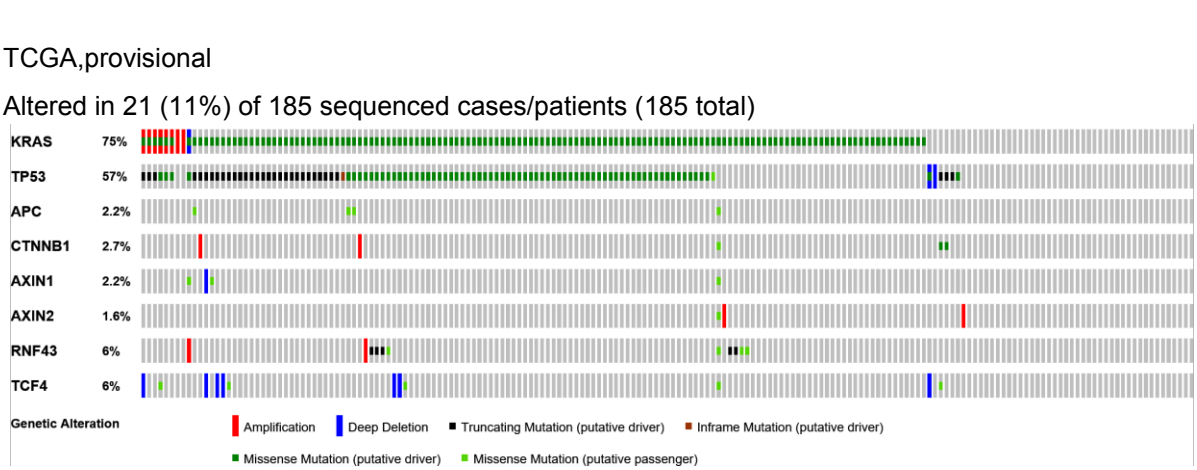
Figure S1

A



B

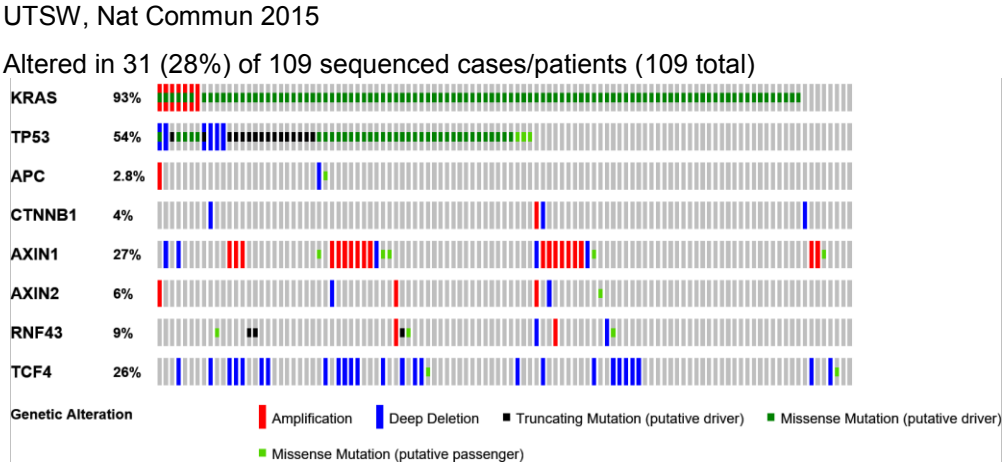


Figure S1. Co-existence of *K-ras* mutation, *p53* loss and alteration of the WNT/ß-catenin signaling molecules in pancreatic cancer.

(**A**)Results of genetic alterations of *K-ras*, *p53* and the WNT/ß-catenin signaling molecules were extracted from the TCGA provisional database and the co-existence of these defects in pancreatic cancer patients was shown. (**B**) Another public UTSW database showed the genetic alterations of *K-ras*, *p53* and the WNT/ß-catenin mediators in 109 pancreatic cancer patients.

Figure S2

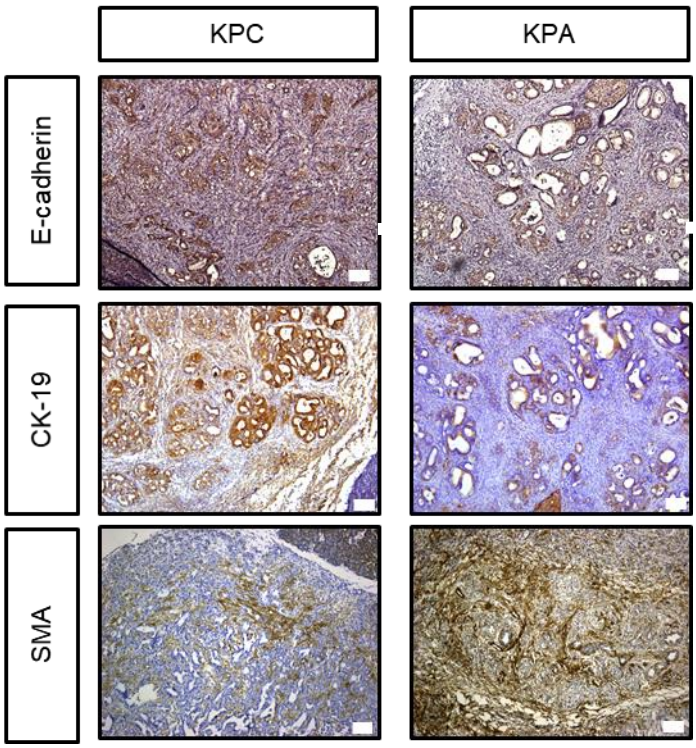


Figure S2. The KPA tumors are poorly differentiated and highly fibrotic.

Tumor tissues obtained from the KPC and KPA mice were subjected to immunohistochemical staining and the expressions of E-cadherin, cytokeratin 19 (CK19) and α-smooth muscle actin (SMA) were compared. The results showed that the staining of CK19 and SMA was increased while the staining of E-cadherin was decreased in the KPA tumors suggesting the KPA tumors are poorly differentiated and highly fibrotic. Scale bars represent 100 μm.

Figure S3

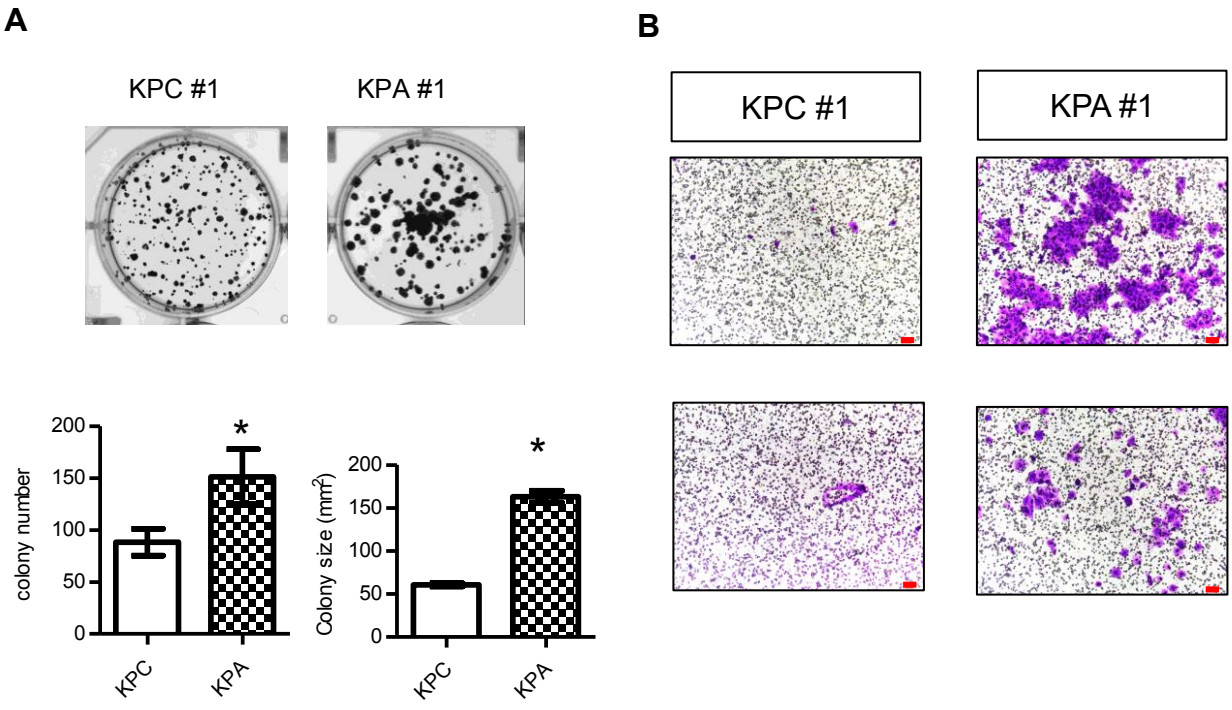


Figure S3. Tumorigenicity and invasion of the KPC and KPA cancer cells.

(A)The KPC and KPA cancer cells were subjected to colony formation assay as previously described (13). The number and size of the colonies were compared between these two groups. The results were expressed as Mean±SEM (n=3). *P<0.05. (B) The KPC and KPA cancer cells were subjected to Transwell assay as previously described (13). The data showed the invasive ability is much higher in the KPA cancer cells. Scale bars represent 50 μm.

Figure S4

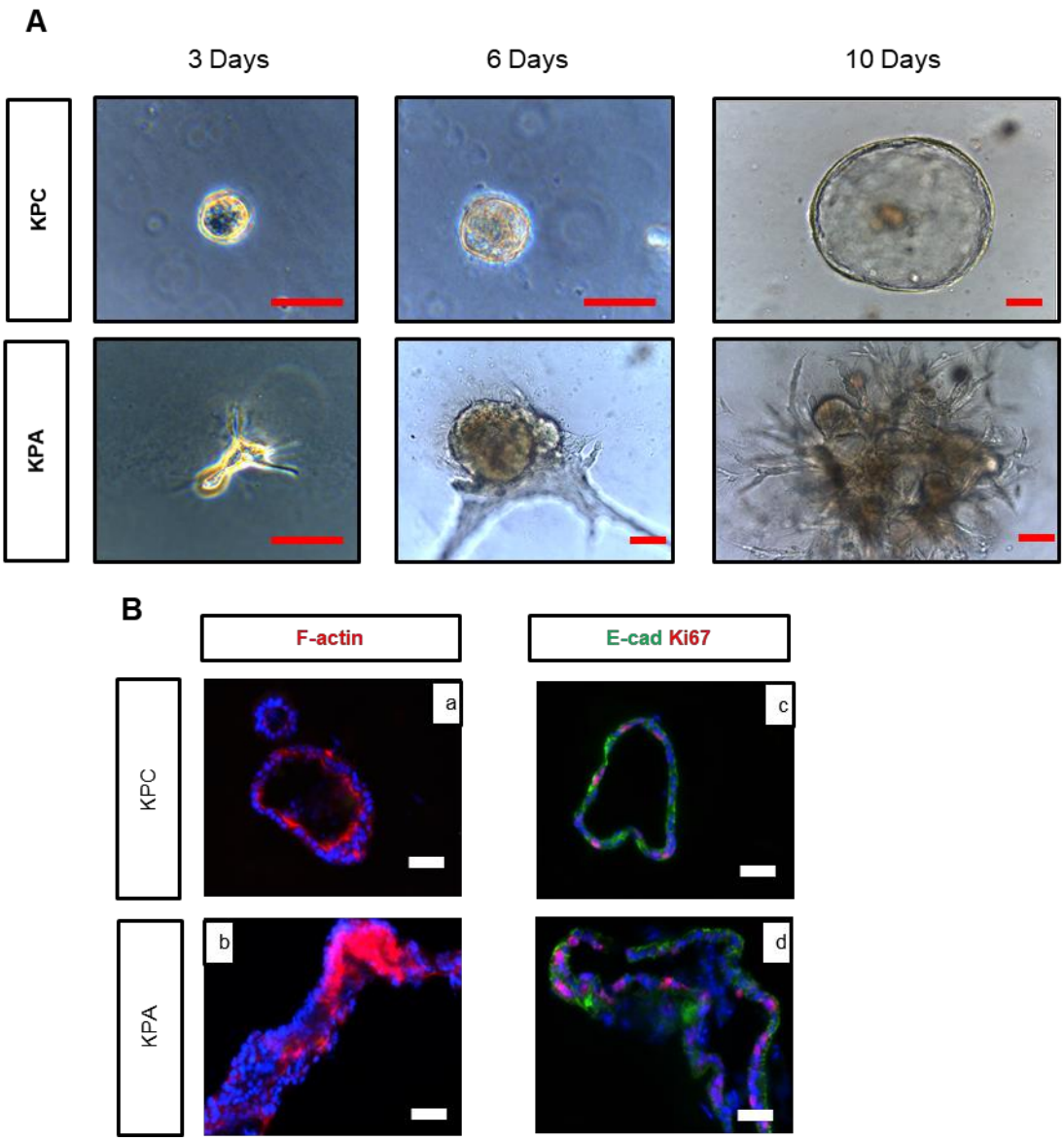


Figure S4. Time-dependent growth of the organoids with proliferative activity and distorted structure. (**A**) Cancer cells were embedded in growth factor-reduced Matrigel and cultured in DMEM medium supplemented with B27, 1.25 mM N-Acetylcysteine,10 nM gastrin and the growth factors: 50 ng/ml EGF, 10% R-spondin 1, 100 ng/ml Noggin, 100 ng/ml FGF10 and 10 mM nicotinamide. The pictures showed the growth of an organoid generated from the KPC and KPA cancer cells at different days after culture. Scale bars represent 75 µm. (**B**) The organoids established from the KPC and KPA cancer cells were processed for cryosection. The distribution and signal intensity of F-actin, E-cadherin and Ki-67 was studied by IF staining. Scale bars represent 50 µm.

Figure S5

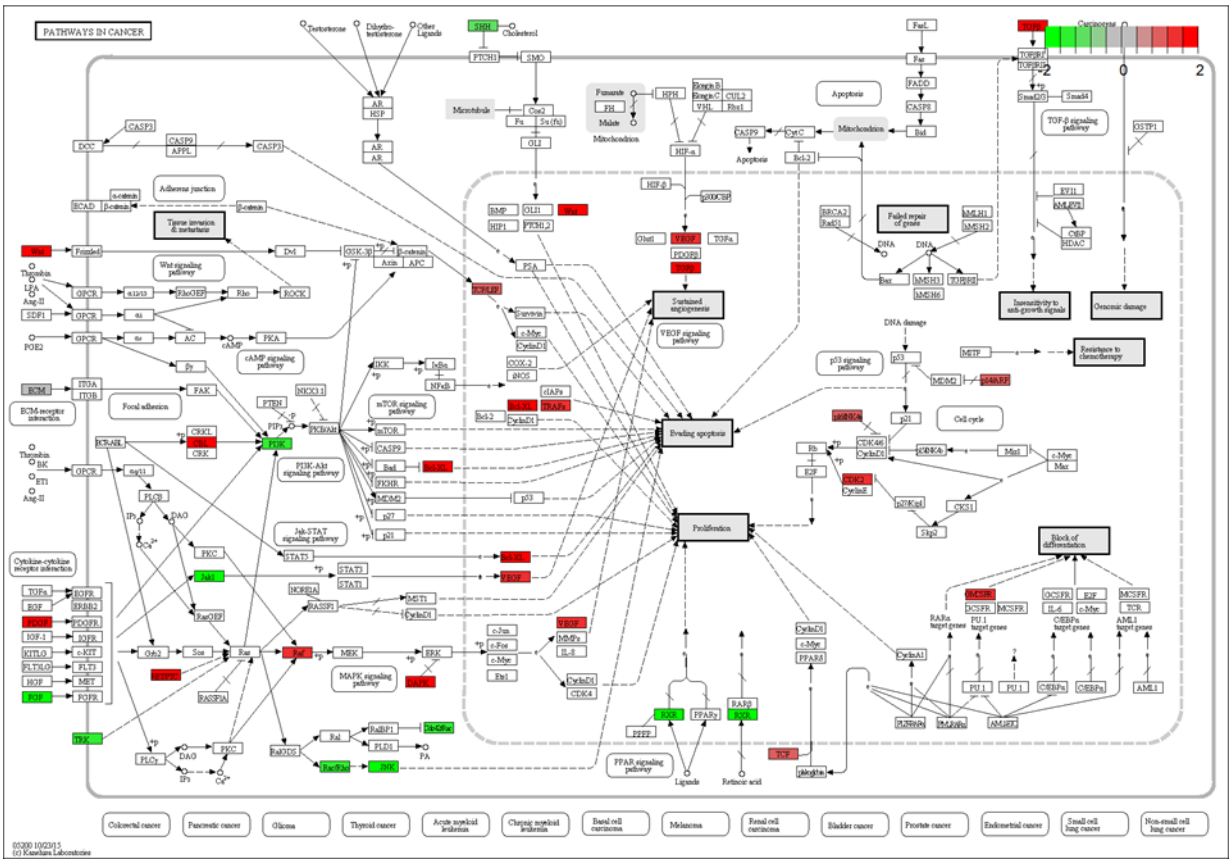


Figure S5. Upregulation of PDGF, VEGF, TGF-β and WNT signaling pathways in the KPA cancer cells. Gene expression profile of the KPC and KPA cancer cells was studied by cDNA microarray and the differentially upregulated pathways were shown. The upregulated genes are marked by red color and the downregulated genes are marked by green color.

Figure S6

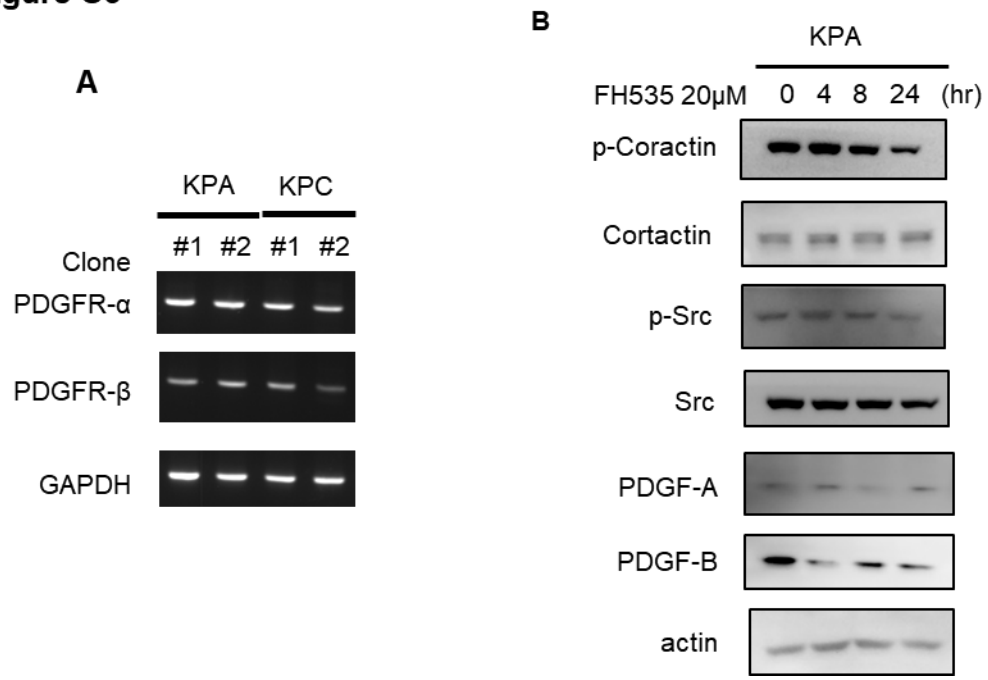


Figure S6. Inhibition of PDGF-B production, Src activation, and cortactin phosphorylation by a β-catenin inhibitor FH535 in the KPA cancer cells. (A) Expression of PDGFR-α and PDGFR-β in the KPC and KPA cancer cells. Total RNAs were extracted from the KPC and KPA cancer cells and expression of PDGFR-α and PDGFR-β was studied by RT-PCR assay. **(B)**The KPA cancer cells were treated with FH535 (20μM) for different times and cellular proteins were harvested for analysis. Phosphorylation of Src and cortactin and intracellular level of PDGF-A and PDGF-B were investigated by Western blotting.

Figure S7

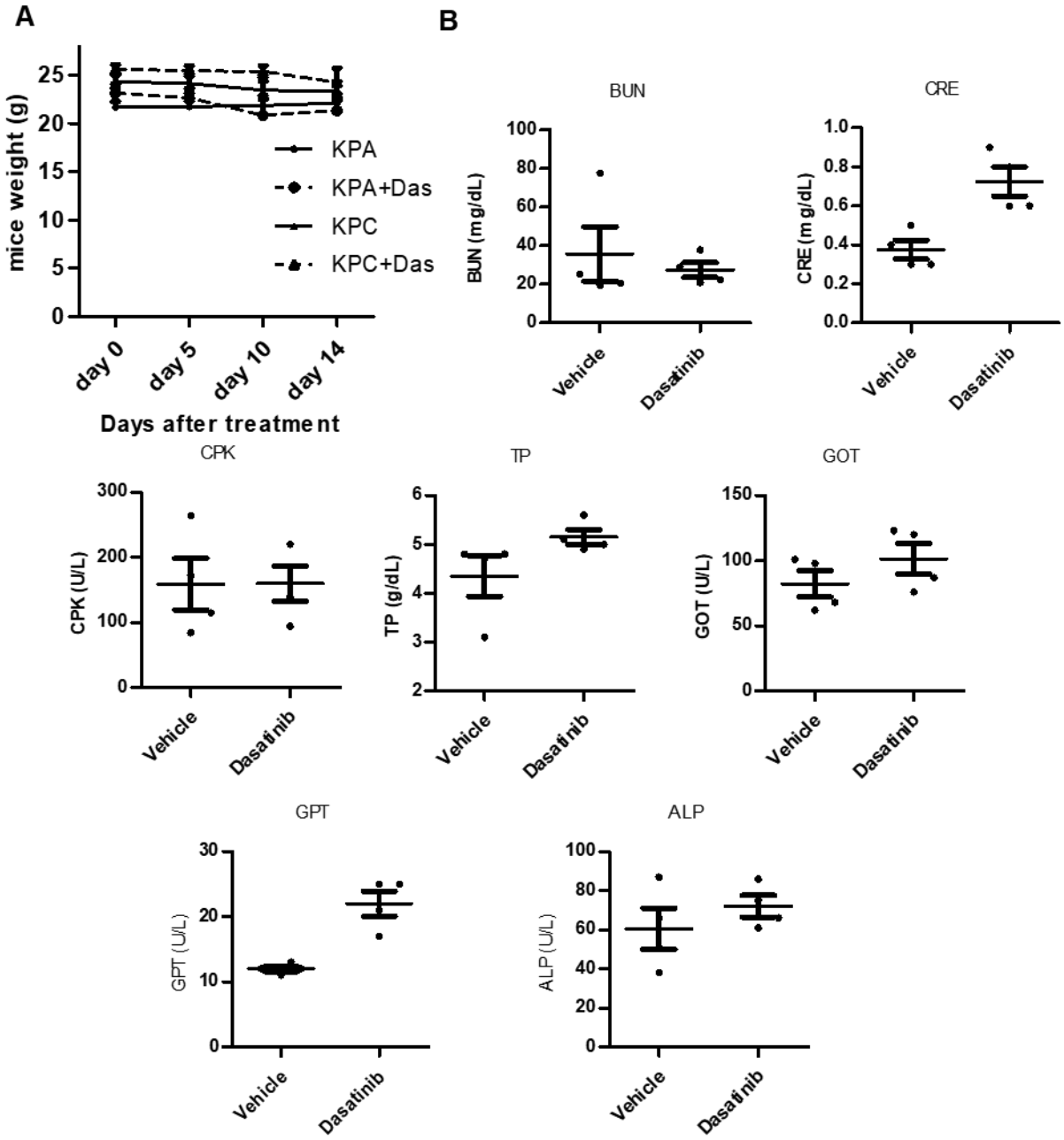


Figure S7. Change of blood chemistry parameters in the KPA mice received PBS or dasatinib treatment for two weeks. Luciferase-tagged KPC and KPA cancer cells (1×10^6 cells) were injected into the pancreas of mice After 1 weeks (day 0), PBS or dasatinib (10 mg/kg) were given to mice by oral gavage daily for 2 weeks, and body weight of the mice was measured every 5 days.(A)Change of body weight of the KPC and KPA mice received PBS or dasatinib treatment for two weeks. (B)Blood samples were collected at animal sacrifice and blood chemistry parameters were analyzed by Fuji Dri-Chem 4000i autoanalyzer of the Taiwan Mouse Clinic (Taipei, Taiwan). Error bars are the means ±s.e.m. (n=5). ALP: Alkaline Phosphatase; BUN: blood urea nitrogen; CRE: creatinine; CPK: Creatine-phospho-kinase; GOT: glutamate oxaloacetate transaminase; GPT: glutamate pyruvate transaminase; TP: total protein.

Figure S8

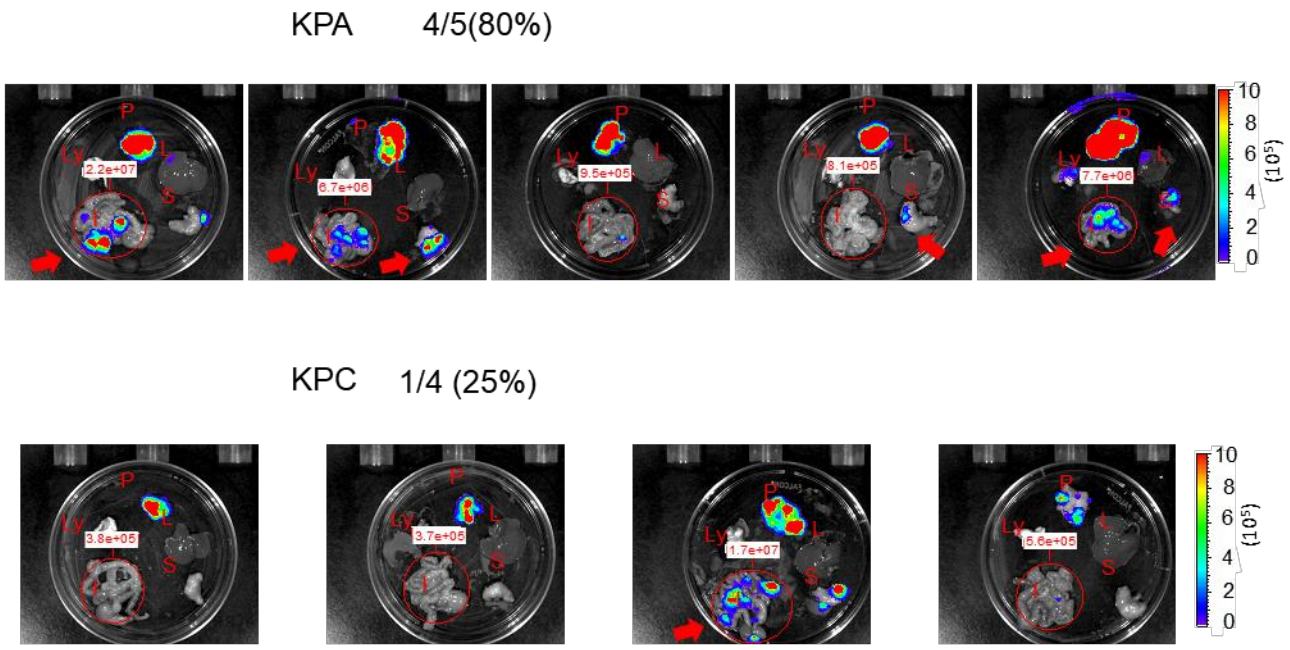


Figure S8. Metastasis of pancreatic tumors to various organs in the KPA and KPC mice. Luciferase-tagged KPC and KPA cancer cells (1×10^6 cells suspended in 50 μL Hank's balanced salt saline) were injected into the pancreas of the mice. Organs including pancreas, liver, intestine, stomach were collected from the mice injected with d-luciferin (150 mg/kg in saline) before sacrifice. Red arrow indicates the metastatic tumors in the organs.

Table S1. Summary of the information and the metastatic status of the KPA mice (n=15).

ID	Age (weeks)	sex	Ascites	Intest	Stoma meta	Liver	Lung
1126	11	F	N	Y	N	N	N
1100	11	M	Y	Y	N	Y	N
1791	11	F	Y	Y	Y	N	N
2010	12	F	N	Y	N	Y	N
2006	15	F	Y	Y	Y	Y	Y
21	15	F	N	Y	Y	N	N
2470	10	F	N	N	N	N	Y
2413	15	M	Y	Y	N	Y	N
2473	15.5	M	Y	N	N	N	Y
2009	8.5	F	N	Y	N	Y	N
2067	12	F	Y	Y	Y	N	N
2232	6	M	N	Y	N	N	N
2378	14	F	Y	Y	Y	N	Y
1127	16	M	Y	N	N	Y	Y
2373	7	M	N	N	N	N	N
Total	11.93	06:09	47%	73%	33%	40%	33%

Table S2. 20 patient with serum clinicopathological features

Characteristic	PDGF+pSrc		Other		*P*
Age, median (range)	65	(52~77)	62	(41~85)	
Sex					**< 0.0001**
Male	4	44%	8	73%	
Female	5	56%	3	27%	
Tumor Location					0.7719
Uncinate	2	22%	3	27%	
Head	4	44%	5	45%	
Neck	0	0%	0	0%	
Body/tail	3	33%	3	27%	
Tumor Location					0.3545
Uncinate/Head	6	67%	8	73%	
Neck/Body/tail	3	33%	3	27%	
Tumor size					**0.015**
< 3 cm	3	33%	2	18%	
≥ 3 cm	6	67%	9	82%	
Lymph nodes status					0.2482
Negative	4	44%	4	36%	
Positive	5	56%	7	64%	
Stage					**0.0021**
T2	0	0%	1	9%	
T3	9	100%	10	91%	
Stage N					0.6554
N0	3	33%	4	36%	
N1	6	67%	7	64%	
Recurrence					1
Yes	9	100%	11	100%	
No	0	0%	0	0%	
CEA,median (range)	7.17	(1.5~20)	8.82	(0.8~12)	
< 5	5	56%	5	45%	0.1198
≥ 5	4	44%	6	55%	
CA19-9,median (range)	1386	(0.6~6730)	605	(0.6~4396)	
< 37	2	22%	7	64%	**< 0.0001**
≥ 37	7	78%	4	36%	

Table S3. Correlation between PDGF/p-Src coexpression and clinicopathological features

Characteristic	PDGF+pSrc		Other		*P*
Age, median (range)	64	(41~77)	61	(38~85)	
Sex					**< 0.0001**
Male	5	38%	43	67%	
Female	8	62%	21	33%	
Tumor Location					0.2026
Uncinate/Head	9	69%	49	77%	
Neck/Body/tail	4	31%	15	23%	
Tumor size					**0.0105**
< 3 cm	6	46%	41	64%	
≥ 3 cm	7	54%	23	36%	
Stage					0.0817
T2	1	8%	10	16%	
T3	12	92%	54	84%	
Stage N					**0.0466**
N0	5	38%	33	52%	
N1	8	62%	31	48%	
Resection Margin					0.1153
R0	10	77%	50	78%	
R1	2	15%	13	20%	
R2	1	8%	1	2%	
Recurrence					**< 0.0001**
Yes	12	92%	44	69%	
No	1	8%	20	31%	
CEA,median (range)	527.8	(1.5~6086)	14	(0.1~494)	
< 5	8	62%	48	75%	**0.0478**
≥ 5	5	38%	16	25%	
CA19-9,median (range)	1095	(0.6~6730)	442	(0.6~5266)	
< 37	3	23%	19	30%	0.2621
≥ 37	10	77%	45	70%	

Table S4. Somatic mutations of *RNF43* and *Axin1* in clinical patients.

Paitient number	Gene	Mutation	Exon	Nucleotide	Protein	PDGF/p-Src
58	*RNF43*	Frameshift deletion	Exon8	198delT	66fs	High
60	*RNF43*	Frameshift insertion	Exon5	515insT	172fs	Low
71	*RNF43*	Frameshift deletion	Exon8	184delT	62fs	High
90	*RNF43*	Frameshift insertion	Exon5	513insTC	171fs	High
85	*RNF43*	Misssense	Exon2	A1058T	L353H	Low
54	*Axin1*	Nonsense	Exon3	C1072A	E358*	High
55	*Axin1*	Misssense	Exon3	G1057A	R353S	High
68	*Axin1*	Misssense	Exon7	G2101A	P701S	Low
71	*Axin1*	Misssense	Exon3	C1058G	R353P	High
79	*Axin1*	Misssense	Exon6	C1916T	G639E	High
90	*Axin1*	Frameshift insertion	Exon3	1093insA	365fs	High

Table S5. List of the primary antibodies used in this study, and information on working dilutions of antibodies in Western blotting (WB), immunohistochemistry (IHC) and immunofluorescence (IF).

Antigen	Species	Source	Catalog#	Dilution		Application	
E-cadherin	Mouse	BD Biosciences	610182	1:100		IHC	
β-catenin	Mouse	Santa Cruz biotechnology	sc-7963	1:50	1:200	IHC	WB
CK19	Mouse	LifeSpan BioSciences,Inc	LS-C180321	1:100		IHC	
α-SMA	Mouse	Sigma	A2547	1:100		IHC	
PDGF-A	Rabbit	Santa Cruz biotechnology	sc-128	1:50	1:200	IHC	WB
PDGF-B	Rabbit	Genetex	GTX100683	1:100	1:1000	IHC	WB
PDGFRα	Rabbit	Genetex	GTX107903	1:1000		WB	
PDGFRβ	Mouse	Santa Cruz biotechnology	SC-374573	1:200		WB	
p-PDGFRβ	Rabbit	LifeSpan BioSciences,Inc	LS-C178098	1:500		WB	
ki67	Rabbit	Spring Bioscience	M3060	1:100		IF	
Phalloidin(F-actin)		Invitrogen	A12381	1:100		IF	
p-Cortactin	Rabbit	Cell Signaling Technology	#4569s	1:100	1:1000	IF WB	
Cortactin	Rabbit	Genetex	GTX100253	1:1000		WB	
p-Src	Rabbit	cell signaling technology	#6943	1:100 1:1000		IHC	WB
Src	Mouse	Upstate	05-184	1:1000		WB	
p-Erk	Rabbit	Cell Signaling Technology	#4370	1:1000		WB	
Erk	Rabbit	Cell Signaling Technology	#4695	1:1000		WB	
p-FAK	Rabbit	Cell Signaling Technology	#8556	1:1000		WB	
FAK	Mouse	BD Biosciences	610087	1:1000		WB	
GAPDH	Mouse	Abcam	ab9485	1:2000		WB	
p-Tyrosine	Mouse	Upstate	05-321	1:1000		WB	
β-Actin	Mouse	Chemicon	MAB1501	1:5000		WB	
APC	Rabbit	Genetex	GTX116009	1:1000		WB	

Table S6 . List of the primers used in this study.

Gene name	Forward Sequence	Reverse Sequence
TGF-β1	TGATACGCCTGAGTGGCTGTCT	CACAAGAGCAGTGAGCGCTGAA
TGF-β2	TTGTTGCCCTCCTACAGACTGG	GTAAAGAGGGCGAAGGCAGCAA
TGFBR3	TCTCCGCTGAATGGCTGTGGTA	CCGACTCCAAATCTTCGTAGCC
PDGF-A	CTGGCTCGAAGTCAGATCCACA	GACTTGTCTCCAAGGCATCCTC
PDGF-B	AATGCTGAGCGACCACTCCATC	TCGGGTCATGTTCAAGTCCAGC
PDGF-C	GAGTCCAACCTGAGCAGCAAGT	GAAACTTCGGGCTGTGGATGCT
PDGF-D	CTGTCAACTGGAAGTCCTGCAC	CCCTTCTCTTGAAATGTCCAGGC
PDGFRα	GCAGTTGCCTTACGACTCCAGA	GGTTTGAGCATCTTCACAGCCAC
PDGFRβ	GTGGTCCTTACCGTCATCTCTC	GTGGAGTCGTAAGGCAACTGCA
GAPDH	CATCACTGCCACCCAGAAGACTG	ATGCCAGTGAGCTTCCCGTTCAG
ACTIN	ACCATCGGCAATGAGCGTTTCC	GCTGTTGTAGGTGGTCTCATGG
TCF4	CCTCCAATCCTTCAACTCCTGTG	TCCAAACGGTCTTCGATTCGGC