

Supplementary Table 1 – mRNA levels (Relative Quantity or RQ as percentage) of targeted proteins for individual and combinatorial silencing in MDA-MB-231 cells (data presented in Figure 3A)

Delivered siRNA	Level of mRNA or Relative Quantity (%)			
	gp130	JAK2	STAT3	Importin α 3
Scrambled	95.7 \pm 6.8	92.4 \pm 5.9	92.6 \pm 2.2	91.3 \pm 4.4
gp130	10.1 \pm 1.3			
JAK2		47.4 \pm 11.6		
STAT3			19.3 \pm 7.8	
Importin α 3				26.1 \pm 13.7
JAK2/gp130	11.1 \pm 3.2	52.5 \pm 5.9		
JAK2/STAT3		50.0 \pm 3.5	30.4 \pm 10.5	
JAK2/Importin α 3		48.5 \pm 6.8		31.8 \pm 5.2

Supplementary Table 2 – mRNA levels (Relative Quantity or RQ as percentage) of targeted proteins for individual and combinatorial silencing in MDA-MB-468 cells (data presented in Figure 3B)

Delivered siRNA	Level of mRNA or Relative Quantity (%)			
	gp130	JAK2	STAT3	Importin α 3
Scrambled	97.2 \pm 1.0	93.2 \pm 5.1	92.0 \pm 1.3	92.3 \pm 6.8
gp130	16.5 \pm 3.7			
JAK2		18.8 \pm 0.3		
STAT3			53.3 \pm 12.8	
Importin α 3				31.3 \pm 3.5
JAK2/gp130	8.3 \pm 6.6	8.8 \pm 0.2		
JAK2/STAT3		32.4 \pm 1.7	23.8 \pm 1.2	
JAK2/Importin α 3		23.5 \pm 13.7		20.6 \pm 2.7

Supplementary Table 3 – mRNA levels (Relative Quantity or RQ as percentage) of antiapoptotic proteins for individual and combinatorial silencing in MDA-MB-231 cells (data presented in **Figure 4A**)

Delivered siRNA	Level of mRNA or Relative Quantity (%)		
	Bcl-2	Bcl-XL	Mcl-1
Scrambled	102.0 ± 4.2	89.4 ± 6.1	101.8 ± 3.4
gp130	63.4 ± 3.7	77.0 ± 0.4	76.3 ± 6.7
JAK2	79.4 ± 9.5	103.6 ± 11.0	96.1 ± 6.8
STAT3	93.5 ± 10.0	106.6 ± 0.7	58.3 ± 4.9
Importin α3	99.8 ± 7.2	74.0 ± 8.8	70.7 ± 1.3
JAK2/gp130	44.3 ± 4.2	32.8 ± 3.2	44.0 ± 1.1
JAK2/STAT3	111.6 ± 7.0	87.0 ± 9.9	119.3 ± 9.8
JAK2/Importin α3	101.5 ± 10.9	86.1 ± 8.4	90.2 ± 8.3

Supplementary Table 4 – mRNA levels (Relative Quantity or RQ as percentage) of antiapoptotic proteins for individual and combinatorial silencing in MDA-MB-468 cells (data presented in **Figure 4B**)

Delivered siRNA	Level of mRNA or Relative Quantity (%)		
	Bcl-2	Bcl-XL	Mcl-1
Scrambled	101.7 ± 0.1	90.2 ± 1.1	102.1 ± 1.2
gp130	40.3 ± 7.8	61.2 ± 10.6	102.6 ± 1.8
JAK2	77.3 ± 7.0	29.4 ± 5.5	77.0 ± 6.3
STAT3	58.3 ± 9.7	57.4 ± 10.4	60.2 ± 9.5
Importin α3	19.3 ± 3.6	31.2 ± 5.3	40.8 ± 8.0
JAK2/gp130	10.3 ± 3.2	12.6 ± 3.7	12.5 ± 0.8
JAK2/STAT3	34.3 ± 10.7	30.0 ± 0.2	46.4 ± 2.2
JAK2/Importin α3	28.7 ± 7.6	26.8 ± 4.7	38.2 ± 7.4

Supplementary Table 5 – Protein expression (normalized compared to the “no treatment” group) of Bcl-2 and Mcl-1 for individual and combinatorial silencing of JAK2 and gp130 in MDA-MB-231 (based on Western Blot results presented in **Figure 4D**)

Delivered siRNA	Protein Expression (%)	
	Bcl-2	Mcl-1
gp130	59.3 ± 6.6	80.1 ± 5.5
JAK2	95.0 ± 4.2	120.6 ± 17.9
JAK2/gp130	21.8 ± 3.3	40.7 ± 4.9

Supplementary Table 6 – mRNA levels (Relative Quantity or RQ as percentage) of pro-apoptotic proteins for individual and combinatorial silencing in MDA-MB-231 cells (data presented in **Figure 5A**)

Delivered siRNA	Level of mRNA or Relative Quantity (%)	
	PTEN	P53
Scrambled	130.6 ± 7.5	92.3 ± 5.4
gp130	159.1 ± 7.0	195.2 ± 10.3
JAK2	95.9 ± 0.2	107.8 ± 0.5
STAT3	115.1 ± 25.0	180.6 ± 4.0
Importin α3	162.7 ± 4.0	176.2 ± 32.2
JAK2/gp130	220.2 ± 5.9	319.0 ± 3.9
JAK2/STAT3	160.4 ± 1.9	173.0 ± 2.3
JAK2/Importin α3	113.9 ± 2.4	190.6 ± 22.4

Supplementary Table 7 – mRNA levels (Relative Quantity or RQ as percentage) of pro-apoptotic proteins for individual and combinatorial silencing in MDA-MB-468 cells (data presented in Figure 5B)

Delivered siRNA	Level of mRNA or Relative Quantity (%)	
	PTEN	P53
Scrambled	110.8 ± 0.8	106.5 ± 3.1
gp130	126.6 ± 2.4	85.5 ± 2.2
JAK2	108.4 ± 1.1	101.2 ± 19.4
STAT3	134.2 ± 22.0	372.7 ± 16.0
Importin α 3	80.4 ± 5.3	99.4 ± 1.7
JAK2/gp130	636.3 ± 43.7	477.4 ± 3.0
JAK2/STAT3	127.2 ± 7.6	279.4 ± 46.6
JAK2/Importin α 3	119.7 ± 53.4	118.5 ± 6.0

Supplementary Table 8 – Protein expression (normalized compared to the “no treatment” group) of PTEN and P53 for individual and combinatorial silencing of JAK2 and gp130 in MDA-MB-231 (based on Western Blot results presented in Figure 5D)

Delivered siRNA	Protein Expression (%)	
	PTEN	P53
gp130	310.4 ± 33.1	522.4 ± 36.0
JAK2	190.2 ± 18.9	409.3 ± 26.5
JAK2/gp130	570.6 ± 31.1	812.5 ± 39.8

Supplementary Table 9 – mRNA levels (Relative Quantity or RQ as percentage) of cell cycle regulator proteins for individual and combinatorial silencing in MDA-MB-231 cells (data presented in Figure 6A)

Delivered siRNA	Level of mRNA or Relative Quantity (%)	
	Cyclin D1	CDK4
Scrambled	90.5 ± 18.7	119.4 ± 3.4
gp130	61.6 ± 2.1	104.4 ± 0.2
JAK2	76.3 ± 12.3	99.3 ± 6.3
STAT3	86.0 ± 4.9	120.8 ± 5.4
Importin α3	79.4 ± 5.4	65.6 ± 5.0
JAK2/gp130	45.6 ± 3.0	60.8 ± 9.0
JAK2/STAT3	60.3 ± 1.1	92.5 ± 7.3
JAK2/Importin α3	85.8 ± 6.5	55.7 ± 6.6

Supplementary Table 10 – mRNA levels (Relative Quantity or RQ as percentage) of cell cycle regulator proteins for individual and combinatorial silencing in MDA-MB-468 cells (data presented in Figure 6B)

Delivered siRNA	Level of mRNA or Relative Quantity (%)	
	Cyclin D1	CDK4
Scrambled	104.6 ± 0.9	85.6 ± 0.6
gp130	77.6 ± 5.2	26.4 ± 7.8
JAK2	64.8 ± 8.4	42.4 ± 7.3
STAT3	58.9 ± 5.1	53.6 ± 8.9
Importin α3	28.0 ± 6.6	36.7 ± 5.6
JAK2/gp130	6.7 ± 0.4	30.8 ± 5.1
JAK2/STAT3	22.1 ± 2.9	51.6 ± 7.3
JAK2/Importin α3	18.6 ± 4.0	32.8 ± 7.2