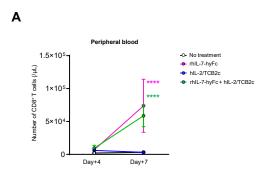
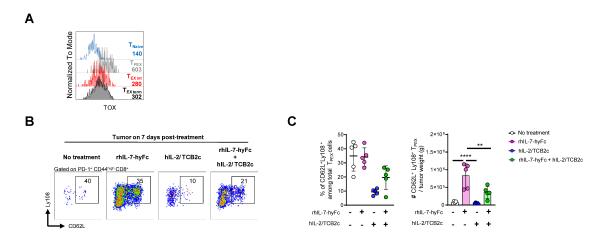
## **Supplemental Figure 1**



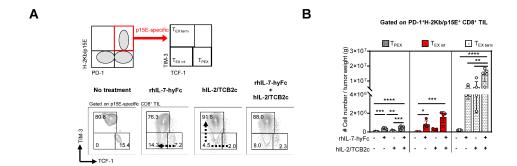
## Supplemental Figure 1. Peripheral blood CD8<sup>+</sup> T cells from multiple groups of tumor-bearing mice. (A) Absolute counts of total CD8<sup>+</sup> T cells in peripheral blood at the indicated date post treatment (n=5 per group). The asterisk (\*) expresses significance compared to the non-treated control. Data are expressed as mean $\pm$ SD and analyzed by one-way ANOVA with Tukey's multiple comparisons test. Statistical significance is indicated as \*p<0.05, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001.

## **Supplemental Figure 2**



Supplemental Figure 2. Characteristics of CD8+  $T_{PEX}$  in the tumor microenvironment. (A) Representative histograms showing TOX protein amounts in  $T_{Naive}$ ,  $T_{PEX}$ ,  $T_{EX int}$ , and  $T_{EX term}$  among CD8+ TIL from non-treated MC38 tumors. The numbers in histograms indicate the geometric MFI of TOX. (B) Representative flow cytometry plots of CD62L+Ly108+ $T_{PEX}$  among PD-1+CD44highCD8+ TILs isolated from MC38 tumor on 7 days post-treatment. (C) Percentages (left panel) and absolute numbers (right panel) of CD62L+Ly108+ $T_{PEX}$ . Absolute numbers were normalized to tumor weight in the four groups. Data are presented as mean  $\pm$  SD (n = 5 per group) and analyzed by one-way ANOVA with Tukey's multiple comparisons test. Statistical significance is indicated as \*p<0.05, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001.

## Supplemental Figure 3



Supplemental Figure 3. Phenotypic changes in p15E-specific CD8<sup>+</sup> T cells within MC38 tumors after treatments. (A) Representative flow cytometry plots and (B) counts of  $T_{PEX}$ ,  $T_{EX int}$ ,  $T_{EX term}$  among PD-1<sup>+</sup>p15E<sup>+</sup> CD8<sup>+</sup> TILs from MC38 tumors 7 days post-treatment. Intratumoral absolute numbers were normalized to tumor weight (g). The data are represented as the mean  $\pm$  SD (n = 5 in each group). Statistical significance is indicated as \*p<0.05, \*\*p<0.01, \*\*\*\*p<0.001, \*\*\*\*p<0.0001.  $T_{PEX}$ , progenitor exhausted T cell.  $T_{EX int}$ , intermediate exhausted T cell.  $T_{EX term}$ , terminally exhausted T cell.

Table S1. List of antibodies used for flow cytometry analysis

Antibody	Fluorochrome	Vendor	Cat No.	Clone	Final dilution	Location
CD16/CD32		BioLegend	101302	93	1:100	extracellular
Live dead Blue	UV	Invitrogen	L34962	fixable blue	1:500	intracellular- unfixed
CD45	BUV496	BD	749889	30-F11	1:250	extracellular
TCRβ	BV650	BioLegend	109251	H57-597	1:100	extracellular
CD3	BV650	BioLegend	100229	17A2	1:100	extracellular
CD4	APC/Fire 810	BioLegend	100480	GK1.5	1:250	extracellular
CD8α	Alexa Fluor 532	BD	58-0081-80	53-6.7	1:125	extracellular
CD11b	BV510	BD	562950	M1/70	1:125	extracellular
NK1.1	APC-eFluor780	invitrogen	47-5941-82	PK136	1:150	extracellular
CD62L	BUV395	BD	740218	MEL-14	1:150	extracellular
CD27	BUV661	BD	741518	LG3A10	1:100	extracellular
CD127	BUV737	BD	612841	SB/199	1:60	extracellular
CD28	BV421	Biolegend	102127	37.51	1:50	extracellular
CD352 (Slamf6)	Pacific Blue	Biolegend	134608	300-AJ	1:100	extracellular
CD183 (CXCR3)	BV480	BD	746651	CXCR3-173	1:25	extracellular
CD44	BV570	Biolegend	103037	IM7	1:150	extracellular
Ly-6A/E (Sca-1)	BV605	BD	563288	D7	1:70	extracellular
CD366 (TIM-3)	BV711	BD	747622	RMT3-23	1:60	extracellular
CD103	BV750	BD	747478	M290	1:80	extracellular
CD226	BV785	Biolegend	133611	Tx42.1	1:60	extracellular
Ly-6C	PerCP	Biolegend	128028	HK1.4	1:150	extracellular
CD195 (CCR5)	PerCP-e710	Invitrogen	46-1951-82	HM-CCR(7A4)	1:20	extracellular
H-2Kb-KSPWFTTL	PE	Immudex	JD3702-PE-150		1:20	extracellular
CD25	PE-Cyanine5	Invitrogen	15-0251-82	PC61.5	1:100	extracellular
CD39	PE-eFluor 610	Invitrogen	61-0391-82	24DMS1	1:100	extracellular
CD69	PE-cy7	BioLegend	104512	H1.2F3	1:60	extracellular
PD-1	APC	BioLegend	135210	29F.1A12	1:50	extracellular
TIGIT	APC-R700	BD	556474	1G9	1:60	extracellular
Ki-67	BV421	BioLegend	151208	11F6	1:250	intracellular
FoxP3	Pacific blue	BioLegend	126410	MF-14	1:125	intracellular
TCF-1	Alexa Fluor 488	Cell signaling	6444	C63D9	1:100	intracellular
Granzyme B	PE-Cyanine5.5	Invitrogen	GRB18	GB11	1:250	intracellular
TNF-α	APC	Invitrogen	17-7321-82	MP6-XT22	1:200	intracellular
IFN-γ	PE-Cyanine7	Invitrogen	25-7311-82	XMG1.2	1:200	intracellular