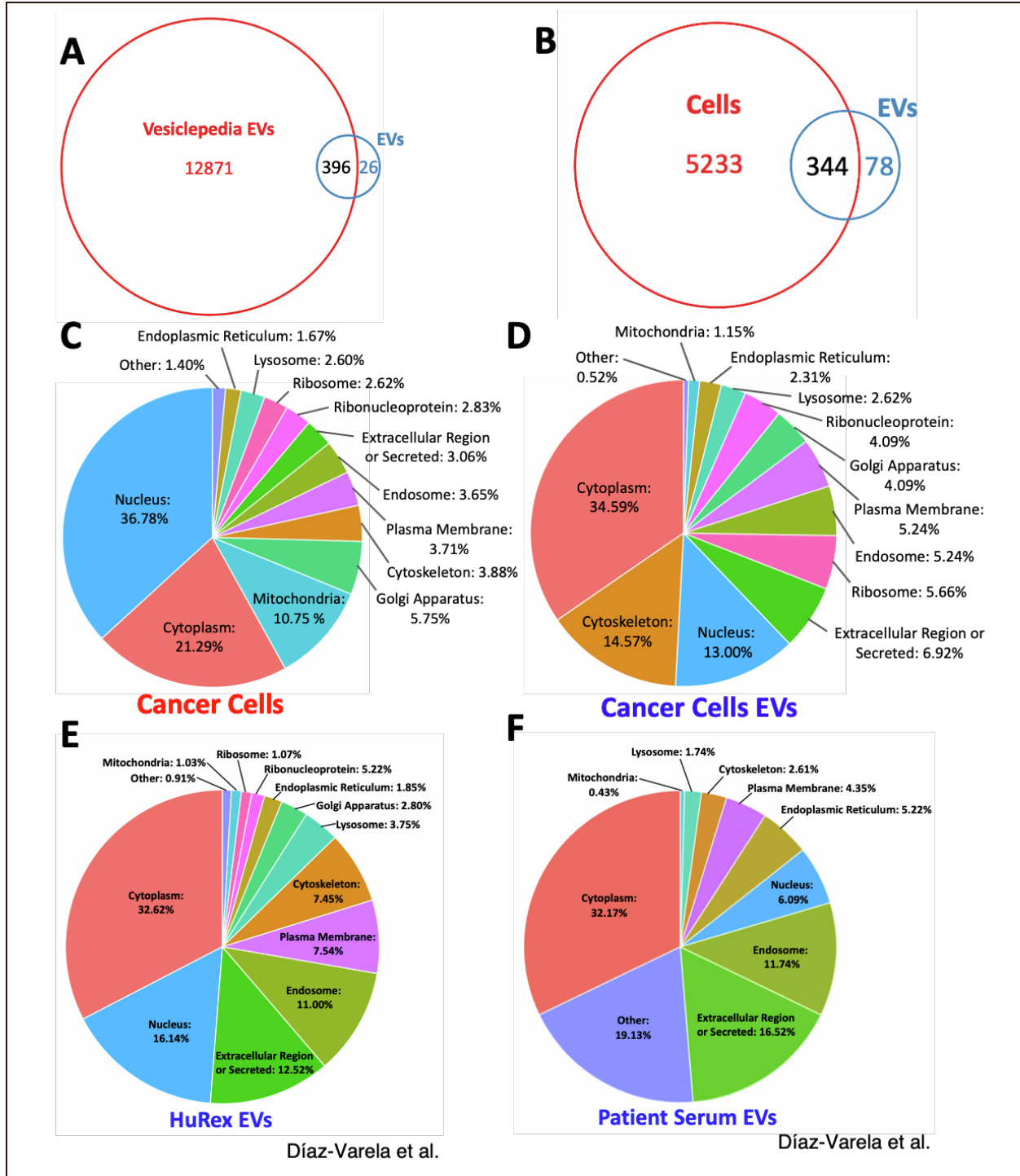


**Supplemental information**

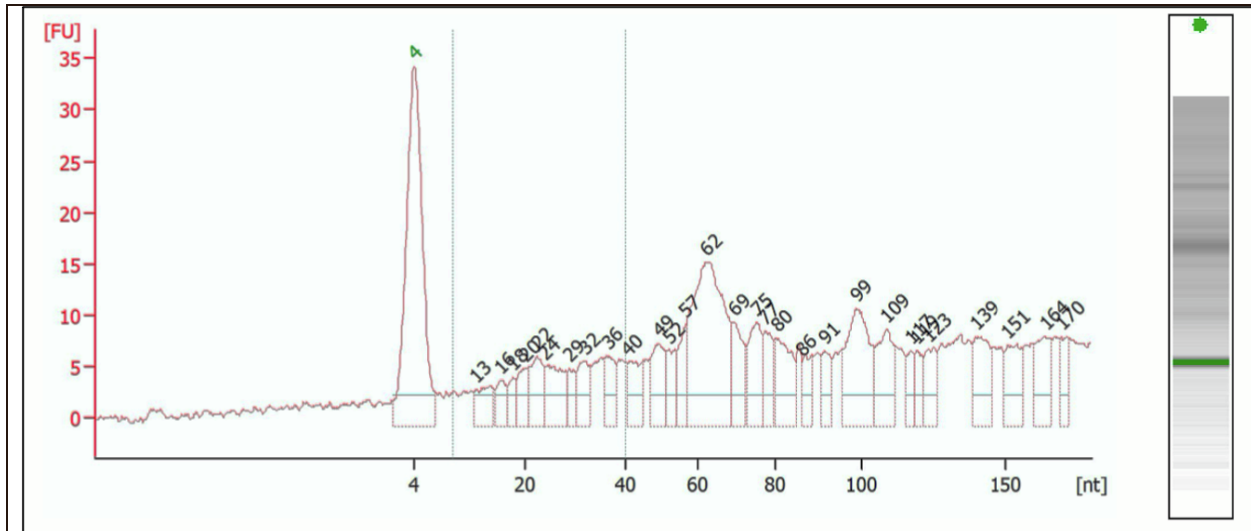
**Extracellular vesicles carry distinct  
proteo-transcriptomic signatures that  
are different from their cancer cell of origin**

**Tzu-Yi Chen, Edgar Gonzalez-Kozlova, Taliah Soleymani, Sabrina La Salvia, Natasha Kyprianou, Susmita Sahoo, Ashutosh K. Tewari, Carlos Cordon-Cardo, Gustavo Stolovitzky, and Navneet Dogra**



**Supplementary figure 1. Proteomic analysis of donor cells and their EVs, related to Figure 3.** (A) Comparative analyses of Vesiclepedia proteomic database of EVs with in-house proteomics of EVs isolated from prostate cancer cell lines, 22RV1. (B) Comparative analyses of EV and their donor cell proteins. (C) Subcellular location of donor cancer cell proteome. (D)

Subcellular location of cancer cell EVs proteome. Analyses of external proteomic data (from Diaz-Varela et al.) from human cord blood reticulocyte-derived (HuRex) exosomes (E) and human serum EVs (F).



**Supplementary figure 2.. Small RNA analyses of EV RNA, related to Figure 4A.** Capillary electrophoresis shows diverse RNA types in EVs ranging from 13-200 nt. Peak at 4nt is a spike-in marker.

Top EV RNA			Interacting RNA and proteins	
Serum EVs (UC)	Serum EVs (nanoDLD)	22rv1 EVs (UC)	EV_RNA	interacting EV_protein
MT-RNR2	TCTE1	VTRNA1-2	VTRNA1-2	IGF2BP2, SRSF1
RNY4	PEX5L	VTRNA1-1	VTRNA1-1	IGF2BP2, SRSF1
VTRNA1-1	CCDC96	RNY1	RNY1	YBX1
AC124068.2	FLNA	MYOCOS	SPEG	let-7
RN7SL2	CELF2	RN7SL2	AC124068.2	
RNY1	SLPI	SPEG	DPP9	snhg16
TCTE1	DBN1	AC124068.2	VTRNA1-3	igf2bp2
PEX5L	MT-RNR2	DPP9	RNY4	ybx1
SLPI	AC124068.2	VTRNA1-3	RNY3	ybx1
CCDC96	AC127164.1	RNY4		
CELF2	AC109466.1	RNY3		
FLNA	ADGRG6	MIR4454		
MYOCOS	KCNIP2	MAP1LC3B		
DBN1	NRXN3	AL049796.1		
MIRLET-7				

**Supplementary Table 1. Interacting RNA and proteins discovered in EVs, related to Figure 6D: Top enriched RNA in EVs and complementary EV proteins.**

Unique EV signatures compared with Vesiclepedia						
UMAD1	H1-0	MT4	AL136295.1	H1-4	SYT4	H2BC11
H3-3A	EPRS1	H4-16	TRAFD1	H1-5	L1RE1	GFP
DEUP1	H2AZ1	H1-10	MACROH2A1	YBX3	CHTOP	
CD59	H2AC11	MVB12A	ATP5F1B	ATP5F1A	DYRK1B	

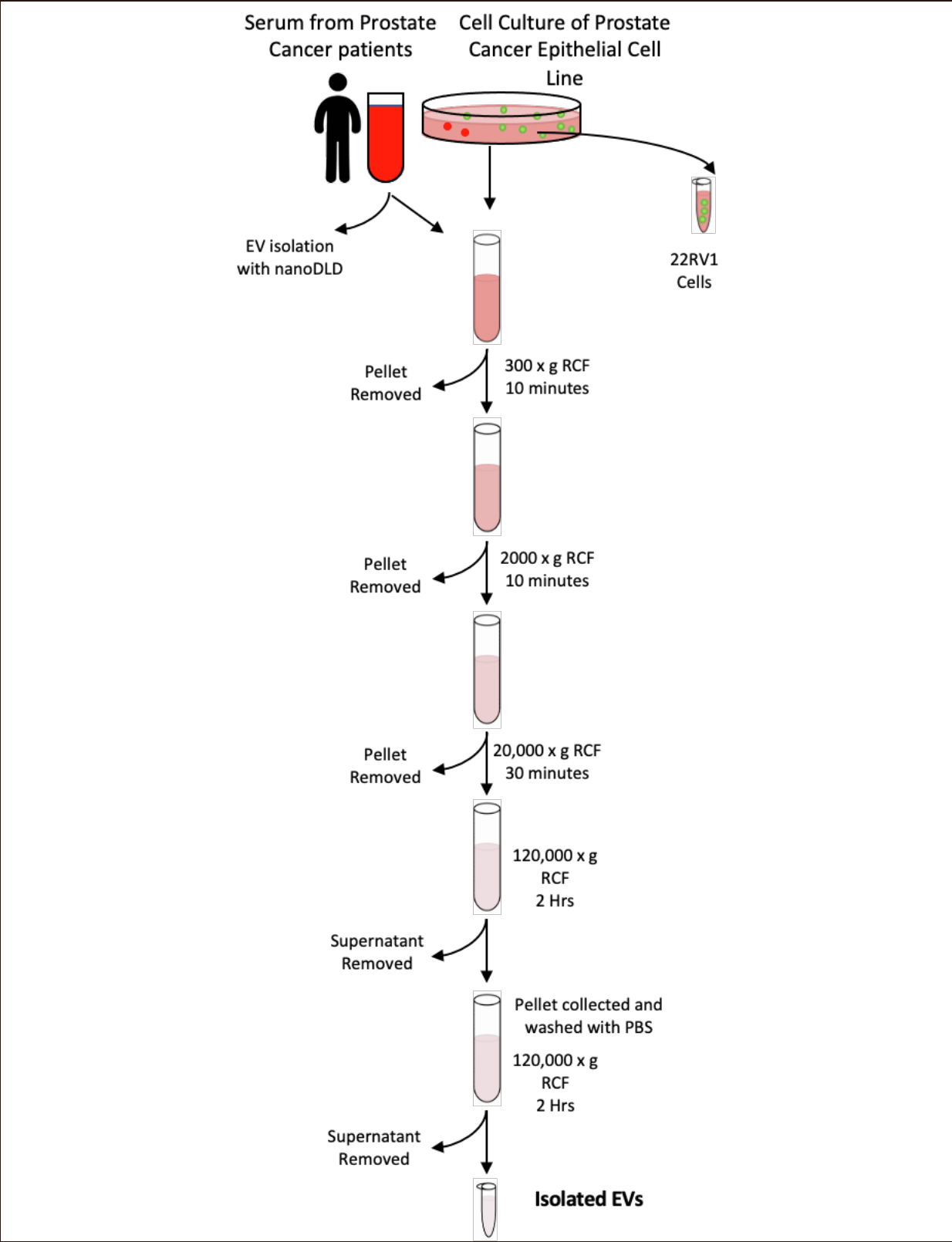
**Supplementary Table 2. A list of ~6% (26) proteins, which are unique to EVs as compared with Vesiclepedia database, related to Figure 3.**

Unique EV signatures as compared to donor 22RV1 cells								
COL1A2	GALNT3	NLRP1	SERPINA3	RRAS	ITGA1	FLG2	MVB12A	VPS37B
FBN2	DEUP1	RELN	HRAS	NAGA	ACTA1	MAST2	ITCH	CALML5
CORIN	CD59	SNRPN	KRAS	FLG	HSPG2	KRT26	ZC3H10	MKRN1
AGRN	UBC	PPL	IGHA1	AZGP1	PKD1	VPS37D	FAM193B	DICER1
LYZ	TUBA1B	WWP2	FN1	DCT	LRP2	NOSTRIN	SH3GL2	DYRK1B
TNXB	HBB	QSOX1	HPX	USP8	PLAUR	PROM2	LAT2	TNFRSF11A
UMAD1	SDCBP	IGSF3	S100A8	GFP	DSC1	SNX33	EPN3	
VPS37C	HCK	FAM13A	ALPL	LGALS7	TRIM26	IGSF8	SMOC1	
EIF1AY	ABCA3	CLDN7	H2AC11	MT4	CEP55	SH3KBP1	THAP9	

**Supplementary Table 3: A list of 78 (22%) proteins, which are unique to EVs as compared with their donor cells, related to Figure 3.**

High in cells						High in EVs					
	Cells	EVs	cell_line	sCellsmbol	ensembl	label	Cells	EVs	cell_line	sCellsmbol	
1	0.90455893	0.19969524	22RV1	MT-TV	ENSG000002	Cells	1	0.10787277	0.83577806	NF	MIR3591
2	0.88258295	0.23594825	22RV1	RELN	ENSG000001	Cells	2	0.23874186	0.76553983	CAF	MIR4508
3	0.88232726	0.13403299	22RV1	MT-TK	ENSG000002	Cells	3	0.10341913	0.72830188	22RV1	SCN4B
4	0.86716709	0.23594825	22RV1	MTRNR2L8	ENSG000002	Cells	4	0	0.72424547	CAF	MIR3591
5	0.85782672	0.23594825	22RV1	MT-RNR1	ENSG000002	Cells	5	0.2231927	0.71202652	CAF	
6	0.85390558	0.19969524	22RV1	MT-TP	ENSG000002	Cells	6	0.10225728	0.68007096	CAF	
7	0.82778252	0.22552475	22RV1	MT-TE	ENSG000002	Cells	7	0.18318049	0.66465689	22RV1	ALDH1A3
8	0.82543984	0.09149175	22RV1	MT-TL1	ENSG000002	Cells	8	0.10341913	0.65589834	22RV1	C1QA
9	0.82097203	0.16205419	22RV1	MTND6P3	ENSG000002	Cells	9	0.21420798	0.64922753	DKs.8	REXO1L1P
10	0.80695857	0.13403299	22RV1	MT-TS2	ENSG000002	Cells	10	0.2457349	0.63661343	DKO.1	REXO1L1P
11	0.76945548	0	22RV1	MT-TM	ENSG000002	Cells	11	0.10341913	0.61763141	22RV1	ADAMTS7
12	0.7609625	0.09149175	22RV1	IL21R	ENSG000001	Cells	12	0.22572863	0.61570638	22RV1	COL4A2
13	0.74018145	0.16205419	22RV1	MT-TD	ENSG000002	Cells	13	0.18112257	0.61124949	CAF	RNU1-22P
14	0.73819892	0.24578448	NF	SNORD61	ENSG000002	Cells	14	0.18112257	0.59728835	CAF	
15	0.73593289	0	NF	SNHG15	ENSG000002	Cells	15	0.15803075	0.5959489	NF	MIR4488
16	0.73271508	0	NF		ENSG000002	Cells	16	0	0.58698526	22RV1	AC006144.1
17	0.72623005	0	22RV1	MT-TA	ENSG000002	Cells	17	0.22572863	0.58083029	22RV1	YEATS2-AS1
18	0.72602815	0.18964622	CAF	SNORD10	ENSG000002	Cells	18	0.10341913	0.58004758	22RV1	RF00019
19	0.71945043	0.22521572	NF	RF00136	ENSG000001	Cells	19	0.19106897	0.57269349	NF	
20	0.71736259	0.22521572	NF	SNORD60	ENSG000002	Cells	20	0.22005261	0.56903857	DKO.1	ESRG
21	0.71509514	0.09149175	22RV1	SNORA73B	ENSG000002	Cells	21	0.15150629	0.56823905	22RV1	KHK
22	0.70883989	0.09149175	22RV1	MT-TR	ENSG000002	Cells	22	0.2231927	0.56510633	CAF	MIR4488
23	0.70082795	0.16205419	22RV1	MTRNR2L2	ENSG000002	Cells	23	0.22572863	0.56509954	22RV1	RF00019
24	0.69936543	0.12945368	CAF	SNORD61	ENSG000002	Cells	24	0.15150629	0.55637744	22RV1	RNY1P11
25	0.69349697	0.22929403	CAF	MIR199B	ENSG000002	Cells	25	0.10341913	0.55404632	22RV1	POU4F2
26	0.68843128	0.11260786	NF	SNHG1	ENSG000002	Cells	26	0.24145446	0.54895051	22RV1	RECQL4
27	0.68393622	0	CAF	RNU5A-6P	ENSG000002	Cells	27	0.23874186	0.54839393	CAF	
28	0.68202929	0.11260786	NF	SNORD59A	ENSG000002	Cells	28	0.2433541	0.54727303	DKO.1	HHLA1
29	0.68146062	0	NF	SNORD18A	ENSG000002	Cells	29	0.22572863	0.54592607	22RV1	IRX3
30	0.68038433	0.13403299	22RV1	MT-TS1	ENSG000002	Cells	30	0.15150629	0.54497293	22RV1	GSTM4
31	0.67997326	0.19969524	22RV1		ENSG000002	Cells	31	0.2327935	0.54274096	DKO.1	SPINK9
32	0.67619049	0.09149175	22RV1	MT-TN	ENSG000002	Cells	32	0.17357232	0.53773875	DKs.8	MUC4
33	0.672547	0	22RV1	MT-TG	ENSG000002	Cells	33	0.15713755	0.53698179	DKs.8	MUC16
34	0.672547	0	22RV1	MTATP8P1	ENSG000002	Cells	34	0.19106897	0.5361891	NF	MIR4508
35	0.66890434	0.16496753	NF	SNORD58A	ENSG000002	Cells	35	0.15150629	0.53451746	22RV1	FBXO45
36	0.66868806	0.19945597	NF	SNORD21	ENSG000002	Cells	36	0.24087803	0.53298657	DKO.1	TPTEP1
37	0.66656565	0.19969524	22RV1	MT-TQ	ENSG000002	Cells	37	0.14980421	0.52891318	CAF	
38	0.66118964	0.1829835	22RV1	MTCO2P12	ENSG000002	Cells	38	0.24375953	0.52856958	DLD.1	TTN
39	0.66034763	0	22RV1	MT-TF	ENSG000002	Cells	39	0.24145446	0.52743161	22RV1	PLEKHG2
40	0.65881276	0.09149175	22RV1	MT-TH	ENSG000002	Cells	40	0.20841342	0.52560988	DKO.1	AL139397.1
41	0.65842688	0	NF	SNORD12C	ENSG000002	Cells	41	0.24087803	0.52518248	DKO.1	TTN
42	0.65829103	0.18964622	CAF	RNU4-2	ENSG000002	Cells	42	0.0996136	0.523759	DKO.1	MUC4
43	0.6552513	0	NF	RNU5A-6P	ENSG000002	Cells	43	0.10341913	0.51837737	22RV1	ADAMTS9
44	0.65441308	0.13403299	22RV1	RF00096	ENSG000002	Cells	44	0.12043901	0.51802033	DKO.1	MUC16
45	0.65375028	0	NF	SNORD14D	ENSG000002	Cells	45	0.23874186	0.51781474	CAF	RNU1-16P
46	0.65375028	0	NF	SNORD12B	ENSG000002	Cells	46	0	0.51771511	22RV1	LCN10
47	0.65299107	0	NF	RNU4-46P	ENSG000002	Cells	47	0.10225728	0.51486874	CAF	MIR4532
48	0.65185636	0.19969524	22RV1	MTCO1P12	ENSG000002	Cells	48	0.23587318	0.51287483	DKs.8	MUC6
49	0.64922826	0.09149175	22RV1	MT-TL2	ENSG000002	Cells	49	0.22572863	0.51150508	22RV1	FZR1
50	0.64917463	0.18964622	CAF	SNORD21	ENSG000002	Cells	50	0	0.51150508	22RV1	CIDEC

**Supplementary Table 4: A list of top 50 RNA enriched EVs and donor cells, related to Figure 4H.**



**EV isolation protocol, related to STAR Methods**