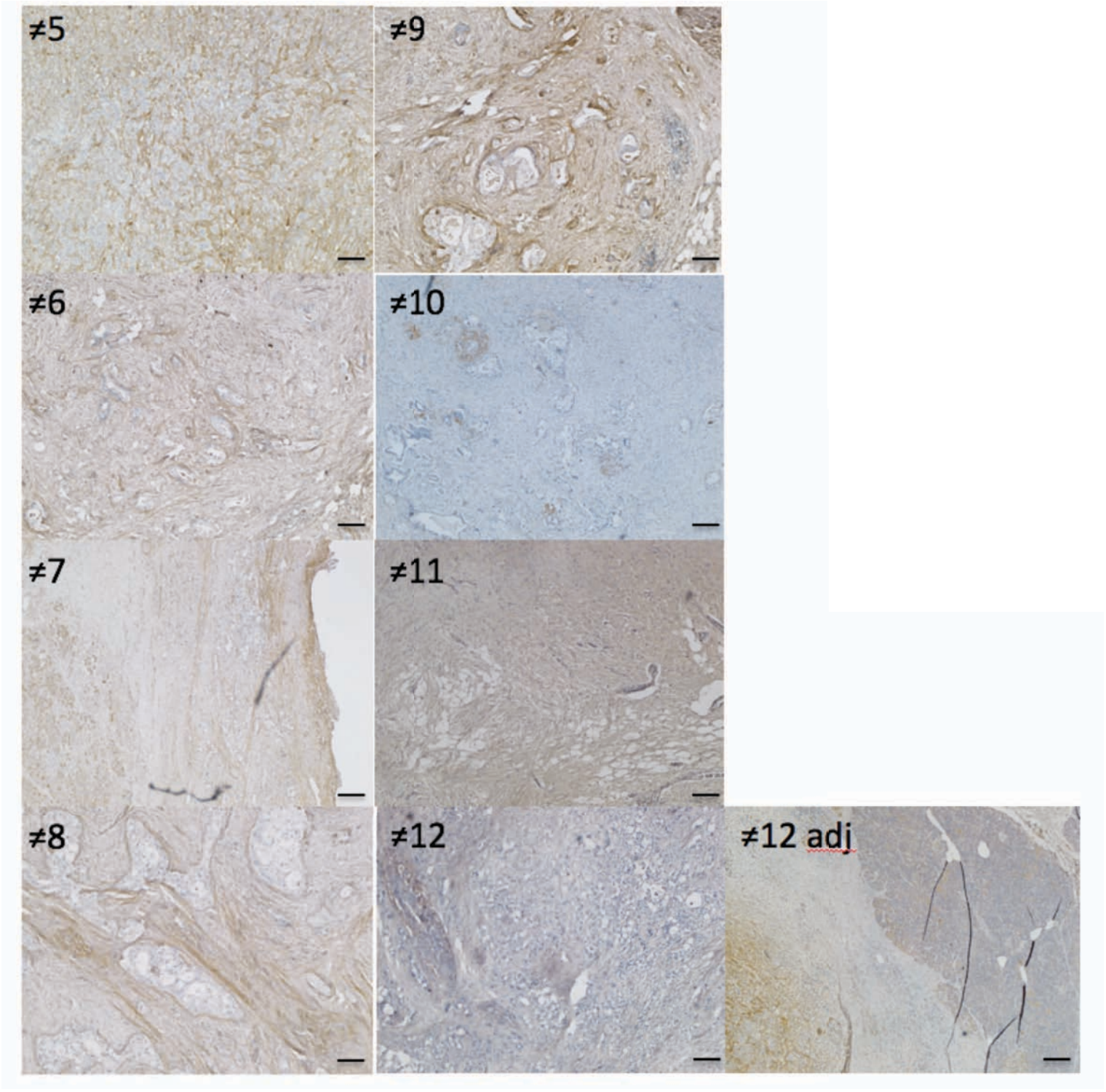
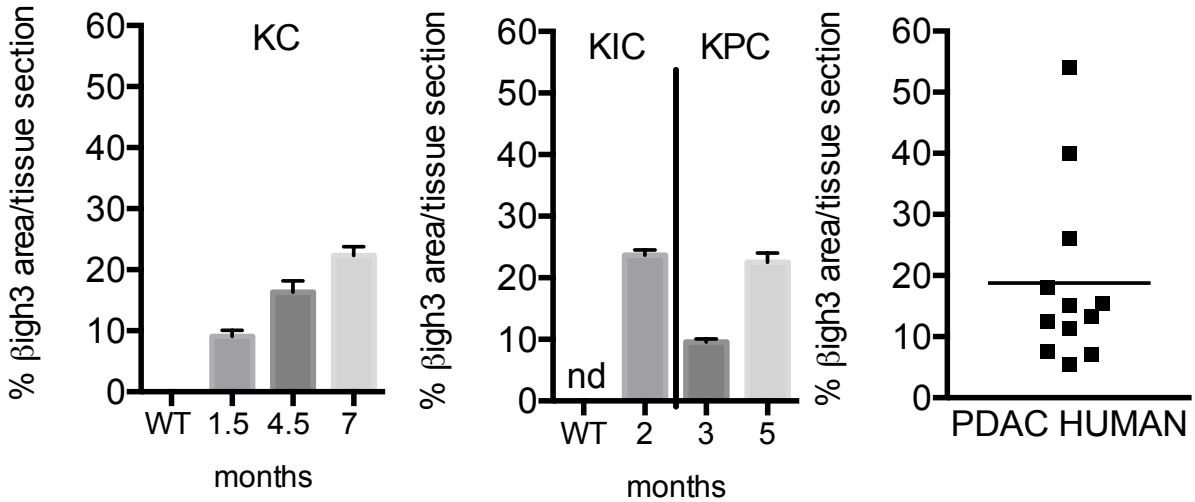
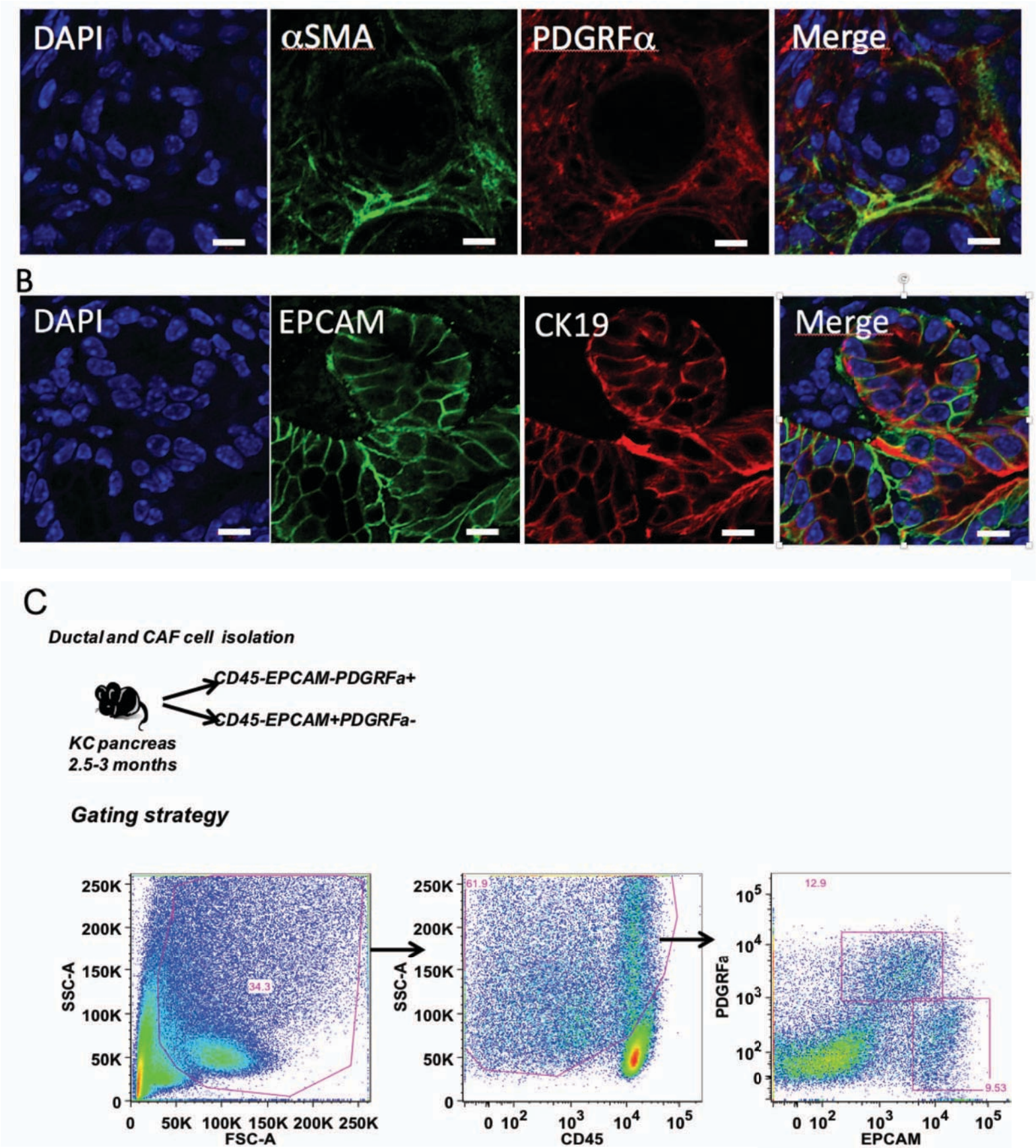
**Supplementary Figure 1**

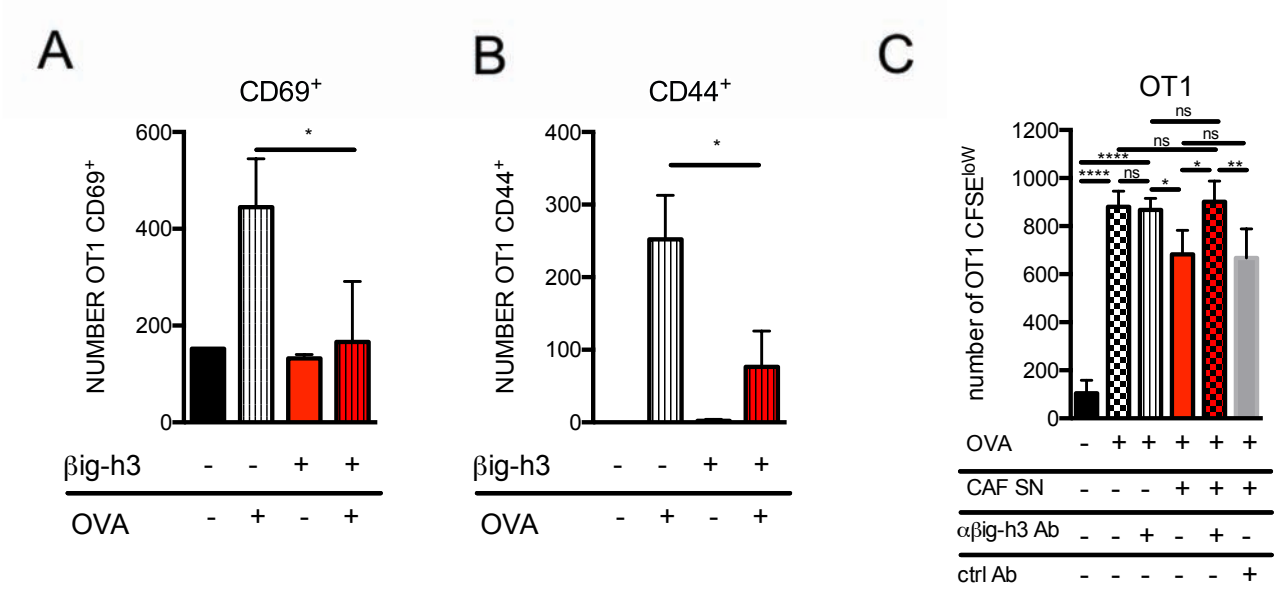


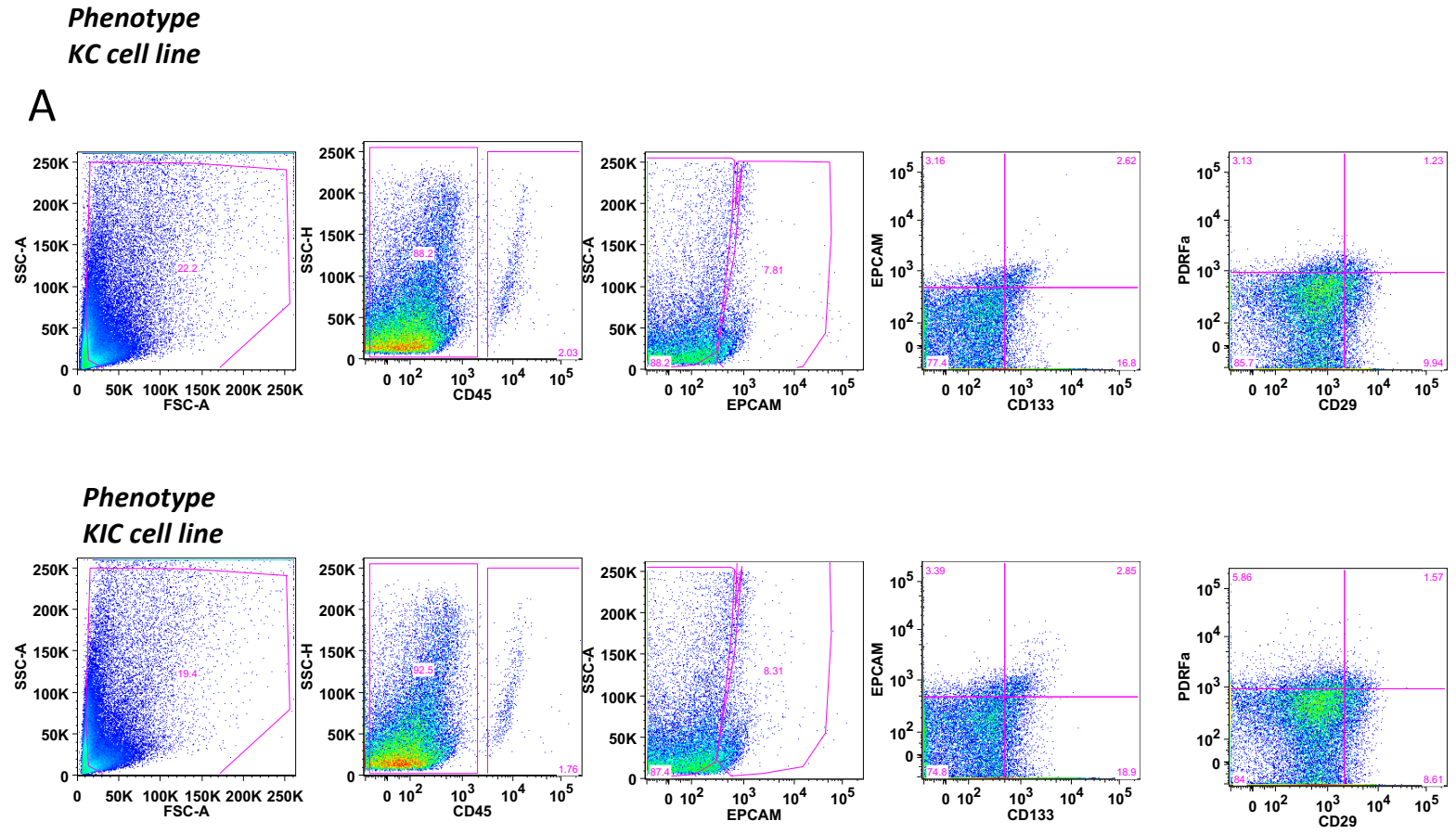
**Supplementary Figure 1.** Representative immunohistochemical staining for βig-h3 in the pancreas in 8 PDA patients. Scale bar, 100 μm. Quantification of the areas of βig-h3 staining in KC mice at different ages, in KIC and KPC mice as well as in a cohort of 12 patients with PDAC. Two representative pictures of patient 12 showing no expression in adjacent non tumoral tissue.

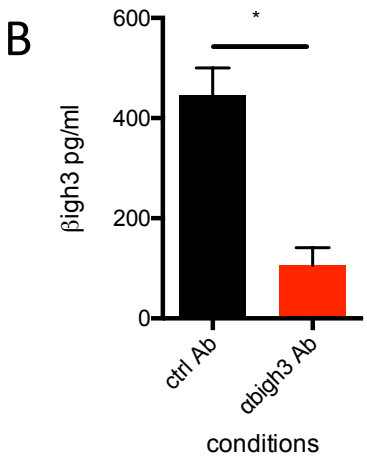



**Supplementary Figure 2.** Representative immunofluorescence labeling in the pancreas in KC mice for αSMA and EPCAM (green), PDGRFα and CK19 (red) and DAPI (blue) (A, B). Scale bar, 10 μm. (C) The gating strategy used to isolate ductal cells and CAFs.



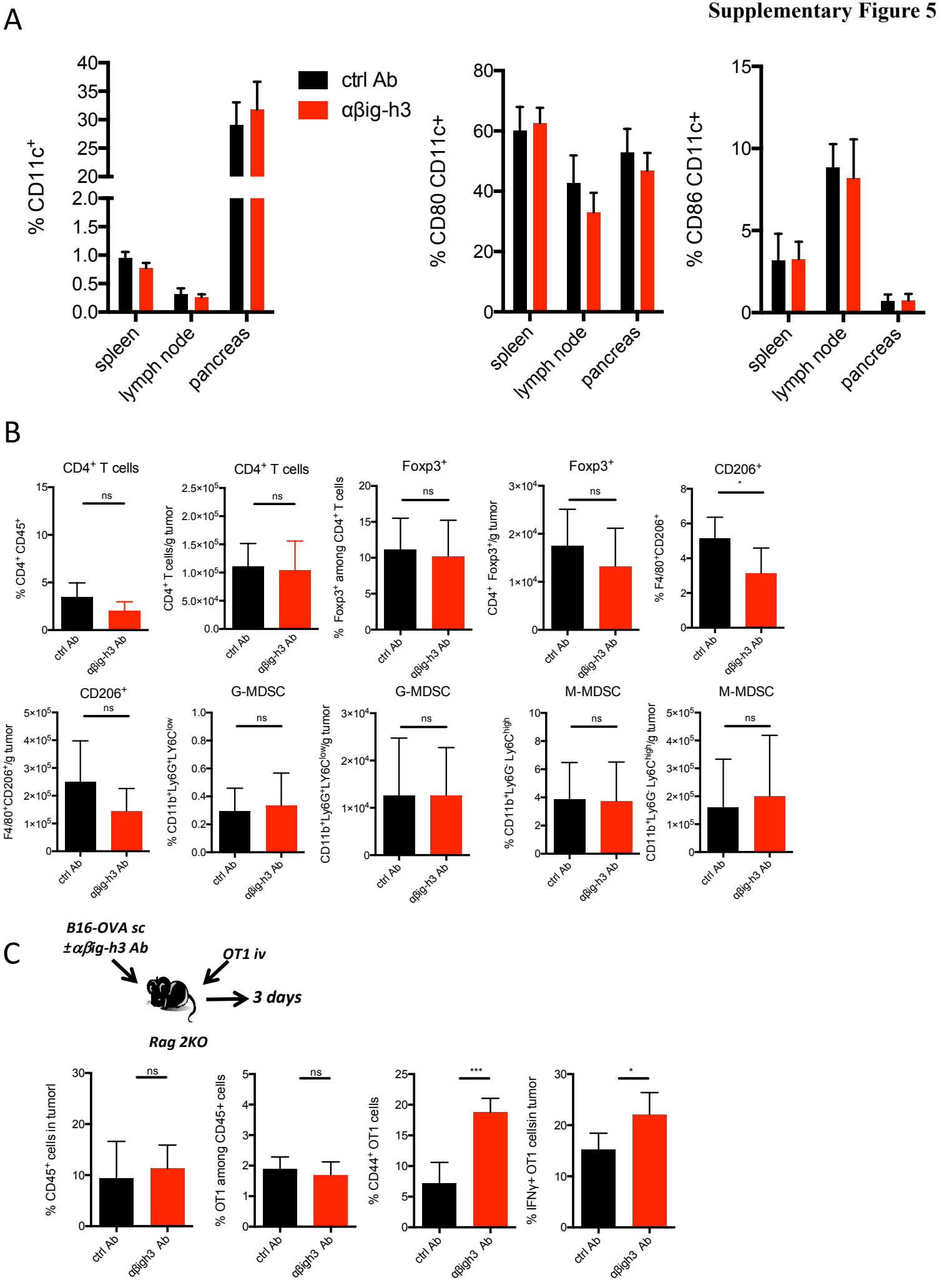

**Supplementary Figure 3** CFSE-labeled OT1 splenocytes were cultured in the presence or absence of rβig-h3 (5 μg/ml) and activated using OVA peptide at a concentration of 1 μg/ml for 72 h. The graphs demonstrate the number of $CFSE^{low}$ OT1 T cells that expressed CD69 (A) or CD44 (B). CFSE-labeled OT1 splenocytes were cultured in the presence/absence of CAF supernatant (C) in the presence of anti-βig-h3 antibodies or ctrl antibodies and activated using OVA peptide (1 μg/ml) for 72 h. The graphs demonstrate the number of $CFSE^{low}$ OT1 cells. One way Anova and Tukey's multiple comparisons tests were performed. **** P< 0.0001, *$P < 0.05$, **$P < 0.01$.



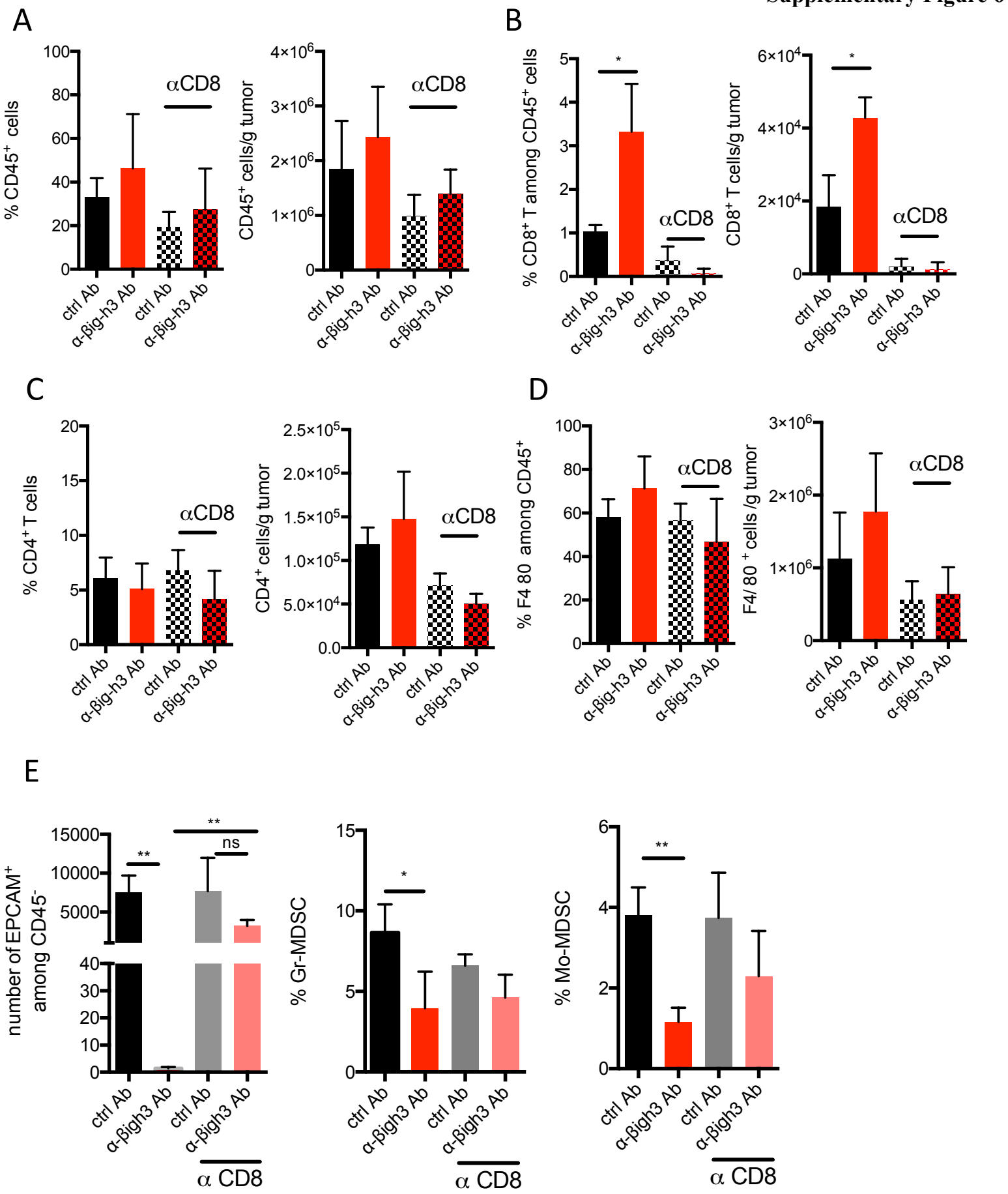

**Supplementary Figure 4.** (A) Representative immunofluorescence labeling of KC and KIC cell lines. (B) ELISA was used to quantify the level of βig-h3 secreted by KC cells incubated in the presence of anti-βig-h3 or ctrl antibodies. *$P < 0.05$

**Supplementary Figure 5**



**Supplementary Figure 5.** FACS analysis of the following immune cell populations: (A) % CD11c, % CD80 among $CD11c^+$ cells, % $CD86^+$ among $CD11c^+$ cells; (B) % and numbers/g tumor $CD4^+$ T cells, $CD4^+$ $Foxp3^+$ T cells, $F4/80^+CD206^+$ macrophages Gr-MDSC, Mo-MDSC in C57Bl6 mice that were subcutaneously injected with KC cells that were treated with ctrl or anti-βig-h3 antibodies. (C) B16 OVA cells (+ anti-βig-h3 Ab or ctrl Ab) were s.c. injected in $Rag2^{KO}$ mice i.v. transferred with OT1 cells. Graphs represent % CD45 cells within the tumor , % OT1 among $CD45^+$ cells, % OT1 $CD44^{high}$ and % OT1 $IFN\gamma^+$, $*P < 0.05$. $***P < 0.001$.

**Supplementary Figure 6**



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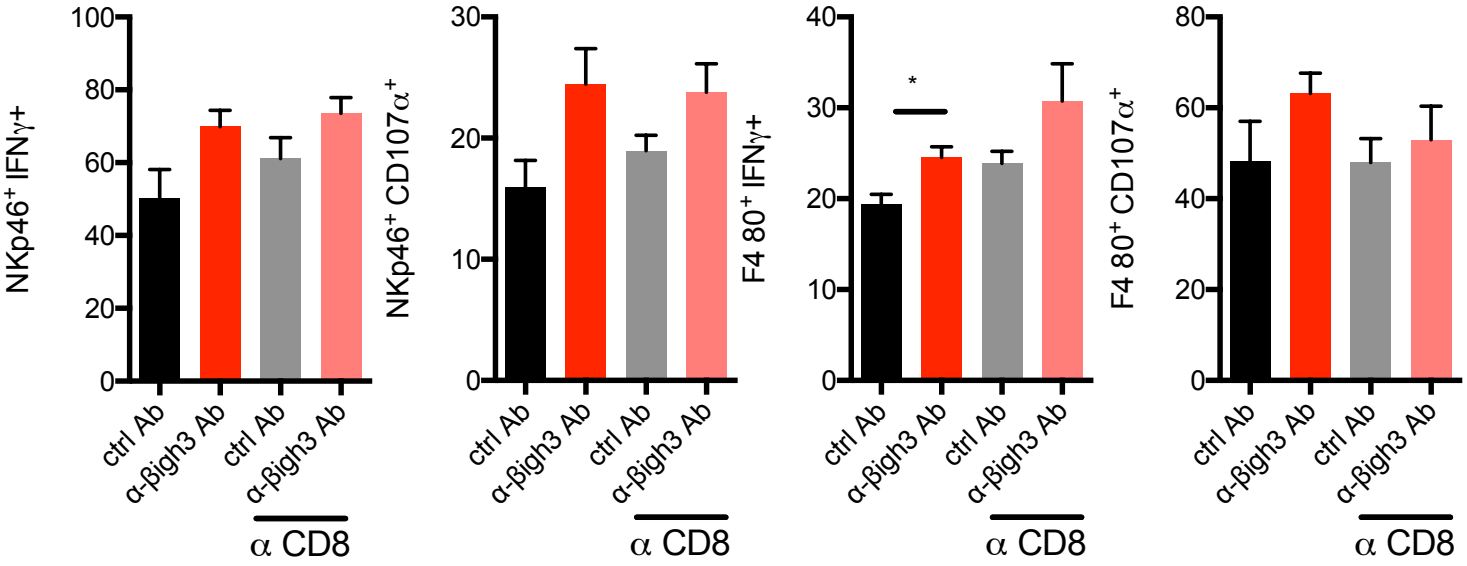
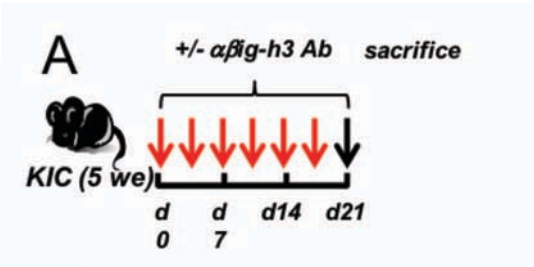
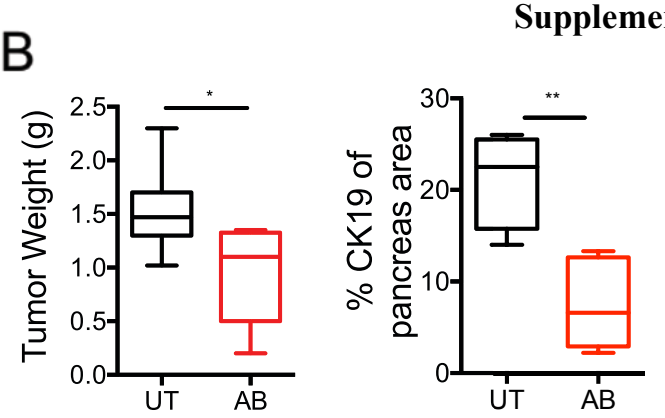
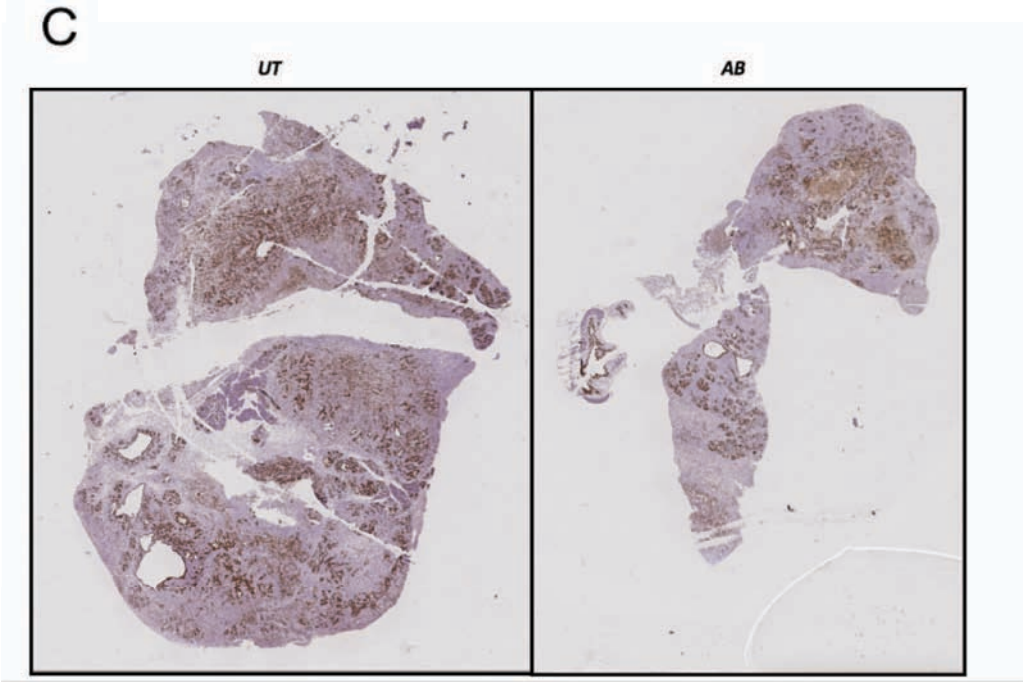


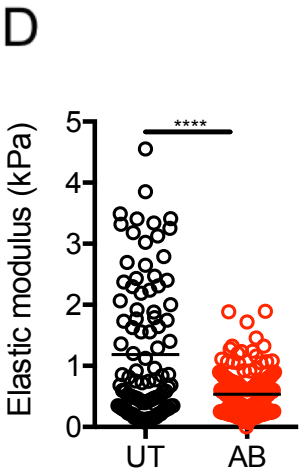

**Supplementary Figure 6.** FACS analysis in KC implantation in C57Bl6 mice (percentages and and numbers/g tumor) of the following immune cell populations: (A) $CD45^+$ T cells, (B) $CD8^+$ T cells, (C) $CD4^+$ T cells and (D) $F4/80^+$ macrophages in C57Bl6 mice that were subcutaneously injected with KC cells that were treated with ctrl or anti-βig-h3 antibodies and then further depleted (or not) via an intravenous injection with anti-CD8 antibodies. $*P < 0.05$. FACS analysis in KIC implantation (percentages and and numbers/g tumor) of the following populations: (E) EPCAM, Gr-MDSC, Mo-MDSC (F) NK cells, $F4/80^+$ macrophages in C57Bl6 mice that were subcutaneously injected with KIC cells that were treated with ctrl or anti-βig-h3 antibodies and then further depleted (or not) via an intravenous injection with anti-CD8 antibodies. $*P < 0.05$. $**P < 0.01$.

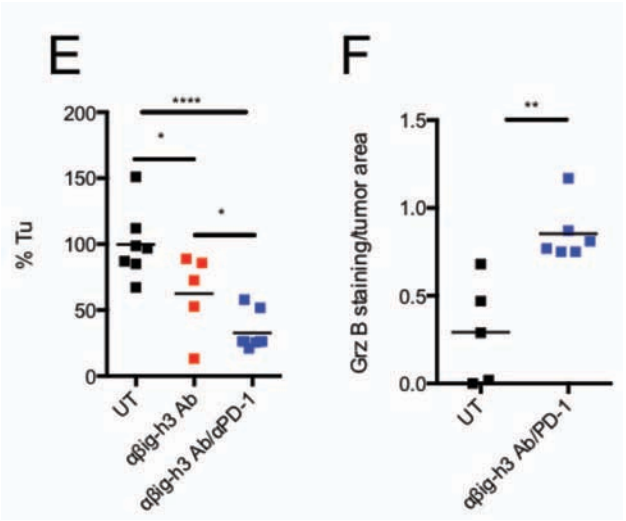
**Supplementary Figure 7**



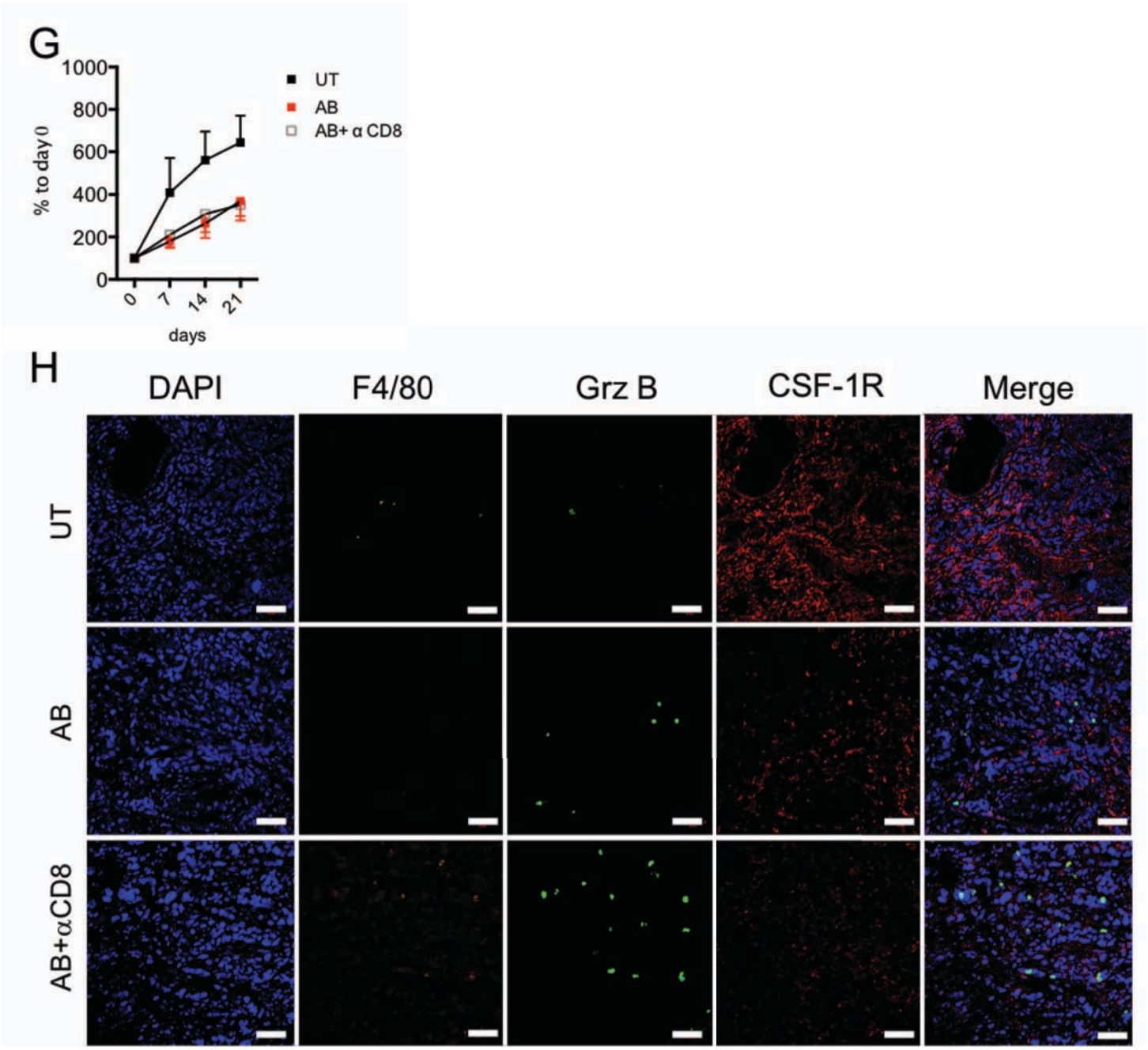



**Supplementary Figure 7**



**Supplementary Figure 7.** The impact of inducing the *in vivo* depletion of βig-h3 in KIC mice. (A) Experimental protocol used to induce antibody depletion. (B) Tumoral weights were quantified at the end of the experiment. (C) Representative scan of immunhistochemistry on whole sectioned pancreas (CK19 staining). (D) Elastic Modulus quantification by AFM coupled with IF (based on CK19 and aSMA staining) in UT and AB treated KIC mice (3 independent mice per group, 100 force curves were measured per interest zone). (E) Impact of the combination anti-βig-h3 and anti-PD-1 Abs. The experiment was performed using 5-6 mice per group. (F) Quantification of the GrzB staining per tumoral area (on whole scan section). (G) Impact of the combination anti-βig-h3 and anti-CD8 Abs in KPC mice. Tumoral volume was quantified using ultrasound (Vevo2100®) in Ab-treated animals and represented in % to day 0. (H) Representative immunofluorescence stainings for F4/ 80, GrzB, CSF-R1 and DAPI in UT, AB and AB+αCD8-treated mice pancreas sections. Scale bar 50 μm *$P < 0.05$, ** $P < 0.01$, **** $P < 0.0001$.

**384 SNP Panel Batch MB-170925KB**

**CR GEMS France Order 2017007016:**
**pk447 Cells (5Log10) in 10% DMSO Comparison to B6J**

**Percent Match to Reference Allelic Profiles of Standard Inbred Strains**

| LTM # - Sample ID | B6J | B6N | NODLJ | C3HHeJ | FVB | BALBcN | BALBcByJ | BALBcJ | DBA2J |
|---|---|---|---|---|---|---|---|---|---|
| 001-pk447 | 94.8% | 93.8% | 46.0% | 40.0% | 39.6% | 39.1% | 39.1% | 39.1% | 35.1% |
| | **94.8%** | **93.8%** | **46.0%** | **40.0%** | **39.6%** | **39.1%** | **39.1%** | **39.1%** | **35.1%** |

**Supplementary Table 1. 384 SNP Panel Batch MB-170925KB (Charles Rivers) was performed by to determine the C57B6J backcross phenotype.**