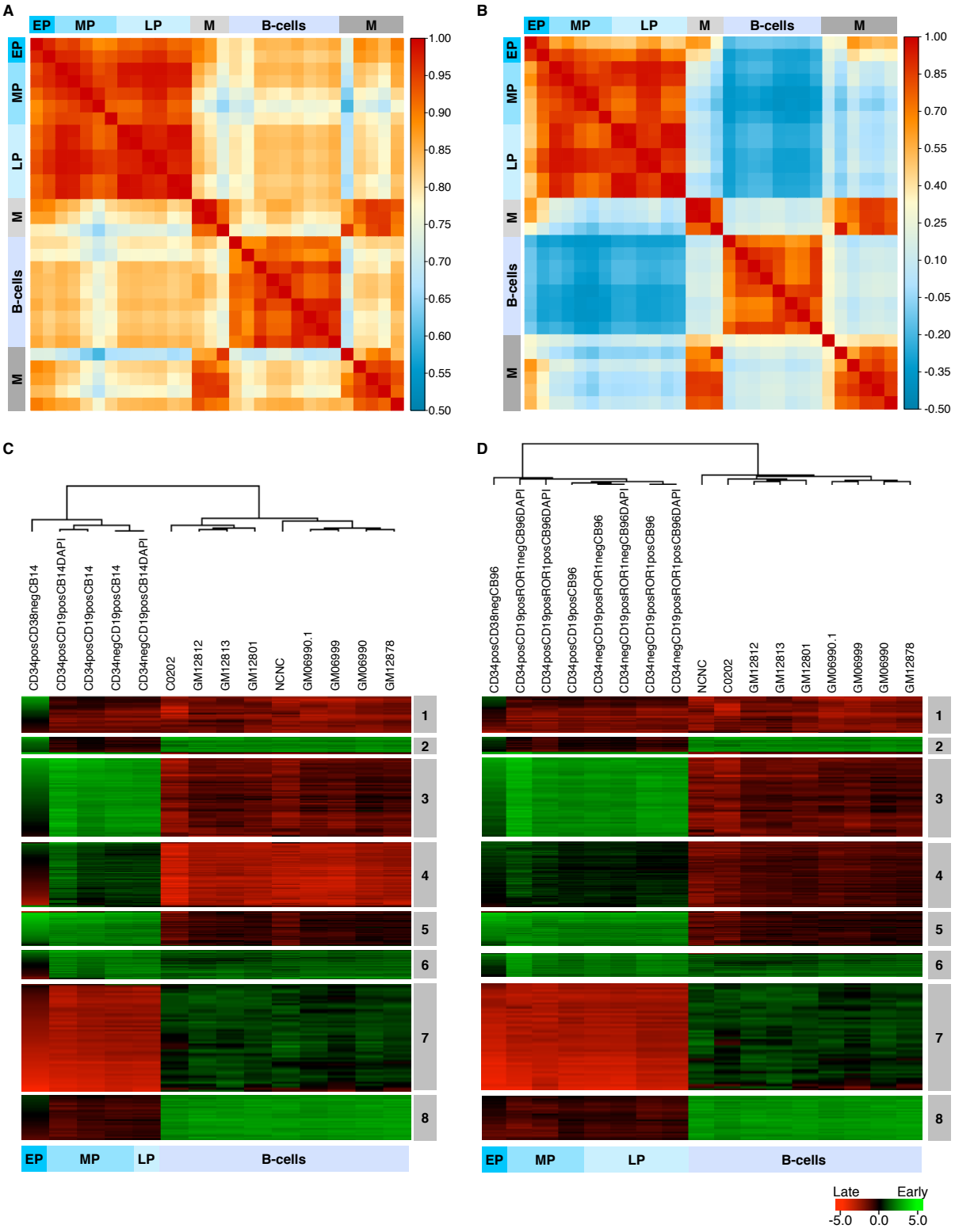
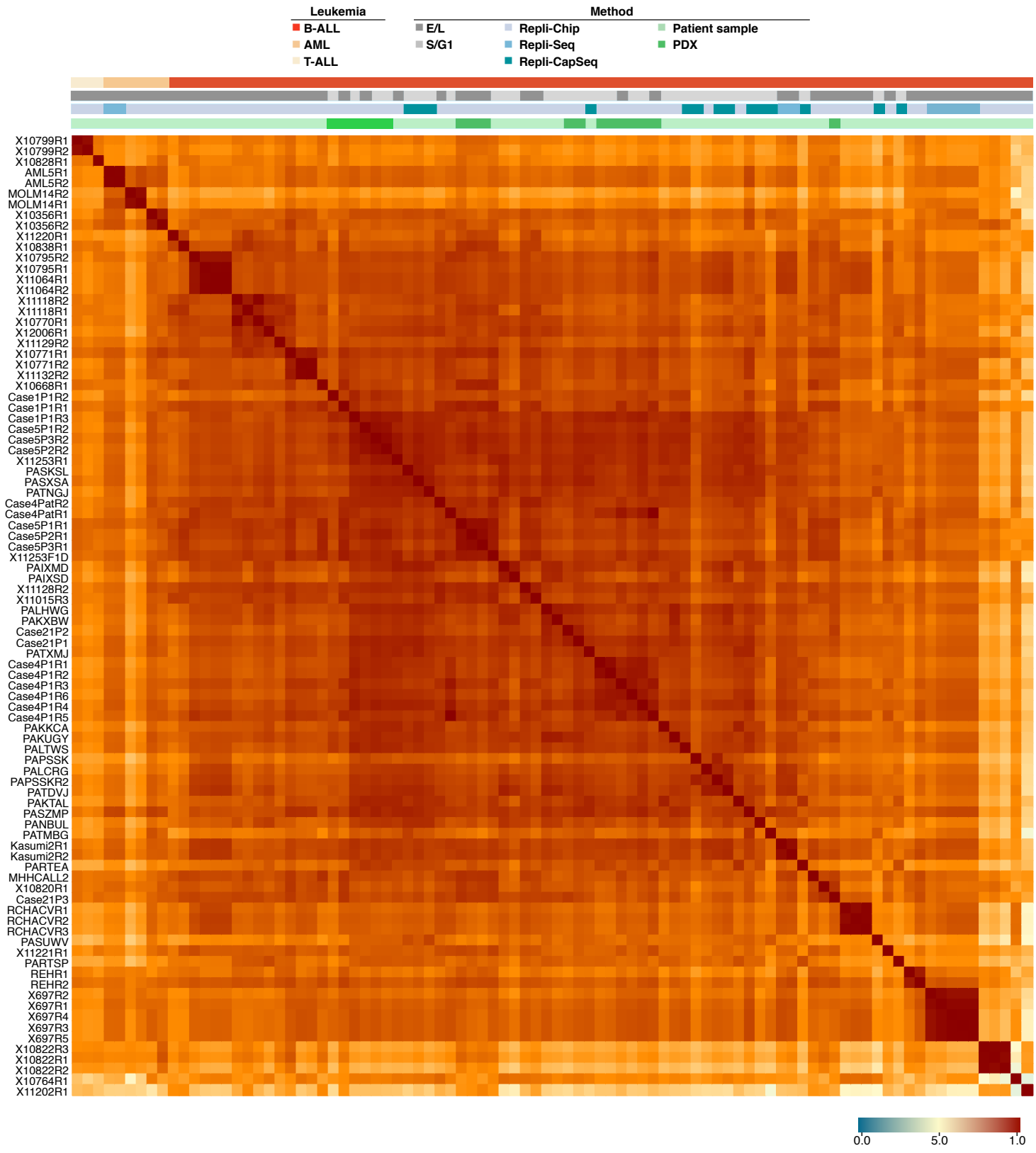
Supplementary Figure S1



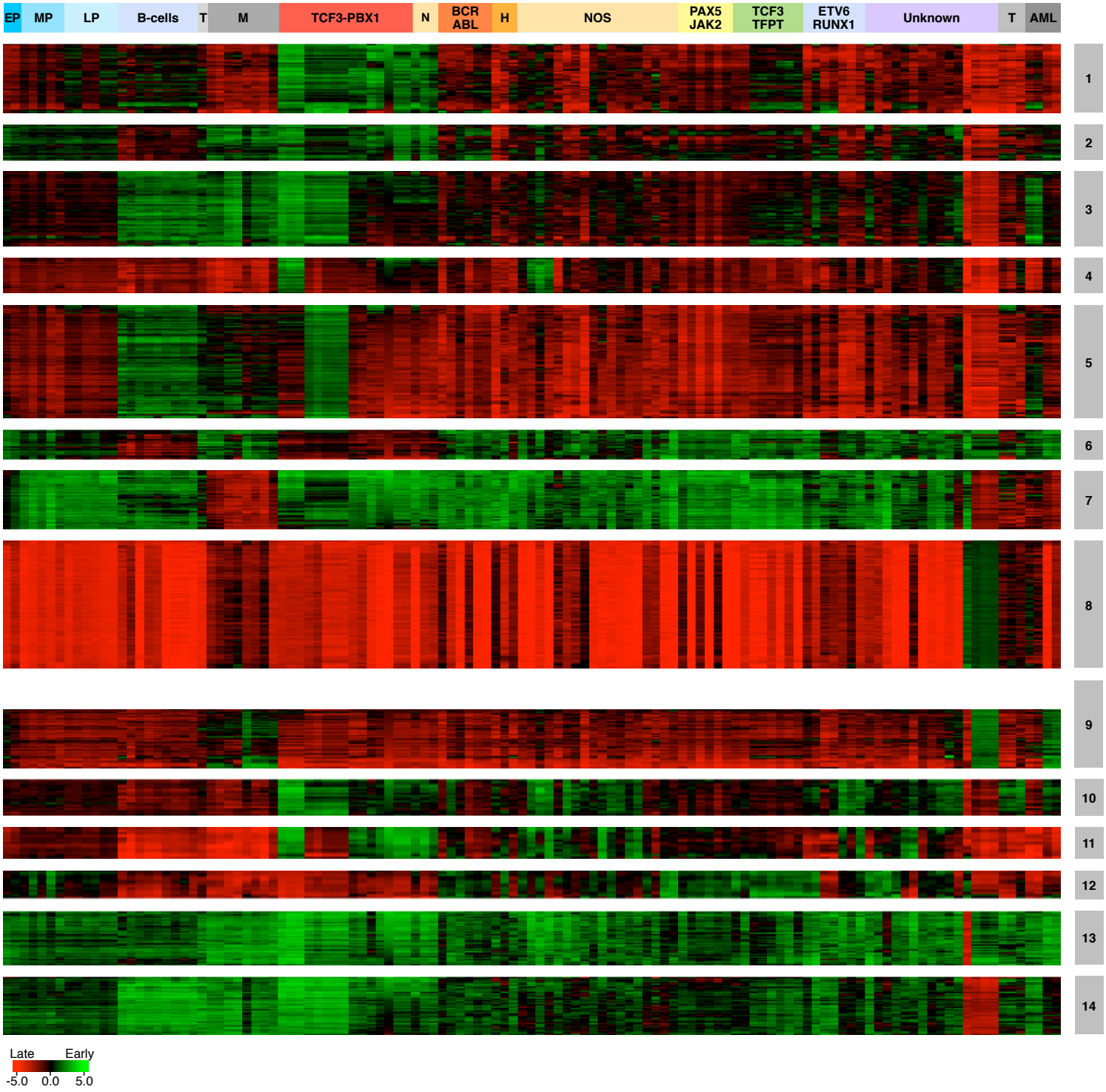
Supplemental Figure S1. Correlation matrix of normal blood cell types. **(A)** Whole genome correlations. **(B)** Correlations using only the RT variable genome segments. **(C-D)** RT signatures per cord blood. EP = early progenitors (CD34+CD38-), MP = middle progenitors (CD34+CD19+), LP = late progenitors (CD34-CD19+), T= normal T-cells, M = myeloid-erythroid progenitors.

Supplementary Figure S2



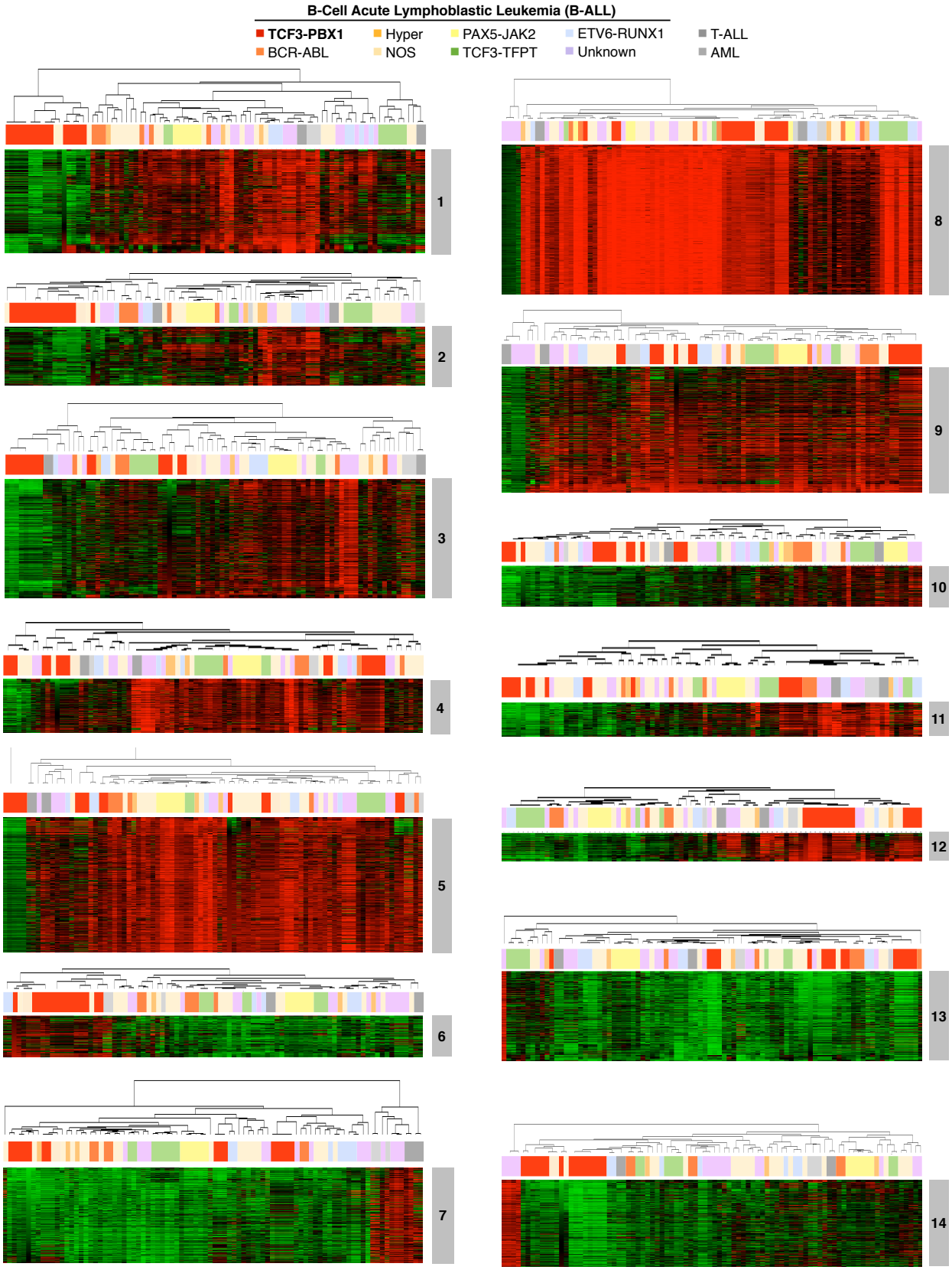
Supplemental Figure S2. Correlation matrix of BCP-ALL patient samples. Genome-wide RT datasets were divided into 55,940 50-kb segments, variable segments were removed and a correlation matrix of constitutive genomic segments was constructed. Datasets were sorted according to their similarity (Pearson's correlation) and are displayed in the same order as in **Figure 2C**.

Supplementary Figure S3



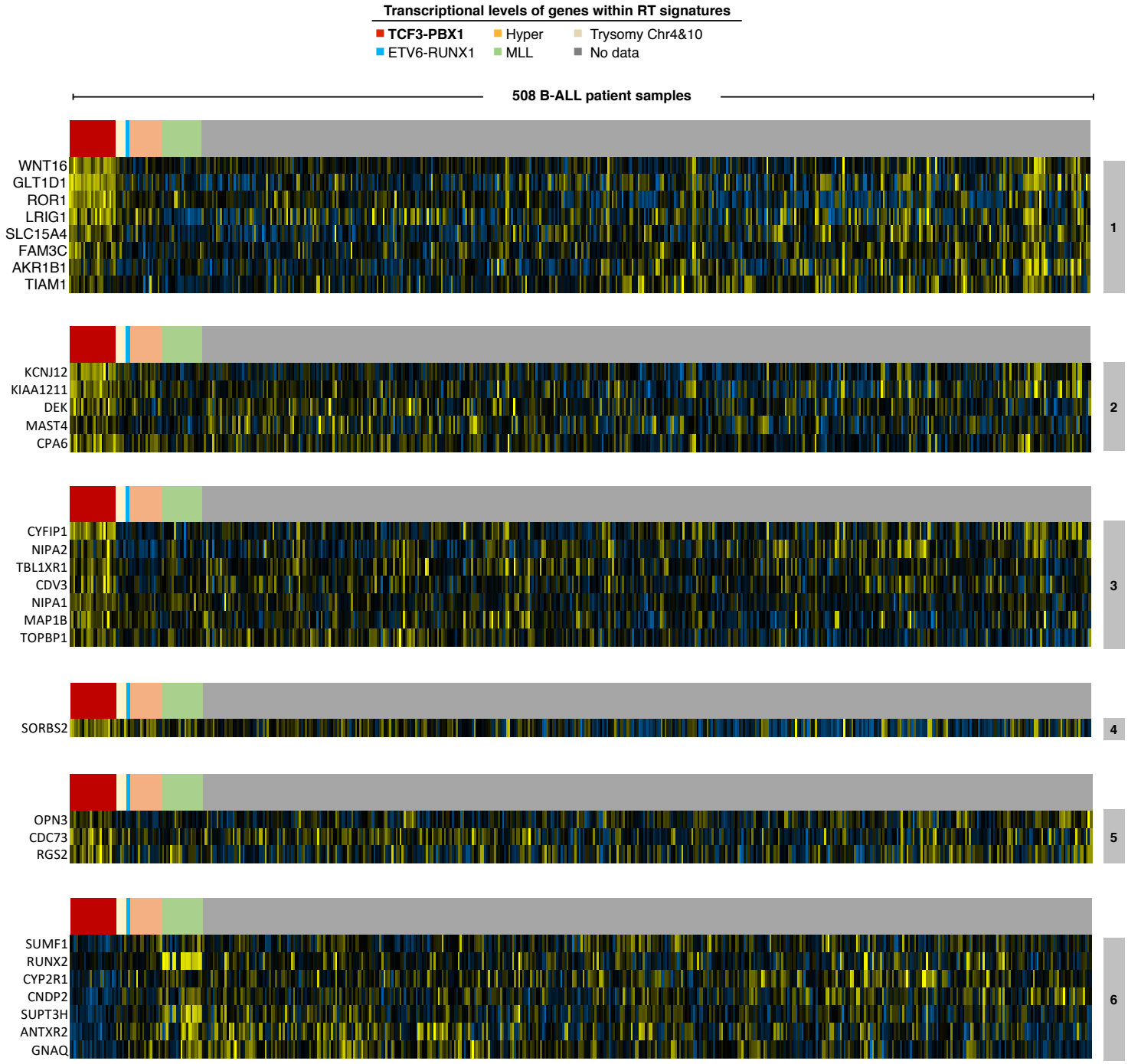
Supplemental Figure S3. RT patterns of BCP-ALL RT signatures in normal blood cell types. RT of all genomic segments from RT signatures shown in **Figure 3A** are displayed together with the data derived from normal B-cell development. EP = early progenitors (CD34+CD38-), MP = middle progenitors (CD34+CD19+), LP = late progenitors (CD34-CD19+), T= normal T-cells, M = myeloid-erythroid progenitors.

Supplementary Figure S4



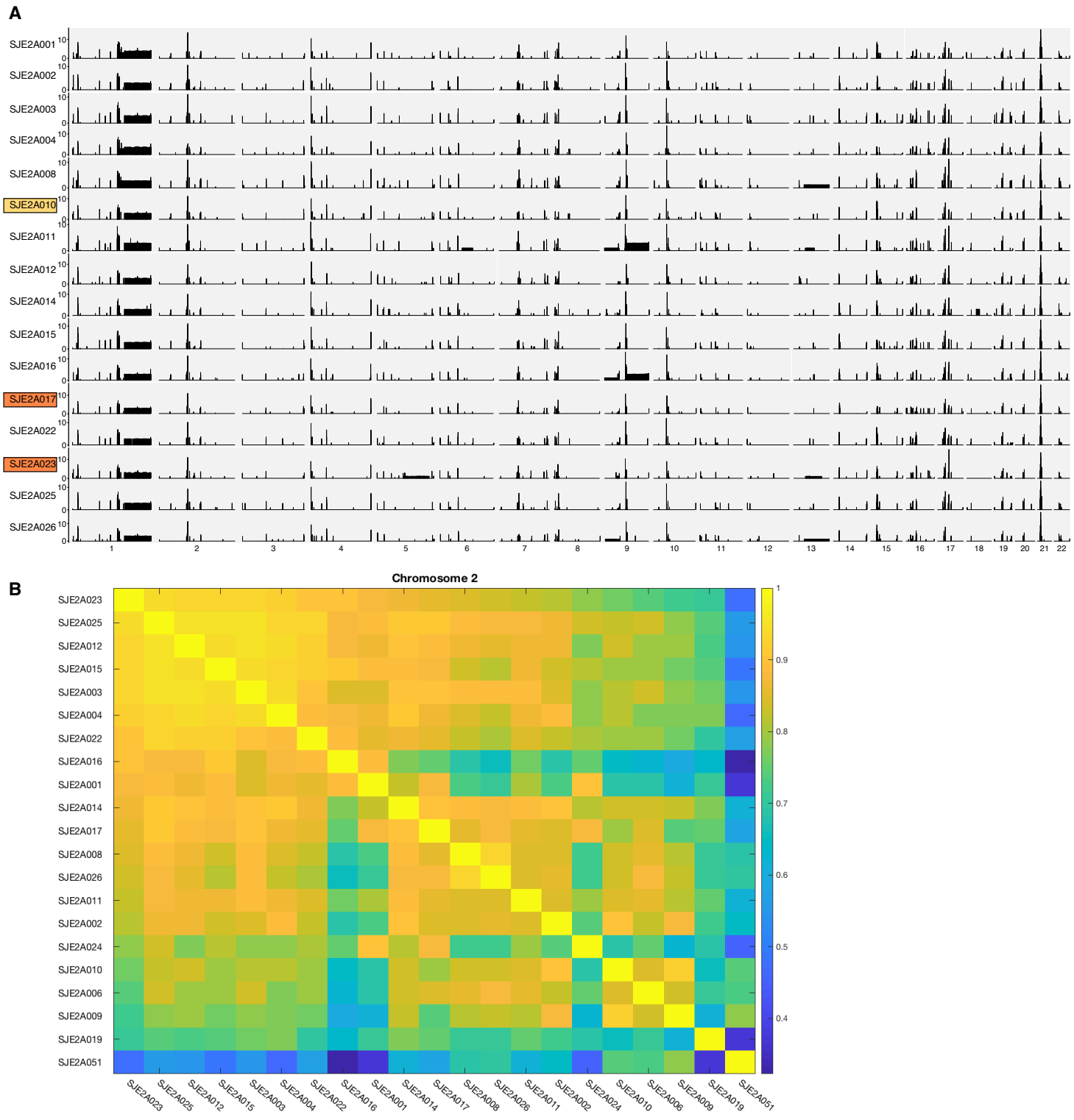
Supplemental Figure S4. Hierarchical clustering analysis for each BCP-ALL RT signature from main **Figure 3A**.

Supplementary Figure S5



Supplemental Figure S5. Gene expression patterns of genes within the BCP-ALL RT signature from main **Figure 3A**. Transcriptome data from 508 B-ALL samples was obtained from the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) (Ma et al., 2018).

Supplementary Figure S6



Supplemental Figure S6. Analysis of whole genome sequencing (WGS) data (28X coverage) from TCF3-PBX1-positive BCP-ALL patients. **(A)** Copy number variation (CNV) per chromosome across TCF3-PBX1-positive patients identified multiple loci amplifications. **(B)** Correlation matrix of the RT programs derived from WGS of TCF3-PBX1-positive BCP-ALL patients. WGS data was obtained from the St. Judes Pediatric Cancer Genome Project (PCGP).