**Supplemental Figures**

**Title: IL-12-producing cytokine factories induce precursor exhausted T cells and elimination of primary and metastatic tumors**

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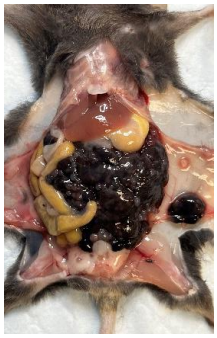

**Fig. S1 – B16LN6 melanoma cells spread rapidly and develop into large tumors when injected into the peritoneal cavity of C57BL/6 mice.** Macroscopic image of the peritoneal cavity of mice inoculated with 1e5 B16LN6 cells and left untreated for 14 days.

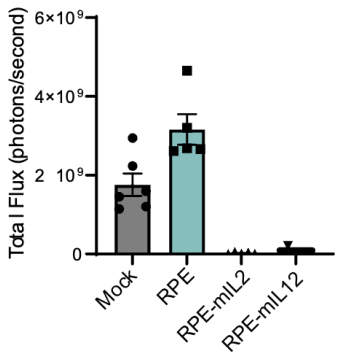


**Fig. S2 – Administration of RPE-mIL12 or RPE-mIL2 reduced IP tumor burden in mice bearing Pan02 tumors.** Total flux (photons/s) quantified from luminescent images acquired 5 days post-treatment and plotted as means ± SEM.

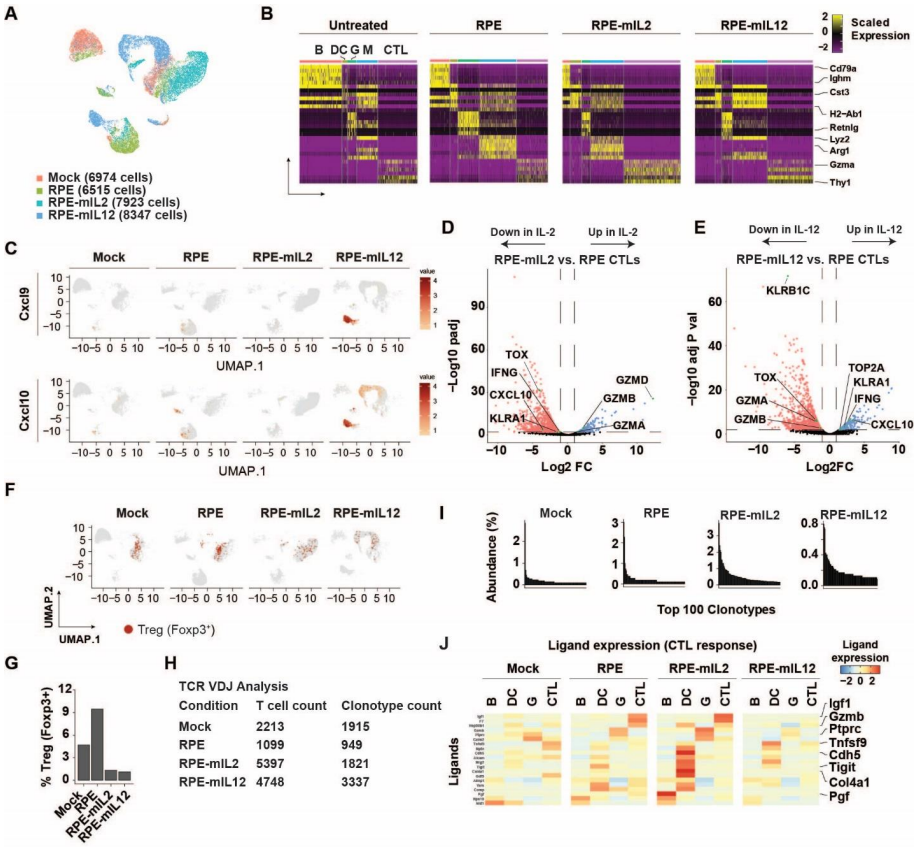


**Fig. S3 – Administration of RPE-mIL2 acts on distinctive cytotoxic lymphocyte populations compared to RPE-mIL12. A)** UMAP embedding of individual cells colored by type of RPE capsule administered. **B)** Single-cell transcriptional profiles clustered into groups by k-means clustering. B, B cells; DC, dendritic cells; G, granulocytes; M, macrophages; CTL, cytotoxic lymphocytes (T and NK cells). **C)** Expression of CTL-recruiting chemokines CXCL10 and CXCL9 across cell types. Gene expression changes in CTLs recruited to **D)** RPE-IL2 or **E)** RPE-IL2-treated tumors versus RPE capsule control. **F)** $T_{reg}$ cells ($Foxp3^{+}$) across conditions. **G)** Percent of total CTLs that are $T_{reg}$ cells across conditions. **H)** Total number of T cells and TCR clonotypes found in each condition. **I)** Relative abundance of the top 100 most abundant BCR clonotypes for each condition. **J)** NicheNet analysis of the expression of CTL-interacting ligands enriched in RPE-IL2 across immune cell types.

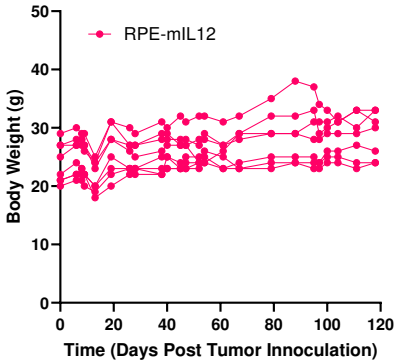


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**Fig. S4 – RPE-mIL12 is well tolerated for 120 days in the intraperitoneal cavity of mice bearing PAN02 tumors.** Body weight of individual C57BL/6 mice (n=8) bearing PAN02 tumor treated with RPE-mIL12 over time.

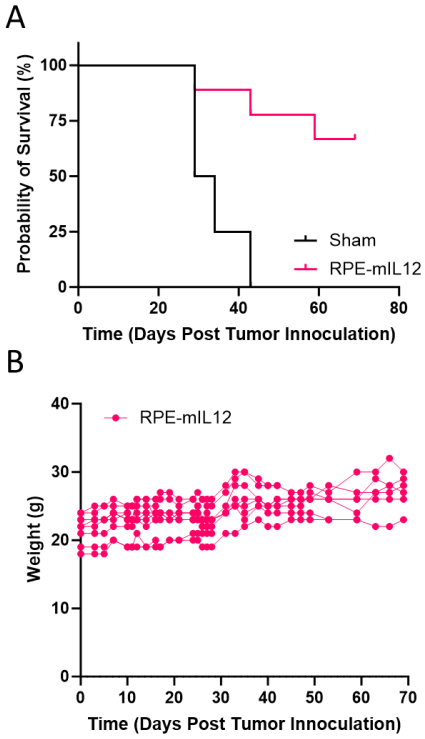


**Fig. S5 – RPE-mIL12 is well tolerated in the intraperitoneal cavity and significantly extends the survival of C57BL/6 mice bearing MC38 tumors.** A. Survival curves (n = 8) depicted as percent survival over time in days after tumor inoculation. Comparison of survival curves was done using the log-rank, Mantel-Cox test. B. Body weight of individual C57BL/6 mice (n=8) bearing MC38 tumors treated with RPE-mIL12 over time.

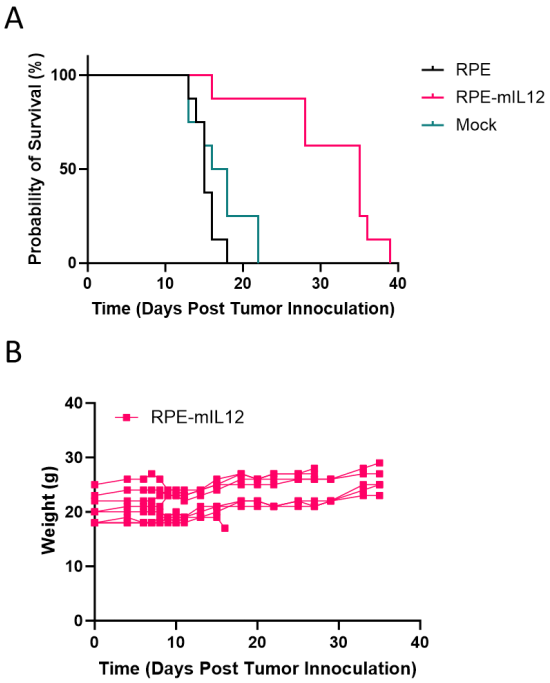


**Fig. S6 – RPE-mIL12 monotherapy treatment is well tolerated and extends the survival of C57BL/6 mice with metastatic melanoma in the peritoneal cavity**. A. Survival curves (n = 8) depicted as percent survival over time in days after tumor inoculation. Comparison of survival curves was done using the log-rank, Mantel-Cox test. B. Body weight of individual C57BL/6 mice (n=8) bearing B16LN6 tumors treated with RPE-mIL12 over time.

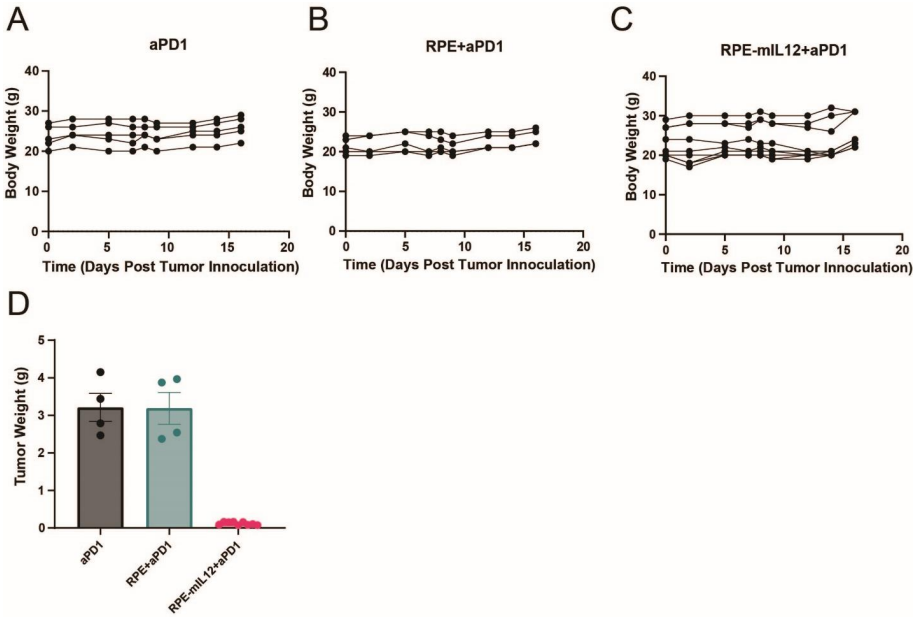


**Fig. S7 – RPE-mIL12+aPD1 treatment is well tolerated and reduces tumor burden in C57BL/6 mice with metastatic melanoma in the peritoneal cavity.** A-C. Body weight of individual C57BL/6 mice bearing B16LN6 tumors treated with aPD1 (n=4), RPE+aPD1(n=4), or RPE-mIL12 (n=8) over time. D. Tumor weight from individual mice one week after treatment with cytokine factories. Tumors were weighted using an analytical balance.