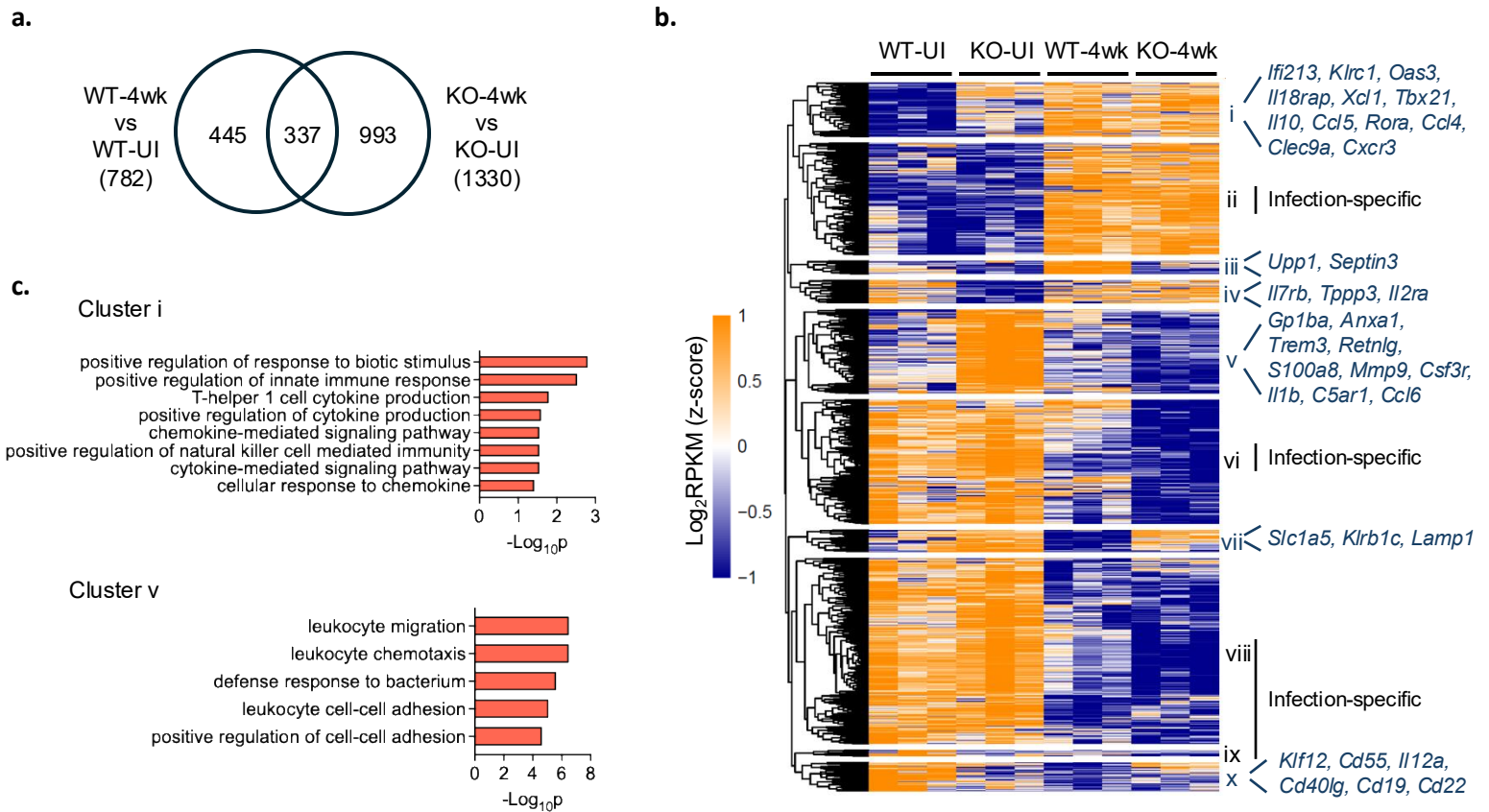


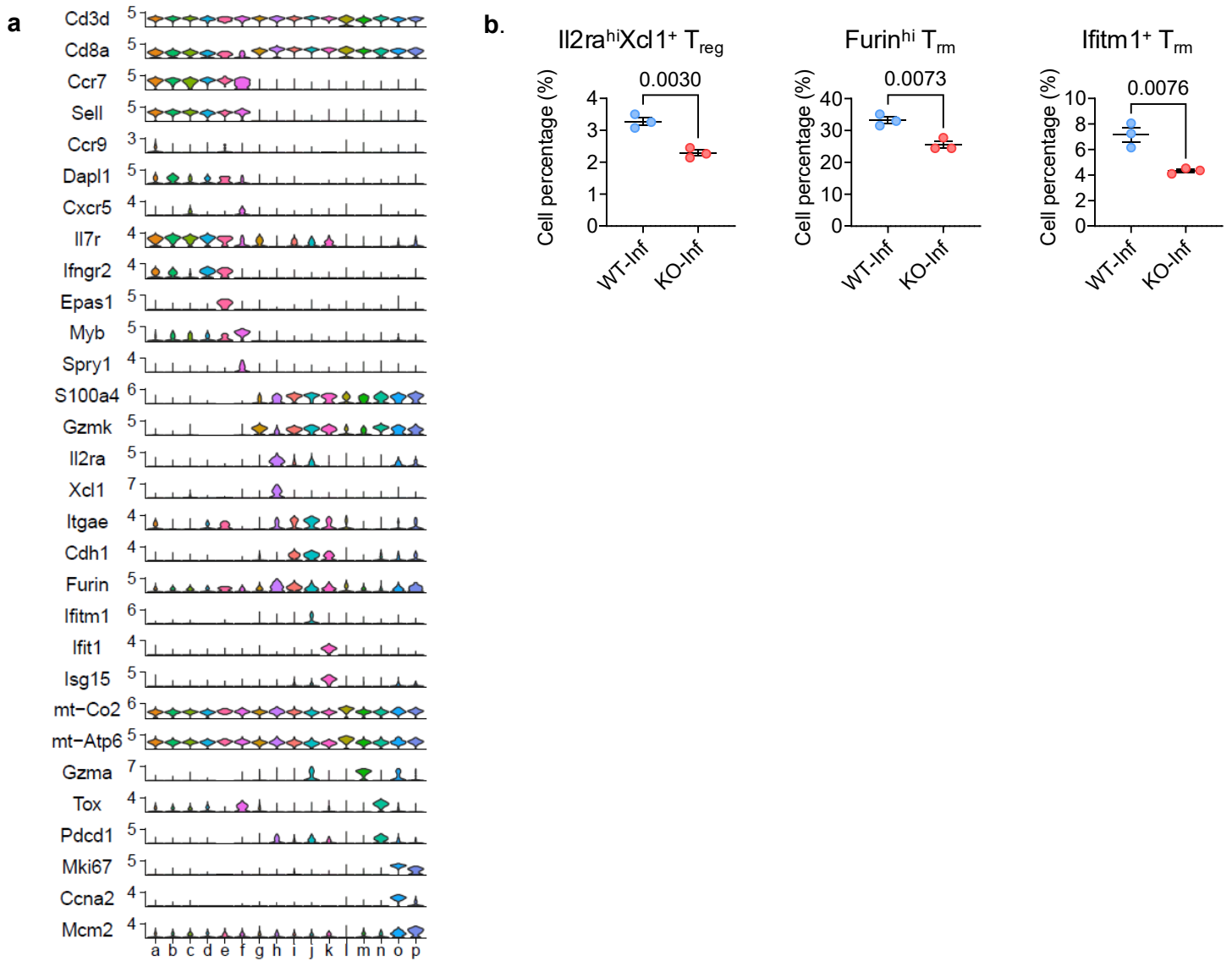
Extended Data Fig. 1 Flow-cytometric gating and quantification of T cell and myeloid subsets in *Nr4a1*-deficient versus WT mice lungs.

a, Lung *Nr4a1* mRNA levels in uninfected (UI) and *Mtb*-infected mice, shown as relative expression (qPCR). *P* value, two-tailed Mann–Whitney. Each dot represents one mouse. Data is mean \pm s.d. **b**, Flow cytometry gating for lung T cells using activation and exhaustion markers. **c**, Gating strategy for analyzing myeloid cells in the lung. **d**, Percentage of CD45⁺ T cells among live lung cells in WT and *Nr4a1*^{-/-} mice. **e–g**, Macrophages (**e**), dendritic cells (**f**) and neutrophils (**g**) as a percentage of CD45⁺ lung leukocytes. Each dot is a mouse; horizontal bar indicates mean \pm s.d. *P* value, two-tailed Mann–Whitney test.



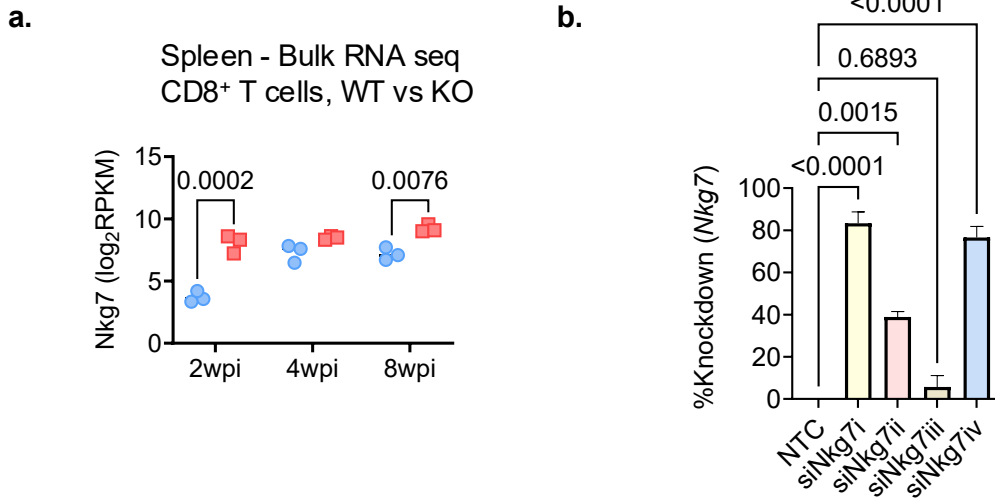
Extended Data Fig. 2 Bulk RNA-seq of spleen CD8⁺ T cells from uninfected and infected (4 wk) Nr4a1^{-/-} and WT mice.

a, Venn diagram showing the overlap of DEGs between 4 wk and uninfected (UI) CD8⁺ T cells from WT and *Nr4a1*^{-/-} mice. **b**, Heatmap of the union of 4 wk vs UI DEGs ($n = 1,775$) identified in panel a. Log₂ RPKM values were z-score-normalized across samples. Genes were grouped into ten clusters (cluster i to x) using *k*-means clustering. Representative genes for clusters not classified as infection-specific are labeled on the right. **c**, GO biological processes among clusters i and v from panel b. Enriched biological processes include pathways related to cytokine-mediated signaling, natural-killer-like effector activity, leukocyte chemotaxis, and antibacterial defense. GO terms shown represent non-redundant categories with the lowest adjusted *P* values.



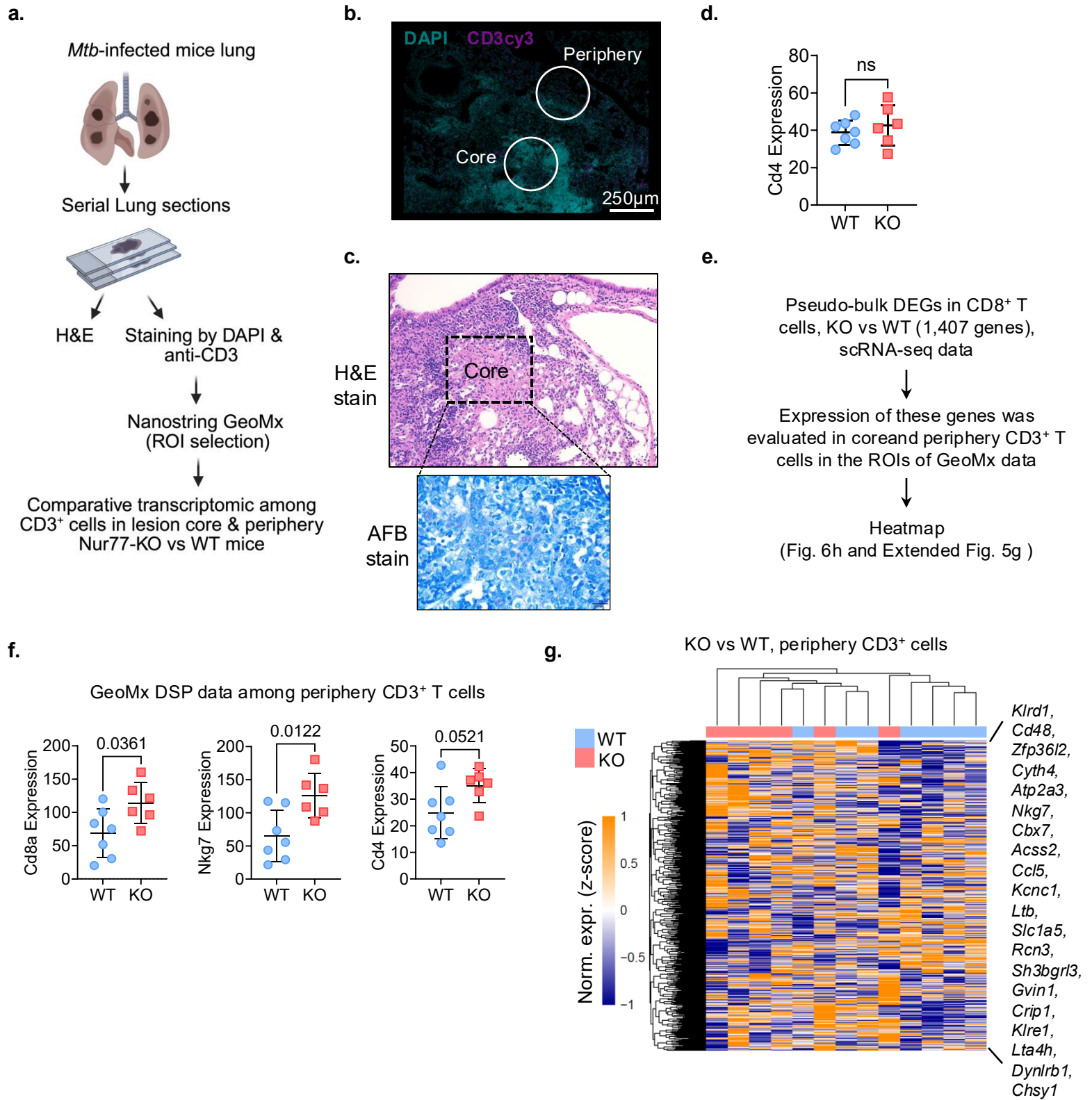
Extended Data Fig. 3 Marker expression and subset frequencies from scRNA-seq data define CD8⁺ T cell states in WT and *Nr4a1*^{-/-} lungs.

a, Expression of markers used to characterize CD8⁺ T cell subtypes (see Methods for gene lists and normalization). **b**, Percentage of Il2ra^{hi}Xcl1⁺ T_m, Furin^{hi} T_m and Ifitm1⁺ T_m in infected lungs (WT versus *Nr4a1*^{-/-}); unpaired two-sided *t*-test; *P* values labeled.



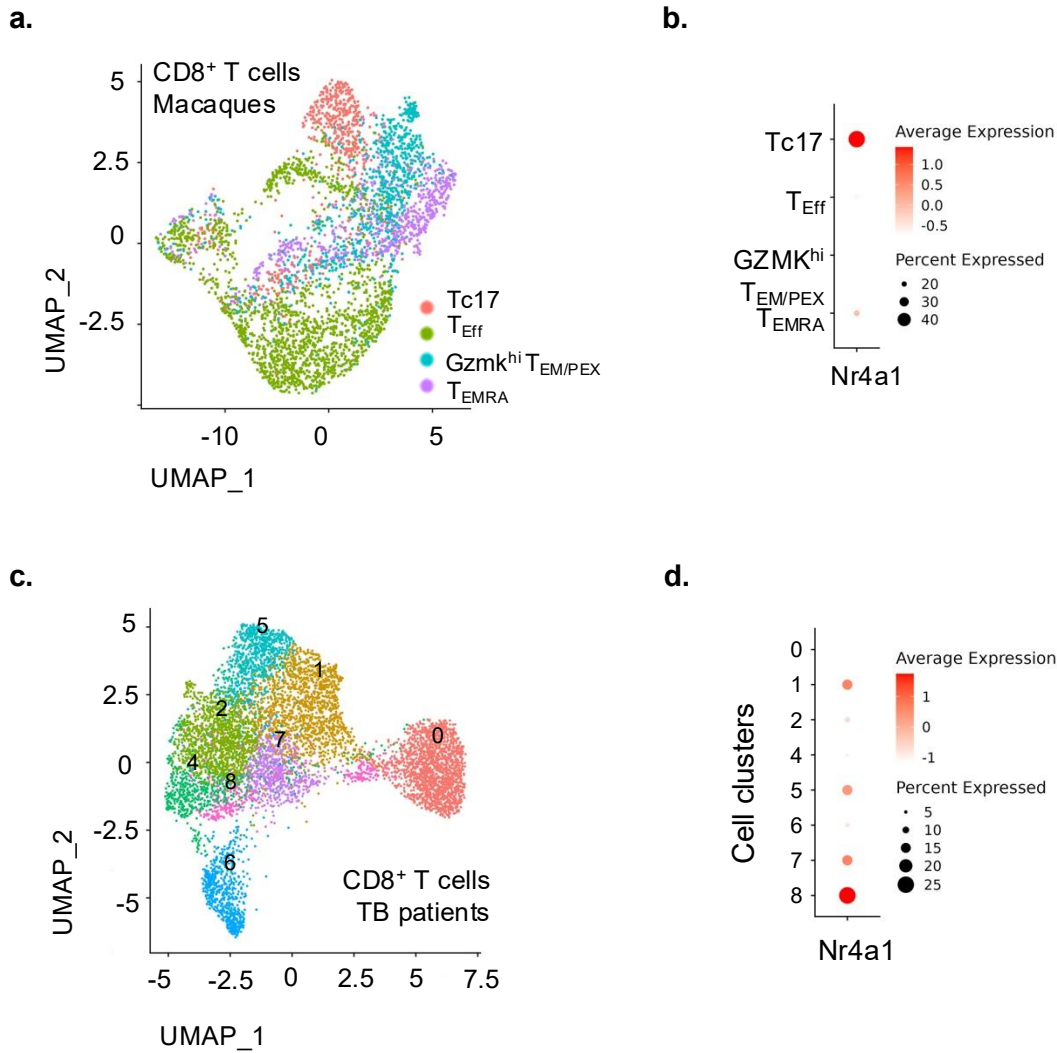
Extended Data Fig. 4 *Nkg7* expression and its knockdown in CD8⁺ T cells.

a, Bulk RNA-seq analysis showing *Nkg7* expression (log₂ RPKM) in splenic CD8⁺ T cells from WT and *Nr4a1*^{-/-} mice at 2, 4, and 8 wk of infection. *P* value, unpaired two-tailed *t* test. **b**, Efficiency of *Nkg7* knockdown in *Nr4a1*^{-/-} CD8⁺ T cells using four independent siRNAs, as measured by RT-qPCR 72 h post-transfection. Data mean \pm s.d.; one-way ANOVA.



Extended Data Fig. 5 Spatial transcriptomic workflow and key readouts in *Mtb*-infected mice lungs.

a, Schematic of GeoMx spatial transcriptomics: serial lung sections; H&E and antibody staining (DAPI, CD3, CD11b) to guide ROI selection; comparative transcriptomics of CD3⁺ and CD11b⁺ cells in lesion core versus periphery, *Nr4a1*^{-/-} versus WT. **b**, Immunofluorescence image showing ROIs in lesion core and periphery defined by DAPI and CD3 (Cy3) signal; scale bar, 250 μ m. **c**, Histology of infected lung sections: H&E (top) and acid-fast bacilli (AFB) stain (bottom). **d**, *Cd4* expression (normalized counts) in CD3⁺ ROIs from WT and *Nr4a1*^{-/-} (KO) lungs (*P* value, two-sided Mann–Whitney test). **e**, Schematic for the heat map generation by taking DEGs from CD8⁺ T cell scRNA-seq data and finding their gene expression in periphery or core CD3⁺ ROIs of spatial transcriptomic data. **f**, Expression levels of *Cd8a*, *Nkg7*, and *Cd4* in peripheral CD3⁺ T cells from WT and *Nr4a1*^{-/-} mice. *P* values, unpaired two-tailed *t* tests. **g**, Heatmap of the pseudo-bulk DEGs identified from total lung CD8⁺ T cell scRNA-seq (Fig. 5b), evaluated in periphery CD3⁺ ROIs from GeoMx spatial transcriptomics of *Mtb*-infected lungs. Distinct clustering of WT (blue) and *Nr4a1*^{-/-} (red) samples was not observed among periphery CD3⁺ ROIs. Representative cytotoxic and activation genes are indicated on right side. See Methods for DEG definition, normalization and clustering parameters.



Extended Data Fig. 6 *Nr4a1* expression across lung CD8⁺ T cell states in macaque and humans with TB, analysis of published scRNA-seq dataset.

a, UMAP of four lung CD8⁺ T cell subtypes in *Mtb*-infected macaques. **b**, Bubble plot summarizing *Nr4a1* expression across the four lung CD8⁺ T cell subtypes in **a** (dot size, percent expressing; color, average normalized expression). **c**, UMAP of eight CD8⁺ T cell clusters in the lungs of active TB patients. **d**, Bubble plot summarizing *Nr4a1* expression across the eight clusters in **c** (dot size, percent expressing; color, average normalized expression). Dataset sources and accessions are listed in Methods.