GEPHE SUMMARY

Gephebase Gene

CCAAT-enhancer-binding protein alpha (CEBPA) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^CCAAT-enhancer-binding protein alpha (CEBPA)^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00001603

Main curator

Prigent

PHENOTYPIC CHANGE

Trait Category

Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)

Trait

Hematopoiesis (blood basophil count) (https://www.gephebase.org/search-criteria?/and+Trait=^Hematopoiesis (blood basophil count)^#gephebase-summary-title)

Trait State in Taxon A

Human - Estonia Biobank

Trait State in Taxon B

Human - Estonia Biobank. Basophil count-decrease

Ancestral State

Unknown

Taxonomic Status

Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)

Taxon A

Latin Name

Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Homo sapiens^#gephebase-summary-title)

Common Name

human

Synonyms

human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo

Parent

Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)

NCBI Taxonomy ID

9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)

is Taxon A an Infraspecies?

Yes

Taxon A Description

Human - Estonia Biobank

Taxon B

Latin Name

Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Homo sapiens^#gephebase-summary-title)

Common Name

human

Synonyms

human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo

Parent

Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)

NCBI Taxonomy ID

9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)

is Taxon B an Infraspecies?

Yes

Taxon B Description

Human - Estonia Biobank. Basophil count-decrease

GENOTYPIC CHANGE

Generic Gene Name

CEBPA

Synonyms

CEBP; C/EBP-alpha

String

9606.ENSP00000427514 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000427514)

Sequence Similarities

Belongs to the bZIP family. C/EBP subfamily.

GO - Molecular Function

GO:0042803 : protein homodimerization activity

UniProtKB Homo sapiens

P49715 (http://www.uniprot.org/uniprot/P49715)

GenebankID or UniProtKB

()

(https://www.ebi.ac.uk/QuickGO/term/GO:0042803)
GO:0001228 : DNA-binding transcription activator activity, RNA polymerase II-specific
(https://www.ebi.ac.uk/QuickGO/term/GO:0001228)
GO:0003700 : DNA-binding transcription factor activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0003700)
GO:0008134 : transcription factor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0008134)
GO:0044212 : transcription regulatory region DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0044212)
GO:0003677 : DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003677)
GO:0000981 : DNA-binding transcription factor activity, RNA polymerase II-specific
(https://www.ebi.ac.uk/QuickGO/term/GO:0000981)
GO:0001077 : proximal promoter DNA-binding transcription activator activity, RNA
polymerase II-specific (https://www.ebi.ac.uk/QuickGO/term/GO:0001077)
GO:0000978 : RNA polymerase II proximal promoter sequence-specific DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0000978)
GO:0003713 : transcription coactivator activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0003713)
GO:0003705 : transcription factor activity, RNA polymerase II distal enhancer sequence-
specific binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003705)
GO:0019900 : kinase binding (https://www.ebi.ac.uk/QuickGO/term/GO:0019900)
GO:0001013 : RNA polymerase I regulatory region DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0001013)

GO - Biological Process

GO:0055088 : lipid homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0055088)
GO:0045944 : positive regulation of transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0045944)
GO:0006091 : generation of precursor metabolites and energy
(https://www.ebi.ac.uk/QuickGO/term/GO:0006091)
GO:0000122 : negative regulation of transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0000122)
GO:0045892 : negative regulation of transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0045892)
GO:0008203 : cholesterol metabolic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0008203)
GO:0008285 : negative regulation of cell proliferation
(https://www.ebi.ac.uk/QuickGO/term/GO:0008285)
GO:0045945 : positive regulation of transcription by RNA polymerase III
(https://www.ebi.ac.uk/QuickGO/term/GO:0045945)
GO:0006351 : transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0006351)
GO:0007219 : Notch signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0007219)
GO:0045669 : positive regulation of osteoblast differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0045669)
GO:0071356 : cellular response to tumor necrosis factor
(https://www.ebi.ac.uk/QuickGO/term/GO:0071356)
GO:0019221 : cytokine-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0019221)
GO:0050729 : positive regulation of inflammatory response
(https://www.ebi.ac.uk/QuickGO/term/GO:0050729)
GO:0045736 : negative regulation of cyclin-dependent protein serine/threonine kinase
activity (https://www.ebi.ac.uk/QuickGO/term/GO:0045736)
GO:0030324 : lung development (https://www.ebi.ac.uk/QuickGO/term/GO:0030324)
GO:0048469 : cell maturation (https://www.ebi.ac.uk/QuickGO/term/GO:0048469)
GO:0001892 : embryonic placenta development
(https://www.ebi.ac.uk/QuickGO/term/GO:0001892)
GO:0007005 : mitochondrion organization
(https://www.ebi.ac.uk/QuickGO/term/GO:0007005)
GO:0006366 : transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0006366)
GO:0001889 : liver development (https://www.ebi.ac.uk/QuickGO/term/GO:0001889)
GO:0045444 : fat cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0045444)
GO:0016032 : viral process (https://www.ebi.ac.uk/QuickGO/term/GO:0016032)
GO:0042593 : glucose homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0042593)
GO:0048839 : inner ear development
(https://www.ebi.ac.uk/QuickGO/term/GO:0048839)
GO:0045600 : positive regulation of fat cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0045600)
GO:0043032 : positive regulation of macrophage activation
(https://www.ebi.ac.uk/QuickGO/term/GO:0043032)
GO:2000144 : positive regulation of DNA-templated transcription, initiation
(https://www.ebi.ac.uk/QuickGO/term/GO:2000144)
GO:0050873 : brown fat cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0050873)
GO:0032436 : positive regulation of proteasomal ubiquitin-dependent protein catabolic
process (https://www.ebi.ac.uk/QuickGO/term/GO:0032436)
GO:0071285 : cellular response to lithium ion

(https://www.ebi.ac.uk/QuickGO/term/GO:0071285)
GO:0071407 : cellular response to organic cyclic compound
(https://www.ebi.ac.uk/QuickGO/term/GO:0071407)
GO:0030851 : granulocyte differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0030851)
GO:0030225 : macrophage differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0030225)
GO:0030099 : myeloid cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0030099)
GO:0006360 : transcription by RNA polymerase I
(https://www.ebi.ac.uk/QuickGO/term/GO:0006360)
GO:0000050 : urea cycle (https://www.ebi.ac.uk/QuickGO/term/GO:0000050)
GO:0050872 : white fat cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0050872)

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:0090575 : RNA polymerase II transcription factor complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0090575)
GO:0043231 : intracellular membrane-bounded organelle
(https://www.ebi.ac.uk/QuickGO/term/GO:0043231)
GO:0005730 : nucleolus (https://www.ebi.ac.uk/QuickGO/term/GO:0005730)

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

Cis-regulatory (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Cis-regulatory^#gephebase-summary-title)

Aberration Type

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

Molecular Details of the Mutation

C>T at the associated SNP which resides 39kb dowstream from CEBPA near a separate enhancer that influences CEBPA expression along various myeloid lineages. T allele was associated with a 28.6% reduction in enhancer activity.

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; Zekavat SM; Buenrostro JD; Natarajan P; Salem RM; Chiarle R; Mitt M; Kals M; PÃ¤rn K; Fischer K; Milani L; MÃ¤gi 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, F2RL2, GATA-binding protein 2 (GATA2), HBS1L-MYB, JAK2, JMJD1C, 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

the enhancer specifically regulates CEBPA expression during basophil differentiation according to CRISPR/Cas9 mutagenesis