Figure 2.

A

No. of DE genes

Downregulated

Upreregulated

Gene knocked out

Dropout TFs

>200 targets

<200 targets

B

39 transcription factors
16,992 regulatory interactions
7,388 gene targets
3,993 coregulated genes
Figure 4.

A: Perturbation(s) diagram with TF1 = Cebpα or Meis1 or Spi1, sgRNA against TF1, β Estr, Infection, sgRNA control, and Control.

B: Equation for gene expression:

\[ Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_1 X_2 + \varepsilon \]

where \( \beta_0 \) is the intercept, \( \beta_1 \) is the coefficient for Perturbation 1 effect, \( \beta_2 \) is the coefficient for Perturbation 2 effect, \( \beta_3 \) is the coefficient for Interaction term, and \( \varepsilon \) is the error term.

C: Heatmaps showing buffering, dominant, and synergy effects.

D: Heatmaps showing 1885 co-regulated genes, 773 co-regulated genes, and 1063 co-regulated genes.

E: Fraction of genes showing interaction classes: additive, buffering, dominant, and synergy.
Figure 5.

A. Heatmap showing enrichment scores for various genes.

B. Bar plots showing downregulated and upregulated genes with enrichment levels.

C. Genomic location of genes AcK27, Erg, Lmo2, Ebf1, and Gata3.

D. Additional genomic location of genes AcK27, Ebf1, and Gata3.
Figure 6.

(A) Gata3 log(esp) vs. Ebf1 log(mrp).

(B) HSPCs, Hoxb8-FL, B cell lineage, T cell lineage.

(C) Scatter plots showing regulation of Gata3 and Ebf1 with 24, 160, and 67 genes.

(D) Li et al. 2018: pre-pro-B, Ebf1, apoptosis, arrested diff.

(E) ChIP-Seq, RNA-Seq, Ebf1 log(fold change) vs. Hoxb8.

(F) Human fetal liver B-cell trajectory (Popescu et al. 2019).

(G) Plot showing scaled log(esp) vs. pseudotime.
Figure 7.

A. Treatment (e.g., TF knockout) → log2(Fold Change): positive/negative

Scaled gene expression (reference)

KIF1

Elane

Dnmt

x 1.7

x -0.5

x -1.5

Direction of state transition (DoT)

Erythroid

HSC

Lymphoid

Myeloid

Cell state vectors

Treatment vector

Viewpoint

s = X ∙ v

s - vector of scores (per cell)

X - scaled expression matrix cells x genes

v - vector of weights - log2(fold change)

B. Mouse LK/LSK

Intermediate progenitors

Unassigned

C. Human BMNC

D. Mono/DC

late B cells

late T cells

Hoxb8 loss

Ery Progenitor

HSC

Meg

IκBα KO

T cells

B cells

Ly
Figure EV3

A

Low stringency

<table>
<thead>
<tr>
<th>TF1</th>
<th>Hoxb8* Interaction</th>
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B

High stringency

<table>
<thead>
<tr>
<th>TF1</th>
<th>Hoxb8* Interaction</th>
</tr>
</thead>
<tbody>
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</table>

C

Meis1

- Interaction

Hoxb8*

- Interaction

CebpA

- Interaction

Hoxb8*

- Interaction

Spi1

- Interaction

Hoxb8*
Figure EV4.

A

Relative fraction of BFP+ cells

B

D

E

G

H

I

Li et al. 2018  
Hoxb-FL  
Revilla-I-Domingo et al. 2012

LMPP  
ALP  
BLP

Mouse early B cell trajectory

Loughran et al. 2017