Supplemental Materials

Supplemental Figures

Supplemental File 1 – SNP IDs, Sentinel SNVs, and associated Phenotypes of MPRA SNPs

Supplemental File 2 – MPRA source data

Supplemental File 3 – 556 reproducible and concordant regulatory variants

Supplemental File 4 – 53 reproducible and concordant regulatory variants at promotors or connected to promoters as determined by promoter CHiC.

Supplemental File 5 – Reference and alternative allele sequences used in dual-luciferase reporter assays

Supplemental File 6 – Nucleic acids associated with MPRA method

Supplemental File 7 – MPRA barcode sequences

Supplemental File 8 – PU.1 binding affinity assay probe sequences

Supplemental File 9 – CRISPR/Cas9 rs1247117 deletion pool sequences

SUPPLEMENTAL FIGURES

Functional investigation of inherited noncoding genetic variation impacting the pharmacogenomics of childhood acute lymphoblastic leukemia treatment

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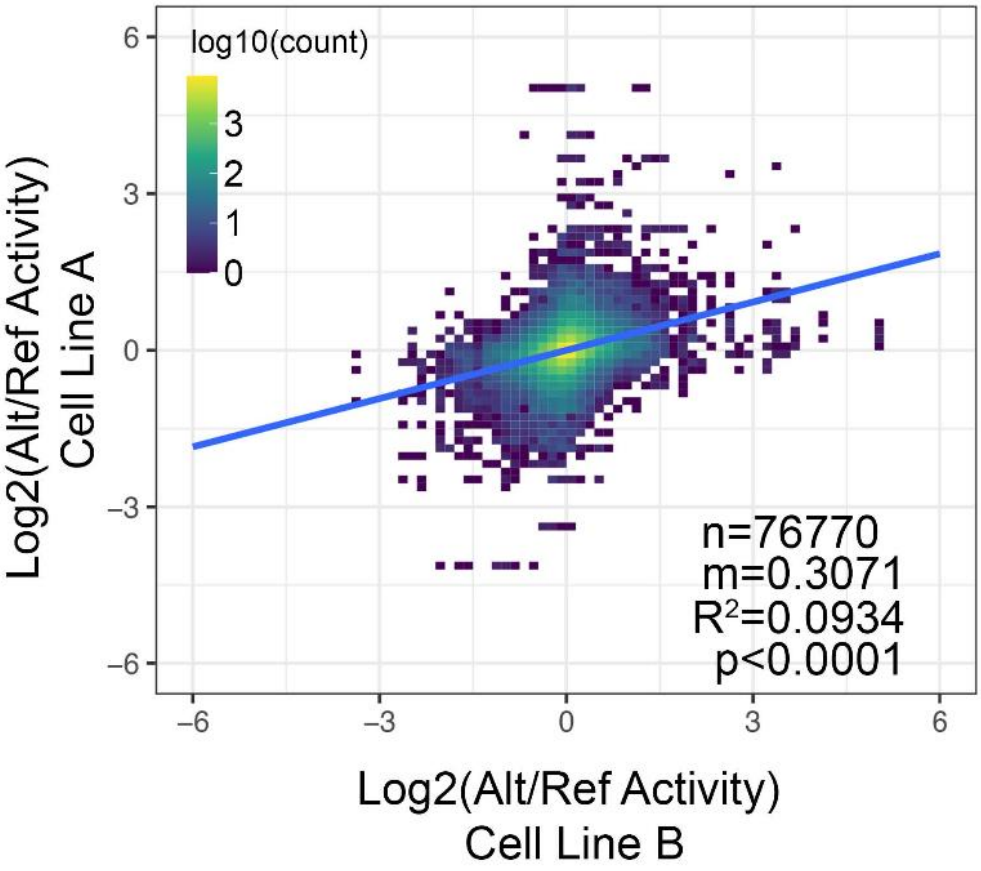
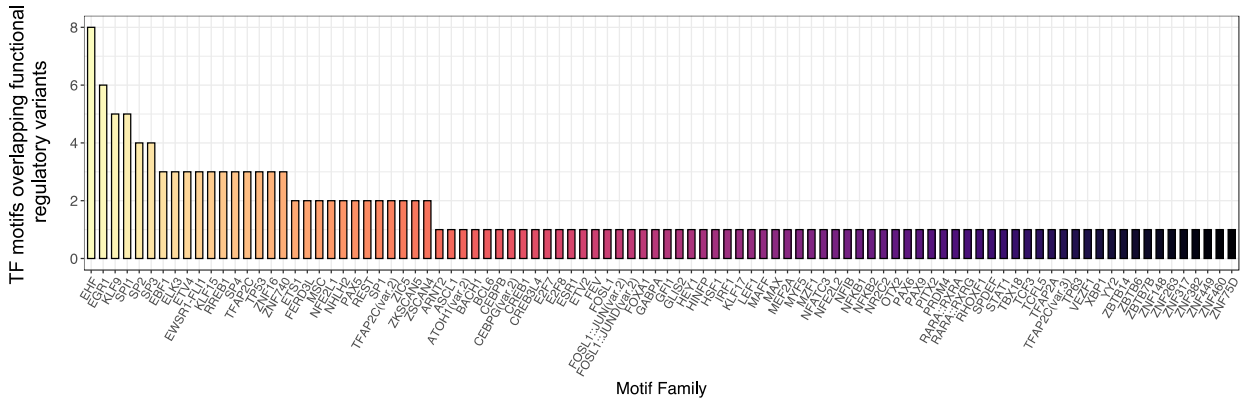
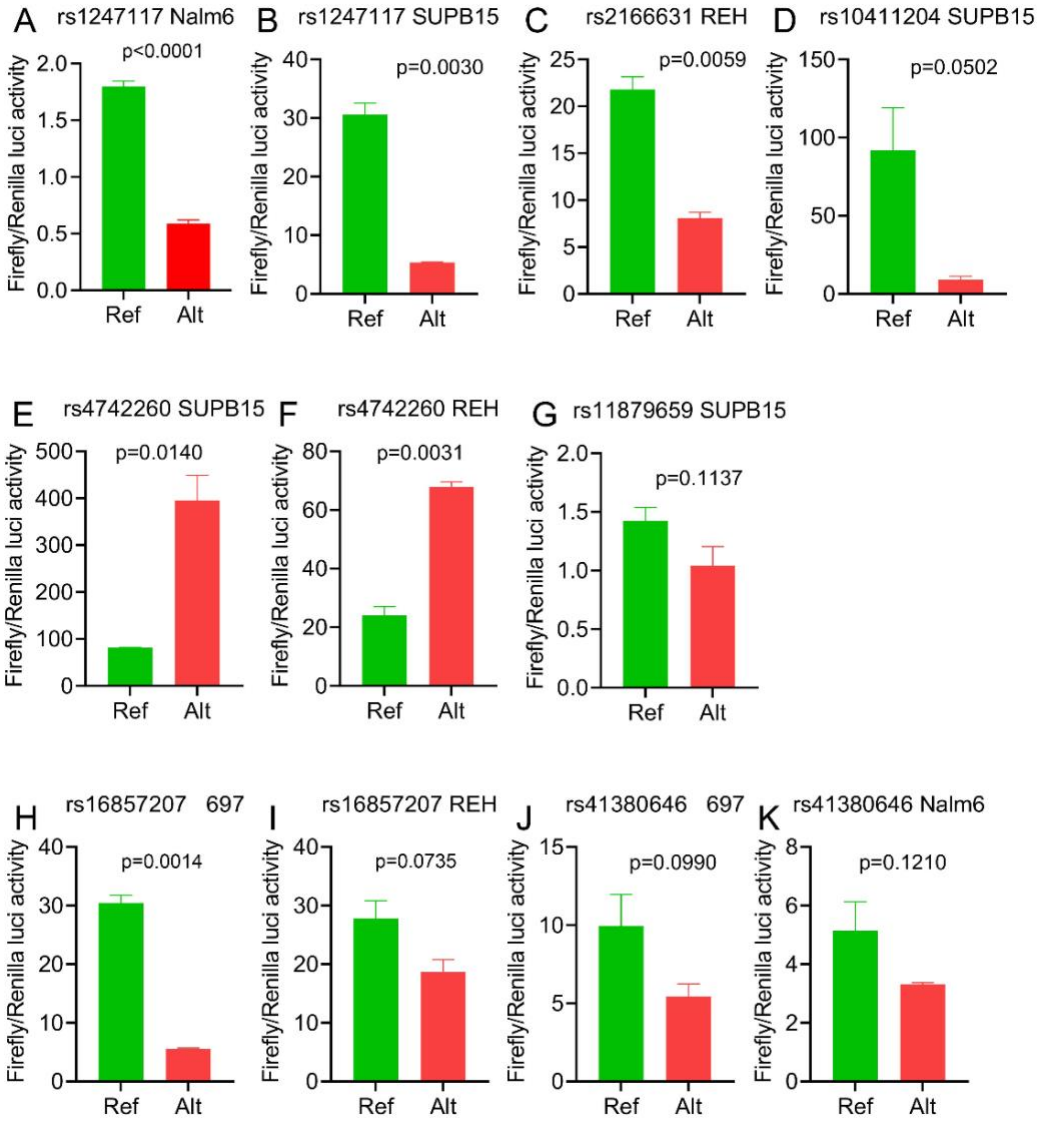
Supplemental Figure 1. MPRA activity comparisons among all cell lines. Pair-wise linear correlation between changes in allele-specific transcriptional activity for all measurements and across all cell lines. R^2 correlation and p-value are provided.



Supplemental Figure 2. Transcription factor footprints at functional regulatory variants. Transcription factor (TF) footprints identified at 54 of 556 functional regulatory variants are shown and ranked by the total number of motifs identified.



Supplemental Figure 3. Dual-luciferase reporter assay validation of the indicated functional regulatory variant. (A-K) Dual-luciferase reporter assays comparing the reference (Ref, in green) and alternate (Alt, in red) alleles ability to drive luciferase expression is depicted. Variant rs number and the ALL cell line the luciferase reporter assay was tested in is provided. Data show the mean +/- SEM of three **(A)** or two **(B-K)** independent experiments. P-value is calculated using a student's t-test.



Supplemental Figure 4. Chromatin accessibility at rs1247117 in primary ALL cells. (A) IGV genome browser image of ATAC-seq chromatin accessibility spanning rs1247117 in diverse molecular subtypes of ALL is provided. **(B)** PU.1 footprint analysis comparing normalized ATAC-seq cut count signal for all bound PU.1 sites (red) compared to unbound (blue) sites across all primary ALL cells from patients. **(C)** Primary ALL cells with SNV genotype information were analyzed (n=69). Normalized ATAC-seq read counts in heterozygous (GA) primary ALL cells (n=12) at rs1247117 compared to homozygous (AA) primary ALL cells (n=57). Mann Whitney U test p-value is provided. **(D)** Normalized ATAC-seq read counts per allele in primary ALL cells for G allele (n=12) and A allele (n=69). Normalized counts for G and A alleles are shown. Mann Whitney U test p-value is provided.