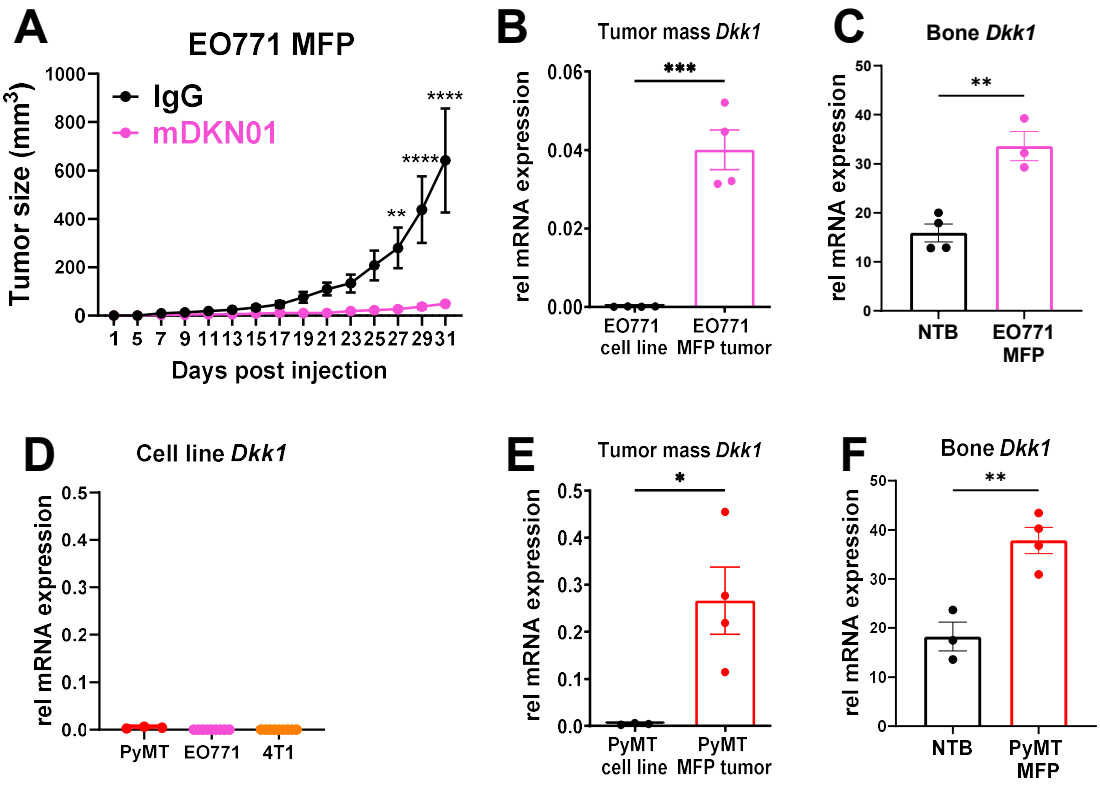
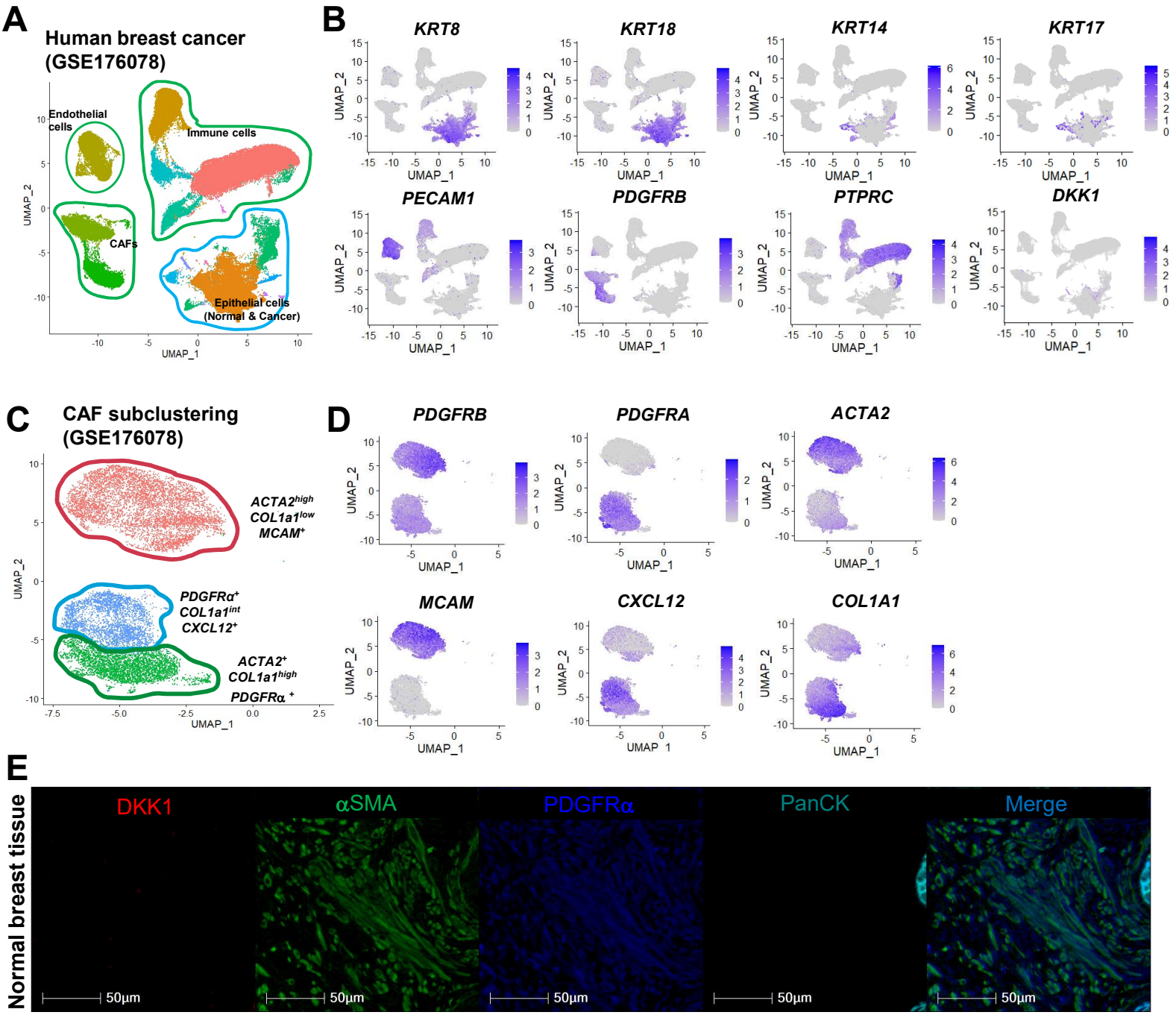
Supplementary Figure 1.



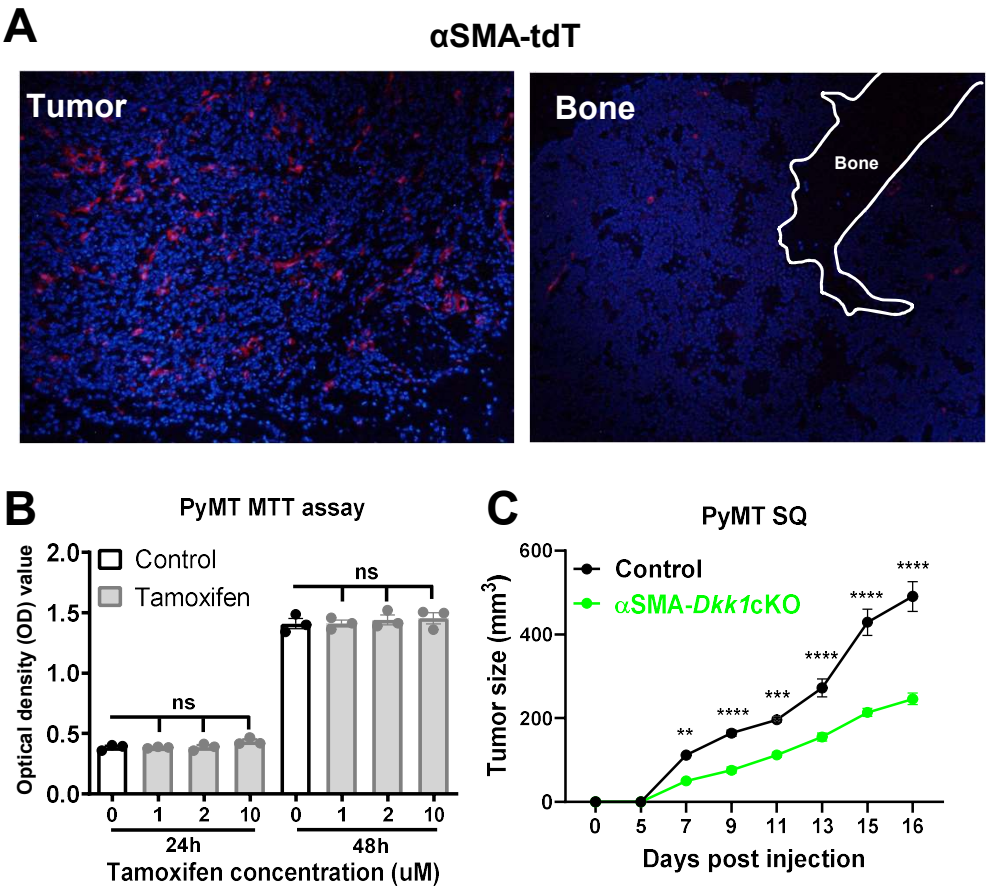
(A) WT mice were inoculated with EO771 (n=4 mice/group) and received mDKN01 (10mg/kg) or control IgG antibody i.p. every other day. Tumor growth was determined by caliper measurements. (B-F) *Dkk1* expression was measured in the primary tumors (B, E), tumor cell lines (D) and bones of no tumor and tumor bearing mice (C, F). Two-way ANOVA followed by Bonferroni multiple-comparison test was used to determine significance in (A), Unpaired t-test for (B-F). * $P < 0.05$, ** $P < 0.01$, **** $P < 0.0001$.

Supplementary Figure 2.



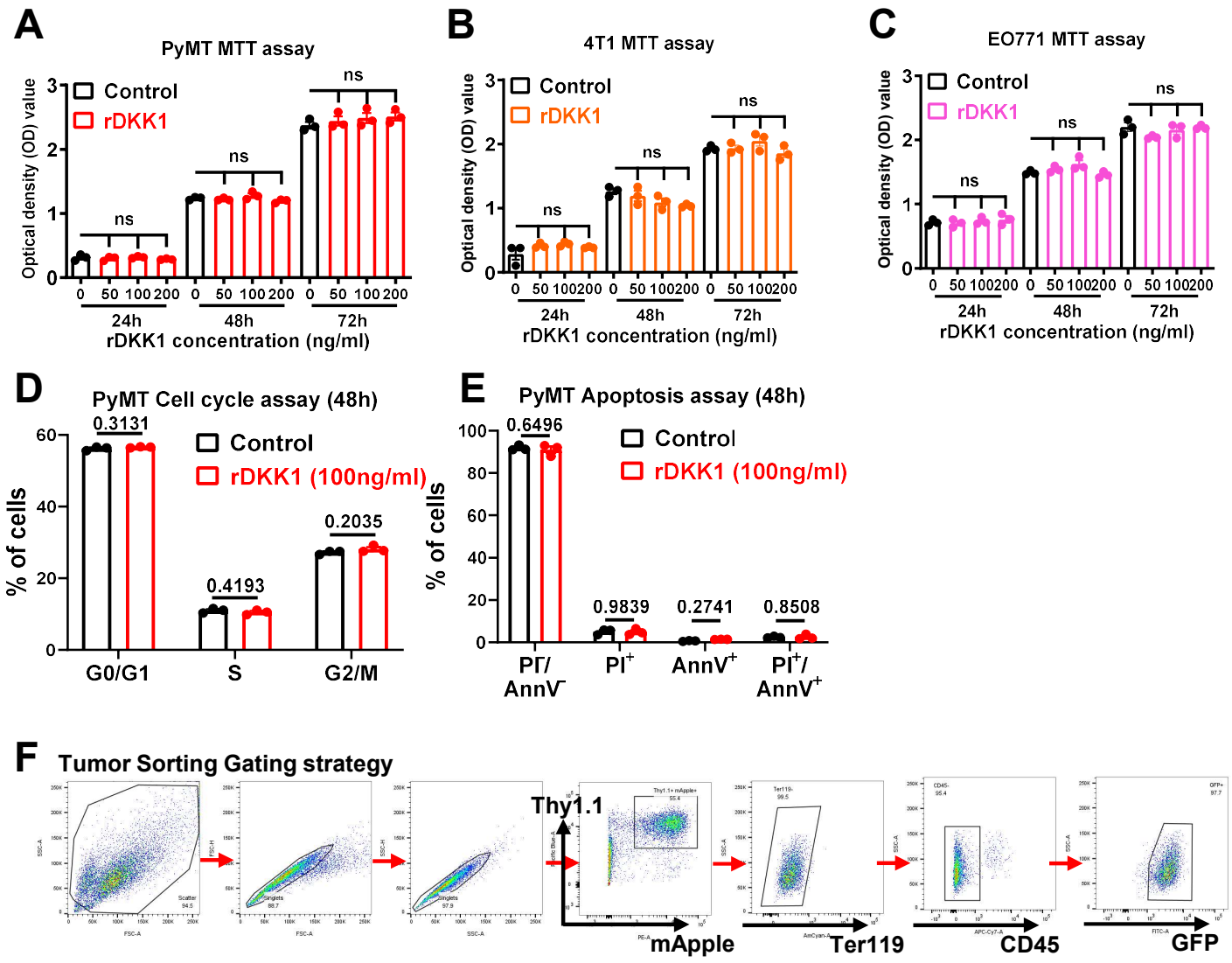
(A, B) UMAP visualization of cell types in human breast cancer (GSE176078). (C, D) UMAP visualization of CAF subset clusters. (E) Multiplex immunohistochemistry of human terminal duct lobular unit in normal breast tissue stained for DKK1 (red), αSMA (green), PDGFRα (blue) and panCK (cyan).

Supplementary Figure 3.



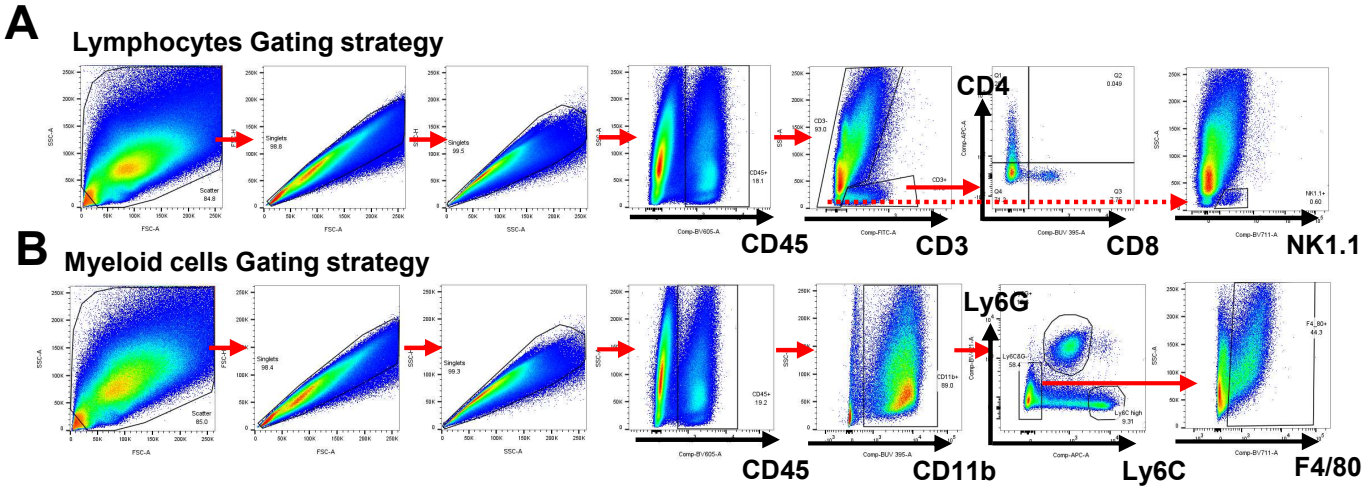
(A) Immunofluorescence analysis of tdT^+ cells (red) and total cells stained with DAPI (blue) from orthotopic PyMT tumors and from bones in 12 weeks old αSMA-tdT mice, receiving tamoxifen at time of tumor inoculation. Trabecular bone depicted by white contour. (B) MTT analysis in PyMT cells stimulated with indicated concentrations of tamoxifen for indicated amount of time. (C) Tumor growth was determined by caliper measurements in 10-12 weeks old, male αSMA-*Dkk1*cKO mice and controls injected with tamoxifen for 5 consecutive days (100mg/kg) starting from the day of subcutaneous PyMT tumor inoculation (n= 5, 8 mice/group). Tumor progression was determined by caliper measurements. Results represent mean +/- SEM. Ordinary one-way ANOVA followed by Dunnett's multiple-comparison test (B), Two-way ANOVA followed by Bonferroni multiple-comparison test was used to determine significance (C) ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$.

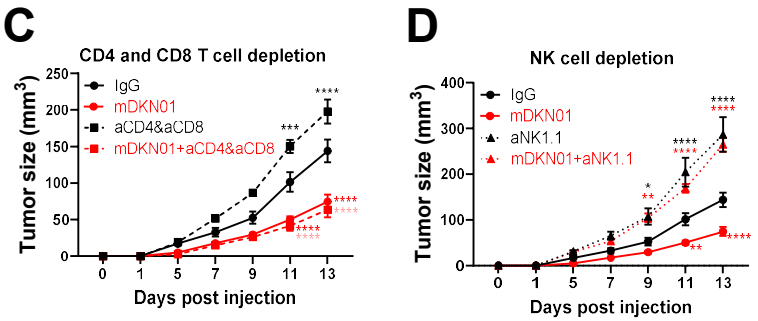
Supplementary Figure 4.



(A-C) MTT analysis in PyMT, (A), 4T1 (B), and EO771 (C) cells stimulated with indicated concentrations of recombinant DKK1 (rDKK1). (D, E) cell cycle and apoptosis analyses in PyMT cells stimulated with indicated concentrations of recombinant DKK1 (rDKK1) for indicated times. Apoptotic cells were analyzed based on positivity for Propidium Iodide (PI) and Annexin V (AnnV). (F) Gating strategies for sorting PyMT-BO1-GFP-fluc-H2B-mApple-Thy1.1 tumor cells injected in the MFP of WT mice. Results represent mean +/- SEM. Ordinary one-way ANOVA followed by Dunnett's multiple-comparison test (A-C), Unpaired t-test (D, E).

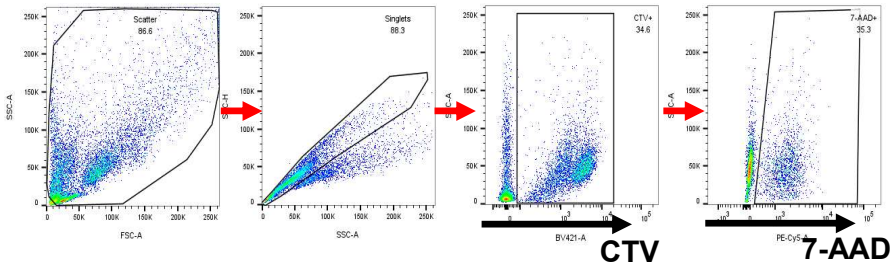
Supplementary Figure 5.





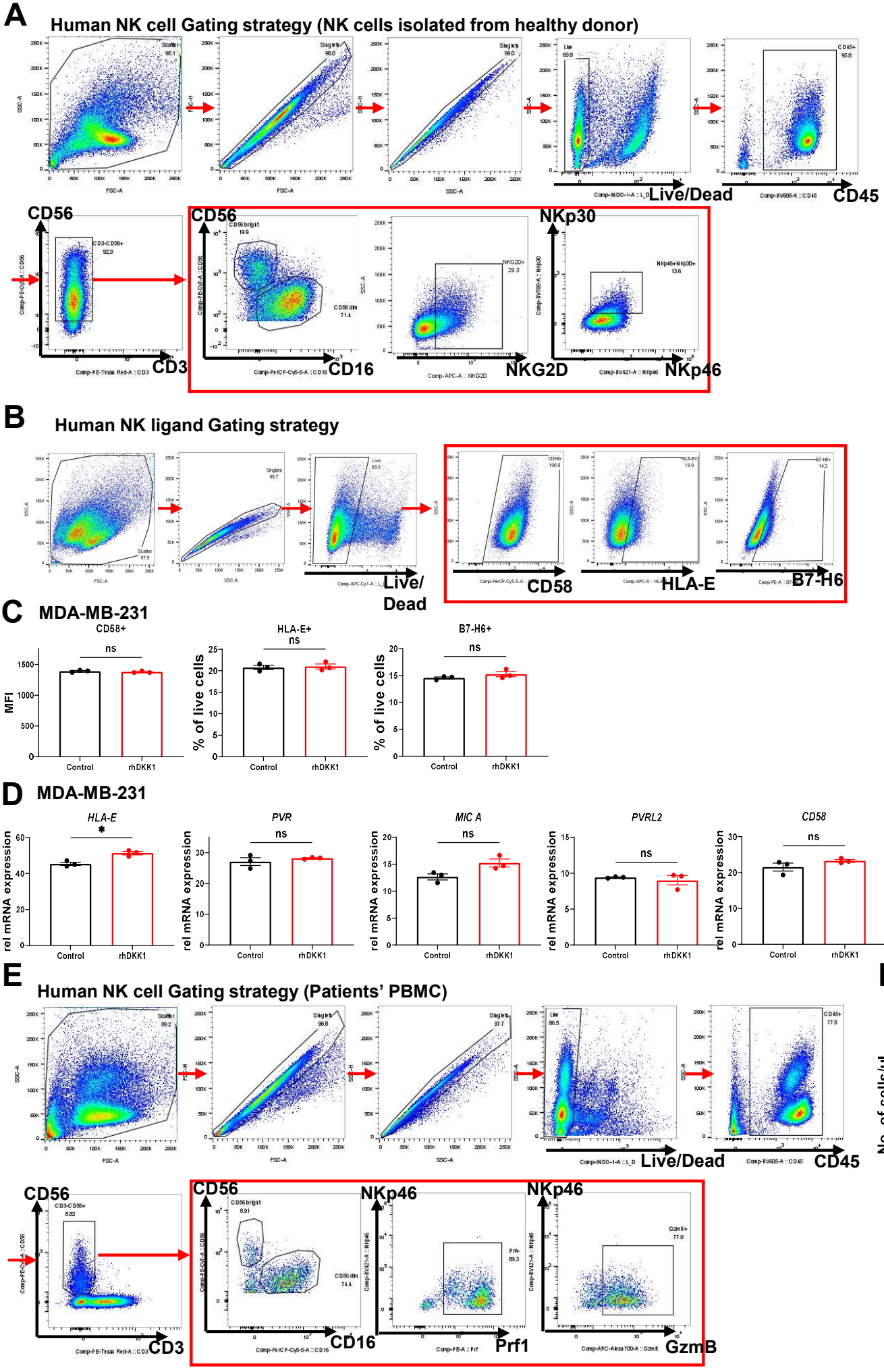
(A, B) Gating strategies for profiling lymphocytes (A) and myeloid cells (B). (C, D) PyMT orthotopic tumor curve determined by caliper measurements in 6-8 weeks WT female mice treated with mDKN01 (10mg/kg) or control IgG antibody every other day along with anti-CD4 and anti-CD8 (C) or NK1.1 (D) (n= 4-9 mice/group). Results represent mean +/- SEM. Two-way ANOVA followed by Bonferroni multiple-comparison test was used to determine significance. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$.

Supplementary Figure 6.



Gating strategies for analyzing Percent Specific Killing of target cells mediated by NK cells.

Supplementary Figure 7.



Supplementary Figure 7.
(A, B) Gating strategies for profiling human NK cells isolated from healthy donor peripheral blood (A) and NK cell ligand expression on MDA-MB-231 cells (B). (C) Quantification of NK ligand expression on MDA-MB-231 cells measured by flow cytometry after 4 hours of incubation with rhDKK1 (200ng/ml). (D) qRT-PCR for NK cell activating/ inhibitory ligand expression in MDA-MB-231 cells after stimulation with rhDKK1 (200ng/ml) for 24 hours. (E) Gating strategies for profiling human NK cells from patient's peripheral blood mononuclear cells. (F) Number of NK cells in blood in patients with regressive/stable (blue) versus progressive bone metastases (red) from initial diagnosis (abbreviated as I) and follow-up visits (abbreviated as F). Results represent mean +/- SEM. Unpaired t-test (C, D) and paired t-test (F) were used to determine significance. * $P < 0.05$.