Disrupting glutamine metabolic pathways to sensitize gemcitabine-resistant pancreatic cancer

Ru Chen^{1*}, Lisa A Lai¹, Yumi Sullivan¹, Melissa Wong¹, Lei Wang¹, Jonah Riddell², Linda Jung², Venu G. Pillarisetty³, Teresa A. Brentnall¹, Sheng Pan¹ *

¹Department of Medicine, University of Washington, Seattle, WA 98195, USA ²Cell Signaling Technology, Inc., Danvers, MA 01923 ³Department of Surgery, University of Washington, Seattle, WA 98195, USA Supplemental Figure 1. Comparison of GEM viability: GEM-R MiaPaCa, GEM-R Panc, MiaPaCa, Panc, HPDE and CAF.



Supplemental Figure 2. Cell proliferation plots normalized to untreated cells.



a. GEM-R MiaPaCa proliferation





Supplemental Figure 3. Multiplex bead based analysis -Graphs illustrate fluorescence intensity as a function of bead size. Squares reflect gating for individual beads. Bead 1: phospho-pRAS40; bead 2: phospho-Akt; bead 3: phospho-S6; bead 4: phospho-p44/p42 MAPK.





Supplemental Table 1. Identification of top twenty five exosome markers

Name	Spectral count			
Name	GEM-R	GEM-R DON		
HSPA8	45	45		
CD9	3	4		
GAPDH	115	100		
АСТВ	98	89		
CD63	0	0		
CD81	2	2		
ANXA2	34	31		
ENO1	33	34		
HSP90AA1	67	55		
EEF1A1	63	50		
PKM2				
YWHAE	15	9		
SDCBP	6	3		
PDCD6IP	11	14		
ALB	51	38		
YWHAZ	9	7		
EEF2	99	97		
ACTG1				
LDHA	15	16		
HSP90AB1	24	23		
ALDOA	24	20		
MSN	19	7		
ANXA5	9	12		
PGK1	34	34		
CFL1	11	5		

Supplemental Table 2. EGF-like domain proteins significantly enriched in the exosomes secreted from GEM-R MiaPaCa cells treated with DON

			Fold			
Term	PValue	Genes	Enrichment	Bonferroni	Benjamini	FDR
IPR000742:Epider		VASN, MATN2, TMEFF2, PEAR1, ATRAID, CD248, ATRN, F7, SCARF1, SLIT2,				
mal growth factor-	3.05E-11	SCARF2, SLIT3, MUC4, HMCN2, LAMA1, NOTCH1, EYS, FAT3, STAB1, FAT4,	4.65	3.22E-08	3.22E-08	4.85E-08
like domain		FBLN2, TENM2, FAT1, TENM3, HEG1, LRP8, LAMC2, MEGF6, LRP5				