

Fig. S1 TRAM KO female septic mice possessed the reduced neutrophil infiltration in spleens and alleviated tissue injuries.

a Flow cytometry analysis of the expression of CD200R, CD86, and CD24 on spleen-resident neutrophils harvested on day 14 from WT and TRAM KO female mice with and without mild sepsis challenged with *E. coli* for 30 minutes (n = 4 or 6).

b Analyses of neutrophil infiltration through flow cytometry. Total spleen cells from WT and TRAM KO female mice with and without mild sepsis challenged with *E. coli* for 30 minutes were harvested and evaluated, and Ly6G⁺ cells were counted as tissue-infiltrated neutrophils (n = 4 or 6).

c The plasma levels of S1P3 in WT and TRAM KO female mice with and without mild sepsis challenged with *E. coli* for 30 minutes (n = 4 or 5).

d The protein concentration in BALF from WT and TRAM KO female mice with and without mild sepsis challenged with *E. coli* for 30 minutes (n = 3, 4, or 6).

****P<0.0001, ***P<0.001, **P<0.01, *P<0.05 using Log-rank test (a) and one-way ANOVA test followed by the post-hoc Sidak multiple comparisons test (a-c). ctrl, control. KO, TRAM KO. CS, cecal slurry i.p. injected.

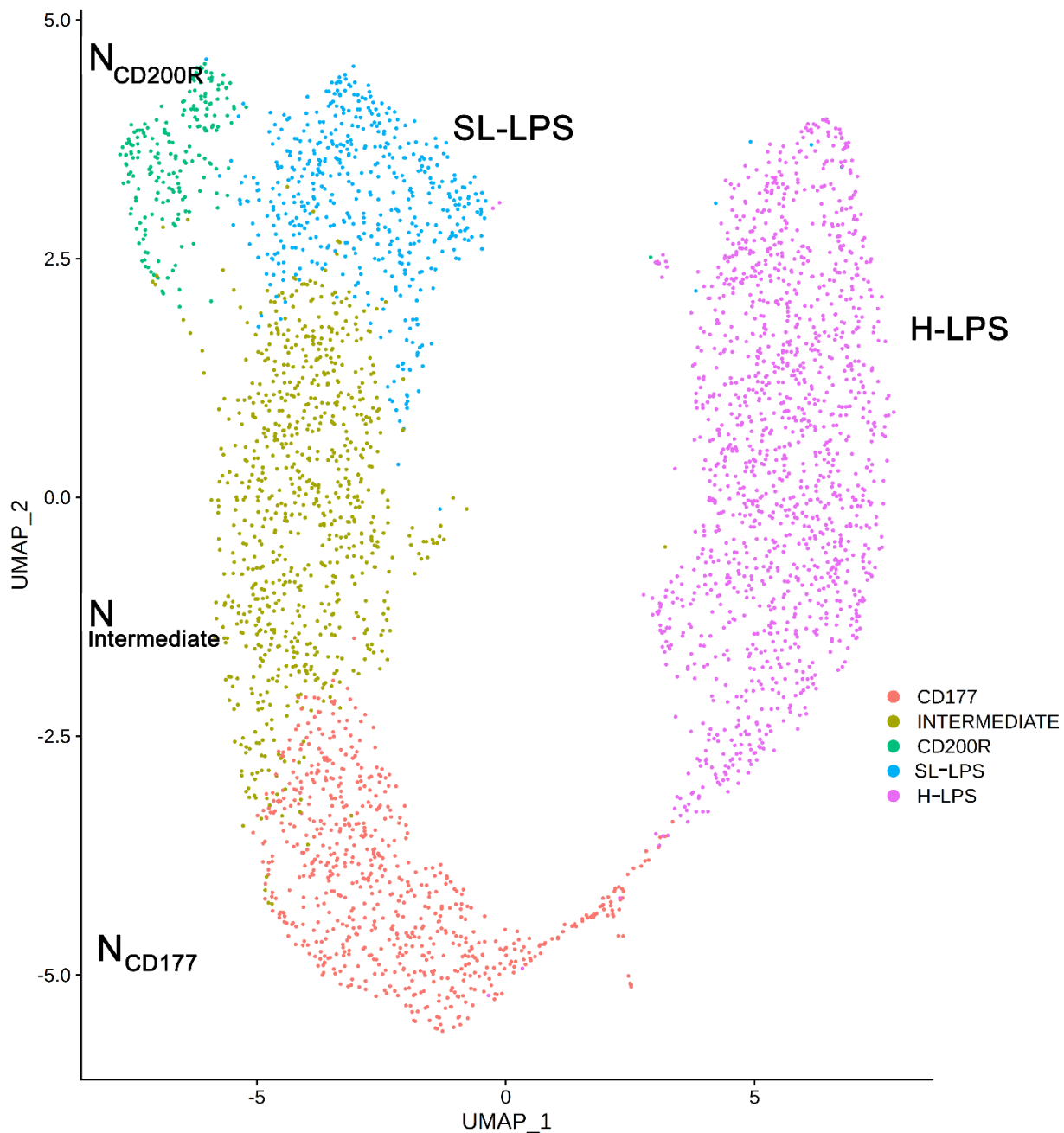


Fig S2a. UMAP cluster analysis of scRNAseq data from wild type neutrophils treated with either PBS, super-low dose LPS (100 pg/ml) or high dose LPS (100 ng/ml). Three clusters of naïve PBS treated neutrophils (CD177, INTERMEDIATE and CD200R), as well as the separate clusters of SL-LPS (super-low dose LPS treated) and H-LPS (high dose LPS treated) were shown.

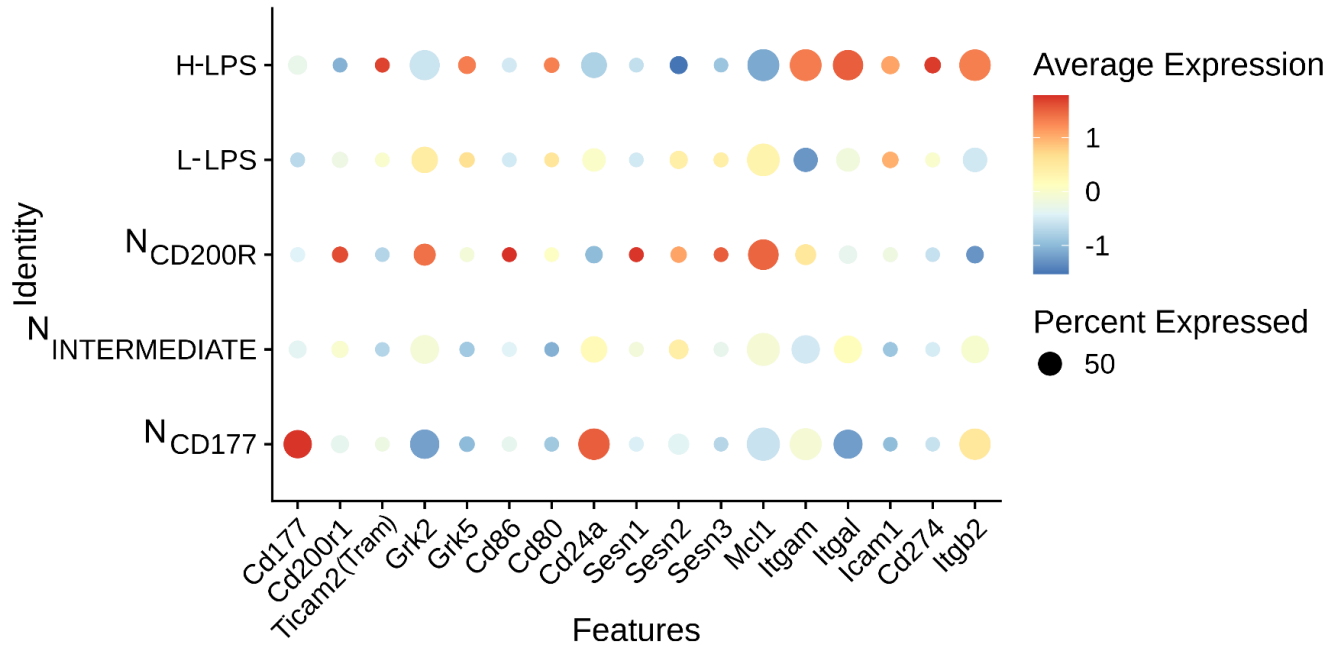


Fig S2b. Bubble plot analyses of selected genes differentially expressed in neutrophils treated with either super-low dose or high dose LPS.

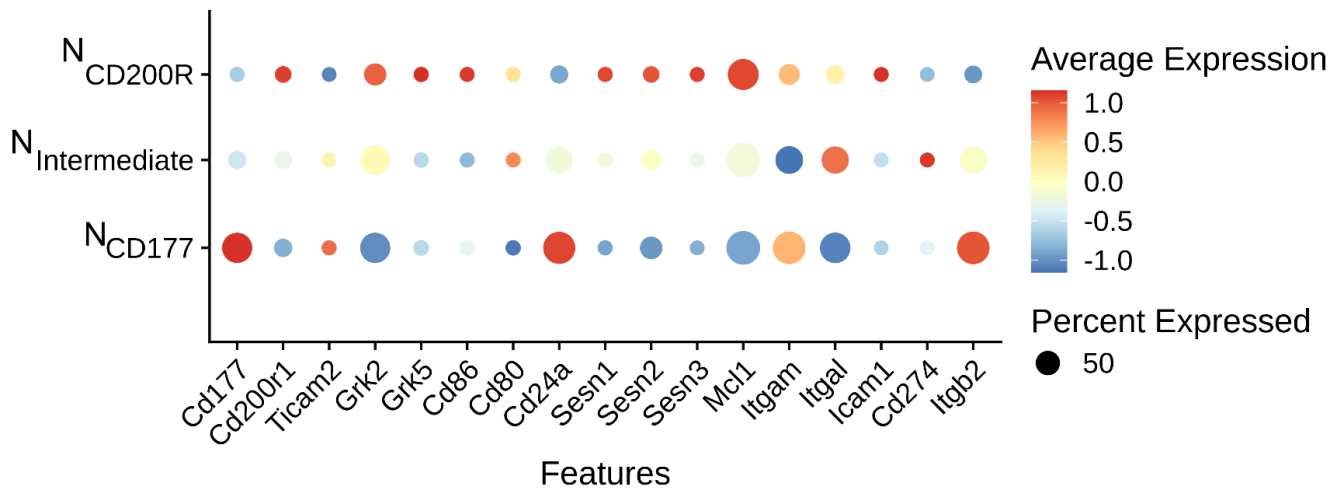


Fig S2c. Bubble plot analyses of selected genes differentially expressed in naïve wild type non-treated neutrophils, showing the N_{200R} subset selectively expresses reduced levels of TRAM.

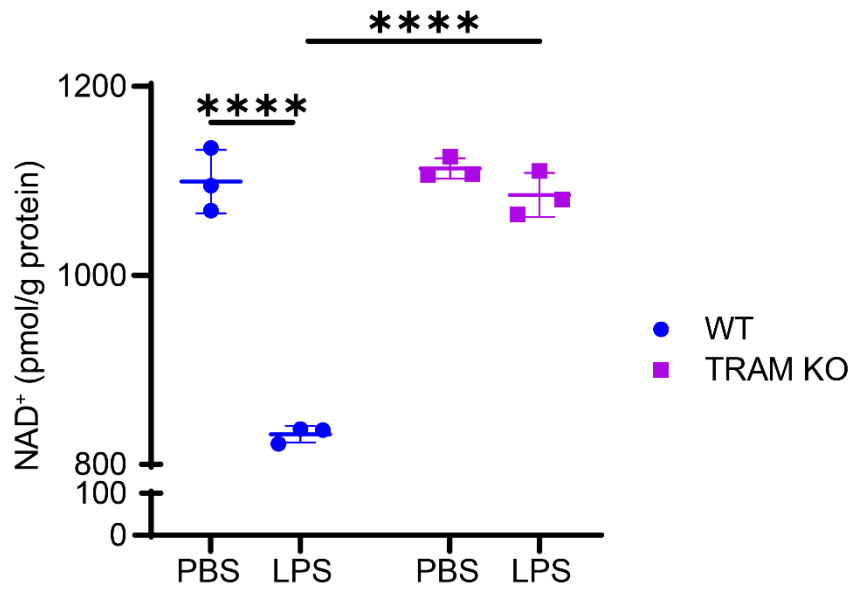


Fig. S3 TRAM KO neutrophils are more resistant to LPS-induced metabolic dysregulation.

The levels of NAD⁺ in WT and TRAM KO neutrophils with or without LPS stimulation for 24 hours (n = 3).

****P<0.0001 using one-way ANOVA test followed by the post-hoc Sidak multiple comparisons test. LPS, lipopolysaccharide.

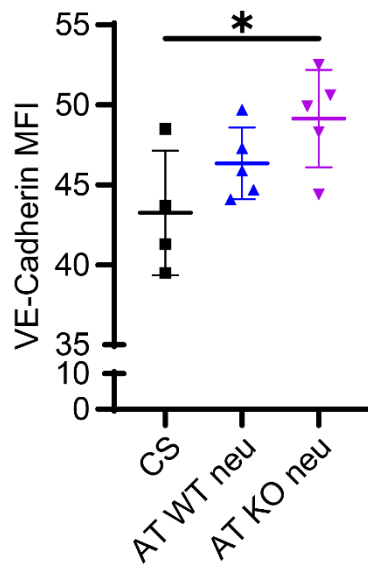


Fig. S4 WT septic mice transfused with TRAM KO neutrophils maintained higher levels of VE-Cadherin, a marker of improved endothelial integrity.

Flow cytometry analysis of the expression of VE-Cadherin on pulmonary endothelial cells harvested on day 14 from WT control mice and WT septic mice with and without neutrophil transfusion challenged with *E. coli* for 30 minutes (n = 3, 4, or 5).

ctrl, control. KO, TRAM KO. CS, cecal slurry i.p. injected. neu, neutrophils. AT, adoptive transfer.

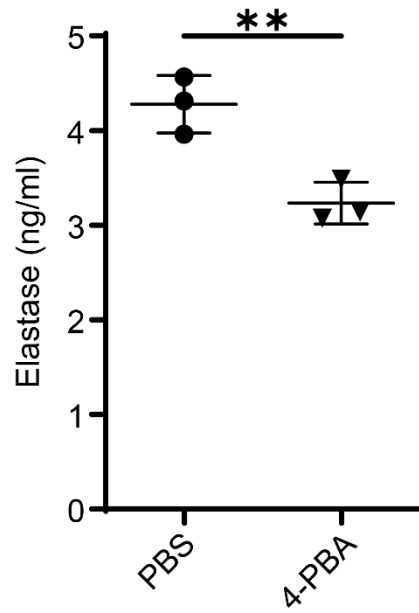


Fig. S5 4-PBA reprogrammed resolving neutrophils expressed decreased elastase secretion.

The secretion of neutrophil elastase by WT neutrophils with or without 2-hour 4-PBA priming followed by 24-hour fMLP stimulation was evaluated by ELISA (n = 3).

**P<0.01 using two-sided Student's t-test.

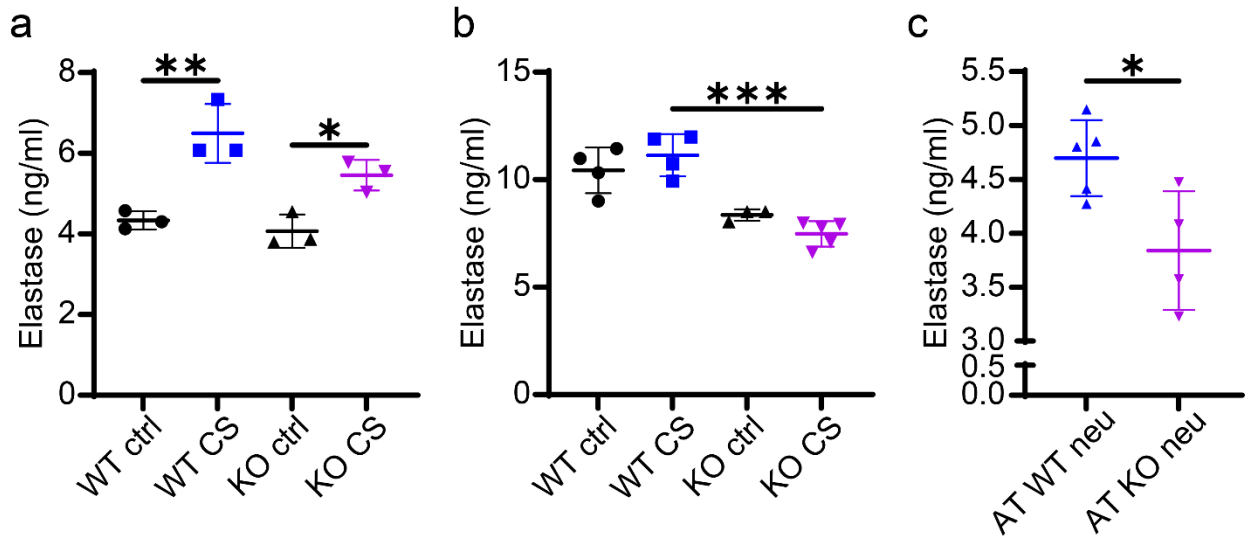


Fig. S6 TRAM KO septic mice exhibited decreased neutrophil elastase in plasma and adoptive transfer of TRAM KO neutrophils downregulated plasma levels of neutrophil elastase.

a&b The plasma levels of neutrophil elastase from WT and TRAM KO male (a) and female (b) mice with and without mild sepsis challenged with *E. coli* for 30 minutes was evaluated by ELISA (n = 3, 4, or 5).

c The levels of neutrophil elastase in plasma from WT control mice and WT septic mice with and without neutrophil transfusion challenged with *E. coli* for 30 minutes (n = 4 or 5).

***P<0.001, **P<0.01, *P<0.05 using one-way ANOVA test followed by the post-hoc Sidak multiple comparisons test. KO, TRAM KO. ctrl, control. neu, neutrophils. CS, cecal slurry i.p. injected. neu, neutrophils. AT, adoptive transfer.