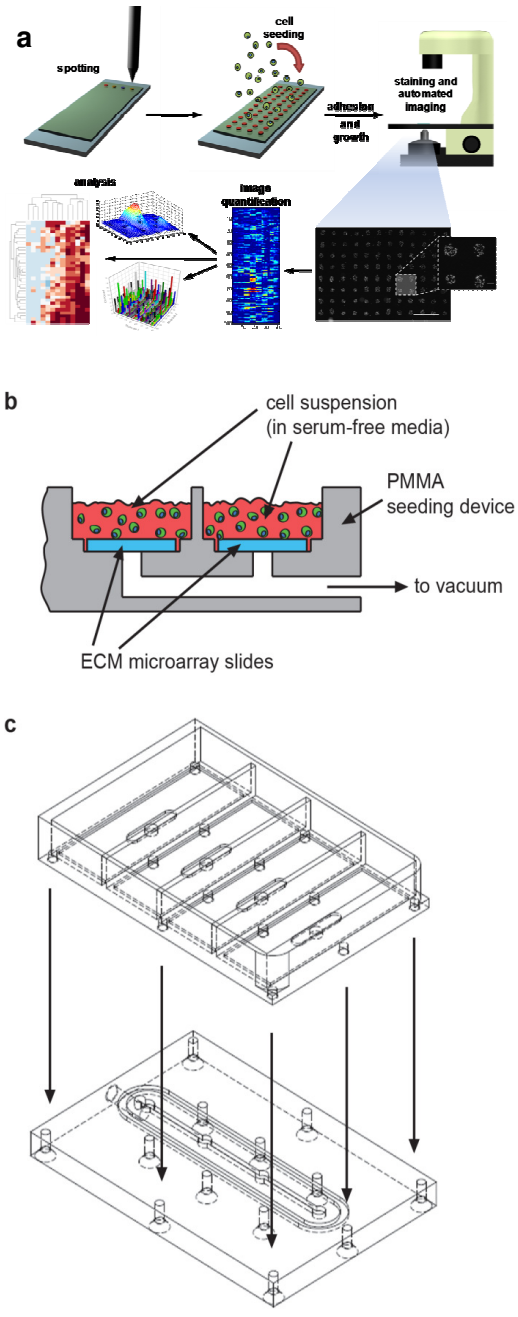
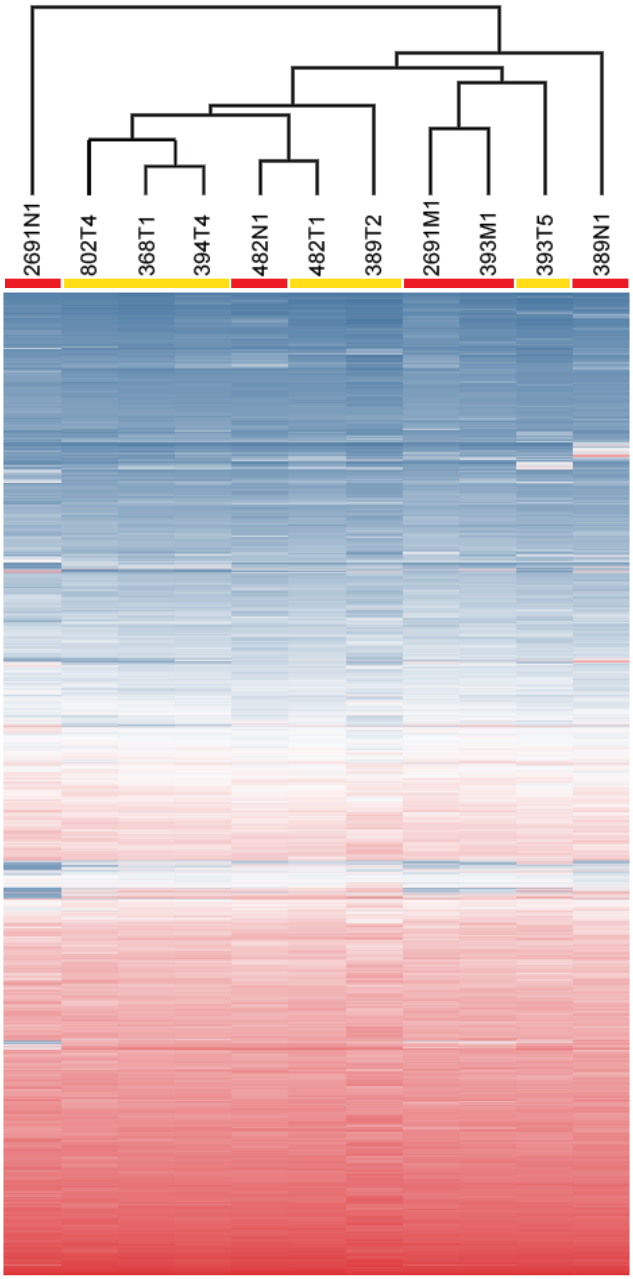
Supplementary Figure S1



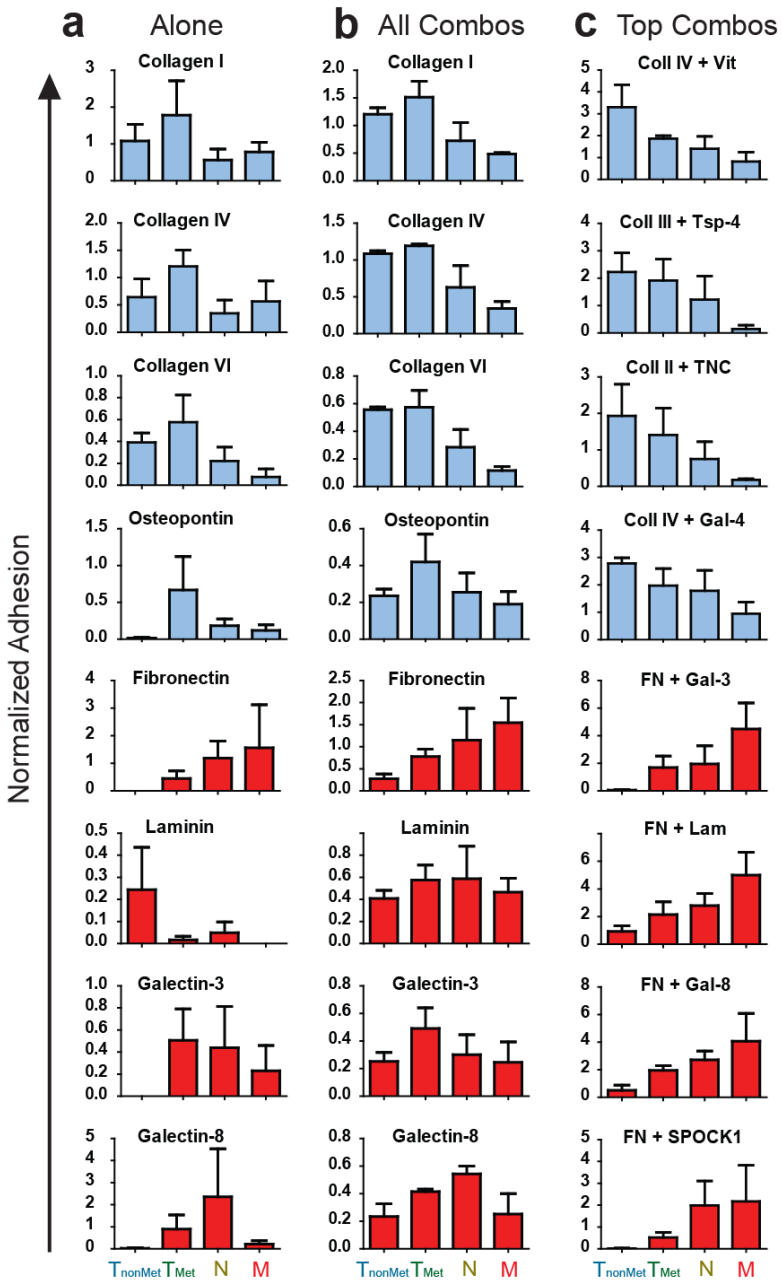
Supplementary Figure S1. Seeding and analyzing ECM microarrays (a) Process flow for ECM microarray experiments: slides are prepared by spotting ECM; cells are seeded onto slides; slides are stained and imaged on an automated microscope; images are quantified and analyzed using custom software. (b) Cross-sectional schematic of seeding device. Slides are held flush with the surface by vacuum. (c) CAD schematic depicting the four chambers of the seeding device.

Supplementary Figure S2



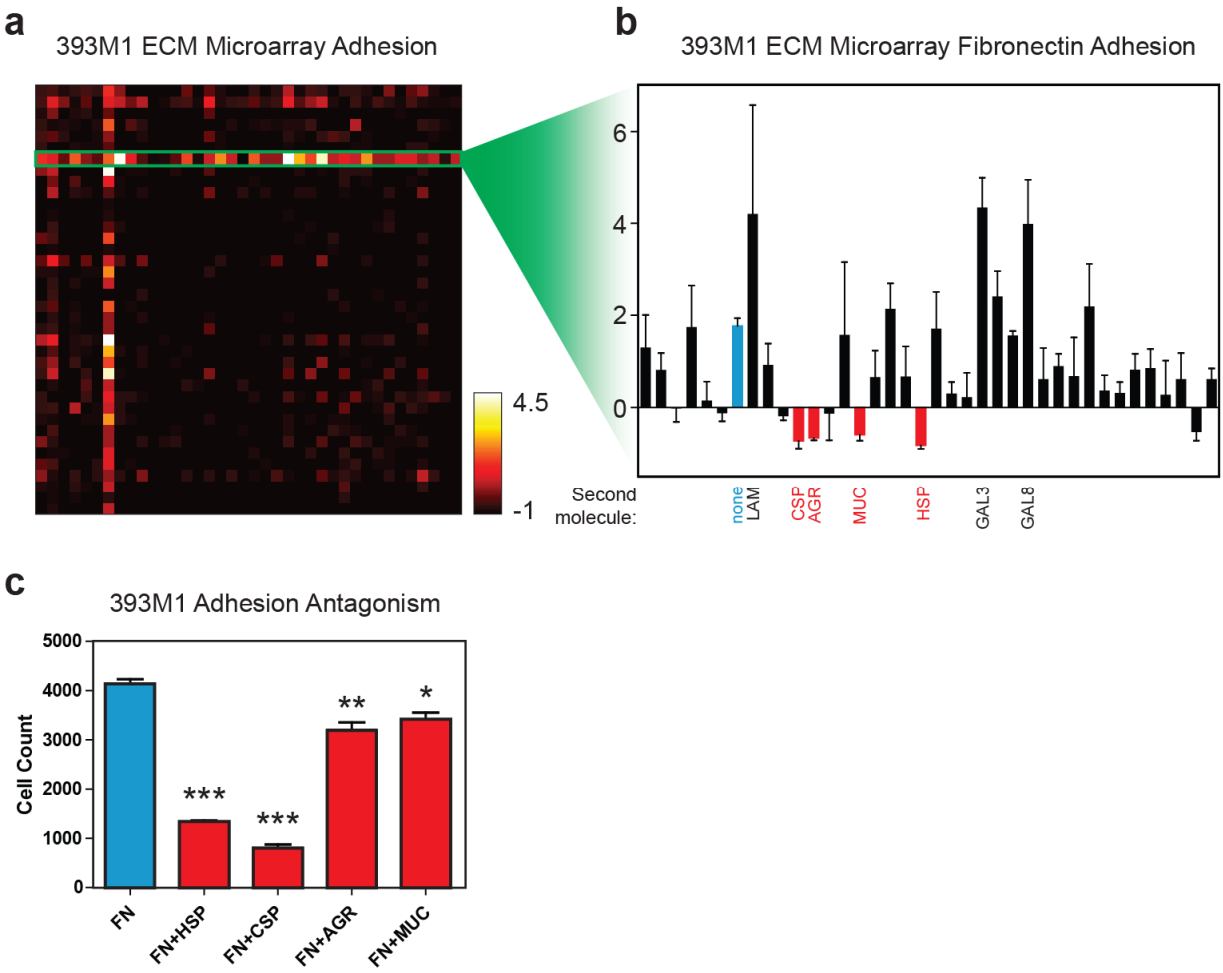
Supplementary Figure S2. Gene Expression Clustering Unsupervised hierarchical clustering of gene expression microarrays. All probesets displaying a variance>0.5 and expression>3.0 were included. Yellow bars demote primary tumor-derived cell lines (T_{nonMet} and T_{Met}) and red bars denote metastasis-derived cell lines (N and M). Clustering is performed using complete linkage analysis with a half square Euclidean distance and average value ordering weight.

Supplementary Figure S3



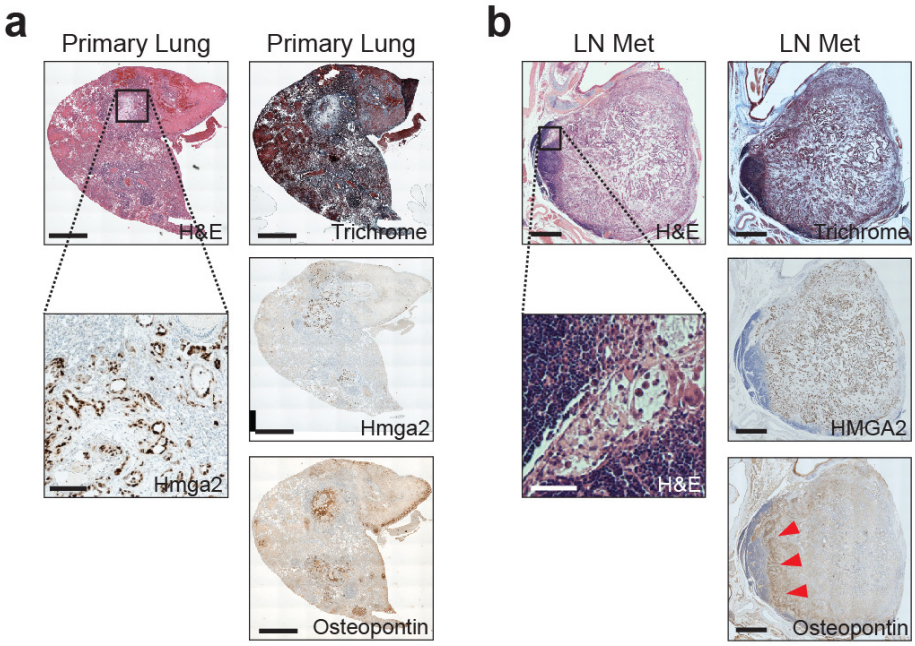
Supplementary Figure S3. Changes in adhesion correlate with metastatic progression
Molecules to which there is a loss of adhesion (blue) or gain of adhesion (red) between the T_{nonMet} ($n = 3$), T_{Met} ($n = 3$), N ($n = 3$), and M ($n = 2$) cell lines when examined alone (a) or as an average of all combinations containing them (b). Combinations that exhibited the greatest gains (red) or losses in adhesion (blue) as determined by linear regression are depicted in (c). Combinations were selected based on the magnitude of the slopes provided that the regressions had r^2 values greater than 0.9. y-axes represent normalized adhesion. Values less than ~0.5 represent very minimal adhesion. Error bars are s.e.m. of the different cell lines of each class.

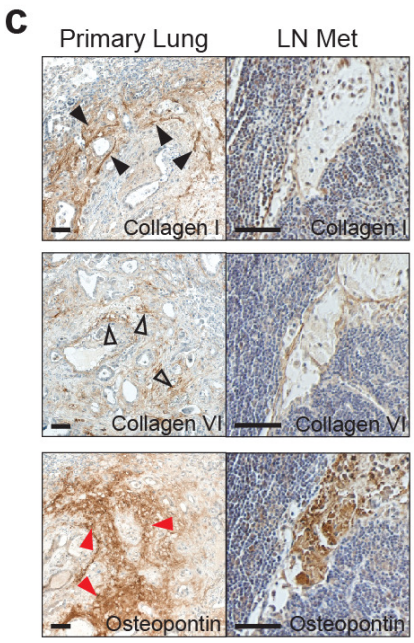
Supplementary Figure S4



Supplementary Figure S4. ECM combinations can have anti-adhesive effects when compared to single molecules (a) Heat map depiction of adhesion profile of the M line 393M1for each ECM combination. (b) All combinations of molecules containing fibronectin. Fibronectin alone is depicted in blue. Four combinations that exhibited significantly decreased adhesion when compared to fibronectin alone are depicted in red. CSP: chondroitin sulfate proteoglycan; AGR: aggrecan; MUC: mucin; HSP: heparin sulfate proteoglycan. The three metastasis-associated ECM combination hits are also denoted (LAM: laminin; GAL3: galectin-3; GAL8: galectin-8). Error bars are s.e.m. of three replicate slides. (c) Verification of anti-adhesive effects of the molecules highlighted in (b) was performed by coating 96-well plates with the molecules and examining adhesion of the 393M1 cell line. Error bars are standard error. ***$P <$ 0.001; **$P < 0.01$; *$P < 0.05$. Significance was determined using one-way ANOVA with Tukey's Multiple Comparisons post-test.

Supplementary Figure S5





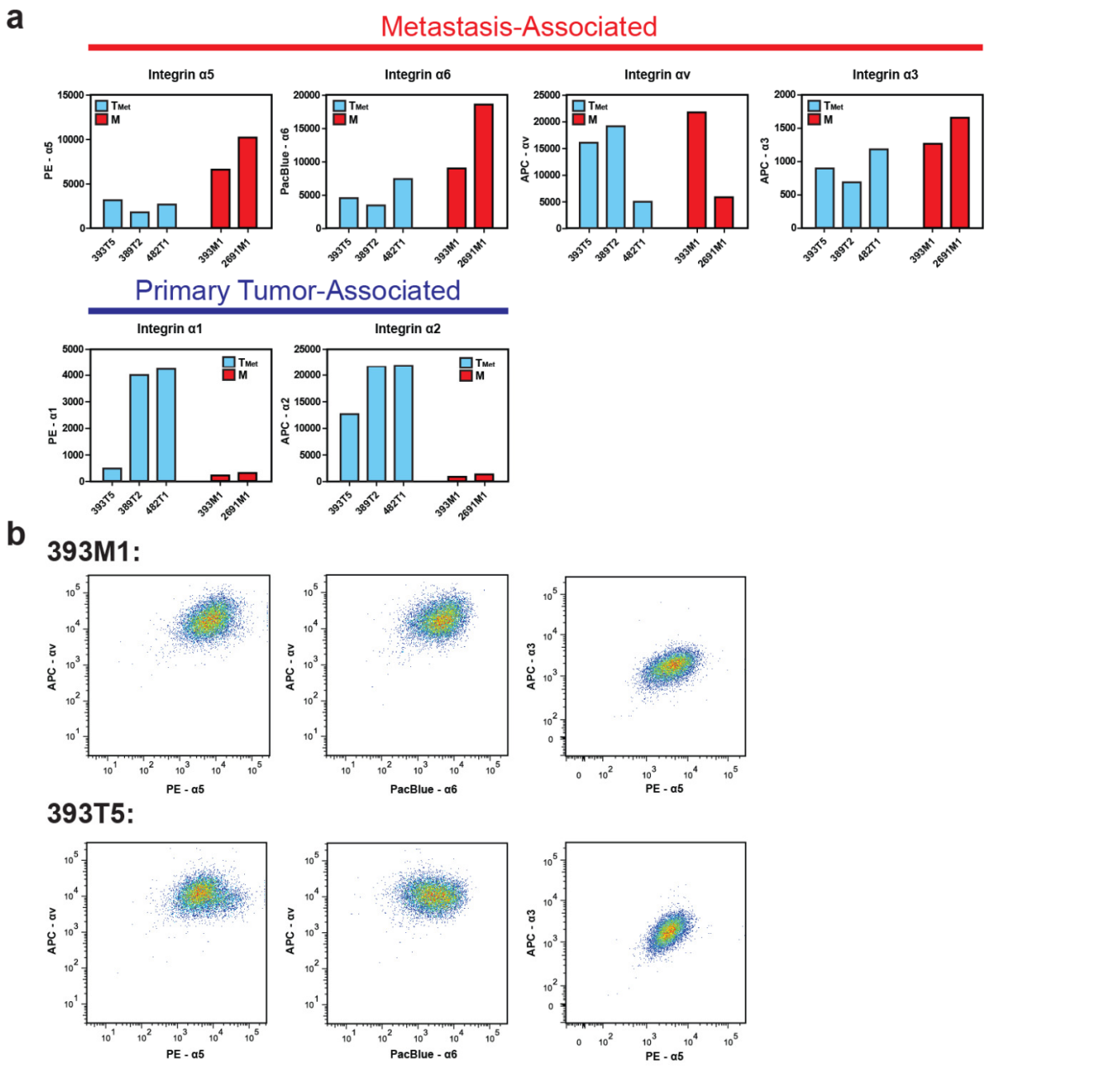
d

	T	N	M
Coll I	+	-	
Coll VI	+	-	
OPN	+	+	
FN	+	+	+
Lam	-	+	+
Gal-3	-	+	+
Gal-8	-	+	+

Supplementary Figure S5. Identified ECM molecules are present in primary tumors and metastases (a) Staining on lungs containing primary lung tumors from *Kras*$^{LSL\text{-}G12D/+}$;*p53*$^{flox/flox}$ mice. (b) Staining of lymph node metastases from the mice. Red arrowheads denote tumor front exhibiting high osteopontin staining. (c) IHC of primary tumor-associated ECM in the lung and lymph node. Black arrowheads: collagen I, open black arrowheads: collagen VI. (d) Summary of IHC results. 'H&E': Hematoxylin and eosin. 'Trichrome': Masson's trichrome. 'Hmga2': High-mobility group AT-hook 2 (marker of metastatic/invasive tumor cells). 'T': primary lung tumor.

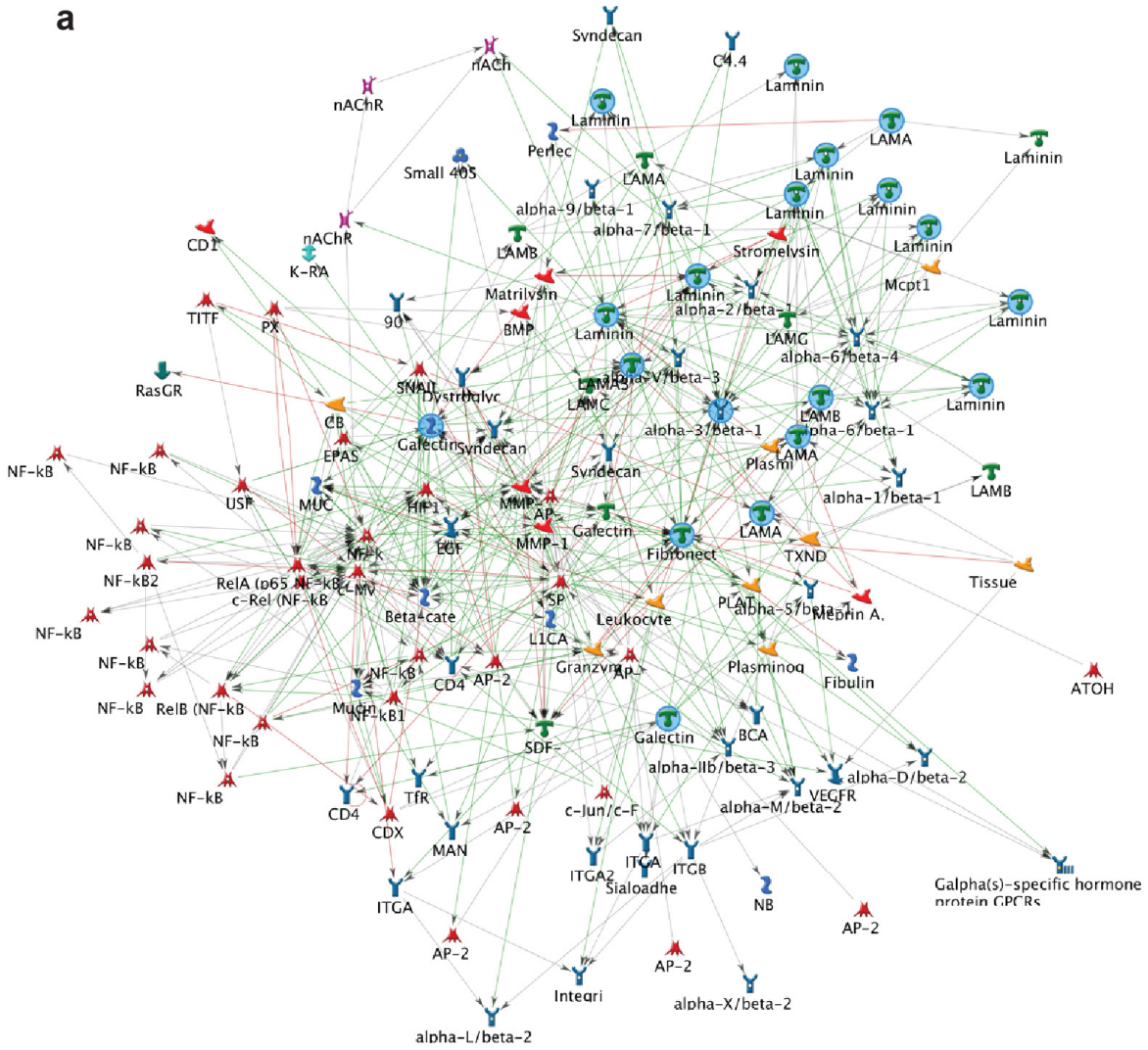
‘N’: lymph node metastasis. ‘M’: distant metastasis. Scale bars: (a) low magnification: 1mm; high magnification: 100μm; (b) low magnification: 500μm; high magnification: 50μm; (c) 50μm.

Supplementary Figure S6



Supplementary Figure S6. Flow cytometry analysis of surface integrin expression (a) Median values for fluorescence intensity of each of the T_{Met} (blue) and M (red) cell lines for the metastasis-associated molecule cognate integrins and primary tumor-associated molecule cognate integrins. (b) Multicolor flow analysis of integrin profiles in the 393M1 and 393T5 for the metastasis-associated molecule cognate integrins shows a lack of discrete subpopulations.

Supplementary Figure S7



b

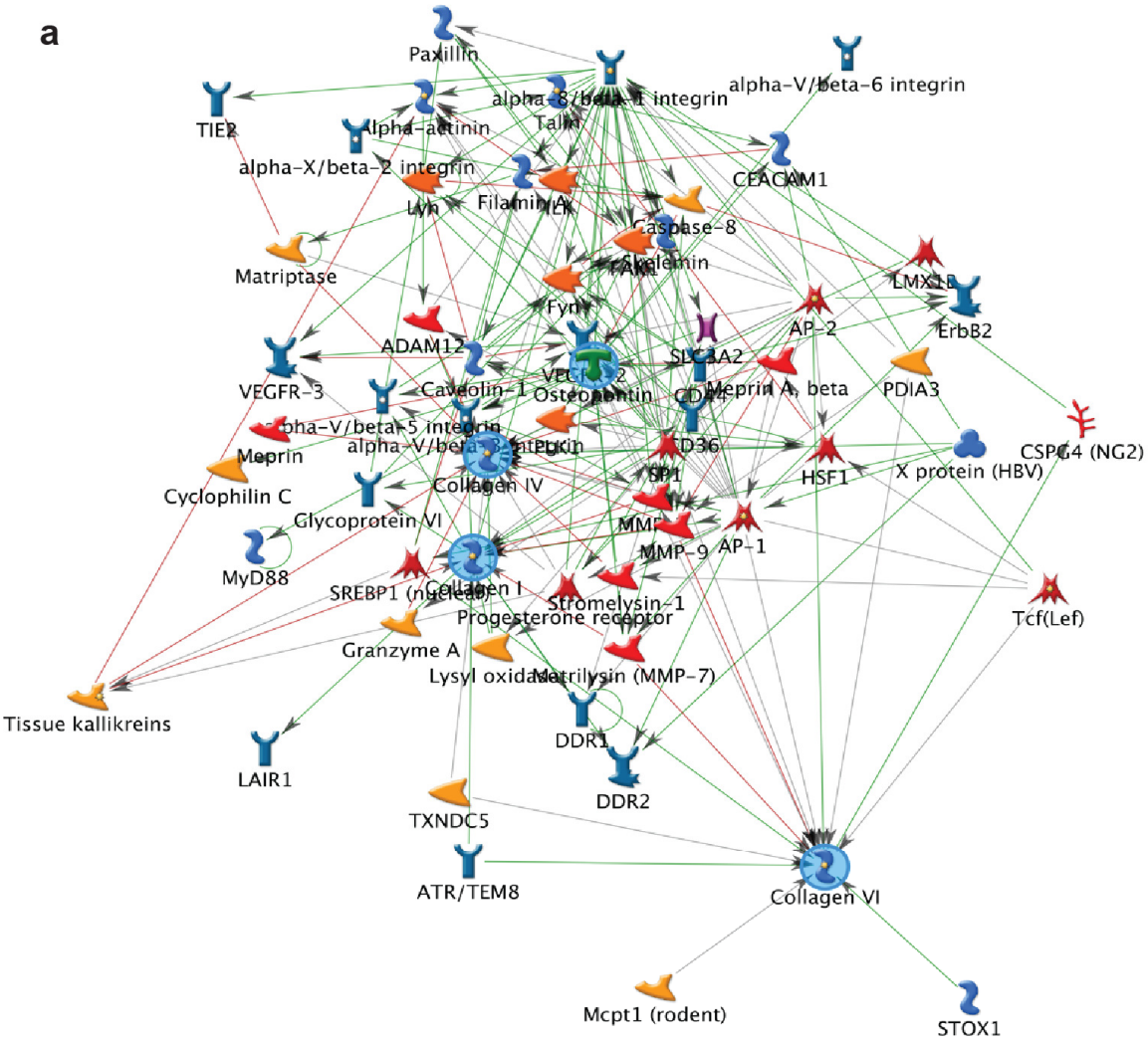
LAM Network

#	Disease	%	p-Value
1	**Neoplasm Metastasis**	**55.28**	**1.094E-45**
2	Neoplastic Processes	55.28	5.054E-44
3	Pathologic Processes	80.49	2.373E-41
4	Genital Diseases, Male	74.8	1.289E-36
5	Skin Diseases	79.67	2.990E-36

Supplementary Figure S7. Metastasis-associated ECM *in silico* network mapping (a) Network map generated in GeneGO (Metacore) generated using an autoexpand algorithm and starting with the metastasis-associated ECM molecules. (b) Disease association rank of the LAM network. P-values determined by hypergeometric test.

Supplementary Figure S8

a



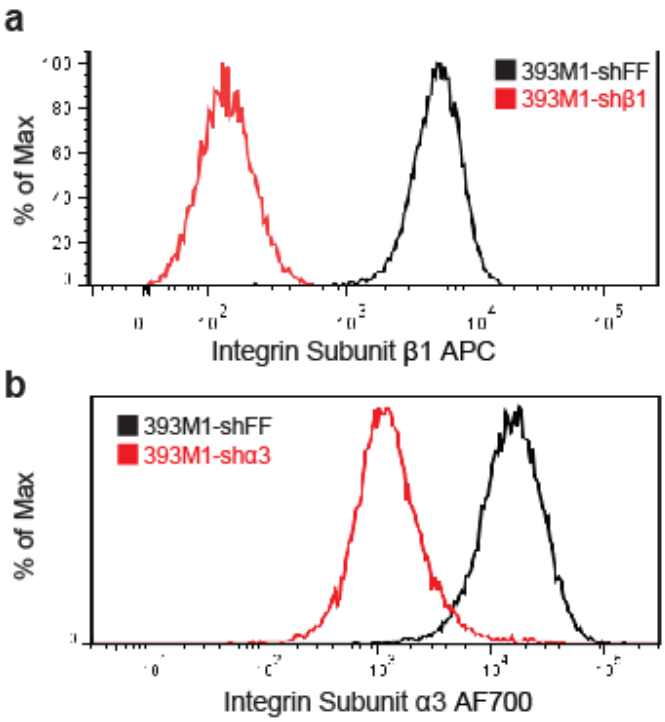
b

Primary Tumor Molecule Network

#	Disease	%	p-Value
1	Wounds and Injuries	56.64	2.507E-41
2	Osteosarcoma	36.28	1.811E-37
3	Neoplasms, Bone Tissue	36.28	4.663E-37
4	Neoplasms, Connective and Soft Tissue	47.79	2.067E-33
5	Neoplasms, Connective Tissue	39.82	1.052E-32

Supplementary Figure S8. Primary tumor-associated ECM *in silico* network mapping (a) Network map generated in GeneGO (Metacore) using the same parameters as the LAM network, but with the primary tumor-associated ECM molecules instead. (b) Disease association rank of the LAM network from Fig. 5c. (b) Disease association rank of the primary tumor molecule network shown in (a). P-values determined by hypergeometric test.

Supplementary Figure S9



Supplementary Figure S9. Knockdown of integrin subunits Flow cytometry analysis of integrin surface expression. (a) knockdown of ITGB1; (b) knockdown of ITGA3. Black: control hairpin against firefly luciferase; red: hairpin against integrin subunits.

Supplementary Table S1. ECM Molecules Present on the Arrays

Collagen I
Collagen II
Collagen III
Collagen IV
Collagen V
Collagen VI
Fibronectin
Laminin
Laminin á2
Tenascin-R
Chondroitin Sulfate Proteooglycans
Aggrecan
Elastin
Keratin
Mucin
Superfibronectin
F-Spondin
Nidogen-2
Heparan Sulfate Proteoglycan (Perlecan)
Biglycan
Decorin
Galectin-1
Galectin-3
Galectin-3c
Galectin-4
Galectin-8
Thrombospondin-4
Osteopontin
Osteonectin
Testican 1
Testican 2
Fibrin
Tenascin-C
Nidogen-1
Vitronectin
Agrin
Hyaluronan
Brevican

Supplementary Table S2. Classification of Cell Lines

Cell Line	Classification
368T1	T_{nonMet}
394T4	T_{nonMet}
802T4	T_{nonMet}
389T2	T_{Met}
393T5	T_{Met}
482T1	T_{Met}
389N1	LN
482N1	LN
2691N1	LN
393M1	Met
2691M1	Met