

Supplemental Figure S1:

- (A) Individual mouse curves in B78 model: Combined individual mouse tumor volume plots, corresponding to data presented in Figure 1A-B, in the B78 model showing each mouse's tumor growth from the two independent experiments along with the percentage of mice from each group that demonstrated a complete response to treatment.
- (B) Percent mice rejecting B78 rechallenge: Mice cured of their initial tumor burden in the experiments corresponding with Figure 1A-B were rechallenged with a second intradermal injection of B78 melanoma cells. The percentage of mice that rejected rechallenge tumor growth, thereby demonstrating anti-tumor immune memory is shown.
- (C) Individual mouse curves in 4T1 model: Combined individual tumor volume plots, corresponding to data presented in Figure 1E-F, in the 4T1 model showing each mouse's tumor growth from two independent experiments along with the percentage of mice from each group that demonstrated a complete response to treatment.
- (D) Individual mouse curves in MOC2 model: Combined individual tumor volume plots, corresponding to data presented in Figure 1C-D, in the MOC2 model showing each mouse's tumor growth from two independent experiments along with the percentage of mice from each group that demonstrated a complete response to treatment.

Supplemental Figure S2: Gating strategy used to analyze immune cell components of spleen.

Gating strategy used in FlowJo to analyze flow cytometry results on splenocytes harvested from tumor bearing mice five days after RT or no RT.

Supplemental Figure S3: Gating strategy used to analyze tumor immune cell infiltrates.

Gating strategy used in FlowJo to analyze flow cytometry results on TILs harvested from mice 14 days after the start of the experiment (i.e. RT d. 0).

Supplemental Figure S4: Peripheral blood analysis confirming *in vivo* immune cell depletion.

Flow cytometry results showing immune cell proportions from peripheral blood evaluated 13 and 34 days after the start of treatment, for mice treated with anti-NK or anti-T cell depleting antibodies or with a control, IgG antibody, demonstrating successful, antibody-specific depletion of NK cells and T cells. Two-way Anova analysis was done to compare depletion effectiveness between groups.

Supplemental Figure S5: NK cell depletion does not impact long term immune memory response in the B78 model.

Corresponding with the data presented in Figure 3A-B, mice cured of their initial tumor burden were rechallenged with a second intradermal injection of B78 melanoma cells. The percentage of mice that rejected rechallenge tumor growth and demonstrated tumor specific immune memory is shown.

Supplemental Figure S6: RT+BEMPEG in TCR alpha KO Mice.

RT+BEMPEG is less effective against B78 tumors in TCR alpha KO mice than in WT C57BL/6 mice

Supplemental Figure S7:

(A) RT+BEMPEG demonstrates superior tumor control over RT+IT IL-2.

Average tumor volume plots (+/- standard error of the mean) from two separate experiments showing group tumor growth following treatment with RT (blue), RT+IT IL-2 (red), or RT+BEMPEG (purple). Survival data from these two experiments together with the data from a similar experiment shown Figure 4A are included in aggregate in Figure 4B. P values calculated using time weighted average analysis. *, $P \leq 0.05$; ** $P \leq 0.01$; *** $P \leq 0.001$;

(B) Individual mouse tumor curves of RT+BEMPEG and RT+IT IL-2 in the B78 model.

Combined individual tumor volume plots from 3 independent experiments, corresponding with the tumor growth data presented in Figure 4A and Figure S7a, in the B78 model showing each mouse's tumor growth from three independent experiments along with the percentage of mice from each group that demonstrated a complete response to treatment.

Supplemental Figure S8: Individual mouse tumor curves in 400 mm³ B78 model.

Combined individual tumor volume plots, corresponding with data presented in Figure 5A-B, in the 400 mm³ B78 model showing each mouse's tumor growth from two independent experiments along with the percentage of mice from each group that demonstrated a complete response to treatment.

Supplemental Figure S9: Individual mouse tumor curves in 1,000 mm³ B78 model.

Combined individual tumor volume plots, corresponding with data presented in Figure 5C-E, in the 1,000 mm³ B78 model showing each mouse's tumor growth from two independent experiments along with the percentage of mice from each group that demonstrated a complete response to treatment.

Supplemental Figure S10: Individual mouse tumor curves of RT+BEMPEG+CTLA-4 in B78 primary with B16 metastases model.

Combined individual tumor plots, corresponding with data presented in Figure 6A-C, in the B78 primary B16 metastasis model showing each mouse's flank tumor growth from two independent experiments along with the percentage of mice from each group that demonstrated a complete response to treatment

Supplemental Figure S11: Individual mouse tumor curves of RT+BEMPEG+CTLA-4 in 4T1 model.

Combined individual tumor plots, corresponding with data presented in Figure 7A-B, in the 4T1 model showing each mouse's tumor growth from two independent experiments along with the percentage of mice from each group that demonstrated a complete response to treatment.

Supplemental Figure S12: Individual mouse curves of RT+BEMPEG+PD-L1 in MOC2 model.

Combined individual tumor plots, corresponding with data presented in Figure 7C-D, in the MOC2 model showing each mouse's tumor growth from two independent experiments along with the percentage of mice from each group that demonstrated a complete response to treatment.

Supplemental Figure S13: Anti-tumor effect of RT+BEMPEG+anti-CTLA-4 in B78 primary B16 metastasis model is T cell mediated.

IVIS imaging on d. 34 of an experiment testing the effect of T cell depletion while treating with RT+BEMPEG+anti-CTLA-4 in the B78 primary, B16 metastasis model. Colorful signals indicated the presence of growing B16 luciferase positive cells.