**SUPPLEMENTARY METHODS**

**Magnetic resonance imaging**

Magnetic resonance imaging (MRI) of liver metastases was performed at 4.7 T (Varian Inc, CA). RF transmission and reception was performed with a 45 mm long 32 mm ID quadrature birdcage coil (Rapid Biomedical GmbH, Germany). Cardio-respiratory gated (CR-gated) 3D balanced SSFP (b-SSFP) scans were performed with TR 2.892 ms, TE 1.446 ms, FOV 48×24×24 mm3, matrix 256×96×96 and RF hard pulse duration 16 μs nominally set to give a 20° flip. Data were acquired in blocks of 32 k-lines lasting 92.544 ms with centric out phase encode ordering starting at detection of each CR-gating signal. The MR steady state was then maintained with a read of the CR-gating signal level during each TR as described previously [22]. Data blocks corrupted by respiration motion were reacquired automatically immediately after each breath. bSSFP data sets were acquired with and without the phase of sequential RF pulses incremented by 180° and the data were combined by maximum intensity projection to reduce SSFP banding.

**Immunofluorescence**

For murine TIMP-1 immunofluorescent staining, following fixation, cells were permeabilised in 0.1% Triton in PBS and stained with 1:200 mouse TIMP-1 antibody (AF980-R&D Systems), followed by anti-goat Alexa Fluor 488 (1:250 Invitrogen). For murine liver Gr-1 staining tissues were fixed in acetone and incubated with anti-mouse Gr1 1:100 for 120 minutes (R&D systems MAB1037) followed by anti-rat Alexa Fluor 546.

# Western blot

# Cells were lysed in RIPA buffer (Sigma) containing 1x Halt protease inhibitor cocktail (Invitrogen). 20 µg of total cell extracts were resolved in 4–12% Bis-Tris Nu-PAGE gels (Invitrogen) and transferred onto PVDF membrane (Millipore) before immunoblotting with 0.5 µg/ml TIMP1 (R&D Biosystems) overnight at 4 °C in 5% skim milk in Tris-buffered saline solution containing 0.1% Tween. Primary antibody detection was carried out by using peroxide-conjugated anti-goat antibody (Jackson Immunoresearch) and autoradiographed on X-ray films (Kodak). All bands were normalized against GAPDH or β-actin as a loading control.

**Flow cytometry**

Tumours and livers were cut into small pieces and dissociated as described (23). Cells were then washed with cold PBS and filtered through a 70 µm nylon strainer. Lysis of red blood cells was carried out for 3 mins at room temperature. Cells were incubated with Fc block (anti-mouse CD16/32)then stained for CD45, CD8, CD4, CXCR2, CD11b, Gr1, CD25 for 1 hour, as well as FoxP3 (all from eBiosciences, UK) following following fixation and permeabilization with FOXP3 staining buffer kit (all from eBiosciences, UK). FACS Calibur and FACS Canto II (BD Biosciences) were used and results were analysed using FlowJo software (Tre Star, Ashland, USA). The percentage of gated cells was assessed.

**Microarray and Oncomine analysis**

Total RNA from PANC1-wild type (WT) and PANC1-KD cells was isolated using the RNeasy mini kit (Qiagen) according to manufacturer’s instructions. The Illumina platform was used for transcriptome analysis with the Human H12 array (Wellcome Trust centre, University of Oxford). The raw bead chip data were processed using GenomeStudio version 1.9.0 and further processed in R 3.2.2. After quantile normalisation and log2 transformation, only probes that had detection p-values ≤ 0.05 for at least one sample were included. Differentially expressed genes were identified using both Linear Models for Microarray Data (LIMMA) and Significance analysis of microarrays in R (SAMR) after which a rank product resulted in the final ranked set of genes. False discovery rate (FDR) was used to correct for multiple testing. GeneCodis was used to perform gene ontology enrichment analysis to identify biological processes that were enriched by the differentially expressed genes. We tested one clone performed 6-fold for the microarray experiment (2 different batches of cells, 1-3 and 4-6, respectively). The clone with the best knockdown indicated a 6-fold decrease in TIMP-1 expression and was chosen for the functional experiments.

In the microarray experiment, standard MIAME guidelines were followed. The full microarray data (GSE94891) are available on GEO.

Publicly available microarray data from human patient samples were analysed using Oncomine (Compendia Bioscience) in human PDAC datasets.

**Real-time quantitative PCR**

RNA was isolated with Trizol (Invitrogen) according to the manufacturer’s instructions, and complementary DNA (cDNA; 2 μg) was synthesized using the MMLV RT (Promega) Real-time PCR reaction mixtures were prepared with the SYBR Green PCR Master Mix (Applied Biosystems)) and performed on a StepOne system (Applied Biosystems). Data were analyzed using the ΔCT method and normalized to the ribosomal protein L32 and GAPDH.

*Primer sequences*

1. hTIMP1

F- 5'- ctgttgttgctgtggctgat-3'

R- 5'- aacttggccctgatgacg-3'

1. hS100A8

F- 5'- gccaagcctaaccgctataa-3'

R-5'- atgatgcccacggacttg -3'

1. hS100A9

F-5'- gtgcgaaaagatctgcaaaa-3'

R- 5'- tcagctgcttgtctgcattt-3'

1. hRIPK2

F-5'- ccactctcaactgcaggaaac-3'

R-5'- tgtcttcccttttgctctgg-3'

1. hGAPDH

F-5'- GACATCAAGAAGGTGGTGAAGC-3'

R-5'- GTCCAACCCTGTTGCTGTAG-3'

1. hL32

F-5'- CATCTCCTTCTCGGCATCA-3'

R-5'- ACCCTGTTGTCAATGCCTC-3'

1. mTIMP1

F-5'- gcaaagagctttctcaaagacc-3'

R-5'- agggatagataaacagggaaacact-3'

1. mL32

F-5'-GAGGTGCTGCTGATGTGC-3'

R-5'- GGCGTTGGGATTGGTGACT-3'

**Invasion towards CAFs**

The assay is described in Supplementary Methods. Millicell cell culture inserts (8 µm) were coated with 500 μl of Matrigel at a concentration of 100µg/cm2 in DMEM and dried overnight. Cells were resuspended in DMEM supplemented with FCS at a concentration of 1 × 106 cells/ml. 250 µl of the cell suspension were then placed into the upper chambers whereas Immortalized Pancreatic CAF-Stellate Cells in VitroPlus III, low serum, completeDMEM conditioned media 500 µl were added to the bottom chambers to act as an attractant. Invasion was measured after overnight incubation at 37°C for 16 h. The top part of the chambers was wiped with cotton wool, and invaded cells on the underside of the membrane were fixed in 100% methanol for 10 min, air dried, stained in crystal violet for 10 min followed by gentle rinsing in water. When dry, the crystal violet stain on membranes was eluted using 0.1M Na citrate in 50% ethanol for 20 min with shaking and absorbance read at 570 nm on the Tecan Infinite® 200 PRO seriesplate reader.The percentage of invaded cells was calculated by dividing the absorbance in test samples by the absorbance from the total number of cells (not wiped) to account for cell proliferative effects.

22. Kinchesh P, G.S., Gomes AL, Kersemans V, Beech J, Allen D, Smart S, *Accelerated imaging of the mouse body using k-space segmentation, cardio-respiratory synchronisation and short, constant TR: Application to b-SSFP.* Proc Intl Soc Mag Reson Med 2016. **24**: p. 1825.