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Supplemental Information

Plasma Cell Fate Is Orchestrated

by Elaborate Changes in Genome

Compartmentalization and Inter-chromosomal Hubs

Alexandra Bortnick, Zhaoren He, Megan Aubrey, Vivek Chandra, Matthew Denholtz, Kenian Chen, Yin C. Lin, and Cornelis Murre

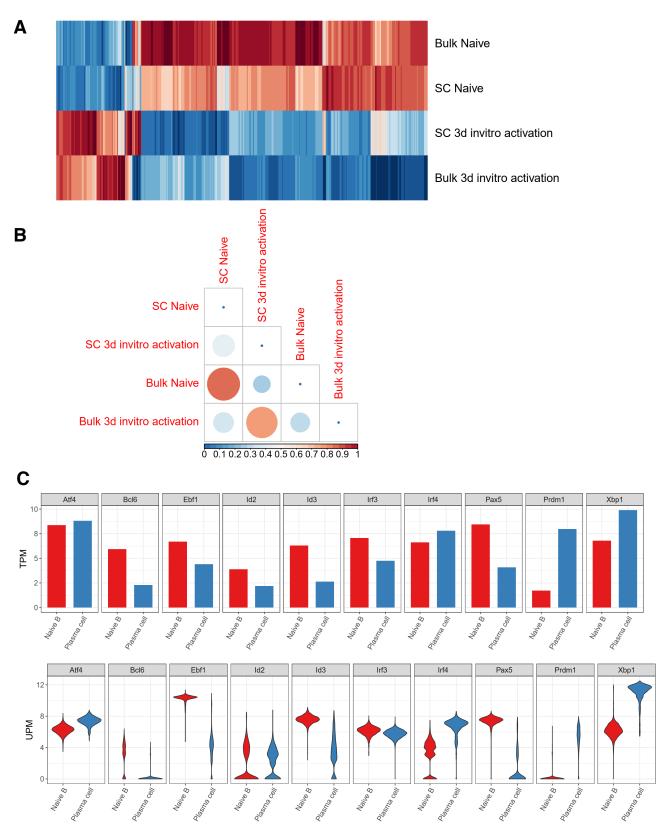
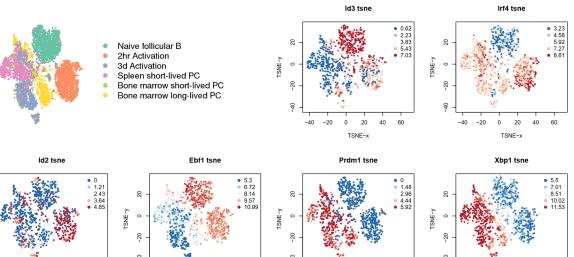
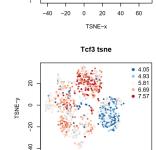
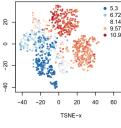


Figure S1. Single Cell RNA-seq Read Density Closely Correlates with Bulk RNA-seq Read Density. (Related to Figure 1). (A) Heatmap of genes expression for each sample. Single cells were merged. Each column is a gene. Gene expression is measured as Z-normalized UPM. (B) Spearman correlation between bulk RNA-seq and pseudo-bulk RNA-seq generated by merging scRNA-seq reads.
(C) Top panel: Bar-plot of bulk RNA-seq for *Atf4*, *Bcl6*, *Ebf1*, *Id2*, *id*, *Irf3*, *Irf4*, *Pax5*, *Prdm1* and *Xbp1*. Bottom panel: Violin plot of single cell RNA-seq *Atf4*, *Bcl6*, *Ebf1*, *Id2*, *id*, *Irf3*, *Irf4*, *Pax5*, *Prdm1* and *Xbp1*.



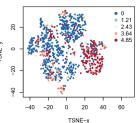




Tcf4 tsne

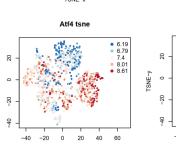
20

TSNE->

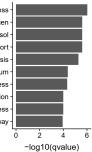




-20



Genes activated in short-lived plasma cells



TSNE

response to endoplasmic reticulum stress antigen processing and presentation of peptide antigen retrograde protein transport, ER to cytosol endoplasmic reticulum to cytosol transport negative regulation of hemopoiesis protein exit from endoplasmic reticulum regulation of catabolic process response to metal ion ER-associated ubiquitin-dependent protein catabolic process ERAD pathway

20

TSNE-

60

10 20 15

-log10(qvalue)

10

20

Genes maintaining follicular naïve B state

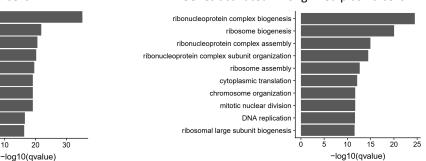
Genes activated in plasma cells

regulation of leukocyte activation leukocyte cell-cell adhesion lymphocyte aggregation leukocyte aggregation regulation of lymphocyte activation lymphocyte differentiation negative regulation of immune system process regulation of leukocyte cell-cell adhesion ribonucleoprotein complex biogenesis

TSNE->

regulation of cell activation

Genes activated in long-lived plasma cells



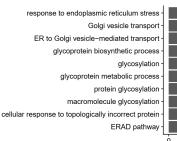


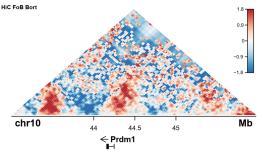
Figure S2. Gene Expression Patterns and GO Analysis for Differentially Expressed Genes. Related Figure 1. (A) TSNE plot of single cell RNA-seq. Each dot is a single cell. The first TSNE plot is labeled to show the origin of each cell. Color in the rest of the plots indicates the expression level of corresponding gene. Expression level unit is UPM. (B) GO term bar-plot for DE gene between naïve B cells and 3d in-vitro activated plasma cells (left). GO term bar-plot for DE gene between bone marrow B220⁻ plasma cell and bone marrow B220⁺ plasma cell (right).

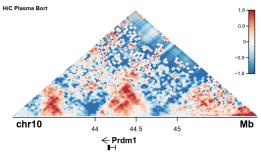
40 -20

TSNE-y

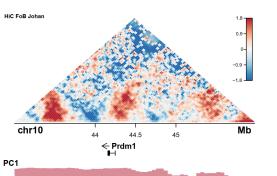
В

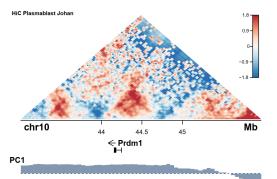
PC1

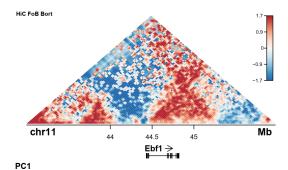








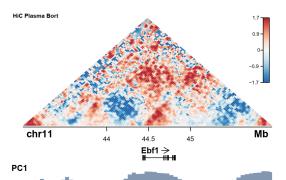




44.5

Ebf1 →

45





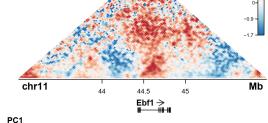


Figure S3. Plasma Cell Fate is Associated with Large-Scale Changes in Chromatin Folding Across the *Prdm1 and Ebf1* **Loci. Related to Figure 3. (A)** Contact map for chromosome 10 across the *Prdm1* locus at 50 kb resolution for follicular B and plasma cells derived from TCC data (top panels) or derived from HiC data (bottom panels). **(B)** Contact map for chromosome 11 across the *Ebf1* locus at 50 kb resolution for plasma cells from TCC data (top panels) or derived from HiC data (bottom panels).

Mb

HiC FoB Johan

chr11

PC1

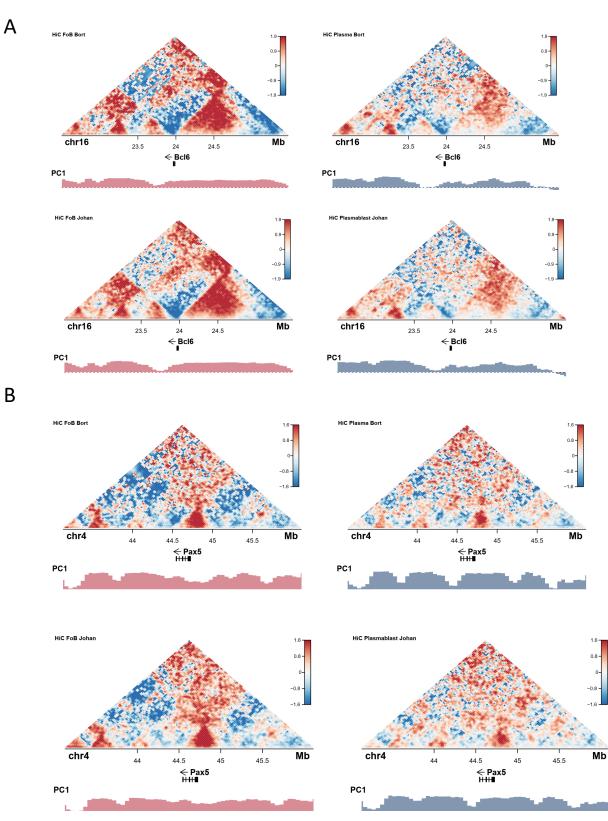


Figure S4. Plasma Cell Fate is Associated with Large-Scale Changes in Chromatin Folding Across the *Bcl6 and Pax5* **Loci. Related to Figure 3. (A)** Contact map for chromosome 10 across the *Bcl6* locus at 50 kb resolution for follicular B and plasma cells derived from TCC data (top panels) or derived from HiC data (bottom panels) (Johanson et al., 2018). **(B)** Contact map for chromosome 11 across the *Pax5* locus at 50 kb resolution for plasma cells from TCC data (top panels) or derived from HiC data (bottom panels) (Johanson et al., 2018).

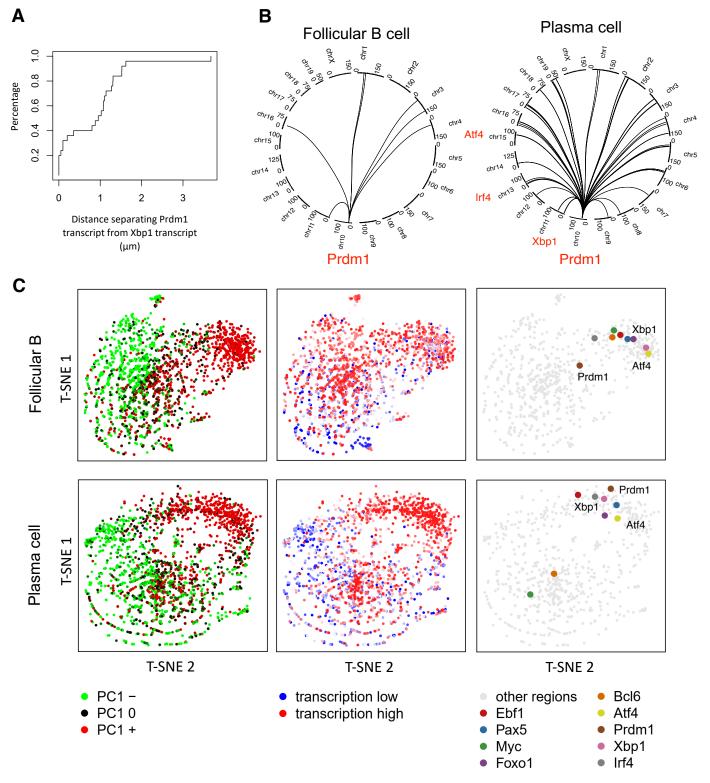


Figure S5. Inter-Chromosomal Associations Involving the *Prdm1* Locus. Related to Figure 5. (A) Cumulative distribution of distance between Prdm1 and Xbp1 intronic RNA-FISH dots in 3d-activated plasma cells. (B) Circos plots for inter-chromosomal association centered on *Prdm1*. Genes contained within the 1 Mb interaction region and that appear in the inter-chromosomal cloud plot are indicated in red. (C) Inter-chromosomal association cloud plots showing the relative inter-chromosomal association preference of all genome regions (computed based on inter-chromosomal TCC reads). Each dot represents a 1 Mb region of the genome. The closer two dots in 2D distance, the more likely they share significant inter-chromosomal association. Dots are colored by PC1 value (left), transcriptional activity (middle) and genes of interest (right).