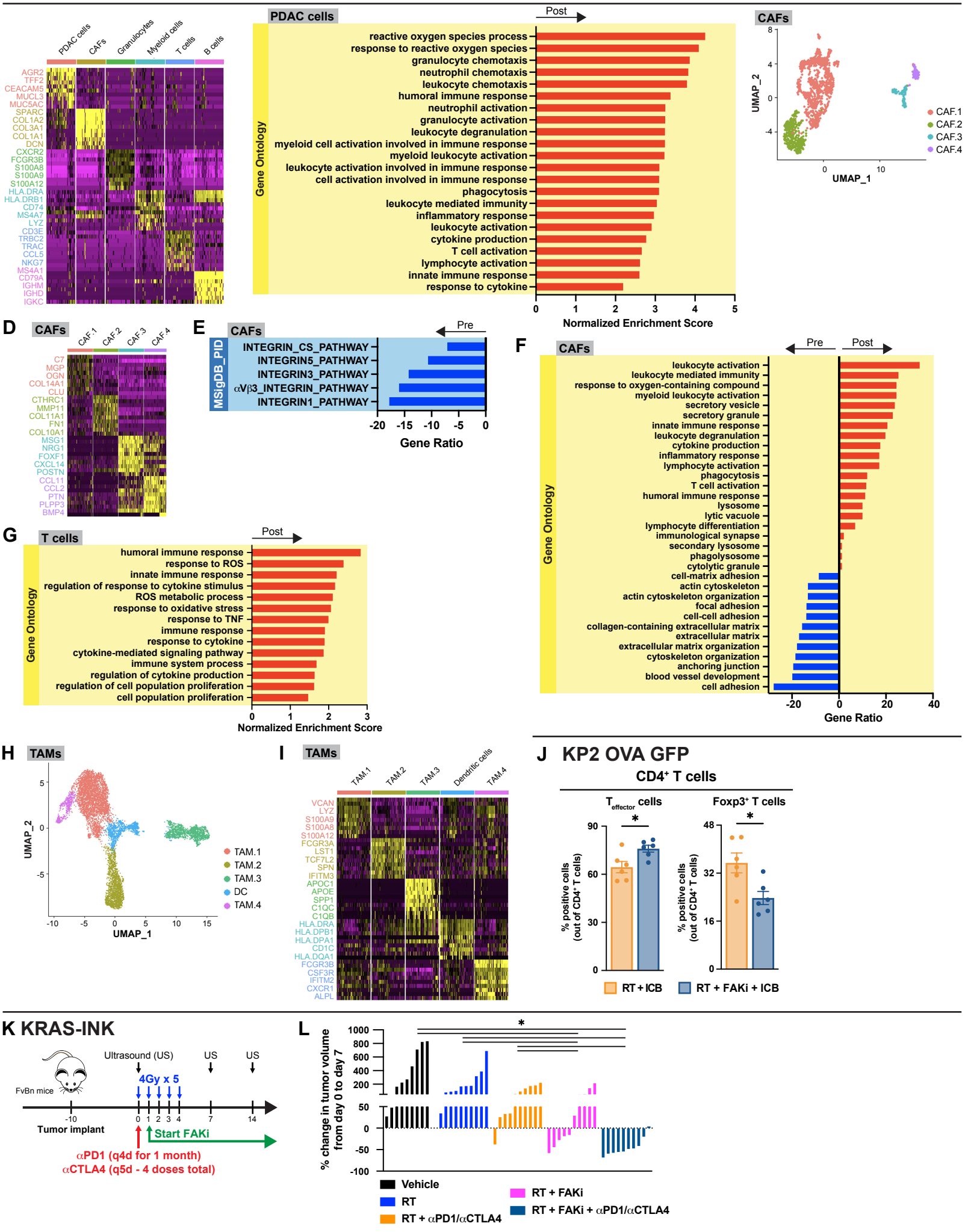
A Clinical Trial
PDAC cells
CAFs
Granulocytes
Myeloid cells
T cells
B cells
AGR2
TFF2
CEACAM5
MUCL3
MUC5AC
SPARC
COL1A2
COL3A1
COL1A1
DCN
CXCR2
FCGR3B
S100A8
S100A9
S100A12
HLA.DRA
HLA.DRB1
CD74
MS4A7
LYZ
CD3E
TRBC2
TRAC
CCL5
NKG7
MS4A1
CD79A
IGHM
IGHD
IGKC
B
PDAC cells
Post
Gene Ontology
reactive oxygen species process
response to reactive oxygen species
granulocyte chemotaxis
neutrophil chemotaxis
leukocyte chemotaxis
humoral immune response
neutrophil activation
granulocyte activation
leukocyte degranulation
myeloid cell activation involved in immune response
myeloid leukocyte activation
leukocyte activation involved in immune response
cell activation involved in immune response
phagocytosis
leukocyte mediated immunity
inflammatory response
leukocyte activation
cytokine production
T cell activation
lymphocyte activation
innate immune response
response to cytokine
0 1 2 3 4 5
Normalized Enrichment Score
C
CAFs
UMAP_2
UMAP_1
CAF.1
CAF.2
CAF.3
CAF.4
D
CAFs
CAF.1
CAF.2
CAF.3
CAF.4
C7
MGP
OGN
COL14A1
CLU
CTHRC1
MMP11
COL11A1
FN1
COL10A1
MSG1
NRG1
FOXF1
CXCL14
POSTN
CCL11
CCL2
PTN
PLPP3
BMP4
E
CAFs
Pre
MSigDB_PID
INTEGRIN_CS_PATHWAY
INTEGRIN5_PATHWAY
INTEGRIN3_PATHWAY
αVβ3_INTEGRIN_PATHWAY
INTEGRIN1_PATHWAY
-20 -15 -10 -5 0
Gene Ratio
F
CAFs
Pre
Post
Gene Ontology
leukocyte activation
leukocyte mediated immunity
response to oxygen-containing compound
myeloid leukocyte activation
secretory vesicle
secretory granule
innate immune response
leukocyte degranulation
cytokine production
inflammatory response
lymphocyte activation
phagocytosis
T cell activation
humoral immune response
lysosome
lytic vacuole
lymphocyte differentiation
immunological synapse
secondary lysosome
phagolysosome
cytolytic granule
cell-matrix adhesion
actin cytoskeleton
actin cytoskeleton organization
focal adhesion
cell-cell adhesion
collagen-containing extracellular matrix
extracellular matrix
extracellular matrix organization
cytoskeleton organization
anchoring junction
blood vessel development
cell adhesion
-20 0 20 40
Gene Ratio
G
T cells
Post
Gene Ontology
humoral immune response
response to ROS
innate immune response
regulation of response to cytokine stimulus
ROS metabolic process
response to oxidative stress
response to TNF
immune response
response to cytokine
cytokine-mediated signaling pathway
immune system process
regulation of cytokine production
regulation of cell population proliferation
cell population proliferation
0 1 2 3
Normalized Enrichment Score
H
TAMs
UMAP_2
UMAP_1
TAM.1
TAM.2
TAM.3
DC
TAM.4
I
TAMs
TAM.1
TAM.2
TAM.3
Dendritic cells
TAM.4
VCAN
LYZ
S100A9
S100A8
S100A12
FCGR3A
LST1
TCF7L2
SPN
IFITM3
APOC1
APOE
SPP1
C1QC
C1QB
HLA.DRA
HLA.DPB1
HLA.DPA1
CD1C
HLA.DQA1
FCGR3B
CSF3R
IFITM2
CXCR1
ALPL
J
KP2 OVA GFP
CD4+ T cells
T effector cells
Foxp3+ T cells
% positive cells (out of CD4+ T cells)
RT + ICB
RT + FAKi + ICB
K
KRAS-INK
FvBn mice
Ultrasound (US)
US
US
4Gy x 5
Tumor implant
Start FAKi
αPD1 (q4d for 1 month)
αCTLA4 (q5d - 4 doses total)
L
% change in tumor volume from day 0 to day 7
Vehicle
RT
RT + αPD1/αCTLA4
RT + FAKi
RT + FAKi + αPD1/αCTLA4

Figure S7: Human PDAC patients and checkpoint blockade

(A) Heatmap displaying top 10 genes of different cell clusters in **Fig. 7B**. **(B)** Bar graph displaying GSEA analysis of DEGs on all the PDAC cells in **Fig. 7B** to known biological functions in GO database. All graphs display comparisons of pre-treatment to post-treatment biopsies. All pathways were filtered with p.adj value < 0.05. **(C)** UMAP analysis of CAFs isolated from **Fig. 7B**. **(D)** Heatmap displaying top 10 genes of different cell clusters in (C). **(E-F)** Bar graphs displaying over-representation analysis of DEGs on all the CAFs in **Fig. 7B** to known biological functions in MSigDB_PID (E) and GO (F) databases. All graphs display comparisons of pre-treatment to post-treatment biopsies. All pathways were filtered with p.adj value < 0.05. **(G)** Bar graph displaying over-representation analysis of DEGs on all the T cells in **Fig. 7B** to known biological functions in GO database. All graphs display comparisons of pre-treatment to post-treatment biopsies. All pathways were filtered with p.adj value < 0.05. **(H)** UMAP analysis of TAMs isolated from **Fig. 7B**. **(I)** Heatmap displaying top 10 genes of different cell clusters in (H). **(J)** Flow cytometry quantification of $CD4^+$ T effector and $CD4^+$ $Foxp3^+$ T regulatory cells from KP2-OVA-GFP tumor bearing mice at day 10 post the start of RT. **(K)** Schematic of RT (4Gy x 5), FAKi (75mg/kg BID), and ICB (αPD1, 200μg and αCTLA4, 200μg) administration and tumor burden monitoring in KRAS-INK orthotopic tumor-bearing mice. Mice were treated and longitudinally assessed for tumor burden by US. **(L)** Waterfall plot of KRAS-INK tumor-bearing mice from (K) evaluating tumor growth difference from day 0 to 7 by US measurement. n = 10 mice/group.

All graphs depict mean +/- SEM. "*" denotes $p < 0.05$ by one-way ANOVA or two-tailed t-test as appropriate.