GEPHE SUMMARY

Gephebase Gene
BAK1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^BAK1^#gephebase-summary-title)
Entry Status
Published

GepheID
GP00001616
Main curator
Prigent

PHENOTYPIC CHANGE

Trait Category
Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)
Trait
Hematopoiesis (blood platelet count) (https://www.gephebase.org/search-criteria?/and+Trait=^Hematopoiesis (blood platelet 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
BAK1
Synonyms
BAK; CDN1; BCL2L7; BAK-LIKE
String
9606.ENSP00000353878 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 9606.ENSP00000353878)
Sequence Similarities
Belongs to the Bcl-2 family.
GO - Molecular Function
GO:0042802 : identical protein binding (https://www.ebi.ac.uk/QuickGO/term/GO:0042802)

UniProtKB Homo sapiens
Q16611 (http://www.uniprot.org/uniprot/Q16611)
GenebankID or UniProtKB
()

GO:0042803 : protein homodimerization activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0042803)
GO:0046982 : protein heterodimerization activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0046982)
GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)
GO:0031072 : heat shock protein binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0031072)
GO:0044325 : ion channel binding (https://www.ebi.ac.uk/QuickGO/term/GO:0044325)
GO:0051087 : chaperone binding (https://www.ebi.ac.uk/QuickGO/term/GO:0051087)
GO:0051400 : BH domain binding (https://www.ebi.ac.uk/QuickGO/term/GO:0051400)

GO - Biological Process

GO:0010629 : negative regulation of gene expression
(https://www.ebi.ac.uk/QuickGO/term/GO:0010629)
GO:0008283 : cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0008283)
GO:0097192 : extrinsic apoptotic signaling pathway in absence of ligand
(https://www.ebi.ac.uk/QuickGO/term/GO:0097192)
GO:0008285 : negative regulation of cell proliferation
(https://www.ebi.ac.uk/QuickGO/term/GO:0008285)
GO:0051881 : regulation of mitochondrial membrane potential
(https://www.ebi.ac.uk/QuickGO/term/GO:0051881)
GO:0071260 : cellular response to mechanical stimulus
(https://www.ebi.ac.uk/QuickGO/term/GO:0071260)
GO:0014070 : response to organic cyclic compound
(https://www.ebi.ac.uk/QuickGO/term/GO:0014070)
GO:0006915 : apoptotic process (https://www.ebi.ac.uk/QuickGO/term/GO:0006915)
GO:0042542 : response to hydrogen peroxide
(https://www.ebi.ac.uk/QuickGO/term/GO:0042542)
GO:0031018 : endocrine pancreas development
(https://www.ebi.ac.uk/QuickGO/term/GO:0031018)
GO:0007568 : aging (https://www.ebi.ac.uk/QuickGO/term/GO:0007568)
GO:0007420 : brain development (https://www.ebi.ac.uk/QuickGO/term/GO:0007420)
GO:0001974 : blood vessel remodeling
(https://www.ebi.ac.uk/QuickGO/term/GO:0001974)
GO:0045471 : response to ethanol (https://www.ebi.ac.uk/QuickGO/term/GO:0045471)
GO:0043065 : positive regulation of apoptotic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0043065)
GO:0051726 : regulation of cell cycle (https://www.ebi.ac.uk/QuickGO/term/GO:0051726)
GO:0097190 : apoptotic signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0097190)
GO:0043496 : regulation of protein homodimerization activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0043496)
GO:0034644 : cellular response to UV
(https://www.ebi.ac.uk/QuickGO/term/GO:0034644)
GO:0035108 : limb morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0035108)
GO:0097202 : activation of cysteine-type endopeptidase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0097202)
GO:0008635 : activation of cysteine-type endopeptidase activity involved in apoptotic process by cytochrome c (https://www.ebi.ac.uk/QuickGO/term/GO:0008635)
GO:0031100 : animal organ regeneration
(https://www.ebi.ac.uk/QuickGO/term/GO:0031100)
GO:1902262 : apoptotic process involved in blood vessel morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:1902262)
GO:0001783 : B cell apoptotic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0001783)
GO:0001782 : B cell homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0001782)
GO:0002352 : B cell negative selection
(https://www.ebi.ac.uk/QuickGO/term/GO:0002352)
GO:0034620 : cellular response to unfolded protein
(https://www.ebi.ac.uk/QuickGO/term/GO:0034620)
GO:0032469 : endoplasmic reticulum calcium ion homeostasis
(https://www.ebi.ac.uk/QuickGO/term/GO:0032469)
GO:0010248 : establishment or maintenance of transmembrane electrochemical gradient
(https://www.ebi.ac.uk/QuickGO/term/GO:0010248)
GO:0044346 : fibroblast apoptotic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0044346)
GO:0008630 : intrinsic apoptotic signaling pathway in response to DNA damage
(https://www.ebi.ac.uk/QuickGO/term/GO:0008630)
GO:0070059 : intrinsic apoptotic signaling pathway in response to endoplasmic reticulum stress (https://www.ebi.ac.uk/QuickGO/term/GO:0070059)
GO:0008053 : mitochondrial fusion (https://www.ebi.ac.uk/QuickGO/term/GO:0008053)
GO:0002262 : myeloid cell homeostasis
(https://www.ebi.ac.uk/QuickGO/term/GO:0002262)
GO:0032471 : negative regulation of endoplasmic reticulum calcium ion concentration
(https://www.ebi.ac.uk/QuickGO/term/GO:0032471)
GO:0033137 : negative regulation of peptidyl-serine phosphorylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0033137)
GO:0010524 : positive regulation of calcium ion transport into cytosol
(https://www.ebi.ac.uk/QuickGO/term/GO:0010524)

GO:1900103 : positive regulation of endoplasmic reticulum unfolded protein response (https://www.ebi.ac.uk/QuickGO/term/GO:1900103)
GO:1903896 : positive regulation of IRE1-mediated unfolded protein response (https://www.ebi.ac.uk/QuickGO/term/GO:1903896)
GO:1901030 : positive regulation of mitochondrial outer membrane permeabilization involved in apoptotic signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:1901030)
GO:0045862 : positive regulation of proteolysis (https://www.ebi.ac.uk/QuickGO/term/GO:0045862)
GO:0090200 : positive regulation of release of cytochrome c from mitochondria (https://www.ebi.ac.uk/QuickGO/term/GO:0090200)
GO:0048597 : post-embryonic camera-type eye morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0048597)
GO:0046902 : regulation of mitochondrial membrane permeability (https://www.ebi.ac.uk/QuickGO/term/GO:0046902)
GO:0043497 : regulation of protein heterodimerization activity (https://www.ebi.ac.uk/QuickGO/term/GO:0043497)
GO:0001836 : release of cytochrome c from mitochondria (https://www.ebi.ac.uk/QuickGO/term/GO:0001836)
GO:0009620 : response to fungus (https://www.ebi.ac.uk/QuickGO/term/GO:0009620)
GO:0010332 : response to gamma radiation (https://www.ebi.ac.uk/QuickGO/term/GO:0010332)
GO:0010046 : response to mycotoxin (https://www.ebi.ac.uk/QuickGO/term/GO:0010046)
GO:0010225 : response to UV-C (https://www.ebi.ac.uk/QuickGO/term/GO:0010225)
GO:0070242 : thymocyte apoptotic process (https://www.ebi.ac.uk/QuickGO/term/GO:0070242)
GO:0060068 : vagina development (https://www.ebi.ac.uk/QuickGO/term/GO:0060068)

GO - Cellular Component

GO:0005829 : cytosol (https://www.ebi.ac.uk/QuickGO/term/GO:0005829)
GO:0005739 : mitochondrion (https://www.ebi.ac.uk/QuickGO/term/GO:0005739)
GO:0005783 : endoplasmic reticulum (https://www.ebi.ac.uk/QuickGO/term/GO:0005783)
GO:0005741 : mitochondrial outer membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005741)
GO:0097145 : BAK complex (https://www.ebi.ac.uk/QuickGO/term/GO:0097145)
GO:0031307 : integral component of mitochondrial outer membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0031307)
GO:0046930 : pore complex (https://www.ebi.ac.uk/QuickGO/term/GO:0046930)

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

A>G 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; 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, CCAAT-enhancer-binding protein alpha (CEBPA), 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