GEPHE SUMMARY

Gephebase Gene
KCNQ1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^KCNQ1^#gephebase-summary-title)
Entry Status
Published

GepheID
GP00000511
Main curator
Martin

PHENOTYPIC CHANGE

Trait Category
Morphology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Morphology^#gephebase-summary-title)
Trait
Body size (height) (https://www.gephebase.org/search-criteria?/and+Trait=^Body size (height)^#gephebase-summary-title)
Trait State in Taxon A
Homo sapiens - Sardinia
Trait State in Taxon B
Homo sapiens - Sardinia
Ancestral State
Data not curated
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?
No

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?
No

GENOTYPIC CHANGE

Generic Gene Name
KCNQ1
Synonyms
WRS; LQT; RWS; LQT1; SQT2; ATFB1; ATFB3; JLNS1; KCNA8; KCNA9; Kv1.9; Kv7.1; KVLQT1
String
9606.ENSP00000155840 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 9606.ENSP00000155840)
Sequence Similarities
Belongs to the potassium channel family. KQT (TC 1.A.1.15) subfamily. Kv7.1/KCNQ1 sub-subfamily.
GO - Molecular Function
GO:0005516 : calmodulin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005516)
GO:0097110 : scaffold protein binding

UniProtKB Homo sapiens
P51787 (http://www.uniprot.org/uniprot/P51787)
GenebankID or UniProtKB
()

(https://www.ebi.ac.uk/QuickGO/term/GO:0097110)
GO:0005249 : voltage-gated potassium channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005249)
GO:0005251 : delayed rectifier potassium channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005251)
GO:0044325 : ion channel binding (https://www.ebi.ac.uk/QuickGO/term/GO:0044325)
GO:0015271 : outward rectifier potassium channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0015271)
GO:0005546 : phosphatidylinositol-4,5-bisphosphate binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005546)
GO:0034236 : protein kinase A catalytic subunit binding (https://www.ebi.ac.uk/QuickGO/term/GO:0034236)
GO:0034237 : protein kinase A regulatory subunit binding (https://www.ebi.ac.uk/QuickGO/term/GO:0034237)
GO:0008157 : protein phosphatase 1 binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008157)
GO:0086089 : voltage-gated potassium channel activity involved in atrial cardiac muscle cell action potential repolarization (https://www.ebi.ac.uk/QuickGO/term/GO:0086089)
GO:0086008 : voltage-gated potassium channel activity involved in cardiac muscle cell action potential repolarization (https://www.ebi.ac.uk/QuickGO/term/GO:0086008)
GO:1902282 : voltage-gated potassium channel activity involved in ventricular cardiac muscle cell action potential repolarization (https://www.ebi.ac.uk/QuickGO/term/GO:1902282)

GO - Biological Process

GO:0071872 : cellular response to epinephrine stimulus (https://www.ebi.ac.uk/QuickGO/term/GO:0071872)
GO:0010460 : positive regulation of heart rate (https://www.ebi.ac.uk/QuickGO/term/GO:0010460)
GO:0008016 : regulation of heart contraction (https://www.ebi.ac.uk/QuickGO/term/GO:0008016)
GO:1901381 : positive regulation of potassium ion transmembrane transport (https://www.ebi.ac.uk/QuickGO/term/GO:1901381)
GO:0035690 : cellular response to drug (https://www.ebi.ac.uk/QuickGO/term/GO:0035690)
GO:0070293 : renal absorption (https://www.ebi.ac.uk/QuickGO/term/GO:0070293)
GO:0048839 : inner ear development (https://www.ebi.ac.uk/QuickGO/term/GO:0048839)
GO:0071805 : potassium ion transmembrane transport (https://www.ebi.ac.uk/QuickGO/term/GO:0071805)
GO:0086014 : atrial cardiac muscle cell action potential (https://www.ebi.ac.uk/QuickGO/term/GO:0086014)
GO:0060048 : cardiac muscle contraction (https://www.ebi.ac.uk/QuickGO/term/GO:0060048)
GO:0072358 : cardiovascular system development (https://www.ebi.ac.uk/QuickGO/term/GO:0072358)
GO:0071320 : cellular response to cAMP (https://www.ebi.ac.uk/QuickGO/term/GO:0071320)
GO:0016458 : gene silencing (https://www.ebi.ac.uk/QuickGO/term/GO:0016458)
GO:0050892 : intestinal absorption (https://www.ebi.ac.uk/QuickGO/term/GO:0050892)
GO:0086011 : membrane repolarization during action potential (https://www.ebi.ac.uk/QuickGO/term/GO:0086011)
GO:0098914 : membrane repolarization during atrial cardiac muscle cell action potential (https://www.ebi.ac.uk/QuickGO/term/GO:0098914)
GO:0086013 : membrane repolarization during cardiac muscle cell action potential (https://www.ebi.ac.uk/QuickGO/term/GO:0086013)
GO:0098915 : membrane repolarization during ventricular cardiac muscle cell action potential (https://www.ebi.ac.uk/QuickGO/term/GO:0098915)
GO:1902260 : negative regulation of delayed rectifier potassium channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:1902260)
GO:1903817 : negative regulation of voltage-gated potassium channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:1903817)
GO:0060452 : positive regulation of cardiac muscle contraction (https://www.ebi.ac.uk/QuickGO/term/GO:0060452)
GO:0097623 : potassium ion export across plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0097623)
GO:0060372 : regulation of atrial cardiac muscle cell membrane repolarization (https://www.ebi.ac.uk/QuickGO/term/GO:0060372)
GO:0060453 : regulation of gastric acid secretion (https://www.ebi.ac.uk/QuickGO/term/GO:0060453)
GO:0006349 : regulation of gene expression by genetic imprinting (https://www.ebi.ac.uk/QuickGO/term/GO:0006349)
GO:0086091 : regulation of heart rate by cardiac conduction (https://www.ebi.ac.uk/QuickGO/term/GO:0086091)
GO:0060306 : regulation of membrane repolarization (https://www.ebi.ac.uk/QuickGO/term/GO:0060306)
GO:0060307 : regulation of ventricular cardiac muscle cell membrane repolarization (https://www.ebi.ac.uk/QuickGO/term/GO:0060307)
GO:0007605 : sensory perception of sound

(https://www.ebi.ac.uk/QuickGO/term/GO:0007605)
GO:0086005 : ventricular cardiac muscle cell action potential
(https://www.ebi.ac.uk/QuickGO/term/GO:0086005)

GO - Cellular Component

GO:0016021 : integral component of membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016021)
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:0045121 : membrane raft (https://www.ebi.ac.uk/QuickGO/term/GO:0045121)
GO:0030659 : cytoplasmic vesicle membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0030659)
GO:0005769 : early endosome (https://www.ebi.ac.uk/QuickGO/term/GO:0005769)
GO:0005783 : endoplasmic reticulum
(https://www.ebi.ac.uk/QuickGO/term/GO:0005783)
GO:0016323 : basolateral plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016323)
GO:0005764 : lysosome (https://www.ebi.ac.uk/QuickGO/term/GO:0005764)
GO:0008076 : voltage-gated potassium channel complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0008076)
GO:0034702 : ion channel complex (https://www.ebi.ac.uk/QuickGO/term/GO:0034702)
GO:0005770 : late endosome (https://www.ebi.ac.uk/QuickGO/term/GO:0005770)

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

Unknown (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Unknown^#gephebase-summary-title)

Aberration Type

Epigenetic Change (https://www.gephebase.org/search-criteria?/and+Aberration Type=^Epigenetic Change^#gephebase-summary-title)

Molecular Details of the Mutation

unknown causative change in an imprinted region - consistent with maternal inheritance detected by the association

Experimental Evidence

Association Mapping (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Association Mapping^#gephebase-summary-title)

Main Reference

Height-reducing variants and selection for short stature in Sardinia. (2015) (https://pubmed.ncbi.nlm.nih.gov/26366551)

Authors

Zoledziewska M; Sidore C; Chiang CWK; Sanna S; Mulas A; Steri M; Busonero F; Marcus JH; Marongiu M; Maschio A; Ortega Del Vecchyo D; Floris M; Meloni A; Delitala A; Concas MP; Murgia F; Biino G; Vaccargiu S; Nagaraja R; Lohmueller KE; ; Timpson NJ; Soranzo N; Tachmazidou I; Dedoussis G; Zeggini E; ; Uzzau S; Jones C; Lyons R; Angius A; Abecasis GR; Novembre J; Schlessinger D; Cucca F

Abstract

We report sequencing-based whole-genome association analyses to evaluate the impact of rare and founder variants on stature in 6,307 individuals on the island of Sardinia. We identify two variants with large effects. One variant, which introduces a stop codon in the GHR gene, is relatively frequent in Sardinia (0.87% versus <0.01% elsewhere) and in the homozygous state causes Laron syndrome involving short stature. We find that this variant reduces height in heterozygotes by an average of 4.2 cm (-0.64 s.d.). The other variant, in the imprinted KCNQ1 gene (minor allele frequency (MAF) = 7.7% in Sardinia versus <1% elsewhere) reduces height by an average of 1.83 cm (-0.31 s.d.) when maternally inherited. Additionally, polygenic scores indicate that known height-decreasing alleles are at systematically higher frequencies in Sardinians than would be expected by genetic drift. The findings are consistent with selection for shorter stature in Sardinia and a suggestive human example of the proposed 'island effect' reducing the size of large mammals.

Additional References

RELATED GEPHE

Related Genes

23 (ADAMTS10, agrecan, CREBRF, DC-STAMP domain containing 2 (DCST2), DYM, EIF2AK3, FTO, GDF5, GHSR, GPR133, Growth Hormone Receptor (GHR), HMGA2, Insulin-like growth factor receptor 1 (IGF1R), JAZF1, LCORL, LIN28B, natriuretic peptide precursor type C (NPPC), natriuretic peptide receptor 3 (NPR3), Patched1 (Ptc1), PPAR-delta, TRIP11 (=GMAP-210), SMAD family member 2 (SMAD2), stanniocalcin 2 (STC2)) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^9606^/and+Trait=Body size/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS