

Figure S1. N-CAFs and R-CAFs were exposed to the indicated concentrations of gemcitabine for 72h, and viability was measured via MTT assay. 3 biologic replicates were included in the experiment. ** $p \leq 0.01$, **** $p \leq 0.0001$

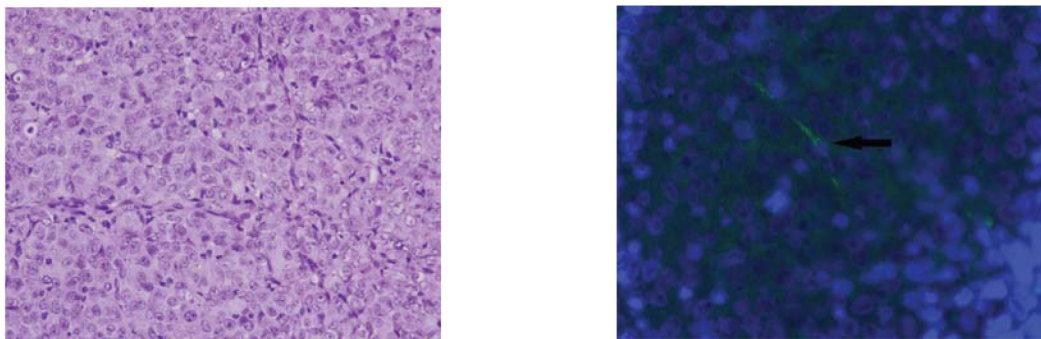


Figure S2. MiaPaCa-2 cells (1×10^5) were subcutaneously injected with N-CAF cells expressing GFP (3×10^5) in NSG mice. At 6 weeks, tumors were harvested and fluorescence microscopy was performed. Representative images of H&E stained sections as well as fluorescence microscopy are displayed. Only occasional GFP+ CAFs were present after 6 weeks.

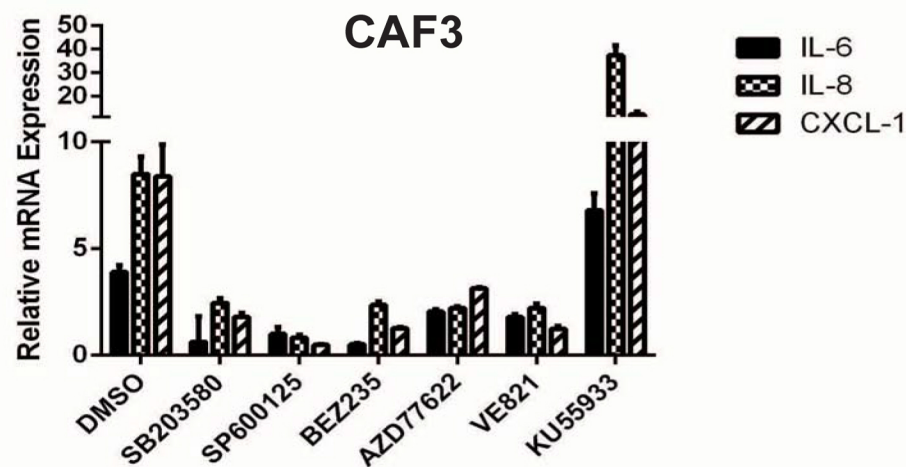
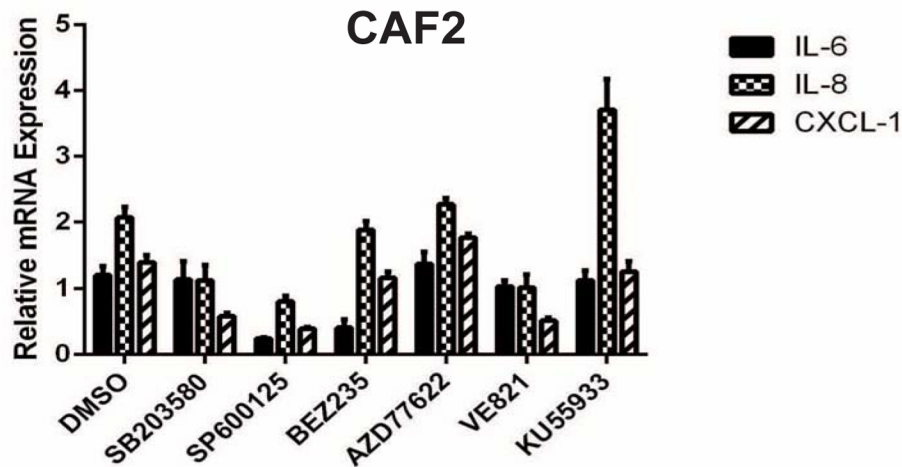
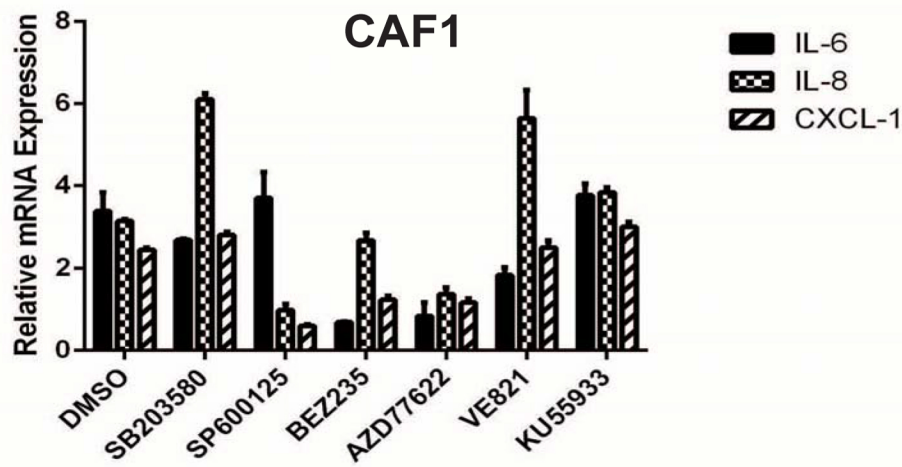


Figure S3. Primary CAFs were treated with 1 μ M GEM plus DMSO or the above listed small molecule inhibitors for 96h and SASP mediator expression was compared to untreated cells via qRT-PCR. Because of limited primary cell numbers, the experiment was performed once in multiple cell lines rather than being replicated in any single line. Drug concentrations and targets: SB203580 10 μ M- P38 MAPK, SP600125 20 μ M- JNK, BEZ235 1 μ M- ATM/ATR/DNA-PK/PI3K/mTOR, AZD77622 200nM- Chk1/Chk2 VE821 2 μ M- ATR, KU55933 20 μ M- ATM.

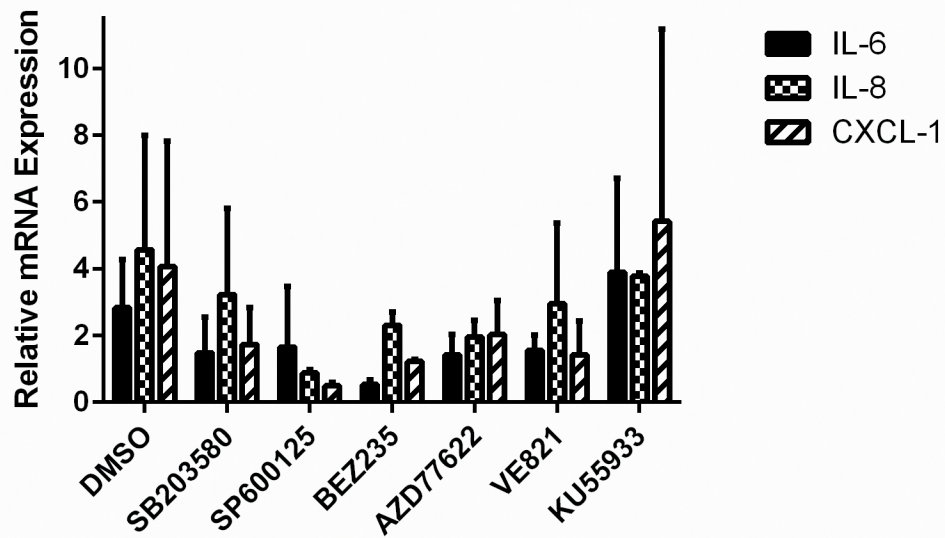


Figure S4. Combined data from Figure S3. The mean normalized expression of each marker from CAF1-3 is displayed. In this combined analysis, none of the changes reached statistical significance.

| Gene | Forward Primer | Reverse Primer |
|---------------|--------------------------|-------------------------|
| CXCL-1 | AGGGAATTCACCCCAAGAAC | ACTATGGGGGATGCAGGATT |
| CXCL-6 | AGAGCTGCGTTGCACTTGTT | GCAGTTTACCAATCGTTTTGGGG |
| ICAM-1 | GCTGACGTGTGCAGTAATACTGG | TTCTGAGACCTCTGGCTTCGT |
| IL-1 α | CGCCAATGACTCAGAGGAAGA | AGGGCGTCATTCAGGATGAA |
| IL-1 β | AAACAGATGAAGTGCTCCTTCC | AAGATGAAGGGAAAGAAGGTGC |
| IL1R1 | ATGAAATTGATGTTTCGTCCCTGT | ACCACGCAATAGTAATGTCCTG |
| IL-6 | AAAGAGGCACTGGCAGAAAA | AGCTCTGGCTTGTTCTCAC |
| IL-8 | ACTGAGAGTGATTGAGAGTGGAC | AACCCTCTGCACCCAGTTTTC |
| SPP1 | GCCGAGGTGATAGTGTGGTT | TGAGGTGATGTCCTCGTCTG |
| RPL13 | CATCGTGGCTAAACAGGTAAGT | GCACGACCTTGAGGGCAGCC |

Table S1. Primer sequences.