Figure S1

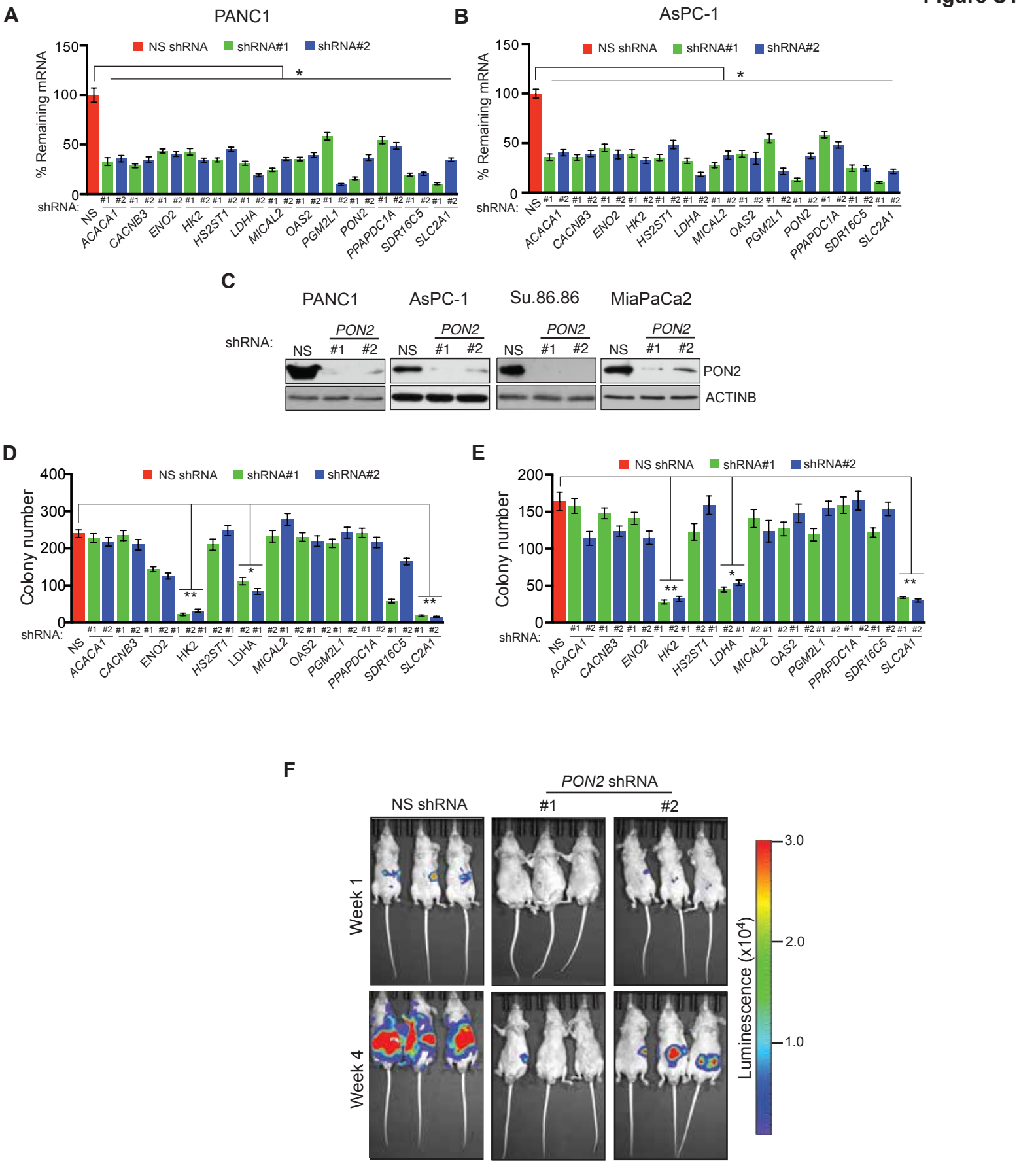
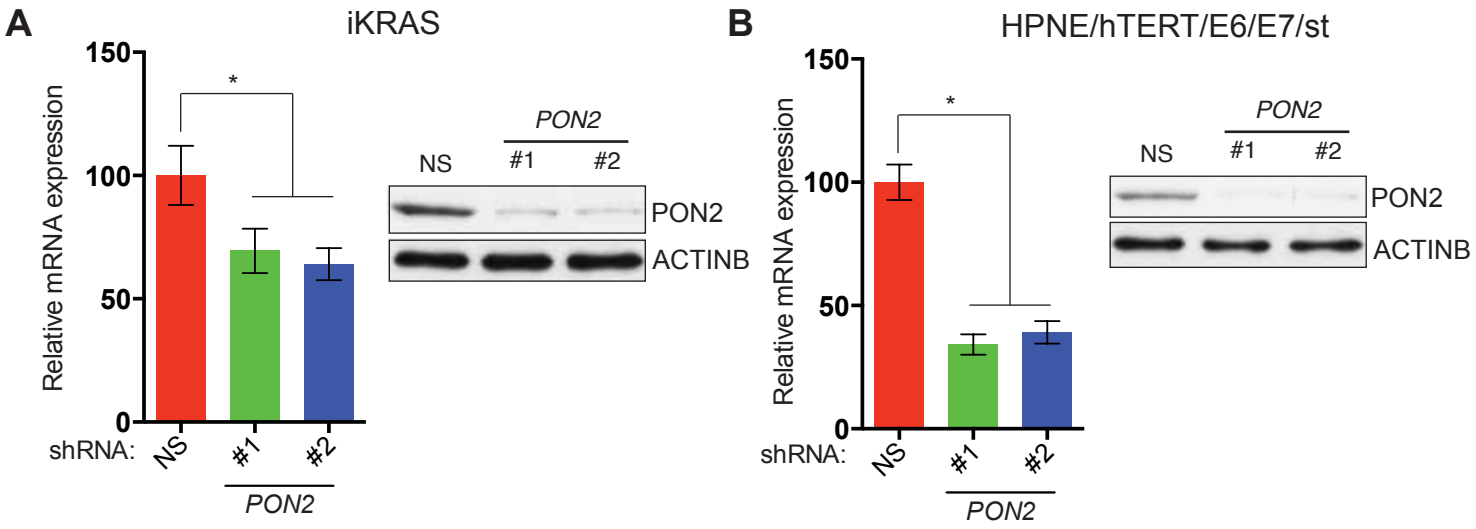
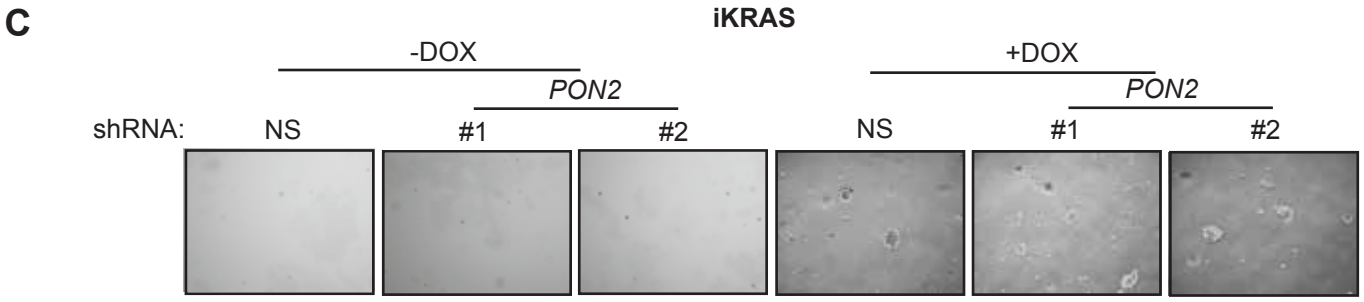
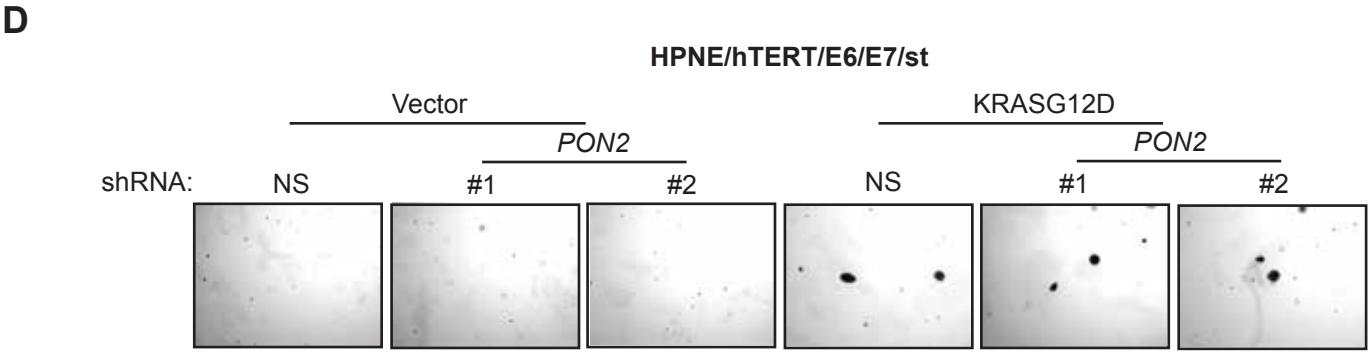

A
PANC1
NS shRNA
shRNA#1
shRNA#2
% Remaining mRNA
150
100
50
0
*
shRNA:
NS
#1 #2
ACACA1
CACNB3
ENO2
HK2
HS2ST1
LDHA
MICAL2
OAS2
PGM2L1
PON2
PPAPDC1A
SDR16C5
SLC2A1
B
AsPC-1
NS shRNA
shRNA#1
shRNA#2
% Remaining mRNA
150
100
50
0
*
shRNA:
NS
#1 #2
ACACA1
CACNB3
ENO2
HK2
HS2ST1
LDHA
MICAL2
OAS2
PGM2L1
PON2
PPAPDC1A
SDR16C5
SLC2A1
C
PANC1
AsPC-1
Su.86.86
MiaPaCa2
shRNA:
PON2
NS
#1
#2
PON2
ACTINB
D
NS shRNA
shRNA#1
shRNA#2
Colony number
400
300
200
100
0
*
**
shRNA:
NS
#1 #2
ACACA1
CACNB3
ENO2
HK2
HS2ST1
LDHA
MICAL2
OAS2
PGM2L1
PPAPDC1A
SDR16C5
SLC2A1
E
NS shRNA
shRNA#1
shRNA#2
Colony number
200
150
100
50
0
*
**
shRNA:
NS
#1 #2
ACACA1
CACNB3
ENO2
HK2
HS2ST1
LDHA
MICAL2
OAS2
PGM2L1
PPAPDC1A
SDR16C5
SLC2A1
F
PON2 shRNA
NS shRNA
#1
#2
Week 1
Week 4
Luminescence (x10⁴)
3.0
2.0
1.0

Figure S2


A
iKRAS
Relative mRNA expression
150
100
50
0
*
shRNA:
NS
#1
#2
PON2
PON2
NS
#1
#2
PON2
ACTINB
B
HPNE/hTERT/E6/E7/st
Relative mRNA expression
150
100
50
0
*
shRNA:
NS
#1
#2
PON2
PON2
NS
#1
#2
PON2
ACTINB


C
iKRAS
-DOX
+DOX
PON2
PON2
shRNA:
NS
#1
#2
NS
#1
#2


D
HPNE/hTERT/E6/E7/st
Vector
KRASG12D
PON2
PON2
shRNA:
NS
#1
#2
NS
#1
#2

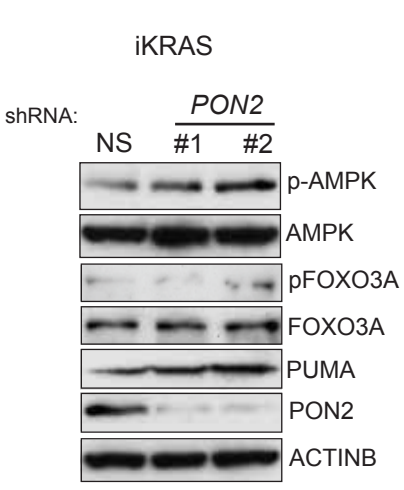

E
iKRAS
shRNA:
PON2
NS
#1
#2
p-AMPK
AMPK
pFOXO3A
FOXO3A
PUMA
PON2
ACTINB

Figure S3

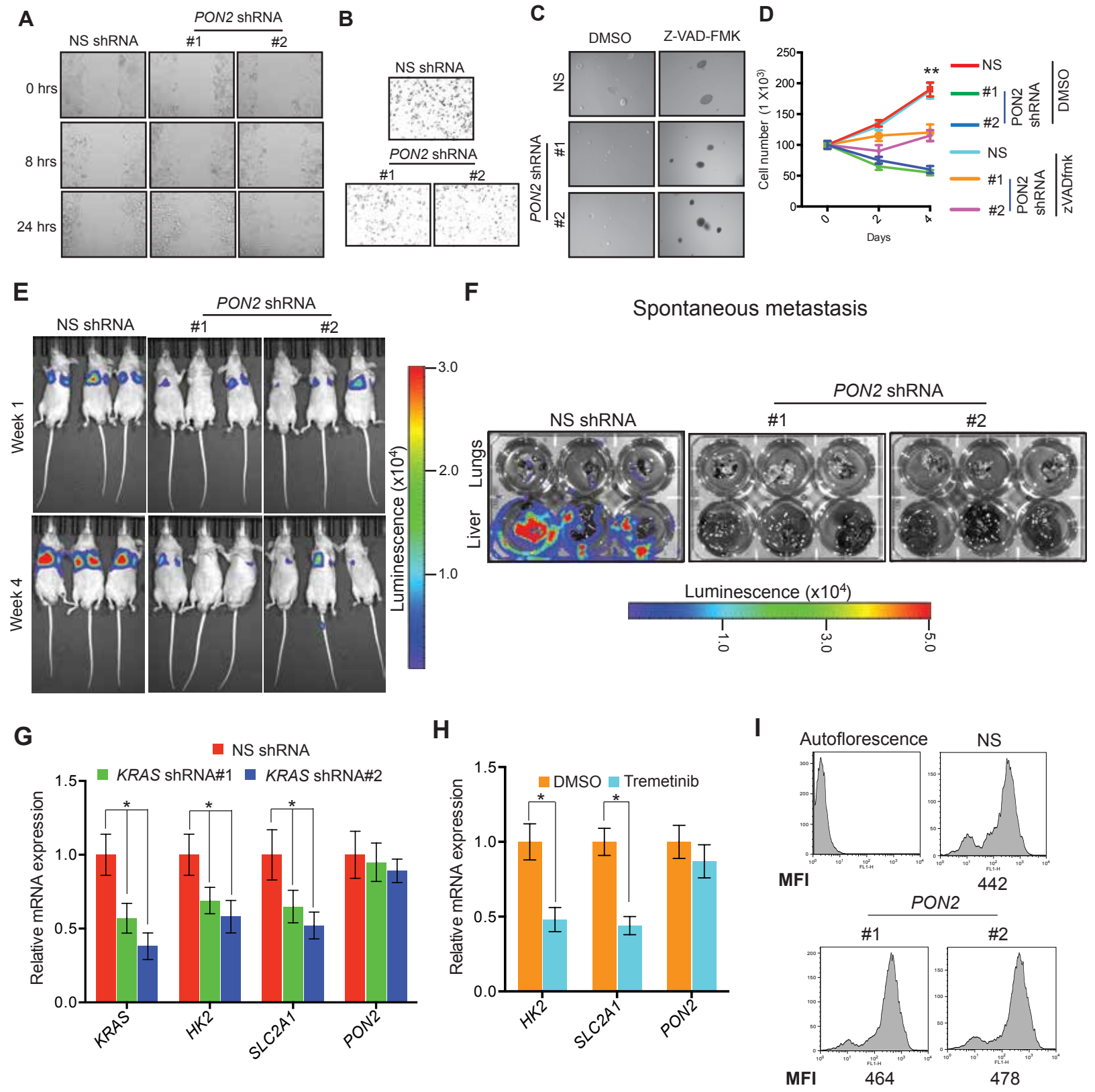

A
PON2 shRNA
NS shRNA
#1
#2
0 hrs
8 hrs
24 hrs
B
NS shRNA
PON2 shRNA
#1
#2
C
DMSO
Z-VAD-FMK
NS
PON2 shRNA
#1
#2
D
Cell number (1 X10^3)
Days
NS
#1
#2
PON2 shRNA
DMSO
zVADfmk
E
PON2 shRNA
NS shRNA
#1
#2
Week 1
Week 4
Luminescence (x10^4)
3.0
2.0
1.0
F
Spontaneous metastasis
PON2 shRNA
NS shRNA
#1
#2
Lungs
Liver
Luminescence (x10^4)
1.0
3.0
5.0
G
NS shRNA
KRAS shRNA#1
KRAS shRNA#2
Relative mRNA expression
KRAS
HK2
SLC2A1
PON2
H
DMSO
Tremetinib
Relative mRNA expression
HK2
SLC2A1
PON2
I
Autoflorescence
NS
MFI
442
PON2
#1
#2
MFI
464
478

Figure S4

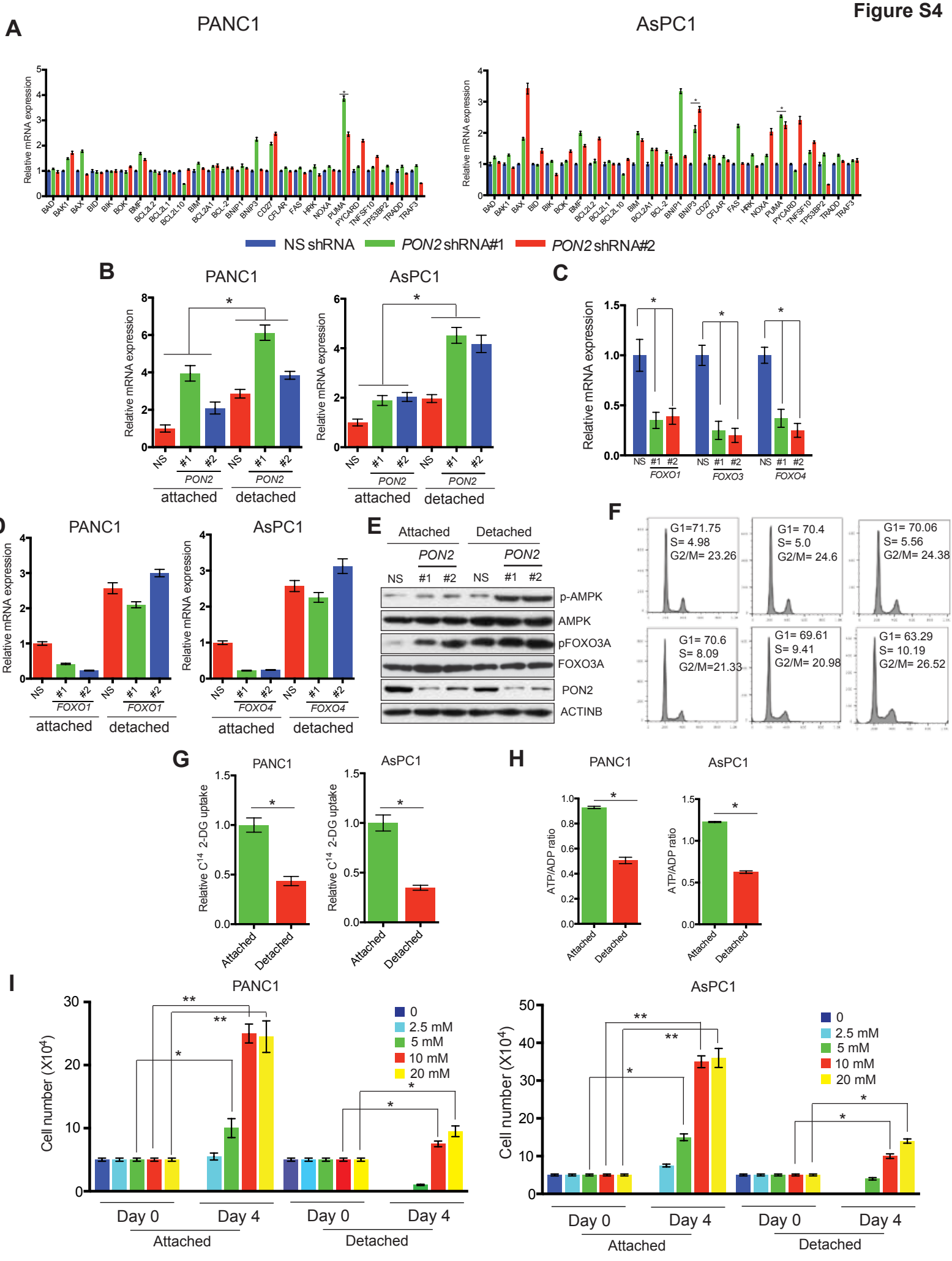

A
PANC1
AsPC1
Relative mRNA expression
BAD BAK1 BAX BID BIK BOK BMF BCL2L2 BCL2L1 BCL2L10 BIM BCL2A1 BCL-2 BNIP1 BNIP3 CD27 CFLAR FAS HRK NOXA PUMA PYCARD TNFSF10 TP53BP2 TRADD TRAF3
NS shRNA
PON2 shRNA#1
PON2 shRNA#2
B
PANC1
AsPC1
Relative mRNA expression
NS #1 #2 NS #1 #2
PON2
attached
detached
C
Relative mRNA expression
NS #1 #2
FOXO1
FOXO3
FOXO4
D
PANC1
AsPC1
Relative mRNA expression
FOXO1
FOXO4
attached
detached
E
Attached
Detached
PON2
NS #1 #2 NS #1 #2
p-AMPK
AMPK
pFOXO3A
FOXO3A
PON2
ACTINB
F
G1=71.75
S= 4.98
G2/M= 23.26
G1= 70.4
S= 5.0
G2/M= 24.6
G1= 70.06
S= 5.56
G2/M= 24.38
G1= 70.6
S= 8.09
G2/M=21.33
G1= 69.61
S= 9.41
G2/M= 20.98
G1= 63.29
S= 10.19
G2/M= 26.52
G
PANC1
AsPC1
Relative C14 2-DG uptake
Attached
Detached
H
PANC1
AsPC1
ATP/ADP ratio
Attached
Detached
I
PANC1
AsPC1
Cell number (X10^4)
0
2.5 mM
5 mM
10 mM
20 mM
Day 0
Day 4
Attached
Detached

Figure S5

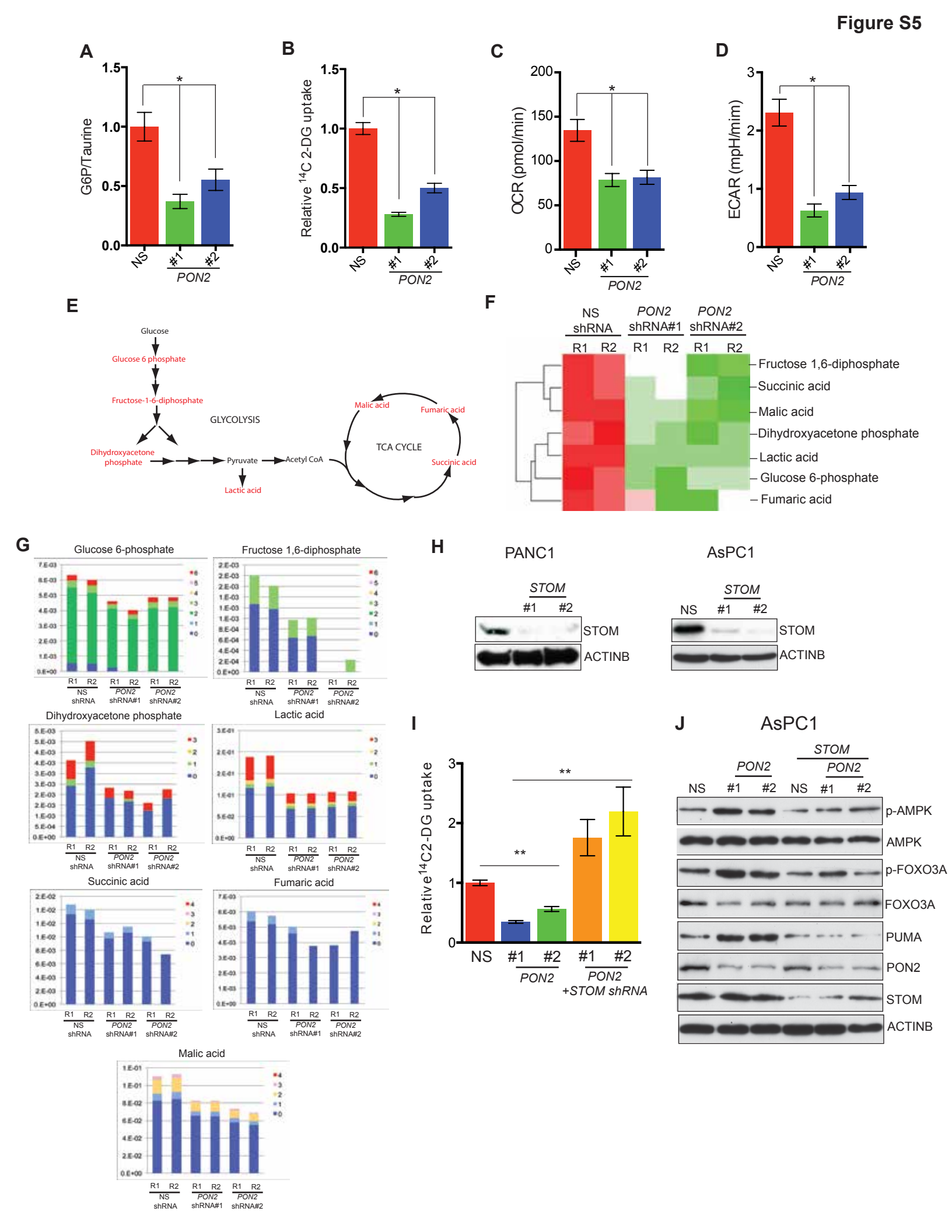
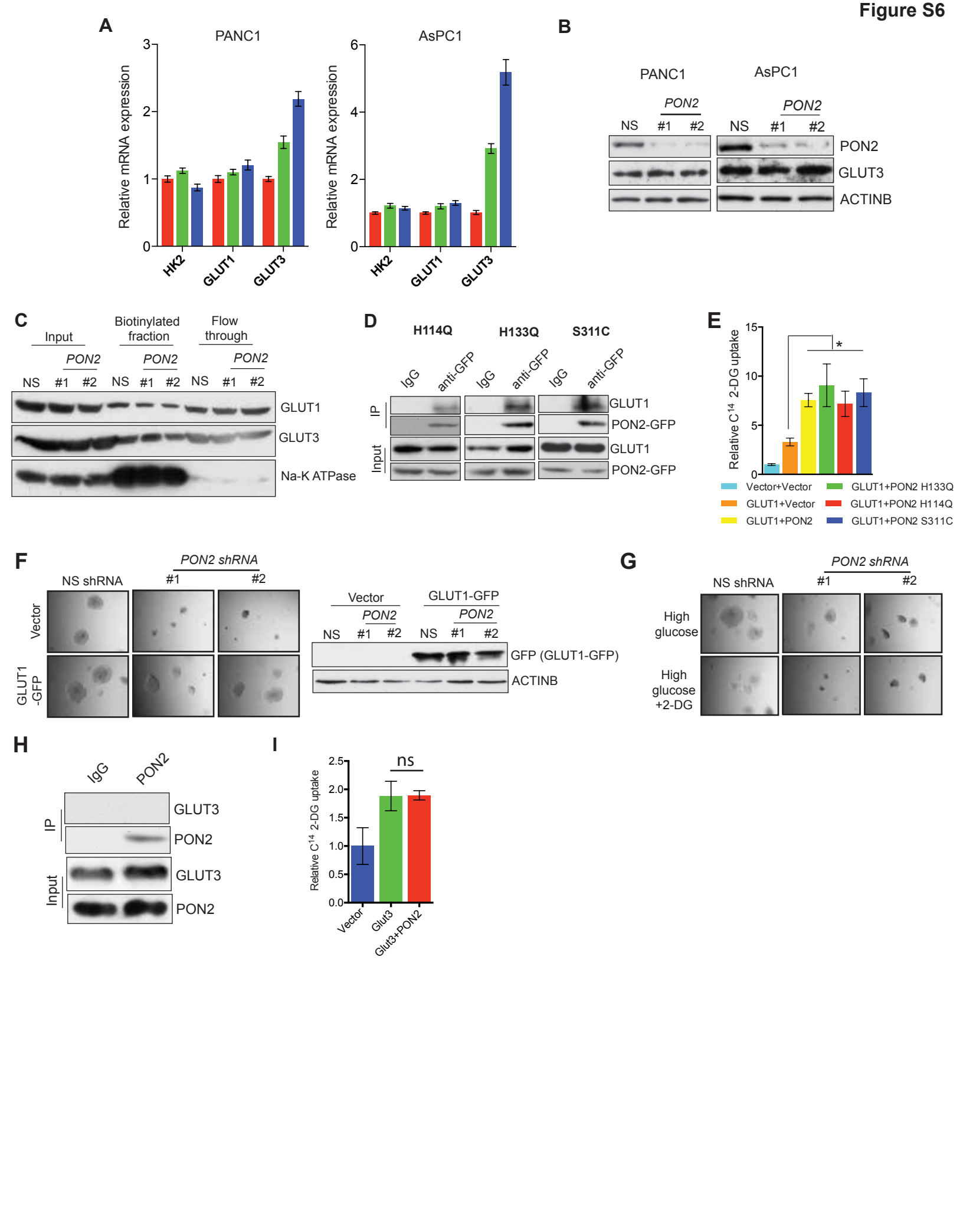
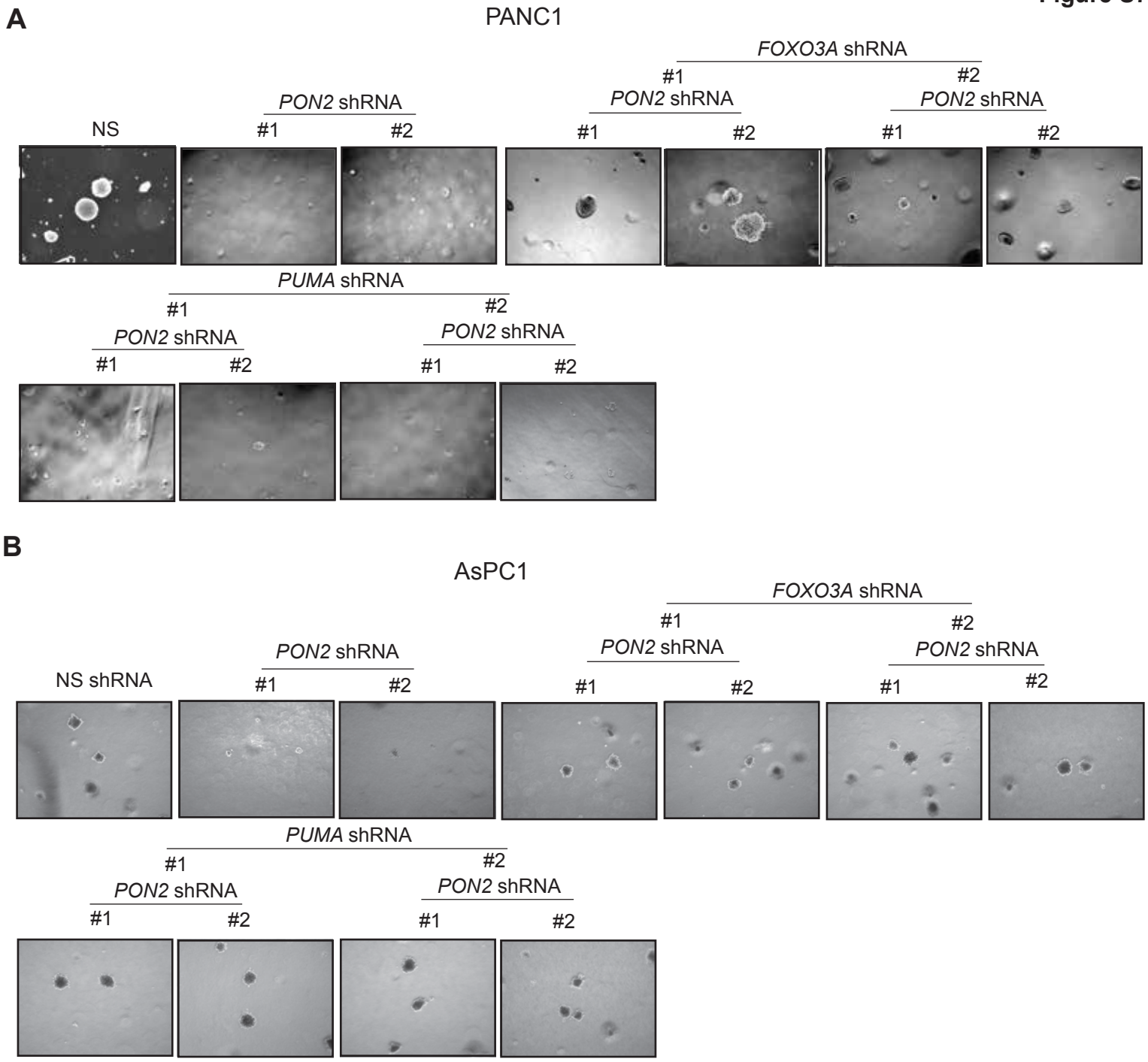

A
G6P/Taurine
NS
#1
#2
PON2
B
Relative 14C 2-DG uptake
C
OCR (pmol/min)
D
ECAR (mpH/mim)
E
Glucose
Glucose 6 phosphate
Fructose-1-6-diphosphate
GLYCOLYSIS
Dihydroxyacetone phosphate
Pyruvate
Acetyl CoA
Lactic acid
TCA CYCLE
Malic acid
Fumaric acid
Succinic acid
F
NS shRNA
PON2 shRNA#1
PON2 shRNA#2
R1
R2
Fructose 1,6-diphosphate
Succinic acid
Malic acid
Dihydroxyacetone phosphate
Lactic acid
Glucose 6-phosphate
Fumaric acid
G
Glucose 6-phosphate
Fructose 1,6-diphosphate
Dihydroxyacetone phosphate
Lactic acid
Succinic acid
Fumaric acid
Malic acid
H
PANC1
AsPC1
STOM
ACTINB
I
Relative 14C2-DG uptake
+STOM shRNA
J
AsPC1
STOM
p-AMPK
AMPK
p-FOXO3A
FOXO3A
PUMA
PON2
STOM
ACTINB

Figure S6


A
PANC1
AsPC1
Relative mRNA expression
HK2
GLUT1
GLUT3
B
PANC1
AsPC1
PON2
NS
#1
#2
PON2
GLUT3
ACTINB
C
Input
Biotinylated fraction
Flow through
PON2
NS
#1
#2
GLUT1
GLUT3
Na-K ATPase
D
H114Q
H133Q
S311C
IgG
anti-GFP
IP
Input
GLUT1
PON2-GFP
E
Relative C14 2-DG uptake
Vector+Vector
GLUT1+Vector
GLUT1+PON2
GLUT1+PON2 H133Q
GLUT1+PON2 H114Q
GLUT1+PON2 S311C
F
PON2 shRNA
NS shRNA
#1
#2
Vector
GLUT1 -GFP
Vector
GLUT1-GFP
GFP (GLUT1-GFP)
ACTINB
G
PON2 shRNA
NS shRNA
High glucose
High glucose +2-DG
H
IgG
PON2
IP
Input
GLUT3
PON2
I
Relative C14 2-DG uptake
ns
Vector
Glut3
Glut3+PON2


A
PANC1
FOXO3A shRNA
#1
#2
PON2 shRNA
#1
#2
NS
PON2 shRNA
#1
#2
PON2 shRNA
#1
#2
PUMA shRNA
#1
#2
PON2 shRNA
#1
#2
PON2 shRNA
#1
#2
B
AsPC1
FOXO3A shRNA
#1
#2
PON2 shRNA
#1
#2
NS shRNA
PON2 shRNA
#1
#2
PON2 shRNA
#1
#2
PUMA shRNA
#1
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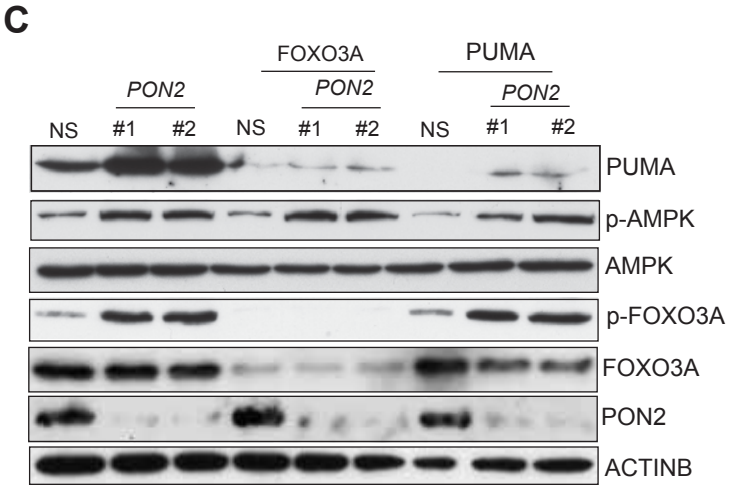
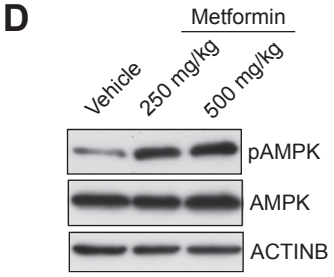
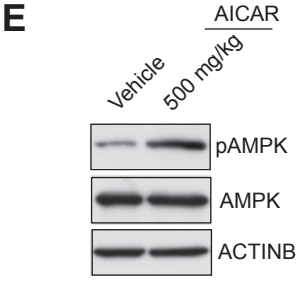
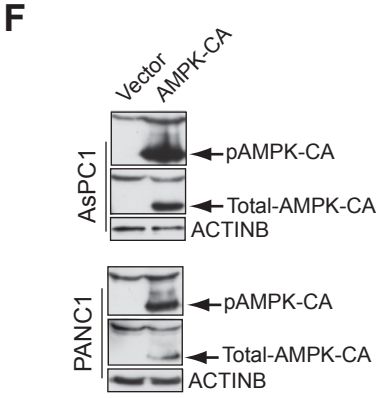
PON2 shRNA
#1
#2
PON2 shRNA
#1
#2


C
FOXO3A
PUMA
PON2
PON2
PON2
NS
#1
#2
NS
#1
#2
NS
#1
#2
PUMA
p-AMPK
AMPK
p-FOXO3A
FOXO3A
PON2
ACTINB


D
Metformin
Vehicle
250 mg/kg
500 mg/kg
pAMPK
AMPK
ACTINB


E
AICAR
Vehicle
500 mg/kg
pAMPK
AMPK
ACTINB


F
Vector
AMPK-CA
AsPC1
pAMPK-CA
Total-AMPK-CA
ACTINB
PANC1
pAMPK-CA
Total-AMPK-CA
ACTINB

SUPPLEMENTARY INFORMATION

SUPPLEMENTARY FIGURE LEGENDS

Figure S1. Related to Figure 1. *PON2* knockdown inhibits PDAC tumor growth

A. PANC1 cells expressing the indicated shRNAs were analyzed by RT-qPCR. The remaining mRNA expression (%) in reference to cells expressing nonspecific (NS) shRNA is shown. **B.** AsPC1 cells expressing the indicated shRNAs were analyzed by RT-qPCR. The remaining gene expression (%) in reference to cells expressing NS shRNA is shown. **C.** PDAC cell lines expressing *PON2* or NS shRNAs were analyzed for PON2 protein by immunoblotting, with ACTINB as a loading control. **D.** PANC1 cells expressing the indicated shRNAs were analyzed for their ability to grow in an anchorage-independent manner in soft agar. Number of colonies is shown. **E.** AsPC-1 cells expressing indicated shRNAs were analyzed for their ability to grow in an anchorage-independent manner in soft agar. Number of colonies is shown. **F.** AsPC-1 cells (1×10^5) expressing either *PON2* or NS shRNA were injected orthotopically into the pancreas of athymic nude mice (n=3), and tumor growth was monitored by bioluminescence imaging. Representative images at week 1 and week 4 are shown. Data are presented as mean ± SEM, *p<0.05, **p<0.005.

Figure S2. Related to Figure 1. PON2 is not necessary for $KRAS^{G12D}$-induced transformation

A. Mouse iKRAS-derived cells expressing *Pon2* or nonspecific (NS) shRNA were analyzed for *Pon2* mRNA levels by RT-qPCR (left) and Pon2 protein levels by immunoblotting (right). **B.** HPNE-hTERT E6/E7/st cells expressing *Pon2* or NS shRNAs

were analyzed for *Pon2* mRNA levels by RT-qPCR (left) or PON2 protein levels by immunoblotting (right). **C.** Mouse iKRAS-derived pancreatic cancer cells expressing *Pon2* or NS shRNAs were analyzed for their ability to grow in an anchorage-independent manner in soft agar assay with without doxycycline (no $KRAS^{G12D}$ activation) or doxycycline ($KRAS^{G12D}$ activation). Representative images are shown. **D.** HPNE-hTERT E6/E7/st cells expressing *PON2* or NS shRNA along with vector expressing $KRAS^{G12D}$ or empty vector were analyzed for their ability to grow in an anchorage-independent manner in soft agar. Representative images are shown. **E.** iKRAS cells expressing *PON2* or NS shRNA were analyzed for indicated proteins by immunoblot analysis. Data are presented as mean ± SEM, *$p<0.05$.

Figure S3. Related to Figure 2. Loss of PON2 does not affect migratory or invasive phenotypes or cellular ROS levels in PDAC cells. A. PANC1 cells expressing *PON2* or nonspecific (NS) shRNAs were analyzed for migration using the wound-healing assay. Representative images are shown. **B.** PANC1 cells expressing *PON2* or NS shRNAs were analyzed for invasion using Matrigel invasion chambers. Representative images are shown. **C.** PANC1 cells expressing *PON2* or NS shRNAs were treated with either DMSO or Z-VAD-FMK (10 μM) and analyzed for anchorage independent growth using soft-agar. Representative wells for indicated conditions is presented. **D.** PDAC cell lines expressing *PON2* or nonspecific (NS) shRNAs were seeded on poly(HEMA)-coated plates and treated with either DMSO or Z-VAD-FMK (10 μM). Viable cells were counted after staining with trypan blue, and the relative numbers of viable cells are plotted at indicated time. **E.** The tail veins of athymic nude mice (n=3) were injected with

PANC1 cells expressing *PON2* or NS shRNAs. Lung metastasis formation was measured by bioluminescence imaging. Representative images for week 1 and week 4 are shown. **F.** Luciferase-tagged AsPC-1 cells carrying *PON2* or NS shRNA were injected into the pancreas of athymic nude mice (n=3). Spontaneous metastasis to liver and lung was analyzed after 6 weeks. Bioluminescence images of the livers and lungs from the mice are shown. **G.** PANC1 cells expressing *KRAS* or NS shRNAs were analyzed for the mRNA expression of indicated genes by RT-qPCR. The relative mRNA expression levels of the indicated genes are shown. **H.** PANC1 cells were treated with 250 nM trametinib or DMSO (control) for 48 hours and analyzed by RT-qPCR. The relative mRNA expression levels of the indicated genes are shown. **I.** PANC1 cells expressing *PON2* or NS shRNAs were analyzed for cellular ROS levels by staining with H2DCFDA followed by fluorescence-activated cell sorting. Representative histograms and mean fluorescent intensities are shown. Data are presented as mean ± SEM, *$p<0.05$, **$p<0.005$.

Figure S4. Related to Figure 4. PON2 loss results in PUMA upregulation in a FOXO3A-dependent manner. A. PANC1 (left) or AsPC-1 (right) cells expressing *PON2* or nonspecific (NS) shRNAs were analyzed for the mRNA expression of the indicated apoptotic genes by RT-qPCR. Relative mRNA expression is shown. **B.** PANC1 (left) or AsPC-1 (Right) cells expressing either *PON2* or NS shRNAs were plated under attached or detached conditions and analyzed for *PUMA* expression by RT-qPCR. Relative PUMA mRNA expression is shown. **C.** PANC1 cells expressing indicated shRNAs were analyzed for the expression of *FOXO1*, *FOXO3A* or *FOXO4* by RT-qPCR. Relative mRNA expression in reference to cells expressing NS shRNA is shown. **D.**

PANC1 or AsPC-1 cells expressing either *FOXO1 (left)*, *FOXO4* (right) or NS shRNA were plated under attached or detached conditions and analyzed for *PUMA* mRNA expression by RT-qPCR. Relative *PUMA* mRNA expression is shown. **E.** AsPC-1 cells expressing *PON2* or NS shRNAs were grown under attached or detached conditions and analyzed for the expression of the indicated proteins by immunoblotting. **F.** Propidium iodide stained PANC1 and AsPC1 cells expressing either a NS shRNA or *PON2* shRNAs were analyzed for cell cycle stages by FACS analysis. % Cell cycle stage is shown. **G.** PANC1 or AsPC1 cells were grown either under attached and detached conditions and ^{14}C-2DG uptake was measured. Relative ^{14}C-2DG uptake for PANC1 and AsPC1 under attached or detached conditions is shown. **H.** PANC1 or AsPC1 cells were grown either under attached and detached conditions and ATP/ADP ratio was measured using ADP/ATP Ratio Assay Kit (Sigma). Relative ATP/ADP ratio for PANC1 and AsPC1 under attached or detached conditions is shown. **I.** PANC1 or AsPC1 cell were seeded on poly(HEMA)-coated plates under indicated glucose concentrations. Viable cells were counted after staining with trypan blue, and the relative numbers of viable cells are plotted at indicated time. Data are presented as mean ± SEM, *$p<0.05$, **$p<0.005$.

Figure S5. Related to Figure 5. Metabolic pathway analysis in PANC1 cells expressing *PON2* or nonspecific shRNA and regulation of GLUT1 activity by PON2

A. Glucose 6-phosphate/taurine ratio in AsPC-1 cells expressing *PON2* or nonspecific (NS) shRNAs. **B.** Relative ^{14}C 2DG uptake in AsPC-1 cells expressing *PON2* or NS shRNAs. **C.** Oxygen consumption rate expressed as pmol/minutes in AsPC-1 cells expressing *PON2* or NS shRNAs. **D.** Extracellular acidification rate (ECAR) expressed

as mpH/minutes in AsPC-1 cells expressing *PON2* or NS shRNAs. **E.** Metabolic pathway highlighting key altered metabolites (red) based on metabolite analysis from PANC1 cells expressing *PON2* or NS shRNAs. **F.** Heatmap for key altered metabolites based on metabolite analysis from PANC1 cells expressing *PON2* or NS shRNAs. **G.** The metabolites labeled in red from glycolytic and TCA cycle are presented in PANC1 cells expressing *PON2* or nonspecific (NS) shRNAs that were grown in 10 mM [U-$^{13}C_6$] glucose and analyzed using CE-TOFMS. The isotope distributions of the metabolites labeled with indicated number of ^{13}C carbon atoms are shown. **H.** Immunoblot analysis of STOM in cells carrying *STOM* or nonspecific (NS) shRNA in PANC1 (left) and AsPC-1 (right) cells. ACTINB was used as a loading control. **I.** Relative ^{14}C 2DG uptake in AsPC-1 expressing *STOM* or *PON2* and *STOM* or NS shRNAs. **J.** Immunoblot analysis to measure indicated proteins in AsPC-1 cells expressing *NS* or *PON2* without or with *STOM* shRNA. Data are presented as mean ± SEM, *p<0.05, **p<0.005.

Figure S6. Related to Figures 5 and 6. PON2 regulates GLUT1 mediated glucose uptake. A. PANC1 (left) or AsPC-1 (right) cells expressing either *PON2* or nonspecific (NS) shRNA were analyzed for *HK2*, *GLUT1* and *GLUT3* mRNA expression by RT-qPCR. **B**. PANC1 (left) or AsPC-1 (right) cells expressing either PON2 or nonspecific (NS) shRNA were analyzed for indicated proteins by immunoblot analysis. **C.** PANC1 cells expressing PON2 or NS shRNAs were analyzed for cell surface GLUT1 and GLUT3 expression, by extraction of the biotinylated fraction followed by immunoblot analysis. **D**. Co-immunoprecipitation assay in PANC1 cells expressing PON2 H114Q-GFP or PON2 H133Q-GFP or PON2 S331C-GFP using IgG or anti-GFP antibody.

Immunoprecipitates and lysates were analyzed for the indicated proteins. **E.** Relative ^{14}C-2DG uptake in PANC1 cells co-expressing GLUT1 along with WT PON2-GFP or PON2 H114Q-GFP or PON2 H133Q-GFP or PON2 S331C-GFP. **F.** (Left) Soft agar assay with PANC1 cells expressing either NS or *PON2* shRNAs along with either stable expression of the empty vector control or GLUT1-GFP. (Right) Immunoblotting showing GFP (GLUT1-GFP) expression under indicated condition. ACTINB was measured as a loading control. **G.** Soft agar assay with PANC1 cells expressing NS or *PON2* shRNAs in DMEM with 75mM glucose or DMEM with 75mM glucose and 10 mM 2-Deoxy-D-glucose (2DG). **H.** Co-immunoprecipitation assay in PANC1 cells using IgG or anti-PON2 antibody. Immunoprecipitates and lysates were analyzed for indicated proteins. **I.** PANC1 cells expressing indicated expression constructs were analyzed for ^{14}C-2DG uptake. Relative ^{14}C-2DG uptake under indicated condition was analyzed. Data are presented as mean ± SEM, *$p<0.05$, ns= not significant.

Figure S7. Related to Figures 6 and 7. *PON2*-loss mediated upregulation of *PUMA* via FOXO3A is necessary for tumor growth inhibition. A. PANC1 cells expressing *PON2* or nonspecific (NS) shRNA alone or along with *FOXO3A* and *PUMA* shRNAs were analyzed for anchorage-independent growth in soft agar. Representative images are shown. **B.** PANC1 cells expressing *PON2* or NS shRNA alone or along with *FOXO3A* and *PUMA* shRNAs were analyzed for anchorage-independent growth in soft agar. Representative images are shown. C. Tumor lysates corresponding to the figure 6A were analyzed for indicated protein by immunoblot analysis. **D.** Immunoblot analysis of tumor lysates for indicated proteins from mice treated with vehicle or indicated concentrations

of metformin. **E.** Immunoblot analysis of tumor lysates for indicated proteins from mice treated with vehicle or AICAR at a concentration of 500mg/Kg body weight. **F.** Immunoblot analysis of PANC1 cells (Top) or AsPC-1 cells (Bottom) expressing vector control or constitutively active AMPKα1 (AMPK-CA).

Table S1. List of 13 metabolic genes shortlisted for functional validation in PDAC cells. Related to Figure 1.

Gene Symbol	Gene Name	Functional Category
ACACA	Acetyl-Coenzyme A Carboxylase Alpha	Fatty acid biosynthesis
CACNB3	Calcium Channel, Voltage-Dependent, Beta 3 Subunit	Calcium ion Transport
ENO2	Enolase 2 (gamma, neuronal)	Glycolysis
HK2	Hexokinase 2	Glycolysis
HS2ST1	Heparan Sulfate 2-O-Sulfotransferase 1	2-O-Sulfation
LDHA	Lactate Dehydrogenase A	Anaerobic Glycolysis
MICAL2	Microtubule associated monoxygenase, calponin and LIM domain containing 2	Redox
OAS2	2'-5'-Oligoadenylate Synthetase 2, 69/71kDa	Nucleotide Metabolism
PGM2L1	Phosphoglucomutase 2-like 1	Glycolysis
PON2	Paraoxonase 2	Antioxidant
PPAPDC1A	Phosphatidic Acid Phosphatase Type 2 Domain Containing 1A	Lipid Phosphatase
SDR16C5	Short-Chain Dehydrogenase/Reductase Family 16C, Member 5	Vitamin A metabolism
SLC2A1	Solute carrier family 2 (facilitated glucose transporter), member 1	Glucose transport

Table S2: Colony number and relative colony size for indicated soft agar assays. Related to Figures 1, 5, 6, S2, S3 and S6.

Figure	Cell Line	Group no	shRNA	Treatment	Colony no.	SEM	P value (compared with)	Relative colony size %	SEM	P value (compared with)
Fig 1B	PANC1	1	NS		240	20.4		100.00	5.2	
		2	PON2#1		42	8.4	<0.005 (1)	17.50	0.6	<0.005 (1)
		3	PON2#2		54	7.2	<0.005 (1)	25.00	1.9	<0.005 (1)
	AsPC-1	4	NS		164	11.1		100.00	6.5	
		5	PON2#1		24	2.5	<0.005 (4)	21.30	1	<0.005 (4)
		6	PON2#2		42	3.2	<0.005 (4)	37.80	1.3	<0.005 (4)
	SU.86.86	7	NS		94	15.5		100.00	5.8	
		8	PON2#1		34	9.9	<0.05 (7)	13.20	1.8	<0.005 (7)
		9	PON2#2		48	7.7	<0.05 (7)	20.60	3	<0.005 (7)
	MiaPaCa2	10	NS		195	18.6		100.00	5.9	
		11	PON2#1		65	8.2	<0.005 (10)	12.30	0.6	<0.005 (10)
		12	PON2#2		72	9.4	<0.005 (10)	19.20	1.4	<0.005 (10)
Fig 1E	iKRAS	1	iKRAS/Vector	Dox-	0					
		2	iKRAS/PON2	Dox-	0					
		3	iKRAS/Vector	Dox+	85	4.5		100.00	8.5	
		4	iKRAS/PON2	Dox+	92	4.9	0.3521 (3)	280.00	16.1	<0.005 (3)
Fig 1F	iKRAS	1	Vector KRASG12D		75	4.6		100.00	7.45	
		2	PON2 KRASG12D		78	3.8	0.6415 (2)	350.00	22.5	<0.005 (2)
Fig 5K	PANC1	1	NS		280	12.6		100.00	7.56	
		2	PON2#1		68	2.85	<0.005 (1)	25.00	2.65	<0.005 (1)
		3	PON2#2		72	3.744	<0.005 (1)	34.38	4.24	<0.005 (1)
		4	NS+STOM		285	13.65		112.50	9.65	ns*
		5	PON2#1+STOM#1		148	5.624	<0.005 (2)	50.00	3.45	<0.005 (2)
		6	PON2#2+STOM#1		165	12.37	<0.005 (2)	53.13	4.56	<0.05 (2)
Fig 6F	PANC1	1	NS	25mM Glu	255	11.65		100.00	6.5	
		2	PON2#1	25mM Glu	78	5.32	<0.005 (1)	38.89	2.1	<0.005 (1)
		3	PON2#2	25mM Glu	94	6.55	<0.005 (1)	44.44	2.25	<0.005 (1)
		4	PON2#1	75mM Glu	156	8.65	<0.005 (2)	77.78	4.5	<0.005 (2)
		5	PON2#2	75mM Glu	144	7.54	<0.005 (3)	94.44	7.8	<0.005 (3)
Fig 7B	PANC1	1	PANC1	UT	261	14.5		100.00	9.5	
		2	PANC1	Metformin	95	7.45	<0.005 (1)	31.00	5.1	<0.005 (1)

	AsPC-1	1	AsPC-1	UT	182	10.25		100.00	8.4	
		2	AsPC-1	Metformin	97	5.65	<0.005 (1)	40.00	4.25	<0.005 (1)
Fig 7D	PANC1	1	PANC1	UT	221	11.5		100.00	7.5	
		2	PANC1	AICAR	74	6.45	<0.005 (1)	61.00	3.5	<0.05 (1)
	AsPC-1	1	AsPC-1	UT	165	13.65		100.00	8.5	
		2	AsPC-1	AICAR	63	3.45	<0.005 (1)	55.00	2.5	<0.05 (1)
Fig 7F	PANC1	1	PANC1	Vec	274	12.25		100.00	8.5	
		2	PANC1	AMPK-CA	225	9.85	<0.005 (1)	71.5	4.5	<0.05 (1)
	AsPC-1	1	AsPC-1	Vec	195	9.5		100.00	9.45	
		2	AsPC-1	AMPK-CA	144	7.5	<0.005 (1)	74.5	5.55	<0.05 (1)
Fig S2C	iKRAS	1	NS	Dox-	0			0.00		
		2	PON2#1	Dox-	0			0.00		
		3	PON2#2	Dox-	0			0.00		
		4	NS	Dox+	78	3.2		100.00	5.45	
		5	PON2#1	Dox+	69	4.1	0.1586 (4)	88.88	4.15	ns* (4)
		6	PON2#2	Dox+	75	3.5	0.5614 (4)	111.11	6.25	ns* (4)
Fig S2D	HPNE	1	NS	Vector	0			0		
		2	PON2#1	Vector	0			0		
		3	PON2#2	Vector	0			0		
		4	NS	KRASG12D	85	3.5		100	4.55	
		5	PON2#1	KRASG12D	78	4.2	0.2363 (4)	95.4	5.2	ns* (4)
		6	PON2#2	KRASG12D	81	4.1	0.4793 (4)	98.33	6.5	ns* (4)
Fig S3C	PANC1	1	NS	DMSO	197	11.35		100.00	7.8	
		2	PON2#1	DMSO	54	5.2	<0.005 (1)	15.30	1.8	<0.005 (1)
		3	PON2#2	DMSO	65	4.2	<0.005 (1)	18.50	2.45	<0.005 (1)
		4	NS	Z-VAD-FMK	221	16.5		124.00	9.55	
		5	PON2#1	Z-VAD-FMK	121	9.3	<0.005 (2)	78.40	6.2	<0.005 (2)
		6	PON2#2	Z-VAD-FMK	183	8.2	<0.005 (3)	76.55	5.9	<0.005 (3)
Fig S6F	PANC1	1	NS	Vector	235	16.54		100.00	7.2	
		2	PON2#1	Vector	67	4.5	<0.005 (1)	35.71	2.89	<0.005 (1)

		3	PON2#2	Vector	72	5.6	<0.005 (1)	28.57	2.45	<0.005 (1)
		4	NS	GLUT1	256	15.25		107.14	6.5	
		5	PON2#1	GLUT1	176	11.25	<0.005 (2)	71.42	5.1	<0.005 (2)
		6	PON2#2	GLUT1	183	10.85	<0.005 (3)	78.57	4.3	<0.005 (3)
FigS6G	PANC1	1	NS	High Glu	225	14.5		100.00	7.45	
		2	PON2#1	High Glu	155	10.55		64.29	5.5	
		3	PON2#2	High Glu	168	9.58		71.43	4.55	
		4	NS	High Glu+2DG	100	6.5	<0.005 (1)	46.43	3.68	<0.005 (1)
		5	PON2#1	High Glu+2DG	35	2.65	<0.005 (2)	25.00	2.95	<0.005 (2)
		6	PON2#2	High Glu+2DG	38	3.2	<0.005 (3)	17.86	2.4	<0.005 (3)
Fig S7A	PANC1	1	NS		215	15.4		100.00	8.5	
		2	PON2#1		53	3.5	<0.005 (1)	25.50	2.3	<0.005 (1)
		3	PON2#2		69	4.5	<0.005 (1)	35.00	3.4	<0.005 (1)
		4	PON2#1	FOXO3A#1	175	7.8	<0.005 (2)	95.70	9.5	<0.005 (2)
		5	PON2#2	FOXO3A#1	145	8.9	<0.005 (3)	92.85	8.2	<0.005 (3)
		6	PON2#1	FOXO3A#2	163	5.9	<0.005 (2)	60.71	6.5	<0.05 (2)
		7	PON2#2	FOXO3A#2	149	8.2	<0.005 (3)	75.00	7.15	<0.05 (3)
		8	PON2#1	PUMA#1	109	6.3	<0.005 (2)	38.55	4.3	ns* (2)
		9	PON2#2	PUMA#1	91	4.5	<0.05 (3)	35.71	4.1	ns* (3)
		10	PON2#1	PUMA#2	84	4.9	<0.05 (2)	39.28	3.33	<0.05 (2)
		11	PON2#2	PUMA#2	117	7.2	<0.005 (3)	42.85	2.89	ns* (3)
Fig S7B	AsPC-1	1	NS		173	11.26		100.00	7.5	
		2	PON2#1		49	3.79	<0.005 (1)	30.55	4.3	<0.005 (1)
		3	PON2#2		63	5.64	<0.005 (1)	33.33	3.35	<0.005 (1)
		4	PON2#1	FOXO3A#1	142	14.5	<0.005 (2)	63.33	7.5	<0.05 (2)
		5	PON2#2	FOXO3A#1	132	10.25	<0.005 (3)	60.55	6.5	<0.05 (3)
		6	PON2#1	FOXO3A#2	133	11.36	<0.005 (2)	65.75	6.5	<0.05 (2)
		7	PON2#2	FOXO3A#2	121	9.8	<0.05 (3)	58.50	4.56	<0.05 (3)
		8	PON2#1	PUMA#1	91	6.3	<0.05 (2)	43.35	3.85	0.0908 (2)
		9	PON2#2	PUMA#1	83	5.5	0.0641 (3)	62.55	5.55	<0.05 (3)
		10	PON2#1	PUMA#2	65	7.2	0.1207 (2)	55.65	3.25	<0.05 (2)
		11	PON2#2	PUMA#2	55	3.45	0.2929 (3)	46.66	3.15	<0.05 (3)

ns*- Not Significant (P value > 0.05)

Table S3: Quantitation for bioluminescent imaging of tumors and metastasis. Related to Figures 1, 2, 6, 7, S1 and S3.

Figure	Group no	Cell line	shRNA	Comment	Weeks post injection	Average Total counts	SEM	P value (Group compared to)
Fig 1D	1	PANC1	NS		Week 1	3808400.00	1324740.37	
	2	PANC1	PON2#1		Week 1	44926.67	32638.40	<0.05 (1)
	3	PANC1	PON2#2		Week 1	67110.00	50905.34	<0.05 (1)
	4	PANC1	NS		Week 4	8173000.00	2656962.87	
	5	PANC1	PON2#1		Week 4	14903.00	4892.25	<0.05 (4)
	6	PANC1	PON2#2		Week 4	100536.67	78690.47	<0.05 (4)
Fig 2D	1	PANC1	NS		Week 1	55613.33	8978.62	
	2	PANC1	PON2#1		Week 1	16990.00	3054.83	<0.05 (1)
	3	PANC1	PON2#2		Week 1	10836.67	142.10	<0.05 (1)
	4	PANC1	NS		Week 4	180733.33	41737.52	
	5	PANC1	PON2#1		Week 4	49070.00	7735.93	<0.05 (4)
	6	PANC1	PON2#2		Week 4	9491.67	524.74	<0.05 (4)
Fig 2E	1	PANC1	NS	Liver		1920333.33	314849.25	
	2	PANC1	PON2#1	Liver		5620.00	2212.86	<0.005 (1)
	3	PANC1	PON2#2	Liver		333716.67	311557.34	<0.05 (1)
Fig 2F	1	PANC1	NS	Lung		898533.33	199600.47	
	2	PANC1	PON2#1	Lung		5945.67	1674.12	<0.05 (1)
	3	PANC1	PON2#2	Lung		23076.67	5332.02	<0.05 (1)
	4	PANC1	NS	Liver		10694000.00	3731717.82	
	5	PANC1	PON2#1	Liver		4734.33	573.77	<0.05 (4)
	6	PANC1	PON2#2	Liver		291296.67	254472.71	<0.05 (4)
Fig 6D	1	PANC1	NS		Week 1	834733.33	55632.93	
	2	PANC1	PON2#1		Week 1	128300.00	21216.63	<0.005 (1)
	3	PANC1	PON2#1 + FOXO3A#1		Week 1	916500.00	267630.53	<0.05 (2)
	4	PANC1	PON2#1 + FOXO3A#2		Week 1	873266.67	139013.45	<0.05 (2)
	5	PANC1	PON2#1 + PUMA#1		Week 1	332700.00	90399.28	ns* (2)
	6	PANC1	PON2#1 + PUMA#2		Week 1	529666.67	129426.10	<0.05 (2)
	7	PANC1	NS		Week 4	6988000.00	1534048.18	
	8	PANC1	PON2#1		Week 4	421666.67	112801.43	<0.05 (7)
	9	PANC1	PON2#1 + FOXO3A#1		Week 4	7235666.67	2236128.97	<0.05 (8)

	10	PANC1	PON2#1 + FOXO3A#2		Week 4	10263000.00	432753.45	<0.005 (8)
	11	PANC1	PON2#1 + PUMA#1		Week 4	1390033.33	275733.15	<0.05 (8)
	12	PANC1	PON2#1 + PUMA#2		Week 4	1308433.33	257991.50	<0.05 (8)
Fig 7A	1	PANC1	NS		Week 1	759133.33	236900.28	
	2	PANC1	NS	+Dox	Week 1	970700.00	392162.36	ns* (1)
	3	PANC1	PON2#1		Week 1	895300.00	333745.62	
	4	PANC1	PON2#1	+Dox	Week 1	1264133.33	214037.32	ns* (3)
	5	PANC1	PON2#2		Week 1	949200.00	163373.34	
	6	PANC1	PON2#2	+Dox	Week 1	1561966.67	382986.04	ns* (5)
	7	PANC1	NS		Week 4	17443333.33	2809571.65	
	8	PANC1	NS	+Dox	Week 4	14679000.00	4802145.47	ns* (7)
	9	PANC1	PON2#1		Week 4	12171000.00	1998634.05	
	10	PANC1	PON2#1	+Dox	Week 4	998966.67	223206.81	<0.05 (9)
	11	PANC1	PON2#2		Week 4	6255666.67	1037122.50	
	12	PANC1	PON2#2	+Dox	Week 4	896066.67	282892.33	<0.05 (11)
Fig S1F	1	AsPC-1	NS		Week 1	5765666.67	401158.29	
	2	AsPC-1	PON2#1		Week 1	25246.67	12431.09	<0.005 (1)
	3	AsPC-1	PON2#2		Week 1	305666.67	14167.90	<0.005 (1)
	4	AsPC-1	NS		Week 4	36556666.67	6100559.34	
	5	AsPC-1	PON2#1		Week 4	221010.67	201360.63	<0.005 (4)
	6	AsPC-1	PON2#2		Week 4	305666.67	14167.90	<0.005 (4)
Fig S3E	1	AsPC-1	NS		Week 1	1755533.33	637021.14	
	2	AsPC-1	PON2#1		Week 1	469876.67	278055.01	ns* (1)
	3	AsPC-1	PON2#2		Week 1	776533.33	482454.07	ns* (1)
	4	AsPC-1	NS		Week 4	14186666.67	2662207.95	
	5	AsPC-1	PON2#1		Week 4	630333.33	413590.70	<0.05 (4)
	6	AsPC-1	PON2#2		Week 4	1427533.33	847301.40	<0.05 (4)
Fig S3F	1	AsPC-1	NS	Lung		508033.33	15462.44	
	2	AsPC-1	PON2#1	Lung		4832.67	586.96	<0.005 (1)
	3	AsPC-1	PON2#2	Lung		5019.00	495.80	<0.005 (1)
	4	AsPC-1	NS	Liver		14243000.00	4747522.99	
	5	AsPC-1	PON2#1	Liver		4765.00	513.59	<0.05 (4)
	6	AsPC-1	PON2#2	Liver		15228.00	7665.27	<0.05 (4)

ns*- Not Significant (P value > 0.05)

Table S4. Summary of immunohistochemistry staining for PON2 in human pancreata and PDAC samples. Related to Figure 3.

Staining	**Cytoplasmic/membranous**					
Density	0	1+	2+	3+		
Percentile	<10%	11-25%	26-50%	>50%		
Non-neoplastic pancreatic tissue						
	Ductal Cells		Acinar Cells		Islet Cells	
4916N			2+	100%		
4417N	1+	5%	1+	20%	1+	100%
4234N	1+	5%	2+	20%		
6492N	0	0	1+	30%		
2820N	1+	20%	1+	80%	2+	100%
Pancreatic ductal adenocracinoma						
7266T	2+	80%				
7261T	2+	90%				
7273T	2+	90%				
7267T	2+	30%	3+	10%		
7265T	2+	60%				
7271T	2+	40%				
7274T	2+	60%	3+	40%		
7275T	2+	80%				
7277T	2+	60%				
7262T	2+	50%	3+	50%		

Table S5. List of RT-qPCR primers of apoptotic genes. Related to Figure S4.

Gene symbol	Species	Forward primer (5'-3')	Reverse primer (5'-3')
BAD	*Human*	CTGGACGCGAGTCTTCCAGT	AGTGGGAACGGGTGGAGTTT
BAK1	*Human*	GCTACCGTCTGGCCCTACAC	CAGAACCACACCCAGAACCA
BAX	*Human*	CAGCAAACTGGTGCTCAAGG	CAACCACCCTGGTCTTGGAT
BID	*Human*	TCCCGCTTGGGAAGAATAGA	TGTGACTGGCCACCTTCTTG
BIK	*Human*	GACCTGGACCCTATGGAGGA	TGGTGAAACCGTCCATGAAA
BOK	*Human*	CCACAGACAAGGAGCTGGTG	CAGACTGCAGGGAGATGTGC
BMF	*Human*	TATGGCAATGCTGGCTATCG	CTGGTGTTGCTGCACATGAA
BCL-W/BCL2L2	*Human*	ACAACGCTTCACCCAGGTCT	CCACTGCTGTGGATCCAGTC
BCL-XL/BCL2L1	*Human*	TGACATCCCAGCTCCACATC	AGAGTGAGCCCAGCAGAACC
DIVA/BCL2L10/ BCL-B	*Human*	GCCGACTACCTGGGGTACTG	ACCGGTGAATCTGCCGTAAC
BIM/BCL2L11	*Human*	ATGCGCCCAGAGATATGGAT	ACCATTCGTGGGTGGTCTTC
BCL2A1	*Human*	TGGATCAGGTCCAAGCAAAA	GGGGCAATTTGCTGTCGTAG
BCL-2	*Human*	CATGTGTGTGGAGAGCGTCA	ATCCCAGCCTCCGTTATCCT
BNIP1	*Human*	GGTGAAGGCGCTTATTCAGG	CATGAGGCCTGATTGCTGAG
BNIP3	*Human*	TCACTGTGACAGCCCACCTC	TTCATGACGCTCGTGTTCCT
CD27	*Human*	CTTCCAAACCCTTCGCTGAC	GGTGGCCAGTGGGTAGAGAG
CFLAR	*Human*	TTCTTGGCCAATTTGCCTGT	CCTCGCTTCTGAGCCTTGAA
FAS	*Human*	CCCTGTCCTCCAGGTGAAAG	TCCGGGTGCAGTTTATTTCC
HRK	*Human*	CTAGGCGACGAGCTGCAC	CACAGCCAAGGCCAGTAGGT
NOXA	*Human*	AAGAAGGCGCGCAAGAAC	TCTGCCGGAAGTTCAGTTTG
PYCARD	*Human*	GGATGCTCTGTACGGGAAGG	GTCCTTGCAGGTCCAGTTCC
TNFSF10	*Human*	CCAACGAGCTGAAGCAGATG	CGGAGTTGCCACTTGACTTG
TP53BP2	*Human*	AAGAATTCCTCGGCCACTCA	TGGATGGGTATGATGGGACA
TRADD	*Human*	CGCTCTGTGGGTCTCAAATG	AGCTCGTTCTCCTCGAGTGC
TRAF3	*Human*	ACCGCCAGCTACAATGGAGT	GCTGGCTGTAAAGGGACAGG

Table S6. Relative area of isotope populations of various metabolites. Related to Figure S5.

Compound name	^{13}C no.	Relative Area					
		NS Rep-1	NS Rep-2	PON2#1 Rep-1	PON2#1 Rep-2	PON2#2 Rep-1	PON2#2 Rep-2
Glucose 6-phosphate	0	6.E-04	5.E-04	3.E-04	N.D.	N.D.	N.D.
	1	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	2	5.E-03	5.E-03	4.E-03	3.E-03	4.E-03	4.E-03
	3	4.E-04	5.E-04	3.E-04	3.E-04	4.E-04	4.E-04
	4	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	5	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	6	4.E-04	4.E-04	2.E-04	3.E-04	3.E-04	3.E-04
Fructose 1,6-diphosphate	0	1.E-03	1.E-03	6.E-04	7.E-04	N.D.	N.D.
	1	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	2	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	3	5.E-04	4.E-04	3.E-04	3.E-04	N.D.	2.E-04
	4	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	5	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	6	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
Dihydroxyacetone phosphate	0	2.E-03	3.E-03	2.E-03	2.E-03	1.E-03	2.E-03
	1	3.E-04	3.E-04	N.D.	1.E-04	N.D.	N.D.
	2	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	3	9.E-04	9.E-04	5.E-04	4.E-04	4.E-04	4.E-04
Lactic acid	0	1.E-01	1.E-01	7.E-02	7.E-02	7.E-02	7.E-02
	1	9.E-03	1.E-02	6.E-03	6.E-03	7.E-03	7.E-03
	2	8.E-03	8.E-03	5.E-03	5.E-03	4.E-03	5.E-03
	3	5.E-02	5.E-02	2.E-02	2.E-02	2.E-02	2.E-02
Succinic acid	0	1.E-02	1.E-02	1.E-02	1.E-02	9.E-03	7.E-03
	1	1.E-03	1.E-03	9.E-04	9.E-04	8.E-04	N.D.
	2	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	3	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	4	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
Fumaric acid	0	5.E-03	5.E-03	5.E-03	4.E-03	4.E-03	5.E-03
	1	7.E-04	6.E-04	4.E-04	N.D.	N.D.	N.D.
	2	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	3	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
	4	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00
Malic acid	0	8.E-02	8.E-02	7.E-02	6.E-02	6.E-02	5.E-02
	1	8.E-03	8.E-03	5.E-03	5.E-03	4.E-03	4.E-03
	2	2.E-02	2.E-02	1.E-02	1.E-02	9.E-03	8.E-03
	3	4.E-03	4.E-03	2.E-03	2.E-03	2.E-03	1.E-03
	4	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00	0.E+00

Table S7. Primers were used for qRT-PCR analysis, ChIP experiments, and cloning. The antibodies were used as indicated. The source and concentrations of chemical inhibitors and biologics used for drug treatment experiments are summarized. Related to STAR methods

PRIMERS			
Gene symbol	**Species**	**Forward primer (5'-3')**	**Reverse primer (5'-3')**
ACACA	Human	GCTGGGACAGAGAACCATCC	AGCCAGTGCAGGACAGTGAA
CACNB3	Human	CCCCATCATCGTCTTTGTCA	CCTCCAGCTGGTTCTCATCC
ENO2	Human	AGCTGAGAGCTTTCGGGATG	CCTTGTCGATGGCTTCCTTC
HK2	Human	AGCTGCTGGAGGTCAAGAGG	CAAGGTCCAAGGCCAAGAAG
HS2ST1	Human	GTCCCGCTCGAAGCTAGAAA	CTTGCCGTTTTGGGAACTCT
LDHA	Human	TGGCCTGTGCCATCAGTATC	TTCCAAGCCACGTAGGTCAA
MICAL2	Human	TCACCTTGCCTCCATGTTTG	TCCTTTCTGGCAGGAGAAGC
OAS2	Human	CCGATGGTACCCTTGTCCTC	TGGATGGTGAACCCATCAAG
PGM2L1	Human	GTGTGGAACCCTGGAATGGT	ATGTCCGACCCCATGAAAAG
PON2	Human	AATCCACATGGCATCAGCAC	CGGTCCAACAGCTGTGATGT
PPAPDC1A	Human	TATCCGGCGAACAGACAAGA	GCAATGCATTTCCGAGTTCA
SDR16C5	Human	CTGGAAGTGGACTCGGAAGG	CCTTCCTTTTGGCTGCAATC
SLC2A1	Human	GATGATGCGGGAGAAGAAGG	GCCTTCTCGAAGATGCTCGT
STOM	Human	CCTGGCTGTGGCAAATATCA	CCTTTATTCCCCAGGCATCA
SDR16C5	Mouse	AAGAACGTTGCCGGTGAGAT	ACTCTGGCAGCTCCTGCTTC
ENO2	Mouse	GGAACTCCGACCTCATCCTG	TGGCATCCTTGCCATACTTG
HK2	Mouse	CGAGGGTGAAGATGTGGTCA	TTCCAGTGCCAACAATGAGG
LDHA	Mouse	GTGCCTGTGTGGAGTGGTGT	ATGGCCCAGGATGTGTAACC
SLC2A1	Mouse	GATGATGCGGGAGAAGAAGG	GCCTTCTCGAAGATGCTCGT
ACACA	Mouse	GGGGTCATGCCTCTGAGAAC	CCACTCCAGGGAAGAGTTGG
CACNB3	Mouse	CGCTCTGTGCTCAACAATCC	AGACGATGATGGGAGCCAGT
PGM2L1	Mouse	TGCTGGAACTGTCCCTGAGA	ATCCACCACCCAAACAAAGC
Cloning			
PON2	pBabe Hygro	CGCGGATCCCCATGGGGCGGCTGG TGGCTGTGGGC	GCGTCGACGAGTTCACAATACAA GGCTCTGTG
PON2	pEGFP-C1	ACCCAAGCTTCGACCATGGGGCGG CTGGTGGCTGTGGGC	CGCGGATCCGAGTTCACAATACA AGGCTCTGTG
PON2 promoter	pGL4.14	AGCCTCGAGACAGGCTCACCACTG CCAGAA	AGTCAGATCTGGCGCGGGAGCCG GGCGC
PUMA promoter	pGL4.14	AGCCTCGAGGGCAGATCACGAGGT CAGGA	AGTCAGATCTACCCAGGCGAGAC ACCTGCA
CHIP			
PON2 promoter p53 binding		TTAATAGAGGCTGGGCATGG	GCTCACTGCAGTCTGGACCT
PUMA		AGGAGGTGACAGGAGTGCAG	CGCACCCCATTGTTTGTAA
Actin		GAGGGGAGAGGGGGTAAAAA	AAAGGCGAGGCTCTGTGCT

Site directed mutation			
PON2 promoter		TTAATAGAGGCTGGGTATAGTGGC TCATTCCTGTA	TACAGGAATGAGCCACTATACCC AGCCTCTATTAA
PUMA promoter		GGCGGGTTTGTTTACAGGGAATGG GGTGCGGGCTCG	CGAGCCCGCACCCCATTCCCTGTA AACAAACCCGCC
CTC primers			
Human Alu		ACGCCTGTAATCCCAGCACTT	TCGCCCAGGCTGGAGTGC
Actin mouse		GCTTCTTTGCAGCTCCTTCGTTG	TTTGCACATGCCGGAGCCGTTGT
RNAi (shRNAs)	**Gene symbol**	**Clone ID**	**Vector**
#1	ACACA	TRCN0000029024	pLKO.1
#2	ACACA	TRCN0000004767	pLKO.1
#1	CACNB3	TRCN0000044066	pLKO.1
#2	CACNB3	TRCN0000044065	pLKO.1
#1	ENO2	TRCN0000156035	pLKO.1
#2	ENO2	TRCN0000158245	pLKO.1
#1	HK2	TRCN0000037672	pLKO.1
#2	HK2	TRCN0000037673	pLKO.1
#1	LDHA	TRCN0000026541	pLKO.1
#2	LDHA	TRCN0000026554	pLKO.1
#1	PGM2L1	TRCN0000049088	pLKO.1
#2	PGM2L1	TRCN0000049091	pLKO.1
#1	PON2	TRCN0000051644	pLKO.1
#2	PON2	TRCN0000051647	pLKO.1
#1	PON2	V2LHS_92265	pGIPZ
#2	PON2	V2LHS_232087	pGIPZ
#1	SDR16C5	TRCN0000028583	pLKO.1
#2	SDR16C5	TRCN0000028656	pLKO.1
#1	SLC2A1	TRCN0000043583	pLKO.1
#2	SLC2A1	TRCN0000043587	pLKO.1
#1	PUMA	V3LHS_342436	pGIPZ
#2	PUMA	V3LHS_342433	pGIPZ
#1	FOXO1	TRCN0000039578	pLKO.1
#2	FOXO1	TRCN0000020707	pLKO.1
#1	FOXO3	TRCN0000010334	pLKO.1
#2	FOXO3	TRCN0000010335	pLKO.1
#1	FOXO4	TRCN0000039718	pLKO.1
#2	FOXO4	TRCN0000039721	pLKO.1

#1	STOM	TRCN0000029160	pLKO.1
#2	STOM	TRCN0000029161	pLKO.1

		Protein symbol	**Antibody source**	**Dilution**
	Immunoblot			
	/CHIP	P53	Santa Cruz Biotechnology #sc-126	1:500
	/IHC	PON2	Santa Cruz Biotechnology #sc-374158	1:1000, 1:500 (IHC)
	/CHIP	FOXO3A	Cell Signaling #2497	1:100
		ß-actin	Cell signaling #4970	1:5000
		Phospho-FOXO3A	Cell Signaling #8174	1:500
		Phospho-AMPK	Cell Signaling #2535	1:1000
		AMPK	Cell Signaling #2532	1:1000
		PARP	Cell Signaling #9542	1:1000
		PUMA	Cell Signaling #4976	1:1000
		GLUT1	Cell Signaling #12939	1:500
		GLUT1	Santa Cruz Biotechnology Sc-7903, sc-377228	1:500
		GLUT3	Santa Cruz Biotechnology Sc-74497	1:500
		STOM	Bethyl Laboratories A304-425A	1:1000

		Inhibitor	**Source**
	Chemical inhibition		
		AMPK inhibitor, Compound C	Calbiochem # 171261
		Metformin	Sigma #D150959
		AICAR	Cayman Chemicals #CAS 2627-69-2
		Trametinib	Selleckchem #S2673
		Z-VAD-FMK	Calbiochem #CAS 187389-52-2