SUPPLEMENTARY FIGURE LEGENDS

Figure S1: **I-BET151 inhibits growth of PDAC cells in three-dimensional collagen. A, B.** AsPC1, CD18 and Panc1 cells were grown in three-dimensional collagen gels and fresh serum-containing medium supplemented with DMSO or I-BET151 was added every other day for 7 days. The effect on colony size was examined by phase contrast microscopy (*A*), and size of the individual colonies measured (*B*). The results are representative of three independent experiments. *, $p < 0.05$.

Figure S2: **I-BET151 decreases growth of CD18-Snail cells in three-dimensional collagen.** CD18-Vector and CD18-Snail cells were grown in three-dimensional collagen gels and fresh serum-containing medium supplemented with DMSO or I-BET151 was added every other day for 7 days. The effect of I-BET151 on colony size in three-dimensional collagen was examined by phase contrast microscopy and size of the individual colonies measured. The results are representative of at least three independent experiments. *, $p < 0.05$.

Figure S3: **JQ1 and I-BET151 decrease growth of AsPC1-Snail cells. A.** Lysates from AsPC1-Vector and AsPC1-Snail cells were analyzed for Snail by Western blotting, and the effect on E-cadherin and vimentin were analyzed by Western blotting. **B,C.** AsPC1-Vector and AsPC1-Snail cells were grown in three-dimensional collagen gels and fresh serum-containing medium supplemented with DMSO, JQ1 or I-BET151 was added every other day for 7 days. The effect of JQ1 (*B*) and I-BET151 (*C*) on colony size in three-dimensional collagen was examined by phase contrast microscopy and size of the individual colonies measured. The results are representative of three independent experiments. *, $p < 0.05$.

Figure S4: **I-BET151 decreases growth of chemoresistant CD18 cells in three-dimensional collagen.** CD18-CR cells were grown in three-dimensional collagen gels and fresh serum-containing medium supplemented with DMSO or I-BET151 was added every other day for 7 days. The effect of JQ1 on colony size in three-dimensional collagen was examined by phase contrast microscopy, and size of the

individual colonies measured. The results are representative of at least three independent experiments. *, $p < 0.05$.

Figure S5: **A**. **I-BET151 decreases expression of *c-MYC* in AsPC1 and CD18 cells, but not in Panc1 cells.** PDAC cells were grown in three-dimensional type I collagen gels in the presence of DMSO (vehicle control), or I-BET151 (1 μM) for 48 hours and *c-MYC* mRNA expression analyzed by qRT-PCR using GAPDH as normalization control. **B. Effect of JQ1 treatment for 8 hours and 24 hours on *c-MYC* mRNA expression in PDAC cells.** PDAC cells were grown in three-dimensional type I collagen gels in the presence of DMSO (vehicle control), or JQ1 (0.5 μM) for 8 hours or 24 hours and *c-MYC* mRNA expression analyzed by qRT-PCR using GAPDH as normalization control. *, $p < 0.05$. **C, D**. **JQ1 represses *c-MYC* in Snail-expressing PDAC cells and chemo-resistant PDAC cells**. PDAC-vector, PDAC-Snail and CD18-CR cells were grown in three-dimensional type I collagen gels in the presence of DMSO (vehicle control), or JQ1 (0.5 μM) for 48 hours and *c-MYC* mRNA expression analyzed by qRT-PCR using GAPDH as normalization control. The results are representative of at least two independent experiments. *, $p < 0.05$.

Figure S6: **A**. **I-BET151 decreases expression of *FOSL1* in PDAC cells.** PDAC cells were grown in three-dimensional type I collagen gels in the presence of DMSO (vehicle control), or I-BET151 (1 μM) for 48 hours and *FOSL1* mRNA expression analyzed by qRT-PCR using GAPDH as normalization control. **B. siRNA BRD4 decreases *FOSL1* mRNA in PDAC cells.** Effect of siBRD4 on *FOSL1* mRNA expression analyzed by qRT-PCR using GAPDH as normalization control. **C. Effect of JQ1 treatment for 8 hours and 24 hours on *FOSL1* mRNA expression in PDAC cells.** PDAC cells were grown in three-dimensional type I collagen gels in the presence of DMSO (vehicle control), or JQ1 (0.5 μM) for 8 hours or 24 hours and *FOSL1* mRNA expression analyzed by qRT-PCR using GAPDH as normalization control. *, $p < 0.05$.

Figure S7: **Effect of JQ1 on BRD4 and RNA polymerase II occupancy on the c-MYC l and FOSL1 loci in Panc1 cells. A, B.** Panc1 cells were treated with JQ1 (0.5 μM) for 24 hours and chromatin immunoprecipitation was performed across MYC and FOSL1 loci with control IgG antibody, anti-BRD4 antibody or anti-RNA polymerase II antibody. Purified DNA was then analyzed by PCR using primers specific for c-MYC or FOSL1 locus, and the PCR products visualized on 2% agarose gels. The results are representative of two independent experiments.

Fig. S1

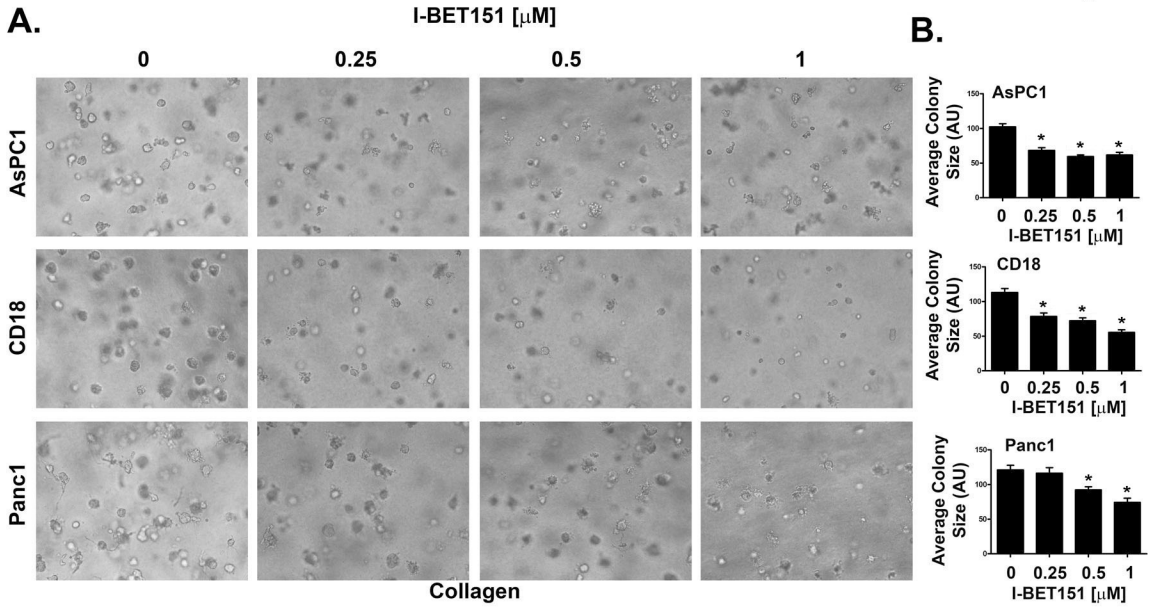

A.
I-BET151 [μM]
0
0.25
0.5
1
AsPC1
CD18
Panc1
Collagen
B.
AsPC1
CD18
Panc1
Average Colony Size (AU)
I-BET151 [μM]
0 0.25 0.5 1
*

Fig. S2

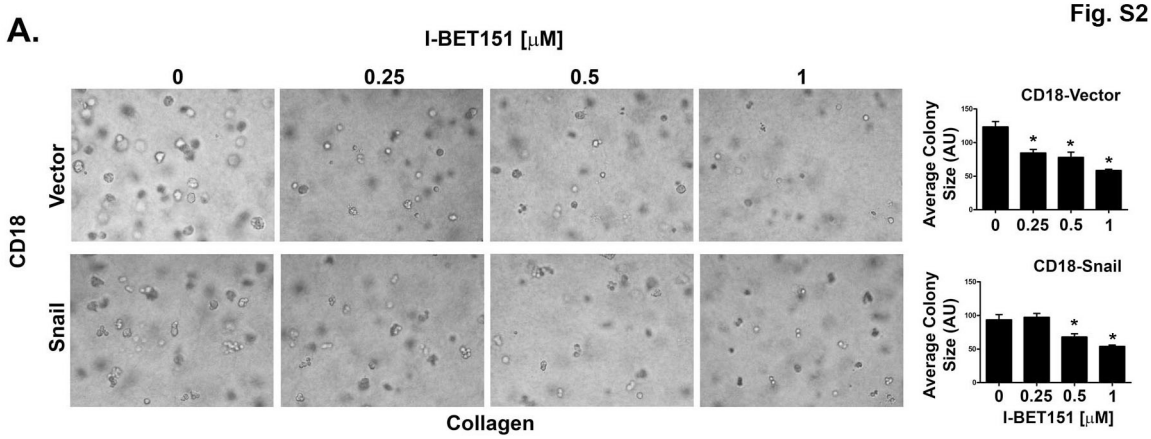

A.
I-BET151 [μM]
0
0.25
0.5
1
CD18
Vector
Snail
Collagen
CD18-Vector
CD18-Snail
Average Colony Size (AU)
150
100
50
0
0 0.25 0.5 1
I-BET151 [μM]
*

Fig. S3

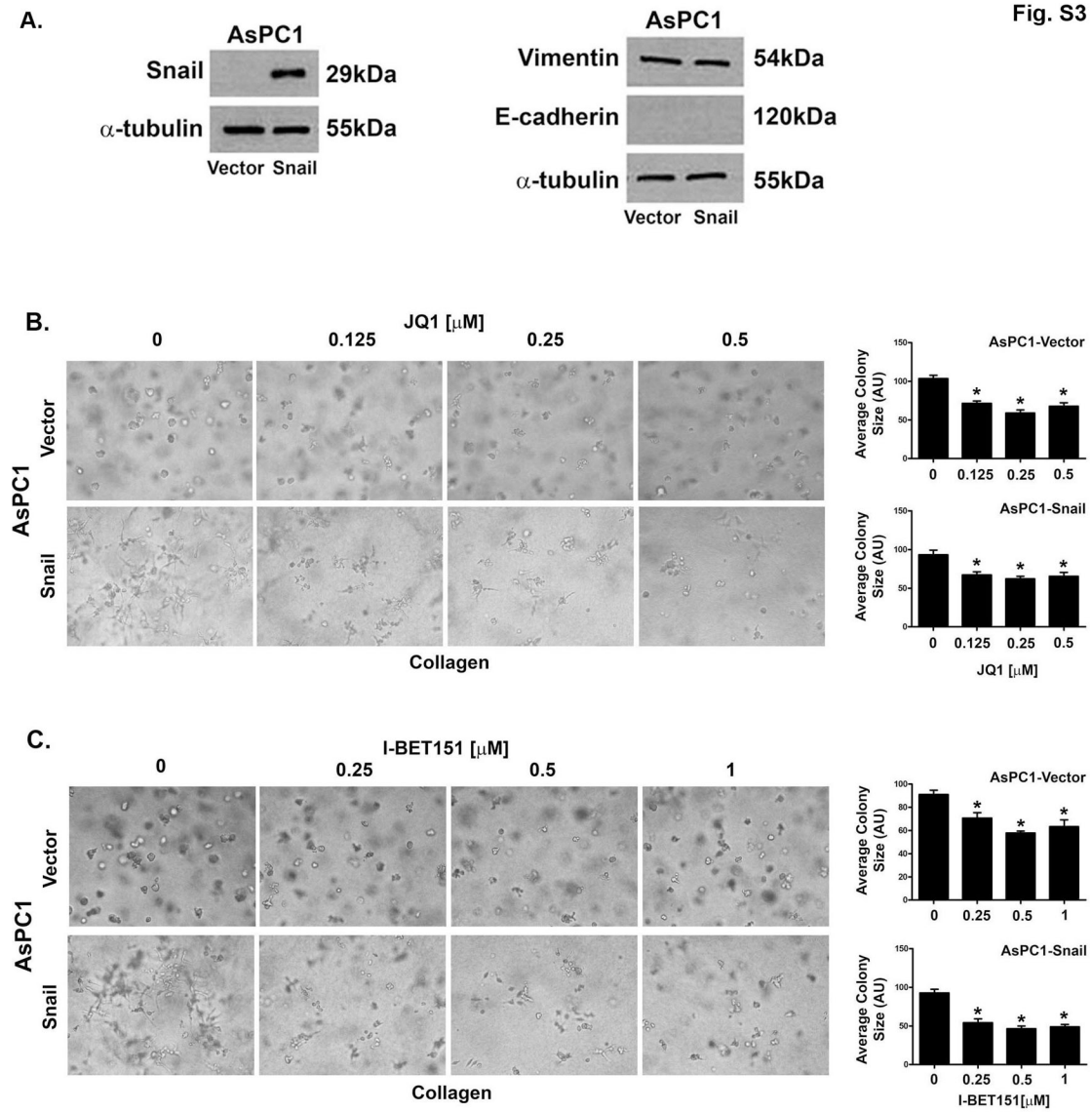

A.
AsPC1
Snail
29kDa
α-tubulin
55kDa
Vector Snail
AsPC1
Vimentin
54kDa
E-cadherin
120kDa
α-tubulin
55kDa
Vector Snail
B.
JQ1 [μM]
0
0.125
0.25
0.5
AsPC1
Vector
Snail
Collagen
AsPC1-Vector
AsPC1-Snail
Average Colony Size (AU)
JQ1 [μM]
C.
I-BET151 [μM]
0
0.25
0.5
1
AsPC1
Vector
Snail
Collagen
AsPC1-Vector
AsPC1-Snail
Average Colony Size (AU)
I-BET151[μM]

Fig. S4

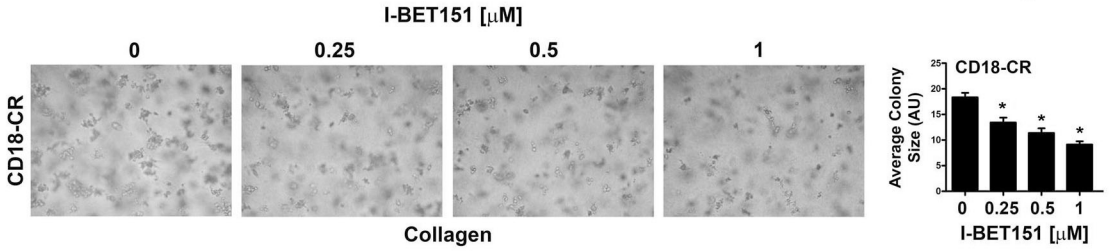

I-BET151 [μM]
0
0.25
0.5
1
CD18-CR
Collagen
CD18-CR
Average Colony Size (AU)
25
20
15
10
5
0
*
*
*
0 0.25 0.5 1
I-BET151 [μM]

Fig. S5

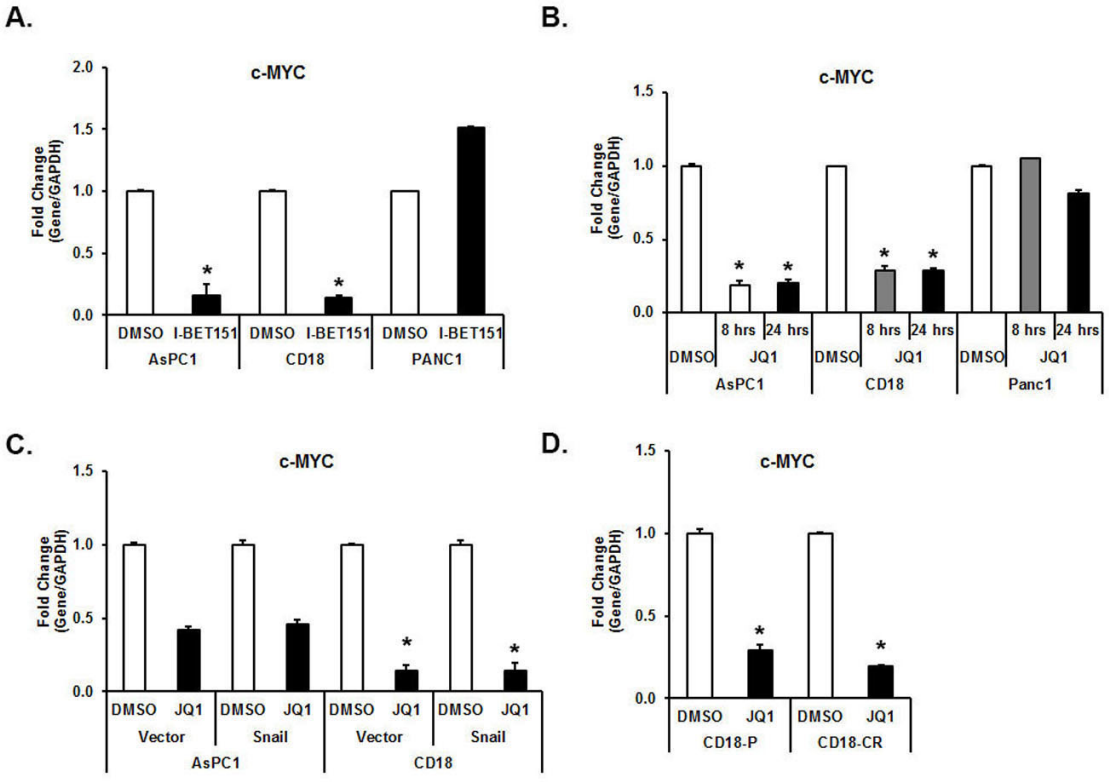

A.
c-MYC
Fold Change (Gene/GAPDH)
2.0
1.5
1.0
0.5
0.0
DMSO I-BET151 DMSO I-BET151 DMSO I-BET151
AsPC1 CD18 PANC1
B.
c-MYC
Fold Change (Gene/GAPDH)
1.5
1.0
0.5
0.0
DMSO 8 hrs 24 hrs DMSO 8 hrs 24 hrs DMSO 8 hrs 24 hrs
JQ1 JQ1 JQ1
AsPC1 CD18 Panc1
C.
c-MYC
Fold Change (Gene/GAPDH)
1.5
1.0
0.5
0.0
DMSO JQ1 DMSO JQ1 DMSO JQ1 DMSO JQ1
Vector Snail Vector Snail
AsPC1 CD18
D.
c-MYC
Fold Change (Gene/GAPDH)
1.5
1.0
0.5
0.0
DMSO JQ1 DMSO JQ1
CD18-P CD18-CR

Fig. S6

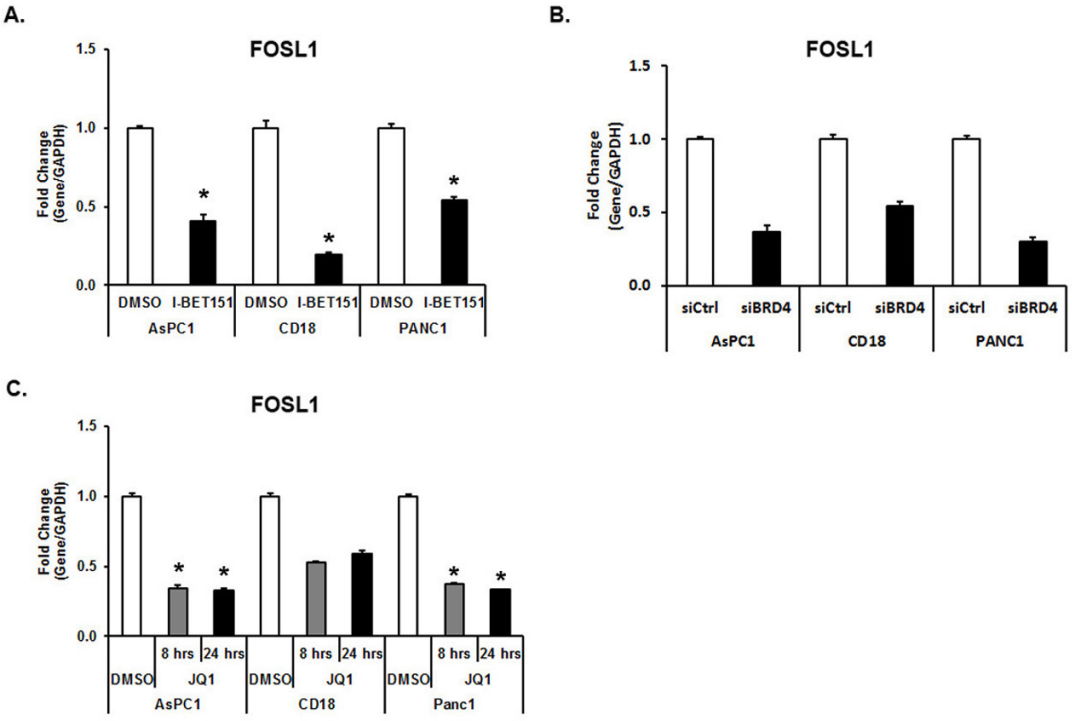
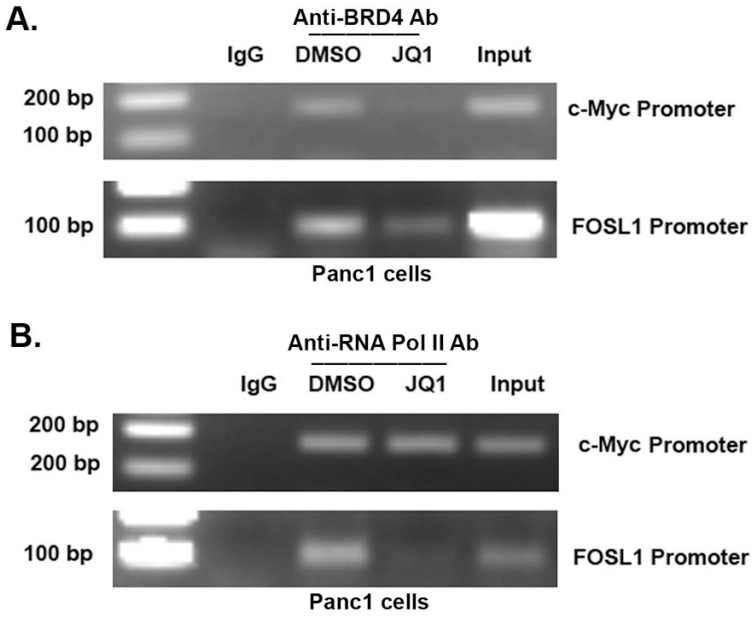

A.
FOSL1
Fold Change (Gene/GAPDH)
1.5
1.0
0.5
0.0
DMSO
I-BET151
AsPC1
CD18
PANC1
B.
FOSL1
Fold Change (Gene/GAPDH)
siCtrl
siBRD4
AsPC1
CD18
PANC1
C.
FOSL1
Fold Change (Gene/GAPDH)
DMSO
8 hrs
24 hrs
JQ1
AsPC1
CD18
Panc1

Fig. S7


A.
Anti-BRD4 Ab
IgG
DMSO
JQ1
Input
200 bp
100 bp
c-Myc Promoter
100 bp
FOSL1 Promoter
Panc1 cells
B.
Anti-RNA Pol II Ab
IgG
DMSO
JQ1
Input
200 bp
200 bp
c-Myc Promoter
100 bp
FOSL1 Promoter
Panc1 cells