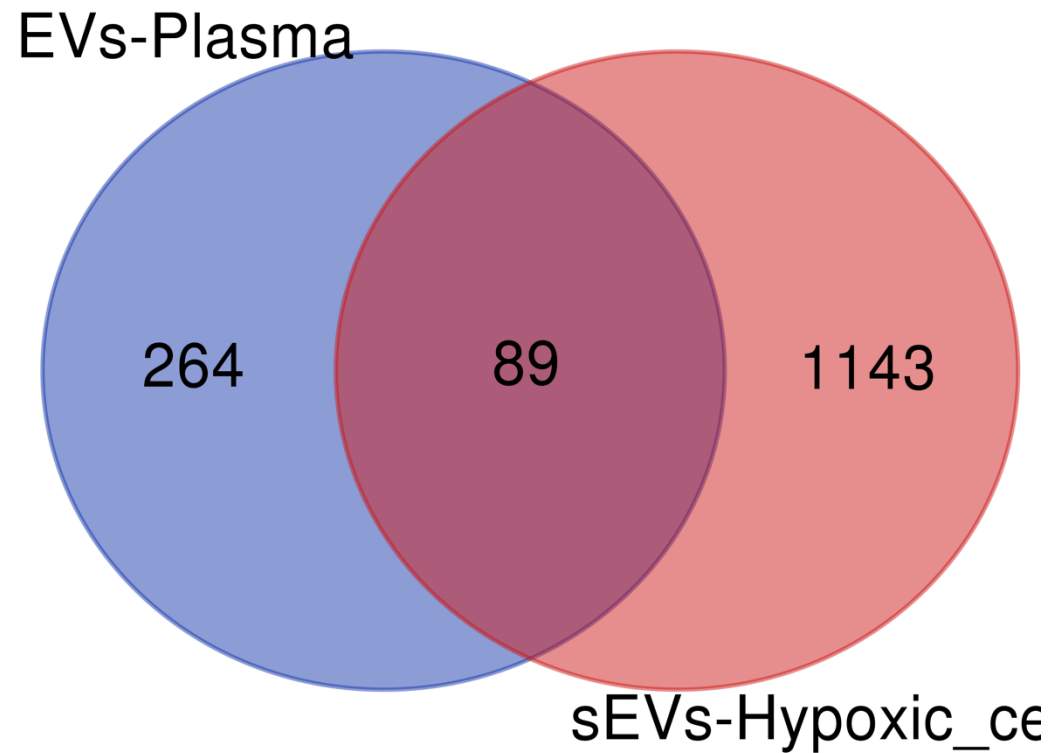
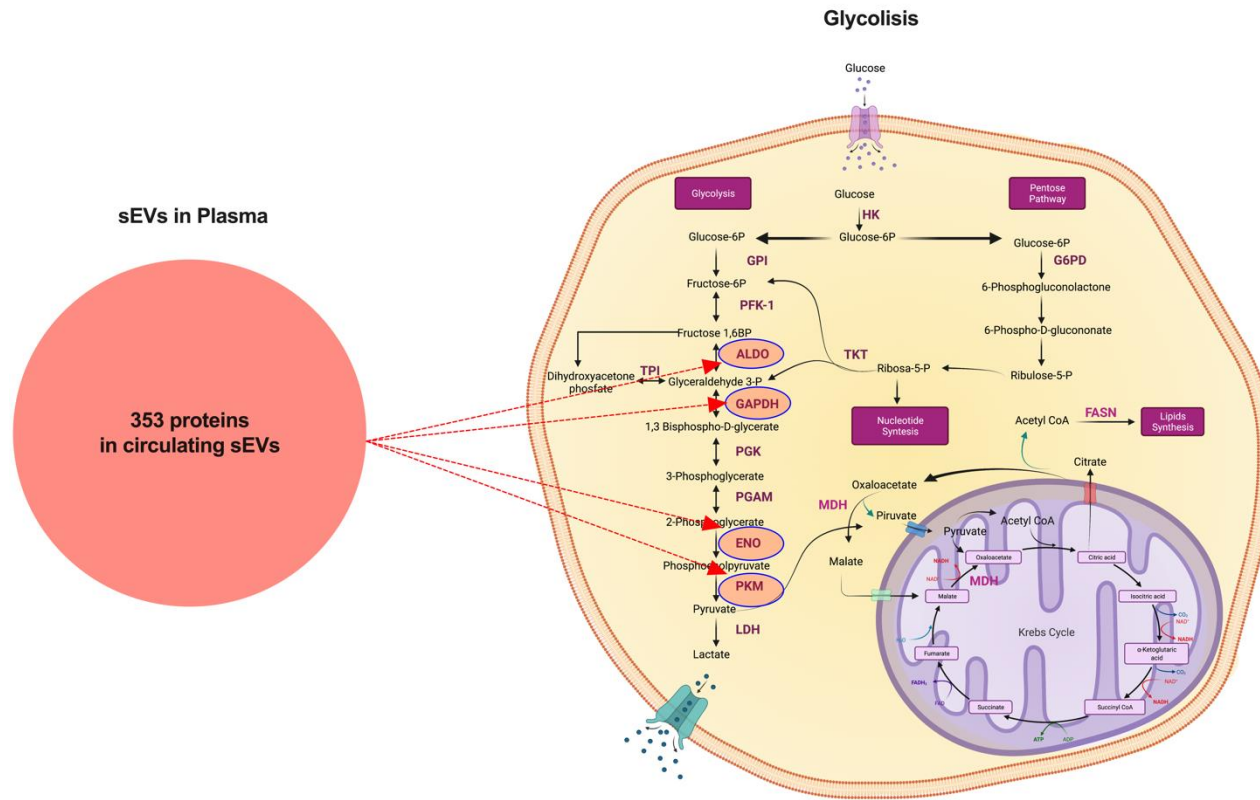


Supplemental Figure S1. Ingenuity Pathway Analysis (IPA) was used to identify signaling pathways associated with changes in proteomic profile in sEVs from cells cultured under hypoxic compared with normoxic conditions. A) Canonical Pathways, and B) Diseases and Bio Functions.



Supplemental Figure S2. Analysis of the protein identified in small extracellular vesicles isolated from cells and plasma. sEVs were isolated from CAOV-3 cells cultured at 1% oxygen, and plasma obtained from patients with ovarian cancer, and global proteomic identification was performed. Venn diagram shown the unique and common protein identified in sEVs from plasma, and from cell-conditioned media.



Supplemental Figure S3. An Ingenuity Pathway Analysis library in circulating small extracellular vesicles identified 4 sEV-associated glycolysis pathway proteins: pyruvate kinase M1/2, enolase 1, glyceraldehyde-3-phosphate dehydrogenase, and aldolase fructose-bisphosphate.

Table S1. Differentially expressed proteins in 1% oxygen CAOV-3 cells compared to 8% oxygen CAOV-3 cells.

Mapped IDs	Peak Name	Gene Name/ Gene Symbol/ Ortholog	PANTHER Family /Subfamily	Pather Protein Class	p-value	Fold Change
P50402	EMD_HUMAN	Emerin;EMD;ortholog	EMERIN (PTHR15171:SF2)		0.0007	0.079345782
Q9P2R7	SUCB1_HUMAN	Succinate--CoA ligase [ADP-forming] subunit beta, mitochondrial;SUCLA2;ortholog	SUCCINATE--COA LIGASE [ADP-FORMING] SUBUNIT BETA, MITOCHONDRIAL (PTHR11815:SF14)	ligase(PC00142)	0.00216	4.721641365
P49588	SYAC_HUMAN	Alanine--tRNA ligase, cytoplasmic;AARS1;ortholog	ALANINE--TRNA LIGASE, CYTOPLASMIC (PTHR11777:SF36)	aminoacyl-tRNA synthetase(PC00047)	0.00603	1.305535801
Q9Y678	COPG1_HUMAN	Coatomer subunit gamma-1;COPG1;ortholog	COATOMER SUBUNIT GAMMA-1 (PTHR10261:SF3)	vesicle coat protein(PC00235)	0.01021	0.589200077
Q9Y376	CAB39_HUMAN	Calcium-binding protein 39;CAB39;ortholog	CALCIUM-BINDING PROTEIN 39 (PTHR10182:SF11)		0.01282	5.893735567
Q08257	QOR_HUMAN	Quinone oxidoreductase;CRYZ;ortholog	QUINONE OXIDOREDUCTASE (PTHR44154:SF1)	oxidoreductase(PC00176)	0.01318	0.654118587
Q9BRP8	PYM1_HUMAN	Partner of Y14 and mago;PYM1;ortholog	PARTNER OF Y14 AND MAGO (PTHR22959:SF0)		0.01539	0.488257721
P11279	LAMP1_HUMAN	Lysosome-associated membrane glycoprotein 1;LAMP1;ortholog	LYSOSOME-ASSOCIATED MEMBRANE GLYCOPROTEIN 1 (PTHR11506:SF27)	membrane trafficking regulatory protein(PC00151)	0.01543	0.10021624
P22626	ROA2_HUMAN	Heterogeneous nuclear ribonucleoproteins A2/B1;HNRNPA2B1;ortholog	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEINS A2/B1 (PTHR48026:SF13)		0.01563	0.22965286
P52823	STC1_HUMAN	Stanniocalcin-1;STC1;ortholog	STANNIOCALCIN-1 (PTHR11245:SF1)	peptide hormone(PC00179)	0.01617	2.894444401
Q8NB59	TXND5_HUMAN	Thioredoxin domain-containing protein 5;TXNDC5;ortholog	THIOREDOXIN DOMAIN-CONTAINING PROTEIN 5 (PTHR45672:SF3)	chaperone(PC00072)	0.01763	0.805404588
P17936	IBP3_HUMAN	Insulin-like growth factor-binding protein 3;IGFBP3;ortholog	INSULIN-LIKE GROWTH FACTOR-BINDING PROTEIN 3 (PTHR11551:SF3)	protease inhibitor(PC00191)	0.01797	2.789064867
Q86TG7	PEG10_HUMAN	Retrotransposon-derived protein PEG10;PEG10;ortholog	RETROTRANSPOSON-DERIVED PROTEIN PEG10 (PTHR15503:SF11)		0.01974	0.143728947
P26006	ITA3_HUMAN	Integrin alpha-3;ITGA3;ortholog	INTEGRIN ALPHA-3 (PTHR23220:SF89)	integrin(PC00126)	0.02445	0.411870465
O94925	GLSK_HUMAN	Glutaminase kidney isoform, mitochondrial;GLS;ortholog	GLUTAMINASE KIDNEY ISOFORM, MITOCHONDRIAL (PTHR12544:SF49)	hydrolase(PC00121)	0.02659	0.664538378
P36542	ATPG_HUMAN	ATP synthase subunit gamma, mitochondrial;ATP5F1C;ortholog	ATP SYNTHASE SUBUNIT GAMMA, MITOCHONDRIAL (PTHR11693:SF31)	ATP synthase(PC00002)	0.02669	2.012627322
Q99961	SH3G1_HUMAN	Endophilin-A2;SH3GL1;ortholog	ENDOPHILIN-A2 (PTHR14167:SF63)		0.02688	3.244213135
Q14764	MVP_HUMAN	Major vault protein;MVP;ortholog	MAJOR VAULT PROTEIN (PTHR14165:SF3)	scaffold/adaptor protein(PC00226)	0.02776	3.309321869
Q9BWD1	THIC_HUMAN	Acetyl-CoA acetyltransferase, cytosolic;ACAT2;ortholog	ACETYL-COA ACETYLTRANSFERASE, CYTOSOLIC (PTHR18919:SF81)	acyltransferase(PC00042)	0.02855	1.842583088

Q92597	NDRG1_HUMAN	Protein NDRG1;NDRG1;ortholog	PROTEIN NDRG1 (PTHR11034:SF18)	serine protease(PC00203)	0.03241	2.897734821
Q9UNN8	EPCR_HUMAN	Endothelial protein C receptor;PROCR;ortholog	ENDOTHELIAL PROTEIN C RECEPTOR (PTHR15349:SF0)	protein-binding activity modulator(PC00095)	0.03415	2.22795871
P69905	HBA_HUMAN	Hemoglobin subunit alpha;HBA2;ortholog	HEMOGLOBIN SUBUNIT ALPHA (PTHR11442:SF48)		0.03428	4.58530993
P11021	BIP_HUMAN	Endoplasmic reticulum chaperone BiP;HSPA5;ortholog	ENDOPLASMIC RETICULUM CHAPERONE BIP (PTHR19375:SF380)		0.03429	1.884856296
Q6X4U4	SOSD1_HUMAN	Sclerostin domain-containing protein 1;SOSTDC1;ortholog	SCLEROSTIN DOMAIN-CONTAINING PROTEIN 1 (PTHR14903:SF5)	intercellular signal molecule(PC00207)	0.03445	0.362794853
P05204	HMG2_HUMAN	Non-histone chromosomal protein HMG-17;HMG2;ortholog	NON-HISTONE CHROMOSOMAL PROTEIN HMG-17 (PTHR23087:SF13)	chromatin/chromatin-binding, or -regulatory protein(PC00077)	0.03665	0.681892896
Q99714	HCD2_HUMAN	3-hydroxyacyl-CoA dehydrogenase type-2;HSD17B10;ortholog	2,4-DIENOYL-COA REDUCTASE, MITOCHONDRIAL-RELATED (PTHR43658:SF8)	oxidoreductase(PC00176)	0.03678	3.63205505
P49321	NASP_HUMAN	Nuclear autoantigenic sperm protein;NASP;ortholog	NUCLEAR AUTOANTIGENIC SPERM PROTEIN (PTHR15081:SF1)	chaperone(PC00072)	0.03969	0.320389344
Q9P258	RCC2_HUMAN	Protein RCC2;RCC2;ortholog	PROTEIN RCC2 (PTHR46207:SF1)		0.04374	1.821171165
P29279	CTGF_HUMAN	CCN family member 2;CCN2;ortholog	CCN FAMILY MEMBER 2 (PTHR11348:SF7)	growth factor(PC00112)	0.04517	1.892568606

Table S2: Differential expressed proteins in sEVs derived from 1% CAO-V-3 cells in compared to exosomes derived from 8% CAO-V-3 cells.

Mapped Ids	Peak Name	Gene Name/ Gene Symbol/ Ortholog	PANTHER Family /Subfamily	Pather Protein Class	p-value	Fold Change
P08697	A2AP_HUMAN	Alpha-2-antiplasmin;SERPINF2;ortholog	ALPHA-2-ANTIPLASMIN (PTHR11461:SF354)	protease inhibitor(PC00191)	0.00083	4.08827906
P01008	ANT3_HUMAN	Antithrombin-III;SERPINC1;ortholog	ANTITHROMBIN-III (PTHR11461:SF53)	protease inhibitor(PC00191)	0.00089	3.72433162
P05141	ADT2_HUMAN	ADP/ATP translocase 2;SLC25A5;ortholog	ADP/ATP TRANSLOCASE 2 (PTHR45635:SF3)	transfer/carrier protein(PC00219)	0.00161	4.82068417
P54920	SNAAP_HUMAN	Alpha-soluble NSF attachment protein;NAPA;ortholog	ALPHA-SOLUBLE NSF ATTACHMENT PROTEIN (PTHR13768:SF23)	membrane traffic protein(PC00150)	0.00253	3.78320567
Q9BWD1	THIC_HUMAN	Protein unc-45 homolog A;UNC45A;ortholog	PROTEIN UNC-45 HOMOLOG A (PTHR45994:SF3)		0.00274	2.74911427
P10909	CLUS_HUMAN	Clusterin;CLU;ortholog	CLUSTERIN (PTHR10970:SF1)		0.0031	3.8284968
P11766	ADHX_HUMAN	Alcohol dehydrogenase class-3;ADH5;ortholog	ALCOHOL DEHYDROGENASE CLASS-3 (PTHR43880:SF4)	dehydrogenase(PC00092)	0.00392	2.17968741
P01130	LDLR_HUMAN	Low-density lipoprotein receptor;LDLR;ortholog	LOW-DENSITY LIPOPROTEIN RECEPTOR (PTHR24270:SF21)	apolipoprotein(PC00052)	0.00401	2.13165456
Q04837	SSBP_HUMAN	Bcl-2-like protein 1;BCL2L1;ortholog	BCL-2-LIKE PROTEIN 1 (PTHR11256:SF12)		0.00478	0.56010098
P08727	K1C19_HUMAN	Keratin, type I cytoskeletal 19;KRT19;ortholog	KERATIN, TYPE I CYTOSKELETAL 19 (PTHR23239:SF14)		0.00514	12.4300286
Q99538	LGMN_HUMAN	Aconitate hydratase, mitochondrial;ACO2;ortholog	ACONITATE HYDRATASE, MITOCHONDRIAL (PTHR43160:SF6)	hydratase(PC00120)	0.00553	6.86414084
P46779	RL28_HUMAN	60S ribosomal protein L28;RPL28;ortholog	60S RIBOSOMAL PROTEIN L28 (PTHR10544:SF12)	ribosomal protein(PC00202)	0.00591	0.20440704
P54819	KAD2_HUMAN	Adenylate kinase 2, mitochondrial;AK2;ortholog	ADENYLATE KINASE 2, MITOCHONDRIAL (PTHR23359:SF227)	nucleotide kinase(PC00172)	0.00616	7.88524548
P23368	MAOM_HUMAN	NAD-dependent malic enzyme, mitochondrial;ME2;ortholog	NAD-DEPENDENT MALIC ENZYME, MITOCHONDRIAL (PTHR23406:SF27)	oxidoreductase(PC00176)	0.0067	2.93587079
P62081	RS7_HUMAN	40S ribosomal protein S7;RPS7;ortholog	40S RIBOSOMAL PROTEIN S7 (PTHR11278:SF5)	ribosomal protein(PC00202)	0.00925	0.13344482
Q15800	MSMO1_HUMAN	26S proteasome non-ATPase regulatory subunit 5;PSMD5;ortholog	26S PROTEASOME NON-ATPASE REGULATORY SUBUNIT 5 (PTHR13554:SF10)	protease(PC00190)	0.00964	3.10769602
P08962	CD63_HUMAN	CD63 antigen;CD63;ortholog	CD63 ANTIGEN (PTHR19282:SF471)		0.01208	2.57763862
P00734	THRB_HUMAN	Prothrombin;F2;ortholog	PROTHROMBIN (PTHR24254:SF10)	serine protease(PC00203)	0.01218	3.75581841
O75822	EIF3J_HUMAN	Eukaryotic translation initiation factor 3 subunit J;EIF3J;ortholog	EUKARYOTIC TRANSLATION INITIATION FACTOR 3 SUBUNIT J (PTHR21681:SF0)	translation initiation factor(PC00224)	0.01281	12.3470777
Q8NG11	TSN14_HUMAN	Programmed cell death 6-interacting protein;PDCD6IP;ortholog	PROGRAMMED CELL DEATH 6-INTERACTING PROTEIN (PTHR23030:SF39)	membrane traffic protein(PC00150)	0.01447	2.69442195
Q8N1G4	LRC47_HUMAN	Tetraspanin-14;TSPAN14;ortholog	TETRASPANIN-14 (PTHR19282:SF261)		0.01484	5.74951622

Q13263	TIF1B_HUMAN	Dynactin subunit 2;DCTN2;ortholog	DYNACTIN SUBUNIT 2 (PTHR15346:SF0)	microtubule binding motor protein(PC00156)	0.0155	17.6460407
Q9UQ80	PA2G4_HUMAN	RuvB-like 1;RUVBL1;ortholog	RUVB-LIKE 1 (PTHR11093:SF6)		0.01561	0.18970385
P11047	LAMC1_HUMAN	Laminin subunit gamma-1;LAMC1;ortholog	LAMININ SUBUNIT GAMMA-1 (PTHR10574:SF270)	extracellular matrix protein(PC00102)	0.01589	2.83518596
Q9UNF1	MAGD2_HUMAN	Proliferation-associated protein 2G4;PA2G4;ortholog	PROLIFERATION-ASSOCIATED PROTEIN 2G4 (PTHR10804:SF130)	protease(PC00190)	0.01767	2.1957425
Q8WUM4	PDC6I_HUMAN	Legumain;LGMN;ortholog	LEGUMAIN (PTHR12000:SF38)	cysteine protease(PC00081)	0.01785	2.43214344
P14209	CD99_HUMAN	CD99 antigen;CD99;ortholog	CD99 ANTIGEN (PTHR15076:SF15)		0.0192	2.75028881
P13995	MTDC_HUMAN	Bifunctional methylenetetrahydrofolate dehydrogenase/cyclohydrolase, mitochondrial;MTHFD2;ortholog	BIFUNCTIONAL METHYLENETETRAHYDROFOLATE DEHYDROGENASE/CYCLOHYDROLASE, MITOCHONDRIAL (PTHR48099:SF15)		0.01934	4.38682582
P43243	MATR3_HUMAN	Matrin-3;MATR3;ortholog	MATRIN-3 (PTHR15592:SF2)		0.02346	2.16067507
O94826	TOM70_HUMAN	Mitochondrial import receptor subunit TOM70;TOMM70;ortholog	MITOCHONDRIAL IMPORT RECEPTOR SUBUNIT TOM70 (PTHR46208:SF1)	primary active transporter(PC00068)	0.02357	0.34372307
Q9H3U1	UN45A_HUMAN	Septin-9;SEPTIN9;ortholog	SEPTIN-9 (PTHR18884:SF47)	cytoskeletal protein(PC00085)	0.02394	3.27024591
Q9UHD8	SEPT9_HUMAN	Multifunctional methyltransferase subunit TRM112-like protein;TRMT112;ortholog	MULTIFUNCTIONAL METHYLTRANSFERASE SUBUNIT TRM112-LIKE PROTEIN (PTHR12773:SF2)		0.02496	1.34614271
O95782	AP2A1_HUMAN	AP-2 complex subunit alpha-1;AP2A1;ortholog	AP-2 COMPLEX SUBUNIT ALPHA-1 (PTHR22780:SF33)	membrane traffic protein(PC00150)	0.02496	2.58909383
Q9BRF8	CPPED_HUMAN	Acetyl-CoA acetyltransferase, cytosolic;ACAT2;ortholog	ACETYL-COA ACETYLTRANSFERASE, CYTOSOLIC (PTHR18919:SF81)	acyltransferase(PC00042)	0.02553	3.55474749
Q9UI30	TR112_HUMAN	Proteasome activator complex subunit 2;PSME2;ortholog	PROTEASOME ACTIVATOR COMPLEX SUBUNIT 2 (PTHR10660:SF6)		0.02636	4.1208149
P01024	CO3_HUMAN	Complement C3;C3;ortholog	COMPLEMENT C3 (PTHR11412:SF81)	protease inhibitor(PC00191)	0.02773	4.41240783
O00232	PSD12_HUMAN	26S proteasome non-ATPase regulatory subunit 12;PSMD12;ortholog	26S PROTEASOME NON-ATPASE REGULATORY SUBUNIT 12 (PTHR10855:SF1)	protease(PC00190)	0.02787	0.19155232
Q9UL46	PSME2_HUMAN	Melanoma-associated antigen D2;MAGED2;ortholog	MELANOMA-ASSOCIATED ANTIGEN D2 (PTHR11736:SF11)	scaffold/adaptor protein(PC00226)	0.02812	3.93921806
P42704	LPPrC_HUMAN	Leucine-rich PPR motif-containing protein, mitochondrial;LRPPRC;ortholog	LEUCINE-RICH PPR MOTIF-CONTAINING PROTEIN, MITOCHONDRIAL (PTHR46669:SF1)		0.02832	2.50153002
Q13561	DCTN2_HUMAN	Nidogen-2;NID2;ortholog	NIDOGEN-2 (PTHR12352:SF3)	calmodulin-related(PC00061)	0.02846	9.68919945
Q14112	NID2_HUMAN	Methylsterol monooxygenase 1;MSMO1;ortholog	METHYLSTEROL MONOOXYGENASE 1 (PTHR11863:SF3)	oxidase(PC00175)	0.02956	2.80446616
Q6WKZ4	RFIP1_HUMAN	Histone H3.2;H3C14;ortholog	HISTONE H3.2 (PTHR11426:SF232)	histone(PC00118)	0.02963	4.20208778
Q13126	MTAP_HUMAN	Transcription intermediary factor 1-beta;TRIM28;ortholog	TRANSCRIPTION INTERMEDIARY FACTOR 1-BETA (PTHR25462:SF274)		0.03141	4.80223729
Q16401	PSMD5_HUMAN	Hexokinase HKDC1;HKDC1;ortholog	HEXOKINASE HKDC1 (PTHR19443:SF28)	kinase(PC00137)	0.03233	3.3350955

Q09666	AHNK_HUMAN	S-methyl-5'-thioadenosine phosphorylase;MTAP;ortholog	S-METHYL-5'-THIOADENOSINE PHOSPHORYLASE (PTHR42679:SF4)	nucleotide kinase(PC00172)	0.03254	3.16204907
Q9Y265	RUVB1_HUMAN	RuvB-like 1, RUVBL1, ortholog	RUVB-LIKE 1 (PTHR11093:SF6)		0.03261	2.38764834
Q07817	B2CL1_HUMAN	Neuroblast differentiation-associated protein AHNAK;AHNAK;ortholog	NEUROBLAST DIFFERENTIATION-ASSOCIATED PROTEIN AHNAK (PTHR23348:SF41)	0.03295	2.46209558	0.39130491
Q2TB90	HKDC1_HUMAN	Rab11 family-interacting protein 1;RAB11FIP1;ortholog	RAB11 FAMILY-INTERACTING PROTEIN 1 (PTHR15746:SF22)		0.03598	3.82367919
O00170	AIP_HUMAN	AH receptor-interacting protein;AIP;ortholog	AH RECEPTOR-INTERACTING PROTEIN (PTHR11242:SF3)	chaperone(PC00072)	0.03726	2.65536185
P19224	UD16_HUMAN	UDP-glucuronosyltransferase 1-6;UGT1A6;ortholog	UDP-GLUCURONOSYLTRANSFERASE 1-6 (PTHR48050:SF7)	glycosyltransferase(PC00111)	0.03841	5.3263806
Q71DI3	H32_HUMAN	Leucine-rich repeat-containing protein 47;LRRC47;ortholog	LEUCINE-RICH REPEAT-CONTAINING PROTEIN 47 (PTHR10947:SF3)	aminoacyl-tRNA synthetase(PC00047)	0.03847	0.07189331
P02749	APOH_HUMAN	Beta-2-glycoprotein 1;APOH;ortholog	BETA-2-GLYCOPROTEIN 1 (PTHR19325:SF549)		0.03894	5.85732831
P19823	ITIH2_HUMAN	Inter-alpha-trypsin inhibitor heavy chain H2;ITIH2;ortholog	INTER-ALPHA-TRYPSIN INHIBITOR HEAVY CHAIN H2 (PTHR10338:SF14)	protease inhibitor(PC00191)	0.03921	4.87285
P34897	GLYM_HUMAN	Serine hydroxymethyltransferase, mitochondrial;SHMT2;ortholog	SERINE HYDROXYMETHYLTRANSFERASE, MITOCHONDRIAL (PTHR11680:SF53)	methyltransferase(PC00155)	0.04049	0.47259358
P43304	GPDM_HUMAN	Glycerol-3-phosphate dehydrogenase, mitochondrial;GPD2;ortholog	GLYCEROL-3-PHOSPHATE DEHYDROGENASE, MITOCHONDRIAL (PTHR11985:SF29)	dehydrogenase(PC00092)	0.04072	5.20909443
Q99798	ACON_HUMAN	Serine/threonine-protein phosphatase CPPED1;CPPED1;ortholog	SERINE/THREONINE-PROTEIN PHOSPHATASE CPPED1 (PTHR43143:SF1)		0.0408	2.64302805
P60842	IF4A1_HUMAN	Eukaryotic initiation factor 4A-I;EIF4A1;ortholog	EUKARYOTIC INITIATION FACTOR 4A-I (PTHR24031:SF221)		0.04115	2.06622701
P51659	DHB4_HUMAN	Peroxisomal multifunctional enzyme type 2;HSD17B4;ortholog	PEROXISOMAL MULTIFUNCTIONAL ENZYME TYPE 2 (PTHR13078:SF56)		0.04359	9.17935303
P41252	SYIC_HUMAN	Isoleucine--tRNA ligase, cytoplasmic;IARS1;ortholog	ISOLEUCINE--TRNA LIGASE, CYTOPLASMIC (PTHR42780:SF1)	aminoacyl-tRNA synthetase(PC00047)	0.04482	2.01765737
O95336	6PGL_HUMAN	6-phosphogluconolactonase;PGLS;ortholog	6-PHOSPHOGLUCONOLACTONASE (PTHR11054:SF0)	hydrolase(PC00121)	0.04518	2.64133289
P17812	PYRG1_HUMAN	CTP synthase 1;CTPS1;ortholog	CTP SYNTHASE 1 (PTHR11550:SF8)	ligase(PC00142)	0.04528	5.42056117
P11908	PRPS2_HUMAN	Ribose-phosphate pyrophosphokinase 2;PRPS2;ortholog	RIBOSE-PHOSPHATE PYROPHOSPHOKINASE 2 (PTHR10210:SF110)	nucleotide kinase(PC00172)	0.04566	3.54000103
P49411	EFTU_HUMAN	Elongation factor Tu, mitochondrial;TUFM;ortholog	ELONGATION FACTOR TU, MITOCHONDRIAL (PTHR43721:SF22)	translation elongation factor(PC00222)	0.04845	4.28367016
Q00325-2	MPCP_HUMAN	Single-stranded DNA-binding protein, mitochondrial;SSBP1;ortholog	SINGLE-STRANDED DNA-BINDING PROTEIN, MITOCHONDRIAL (PTHR10302:SF0)	DNA metabolism protein(PC00009)	0.04862	4.70816339
O15355	PPM1G_HUMAN	Protein phosphatase 1G;PPM1G;ortholog	PROTEIN PHOSPHATASE 1G (PTHR13832:SF805)	protein phosphatase(PC00195)	0.04977	1.96627827

Table S3. A comparison of proteins differentially expressed in 1% O₂ sEVs and 8% O₂ sEVs.

Protein	p-value	Fold change
Glycolysis related proteins		
Hexokinase (HK)	0.036	3.82
UDP-glucuronosyltransferase 1-6 (UD16)	0.038	5.33
6-phosphogluconolactonase (6PGL)	0.045	2.64
CTP synthase 1 (PYRG1)	0.045	5.42
Detoxification associated proteins		
Alcohol dehydrogenase class-3 (ADH5)	0.004	2.18
NAD-dependent malic enzyme (MAMO)	0.007	2.93
Bifunctional methylenetetrahydrofolate dehydrogenase/cyclohydrolase (MTDC)	0.019	4.39
Peroxisomal multifunctional enzyme type 2 (DHB4)	0.044	9.18

Table S4. Target Set of Metabolic and Reference Proteins.

Pathways	Peptides	Protein code
Main glycolysis pathway	NLVTEDVMR	GPI
	SNTPILVDGK	GPI
	TFTTQETITNAETAK	GPI
	GQLESIVENIR	PFKL
	EWSGLLEELAR	PFKP
	TFVLEVMMGR	PFKP
	YLEEIATQMR	PFKP
	ALANSLACQ GK	ALDO
	QLLLTADDR	ALDO
	ELSDIAHR	ALDOA
	GILAADESTGSIK	ALDOA
	LQSIGTENTEENR	ALDOA
	HVFGESDELIGQK	TP1
	IYGGSVTGATCK	TP1
	VVLAYEPVWAIGTGK	TP1
	FFVGGNWK	TPI
	QSLGELIGTLNAK	TPI
	TATPQQAQEVHEK	TPI
	VVFEQTK	TPI
	IISNASCTTNCLAPLAK	GAPDH
	VPTANVSVDLTCR	GAPDH
	ALMDEVVK	PGK1
	ELNYFAK	PGK1

	LGDVYVNDAFGTAHR	PGK1
	VDFNVPMK	PGK1
	VSHVSTGGGASLELEGK	PGK1
	AHSSMVGVNLPQK	PGK1
	ALPFWNEEIVPQIK	PGAM
	YADLTEDQLPSCESLK	PGAM1
	TIAPALVSK	ENO
	VVIGMDVAASEFFR	ENO
	AAVPSGASTGIYEALER	ENO1
	LMIEMDG TENK	ENO1
	VNQIGSVTESLQACK	ENO1
	YISPDQLADLYK	ENO1
	CCSGAIIVLTK	PKM2
	GDLGIEIPA EK	PKM2
	GDYPLEAVR	PKM2
	GIFPVLCK	PKM2
	GSGTAEVELK	PKM2
	ITLDNAYMEK	PKM2
	IYVDDGLISLQVK	PKM2
	LDIDSPPI TAR	PKM2
	NTGI ICTIGPASR	PKM2
Glycolysis branching pathways	FIIPNVVK	LDHA
	LVIITAGAR	LDHA
	QVVESAYEVIK	LDHA
	SLADELALVDVLEDK	LDHA
	VIGSGCNLDSAR	LDHA

	GGYFDEFGIIR	G6PD
	GPTEADELMK	G6PD
	GYLDDPTVPR	G6PD
	HQPTAIIAK	TKT
	NSTFSEIFK	TKT
Other metabolic proteins	AALQEELQLCK	FASN
	ACLDTAVENMPSLK	FASN
	AQVADVVSRR	FASN
	SLLVNPEGPTLMR	FASN
	VLEALLPLK	FASN
	FVEGLPINDFSR	MDH1
	GEFVTTVQQR	MDH1
Reference proteins	GYSFTTTAER	ACTAB
	HQGVMMVGMGQK	ACTAB
	QEYDESGPSIVHR	ACTAB
	AGFAGDDAPR	ACTAB
	EITALAPSTMK	ACTAB
	IIQLDDYPK	RLPL0
	EGMNIVEAMER	PPIA
	FEDENFILK	PPIA
	IIPGFMCQGGDFTR	PPIA
	FLIPNASQAESK	YWHAZ

Table S5. Differentially expressed proteins in cells incubated with hypoxic exosomes compared to cells incubated with normoxic sEVs

Mapped Ids	Peak Name	Gene Name/ Gene Symbol/ Ortholog	PANTHER Family /Subfamily	Pather Protein Class	p-value	Fold Change
O43242	RS14_HUMAN	40S ribosomal protein S14;RPS14;ortholog	40S RIBOSOMAL PROTEIN S14 (PTHR11759:SF58)	ribosomal protein(PC00202)	0.00000227	0.267584
P08670	COMP_HUMAN	Cartilage oligomeric matrix protein;COMP;ortholog	CARTILAGE OLIGOMERIC MATRIX PROTEIN (PTHR10199:SF88)	NA	0.00024	0.765258
P55036	HSPB1_HUMAN	Heat shock protein beta-1;HSPB1;ortholog	HEAT SHOCK PROTEIN BETA-1 (PTHR45640:SF7)	NA	0.00041	1.131776
P45880	ECI1_HUMAN	Enoyl-CoA delta isomerase 1, mitochondrial;ECI1;ortholog	ENOYL-COA DELTA ISOMERASE 1, MITOCHONDRIAL (PTHR11941:SF45)	hydratase(PC00120)	0.00055	0.879293
P40429	RL5_HUMAN	60S ribosomal protein L5;RPL5;ortholog	60S RIBOSOMAL PROTEIN L5 (PTHR23410:SF24)	ribosomal protein(PC00202)	0.0006	1.231754
Q86VP6	EPCR_HUMAN	Endothelial protein C receptor;PROCR;ortholog	ENDOTHELIAL PROTEIN C RECEPTOR (PTHR15349:SF0)	protein-binding activity modulator(PC00095)	0.00066	0.695279
Q06481	ALDOC_HUMAN	Fructose-bisphosphate aldolase C;ALDOC;ortholog	FRUCTOSE-BISPHOSPHATE ALDOLASE C (PTHR11627:SF3)	aldolase(PC00044)	0.00067	1.664374
P49588	VDAC2_HUMAN	Voltage-dependent anion-selective channel protein 2;VDAC2;ortholog	VOLTAGE-DEPENDENT ANION-SELECTIVE CHANNEL PROTEIN 2 (PTHR11743:SF12)	voltage-gated ion channel(PC00241)	0.00077	1.15718
P78347	COPB_HUMAN	Coatomer subunit beta;COPB1;ortholog	COATOMER SUBUNIT BETA (PTHR10635:SF0)	vesicle coat protein(PC00235)	0.00081	0.796536
Q9UJS0	NPM_HUMAN	Nucleophosmin;NPM1;ortholog	NUCLEOPHOSMIN (PTHR22747:SF28)	chaperone(PC00072)	0.00091	0.857056
Q9NR96	RS8_HUMAN	40S ribosomal protein S8;RPS8;ortholog	40S RIBOSOMAL PROTEIN S8 (PTHR10394:SF12)	ribosomal protein(PC00202)	0.00112	1.139647
Q6X4U4	RL28_HUMAN	60S ribosomal protein L28;RPL28;ortholog	60S RIBOSOMAL PROTEIN L28 (PTHR10544:SF12)	ribosomal protein(PC00202)	0.00117	1.247209
P11279	RAB32_HUMAN	Ras-related protein Rab-32;RAB32;ortholog	RAS-RELATED PROTEIN RAB-32 (PTHR24073:SF1176)	NA	0.00125	1.258191
P09496	PARP1_HUMAN	Poly [ADP-ribose] polymerase 1;PARP1;ortholog	POLY [ADP-RIBOSE] POLYMERASE 1 (PTHR10459:SF112)	DNA metabolism protein(PC00009)	0.00126	0.870104
P53602	KCC2D_HUMAN	Calcium/calmodulin-dependent protein kinase type II subunit delta;CAMK2D;ortholog	CALCIUM/CALMODULIN-DEPENDENT PROTEIN KINASE TYPE II SUBUNIT DELTA (PTHR24347:SF365)	non-receptor serine/threonine protein kinase(PC00167)	0.00183	1.23107
Q8N163	PUR6_HUMAN	Multifunctional protein ADE2;PAICS;ortholog	MULTIFUNCTIONAL PROTEIN ADE2 (PTHR43599:SF3)	NA	0.00253	1.129759

Q13620	COPD_HUMAN	Coatomer subunit delta;ARC1;ortholog	COATOMER SUBUNIT DELTA (PTHR10121:SF0)	vesicle coat protein(PC00235)	0.00287	0.723674
P19105	CMC2_HUMAN	Calcium-binding mitochondrial carrier protein Aralar2;SLC25A13;ortholog	CALCIUM-BINDING MITOCHONDRIAL CARRIER PROTEIN ARALAR2 (PTHR45678:SF12)	secondary carrier transporter(PC00258)	0.00288	1.27725
P11169	HMCS1_HUMAN	Hydroxymethylglutaryl-CoA synthase, cytoplasmic;HMGCS1;ortholog	HYDROXYMETHYLGLUTARYL-COA SYNTHASE, CYTOPLASMIC (PTHR43323:SF4)	NA	0.00341	0.76832
P51858	IMA3_HUMAN	Importin subunit alpha-3;KPNA4;ortholog	IMPORTIN SUBUNIT ALPHA-3 (PTHR23316:SF7)	transporter(PC00227)	0.00372	3.844421
O00767	1433B_HUMAN	14-3-3 protein beta/alpha;YWHAB;ortholog	14-3-3 PROTEIN BETA/ALPHA (PTHR18860:SF28)	scaffold/adaptor protein(PC00226)	0.00383	0.857004
P09874	RU2A_HUMAN	U2 small nuclear ribonucleoprotein A';SNRPA1;ortholog	U2 SMALL NUCLEAR RIBONUCLEOPROTEIN A' (PTHR10552:SF6)	RNA splicing factor(PC00148)	0.00418	0.895571
P42126	RB11B_HUMAN	Ras-related protein Rab-11B;RAB11B;ortholog	RAS-RELATED PROTEIN RAB-11B (PTHR47979:SF41)	NA	0.00429	0.910052
P53999	TRA2B_HUMAN	Transformer-2 protein homolog beta;TRA2B;ortholog	TRANSFORMER-2 PROTEIN HOMOLOG BETA (PTHR48034:SF1)	NA	0.00435	0.350914
P04181	SYRC_HUMAN	Arginine--tRNA ligase, cytoplasmic;RARS1;ortholog	ARGININE--TRNA LIGASE, CYTOPLASMIC (PTHR11956:SF5)	aminoacyl-tRNA synthetase(PC00047)	0.00453	0.773548
P22234	CH60_HUMAN	60 kDa heat shock protein, mitochondrial;HSPD1;ortholog	60 KDA HEAT SHOCK PROTEIN, MITOCHONDRIAL (PTHR45633:SF17)	NA	0.00479	0.779151
P62263	ROA2_HUMAN	Heterogeneous nuclear ribonucleoproteins A2/B1;HNRNPA2B1;ortholog	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEINS A2/B1 (PTHR48026:SF13)	NA	0.00547	0.902825
Q13200	GCP2_HUMAN	Gamma-tubulin complex component 2;TUBGCP2;ortholog	GAMMA-TUBULIN COMPLEX COMPONENT 2 (PTHR19302:SF13)	non-motor microtubule binding protein(PC00166)	0.00547	0.779102
Q01581	CAND1_HUMAN	Cullin-associated NEDD8-dissociated protein 1;CAND1;ortholog	CULLIN-ASSOCIATED NEDD8-DISSOCIATED PROTEIN 1 (PTHR12696:SF1)	ubiquitin-protein ligase(PC00234)	0.0055	0.918307
O15269	TALDO_HUMAN	Transaldolase;TALDO1;ortholog	TRANSALDOLASE (PTHR10683:SF18)	aldolase(PC00044)	0.00629	1.211286
Q92598	COX2_HUMAN	Cytochrome c oxidase subunit 2;MT-CO2;ortholog	CYTOCHROME C OXIDASE SUBUNIT 2 (PTHR22888:SF9)	oxidoreductase(PC00176)	0.00652	0.791912
P11142	OAT_HUMAN	Ornithine aminotransferase, mitochondrial;OAT;ortholog	ORNITHINE AMINOTRANSFERASE, MITOCHONDRIAL (PTHR11986:SF118)	transaminase(PC00216)	0.00733	1.162815
Q96M27	RS6_HUMAN	40S ribosomal protein S6;RPS6;ortholog	40S RIBOSOMAL PROTEIN S6 (PTHR11502:SF33)	ribosomal protein(PC00202)	0.00788	1.301697
Q9NR30	GCSH_HUMAN	Glycine cleavage system H protein, mitochondrial;GCSH;ortholog	GLYCINE CLEAVAGE SYSTEM H PROTEIN, MITOCHONDRIAL (PTHR11715:SF28)	NA	0.00829	1.441947
P53618	CAH2_HUMAN	Carbonic anhydrase 2;CA2;ortholog	CARBONIC ANHYDRASE 2 (PTHR18952:SF120)	NA	0.0084	1.224134
O60762	MVD1_HUMAN	Diphosphomevalonate decarboxylase;MVD;ortholog	DIPHOSPHOMEVALONATE DECARBOXYLASE (PTHR10977:SF3)	decarboxylase(PC00089)	0.00865	0.730017

O75533	RL23_HUMAN	60S ribosomal protein L23;RPL23;ortholog	60S RIBOSOMAL PROTEIN L23 (PTHR11761:SF22)	ribosomal protein(PC00202)	0.00905	0.90547
P26373	PFKAL_HUMAN	ATP-dependent 6-phosphofructokinase, liver type;PFKL;ortholog	ATP-DEPENDENT 6-PHOSPHOFRUCTOKINASE, LIVER TYPE (PTHR13697:SF14)	carbohydrate kinase(PC00065)	0.00906	0.669557
Q16186	SPTC1_HUMAN	Serine palmitoyltransferase 1;SPTLC1;ortholog	SERINE PALMITOYLTRANSFERASE 1 (PTHR13693:SF2)	transaminase(PC00216)	0.00911	1.085099
Q9NSD9	CLCA_HUMAN	Clathrin light chain A;CLTA;ortholog	CLATHRIN LIGHT CHAIN A (PTHR10639:SF1)	vesicle coat protein(PC00235)	0.00927	0.815368
P49327	HM13_HUMAN	Minor histocompatibility antigen H13;HM13;ortholog	MINOR HISTOCOMPATIBILITY ANTIGEN H13 (PTHR12174:SF23)	aspartic protease(PC00053)	0.01001	1.18603
Q12874	PGBM_HUMAN	Basement membrane-specific heparan sulfate proteoglycan core protein;HSPG2;ortholog	BASEMENT MEMBRANE-SPECIFIC HEPARAN SULFATE PROTEOGLYCAN CORE PROTEIN (PTHR10574:SF273)	extracellular matrix protein(PC00102)	0.01079	1.14086
P62753	GTR3_HUMAN	Solute carrier family 2, facilitated glucose transporter member 3;SLC2A3;ortholog	SOLUTE CARRIER FAMILY 2, FACILITATED GLUCOSE TRANSPORTER MEMBER 3 (PTHR23503:SF99)	NA	0.01171	0.886411
P09661	NDRG1_HUMAN	Protein NDRG1;NDRG1;ortholog	PROTEIN NDRG1 (PTHR11034:SF18)	serine protease(PC00203)	0.01195	0.811879
P83731	SYSC_HUMAN	Serine--tRNA ligase, cytoplasmic;SARS1;ortholog	SERINE--TRNA LIGASE, CYTOPLASMIC-RELATED (PTHR11778:SF7)	aminoacyl-tRNA synthetase(PC00047)	0.01277	0.682187
Q9NS69	VIME_HUMAN	Vimentin;VIM;ortholog	VIMENTIN (PTHR45652:SF5)	NA	0.01328	0.684403
P22626	1433G_HUMAN	14-3-3 protein gamma;YWHAG;ortholog	14-3-3 PROTEIN GAMMA (PTHR18860:SF22)	scaffold/adaptor protein(PC00226)	0.01357	1.061605
Q9UBM7	DHB12_HUMAN	Very-long-chain 3-oxoacyl-CoA reductase;HSD17B12;ortholog	VERY-LONG-CHAIN 3-OXOACYL-COA REDUCTASE (PTHR43899:SF14)	NA	0.01437	0.337966
P31946	PRS6A_HUMAN	26S proteasome regulatory subunit 6A;PSMC3;ortholog	26S PROTEASOME REGULATORY SUBUNIT 6A (PTHR23073:SF90)	protease(PC00190)	0.01479	0.911007
P53801	PLEC_HUMAN	Plectin;PLEC;ortholog	PLECTIN (PTHR23169:SF20)	intermediate filament binding protein(PC00130)	0.01513	1.214068
P61221	UGPA_HUMAN	UTP--glucose-1-phosphate uridylyltransferase;UGP2;ortholog	UTP--GLUCOSE-1-PHOSPHATE URIDYLYLTRANSFERASE (PTHR43511:SF4)	NA	0.01515	1.244052
P49736	SF3B1_HUMAN	Splicing factor 3B subunit 1;SF3B1;ortholog	SPLICING FACTOR 3B SUBUNIT 1 (PTHR12097:SF0)	RNA splicing factor(PC00148)	0.01517	1.095972
Q15149	SOSD1_HUMAN	Sclerostin domain-containing protein 1;SOSTDC1;ortholog	SCLEROSTIN DOMAIN-CONTAINING PROTEIN 1 (PTHR14903:SF5)	intercellular signal molecule(PC00207)	0.0162	0.848756
P46779	ABCE1_HUMAN	ATP-binding cassette sub-family E member 1;ABCE1;ortholog	ATP-BINDING CASSETTE SUB-FAMILY E MEMBER 1 (PTHR19248:SF16)	NA	0.01628	0.867793
Q9UBI6	CUL4B_HUMAN	Cullin-4B;CUL4B;ortholog	CULLIN-4B (PTHR11932:SF66)	ubiquitin-protein ligase(PC00234)	0.01713	1.156406
P00403	COPZ1_HUMAN	Coatomer subunit zeta-1;COPZ1;ortholog	COATOMER SUBUNIT ZETA-1 (PTHR11043:SF2)	vesicle coat protein(PC00235)	0.01721	0.888619
P13726	RL35A_HUMAN	60S ribosomal protein L35a;RPL35A;ortholog	60S RIBOSOMAL PROTEIN L35A (PTHR10902:SF30)	ribosomal protein(PC00202)	0.01739	0.688932

P16949	EIF3H_HUMAN	Eukaryotic translation initiation factor 3 subunit H;EIF3H;ortholog	EUKARYOTIC TRANSLATION INITIATION FACTOR 3 SUBUNIT H (PTHR10410:SF3)	translation initiation factor(PC00224)	0.01757	1.165479
O15372	UBP5_HUMAN	Ubiquitin carboxyl-terminal hydrolase 5;USP5;ortholog	UBIQUITIN CARBOXYL-TERMINAL HYDROLASE 5 (PTHR24006:SF655)	cysteine protease(PC00081)	0.01776	1.109794
Q9NQ88	LAMP1_HUMAN	Lysosome-associated membrane glycoprotein 1;LAMP1;ortholog	LYSOSOME-ASSOCIATED MEMBRANE GLYCOPROTEIN 1 (PTHR11506:SF27)	membrane trafficking regulatory protein(PC00151)	0.01795	1.120998
Q04446	MCM2_HUMAN	DNA replication licensing factor MCM2;MCM2;ortholog	DNA REPLICATION LICENSING FACTOR MCM2 (PTHR11630:SF44)	DNA metabolism protein(PC00009)	0.01818	0.932507
P08134	TIM44_HUMAN	Mitochondrial import inner membrane translocase subunit TIM44;TIMM44;ortholog	MITOCHONDRIAL IMPORT INNER MEMBRANE TRANSLOCASE SUBUNIT TIM44 (PTHR10721:SF1)	transporter(PC00227)	0.01894	0.811457
P17980	ROAA_HUMAN	Heterogeneous nuclear ribonucleoprotein A/B;HNRNPAB;ortholog	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A/B (PTHR48033:SF1)	NA	0.01914	0.230408
P49721	CDC42_HUMAN	Cell division control protein 42 homolog;CDC42;ortholog	CELL DIVISION CONTROL PROTEIN 42 HOMOLOG (PTHR24072:SF136)	small GTPase(PC00208)	0.01927	1.062811
Q9Y3A5	DPM1_HUMAN	Dolichol-phosphate mannosyltransferase subunit 1;DPM1;ortholog	DOLICHOL-PHOSPHATE MANNOSYLTRANSFERASE SUBUNIT 1 (PTHR43398:SF1)	glycosyltransferase(PC00111)	0.0194	0.666285
Q8TC12	RL18A_HUMAN	60S ribosomal protein L18a;RPL18A;ortholog	60S RIBOSOMAL PROTEIN L18A (PTHR10052:SF50)	ribosomal protein(PC00202)	0.01969	0.682036
P25205	HEX1_HUMAN	Protein HEXIM1;HEXIM1;ortholog	PROTEIN HEXIM1 (PTHR13469:SF7)	NA	0.02003	0.698776
Q9HB07	ACLY_HUMAN	ATP-citrate synthase;ACLY;ortholog	ATP-CITRATE SYNTHASE (PTHR23118:SF0)	transferase(PC00220)	0.02008	0.319368
P17858	TLR9_HUMAN	Toll-like receptor 9;TLR9;ortholog	TOLL-LIKE RECEPTOR 9 (PTHR47410:SF3)	transmembrane signal receptor(PC00197)	0.02017	0.391474
P61923	ACOD_HUMAN	Acyl-CoA desaturase;SCD;ortholog	ACYL-COA DESATURASE (PTHR11351:SF73)	NA	0.02051	0.749126
Q9BXW7	CGL_HUMAN	Cystathionine gamma-lyase;CTH;ortholog	CYSTATHIONINE GAMMA-LYASE (PTHR11808:SF15)	lyase(PC00144)	0.0213	0.22855
P04792	RRP1_HUMAN	Ribosomal RNA processing protein 1 homolog A;RRP1;ortholog	RIBOSOMAL RNA PROCESSING PROTEIN 1 HOMOLOG A (PTHR13026:SF1)	NA	0.02226	0.791443
P49747	SBDS_HUMAN	Ribosome maturation protein SBDS;SBDS;ortholog	RIBOSOME MATURATION PROTEIN SBDS (PTHR10927:SF1)	RNA metabolism protein(PC00031)	0.02296	0.659036
Q99729	SYFB_HUMAN	Phenylalanine--tRNA ligase beta subunit;FARSB;ortholog	PHENYLALANINE--TRNA LIGASE BETA SUBUNIT (PTHR10947:SF0)	aminoacyl-tRNA synthetase(PC00047)	0.02334	0.214782
P62995	PRRC1_HUMAN	Protein PRRC1;PRRC1;ortholog	PROTEIN PRRC1 (PTHR23276:SF2)	NA	0.0237	0.821451
Q16851	HS105_HUMAN	Heat shock protein 105 kDa;HSPH1;ortholog	HEAT SHOCK PROTEIN 105 KDA (PTHR45639:SF2)	NA	0.02479	1.133302
Q07954	SEP11_HUMAN	Septin-11;SEPTIN11;ortholog	SEPTIN-11 (PTHR18884:SF48)	cytoskeletal protein(PC00085)	0.02572	0.325575
Q13557	ARF4_HUMAN	ADP-ribosylation factor 4;ARF4;ortholog	ADP-RIBOSYLATION FACTOR 4 (PTHR11711:SF110)	G-protein(PC00020)	0.02602	1.166569

P52789	HDHD5_HUMAN	Haloacid dehalogenase-like hydrolase domain-containing 5;HDHD5;ortholog	HALOACID DEHALOGENASE-LIKE HYDROLASE DOMAIN-CONTAINING 5 (PTHR14269:SF17)	transferase(PC00220)	0.02732	0.896284
Q9BSJ2	DSG1_HUMAN	Desmoglein-1;DSG1;ortholog	DESMOGLEIN-1 (PTHR24025:SF9)	cadherin(PC00057)	0.02746	0.887029
P18077	MARE1_HUMAN	Microtubule-associated protein RP/EB family member 1;MAPRE1;ortholog	MICROTUBULE-ASSOCIATED PROTEIN RP/EB FAMILY MEMBER 1 (PTHR10623:SF20)	non-motor microtubule binding protein(PC00166)	0.02755	0.791303
P56182	UGDH_HUMAN	UDP-glucose 6-dehydrogenase;UGDH;ortholog	UDP-GLUCOSE 6-DEHYDROGENASE (PTHR11374:SF3)	dehydrogenase(PC00092)	0.02804	1.086134
Q15907	STMN1_HUMAN	Stathmin;STMN1;ortholog	STATHMIN (PTHR10104:SF5)	NA	0.02811	1.256738
Q9UBN6	LRP1_HUMAN	Prolow-density lipoprotein receptor-related protein 1;LRP1;ortholog	PROLOW-DENSITY LIPOPROTEIN RECEPTOR-RELATED PROTEIN 1 (PTHR24270:SF23)	apolipoprotein(PC00052)	0.02814	1.123403
P10809	HSP7C_HUMAN	Heat shock cognate 71 kDa protein;HSPA8;ortholog	HEAT SHOCK COGNATE 71 KDA PROTEIN (PTHR19375:SF379)	NA	0.02828	0.915755
P62829	PSB2_HUMAN	Proteasome subunit beta type-2;PSMB2;ortholog	PROTEASOME SUBUNIT BETA TYPE-2 (PTHR11599:SF6)	protease(PC00190)	0.02885	0.913065
Q8TCT9	G3BP1_HUMAN	Ras GTPase-activating protein-binding protein 1;G3BP1;ortholog	RAS GTPASE-ACTIVATING PROTEIN-BINDING PROTEIN 1 (PTHR10693:SF21)	RNA metabolism protein(PC00031)	0.02908	0.689067
Q13283	MYG1_HUMAN	MYG1 exonuclease;MYG1;ortholog	MYG1 EXONUCLEASE (PTHR11215:SF1)	hydrolase(PC00121)	0.02976	1.105623
Q01082	ML12A_HUMAN	Myosin regulatory light chain 12A;MYL12A;ortholog	MYOSIN REGULATORY LIGHT CHAIN 12A (PTHR23049:SF57)	actin or actin-binding cytoskeletal protein(PC00041)	0.03133	0.768661
Q9UGI8	APLP2_HUMAN	Amyloid-like protein 2;APLP2;ortholog	AMYLOID-LIKE PROTEIN 2 (PTHR23103:SF14)	protease inhibitor(PC00191)	0.03172	2.592006
P53396	ADRM1_HUMAN	Proteasomal ubiquitin receptor ADRM1;ADRM1;ortholog	PROTEASOMAL UBIQUITIN RECEPTOR ADRM1 (PTHR12225:SF0)	NA	0.03229	0.872436
P06748	ECH1_HUMAN	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial;ECH1;ortholog	DELTA(3,5)-DELTA(2,4)-DIENOYL-COA ISOMERASE, MITOCHONDRIAL (PTHR43149:SF1)	hydratase(PC00120)	0.03299	0.847672
Q92575	RDH11_HUMAN	Retinol dehydrogenase 11;RDH11;ortholog	RETINOL DEHYDROGENASE 11 (PTHR24320:SF108)	dehydrogenase(PC00092)	0.03303	1.186658
O00629	TIGAR_HUMAN	Fructose-2,6-bisphosphatase TIGAR;TIGAR;ortholog	FRUCTOSE-2,6-BISPHOSPHATASE TIGAR (PTHR46517:SF1)	phosphatase(PC00181)	0.03319	1.388604
Q02543	RL13A_HUMAN	60S ribosomal protein L13a;RPL13A;ortholog	60S RIBOSOMAL PROTEIN L13A (PTHR11545:SF30)	ribosomal protein(PC00202)	0.03326	0.594694
P09972	RL13_HUMAN	60S ribosomal protein L13;RPL13;ortholog	60S RIBOSOMAL PROTEIN L13 (PTHR11722:SF4)	ribosomal protein(PC00202)	0.03334	0.884622
O94992	GTF2I_HUMAN	General transcription factor II-I;GTF2I;ortholog	GENERAL TRANSCRIPTION FACTOR II-I (PTHR46304:SF2)	general transcription factor(PC00259)	0.03337	1.185212
P98160				NA	0.03486	0.761527

Q92504	PSMD4_HUMAN	26S proteasome non-ATPase regulatory subunit 4;PSMD4;ortholog	26S PROTEASOME NON-ATPASE REGULATORY SUBUNIT 4 (PTHR10223:SF7)	protease(PC00190)	0.03504	1.591623
Q02413	PTTG_HUMAN	Pituitary tumor-transforming gene 1 protein-interacting protein;PTTG1IP;ortholog	PITUITARY TUMOR-TRANSFORMING GENE 1 PROTEIN-INTERACTING PROTEIN (PTHR15191:SF2)	NA	0.03604	0.529322
Q13637	HNRPK_HUMAN	Heterogeneous nuclear ribonucleoprotein K;HNRNPK;ortholog	HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN K (PTHR10288:SF307)	RNA metabolism protein(PC00031)	0.03713	0.472748
Q13011	PSMD3_HUMAN	26S proteasome non-ATPase regulatory subunit 3;PSMD3;ortholog	26S PROTEASOME NON-ATPASE REGULATORY SUBUNIT 3 (PTHR10758:SF2)	protease(PC00190)	0.03726	0.917002
Q9UNN8	CCAR2_HUMAN	Cell cycle and apoptosis regulator protein 2;CCAR2;ortholog	CELL CYCLE AND APOPTOSIS REGULATOR PROTEIN 2 (PTHR14304:SF12)	chromatin/chromatin-binding, or -regulatory protein(PC00077)	0.03743	2.514653
O60701	FAS_HUMAN	Fatty acid synthase;FASN;ortholog	FATTY ACID SYNTHASE (PTHR43775:SF7)	NA	0.03763	1.12561
P61978	TES_HUMAN	Testin;TES;ortholog	TESTIN (PTHR24211:SF1)	scaffold/adaptor protein(PC00226)	0.03775	1.164893
O94826	TCP4_HUMAN	Activated RNA polymerase II transcriptional coactivator p15;SUB1;ortholog	ACTIVATED RNA POLYMERASE II TRANSCRIPTIONAL COACTIVATOR P15 (PTHR13215:SF0)	general transcription factor(PC00259)	0.03811	0.621374
P49591	DHCR7_HUMAN	7-dehydrocholesterol reductase;DHCR7;ortholog	7-DEHYDROCHOLESTEROL REDUCTASE (PTHR21257:SF38)	reductase(PC00198)	0.03902	0.921808
Q12797	GBG12_HUMAN	Guanine nucleotide-binding protein G(I)/G(S)/G(O) subunit gamma-12;GNG12;ortholog	GUANINE NUCLEOTIDE-BINDING PROTEIN G(I)/G(S)/G(O) SUBUNIT GAMMA-12 (PTHR13809:SF9)	heterotrimeric G-protein(PC00117)	0.03937	5.053687
P62241	DDX21_HUMAN	Nucleolar RNA helicase 2;DDX21;ortholog	NUCLEOLAR RNA HELICASE 2 (PTHR47958:SF109)	NA	0.03971	1.251012
P00918	RL24_HUMAN	60S ribosomal protein L24;RPL24;ortholog	60S RIBOSOMAL PROTEIN L24 (PTHR10792:SF44)	ribosomal protein(PC00202)	0.03983	1.16354
P60953	MCM3_HUMAN	DNA replication licensing factor MCM3;MCM3;ortholog	DNA REPLICATION LICENSING FACTOR MCM3 (PTHR11630:SF46)	DNA metabolism protein(PC00009)	0.04021	1.238328
P23434	VAPB_HUMAN	Vesicle-associated membrane protein-associated protein B/C;VAPB;ortholog	VESICLE-ASSOCIATED MEMBRANE PROTEIN-ASSOCIATED PROTEIN B/C (PTHR10809:SF12)	membrane trafficking regulatory protein(PC00151)	0.04089	0.699019
P48444	HXK2_HUMAN	Hexokinase-2;HK2;ortholog	HEXOKINASE-2 (PTHR19443:SF4)	kinase(PC00137)	0.04144	0.875105
O95292	PSMD2_HUMAN	26S proteasome non-ATPase regulatory subunit 2;PSMD2;ortholog	26S PROTEASOME NON-ATPASE REGULATORY SUBUNIT 2 (PTHR10943:SF11)	protease(PC00190)	0.04195	2.668984
Q9NVA2	SYAC_HUMAN	Alanine--tRNA ligase, cytoplasmic;AARS1;ortholog	ALANINE--TRNA LIGASE, CYTOPLASMIC (PTHR11777:SF36)	aminoacyl-tRNA synthetase(PC00047)	0.04205	0.917524
Q53GQ0	TOM70_HUMAN	Mitochondrial import receptor subunit TOM70;TOMM70;ortholog	MITOCHONDRIAL IMPORT RECEPTOR SUBUNIT TOM70 (PTHR46208:SF1)	primary active transporter(PC00068)	0.04411	1.122194
P45974	TF_HUMAN	Tissue factor;F3;ortholog	TISSUE FACTOR (PTHR20859:SF22)	transmembrane signal receptor(PC00197)	0.04428	0.756568

P54136	SF3A3_HUMAN	Splicing factor 3A subunit 3;SF3A3;ortholog	SPLICING FACTOR 3A SUBUNIT 3 (PTHR12786:SF3)	RNA splicing factor(PC00148)	0.04483	3.710812
P37837	PYR1_HUMAN	CAD protein;CAD;ortholog	CAD PROTEIN (PTHR11405:SF5)	ligase(PC00142)	0.04487	1.234783
P32929	TR10D_HUMAN	Tumor necrosis factor receptor superfamily member 10D;TNFRSF10D;ortholog	TUMOR NECROSIS FACTOR RECEPTOR SUPERFAMILY MEMBER 10D (PTHR46330:SF10)	transmembrane signal receptor(PC00197)	0.04537	1.101144
Q15691	HDGF_HUMAN	Hepatoma-derived growth factor;HDGF;ortholog	HEPATOMA-DERIVED GROWTH FACTOR (PTHR12550:SF41)	transcription cofactor(PC00217)	0.04544	0.953502
O43615	S39A7_HUMAN	Zinc transporter SLC39A7;SLC39A7;ortholog	ZINC TRANSPORTER SLC39A7 (PTHR16950:SF25)	primary active transporter(PC00068)	0.04568	0.882531
P21741	TOM22_HUMAN	Mitochondrial import receptor subunit TOM22 homolog;TOMM22;ortholog	MITOCHONDRIAL IMPORT RECEPTOR SUBUNIT TOM22 HOMOLOG (PTHR12504:SF3)	primary active transporter(PC00068)	0.04581	0.895941
P61981	RHOC_HUMAN	Rho-related GTP-binding protein RhoC;RHOC;ortholog	RHO-RELATED GTP-BINDING PROTEIN RHOC (PTHR24072:SF100)	small GTPase(PC00208)	0.04582	0.870883
P27708	UBXN4_HUMAN	UBX domain-containing protein 4;UBXN4;ortholog	UBX DOMAIN-CONTAINING PROTEIN 4 (PTHR46424:SF1)	NA	0.04618	0.959065
P18085	SPTB2_HUMAN	Spectrin beta chain, non-erythrocytic 1;SPTBN1;ortholog	SPECTRIN BETA CHAIN, NON-ERYTHROCYTIC 1 (PTHR11915:SF226)	NA	0.0466	0.773288
Q92597	MK_HUMAN	Midkine;MDK;ortholog	MIDKINE (PTHR13850:SF2)	growth factor(PC00112)	0.04843	1.167836
P46777	GLGB_HUMAN	1,4-alpha-glucan-branching enzyme;GBE1;ortholog	1,4-ALPHA-GLUCAN-BRANCHING ENZYME (PTHR43651:SF3)	amylase(PC00048)	0.04917	1.101776

Table S6. Clinical characteristics of the patients involved in this study.

Variables	Controls (n=22)	Cancer recurrence (n=9)	ANOVA
Age, years, Mean (SD)	n=22 61.09 (13.15)	n=9 57.89 (21.46)	p= 0.9405
Pre-Op CA-125, U/mL, Mean (SD)	n=14 423.60 (460.20)	n=9 645.60 (869.50)	p= 0.5571
Post-Op CA-125, U/mL, Mean (SD)	n=13 39.54 (33.01)	n=3 211.70 (197.10)	p= 0.3571
Post-Chemo CA-125, U/mL, Mean (SD)	n=11 11.46 (7.69)	n=4 52.43 (82.44)	p= 0.2637
Serous, n	16	9	-
Mucinous, n	2	-	-
Clear Cell, n	1	-	-
Endometrioid, n	3	-	-

Clinical characteristics of patient samples. Data are presented as mean (SD). Groups were classified according to patients that were Alive without Disease (AWOD) or patients that presented with Recurrent Disease (RD). (-) Not applicable. Clinical data was not available for all samples.

Table S7. Proteins identified in circulating sEVs isolated from plasma.

ID	Symbol	Entrez Gene Name	Location	Type(s)
A1BG_HUMAN	A1BG	alpha-1-B glycoprotein	Extracellular Space	other
A2MG_HUMAN	A2M	alpha-2-macroglobulin	Extracellular Space	transporter
ACES_HUMAN	ACHE	acetylcholinesterase (Cartwright blood group)	Plasma Membrane	enzyme
ACTB_HUMAN	ACTB	actin beta	Cytoplasm	other
ACTC_HUMAN	ACTC1	actin alpha cardiac muscle 1	Cytoplasm	enzyme
ACTN1_HUMAN	ACTN1	actinin alpha 1	Cytoplasm	transcription regulator
ADIPO_HUMAN	ADIPOQ	adiponectin, C1Q and collagen domain containing	Extracellular Space	other
AFAM_HUMAN	AFM	afamin	Extracellular Space	transporter
ANGT_HUMAN	AGT	angiotensinogen	Extracellular Space	growth factor
FETUA_HUMAN	AHSG	alpha 2-HS glycoprotein	Extracellular Space	other
ALBU_HUMAN	ALB	albumin	Extracellular Space	transporter
ALDOA_HUMAN	ALDOA	aldolase, fructose-bisphosphate A	Cytoplasm	enzyme
AMBP_HUMAN	AMBP	alpha-1-microglobulin/bikunin precursor	Extracellular Space	transporter
ANK1_HUMAN	ANK1	ankyrin 1	Plasma Membrane	other
AMPN_HUMAN	ANPEP	alanyl aminopeptidase, membrane	Plasma Membrane	peptidase
ANXA2_HUMAN	ANXA2	annexin A2	Plasma Membrane	other
SAMP_HUMAN	APCS	amyloid P component, serum	Extracellular Space	other
APMAP_HUMAN	APMAP	adipocyte plasma membrane associated protein	Plasma Membrane	enzyme
APOA1_HUMAN	APOA1	apolipoprotein A1	Extracellular Space	transporter
APOA2_HUMAN	APOA2	apolipoprotein A2	Extracellular Space	transporter
APOA4_HUMAN	APOA4	apolipoprotein A4	Extracellular Space	transporter
APOB_HUMAN	APOB	apolipoprotein B	Extracellular Space	transporter
APOC1_HUMAN	APOC1	apolipoprotein C1	Extracellular Space	transporter
APOC2_HUMAN	APOC2	apolipoprotein C2	Extracellular Space	transporter
APOC3_HUMAN	APOC3	apolipoprotein C3	Extracellular Space	transporter

APOC4_HUMAN	APOC4	apolipoprotein C4	Extracellular Space	transporter
APOD_HUMAN	APOD	apolipoprotein D	Extracellular Space	transporter
APOE_HUMAN	APOE	apolipoprotein E	Extracellular Space	transporter
APOF_HUMAN	APOF	apolipoprotein F	Extracellular Space	transporter
APOH_HUMAN	APOH	apolipoprotein H	Extracellular Space	transporter
APOL1_HUMAN	APOL1	apolipoprotein L1	Extracellular Space	transporter
APOM_HUMAN	APOM	apolipoprotein M	Plasma Membrane	transporter
ARG1_HUMAN	ARG1	arginase 1	Cytoplasm	enzyme
ATRN_HUMAN	ATRN	atractin	Extracellular Space	other
ZA2G_HUMAN	AZGP1	alpha-2-glycoprotein 1, zinc-binding	Extracellular Space	transporter
CHLE_HUMAN	BCHE	butyrylcholinesterase	Plasma Membrane	enzyme
BLVRB_HUMAN	BLVRB	biliverdin reductase B	Cytoplasm	enzyme
XP32_HUMAN	C1orf68	chromosome 1 open reading frame 68	Cytoplasm	other
C1QA_HUMAN	C1QA	complement C1q A chain	Extracellular Space	other
C1QB_HUMAN	C1QB	complement C1q B chain	Extracellular Space	other
C1QC_HUMAN	C1QC	complement C1q C chain	Extracellular Space	other
C1R_HUMAN	C1R	complement C1r	Extracellular Space	peptidase
C1S_HUMAN	C1S	complement C1s	Extracellular Space	peptidase
CO2_HUMAN	C2	complement C2	Extracellular Space	peptidase
CO3_HUMAN	C3	complement C3	Extracellular Space	peptidase
CO4A_HUMAN	C4A/C4B	complement C4A (Rodgers blood group)	Extracellular Space	other
CO4B_HUMAN	C4A/C4B	complement C4A (Rodgers blood group)	Extracellular Space	other
C4BPA_HUMAN	C4BPA	complement component 4 binding protein alpha	Extracellular Space	other
CO5_HUMAN	C5	complement C5	Extracellular Space	cytokine
CO6_HUMAN	C6	complement C6	Extracellular Space	other
CO7_HUMAN	C7	complement C7	Extracellular Space	other
CO8A_HUMAN	C8A	complement C8 alpha chain	Extracellular Space	other
CO8B_HUMAN	C8B	complement C8 beta chain	Extracellular Space	other
CO8G_HUMAN	C8G	complement C8 gamma chain	Extracellular Space	transporter
CO9_HUMAN	C9	complement C9	Extracellular Space	other
CAH1_HUMAN	CA1	carbonic anhydrase 1	Cytoplasm	enzyme
CAH2_HUMAN	CA2	carbonic anhydrase 2	Cytoplasm	enzyme
CAMP_HUMAN	CAMP	cathelicidin antimicrobial peptide	Cytoplasm	other

CAP1_HUMAN	CAP1	cyclase associated actin cytoskeleton regulatory protein 1	Plasma Membrane	other
CASPE_HUMAN	CASP14	caspase 14	Cytoplasm	peptidase
CATA_HUMAN	CAT	catalase	Cytoplasm	enzyme
CAVN2_HUMAN	CAVIN2	caveolae associated protein 2	Plasma Membrane	other
CD36_HUMAN	CD36	CD36 molecule	Plasma Membrane	transmembrane receptor
CD59_HUMAN	CD59	CD59 molecule (CD59 blood group)	Plasma Membrane	other
CD5L_HUMAN	CD5L	CD5 molecule like	Plasma Membrane	transmembrane receptor
CD9_HUMAN	CD9	CD9 molecule	Plasma Membrane	other
CDC42_HUMAN	CDC42	cell division cycle 42	Cytoplasm	enzyme
CFA46_HUMAN	CFAP46	cilia and flagella associated protein 46	Cytoplasm	other
CFAB_HUMAN	CFB	complement factor B	Extracellular Space	peptidase
CFAH_HUMAN	CFH	complement factor H	Extracellular Space	other
FHR1_HUMAN	CFHR1	complement factor H related 1	Extracellular Space	other
FHR4_HUMAN	CFHR4	complement factor H related 4	Extracellular Space	transporter
FHR5_HUMAN	CFHR5	complement factor H related 5	Extracellular Space	other
CFAI_HUMAN	CFI	complement factor I	Extracellular Space	peptidase
COF1_HUMAN	CFL1	cofilin 1	Nucleus	other
PROP_HUMAN	CFP	complement factor properdin	Extracellular Space	other
CLUS_HUMAN	CLU	clusterin	Cytoplasm	other
CO6A3_HUMAN	COL6A3	collagen type VI alpha 3 chain	Extracellular Space	other
COL11_HUMAN	COLEC11	collectin subfamily member 11	Extracellular Space	other
COMP_HUMAN	COMP	cartilage oligomeric matrix protein	Extracellular Space	other
CERU_HUMAN	CP	ceruloplasmin	Extracellular Space	enzyme
CBPN_HUMAN	CPN1	carboxypeptidase N subunit 1	Extracellular Space	peptidase
CPN2_HUMAN	CPN2	carboxypeptidase N subunit 2	Extracellular Space	peptidase
CRP_HUMAN	CRP	C-reactive protein	Extracellular Space	other
DOPO_HUMAN	DBH	dopamine beta-hydroxylase	Cytoplasm	enzyme
DCD_HUMAN	DCD	dermcidin	Extracellular Space	other
DEF3_HUMAN	DEFA1 (includes others)	defensin alpha 1	Cytoplasm	other
DSC1_HUMAN	DSC1	desmocollin 1	Plasma Membrane	other
DSG1_HUMAN	DSG1	desmoglein 1	Plasma Membrane	other

DESP_HUMAN	DSP	desmoplakin	Plasma Membrane	other
ECM1_HUMAN	ECM1	extracellular matrix protein 1	Extracellular Space	transporter
ENOA_HUMAN	ENO1	enolase 1	Cytoplasm	enzyme
41_HUMAN	EPB41	erythrocyte membrane protein band 4.1	Plasma Membrane	other
EPB42_HUMAN	EPB42	erythrocyte membrane protein band 4.2	Plasma Membrane	transporter
FA10_HUMAN	F10	coagulation factor X	Extracellular Space	peptidase
F13A_HUMAN	F13A1	coagulation factor XIII A chain	Extracellular Space	enzyme
F13B_HUMAN	F13B	coagulation factor XIII B chain	Extracellular Space	enzyme
THRB_HUMAN	F2	coagulation factor II, thrombin	Extracellular Space	peptidase
FA5_HUMAN	F5	coagulation factor V	Extracellular Space	other
FABP5_HUMAN	FABP5	fatty acid binding protein 5	Cytoplasm	transporter
FBLN1_HUMAN	FBLN1	fibulin 1	Extracellular Space	other
FCGBP_HUMAN	FCGBP	Fc fragment of IgG binding protein	Extracellular Space	other
FCN2_HUMAN	FCN2	ficolin 2	Extracellular Space	other
FCN3_HUMAN	FCN3	ficolin 3	Extracellular Space	other
URP2_HUMAN	FERMT3	fermitin family member 3	Cytoplasm	enzyme
FIBA_HUMAN	FGA	fibrinogen alpha chain	Extracellular Space	other
FIBB_HUMAN	FGB	fibrinogen beta chain	Extracellular Space	other
FIBG_HUMAN	FGG	fibrinogen gamma chain	Extracellular Space	other
FILA_HUMAN	FLG	filaggrin	Cytoplasm	other
FILA2_HUMAN	FLG2	filaggrin family member 2	Cytoplasm	other
FLNA_HUMAN	FLNA	filamin A	Cytoplasm	other
FINC_HUMAN	FN1	fibronectin 1	Extracellular Space	enzyme
G3P_HUMAN	GAPDH	glyceraldehyde-3-phosphate dehydrogenase	Cytoplasm	enzyme
VTDB_HUMAN	GC	GC vitamin D binding protein	Extracellular Space	transporter
GNAI2_HUMAN	GNAI2	G protein subunit alpha i2	Plasma Membrane	enzyme
GP1BA_HUMAN	GP1BA	glycoprotein Ib platelet subunit alpha	Plasma Membrane	transmembrane receptor
GP1BB_HUMAN	GP1BB	glycoprotein Ib platelet subunit beta	Plasma Membrane	other
GPIX_HUMAN	GP9	glycoprotein IX platelet	Plasma Membrane	other
PHLD_HUMAN	GPLD1	glycosylphosphatidylinositol specific phospholipase D1	Cytoplasm	enzyme
GELS_HUMAN	GSN	gelsolin	Extracellular Space	other
GLPA_HUMAN	GYPA	glycophorin A (MNS blood group)	Plasma Membrane	other

GLPC_HUMAN	GYPC	glycophorin C (Gerbich blood group)	Plasma Membrane	other
H2AJ_HUMAN	H2AJ	H2A.J histone	Cytoplasm	other
H2B2F_HUMAN	H2BC18	H2B clustered histone 18	Nucleus	other
HBB_HUMAN	HBB	hemoglobin subunit beta	Cytoplasm	transporter
HBD_HUMAN	HBD	hemoglobin subunit delta	Other	transporter
HBG2_HUMAN	HBG2	hemoglobin subunit gamma 2	Cytoplasm	other
HPT_HUMAN	HP	haptoglobin	Extracellular Space	peptidase
HPTR_HUMAN	HPR	haptoglobin-related protein	Extracellular Space	peptidase
HEMO_HUMAN	HPX	hemopexin	Extracellular Space	transporter
HRG_HUMAN	HRG	histidine rich glycoprotein	Extracellular Space	other
HORN_HUMAN	HRNR	hornerin	Cytoplasm	other
HSP7C_HUMAN	HSPA8	heat shock protein family A (Hsp70) member 8	Cytoplasm	enzyme
ALS_HUMAN	IGFALS	insulin like growth factor binding protein acid labile subunit	Extracellular Space	other
IGHA1_HUMAN	IGHA1	immunoglobulin heavy constant alpha 1	Extracellular Space	other
IGHA2_HUMAN	IGHA2	immunoglobulin heavy constant alpha 2 (A2m marker)	Extracellular Space	other
IGHD_HUMAN	IGHD	immunoglobulin heavy constant delta	Extracellular Space	other
IGHG1_HUMAN	IGHG1	immunoglobulin heavy constant gamma 1 (G1m marker)	Extracellular Space	other
IGHG2_HUMAN	IGHG2	immunoglobulin heavy constant gamma 2 (G2m marker)	Plasma Membrane	other
IGHG3_HUMAN	IGHG3	immunoglobulin heavy constant gamma 3 (G3m marker)	Extracellular Space	other
IGHG4_HUMAN	IGHG4	immunoglobulin heavy constant gamma 4 (G4m marker)	Extracellular Space	other
IGHM_HUMAN	IGHM	immunoglobulin heavy constant mu	Plasma Membrane	transmembrane receptor
HV118_HUMAN	IGHV1-18	immunoglobulin heavy variable 1-18	Other	other
HV124_HUMAN	IGHV1-24	immunoglobulin heavy variable 1-24	Other	other
HV103_HUMAN	IGHV1-3	immunoglobulin heavy variable 1-3	Other	other
HV146_HUMAN	IGHV1-46	immunoglobulin heavy variable 1-46	Other	other
HV158_HUMAN	IGHV1-58	immunoglobulin heavy variable 1-58	Other	other
HV692_HUMAN	IGHV1-69-2	immunoglobulin heavy variable 1-69-2	Other	other
HV69D_HUMAN	IGHV1-69D	immunoglobulin heavy variable 1-69D	Other	other
HV226_HUMAN	IGHV2-26	immunoglobulin heavy variable 2-26	Other	other
HV205_HUMAN	IGHV2-5	immunoglobulin heavy variable 2-5	Other	other

HV70D_HUMAN	IGHV2-70D	immunoglobulin heavy variable 2-70D	Other	other
HV315_HUMAN	IGHV3-15	immunoglobulin heavy variable 3-15	Other	other
HV320_HUMAN	IGHV3-20	immunoglobulin heavy variable 3-20	Other	other
HV323_HUMAN	IGHV3-23	immunoglobulin heavy variable 3-23	Extracellular Space	other
HV335_HUMAN	IGHV3-35	immunoglobulin heavy variable 3-35 (non-functional)	Other	other
HV349_HUMAN	IGHV3-49	immunoglobulin heavy variable 3-49	Other	other
HV364_HUMAN	IGHV3-64	immunoglobulin heavy variable 3-64	Other	other
HV64D_HUMAN	IGHV3-64D	immunoglobulin heavy variable 3-64D	Other	other
HV366_HUMAN	IGHV3-66	immunoglobulin heavy variable 3-66	Other	other
HV307_HUMAN	IGHV3-7	immunoglobulin heavy variable 3-7	Extracellular Space	other
HV372_HUMAN	IGHV3-72	immunoglobulin heavy variable 3-72	Other	other
HV373_HUMAN	IGHV3-73	immunoglobulin heavy variable 3-73	Other	other
HV374_HUMAN	IGHV3-74	immunoglobulin heavy variable 3-74	Other	other
HV434_HUMAN	IGHV4-34	immunoglobulin heavy variable 4-34	Other	other
HV5X1_HUMAN	IGHV5-10-1	immunoglobulin heavy variable 5-10-1	Other	other
HV551_HUMAN	IGHV5-51	immunoglobulin heavy variable 5-51	Other	other
HV601_HUMAN	IGHV6-1	immunoglobulin heavy variable 6-1	Other	other
IGKC_HUMAN	IGKC	immunoglobulin kappa constant	Extracellular Space	other
KVD16_HUMAN	IGKC	immunoglobulin kappa constant	Extracellular Space	other
KV113_HUMAN	IGKV1-13	immunoglobulin kappa variable 1-13 (gene/pseudogene)	Other	other
KV106_HUMAN	IGKV1-6	immunoglobulin kappa variable 1-6	Other	other
KV133_HUMAN	IGKV1D-33	immunoglobulin kappa variable 1D-33	Extracellular Space	other
KVD08_HUMAN	IGKV1D-8	immunoglobulin kappa variable 1D-8	Other	other
KV224_HUMAN	IGKV2-24	immunoglobulin kappa variable 2-24	Other	other
KV230_HUMAN	IGKV2-30	immunoglobulin kappa variable 2-30	Extracellular Space	other
KVD40_HUMAN	IGKV2-40	immunoglobulin kappa variable 2-40	Extracellular Space	other
KVD29_HUMAN	IGKV2D-29	immunoglobulin kappa variable 2D-29	Other	other
KV320_HUMAN	IGKV3-20	immunoglobulin kappa variable 3-20	Extracellular Space	other
KV311_HUMAN	IGKV3D-11	immunoglobulin kappa variable 3D-11	Extracellular Space	other
KVD15_HUMAN	IGKV3D-15	immunoglobulin kappa variable 3D-15 (gene/pseudogene)	Other	other
KVD20_HUMAN	IGKV3D-20	immunoglobulin kappa variable 3D-20	Extracellular Space	other

KVD07_HUMAN	IGKV3D-7	immunoglobulin kappa variable 3D-7	Other	other
KV401_HUMAN	IGKV4-1	immunoglobulin kappa variable 4-1	Extracellular Space	other
KVD21_HUMAN	IGKV6D-21	immunoglobulin kappa variable 6D-21 (non-functional)	Other	other
IGLC3_HUMAN	IGLC3	immunoglobulin lambda constant 3 (Kern-Oz+ marker)	Extracellular Space	other
IGLC7_HUMAN	IGLC7	immunoglobulin lambda constant 7	Extracellular Space	other
IGLL5_HUMAN	IGLL1/IGLL5	immunoglobulin lambda like polypeptide 1	Plasma Membrane	other
LV136_HUMAN	IGLV1-36	immunoglobulin lambda variable 1-36	Other	other
LV140_HUMAN	IGLV1-40	immunoglobulin lambda variable 1-40	Other	other
LV147_HUMAN	IGLV1-47	immunoglobulin lambda variable 1-47	Extracellular Space	other
LV151_HUMAN	IGLV1-51	immunoglobulin lambda variable 1-51	Extracellular Space	other
LVX54_HUMAN	IGLV10-54	immunoglobulin lambda variable 10-54	Other	other
LV211_HUMAN	IGLV2-11	immunoglobulin lambda variable 2-11	Extracellular Space	other
LV218_HUMAN	IGLV2-18	immunoglobulin lambda variable 2-18	Other	other
LV310_HUMAN	IGLV3-10	immunoglobulin lambda variable 3-10	Other	other
LV319_HUMAN	IGLV3-19	immunoglobulin lambda variable 3-19	Extracellular Space	other
LV321_HUMAN	IGLV3-21	immunoglobulin lambda variable 3-21	Extracellular Space	other
LV327_HUMAN	IGLV3-27	immunoglobulin lambda variable 3-27	Other	other
LV469_HUMAN	IGLV4-69	immunoglobulin lambda variable 4-69	Other	other
LV657_HUMAN	IGLV6-57	immunoglobulin lambda variable 6-57	Extracellular Space	other
LV746_HUMAN	IGLV7-46	immunoglobulin lambda variable 7-46 (gene/pseudogene)	Other	other
LV861_HUMAN	IGLV8-61	immunoglobulin lambda variable 8-61	Other	other
LV949_HUMAN	IGLV9-49	immunoglobulin lambda variable 9-49	Other	other
ITA2B_HUMAN	ITGA2B	integrin subunit alpha 2b	Plasma Membrane	transmembrane receptor
ITB1_HUMAN	ITGB1	integrin subunit beta 1	Plasma Membrane	transmembrane receptor
ITB3_HUMAN	ITGB3	integrin subunit beta 3	Plasma Membrane	transmembrane receptor
ITIH1_HUMAN	ITIH1	inter-alpha-trypsin inhibitor heavy chain 1	Extracellular Space	other
ITIH2_HUMAN	ITIH2	inter-alpha-trypsin inhibitor heavy chain 2	Extracellular Space	other
ITIH3_HUMAN	ITIH3	inter-alpha-trypsin inhibitor heavy chain 3	Extracellular Space	other
ITIH4_HUMAN	ITIH4	inter-alpha-trypsin inhibitor heavy chain 4	Extracellular Space	other
IGJ_HUMAN	JCHAIN	joining chain of multimeric IgA and IgM	Extracellular Space	other
PLAK_HUMAN	JUP	junction plakoglobin	Plasma Membrane	other

KLKB1_HUMAN	KLKB1	kallikrein B1	Extracellular Space	peptidase
KNG1_HUMAN	KNG1	kininogen 1	Extracellular Space	other
KNG1_HUMAN	KNG1	kininogen 1	Extracellular Space	other
KPRP_HUMAN	KPRP	keratinocyte proline rich protein	Cytoplasm	other
K2C1_HUMAN	KRT1	keratin 1	Cytoplasm	other
K1C10_HUMAN	KRT10	keratin 10	Cytoplasm	other
K1C14_HUMAN	KRT14	keratin 14	Cytoplasm	other
K1C16_HUMAN	KRT16	keratin 16	Cytoplasm	other
K1C17_HUMAN	KRT17	keratin 17	Cytoplasm	other
K22E_HUMAN	KRT2	keratin 2	Cytoplasm	other
K1H1_HUMAN	KRT31	keratin 31	Cytoplasm	other
KT33A_HUMAN	KRT33A	keratin 33A	Extracellular Space	other
KT33B_HUMAN	KRT33B	keratin 33B	Extracellular Space	other
KRT34_HUMAN	KRT34	keratin 34	Cytoplasm	other
KRT35_HUMAN	KRT35	keratin 35	Cytoplasm	other
KRT36_HUMAN	KRT36	keratin 36	Cytoplasm	other
K2C4_HUMAN	KRT4	keratin 4	Cytoplasm	other
K2C5_HUMAN	KRT5	keratin 5	Cytoplasm	other
K2C6B_HUMAN	KRT6B	keratin 6B	Cytoplasm	other
K2C73_HUMAN	KRT73	keratin 73	Extracellular Space	other
K2C1B_HUMAN	KRT77	keratin 77	Cytoplasm	other
K2C78_HUMAN	KRT78	keratin 78	Cytoplasm	other
K2C80_HUMAN	KRT80	keratin 80	Cytoplasm	other
KRT82_HUMAN	KRT82	keratin 82	Cytoplasm	other
KRT83_HUMAN	KRT83	keratin 83	Cytoplasm	other
KRT85_HUMAN	KRT85	keratin 85	Extracellular Space	other
KRT86_HUMAN	KRT86	keratin 86	Cytoplasm	other
KR87P_HUMAN	KRT87P	keratin 87 pseudogene	Extracellular Space	other
K1C9_HUMAN	KRT9	keratin 9	Cytoplasm	other
KRA21_HUMAN	KRTAP2-1	keratin associated protein 2-1	Cytoplasm	other
LAMB1_HUMAN	LAMB1	laminin subunit beta 1	Extracellular Space	other
LBP_HUMAN	LBP	lipopolysaccharide binding protein	Plasma Membrane	transporter
LBX2_HUMAN	LBX2	ladybird homeobox 2	Nucleus	transcription regulator

LDHB_HUMAN	LDHB	lactate dehydrogenase B	Cytoplasm	enzyme
LG3BP_HUMAN	LGALS3BP	galectin 3 binding protein	Plasma Membrane	transmembrane receptor
APOA_HUMAN	LPA	lipoprotein(a)	Extracellular Space	other
A2GL_HUMAN	LRG1	leucine rich alpha-2-glycoprotein 1	Extracellular Space	other
TRFL_HUMAN	LTF	lactotransferrin	Extracellular Space	peptidase
LUM_HUMAN	LUM	lumican	Extracellular Space	other
LYSC_HUMAN	LYZ	lysozyme	Extracellular Space	enzyme
MASP1_HUMAN	MASP1	mannan binding lectin serine peptidase 1	Extracellular Space	peptidase
MASP1_HUMAN	MASP1	mannan binding lectin serine peptidase 1	Extracellular Space	peptidase
MBL2_HUMAN	MBL2	mannose binding lectin 2	Extracellular Space	other
MMRN1_HUMAN	MMRN1	multimerin 1	Extracellular Space	other
PERM_HUMAN	MPO	myeloperoxidase	Cytoplasm	enzyme
EM55_HUMAN	MPP1	membrane palmitoylated protein 1	Plasma Membrane	kinase
MUC1_HUMAN	MUC1	mucin 1, cell surface associated	Plasma Membrane	other
MUC16_HUMAN	MUC16	mucin 16, cell surface associated	Cytoplasm	other
MUC5A_HUMAN	MUC5AC	mucin 5AC, oligomeric mucus/gel-forming	Cytoplasm	peptidase
MUC5B_HUMAN	MUC5B	mucin 5B, oligomeric mucus/gel-forming	Extracellular Space	peptidase
MYH9_HUMAN	MYH9	myosin heavy chain 9	Cytoplasm	enzyme
NOP53_HUMAN	NOP53	NOP53 ribosome biogenesis factor	Cytoplasm	other
A1AG1_HUMAN	ORM1	orosomucoid 1	Extracellular Space	other
A1AG2_HUMAN	ORM2	orosomucoid 2	Extracellular Space	other
PDIA1_HUMAN	P4HB	prolyl 4-hydroxylase subunit beta	Cytoplasm	enzyme
PCYOX_HUMAN	PCYOX1	prenylcysteine oxidase 1	Cytoplasm	enzyme
PECA1_HUMAN	PECAM1	platelet and endothelial cell adhesion molecule 1	Plasma Membrane	other
PLF4_HUMAN	PF4	platelet factor 4	Extracellular Space	cytokine
PROF1_HUMAN	PFN1	profilin 1	Cytoplasm	other
PGRP2_HUMAN	PGLYRP2	peptidoglycan recognition protein 2	Plasma Membrane	transmembrane receptor
PI16_HUMAN	PI16	peptidase inhibitor 16	Extracellular Space	other
PIGR_HUMAN	PIGR	polymeric immunoglobulin receptor	Plasma Membrane	transporter
PIP_HUMAN	PIP	prolactin induced protein	Extracellular Space	peptidase
KPYM_HUMAN	PKM	pyruvate kinase M1/2	Cytoplasm	kinase
PKP1_HUMAN	PKP1	plakophilin 1	Plasma Membrane	other
PLEK_HUMAN	PLEK	pleckstrin	Cytoplasm	other

PLMN_HUMAN	PLG	plasminogen	Extracellular Space	peptidase
PLTP_HUMAN	PLTP	phospholipid transfer protein	Extracellular Space	enzyme
POF1B_HUMAN	POF1B	POF1B actin binding protein	Plasma Membrane	other
PON1_HUMAN	PON1	paraoxonase 1	Extracellular Space	phosphatase
PPIA_HUMAN	PPIA	peptidylprolyl isomerase A	Cytoplasm	enzyme
PRDX2_HUMAN	PRDX2	peroxiredoxin 2	Cytoplasm	enzyme
PRDX6_HUMAN	PRDX6	peroxiredoxin 6	Cytoplasm	enzyme
PRG4_HUMAN	PRG4	proteoglycan 4	Extracellular Space	other
PROS_HUMAN	PROS1	protein S	Extracellular Space	other
PZP_HUMAN	PZP	PZP alpha-2-macroglobulin like	Extracellular Space	other
QSOX1_HUMAN	QSOX1	quiescin sulfhydryl oxidase 1	Cytoplasm	enzyme
RAB1B_HUMAN	RAB1B	RAB1B, member RAS oncogene family	Cytoplasm	other
RAP1B_HUMAN	RAP1B	RAP1B, member of RAS oncogene family	Cytoplasm	enzyme
RAP2B_HUMAN	RAP2B	RAP2B, member of RAS oncogene family	Plasma Membrane	enzyme
RHAG_HUMAN	RHAG	Rh associated glycoprotein	Plasma Membrane	peptidase
RHD_HUMAN	RHCE/RHD	Rh blood group D antigen	Plasma Membrane	transporter
RS27A_HUMAN	RPS27A	ribosomal protein S27a	Cytoplasm	other
S10A8_HUMAN	S100A8	S100 calcium binding protein A8	Cytoplasm	other
S10A9_HUMAN	S100A9	S100 calcium binding protein A9	Cytoplasm	other
SAA1_HUMAN	SAA1	serum amyloid A1	Extracellular Space	transporter
SAA2_HUMAN	SAA2	serum amyloid A2	Extracellular Space	other
SAA4_HUMAN	SAA4	serum amyloid A4, constitutive	Extracellular Space	transporter
A1AT_HUMAN	SERPINA1	serpin family A member 1	Extracellular Space	other
ZPI_HUMAN	SERPINA10	serpin family A member 10	Extracellular Space	other
AACT_HUMAN	SERPINA3	serpin family A member 3	Extracellular Space	other
CBG_HUMAN	SERPINA6	serpin family A member 6	Extracellular Space	other
SPB12_HUMAN	SERPINB12	serpin family B member 12	Cytoplasm	other
ANT3_HUMAN	SERPINC1	serpin family C member 1	Extracellular Space	enzyme
HEP2_HUMAN	SERPIND1	serpin family D member 1	Extracellular Space	other
PEDF_HUMAN	SERPINF1	serpin family F member 1	Extracellular Space	other
A2AP_HUMAN	SERPINF2	serpin family F member 2	Extracellular Space	other
IC1_HUMAN	SERPING1	serpin family G member 1	Extracellular Space	other
SHBG_HUMAN	SHBG	sex hormone binding globulin	Extracellular Space	other

S29A1_HUMAN	SLC29A1	solute carrier family 29 member 1 (Augustine blood group)	Plasma Membrane	transporter
GTR1_HUMAN	SLC2A1	solute carrier family 2 member 1	Plasma Membrane	transporter
GTR14_HUMAN	SLC2A14	solute carrier family 2 member 14	Nucleus	transporter
B3AT_HUMAN	SLC4A1	solute carrier family 4 member 1 (Diego blood group)	Plasma Membrane	transporter
SPR2G_HUMAN	SPRR2G	small proline rich protein 2G	Cytoplasm	other
SPTA1_HUMAN	SPTA1	spectrin alpha, erythrocytic 1	Cytoplasm	other
SPTB1_HUMAN	SPTB	spectrin beta, erythrocytic	Plasma Membrane	other
SRGN_HUMAN	SRGN	serglycin	Cytoplasm	other
SRCRL_HUMAN	SSC5D	scavenger receptor cysteine rich family member with 5 domains	Plasma Membrane	transmembrane receptor
STOM_HUMAN	STOM	stomatin	Plasma Membrane	other
SYNE2_HUMAN	SYNE2	spectrin repeat containing nuclear envelope protein 2	Nucleus	other
TAGL2_HUMAN	TAGLN2	transgelin 2	Cytoplasm	other
TRFE_HUMAN	TF	transferrin	Extracellular Space	transporter
TFR1_HUMAN	TFRC	transferrin receptor	Plasma Membrane	transporter
BGH3_HUMAN	TGFBI	transforming growth factor beta induced	Extracellular Space	other
TGM3_HUMAN	TGM3	transglutaminase 3	Cytoplasm	enzyme
TSP1_HUMAN	THBS1	thrombospondin 1	Extracellular Space	other
TLN1_HUMAN	TLN1	talin 1	Plasma Membrane	other
TENA_HUMAN	TNC	tenascin C	Extracellular Space	other
TSN1_HUMAN	TSPAN1	tetraspanin 1	Cytoplasm	other
TTHY_HUMAN	TTR	transthyretin	Extracellular Space	transporter
TBA1B_HUMAN	TUBA1B	tubulin alpha 1b	Cytoplasm	other
TBA4A_HUMAN	TUBA4A	tubulin alpha 4a	Cytoplasm	other
TBB5_HUMAN	TUBB	tubulin beta class I	Cytoplasm	other
TBB1_HUMAN	TUBB1	tubulin beta 1 class VI	Cytoplasm	other
VCAM1_HUMAN	VCAM1	vascular cell adhesion molecule 1	Plasma Membrane	transmembrane receptor
VINC_HUMAN	VCL	vinculin	Plasma Membrane	enzyme
TERA_HUMAN	VCP	valosin containing protein	Cytoplasm	enzyme
VIME_HUMAN	VIM	vimentin	Cytoplasm	other
VTNC_HUMAN	VTN	vitronectin	Extracellular Space	other
VWF_HUMAN	VWF	von Willebrand factor	Extracellular Space	other

1433E_HUMAN	YWHAE	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein epsilon	Cytoplasm	other
1433G_HUMAN	YWHAG	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein gamma	Cytoplasm	other
1433F_HUMAN	YWHAH	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein eta	Cytoplasm	transcription regulator
1433Z_HUMAN	YWHAZ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein zeta	Cytoplasm	enzyme
ZFHX2_HUMAN	ZFHX2	zinc finger homeobox 2	Nucleus	transcription regulator

Table S8. Peptide separation was performed at a total flow rate of 5 $\mu\text{L}/\text{mL}$ according to the gradient conditions listed below.

Time (min)	Mobile phase A %	Mobile phase B %
0	97	3
15	60	40
18	5	95
22	5	95
25	97	3
30	97	3

Table S9. Chromatography was performed with solvent A (100% H_2O , 0.1% FA) and solvent B (100% ACN, 0.1% FA) at a total flow rate of 15 $\mu\text{L}/\text{mL}$ according to the gradient conditions listed below.

Time (min)	Mobile phase A %	Mobile phase B %
0	95	5
1	90	10
8.5	60	40
9.5	10	90
11.5	10	90
12	95	5
18	95	5

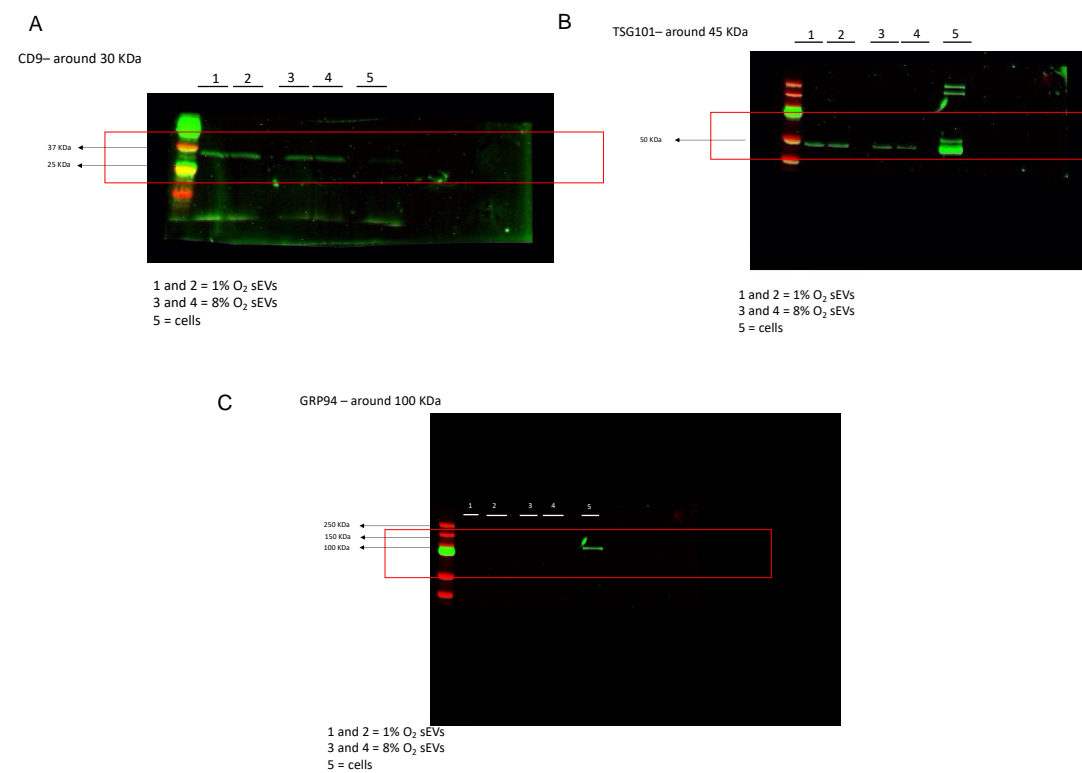


Figure S4. Original Western blots used in Figure 3B. A) CD9, B) TSG101, and C) GRP94.