GEPHE SUMMARY

Gephebase Gene

GATA-binding protein 2 (GATA2) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^GATA-binding protein 2 (GATA2)^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00001610

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

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

GENOTYPIC CHANGE

Generic Gene Name

GATA2

Synonyms

DCML; IMD21; NFE1B; MONOMAC

String

9606.ENSP00000345681 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 9606.ENSP00000345681)

Sequence Similarities

-

GO - Molecular Function

GO:0003700 : DNA-binding transcription factor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0003700)

UniProtKB Homo sapiens

P23769 (http://www.uniprot.org/uniprot/P23769)

GenebankID or UniProtKB

()

GO:0008134 : transcription factor binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008134)
GO:0008270 : zinc ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008270)
GO:0003682 : chromatin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003682)
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:0000980 : RNA polymerase II distal enhancer sequence-specific DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0000980)
GO:0070742 : C2H2 zinc finger domain binding (https://www.ebi.ac.uk/QuickGO/term/GO:0070742)
GO:0001158 : enhancer sequence-specific DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0001158)

GO - Biological Process

GO:0045944 : positive regulation of transcription by RNA polymerase II (https://www.ebi.ac.uk/QuickGO/term/GO:0045944)
GO:0000122 : negative regulation of transcription by RNA polymerase II (https://www.ebi.ac.uk/QuickGO/term/GO:0000122)
GO:0010629 : negative regulation of gene expression (https://www.ebi.ac.uk/QuickGO/term/GO:0010629)
GO:0010628 : positive regulation of gene expression (https://www.ebi.ac.uk/QuickGO/term/GO:0010628)
GO:0006351 : transcription, DNA-templated (https://www.ebi.ac.uk/QuickGO/term/GO:0006351)
GO:0007204 : positive regulation of cytosolic calcium ion concentration (https://www.ebi.ac.uk/QuickGO/term/GO:0007204)
GO:0045666 : positive regulation of neuron differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0045666)
GO:0007596 : blood coagulation (https://www.ebi.ac.uk/QuickGO/term/GO:0007596)
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:0021902 : commitment of neuronal cell to specific neuron type in forebrain (https://www.ebi.ac.uk/QuickGO/term/GO:0021902)
GO:0042472 : inner ear morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0042472)
GO:0033993 : response to lipid (https://www.ebi.ac.uk/QuickGO/term/GO:0033993)
GO:0045766 : positive regulation of angiogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0045766)
GO:2000352 : negative regulation of endothelial cell apoptotic process (https://www.ebi.ac.uk/QuickGO/term/GO:2000352)
GO:0043306 : positive regulation of mast cell degranulation (https://www.ebi.ac.uk/QuickGO/term/GO:0043306)
GO:0035019 : somatic stem cell population maintenance (https://www.ebi.ac.uk/QuickGO/term/GO:0035019)
GO:0006909 : phagocytosis (https://www.ebi.ac.uk/QuickGO/term/GO:0006909)
GO:0021983 : pituitary gland development (https://www.ebi.ac.uk/QuickGO/term/GO:0021983)
GO:1902895 : positive regulation of pri-miRNA transcription by RNA polymerase II (https://www.ebi.ac.uk/QuickGO/term/GO:1902895)
GO:0001709 : cell fate determination (https://www.ebi.ac.uk/QuickGO/term/GO:0001709)
GO:0045746 : negative regulation of Notch signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0045746)
GO:0045599 : negative regulation of fat cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0045599)
GO:0021533 : cell differentiation in hindbrain (https://www.ebi.ac.uk/QuickGO/term/GO:0021533)
GO:0021954 : central nervous system neuron development (https://www.ebi.ac.uk/QuickGO/term/GO:0021954)
GO:0090102 : cochlea development (https://www.ebi.ac.uk/QuickGO/term/GO:0090102)
GO:0060216 : definitive hemopoiesis (https://www.ebi.ac.uk/QuickGO/term/GO:0060216)
GO:0035854 : eosinophil fate commitment (https://www.ebi.ac.uk/QuickGO/term/GO:0035854)
GO:0097154 : GABAergic neuron differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0097154)
GO:0048873 : homeostasis of number of cells within a tissue (https://www.ebi.ac.uk/QuickGO/term/GO:0048873)
GO:0070345 : negative regulation of fat cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0070345)
GO:0045650 : negative regulation of macrophage differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0045650)
GO:2000178 : negative regulation of neural precursor cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:2000178)
GO:0001764 : neuron migration (https://www.ebi.ac.uk/QuickGO/term/GO:0001764)

GO:1903589 : positive regulation of blood vessel endothelial cell proliferation involved in sprouting angiogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:1903589)
GO:0090050 : positive regulation of cell migration involved in sprouting angiogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0090050)
GO:0045648 : positive regulation of erythrocyte differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0045648)
GO:0045654 : positive regulation of megakaryocyte differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0045654)
GO:0050766 : positive regulation of phagocytosis (https://www.ebi.ac.uk/QuickGO/term/GO:0050766)
GO:0060100 : positive regulation of phagocytosis, engulfment (https://www.ebi.ac.uk/QuickGO/term/GO:0060100)
GO:2000977 : regulation of forebrain neuron differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:2000977)
GO:1902036 : regulation of hematopoietic stem cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:1902036)
GO:0035065 : regulation of histone acetylation (https://www.ebi.ac.uk/QuickGO/term/GO:0035065)
GO:0010725 : regulation of primitive erythrocyte differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0010725)
GO:0060872 : semicircular canal development (https://www.ebi.ac.uk/QuickGO/term/GO:0060872)
GO:0001655 : urogenital system development (https://www.ebi.ac.uk/QuickGO/term/GO:0001655)
GO:0021514 : ventral spinal cord interneuron differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0021514)

GO - Cellular Component

GO:0005737 : cytoplasm (https://www.ebi.ac.uk/QuickGO/term/GO:0005737)
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:0032991 : protein-containing complex (https://www.ebi.ac.uk/QuickGO/term/GO:0032991)

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

G>A at the associated SNP. Another variant (rs6782812) in a pleiotropic myeloid enhancer near GATA2 reduced enhancer activity by 69%

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, CCAAT-enhancer-binding protein alpha (CEBPA), F2RL2, 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