

Table 1 ESI. Clinical characteristic of enrolled ccRCC patients; concentration of urinary exosomal proteins and creatinine.

Patient Code	Age	Sex	pT	N	G	Exosomal proteins (µg/ml)	Creatinine (mg/dl)	Pool
34	52	M	1b	X	3	6,82	161	
40	40	F	1b	X	2	7,91	29,6	
46	69	F	2a	X	2	2,11	32,8	
51	67	M	1b	X	2	16,0	115	X
56	55	F	1a	X	2	3,17	58,0	X
58	53	F	1b	X	2	7,46	47,1	
61	62	M	1b	X	2	3,00	57,5	X
63	70	M	1b	0	3	10,4	182	
65	61	M	1b	X	2	2,11	60,9	X
67	59	F	2a	0	2	7,85	62,8	X
70	68	M	1b	X	3	n.a.	5,96	
74	72	M	1b	X	2	n.a.	208	
76	78	M	2b	X	3	3,56	177	
84	46	M	1a	0	2	3,33	27,1	
85	48	F	2a	0	2	3,09	69,4	X
86	53	M	1b	X	2	5,74	236	
91	79	M	2a	X	2	5,00	63,0	X
93	59	M	1a	X	2	2,22	129	
97	72	M	2a	X	2	3,49	54,4	
98	71	M	1b	0	2	10,5	99,5	
103	78	F	1b	X	2-3	3,40	66,1	X
111	54	M	2a	X	3	n.a.	69,7	
112	58	M	2a	0	1	2,95	81,8	
113	57	F	1b	0	2	4,15	92,6	
120	80	M	1a	X	3	0,99	26,3	
136	86	F	1a	X	2	3,35	26,1	
146	38	M	2a	X	2	3,25	29,9	
147	84	F	1b	0	2	5,43	32,6	X
152	72	M	1a	X	2	2,29	n.a.	

Pool = urinary exosome samples selected to constitute RCC exosome pool

Exosomal proteins (µg/ml) = concentration of urinary exosomal proteins referred to the initial urine volume

Creatinine (mg/dl) = concentration of urinary creatinine

n.a. = not available

Table 2 ESI. Characteristic of control healthy subjects; concentration of urinary exosomal proteins and creatinine.

Control Code	Age	Sex	Exosomal proteins (µg/ml)	Creatinine (mg/dl)	Pool
DB	52	F	10,2	198	
MK	40	F	10,4	206	
PK	69	M	n.a.	132	
AR	67	F	4.67	177	
VC	55	M	3.00	108	
LR	53	M	4.33	173	
ET	62	F	5.53	177	
SN	70	M	8.55	145	X
PG	61	M	3.03	180	X
NG	59	F	4.95	117	X
GG	68	M	4.78	173	X
OA	72	F	7.59	155	X
PL	78	F	3.94	63.4	X
CC	46	M	11.8	168	
AC	48	F	2.78	53.8	
ZC	53	F	11.1	146	
EB	79	M	11.1	68.8	
BC	59	M	10.7	87.9	
MB	72	M	3.36	94.1	X
MI	71	M	4.69	n.a.	X
PP	78	F	3.49	110	
FM	54	M	9.70	190	X

Pool = urinary exosome samples selected to constitute RCC exosome pool

Exosomal proteins (µg/ml) = concentration of urinary exosomal proteins referred to the initial urine volume

Creatinine (mg/dl) = concentration of urinary creatinine

n.a. = not available

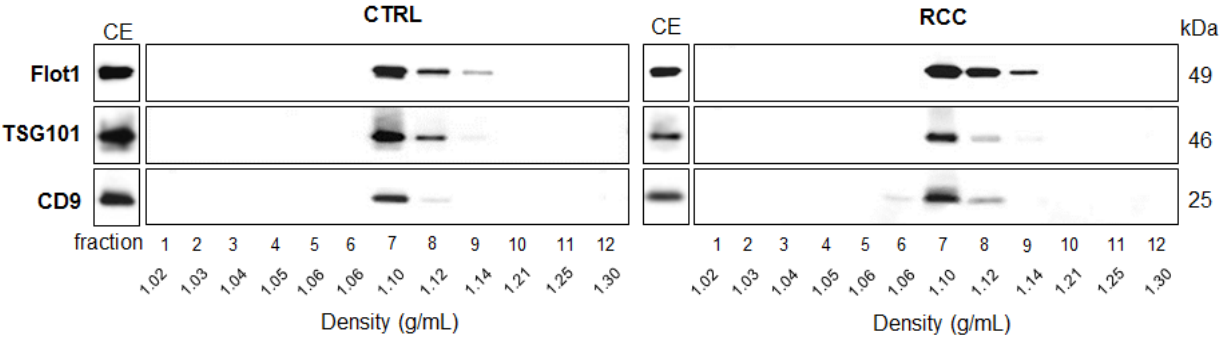


Fig. 1 ESI. OptiPrep density gradient separation of crude exosomes (CE). Western Blot analysis of urinary exosomal markers (CD9, TSG101 and Flot1) along gradient fractions.

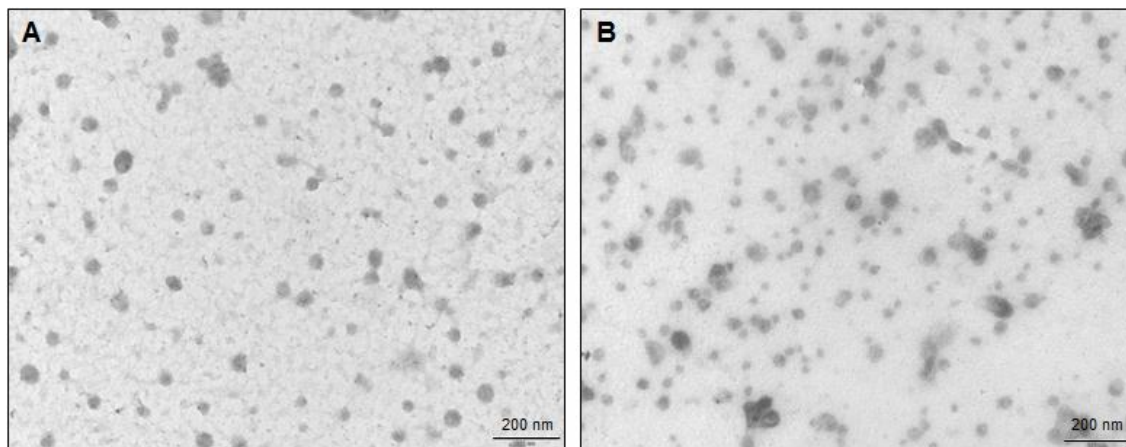


Fig. 2 ESI. Morphological characterization of urinary exosomes. Electron micrographs of crude exosomes (A) and exosomes after Optiprep gradient purification (B) of a control subject. Exosomes were doubly stained with uranyl acetate and lead citrate, and examined by transmission electron microscope CM 10 Philips.

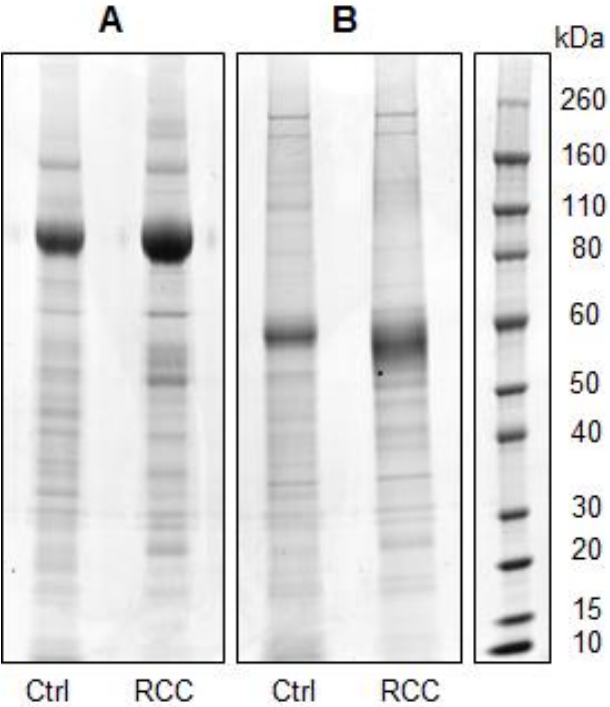


Fig. 3 ESI. Protein patterns of urinary exosome pools (NuPAGE 4-12%), before (A) and after deglycosilation (B).

Table 3 ESI. List of proteins identified in urinary exosomes isolated from control subject urines.

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	RCC	Exocarta	Localization
1	Histone H4	P62805	11360	111	41	5			Oth/Unk
1	Proactivator polypeptide	P07602	59899	97	5	3			Org
1	Protein S100-A6	P06703	10230	33	8	1		X	Cyt
1	Protein S100-A8	P05109	10885	274	52	14	X	X	Cyt
2	Acid ceramidase	Q13510	45087	82	11	6	X	X	Org
2	Histone H2A type 1-A	Q96QV6	14225	26	6	1		X	Oth/Unk
2	Histone H3.1t	Q16695	15613	37	10	2			Oth/Unk
2	Macrophage migration inhibitory factor	P14174	12639	50	17	2	X	X	Secr
2	Mannan-binding lectin serine protease 2	O00187	77224	116	7	6		X	Secr
2	Thioredoxin	P10599	12015	83	31	4		X	Cyt
2	Tubulin polyglutamylase TTLL7 *	Q6ZT98	103846	32	1	1		X	CySk
2	Uroplakin-2	O00526	19540	83	24	7		X	Pm
2	Vesicle-associated membrane protein 8	Q9BV40	11488	36	19	2		X	Pm
3	14225	Q9H1C7	10966	86	11	2		X	Oth/Unk
3	Cystatin-C	P01034	16017	70	19	2	X	X	Secr
3	PDZK1-interacting protein 1	Q13113	12333	51	9	1		X	Pm
3	Profilin-1	P07737	15216	30	47	6		X	CySk
3	Protein S100-A9	P06702	13291	82	50	7		X	Cyt
4	Hemoglobin subunit α	P69905	15305	41	16	2	X		Oth/Unk
4	Prolactin-inducible protein	P12273	16847	33	17	2		X	Secr
4	Retinol-binding protein 5	P82980	16092	39	13	2		X	Cyt
4	UPF0467 protein C5orf32	Q9H1C7	10966	26	10	1	X		Oth/Unk
5	ADP-ribosylation factor 1	P84077	20741	58	11	2	X	X	Org
5	ADP-ribosylation factor 6	P62330	20183	62	12	2		X	Org
5	CD59 glycoprotein	P13987	14795	54	15	2	X	X	Pm
5	CD9 antigen	P21926	25969	83	9	4	X	X	Pm

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	RCC	Exocarta	Localization
5	Cofilin-1	P23528	18719	45	6	1		X	Cyt
5	Lysosomal protective protein	P10619	54944	59	2	1		X	Org
5	Non-secretory ribonuclease	P10153	18855	37	8	1		X	Org
5	Peptidyl-prolyl cis-trans isomerase A	P62937	18229	85	35	9	X	X	Cyt
5	Rho guanine nucleotide exchange factor 10-like protein *	Q9HCE6	141873	26	0	1			Cyt
5	Semenogelin-2	Q02383	65519	27	5	3			Secr
5	Transforming protein RhoA	P61586	22096	26	3	2		X	Pm
5	Transmembrane protein C19orf77	O75264	15012	53	26	2			Pm
6	ADP-ribosylation factor-like protein 3	P36405	20614	78	6	1	X	X	CySk
6	Perlecan	P98160	479221	29	0	3			Secr
6	Cell division control protein 42	P60953	21696	33	5	3	X	X	Pm
6	Glutathione S-transferase P	P09211	23569	32	4	1		X	Oth/Unk
6	Immunoglobulin J chain	P01591	18543	100	26	4	X		Secr
6	Peroxiredoxin-1	Q06830	22324	35	20	5			Cyt
6	Phosphatidylethanolamine-binding protein 1	P30086	21158	108	21	9		X	Cyt
6	Programmed cell death protein 6	O75340	21912	21	5	1	X	X	Pm
6	Prostate stem cell antigen	O43653	13474	33	8	1	X	X	Pm
6	Ras-related C3 botulinum toxin substrate 2	P15153	21814	36	5	1		X	Cyt
6	Ras-related protein Rab-2A	P61019	23702	36	6	1		X	Org
6	Ras-related protein Rab-7a	P51149	23760	21	18	5		X	Pm
6	Ras-related protein Rab-8B	Q92930	23740	45	11	2		X	Pm
6	Ras-related protein Rap-1A	P62834	21316	63	12	2			Pm
7	Apolipoprotein D	P05090	21547	154	30	8	X	X	Secr
7	Mps one binder kinase activator-like 1A	Q7L9L4	25246	30	5	1	X		Cyt
7	Mucin-1	P15941	122200	111	1	5	X	X	Pm
7	Ras-related protein Rab-10	P61026	22755	92	24	5		X	Pm
7	Ras-related protein Rab-11A	P62491	24492	71	18	4			Pm
7	Ras-related protein Rab-1A *	P62820	22891	78	18	4		X	Org
7	Uroplakin-1a	O00322	29429	32	17	4		X	Pm

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	RCC	Exocarta	Localization
7	Vacuolar protein sorting-associated protein 28	Q9UK41	25694	65	8	3		X	Pm
8	Cardiotrophin-like cytokine factor 1	Q9UBD9	25388	44	3	1	X		Secr
8	Collagen α -1(XV) chain	P39059	142202	25	0	1	X	X	Secr
8	Glutathione S-transferase A2	P09210	25648	74	22	7		X	Cyt
8	Glutathione S-transferase Mu 3	P21266	26998	92	17	4	X	X	Cyt
8	Ig kappa chain C	P01834	11773	130	51	5	X		Secr
8	Peroxiredoxin-6	P30041	25133	66	17	4	X	X	Cyt
8	Ras-related protein Rab-11B	Q15907	24588	53	24	5		X	Pm
8	Ras-related protein Rab-5C	P51148	23696	145	28	5		X	Pm
8	Ras-related protein Ral-A	P11233	23723	47	16	3	X	X	Pm
8	Semenogelin-1	P04279	52157	44	4	2			Secr
8	Transmembrane protease serine 2	O15393	55079	39	1	1		X	Pm
9	3-hydroxybutyrate dehydrogenase type 2	Q9BUT1	27049	51	8	2		X	Cyt
9	Cytochrome b reductase 1	Q53TN4	31735	32	3	1		X	Pm
9	Dihydropteridine reductase	P09417	26001	31	4	1			Cyt
9	Glutathione S-transferase A1 *	P08263	25672	30	19	5	X	X	Cyt
9	Heat shock protein β -1	P04792	22826	61	14	3	X	X	Cyt
9	Ig kappa chain V-I region Lay *	P01605	11941	23	8	1	X		Secr
9	Ig kappa chain V-II region Cum	P01614	12782	54	11	2	X		Secr
9	Ig lambda chain V-I region HA	P01700	12003	39	11	1	X		Secr
9	L-xylulose reductase	Q7Z4W1	26182	35	4	1	X	X	Pm
9	Programmed cell death protein 10	Q9BUL8	24686	34	14	3		X	Pm
9	Ras-related protein Rab-3A	P20336	25196	53	10	2		X	Pm
9	Ras-related protein Rab-5B	P61020	23920	47	11	2		X	Pm
9	Ras-related protein Ral-B	P11234	23508	53	19	5		X	Pm
9	Ras-related protein R-Ras2 *	P62070	23613	42	5	1		X	Pm
9	Triosephosphate isomerase	P60174	26938	111	26	6		X	Oth/Unk
10	14-3-3 protein β/α	P31946	28179	35	20	5	X	X	Cyt
10	15-hydroxyprostaglandin dehydrogenase [NAD+]	P15428	29187	59	9	2		X	Cyt

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	RCC	Exocarta	Localization
10	Azurocidin	P20160	27325	26	6	2		X	Cyt
10	Carboxymethylenebutenolidase homolog	Q96DG6	28372	24	3	1		X	Cyt
10	Charged multivesicular body protein 1b	Q7LBR1	22152	112	13	7		X	Org
10	Glutathione S-transferase omega-1	P78417	27833	33	4	1		X	Cyt
10	Ig lambda-2 chain C	P0CG05	11458	155	41	7	X		Secr
10	MIT domain-containing protein 1	Q8WV92	29638	67	16	4		X	Org
11	14-3-3 protein z/δ	P63104	27899	74	12	3		X	Cyt
11	ADP-ribosyl cyclase 2*	Q10588	36328	44	5	2		X	Pm
11	Calbindin*	P05937	30291	46	13	4		X	Cyt
11	Carbonic anhydrase 2	P00918	29285	81	15	5	X	X	Cyt
11	Carbonyl reductase [NADPH] 1	P16152	30641	43	12	3	X	X	Cyt
11	Charged multivesicular body protein 2a	O43633	25088	81	22	9		X	Org
11	Charged multivesicular body protein 2b	Q9UQN3	23948	48	14	3	X	X	Org
11	Charged multivesicular body protein 5	Q9NZZ3	24612	51	7	1		X	Org
11	Chloride intracellular channel protein 1	O00299	27248	40	8	2	X	X	Pm
11	Chloride intracellular channel protein 4 *	Q9Y696	28982	31	7	2		X	Pm
11	Erythrocyte band 7 integral membrane protein	P27105	31882	59	19	5	X	X	Pm
11	Galectin-3 *	P17931	26193	27	7	2			Cyt
11	Protein MAL2	Q969L2	19341	51	6	1		X	Pm
11	Vacuolar protein sorting-associated protein 37D	Q86XT2	27941	82	14	3		X	Org
11	Vesicular integral-membrane protein VIP36 *	Q12907	40545	27	2	1	X	X	Org
12	14-3-3 protein ε *	P31946	29326	56	23	5		X	Cyt
12	Actin-related protein 2/3 complex subunit 2	O15144	34426	37	3	1		X	CySk
12	Annexin A4	P09525	36088	340	43	15		X	Cyt
12	Annexin A5	P08758	35971	339	35	18	X	X	Cyt
12	Aquaporin-2	P41181	29047	45	7	3		X	Pm
12	Charged multivesicular body protein 4b	Q9H444	24935	148	20	5		X	Org
12	Insulin-like growth factor-binding protein 7	Q16270	30138	28	5	1			Secr
12	L-lactate dehydrogenase B chain	P07195	36900	260	23	8	X	X	Cyt

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	RCC	Exocarta	Localization
12	Multivesicular body subunit 12A	Q96EY5	29107	56	5	1			Org
12	Peflin *	Q9UBV8	30646	46	9	5		X	Cyt
12	Protein AMBP	P02760	39886	181	14	6	X	X	Secr
12	Syntenin-1	O00560	32595	246	27	12	X	X	CySk
12	Tetraspanin-1	O60635	26910	68	5	1		X	Pm
12	Thy-1 membrane glycoprotein	P04216	18151	117	14	4	X	X	Pm
12	Toll-interacting protein	Q9H0E2	30490	78	9	3		X	Cyt
13	Napsin-A *	O96009	45700	54	4	2	X	X	Secr
14	1,5-anhydro-D-fructose reductase	Q96JD6	37136	21	2	1			Cyt
14	Alcohol dehydrogenase [NADP+]	P14550	36892	21	10	3		X	Oth/Unk
14	Annexin A2	P07355	38808	98	20	6	X	X	Pm
14	Calcium-binding protein 39	Q9Y376	40015	94	18	7	X	X	Cyt
14	Fructose-1,6-bisphosphatase 1	P09467	37218	31	4	1		X	Cyt
14	Glyceraldehyde-3-phosphate dehydrogenase	P04406	36201	118	22	7	X	X	Cyt
14	G-protein G(I)/G(S)/G(T) subunit β -1	P62873	38151	29	3	1	X	X	Pm
14	G-protein G(I)/G(S)/G(T) subunit β -2 *	P62879	38048	69	16	5			Pm
14	L-lactate dehydrogenase A chain *	P00338	36950	26	3	1	X	X	Cyt
14	Putative β -actin-like protein 3 *	Q9BYX7	42331	42	3	1			CySk
14	Vacuolar protein sorting-associated protein VTA1 homolog	Q9NP79	34143	39	9	3		X	Org
15	Clusterin	P10909	53031	24	2	1	X	X	Secr
15	Fructose-bisphosphate aldolase B	P05062	39961	63	10	4	X	X	Cyt
15	Glycerol-3-phosphate dehydrogenase [NAD+] *	P21695	38171	27	2	1		X	Cyt
15	G-protein G(i) subunit α -2	P04899	40995	86	9	3			Pm
15	Macrophage-capping protein	P40121	38779	32	3	1		X	Cyt
15	Prostasin	Q16651	37093	71	6	2	X		Pm
15	Sorbitol dehydrogenase	Q00796	38927	33	4	2	X	X	Org
16	Actin	P60709	42052	415	32	16	X	X	CySk
16	Brevican core protein *	Q96GW7	100539	22	0	1			Secr
16	Chromobox protein homolog 2	Q14781	56388	21	2	1			Oth/Unk

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16	Fructose-bisphosphate aldolase A	P04075	39851	41	7	2	X	X	Cyt
16	γ -butyrobetaine dioxygenase	O75936	45200	32	2	1			Cyt
16	G-protein coupled receptor family C group 5 member B	Q9NZH0	45279	140	6	3			Pm
16	G-protein G(i) subunit α -1 *	P63096	40905	73	13	5	X	X	Pm
16	G-protein G(q) subunit α *	P50148	42400	74	3	1	X	X	Pm
16	G-protein subunit α -13	Q14344	44364	48	8	3		X	Pm
16	Prostatic acid phosphatase *	P15309	44880	40	4	1	X		Secr
16	Tripeptidyl-peptidase 1 *	O14773	61723	69	4	2	X	X	Org
16	V-type proton ATPase subunit C 1	P21283	44085	21	2	1			Org
18	Aminoacylase-1	Q03154	46084	31	3	2	X	X	Cyt
18	Betaine--homocysteine S-methyltransferase 1	Q93088	45426	30	1	1	X	X	Cyt
18	BRO1 domain-containing protein BROX	Q5VW32	46960	121	18	8	X	X	Pm
18	Isocitrate dehydrogenase [NADP] Cytoplasmic	O75874	46915	37	7	3	X	X	Cyt
18	IST1 homolog	P53990	39897	131	20	8	X	X	Org
19	α -enolase	P06733	47481	75	21	9	X	X	Pm
19	Annexin A7	P20073	52991	108	14	8		X	Secr
19	Elongation factor 1- α 1	P68104	50451	53	6	3		X	Cyt
19	Fidgetin-like protein 1	Q6PIW4	74829	24	1	1		X	Oth/Unk
19	G-protein coupled receptor family C group 5 member C	Q9NQ84	48732	103	7	4		X	Pm
19	Hsc70-interacting protein	P50502	41477	72	6	2			Cyt
19	N-acetyllactosaminide β -1,3-N-acetylglucosaminyltransferase	O43505	47545	37	2	1	X		Org
19	Plasma serine protease inhibitor	P05154	45787	90	11	5	X		Secr
19	Probable serine carboxypeptidase CPVL	Q9H3G5	54414	38	1	1	X		Oth/Unk
19	Ribonuclease inhibitor	P13489	51766	28	2	1		X	Cyt
19	Tumor susceptibility gene 101 protein	Q99816	44088	59	12	4	X	X	Pm
20	Ubiquitin-conjugating enzyme E2 variant 3	Q8IX04	52516	29	4	2		X	Oth/Unk
21	Brain acid soluble protein 1	P80723	22680	116	38	5		X	Pm
21	Cytsolic non-specific dipeptidase	Q96KP4	53187	31	5	2	X	X	Cyt
21	Ig γ -1 chain C region	P01857	36596	94	18	5	X		Secr

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21	Ig γ -2 chain C region	P01859	36505	112	12	4	X		Secr
21	Selenium-binding protein 1	Q13228	52928	43	4	2		X	Cyt
21	Tyrosine-protein kinase FRK	P42685	58673	35	3	2		X	Cyt
21	Vacuolar protein sorting-associated protein 4A	Q9UN37	49152	77	17	8		X	Org
21	Vacuolar protein sorting-associated protein 4B	O75351	49443	218	28	13	X	X	Org
21	V-type proton ATPase subunit B, kidney isoform	P15313	57196	26	2	1		X	Org
21	Xaa-Pro dipeptidase	P12955	55311	25	2	1		X	Pm
22	Annexin A11	P50995	54697	655	35	22		X	CySk
22	Dipeptidase 1	P16444	46101	189	24	8	X	X	Pm
22	Pancreatic α -amylase	P04746	58354	26	2	2	X		Secr
22	V-type proton ATPase subunit B, brain isoform	P21281	56807	24	5	2			Org
23	α -1-antichymotrypsin	P01011	47792	33	2	1	X		Secr
23	β -galactosidase	P16278	76483	373	21	13	X	X	Cyt
23	Copine-3	O75131	60947	68	11	6		X	Cyt
23	Glucose-6-phosphate isomerase	P06744	63335	36	5	3		X	Cyt
23	Ig α -1 chain C region	P01876	38486	393	38	11	X		Secr
23	Kininogen-1	P01042	72996	270	17	10	X	X	Secr
23	Mannosyl-oligosaccharide 1,2- α -mannosidase 1A	P33908	73150	48	7	4	X		Org
23	Myeloperoxidase	P05164	84784	61	2	2		X	Org
23	Proto-oncogene tyrosine-protein kinase Src	P12931	60310	33	5	3		X	Pm
23	WD repeat-containing protein 1	O75083	66836	23	1	1		X	Cyt
24	Bifunctional ATP-dep. dihydroxyacetone kinase/FAD-AMP lyase (cyclizing)	Q3LXA3	59252	38	2	1	X		Cyt
24	Brain-specific angiogenesis inhibitor 1- associated protein 2	Q9UQB8	61115	40	10	6		X	Cyt
24	Copine-8	Q86YQ8	63638	34	8	5		X	Oth/Unk
24	EH domain-containing protein 1	Q9H4M9	60646	84	8	4		X	Pm
24	Ig α -2 chain C region	P01877	37301	213	20	8	X		Secr
24	Pyruvate kinase isozymes M1/M2	P14618	58470	60	12	6			Cyt
25	Calpain-7	Q9Y6W3	93335	40	2	2		X	Oth/Unk
25	EH domain-containing protein 4	Q9H223	61365	107	10	5		X	Pm

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	RCC	Exocarta	Localization
25	γ -glutamyltransferase 1	P19440	61714	86	6	4	X	X	Pm
25	Vitamin K-dependent protein Z	P22891	46026	26	4	2		X	Secr
26	Heat shock 70 kDa protein 1-like	P34931	70730	44	1	1			Cyt
26	Na(+)/H(+) exchange regulatory cofactor	Q5T2W1	57379	21	7	2		X	Pm
26	Plastin-1	Q14651	70608	59	1	1	X	X	Cyt
26	Serum albumin	P02768	66170	630	40	27	X	X	Secr
27	Galectin-3-binding protein	Q08380	66202	188	18	12	X		Secr
27	Heat shock 70 kDa protein 1A/1B	P08107	70294	194	13	10	X	X	Cyt
27	Heat shock cognate 71 kDa protein	P11142	71082	292	25	14	X		Cyt
27	Olfactomedin-4	Q6UX06	57529	177	11	5	X	X	Secr
27	Solute carrier family 23 member 1	Q9UHI7	65644	27	1	1		X	Pm
27	V-type proton ATPase catalytic subunit A	P38606	68660	30	5	3	X	X	Org
28	Annexin A6	P08133	76168	97	11	9		X	Cyt
28	Kinesin-like protein KIF12	Q96FN5	71813	29	4	3		X	CySk
28	Moesin	P26038	67892	211	13	12	X	X	Pm
29	α -N-acetylglucosaminidase	P54802	82571	30	1	1	X	X	Org
29	Ezrin	P15311	69484	211	23	18	X	X	Pm
29	Ig mu chain C region	P01871	49960	39	6	3	X		Secr
29	Protein-glutamine γ -glutamyltransferase 4	P49221	77951	84	5	3	X	X	Oth/Unk
29	Radixin	P35241	68635	100	11	9		X	Pm
30	CD2-associated protein	Q9Y5K6	71635	43	3	2		X	CySk
30	Choline transporter-like protein 2	Q8IWA5	81610	40	4	5	X		Pm
30	Proton-coupled amino acid transporter 2	Q495M3	53809	37	3	3			Pm
30	Solute carrier family 22 member 2	O15244	63265	30	1	1		X	Pm
30	Xaa-Pro aminopeptidase 2	O43895	76090	32	10	8			Pm
31	Polymeric immunoglobulin receptor	P01833	84429	167	9	7	X	X	Pm
31	Probable Xaa-Pro aminopeptidase 3	Q9NQH7	57624	25	1	1			Org
31	Uromodulin	P07911	72451	1753	30	76	X	X	Pm
32	Lysosome-associated membrane glycoprotein 1	P11279	45367	75	4	2		X	Org

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	RCC	Exocarta	Localization
32	Neprilysin	P08473	86144	151	15	12			Pm
32	Programmed cell death 6-interacting protein	Q8WUM4	96590	271	22	14	X	X	Cyt
33	Centrosomal protein of 290 kDa *	O15078	290892	27	0	1			Cyt
33	Plasma protease C1 inhibitor	P05155	55347	61	9	4	X		Secr
33	Pro-epidermal growth factor	P01133	137613	154	5	7	X	X	Pm
34	Dipeptidyl peptidase 4	P27487	88907	463	26	27	X	X	Pm
34	Prominin-2	Q8N271	93079	54	2	2	X	X	Pm
35	Coiled-coil and C2 domain-containing protein 1A	Q6P1N0	104397	45	1	1			Cyt
35	Collagen α -1(VI) chain	P12109	109602	44	4	3	X	X	Secr
35	Electrogenic sodium bicarbonate cotransporter 1	Q9Y6R1	122295	25	0	1			Pm
35	Myosin-1c	O00159	122503	156	8	8		X	Cyt
35	Nck-associated protein 1	Q9Y2A7	130018	48	1	1		X	Org
35	Prominin-1	O43490	98395	224	15	12	X	X	Pm
35	Solute carrier family 12 member 3	P55017	114193	70	3	3		X	Pm
35	WASH complex subunit strumpellin	Q12768	135113	34	0	1			Org
36	Ankyrin repeat and FYVE domain-containing protein 1	Q9P2R3	129915	69	1	2		X	Org
36	Cullin-associated NEDD8-dissociated protein 1	Q86VP6	137999	36	1	1		X	Oth/Unk
36	DNA excision repair protein ERCC-6	Q03468	169452	27	0	1			Oth/Unk
36	Nesprin-1 *	Q8NF91	1017069	18	0	1			CySk
36	Thyrotropin-releasing hormone-degrading ectoenzyme	Q9UKU6	117439	24	0	1	X		Pm
37	Aminopeptidase N	P15144	109870	998	29	50	X		Pm
37	Glutamyl aminopeptidase	Q07075	109689	30	3	3	X	X	Pm
37	Podocalyxin	O00592	59055	175	12	7	X	X	Pm
37	Solute carrier family 12 member 1	Q13621	122627	122	6	7	X	X	Pm
38	Multidrug resistance protein 1	P08183	141788	65	4	6		X	Pm
39	Angiotensin-converting enzyme	P12821	150418	43	2	4	X	X	Pm
41	THAP domain-containing protein 4	Q8WY91	63535	23	1	2		X	Oth/Unk
42	Cubilin	O60494	407262	59	2	6	X	X	Org
42	Low-density lipoprotein receptor-related protein 2	P98164	540376	67	1	9	X	X	Pm

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	RCC	Exocarta	Localization
42	Maltase-glucoamylase	O43451	211031	94	4	9		X	Pm
44	Annexin A1	P04083	38918	105	19	7		X	Pm
44	Desmoplakin	P15924	334021	29	0	1		X	CySk

Mascot Score = Mascot threshold score for identity were used as peptide level filters of peptide significance. Protein identifications with a Mascot score above the significant hit threshold ($p < 0.05$) and at least one identical peptide were considered significant.

Cov. % = % of protein coverage.

RCC = protein identified also in RCC urinary exosome sample.

Exocarta = protein also identified in Exocarta database in the section regarding UE²⁸.

Localization = subcellular localization based on UniProtKB. **Pm** = plasmamembrane; **CySk** = Cytoskeleton; **Org** = Organelles; **Cyt** = Cytosol; **Secr** = Secreted; **Oth/Unk** = Other/ Unknown.

***** = protein identified only after deglycosilation treatment.

Table 4 ESI. List of proteins identified in urinary exosomes isolated from RCC patient urines.

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	CTRL	Exocarta	Localization
1	Protein S100-A8	P05109	10885	135	38	6	X	X	Cyt
2	Macrophage migration inhibitory factor	P14174	12639	49	17	2	X	X	Secr
2	Nuclear transport factor 2	P61970	14640	34	6	1		X	Cyt
3	Cystatin-C	P01034	16017	38	7	1	X	X	Secr
3	UPF0467 protein C5orf32	Q9H1C7	10966	60	11	2	X		Oth/Unk
3	Uromodulin	P07911	72451	1661	30	81	X	X	Pm
4	CD59 glycoprotein	P13987	14795	25	15	2	X	X	Pm
4	Haptoglobin	P00738	45861	34	6	2		X	Secr
4	Hemoglobin subunit α	P69905	15305	141	61	8	X		Oth/Unk
4	Hemoglobin subunit β	P68871	16102	72	31	3		X	Oth/Unk
5	Actin-related protein 2/3 complex subunit 4	P59998	19768	27	11	2		X	CySk
5	ADP-ribosylation factor 1	P84077	20741	41	6	1	X	X	Org
5	CD9 antigen	P21926	25969	87	9	4	X	X	Pm
5	Ganglioside GM2 activator	P17900	21281	51	5	1		X	Org
5	Mannan-binding lectin serine protease 2	O00187	77224	68	8	9	X	X	Secr
5	Multimerin-2	Q9H8L6	105028	38	0	1		X	Secr
5	Peptidyl-prolyl cis-trans isomerase A	P62937	18229	50	18	3	X	X	Cyt
5	Prostate stem cell antigen	O43653	13474	28	8	1	X	X	Pm
6	ADP-ribosylation factor-like protein 3	P36405	20614	50	6	1	X	X	CySk
6	Cell division control protein 42	P60953	21696	24	11	3	X	X	Pm
6	Immunoglobulin J	P01591	18543	108	13	3	X		Secr
6	Peroxiredoxin-2	Q06830	22049	46	9	2			Cyt
6	Programmed cell death protein 6	O75340	21912	42	5	1	X	X	Pm
6	Prostate-specific antigen	P07288	29293	27	4	1			Secr
6	Ras-related C3 botulinum toxin substrate 1	P63000	21835	25	9	2		X	Pm
7	Abhydrolase domain-containing protein 14B	Q96IU4	22446	47	10	3		X	Cyt

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	CTRL	Exocarta	Localization
7	Apolipoprotein D	P05090	21547	184	34	10	X	X	Secr
7	Collagen α -3(VI) chain	P12111	345167	44	0	2		X	Secr
7	Cytochrome b561	P49447	27713	24	3	1		X	Pm
7	Mps one binder kinase activator-like 1A	Q7L9L4	25246	24	5	1	X		Cyt
7	Ras-related protein Rab-1A	P62820	22891	66	5	2		X	Org
8	Apolipoprotein A-I	P02647	30759	71	20	6		X	Secr
8	Eukaryotic translation initiation factor 6	P56537	27095	35	4	1		X	Cyt
8	Glutathione S-transferase A1	P08263	25672	23	7	2	X	X	Cyt
8	Glutathione S-transferase Mu 3	P21266	26998	34	8	2	X	X	Cyt
8	Heat shock protein β -1	P04792	22826	32	4	1	X	X	Cyt
8	Ig κ chain C	P01834	11773	389	68	13	X		Secr
8	Ig κ chain V-I region Lay	P01605	11941	45	8	1	X	X	Secr
8	Ig κ chain V-III region SIE	P01620	11882	100	24	3		X	Secr
8	Ig κ chain V-III region VG (Fragment)	P04433	12681	38	7	1		X	Secr
8	Ig κ chain V-IV region Len	P01625	12746	39	23	2		X	Secr
8	Ig λ chain V-III region LOI	P80748	12042	33	14	1		X	Secr
8	Mucin-1	P15941	122200	97	6	6	X	X	Pm
8	Peroxiredoxin-6	P30041	25133	70	8	2	X	X	Cyt
8	Ras-related protein Ral-A	P11233	23723	41	3	1	X	X	Pm
8	Serum amyloid P-component	P02743	25485	37	14	3		X	Secr
9	Dapper homolog 1	Q9NYF0	91145	31	0	1		X	Cyt
9	Ig κ chain V-II region Cum	P01614	12782	87	11	1	X		Secr
9	Ig κ chain V-IV region (Fragment)	P06312	13486	49	7	1		X	Secr
9	Ig λ chain V-I region HA	P01700	12003	51	11	1	X		Secr
9	Ig λ -2 chain C regions	P0CG05	11458	326	63	13	X		Secr
9	L-xylulose reductase	Q7Z4W1	26182	30	8	2	X	X	Pm
9	Peptidoglycan recognition protein 1	O75594	22116	73	12	3		X	Secr
9	Ras-related protein Rab-5A *	P20339	23872	23	5	1		X	Pm
9	TIR domain-containing adapter molecule 1	Q8IUC6	77343	17	1	1		X	Pm

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	CTRL	Exocarta	Localization
10	14-3-3 protein β/α	P31946	28179	25	16	4	X	X	Cyt
10	6-phosphogluconolactonase	O95336	27815	123	39	8		X	Cyt
10	Collagen α -1(XV) chain	P39059	142202	41	2	3	X	X	Secr
10	Retinoid-inducible serine carboxypeptidase	Q9HB40	51083	48	2	1			Secr
11	Carbonic anhydrase 1	P00915	28909	21	11	3			Cyt
11	Carbonic anhydrase 2	P00918	29285	61	15	4	X	X	Cyt
11	Carbonyl reductase [NADPH] 1	P16152	30641	25	9	3	X	X	Cyt
11	Charged multivesicular body protein 2b	Q9UQN3	23948	32	4	1	X	X	Org
11	Chloride intracellular channel protein 1	O00299	27248	37	8	2	X	X	Pm
11	Probable serine carboxypeptidase CPVL	Q9H3G5	54414	27	7	4	X		Oth/Unk
11	Transmembrane protein 44	Q2T9K0	53061	21	1	1		X	Pm
12	Annexin A5	P08758	35971	44	8	3	X	X	Cyt
12	L-lactate dehydrogenase B chain	P07195	36900	166	17	6	X	X	Cyt
12	Protein AMBP	P02760	39886	88	13	4	X	X	Secr
12	Syntenin-1	O00560	32595	27	15	6	X	X	Pm
12	Vesicular integral-membrane protein VIP36	Q12907	40545	33	5	2	X	X	Org
14	Acid ceramidase	Q13510	45087	67	4	2	X	X	Org
14	Annexin A2	P07355	38808	46	8	3	X	X	Pm
14	Annexin A3	P12429	36524	35	2	1		X	Secr
14	Clusterin	P10909	53031	54	11	5	X	X	Secr
14	Deoxyribonuclease-1	P24855	31642	86	11	3		X	Secr
14	F-actin-capping protein subunit α -1	P52907	33073	51	3	1		X	Cyt
14	G-protein G(I)/G(S)/G(T) subunit β -1	P62873	38151	79	16	5	X	X	Pm
14	Inter- α -trypsin inhibitor heavy chain H4	Q14624	103521	132	4	4		X	Secr
14	L-lactate dehydrogenase A chain *	P00338	36900	30	6	2	X	X	Cyt
14	Napsin-A	O96009	45700	37	4	2	X	X	Secr
15	Calcium-binding protein 39	Q9Y376	39869	19	1	1	X	X	Cyt
15	Endothelial protein C receptor	Q9UNN8	26997	66	3	1		X	Pm
15	Fructose-bisphosphate aldolase B	P05062	39961	87	7	2	X	X	Cyt

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	CTRL	Exocarta	Localization
15	Glyceraldehyde-3-phosphate dehydrogenase	P04406	36201	46	17	5	X	X	Cyt
15	G-protein G(q) subunit α	P50148	42400	59	3	1	X	X	Pm
15	G-protein G(s) subunit α isoforms XLas	Q5JWF2	11025	79	1	2		X	Pm
15	Integrator complex subunit 4-like protein 1 *	Q96LV5	49382	24	1	1			Cyt
15	N-acetylgalactosamine-6-sulfatase	P34059	58445	26	1	1		X	Org
15	Prostasin	Q16651	37093	33	4	1	X		Pm
15	Sorbitol dehydrogenase	Q00796	38927	26	2	1	X	X	Org
16	Actin	P60709	42052	309	31	13	X	X	CySk
16	Fructose-bisphosphate aldolase A *	P04075	39851	44	3	1	X	X	Cyt
16	G-protein G(i) subunit α -1 *	P63096	40905	80	5	2	X	X	Pm
16	Pepsin A	P00790	42350	43	4	2			Secr
16	Tripeptidyl-peptidase 1 *	O14773	61723	56	2	1	X	X	Org
17	Aspartate aminotransferase	P17174	46447	23	3	1		X	Cyt
17	Erythrocyte band 7 integral membrane protein	P27105	31882	114	13	3	X	X	Pm
18	Aminoacylase-1	Q03154	46084	69	9	4	X	X	Cyt
18	Betaine-homocysteine S-methyltransferase 1	Q93088	45426	57	12	5	X	X	Cyt
18	BRO1 domain-containing protein BROX	Q5VW32	46960	41	7	3	X	X	Cyt
18	Cathepsin	P07339	45037	35	11	5		X	Org
18	Chondroitin sulfate proteoglycan 4	Q6UVK1	251067	95	1	3			Pm
18	Isocitrate dehydrogenase [NADP] Cyt	O75874	46915	33	13	5	X	X	Cyt
18	IST1 homolog	P53990	39897	59	13	5	X	X	Org
18	Phosphoglycerate kinase 1	P00558	44985	28	11	6		X	Cyt
18	Serpin B3	P29508	44594	103	12	5		X	Cyt
19	α -enolase	P06733	47481	95	9	4	X	X	Pm
19	Fibrinogen γ chain	P02679	52106	31	1	1		X	Secr
19	Leucine-rich α -2-glycoprotein	P02750	38382	72	10	4		X	Secr
19	Lysosomal acid phosphatase	P11117	48713	115	12	6		X	Org
19	Monocyte differentiation antigen CD14	P08571	40678	30	7	3		X	Pm
19	N-acetylglucosaminide β -1,3-N-acetylglucosaminyltransferase	O43505	47545	44	3	2	X		Org

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	CTRL	Exocarta	Localization
20	Ig γ -3 chain C region *	P01860	42287	89	10	4			Oth/Unk
20	Plasma serine protease inhibitor	P05154	45787	147	16	7	X		Secr
20	Tissue α -L-fucosidase*	P04066	53940	25	4	2		X	Org
20	Tumor susceptibility gene 101 protein *	Q99816	44088	52	6	2	X	X	Pm
21	Cytosolic non-specific dipeptidase	Q96KP4	53187	48	6	2	X	X	Cyt
21	Dipeptidase 1	P16444	46101	69	4	2	X	X	Pm
21	Ig γ -1 chain C	P01857	36596	472	54	16	X		Secr
21	Ig γ -2 chain C region	P01859	36505	359	38	13	X		Secr
21	Ig heavy chain V-III region TIL	P01765	12462	85	16	2			Secr
21	Ig heavy chain V-III region VH26 *	P01764	12745	54	18	2			Secr
21	Pancreatic α -amylase	P04746	58354	179	21	10	X		Secr
21	Prostatic acid phosphatase	P15309	44880	115	15	5	X		Org
22	1-acyl-sn-glycerol-3-phosphate acyltransferase α *	Q99943	32038	32	3	1		X	Pm
22	α -1-antitrypsin	P01009	46878	354	33	17		X	Secr
22	Antithrombin-III	P01008	53025	41	2	1			Secr
22	Dipeptidyl peptidase 2	Q9UHL4	54763	19	5	2		X	Org
22	Fibrinogen β chain	P02675	56577	36	13	6			Secr
22	Kininogen-1	P01042	72996	254	12	8	X	X	Secr
23	α -1-antichymotrypsin	P01011	47792	192	13	6	X		Secr
23	β -galactosidase	P16278	76483	122	11	7	X	X	Cyt
23	Dickkopf-related protein 4	Q9UBT3	26057	14	5	1		X	Secr
23	Ig α -1 chain C	P01876	38486	533	38	14	X		Secr
23	Ig α -2 chain C	P01877	37301	361	25	10	X		Secr
23	Mannosyl-oligosaccharide 1,2- α -mannosidase 1A	P33908	73150	61	4	2	X		Org
23	Receptor activity-modifying protein 2 *	O60895	19880	21	4	1			Pm
24	Angiotensinogen	P01019	53406	22	3	1		X	Secr
24	Bifunctional ATP-dependent dihydroxyacetone kinase/FAD-AMP lyase (cyclizing)	Q3LXA3	59252	32	2	1	X		Cyt
24	Thy-1 membrane glycoprotein	P04216	18151	36	6	1	X	X	Pm
25	γ -glutamyltransferase 1	P19440	61714	22	3	2	X	X	Pm

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	CTRL	Exocarta	Localization
25	Hemopexin	P02790	52385	24	2	1		X	Secr
26	Protein-glutamine γ -glutamyltransferase 4	P49221	77951	41	7	4	X	X	Oth/Unk
26	Serum albumin	P02768	71317	592	43	30	X	X	Secr
27	Complement component C9	P02748	64615	32	3	2		X	Pm
27	Galectin-3-binding protein	Q08380	66202	33	4	2	X		Secr
27	Heat shock 70 kDa protein 1A/1B	P08107	70294	61	13	7	X	X	Cyt
27	Heat shock-related 70 kDa protein 2	P54652	70263	56	12	6		X	Oth/Unk
27	Olfactomedin-4	Q6UX06	57529	112	13	8	X	X	Secr
27	Plastin-1	Q14651	70608	23	1	1	X	X	Cyt
27	Vacuolar protein sorting-associated protein 4B	O75351	49443	38	4	1	X	X	Org
28	Cardiotrophin-like cytokine factor 1	Q9UBD9	25388	27	3	1	X		Secr
28	Complement C4-A	P0C0L4	194247	52	5	11		X	Secr
28	Heat shock cognate 71 kDa protein	P11142	71082	87	15	8	X		Cyt
28	Moesin	P26038	67892	51	6	5	X	X	Pm
29	Ezrin	P15311	69484	70	9	6	X	X	Pm
29	Ig μ chain C region	P01871	49960	67	16	7	X		Secr
29	Thyroxine-binding globulin	P05543	46637	21	3	1		X	Secr
29	V-type proton ATPase catalytic subunit A	P38606	68660	39	1	1	X	X	Org
30	α -N-acetylglucosaminidase	P54802	82571	31	2	2	X	X	Org
30	Choline transporter-like protein 2	Q8IWA5	81610	24	2	2	X		Pm
30	Thyrotropin-releasing hormone-degrading ectoenzyme	Q9UKU6	117439	23	0	1	X		Pm
31	Plasma protease C1 inhibitor	P05155	55347	85	7	4	X		Secr
31	Polymeric immunoglobulin receptor	P01833	84429	266	16	10	X	X	Pm
32	Programmed cell death 6-interacting protein X	Q8WUM4	96590	50	3	3	X	X	Cyt
32	Vasorin	Q6EMK4	72751	72	6	4		X	Pm
34	Bile salt-activated lipase	P19835	79614	29	1	1			Secr
34	Dipeptidyl peptidase 4	P27487	88907	132	9	9	X	X	Pm
34	Prominin-1	O43490	98395	17	2	2	X	X	Pm
34	Prominin-2	Q8N271	93079	50	2	2	X	X	Pm

Band No	Name	Accession (UNIPROT)	MW (Da)	Mascot Score	Cov. (%)	Matched Peptides	CTRL	Exocarta	Localization
35	Complement C3	P01024	188569	231	14	26		X	Secr
35	Protein archease*	Q8IWT0	19535	35	4	2			Oth/Unk
36	Glutamyl aminopeptidase	Q07075	109689	36	1	2	X	X	Pm
37	Aminopeptidase N	P15144	109870	790	25	38	X		Pm
37	Ceruloplasmin	P00450	122983	274	14	15		X	Secr
37	Collagen α -1(VI) chain	P12109	109602	314	10	10	X	X	Secr
37	Podocalyxin	O00592	59055	33	8	4	X	X	Pm
37	Pro-epidermal growth factor	P01133	137613	750	22	33	X	X	Pm
37	Solute carrier family 12 member 1	Q13621	122627	62	2	2	X	X	Pm
37	Transthyretin	P02766	15991	48	9	2		X	Secr
39	α -2-macroglobulin	P01023	164613	226	9	12		X	Secr
39	Angiotensin-converting enzyme	P12821	150418	44	1	2	X	X	Pm
40	Serotransferrin	P02787	79280	349	30	19		X	Secr
42	Cubilin	O60494	407262	43	1	6	X	X	Org
44	Low-density lipoprotein receptor-related protein 2	P98164	540376	79	1	7	X	X	Pm

Mascot Score = Mascot threshold score for identity were used as peptide level filters of peptide significance. Protein identifications with a Mascot score above the significant hit threshold ($p < 0.05$) and at least one identical peptide were considered significant.

Cov. % = % of protein coverage.

CTRL = protein identified also in control urinary exosome sample.

Exocarta = protein also identified in Exocarta database in the section regarding UE²⁸.

Localization = subcellular localization based on UniProtKB. **Pm** = plasmamembrane; **CySk** = Cytoskeleton; **Org** = Organelles; **Cyt** = Cytosol; **Secr** = Secreted; **Oth/Unk** = Other/ Unknown.

* = protein identified only after deglycosilation treatment.

