Supplementary Figure Legends:

Supplementary Figure 1: (A) Kaplan-Meier survival curves for PDAC patients with negative (blue) and positive FAM49B expression (red). Comparison of effects of negative vs positive FAM49B expression on overall survival. Cox model adjusted for age (as a continuous variable) and tumor grade (B) FAM49B protein expression in four different normal duct cell lysates was analyzed by western blotting. Actin was used as a loading control. (C) FAM49B expression in the K8484 murine PDAC cell line, as determined by qPCR. Actin was used as a reference gene. (D) Light microscopic images of the 3D cultures of the CFPAC1 and T3M4 and K8484 PDAC cell lines and fluorescence channels for F-actin (green) at 14 days of culture, Hoechst-stained nuclei are shown in blue. Scale bar respresent 10- µm. (E) FAM49B expression in CFPAC1 and T3M4 PDAC cells and normal HPDE cells cultured on plates coated Matrigel (3D base) or plates with no coating (2D) monolayer cultures, expression levels was analyzed by qPCR. Actin was used as a reference gene. All graphs illustrate the mean results of three independent experiments ±SEM (*p<0.05; **p<0.001, ***p<0.0001, Student's t-test)

Supplementary Figure 2: (A) FAM49B protein expression in CFPAC1, T3M4 PDAC cells, normal HPDE cells and Murine PDAC cell line K8484 cultured without (untreated UT) or with MG132 5 µM (treated for 6h and 12 h). (B) FAM49B protein expression in CFPAC1 human PDAC cells, normal HPDE cells and Murine PDAC cell line K8484 cultured in 3D culture with or without MG132 and compare with 2D cultures as control. Beta catenin levels were analysed as positive reponse of MG132 treatment. (C) qPCR analysis of relative FAM49B expression levels in the PDAC cell lines CFPAC1,T3M4 and HPDE cells which were transfected with shCNTRL, shFAM49B1 or shFAM49B2. Actin was used as a reference gene. The bars represent the mean values ±SDs of three experiments. (D) Immunoblotting for FAM49B expression, which was normalized against actin, in the PDAC cell lines CFPAC, T3M4 and HPDE cells which were transfected with shCNTRL, shFAM49B1 or shFAM49B2. The data represent the mean values ±SDs of three experiments (*p<0.05; **p<0.001, ***p<0.0001, Student's t-test).

Supplementary Figure 3: (A) MTT proliferation assay of shCTRL (Grey circle) and shFAM49B HPDE cells (Black circle). The data are shown as the mean ±SEM of three independent experiments (*p<0.05, t-test). (B) Wound-healing assays of shCNTRL and shFAM49B HPDE cells. The dotted lines indicate the wound edge at 0 h. Migration of individual cells over 18-24 h was tracked using ImageJ. The data represent the mean

values ±SDs of three experiments (C) Expression of various EMT markers, as demonstrated by real-time PCR in shCTRL and shFAM49B in HPDE cell line. Actin was used as a reference gene. All graphs illustrate the mean results of three independent experiments ±SEM (*p<0.05; **p<0.001, ***p<0.0001, Student's t-test)

Supplementary Figure 4: (A) Subcellular localization of GFP-tagged FAM49B, as shown by fluorescence microscopy. 293T cells transfected with GFP- tagged FAM49B were subjected to protease protection assay, which confirmed the subcellular distribution patterns of FAM49B. (B) Electron micrograph showing FAM49B localization in the mitochondria of 293T cells transfected with GFP-tagged FAM49B. Scale bar represents 500nm. (C) Flow cytometry analysis of mitochondrial membrane potential in shCTRL and shFAM49B CFPAC, T3M4 and HPDE cells, as demonstrated by JC1 staining. (D) Western blot analysis of Cytochrome C on cytosolic and mitochondrial fractions of the shCTRL and shFAM49B CFPAC1, T3M4 and HPDE cells. (E) Caspase 3 and Caspase 9 activity measured with flouroscence probe in shCTRL and shFAM49B CFPAC, T3M4 and HPDE cells. (F) MitoTracker staining was used for analysis of mitochondrial morphology in the HPDE cell lines silenced for FAM49B with a control vector or His FAM49B vector. Tissue sections were analyzed with a laser-scanning microscope (Zeiss LSM5 Pascal). The data represent the mean values ±SDs of three experiments (*p<0.05; **p<0.001, ***p<0.0001, Student's t-test).