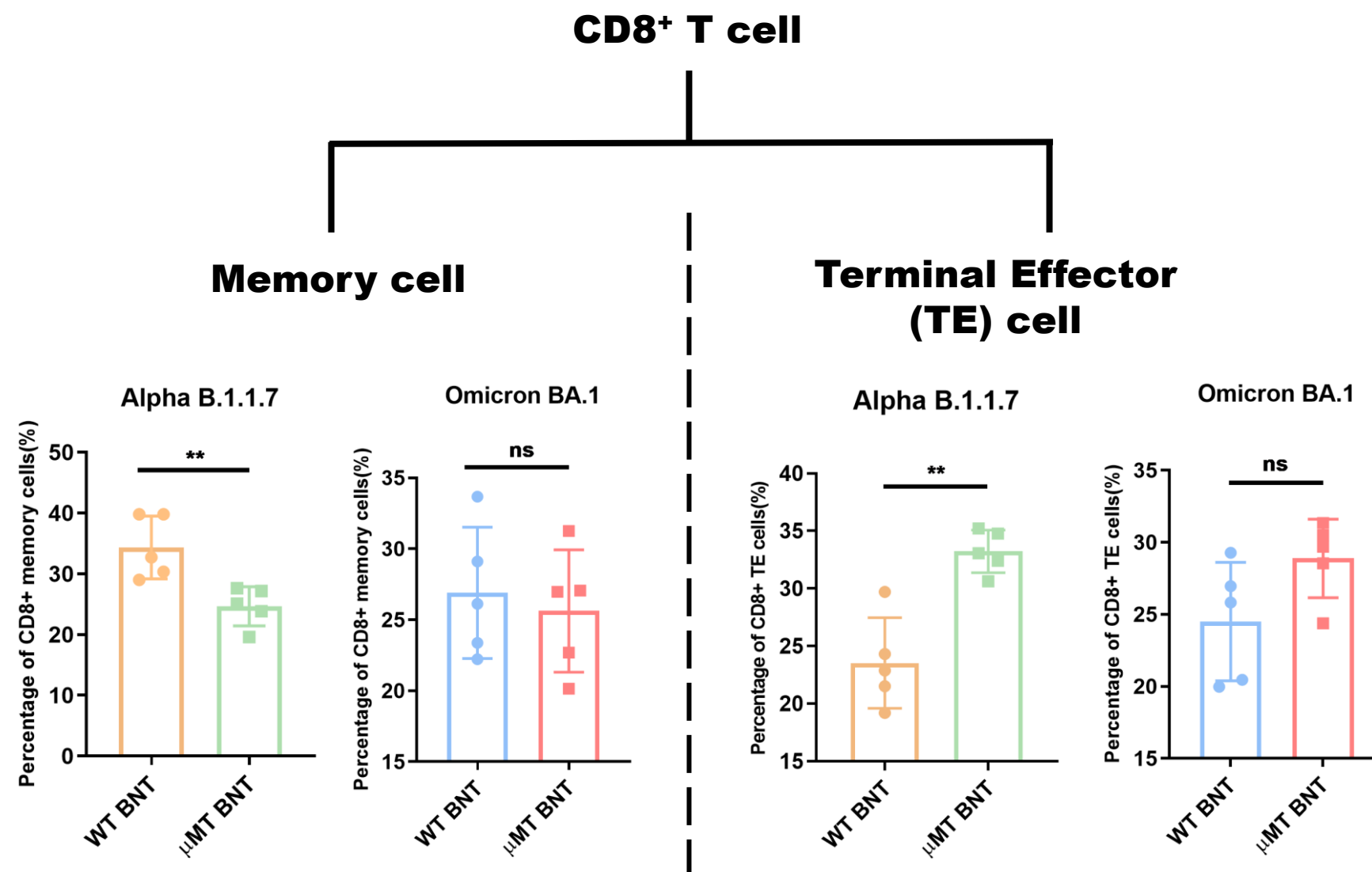
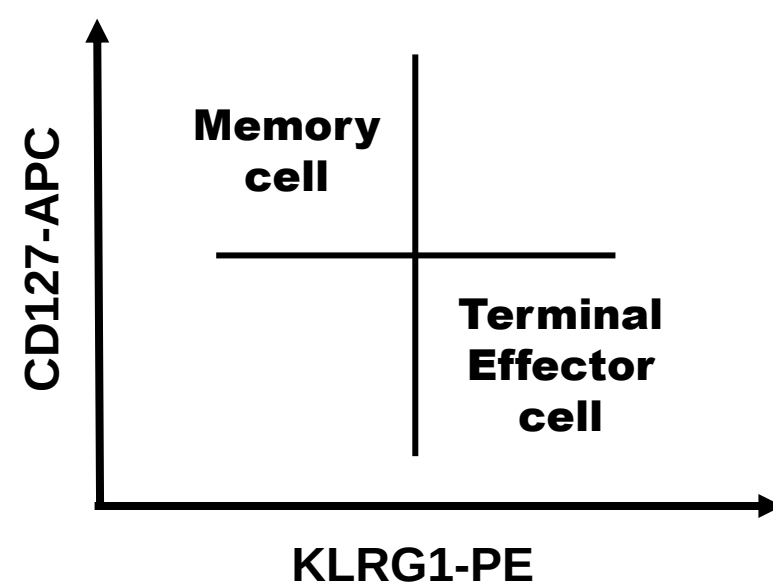


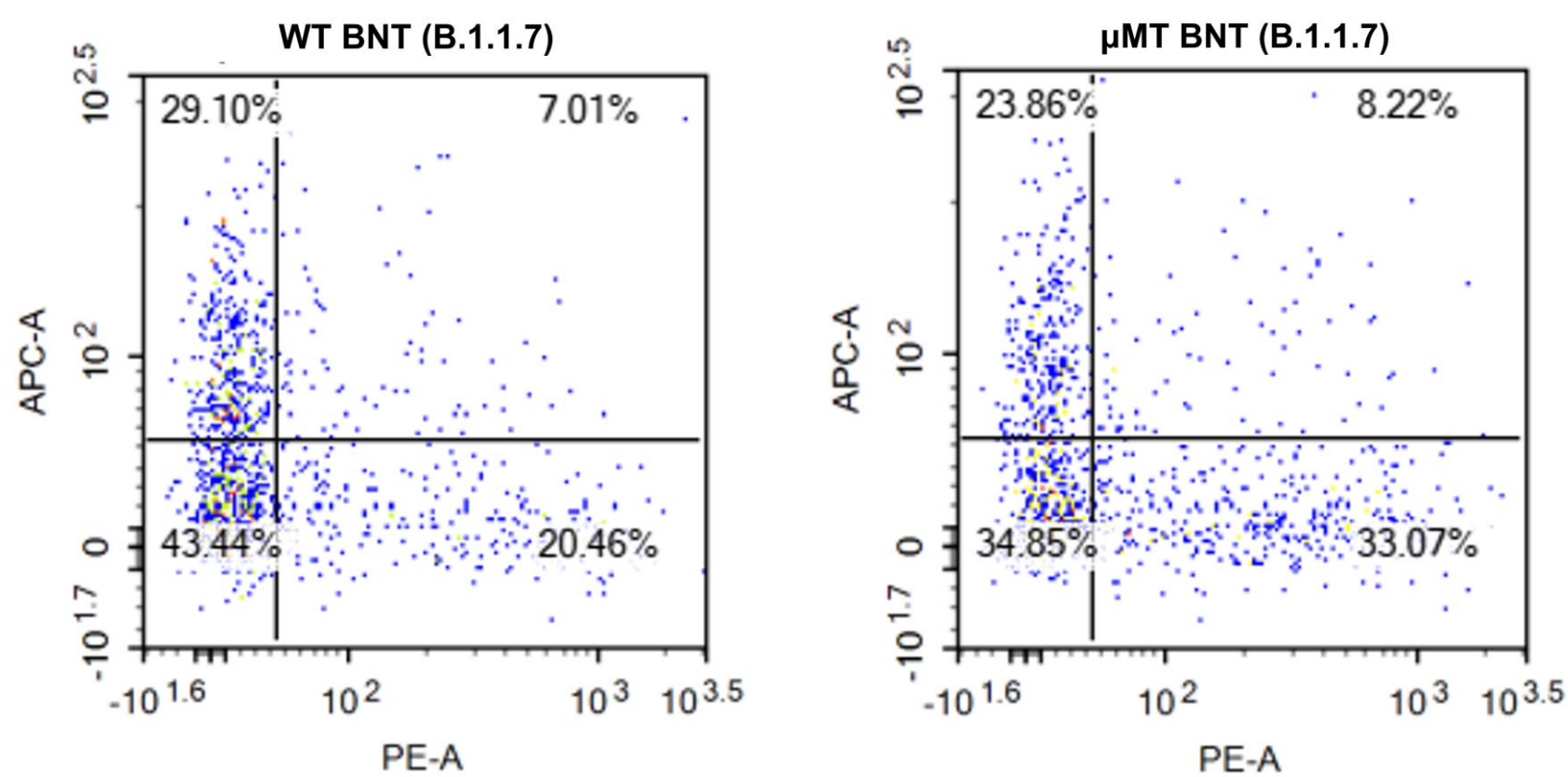
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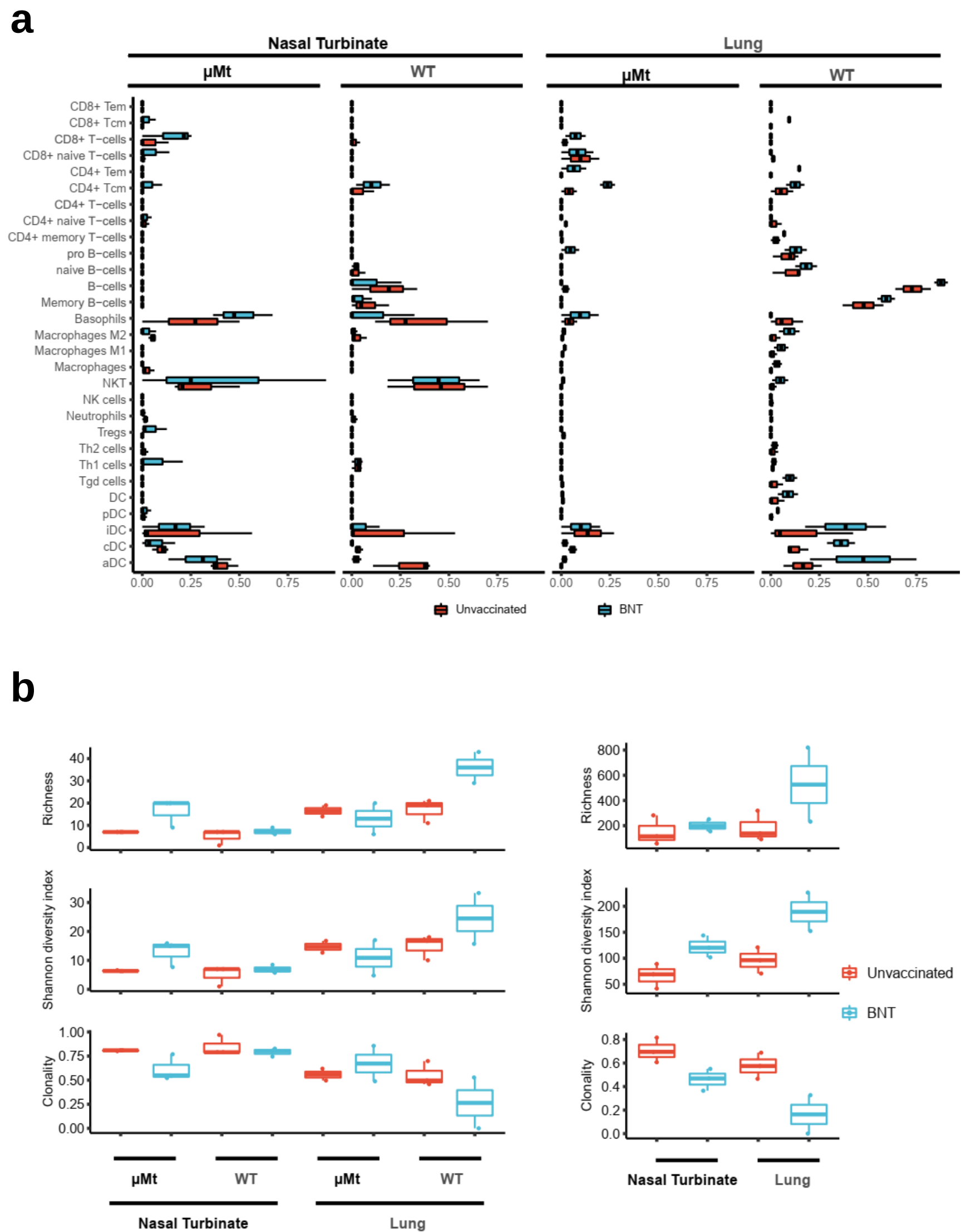
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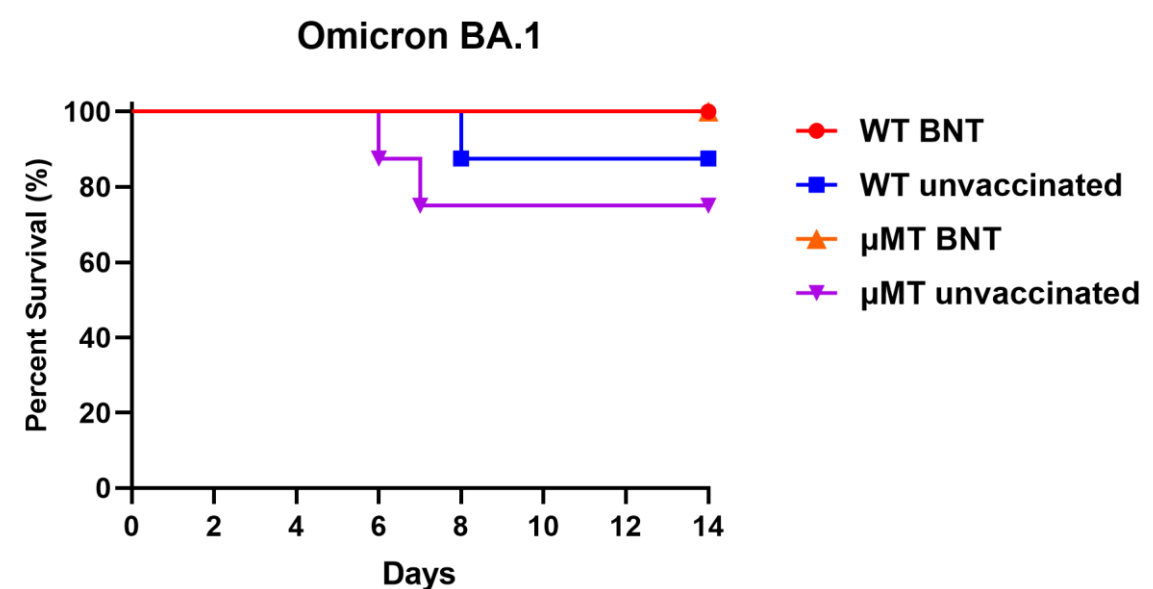
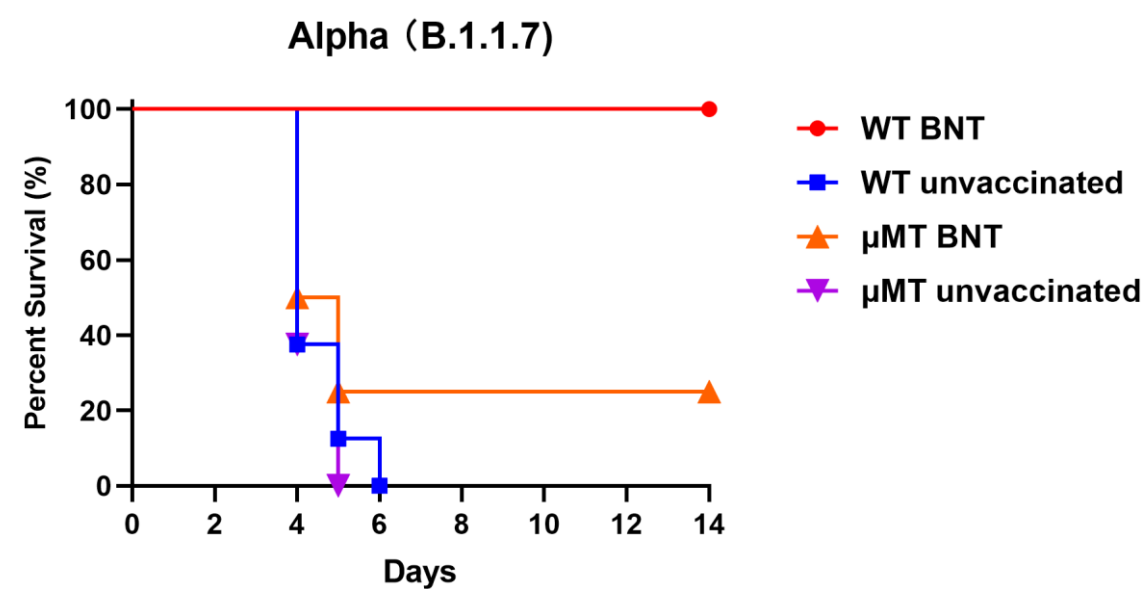
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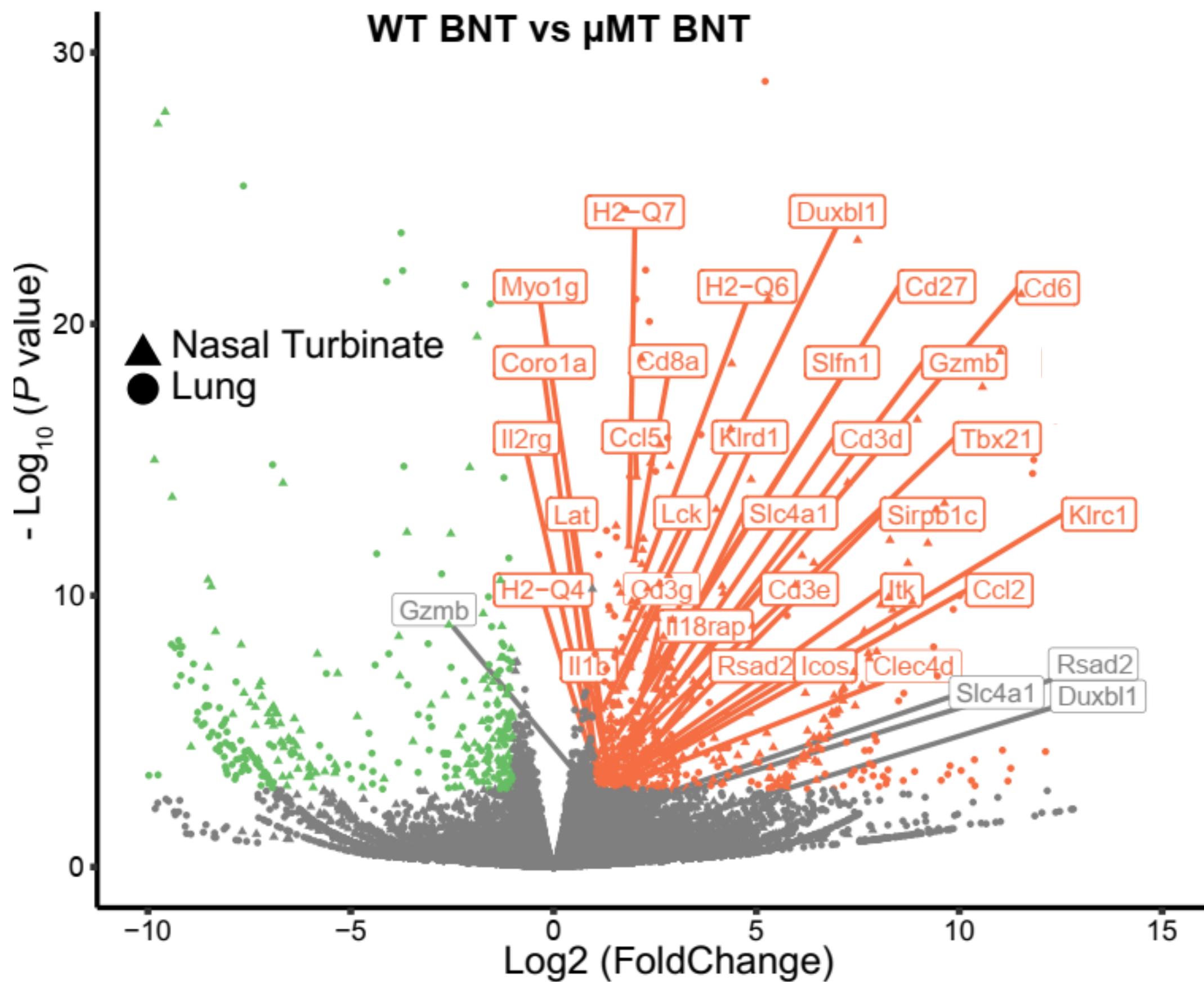
**Fig. S1 Spike protein of SARS-CoV-2 induced the differentiation of CD8<sup>+</sup> T memory cell in spleen of vaccinated WT and μMT mice in vitro.** (a) The percentage of CD8<sup>+</sup> T cell subsets in spleen of vaccinated WT and μMT mice after spike protein stimulation (Alpha and Omicron BA.1). (n=5) (b) Schematic diagram of characterization of CD8<sup>+</sup> T memory cell subsets by flow cytometry. CD127<sup>-</sup> KLRG1<sup>+</sup> — TE cell; CD127<sup>+</sup> KLRG1<sup>-</sup> — memory cell. (c) Representative dot plots showing CD8<sup>+</sup> T memory cell differentiation in spleen of vaccinated WT and μMT mice. Statistical significance was determined using two-tailed Student's t-tests.



**Fig. S2 Cell type enrichment analysis and immune repertoire richness/diversity analysis of the RNA-seq data.** (a) Cell type enrichment analysis of RNA-seq data indicated the function enrich scores of each cell type for vaccinated and unvaccinated WT and  $\mu$ MT mice. (b) Immune repertoire richness and diversity analysis of the samples. IGH results were not showed in  $\mu$ MT mice due to the missing B cell receptor gene expression.

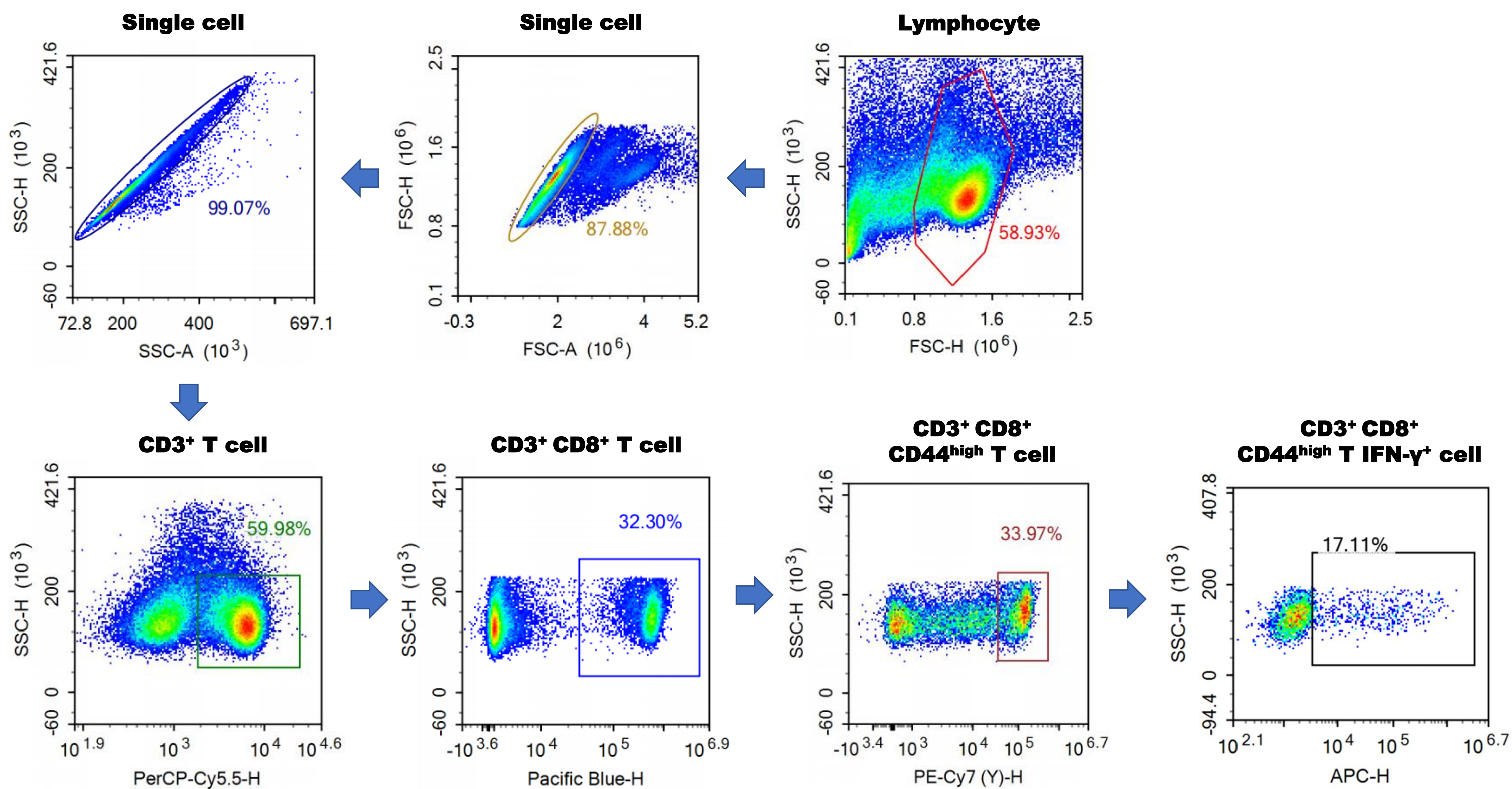


**Fig. S3 BNT162b2 vaccination increased the survival of K18-hACE2 WT and  $\mu$ MT mice.** The survival of vaccinated and unvaccinated WT and  $\mu$ MT mice against Alpha (a) and Omicron BA.1 (b) challenge. (n=8). Statistical significance was determined using log-rank (Mantel–Cox) tests.



**Fig. S4** Volcano plot showing differential expression genes comparing transcriptome of C57BL/6J  $\mu$ MT to WT mice in both NT and lung after BNT162b2 vaccination. Genes with orange labels were significantly up regulated in NT or lung of vaccinated  $\mu$ MT mice (adjusted P value < 0.05 and gene expression fold change > 2), scatters with grey labels indicated gene up regulated in both NT and lung of vaccinated WT mice (P value < 0.05 and gene expression fold change > 2).





**Fig. S5 Gating strategy for detection of CD3<sup>+</sup> CD8<sup>+</sup> CD44<sup>high</sup> IFN-γ<sup>+</sup> T cells in spleen of vaccinated C57BL/6J WT and μMT mice after spike protein stimulation.**