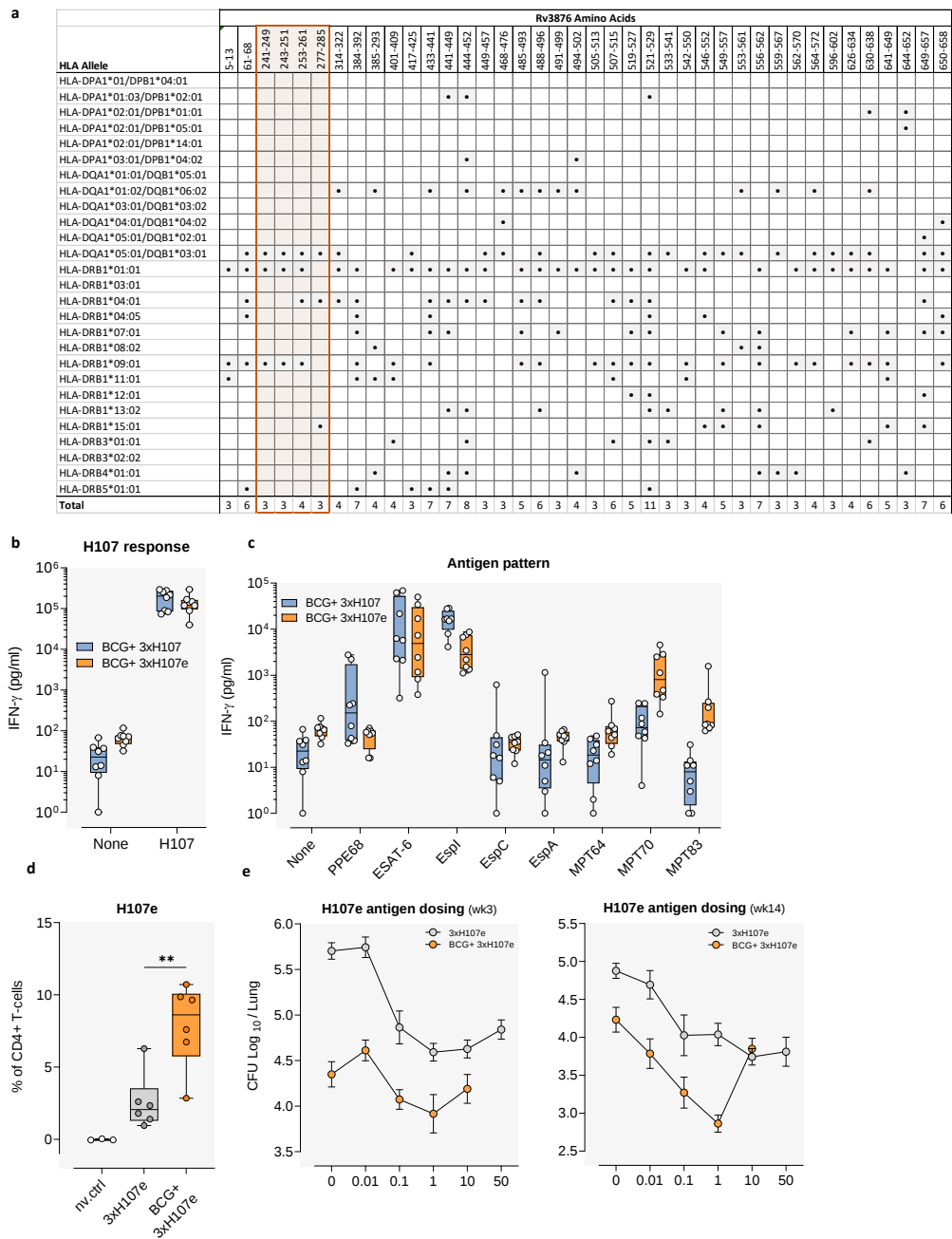


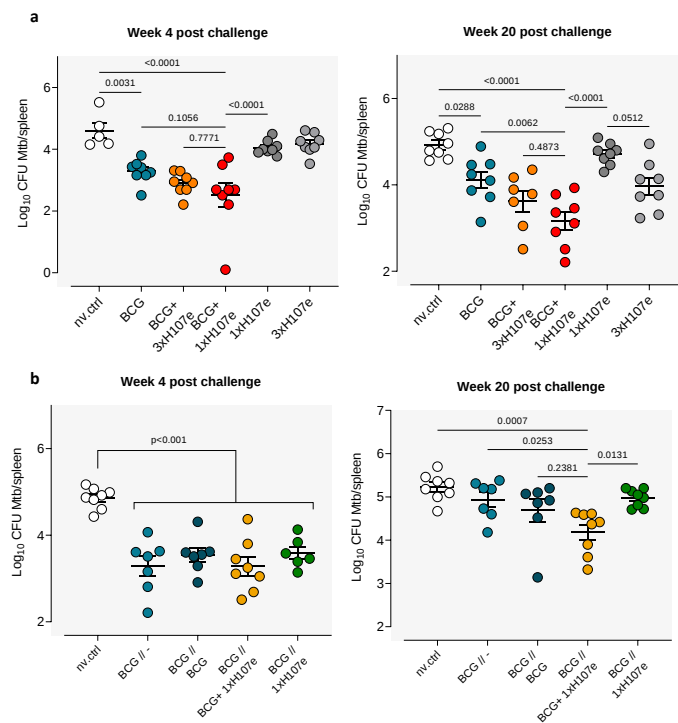
Supplementary Figure 1.



Supplementary Figure 1

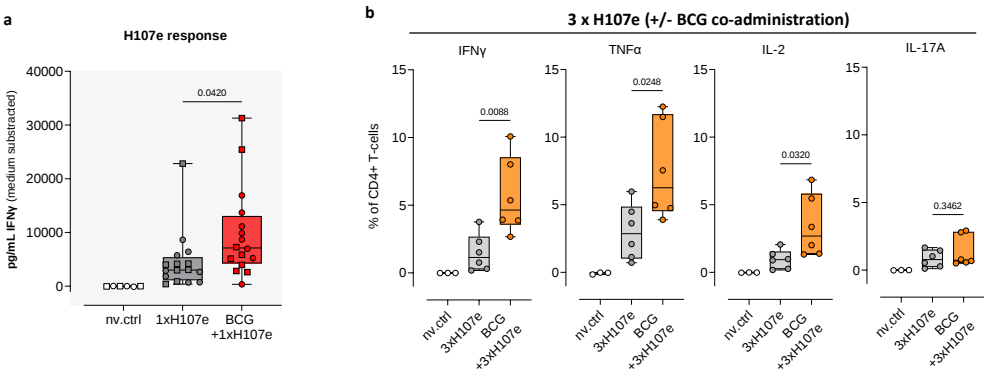
a In silico MHC class II prediction of binding epitopes in Rv3876. The amino acid sequence of Rv3876 was obtained from the Mycobrowser server and analyzed for potential HLA binding epitopes using the SMM-align and NN-align methods. Columns in the checkerboard table show 9-mer core peptides identified as binding epitopes within antigenic stretches of the Rv3876 antigen. Each row shows identified HLA binding alleles among 27 common HLA DRA, DQ and DP molecules. IC50 values <500nM were employed as cutoff for identified binding epitopes (shown as dots). Area marked by orange box signify the deleted proline-rich fraction in the Rv3876 antigen (Δ 75-294) in H107e relative to H107. **b** H107/H107e specific IFN- γ production by splenocytes from animals vaccinated with BCG+ 3xH107/CAF[®]01 or BCG+ 3xH107e/CAF[®]01, as measured by ELISA. Data graphed as box plots with line at median, boxes indicating interquartile range, and whiskers delineating minimum and maximum values (n=8). **c** IFN- γ release after ex vivo stimulation with single antigen components of H107(e) by splenocytes from animals vaccinated with BCG+ 3xH107/CAF[®]01 or BCG+ 3xH107e/CAF[®]01, as measured by ELISA. Data graphed as box plots with line at median, boxes indicating interquartile range, and whiskers delineating minimum and maximum values (n=8). **d** Cumulative frequency of cytokine-positive (IFN- γ , TNF- α , IL-2 and/or IL-17A) CD4 T cells in spleen after stimulation with H107e protein in mice immunized with 3x H107e/CAF[®]01 compared to BCG+ 3x H107e/CAF[®]01. Box plots with line at median, boxes indicating interquartile range, and whiskers showing minimum and maximum values (n=3-6). Statistical significance of group differences determined by Student's T-test. **e** Lung bacterial burden at week three (left) and fourteen (right) post aerosol challenge with Mtb Erdman in mice immunized with 3x H107e/CAF[®]01 in a range of doses administered with or without BCG co-administration. Data plotted as mean $\pm$ SEM (n=6-8).

Supplementary Figure 2



Supplementary Figure 2

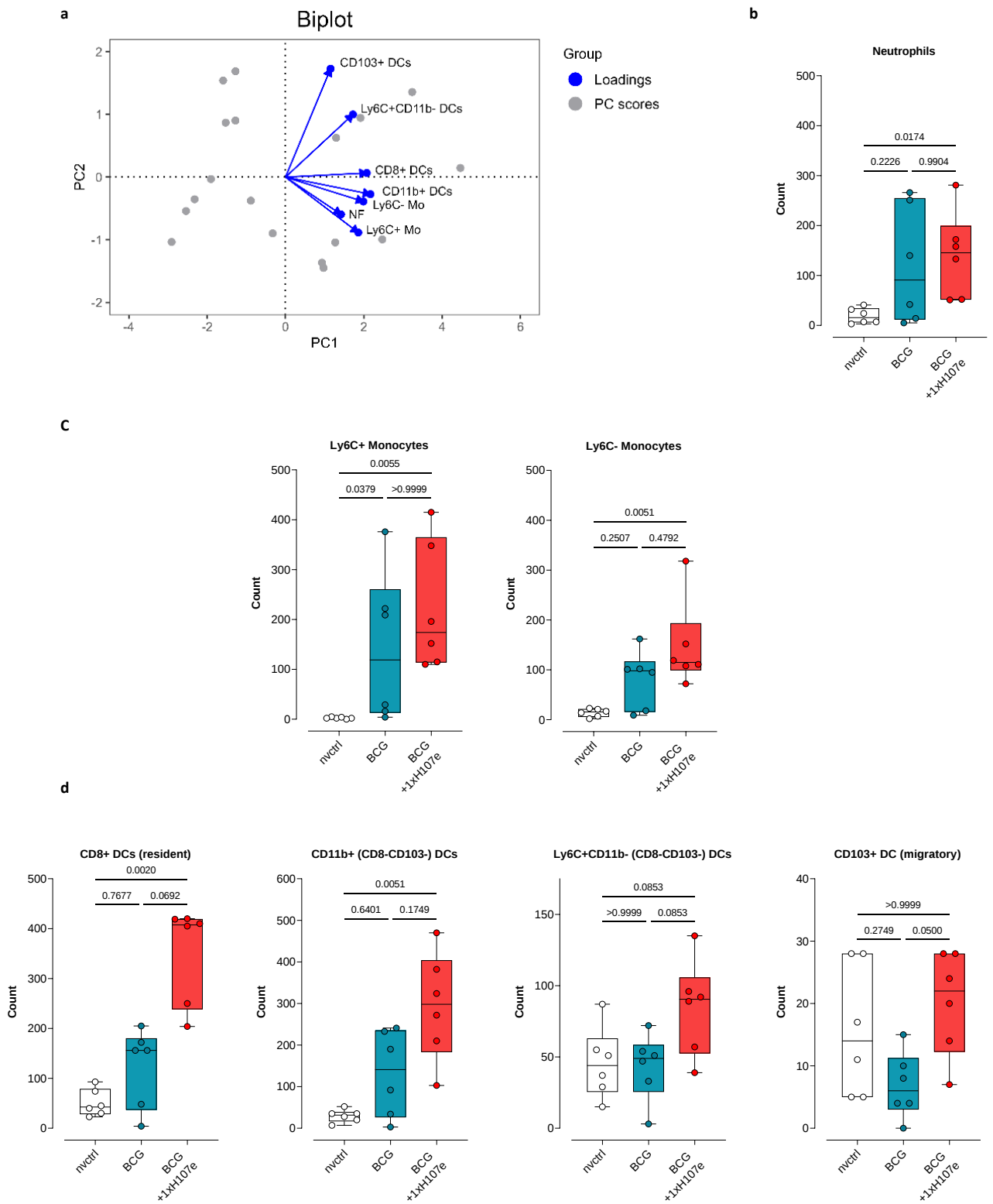
a Spleen bacterial loads of the animals from the study described in **Figure 2**, 4 (left panel) and 20 weeks (right panel) after challenge with Mtb. **b** Spleen bacterial loads of the animals from the study described in **Figure 3**, 4 (left panel) and 20 weeks (right panel) after challenge with Mtb. Line and error bars depict mean and SEM. Statistical significance of group differences was determined via one-way ANOVA and Tukey's multiple comparison test



Supplementary Figure 3

a H107e specific IFN- γ production by splenocytes from animals vaccinated with 1xH107e/CAF $^{\text{®}}$ 01 or BCG+ 1xH107e/CAF $^{\text{®}}$ 01, as measured by ELISA. Data pooled from two independent studies, differentiated by symbol shape, and graphed as box plots with line at median, boxes indicating interquartile range, and whiskers delineating minimum and maximum values. **b** Comparison of individual cytokine responses between the animals vaccinated with 3xH107e/CAF $^{\text{®}}$ 01 versus BCG+ 3xH107e/CAF $^{\text{®}}$ 01, 1 week after vaccination. Data graphed as box plots with line at median, boxes indicating interquartile range, and whiskers delineating minimum and maximum values. Statistical significance of group differences determined via unpaired t-test

Supplementary Figure 4



Supplementary Figure 4

a Loadings from PCA on neutrophil, Ly6C- and Ly6C+ monocyte, CD8a+-resident, CD103+-migratory, CD11b+ and Ly6C+ DC cell numbers in vaccine-draining lymph nodes at week 5 post immunization among BCG and BCG +1x H107e/CAF®01 immunized relative to non-immunized mice. **b** Number of neutrophilic cells **c** Number of Ly-6C+ (left) and Ly-6C- (right) monocytes. **d** Number of DC subsets. From left to right, plots show: 1) CD8a+ resident DCs, 2) CD11b+ (CD8a-CD103-) DCs, 3) Ly-6C+CD11b+ (CD8a-CD103-) DCs and 4) CD103+ migratory DCs. Data are in all cases graphed as box plots showing median $\pm$ IQR with whiskers signifying the range of responses. Statistical significant differences between groups determined using Kruskal-Wallis and Dunn's multiple comparison test, n=6.