

## Electronic Supplementary Information

# A new integrated method for tissue extracellular vesicle enrichment and proteome profiling

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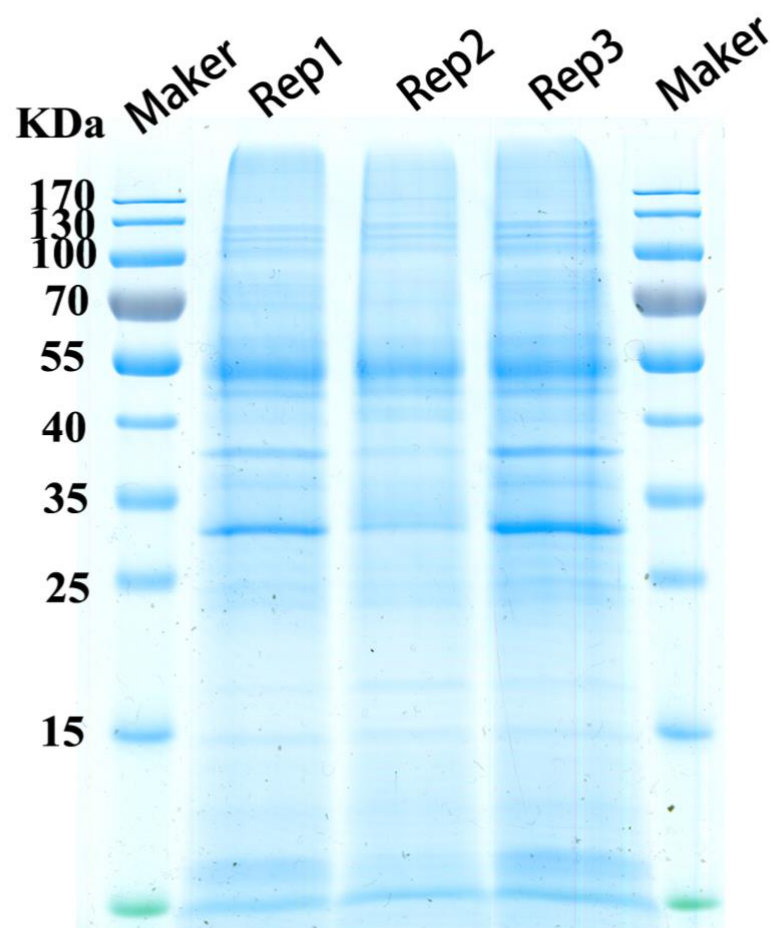
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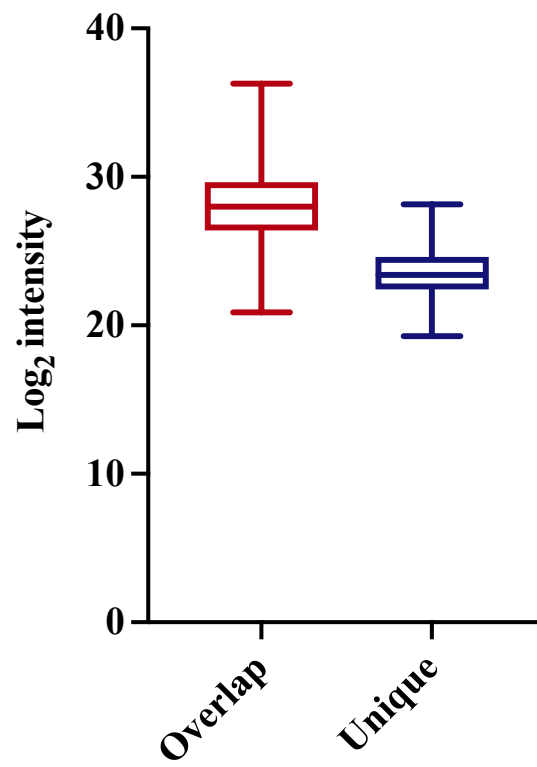
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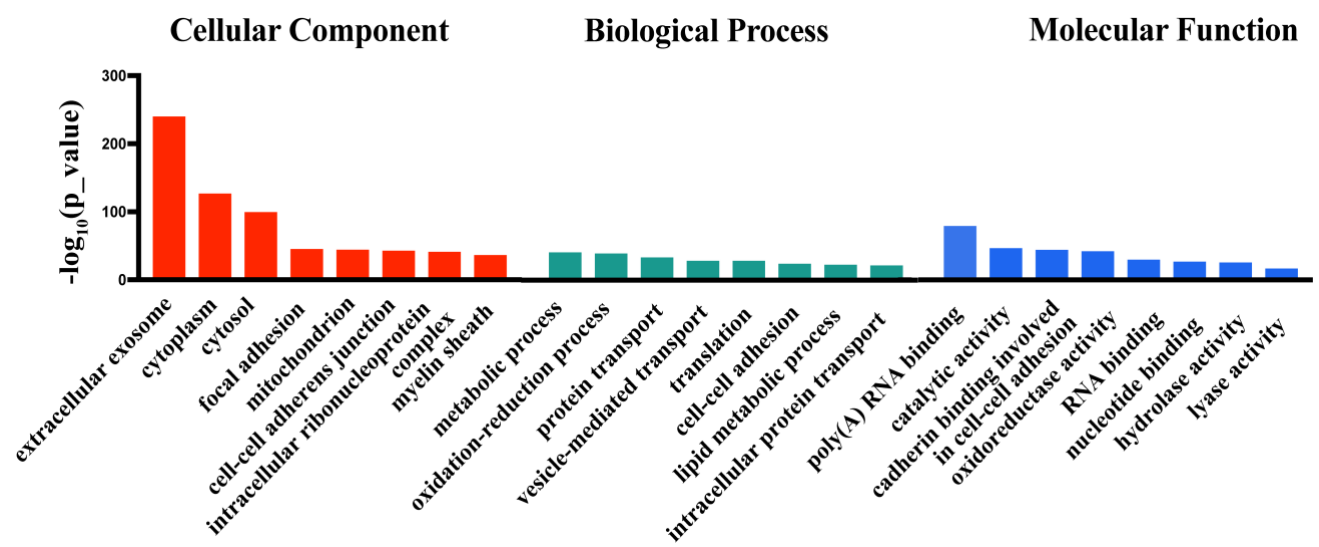
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**Figure S1.** Separation of liver tissue EV proteins in triplicates by SDS-PAGE (blue-stained).



**Figure S2.** Box plot showing the intensity of EV proteins detected by all the four methods and by kit-TiO<sub>2</sub> approach alone.



**Figure S3.** The gene ontology analysis of the identified tissue EV proteins by the kit–TiO<sub>2</sub> series method.

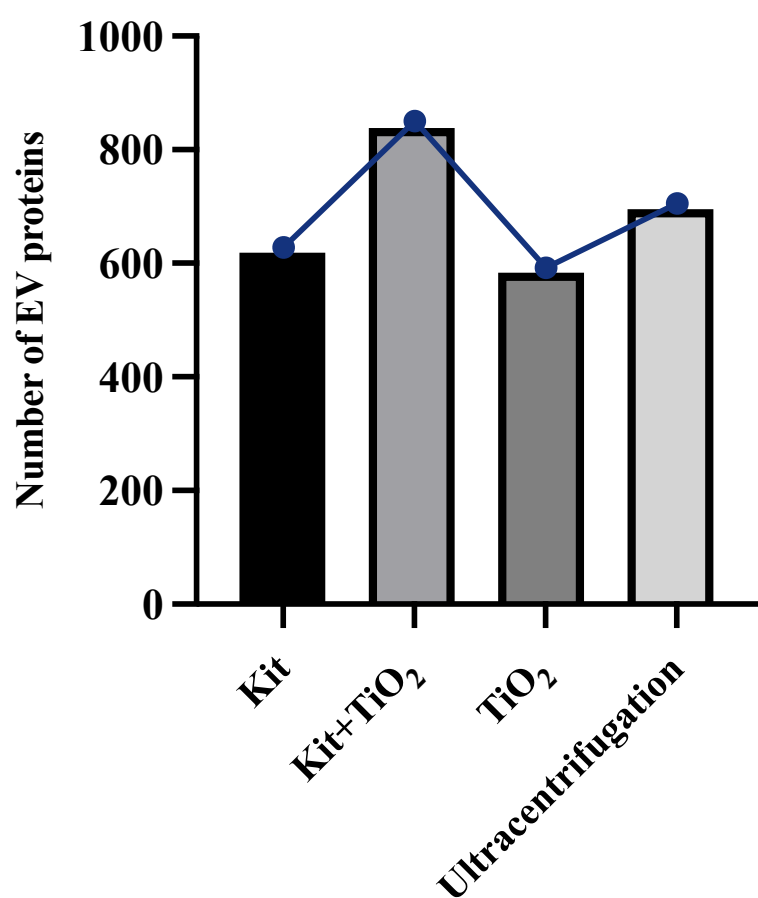


Figure S4. The number of EV proteins in cellular compartments of GO analysis for the different extraction methods.

**Table S1.** differentially expressed proteins of tissue EV from the healthy and HCC Mice

Uniprot ID	Gene names	logFC	logCPM	PValue	FDR
P97500	Myt1	6.576232	6.676787	2.43E-18	2.03E-15
O80358	FPG1	6.471748	6.573426	7.25E-18	3.02E-15
Q3URU2	Peg3	5.760498	5.872382	3.54E-12	9.84E-10
Q80UW5	Cdc42bpg	4.82743	5.327343	2.07E-06	9.06E-05
P04776	GY1	4.721327	7.213106	3.49E-05	0.000939
Q9CWJ9	Atic	3.806736	3.991827	5.02E-08	5.23E-06
Q27IK6	KIN12D	3.707794	5.072426	0.000198	0.003951
P04405	GY2	3.18414	8.15941	0.004317	0.045245
Q8CIE6	Copa	2.320275	6.92623	0.001219	0.015864
Q91YT0	Ndufv1	2.180942	8.684168	0.000306	0.005666
P06801	Me1	1.971252	9.851786	1.66E-05	0.000533
Q8BWP8	B4gat1	1.925424	2.955314	0.008034	0.071964
P09811	Pygl	1.90594	11.02188	4.10E-05	0.001035
Q8K0V4	Cnot3	1.867488	7.592016	0.001389	0.017265
O35639	Anxa3	1.819554	7.019045	0.003405	0.037316
Q9D6J6	Ndufv2	1.808295	9.669767	0.000374	0.0065
P09528	Fth1	1.751346	9.531872	6.70E-05	0.00155
Q99LB7	Sardh	1.732996	8.926328	0.000614	0.009843
P48036	Anxa5	1.659633	11.37893	9.30E-05	0.002094
P67778	Phb1	1.649297	12.14927	3.93E-05	0.001023
P29391	Ftl1	1.626707	10.7031	6.06E-05	0.001443
Q8BWT1	Acaa2	1.596736	10.92431	0.000375	0.0065
O04291	ATHB-14	1.538602	10.3154	4.67E-05	0.001144
Q9D3D9	Atp5f1d	1.52851	9.382788	0.001146	0.01515
P26443	Glud1	1.511104	10.57208	0.0002	0.003951
Q8VC30	Tkfc	-1.51858	9.559122	0.008485	0.075195
Q9WVJ2	Psm13	-1.53305	9.528347	0.000362	0.0065
Q8K157	Galm	-1.82291	2.826816	0.00633	0.05992
Q91WG4	Elp2	-1.92713	2.90871	0.004544	0.046135
Q9QUI0	Rhoa	-2.05601	3.011694	0.007245	0.066322
P58044	Idi1	-2.11684	3.060923	0.001917	0.022815
O54774	Ap3d1	-2.15786	3.837691	0.004345	0.045245
Q9CY64	Blvra	-2.20043	3.12922	0.001375	0.017265
Q61553	Fscn1	-2.21636	4.074914	0.00538	0.053348
Q922H4	Gmppa	-2.28484	3.198905	0.00086	0.012547
O08692	Ngp	-2.32189	6.456339	0.001609	0.019419
Q91WT9	Cbs	-2.34083	8.635732	2.21E-07	1.68E-05

Uniprot ID	Gene names	logFC	logCPM	PValue	FDR
P46460	Nsf	-2.36294	3.264	0.000577	0.009616
Q9CYH2	Prxl2a	-2.3829	3.751514	0.000797	0.011849
Q61543	Glg1	-2.54037	3.414002	0.000219	0.00414
P62264	Rps14	-2.54801	3.420522	0.000204	0.003951
Q9D819	Ppa1	-2.58664	4.847157	0.003207	0.036593
Q80TA6	Mtmr12	-2.6011	3.465978	0.000164	0.003511
P47758	Srprb	-2.61531	3.478189	0.000173	0.003609
Q9D4H8	Cul2	-2.65042	3.50842	0.000139	0.003039
Q501J6	Ddx17	-2.88488	4.279651	1.21E-05	0.000439
P26883	Fkbp1a	-2.92407	3.747416	2.87E-05	0.000853
Q9EQP6	Arr3	-2.9776	6.056333	3.30E-05	0.000916
Q922D8	Mthfd1	-2.99898	3.813802	2.01E-05	0.00062
O08600	Endog	-3.13708	4.914939	0.000733	0.011104
P63087	Ppp1cc	-3.14668	3.945803	1.33E-05	0.000461
Q9CQC6	Bzw1	-3.16966	3.966469	9.75E-06	0.000369
O55135	Eif6	-3.18406	6.222929	1.64E-06	7.59E-05
P20060	Hexb	-3.20593	3.999156	1.45E-05	0.000483
Q64458	Cyp2c29	-3.24863	5.868282	0.000703	0.010847
Q9D8L5	Ccdc91	-3.29284	4.077791	4.30E-06	0.00017
Q7SIB2	COL4A1	-3.60271	4.361613	8.35E-07	4.09E-05
O89112	Lancl1	-3.61371	4.371775	7.14E-07	3.72E-05
Q62186	Ssr4	-3.64042	4.396491	2.36E-06	9.85E-05
P10605	Ctsb	-3.66676	4.420888	3.18E-05	0.000913
Q6WVG3	Kctd12	-3.67902	4.432254	7.13E-07	3.72E-05
Q91VS7	Mgst1	-3.70778	4.458957	4.68E-07	2.78E-05
Q99L13	Hibadh	-3.80537	5.306542	2.84E-07	1.97E-05
P62700	Ypel5	-3.84779	4.589449	3.89E-07	2.49E-05
P14431	H2-Q9	-4.12981	4.854729	1.50E-07	1.25E-05
Q91W43	Gldc	-4.25102	4.969649	7.27E-08	6.73E-06
Q8BMJ2	Lars1	-4.36799	5.081001	3.14E-08	3.73E-06
Q9CWG9	Bloc1s2	-4.45656	5.165596	1.93E-08	2.67E-06
Q9DCQ2	Aspdh	-4.57121	5.275438	1.17E-08	1.94E-06
Q94AY3	DRIP2	-4.90504	5.597182	9.17E-10	1.91E-07