

Table W1. List of Antibodies.

Antibody	Supplier	Antibody	Supplier
$\alpha 6\beta 4$	Clone B5.5 [1]	EpCAM	Clone D5.7 [1]
ADAM10	Santa Cruz Biotechnology (Heidelberg, Germany)	Fibulin	Santa Cruz Biotechnology
ADAM17	Santa Cruz Biotechnology	Fibronectin	BD (Heidelberg, Germany)
ADAMTS1	Santa Cruz Biotechnology	Follistatin	Santa Cruz Biotechnology
ADAMTS5	Santa Cruz Biotechnology	GADD45G	Santa Cruz Biotechnology
ADAMTS8	Santa Cruz Biotechnology	Gal.bind. 4	Santa Cruz Biotechnology
ALDH3a1	Santa Cruz Biotechnology	Hyaluronan	Rockland (Gilbertsville, PA)
Anillin	Santa Cruz Biotechnology	HGF	Santa Cruz Biotechnology
bFGF	Oncogene (Boston, MA)	HGDF	Santa Cruz Biotechnology
BTG2	Santa Cruz Biotechnology	IGF	Santa Cruz Biotechnology
CA5B	Santa Cruz Biotechnology	IL1R1	Santa Cruz Biotechnology
C4.4A	Clone C4.4 [1]	Laminin 1	Rockland
Caveolin	Santa Cruz Biotechnology	MAL	Santa Cruz Biotechnology
CD9	BD	MDR1	Santa Cruz Biotechnology
CD11a	BD	MMP2	Dianova (Hamburg, Germany)
CD11b	Clone Ox42 (EAACC)*	MMP3	Santa Cruz Biotechnology
CD11c	Clone Ox41 (EAACC)*	MMP9	Dianova
CD18	BD	MMP13	Dianova
CD24	BD	MMP14	Dianova
CD29	BD	Metallothio.	Santa Cruz Biotechnology
CD44s	Clone Ox50 (EAACC)*	Neuropilin	Santa Cruz Biotechnology
CD44v6	Clone A2.6 [1]	Osteopontin	Santa Cruz Biotechnology
CD49a	BD	Palladin	Santa Cruz Biotechnology
CD49b	BD	Pan cadherin	Santa Cruz Biotechnology
CD49c	BD	PDGF	BD
CD49d	BD	PDGFR	BD
CD49e	BD	Periostin	Santa Cruz Biotechnology
CD49f	Abcam (Cambridge, United Kingdom)	PG-Synth. 3	Santa Cruz Biotechnology
CD53	Clone Ox44 (EAACC)*	Phospholip.A2	Santa Cruz Biotechnology
CD54	Biozol (Eching, Germany)	Properdin	Santa Cruz Biotechnology
CD56	BD	SDF1	Abcam
CD61	Biozol	SLPI	Santa Cruz Biotechnology
CD62L	BD	SOD2	Santa Cruz Biotechnology
CD63	BD	Tenascin	LabVision (Fremont, CA)
CD81	Santa Cruz Biotechnology	TF	Santa Cruz Biotechnology
CD104	BD	TGF β	Santa Cruz Biotechnology
CD106	Biozol	TRAF4	Santa Cruz Biotechnology
CD151	[2]	uPA	Calbiochem (Darmstadt, Germany)
Cdc2a	Santa Cruz Biotechnology	uPAR	Calbiochem
Claudin-4	Santa Cruz Biotechnology	VEGF	Biotrend (Köln, Germany)
Claudin-6	Santa Cruz Biotechnology	VEGFR1	Biotrend
Collagen I	Rockland	VEGFR2	Biotrend
Collagen II	LabVision	Vitronectin	Biotrend
Collagen IV	Rockland	vWF	Abcam
CXCR4	Santa Cruz Biotechnology	mIgG [†]	Dianova
CyclinB2	Santa Cruz Biotechnology	mIgM [†]	Dianova
D6.1A	Clone D6.1 [1]	Rabbit IgG [†]	Dianova
Endothelin	BD	Goat IgG [†]	Dianova
		Streptavidin [†]	Dianova

References:

[1] Martzku S, Wenzel A, Liu S, and Zöller M (1989). Antigenic differences between metastatic and non-metastatic rat tumor variants characterized by monoclonal antibodies. *Cancer Res* **49**, 1294–1299.

[2] Claas C, Wahl J, Orlicky D, Karaduman H, Schnölzer M, Kempf T, and Zöller M (2005). The tetraspanin D6.1A and its molecular partners on rat carcinoma cells. *Biochem J* **389**, 99–110.

*EAACC, European Association of Animal Cell Cultures, Porton Down, United Kingdom.

[†]Secondary antibodies and streptavidin were fluorescein isothiocyanate, phycoerythrin (PE), biotin, or HRP labeled.

Table W2. Primers.

Primers for qRT-PCR

GAPDH

Forward primer: cttctccatggtggtgaagac

Reverse primer: gacccttcattgacctcaac

Cdh17

Forward primer: cctgggtctctgtgaagg

Reverse primer: gtgattttgatgggtgagg

MAL

Forward primer: ttctccgtctctgcacctt

Reverse primer: gtctccccaccatgagtacc

KLF4

Forward primer: gcaagtcctctctccatt

Reverse primer: ggtaaggtttctgcctgtg

MMP3

Forward primer: ggctgaagatgacaggaag

Reverse primer: caatggcagaatccacactc

MT1a

Forward primer: accccaactgctctgct

Reverse primer: actgtccgagccactt

ADAMTS1

Forward primer: gccactgcttctactctgg

Reverse primer: gtgcgattgactcctcttc

TRAF4

Forward primer: gctgctggaggctgcaa

Reverse primer: atctgtctgggtctctg

4.5SRNA

Forward primer: aatgccccaaaacagtcaa

Reverse primer: acctccagttgaaccagcac

C4.4A

Forward primer: attcactcagcggttct

Reverse primer: gtggtggcttgatgtag

Stem loop primers

Universal reverse miRNA primer: 5' gtcagggtccgaggt 3'

Stem loop miR-300-5p:

Forward primer: 5' gttgctctggtgcagggtccgaggtattcgaccagagccaacacaag 3'

Stem loop miR-296:

Forward primer: 5' gttgctctggtgcagggtccgaggtattcgaccagagccaacggagag 3'

Stem loop miR-300-5p:

Forward primer: 5' gtttggttgaagagaggttacc 3'

Stem loop miR-296:

Forward primer: 5' ttggagggttgggtggag 3'

Oligos and primers for the reporter assay

300-5p binding oligo

Sense: 5' aaactagcggccgctagtacaaggataacctcttcaat 3'

Antisense: 5' ctgattgaagagaggttacctttagctagcggccgctagttt 3'

Cdh17

3'UTR cdh17 fw Pme1: gtttaactcccttctgtttccacctg

3'UTR cdh17 rev Xba1: tctagaccacgtacatcttctg

MAL

3'UTR MAL fw Pme1: gtttaaacacagcagattggagct

3'UTR MAL rev Xba1: tctagatggtgggtgaatttcagtg

Sequences of the 3'UTR with binding sites and SVR score

3'UTR MAL

gacagcagattggagctgaaccagagcaattaactggtcagcctgctctcccattacttctggaacagactgaatggaggagaaaagaaa
caagccaaaagaaaacaaacagacacaaaaaaaagaaacatgtrtcgagctcttgggtgttacgtttaccttctgtagggttttagggttg
ctgaatttaacttccagcaaaaggagaaagagttgcttggcggcccttctgccccttgaccaggaacaggggtgggagcttggaaacctgac
tgaagaatgacaatttcccttgacccttggagcaggtcctaacaattgcttgggaattttccacaagctctttgaccactatccccggcata
tcttagattttggatagcttaggtgacagggcactgaaattcaccaca

gacagcagattggagc: target site miR-494 (mirSVR score: -0.9472)

3'UTR Cdh17

tcccttctggttccacctgcccctgattctcagcattac**attaattt**aaatg**gtgcaca**caaaagacaaagtgaagtcttgggggggtgtt
gctaagtgacagcctattcttttagacacaaacagcttctctggtgtgtcatcttaatagaggtctccagcttggctatggtgtagacctggg
gaggtacaatacaactccgtrttcaagaagacctactctatgaggcacaggaactgacgagctgctgggtttactcactactccgtgctta
catcatgctgtacatgttttttgtatattgaagttttgtatatttatcatgtggaggaagacgaaagcatgtacgtgggtg

attaatttaaatg**gtgcaca**: target site miR-542-3P (mirSVR score: -0.1085)

atacatgctgtacatgtttta: target site miR 494 (mirSVR score: -0.1085)

Table W3. mRNA Recovery in ASML^{wt} and ASML-CD44^{kd} Exosomes (Signal Strength 10,000).

mRNA	Mean Signal Strength*	
	ASML ^{wt} Exosomes	ASML-CD44 ^{kd} Exosomes
Acidic ribosomal phosphoprotein P0 (Arbp)	36,537	34,209
Pred. similar to LRRG00135	28,102	17,532
Pred. similar to Ab2-143	26,757	13,956
Pred. similar to 60S ribosomal protein L37a	25,511	27,156
Pred. similar to LRRG00135	25,318	15,450
Pred. similar to restin (LOC503278)	24,223	12,457 [†]
Pred. similar to RIKEN cDNA 2410116I05	23,944	21,405
Ribosomal protein S15a (Rps15a)	22,854	25,011
Pred. ribosomal protein L27a (Rpl27a)	21,294	25,079
Pred. ribosomal protein L37a (Rpl37a)	20,655	26,661
Pred. similar to 60S ribosomal protein L7a	18,819	24,078
Ribosomal protein S14 (Rps14)	18,335	22,643
Eukaryotic translation elongation factor 1 alpha 1	17,840	20,172
Pred. similar to ORF4	17,709	8,172 [†]
Pred. similar to 60S ribosomal protein L23a	17,248	22,830
Pred. similar to ribosomal protein L19	16,799	21,770
Pred. similar to ORF4 (LOC361942)	16,503	7,596 [†]
Ribosomal protein S18 (Rps18)	16,501	16,624
Pred. similar to testis-derived transcript	16,125	25,111
Pred. ribosomal protein L10 (Rpl10)	16,056	14,972
Ribosomal protein L41 (Rpl41)	15,816	15,564
Pred. S100 calcium-binding protein A11 (S100a11)	15,812	20,179
Pred. similar to 40S ribosomal protein S3	15,623	14,168
Ribosomal protein S4, X-linked (Rps4x)	15,608	22,525
Pred. ribosomal protein s25 (Rps25)	15,597	15,107
Pred. similar to Ac1262	15,361	6,541 [†]
Ribosomal protein L9 (Rpl9)	15,328	15,018
Tumor protein, translationally controlled 1 (Tpt1)	14,796	15,898
Pred. similar to 60S ribosomal protein L7a	14,785	18,844
Ferritin, heavy polypeptide 1 (Fth1)	14,268	13,168
Ribosomal protein L29 (Rpl29)	14,249	19,063
Eukaryotic translation elongation factor 1 alpha 1	14,047	15,670
Pred. ribosomal protein S5 (Rps5)	13,772	12,954
Ribosomal protein L3 (Rpl3)	13,516	17,927
Laminin receptor 1 (ribosomal protein SA) (Lamr1)	13,281	16,180
Ribosomal protein S3 (Rps3)	13,274	13,387
Ribosomal protein L32 (Rpl32)	13,223	14,601
Ribosomal protein L6 (Rpl6)	13,023	13,800
Pred. similar to glyceraldehyde-3-phosphate dehydrogenase	12,883	20,653
Ribosomal protein S10 (Rps10)	12,629	15,551
Ribosomal protein S29 (Rps29)	12,375	14,993
Ribosomal protein S20 (Rps20)	12,191	16,162
Pred. Similar to 60S ribosomal protein L9	12,045	11,228
Pred. similar to 60S ribosomal protein L6 (neoplasm-related protein C140)	12,002	11,535
Pred. similar to ribosomal protein S7	11,952	16,878
Pred. similar to 40S ribosomal protein S20	11,767	13,423
Pred. similar to ribosomal protein S23	11,758	14,377
Pred. similar to ribosomal protein S26	11,619	11,565
Ribosomal protein L17 (Rpl17)	11,387	14,337
Pred. similar to ribosomal protein L15	11,382	10,145
Ubiquitin A-52 residue ribosomal protein fusion product 1	11,277	10,050
Pred. similar to Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV) ubiquitously expressed (fox derived)	11,094	13,392
Ribosomal protein S8 (Rps8)	11,085	17,872
Ribosomal protein L22 (Rpl22)	11,074	15,648
Pred. similar to ribosomal protein L31	11,007	12,825
Pred. similar to 60S ribosomal protein L32	10,602	12,524
Ribosomal protein, large, P1 (Rplp1)	10,529	9,656
Ribosomal protein S26 (Rps26)	10,390	11,011
Peptidylprolyl isomerase A (Ppia)	10,363	18,435
Ribosomal protein L27 (Rpl27)	10,242	14,789
Pred. Finkel-Biskis-Reilly murine sarcoma virus ubiquitously expressed (Fau)	10,237	13,329
Pred. similar to 60S ribosomal protein L17 (L23) (amino acid starvation-induced protein) (ASI)	10,203	12,418
Pred. similar to tubulin alpha-2 chain (alpha-tubulin 2)	8,769	20,050 [†]
Actin, beta (Actb)	7,779	14,422
Ribosomal protein L19 (Rpl19)	9,245	12,973
Pred. similar to l-lactate dehydrogenase A chain	8,749	12,938
Pred. capping protein (actin filament) muscle Z-line, alpha 2	9,542	12,599
Pred. similar to ribosomal protein S12	9,387	12,278
Pred. similar to 60S acidic ribosomal protein P2	8,699	12,266
Calmodulin 2 (Calm2)	7,108	12,054
Pred. similar to 60S ribosomal protein L7a	9,513	12,043
Ribosomal protein L21 (Rpl21)	8,710	11,910

Table W3. (continued)

mRNA	Mean Signal Strength*	
	ASML ^{wt} Exosomes	ASML-CD44 ^{kd} Exosomes
Pred. similar to ribosomal protein L21	9,121	11,850
Pred. triosephosphate isomerase 1 (Tpi1)	5,867	11,739 [†]
PAI-1 mRNA-binding protein (Pairbp1)	5,297	11,647 [†]
Pred. glutathione S-transferase, pi 1 (Gstp1)	7,189	11,480
Pred. similar to glyceraldehyde-3-phosphate dehydrogenase	9,042	11,083
Ribosomal protein S6 (Rps6)	8,109	10,953
Pred. similar to ribosomal protein S19	7,851	10,950
Large subunit ribosomal protein L36a (Rpl36a)	8,625	10,804
Pred. actin, gamma, cytoplasmic (Actg)	8,184	10,751
Similar to 60S ribosomal protein L21	7,251	10,610
Pred. similar to 40S ribosomal protein S3a (V-fos transformation effector protein)	6,252	10,107
Ornithine decarboxylase antizyme 1 (Oaz1)	6,971	10,027

*Mean signal strength was calculated from duplicates, respectively, triplicates, of two independently performed arrays after normalization (Chipster analysis and Agilent annotation). Only exosomal mRNA with a signal strength of >10,000 is shown.

[†]Signal strength with a more than two-fold change between ASML^{wt} and ASML-CD44^{kd} exosomes.

Table W4. mRNA Expression in ASML^{wt} and ASML-CD44^{kd} Cells (Signal Strength > 50,000).

mRNA	Mean Signal Strength*	
	ASML ^{wt} Cells	ASML-CD44 ^{kd} Cells
Hypothetical protein LOC310926	299,044	309,590
Actin, gamma 1 (Actg1)	296,979	221,969
Stefin A2 (Stfa2)	294,927	329,519
Ferritin, light polypeptide (Ftl)	246,290	277,091
Heat shock protein 8 (Hspa8)	246,290	143,431
Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV)	223,513	182,812
Similar to TRAF-binding protein	217,401	260,333
Testis-derived transcript (Tes)	214,408	143,431
Ferritin light chain 1-like	209,996	217,401
Similar to Ac1147	205,674	221,969
Carcinoembryonic antigen-related cell adhesion molecule 9 (Ceacam9)	202,842	249,728
Similar to glyceraldehyde-3-phosphate dehydrogenase	193,235	180,295
Similar to Rpl7a protein	193,235	179,050
Eukaryotic translation elongation factor 1 gamma (Eef1g)	168,221	91,406
Enolase 1 alpha	165,905	200,050
Ferritin heavy polypeptide 1 (Fth1)	162,491	121,450
Ubiquitin A-52 residue ribosomal protein fusion product 1 (Uba52)	162,491	133,826
Phosphoglycerate mutase 1 (brain) (Pgam1)	159,147	90,775
Similar to sex-determination protein homolog Fem1a	158,048	155,872
Similar to DKFZP434B168 protein	155,872	134,757
Peptidylprolyl isomerase A (cyclophilin A) (Ppia)	151,609	182,812
Coiled-coil-helix-coiled-coil-helix domain containing 2 (Chchd2)	150,562	111,757
Eukaryotic translation elongation factor 1 alpha 1 (Eef1a1)	147,464	151,609
Annexin A2 (Anxa2)	145,433	133,826
Similar to cleavage and polyadenylation factor 73 kDa (CPSF73kDa)	142,441	136,638
Phosphoglycerate kinase 1 (Ppk1)	136,638	100,721
Lactate dehydrogenase A (Ldha)	135,694	95,950
Similar to glyceraldehyde-3-phosphate dehydrogenase	135,694	118,129
Annexin A1 (Anxa1)	129,267	101,421
Heat shock protein HSP 90-beta	125,733	85,878
Transketolase (Tkt)	125,733	107,204
Capping protein (actin filament) muscle Z-line, alpha 2 (Capza2)	122,295	73,732
Eukaryotic translation initiation factor 2B, subunit 2 beta (Eif2b2)	120,611	105,728
Similar to elongation factor 1-alpha 1 (EF-1-alpha-1)	117,313	107,950
Heat shock cognate 71 kDa protein	115,698	66,451
Cathepsin D (Ctsd)	114,105	153,726
Similar to peptidylprolyl isomerase A (cyclophilin A)	110,985	137,588
Actin, beta (Actb)	106,464	48,645 [†]
Ubiquitin C (Ubc)	106,464	146,445
Tumor protein translationally controlled 1 (Tpr1)	104,273	153,726
Eukaryotic translation elongation factor 1 beta 2 (Eef1b2)	100,721	102,127
Ubiquitin B (Ubb)	97,290	95,950
Keratin 18 (Krt18)	95,950	19,216 [†]
Hypothetical gene supported by AF152002 (LOC290595)	94,629	56,267
Tubulin beta 4B class IVb (Tubb4b)	93,976	72,717
Transmembrane emp24-like trafficking protein 10 (Tmed10)	91,406	131,984
Interferon gamma-induced GTPase (Igtip)	90,775	113,317

Table W4. (continued)

mRNA	Mean Signal Strength*	
	ASML ^{wt} Cells	ASML-CD44 ^{kd} Cells
Similar to elongation factor 1-gamma (EF-1-gamma)	90,775	40,342 [†]
Glutathione S-transferase pi 1 (Gstp1)	86,475	53,232
Heat shock protein 1 (chaperonin 10) (Hspe1)	86,475	50,360
Glutathione peroxidase 2 (Gpx2)	85,285	13,401 [†]
Nucleophosmin (nucleolar phosphoprotein B23, Numatrin) (Npm1)	84,111	92,682
RAN member RAS oncogene family (Ran)	84,111	69,273
Progressive external ophthalmoplegia 1 (Peo1)	81,811	182,812 [†]
Hypothetical protein LOC687872	79,024	71,220
Eukaryotic translation elongation factor 1 delta (Eef1d)	77,398	60,725
Poly(A)-binding protein, cytoplasmic 1 (Pabpc1)	77,398	115,698
Eukaryotic translation elongation factor 2 (Eef2)	76,863	38,166 [†]
Guanine nucleotide binding protein beta polypeptide 2 like 1 (Gnb2l1)	76,332	39,512
Cytochrome c oxidase subunit VIa polypeptide 1 (Cox6a1)	75,281	139,509
NADH-ubiquinone oxidoreductase chain 1	74,761	209,996 [†]
Cytochrome c oxidase subunit VIIa polypeptide 2 like (Cox7a2l)	73,732	64,634
Mitogen-activated protein kinase 3 (MAPK3)	73,732	80,684
Galactoside-binding soluble 3 (Lgals3)	73,223	80,684
Cytochrome b	72,717	181,549 [†]
Non-metastatic cells 2 protein (NM23B) (Nme2)	72,717	65,083
Myosin light polypeptide 6 smooth muscle and non-muscle-like (Myf6)	72,214	105,728
RT1 class Ia, locus A1 (RT1-A1)	71,716	90,775
Cell division cycle 37 homolog (Cdc37)	69,755	46,988
Glyceraldehyde-3-phosphate dehydrogenase (GAPDH)	69,755	52,864
CD24	69,273	28,725
Complement component 1q subcomponent binding protein (C1qbp)	69,273	67,847
Hematological and neurological expressed 1 (Hn1)	69,273	22,073 [†]
ATP synthase, H ⁺ transporting, mitochondrial Fo complex C2 (Atp5g2)	68,794	53,602
Phosphoglycerate dehydrogenase (Phgdh)	68,319	72,214
Proteasome subunit beta type 4 (Psmb4)	68,319	39,512
Heat shock protein 90 alpha class B member 1 (Hsp90ab1)	67,378	44,762
Ornithine decarboxylase antizyme 1 (Oaz1)	67,378	62,432
Similar to glyceraldehyde-3-phosphate dehydrogenase	67,378	52,864
ATP synthase, H ⁺ transporting, mitochondrial Fo complex d (Atp5h)	66,913	72,214
Thymosin beta 4. X-linked (Tmsb4x)	66,913	55,109
High-mobility group nucleosome binding domain 1 (Hmgn1)	65,992	85,878
Phosphatidylethanolamine-binding protein 1 (Pebp1)	65,992	76,332
Histidine triad nucleotide-binding protein 1 (Hint1)	65,536	74,761
Eukaryotic translation initiation factor 3, subunit I (Eif3i)	65,083	59,889
ATP synthase subunit d	64,634	65,992
Heat shock protein 1 (chaperonin) (Hspd1)	64,187	50,360
Similar to RIKEN cDNA 3100001N19 (LOC306079)	63,304	54,728
H6 family homeobox 1 (Hmx1)	62,866	59,064
GNAS complex locus (Gnas), transcript variant 3	62,432	120,611
Ly6/Plaur domain containing 3 (Lypd3)	62,432	45,703
ATP synthase, H ⁺ transporting, mitochondrial Fo complex E (Atp5i)	61,573	64,187
Similar to glyceraldehyde-3-phosphate dehydrogenase (LOC305194)	61,573	47,315
Prothymosin alpha (Ptma)	59,475	59,889
Family with sequence similarity 49, member B (Fam49b)	58,251	49,667
ADP-ribosylation factor 5 (Arf5)	57,449	32,317
GTPase IMAP family member 9 (Gimap9)	57,449	75,805
Enolase 1alpha (Eno1) transcript variant 2	57,052	70,728
Cysteine-rich protein 2 (Crip2)	56,658	42,055
ATP synthase, H ⁺ transporting, F1 complex α 1 cardiac muscle (Atp5a1)	55,878	67,378
Reactive oxygen species modulator 1 (Romo1)	55,878	32,768
Proteasome 26S subunit ATPase 5 (Psmc5)	55,492	26,801 [†]
TIMP metalloproteinase inhibitor 2 (Timp2)	55,109	214,408 [†]
Cytochrome c oxidase subunit 1	53,975	190,575 [†]
Eukaryotic translation initiation factor 4H (Eif4h)	51,776	21,469 [†]
T-box 21 (Tbx21)	51,776	48,983
Dextrin (Dstn)	51,419	36,358
Similar to keratin complex 1 acidic gene 18	51,419	7,913 [†]
Mesothelin (Msln)	51,063	58,251
Tubulin, alpha 1B (Tuba1b)	50,012	63,744
ATP synthase subunit a	38,699	208,545 [†]
Cytochrome c oxidase subunit 3	42,348	167,059 [†]
S100 calcium-binding protein A6 (S100a6)	40,623	165,905 [†]
Caveolin 1 (Cav1)	43,238	155,872 [†]
Cytochrome c oxidase subunit 2	39,787	146,445 [†]
NADH-ubiquinone oxidoreductase chain 4	34,397	128,375 [†]
Kelch domain containing 2 (Klhd2)	38,431	100,721 [†]
ATP synthase F1 complex epsilon (Atp5e)	40,623	94,629 [†]
Growth arrest specific 5 (Gas5)	42,055	93,976 [†]

Table W4. (continued)

mRNA	Mean Signal Strength*	
	ASML ^{wt} Cells	ASML-CD44 ^v ^{kd} Cells
S100 calcium-binding protein A4 (S100a4)	5,405	90,148 [†]
Serum deprivation response (Sdpr)	24,154	85,285 [†]
Dynein heavy-10 (Dnah10)	49,667	78,478
Rap GEF 6 (Rapgef6)	48,983	77,936
NADH-ubiquinone oxidoreductase chain 2	7,750	72,717 [†]
SMT3 suppressor of mif two 3 homolog 2 (Sumo2)	49,667	70,728
Caveolin 2 (Cav2)	23,170	68,794 [†]
Thioredoxin 1 (Txn1)	44,453	66,913
Myosin light chain 6 (Myl6)	46,341	65,992
Translationally controlled tumor protein (TCTP)	43,538	65,536
Hepatocyte malignant transforming factor	38,431	65,083
Ubiquinol-cytochrome c reductase complex isoform b	43,841	62,866
Eukaryotic translation initiation factor 4E binding protein 1 (Eif4ebp1)	34,397	62,432
Cathepsin B (Ctsb)	36,611	60,725
Stearoyl-CoA desaturase delta (Scd)	23,494	59,064 [†]
Parkinson protein 7 (Park7)	37,902	57,849
Glutathione peroxidase 4 (Gpx4)	46,021	57,449
Acidic (leucine-rich) nuclear phosphoprotein 32B (Anp32b)	27,175	57,449
Clathrin light chain A (Clta)	29,944	56,267
Suppressor of initiator codon mutations	33,225	54,728
Aminolevulinate dehydratase (Alad)	38,699	54,350
Protein tyrosine phosphatase F (Ptpnf)	15,076	53,602 [†]
H1 histone family member 0 (H1f0)	5,043	53,232 [†]
Histone cluster 1 H2ak (Hist1h2ak)	44,762	52,864
2-5 oligoadenylate synthetase 1B (Oas1b)	35,120	52,499
Eukaryotic translation initiation factor 3K (Eif3k)	48,645	50,711
Cyclin-dependent kinase inhibitor 2A (Cdkn2a)	27,746	50,711
Programmed cell death 5 (Pcd5)	28,329	50,360

*Mean signal strength was calculated from duplicates, respectively, triplicates, after normalization (Chipster analysis and Agilent annotation) of two independently performed microarray analyses. Only cellular mRNA with a signal strength of >50,000 is shown.

[†]Signal strength with a more than two-fold change between ASML^{wt} and ASML-CD44^v^{kd} cells.

Table W5. Distinctly Recovered mRNA in ASML^{wt} and ASML-CD44^v^{kd} Exosomes *versus* Cells.

mRNA	Mean Signal Strength*		ASML ^{wt} Exosomes <i>versus</i> Cells	Mean Signal Strength*		ASML-CD44 ^v ^{kd} Exosomes <i>versus</i> Cells
	ASML ^{wt}			ASML-CD44 ^v ^{kd}		
	Exosomes	Cells		Exosomes	Cells	
Translationally controlled tumor protein 1 (Tprt1)	21,555	104,273	0.21	20,863	153,726	0.14
Ferritin 1 (Fth1)	21,061	169	124.70	18,061	131	138.20
Laminin receptor 1 (Lamr1)	19,878	nd [†]	∞	20,967	nd	∞
Keratin complex 1-19 (Krt1-19)	14,348	73	197.89	13,274	79	168.47
Actin, beta (Actb)	12,963	106,464	0.12	18,280	48,645	0.38
Calmodulin 2 (Calm2)	12,033	51,776	0.23	15,726	60,725	0.26
Ornithine decarboxylase antizyme 1 (Oaz1)	11,924	90	132.67	13,427	80	166.90
Metallothionein (MT1a)	9,659	596	16.20	5,546	526	10.54
Peroxiredoxin 1 (Prdx1)	9,436	77	122.27	12,336	104	118.65
Non-metastatic cells 2 (Nme2)	9,417	nd	∞	9,113	nd	∞
Phosphoglycerate kinase 1 (Pgk1)	9,391	89	105.21	12,013	131	91.92
Annexin A2 (Anxa2)	9,196	145,433	0.06	8,734	133,826	0.07
Synaptic vesicle glycoprotein 2b (Sv2b)	9,153	nd	∞	3,304	nd	∞
Annexin A1 (Anxa1)	9,072	129,267	0.07	9,408	101,421	0.09
Villin 2 (Vil2)	9,071	nd	∞	7,751	nd	∞
Diazepam binding inhibitor (Dbi)	8,840	80	109.88	10,165	78	130.81
Macrophage migration inhibitory factor (Mif)	8,578	135	63.40	9,533	85	112.10
Galactose binding lectin, soluble 3 (Lgals3)	8,566	72	119.79	6,559	68	96.29
Peroxiredoxin 2 (Prdx2)	8,476	370	22.93	10,633	187	56.74
Cell division cycle 37 homolog (Cdc37)	8,377	405	20.71	11,208	269	41.71
S100 calcium-binding protein A6 (S100a6)	8,297	1,287	6.44	7,497	357	21.00
Brain protein I3 (Bri3)	8,064	21,028	0.38	10,520	15,936	0.66
Cofilin 1 (Cfl1)	8,043	46,988	0.17	12,817	25,709	0.50
Basic keratin complex 2-8 (Krt2-8)	8,015	nd	∞	7,486	nd	∞
Phosphatidylethanolamine-binding protein (Pbp)	7,653	843	9.07	8,791	867	10.14
Proteasome subunit beta 1 (Psm1)	7,626	80	95.46	8,227	68	121.61
Aldose reductase 1-B4 (Akr1b4)	7,411	4,096	1.81	8,827	2,937	3.01

Table W5. (continued)

mRNA	Mean Signal Strength*		ASML ^{wt} Exosomes versus Cells	Mean Signal Strength*		ASML-CD44v ^{kd} Exosomes versus Cells
	ASML ^{wt}			ASML-CD44v ^{kd}		
	Exosomes	Cells		Exosomes	Cells	
Profilin 1 (Pfn1)	6,662	187	35.55	5,998	67	89.27
Heat shock protein 8 (Hspa8)	6,577	6,165	1.06	4,584	3,236	1.41
Cell division cycle 42 (Cdc42)	6,492	519	12.51	10,242	298	34.35
Glutathione peroxidase 2 (Gpx2)	6,434	1,226	5.25	4,124	1,209	3.41
Cytochrome c, somatic (Cycs)	6,401	343	18.69	8,157	910	8.96
Protein phosphatase 1-14B (Ppp1r14b)	6,280	34,397	0.18	4,807	22,227	0.22
Adaptor-related protein complex 2-sigma 1 (Ap2s1)	6,237	21,619	0.29	7,003	12,944	0.54
Transmembrane trafficking protein 21 (Ttmp21)	6,161	nd	∞	5,505	nd	∞
Proliferating cell nuclear antigen (Pcna)	5,845	21,469	0.27	7,698	11,426	0.67
Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta (Ywhaz)	5,843	4,012	1.46	7,178	5,293	1.36
Proteasome beta-4 (Psmb4)	5,697	5,113	1.11	6,876	1,053	6.53
Superoxide dismutase 1 (Sod1)	5,639	49,324	0.11	6,120	33,225	0.18
ATPase, H+ transporting, V0-C (Atp6v0c)	5,550	13,777	0.40	5,220	10,441	0.50
Proteolipid protein 2 (Plp2)	5,549	3,692	1.50	4,413	4,939	0.89
Non-metastatic cells 1 (Nme1)	5,487	20,453	0.27	5,242	16,845	0.31
C-terminal binding protein 1 (Ctbp1)	5,416	24,492	0.22	8,964	11,191	0.80
ARP2 actin-related 2 (Actr2)	5,387	5,914	0.91	7,636	5,480	1.39
Cytochrome c oxidase VIIIb (Cox7b)	5,263	74	71.59	5,238	69	75.83
Integrin beta 4 binding protein (Itgb4bp)	5,252	8,719	0.60	4,039	27,939	0.14
Proteasome beta 2 (Psmb2)	5,169	176	29.36	5,941	74	80.81
Radixin (Rdx)	5,165	17,929	0.29	4,787	187	25.54
Cyclin D1 (Cnd1)	5,160	4,576	1.13	8,670	1,783	4.86
Peptidylprolyl isomerase B (Ppib)	5,083	68	75.14	3,001	72	41.68
S-phase kinase-associated 1A (Skp1a)	4,916	10,369	0.47	5,992	5,914	1.01
Tubulin beta 2 (Tubb2)	4,851	609	7.97	6,840	1,160	5.90
SMT3 suppressor of mif two 3-1 (Sumo1)	4,843	7,913	0.61	7,168	8,192	0.88
Glutathione peroxidase 4 (Gpx4)	4,840	93	52.01	4,487	75	60.19
Chromobox homolog 3 (Cbx3)	4,839	1,113	4.35	5,945	798	7.45
Poly(A)-binding protein 1 (Pabpc1)	4,788	186	25.73	3,177	239	13.30
Dynein light chain 2A (Dncl2a)	4,747	2,320	2.05	3,733	1,003	3.72
Aldo-keto reductase 1-A1 (Akr1a1)	4,656	9,345	0.50	7,095	12,161	0.58
Tyrosine 3/tryptophan 5-monooxygenase ε (Ywhae)	4,646	31,433	0.15	9,089	33,689	0.27
MAP kinase kinase 2 (Map2k2)	4,573	30,362	0.15	4,357	26,801	0.16
S100 calcium-binding protein A4 (S100a4)	4,495	92	48.98	4,424	1,261	3.51
Dynein light chain 1 (Dncl1)	4,444	333	13.34	3,237	508	6.37
ATX1-1 (Atox1)	4,389	13,308	0.33	3,323	6,383	0.52
Beta-2 microglobulin (B2m)	4,380	26,987	0.16	3,997	22,694	0.18
Aldolase A (Aldoa)	4,313	19,619	0.22	2,549	8,841	0.29
Lactate dehydrogenase A (Ldha)	4,278	333	12.84	3,623	498	7.28
RAN, member RAS oncogene family (Ran)	4,266	72	59.66	4,704	167	28.24
Hepatoma-derived growth factor (Hdgf)	4,232	48,309	0.09	5,068	35,364	0.14
Catenin alpha 1 (Ctnn1)	4,168	3,169	1.32	7,307	3,083	2.37
Complement component 1q (C1qbp)	4,158	516	8.07	4,389	2,759	1.59
Fertility protein SP22 (Park7)	4,146	nd	∞	5,720	nd	∞
Thioredoxin 1 (Txn1)	4,141	44,453	0.09	3,567	66,913	0.05
Chaperonin subunit 4 (Cct4)	4,101	127	32.26	4,233	162	26.13
Transaldolase 1 (Taldo1)	3,997	10,441	0.38	6,234	13,308	0.47
NADH dehydrogenase 1 alpha-5 (Ndufa5)	3,923	83	47.43	4,170	73	57.12
Cytochrome c oxidase Va (Cox5a)	3,901	452	8.63	2,557	252	10.13
cAMP-regulated phosphoprotein 19 (Arpp19)	3,899	15,608	0.25	2,628	7,132	0.37
Proteasome 26S subunit 3 (Psm3)	3,880	556	6.97	4,621	85	54.34
Cytochrome c oxidase subunit IV-1 (Cox4i1)	3,864	79	49.04	3,441	77	44.59
Amino-terminal enhancer of split (Aes)	3,864	1,287	3.00	3,421	750	4.56
Proteasome beta-3 (Psm3)	3,860	2,610	1.48	5,159	152	33.89
Myelocytomatosis viral oncogene- (Myc)	3,854	792	4.86	3,028	508	6.00
LIM domain only 4 (Lmo4)	3,812	322	11.85	4,896	413	11.85
Cyclin-dependent kinase 4 (Cdk4)	3,807	639	5.96	4,695	942	4.98
Spastic paraplegia 21 (Spg21)	3,786	3,421	1.11	3,641	1,351	2.69
Proteasome alpha-6 (Psm6)	3,740	311	12.03	4,015	81	49.56
FK506 binding protein 1a (Fkbp1a)	3,734	91	41.26	3,195	91	35.06
Cold shock domain protein A (CsdA)	3,682	107	34.45	4,488	81	55.40
Neural precursor cell expressed, developmentally downregulated 8 (Nedd8)	3,674	4,705	0.78	2,801	9,675	0.29
Rho GDP dissociation inhibitor (GDI) alpha	3,662	202	18.11	5,106	95	53.74
Guanine nucleotide binding protein α inhibitor 2 (Gnai2)	3,635	1,846	2.00	3,602	1,399	2.57
Peroxiredoxin 5 (Prdx5)	3,602	71	51.07	3,060	71	43.09
DnaJ (Hsp40)subfamily A-2 (Dnaja2)	3,586	76	47.44	5,134	78	65.61
Spermidine/spermine N ¹ -acetyl transferase (Sat)	3,571	7,332	0.49	3,937	15,500	0.25

Table W5. (continued)

mRNA	Mean Signal Strength*		ASML ^{wt} Exosomes versus Cells	Mean Signal Strength*		ASML-CD44 ^{kd} Exosomes versus Cells
	ASML ^{wt}			ASML-CD44 ^{kd}		
	Exosomes	Cells		Exosomes	Cells	
CD24	3,455	2,353	1.47	4,445	3,541	1.26
Aldo-keto reductase 1-B8 (Akr1b8)	3,432	30,153	0.11	1,313	6,794	0.19
Annexin A4 (Anxa4)	3,421	101	33.83	4,578	90	50.94
Tubulin alpha 1 (Tuba1)	3,388	28,924	0.12	5,870	14,869	0.39
Galactokinase 1 (Galk1)	3,366	91	37.19	4,419	95	46.51
ARP10 actin-related protein 10 (Actr10)	3,336	11,666	0.29	4,332	5,793	0.75
S-adenosylhomocysteine hydrolase (Ahcy)	3,328	nd	∞	2,459	nd	∞
NADH dehydrogenase 1 alpha 11 (Ndufa11)	3,324	180	18.49	3,244	155	20.87
t-complex protein 1 (Tcpl)	3,294	25,709	0.13	3,109	21,769	0.14
Phosphoserine phosphatase (Psp)	3,287	107	30.75	3,115	94	33.01
Inosine 5-monophosphate dehydrog.2 (Impdh2)	3,261	nd	∞	2,763	nd	∞
Chaperonin subunit 3 (Cct3)	3,249	5,753	0.56	4,492	5,955	0.75
Protein phosphatase 2a alpha (Ppp2ca)	3,218	2,402	1.34	3,835	2,353	1.63
Upregulated by 1,25-dihydroxyvitamin D-3 (Txnip)	3,214	3,492	0.92	6,130	6,039	1.02
Microtubule-associated protein light chain 1A/1B light 3 (Map1lc3b)	3,176	1,438	2.21	6,066	449	13.51
Glucose phosphate isomerase (Gpi)	3,158	71	44.78	3,444	87	39.39
Annexin A5 (Anxa5)	3,115	5,634	0.55	2,642	3,566	0.74
Coated vesicle membrane protein (Rnp24)	3,115	nd	∞	2,593	nd	∞
Peroxiredoxin 6 (Prdx6)	3,108	74	41.98	3,706	67	55.54
GDP dissociation inhibitor 2 (Gdi2)	3,077	70	44.24	5,625	69	81.43
Cytochrome c oxidase subunit Vb (Cox5b)	3,037	83	36.46	2,219	74	30.19
MAP kinase-interacting serine/threonine kinase 2 (Mknk2)	3,025	nd	∞	3,221	nd	∞

*mRNA was ordered according to the signal strength in ASML^{wt} exosomes (mean signal strength was calculated from duplicates, respectively, triplicates, after normalization of two independently performed microarray analyses. Only defined mRNA with a mean signal strength of >3000 was included.

†nd: below the detection limit in cell extract. There has been no ASML-CD44^{kd} mRNA opposing regulated in cells versus exosomes.

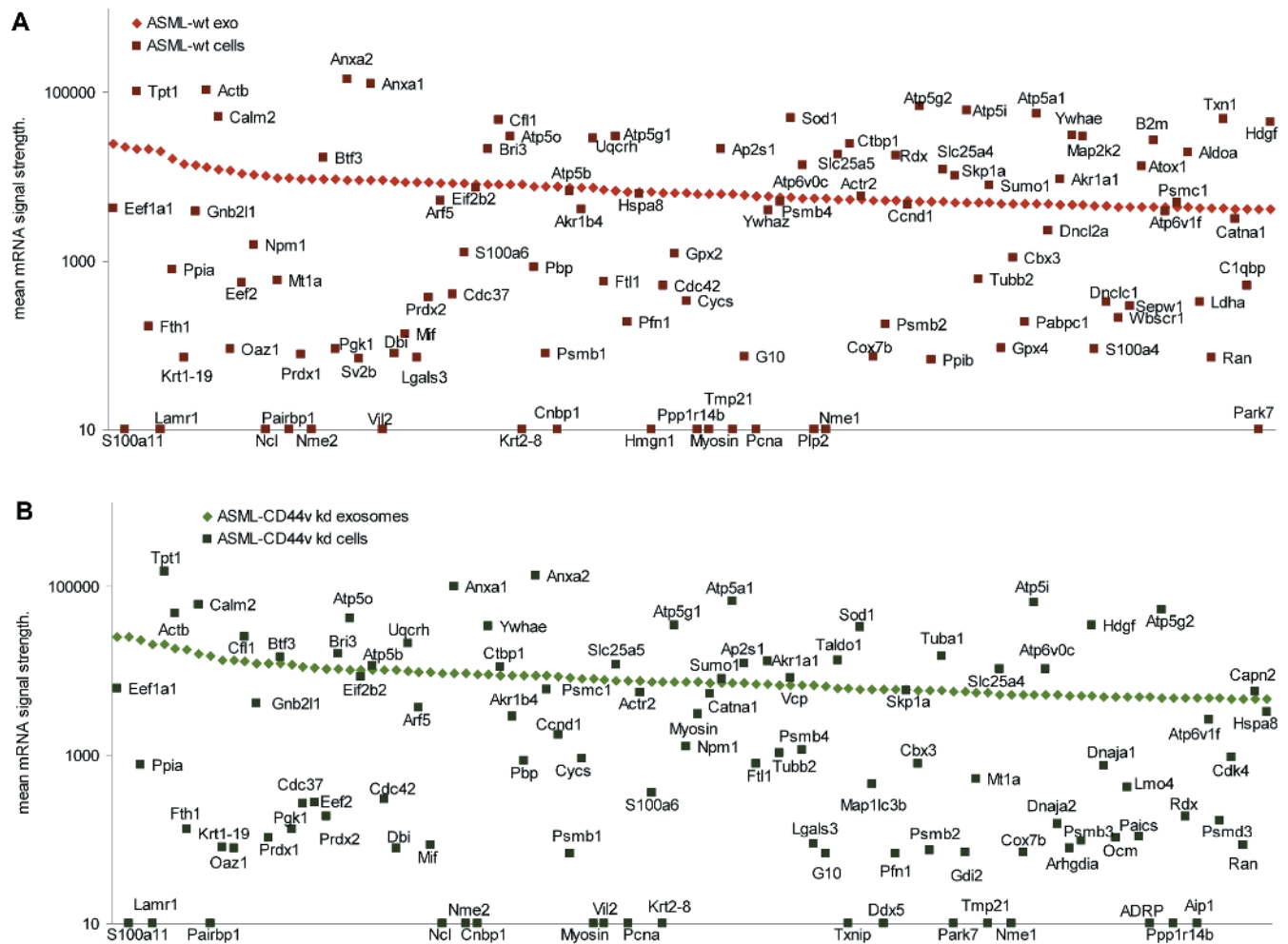


Figure W1. Comparison of ASML^{wt} and ASML-CD44v^{kd} exosomal *versus* cellular mRNA. (A) The 100 exosomal ASML^{wt} mRNAs with the highest signal strength and, for comparison, the corresponding cellular mRNAs and (B) the 100 exosomal ASML-CD44v^{kd} mRNAs with the highest signal strength and, for comparison, the corresponding cellular mRNAs are shown. The mean signal strength of duplicates, respectively, triplicates, of two independent microarray analyses is shown. For more detailed information and full names, see Table W5. Independent of CD44v expression, the composition of exosomal and cellular mRNAs differs strongly.

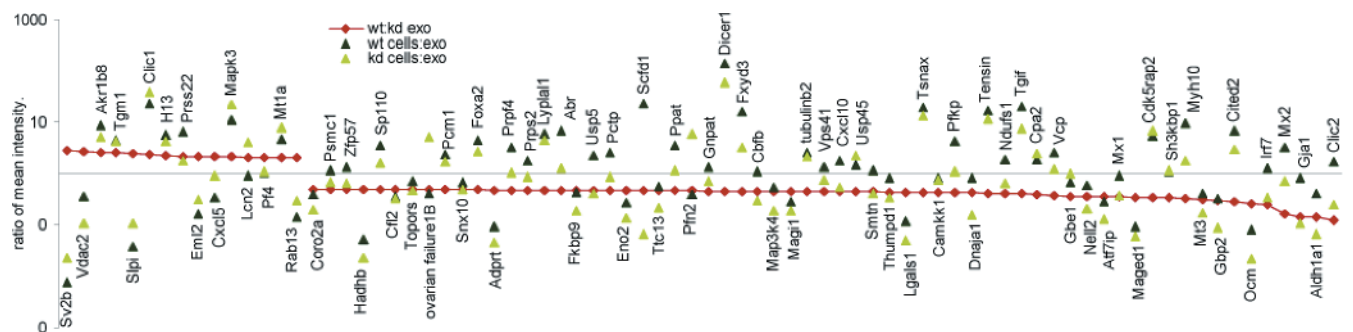


Figure W2. Comparison of the ratio of exosomal ASML^{wt} to ASML-CD44v^{kd} mRNA with the ratio of cellular to exosomal mRNA: Scatter blot of exosomal mRNA that differs more than two-fold between ASML^{wt} *versus* ASML-CD44v^{kd} exosomes as well as the ratios of the ASML^{wt} and ASML-CD44v^{kd} cellular to exosomal mRNA. For abbreviations, see Tables W4 and W5. With four exceptions (ovarian failure1B, Scfd1, Pfn2, and Clic2), signals for both ASML^{wt} and ASML-CD44v^{kd} cellular mRNA are either enriched or reduced compared to the exosomal mRNA signal strength. This finding strongly argues against CD44v being directly engaged in mRNA recruitment into MVB.

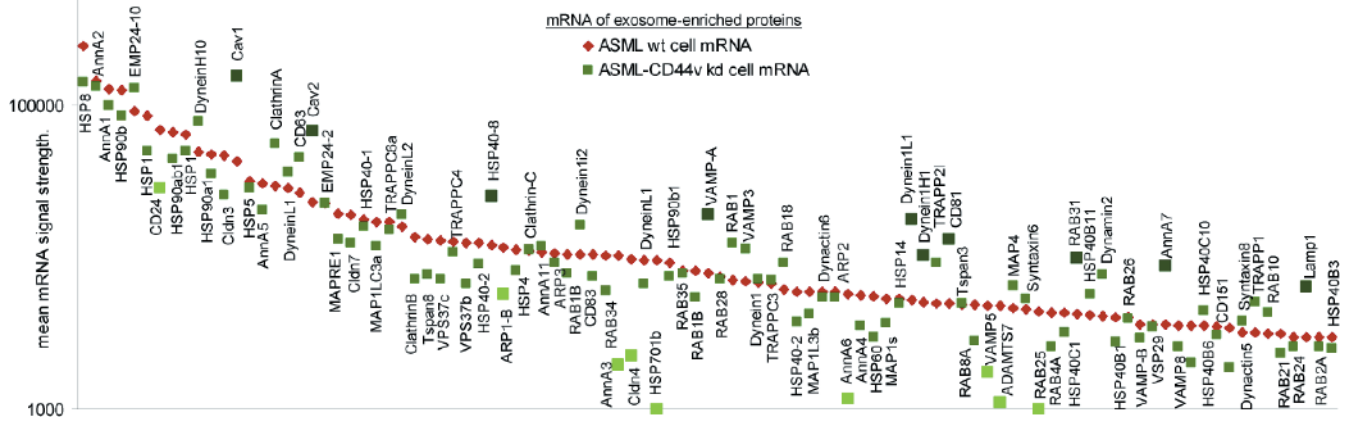


Figure W3. Comparison of cellular ASML^{wt} and ASML-CD44v^{kd} mRNA whose proteins are enriched in exosomes: Scatter blot of mean cellular mRNA signal strength in ASML^{wt} and ASML-CD44v^{kd} cells. Only mRNAs whose proteins are known to be enriched in exosomes are shown, where from 164 mRNAs the 100 with high signal strength have been selected. The mean signal strength of duplicates, respectively, triplicates, of two independent microarray analyses is shown. mRNAs with a more than two-fold change in the signal strength between ASML^{wt} *versus* ASML-CD44v^{kd} cells are indicated by larger symbols. For abbreviations, see Table W3. In comparison to the impact of CD44v on the total cellular mRNA, CD44v rather abundantly affects mRNA, where translation products are enriched in exosomes.

Table W6. miRNA in ASML^{wt} and ASML-CD44v^{kd} Exosomes and Cells.

(A) Exosomal miRNA			
miRNA	Mean Signal Strength*		ASML ^{wt} /ASML-CD44v ^{kd} Exosomes
	ASML ^{wt}	ASML-CD44v ^{kd}	
Exosomes			
let-7a	2,710	2,808	0.97
let-7b	5,038	14,760	0.34 [†]
let-7c	24,097	29,257	0.82
let-7d	1,148	377	3.04 [†]
let-7e	12,646	32,111	0.39 [†]
let-7f	961	971	0.99
let-7i	346	561	0.62
miR-101b	285	853	0.33 [†]
miR-103	1,468	637	2.30 [†]
miR-106b	1,520	2,228	0.68
miR-10a-3p	425	484	0.88
miR-10a-5p	166	445	0.37 [†]
miR-122	236	400	0.59
miR-124	2,332	1,163	2.00 [†]
miR-125a-3p	1,574	1,815	0.87
miR-125a-5p	9,079	2,077	4.37 [†]
miR-125b-3p	29,549	5,541	5.33 [†]
miR-125b-5p	2,144	1,825	1.18
miR-127	1,209	356	3.40 [†]
miR-129	15,607	7,956	1.96
miR-130b	3,032	2,086	1.45
miR-138	1,791	3,036	0.59
miR-142-5p	541	990	0.55
miR-147	337	496	0.68
miR-148b-3p	1,924	528	3.64 [†]
miR-150	2,415	2,151	1.12
miR-183	429	292	1.47
miR-184	5,936	7,438	0.80
miR-185	655	1,510	0.43 [†]
miR-193	416	191	2.17 [†]
miR-196a	293	416	0.70
miR-200b	492	339	1.45
miR-200c	697	511	1.36
miR-204	24,335	23,711	1.03
miR-206	6,513	4,944	1.32
miR-207	4,876	8,012	0.61
miR-208	686	941	0.73
miR-21	11,462	5,333	2.15 [†]
miR-214	9,826	3,482	2.82 [†]
miR-22	427	945	0.45 [†]
miR-221	1,421	979	1.45
miR-222	848	909	0.93
miR-23a	692	754	0.92
miR-23b	1,401	1,120	1.25
miR-24	35,571	6,978	5.10 [†]
miR-26b	7,022	26,350	0.27
miR-290	12,052	11,948	1.01
miR-291a-5p	5,534	627	8.83 [†]
miR-296	33,359	9,235	3.61 [†]
miR-298	266	454	0.59
miR-29a	1,808	911	1.99
miR-29b	1,281	676	1.90
miR-29c	1,118	533	2.10 [†]
miR-300-3p	1,951	1,213	1.61
miR-300-5p	65,490	7,287	8.99 [†]
miR-30b-3p	2,348	5,402	0.43 [†]
miR-30b-5p	345	401	0.86
miR-30c	5,715	1,870	3.06 [†]
miR-31	533	563	0.95
miR-323	1,910	964	1.98
miR-325-3p	7,129	5,608	1.27
miR-325-5p	522	1,617	0.32 [†]
miR-327	463	392	1.18
miR-329	745	1,048	0.71
miR-330	285	1,181	0.24 [†]
miR-331	585	4,471	0.13
miR-341	13,956	9,369	1.49
miR-342-5p	404	999	0.40 [†]
miR-347	801	1,084	0.74
miR-34a	650	5,420	0.12 [†]

Table W6. (continued)

(A) Exosomal miRNA			
miRNA	Mean Signal Strength*		ASML ^{wt} /ASML-CD44v ^{kd} Exosomes
	ASML ^{wt}	ASML-CD44v ^{kd}	
Exosomes			
miR-34c	410	565	0.72
miR-350	245	455	0.54
miR-351	3,707	1,558	2.38 [†]
miR-352	435	525	0.83
miR-361	777	950	0.82
miR-363	1,692	181	9.34 [†]
miR-370	98	579	0.17 [†]
miR-377	324	753	0.43 [†]
miR-381	433	480	0.90
miR-382	18,070	3,630	4.98 [†]
miR-409-5p	375	1,801	0.21 [†]
miR-423	4,548	1,448	3.14 [†]
miR-466c	403	674	0.60
miR-471	432	826	0.52
miR-494	31,123	14,605	2.13 [†]
miR-500	1,225	548	2.24 [†]
miR-503	14,520	7,329	1.98
miR-540	378	578	0.66
miR-542-3p	14,225	2,133	6.67 [†]
miR-542-5p	463	213	2.18 [†]
miR-551b	1,794	2,050	0.87
miR-652	436	129	3.38 [†]
miR-664	386	592	0.65
miR-743a	247	611	0.40 [†]
miR-743b	277	497	0.56
miR-7a	569	5,188	0.11 [†]
miR-872	851	706	1.21
miR-874	3,096	1,075	2.88 [†]
miR-877	4,763	4,625	1.03
miR-96	417	118	3.54 [†]
miR-98	453	559	0.81
miR-99b	1,359	5,133	0.26 [†]

(B) Cellular miRNA			
miRNA	Mean Signal Strength*		ASML ^{wt} /ASML-CD44v ^{kd} Cells
	ASML ^{wt}	ASML-CD44v ^{kd}	
Cells			
let-7a	13,560	15,699	0.86
let-7b	7,125	10,683	0.67
let-7c	7,963	15,121	0.53
let-7d	6,440	5,844	1.10
let-7e	1,158	3,018	0.38 [†]
let-7f	15,565	16,357	0.95
let-7i	4,485	5,129	0.87
miR-100	935	1,401	0.67
miR-101b	700	488	1.43
miR-103	2,369	2,380	1.00
miR-106b	4,409	4,475	0.99
miR-107	2,664	2,503	1.06
miR-10a-5p	5,116	6,966	0.73
miR-1224	992	566	1.75
miR-125a-5p	630	1,424	0.44 [†]
miR-125b-5p	32,799	46,281	0.71
miR-128	491	429	1.15
miR-130a	3,199	5,535	0.58
miR-130b	1,396	1,288	1.08
miR-140	689	814	0.85
miR-141	1,744	607	2.87 [†]
miR-148b-3p	501	466	1.08
miR-151	857	1,056	0.81
miR-15b	5,295	5,005	1.06
miR-16	10,127	9,008	1.12
miR-181c	428	708	0.60
miR-181d	453	467	0.97
miR-182	948	845	1.12
miR-183	1,854	2,431	0.76

Table W6. (continued)

miRNA	Mean Signal Strength*		ASML ^{wt} /ASML-CD44 ^{kd} Cells
	ASML ^{wt}	ASML-CD44 ^{kd}	
	Cells		
miR-185	749	432	1.73
miR-186	1,606	610	2.63 [†]
miR-193	329	498	0.66
miR-1949	2,018	614	3.29 [†]
miR-196c	793	456	1.74
miR-200a	2,646	560	4.73 [†]
miR-200b	4,467	949	4.71 [†]
miR-200c	1,192	186	6.40 [†]
miR-203	1,524	2,645	0.58
miR-207	286	523	0.55
miR-21	57,732	47,159	1.22
miR-210	747	1,056	0.71
miR-218a	307	548	0.56
miR-22	4,177	5,884	0.71
miR-221	2,233	5,340	0.42
miR-222	1,217	1,459	0.83
miR-23a	12,378	22,556	0.55
miR-23b	4,652	5,909	0.79
miR-24	6,898	13,293	0.52
miR-25	4,572	3,947	1.16
miR-26a	3,053	4,094	0.75
miR-26b	2,252	3,084	0.73
miR-27a	4,819	12,832	0.38 [†]
miR-27b	2,823	3,969	0.71
miR-28	555	431	1.29
miR-29a	37,744	37,658	1.00
miR-29b	11,953	24,913	0.48 [†]
miR-29c	2,719	2,862	0.95
miR-301a	469	1,559	0.30 [†]
miR-30a	928	1,013	0.92
miR-30b-5p	1,262	1,222	1.03
miR-30c	2,404	2,207	1.09
miR-30d	492	478	1.03
miR-30e	1,160	1,407	0.82
miR-31	8,921	1,2526	0.71
miR-32	378	623	0.61

Table W6. (continued)

miRNA	Mean Signal Strength*		ASML ^{wt} /ASML-CD44 ^{kd} Cells
	ASML ^{wt}	ASML-CD44 ^{kd}	
	Cells		
miR-322	614	453	1.36
miR-324-3p	971	1,041	0.93
miR-335	433	531	0.82
miR-34a	597	1,305	0.46 [†]
miR-34b	669	355	1.89
miR-34c	720	320	2.25 [†]
miR-361	414	436	0.95
miR-365	1,493	1,426	1.05
miR-374	539	418	1.29
miR-425	386	547	0.71
miR-429	2,625	544	4.83 [†]
miR-466b-1	1,129	1,481	0.76
miR-466b-2	1,296	1,643	0.79
miR-466c	1,015	1,430	0.71
miR-485	312	579	0.54
miR-494	707	417	1.70
miR-500	432	457	0.95
miR-582	407	92	4.44 [†]
miR-652	1,366	1,756	0.78
miR-672	394	1,063	0.37 [†]
miR-741-3p	11	857	0.01 [†]
miR-764	312	647	0.48 [†]
miR-7a	1,850	373	4.96 [†]
miR-872	692	748	0.92
miR-883	7	438	0.02 [†]
miR-9	486	387	1.25
miR-93	1,936	1,727	1.12
miR-96	5,737	5,758	1.00
miR-98	1,139	1,932	0.59
miR-99a	152	4,253	0.04 [†]
miR-99b	528	891	0.59

*All miRNAs (in alphabetic order) with a mean signal strength (quadruplicates, two independently performed microarray analyses) after normalization (Chipster analysis and Agilent annotation by Agilent Feature Extraction software) of >400 in ASML^{wt} or ASML-CD44^{kd} exosomes or cells are shown. [†]miRNA that differs between ASML^{wt} versus ASML-CD44^{kd} exosomes or cells in signal intensity by more than two-fold.

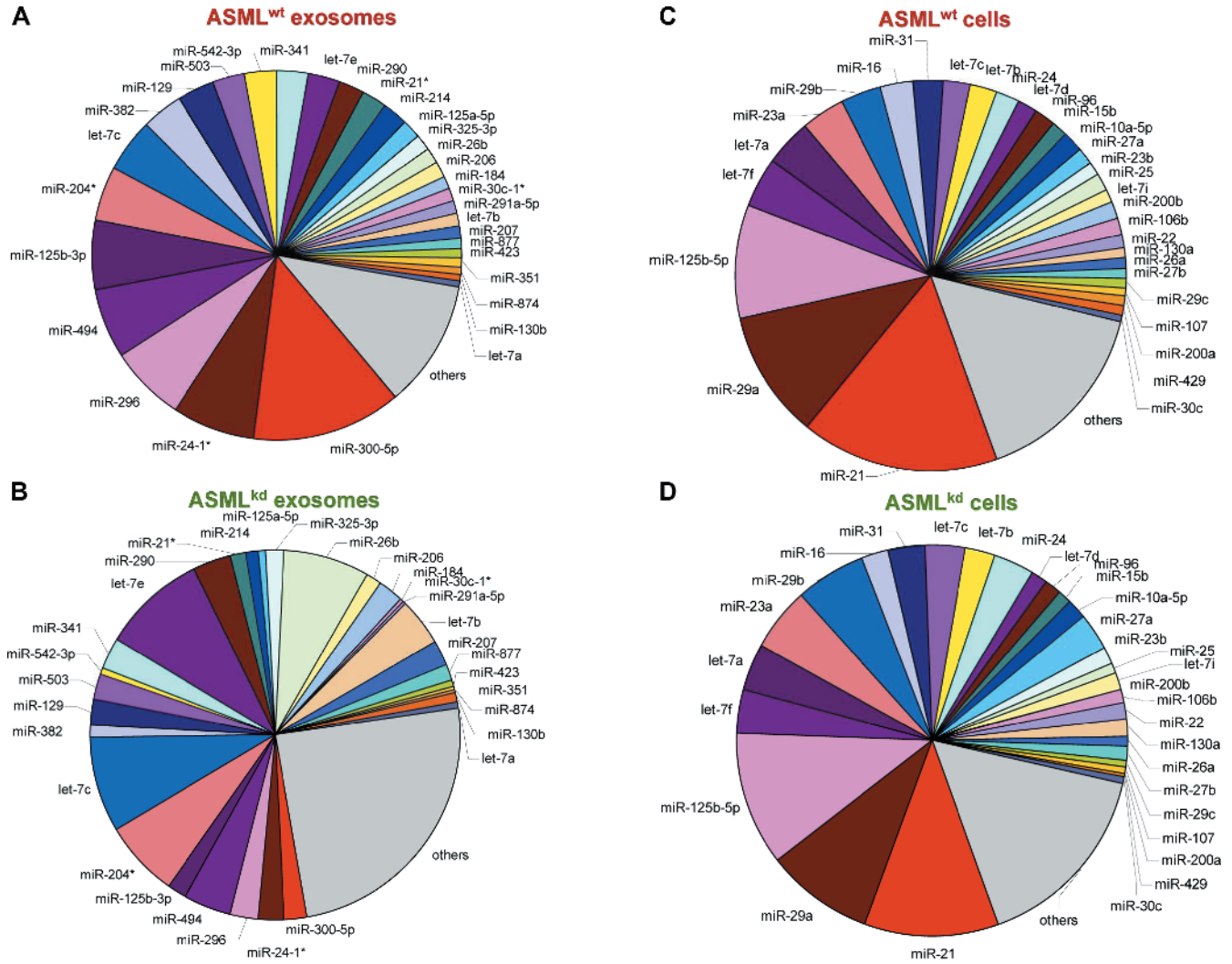


Figure W4. Comparative analysis of ASML^{wt} and ASML-CD44^{kd} cellular and exosomal miRNAs. (A–D) Presentation of the most abundant miRNA in ASML^{wt} and, for comparison, in ASML-CD44^{kd} cells and exosomes. The mean signal strength of quadruplicates of two independent microarray analyses is shown. ASML exosomes and cells contain a limited number of miRNA that differ significantly between cells and exosomes and in dependence on CD44v expression.

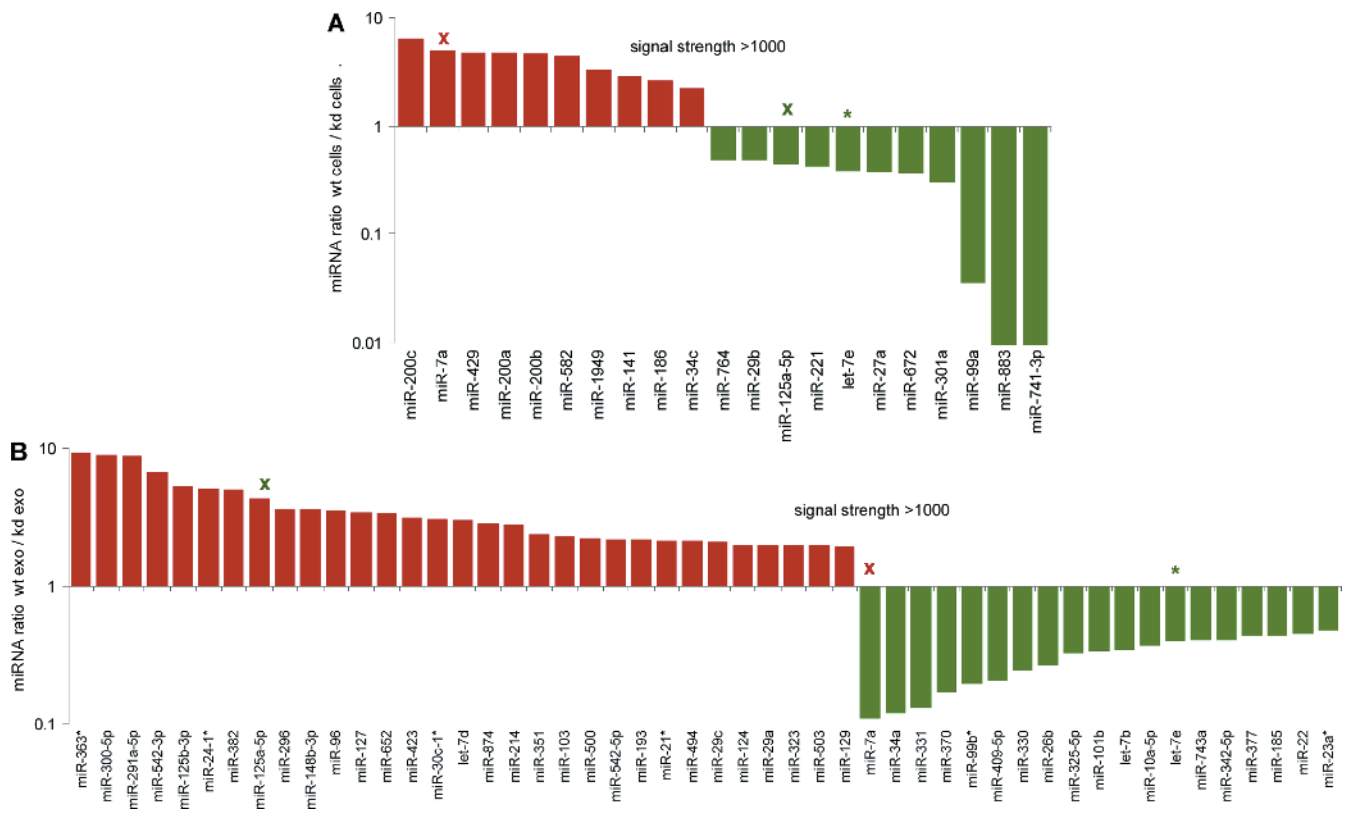


Figure W5. Comparison of miRNA in ASML^{wt} versus ASML-CD44^{kd} cells and exosomes. (A) Cellular and (B) exosomal miRNAs with a signal strength > 1000 and a more than two-fold difference in signal strength in ASML^{wt} versus ASML-CD44^{kd} cells or exosomes (mean signal strength of quadruplicates of two independent microarray analyses) is shown; Oppositely regulated miRNA in cells versus exosomes are indicated by X and aliquote regulated miRNA by asterisk. Independent of CD44v expression, most abundantly recovered cellular and exosomal miRNAs differ significantly, confirming the selectivity of miRNA recruitment.

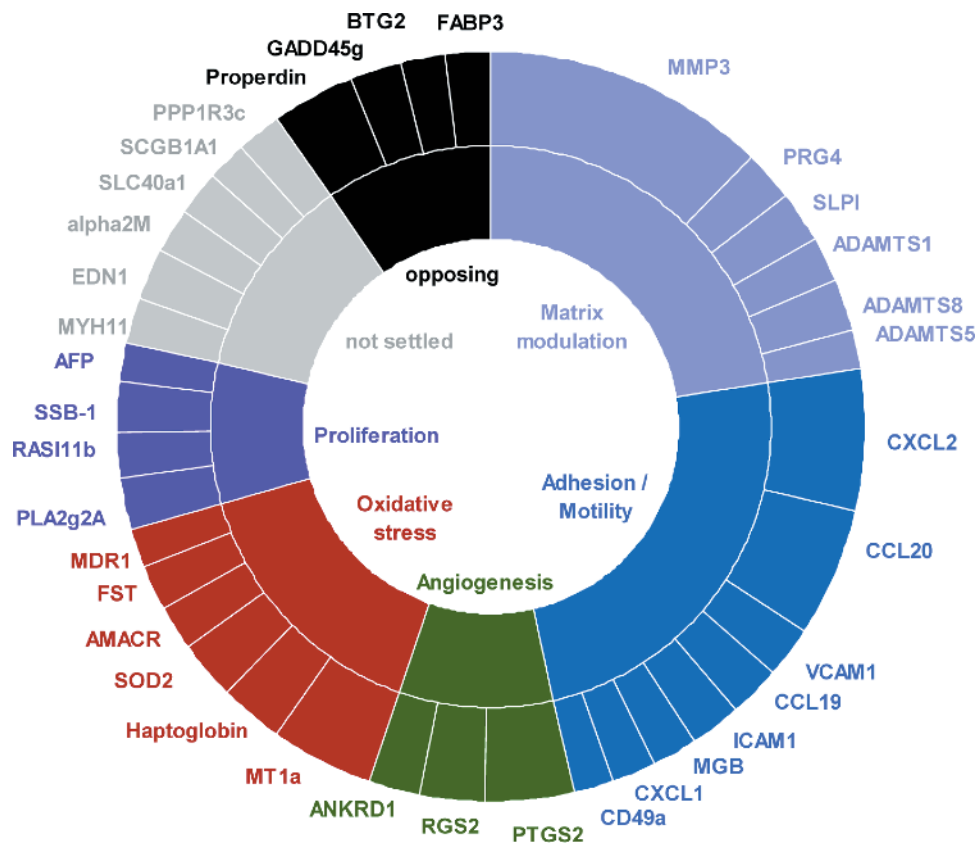


Figure W6. Exosome transfer-promoted activities of target cells in the premetastatic niche. Exosome uptake-induced upregulated mRNAs in LnStr were grouped according to main functional activities and are presented according to the fold up-regulation. Short comments on the main activity of upregulated genes and related references are given below.

Matrix modulation

MMP3 (matrix metalloproteinase 3): matrix degradation, well organized role in invasion and metastasis

Hua H, Li M, Luo T, Yin Y, and Jiang Y (2011). Matrix metalloproteinases in tumorigenesis: an evolving paradigm. *Cell Mol Life Sci* **68**, 3853–3868.

PRG4 (proteoglycan 4): co-receptor for integrins, co-operates with MT1-MMP in collagen modulation.

Vuoriluoto K, Högnäs G, Meller P, Lehti K, and Ivaska J (2011). Syndecan-1 and -4 differentially regulate oncogenic K-ras dependent cell invasion into collagen through $\alpha 2\beta 1$ integrin and MT1-MMP. *Matrix Biol* **30**, 207–217.

SLPI (secretory leukocyte peptidase inhibitor): often upregulated in cancer, induces MMP9 transcription.

Nukiwa T, Suzuki T, Fukuhara T, and Kikuchi T (2008). Secretory leukocyte peptidase inhibitor and lung cancer. *Cancer Sci* **99**, 849–855.

Hoskins E, Rodriguez-Canales J, Hewitt SM, Elmasri W, Han J, Han S, Davidson B, and Kohn EC (2011). Paracrine SLPI secretion upregulates MMP-9 transcription and secretion in ovarian cancer cells. *Gynecol Oncol* **122**, 656–662.

ADAMTS1 (a disintegrin-like and metalloprotease with thrombospondin type 1, motif 1); ADAMTS8 (a disintegrin-like and metalloprotease with thrombospondin type 1, motif 8); ADAMTS5 (a disintegrin-like and metalloprotease with thrombospondin type 1, motif 5): procollagen maturation, extracellular matrix proteolysis related to angiogenesis and metastasis.

Apte SS (2009). A disintegrin-like and metalloprotease (reprolysin-type) with thrombospondin type 1 motif (ADAMTS) superfamily: functions and mechanisms. *J Biol Chem* **284**, 31493–31497.

Adhesion/motility

CXCL2 (C-X-C chemokine ligand 2), CCL20 (C-C chemokine ligand 20), CCL19 (C-C chemokine ligand 19), CXCL1 (CXC chemokine ligand 1): chemokines and their ligands largely determine organ specificity of metastases, facilitating migration and extravasation; they can be involved in tumor cell proliferation and survival.

Ben-Baruch A (2008). Organ selectivity in metastasis: regulation by chemokines and their receptors. *Clin Exp Metastasis* **25**, 345–356.

VCAM1 (vascular cell adhesion molecule 1); ICAM1 (intercellular adhesion molecule 1): metastasis promoting by engagement in migration, proliferation, angiogenesis, and thrombosis.

Mousa SA (2008). Cell adhesion molecules: potential therapeutic & diagnostic implications. *Mol Biotechnol* **38**, 33–40.

MGP (matrix Gla protein): migration promoting, overexpressed in cancer.

Mertsch S, Schurgers LJ, Weber K, Paulus W, and Senner V (2009). Matrix gla protein (MGP): an overexpressed and migration-promoting mesenchymal component in glioblastoma. *BMC Cancer* **9**, 302.

CD49a (integrin alpha 1): supports tumor cell migration.

Madsen CD and Sahai E (2010). Cancer dissemination—lessons from leukocytes. *Dev Cell* **19**, 13–26.

Angiogenesis

PTGS2/COX2 (prostaglandin-endoperoxide synthase 2): involved in inflammation, increased in more aggressive forms of colorectal cancer, known to promote angiogenesis.

Wang S, Liu Z, Wang L, and Zhang X (2009). NF-kappaB signaling pathway, inflammation and colorectal cancer. *Cell Mol Immunol* **6**, 327–334.

RGS2 (regulator of G-protein signaling 2): critical regulator of proangiogenic function of MDSC.

Boelte KC, Gordy LE, Joyce S, Thompson MA, Yang L, and Lin PC (2011). Rgs2 mediates pro-angiogenic function of myeloid derived suppressor cells in the tumor microenvironment via upregulation of MCP-1. *PLoS One* **6**, e18534.

ANKRD1 (ankyrin repeat domain 1): co-transcription factor involved in angiogenesis.

Samaras SE, Shi Y, and Davidson JM (2006). CARP: fishing for novel mechanisms of neovascularization. *J Invest Dermatol Symp Proc* **11**, 124–131.

Oxidative stress

MT1a (metallothionein): contributes to protective reactions with chemotherapeutic agents that are electrophiles or can generate reactive oxygen species.

Namdarghanbari M, Wobig W, Krezoski S, Tabatabai NM, and Petering DH (2011). Mammalian metallothionein in toxicology, cancer, and cancer chemotherapy. *J Biol Inorg Chem* **16**, 1087–1101.

Haptoglobin: CD163 clearance and metabolism of “free” hemoglobin released during intravascular hemolysis. This scavenging system counteracts the potentially harmful oxidative and NO-scavenging effects associated with “free” hemoglobin.

Nielsen MJ and Moestrup SK (2009). Receptor targeting of hemoglobin mediated by the haptoglobins: roles beyond heme scavenging. *Blood* **114**, 764–771.

SOD2 (superoxide dismutase 2): catalysis oxidative stress, upregulated in metastasis.

Hempel N, Carrico PM, and Melendez JA (2011). Manganese superoxide dismutase (Sod2) and redox-control of signaling events that drive metastasis. *Anticancer Agents Med Chem* **11**, 191–201.

AMACR (α -methylacyl-CoA racemase): catalyzes the chiral inversion of a diverse number of 2-methyl acids (as their CoA esters) and regulates the entry of branched-chain lipids into the peroxisomal and mitochondrial β -oxidation pathways; linked with prostate, breast, colon, and other cancers.

Lloyd MD, Darley DJ, Wierzbicki AS, and Threadgill MD (2008). Alpha-methylacyl-CoA racemase—an ‘obscure’ metabolic enzyme takes centre stage. *FEBS J* **275**, 1089–1102.

FST (follistatin): Localization of FST to the nucleolus attenuates rRNA synthesis, a key process for cellular energy homeostasis and cell survival. Overexpression of FST delays glucose deprivation-induced apoptosis and promotes survival.

Gao X, Wei S, Lai K, Sheng J, Su J, Zhu J, Dong H, Hu H, and Xu Z (2010). Nucleolar follistatin promotes cancer cell survival under glucose-deprived conditions through inhibiting cellular rRNA synthesis. *J Biol Chem* **285**, 36857–36864.

MDR1 (ATP-binding cassette, subfamily B, member 1): promotes drug resistance, high expression frequently associated with metastasizing cancer-initiating cells.

Adhikari AS, Agarwal N, and Iwakuma T (2011). Metastatic potential of tumor-initiating cells in solid tumors. *Front Biosci* **16**, 1927–1938.

Proliferation

PLA2g2A (phospholipase A2, group 2A): contributes to EGFR activation.

Hernández M, Martín R, García-Cubillas MD, Maeso-Hernández P, and Nieto ML (2010). Secreted PLA2 induces proliferation in astrocytoma through the EGF receptor: another inflammation-cancer link. *Neuro Oncol* **12**, 1014–1023.

RASL11b (RAS-like family 11 member B): RasL11b acts in concert with UBF to facilitate initiation and/or elongation by RNA polymerase II, suggested to be upregulated in cancer.

Stolle K, Schnoor M, Fuellen G, Spitzer M, Cullen P, and Lorkowski S (2010). Cloning, genomic organization, and tissue-specific expression of the RASL11B gene. *Biochim Biophys Acta* **1769**, 514–524.

Pistoni M, Verrecchia A, Doni M, Guccione E, and Amati B (2010). Chromatin association and regulation of rDNA transcription by the Ras-family protein RasL11a. *EMBO J* **29**, 1215–1224.

SSB1 (similar to SPRY domain-containing SOCS box protein): binds to MET and enhances the HGF-induced Erk–Elk-1–SRE pathway.

Wang D, Li Z, Messing EM, and Wu G (2005). The SPRY domain-containing SOCS box protein 1 (SSB-1) interacts with MET and enhances the hepatocyte growth factor-induced Erk–Elk-1–serum response element pathway. *J Biol Chem* **280**, 16393–16401.

AFP (alpha-fetoprotein): tumor growth enhancing, possesses proangiogenic properties.

Mizejewski GJ (2007). Physiology of alpha-fetoprotein as a biomarker for perinatal distress: relevance to adverse pregnancy outcome. *Exp Biol Med* **232**, 993–1004.

Not settled

MYH11 (myosin heavy chain 11): not settled, known to fuse with CBF in leukemia.

Weckerle AB, Santra M, Ng MC, Koty PP, and Wang YH (2011). *CBFB* and *MYH11* in inv(16)(p13q22) of acute myeloid leukemia displaying close spatial proximity in interphase nuclei of human hematopoietic stem cells. *Genes Chromosomes Cancer* **50**, 746–755.

EDN1 (endothelin 1): not settled, peptide hormone signaling through its cognate receptor, the endothelin-A receptor, critical for patterning, relation to cancer unknown.

Clouthier DE, Garcia E, and Schilling TF (2010). Regulation of facial morphogenesis by endothelin signaling: insights from mice and fish. *Am J Med Genet A* **152A**, 2962–2973.

α 2M (alpha-2-macroglobulin): interacts and captures virtually any proteinase.

Woessner JF Jr (1991). Matrix metalloproteinases and their inhibitors in connective tissue remodeling. *FASEB J* **5**, 2145–2154.

SLC40a1 (solute carrier family 39 iron-regulated transporter, member 1): iron export, may inhibit metastasis.

Jiang XP, Elliott RL, and Head JF (2010). Manipulation of iron transporter genes results in the suppression of human and mouse mammary adenocarcinomas. *Anticancer Res* **30**, 759–765.

SCGB1A1 (secretoglobin, family 1A, member 1): downstream target for a homeodomain transcription factor NKX2-1, which is critical for the development of lung, thyroid, and ventral forebrain, upregulated in lung cancer.

Kurotani R, Kumaki N, Naizhen X, Ward JM, Linnoila RI, and Kimura S (2011). Secretoglobin 3A2/uteroglobin-related protein 1 is a novel marker for pulmonary carcinoma in mice and humans. *Lung Cancer* **71**, 42–48.

PPP1R3C (protein phosphatase 1, regulatory (inhibitor) subunit 3C): correlates with glycogen accumulation under hypoxia, described as a candidate tumor suppressor.

Shen GM, Zhang FL, Liu XL, and Zhang JW (2010). Hypoxia-inducible factor 1-mediated regulation of PPP1R3C promotes glycogen accumulation in human MCF-7 cells under hypoxia. *FEBS Lett* **584**, 4366–4372.

Bonazzi VF, Irwin D, and Hayward NK (2009). Identification of candidate tumor suppressor genes inactivated by promoter methylation in melanoma. *Genes Chromosomes Cancer* **48**, 10–21.

Metastasis opposing

Properdin: antiangiogenic.

Kemper C, Atkinson JP, and Hourcade DE (2010). Properdin: emerging roles of a pattern-recognition molecule. *Annu Rev Immunol* **28**, 131–155.

GADD45g (growth arrest and DNA-damage-inducible 45γ): supposed to function as metastasis inhibitor.

Ying J, Srivastava G, Hsieh WS, Gao Z, Murray P, Liao SK, Ambinder R, and Tao Q (2005). The stress-responsive gene GADD45G is a functional tumor suppressor, with its response to environmental stresses frequently disrupted epigenetically in multiple tumors. *Clin Cancer Res* **11**, 6442–6449.

BTG2 (B-cell translocation gene 2): antiproliferative, pan cell cycle modulator and endogenous cell death molecule, downregulated in cancer.

Lim IK (2006). TIS21 (/BTG2/PC3) as a link between ageing and cancer: cell cycle regulator and endogenous cell death molecule. *J Cancer Res Clin Oncol* **132**, 417–426.

FABP3 (fatty acid binding protein 3): inhibits proliferation and promotes apoptosis

Zhu C, Hu DL, Liu YQ, Zhang QJ, Chen FK, Kong XQ, Cao KJ, Zhang JS, and Qian LM (2011). Fabp3 inhibits proliferation and promotes apoptosis of embryonic myocardial cells. *Cell Biochem Biophys* **60**, 259–266.

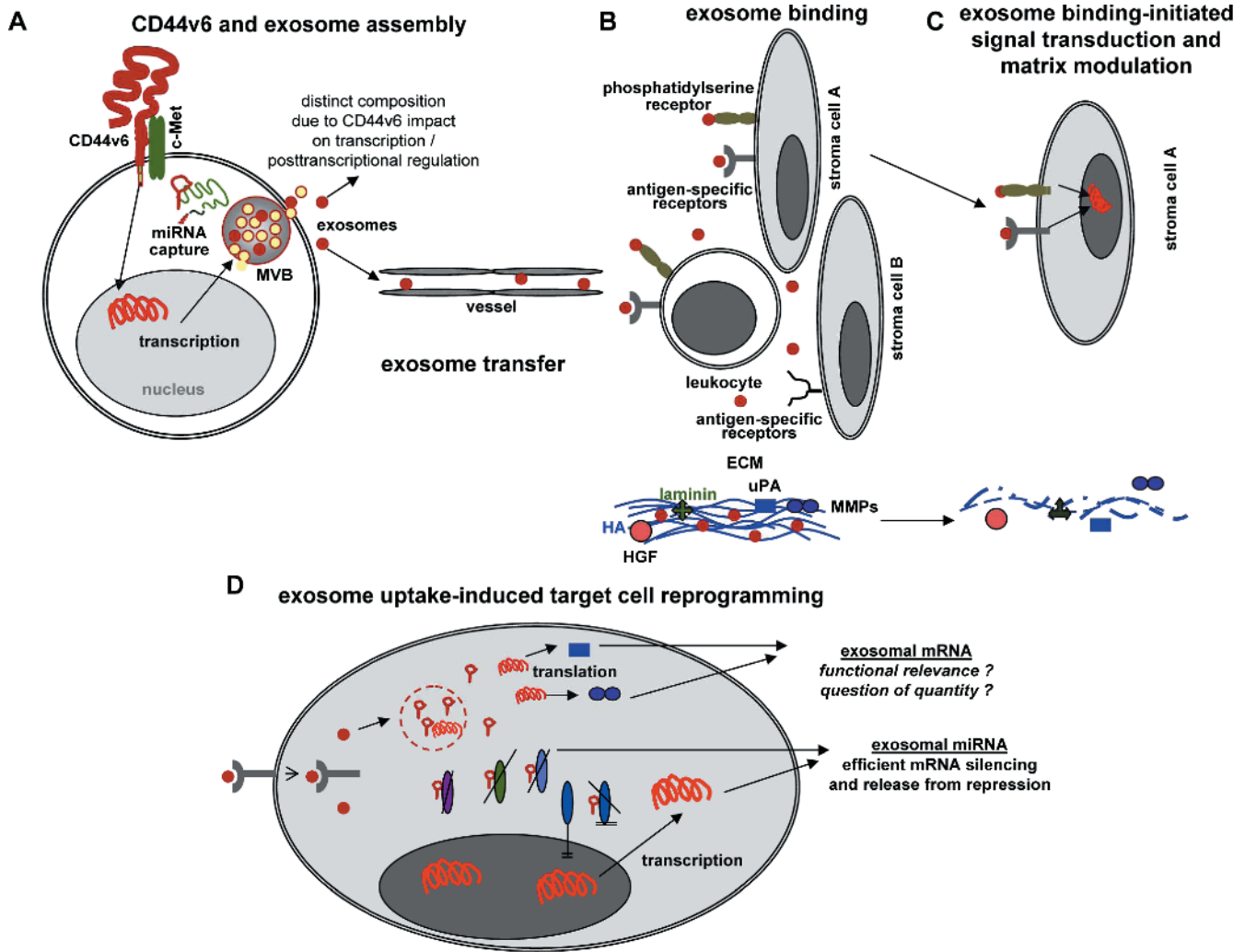


Figure W7. A metastasis-associated gene, its impact on exosome shaping, and the impact on host cells: (A) CD44v6 influences gene transcription and posttranscriptional modulation. This influences the protein [1,2], mRNA, and miRNA composition of exosomes. Exosomes reach premetastatic organs from a distantly located primary tumor (demonstrated for draining lymph nodes, accounts equally for other metastatic organs and the bone marrow, as well as for transfer through the blood [2,3]). (B) Exosomes bind selected target cells (demonstrated for LnStr and LuFb, additional preferred targets for ASML exosomes are monocytes/monocyte progenitors [3]). (C) Exosome binding is supposed to initiate signal transduction in target cells [4] (not approached in the present manuscript) and severely affect the host matrix (unpublished). (D) Exosomes are taken up and uptaken mRNA and miRNA are recovered in the target cell. According to our findings, uptaken miRNA severely modulates the target cell, fitting the demands for premetastatic niche formation (only demonstrated for metastatic organ stroma cells but accounts equally well for hematopoietic cells).

Taken that tumor exosomes are recovered in patients' sera [5] and exhibit very selective binding implies that functional activity of exosomes has to be taken into account at sites distant from the tumor (e.g., premetastatic organs), where the selectivity of exosome uptake will greatly facilitate therapeutic interference. However and notably, as the exosome composition becomes significantly influenced also by proteins of the tumor cell that are not engaged in exosome assembly or transport, it is essential to characterize the individual patient's exosomes in advance, which can be approached by tumor exosomes in the patient's serum.

[1] Jung T, Castellana D, Klingbeil P, Cuesta Hernández I, Vitacolonna M, Orlicky DJ, Roffler SR, Brodt P, and Zöller M (2009). CD44v6 dependence of premetastatic niche preparation by exosomes. *Neoplasia* **11**, 1093–1105.

[2] Zech D, Rana S, Büchler MW, and Zöller M (2012). Tumor-exosomes and leukocyte activation: an ambivalent crosstalk. *Cell Commun Signal* **10**, 37.

[3] Rana S, Shijing Y, Stadel D, and Zöller M (2012). Toward tailored exosomes: The exosomal tetraspanin web contributes to target cell selection. *Int J Biochem Cell Biol* **44**, 1574–1584.

[4] Hupalowska A and Miaczynska M (2012). The new faces of endocytosis in signaling. *Traffic* **13**, 9–18.

[5] Wittmann J and Jäck HM (2010). Serum microRNAs as powerful cancer biomarkers. *Biochim Biophys Acta* **1806**, 200–207.