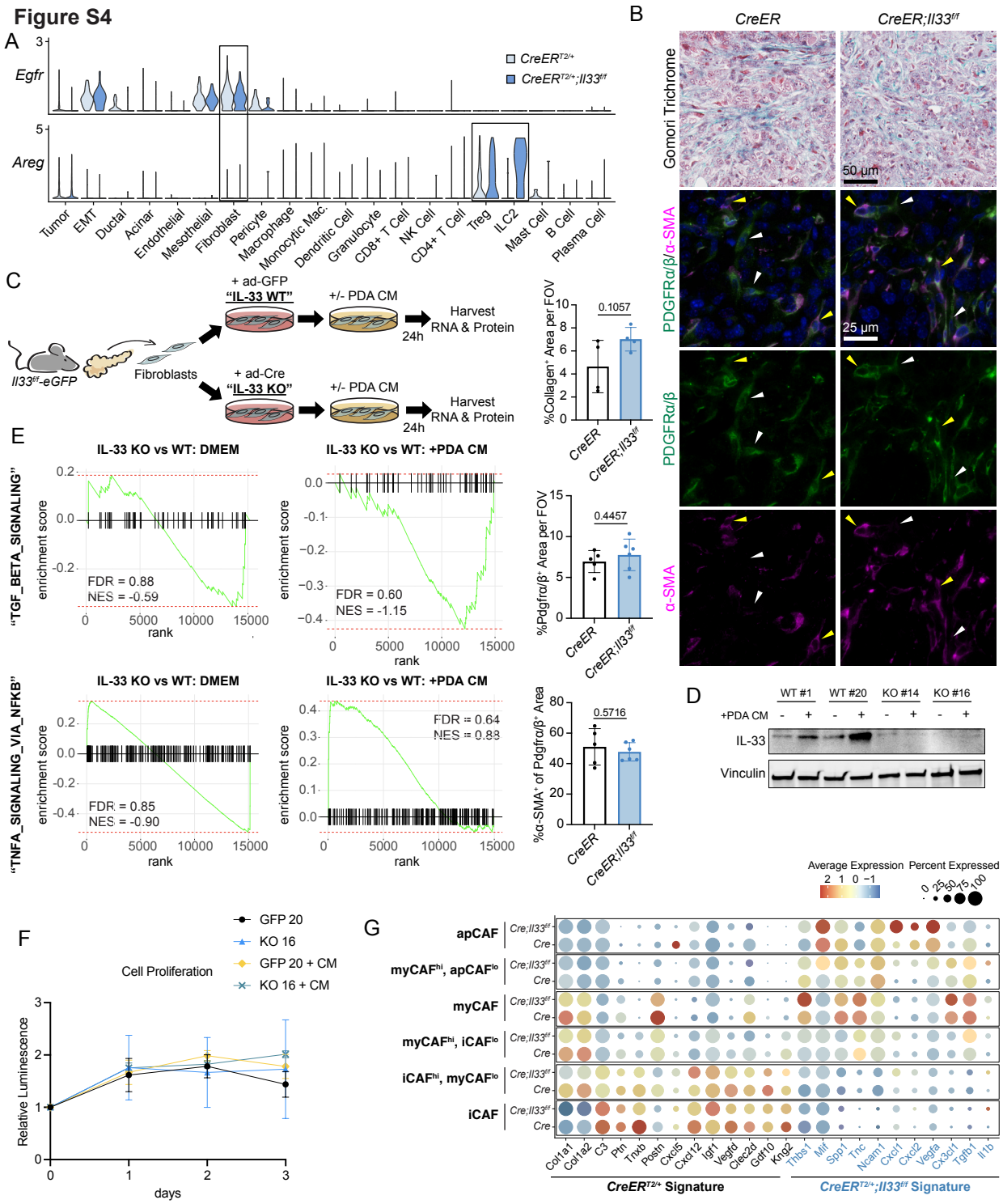
Figure S4
A
Egfr
Areg
CreER^T2/+
CreER^T2/+;Il33^f/f
Tumor
EMT
Ductal
Acinar
Endothelial
Mesothelial
Fibroblast
Pericyte
Macrophage
Monocytic Mac.
Dendritic Cell
Granulocyte
CD8+ T Cell
NK Cell
CD4+ T Cell
Treg
ILC2
Mast Cell
B Cell
Plasma Cell
B
CreER
CreER;Il33^f/f
Gomori Trichrome
50 μm
PDGFRα/β/α-SMA
25 μm
PDGFRα/β
α-SMA
C
+ ad-GFP
"IL-33 WT"
+/- PDA CM
Harvest RNA & Protein
24h
Il33^f/f-eGFP
Fibroblasts
+ ad-Cre
"IL-33 KO"
%Collagen⁺ Area per FOV
0.1057
%Pdgfrα/β⁺ Area per FOV
0.4457
%α-SMA⁺ of Pdgfrα/β⁺ Area
0.5716
E
IL-33 KO vs WT: DMEM
IL-33 KO vs WT: +PDA CM
"TGF_BETA_SIGNALING"
"TNFA_SIGNALING_VIA_NFKB"
enrichment score
rank
FDR = 0.88
NES = -0.59
FDR = 0.60
NES = -1.15
FDR = 0.85
NES = -0.90
FDR = 0.64
NES = 0.88
D
WT #1
WT #20
KO #14
KO #16
+PDA CM
IL-33
Vinculin
Average Expression
Percent Expressed
F
Cell Proliferation
GFP 20
KO 16
GFP 20 + CM
KO 16 + CM
Relative Luminescence
days
G
apCAF
myCAF^hi, apCAF^lo
myCAF
myCAF^hi, iCAF^lo
iCAF^hi, myCAF^lo
iCAF
Cre;Il33^f/f
Cre
Col1a1
Col1a2
C3
Ptn
Tnxb
Postn
Cxcl5
Cxcl12
Igf1
Vegfd
Ccl21
Gdf10
Kng2
Thbs1
Mif
Spp1
Tnc
Ncam1
Cxcl1
Cxcl2
Vegfa
Cx3cl1
Tgfb1
Il1b
CreER^T2/+ Signature
CreER^T2/+;Il33^f/f Signature

Figure S4: Loss of stromal IL-33 alters the ST2^{+} immune cell secretome, resulting in a shift in CAF differentiation. (A) Expression of *Areg* and *Egfr* across cell types in the *CreER* and *CreER;Il33$^{f/f}$* scRNAseq datasets. (B) Immunostaining of *CreER* and *CreER;Il33$^{f/f}$* tumors. Top = Gomori trichrome staining, bottom = Co-IF staining of PDGFRα/β (green), α-SMA (magenta), and DAPI (blue); arrows denote representative PDGFRα/β^{+} α-SMA^{+} cells (yellow) or PDGFRα/β^{+} α-SMA^{-} cells (white). (C) Diagram depicting generation and treatment of IL-33 WT and IL-33 KO fibroblast lines. (D) Protein expression from fibroblasts in (C). (E) GSEA enrichment plots from bulk RNAseq of fibroblasts from (C). (F) Proliferation of IL-33 WT and KO fibroblasts with and without PDA CM treatment. (G) Gene expression of differentially expressed ligands from **Figure 3H** grouped by CAF subtype and split by experimental group. For staining quantification, each dot represents one animal, and values were compared using two-tailed Student's *t* test. Histogram data are mean ±standard deviation.