GEPHE SUMMARY

Gephebase Gene
TMPRSS6

GephelD
GP00001618

Entry Status
Published

Main curator
Prigent

PHENOTYPIC CHANGE

Trait Category
Physiology

Trait
Hematopoiesis (mean blood corpuscular hemoglobin)

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
TMPRSS6

Synonyms
IRIDA; UNQ354/PRO618

String
9606.ENSP00000334962

Sequence Similarities
Belongs to the peptidase S1 family.

GO - Molecular Function
GO:0004222 : metalloendopeptidase activity
GO:0004252 : serine-type endopeptidase activity

GO - Biological Process
GO:0045944 : positive regulation of transcription by RNA polymerase II
GO:0030198 : extracellular matrix organization

UniProtKB Homo sapiens
Q8IU80

GenebankID or UniProtKB

GO:0006508 : proteolysis
GO:0000122 : negative regulation of transcription by RNA polymerase II
GO:0045892 : negative regulation of transcription, DNA-templated
GO:0006879 : cellular iron ion homeostasis
GO:0001525 : angiogenesis
GO:0055072 : iron ion homeostasis
GO:0035556 : intracellular signal transduction
GO:0030574 : collagen catabolic process
GO:0022617 : extracellular matrix disassembly
GO:0042730 : fibrinolysis
GO:0033619 : membrane protein proteolysis
GO:0030514 : negative regulation of BMP signaling pathway
GO:0097264 : self proteolysis

GO - Cellular Component
GO:0016021 : integral component of membrane
GO:0005886 : plasma membrane
GO:0005615 : extracellular space

Presumptive Null
No

Molecular Type
Coding

Aberration Type
SNP

SNP Coding Change
Nonsynonymous

Molecular Details of the Mutation
T>C at the associated SNP. Another SNP variant in strong LD p.V736A previously reported to influence iron homeostasis

Experimental Evidence
Association Mapping

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	-	-	-

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, GATA-binding protein 2 (GATA2), HBS1L-MYB, JAK2, JMJD1C, LPAR1, PIK3CG, PSMD13, WDR66)
Related Haplotypes
No matches found.

EXTERNAL LINKS

COMMENTS