## Supplementary

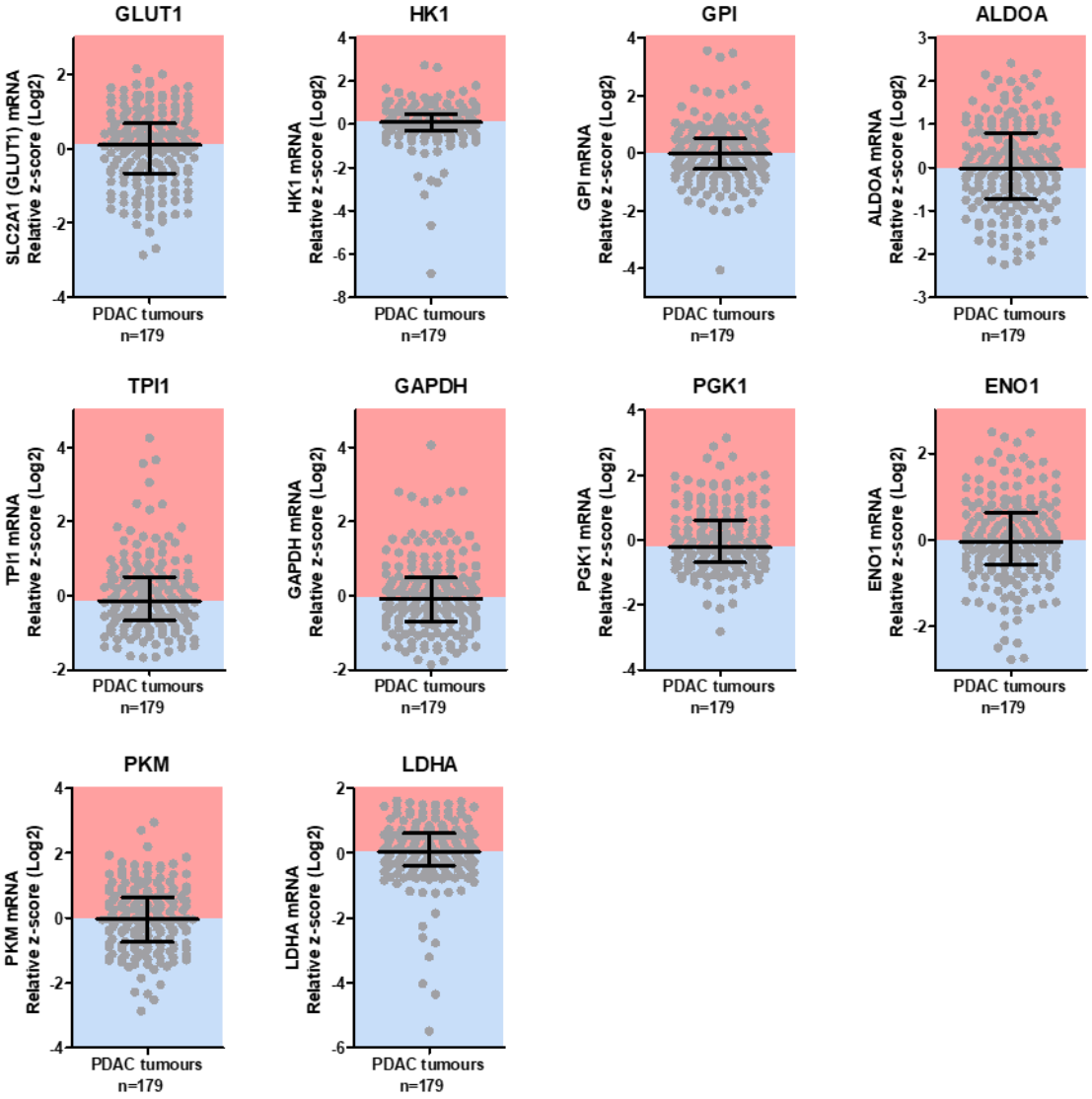


**Figure S1.** Gene expression of glycolysis enzymes (GLUT1, HK1, G6PD, ALDOA, TPI1, GAPDH, PGK1, ENO1, PKM and LDHA) split into high (red shading) and low (blue shading) based on median, for n=179 PDAC tumors (TCGA data).

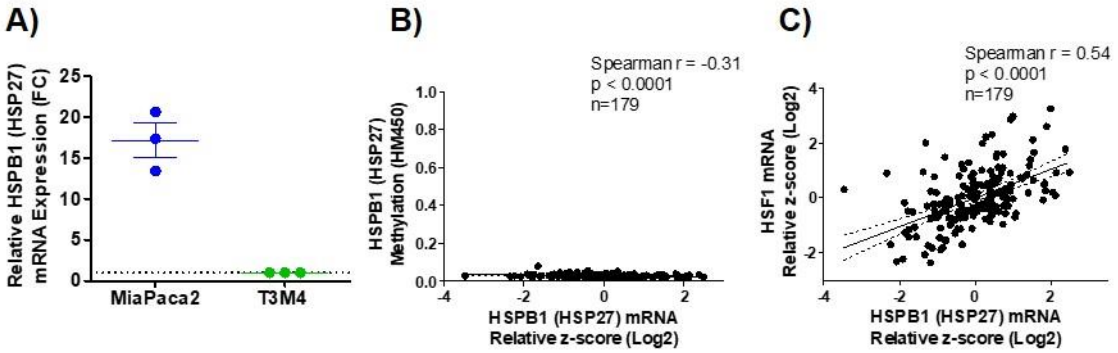


**Figure S2. (A)** mRNA levels of HSP27 (*HSPB1*) assessed by RT-qPCR in parental T3M4 and MiaPaca2 cells. mRNA levels are shown as relative to parental T3M4 cells and data were analyzed using paired t-test and shown as mean values ± SEM of three independent experiments; *p < 0.05. Correlation between HSP27 (*HSPB1*) mRNA levels and **(B)** HSP27 (*HSPB1*) gene methylation (HM450) and **(C)** *HSF1* mRNA levels across n=179 PDAC tumors (TCGA data). Data were analyzed by linear regression; statistical significance indicated.

**Table S1.** List of antibodies.

| Antibody | Concentration | Company | Identifier |
|---|---|---|---|
| ArgP | 1 in 10,000 | Oya et al. 1999 | Cat# mAb6B |
| β-actin | 1 in 5,000 | Sigma-Aldrich | Cat# A5441 |
| GLO1 | 1 in 1,000 | BioMAC | Cat# 02-14 |
| GLUT1 | 1 in 1,000 | Cell Signaling | Cat# 12939 |
| HSF1 | 1 in 1,000 | Cell Signaling | Cat# 12972 |
| HSP27 | 1 in 3,000 | Enzo Life Sciences | Cat# ADI-SPA-803-D |
| HSP90 | 1 in 1,000 | Cell Signaling | Cat# 4877 |
| LDHA | 1 in 1,000 | Cell Signaling | Cat# 3582 |
| MGHs | 1 in 1,000 | Cell Biolabs | Cat# STA-011 |

**Table S2.** Oncogenic mutations investigated in parental and gemcitabine resistant cells.

| Gene | Variant | Classification | Exon | Consequence | External IDs | Cell lines | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | T3M4 | | MiaPaca2 | |
| | | | | | | P | GR | P | GR |
| *ALK* | c.4587C>G (p.Asp1529Glu) | Benign | 29 of 29 | Missense Variant | rs1881421 | + | + | + | + |
| *ALK* | c.4472A>G (p.Lys1491Arg) | Benign | 29 of 29 | Missense Variant | rs1881420 | + | + | + | + |
| *ALK* | c.4381A>G (p.Ile1461Val) | Benign | 29 of 29 | Missense Variant | rs1670283 | + | + | + | + |
| *ALK* | c.3375C>A | Benign | 21 of 29 | Synonymous Variant | rs3795850 | + | + | + | + |
| *PDGFRA* | c.1701A>G | Benign | 12 of 23 | Synonymous Variant | rs1873778 | + | + | + | + |
| *PDGFRA* | c.2472C>T | Benign | 18 of 23 | Synonymous Variant | rs2228230 | + | + | - | - |
| *MET* | c.3912C>T | Benign | 20 of 21 | Synonymous Variant | rs41736 | + | + | - | - |
| *MET* | c.534C>T | Benign | 2 of 21 | Synonymous Variant | rs35775721 | - | - | + | + |
| *HRAS* | c.81T>C | Benign | 2 of 6 | Synonymous Variant | rs12628 | + | + | + | + |
| *DDR2* | c.1260C>G | Probably Benign | 12 of 19 | Synonymous Variant | rs2298258 | + | + | - | - |
| *FGFR3* | c.1959G>A | Probably Benign | 14 of 18 | Synonymous Variant | rs7688609 | + | + | + | + |
| *KIT* | c.1621A>C (p.Met541Leu) | Probably Benign | 10 of 21 | Missense Variant | rs3822214 | + | + | - | - |
| *KIT* | c.2586G>C | Probably Benign | 18 of 21 | Synonymous Variant | rs3733542 | + | + | - | - |
| *HIST1H3B* | c.*10C>T | Probably Benign | 1 of 1 | 3' UTR Variant | rs2213284 | + | + | - | - |
| *EGFR* | c.2361G>A | Probably Benign | 20 of 28 | Synonymous Variant | rs1050171 | - | - | + | + |
| *KRAS* | c.183A>C (p.Gln61His) | Pathogenic | 3 of 6 | Missense Variant | rs17851045 | + | + | - | - |
| *KRAS* | c.34G>T (p.Gly12Cys) | Pathogenic | 2 of 6 | Missense Variant | rs121913530 | - | - | + | + |

+ Mutation is present; - Mutation is not present; P= parental; GR= gemcitabine resistant. Additional oncogenes investigated, no mutations evidenced: AKT1, BRAF, CDKN2A, CTNNB1, ERBB2, ERBB4, FGFR2, H3F3A, IDH1, IDH2, MAP2K1, NRAS, PIK3CA, PIK3R1, PTEN, STK11.