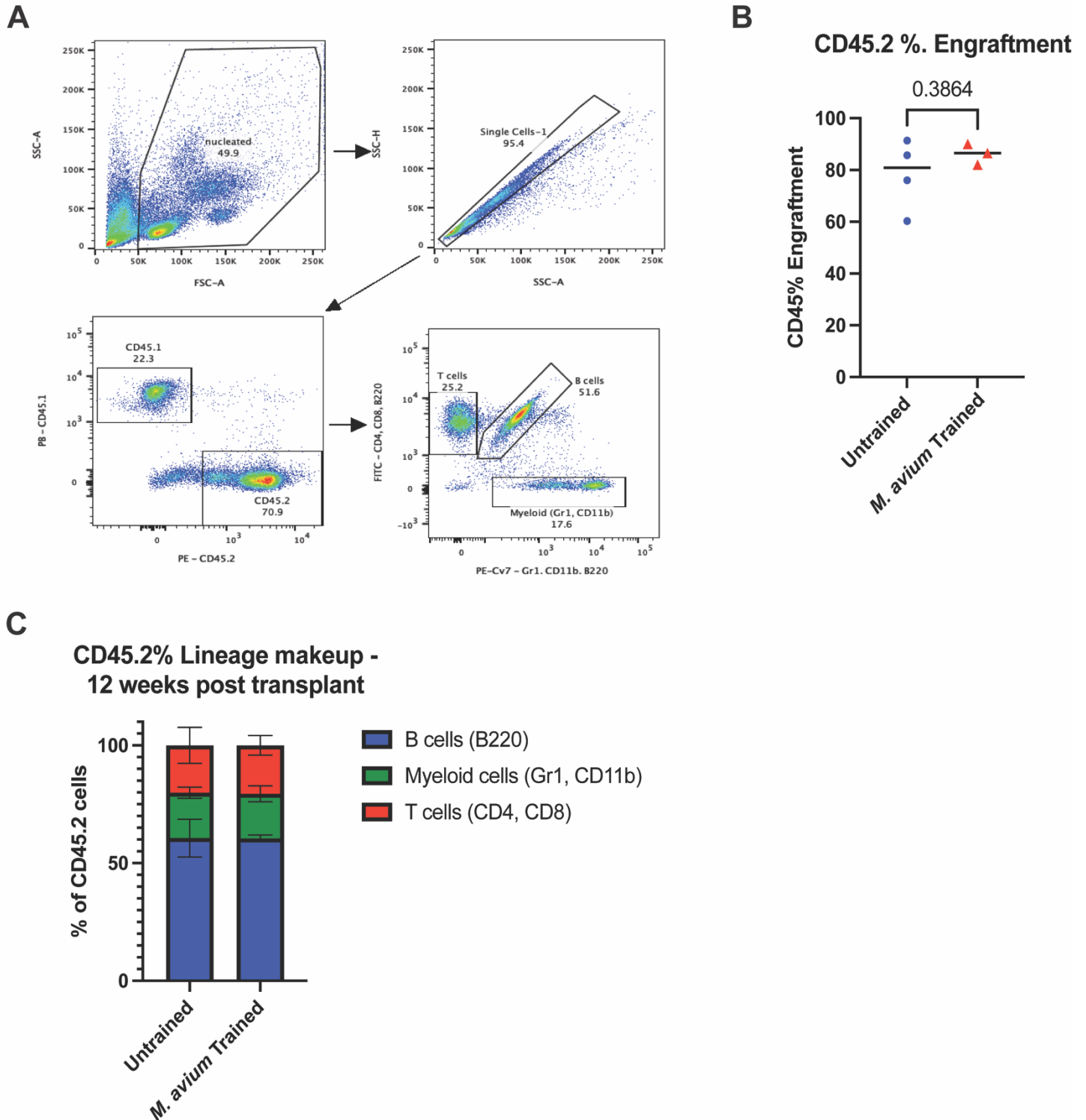


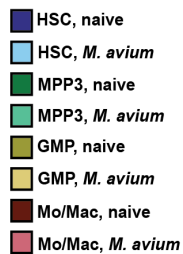
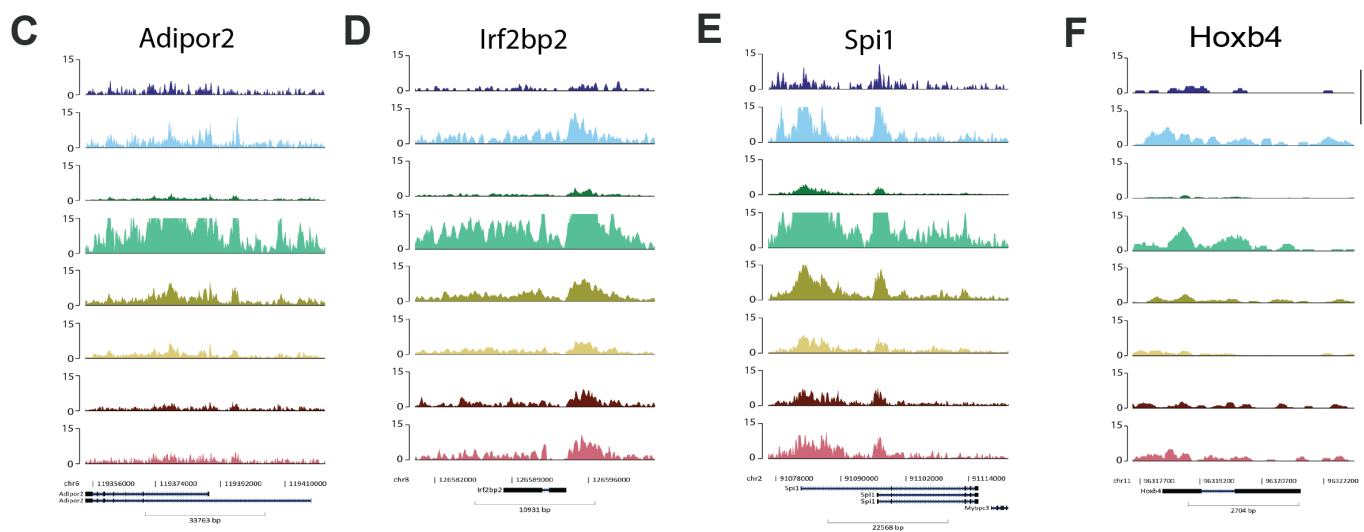
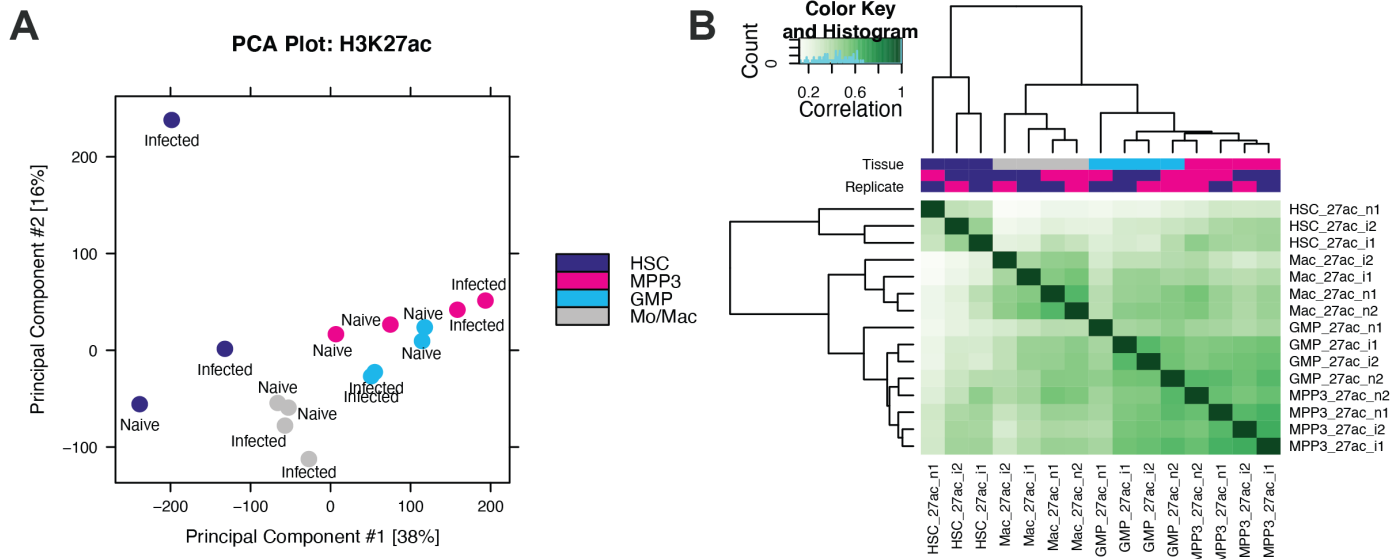
Supplemental Figures

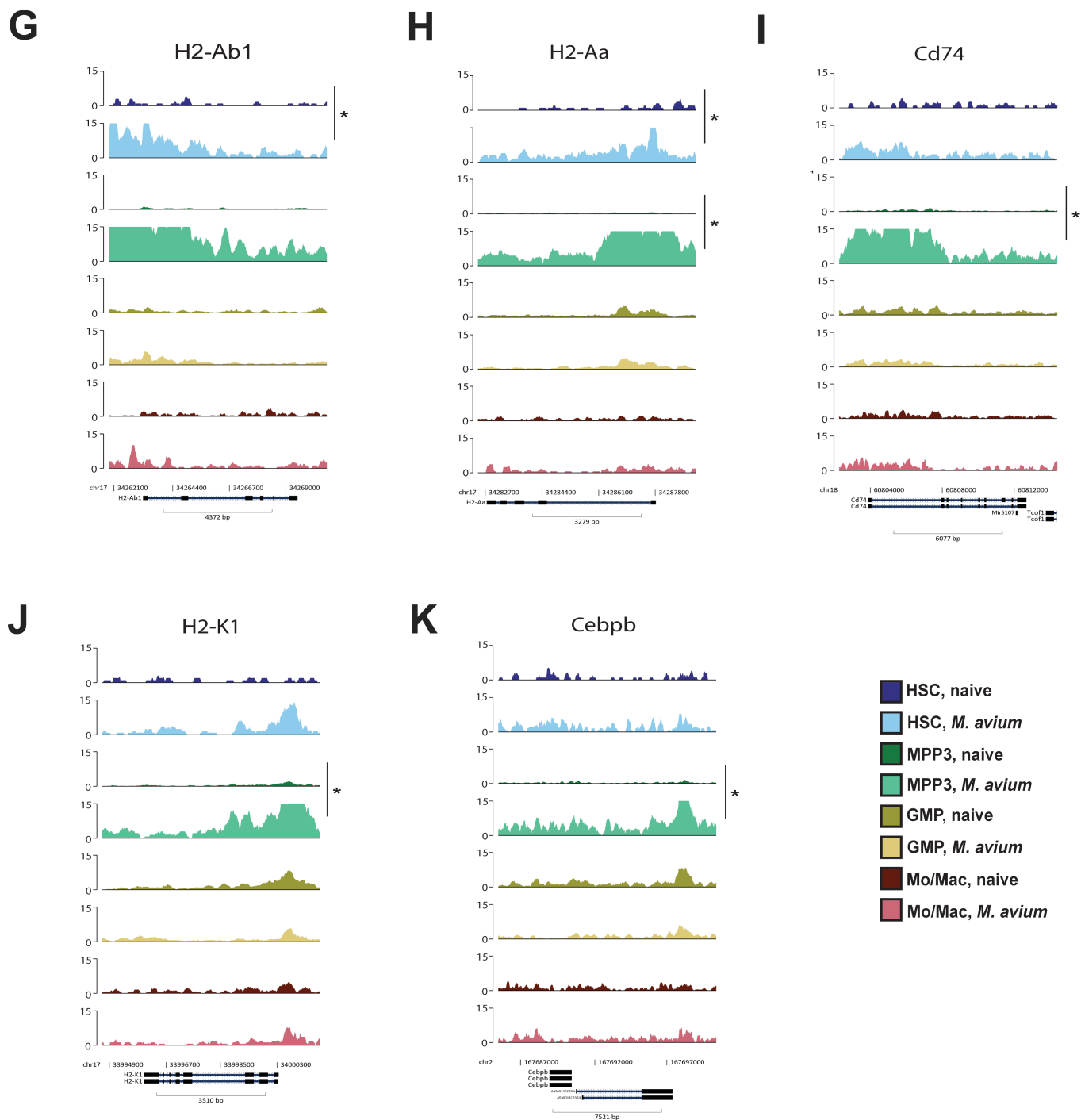


Supplemental Figure 1: Analysis of transplant engraftment of trained immunity transplant experiments.

(A) Peripheral blood engraftment flow cytometry gating strategy to identify donor distinct cells and trilineage production. **(B)** Percentage of CD45.2 bone marrow compared to total CD45.2 and CD45.1

cells. Representative engraftment of two independent experiments. **(C)** Lineage breakdown of CD45.2 positive cells within untrained and *M. avium* trained groups. Figure representative of two independent experiments. Unpaired Student's t test was used for **(B)**, showing no significant differences in CD45.2 engraftment.



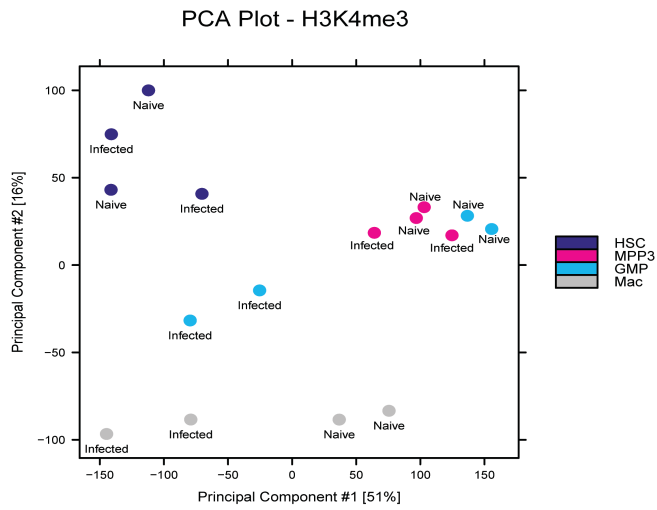
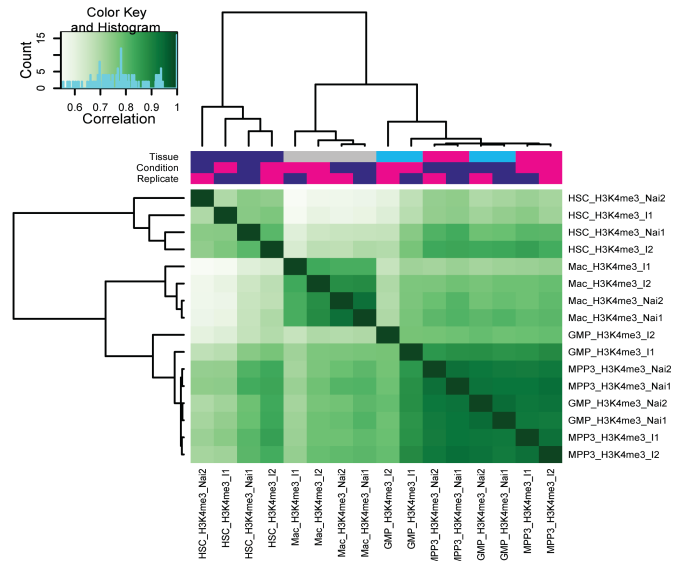
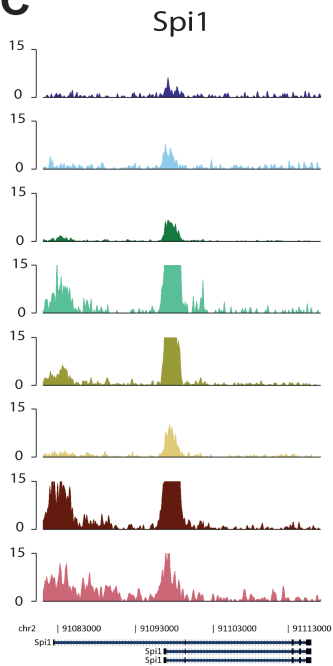
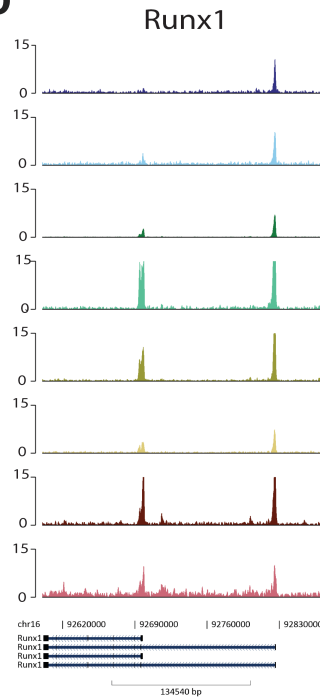
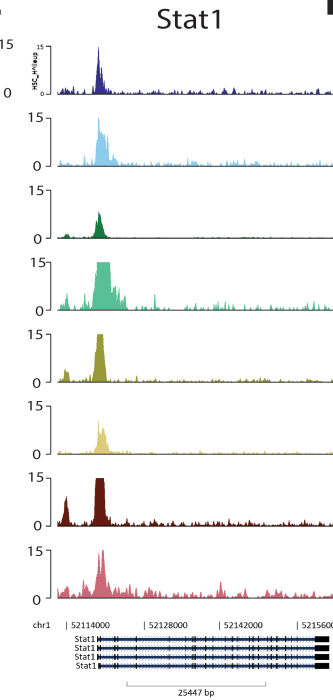
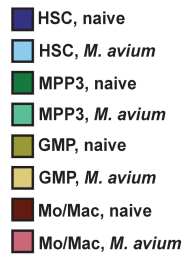
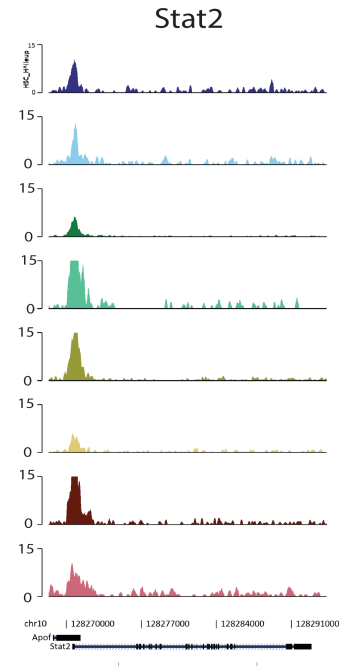


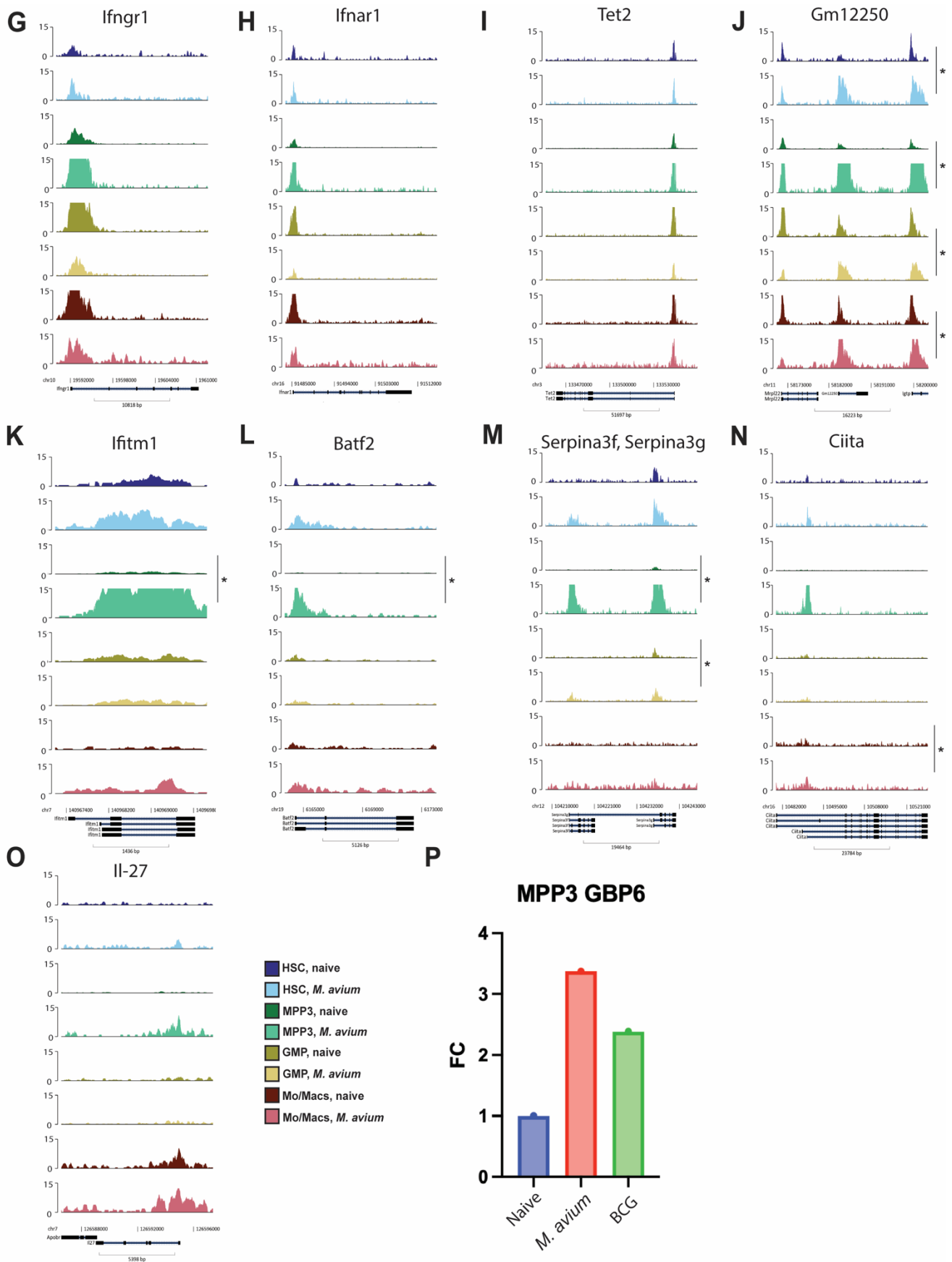
Supplemental Figure 2: Analysis of CUT&RUN-sequenced H3K27ac libraries and genomic coverage from *M. avium* infected and naive samples.

(A) PCA Plot of H3K27ac libraries in both *M. avium* infected and naïve groups **(B)** Pearson correlation plot of H3K27ac sample libraries **(C-D)** Coverage plots of *Adipor2* **(C)**, *Irf2bp2* **(D)**, *Spi1* **(E)**, and *Hoxb4* **(F)**. Comparisons marked with an asterisk were found to be significant at least at FDR

< 0.05. **(G-K)** Coverage plots of *H2-Ab1* **(G)**, *H2-Aa* **(H)**, *Cd74* **(I)**, *H2-K1* **(J)**, and *Cebpb* **(K)**.

Comparisons marked with an asterisk were considered significant at least at an FDR < 0.05.

A**B****C****D****E****F**



Supplemental Figure 3: Analysis of CUT&RUN-sequenced H3K4me3 libraries and genomic coverage from *M. avium* infected and naive samples.

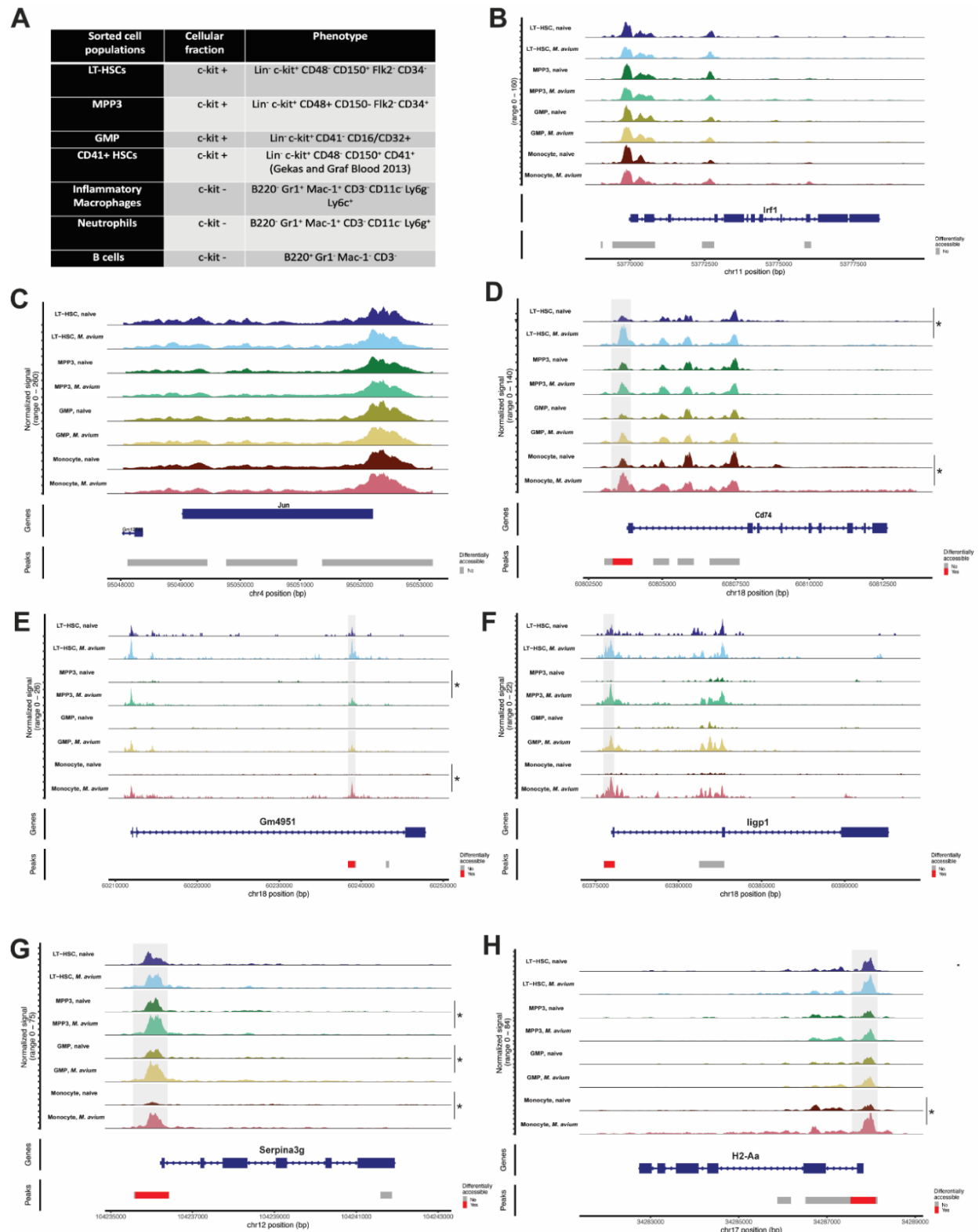
(A) PCA Plot of H3K4me3 libraries across cell types across naïve and *M. avium* infected conditions

(B) Pearson correlation plot of H3K4me3 libraries across cell types in naïve and *M. avium* infected conditions

(C-F) Coverage plots of *Spi1* **(C)**, *Runx1* **(D)**, *Stat1* **(E)**, and *Stat2* **(F)**. Comparisons marked with an asterisk were considered significant at least at an FDR < 0.05

(G-O) Coverage plots of *Ifngr1* **(G)**, *Ifnar1* **(H)**, *Tet2* **(I)**, *Gm12250* **(J)**, *Ifitm1* **(K)**, *Batf2* **(L)**, *Serpina3f*, *Serpina3g* **(M)**, *Ciita* **(N)**, and *Il-27* **(O)** Comparisons marked with an asterisk were considered significant with at least an FDR < 0.05.

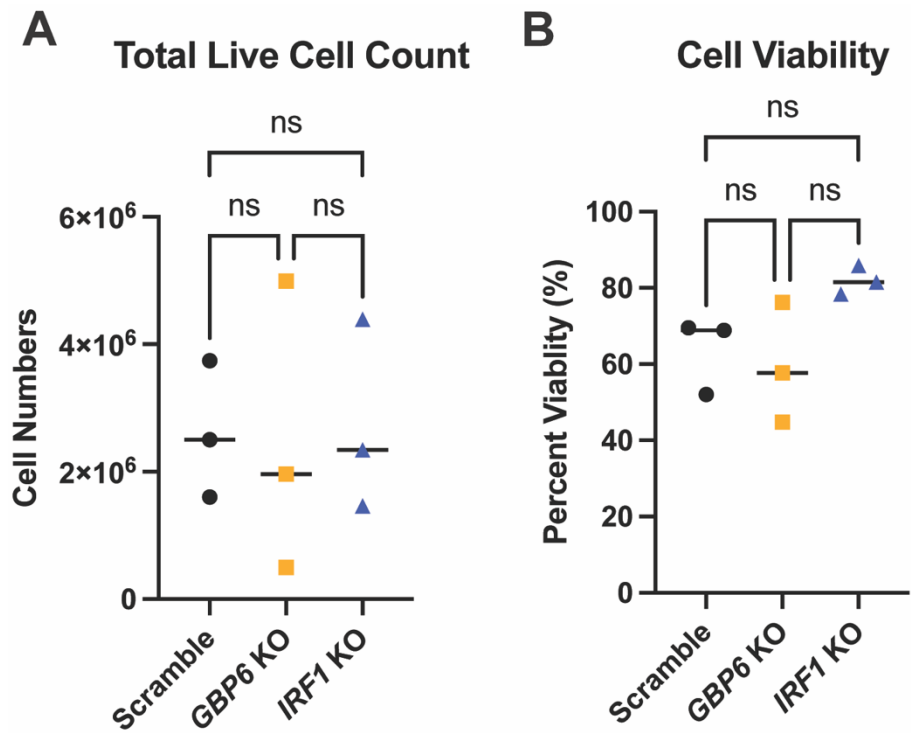
(P) Relative H3K4me3 marks at GBP6 in MPP3s after 2-week *M. avium* or BCG exposure.



Supplemental Fig.4: Genomic coverage and peakcalling of chromatin accessibility across *M. avium* infected and naive cell populations.

(A) Cell sorting table indicating cell surface markers used to specially sort cell populations via FACS

(B-G) Genomic coverage plots of *Irf1* **(B)**, *Jun* **(C)**, *Cd74* **(D)**, *Gm4951* **(E)**, *ligp2* **(F)**, *Serpina3g* **(G)**, *H2-Aa* **(H)**.



Supplemental Figure 5: PMA treatment of IRF1 KO and GBP6 KO THP-1 cells induces varying differentiation responses.

(A) Total live cell counts per group. Each dot represents the cell number from an independent experiment. n= 3 **(B)** Percent live cells based on AOPI staining of PMA-treated THP1 cells after three days stimulation. Each dot represents the percent cell viability from an independent experiment. n = 3 ns; not significant by one-way ANOVA.