**Supplementary Figure Legends**

**Supplementary Figure 1. Identification of FAP+ cancer-associated stromal cells in desmoplastic A549 tumors.** A549 tumor cells mixed with matrigel were injected into the flanks of NSG-FAP intact and NSG-FAP null mice. Established tumors were harvested and dissociated with a collagenase cocktail to obtain single cell suspension. Cells were stained with anti-CD45, anti-CD90, anti-F4/80, anti-CD206 and anti-FAP antibodies. Dead cells were excluded by propidium iodide staining. Flow cytometry was performed to (A) identify CD90+ stromal cells and CD45+ hematopoietic cells that express FAP and (B) identify F4/80+ CD206+ cells that have enriched FAP expression in CD45+ hematopoietic cells. (C) A549 frozen tumor sections were subjected to immunofluorescence staining with FAP and SMA to determine mesenchymal stromal cells present in the tumor. Scale: 100 m. (D) Expression of mesenchymal stem cell marker CD105 and CD44 by a subpopulation of FAP+ cells in A549 tumor xenografts.

**Supplementary Figure 2. The adaptive immune response plays a critical role in FAP-CAR T cell-mediated anti-tumor activity in immunogenic AE17.OVA tumors.** (A) Syngeneic C57BL/6 mice bearing established AE17.OVA tumors were injected intravenously with FAP-CAR or MigR1 T cells. (B) NSG mice bearing established AE17.OVA tumors were injected intravenously with FAP-CAR T cells. Tumor measurements were then taken. These figures were reproduced from our previous report in accordance with guidelines of AACR Journals (44). (C) AE17.OVA tumor tissues from syngeneic C57BL/6 mice treated with FAP-CAR or MigR1 mouse T cells intravenously or left untreated were harvested 9 days post-adoptive T cell transfer. Histopathology was examined by H&E staining. Scale: 100 m. # Denotes statistical significance between untreated, MigR1-treated and FAP-CAR-treated samples, p value < 0.05.

**Supplementary Figure 3. FAP-CAR T cells restrict AE17.OVA tumor growth through reduced proliferation, increased apoptosis and altered tumor stroma.** Established AE17.OVA tumor-bearing mice were administered with FAP-CAR or MigR1 mouse T cells intravenously, or left untreated. Tumor tissues were harvested 9 days post-adoptive T cell transfer. (A) Tumor sections were stained with an anti-ki-67 antibody. Proliferation index was calculated by the ratio of ki-67+ cells to hematoxylin+ cells. (B) AE17.OVA tumor tissues were stained with an anti-cleaved caspase-3 (CC-3) antibody. Apoptotic index was calculated by the ratio of CC-3+ cells to hematoxylin+ cells. (C) Masson’s trichrome was performed to determine collagen content. (D) Hyaluronan content was determined by HABP immunohistochemistry. (E) Tumor tissues were also stained with an antibody against CD31 and vessel number was quantified by counting immuno-reactive vessels. Scale: 100 m. Results are shown as mean ± SEM (n=3 per group). # Denotes significant difference between untreated, MigR1 and FAP-CAR T cell-treated group, p value < 0.05.

**Supplementary Figure 4. Alteration of tumor structure by FAP-CAR T cells in A549 tumors.** Established A549 tumor-bearing mice were treated with FAP-CAR human T cells. Tumor tissues were harvested 8 days post-adoptive T cell transfer. Histopathology was examined by H&E staining. Scale: 100 m. H&E stained slides were evaluated by two board-certified veterinary pathologists (ACD, ELB). Lung tumors were evaluated in 9 consecutive 40X HPF images. Well-differentiated tumors formed distinct tubular structures; moderately differentiated tumors contained variably distinct tubules, with cell piling or attenuation; poorly differentiated tumor cells were arranged in solid nests or individualized neoplastic cells. \* Denotes significant difference between untreated and FAP-CAR T cell-treated group, p value < 0.05.

**Supplementary Figure 5. Analysis of immune infiltrating cells in 4662 tumors following FAP-CAR Therapy.** Established 4662 PDA-bearing mice were treated with 2 doses of either MigR1 or FAP-CAR mouse T cells or left untreated. (A) Tumor growth in untreated B6 and NSG mice was comparable. (B) Tumor tissues were harvested 7 days post second dose of T cell transfer for single cell preparation. Flow cytometry was performed to identify CD11b+ F4/80+ macrophages, CD11b+ Ly6G+ neutrophils and (C) GFP- CD8+ host T cells and GFP+ adoptive transferred FAP-CAR T or MigR1 T cells. # Denotes significant difference between untreated, MigR1 and FAP-CAR T cell-treated group, p value < 0.05.

**Supplementary Figure 6. Alteration of tumor structure by FAP-CAR T cells in murine PDAs.** Established 4662 tumor-bearing mice and autochthonous PDA-bearing KPC mice were treated with 2 doses of FAP-CAR mouse T cells. Tumor tissues were harvested 3 days post second dose of adoptive T cell transfer. Histopathology was examined by H&E staining. Scale: 100 m. H&E stained slides were evaluated by two board-certified veterinary pathologists (ACD, ELB).  For each PDA tumor, 10 consecutive 40X HPF images were evaluated and scored based on the predominant tumor phenotype (greater than 50% of the field of view): necrosis, well-differentiated, moderately differentiated, and poorly differentiated (34). \* and # denote statistical significance between MigR1 and FAP-CAR T cell-treated samples, p value < 0.01 and p value = 0.05, respectively.

**Supplementary Figure 7. Identification of tumor stroma by FAP and SMA reveals stromal cell heterogeneity in human and murine PDA.** (A) Human and murine PDA frozen tumor sections were subjected to immunofluorescence staining with FAP, SMA or CD45 to determine the overall immune infiltrating cells and mesenchymal stromal cells present in the tumor. The majority of stromal cells express either FAP or SMA. Arrows indicate co-localization of indicated markers. Scale: 100 m. FAP+ cells also express mesenchymal stem cell marker CD105. (B) Human PDA-associated stromal cells were isolated from tumor explants and stained with FAP and SMA. Scale: 50 m.

**Supplementary Figure 8. Combination of FAP-CAR T cells and gemcitabine treatment augments anti-tumor response in 4662 tumors**. 4662 tumor cells were inoculated into the right flanks of C57BL/6 mice. When tumors reached 100 mm3, one dose of FAP-CAR T cells were given intravenously; second dose was administered after initial dose (blue arrow). A cohort of 4662 tumor-bearing mice received gemcitabine (120mg/kg) treatment through i.p. on day 4 (orange arrow). For combination therapy, 4662 tumor-bearing mice were given gemcitabine 4 days post 2nd dose of FAP-CAR T cells (red arrow). Tumor measurements followed. The values are expressed as the mean ± SEM (n=5). \* Significant difference between FAP-CAR, gemcitabine and the combo groups (P < 0.05).