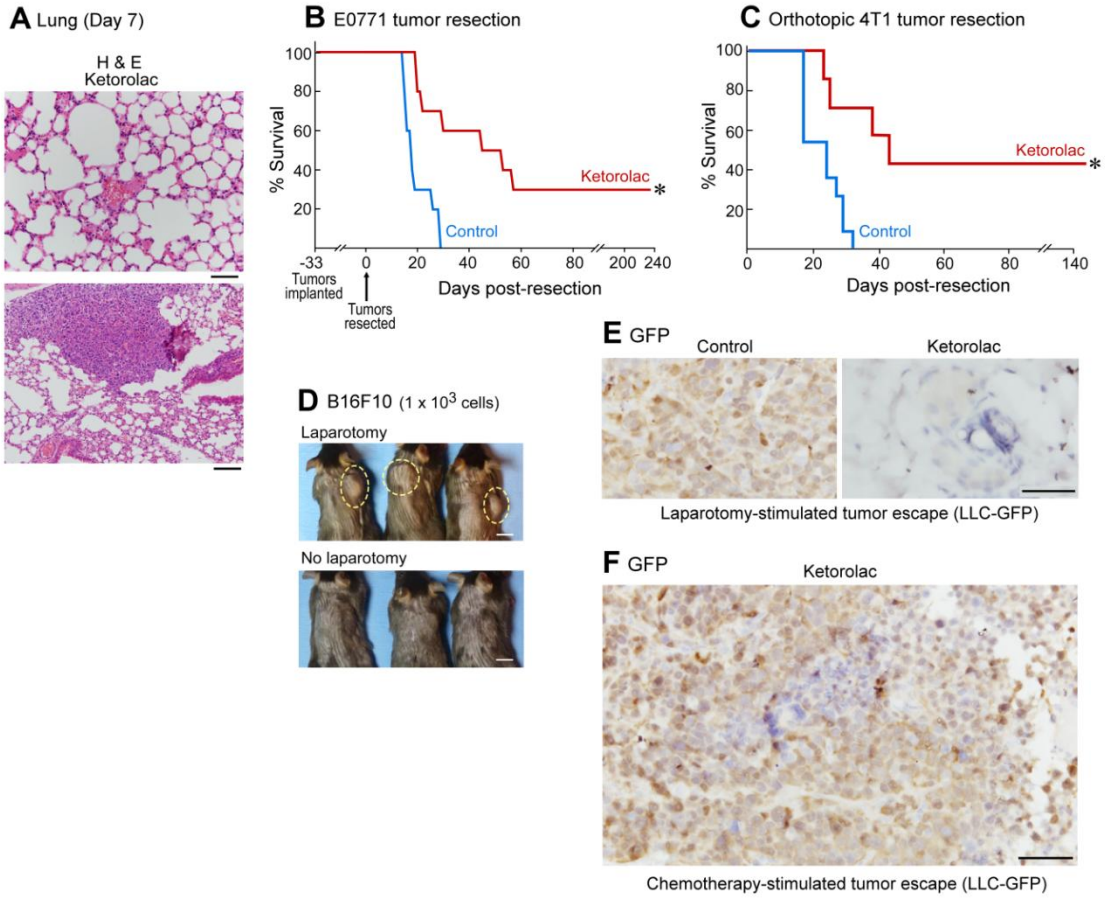

Figure S1. Pre-operative ketorolac eradicates micrometastases and promotes long-term survival in multiple tumor resection models.

(A) H&E staining of lungs from pre-operative ketorolac-treated mice 7 days post-LLC tumor resection with non-detectable (top) or detectable (bottom) LLC tumor cells. n=5 mice/group. Scale bar: 50 μm. **(B)** Pre-operative ketorolac on survival of female C57BL/6J mice in a spontaneous E0771 breast cancer metastasis model after orthotopic tumor resection. n=10 mice/group. *p<0.05 ketorolac vs. control. **(C)** Pre-operative ketorolac on survival of female BALB/cJ mice after orthotopic 4T1 breast cancer resection. n=7-12 mice/group. *p<0.05 ketorolac vs. control. **(D)** Images of representative mice injected with 10^3 B16F10 subjected to laparotomies (day 0 and 21 post-injection) (top) or no laparotomy (bottom) on day 35 post-injection. n=3 mice/group. Dashed circles indicate macroscopic tumors. Scale bar: 1 cm. **(E)** Immunohistochemistry analysis of GFP-labeled tumor cells (brown DAB staining) in control or pre-operative ketorolac-treated mice injected with 10^4 LLC-GFP tumor cells and subjected to a laparotomy. Laparotomy was performed on day of injection. Images were taken of sections harvested from the tumor implantation site 38 days post-injection. Scale bar: 50 μm. n=4-5 mice/group. **(F)** Immunohistochemistry analysis of GFP-labeled tumor cells (brown DAB staining) in mice injected with 10^4 LLC-GFP tumor cells and treated with ketorolac and chemotherapy. Systemic chemotherapy (cisplatin) initiated on day of tumor cell injection. Ketorolac was administered the day before, day of, and day after chemotherapy. Images were taken of sections from the tumor implantation site on day 30 post-injection. Scale bar: 50 μm. n=4 mice/group.

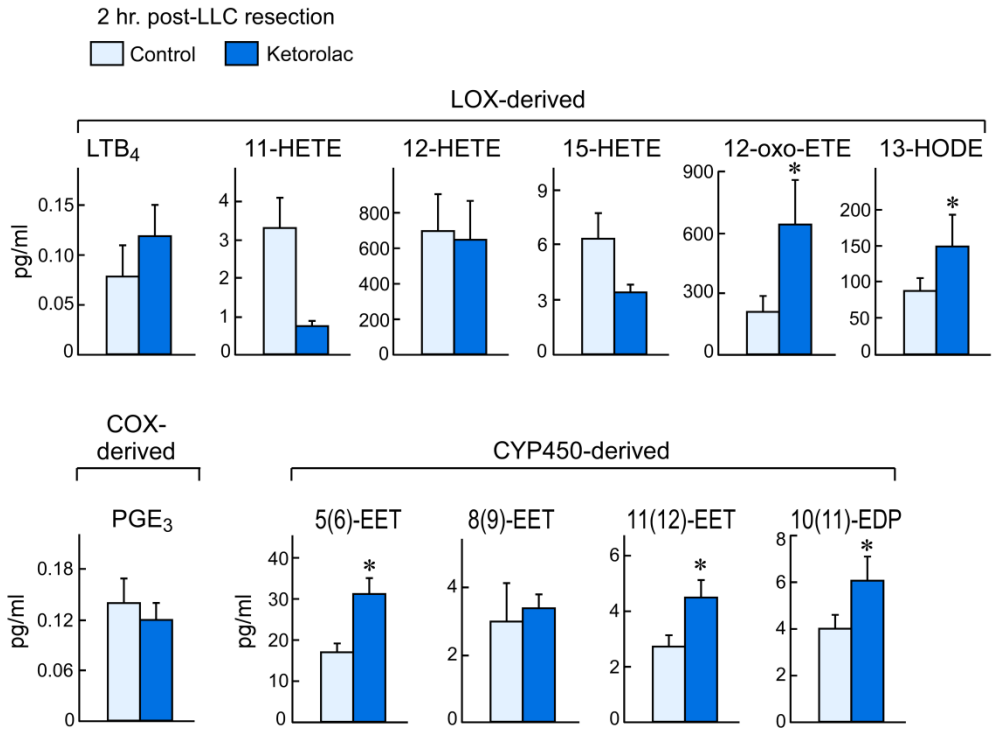

Figure S2. Pre-operative ketorolac induced shunting of the arachidonic acid cascade to the LOX and CYP pathways.

LC-MS/MS-based oxylipin profiling of plasma 2 hours post-LLC tumor resection from pre-operative ketorolac-treated or control mice. n= 5-6 mice/group. *p<0.05 vs. control.

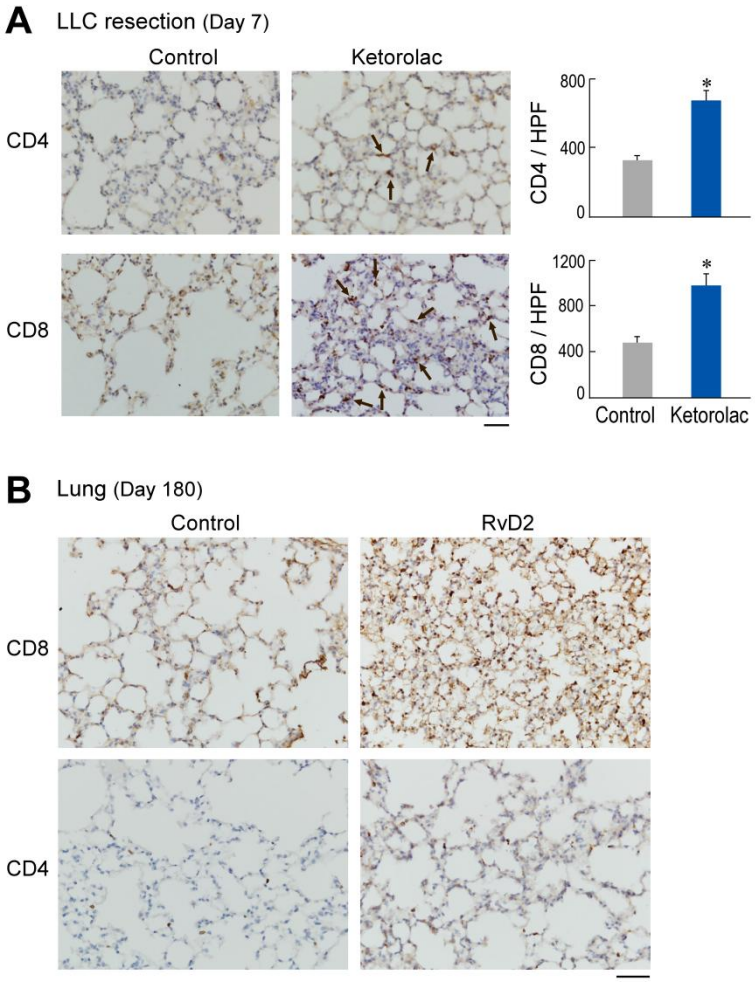

Figure S3. Resolvins increase anti-tumor immunity.

(A) Immunohistochemistry analysis of CD4 and CD8 cells in lungs from pre-operative ketorolac-treated or control mice on day 7 post-LLC tumor resection. n=4-5 mice/group. Arrows indicate brown DAB staining for CD4+ or CD8+ cells. Scale bar: 100 μm. Immune cell quantification is represented as means ± SEM. *p<0.05 vs. control. **(B)** Immunohistochemistry analysis of CD4 and CD8 cells (brown DAB staining) in lungs from pre-operative RvD2-treated mice on day 180 post-LLC tumor resection or age-matched naïve mice. n=5-6 mice/group. Scale bar: 100 μm.

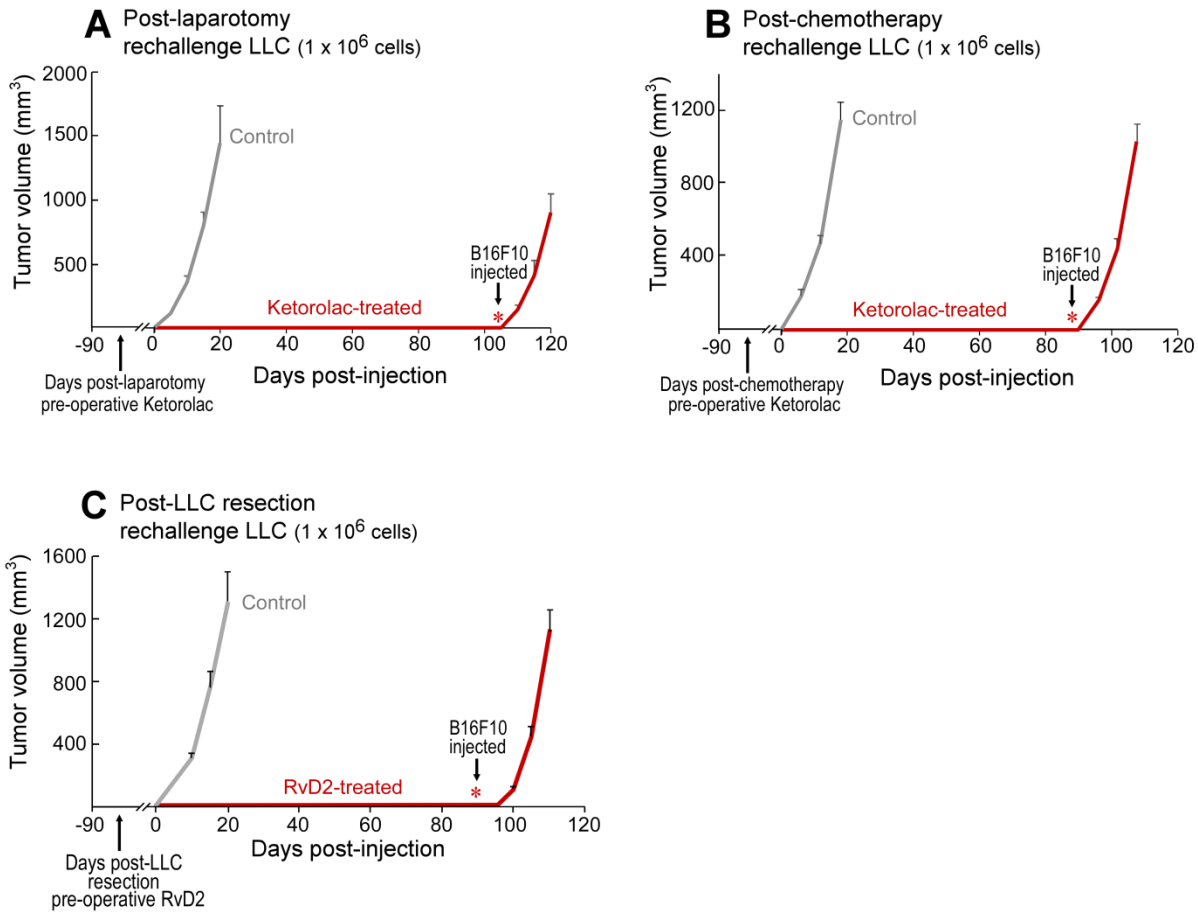

Figure S4. Ketorolac restores anti-tumor immunity after surgery or chemotherapy.

Long-term surviving pre-operative ketorolac-treated mice injected with a subthreshold inoculum of 10^4 LLC at 90 days **(A)** post-laparotomy or **(B)** post-chemotherapy (e.g., cisplatin) were injected with LLC (10^6 cells) (red) and compared to naïve control mice (gray). Ketorolac-treated mice were injected 90 days later with B16F10 (10^6 cells). n=4-12 mice/group. *p<0.05 vs. control. **(C)** Long-term surviving pre-operative RvD2-treated mice at 90 days post-LLC tumor resection (n=3/5 mice) were injected with LLC (10^6 cells) (red) and compared to naïve control mice (n=5 mice; gray). Ninety days later, RvD2-treated mice were injected with B16F10 (10^6 cells). *p<0.05 vs. control.

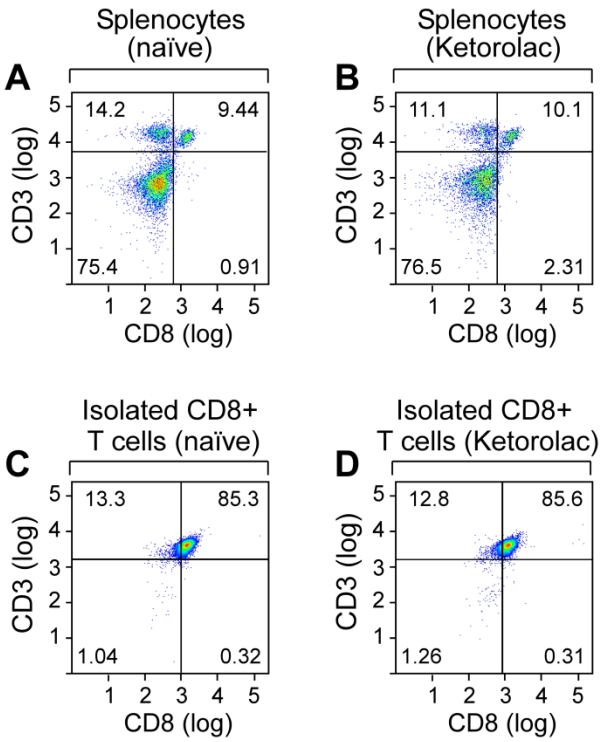

Figure S5. Characterization of T cells in spleens from pre-operative ketorolac-treated long-term survivors post-LLC resection vs. naïve control mice.

FACS analysis of total splenocytes from **(A)** naïve or **(B)** pre-operative ketorolac-treated long-term survivors post-LLC resection stained for CD3 and CD8. FACS analysis of isolated CD8+ T cells from total splenocytes of **(C)** naïve or **(D)** pre-operative ketorolac-treated long-term survivors post-LLC resection stained for CD3 and CD8. Panels A-D are derived from the same experiment. n=3-4 mice/group.

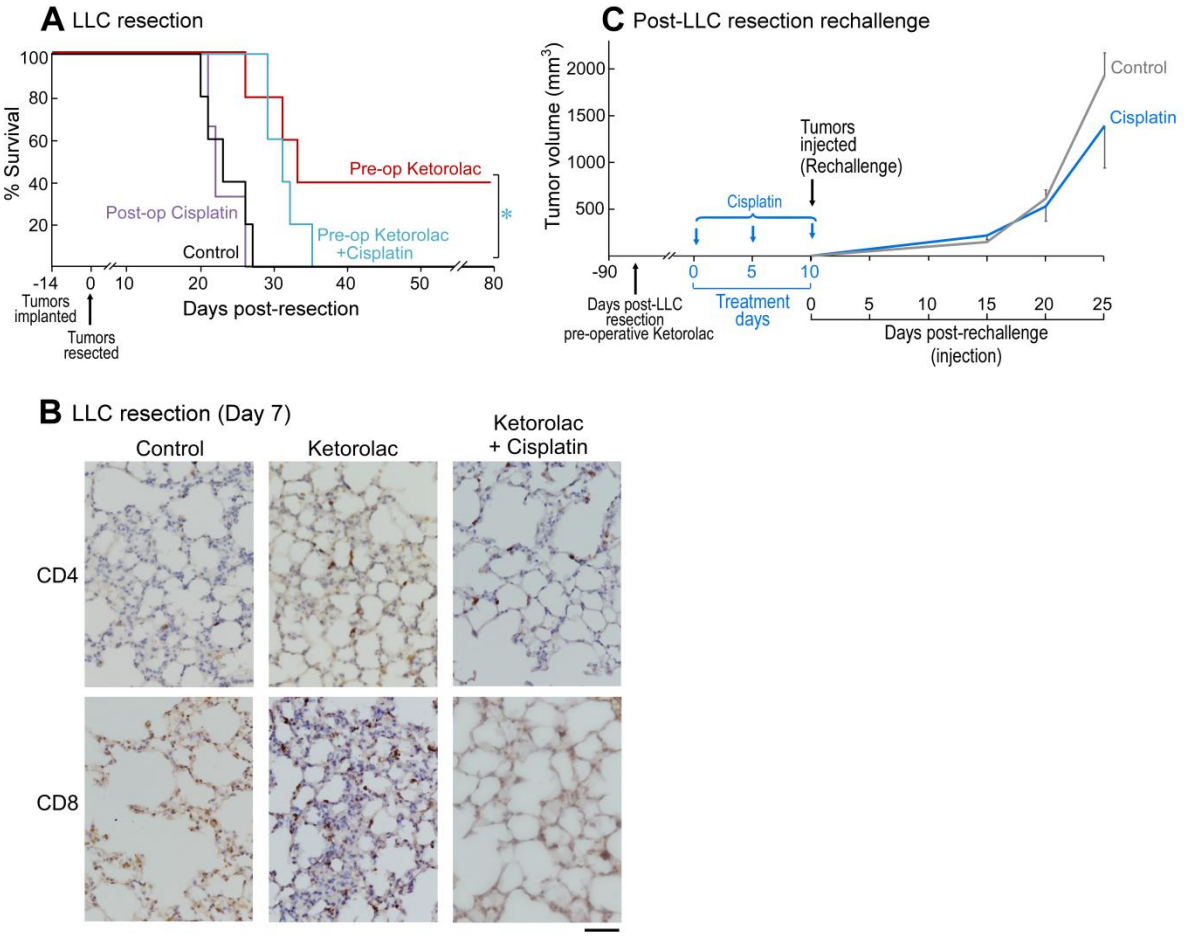

Figure S6. Adjuvant chemotherapy disrupts ketorolac-induced tumor-specific anti-tumor immunity.

(A) Pre-operative ketorolac and/or post-operative cisplatin on survival post-LLC tumor resection. Cisplatin (5 mg/kg) was administered 7 days post-LLC tumor resection. n=5 mice/group. *p<0.05 ketorolac and cisplatin vs. ketorolac. **(B)** Immunohistochemistry analysis of CD4+ and CD8+ T cells (brown DAB staining) in lungs from mice treated with control or pre-operative ketorolac with and without cisplatin on day 7 post-LLC tumor resection. n=4-5 mice/group. Scale bar: 100 μm. Control and ketorolac (CD4 and CD8) panels are taken from the same experiment presented in Figure S3A. **(C)** Growth of LLC (10^6 cells) in long-term surviving pre-operative ketorolac-treated mice at 90 days post-LLC resection administered 3 cycles of cisplatin (5 mg/kg q 5 days) prior to rechallenge with LLC vs. age-matched naïve control mice. n=3-5 mice/group.

Category	Name	Ketorolac z-score	Control z-score
Pathway	Triacylglycerol biosynthesis	-1.342	2.000
Functions	Lipid secretion	-2.476	1.766
	Carbohydrate metabolism	-1.484	2.594
	Triacylglycerol metabolism	-1.334	2.190
	Lipid synthesis	-0.882	2.546
	Fatty acid metabolism	-0.880	2.201
	Cell death	2.759	-0.687
	Organismal death	3.825	-5.193

Supplementary Table 1. Pathway and functions enrichment analysis of genes that are significantly dysregulated in Ly6G+ granulocytes from control and ketorolac-treated samples. Table depicts the activation (positive z-score) or inhibition (negative z-score) of selected pathways/functions in the control and ketorolac-treated T cell clusters. The z-scores of pathways and functions were calculated using ingenuity pathways analysis systems.