GEPHE SUMMARY

Gephebase Gene
GATA-binding protein 2 (GATA2)

GephelD
GP00001610

Entry Status
Published

Main curator
Prigent

PHENOTYPIC CHANGE

Trait Category
Physiology

Trait
Hematopoiesis (blood basophil count)

Trait State in Taxon A
Human - Estonia Biobank

Trait State in Taxon B
Human - Estonia Biobank

Ancestral State
Unknown

Taxonomic Status
Intraspecific

Taxon A

Latin Name
Homo sapiens

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)

NCBI Taxonomy ID
9606

is Taxon A an Infraspecies?
Yes

Taxon A Description
Human - Estonia Biobank

Taxon B

Latin Name
Homo sapiens

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)

NCBI Taxonomy 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

Sequence Similarities
-

GO - Molecular Function
GO:0003700 : DNA-binding transcription factor activity
GO:0008134 : transcription factor binding
GO:0008270 : zinc ion binding
GO:0003682 : chromatin binding
GO:0000981 : DNA-binding transcription factor activity, RNA polymerase II-specific

UniProtKB Homo sapiens
P23769

GenebankID or UniProtKB

GO:0001077 : proximal promoter DNA-binding transcription activator activity, RNA polymerase II-specific
GO:0000978 : RNA polymerase II proximal promoter sequence-specific DNA binding
GO:0000980 : RNA polymerase II distal enhancer sequence-specific DNA binding
GO:0070742 : C2H2 zinc finger domain binding
GO:0001158 : enhancer sequence-specific DNA binding

GO - Biological Process
GO:0045944 : positive regulation of transcription by RNA polymerase II
GO:0000122 : negative regulation of transcription by RNA polymerase II
GO:0010629 : negative regulation of gene expression
GO:0010628 : positive regulation of gene expression
GO:0006351 : transcription, DNA-templated
GO:0007204 : positive regulation of cytosolic calcium ion concentration
GO:0045666 : positive regulation of neuron differentiation
GO:0007596 : blood coagulation
GO:0048469 : cell maturation
GO:0001892 : embryonic placenta development
GO:0021902 : commitment of neuronal cell to specific neuron type in forebrain
GO:0042472 : inner ear morphogenesis
GO:0033993 : response to lipid
GO:0045766 : positive regulation of angiogenesis
GO:2000352 : negative regulation of endothelial cell apoptotic process
GO:0043306 : positive regulation of mast cell degranulation
GO:0035019 : somatic stem cell population maintenance
GO:0006909 : phagocytosis
GO:0021983 : pituitary gland development
GO:1902895 : positive regulation of pri-miRNA transcription by RNA polymerase II
GO:0001709 : cell fate determination
GO:0045746 : negative regulation of Notch signaling pathway
GO:0045599 : negative regulation of fat cell differentiation
GO:0021533 : cell differentiation in hindbrain
GO:0021954 : central nervous system neuron development
GO:0090102 : cochlea development
GO:0060216 : definitive hemopoiesis
GO:0035854 : eosinophil fate commitment
GO:0097154 : GABAergic neuron differentiation
GO:0048873 : homeostasis of number of cells within a tissue
GO:0070345 : negative regulation of fat cell proliferation
GO:0045650 : negative regulation of macrophage differentiation
GO:2000178 : negative regulation of neural precursor cell proliferation
GO:0001764 : neuron migration
GO:1903589 : positive regulation of blood vessel endothelial cell proliferation involved in sprouting angiogenesis
GO:0090050 : positive regulation of cell migration involved in sprouting angiogenesis
GO:0045648 : positive regulation of erythrocyte differentiation
GO:0045654 : positive regulation of megakaryocyte differentiation
GO:0050766 : positive regulation of phagocytosis
GO:0060100 : positive regulation of phagocytosis, engulfment
GO:2000977 : regulation of forebrain neuron differentiation
GO:1902036 : regulation of hematopoietic stem cell differentiation
GO:0035065 : regulation of histone acetylation
GO:0010725 : regulation of primitive erythrocyte differentiation
GO:0060872 : semicircular canal development
GO:0001655 : urogenital system development
GO:0021514 : ventral spinal cord interneuron differentiation

GO - Cellular Component
GO:0005737 : cytoplasm
GO:0005654 : nucleoplasm
GO:0005634 : nucleus
GO:0032991 : protein-containing complex

Presumptive Null
No

Molecular Type
Cis-regulatory

Aberration Type
SNP

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

Main Reference
Comprehensive population-based genome sequencing provides insight into hematopoietic regulatory mechanisms. (2017)

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)

Related Haplotypes

No matches found.

COMMENTS