GEPHE SUMMARY

Gephebase Gene

JAK2 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^JAK2^#gephebase-summary-title)

GepheID

GP00001613

Entry Status

Published

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

JAK2

Synonyms

JTK10; THCYT3

String

9606.ENSP00000371067 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000371067)

Sequence Similarities

Belongs to the protein kinase superfamily. Tyr protein kinase family. JAK subfamily.

GO - Molecular Function

GO:0005524 : ATP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005524)
GO:0042802 : identical protein binding

UniProtKB Homo sapiens

O60674 (http://www.uniprot.org/uniprot/O60674)

GenebankID or UniProtKB

()

(https://www.ebi.ac.uk/QuickGO/term/GO:0042802)
GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)
GO:0005088 : Ras guanyl-nucleotide exchange factor activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0005088)
GO:0005102 : signaling receptor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0005102)
GO:0019901 : protein kinase binding (https://www.ebi.ac.uk/QuickGO/term/GO:0019901)
GO:0020037 : heme binding (https://www.ebi.ac.uk/QuickGO/term/GO:0020037)
GO:0004672 : protein kinase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004672)
GO:0031702 : type 1 angiotensin receptor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0031702)
GO:0004713 : protein tyrosine kinase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0004713)
GO:0042169 : SH2 domain binding (https://www.ebi.ac.uk/QuickGO/term/GO:0042169)
GO:0043560 : insulin receptor substrate binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0043560)
GO:0043548 : phosphatidylinositol 3-kinase binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0043548)
GO:0004715 : non-membrane spanning protein tyrosine kinase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0004715)
GO:0008022 : protein C-terminus binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0008022)
GO:0033130 : acetylcholine receptor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0033130)
GO:0005131 : growth hormone receptor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0005131)
GO:0042393 : histone binding (https://www.ebi.ac.uk/QuickGO/term/GO:0042393)
GO:0035401 : histone kinase activity (H3-Y41 specific)
(https://www.ebi.ac.uk/QuickGO/term/GO:0035401)
GO:0005143 : interleukin-12 receptor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0005143)
GO:0051428 : peptide hormone receptor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0051428)

GO - Biological Process

GO:0007165 : signal transduction (https://www.ebi.ac.uk/QuickGO/term/GO:0007165)
GO:0030154 : cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0030154)
GO:0007186 : G protein-coupled receptor signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0007186)
GO:0043524 : negative regulation of neuron apoptotic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0043524)
GO:0000165 : MAPK cascade (https://www.ebi.ac.uk/QuickGO/term/GO:0000165)
GO:0050731 : positive regulation of peptidyl-tyrosine phosphorylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0050731)
GO:0046579 : positive regulation of Ras protein signal transduction
(https://www.ebi.ac.uk/QuickGO/term/GO:0046579)
GO:0008285 : negative regulation of cell proliferation
(https://www.ebi.ac.uk/QuickGO/term/GO:0008285)
GO:0045597 : positive regulation of cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0045597)
GO:0007204 : positive regulation of cytosolic calcium ion concentration
(https://www.ebi.ac.uk/QuickGO/term/GO:0007204)
GO:0006468 : protein phosphorylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0006468)
GO:0032496 : response to lipopolysaccharide
(https://www.ebi.ac.uk/QuickGO/term/GO:0032496)
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:0007596 : blood coagulation (https://www.ebi.ac.uk/QuickGO/term/GO:0007596)
GO:0007498 : mesoderm development
(https://www.ebi.ac.uk/QuickGO/term/GO:0007498)
GO:0006915 : apoptotic process (https://www.ebi.ac.uk/QuickGO/term/GO:0006915)
GO:0033209 : tumor necrosis factor-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0033209)
GO:0006919 : activation of cysteine-type endopeptidase activity involved in apoptotic
process (https://www.ebi.ac.uk/QuickGO/term/GO:0006919)
GO:0046777 : protein autophosphorylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0046777)
GO:0002250 : adaptive immune response
(https://www.ebi.ac.uk/QuickGO/term/GO:0002250)
GO:0030218 : erythrocyte differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0030218)
GO:0120162 : positive regulation of cold-induced thermogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0120162)
GO:0018108 : peptidyl-tyrosine phosphorylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0018108)
GO:0032024 : positive regulation of insulin secretion

(https://www.ebi.ac.uk/QuickGO/term/GO:0032024)
GO:0042976 : activation of Janus kinase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0042976)
GO:0060396 : growth hormone receptor signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0060396)
GO:0007259 : JAK-STAT cascade (https://www.ebi.ac.uk/QuickGO/term/GO:0007259)
GO:0060397 : JAK-STAT cascade involved in growth hormone signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0060397)
GO:0042531 : positive regulation of tyrosine phosphorylation of STAT protein
(https://www.ebi.ac.uk/QuickGO/term/GO:0042531)
GO:0030335 : positive regulation of cell migration
(https://www.ebi.ac.uk/QuickGO/term/GO:0030335)
GO:0045429 : positive regulation of nitric oxide biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0045429)
GO:0060333 : interferon-gamma-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0060333)
GO:0043392 : negative regulation of DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0043392)
GO:0035556 : intracellular signal transduction
(https://www.ebi.ac.uk/QuickGO/term/GO:0035556)
GO:0014068 : positive regulation of phosphatidylinositol 3-kinase signaling
(https://www.ebi.ac.uk/QuickGO/term/GO:0014068)
GO:0043388 : positive regulation of DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0043388)
GO:0033160 : positive regulation of protein import into nucleus, translocation
(https://www.ebi.ac.uk/QuickGO/term/GO:0033160)
GO:1904707 : positive regulation of vascular smooth muscle cell proliferation
(https://www.ebi.ac.uk/QuickGO/term/GO:1904707)
GO:0045428 : regulation of nitric oxide biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0045428)
GO:0051091 : positive regulation of DNA-binding transcription factor activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0051091)
GO:0030041 : actin filament polymerization
(https://www.ebi.ac.uk/QuickGO/term/GO:0030041)
GO:0045822 : negative regulation of heart contraction
(https://www.ebi.ac.uk/QuickGO/term/GO:0045822)
GO:0032760 : positive regulation of tumor necrosis factor production
(https://www.ebi.ac.uk/QuickGO/term/GO:0032760)
GO:0000186 : activation of MAPKK activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0000186)
GO:0046677 : response to antibiotic (https://www.ebi.ac.uk/QuickGO/term/GO:0046677)
GO:0034612 : response to tumor necrosis factor
(https://www.ebi.ac.uk/QuickGO/term/GO:0034612)
GO:0008631 : intrinsic apoptotic signaling pathway in response to oxidative stress
(https://www.ebi.ac.uk/QuickGO/term/GO:0008631)
GO:0031103 : axon regeneration (https://www.ebi.ac.uk/QuickGO/term/GO:0031103)
GO:0097296 : activation of cysteine-type endopeptidase activity involved in apoptotic
signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0097296)
GO:0007167 : enzyme linked receptor protein signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0007167)
GO:0097191 : extrinsic apoptotic signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0097191)
GO:0035409 : histone H3-Y41 phosphorylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0035409)
GO:0035722 : interleukin-12-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0035722)
GO:0038155 : interleukin-23-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0038155)
GO:0070106 : interleukin-27-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0070106)
GO:0070757 : interleukin-35-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0070757)
GO:0070102 : interleukin-6-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0070102)
GO:0061180 : mammary gland epithelium development
(https://www.ebi.ac.uk/QuickGO/term/GO:0061180)
GO:0031959 : mineralocorticoid receptor signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0031959)
GO:0050804 : modulation of chemical synaptic transmission
(https://www.ebi.ac.uk/QuickGO/term/GO:0050804)
GO:0010667 : negative regulation of cardiac muscle cell apoptotic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0010667)
GO:0022408 : negative regulation of cell-cell adhesion
(https://www.ebi.ac.uk/QuickGO/term/GO:0022408)
GO:0048008 : platelet-derived growth factor receptor signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0048008)
GO:0050867 : positive regulation of cell activation
(https://www.ebi.ac.uk/QuickGO/term/GO:0050867)

GO:0010811 : positive regulation of cell-substrate adhesion (https://www.ebi.ac.uk/QuickGO/term/GO:0010811)
GO:1904037 : positive regulation of epithelial cell apoptotic process (https://www.ebi.ac.uk/QuickGO/term/GO:1904037)
GO:1902728 : positive regulation of growth factor dependent skeletal muscle satellite cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:1902728)
GO:0060399 : positive regulation of growth hormone receptor signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0060399)
GO:0032731 : positive regulation of interleukin-1 beta production (https://www.ebi.ac.uk/QuickGO/term/GO:0032731)
GO:0051770 : positive regulation of nitric-oxide synthase biosynthetic process (https://www.ebi.ac.uk/QuickGO/term/GO:0051770)
GO:0032516 : positive regulation of phosphoprotein phosphatase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0032516)
GO:0099527 : postsynapse to nucleus signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0099527)
GO:0050727 : regulation of inflammatory response (https://www.ebi.ac.uk/QuickGO/term/GO:0050727)
GO:0060334 : regulation of interferon-gamma-mediated signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0060334)
GO:0046425 : regulation of JAK-STAT cascade (https://www.ebi.ac.uk/QuickGO/term/GO:0046425)
GO:0033194 : response to hydroperoxide (https://www.ebi.ac.uk/QuickGO/term/GO:0033194)
GO:0070671 : response to interleukin-12 (https://www.ebi.ac.uk/QuickGO/term/GO:0070671)
GO:0007260 : tyrosine phosphorylation of STAT protein (https://www.ebi.ac.uk/QuickGO/term/GO:0007260)

GO - Cellular Component

GO:0005886 : plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005886)
GO:0005737 : cytoplasm (https://www.ebi.ac.uk/QuickGO/term/GO:0005737)
GO:0005829 : cytosol (https://www.ebi.ac.uk/QuickGO/term/GO:0005829)
GO:0005925 : focal adhesion (https://www.ebi.ac.uk/QuickGO/term/GO:0005925)
GO:0045121 : membrane raft (https://www.ebi.ac.uk/QuickGO/term/GO:0045121)
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:0098978 : glutamatergic synapse (https://www.ebi.ac.uk/QuickGO/term/GO:0098978)
GO:0005856 : cytoskeleton (https://www.ebi.ac.uk/QuickGO/term/GO:0005856)
GO:0005901 : caveola (https://www.ebi.ac.uk/QuickGO/term/GO:0005901)
GO:0098794 : postsynapse (https://www.ebi.ac.uk/QuickGO/term/GO:0098794)
GO:0031904 : endosome lumen (https://www.ebi.ac.uk/QuickGO/term/GO:0031904)
GO:0016363 : nuclear matrix (https://www.ebi.ac.uk/QuickGO/term/GO:0016363)

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

G>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; 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, GATA-binding protein 2 (GATA2), HBS1L-MYB, 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