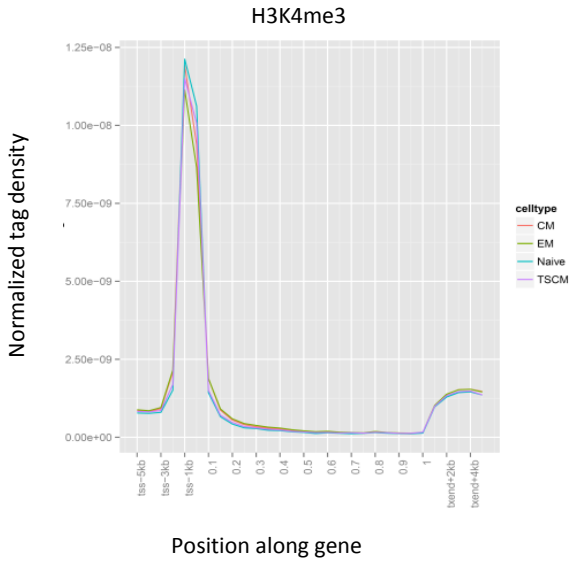
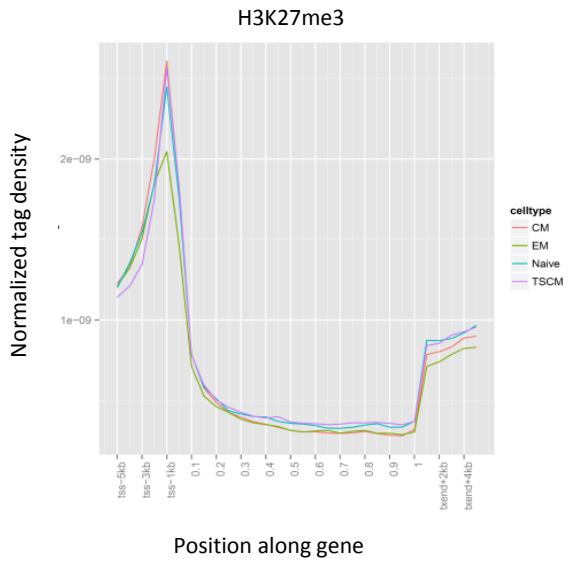
A)



B)



Supplemental Figure 1. Enrichment of H3K4me3 and H3K27me3 islands near transcription start sites Counts of modification tags falling in windows defined along the gene bodies and gene promoter regions (see Methods) were computed, and the tag count of each window normalized by the total number of bases in the window and the total number of genome-mapped and island-filtered ChIP-seq reads in the given library to obtain the normalized tag density profiles shown here for **(A)** H3K4me3 and **(B)** H3K27me3.

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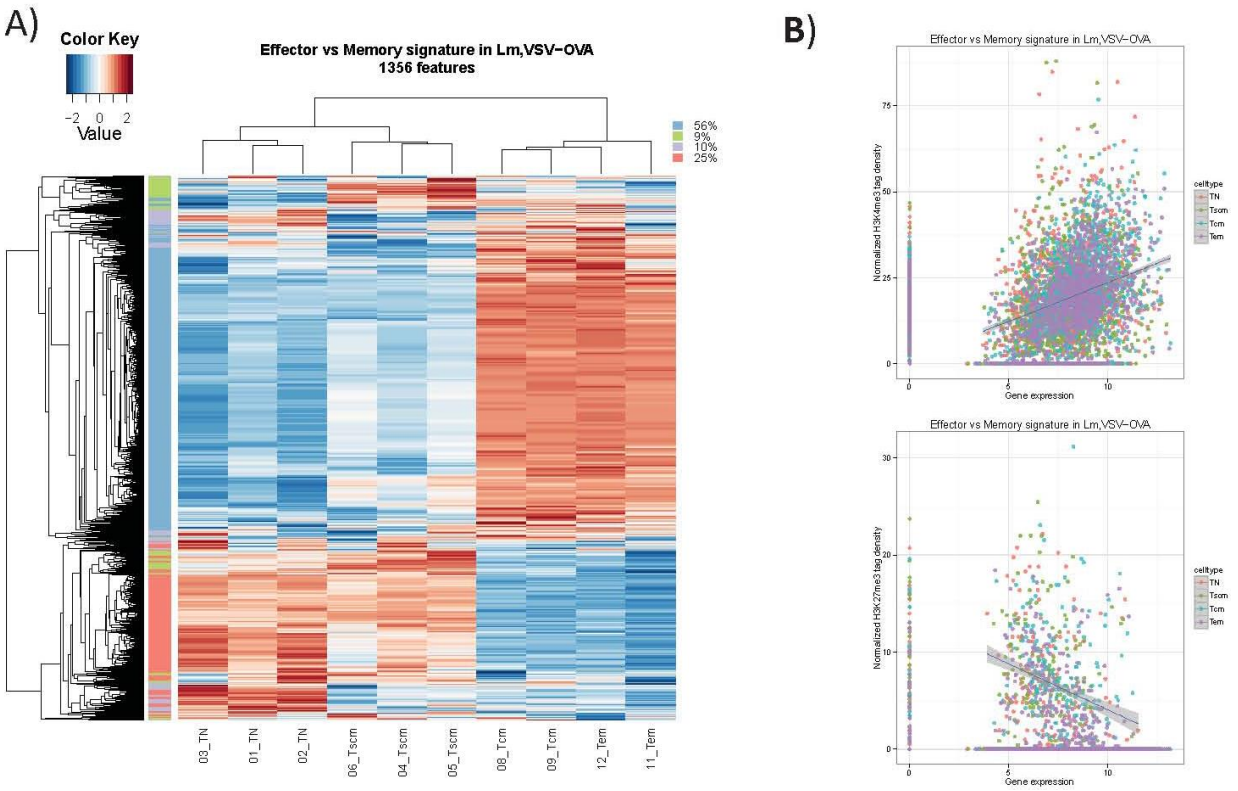

Supplemental Figure 2. Behavior of Immgen *in vivo* signature genes in our *in vitro* expression data. Clustering of our *in vitro*-derived T cell subsets using genes derived from comparison of memory versus effector transcriptomic data of *in vivo*-generated T cells from the Immgen Consortium (23). **(A)** Heat map of our expression data among the *in vivo* Immgen signature genes. Genes with similar patterns across the cell types are grouped using k-means algorithm and marked by colors alongside the rows. **(B**) Scatter plot showing H3K4me3 or H3K27me3 normalized tag density and its correlation with gene expression in indicated antigen-experienced CD8+ T cell subsets.

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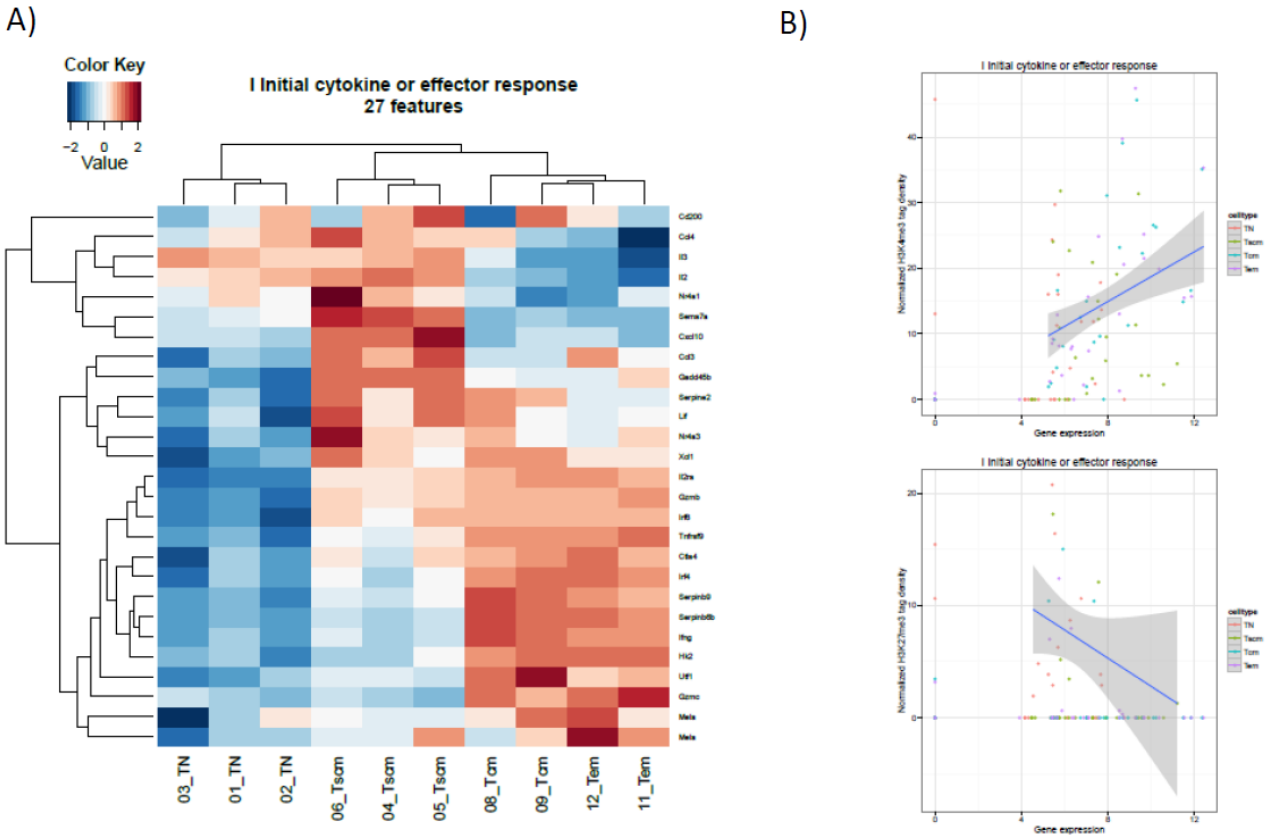

Supplemental Figure 3. Correlation between histone modification and expression levels of genes associated with initial cytokine or effector response (from Immgen *in vivo* clusters) (23). **(A)** Heat map of our expression data among the cluster genes and **(B**) Scatter plot showing H3K4me3 or H3K27me3 normalized tag density and its correlation with gene expression in indicated antigen-experienced CD8+ T cell subsets.

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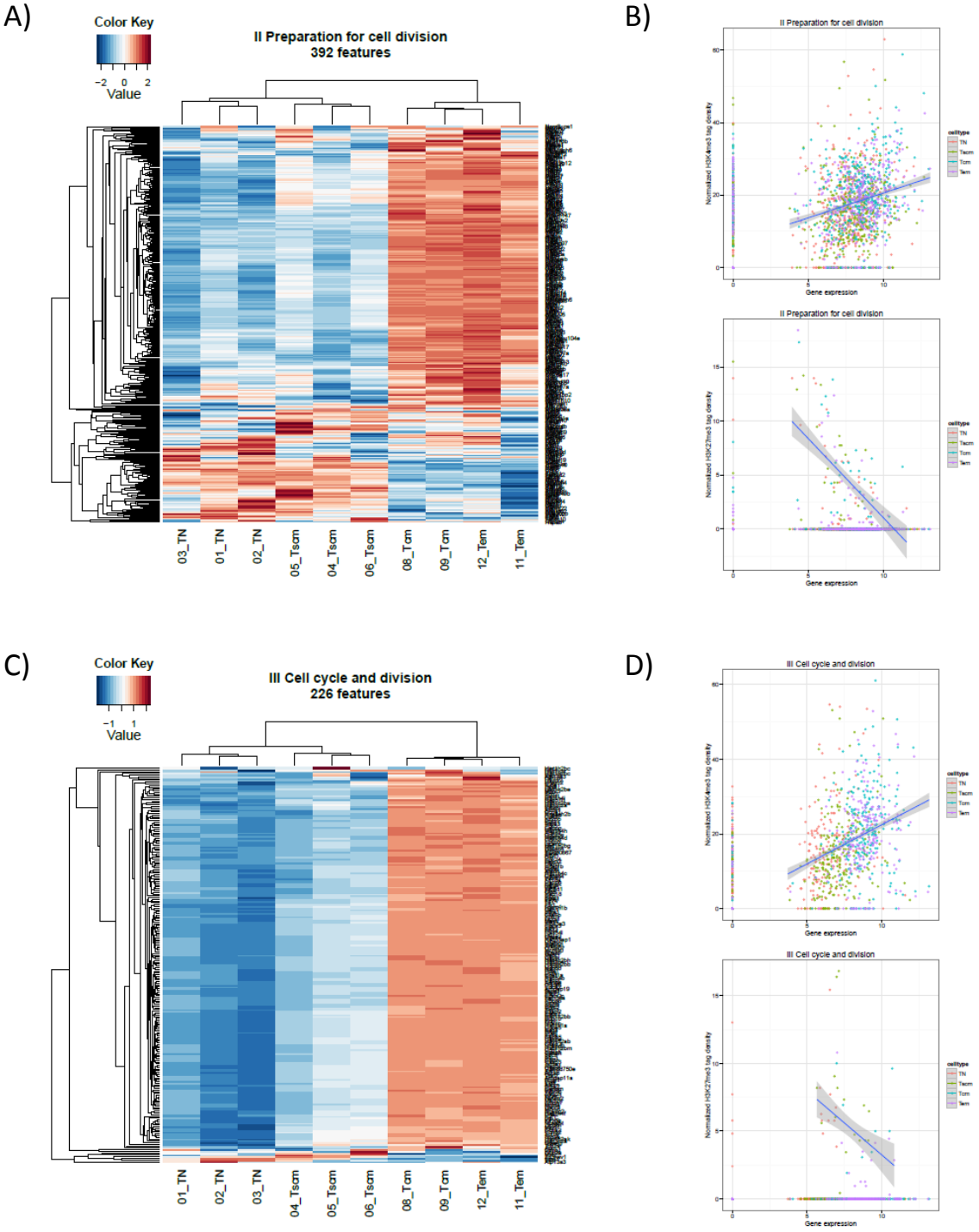
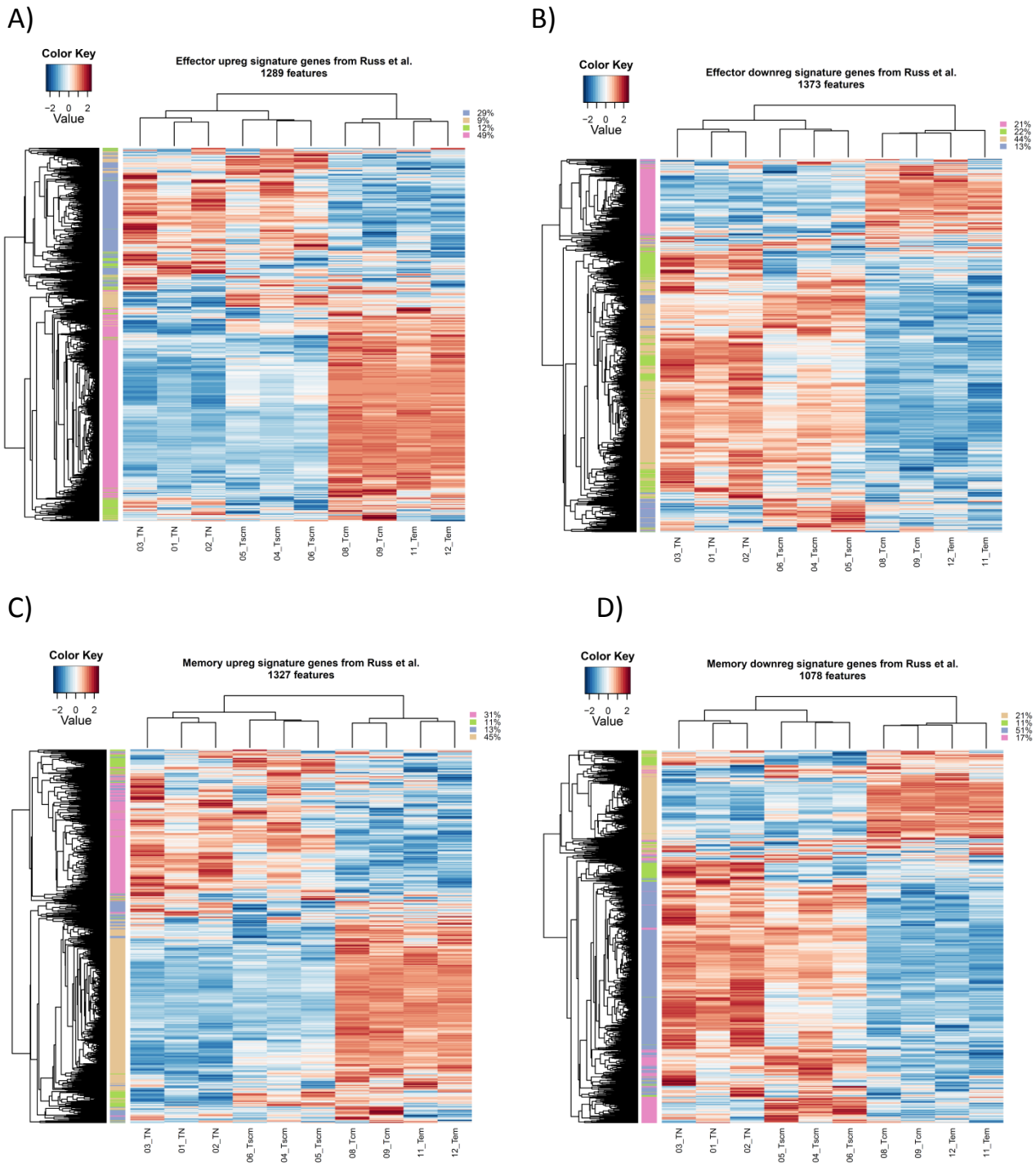
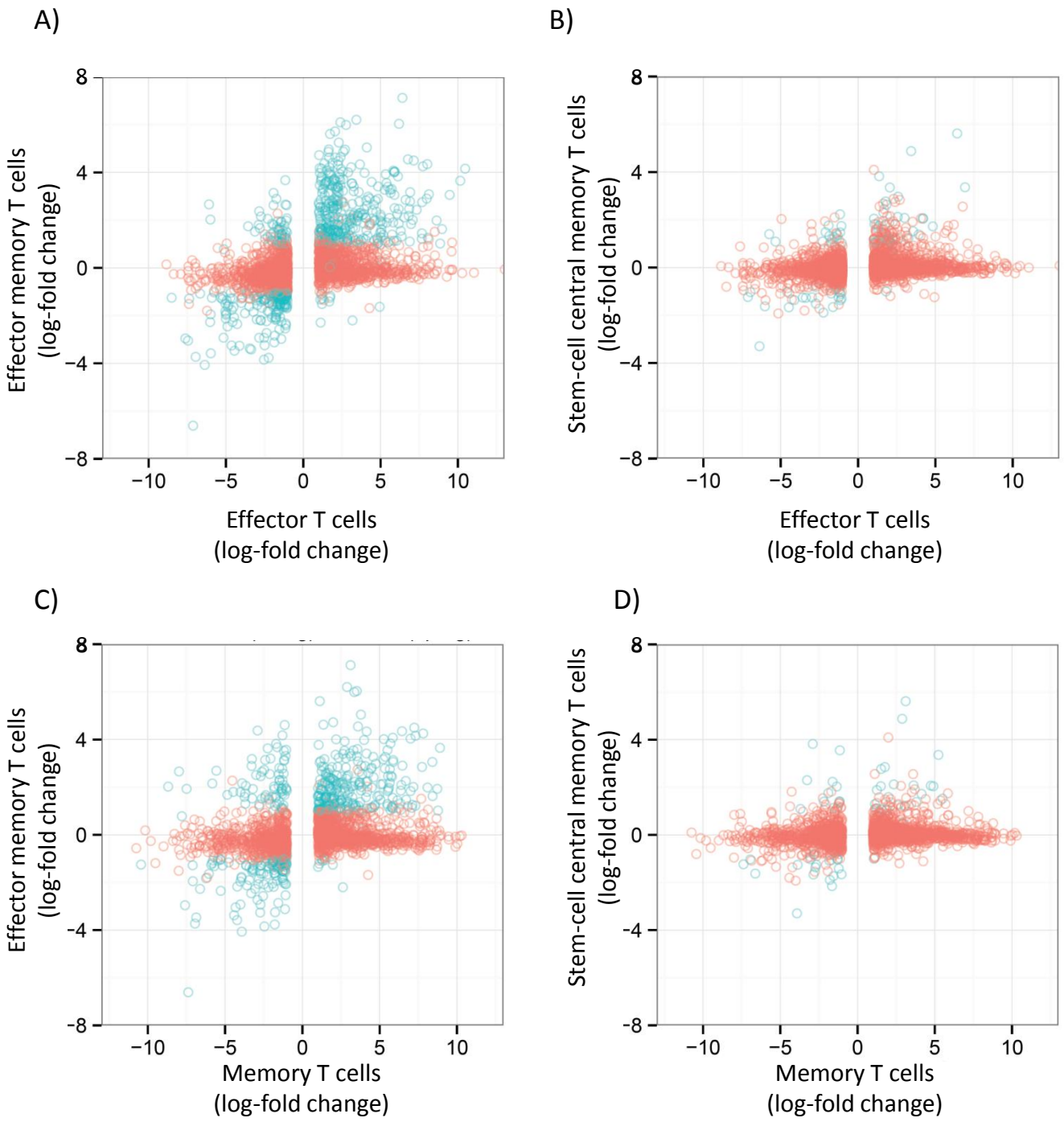


Supplemental Figure 4. Correlation between histone modification and expression levels of genes associated with preparation for cell division and cell cycle (from Immgen *in vivo* clusters) (23). **(A)** Heat map of our expression data among the Immgen cluster genes associated with "preparation for cell division" and **(B**) Scatter plot showing H3K4me3 or H3K27me3 normalized tag density and its correlation with gene expression of genes associated with "preparation for cell division" in indicated antigen-experienced CD8+ T cell subsets. **(C)** Heat map of our expression data among the Immgen cluster genes associated with "cell cycle and division" and **(D**) Scatter plot showing H3K4me3 or H3K27me3 normalized tag density and its correlation with gene expression of genes associated with "cell cycle and division" in indicated antigen-experienced CD8+ T cell subsets.



Supplemental Figure 5. Evaluation in our T cell subsets of genes that were recently reported (in ref 24) to either be upregulated or downregulated in *ex vivo*-isolated memory and effector T cells. Heat maps showing expression of genes (A) upregulated in effector T cells (B) downregulated in effector T cells (C) upregulated in memory T cells or (D) downreglated in memory T cells—among antigen-experienced subsets of CD8 T cells: naïve (T_N), stem-cell memory (T_{SCM}), central memory (T_{CM}), and effector memory (T_{EM}).



Supplemental Figure 6. Correlation between gene expression in our T cells subsets with genes that were recently reported (in ref 24) to either be upregulated or downregulated in *ex vivo*-isolated memory and effector T cells. Scatter plots showing correlation of log fold-change in indicated subset compared to naïve T cells: **(A)** effector memory (T_{EM}) versus effector T cells (ref. 24). P= $3.8e^{-69}$ (dnreg), P=$7.3e^{-163}$ (upreg) **(B)** stem-cell memory (T_{SCM}) versus effector T cells (ref. 24). P= $4.1e^{-12}$ (dnreg), P=$8.5e^{-21}$ (upreg) **(C)** effector memory (T_{EM}) versus memory T cells (ref. 24). P= $2.1e^{-46}$ (dnreg), P=$1.2e^{-87}$ (upreg) or **(D)** stem-cell memory (T_{SCM}) versus effector T cells (ref. 24). P= $1.6e^{-13}$ (dnreg), P=$1.3e^{-08}$ (upreg) Both signature sets were obtained using the same criteria of Benjamini-Hochberg-adjusted p value (FDR) < 0.05 and absolute fold change of at least 2 when comparing subsets with naïve T cells. The p values in these figures show the significance (hypergeometric P value) of overlap between the corresponding signatures from both studies.