

Protein Corona over Mesoporous Silica Nanoparticles: Influence of the Pore Diameter on Competitive Adsorption and Application to Prostate Cancer Diagnostic

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1. Materials

All materials were purchased from Sigma Aldrich unless otherwise noted, and used as received.

2. Synthesis & Characterization of Nanoparticles

Synthesis of Dense Silica Nanoparticles (SNP). This synthesis was conducted by modifying the Stöber method.¹ EtOH (100%, 20 mL) was mixed with NH₄OH (12.9 M, 1.5 mL) at room temperature in a 100 mL round-bottom flask equipped with a magnetic stir bar. This mixture was stirred briefly to equilibrate, and then tetraethyl orthosilicate (TEOS, 2 mL in 5 mL EtOH, 7 mL, 8.93 mmol) was added to the solution. The obtained gel was 1:2.24:4.70:45.5 SiO₂/NH₄OH/H₂O/EtOH. This mixture was stirred for 1 h at room temperature. Afterwards, the precipitate was isolated by centrifugation (14 800 rpm, 5 min) and resuspended in EtOH. This process was repeated three times in order to remove as much unreacted reagent as possible. Finally, EtOH was removed and the obtained white powder was freeze-dried at -55 °C for 16 h.

Synthesis of Medium Pore Silica Nanoparticles (MSN). This protocol was adapted from a previous recipe.² Hexadecyltrimethylammonium bromide (CTAB, 1.00 g) was dissolved in 500 mL of NaOH 14 mM at 80 °C with strong stirring. Then, 5.0 mL of tetraethyl orthosilicate (TEOS) was dropped slowly. The obtained gel was 1:0.12:0.31:1245 SiO₂/CTAB/NaOH/H₂O. After 2 h the resulting mixture was cooled in ice, filtered off and washed with water and methanol. The solid was freeze-dried at -55 °C for 16 h.

Synthesis of Large Pore Silica Nanoparticles (LPS). According to our former work,³ mesoporous silica nanoparticles with large pores were synthesized by using a block copolymer (Pluronic F127) and a fluorocarbon surfactant (FC-4, Yick-Vik) as internal and external templates, respectively. For the synthesis of LPS-1, 0.25 g of F127 and 0.70 g of FC-4 were dissolved in 30 mL of HCl aqueous solution (0.02 M), followed by the introduction of 0.20 g of 1,3,5-trimethylbenzene (TMB) into the solution. The mixture was stirred for 2h at 15 °C. Then, 1.50 g of tetraethyl orthosilicate (TEOS) was dropped slowly to the solution and stirred for 24 h at 10 °C. The molar ratio of the reactants was 1:0.0028:0.24:0.12:0.08:232 TEOS/F127/TMB/FC-4/HCl/H₂O. The solution along with the precipitate was then introduced into an autoclave and hydrothermally treated at 135 °C for 24 h. The as-prepared product was filtered and washed first with water and subsequently with ethanol and dried in air. For the other LPS samples, the hydrothermal treatment was carried out at 150 °C, and after solid recovery a second hydrothermal treatment was carried out at 100 °C (LPS-2), 120 °C (LPS-3) or 150 °C (LPS-4). For this sake, 0.50 g of as-prepared product was added to a solution of 30 mL of HCl 2M in an autoclave,

and the mixture was heated at 140 °C for 48 h. Subsequently, template removal was done by microwave-assisted digestion. 0.40 g of the as-prepared sample was introduced into a Teflon vessel with 6 mL of HNO₃ (15 M) and 4 mL of H₂O₂ (9 M), and the mixture was treated in a microwave oven MARS-5 at 800 W, 2245 MHz, and 220 V. The maximum temperature (150 °C) was held for 2 min. The solid was recovered by filtration, washed with water and ethanol, and finally dried overnight at room temperature under vacuum.

Surface Modification of Nanoparticles. MSN adsorption properties were modified by surface decoration with variable organic functionalities. Here, the incorporation of amine or carboxylate groups (respectively, MSN-NH₂ or MSN-COOH samples) was carried out by following methods reported elsewhere.⁴ For preparation of thiol derivatized MSN (MSN-SH) 500 mg of particles MSN-OH were dried under vacuum with a temperature of 350 °C for 3 hours. Then 15 mL of anhydrous toluene was added under stirring at 120 °C and inert atmosphere. Finally 932 µL of (3-mercaptopropyl) trimethoxysilane were added and allowed to stir for 16 h. The solid obtained was filtered, washed with toluene and methanol and freeze-dried at -55 °C for 16 h.

Nanoparticle Characterization. Nanoparticle morphology and size were studied by transmission electron microscopy (TEM) in a JEOL JEM 2100F microscope operating at 200 kV. Samples were dispersed in isopropanol and transferred to carbon coated copper grids. Nitrogen gas adsorption isotherms were measured in a Micromeritics Flowsorb apparatus. Surface area calculations were carried out using the BET method, whereas pore size distribution was calculated according the BJH algorithm.⁵ Particle size and Z-Potential measurements were conducted by diffuse light scattering (DLS) in a Zetasizer Nano ZS (Malvern Instruments Ltd., Worcestershire, UK). Dried materials were re-suspended in deionized water at a concentration of 5 µg/mL and measurements were performed at 25 °C. The mean hydrodynamic diameter was determined by cumulant analysis. Surface coverage of organic groups (R-NH₂, R-COOH, R- and R-SH) was calculated from carbon elemental analysis determination (FISONS, EA 1108 CHNS-O). The organic content on the different samples before and after protein adsorption was quantified by thermogravimetric analysis in a Mettler-Toledo TGA/SDTA 851_e apparatus.

3. Supplementary Tables

Table S1. Protein adsorption onto silica nanoparticles from human serum as a function of pore diameter. Values (mg/g SiO₂) corresponding to the mean \pm standard deviation (SD) were calculated by multiplying the normalized spectral counts (NSpC) obtained from liquid chromatography tandem-mass spectrometry (LC-MS/MS) by the total mass of the protein corona (PC) obtained from thermogravimetric analysis (TGA).

Proteomic Fraction (%)	Pore Diameter (nm)					
	0	2.7	4.8	6.2	7.4	14.0
Mw < 50 kDa	64.7 \pm 8.8	84.9 \pm 3.8	86.9 \pm 4.0	84.8 \pm 6.8	85.1 \pm 5.0	79.9 \pm 10.7
Mw 50-70 kDa	28.9 \pm 4.4	11.8 \pm 1.1	9.2 \pm 0.7	11.0 \pm 0.7	11.6 \pm 0.9	16.1 \pm 1.6
Mw 70-140 kDa	4.2 \pm 0.6	2.1 \pm 0.2	2.5 \pm 0.2	2.5 \pm 0.8	2.0 \pm 0.2	1.9 \pm 0.9
Mw > 140 kDa	2.2 \pm 0.6	1.1 \pm 0.1	1.3 \pm 0.4	1.7 \pm 0.5	1.3 \pm 0.1	2.1 \pm 0.6

Table S2. Values of NSpC x TGA for all proteins found in protein corona analysis of silica nanoparticles with variable pore diameter. Total protein content determined by TGA is indicated at the end of the list for every sample. Data in mg/g.

PROTEIN NAME	Mw	SNP	MSN	LPS-1	LPS-2	LPS-3	LPS-4
Immunoglobulin lambda-like polypeptide 5 OS=Homo sapiens GN=IGLL5 PE=2 SV=2	8.843	0.299	0.000	1.717	0.000	0.000	0.000
Apolipoprotein C-I OS=Homo sapiens GN=APOC1 PE=1 SV=1	9.332	0.590	16.978	18.864	14.965	12.733	3.552
Neutrophil defensin 3 OS=Homo sapiens GN=DEFA3 PE=1 SV=1	10.245	0.000	0.000	0.016	0.014	0.000	0.000
Platelet factor 4 OS=Homo sapiens GN=PF4 PE=1 SV=2	10.850	0.123	0.117	0.364	0.535	0.499	0.630
Apolipoprotein C-III OS=Homo sapiens GN=APOC3 PE=1 SV=1	10.852	0.079	8.481	4.577	3.116	2.095	0.535
Apolipoprotein A-II OS=Homo sapiens GN=APOA2 PE=1 SV=1	11.175	7.481	17.874	14.088	13.302	14.543	22.426
Ig lambda-3 chain C regions OS=Homo sapiens GN=IGLC3 PE=1 SV=1	11.238	0.000	0.351	0.880	1.774	0.627	0.545
Apolipoprotein C-II OS=Homo sapiens GN=APOC2 PE=1 SV=1	11.284	0.114	5.522	2.607	1.632	1.048	0.398
Ig lambda-1 chain C regions OS=Homo sapiens GN=IGLC1 PE=1 SV=1	11.348	0.000	0.000	0.000	0.000	0.932	0.853
Platelet factor 4 variant OS=Homo sapiens GN=PF4V1 PE=1 SV=1	11.553	0.000	0.115	0.000	0.000	0.000	0.000
Ig kappa chain C region OS=Homo sapiens GN=IGKC PE=1 SV=1	11.609	0.959	0.632	2.127	1.727	1.872	1.368
Immunoglobulin lambda variable 1-47 OS=Homo sapiens GN=IGLV1-47 PE=1 SV=2	12.284	0.014	0.000	0.040	0.024	0.035	0.017
Immunoglobulin kappa variable 3-15 OS=Homo sapiens GN=IGKV3-15 PE=1 SV=2	12.496	0.000	0.000	0.031	0.030	0.030	0.000
Immunoglobulin kappa variable 3-20 OS=Homo sapiens GN=IGKV3-20 PE=1 SV=2	12.557	0.011	0.000	0.054	0.000	0.043	0.035
Immunoglobulin kappa variable 3-11 OS=Homo sapiens GN=IGKV3-11 PE=1 SV=1	12.575	0.000	0.000	0.038	0.023	0.021	0.000
Vesicle-associated membrane protein 5 OS=Homo sapiens GN=VAMP5 PE=1 SV=1	12.805	0.000	0.000	0.000	0.000	0.058	0.000
Apolipoprotein M OS=Homo sapiens GN=APOM PE=1 SV=2	13.051	0.008	0.016	0.045	0.041	0.061	0.064
Protein FAM27E3 OS=Homo sapiens GN=FAM27E3 PE=1 SV=1	13.507	0.000	0.000	0.000	0.010	0.012	0.128
Serum amyloid A-2 protein OS=Homo sapiens GN=SAA2 PE=1 SV=1	13.527	0.000	1.030	0.650	0.554	0.474	0.252
Serum amyloid A-1 protein OS=Homo sapiens GN=SAA1 PE=1 SV=1	13.532	0.029	1.658	1.198	1.007	0.822	0.318
Beta-2-microglobulin OS=Homo sapiens GN=B2M PE=1 SV=1	13.715	0.000	0.004	0.023	0.035	0.038	0.000
Platelet basic protein OS=Homo sapiens GN=PPBP PE=1 SV=3	13.890	0.106	0.043	0.843	0.677	0.731	0.621
Apolipoprotein C-IV OS=Homo sapiens GN=APOC4 PE=1 SV=1	14.553	0.023	0.215	0.269	0.362	0.293	0.391
Serum amyloid A-4 protein OS=Homo sapiens GN=SAA4 PE=1 SV=2	14.747	0.066	0.580	0.704	0.406	0.632	0.745
Cystatin-C OS=Homo sapiens GN=CT3 PE=1 SV=1	15.800	0.017	0.126	0.141	0.193	0.137	0.131
Transthyretin OS=Homo sapiens GN=TTR PE=1 SV=1	15.887	0.000	0.551	0.621	0.239	0.297	0.063
Hemoglobin subunit gamma-2 OS=Homo sapiens GN=HBG2 PE=1 SV=2	16.126	0.006	0.000	0.000	0.000	0.013	0.019
Lysozyme C OS=Homo sapiens GN=LYZ PE=1 SV=1	16.537	0.012	14.563	0.033	0.058	0.056	0.047
Angiogenin OS=Homo sapiens GN=ANG PE=1 SV=1	16.561	0.017	0.000	0.024	0.043	0.040	0.000
Ribonuclease 4 OS=Homo sapiens GN=RNASE4 PE=1 SV=3	16.925	0.000	0.000	0.000	0.026	0.019	0.024
Immunoglobulin J chain OS=Homo sapiens GN=JCHAIN PE=1 SV=4	18.099	0.000	0.000	0.000	0.000	0.004	0.000
Cofilin-1 OS=Homo sapiens GN=CFL1 PE=1 SV=3	18.502	0.002	0.016	0.017	0.032	0.033	0.030
Retinoic acid receptor responder protein 2 OS=Homo sapiens GN=RARRES2 PE=1 SV=1	18.618	0.014	0.032	0.037	0.045	0.036	0.051
REVERSED Transmembrane and coiled-coil domain-containing protein 2 OS=Homo sapiens GN=TMCO2 PE=2 SV=1	20.071	0.000	0.008	0.000	0.000	0.000	0.000
Insulin-like growth factor II OS=Homo sapiens GN=IGF2 PE=1 SV=1	20.274	0.008	0.055	0.047	0.027	0.015	0.034
Apolipoprotein D OS=Homo sapiens GN=APOD PE=1 SV=1	21.276	0.015	0.047	0.112	0.043	0.091	0.160
Insulin-like growth factor 1 OS=Homo sapiens GN=IGF1 PE=1 SV=1	21.841	0.000	0.000	0.000	0.000	0.021	0.024
Complement component C8 gamma chain OS=Homo sapiens GN=C8G PE=1 SV=3	22.277	0.044	0.000	0.000	0.000	0.000	0.000
Transgelin-2 OS=Homo sapiens GN=TAGLN2 PE=1 SV=3	22.391	0.000	0.000	0.010	0.000	0.000	0.001
Tetranectin OS=Homo sapiens GN=CLEC3B PE=1 SV=3	22.537	0.181	1.112	0.496	0.304	0.312	0.247
Retinol-binding protein 4 OS=Homo sapiens GN=RBP4 PE=1 SV=3	23.010	0.000	0.000	0.000	0.008	0.013	0.042
Insulin-like growth factor-binding protein 6 OS=Homo sapiens GN=IGFBP6 PE=1 SV=1	25.320	0.000	0.001	0.013	0.010	0.009	0.000
Serum amyloid P-component OS=Homo sapiens GN=APCS PE=1 SV=2	25.387	0.051	0.000	0.000	0.000	0.000	0.000
Glutathione peroxidase 3 OS=Homo sapiens GN=GPX3 PE=1 SV=2	25.552	0.008	0.075	0.054	0.027	0.023	0.047
Complement C1q subcomponent subunit C OS=Homo sapiens GN=C1QC PE=1 SV=3	25.774	0.000	0.000	0.013	0.011	0.006	0.029
Complement C1q subcomponent subunit B OS=Homo sapiens GN=C1QB PE=1 SV=3	26.722	0.000	0.000	0.007	0.000	0.006	0.000
Complement factor D OS=Homo sapiens GN=CFD PE=1 SV=5	27.870	0.031	0.039	0.090	0.056	0.059	0.181
Insulin-like growth factor-binding protein 4 OS=Homo sapiens GN=IGFBP4 PE=1 SV=2	27.940	0.001	0.000	0.012	0.014	0.012	0.000
Insulin-like growth factor-binding protein 5 OS=Homo sapiens GN=IGFBP5 PE=1 SV=1	30.570	0.003	0.000	0.000	0.004	0.000	0.009
Complement factor H-related protein 2 OS=Homo sapiens GN=CFHR2 PE=1 SV=1	30.651	0.113	0.086	0.075	0.069	0.000	0.000
Apolipoprotein A-I OS=Homo sapiens GN=APOA1 PE=1 SV=1	30.778	9.106	90.776	78.863	59.483	65.113	71.728
Insulin-like growth factor-binding protein 3 OS=Homo sapiens GN=IGFBP3 PE=1 SV=2	31.674	0.009	0.015	0.011	0.011	0.009	0.016
Insulin-like growth factor-binding protein 2 OS=Homo sapiens GN=IGFBP2 PE=1 SV=2	34.814	0.003	0.000	0.000	0.000	0.005	0.008
Apolipoprotein F OS=Homo sapiens GN=APOF PE=1 SV=2	35.399	0.000	0.062	0.025	0.008	0.011	0.000
Ig gamma-2 chain C region OS=Homo sapiens GN=IGHG2 PE=1 SV=2	35.901	0.424	0.000	0.600	0.684	0.671	0.474
Ig gamma-4 chain C region OS=Homo sapiens GN=IGHG4 PE=1 SV=1	35.941	0.000	0.185	0.000	0.000	0.000	0.923
Ig gamma-1 chain C region OS=Homo sapiens GN=IGHG1 PE=1 SV=1	36.106	1.351	0.373	1.884	2.016	1.777	1.443
Apolipoprotein E OS=Homo sapiens GN=APOE PE=1 SV=1	36.154	0.670	4.835	5.497	4.659	4.380	6.401
Complement factor H-related protein 1 OS=Homo sapiens GN=CFHR1 PE=1 SV=2	37.651	0.196	0.291	0.172	0.144	0.160	0.197
Ig alpha-1 chain C region OS=Homo sapiens GN=IGHA1 PE=1 SV=2	37.663	0.026	0.162	0.056	0.062	0.095	0.120
Beta-2-glycoprotein 1 OS=Homo sapiens GN=APOH PE=1 SV=3	38.298	0.507	0.616	0.181	0.085	0.058	0.253
Protein AMBP OS=Homo sapiens GN=AMBP PE=1 SV=1	38.999	0.009	0.056	0.029	0.012	0.009	0.014
Alpha-2-HS-glycoprotein OS=Homo sapiens GN=AHSG PE=1 SV=1	39.325	0.670	5.589	3.006	1.790	1.606	3.363
Serum paraoxonase/arylesterase 1 OS=Homo sapiens GN=PON1 PE=1 SV=3	39.731	0.025	0.071	0.070	0.035	0.064	0.067
Ig gamma-3 chain C region OS=Homo sapiens GN=IGHG3 PE=1 SV=2	41.287	0.723	0.293	1.512	1.542	1.292	0.997
Actin, cytoplasmic 2 OS=Homo sapiens GN=ACTG1 PE=1 SV=1	41.793	0.000	0.003	0.000	0.000	0.000	0.000
Putative beta-actin-like protein 3 OS=Homo sapiens GN=POTEKP PE=5 SV=1	42.016	0.000	0.011	0.000	0.000	0.000	0.000
Haptoglobin-related protein OS=Homo sapiens GN=HPR PE=2 SV=2	43.078	0.000	0.171	0.018	0.024	0.037	0.088
Selenoprotein P OS=Homo sapiens GN=SEPP1 PE=1 SV=3	43.174	0.059	0.304	0.204	0.194	0.198	0.364
Apolipoprotein L1 OS=Homo sapiens GN=APOLI1 PE=1 SV=5	43.974	0.002	0.034	0.017	0.017	0.017	0.021
Haptoglobin OS=Homo sapiens GN=HP PE=1 SV=1	45.205	0.008	0.325	0.017	0.019	0.033	0.037
Apolipoprotein A-IV OS=Homo sapiens GN=APOA4 PE=1 SV=3	45.399	0.411	5.133	4.867	2.873	2.764	1.479
Plasma serine protease inhibitor OS=Homo sapiens GN=SERPINA5 PE=1 SV=3	45.680	0.000	0.000	0.000	0.009	0.014	0.044
Pigment epithelium-derived factor OS=Homo sapiens GN=SERPINF1 PE=1 SV=4	46.312	0.107	0.007	0.057	0.028	0.027	0.076
Alpha-1-antitrypsin OS=Homo sapiens GN=SERPINA1 PE=1 SV=3	46.737	0.002	0.187	0.155	0.067	0.066	0.042
Keratin, type I cuticular Ha1 OS=Homo sapiens GN=KRT31 PE=1 SV=3	47.237	0.000	0.000	0.000	0.000	0.000	0.017
Alpha-1-antichymotrypsin OS=Homo sapiens GN=SERPINA3 PE=1 SV=2	47.651	0.004	0.000	0.000	0.000	0.000	0.002
Procollagen C-endopeptidase enhancer 1 OS=Homo sapiens GN=PCOLCE PE=1 SV=2	47.972	0.002	0.000	0.006	0.006	0.012	0.064
Kallistatin OS=Homo sapiens GN=SERPINA4 PE=1 SV=3	48.542	0.003	0.000	0.000	0.000	0.000	0.000
Ig mu chain C region OS=Homo sapiens GN=IGHM PE=1 SV=3	49.307	0.023	0.007	0.010	0.030	0.042	0.088
REVERSED Adenyltransferase and sulfatransferase MOCS3 OS=Homo sapiens GN=MOCS3 PE=1 SV=1	49.669	0.000	0.051	0.000	0.000	0.000	0.000
RUN domain-containing protein 3A OS=Homo sapiens GN=RUNC3A PE=1 SV=2	49.747	0.000	0.014	0.021	0.027	0.027	0.098
Fibrinogen gamma chain OS=Homo sapiens GN=FGG PE=1 SV=3	51.512	0.000	0.000	0.000	0.000	0.000	0.000
Hemopexin OS=Homo sapiens GN=HPX PE=1 SV=2	51.676	0.071	0.133	0.510	0.269	0.194	0.151
Coagulation factor IX OS=Homo sapiens GN=F9 PE=1 SV=2	51.778	0.000	0.001	0.000	0.000	0.000	0.000
Adenylyl cyclase-associated protein 1 OS=Homo sapiens GN=CAPI1 PE=1 SV=5	51.901	0.000	0.000	0.004	0.002	0.012	0.000
Ig lambda-2 chain C regions OS=Homo sapiens GN=IGLC2 PE=1 SV=1	52.199	0.067	0.140	0.330	0.174	0.183	0.237
Clusterin OS=Homo sapiens GN=CLU PE=1 SV=1	52.495	0.091	1.173	0.313	0.173	0.160	0.074
FAS-associated factor 2 OS=Homo sapiens GN=FAF2 PE=1 SV=2	52.623	0.000	0.000	0.000	0.000	0.001	0.000
Vitamin D-binding protein OS=Homo sapiens GN=GC PE=1 SV=1	52.964	0.025	0.558	0.159	0.033	0.027	0.017
Angiotensinogen OS=Homo sapiens GN=AGT PE=1 SV=1	53.154	0.000	0.004	0.000	0.000	0.000	0.000
Lipopolysaccharide-binding protein OS=Homo sapiens GN=LBP PE=1 SV=3	53.319	0.005	0.001	0.000	0.000	0.000	0.003
Keratin, type II cuticular Hb6 OS=Homo sapiens GN=KRT86 PE=1 SV=1	53.501	0.000	0.000	0.000	0.000	0.000	0.012
Alpha-1B-glycoprotein OS=Homo sapiens GN=A1BG PE=1 SV=4	54.254	0.000	0.025	0.000	0.000	0.000	0.000

Vitronectin OS=Homo sapiens GN=VTN PE=1 SV=1	54.306	0.282	1.295	0.409	0.235	0.261	0.229
Alpha-2-antiplasmin OS=Homo sapiens GN=SERPINF2 PE=1 SV=3	54.566	0.000	0.040	0.000	0.002	0.004	0.000
EGF-containing fibulin-like extracellular matrix protein 1 OS=Homo sapiens GN=EFEMP1 PE=1 SV=2	54.641	0.000	0.028	0.000	0.000	0.000	0.000
Plasma protease C1 inhibitor OS=Homo sapiens GN=SERPING1 PE=1 SV=2	55.154	0.007	0.000	0.000	0.000	0.000	0.000
Sperm-associated antigen 6 OS=Homo sapiens GN=SPAG6 PE=2 SV=1	55.476	0.001	0.000	0.003	0.002	0.002	0.000
Fibrinogen beta chain OS=Homo sapiens GN=FGB PE=1 SV=2	55.928	0.006	0.000	0.000	0.000	0.000	0.000
Heparin cofactor 2 OS=Homo sapiens GN=SERPIND1 PE=1 SV=3	57.071	0.003	0.016	0.001	0.002	0.001	0.001
Histidine-rich glycoprotein OS=Homo sapiens GN=HRG PE=1 SV=1	59.578	3.413	7.937	8.932	10.002	11.133	18.933
REVERSED Histone H4 transcription factor OS=Homo sapiens GN=HNFPP PE=1 SV=2	59.678	0.004	0.000	0.000	0.016	0.017	0.069
REVERSED Glucosylceramidase OS=Homo sapiens GN=GBA PE=1 SV=3	59.716	0.000	0.000	0.000	0.002	0.000	0.000
ATP synthase subunit alpha, mitochondrial OS=Homo sapiens GN=ATP5A1 PE=1 SV=1	59.751	0.000	0.000	0.000	0.000	0.001	0.000
Keratin, type II cytoskeletal 6C OS=Homo sapiens GN=KRT6C PE=1 SV=3	60.025	0.000	0.001	0.000	0.000	0.000	0.000
Keratin, type II cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3	62.064	0.000	0.014	0.000	0.000	0.000	0.000
N-acetylmuramoyl-L-alanine amidase OS=Homo sapiens GN=PGLYRP2 PE=1 SV=1	62.219	0.001	0.004	0.000	0.000	0.000	0.000
Leucine-rich repeat LG1 family member 2 OS=Homo sapiens GN=LG12 PE=2 SV=1	62.298	0.000	0.000	0.000	0.015	0.000	0.000
Hyaluronan-binding protein 2 OS=Homo sapiens GN=HABP2 PE=1 SV=1	62.672	0.002	0.000	0.000	0.000	0.000	0.000
Complement component C9 OS=Homo sapiens GN=C9 PE=1 SV=2	63.173	0.032	0.022	0.004	0.001	0.000	0.008
C4b-binding protein alpha chain OS=Homo sapiens GN=C4BPA PE=1 SV=2	64.283	0.000	0.000	0.074	0.045	0.038	0.004
Complement factor H-related protein 5 OS=Homo sapiens GN=CFHR5 PE=1 SV=1	64.430	0.000	0.025	0.000	0.000	0.000	0.000
REVERSED Zinc finger protein 211 OS=Homo sapiens GN=ZNF211 PE=2 SV=2	64.535	0.000	0.000	0.000	0.008	0.000	0.000
Complement component C8 alpha chain OS=Homo sapiens GN=C8A PE=1 SV=2	65.163	0.010	0.000	0.000	0.000	0.000	0.000
Coiled-coil domain-containing protein 38 OS=Homo sapiens GN=CCDC38 PE=2 SV=1	65.315	0.000	0.000	0.000	0.000	0.003	0.000
Keratin, type II cytoskeletal 2 epidermal OS=Homo sapiens GN=KRT2 PE=1 SV=2	65.433	0.004	0.000	0.000	0.000	0.000	0.000
Complement factor I OS=Homo sapiens GN=CFI PE=1 SV=2	65.750	0.006	0.003	0.000	0.000	0.000	0.000
Insulin-like growth factor-binding protein complex acid labile subunit OS=Homo sapiens GN=IGFALS PE=1 SV=1	66.035	0.011	0.001	0.001	0.004	0.009	0.028
Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6	66.039	0.010	0.023	0.000	0.000	0.000	0.027
All-trans-retinol 13,14-reductase OS=Homo sapiens GN=RETSAT PE=1 SV=2	66.820	0.000	0.000	0.000	0.005	0.007	0.000
Complement component C8 beta chain OS=Homo sapiens GN=C8B PE=1 SV=3	67.047	0.013	0.000	0.000	0.000	0.000	0.000
Probable ATP-dependent RNA helicase DDX52 OS=Homo sapiens GN=DDX52 PE=1 SV=3	67.498	0.000	0.000	0.000	0.000	0.189	0.000
Coagulation factor XII OS=Homo sapiens GN=F12 PE=1 SV=3	67.792	0.220	0.763	0.403	0.328	0.465	0.547
Afamin OS=Homo sapiens GN=AFM PE=1 SV=1	69.070	0.000	0.003	0.000	0.000	0.000	0.000
Serum albumin OS=Homo sapiens GN=ALB PE=1 SV=2	69.367	6.775	12.932	4.630	3.596	3.304	3.659
Prothrombin OS=Homo sapiens GN=F2 PE=1 SV=2	70.037	0.026	0.383	0.164	0.111	0.097	0.053
Coagulation factor XI OS=Homo sapiens GN=F11 PE=1 SV=1	70.109	0.000	0.000	0.000	0.000	0.000	0.000
Hepatocyte growth factor activator OS=Homo sapiens GN=HGFA PE=1 SV=1	70.682	0.014	0.020	0.039	0.049	0.057	0.102
Secretogranin-2 OS=Homo sapiens GN=SG2 PE=1 SV=2	70.941	0.000	0.000	0.000	0.000	0.006	0.000
Plasma kallikrein OS=Homo sapiens GN=KLKB1 PE=1 SV=1	71.370	0.009	0.044	0.014	0.006	0.009	0.000
Cartilage acidic protein 1 OS=Homo sapiens GN=CRTAC1 PE=1 SV=2	71.421	0.000	0.000	0.000	0.000	0.000	0.003
Kininogen-1 OS=Homo sapiens GN=KNG1 PE=1 SV=2	71.957	0.232	1.333	0.633	0.905	0.486	0.185
REVERSED Differentially expressed in FDPC 6 homolog OS=Homo sapiens GN=DEF6 PE=1 SV=1	73.910	0.000	0.027	0.000	0.026	0.000	0.046
Complement C1s subcomponent OS=Homo sapiens GN=C1S PE=1 SV=1	76.684	0.000	0.004	0.000	0.000	0.000	0.000
Serotransferrin OS=Homo sapiens GN=TF PE=1 SV=3	77.064	0.068	0.028	0.046	0.055	0.071	0.135
REVERSED Endoplasmic reticulum mannosyl-oligosaccharide 1,2-alpha-mannosidase OS=Homo sapiens GN=MAN1B1 PE=1 SV=2	79.580	0.000	0.000	0.000	0.000	0.001	0.000
Putative macrophage stimulating 1-like protein OS=Homo sapiens GN=MS1L PE=2 SV=2	79.694	0.002	0.000	0.000	0.000	0.000	0.000
Complement C1r subcomponent OS=Homo sapiens GN=C1R PE=1 SV=2	80.119	0.000	0.000	0.000	0.000	0.000	0.000
SEC14-like protein 1 OS=Homo sapiens GN=SEC14L1 PE=1 SV=2	81.250	0.000	0.009	0.000	0.000	0.000	0.000
Sulfhydryl oxidase 1 OS=Homo sapiens GN=SOX1 PE=1 SV=3	82.578	0.001	0.000	0.000	0.000	0.000	0.000
Complement C2 OS=Homo sapiens GN=C2 PE=1 SV=2	83.266	0.030	0.061	0.052	0.012	0.016	0.036
Complement factor B OS=Homo sapiens GN=CFB PE=1 SV=2	85.533	0.265	0.175	0.041	0.017	0.021	0.003
Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1	85.698	0.495	1.337	1.828	1.240	0.943	0.781
REVERSED tRNA (cytosine[34]-C[5])-methyltransferase OS=Homo sapiens GN=NSUN2 PE=1 SV=2	86.471	0.000	0.000	0.000	0.000	0.000	0.005
Plasminogen OS=Homo sapiens GN=PLG PE=1 SV=2	90.569	0.341	0.387	0.801	0.667	0.660	0.765
Complement component C7 OS=Homo sapiens GN=C7 PE=1 SV=2	93.518	0.000	0.000	0.000	0.000	0.000	0.000
Fibrinogen alpha chain OS=Homo sapiens GN=FGA PE=1 SV=2	94.973	0.000	0.277	0.276	0.217	0.235	0.127
Rab GTPase-binding effector protein 1 OS=Homo sapiens GN=RABEP1 PE=1 SV=2	99.290	0.000	0.000	0.000	0.000	0.000	0.003
Inter-alpha-trypsin inhibitor heavy chain III OS=Homo sapiens GN=ITHI1 PE=1 SV=3	101.389	0.012	0.026	0.005	0.002	0.004	0.002
Inter-alpha-trypsin inhibitor heavy chain H4 OS=Homo sapiens GN=ITH4 PE=1 SV=4	103.357	0.050	0.163	0.188	0.101	0.103	0.562
Complement component C6 OS=Homo sapiens GN=C6 PE=1 SV=3	104.786	0.016	0.063	0.080	0.009	0.010	0.004
Inter-alpha-trypsin inhibitor heavy chain H2 OS=Homo sapiens GN=ITH2 PE=1 SV=2	106.463	0.017	0.034	0.006	0.010	0.003	0.000
Ankyrin repeat domain-containing protein 35 OS=Homo sapiens GN=ANKRD35 PE=2 SV=2	109.966	0.000	0.016	0.023	0.016	0.011	0.006
ADAMTS-like protein 4 OS=Homo sapiens GN=ADAMTSL4 PE=1 SV=2	116.545	0.000	0.002	0.000	0.000	0.001	0.000
POTE ankyrin domain family member E OS=Homo sapiens GN=POTEE PE=2 SV=3	121.363	0.000	0.001	0.000	0.000	0.000	0.000
Ceruloplasmin OS=Homo sapiens GN=CP PE=1 SV=1	122.205	0.022	0.000	0.000	0.000	0.000	0.000
Thrombospondin-1 OS=Homo sapiens GN=THBS1 PE=1 SV=2	129.390	0.000	0.001	0.002	0.000	0.000	0.006
Partner and localizer of BRCA2 OS=Homo sapiens GN=PALB2 PE=1 SV=1	131.295	0.000	0.000	0.000	0.000	0.001	0.000
Sperm-associated antigen 5 OS=Homo sapiens GN=SPAG5 PE=1 SV=2	134.422	0.000	0.000	0.000	0.010	0.000	0.000
Complement factor H OS=Homo sapiens GN=CFH PE=1 SV=4	139.096	0.021	0.166	0.020	0.002	0.009	0.016
Sterol regulatory element-binding protein cleavage-activating protein OS=Homo sapiens GN=SCAP PE=1 SV=4	139.729	0.000	0.005	0.000	0.000	0.000	0.000
Proteoglycan 4 OS=Homo sapiens GN=PRG4 PE=1 SV=2	151.077	0.010	0.123	0.023	0.021	0.019	0.024
REVERSED Tensin-2 OS=Homo sapiens GN=TNS2 PE=1 SV=2	152.580	0.000	0.000	0.002	0.000	0.002	0.000
Uncharacterized protein KIAA1107 OS=Homo sapiens GN=KIAA1107 PE=1 SV=2	155.681	0.000	0.000	0.001	0.000	0.000	0.000
Alpha-2-macroglobulin OS=Homo sapiens GN=A2M PE=1 SV=3	163.291	0.003	0.002	0.004	0.010	0.009	0.011
Complement C3 OS=Homo sapiens GN=C3 PE=1 SV=2	187.148	0.568	1.676	1.222	1.271	1.084	1.554
Complement C4-B OS=Homo sapiens GN=C4B PE=1 SV=2	192.751	0.099	0.539	0.454	0.345	0.000	0.497
Complement C4-A OS=Homo sapiens GN=C4A PE=1 SV=2	192.785	0.120	0.000	0.470	0.470	0.471	0.560
Protein TANC1 OS=Homo sapiens GN=TANC1 PE=1 SV=3	202.219	0.000	0.001	0.000	0.000	0.000	0.000
Protein NLRC5 OS=Homo sapiens GN=NLRC5 PE=1 SV=3	204.595	0.000	0.000	0.000	0.000	0.001	0.000
Periplakin OS=Homo sapiens GN=PPL PE=1 SV=4	204.747	0.000	0.000	0.000	0.001	0.000	0.000
Coagulation factor V OS=Homo sapiens GN=F5 PE=1 SV=4	251.700	0.001	0.003	0.001	0.001	0.002	0.000
Fibronectin OS=Homo sapiens GN=FN1 PE=1 SV=4	262.622	0.001	0.002	0.002	0.000	0.000	0.000
REVERSED Myomegalin OS=Homo sapiens GN=PDE4DIP PE=1 SV=1	265.080	0.001	0.000	0.000	0.000	0.000	0.000
Talin-1 OS=Homo sapiens GN=TLN1 PE=1 SV=3	269.767	0.000	0.000	0.001	0.002	0.002	0.001
Nucleosome-remodeling factor subunit BPTF OS=Homo sapiens GN=BPTF PE=1 SV=3	338.262	0.000	0.000	0.000	0.000	0.002	0.000
Apolipoprotein(a) OS=Homo sapiens GN=LPA PE=1 SV=1	501.319	0.004	0.000	0.000	0.000	0.001	0.003
Dynein heavy chain 8, axonemal OS=Homo sapiens GN=DNAH8 PE=1 SV=2	514.664	0.000	0.000	0.000	0.001	0.000	0.000
Apolipoprotein B-100 OS=Homo sapiens GN=APOB PE=1 SV=2	515.605	0.035	0.026	0.108	0.190	0.172	0.548
TOTAL PROTEIN CONTENT (mg/g)	38.290	212.851	170.295	135.990	137.664	149.406	

Table S3. Values of NSpC x TGA for all proteins found in protein corona analysis of PCa patient serum samples. Total protein content determined by TGA is indicated at the end of the list for every patient. Data in mg/g.

PROTEIN NAME	Mw	PA-1	PA-2	PA-3	PA-4	PA-5	PA-6	PA-7	PA-8	PA-9	PA-10	PA-11	PA-12	PA-13	PA-14	PA-15	PA-16	PA-17	PA-18	PA-19	PA-20	PA-21	PA-22	
Nephrilkinin-3	1.088	0.000	0.000	0.000	0.000	0.752	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Thymosin beta-4	5.053	0.000	0.000	0.000	0.000	0.000	3.518	0.000	0.000	0.000	0.000	0.719	1.288	0.136	1.204	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Neurogranin	7.618	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.021	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
IgG-exposed antimicrobial peptide 2	8.843	0.000	0.000	0.000	0.000	0.60	0.000	0.188	0.000	0.000	0.24	0.124	0.123	0.008	0.124	0.008	0.124	0.008	0.124	0.008	0.124	0.008	0.124	0.008
Immunoglobulin lambda-like polypeptide 5	8.843	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	5.835	2.654	0.000	0.000	0.000	7.813	0.000	0.000	0.000	0.948	20.179	3.188	11.371	133.690	
Guanine nucleotide-binding protein subunit gamma	9.058	0.000	0.000	0.000	0.000	0.000	0.000	2.420	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Apolipoprotein C-I	9.332	0.872	2.625	0.770	0.000	3.232	0.000	0.000	1.588	6.954	6.172	6.472	6.646	18.530	3.725	15.283	4.883	3.969	7.992	6.652	1.597	0.000	0.000	0.000
Putative membrane protein insertion efficiency factor	9.378	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.423	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Hepcidin	9.408	0.000	0.000	0.000	0.000	0.122	0.699	0.000	0.000	0.000	0.639	1.011	1.957	1.422	1.221	1.481	1.015	1.047	0.000	0.000	1.436	1.160	0.000	0.000
Defensin-5	10.071	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Neutrophil defensin 1	10.201	0.000	0.000	0.000	0.000	2.562	4.354	3.610	2.369	3.953	4.713	0.850	2.993	5.726	1.911	3.887	2.868	1.916	3.627	2.998	2.826	1.435	1.297	0.000
Neutrophil defensin 3	10.245	0.000	0.000	0.000	0.000	0.000	0.469	0.000	0.000	1.863	4.576	1.110	0.000	7.552	0.000	0.000	0.000	1.746	0.000	0.000	0.000	1.429	0.591	0.000
Stromal cell-derived factor 1	10.666	0.000	0.000	0.000	0.000	0.030	0.000	0.000	0.000	0.000	0.036	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Ig kappa chain V-III region NG9 (Fragment)	10.729	0.000	0.000	0.000	0.000	0.271	0.000	0.000	0.000	0.461	0.112	0.565	0.000	0.000	0.000	0.000	0.204	0.215	0.000	0.000	0.000	0.133	0.000	0.000
5S ribosomal protein L30e	10.766	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.626	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Platelet factor 4	10.850	3.550	8.543	0.394	7.163	39.277	32.770	18.140	10.785	30.760	33.557	20.286	16.047	31.303	39.702	31.248	36.603	19.713	16.820	12.846	19.219	29.117	11.406	0.000
Apolipoprotein C-III	10.852	0.890	1.401	2.441	2.340	7.331	3.461	9.648	6.444	10.925	9.537	6.373	11.706	21.120	8.915	5.769	6.661	17.421	22.594	9.764	11.448	10.268	4.367	0.000
Apolipoprotein A-II	11.175	56.887	6.242	20.299	70.436	7.717	23.306	19.465	61.325	16.471	22.751	6.781	16.529	8.464	7.211	5.213	9.620	32.624	37.331	27.445	21.455	24.077	18.602	0.000
Ig lambda-3 chain C regions	11.238	1.205	2.666	0.167	1.007	1.509	0.000	2.597	2.791	3.169	1.466	4.879	3.484	4.862	3.134	4.620	1.505	0.327	2.037	2.046	3.886	0.358	0.000	0.000
Apolipoprotein C-II	11.284	0.000	0.000	0.000	0.000	0.295	0.000	0.676	1.824	0.973	0.690	0.815	3.283	0.959	0.000	0.500	1.199	4.020	0.820	2.767	0.713	0.000	0.000	0.000
Densinidin	11.284	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.138	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Ig lambda-2 chain C regions	11.294	0.000	0.082	0.000	0.000	2.016	2.224	2.379	5.193	0.221	0.185	2.921	1.994	2.142	0.359	3.585	4.135	1.019	1.883	2.435	2.976	4.592	3.094	0.000
Ig lambda-7 chain C region	11.303	0.000	0.000	0.000	0.000	0.000	0.000	0.108	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Ig lambda-1 chain C regions	11.348	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	2.027	7.833	0.210
Ig lambda chain V-III region SH	11.393	0.000	0.000	0.000	0.000	0.036	0.000	0.000	0.000	0.000	0.000	0.000	0.045	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Ig lambda chain V-III region NG-58	11.455	0.000	0.000	0.000	0.000	0.000	0.000	0.052	0.197	0.000	0.045	0.296	0.120	0.302	0.206	0.000	0.000	0.000	0.000	0.000	0.225	0.435	3.528	0.000
Ig lambda chain V-III region BUR	11.506	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.143	0.000	0.000	0.000	0.000	0.340	9.122	0.000	0.000
Ig lambda chain V-IV region HI	11.519	0.000	0.000	0.000	0.000	0.174	0.000	0.000	0.178	0.067	0.000	0.237	0.000	0.121	0.048	0.000	0.085	0.133	0.158	0.000	0.008	0.319	0.000	0.000
Platelet factor 4 variant	11.553	0.000	0.000	0.000	0.000	23.962	0.000	0.000	0.000	0.000	0.000	0.000	15.173	0.000	20.440	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Ig lambda chain V-II region TRO	11.561	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.354	3.269	0.000
Ig kappa chain C region	11.609	1.198	3.822	0.381	0.449	4.086	7.210	12.572	23.778	8.499	3.828	17.390	6.874	2.434	13.988	12.545	4.848	4.324	0.530	3.677	3.093	10.610	10.759	0.000
Ig lambda chain V-II region BOH	11.650	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.352	2.217	0.000
Ig lambda chain V-I region WAH	11.729	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Ig kappa chain V-II region WAT	11.737	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Ig kappa chain V-III region WOL	11.746	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.122	0.000	0.000
Ig kappa chain V-III region SIE	11.775	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.122	0.000	0.000
Ig kappa chain V-III region TI	11.788	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.121	0.000	0.000
Ig kappa chain V-III region GOL	11.830	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.293	0.281	0.000	0.000	0.000	0.000	0.061	0.000	0.000	0.000	0.000	0.000	0.000	0.121	0.000	0.000
Ig lambda chain V-III region LOI	11.935	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.173	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Colipase	11.954	0.000	0.000	0.000	0.000	0.041	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Ig kappa chain V-IV region Len	12.080	0.000	0.000	0.000	0.000	0.290	0.000	0.134	0.290	0.000	0.045	0.000	0.000	0.000	0.000	0.000	0.136	0.000	0.000	0.000	0.435	17.129	0.000	0.000
Ig heavy chain V-II region TUR	12.190	0.072	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.113	0.034	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
REVERSED 5S ribosomal protein L24	12.236	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.026	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Ig kappa chain V-II region TEW	12.316	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Matrix Gla protein	12.353	0.000	0.000	0.000	0.000	0.071	0.000	0.000	0.233	0.000	0.051	0.043	0.146	0.025	0.074	0.080	0.125	0.019	0.137	0.000	0.000	0.155	1.524	0.000
Ig heavy chain V-I region EU	12.472	0.000	0.000	0.000	0.000	0.176	0.000	0.246	0.235	0.072	0.000	0.207	0.000	0.000	0.116	0.138	0.077	0.269	0.000	0.000	0.000	0.000	0.000	0.000
Hepatocyte growth factor-like protein	12.802	0.156	0.000	0.000	0.000	0.013	0.000	0.000																

Table S4. Observed up and down-regulated proteins with reported cancer biomarker potential.⁶

Protein	Gene	Function	Cancer biomarker	Observed tag
Apolipoprotein C-I	APOC1	Lipid metabolism regulator	Up-regulated in gastric cancer	Up-regulated in B- Down-regulated in B+/M
Prothrombin	F2	Coagulation factor	Up-regulated in cancer with thrombosis	Up-regulated in B+ Down-regulated in M
Neutrophil defensin 1	DEFA1	Antimicrobial	Up-regulated in colon cancer	Up-regulated in B+ Down-regulated in M
Platelet factor 4 variant	PF4V1	Promotes coagulation	Up-regulated in cancer	Up-regulated in B+
Inter-alpha trypsin inhibitor heavy chain H1	ITIH1	Hyaluronan carrier	Up-regulated in ovarian cancer	Up-regulated in M
Plasma serine protease inhibitor	SERPINA5	Serine proteases inactivation	Up-regulated in prostate cancer	Up-regulated in B+ Down-regulated in M
Histidine-rich glycoprotein	HRG	Angiogenesis, Immune system	Up-regulated in cancer	Up-regulated in M

4. Supplementary Figures

Figure S1. Particle hydrodynamic diameter of as-synthesized materials as determined in water by DLS (intensity output).

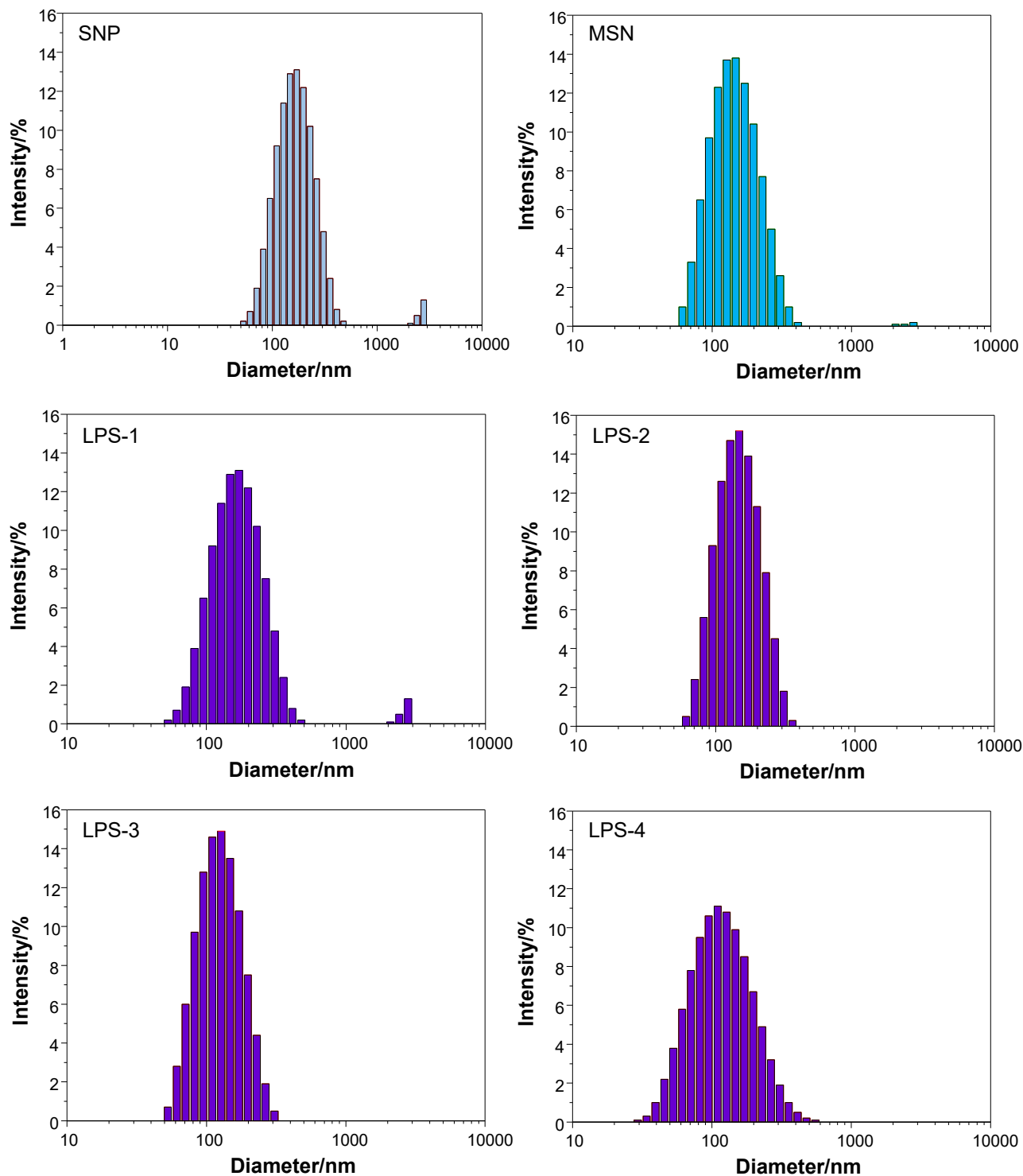


Figure S2. BET N₂ adsorption-desorption isotherms of as-synthesized materials.

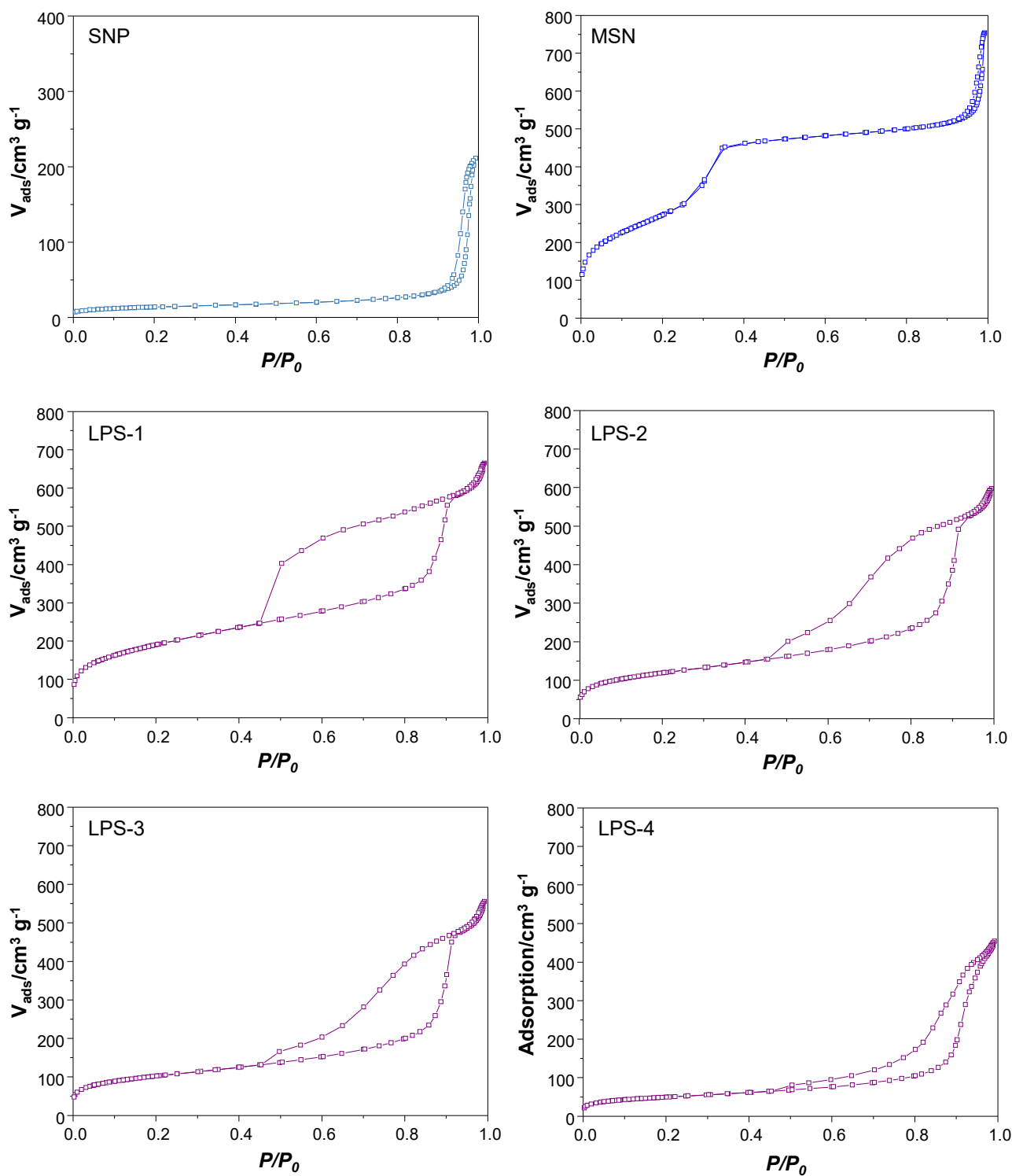


Figure S3. Pore size distribution in as-synthesized materials as determined by BJH method. Legend: (□) Pore size as determined by N₂ adsorption isotherms. In the case of LPS materials, these data correspond to internal cavity size distribution. (○) Pore size as determined by desorption isotherms. In the case of LPS materials, these data correspond to pore entrance size distribution.

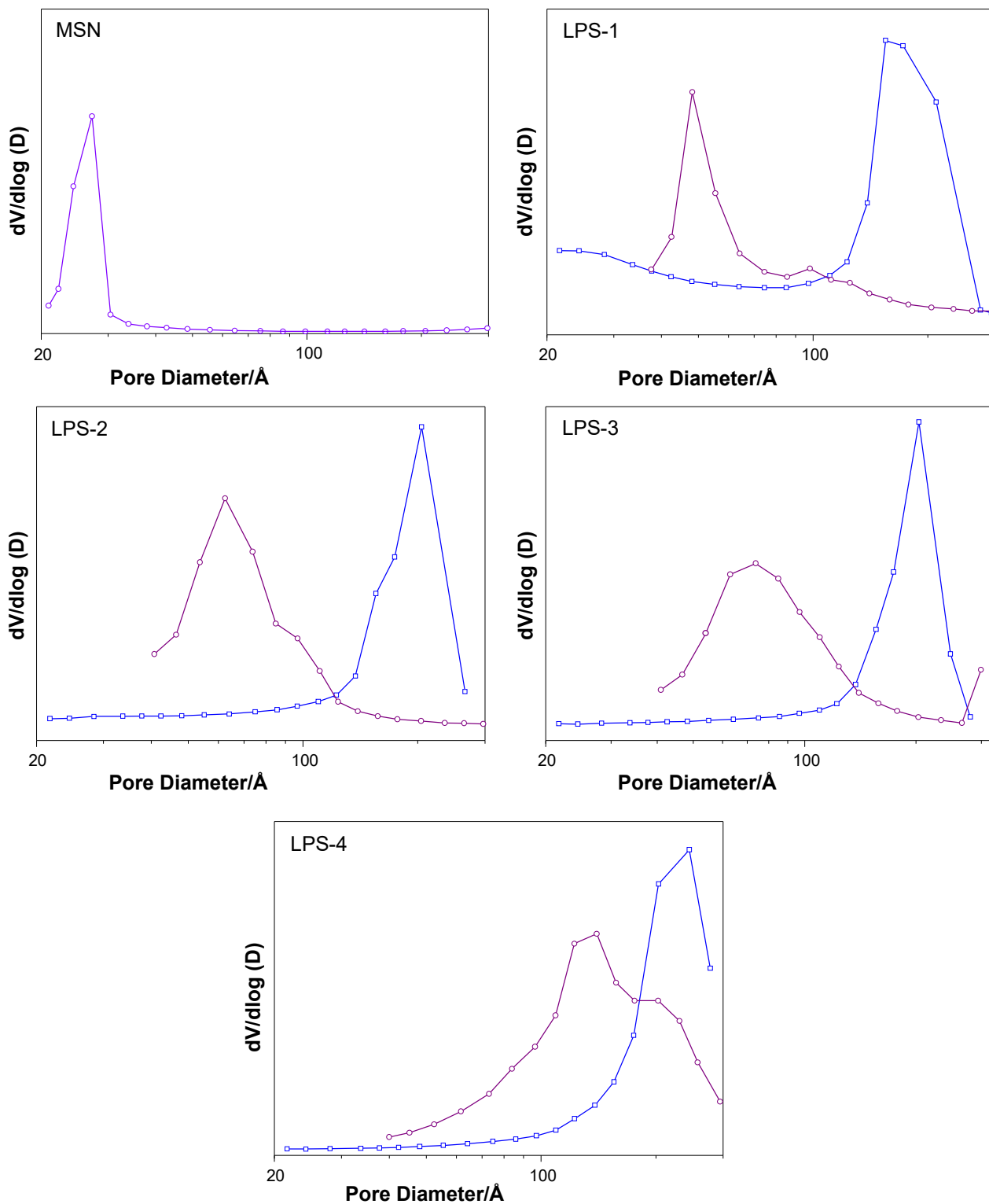


Figure S4. SDS-PAGE of isolated corona proteins from silica nanoparticles with variable pore diameter.

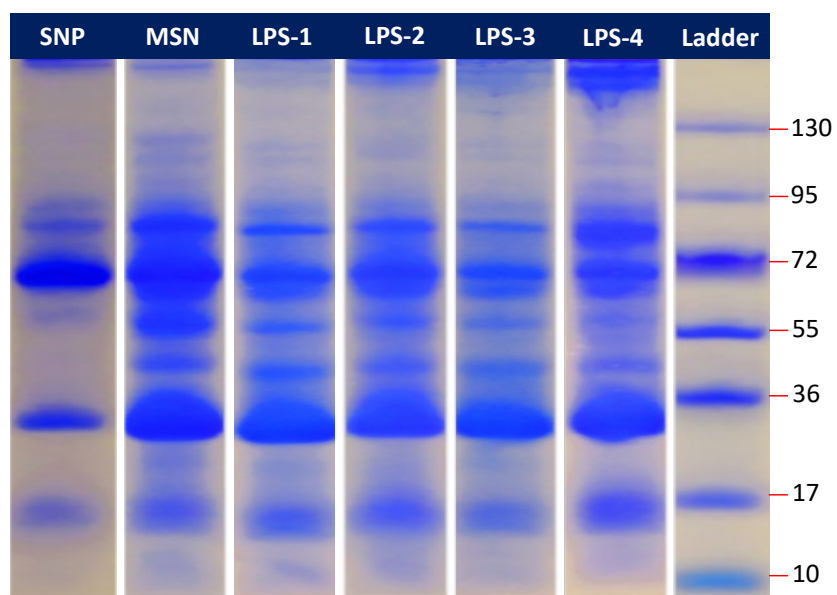


Figure S5. Comparison of the weight percent of the protein corona (NSpC x TGA) across the different surface modified MSN with respect to molecular weight (MW). As show, in all cases, low MW proteins composed the highest percentage of the isolated proteome.

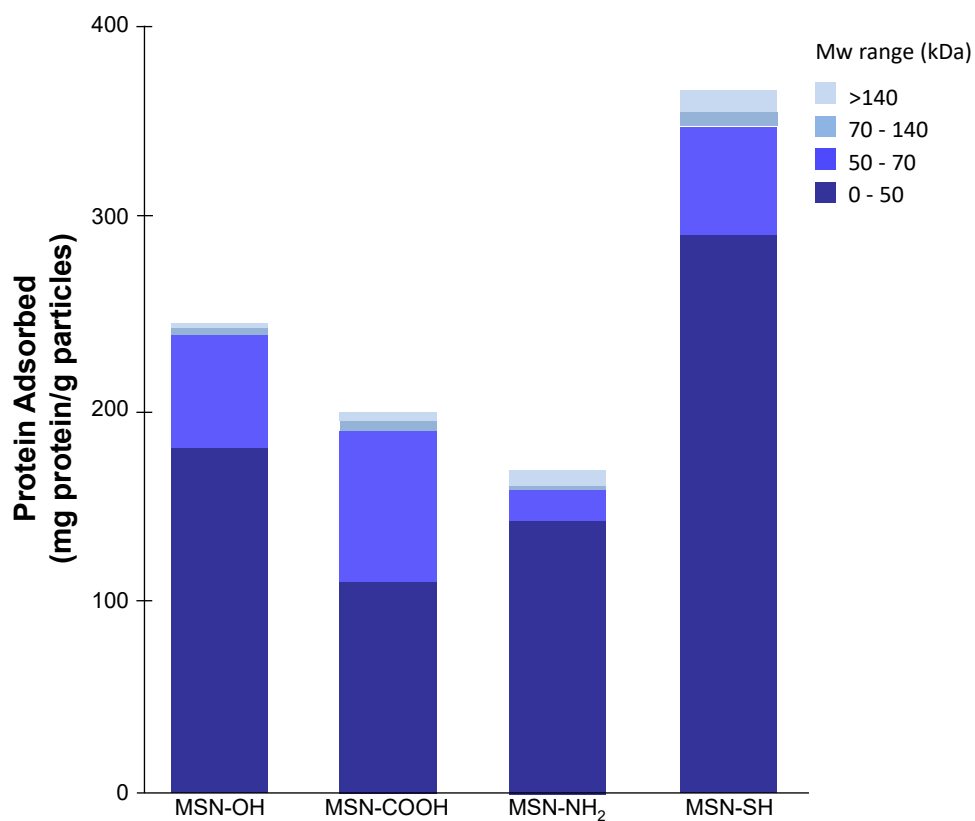
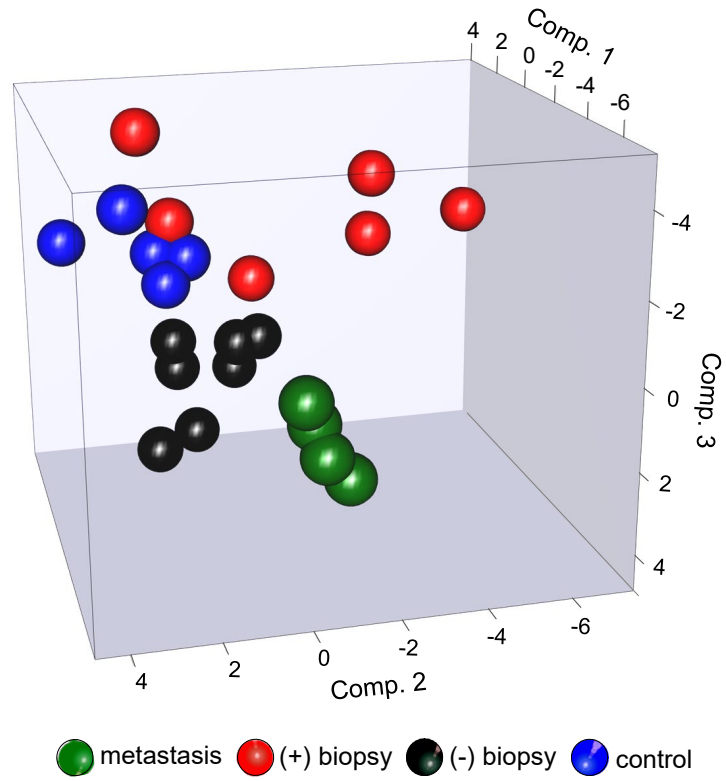


Figure S6. Principal Component Analysis (PCA) representation of experimental data. The first three components of the projection are represented in a tri-coordinate system where the different patient groups are clearly split.



5. References

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