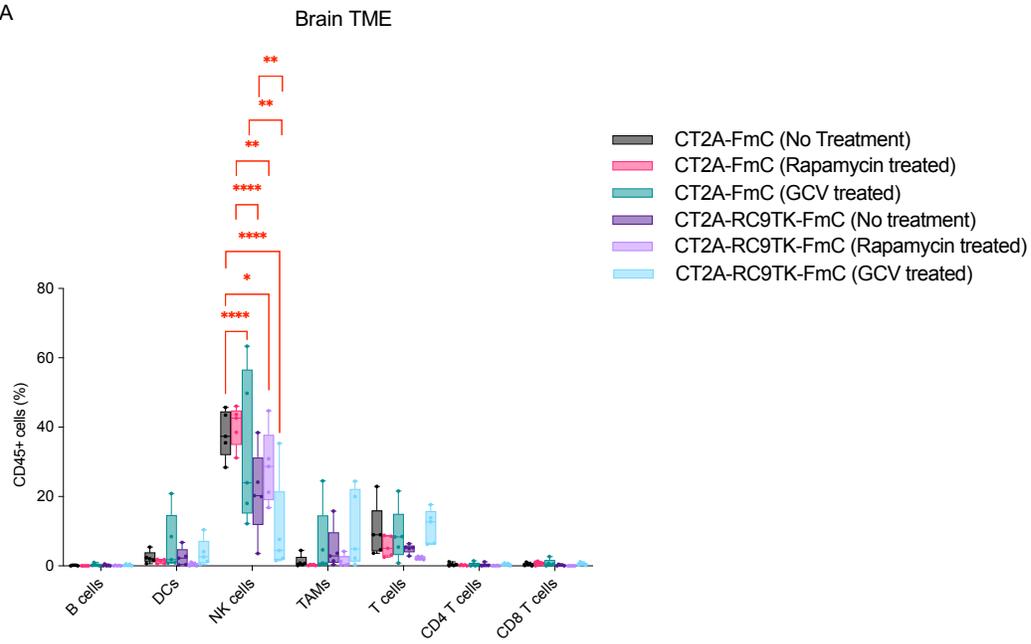
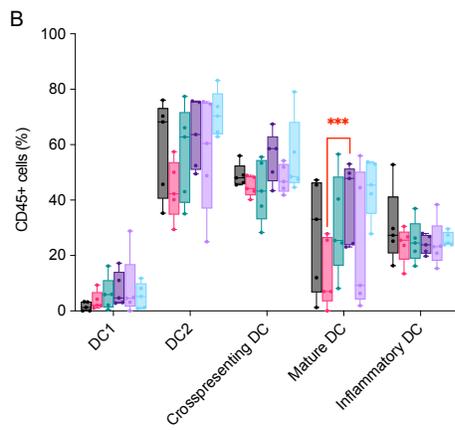


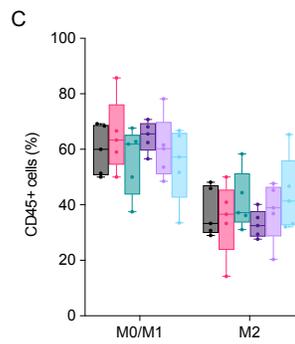
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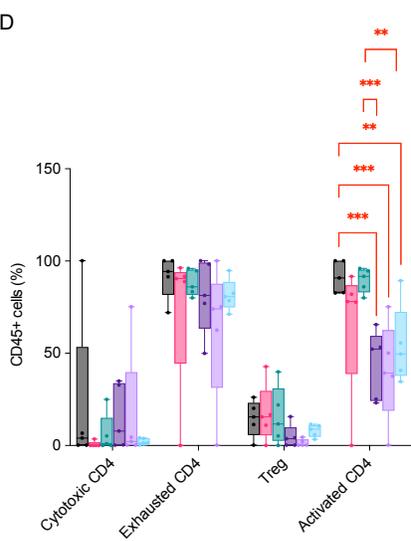
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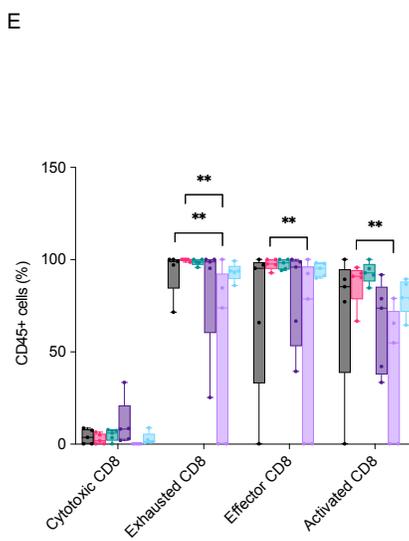
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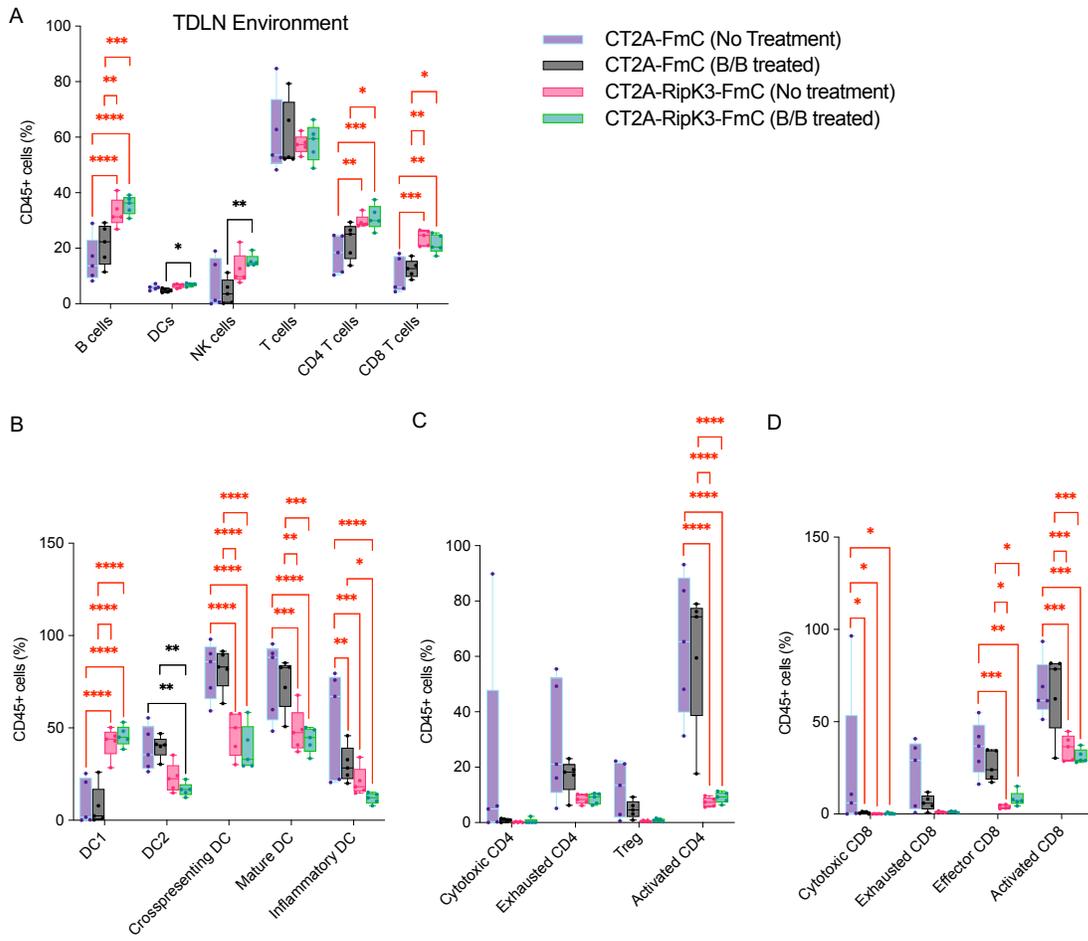


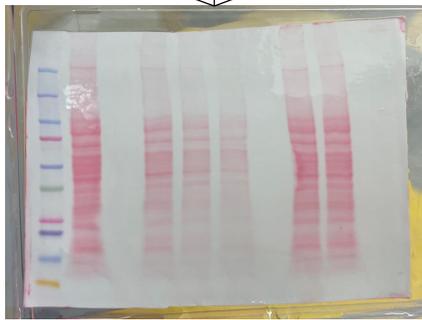
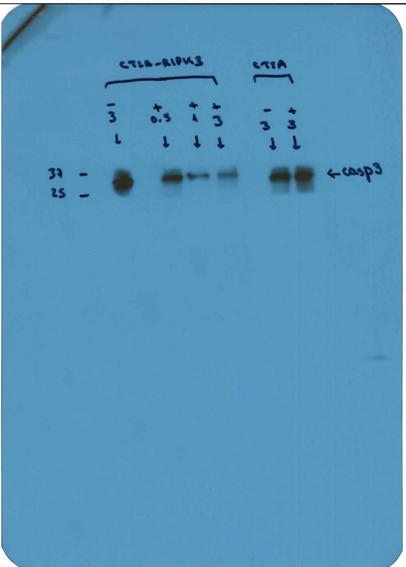
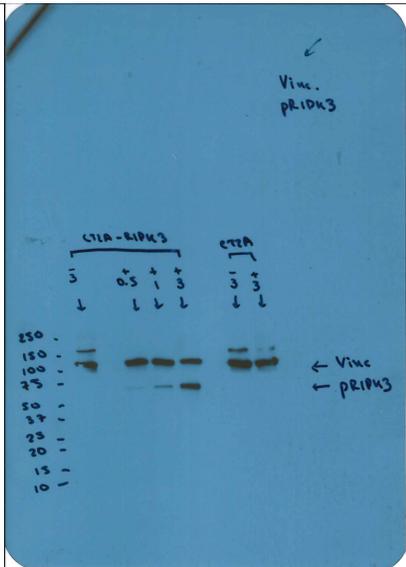
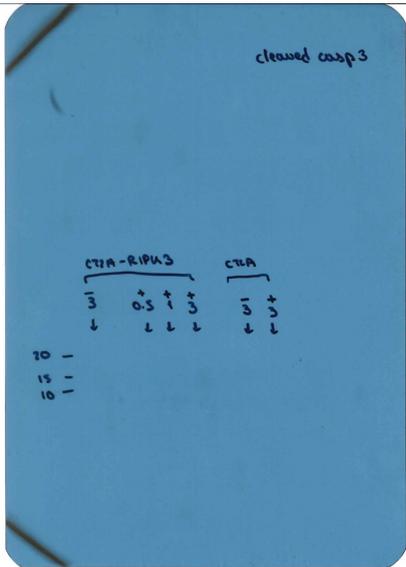
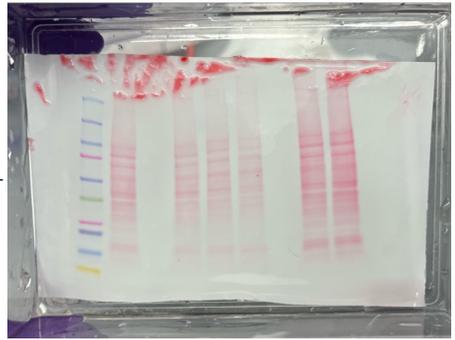
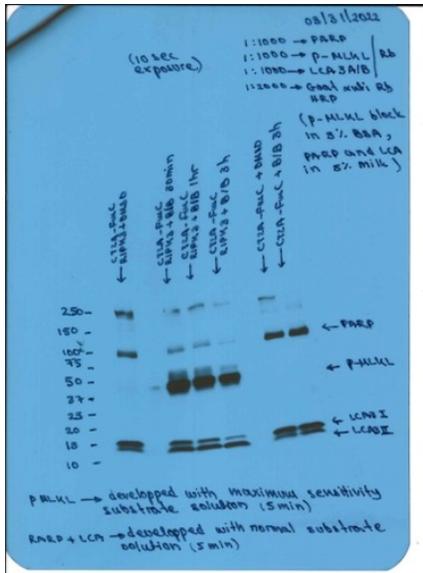
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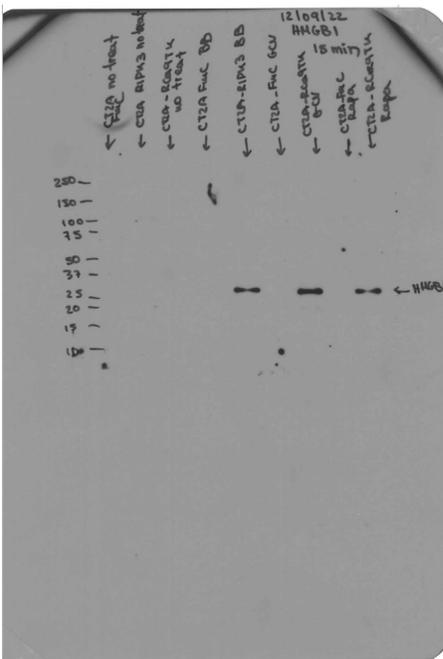
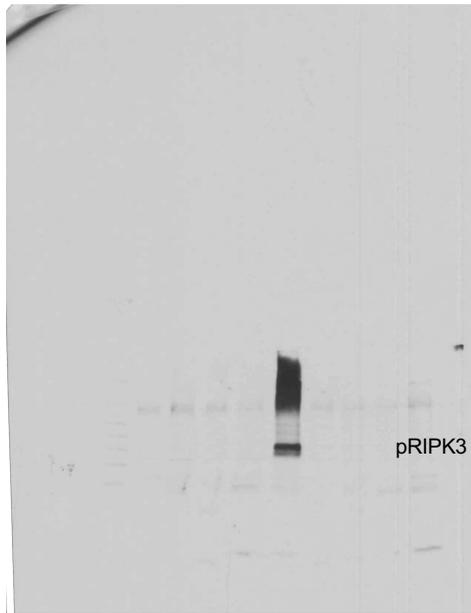
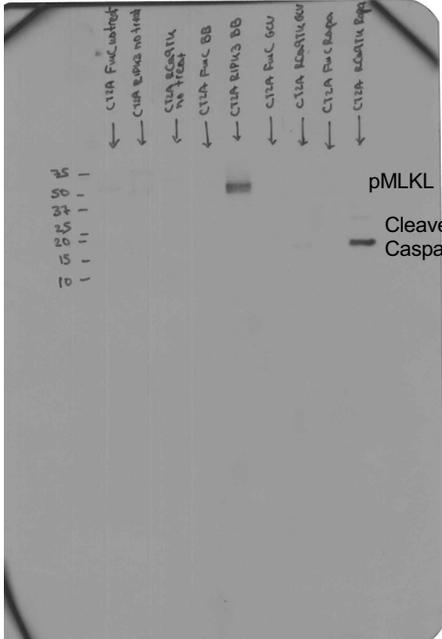
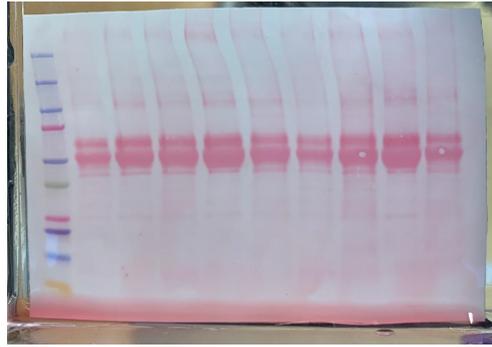
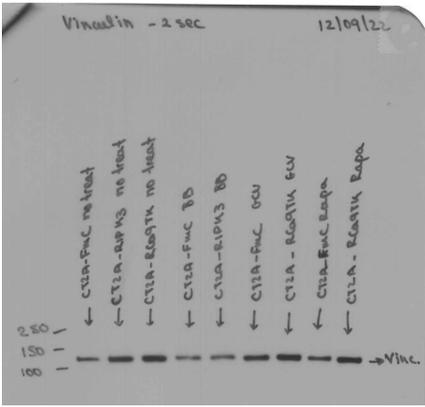


E









Supplementary Figures and Legends

Figure. S1 Flow plots demonstrate the gating strategy for immune profiling on tissues harvested from the mouse brain and TDLN.

Figure. S2 Cell death induced by RapaCas9 and HSV-TK safety switches has minimal effects on tumor immune microenvironment in vivo. (A) Boxplot showing immune profiling of tumor tissues harvested from the mouse brain 5 days post prodrug treatment for the groups of CT2A with rapamycin treatment (n=5), GCV treatment (n=5), and without any treatment (n=5), and CT2A-RC9TK with rapamycin treatment (n=5), GCV treatment (n=5), and without any treatment (n=5) (B) Boxplot showing the profile of DC subpopulations from the experiment in (A). (C) Boxplot showing the profile of TAM subpopulations from the experiment in (A). (D) Boxplot showing the profile of CD4 T subpopulations from the experiment in (A). (E) Boxplot showing the profile of CD8 T subpopulations from the experiment in (A). The whiskers represent minimum to maximum. Data were analyzed by 2-Way ANOVA with the two-stage step-up method of Benjamini, Krieger and Yekutieli test for multiple comparison correction. * = $P < 0.05$, ** = $P < 0.01$, *** = $P < 0.001$. The significance line in black represents changes due to the activation of the suicide system, whereas in red represents changes due to differences in cell type or drug.

Figure. S3 Cell death induced by RIPK3 safety switch reinvigorates TDLN environment in vivo. (A) Boxplot showing immune profiling of TDLN harvested from the mice 5 days post prodrug treatment for the groups of CT2A with (n=5) or without (n=5) B/B treatment and the groups of the mixture of CT2A and CT2A-RIPK3 with (n=5) or without (n=5) B/B treatment. (B) Boxplot showing the profile of DC subpopulations from the experiment in (A). (C) Boxplot showing the profile of CD4 T subpopulations from the experiment in (A). (D) Boxplot showing the profile of CD8 T subpopulations from the experiment in (A). The whiskers represent minimum to maximum. Data were analyzed by 2-Way ANOVA with the two-stage step-up method of Benjamini, Krieger and Yekutieli test for multiple comparison correction. * = $P < 0.05$, ** = $P < 0.01$, *** = $P < 0.001$. The significance line in black represents changes due to the activation of RIPK3 safety switch, whereas in red represents changes due to differences in cell type or drug.

Figure. S4 Unedited blots for Fig. 1I.

Figure. S5 Unedited blots for Fig. 2F.