Figure S1. Primary human erythroid cells and Hi-C profiles.
(A) Giemsa staining of in vitro cultured primary human erythroid cells derived from fetal and adult sources.
(B) Flow cytometry results of CD235a staining of in vitro cultured human fetal and adult erythroid cells.
(C) Scatter plots of RNA-seq results comparing fetal and adult erythroid cells at different differentiation time points.
(D) Scatter plots of RNA-seq results comparing maturation stages.
(E) RNA-seq expression levels of representative erythroid genes at day 11.
Figure S2. Examples of dynamic chromatin structures in human erythroblasts during development.
(A) Correlations of normalized Hi-C interaction frequencies between two biological replicates.
(B) Fractions of genome with switched chromatin compartments from fetal to adult stage.
(C) Expression ratios of genes within switched and stable chromatin compartments during development. P-values were calculated by Wilcoxon test.
(D, E) RNA-seq expression levels of LIN28B (D) and THRB (E).
(F, G) Hi-C interactions and PC1 values of LIN28B (F) and THRB (G) locus.
Figure S3. CTCF binding profiles in human erythroblasts during development.
(A) Overlap of CTCF peaks of human fetal and adult erythroblasts.
(B) Heatmaps of CTCF signals across the peaks in human fetal and adult erythroblasts.
(C) CTCF peaks across the TAD boundaries.
Figure S4. Chromatin interactions and CTCF binding profiles of β-globin locus in different cell types.

(A) Heatmaps of normalized Hi-C interactions of β-globin locus from eight human cell lines. The chromatin interactions between CTCF binding sites in primary erythroblasts (Fig. 3A) are highlighted by dashed circles.

(B) CTCF binding profiles of the corresponding cells (ChIP-seq data are obtained from ENCODE). Olfactory receptor genes are shown by black boxes. CTCF binding sites are highlighted by light purple. The orientations of CTCF binding motifs are indicated by blue and green arrows.
Figure S5. Chromatin interactions of β-globin and γ-globin genes in erythroblasts during development.

(A) Hi-C heatmaps of β-globin locus. Dynamic chromatin interactions involving the HBBP1 region are highlighted by blue dashed boxes.

(B) Capture-C interaction profiles of Gγ- and β-globin promoters. The anchor positions are indicated by black arrows. Olfactory receptor genes are shown as black boxes.

(C) RNA-seq expression profiles of the genes within β-globin locus.
Figure S6. Genome editing of HBBP1 region in HUDEP-2 cells.
(A) Diagram of human β-globin locus and HPFH deletions. HPFH coordinates were obtained from Globin Gene Server (globin.cse.psu.edu).
(B, C) Genotyping sequences of HBBP1 (B) and TSS (C) deletion clones. Guide RNA targets are highlighted in red, PAM sequences are shown in bold.
(D) The expression levels of HBBP1, α-globin and representative erythroid genes in the control and HUDEP-2 mutant clones. Results are shown as mean ± SD (n ≥ 3). Statistically difference from control by one-way ANOVA test: * P < 0.05; ** P < 0.01; n.s. not significant.
Figure S7. Genome editing of BCL11A in HUDEP-2 cells.
(A) Genotyping sequences of BCL11A knockout clones. Guide RNA sequences targeted to the second exon of BCL11A are highlighted in red, PAM sequences are shown in bold. (B) The expression percentage of γ-globin in the control and BCL11A knockout clones. Results are shown as mean ± SD (n=3). (C) Subtraction of normalized BGLT3 Capture-C interactions of control and mutant clones (Fig. 6B). OR: olfactory receptor genes.