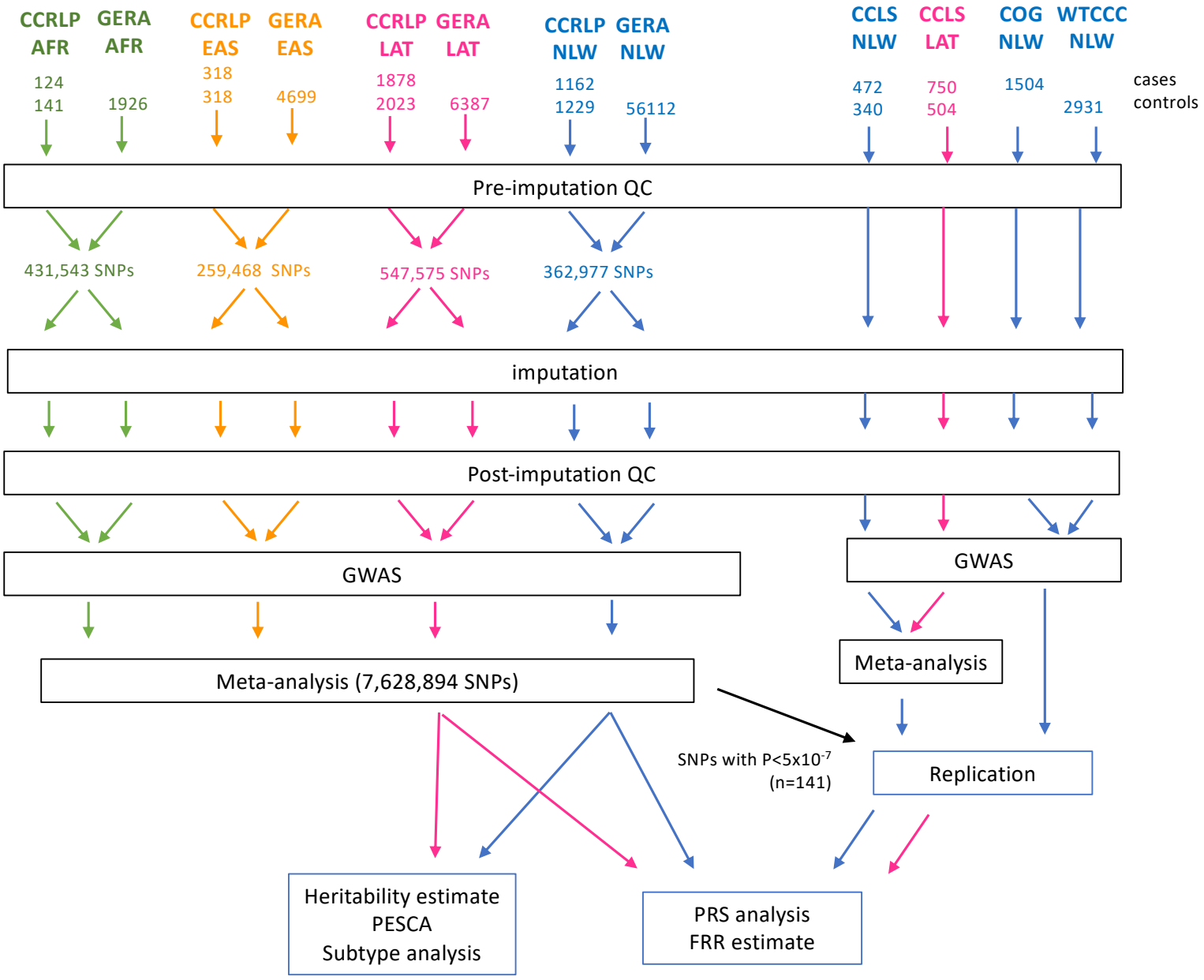


Figure S1. Summary of Study Design and Analysis
The flowchart details different cohorts used for various analyses through different stages of the study. The colors are based on populations – green, orange, red, blue for AFR, EAS, LAT, NLW respectively. AFR: African Americans; EAS: East Asian Americans; LAT: Latino Americans; NLW: non-Latino White Americans; PRS: Polygenic Risk Score; FRR: Familial risk ratio

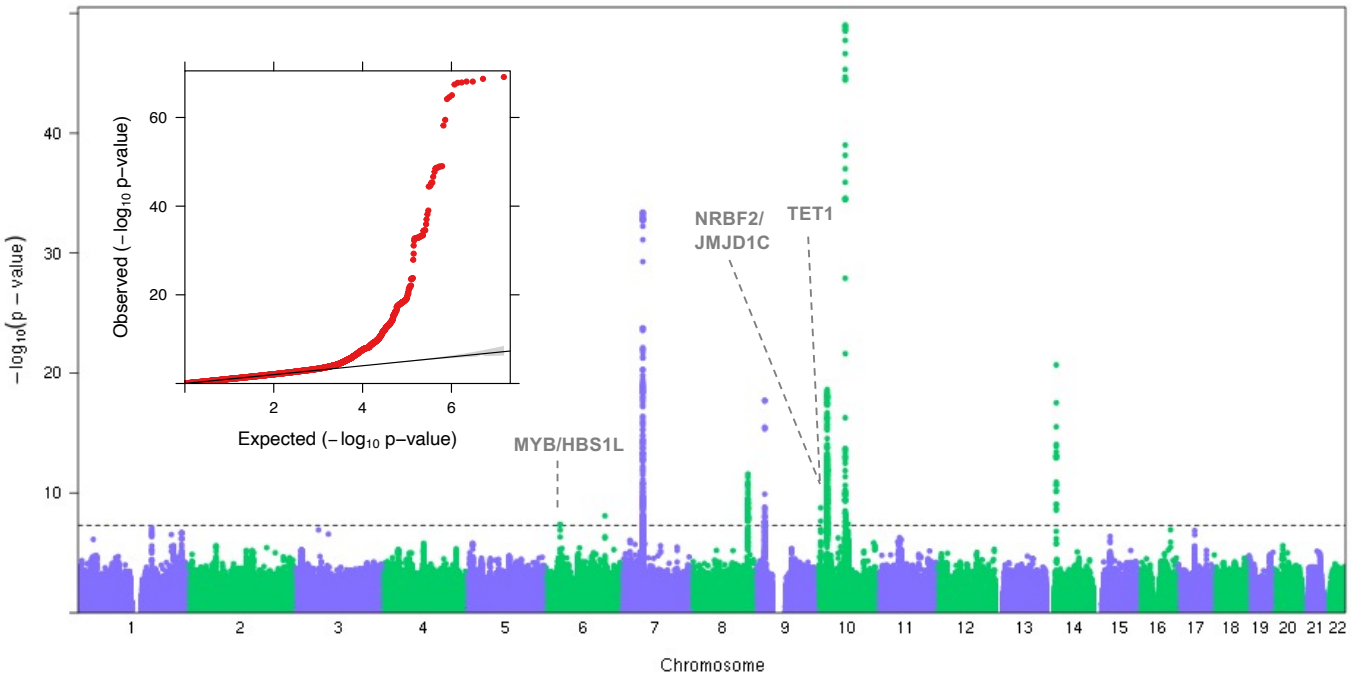


Figure S2. Summary result of the trans-ethnic meta-analysis on ALL.
Results of the meta-analysis is represented by the Manhattan plot. The novel loci from this study are marked with dotted lines and labeled with the nearest genes. Significance threshold at genome-wide significance level ($5x10^{-8}$) is marked with a horizontal dashed grey line in the Manhattan plot. The y-axis is truncated at $-log10(1x10^{-50})$ to improve readability. The insert shows the Quantile-Quantile plot. Deviation from the expected p-value distribution is evident only in the tail.

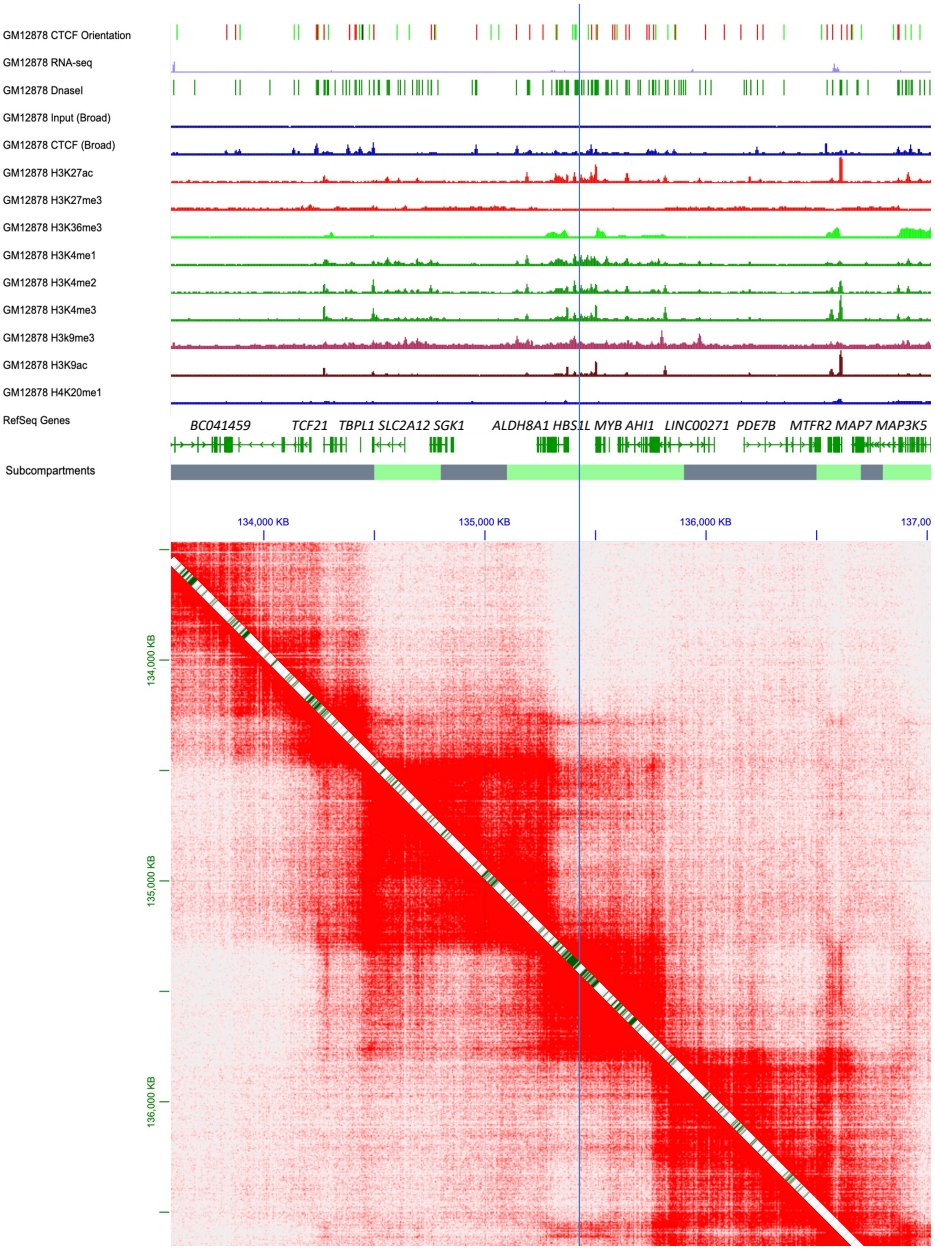


Figure S3: Chromatin structure surrounding the MYB/HBS1L region. The region surrounding rs9376090, including high resolution 3-dimensional map of chromatin connections constructed using Hi-C and sequencing (Rao et all., Cell, 159(7):1665, 2014) is displayed, along with ENCODE histone modifications in the same B-lymphoblastoid cell line (GM12878). The SNP is indicated with a vertical blue line, which exists within a chromatin subcompartment (indicated on lowest track above the chromatin map) with *ALDH8A1, HBS1L, MYB, AHI1*, and *LINC00271* within this compartment. Known SNPs with any condition (from the GWAS catalog) are indicated with a diagonal line through the chromatin connection map, showing a high density of GWAS SNPs proximal to rs9376090.

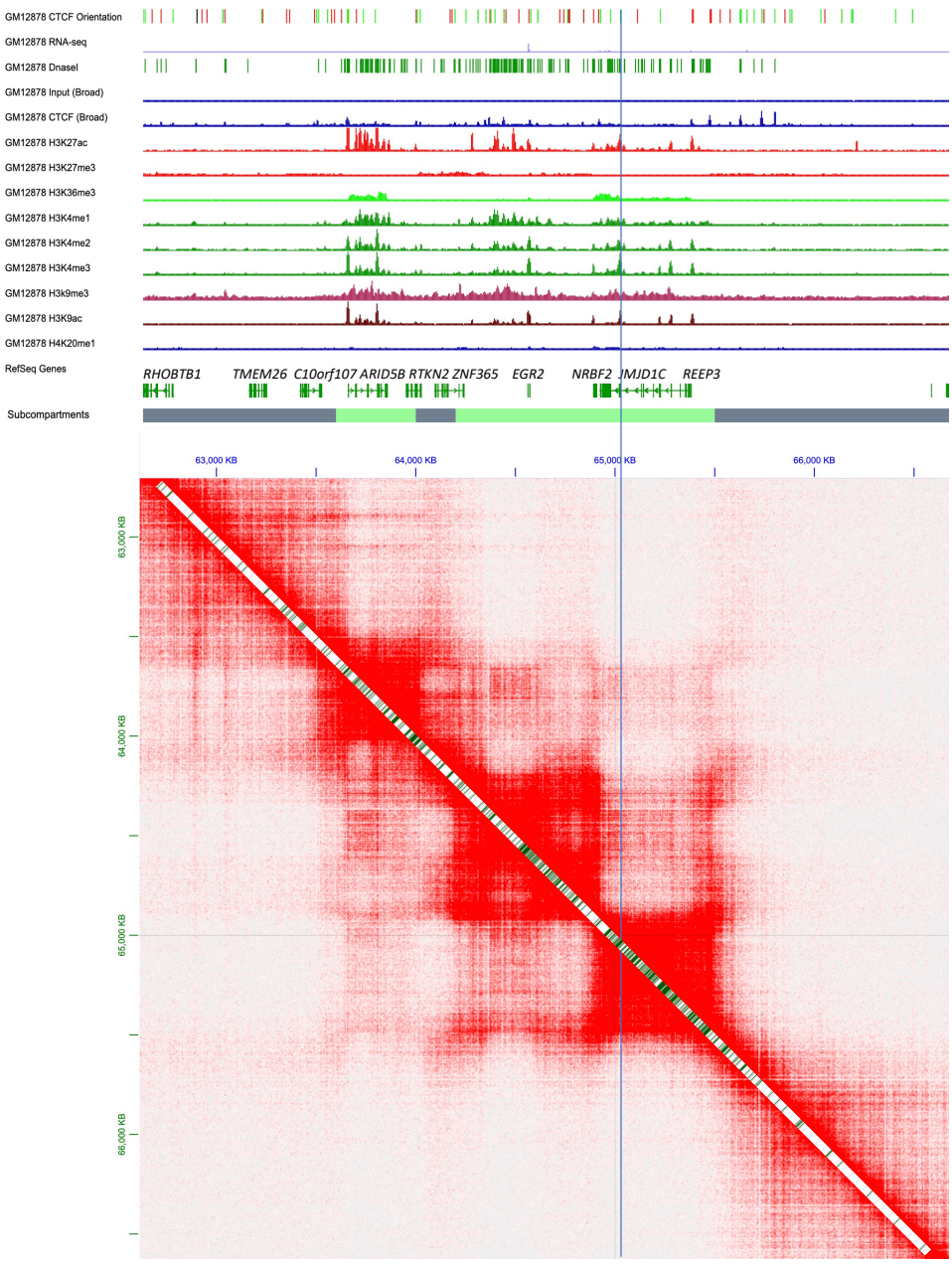


Figure S4: Chromatin structure surrounding the NRBF2/JMJD1C region. The region surrounding rs9415680 , including high resolution 3-dimensional map of chromatin connections constructed using Hi-C and sequencing (Rao et all., Cell, 159(7):1665, 2014) is displayed, along with ENCODE histone modifications in the same B-lymphoblastoid cell line (GM12878). As in Figure S6, the SNP is indicated with a vertical blue line, which exists within a chromatin subcompartment (indicated on lowest track above the chromatin map) with *ZNF365, EGR2, ADO, NRBF2, JMJD1C, AX747628, MIR1296, JMD1C-AS1*, and *REEP3* (not all shown in the figure) within this compartment. Known SNPs with any condition (from the GWAS catalog) are indicated with a diagonal line through the chromatin connection map.

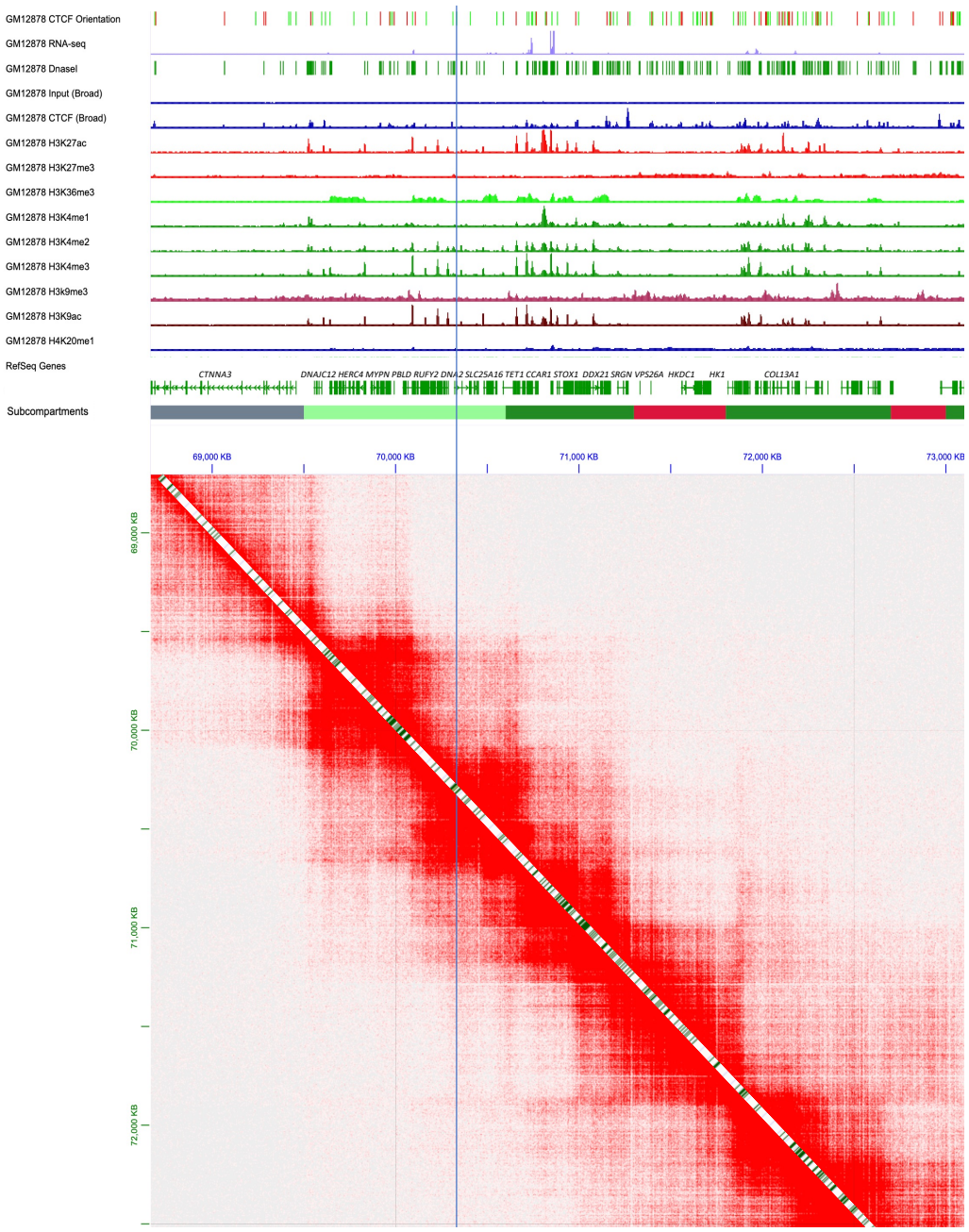
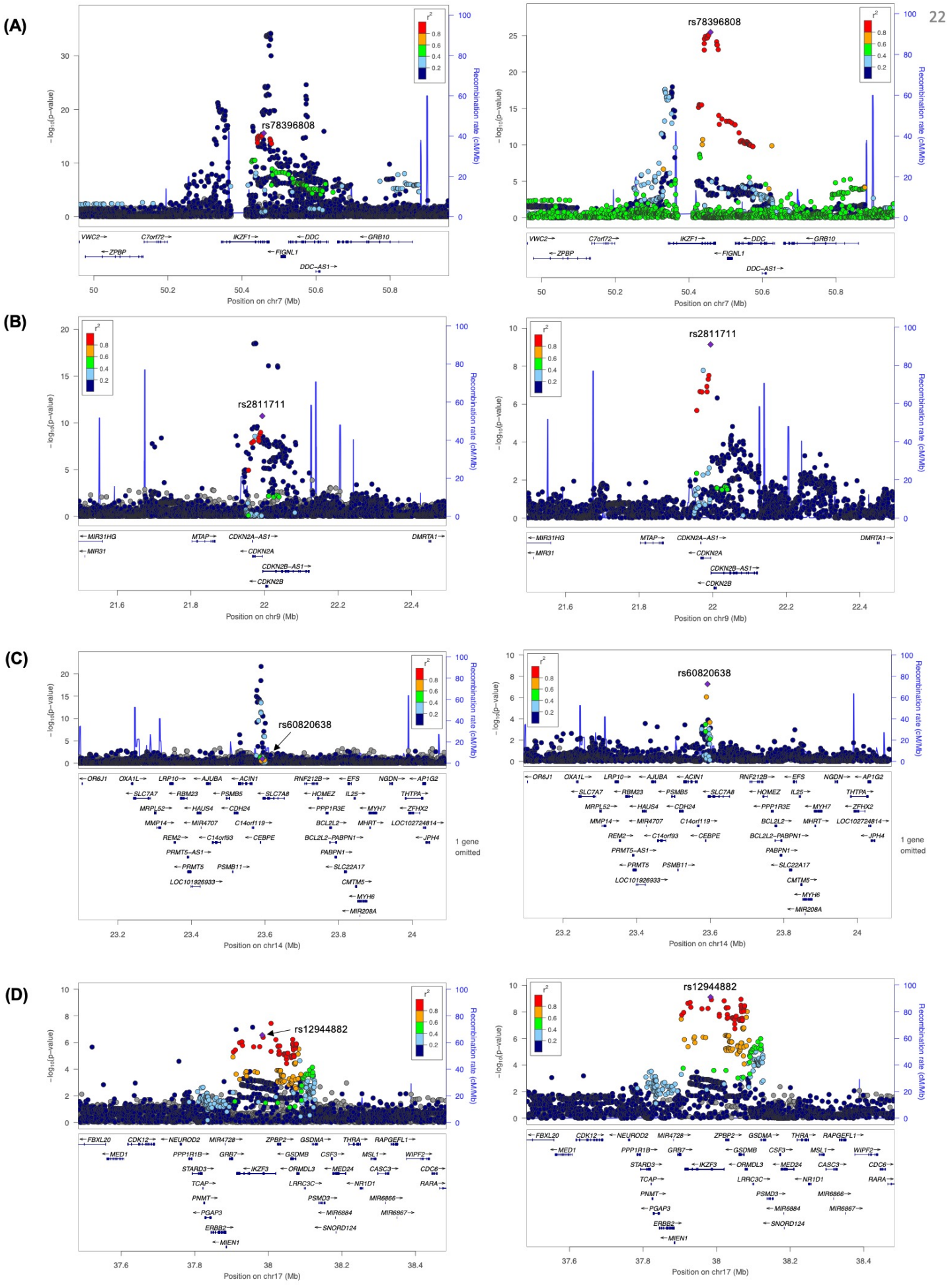


Figure S5: Chromatin structure surrounding the region. The region surrounding rs10998283 , including high resolution 3-dimensional map of chromatin connections constructed using Hi-C and sequencing (Rao et all., Cell, 159(7):1665, 2014) is displayed, along with ENCODE histone modifications in the same B-lymphoblastoid cell line (GM12878). As in Figure S6, the SNP is indicated with a vertical blue line, which exists within a chromatin subcompartment (indicated on lowest track above the chromatin map) with *DNAJC12, SIRT1, HERC4, MYPN, PBLD, HNRNPH3, RUFY2, DNA2, SLC25A16, TET1, and CCAR1* (not all shown in the figure) within this compartment. Known SNPs with any condition (from the GWAS catalog) are indicated with a diagonal line through the chromatin connection map.

Figure S6. Secondary association signal ($p < 5x10^{-8}$) with ALL found in previously known loci through conditional analysis. LocusZoom plot displaying the 1 Mb region found to harbor a second novel variant associated with ALL through conditional analysis: (A) IKZF1 (B) CDKN2A (C) CEBPE (D) IKZF3. For each locus, we display the pattern of association before(left) and after(right) conditioning on the top associated variant in the locus. In both cases, diamond indicates the lead SNP in the conditional analysis. Color of the remaining SNPs is based on linkage disequilibrium (LD) with the lead variant in the conditional analysis in non-Latino white. Genomic coordinates on x-axis are in hg19.


(A)
rs78396808
rs78396808
Position on chr7 (Mb)
(B)
rs2811711
rs2811711
Position on chr9 (Mb)
(C)
rs60820638
rs60820638
1 gene omitted
1 gene omitted
Position on chr14 (Mb)
(D)
rs12944882
rs12944882
Position on chr17 (Mb)
Recombination rate (cM/Mb)

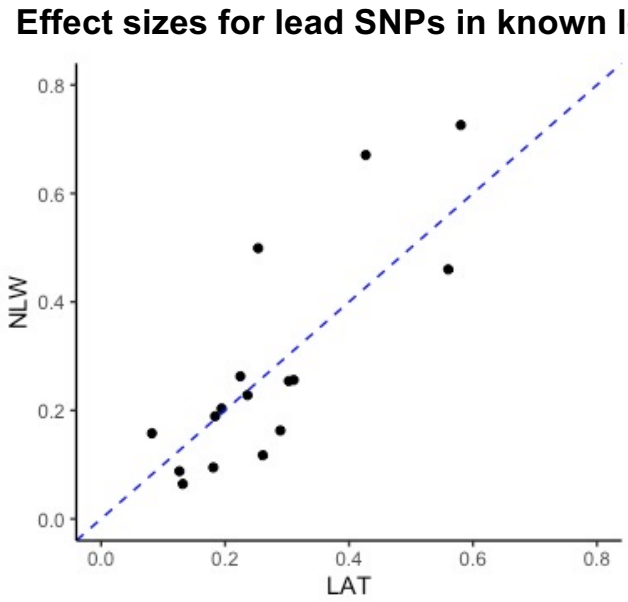


Figure S7. **Effect sizes for lead SNPs in each of the 16 known loci**. The effect size estimates(Beta) from GWAS in only the LAT or NLW subset from our discovery cohort are shown. The correlation coefficient (r) is 0.819. The dashed blue line is y=x.