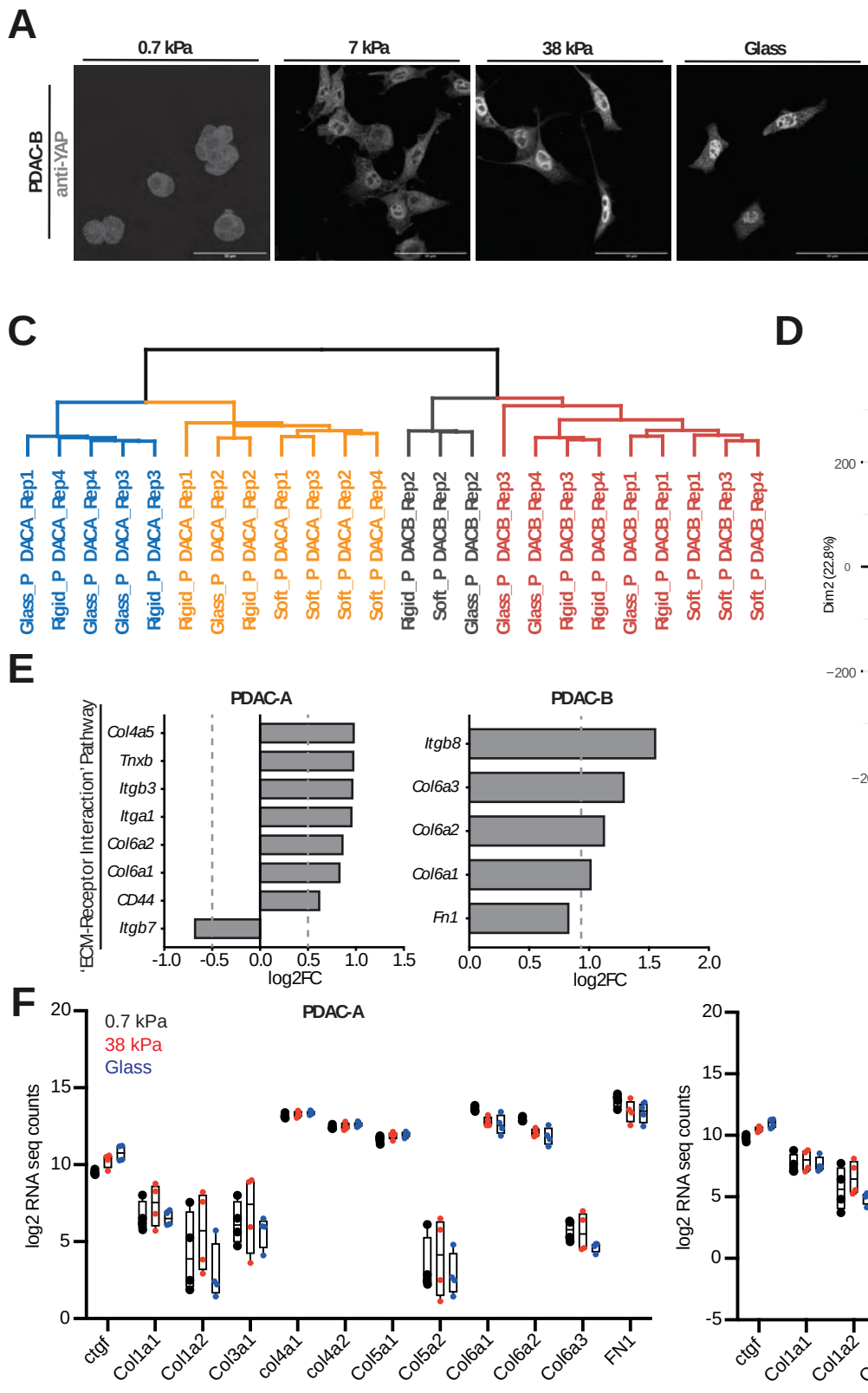
A
0.7 kPa
7 kPa
38 kPa
Glass
PDAC-B
anti-YAP
B
PDAC-B
Nuclear / Cytosolic YAP
p<0.0001
0.7kPa
7kPa
38kPa
Glass
C
Glass_P DACA_Rep1
Rigid_P DACA_Rep4
Glass_P DACA_Rep4
Glass_P DACA_Rep3
Rigid_P DACA_Rep3
Rigid_P DACA_Rep1
Glass_P DACA_Rep2
Rigid_P DACA_Rep2
Soft_P DACA_Rep1
Soft_P DACA_Rep3
Soft_P DACA_Rep2
Soft_P DACA_Rep4
Rigid_P DACB_Rep2
Soft_P DACB_Rep2
Glass_P DACB_Rep2
Glass_P DACB_Rep3
Glass_P DACB_Rep4
Rigid_P DACB_Rep3
Rigid_P DACB_Rep4
Glass_P DACB_Rep1
Rigid_P DACB_Rep1
Soft_P DACB_Rep1
Soft_P DACB_Rep3
Soft_P DACB_Rep4
D
Groups
Glass_PDACA
Glass_PDACB
Rigid_PDACA
Rigid_PDACB
Soft_PDACA
Soft_PDACB
PDAC-B
PDAC-A
Dim1 (39.8%)
Dim2 (22.8%)
E
PDAC-A
PDAC-B
'ECM-Receptor Interaction' Pathway
Col4a5
Tnxb
Itgb3
Itga1
Col6a2
Col6a1
CD44
Itgb7
Itgb8
Col6a3
Col6a2
Col6a1
Fn1
log2FC
F
0.7 kPa
38 kPa
Glass
PDAC-A
PDAC-B
log2 RNA seq counts
ctgf
Col1a1
Col1a2
Col3a1
col4a1
col4a2
Col5a1
Col5a2
Col6a1
Col6a2
Col6a3
FN1

Fig. S1. Low substrate stiffness alters the expression of matrisome-related genes in PDAC cells.

A: Immunofluorescence of PDAC-B cells cultured atop of 0.7 kPa, 7 kPa or 38 kPa fibronectin-coated polyacrylamide hydrogels for 24 hours, showing YAP1 (grey). Scale bars, 50 µm.

B: Quantification of 'nuclear YAP1'/ 'cytosolic YAP1' intensity ratio for cells in (A). Values are mean ± s.e.m. from n= 52 cells, 0.7kPa; n= 68, 7kPa; n= 42, 38kPa; n= 46, glass. Cells are from 3 independent experiments. Statistical significance was assessed by Kruskal-Wallis test with Dunn's multiple comparisons test.

C: Hierarchical clustering of RNA sequencing signatures from PDAC-A and PDAC-B cells cultured on fibronectin-coated 0.7 kPa, 38 PAAm hydrogels and glass coverslips for 24 hours.

D: PCA clustering of cells from **(C)**.

E: Bar plot displaying differentially expressed genes ($p_{adj} < 0.05$; log2 fold change >1) from the 'ECM-Receptor Interaction' KEGG pathway that were enriched in cells from **(C)**. Data is organised by log2 fold change.

F: log2 RNA seq counts of indicated genes genes of PDAC-A (left) and PDAC-B (right) cells cultured on 0.7 kPa, 38 kPa hydrogels and glass coverslips. Data is from n = 4 independent replicates per condition for each cell line.

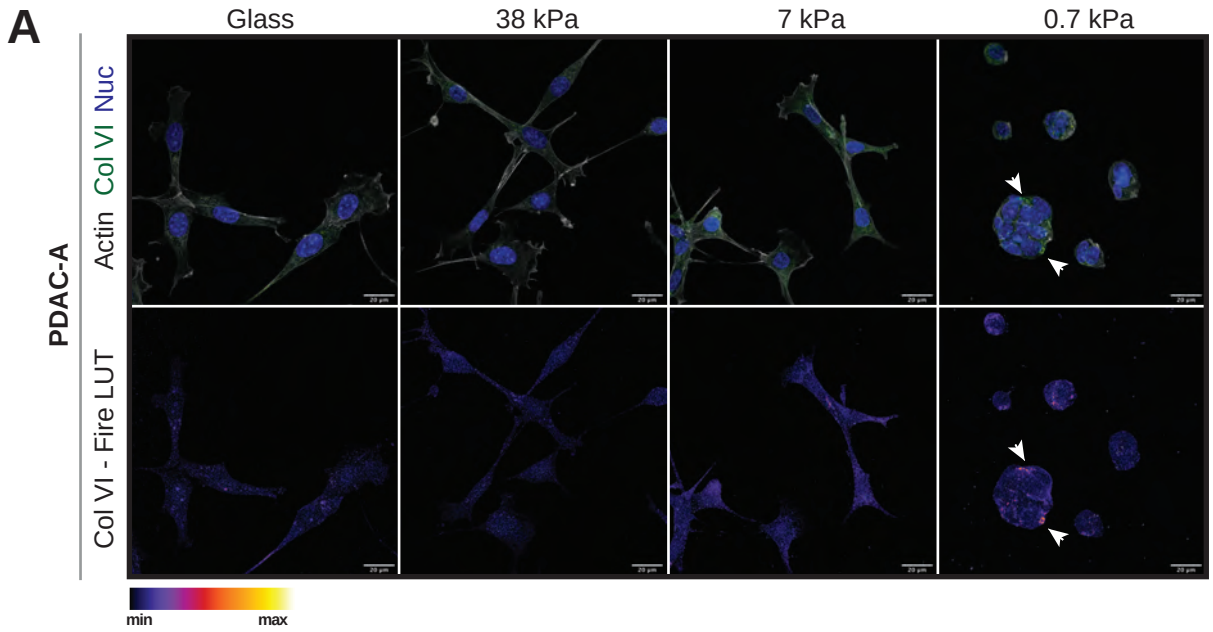
A
Glass
38 kPa
7 kPa
0.7 kPa
PDAC-A
Actin Col VI Nuc
Col VI - Fire LUT
min
max
B
Glass
38 kPa
7 kPa
0.7 kPa
PANC-1
Actin ColVI Nuc
ColVI

Fig. S2. Collagen VI is upregulated in PDAC cells upon low substrate stiffness

A: Top; Immunofluorescence of PDAC-A cells cultured on glass coverslips, 0.7-, 7- and 38-kPa fibronectin-coated hydrogels, showing Collagen VI (green), Actin (grey) and nuclei (blue). Representative pictures from 3 independent experiments. Bottom; Individual Collagen VI channel (Fire LUT). Scale bars, 20µm. Arrowheads indicate Collagen VI enrichment.

B: Top; Immunofluorescence of PANC-1 cells cultured on glass coverslips, 0.7-, 7- and 38-kPa fibronectin-coated hydrogels, showing Collagen VI (green), Actin (grey) and nuclei (blue). Representative pictures from 3 independent experiments. Bottom; Individual Collagen VI channel (Green). Scale bars, 20µm.

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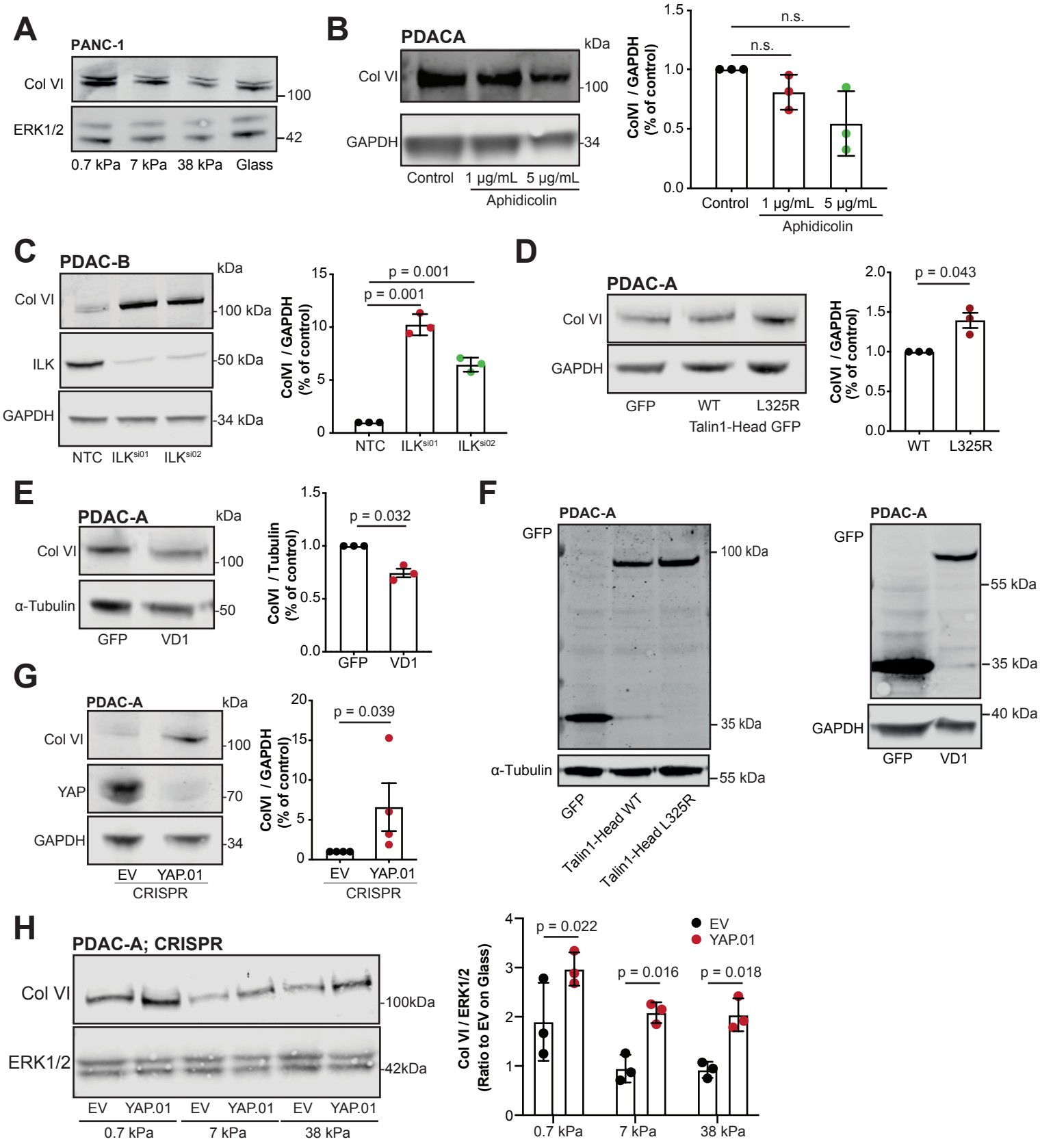
A
PANC-1
Col VI
ERK1/2
100
42
0.7 kPa 7 kPa 38 kPa Glass
B
PDACA
kDa
Col VI
GAPDH
100
34
Control 1 µg/mL 5 µg/mL
Aphidicolin
ColVI / GAPDH (% of control)
n.s.
n.s.
Control 1 µg/mL 5 µg/mL
Aphidicolin
C
PDAC-B
kDa
Col VI
ILK
GAPDH
100 kDa
50 kDa
34 kDa
NTC ILKsi01 ILKsi02
ColVI / GAPDH (% of control)
p = 0.001
p = 0.001
NTC ILKsi01 ILKsi02
D
PDAC-A
Col VI
GAPDH
GFP WT L325R
Talin1-Head GFP
ColVI / GAPDH (% of control)
p = 0.043
WT L325R
E
PDAC-A
kDa
Col VI
α-Tubulin
100
50
GFP VD1
ColVI / Tubulin (% of control)
p = 0.032
GFP VD1
F
PDAC-A
GFP
100 kDa
35 kDa
α-Tubulin
55 kDa
GFP Talin1-Head WT Talin1-Head L325R
PDAC-A
GFP
55 kDa
35 kDa
GAPDH
40 kDa
GFP VD1
G
PDAC-A
kDa
Col VI
YAP
GAPDH
100
70
34
EV YAP.01
CRISPR
ColVI / GAPDH (% of control)
p = 0.039
EV YAP.01
CRISPR
H
PDAC-A; CRISPR
Col VI
ERK1/2
100kDa
42kDa
EV YAP.01 EV YAP.01 EV YAP.01
0.7 kPa 7 kPa 38 kPa
Col VI / ERK1/2 (Ratio to EV on Glass)
EV
YAP.01
p = 0.022
p = 0.016
p = 0.018
0.7 kPa 7 kPa 38 kPa

Fig. S3. Loss of ECM adhesion and mechanosensing upregulates Collagen VI expression in PDAC cells.

A: Collagen VI protein expression in PANC-1 cells measured by immunoblotting for Collagen VI (Col VI) and ERK1/2 (loading control). Blots are representative of two independent experiments.

B: Left; PDAC-A cells were treated with 1 µg/mL and 5 µg/mL aphidicolin for 24 hours and immunoblotted for Collagen VI and GAPDH (loading control). Right; Densitometric quantification of protein expression. Values are mean ± s.d.

C: Left; Control (NTC) or ILK silenced (*Ilk*^{si01}, *Ilk*^{si02}) PDAC-B cells were immunoblotted for Collagen VI, ILK and α-Tubulin (loading control). Right; Densitometric quantification of protein expression. Values are mean ± s.d.

D: Left; PDAC-A cells expressing either GFP or GFP-tagged Talin 1-head domain (WT, control) or Talin-head L325R mutant (L325R) were immunoblotted for Collagen VI and GAPDH (loading control). Right; Densitometric quantification of protein expression. Values are mean ± s.d.

E: Left; PDAC-A cells expressing either GFP (control) or GFP-tagged Vinculin Domain 1 (VD1) were immunoblotted for Collagen VI and α-Tubulin (loading control). Right; Densitometric quantification of protein expression. Values are mean ± s.d.

F: Left; PDAC-A cells expressing expressing either GFP or GFP-tagged Talin 1-head domain (WT, control) or Talin-head L325R mutant (L325R) were immunoblotted for GFP and α-Tubulin (loading control). Right; PDAC-A cells expressing either GFP or GFP-tagged Vinculin Domain 1 (VD1) were immunoblotted for GFP and GAPDH (loading control).

G: Left; Control (EV) or YAP-depleted (YAP.01) PDAC-A cells were immunoblotted for Collagen VI, YAP and GAPDH (loading control). Pictures are representative of 4 independent experiments. Right; Densitometric quantification of ColVI protein expression. Values are mean ± s.d.

H: Left; Control (EV) or YAP-depleted (YAP.01) PDAC-A cells were cultured on fibronectin-coated 0.7- , 7- and 38-kPa hydrogels and were immunoblotted for Collagen VI and ERK1/2 (loading control). Right; Densitometric quantification of protein. Values are mean ± s.d. and representative from 3 independent experiments. Statistical significance was assessed by two-way ANOVA and p-values were corrected for multiple comparisons by Šídák's test.

All data in B-E are from 3 independent experiments. Statistical significance was assessed by two-tailed one-sample *t*-test on natural log-transformed values.

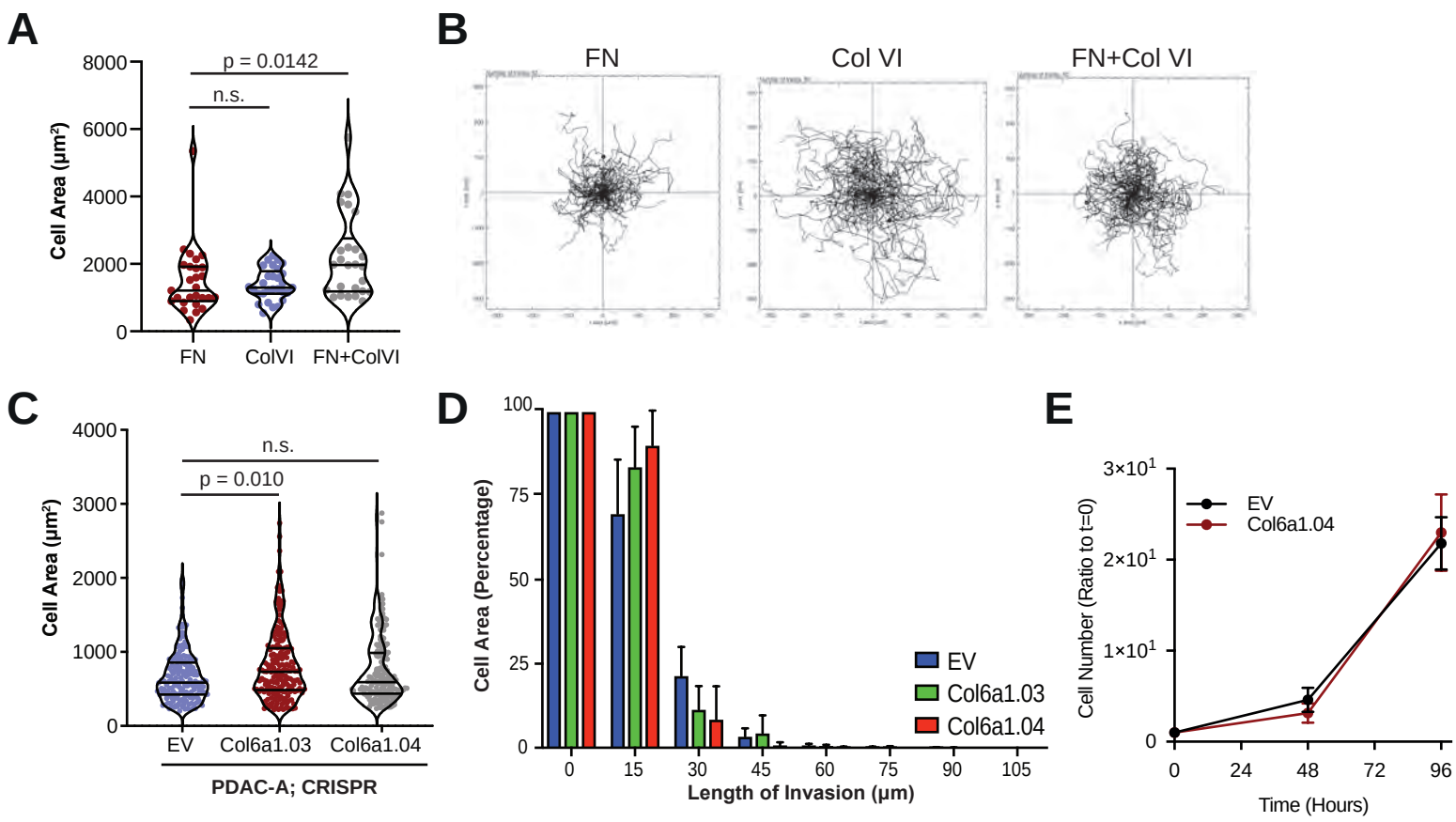

Fig. S4. Collagen VI ECM supports migratory behaviour of PDAC cells *in vitro* and loss of Col6a1 expression delays invasion through recombinant basement membrane ECM.

A: Cell area (µm^2) quantification of PDAC-A cells cultured on fibronectin (FN), collagen VI (ColVI) or fibronectin and collagen VI (FN+ColVI) glass coverslips. Values are from $n = 27$ FN cells;$n = 29$, ColVI; $n =$ 26, Fn+ColVI cells. Cells are from three independent experiments. Statistical significance was assessed by Kruskal-Wallis with Dunn's multiple comparisons test.

B: Tracks (spider plots) of PDAC-A cells migrating on fibronectin (FN), collagen VI (ColVI) or fibronectin and collagen VI (FN+ColVI) glass coverslips for 16 hours.ho

C: Cell area (µm^2) quantification of Control (EV) or Collagen VI depleted (Col6a1.03 and Col6a1.04) mouse PDAC-A cells. Values are mean ± s.d. from n=170 EV, n=191 Col6a1.03 and n=183 Col6a1.04 cells from 3 independent experiments. Statistical significance was assessed by Kruskal-Wallis with Dunn's multiple comparisons test.

D: Quantification of invaded area of Control (EV) or Collagen VI depleted (Col6a1.03 and Col6a1.04) mouse PDAC-A cells invading through the inverted invasion assay setup. Intensity for each depth is reported as a percentage of intensity at 0 µm. Values are me an ± s.d. from 3 independent experiments.

E: Cell number (Ratio to t=0) over time of control (EV) or Collagen VI depleted (Col6a1.01-04) PDAC-B cells. Values are mean ± SD from n = 3 independent experiments.

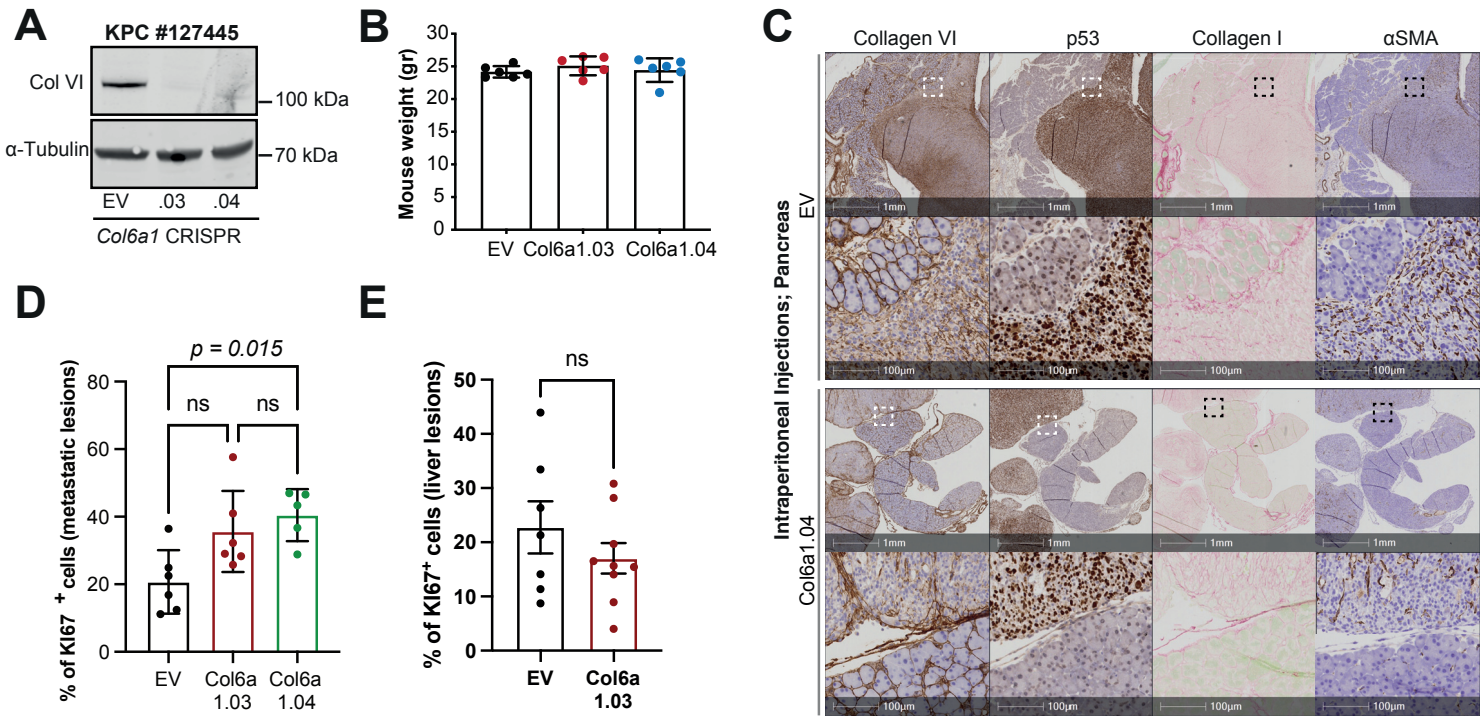

Fig. S5. Collagen VI expression supports establishment of pancreatic metastasis in vivo.

A: Control (EV) or Collagen VI depleted (Col6a1.01-04) KPC cells were immunoblotted for Collagen VI and α-Tubulin (loading control).

B: Weight (gr) per mouse as indicated from intraperitoneal injection of control (EV) or Collagen VI depleted (Col6a1.03 and Col6a1.04) KPC cells after sacrifice. Values are mean ± SD from n = 6 EV, n = 6 Col6a1.03 and n = 6 Col6a1.04 mice.

C: Representative immunohistochemistry images showing Collagen VI, p53, Collagen I and α-SMA expression in tumors formed in the pancreas by intraperitoneal injection of control (EV) (top 2 panels) or Collagen VI depleted (bottom 2 panels) KPC cells. Scale bars, 1mm and 100μm.

D: Quantifications of $KI67^+$ cells in metastatic lesions of nude mice intraperitoneally injected with control (EV), or Collagen VI depleted KPC cells (Col6a1.03 and Col6a1.04). Mean ± s.e.m. from n = 6 EV, n = 6 Col6a1.03 and n = 5 Col6a1.04 mice. Statistical significance was assessed with Brown-Forsythe and Welch ANOVA test with Dunnett's multiple comparison test.

E: Quantifications of $KI67^+$ cells in metastatic lesions of nude mice intrasplenically injected with control (EV), or Collagen VI depleted PDAC-B (Col6a1.03). Mean ± s.e.m. from n = 7 EV and n = 9 Col6a1.03 mice. Statistical significance was assessed with two-tailed Welch's t-test.

F: Representative immunohistochemistry images showing Collagen VI, Fibronectin, Collagen I, α-SMA, Ly6G and F4/80 expression in liver metastatic nodules formed by intrasplenic injection of control (EV; top) or Collagen VI depleted (Col6a1.03; bottom) KPC cells. Red line denotes liver (L) and metastasis (M) boundary. Scale bars, 100μm.

G: Quantification of positively stained regions over tumor area (%) from D. Values are mean ± s.e.m. from n = 5 control (EV) and n = 4 Col6a1.03 mice. Statistical significance was assessed by Mann-Whitney test (Collagen VI) and unpaired t-test (Fibronectin, Collagen I, αSMA, Ly6G and F4/80).

Table S1. Mice Information

Mouse ID	Strain	Genotype	Sex	Genetic Background	Age (days)	Application	Source
KPC endpoint PDAC							
FPZPR 103996	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Male	C57BL/6J	118	IHC	CRUK Beatson Institute
BALF 162992	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Male	C57BL/6J	123	IHC	CRUK Beatson Institute
BALF 192959	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Male	C57BL/6J	233	IHC	CRUK Beatson Institute
BALF 192970	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	114	IHC	CRUK Beatson Institute
BALA 27356	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Male	C57BL/6J	140	IHC	CRUK Beatson Institute
BALA 32316	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	152	IHC	CRUK Beatson Institute
BALA 32329	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	94	IHC	CRUK Beatson Institute
BALF 6.1b	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Male	C57BL/6J	170	IHC	CRUK Beatson Institute
BALF 6.1e	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	166	IHC	CRUK Beatson Institute
BALA 22160	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	99	IHC	CRUK Beatson Institute
BALA 24900	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	94	IHC	CRUK Beatson Institute
BALA 32310	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Male	C57BL/6J	139	IHC	CRUK Beatson Institute
Normal							
BALF 170396	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras +/+;LSL-p53 +/+	Male	C57BL/6J	204	IHC	CRUK Beatson Institute
BALF 171667	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras +/+;LSL-p53 +/+	Female	C57BL/6J	202	IHC	CRUK Beatson Institute
BALF 80410	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras +/+;LSL-p53 +/+	Male	C57BL/6J	46	IHC	CRUK Beatson Institute
BALF 80418	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras +/+;LSL-p53 +/+	Female	C57BL/6J	46	IHC	CRUK Beatson Institute
KPC 10-week PanIN							
BAJD 67.3c	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Male	C57BL/6J	68	IHC	CRUK Beatson Institute
BAJD 91.1a	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	69	IHC	CRUK Beatson Institute
BAJD 91.1d	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	69	IHC	CRUK Beatson Institute
BAJD 91.1f	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	69	IHC	CRUK Beatson Institute
BAJD 91.2b	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	69	IHC	CRUK Beatson Institute
KPC 15-week PanIN							
BALF 11.2g	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	104	IHC	CRUK Beatson Institute
BALF 18.2b	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	103	IHC	CRUK Beatson Institute
BALF 18.2d	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	103	IHC	CRUK Beatson Institute
BALF 18.2e	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Female	C57BL/6J	103	IHC	CRUK Beatson Institute
BALF 11.2a	Pdx-1::Cre;LSL-Kras G12D;LSL-p53 R172H (KPC)	Pdx-1::Cre+;LSL-Kras G12D/+;LSL-p53 R172H/+ (KPC)	Male	C57BL/6J	104	IHC	CRUK Beatson Institute
Intraperitoneal Injection Model - KPC cells							
BVCD3.1a	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.1b	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.1c	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.2a	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.2b	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.2c	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.3a	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.3b	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.3c	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.4a	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCF3.4b	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.4c	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.5a	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.5b	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.5c	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.6a	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.6b	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
BVCD3.6c	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Intrasplenic Transplantation Model - KPC cells							
Cage 1 NM	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 1 L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 1 R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 1 L+R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 2 NM	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 2 L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 2 R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 2 L+R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 3 NM	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 3 L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 3 R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 3 L+R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected KPC Col6a1.04 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Intrasplenic Transplantation Model - PDAC B cells							
Cage 1 NM	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 1 L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 1 R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 1 L+R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 1 2L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 2 NM	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 2 L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 2 R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 2 L+R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 2 2L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B EV (WT) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 3 NM	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 3 L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 3 R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 3 L+R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 3 2L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 4 NM	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 4 L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 4 R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 4 L+R	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories
Cage 4 2L	Foxn1-nu:Hom (CD1-nu)	Foxn1-nu:Hom (CD1-nu); Injected PDAC-B Col6a1.03 (KO) cells	Female	CD1	62	Intrasplenic	Charles River Laboratories

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Table S2. Raw data, including RNA sequencing data.

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