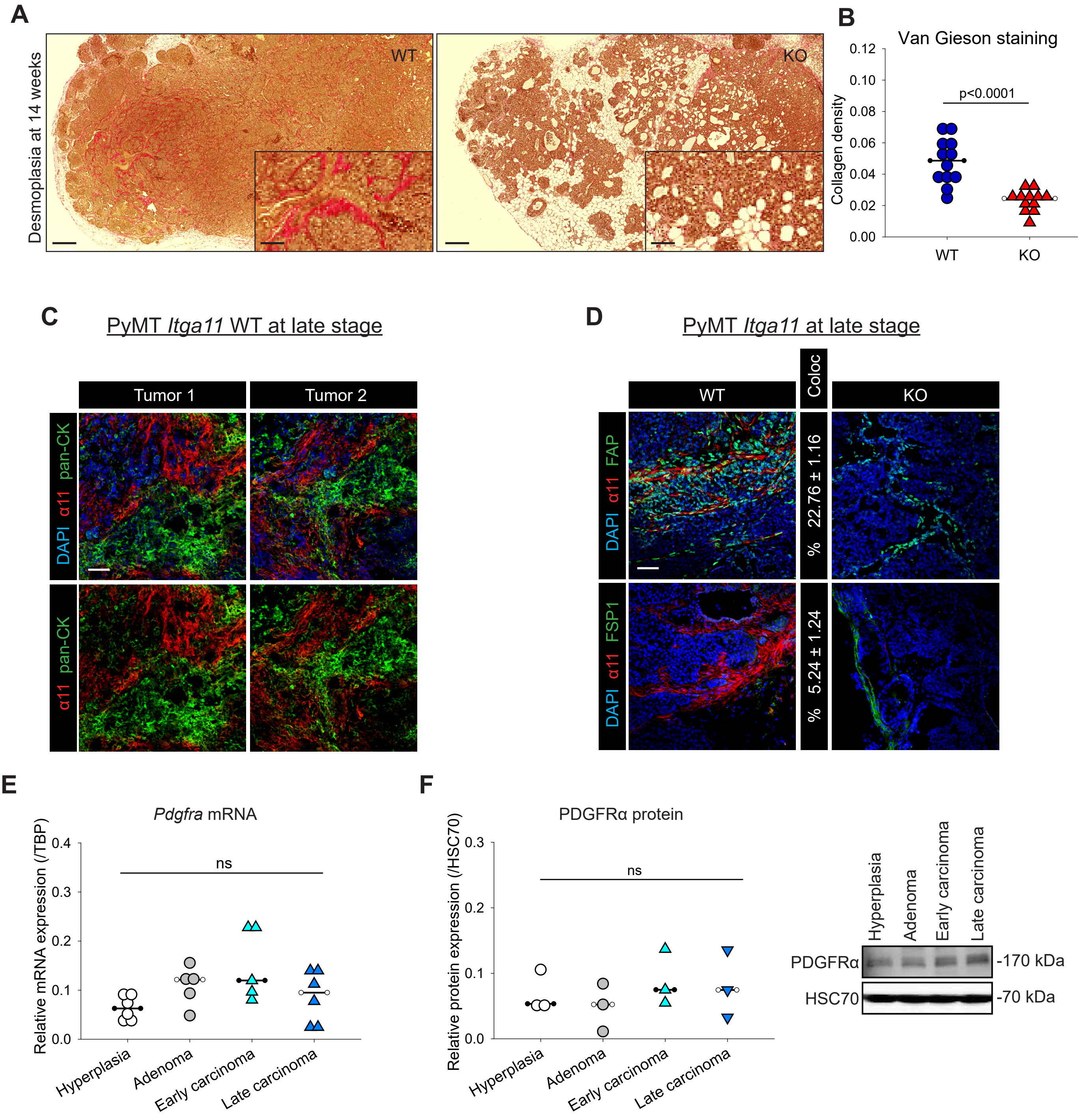
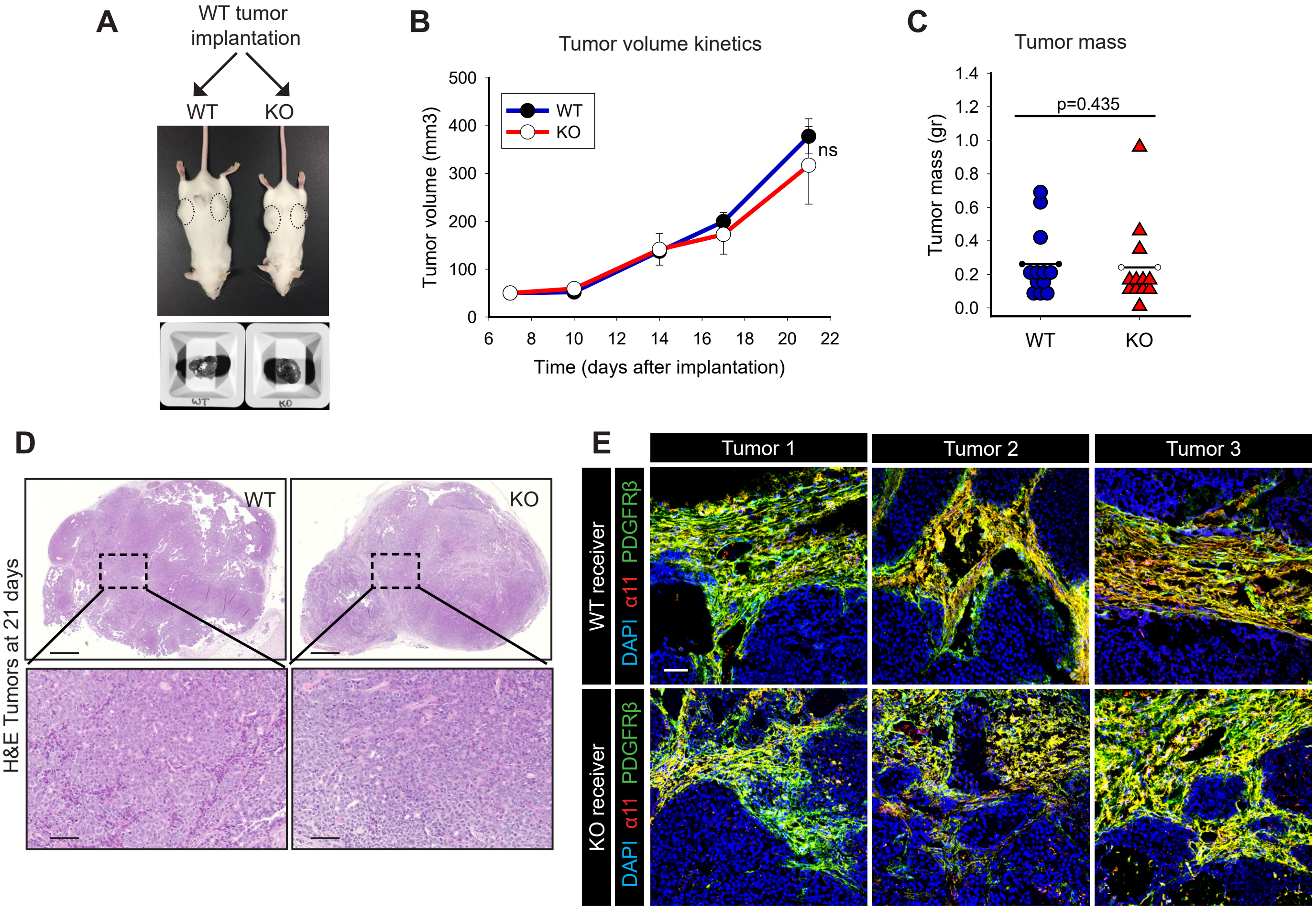
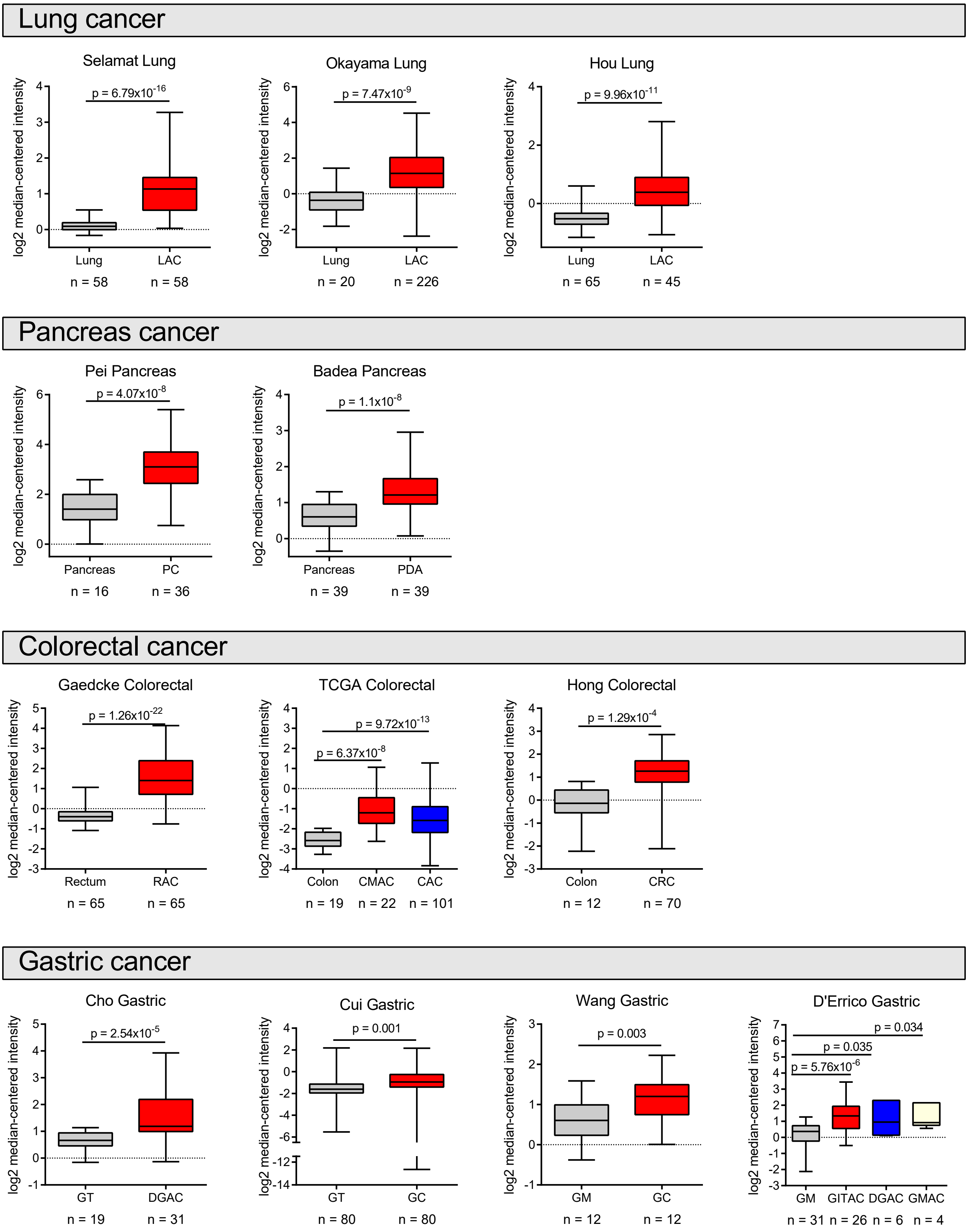


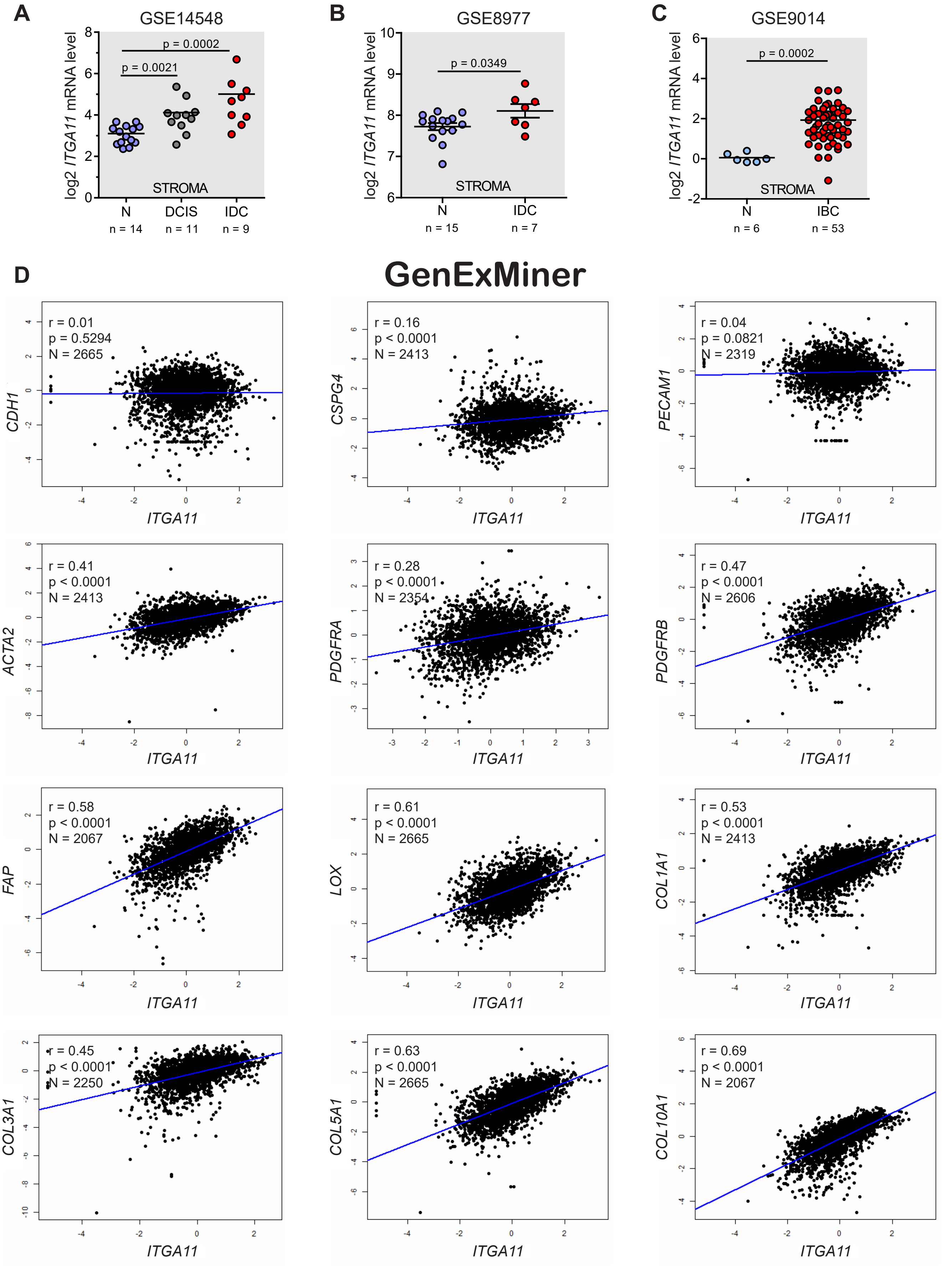
Supplemental Figure 1 corresponding to Figure 1 and 3: Integrin α11 expression is associated with stroma in PyMT tumors. (**A-B**) corresponding to Figure 1: Representative images of desmoplasia (pink) (**A**) and its quantification (**B**) by Van Gieson staining. Bar scale: 250 µm (original); 50 µm (zoom). Data presented as collagen density (collagen-stained area/tumor area), (n = 12 mice/genotype). Mann-Whitney test. (**C**) corresponding to Figure 3A: Representative confocal pictures showing the co-staining of integrin α11 (red) and pan-cytokeratin (CK) (green) of two individual PyMT *Itga11* WT tumors at late stage (14 weeks). Nuclei were counterstained with DAPI (blue). Scale bar: 50 µm. (**D**) corresponding to Figure 3A: Immunofluorescence confocal pictures showing the co-staining of integrin α11 (red) and FAP (upper panels) or FSP1 (lower panels) (green) of PyMT *Itga11* WT and KO tumors at late stage (14 weeks). Nuclei were stained with DAPI (blue). Scale bar: 50 µm. The % of cells positive for integrin α11 and a second marker compared to the total amount of α11+ cells are indicated on the figure (“coloc”). Colocalisation was determined by a computerized method on > 12 stromal fields/tumor (n = 8-10 for each genotype). (**E-F**) corresponding to Figure 3, B and C: Quantification of PDGFRα mRNA levels (qRT-PCR, data normalized to TBP) (n = 6) (**E**), and protein levels (Western blot, data normalized to HSC-70) (n = 3) (**F**) in PyMT tumors at different stages. 1-way ANOVA with Holm-Sidak multiple comparison test. Representative pictures of Western blots are shown in right panels.



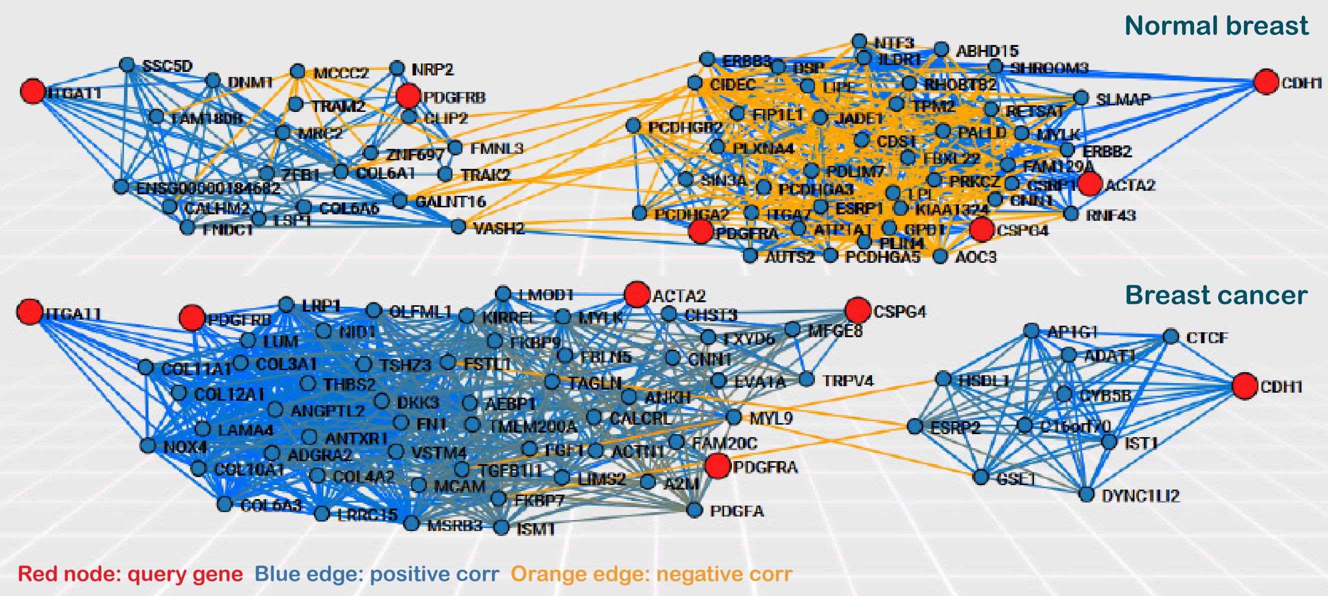
Supplemental Figure 2 corresponding to Figure 1 and 3: Resident integrin α11+ fibroblasts in PyMT tumors promote tumor progression. (**A**) Representative pictures of *Itga11* WT and KO mice with *Itga11* WT PyMT tumor fragments at 21 days after implantation. Corresponding tumors at sacrifice are shown in the lower pannel. (**B**) Tumor growth kinetics after implantation. n = 6 mice/genotype. 2-Way ANOVA test with Holm-Sidak multiple comparison test. (**C**) Tumor mass of transplanted tumors at sacrifice. Median of tumor mass. n = 12/ genotype. Mann-Whitney test. (**D**) Representative pictures of haematoxylin & eosin staining of the resected tumors at sacrifice. Scale bar: 2 mm (original); 0.5 mm (zoom). (**E**) corresponding to Figure 3: Immunofluorescence confocal pictures showing the co-staining of integrin α11 (red) and PDGFRβ (green) of PyMT *Itga11* WT transplanted tumors. Nuclei were stained with DAPI (blue). Scale bar: 50 μm.



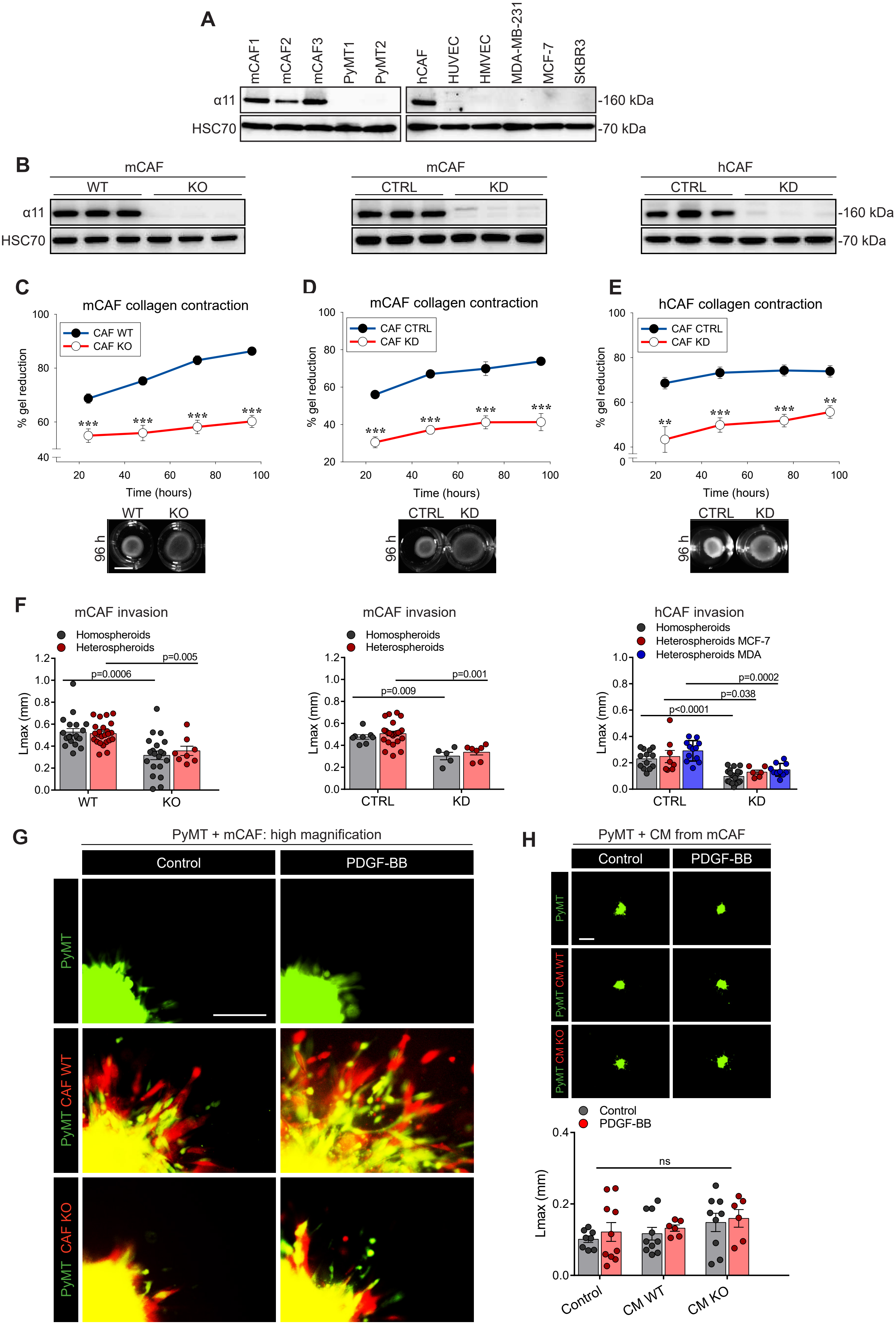
Supplemental Figure 3 corresponding to Figure 4: Integrin α11 is overexpressed in different human cancers. Various Oncomine microarray datasets were used to analyze *ITGA11* mRNA expression in different types of cancer in relation to the matched normal tissues. Increased integrin α11 expression is detected in lung adenocarcinoma (LAC), pancreatic cancer (PC: pancreatic carcinoma; PDA: pancreatic ductal adenocarcinoma), colorectal cancer (RAC: rectal adenocarcinoma; CMAC: colon mucinous adenocarcinoma; CAC: colon adenocarcinoma; CRC: colorectal carcinoma) and gastric cancer (DGAC: diffuse gastric adenocarcinoma; GT: gastric tissue; GC: gastric cancer; GITAC: gastric intestinal type adenocarcinoma ; GM: gastric mucosa ; GMAC: gastric mixed adenocarcinoma). Data (log2 median-centered intensity) were obtained from the Oncomine portal. The boxes show the median (horizontal line across the box) and interquartile range, the whiskers represent the 10th and 90th percentiles. Significance was measured by a 2-sided *t*-test for two class differential expression analyses and Pearson's correlation for multiclass analyses. *P*-values are corrected for multiple hypothesis testing using the false discovery rate method.



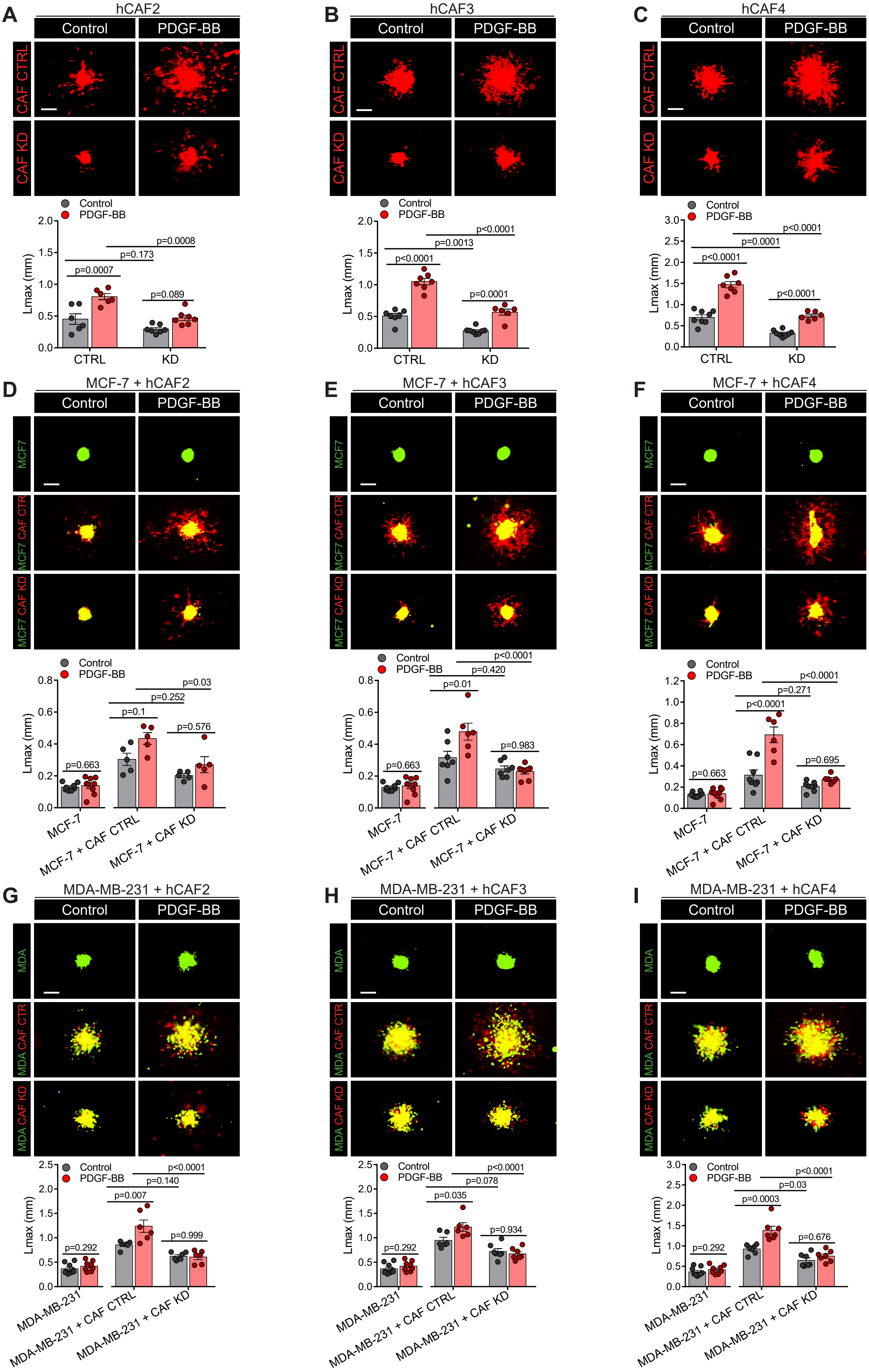
Supplemental Figure 4 corresponding to Figure 5: Integrin α11 expression is correlated with a stromal gene signature in human breast cancer. (**A-C**) corresponding to Figure 5, A-D: *ITGA11* mRNA expression in microdissected stromal compartment from normal breast (N), ductal carcinoma *in situ* (DCIS) and invasive ductal (IDC)/invasive breast (IBC) carcinonoma issued from GSE14548 (**A**), GSE8977 (**B**) and GSE9014 (**C**) datasets. The $\log_2$ transformed expression values of *ITGA11* were exported from GEO2R and analysed in GraphPad Prism. Data were analysed by ANOVA Kruskal-Wallis test with Dunn's multiple comparisons test (**A**), Unpaired 2-tailed *t*-test (**B**) and Mann Whitney test (**C**). (**D**) corresponding to Figure 5G: Pairwise-Pearson single plot correlation for each of the twelve analysed genes. Gene expression levels, *r* and *P*-values were retrieved from bc-GenExMiner.



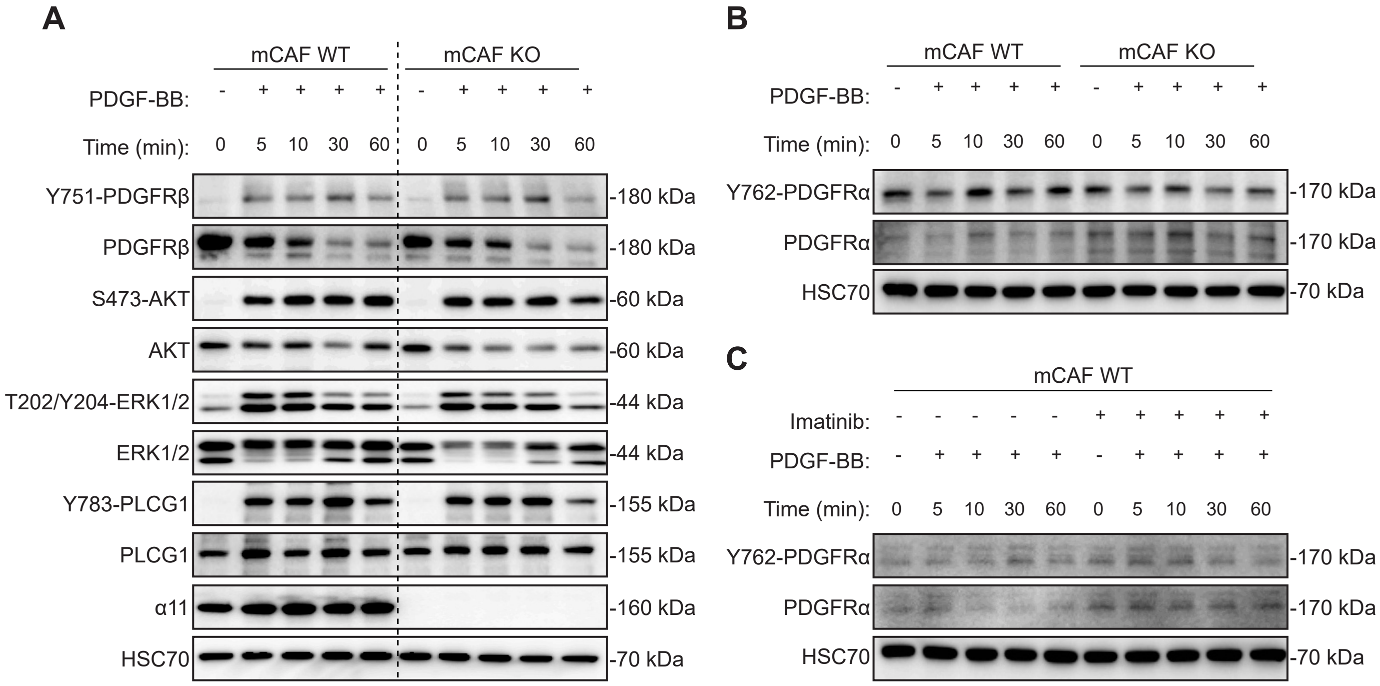
Supplemental Figure 5 corresponding to Figure 5. Integrin α11 expression correlates with a stromal gene signature in human breast cancer. TCSBN integrative co-expression network in normal tissue and BC of *ITGA11* and query genes: *CDH1 (*E-cadherin), *CSPG4* (Chondroitin sulphate proteoglycan 4), *ACTA2* (alpha smooth muscle actin), *PDGFRA* (platelet-derived growth factor receptor α) and *PDGFRB* (platelet-derived growth factor receptor β). Maximum number of nodes/gene = 10; Edge pruning parameter ($-\log_{10}p$) = 15; $P < 1.0\text{e-}15$.


A
mCAF1
mCAF2
mCAF3
PyMT1
PyMT2
hCAF
HUVEC
HMVEC
MDA-MB-231
MCF-7
SKBR3
α11
HSC70
-160 kDa
-70 kDa
B
mCAF
WT
KO
mCAF
CTRL
KD
hCAF
CTRL
KD
α11
HSC70
-160 kDa
-70 kDa
C
mCAF collagen contraction
CAF WT
CAF KO
% gel reduction
Time (hours)
***
WT
KO
96 h
D
mCAF collagen contraction
CAF CTRL
CAF KD
% gel reduction
Time (hours)
***
CTRL
KD
96 h
E
hCAF collagen contraction
CAF CTRL
CAF KD
% gel reduction
Time (hours)
**
***
CTRL
KD
96 h
F
mCAF invasion
Homospheroids
Heterospheroids
Lmax (mm)
p=0.0006
p=0.005
WT
KO
mCAF invasion
Homospheroids
Heterospheroids
Lmax (mm)
p=0.009
p=0.001
CTRL
KD
hCAF invasion
Homospheroids
Heterospheroids MCF-7
Heterospheroids MDA
Lmax (mm)
p<0.0001
p=0.038
p=0.0002
CTRL
KD
G
PyMT + mCAF: high magnification
Control
PDGF-BB
PyMT
PyMT CAF WT
PyMT CAF KO
H
PyMT + CM from mCAF
Control
PDGF-BB
PyMT
PyMT CM WT
PyMT CM KO
Control
PDGF-BB
Lmax (mm)
ns
Control
CM WT
CM KO

Supplemental Figure 6 corresponding to Figure 7: Integrin α11 regulates CAF properties. (**A**) Integrin α11 protein expression by Western Blot in mouse primary PyMT CAFs (mCAF) and tumor cells (PyMT) (left panel), and in human cells (right panel): breast CAFs (hCAF), blood endothelial cells (HUVEC), lymphatic cells (HMVEC) and breast cancer cell lines (MDA-MB-231, MCF-7, SKBR3). (**B**) Validation of integrin α11 knock-out/down (KO/KD) in mCAFs and hCAFs by Western blot (3 replicates). Integrin α11 protein expression in CAFs KD was analysed after 72 h of siRNA treatment. (**C-E**) Collagen contraction assay of mCAFs WT and KO (**C**), mCAFs CTRL and KD (**D**) and hCAFs CTRL and KD (**E**) at 24, 48, 72 and 96 h. Representative pictures of contracted gels are shown in lower panels n = 9-10 (**C**); n = 6 (**D**); n = 4-5 gels (**E**). Scale bar: 1cm. Data are expressed as % of area gel reduction normalized to time 0 h. ***$P < 0.001$; **$P < 0.01$; 2-Way ANOVA test with Holm-Sidak multiple comparison test. (**F**) corresponding to Figure 7 panels D-F: Quantification of CAF invasion in homo- *vs* heterospheroids for mCAFs WT and KO (n = 11-24), mCAFs CTRL and KD (n = 5-18) and hCAFs CTRL and KD (n = 8-10). Kruskal-Wallis with Dunn's multiple comparison (mCAF WT/KO) and 1-way ANOVA with Tukey's multiple comparison (CAF CTRL/KD) tests. (**G**) corresponding to Figure 7D: Additional high magnification homo- and heterospheroid pictures of green-tracked PyMT tumor cells and red-tracked mCAFs WT and KO issued from the panel of Figure 7D. Scale bar: 100 µm. (**H**) Representative homospheroid pictures of green-tracked PyMT tumor cells cultured for 20 h with conditioned medium (CM) from PDGF-BB-pre-treated CAFs WT or KO. Scale bar: 200 µm. Quantification of tumor cell invasion is presented in the lower panel. Data are expressed as cell distribution from the border of the spheroid until the maximal distance (Lmax). (n = 6-10). 1-way ANOVA with Tukey's multiple comparison test.


A
hCAF2
Control
PDGF-BB
CAF CTRL
CAF KD
Control
PDGF-BB
Lmax (mm)
2.0
1.5
1.0
0.5
0.0
p=0.0008
p=0.173
p=0.0007
p=0.089
CTRL
KD
B
hCAF3
Control
PDGF-BB
CAF CTRL
CAF KD
Control
PDGF-BB
Lmax (mm)
p<0.0001
p=0.0013
p<0.0001
p=0.0001
CTRL
KD
C
hCAF4
Control
PDGF-BB
CAF CTRL
CAF KD
Control
PDGF-BB
Lmax (mm)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
p<0.0001
p=0.0001
p<0.0001
p<0.0001
CTRL
KD
D
MCF-7 + hCAF2
Control
PDGF-BB
MCF7
MCF7 CAF CTR
MCF7 CAF KD
Control
PDGF-BB
Lmax (mm)
0.8
0.6
0.4
0.2
0.0
p=0.03
p=0.252
p=0.1
p=0.576
p=0.663
MCF-7
MCF-7 + CAF CTRL
MCF-7 + CAF KD
E
MCF-7 + hCAF3
Control
PDGF-BB
MCF7
MCF7 CAF CTR
MCF7 CAF KD
Control
PDGF-BB
p<0.0001
p=0.420
p=0.01
p=0.983
p=0.663
Lmax (mm)
MCF-7
MCF-7 + CAF CTRL
MCF-7 + CAF KD
F
MCF-7 + hCAF4
Control
PDGF-BB
MCF7
MCF7 CAF CTR
MCF7 CAF KD
Control
PDGF-BB
Lmax (mm)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
p<0.0001
p=0.271
p<0.0001
p=0.695
p=0.663
MCF-7
MCF-7 + CAF CTRL
MCF-7 + CAF KD
G
MDA-MB-231 + hCAF2
Control
PDGF-BB
MDA
MDA CAF CTR
MDA CAF KD
Control
PDGF-BB
Lmax (mm)
2.5
2.0
1.5
1.0
0.5
0.0
p<0.0001
p=0.140
p=0.007
p=0.999
p=0.292
MDA-MB-231
MDA-MB-231 + CAF CTRL
MDA-MB-231 + CAF KD
H
MDA-MB-231 + hCAF3
Control
PDGF-BB
MDA
MDA CAF CTR
MDA CAF KD
Control
PDGF-BB
Lmax (mm)
p<0.0001
p=0.078
p=0.035
p=0.934
p=0.292
MDA-MB-231
MDA-MB-231 + CAF CTRL
MDA-MB-231 + CAF KD
I
MDA-MB-231 + hCAF4
Control
PDGF-BB
MDA
MDA CAF CTR
MDA CAF KD
Control
PDGF-BB
Lmax (mm)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
p<0.0001
p=0.03
p=0.0003
p=0.676
p=0.292
MDA-MB-231
MDA-MB-231 + CAF CTRL
MDA-MB-231 + CAF KD

Supplemental Figure 7 corresponding to Figure 7C, E and F. Integrin α11-expressing CAFs promote *in vitro* tumor cell invasion in response to PDGF-BB. (**A-C**) corresponding to Figure 7C: Representative spheroid pictures of red-tracked hCAFs CTRL and KD issued from different patients: hCAF2 (**A**), hCAF3 (**B**), hCAF4 (**C**) after 20 h of invasion in a 3D collagen matrix in response to PDGF-BB (10 ng/ml). Scale bar: 200 µm. Quantification of cell invasion is presented in the lower panels. Data are expressed as maximal distance of invasion from the border of the spheroid (Lmax). n = 5-8. 1-way ANOVA with Tukey's multiple comparison test. (**D-I**) Representative homo- and heterospheroid pictures of green-tracked MCF-7 (**D-F**) corresponding to Figure 7E and MDA-MB-231 tumor cells (**G-I**) corresponding to Figure 7F and red-tracked hCAF2-4 CTRL and KD after 20 h of seeding in a 3D collagen matrix. Scale bar: 200 µm. Quantification of tumor cell invasion (Lmax) is presented in the lower panels. n = 5-8. Disclosure: same MCF-7 (**D-F**) and MDA-MB-231 (**G-I**) (Control and PDGF-BB-treated) homospheroid samples were used for the quantification graphs of each hCAF analysis. 1-way ANOVA with Tukey's multiple comparison test.



Supplemental Figure 8 corresponding to Figure 9: Integrin α11 regulates PDGFRβ signaling in CAFs. (**A**) corresponding to Figure 9A: Western blot of protein phosphorylation for PDGFRβ (Y751), AKT (S473), ERK1-2 (T202/Y204) and PLCG1 (Y783) after 0, 5, 10, 30 and 60 min of PDGF-BB (10 ng/ml) stimulation in mCAFs WT and KO. (**B**) corresponding to Figure 9A: Western blot of protein phosphorylation for PDGFRα (Y762) after PDGF-BB (10 ng/ml) stimulation in mCAFs WT and KO. (**C**) corresponding to Figure 9C: Western blot of protein phosphorylation for PDGFRα (Y762) after PDGF-BB (10 ng/ml) stimulation in mCAFs WT pre-treated or not with Imatinib (5 μM) for 1.5 h.

Supplemental Table 1: Meta-analysis datasets

	Sample sets	**Oncomine dataset**	**Journal & date**	**Study description**	**Ref**
1	Invasive ductal breast carcinoma	Curtis Breast	Nature 2012/04/18	One thousand nine hundred nintey-two (1,992) breast carcinoma samples and 144 paired normal breast samples were analyzed for the METABRIC project. Sample data includes ER/PR/ERBB2 status, overall survival status and followup time, stage, grade, and others.	1
2	Tubular breast carcinoma	Curtis Breast	Nature 2012/04/18	One thousand nine hundred nintey-two (1,992) breast carcinoma samples and 144 paired normal breast samples were analyzed for the METABRIC project. Sample data includes ER/PR/ERBB2 status, overall survival status and followup time, stage, grade, and others.	1
3	Invasive breast carcinoma stroma	Finak Breast	Nat Med 2008/05/01	Fifty-three (53) breast tumor stroma samples and six (6) normal breast stroma samples were analyzed on Agilent 44K microarrays. Sample data includes outcome, recurrence, grade, ER status, PR status, ERBB2 status, lymph node status, age, tumor size, and others. This data was from a dye swap study. The data in Oncomine has been processed by inversing the ratios and averaging the two values per sample.	2
4	Invasive breast carcinoma	Gluck Breast	Breast Cancer Res Treat 2011/03/04	One hundred fifty-four (154) invasive breast carcinoma samples and 4 normal breast samples were analyzed. Sample data includes intrinsic subtype, TP53 mutation status, TP53 IHC status, grade, tumor size, ER status, PR status, ERBB2 status, and response to capecitabine/docetaxel + trastuzumab or capecitabine/docetaxel.	3
5	Invasive ductal breast carcinoma stroma	Karnoub Breast	Nature 2007/10/04	Twenty-two (22) breast samples, including 15 non-tumor breast stroma samples and 7 primary invasive ductal breast carcinoma stroma samples, were analyzed on Affymetrix U133 Plus 2.0 microarrays.	4
6	Ductal breast carcinoma *in situ* stroma	Ma	Breast Cancer Res 2009/02/02	Twenty (20) ductal breast carcinoma in situ, 18 invasive ductal breast carcinoma, and 28 normal breast samples were analyzed from 14 patients, many with paired epithelial and stromal tissues. Sample data includes estrogen, progesterone and ERBB2 status; age, grade, and N stage. Refer to Ma Breast for corresponding samples that were previously analyzed on cDNA microarrays.	5
7	Invasive ductal breast carcinoma stroma	Ma	Cancer Res 2009/02/02	Twenty (20) ductal breast carcinoma in situ, 18 invasive ductal breast carcinoma, and 28 normal breast samples were analyzed from 14 patients, many with paired epithelial and stromal tissues. Sample data includes estrogen, progesterone and ERBB2 status; age, grade, and N stage. Refer to Ma Breast for corresponding samples that were previously analyzed on cDNA microarrays.	5
8	Invasive breast carcinoma	TCGA Breast	No Associated Paper 2011/09/02	Five hundred thirty-two (532) invasive breast carcinoma, 61 paired normal breast tissue and 3 paired metastatic samples were analyzed. Sample data includes age, histology, TNM stage, ER/PR/ERBB2 status, sex, stage, and others. This dataset consists of Level 2 (processed) data from the TCGA data portal.	-
9	Invasive ductal breast carcinoma	TCGA Breast	No Associated Paper 2011/09/02	Five hundred thirty-two (532) invasive breast carcinoma, 61 paired normal breast tissue and 3 paired metastatic samples were analyzed. Sample data includes age, histology, TNM stage, ER/PR/ERBB2 status, sex, stage, and others. This dataset consists of Level 2 (processed) data from the TCGA data portal.	-
10	Invasive lobular breast carcinoma	TCGA Breast	No Associated Paper 2011/09/02	Five hundred thirty-two (532) invasive breast carcinoma, 61 paired normal breast tissue and 3 paired metastatic samples were analyzed. Sample data includes age, histology, TNM stage, ER/PR/ERBB2 status, sex, stage, and others. This dataset consists of Level 2 (processed) data from the TCGA data portal.	-
11	Mixed lobular and ductal breast carcinoma	TCGA Breast	No Associated Paper 2011/09/02	Five hundred thirty-two (532) invasive breast carcinoma, 61 paired normal breast tissue and 3 paired metastatic samples were analyzed. Sample data includes age, histology, TNM stage, ER/PR/ERBB2 status, sex, stage, and others. This dataset consists of Level 2 (processed) data from the TCGA data portal.	-
12	Invasive ductal breast carcinoma	Turashvili Breast	BMC Cancer 2007/03/27	Tissue samples from breast carcinomas of the duct (n=5) and lobules (n=5), as well as normal adjacent duct (n=10) and normal adjacent lobules (n=10) were analyzed on Affymetrix HG U133 Plus 2.0 arrays. Sample data includes cancer type, Nottingham grade, accompanying changes, lymph node status, estrogen receptor status, progesterone receptor status, HER2 status, Bcl-2 status, patient ID, and E-cadherin status.	6
References					
1.	**Curtis C. et al, Nature 486:346-352.**				
2.	**Finak G. et al, Nat Med. 14:518-527.**				
3.	**Glück S. et al, Breast Cancer Res Treat. 132:781-791.**				
4.	**Karnoub AE. et al, Nature 449 :557-563.**				
5.	**Ma XJ. et al, Breast Cancer Res. 11:R7.**				
6.	**Turashvili G. et al, BMC Cancer 7: 55.**				

Supplemental Table 2: Gene correlation

TCGA Breast			Metabric			GenExMiner			*ITGA11*-associated gene signature
Gene Symbol	Pearson Score	No. patients	Gene Symbol	Pearson Score	No. patients	Gene symbol	Pearson Score	No. patients	
COL10A1	0.89	817	*COL11A1*	0.84	2509	*COL10A1*	0.6934	2067	*ADAMTS2*
COL11A1	0.86	817	*COL8A2*	0.81	2509	*AEBP1*	0.6870	2412	*AEBP1*
ANTXR1	0.86	817	*COL12A1*	0.8	2509	*COL11A1*	0.6737	2067	*ANGPTL2*
THBS2	0.84	817	*LRRC15*	0.78	2509	*COL8A2*	0.6705	2007	*ANTXR1*
AEBP1	0.83	817	*SYNDIG1*	0.78	2509	*ANTXR1*	0.6567	2413	*C1QTNF3*
COL12A1	0.82	817	*COL8A1*	0.77	2509	*THBS2*	0.6487	2665	*C1QTNF6*
LUM	0.82	817	*ANTXR1*	0.77	2509	*FBN1*	0.6424	2413	*CDH11*
LRRC15	0.81	817	*AEBP1*	0.76	2509	*LRRC15*	0.6326	2413	*CMTM3*
COL8A2	0.81	817	*THBS2*	0.75	2509	*SYNDIG1*	0.6326	2067	*COL10A1*
FBN1	0.8	817	*NKX3-2*	0.73	2509	*COL5A1*	0.6318	2665	*COL11A1*
NOX4	0.8	817	*COL5A1*	0.73	2509	*COL5A2*	0.6308	2665	*COL12A1*
CALHM5	0.8	817	*COL10A1*	0.73	2509	*MFAP5*	0.6276	2067	*COL1A1*
FN1	0.79	817	*FBN1*	0.73	2509	*NOX4*	0.6274	2067	*COL1A2*
CDH11	0.78	817	*MFAP5*	0.73	2509	*VCAN*	0.6134	2413	*COL5A1*
COL5A2	0.78	817	*NOX4*	0.73	2509	*LOC102725271*	0.6113	1758	*COL5A2*
DACT1	0.78	817	*COL5A2*	0.72	2509	*THY1*	0.6104	2665	*COL8A1*
ITGBL1	0.77	817	*MMP11*	0.72	2509	*MXRA5*	0.6088	2067	*COL8A2*
MFAP5	0.76	817	*PLAU*	0.72	2509	*CDH11*	0.6054	2665	*COMP*
CORIN	0.76	817	*CORIN*	0.72	2509	*ASPN*	0.6017	2067	*CORIN*
NTM	0.76	817	*NTM*	0.72	2509	*GLT8D2*	0.6008	2067	*DACT1*
COL8A1	0.75	817	*SGIP1*	0.72	2509	*PLAU*	0.5952	2665	*DKK3*
SYNDIG1	0.75	817	*COL1A1*	0.71	2509	*ST6GAL2*	0.5942	1859	*DPYSL3*
GLT8D2	0.75	817	*COMP*	0.7	2509	*COMP*	0.5941	2413	*EDNRA*
MXRA5	0.75	817	*SCARF2*	0.69	2509	*DACT1*	0.5913	2066	*FAP*
CYS1	0.75	817	*MXRA5*	0.69	2509	*CYS1*	0.5904	1808	*FBN1*
RASGRF2	0.73	817	*PLPP4*	0.69	2509	*PPAPDC1A*	0.5902	2312	*FNDC1*
FAP	0.72	817	*THY1*	0.68	2509	*COL1A1*	0.5854	2665	*GLT8D2*
GPR1	0.72	817	*DPYSL3*	0.67	2509	*FAP*	0.5839	2067	*HTRA1*
NID2	0.72	817	*GJB2*	0.67	2509	*NID2*	0.5836	2413	*HTRA3*
PLPP4	0.72	817	*SPOCK1*	0.67	2509	*COL12A1*	0.5825	2319	*LOX*
HSD17B6	0.71	817	*C1QTNF3*	0.67	2509	*MMP11*	0.5709	2665	*LOXL1*
DKK3	0.71	817	*C1QTNF5*	0.67	2509	*HTRA3*	0.5707	2413	*LRRC15*
VCAN	0.7	817	*COL1A2*	0.66	2509	*FNDC1*	0.5664	1966	*MFAP5*
DCN	0.7	817	*SUGCT*	0.66	2509	*ITGBL1*	0.5645	2413	*MMP11*
DPYSL3	0.7	817	*LOXL1*	0.65	2509	*ADAMTS2*	0.5591	2413	*MXRA5*
SPOCK1	0.7	817	*CEMIP*	0.65	2509	*SPOCK1*	0.5583	2413	*NOX4*

TIMP2	0.7	817	*SRPX2*	0.65	2509	*ADAM12*	0.5579	2067	*NUAK1*
ST6GAL2	0.7	817	*MXRA8*	0.64	2509	*GJB2*	0.5578	2067	*PDPN*
COL1A2	0.69	817	*SULF1*	0.64	2509	*COL6A2*	0.5562	2413	*PLAU*
COL5A1	0.69	817	*CMTM3*	0.64	2509	*C1QTNF3*	0.5550	2413	*PRRX1*
INHBA	0.69	817	*MFAP2*	0.63	2509	*SULF1*	0.5550	2067	*SERPINF1*
C1QTNF3	0.69	817	*TGFB1I1*	0.63	2509	*WISP1*	0.5542	2413	*SFRP2*
AXL	0.68	817	*DACT1*	0.63	2509	*COL1A2*	0.5534	2662	*SPOCK1*
ADAMTS12	0.68	817	*FNDC1*	0.63	2509	*SPON1*	0.5528	2067	*SULF1*
ANGPTL2	0.68	817	*GRP*	0.62	2509	*SPARC*	0.5518	2665	*SYNDIG1*
F13A1	0.67	817	*GLIS3*	0.62	2509	*DPYSL3*	0.5510	2665	*THBS2*
LOX	0.67	817	*HSD17B6*	0.62	2509	*FIBIN*	0.5504	2413	*THY1*
PRRX1	0.67	817	*NUAK1*	0.62	2509	*UNC5B*	0.5499	2413	*TIMP2*
C14ORF37	0.67	817	*C1QTNF6*	0.62	2509	*LUM*	0.5451	2665	*TSHZ3*
CTHRC1	0.67	817	*KIF26B*	0.62	2509	*SFRP2*	0.5426	2413	*UNC5B*
CEMIP	0.67	817	*CDH11*	0.61	2509	*ANGPTL2*	0.5414	2413	*VCAN*
COL6A3	0.66	817	*FAP*	0.61	2509	*OLFML2B*	0.5410	2413	
ECM2	0.66	817	*FN1*	0.61	2509	*EFEMP2*	0.5398	2413	
SERPINF1	0.66	817	*ISLR*	0.61	2509	*CILP2*	0.5373	1286	
WNT2	0.66	817	*GLT8D2*	0.61	2509	*PRRX1*	0.5372	2413	
OMD	0.65	817	*CERCAM*	0.61	2509	*COPZ2*	0.5359	2413	
SPARC	0.65	817	*COPZ2*	0.61	2509	*MXRA8*	0.5357	1918	
CHSY3	0.65	817	*OLFML2B*	0.61	2509	*POSTN*	0.5335	2606	
P4HA3	0.65	817	*HTRA3*	0.61	2509	*ISLR*	0.5328	2067	
FIBIN	0.65	817	*BGN*	0.6	2509	*HTRA1*	0.5326	2665	
COL1A1	0.64	817	*PCOLCE*	0.6	2509	*C1QTNF6*	0.5306	2412	
COL3A1	0.64	817	*SDC1*	0.6	2509	*LOX*	0.5306	2413	
GPR21	0.64	817	*MYL9*	0.6	2509	*PDPN*	0.5305	2413	
MMP11	0.64	817	*DKK3*	0.6	2509	*LOXL1*	0.5293	2665	
SGCD	0.64	817	*COL3A1*	0.59	2509	*CTSK*	0.5282	2412	
RECK	0.64	817	*COL6A1*	0.59	2509	*GRP*	0.5269	2412	
ADAMTS2	0.64	817	*COL6A2*	0.59	2509	*CORIN*	0.5266	2412	
OLFML1	0.64	817	*VCAN*	0.59	2509	*LOC101929504*	0.5266	1036	
ASPN	0.64	817	*PRRX1*	0.59	2509	*DKK3*	0.5250	2413	
ZFPM2	0.64	817	*PDPN*	0.59	2509	*TSHZ3*	0.5162	2017	
PDPN	0.63	817	*PPEF1*	0.58	2509	*EMILIN1*	0.5152	2413	
GLIS2	0.63	817	*HTRA1*	0.58	2509	*RUNX2*	0.5143	2413	
CMTM3	0.63	817	*SPON1*	0.58	2509	*PCOLCE*	0.5132	2665	
SRPX2	0.63	817	*C14ORF37*	0.58	2509	*COL8A1*	0.5087	2665	
LOXL2	0.62	817	*MSRB3*	0.58	2509	*SERPINF1*	0.5084	2413	
MMP2	0.62	817	*RCN3*	0.58	2509	*GXYLT2*	0.5078	2104	
NID1	0.62	817	*P3H1*	0.58	2509	*CTHRC1*	0.5076	2413	
PDGFRB	0.62	817	*EDNRA*	0.57	2509	*CMTM3*	0.5067	2067	

GXYLT2	0.62	817	*MMP2*	0.57	2509	*TIMP2*	0.5063	2413
TNFSF4	0.62	817	*TPM2*	0.57	2509	*SALL4*	0.5050	2067
ADAM12	0.62	817	*TNFSF4*	0.57	2509	*BGN*	0.5022	2665
MRVI1	0.62	817	*EMILIN1*	0.57	2509	*NUAK1*	0.5022	2008
POSTN	0.62	817	*TM6SF2*	0.57	2509	*EDNRA*	0.5007	2067
FSTL1	0.61	817	*PALLD*	0.57	2509			
SUGCT	0.61	817	*UNC5B*	0.57	2509			
MSRB3	0.61	817	*KIAA1217*	0.57	2509			
LAMA4	0.6	817	*TSHZ3*	0.57	2509			
PDGFRL	0.6	817	*AXL*	0.56	2509			
TBX5	0.6	817	*BMP1*	0.56	2509			
KLKP1	0.6	817	*COL6A3*	0.56	2509			
TM6SF2	0.6	817	*EVC*	0.56	2509			
BNC2	0.6	817	*MMP13*	0.56	2509			
GPX8	0.59	817	*PTPRD*	0.56	2509			
PLAU	0.59	817	*ADAMTSL2*	0.56	2509			
TIMP3	0.59	817	*MXRA7*	0.56	2509			
SGIP1	0.59	817	*SYDE1*	0.56	2509			
FNDC1	0.59	817	*NINJ2*	0.55	2509			
PALLD	0.59	817	*RARRES2*	0.55	2509			
JCAD	0.59	817	*TIMP2*	0.55	2509			
SLC24A2	0.59	817	*TIMP3*	0.55	2509			
CCIN	0.58	817	*HEPH*	0.55	2509			
COMP	0.58	817	*FST*	0.55	2509			
EDNRA	0.58	817	*SALL4*	0.55	2509			
LRP1	0.58	817	*GPR1*	0.54	2509			
HTRA1	0.58	817	*SFRP2*	0.54	2509			
ALPK2	0.58	817	*WNT2*	0.54	2509			
EVC	0.57	817	*SH3PXD2A*	0.54	2509			
LINC00922	0.57	817	*ZNF668*	0.54	2509			
UNC5B	0.57	817	*SPSB1*	0.54	2509			
TSHZ3	0.57	817	*CAVIN1*	0.54	2509			
HTRA3	0.57	817	*ANGPTL2*	0.54	2509			
ARSB	0.56	817	*CTSK*	0.53	2509			
RUNX2	0.56	817	*LAMA4*	0.53	2509			
CD55	0.56	817	*PDGFRB*	0.53	2509			
LOXL1	0.56	817	*TNFAIP6*	0.53	2509			
MMP14	0.56	817	*ADAMTS2*	0.53	2509			
PTPRD	0.56	817	*FSTL1*	0.53	2509			
SLIT3	0.56	817	*CNTN1*	0.52	2509			
SFRP2	0.55	817	*ITGA5*	0.52	2509			
PODNL1	0.55	817	*LOX*	0.52	2509			

HMCN1	0.55	817	*CD99*	0.52	2509
CALD1	0.54	817	*PXDN*	0.52	2509
TCF4	0.54	817	*PDLIM7*	0.52	2509
THBS1	0.54	817	*COL5A3*	0.52	2509
MARVELD1	0.54	817	*SERPINH1*	0.51	2509
GREM1	0.54	817	*EPYC*	0.51	2509
VSTM4	0.53	817	*SERPINF1*	0.51	2509
EPYC	0.53	817	*TAGLN*	0.51	2509
GLIS3	0.53	817	*CRISPLD2*	0.51	2509
THY1	0.53	817	*PMEPA1*	0.51	2509
WISP1	0.53	817	*FKBP9P1*	0.51	2509
NUAK1	0.53	817			
PLXNC1	0.53	817			
SEC23A	0.53	817			
ACKR4	0.53	817			
KIF26B	0.53	817			
PARVA	0.53	817			
NEXN	0.53	817			
DSE	0.53	817			
NAP1L3	0.52	817			
PRKG1	0.52	817			
ZEB1	0.52	817			
FILIP1L	0.52	817			
C1QTNF6	0.52	817			
GALNT15	0.52	817			
SULF1	0.52	817			
MITF	0.51	817			
PRKG2	0.51	817			
SLC6A1	0.51	817			
MICAL2	0.51	817			
BICC1	0.51	817			
FKBP7	0.51	817			
HEG1	0.51	817			

Supplemental Table 3: Reactome pathway

Pathway identifier	Pathway name	found	total	#Interactors found	#Interactors total	ratio	pValue	FDR	#Reactions found	#Reactions total	Reactions ratio	Submitted entities
R-HSA-1474244	Extracellular matrix organization	34	329	4	394	0.02435	1.5,85.811E-16	2.75E-14	157	318	0.0286	*SPARC;LAMA4;COL11A1; COL12A1;HTRA1;NID2; LOXL1;COMP;ADAMTS2;CTSK; TIMP2;COL10A1; EMILIN1;LUM;MMP2;FN1;BGN; PCOLCE;ASPN;COL1A1;MFAP5;MMP11;COL3A1;VCAN; COL1A2;COL5A1;LOX;COL6A2; COL5A2;ADAM12;COL8A2;COL8A1;COL6A3;FBN1*
R-HSA-2022090	Assembly of collagen fibrils and other multimeric structures	15	67	0	5	0.00496	2.22E-16	2.75E-14	19	26	0.0023	*COL11A1;COL12A1;PCOLCE;LOXL1;COL1A1;COL3A1;COL1A2;LOX;COL5A1;COL6A2;COL5A2;COL8A2;COL10A1;COL8A1;COL6A3*
R-HSA-1442490	Collagen degradation	15	69	0	6	0.00511	2.22E-16	2.75E-14	21	34	0.0031	*MMP2;COL11A1;COL12A1;COL1A1;MMP11;COL3A1;COL1A2; COL5A1;COL6A2;CTSK;COL5A2;COL8A2;COL10A1;COL8A1;COL6A3*
R-HSA-1474228	Degradation of the extracellular matrix	19	148	1	44	0.01095	5.55E-15	5.16E-13	52	105	0.0095	*MMP2;COL11A1;COL12A1;HTRA1;FN1;COL1A1;MMP11;COL3A1;COL1A2;COL5A1;COL6A2;CTSK;COL5A2;TIMP2;COL8A2;COL10A1;COL8A1;COL6A3;FBN1*
R-HSA-8948216	Collagen chain trimerization	12	44	0	0	0.00326	8.33E-15	6.16E-13	9	28	0.0025	*COL1A1;COL3A1;COL1A2;COL5A1;COL6A2;COL11A1;COL5A2;COL12A1;COL8A2;COL10A1;COL8A1;COL6A3*
R-HSA-1474290	Collagen formation	16	104	0	13	0.00770	9.99E-15	6.20E-13	50	77	0.0069	*COL11A1;COL12A1;PCOLCE;LOXL1;COL1A1;ADAMTS2;COL3A1;COL1A2;LOX;COL5A1;COL6A2;COL5A2;COL8A2;COL10A1;COL8A1;COL6A3*
R-HSA-1650814	Collagen biosynthesis and modifying enzymes	14	76	0	8	0.00562	3.52E-14	1.87E-12	31	51	0.0046	*COL11A1;COL12A1;PCOLCE;COL1A1;ADAMTS2;COL3A1;COL1A2;COL5A1;COL6A2;COL5A2;COL8A2;COL10A1;COL8A1;COL6A3*
R-HSA-3000178	ECM proteoglycans	15	78	1	31	0.00577	4.92E-14	2.26E-12	12	22	0.0020	*SPARC;LUM;LAMA4;FN1;BGN; ASPN;COL1A1;COMP;VCAN;COL3A1;COL1A2;COL5A1;COL6A2;COL5A2;COL6A3*
R-HSA-216083	Integrin cell surface interactions	14	87	1	261	0.00644	1.34E-06	5.51E-05	10	55	0.0050	*LUM;FN1;COL1A1;COMP;COL3A1;COL1A2;COL5A1;COL6A2;COL5A2;COL8A2;COL10A1;COL8A1;COL6A3;FBN1*
R-HSA-2243919	Crosslinking of collagen fibrils	5	24	0	0	0.00178	2.45E-06	8.34E-05	12	13	0.0012	*COL1A1;COL1A2;LOX;PCOLCE;LOXL1*
R-HSA-8875878	MET promotes cell motility	8	45	0	69	0.00333	5.17E-06	1.60E-04	1	12	0.0011	*COL1A1;COL3A1;COL1A2;COL5A1;LAMA4;COL11A1;COL5A2; FN1*
R-HSA-1566948	Elastic fibre formation	6	46	1	12	0.00340	7.68E-06	2.15E-04	13	17	0.0015	*MFAP5;LOX;FN1;EMILIN1;LOXL1;FBN1*
R-HSA-3000171	Non-integrin membrane-ECM interactions	9	61	1	107	0.00451	1.31E-05	3.40E-04	8	22	0.0020	*COL1A1;COL3A1;COL1A2;COL5A1;LAMA4;COL11A1;COL5A2; FN1;COL10A1*
R-HSA-419037	NCAM1 interactions	5	44	0	12	0.00326	1.25E-04	0.002881196	1	10	0.0009	*COL3A1;COL5A1;COL6A2;COL5A2;COL6A3*
R-HSA-2129379	Molecules associated with elastic fibres	4	38	0	2	0.00281	4.26E-04	0.009381006	6	10	0.0009	*MFAP5;FN1;EMILIN1;FBN1*
R-HSA-3000170	Syndecan interactions	6	29	1	92	0.00215	5.19E-04	0.010379892	3	15	0.0014	*COL1A1;COL3A1;COL1A2;COL5A1;COL5A2;FN1*
R-HSA-186797	Signaling by PDGF	7	69	0	127	0.00511	0.001215842	0.023101006	21	28	0.0025	*PDGFRB;COL3A1;COL5A1;COL6A2;COL5A2;COL6A3;THBS2*
R-HSA-1592389	Activation of Matrix Metalloproteinases	4	35	1	24	0.00259	0.001571342	0.028284155	12	27	0.0024	*MMP11;CTSK;MMP2;TIMP2*
R-HSA-8957275	Post-translational protein phosphorylation	5	109	0	0	0.00807	0.002648245	0.045020159	1	1	0.0001	*VCAN;FN1;MXRA8;FSTL1;FBN1*
R-HSA-381426	Regulation of IGF transport and uptake by IGFBPs	6	127	0	40	0.00940	0.003292029	0.048406843	2	14	0.0013	*VCAN;MMP2;FN1;MXRA8;FSTL1;FBN1*

Supplemental Table 4: Primers

RT-qPCR Primers

Gene	**Type**	**Sequence**
Itga11	Forward	5’-*CTGAGCCTTGCCACCAAC*-3’
	Reverse	5’-*CACTCGTGCGACCAGAGA*-3’
Pdgfra	Forward	5’-*CAGACATTGACCCTGTTCCA*-3’
	Reverse	5’-*CTTCCGAAGTCTGTGAGCTGT*-3’
Pdgfrb	Forward	5’-*GCGTATCTATATCTTTGTGCCAGA*-3’
	Reverse	5’-*ACAGGTCCTCGGAGTCCAT*-3’
Tbp	Forward	5’-*GGCGGTTTGGCTAGGTTT*-3’
	Reverse	5’-*GGGTTATCTTCACACACCATGA*-3’

Genotyping Primers

Gene	**Type**	**Sequence**
Itga11	WT-Forward	5’-*CCATCAGAAGACAGGAGACGTATAACA*-3’
	WT-Reverse	5’-*TGGTCAGTGGATGGGTTAGGAAG*-3’
	LacZ-1	5’-*GTGGTGGTTATGCCGATCGC*-3’
	LacZ-2	5’-*TACCACAGCGGATGGTTCGG*-3’
PyMT	PymT3p	5’-*CGGCGGAGCGAGGAACTGAGGAGAG*-3’
	PymT4m	5’-*TCAGAAGACTCGGCAGTCTTAGGCG*-3’

Supplemental Table 5:

Antibody	Specificity	Brand source	Ref.	Type	Dilution			
					IF	**WB**	**IP**	**IHC**
ITGA11	mouse	R&D systems	AF6498	Polyclonal	1 :20	1 :200		
ITGA11	human	Patent EP18155716	Mab 203 E1H5	Monoclonal	1 :150			
NG2	mouse	Milipore	AB5320	Polyclonal	1 :100			
pan-cytokeratin	mouse	Abcam	AB7753	Monoclonal	1 :50			
FAP	mouse	Abcam	AB53066	Polyclonal	1 :50			
FSP1	mouse	Abcam	AB41532	Polyclonal	1 :50			
aSMA-FITC	mouse	Sigma Aldrich	F3777	Monoclonal clone 1A4	1 :50			1 :200
PDGFRα	mouse	eBiosciences	14-1401-82	Monoclonal clone APA5	1 :50			
PDGFRα	mouse	Cell Signalling	3174	Monoclonal D1E1E		1 :1000		
PDGFRα-Y762	mouse	Cell Signalling	24188	Monoclonal D9B1N		1 :1000		
PDGFRβ	mouse	eBiosciences	14-1402-82	Monoclonal APB5	1 :50			
PDGFRβ	human	Cell Signalling	3169	Monoclonal 28E1	1 :50			
PDGFRβ	mouse	Cell Signalling	3175	Monoclonal clone 2B3		1 :1000	1 :50	
PDGFRβ-Y771	mouse	Cell Signalling	3173	Monoclonal clone 76D6		1 :1000		
PDGFRβ-Y751	mouse	Cell Signalling	3166	Monoclonal clone 88H8		1 :1000		
CRK	mouse	Cell Signalling	3492	Polyclonal		1 :1000		
CRK-Y221	mouse	Cell Signalling	3491	Polyclonal		1 :1000		
SRC	mouse	Cell Signalling	2109	Monoclonal clone 36D10		1 :1000		
SRC-Y416	mouse	Cell Signalling	2101	Polyclonal		1 :1000		
JNK/SAPK	mouse	Cell Signalling	9252	Polyclonal		1 :1000		
JNK/SAPK-T183/Y185	mouse	Cell Signalling	9251	Polyclonal		1 :1000		
AKT	mouse	Cell Signalling	9272	Polyclonal		1 :1000		
AKT-S473	mouse	Cell Signalling	9271	Polyclonal		1 :1000		
ERK1/2	mouse	Cell Signalling	4695	Monoclonal clone 137F5		1 :1000		
ERK1/2-T202/Y204	mouse	Cell Signalling	4370	Monoclonal clone D13.14.4E		1 :1000		
PLCG1	mouse	Cell Signalling	5690	Monoclonal clone D9H10		1 :1000		
PLCG1-y783	mouse	Cell Signalling	14008	Monoclonal clone D6M9S		1 :1000		
TNC	mouse	R&S Systems	MAB2138	Clone 578	1 :50	1 :500		
TNC	human	R&S Systems	AF3358	Polyclonal	1 :100			
HSC70	mouse	Santa Cruz	sc-7298	Monoclonal clone B6		1 :2000		

**All secondary HRP-linked antibodies for Western Blot detection were purchased from Cell Signaling Technology. All secondary antibodies for immunofluorescence were AlexaFluor488/594 purchased from Invitrogen (Thermo Fisher). All antibodies were diluted and used according manufacturer's recommendations*