



GO:0051213 : dioxygenase activity (<https://www.ebi.ac.uk/QuickGO/term/GO:0051213>)  
 GO:0000976 : transcription regulatory region sequence-specific DNA binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0000976>)  
 GO:0031490 : chromatin DNA binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0031490>)  
 GO:0032454 : histone demethylase activity (H3-K9 specific) (<https://www.ebi.ac.uk/QuickGO/term/GO:0032454>)  
 GO:0046966 : thyroid hormone receptor binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0046966>)

GO - Biological Process

GO:0006355 : regulation of transcription, DNA-templated (<https://www.ebi.ac.uk/QuickGO/term/GO:0006355>)  
 GO:0007596 : blood coagulation (<https://www.ebi.ac.uk/QuickGO/term/GO:0007596>)  
 GO:0033169 : histone H3-K9 demethylation (<https://www.ebi.ac.uk/QuickGO/term/GO:0033169>)

GO - Cellular Component

GO:0005654 : nucleoplasm (<https://www.ebi.ac.uk/QuickGO/term/GO:0005654>)  
 GO:0005634 : nucleus (<https://www.ebi.ac.uk/QuickGO/term/GO:0005634>)  
 GO:0005622 : intracellular (<https://www.ebi.ac.uk/QuickGO/term/GO:0005622>)  
 GO:0000785 : chromatin (<https://www.ebi.ac.uk/QuickGO/term/GO:0000785>)

Presumptive Null

Unknown (<https://www.gephebase.org/search-criteria?/and+Presumptive Null=~Unknown^#gephebase-summary-title>)

Molecular Type

Unknown (<https://www.gephebase.org/search-criteria?/and+Molecular Type=~Unknown^#gephebase-summary-title>)

Aberration Type

Unknown (<https://www.gephebase.org/search-criteria?/and+Aberration Type=~Unknown^#gephebase-summary-title>)

Molecular Details of the Mutation

T>A at the associated SNP

Experimental Evidence

Association Mapping (<https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Association Mapping^#gephebase-summary-title>)

Main Reference

Comprehensive population-based genome sequencing provides insight into hematopoietic regulatory mechanisms. (2017) (<https://pubmed.ncbi.nlm.nih.gov/28031487>)

Authors

Guo MH; Nandakumar SK; Ulirsch JC; Žekavat SM; Buenrostro JD; Natarajan P; Salem RM; Chiarle R; Mitt M; Kals M; PÄrrn K; Fischer K; Milani L; MÄrqi R; Palta P; Gabriel SB; Metspalu A; Lander ES; Kathiresan S; Hirschhorn JN; Esko T; Sankaran VG

Abstract

Genetic variants affecting hematopoiesis can influence commonly measured blood cell traits. To identify factors that affect hematopoiesis, we performed association studies for blood cell traits in the population-based Estonian Biobank using high-coverage whole-genome sequencing (WGS) in 2,284 samples and SNP genotyping in an additional 14,904 samples. Using up to 7,134 samples with available phenotype data, our analyses identified 17 associations across 14 blood cell traits. Integration of WGS-based fine-mapping and complementary epigenomic datasets provided evidence for causal mechanisms at several loci, including at a previously undiscovered basophil count-associated locus near the master hematopoietic transcription factor CEBPA. The fine-mapped variant at this basophil count association near CEBPA overlapped an enhancer active in common myeloid progenitors and influenced its activity. In situ perturbation of this enhancer by CRISPR/Cas9 mutagenesis in hematopoietic stem and progenitor cells demonstrated that it is necessary for and specifically regulates CEBPA expression during basophil differentiation. We additionally identified basophil count-associated variation at another more pleiotropic myeloid enhancer near GATA2, highlighting regulatory mechanisms for ordered expression of master hematopoietic regulators during lineage specification. Our study illustrates how population-based genetic studies can provide key insights into poorly understood cell differentiation processes of considerable physiologic relevance.

Additional References

RELATED GEPHE

Related Genes

12 (ARHGEF3, BAK1, CCAAT-enhancer-binding protein alpha (CEBPA), F2RL2, GATA-binding protein 2 (GATA2), HBS1L-MYB, JAK2, LPAR1, PIK3CG, PSMD13, TMPRSS6, WDR66) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=~9606^/and+Trait=Hematopoiesis/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

