteins

After initial centrifugation

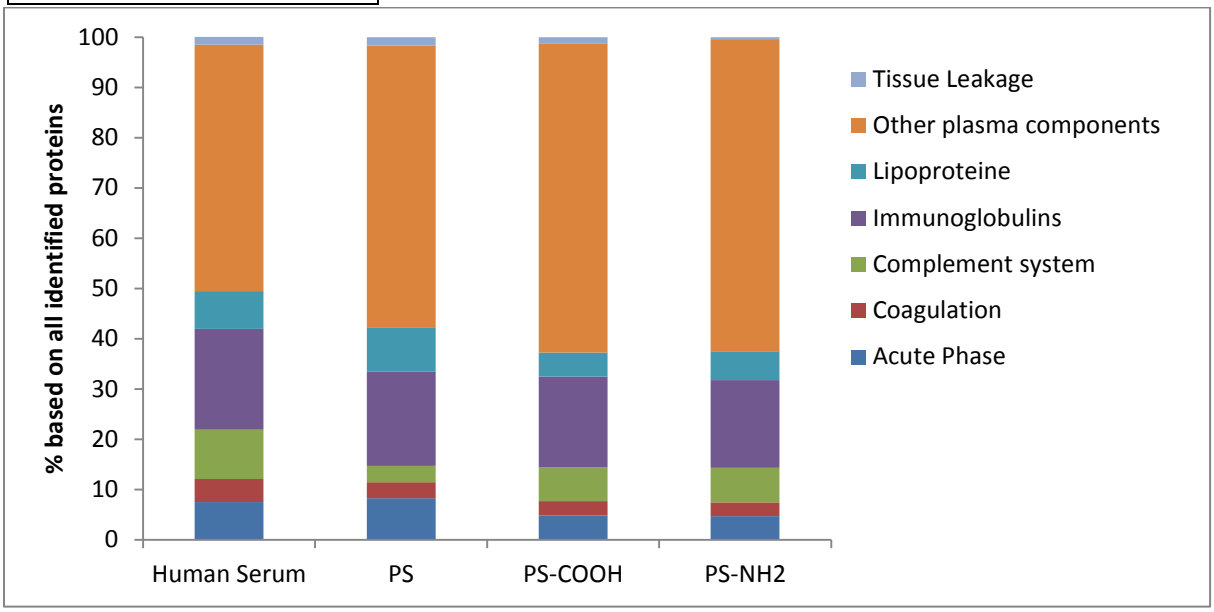

Figure 10: LC-MS Protein classification of proteins associated with nanoparticles after the first centrifugation (A). There is no significant difference in the protein pattern for all nanoparticles.

After 3. wash

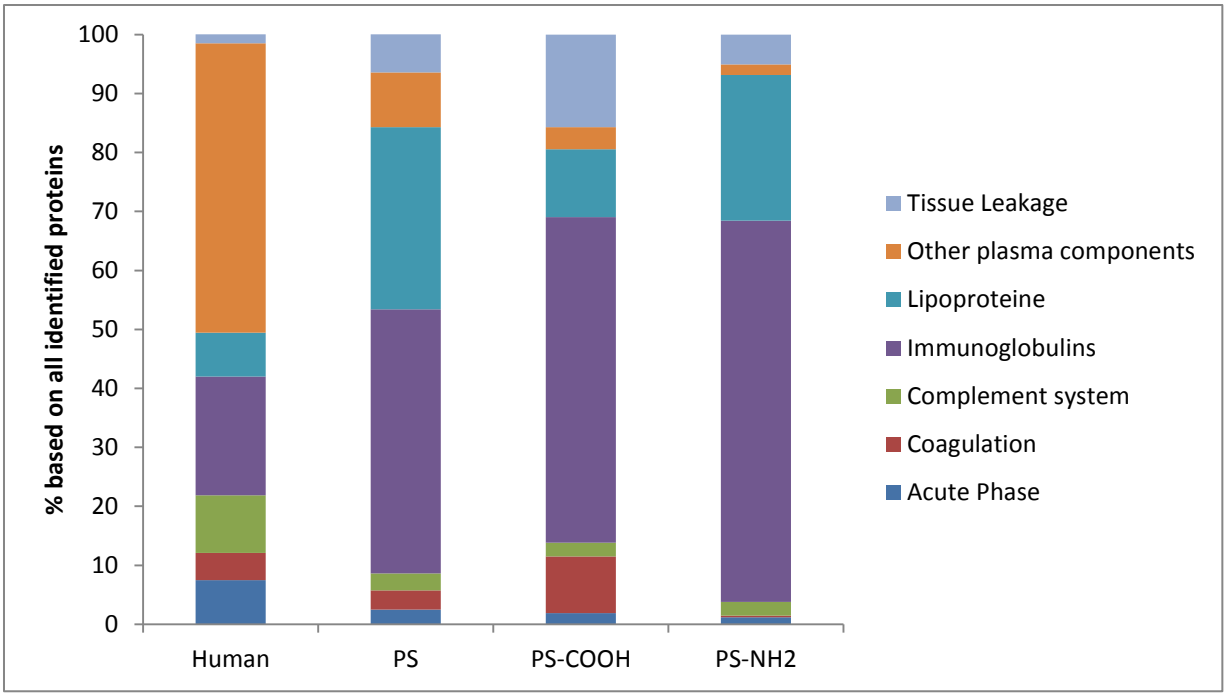

Figure 11: LC-MS Protein classification of proteins associated with nanoparticles after the third wash (D). The distinct hard protein corona profile depends on surface functionalization of nanoparticles and highly differs from the protein composition in human serum.

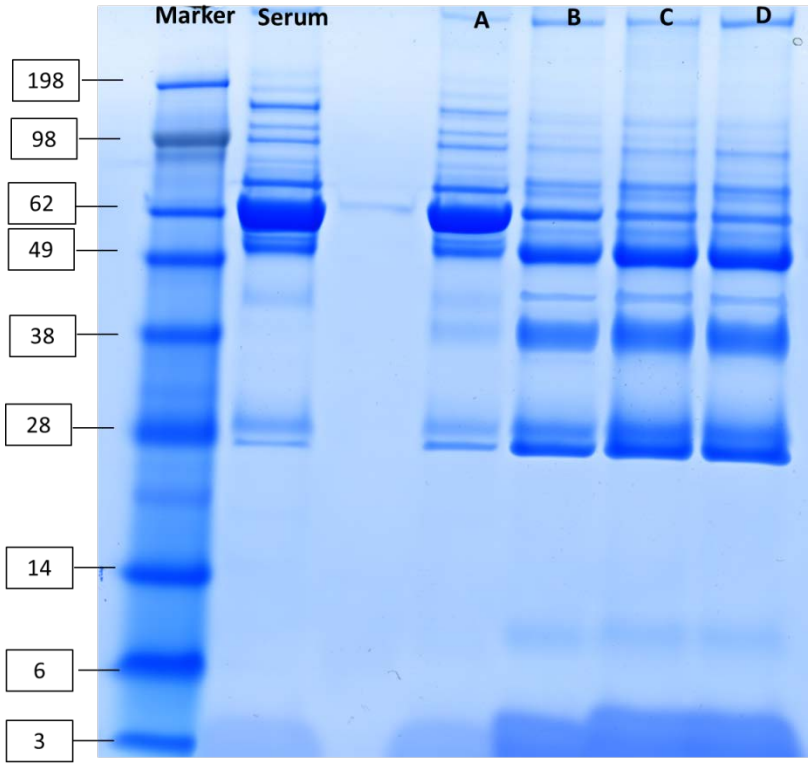

Figure 12: Evolution of the hard corona profil after each purification step for un-functionalized PS nanoparticles visualized by SDS-PAGE. (A = First centrifugation, B = 1. Wash, C = 2. Wash, D = Third wash)

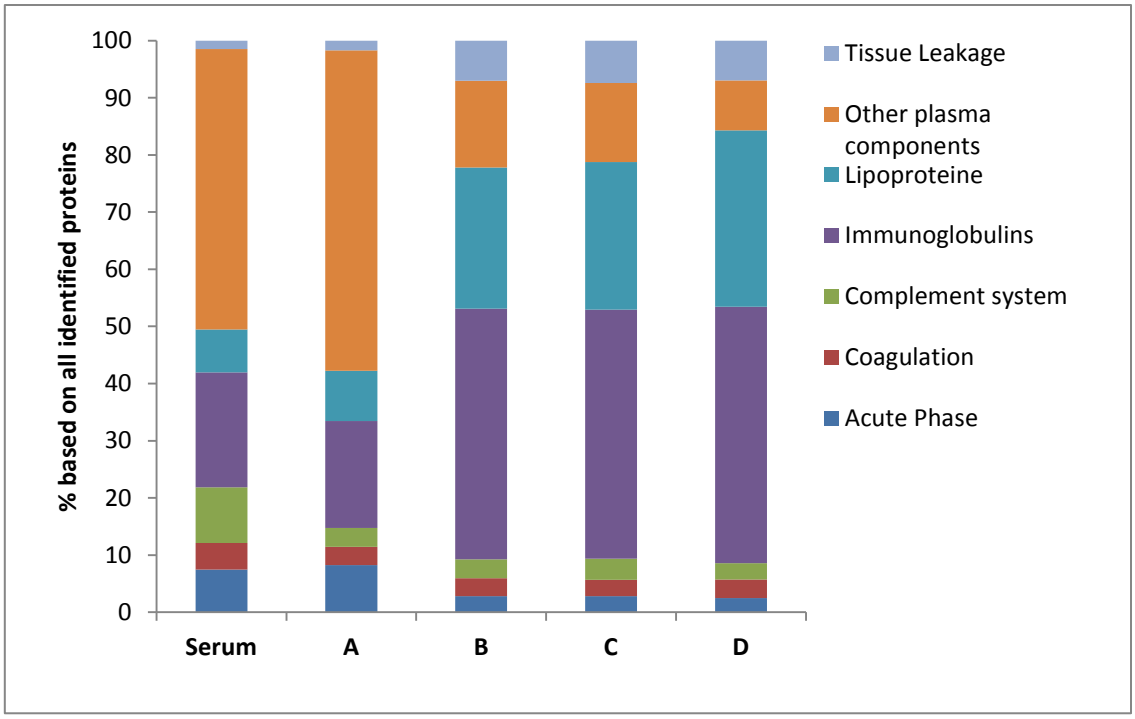

Figure 13: LC-MS Protein classification of proteins associated with un-functionalized PS nanoparticles after each purification step. (A = First centrifugation, B = 1. Wash, C = 2. Wash, D = Third wash)

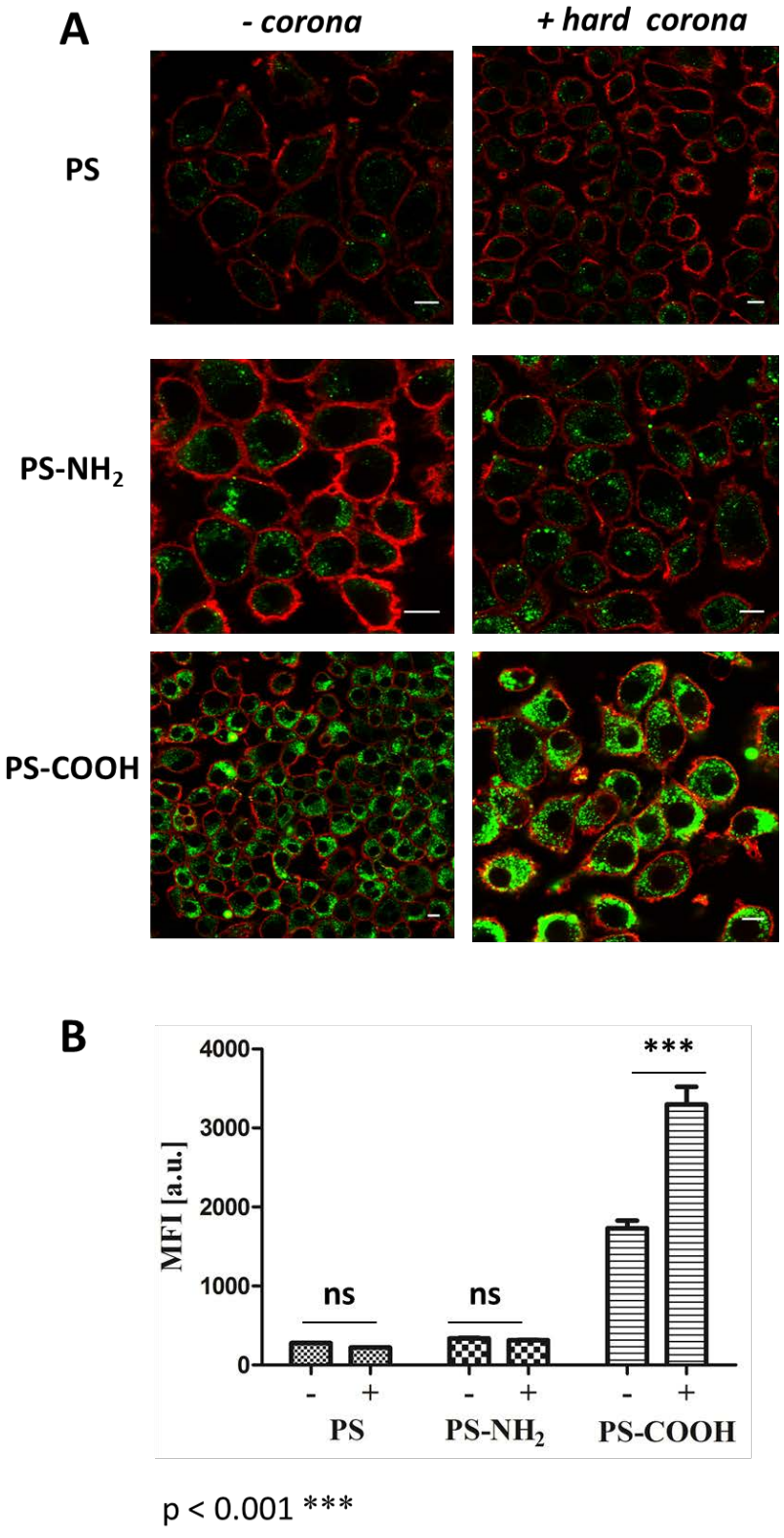

Figure 14: A. Confocal laser scanning microscopy images: RAW264.7 cells were incubated with un-functionalized or functionalized polystyrene nanoparticles (300µg/mL) for 1h. Prior to cellular uptake studies, nanoparticles were incubated with human serum for 1h at 37°C, centrifuged and washed to remove unbound proteins. Isolated hard corona coated nanoparticles (+) or uncoated nanoparticles (-) were added to serum free cell culture medium. Scale

bar: 10µm **B.** Flow cytometry experiments: RAW264.7 cells were incubated with un-functionalized or functionalized polystyrene nanoparticles coated with (+/-) or without hard protein corona (300µg/mL) for 1h. The average of the median fluorescence intensity of three independent experiments is shown (n=3). GraphPad Prism 5 Software was used for statistical analysis using a one-way ANOVA followed by Tukey's post-hoc multiple comparisons test. A *p*-value of < 0.001 was considered as highly significant***.

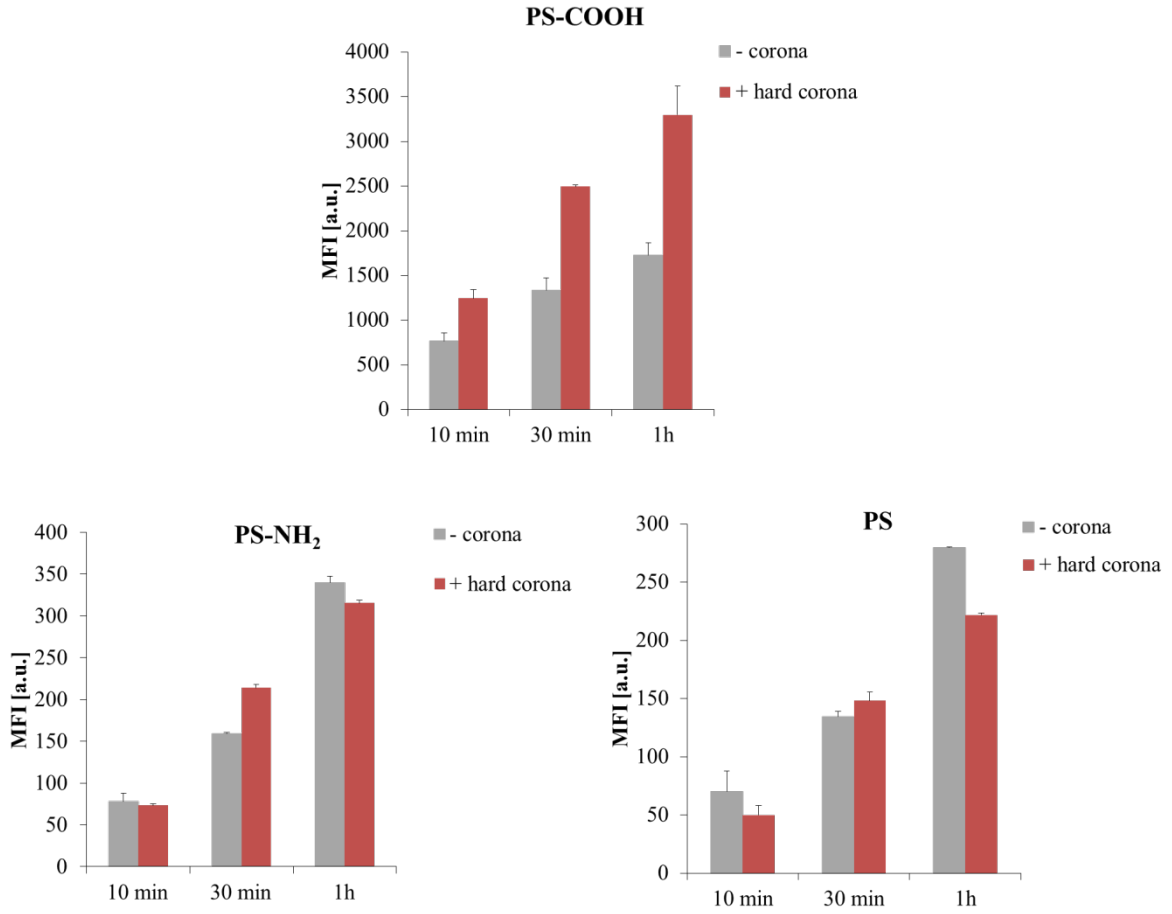

Figure 15: Flow cytometry analysis: RAW264.7 cells were incubated with un-functionalized or functionalized polystyrene nanoparticles (300µg/mL) for 10 min, 30 mins or 1h. Prior to cellular uptake studies, nanoparticles were incubated with human serum for 1h at 37°C, centrifuged and washed to remove unbound proteins. Isolated hard corona coated nanoparticles (+) or uncoated nanoparticles (-) were added to serum free cell culture medium. The average of the median fluorescence intensity (MFI) of three independent experiments is shown (n=3).

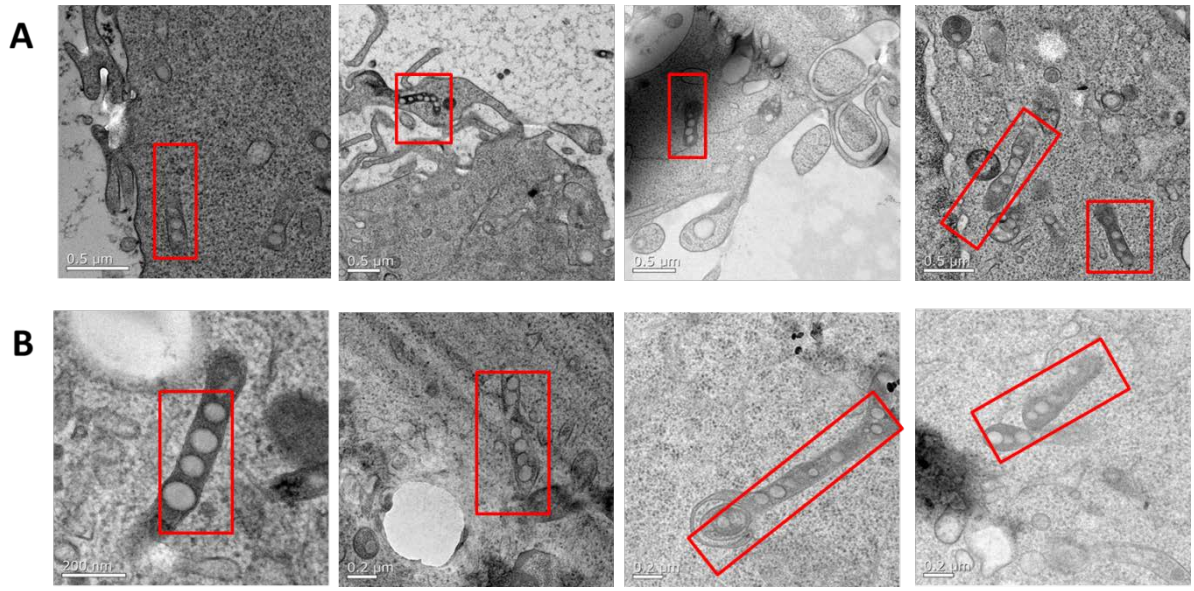

Figure 16: TEM micrographs of high-pressure frozen macrophages treated with 300 µg/mL of un-functionalized nanoparticles **without** (-) hard protein corona for 1h. Scale bar: **A** = 0.5µm; **B** = 200nm. Numerous un-functionalized polystyrene nanoparticles were packed in long membrane structures (CLIC/GEEC endocytosis pathway).

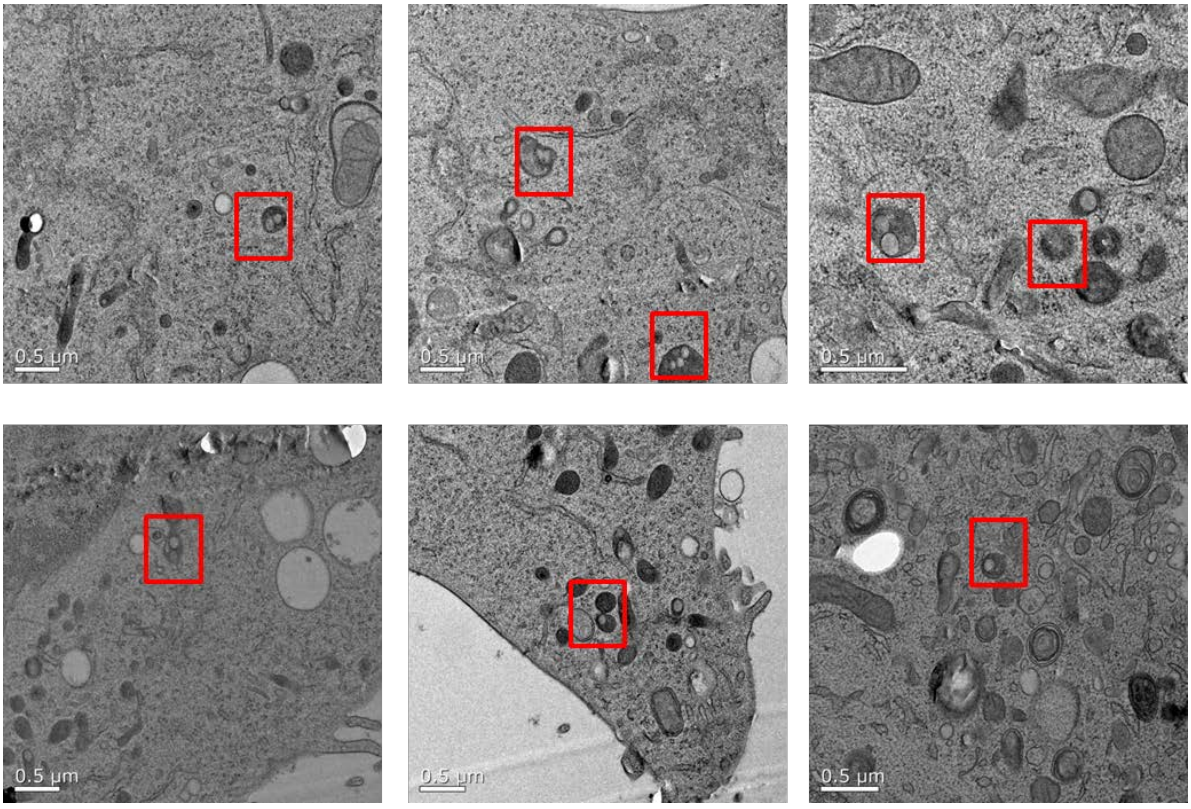

Figure 17: TEM micrographs of high-pressure frozen macrophages treated with 300 µg/mL of un-functionalized nanoparticles **with** (+) hard protein corona for 1h. (+). Scale bar: 0.5µm Hard corona coated un-functionalized PS-NPs were packed in small vesicles (either individually or in a group of 2-3).

LC MS Analysis

Table 7: LC MS Analysis: All identified corona proteins associated with unfunctionalized nanoparticles (PS) after each purification step in comparison to human serum. Values are presented in % based on all identified proteins (in fmol**).**

			PS			
Annotation	**Description**	**Human Serum**	**1st Cent**	**1st Wash**	**2nd Wash**	**3rd Wash**
Acute Phase	Alpha-1-acid glycoprotein 1	0.61	0.54	0.07	0.04	0.04
Acute Phase	Alpha-1-acid glycoprotein 2	0.23	0.25	0.08	0.05	0.04
Acute Phase	Alpha-1-antichymotrypsin	0.33	2.71	0.00	0.00	0.00
Acute Phase	Alpha-2-macroglobulin	0.87	0.58	0.78	0.91	0.58
Acute Phase	Ceruloplasmin	0.32	0.64	0.05	0.03	0.02
Acute Phase	Fibronectin	0.05	0.00	0.00	0.00	0.00
Acute Phase	Haptoglobin	2.03	0.85	0.58	0.53	0.60
Acute Phase	Haptoglobin-related protein	0.18	0.32	0.06	0.06	0.04
Acute Phase	Lipopolysaccharide-binding protein	0.00	0.00	0.00	0.00	0.00
Acute Phase	Platelet basic protein	0.00	0.00	0.00	0.00	0.00
Acute Phase	Serum amyloid A-1 protein	0.00	0.00	0.03	0.04	0.04
Acute Phase	Serum amyloid P-component	0.00	0.67	0.63	0.44	0.46
Coagulation	Alpha-2-antiplasmin	0.00	0.00	0.00	0.00	0.00
Coagulation	Antithrombin-III	0.10	1.17	2.47	2.61	3.02
Coagulation	Carboxypeptidase B2	0.00	0.00	0.08	0.09	0.08
Coagulation	Coagulation factor V	0.00	0.00	0.04	0.04	0.04
Coagulation	Coagulation factor XI	0.00	0.00	0.00	0.00	0.00
Coagulation	Fibrinogen alpha chain	0.00	0.00	0.00	0.00	0.00
Coagulation	Heparin cofactor 2	0.00	0.00	0.00	0.00	0.00
Coagulation	Histidine-rich glycoprotein	0.08	0.04	0.00	0.00	0.00
Coagulation	Integrin alpha-IIb	0.00	0.00	0.00	0.00	0.00
Coagulation	Integrin beta-3	0.00	0.00	0.00	0.00	0.00
Coagulation	Plasma serine protease inhibitor	0.00	0.00	0.00	0.00	0.00
Coagulation	Plasminogen	0.44	0.46	0.00	0.00	0.00
Coagulation	Platelet factor 4	0.00	0.00	0.00	0.00	0.00
Coagulation	Prothrombin	0.13	1.42	0.58	0.59	0.62
Complement system	C4b-binding protein alpha chain	0.13	0.08	0.00	0.00	0.00
Complement system	Calmodulin-like protein 5	0.00	0.00	0.00	0.00	0.00
Complement system	Complement C1q subcomponent subunit B	0.00	0.00	0.76	0.94	0.50
Complement system	Complement C1q subcomponent subunit C	0.05	0.09	0.23	0.22	0.16
Complement system	Complement C1r subcomponent	0.00	0.00	0.08	0.07	0.06
Complement	Complement C1s subcomponent	0.00	0.00	0.29	0.35	0.20

system						
Complement system	Complement C3	1.31	1.03	0.25	0.22	0.14
Complement system	Complement C4-A	0.00	0.00	0.00	0.00	0.00
Complement system	Complement C4-A	0.19	1.51	0.00	0.00	0.00
Complement system	Complement C4-B	0.00	0.00	0.00	0.00	0.00
Complement system	Complement C4-B	0.00	0.00	0.60	0.59	0.42
Complement system	Complement C5	0.00	0.00	0.00	0.00	0.00
Complement system	Complement component C6	0.00	0.00	0.00	0.00	0.00
Complement system	Complement component C7	0.00	0.00	0.00	0.00	0.00
Complement system	Complement component C8	0.00	0.00	0.00	0.00	0.00
Complement system	Complement component C8 alpha chain	0.00	0.00	0.00	0.00	0.00
Complement system	Complement component C8 gamma chain	0.00	0.00	0.02	0.02	0.02
Complement system	Complement component C9	0.00	0.00	0.57	0.65	0.71
Complement system	Complement factor B	0.15	0.04	0.00	0.00	0.00
Complement system	Complement factor H	0.12	0.20	0.15	0.18	0.17
Complement system	Complement factor H-related protein 1	0.00	0.00	0.00	0.00	0.00
Complement system	Complement factor H-related protein 5	0.00	0.00	0.00	0.00	0.00
Complement system	Ig lambda chain V-I	0.00	0.00	0.00	0.00	0.00
Complement system	Mannan-binding lectin serine protease 1	0.00	0.00	0.00	0.00	0.00
Complement system	Plasma protease C1 inhibitor	0.18	0.18	0.25	0.22	0.20
Complement system	Properdin	0.00	0.00	0.06	0.06	0.06
Immunoglobulins	Ig alpha-1 chain C	1.46	0.65	0.23	0.20	0.11
Immunoglobulins	Ig alpha-2 chain C	0.10	0.00	0.00	0.00	0.00
Immunoglobulins	Ig delta chain C	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig gamma-1 chain C	7.87	4.98	20.41	20.29	20.70
Immunoglobulins	Ig gamma-2 chain C	2.58	0.73	0.61	0.63	0.80
Immunoglobulins	Ig gamma-3 chain C	0.70	0.34	1.48	1.43	1.57
Immunoglobulins	Ig gamma-4 chain C	0.06	0.58	0.83	0.91	0.97
Immunoglobulins	Ig gamma-4 chain C	0.00	0.00	0.19	0.21	0.18
Immunoglobulins	Ig heavy chain V-I	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig heavy chain V-I	0.00	0.00	0.21	0.24	0.21
Immunoglobulins	Ig heavy chain V-I	0.00	0.00	0.04	0.05	0.04
Immunoglobulins	Ig heavy chain V-II	0.00	0.12	0.27	0.25	0.20
Immunoglobulins	Ig heavy chain V-II	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig heavy chain V-II	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig heavy chain V-II	0.00	0.00	0.00	0.00	0.00

Immunoglobulins	Ig heavy chain V-II	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig heavy chain V-III	0.30	0.30	1.80	1.93	1.70
Immunoglobulins	Ig kappa chain C	9.85	6.38	19.49	20.11	19.86
Immunoglobulins	Ig kappa chain V-II	0.00	0.00	0.13	0.13	0.13
Immunoglobulins	Ig kappa chain V-II	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-II	0.00	0.17	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-II	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-II	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-II	0.00	0.00	0.24	0.24	0.24
Immunoglobulins	Ig kappa chain V-III 1	0.69	0.13	0.88	0.93	0.83
Immunoglobulins	Ig kappa chain V-IV	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-IV	0.18	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-IV	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-IV	0.00	0.00	0.50	0.44	0.28
Immunoglobulins	Ig kappa chain V-IV	0.00	0.00	0.13	0.12	0.14
Immunoglobulins	Ig kappa chain V-IV	0.00	0.09	0.00	0.00	0.00
Immunoglobulins	Ig lambda chain V-I	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig lambda chain V-I	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig lambda chain V-II	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig lambda chain V-III	0.11	0.00	0.00	0.00	0.00
Immunoglobulins	Ig lambda chain V-III	0.14	0.00	0.11	0.11	0.10
Immunoglobulins	Ig lambda-2 chain C	1.72	0.00	0.00	0.00	0.00
Immunoglobulins	Ig lambda-3 chain C	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Ig lambda-7 chain C	0.00	0.00	0.67	0.61	0.73
Immunoglobulins	Ig mu chain C	0.00	0.00	1.90	0.92	0.79
Immunoglobulins	Ig mu chain C region	0.87	1.03	0.00	0.00	0.00
Immunoglobulins	Ig mu heavy chain disease protein	0.00	0.00	0.06	0.03	0.03
Immunoglobulins	Immunoglobulin J	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Immunoglobulin J	0.00	0.00	0.00	0.00	0.00
Immunoglobulins	Immunoglobulin lambda-like polypeptide 5	0.88	1.43	2.34	2.57	2.30
Immunoglobulins	Plasma kallikrein	0.00	0.00	0.00	0.00	0.00
Lipoproteins	Apolipoprotein A-I	1.88	1.75	8.65	10.29	12.90
Lipoproteins	Apolipoprotein A-II	0.00	0.08	0.13	0.13	0.15
Lipoproteins	Apolipoprotein A-IV	0.09	1.33	0.78	0.89	0.84
Lipoproteins	Apolipoprotein A-V	0.00	0.00	0.00	0.00	0.00
Lipoproteins	Apolipoprotein B-100	0.20	2.03	1.03	1.01	1.23
Lipoproteins	Apolipoprotein C-II	0.00	0.00	0.07	0.07	0.08
Lipoproteins	Apolipoprotein C-III	0.00	0.00	1.37	1.77	1.94
Lipoproteins	Apolipoprotein C-IV	0.00	0.00	0.00	0.00	0.00
Lipoproteins	Apolipoprotein D	0.00	0.00	0.11	0.14	0.10
Lipoproteins	Apolipoprotein E	0.00	0.32	0.52	0.56	0.65
Lipoproteins	Apolipoprotein L1	0.00	0.00	0.00	0.00	0.00
Lipoproteins	Apolipoprotein M	0.00	0.00	0.05	0.03	0.04
Lipoproteins	Beta-2-glycoprotein 1	0.23	0.89	0.09	0.07	0.06
Lipoproteins	Clusterin	0.23	2.11	14.89	14.99	16.77
Lipoproteins	Phospholipid transfer protein	0.00	0.00	0.63	0.57	0.49
Lipoproteins	Serum paraoxonase/arylesterase 1	0.10	0.04	0.00	0.00	0.00

Other Plasma components	Actin, cytoplasmic 1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Actin, gamma-enteric smooth muscle	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Alpha-1-antitrypsin	1.74	1.24	0.28	0.25	0.18
Other Plasma components	Alpha-1B-glycoprotein	0.21	0.16	0.00	0.00	0.00
Other Plasma components	Alpha-2-HS-glycoprotein	0.61	0.27	0.00	0.00	0.00
Other Plasma components	Angiotensinogen	0.12	0.57	0.00	0.00	0.00
Other Plasma components	Annexin A2	0.00	0.00	0.00	0.00	0.00
Other Plasma components	AP-1 complex subunit sigma-2	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Bone morphogenetic protein 8B	0.00	0.00	0.00	0.00	0.00
Other Plasma components	BPI fold-containing family A member 1	0.00	0.00	0.08	1.06	0.06
Other Plasma components	Brain and acute leukemia cytoplasmic protein	0.00	0.00	0.00	0.00	0.00
Other Plasma components	BTB/POZ domain-containing protein	0.00	1.33	0.00	0.00	0.00
Other Plasma components	Calcium-transporting ATPase type 2C member 2	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Carbonyl reductase [NADPH] 1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Caspase-14	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Cofilin-2	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Cytohesin-1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	DnaJ homolog subfamily B member 4	0.00	0.00	0.00	0.00	0.00
Other Plasma components	E3 SUMO-protein ligase PIAS3	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Eukaryotic translation initiation factor 1b	0.00	0.00	0.00	0.00	0.00
Other Plasma components	F-actin-capping protein subunit alpha-2	0.00	0.18	0.00	0.00	0.00
Other Plasma components	Frataxin, mitochondrial	0.00	0.13	0.00	0.00	0.00
Other Plasma components	Ganglioside-induced differentiation-associated protein 1-like 1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Glutathione peroxidase 3	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Hemoglobin subunit beta	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Hemoglobin subunit beta	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Hemoglobin subunit delta	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Hemoglobin subunit gamma-2	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Hemopexin	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Hemopexin	1.43	0.91	0.18	0.15	0.09
Other Plasma	Homeobox protein Meis1	0.00	0.00	0.00	0.00	0.00

components						
Other Plasma components	Inactive ubiquitin carboxyl-terminal hydrolase 17-like protein 7	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Insulin-like growth factor-binding protein complex acid labile subunit	0.02	0.01	0.02	0.02	0.02
Other Plasma components	Inter-alpha-trypsin inhibitor heavy chain H1	0.20	0.33	0.00	0.00	0.00
Other Plasma components	Inter-alpha-trypsin inhibitor heavy chain H2	0.18	0.21	0.00	0.00	0.00
Other Plasma components	Inter-alpha-trypsin inhibitor heavy chain H4	0.13	0.17	0.00	0.00	0.00
Other Plasma components	Keratin	0.37	0.54	0.62	0.83	0.65
Other Plasma components	LIM domain only protein 3	0.00	0.00	0.00	0.00	0.00
Other Plasma components	L-lactate dehydrogenase C	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Lysozyme C	0.00	0.00	0.00	0.04	0.00
Other Plasma components	Microtubule-associated protein RP/EB family member 3	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Multimerin-1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Myb/SANT-like DNA-binding domain-containing protein 4	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Neuroblastoma breakpoint family member 4	0.00	0.11	0.00	0.00	0.00
Other Plasma components	Neutrophil gelatinase-associated lipocalin	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Oxidoreductase NAD-binding domain-containing protein 1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Paired mesoderm homeobox protein 1	0.00	0.07	0.00	0.00	0.00
Other Plasma components	Pancreatic secretory trypsin inhibitor	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Platelet factor 4 variant	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Platelet glycoprotein 4	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Pleckstrin	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Polymeric immunoglobulin receptor	0.00	0.00	0.02	0.11	0.01
Other Plasma components	POTE ankyrin domain family member E	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Pregnancy zone protein	0.00	0.34	0.00	0.00	0.00
Other Plasma components	Probable ribonuclease 11	0.00	0.02	0.00	0.00	0.00
Other Plasma components	Procollagen C-endopeptidase enhancer 1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Protein AMBP	0.13	0.15	0.00	0.00	0.00
Other Plasma components	Protein Njmu-R1	0.00	2.36	0.00	0.00	0.00
Other Plasma components	Protein slowmo homolog 1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Protein SSX9	0.00	0.03	0.00	0.00	0.00
Other Plasma components	Putative annexin A2-like protein	0.00	0.00	0.00	0.00	0.00

Other Plasma components	Putative Polycomb group protein ASXL1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Ragulator complex protein	0.00	1.02	0.00	0.00	0.00
Other Plasma components	Reticulocalbin-3	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Retinol-binding protein 4	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Ribonuclease 4	0.00	0.00	0.00	0.00	0.00
Other Plasma components	RNA-binding protein Musashi homolog 1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Selenoprotein P	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Serotransferrin	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Serum albumin	53.28	40.84	6.94	3.54	1.65
Other Plasma components	Sideroflexin-5	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Synapsin-1	0.00	0.00	0.00	0.00	0.00
Other Plasma components	TRAF family member-associated NF-kappa-B activator	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Transgelin-2	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Transmembrane domain-containing protein	0.00	6.78	0.00	0.00	0.00
Other Plasma components	Transmembrane protein 43	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Transthyretin	0.40	0.37	0.13	0.12	0.09
Other Plasma components	Ubiquitin-conjugating enzyme E2	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Uncharacterized protein C10orf88	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Uncharacterized protein C11orf70	0.00	0.00	0.00	0.00	0.00
Other Plasma components	Vitamin D-binding protein	0.35	0.15	0.00	0.00	0.00
Other Plasma components	Zinc-alpha-2-glycoprotein	0.10	0.17	0.02	0.02	0.00
Other Plasma components	Zymogen granule protein 16 homolog B	0.00	0.00	0.00	0.03	0.00
Tissue Leakage	14-3-3 protein zeta/delta	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	ADP-ribosylation factor 1	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	ADP-ribosylation factor 3	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	ADP-ribosylation factor 5	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Angiogenin	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Calcineurin subunit B type 1	0.00	0.07	0.00	0.00	0.00
Tissue Leakage	Cathelicidin antimicrobial peptide	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	CD5 antigen-like	0.04	0.02	0.07	0.04	0.03
Tissue Leakage	Cell division cycle 5-like protein	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Choriogonadotropin subunit beta	0.00	0.78	0.00	0.00	0.00
Tissue Leakage	Cofilin-1	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Complement C1q subcomponent subunit A	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Erythrocyte band 7 integral membrane	0.00	0.00	0.00	0.00	0.00

	protein					
Tissue Leakage	Fermitin family homolog 3	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Gelsolin	0.03	0.00	0.05	0.05	0.04
Tissue Leakage	Glyceraldehyde-3-phosphate dehydrogenase	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	GTPase IMAP family member 7	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Hemoglobin subunit beta	0.00	0.00	0.09	0.08	0.09
Tissue Leakage	Heterogeneous nuclear ribonucleoprotein A3	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Insulin-like growth factor-binding protein 4	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Insulin-like growth factor-binding protein 5	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Killer cell immunoglobulin-like receptor	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Lactotransferrin	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Microtubule-associated protein RP/EB family member 2	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Multifunctional methyltransferase subunit	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Peflin	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Platelet factor 4	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Probable ATP-dependent RNA helicase	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Profilin-1	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Prolactin-inducible protein	0.00	0.00	0.01	0.13	0.01
Tissue Leakage	Proteoglycan 4	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Putative UPF0607	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Ras-related protein Rap-1A	0.00	0.00	0.09	0.10	0.09
Tissue Leakage	Ras-related protein Rap-1b	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	rRNA methyltransferase 2, mitochondrial	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Serine racemase	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Serotransferrin	2.61	2.05	0.48	0.33	0.25
Tissue Leakage	Serum amyloid A-2 protein	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Small integral membrane protein 7	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Tetranectin	0.00	0.00	0.00	0.00	0.00
Tissue Leakage	Vitronectin	0.33	0.37	0.66	0.61	0.60
Tissue Leakage	Zinc finger protein basonuclin-2	0.00	0.00	0.69	0.67	0.78

Table 8: LC MS Analysis: All identified corona proteins associated with functionalized nanoparticles (PS-COOH and PS-NH_2) after each purification step in comparison to human serum. Values are presented in % based on all identified proteins (in fmol).

		PS-COOH		PS-NH_2	
Annotation	**Description**	**1st Cent**	**3rd Wash**	**1st Cent**	**3rd Wash**
Acute Phase	Alpha-1-acid glycoprotein 1	0.47	0.00	0.37	0.02
Acute Phase	Alpha-1-acid glycoprotein 2	0.20	0.00	0.14	0.03
Acute Phase	Alpha-1-antichymotrypsin	0.56	0.00	0.31	0.04
Acute Phase	Alpha-2-macroglobulin	0.57	0.03	0.61	0.03
Acute Phase	Ceruloplasmin	0.41	0.00	0.41	0.04
Acute Phase	Fibronectin	0.00	0.00	0.00	0.00

Acute Phase	Haptoglobin	1.05	0.00	1.17	0.07
Acute Phase	Haptoglobin-related protein	0.16	0.00	0.18	0.04
Acute Phase	Lipopolysaccharide-binding protein	0.08	0.26	0.01	0.00
Acute Phase	Platelet basic protein	0.00	0.17	0.00	0.04
Acute Phase	Serum amyloid A-1 protein	0.00	0.04	0.00	0.01
Acute Phase	Serum amyloid P-component	0.56	1.37	0.58	0.92
Coagulation	Alpha-2-antiplasmin	0.00	0.03	0.00	0.00
Coagulation	Antithrombin-III	0.48	3.26	0.33	0.06
Coagulation	Carboxypeptidase B2	0.00	0.13	0.00	0.01
Coagulation	Coagulation factor V	0.00	0.17	0.00	0.09
Coagulation	Coagulation factor XI	0.00	0.40	0.00	0.00
Coagulation	Fibrinogen alpha chain	0.00	0.00	0.00	0.01
Coagulation	Heparin cofactor 2	0.00	0.04	0.00	0.00
Coagulation	Histidine-rich glycoprotein	0.00	0.02	0.00	0.00
Coagulation	Integrin alpha-IIb	0.00	0.00	0.00	0.03
Coagulation	Integrin beta-3	0.00	0.00	0.00	0.01
Coagulation	Plasma serine protease inhibitor	0.00	0.18	0.00	0.00
Coagulation	Plasminogen	0.42	0.45	0.70	0.00
Coagulation	Platelet factor 4	0.00	2.27	0.00	0.00
Coagulation	Prothrombin	0.75	2.81	0.37	0.10
Complement system	C4b-binding protein alpha chain	0.10	0.00	0.09	0.06
Complement system	Calmodulin-like protein 5	0.00	0.24	0.00	0.00
Complement system	Complement C1q subcomponent subunit B	0.00	0.26	0.00	0.16
Complement system	Complement C1q subcomponent subunit C	0.00	0.27	0.00	0.36
Complement system	Complement C1r subcomponent	0.00	0.12	0.00	0.10
Complement system	Complement C1s subcomponent	0.00	0.12	0.00	0.09
Complement system	Complement C3	0.65	0.29	0.55	0.28
Complement system	Complement C4-A	0.00	0.00	0.00	0.11
Complement system	Complement C4-A	0.00	0.61	0.00	0.00
Complement system	Complement C4-B	0.00	0.00	0.00	0.02
Complement system	Complement C4-B	4.91	0.00	4.77	0.00
Complement system	Complement C5	0.00	0.00	0.00	0.04
Complement system	Complement component C6	0.00	0.00	0.00	0.01
Complement system	Complement component C7	0.00	0.00	0.00	0.02
Complement system	Complement component C8	0.00	0.02	0.00	0.00
Complement system	Complement component C8 alpha chain	0.00	0.00	0.00	0.02
Complement system	Complement component C8 gamma chain	0.00	0.02	0.00	0.03
Complement	Complement component C9	0.00	0.04	0.00	0.27

system					
Complement system	Complement factor B	0.13	0.00	0.11	0.00
Complement system	Complement factor H	0.26	0.19	0.20	0.14
Complement system	Complement factor H-related protein 1	0.00	0.15	0.00	0.02
Complement system	Complement factor H-related protein 5	0.00	0.09	0.00	0.02
Complement system	Ig lambda chain V-I	0.00	0.00	0.00	0.20
Complement system	Mannan-binding lectin serine protease 1	0.50	0.00	1.02	0.00
Complement system	Plasma protease C1 inhibitor	0.17	0.08	0.12	0.07
Complement system	Properdin	0.00	0.08	0.00	0.20
Immunoglobulins	Ig alpha-1 chain C	0.63	0.09	0.67	0.17
Immunoglobulins	Ig alpha-2 chain C	0.04	0.00	0.04	0.02
Immunoglobulins	Ig delta chain C	0.00	0.00	0.00	0.01
Immunoglobulins	Ig gamma-1 chain C	5.40	23.51	5.37	26.76
Immunoglobulins	Ig gamma-2 chain C	1.11	2.63	1.14	3.22
Immunoglobulins	Ig gamma-3 chain C	0.43	3.10	0.43	3.04
Immunoglobulins	Ig gamma-4 chain C	0.32	0.14	0.31	0.21
Immunoglobulins	Ig gamma-4 chain C	0.00	0.13	0.00	0.00
Immunoglobulins	Ig heavy chain V-I	0.00	0.01	0.00	0.02
Immunoglobulins	Ig heavy chain V-I	0.00	0.13	0.00	0.15
Immunoglobulins	Ig heavy chain V-I	0.00	0.11	0.00	0.11
Immunoglobulins	Ig heavy chain V-II	0.00	0.18	0.00	0.08
Immunoglobulins	Ig heavy chain V-II	0.00	0.01	0.00	0.02
Immunoglobulins	Ig heavy chain V-II	0.00	0.07	0.00	0.00
Immunoglobulins	Ig heavy chain V-II	0.00	0.00	0.00	0.02
Immunoglobulins	Ig heavy chain V-II	0.04	0.00	0.04	0.00
Immunoglobulins	Ig heavy chain V-III	0.35	1.52	0.33	1.78
Immunoglobulins	Ig kappa chain C	6.43	21.24	5.98	22.01
Immunoglobulins	Ig kappa chain V-II	0.03	0.00	0.02	0.02
Immunoglobulins	Ig kappa chain V-II	0.00	0.01	0.00	0.00
Immunoglobulins	Ig kappa chain V-II	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-II	0.00	0.00	0.00	0.39
Immunoglobulins	Ig kappa chain V-II	0.00	0.03	0.00	0.13
Immunoglobulins	Ig kappa chain V-II	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-III 1	0.33	0.55	0.27	1.28
Immunoglobulins	Ig kappa chain V-IV	0.10	0.33	0.11	0.00
Immunoglobulins	Ig kappa chain V-IV	0.00	0.00	0.00	0.38
Immunoglobulins	Ig kappa chain V-IV	0.00	0.00	0.00	0.03
Immunoglobulins	Ig kappa chain V-IV	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-IV	0.00	0.00	0.00	0.00
Immunoglobulins	Ig kappa chain V-IV	0.00	0.00	0.00	0.00
Immunoglobulins	Ig lambda chain V-I	0.00	0.02	0.00	0.00
Immunoglobulins	Ig lambda chain V-I	0.00	0.00	0.00	0.04

Immunoglobulins	Ig lambda chain V-II	0.00	0.03	0.00	0.00
Immunoglobulins	Ig lambda chain V-III	0.00	0.00	0.00	0.14
Immunoglobulins	Ig lambda chain V-III	0.00	0.07	0.00	0.08
Immunoglobulins	Ig lambda-2 chain C	1.45	0.00	1.32	0.00
Immunoglobulins	Ig lambda-3 chain C	0.00	0.00	0.00	0.00
Immunoglobulins	Ig lambda-7 chain C	0.00	0.01	0.00	0.01
Immunoglobulins	Ig mu chain C	0.00	0.38	0.00	0.00
Immunoglobulins	Ig mu chain C region	0.98	0.00	0.98	1.16
Immunoglobulins	Ig mu heavy chain disease protein	0.00	0.01	0.00	0.00
Immunoglobulins	Immunoglobulin J	0.00	0.03	0.00	0.00
Immunoglobulins	Immunoglobulin J	0.00	0.03	0.00	0.05
Immunoglobulins	Immunoglobulin lambda-like polypeptide 5	0.40	1.70	0.38	1.65
Immunoglobulins	Plasma kallikrein	1.21	0.20	1.38	0.00
Lipoproteins	Apolipoprotein A-I	2.02	3.28	2.46	8.58
Lipoproteins	Apolipoprotein A-II		0.00	0.00	0.07
Lipoproteins	Apolipoprotein A-IV	0.48	0.02	0.68	0.31
Lipoproteins	Apolipoprotein A-V	0.00	0.00	0.00	0.02
Lipoproteins	Apolipoprotein B-100	1.01	0.14	1.00	0.11
Lipoproteins	Apolipoprotein C-II	0.00	0.00	0.00	0.04
Lipoproteins	Apolipoprotein C-III	0.00	0.26	0.00	0.85
Lipoproteins	Apolipoprotein C-IV	0.00	0.06	0.00	0.01
Lipoproteins	Apolipoprotein D	0.00	0.00	0.00	0.04
Lipoproteins	Apolipoprotein E	0.16	2.94	0.07	0.56
Lipoproteins	Apolipoprotein L1	0.00	0.00	0.00	0.03
Lipoproteins	Apolipoprotein M	0.00	0.00	0.00	0.02
Lipoproteins	Beta-2-glycoprotein 1	0.73	2.72	0.21	0.05
Lipoproteins	Clusterin	0.35	2.09	1.34	13.76
Lipoproteins	Phospholipid transfer protein	0.00	0.00	0.00	0.05
Lipoproteins	Serum paraoxonase/arylesterase 1	0.00	0.00	0.00	0.02
Other Plasma components	Actin, cytoplasmic 1	0.00	0.00	0.00	0.04
Other Plasma components	Actin, gamma-enteric smooth muscle	0.00	0.00	0.00	0.03
Other Plasma components	Alpha-1-antitrypsin	0.77	0.03	0.91	0.05
Other Plasma components	Alpha-1B-glycoprotein	0.11	0.00	0.10	0.00
Other Plasma components	Alpha-2-HS-glycoprotein	0.22	0.00	0.20	0.00
Other Plasma components	Angiotensinogen	0.20	0.00	0.21	0.00
Other Plasma components	Annexin A2	0.00	0.08	0.00	0.00
Other Plasma components	AP-1 complex subunit sigma-2	0.00	0.00	0.00	0.01
Other Plasma components	Bone morphogenetic protein 8B	0.00	0.00	0.00	0.00
Other Plasma components	BPI fold-containing family A member 1	0.00	0.00	0.00	0.00
Other Plasma components	Brain and acute leukemia cytoplasmic protein	0.00	0.00	0.00	0.01
Other Plasma	BTB/POZ domain-containing protein	0.00	0.00	0.00	0.00

components					
Other Plasma components	Calcium-transporting ATPase type 2C member 2	0.07	0.00	0.07	0.00
Other Plasma components	Carbonyl reductase [NADPH] 1	2.70	0.00	3.17	0.00
Other Plasma components	Caspase-14	0.00	0.01	0.00	0.00
Other Plasma components	Cofilin-2	0.00	0.00	0.00	0.00
Other Plasma components	Cytohesin-1	0.00	0.00	0.00	0.00
Other Plasma components	DnaJ homolog subfamily B member 4	0.00	0.04	0.00	0.00
Other Plasma components	E3 SUMO-protein ligase PIAS3	0.31	0.00	0.20	0.00
Other Plasma components	Eukaryotic translation initiation factor 1b	0.00	0.00	0.00	0.00
Other Plasma components	F-actin-capping protein subunit alpha-2	0.00	0.00	0.00	0.00
Other Plasma components	Frataxin, mitochondrial	0.00	0.00	0.00	0.00
Other Plasma components	Ganglioside-induced differentiation-associated protein 1-like 1	0.04	0.00	0.04	0.00
Other Plasma components	Glutathione peroxidase 3	0.00	0.00	0.00	0.02
Other Plasma components	Hemoglobin subunit beta	0.00	0.00	0.00	0.05
Other Plasma components	Hemoglobin subunit beta	0.03	0.00	0.04	0.00
Other Plasma components	Hemoglobin subunit delta	0.00	0.00	0.00	0.01
Other Plasma components	Hemoglobin subunit gamma-2	0.00	0.00	0.00	0.01
Other Plasma components	Hemopexin	0.00	0.01	0.00	0.00
Other Plasma components	Hemopexin	0.93	0.01	0.81	0.03
Other Plasma components	Homeobox protein Meis1	0.00	0.01	0.00	0.00
Other Plasma components	Inactive ubiquitin carboxyl-terminal hydrolase 17-like protein 7	0.00	0.00	0.00	0.04
Other Plasma components	Insulin-like growth factor-binding protein complex acid labile subunit	0.00	0.00	0.00	0.01
Other Plasma components	Inter-alpha-trypsin inhibitor heavy chain H1	1.27	0.00	0.57	0.00
Other Plasma components	Inter-alpha-trypsin inhibitor heavy chain H2	0.28	0.00	0.38	0.00
Other Plasma components	Inter-alpha-trypsin inhibitor heavy chain H4	0.36	1.98	0.15	0.04
Other Plasma components	Keratin	1.74	1.54	1.51	2.03
Other Plasma components	LIM domain only protein 3	0.06	0.00	0.01	0.00
Other Plasma components	L-lactate dehydrogenase C	0.72	0.00	1.03	0.00
Other Plasma components	Lysozyme C	0.00	0.05	0.00	0.00
Other Plasma components	Microtubule-associated protein RP/EB family member 3	0.60	0.00	0.56	0.00
Other Plasma components	Multimerin-1	0.00	0.05	0.00	0.00

Other Plasma components	Myb/SANT-like DNA-binding domain-containing protein 4	0.00	0.04	0.00	0.00
Other Plasma components	Neuroblastoma breakpoint family member 4	0.00	0.00	0.00	0.00
Other Plasma components	Neutrophil gelatinase-associated lipocalin	0.00	0.01	0.00	0.00
Other Plasma components	Oxidoreductase NAD-binding domain-containing protein 1	0.15	0.00	0.20	0.00
Other Plasma components	Paired mesoderm homeobox protein 1	0.00	0.00	0.00	0.00
Other Plasma components	Pancreatic secretory trypsin inhibitor	0.00	0.00	0.00	0.00
Other Plasma components	Platelet factor 4 variant	0.00	0.16	0.00	0.00
Other Plasma components	Platelet glycoprotein 4	0.00	0.00	0.00	0.01
Other Plasma components	Pleckstrin	0.00	0.02	0.00	0.00
Other Plasma components	Polymeric immunoglobulin receptor	0.00	0.00	0.00	0.00
Other Plasma components	POTE ankyrin domain family member E	0.00	0.00	0.00	0.08
Other Plasma components	Pregnancy zone protein	0.63	0.00	0.62	0.00
Other Plasma components	Probable ribonuclease 11	0.00	0.00	0.00	0.00
Other Plasma components	Procollagen C-endopeptidase enhancer 1	0.00	0.05	0.00	0.00
Other Plasma components	Protein AMBP	0.08	0.10	0.07	0.00
Other Plasma components	Protein Njmu-R1	0.61	0.00	0.58	0.00
Other Plasma components	Protein slowmo homolog 1	0.00	0.00	0.00	0.01
Other Plasma components	Protein SSX9	0.00	0.00	0.00	0.00
Other Plasma components	Putative annexin A2-like protein	0.00	0.00	0.00	0.08
Other Plasma components	Putative Polycomb group protein ASXL1	0.00	0.00	0.00	0.05
Other Plasma components	Ragulator complex protein	0.00	0.00	0.00	0.00
Other Plasma components	Reticulocalbin-3	0.00	0.00	0.00	0.01
Other Plasma components	Retinol-binding protein 4	0.04	0.00	0.04	0.00
Other Plasma components	Ribonuclease 4	0.00	0.04	0.00	0.00
Other Plasma components	RNA-binding protein Musashi homolog 1	0.00	0.15	0.00	0.00
Other Plasma components	Selenoprotein P	0.00	0.04	0.00	0.00
Other Plasma components	Serotransferrin	0.00	0.09	0.00	0.00
Other Plasma components	Serum albumin	47.74	0.69	49.31	1.31
Other Plasma components	Sideroflexin-5	0.03	0.00	0.02	0.00
Other Plasma components	Synapsin-1	0.01	0.00	0.01	0.00
Other Plasma	TRAF family member-associated NF-kappa-B	0.00	0.00	0.00	0.00

components	activator				
Other Plasma components	Transgelin-2	0.00	0.00	0.00	0.01
Other Plasma components	Transmembrane domain-containing protein	0.00	0.00	0.00	0.00
Other Plasma components	Transmembrane protein 43	0.17	0.00	0.13	0.00
Other Plasma components	Transthyretin	0.25	0.05	0.24	0.05
Other Plasma components	Ubiquitin-conjugating enzyme E2	0.00	0.01	0.00	0.00
Other Plasma components	Uncharacterized protein C10orf88	0.00	0.00	0.00	0.03
Other Plasma components	Uncharacterized protein C11orf70	0.16	0.00	0.16	0.00
Other Plasma components	Vitamin D-binding protein	0.13	0.00	0.14	0.01
Other Plasma components	Zinc-alpha-2-glycoprotein	0.04	0.00	0.03	0.00
Other Plasma components	Zymogen granule protein 16 homolog B	0.00	0.00	0.00	0.00
Tissue Leakage	14-3-3 protein zeta/delta	0.00	0.00	0.00	0.00
Tissue Leakage	ADP-ribosylation factor 1	0.00	0.00	0.00	0.02
Tissue Leakage	ADP-ribosylation factor 3	0.00	0.01	0.00	0.00
Tissue Leakage	ADP-ribosylation factor 5	0.00	0.00	0.00	0.00
Tissue Leakage	Angiogenin	0.00	0.42	0.00	0.00
Tissue Leakage	Calcineurin subunit B type 1	0.00	0.00	0.00	0.00
Tissue Leakage	Cathelicidin antimicrobial peptide	0.00	0.05	0.00	0.00
Tissue Leakage	CD5 antigen-like	0.00	0.03	0.00	0.11
Tissue Leakage	Cell division cycle 5-like protein	0.00	0.11	0.00	0.00
Tissue Leakage	Choriogonadotropin subunit beta	0.00	0.00	0.00	0.00
Tissue Leakage	Cofilin-1	0.00	0.03	0.00	0.00
Tissue Leakage	Complement C1q subcomponent subunit A	0.00	0.10	0.00	0.07
Tissue Leakage	Erythrocyte band 7 integral membrane protein	0.05	0.00	0.04	0.02
Tissue Leakage	Fermitin family homolog 3	0.00	0.04	0.00	0.00
Tissue Leakage	Gelsolin	0.00	0.47	0.00	0.11
Tissue Leakage	Glyceraldehyde-3-phosphate dehydrogenase	0.00	0.04	0.00	0.00
Tissue Leakage	GTPase IMAP family member 7	0.00	0.00	0.00	0.01
Tissue Leakage	Hemoglobin subunit beta	0.00	0.00	0.00	0.00
Tissue Leakage	Heterogeneous nuclear ribonucleoprotein A3	0.00	0.00	0.00	1.38
Tissue Leakage	Insulin-like growth factor-binding protein 4	0.00	0.03	0.00	0.00
Tissue Leakage	Insulin-like growth factor-binding protein 5	0.00	0.04	0.00	0.00
Tissue Leakage	Killer cell immunoglobulin-like receptor	0.00	0.00	0.00	0.01
Tissue Leakage	Lactotransferrin	0.00	0.37	0.00	0.00
Tissue Leakage	Microtubule-associated protein RP/EB family member 2	0.00	0.00	0.00	0.01
Tissue Leakage	Multifunctional methyltransferase subunit	0.00	0.00	0.00	0.09
Tissue Leakage	Peflin	0.00	0.00	0.00	1.20
Tissue Leakage	Platelet factor 4	0.21	0.00	0.01	0.06
Tissue Leakage	Probable ATP-dependent RNA helicase	0.00	0.00	0.00	0.22
Tissue Leakage	Profilin-1	0.00	0.00	0.00	0.01
Tissue Leakage	Prolactin-inducible protein	0.00	0.00	0.00	0.00

Tissue Leakage	Proteoglycan 4	0.00	0.13	0.00	0.00
Tissue Leakage	Putative UPF0607	0.00	0.05	0.00	0.00
Tissue Leakage	Ras-related protein Rap-1A	0.00	0.01	0.00	0.00
Tissue Leakage	Ras-related protein Rap-1b	0.00	0.00	0.00	0.06
Tissue Leakage	rRNA methyltransferase 2, mitochondrial	0.00	0.00	0.00	0.07
Tissue Leakage	Serine racemase	0.00	0.00	0.00	0.00
Tissue Leakage	Serotransferrin	1.66	0.09	1.47	0.18
Tissue Leakage	Serum amyloid A-2 protein	0.00	0.00	0.00	0.00
Tissue Leakage	Small integral membrane protein 7	0.00	0.00	0.00	0.01
Tissue Leakage	Tetranectin	0.00	0.00	0.00	0.00
Tissue Leakage	Vitronectin	1.18	10.73	0.36	0.36
Tissue Leakage	Zinc finger protein basonuclin-2	0.00	0.00	0.00	0.68

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