

GEPHE SUMMARY

	Gephebase Gene	GepheID
Growth Hormone Receptor (GHR) (<a +growth+hormone+receptor+(ghr)+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=">https://www.gephebase.org/search-criteria?/and+Gene+Gephebase="+Growth+Hormone+Receptor+(GHR)+"#gephebase-summary-title)	GP00000415	
	Entry Status	Main curator
Published	Martin	

PHENOTYPIC CHANGE

	Trait Category		
Morphology (<a +morphology+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait+Category=">https://www.gephebase.org/search-criteria?/and+Trait+Category="+Morphology+"#gephebase-summary-title)		Trait	
Body size (height) (<a +body+size+(height)+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait=">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 (<a +intraspecific+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=">https://www.gephebase.org/search-criteria?/and+Taxonomic+Status="+Intraspecific+"#gephebase-summary-title)			
	Taxon A		Taxon B
	Latin Name		Latin Name
Homo sapiens (<a +homo+sapiens+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms="+Homo+sapiens+"#gephebase-summary-title)		Homo sapiens (<a +homo+sapiens+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms="+Homo+sapiens+"#gephebase-summary-title)	
	Common Name		Common Name
human		human	
	Synonyms		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		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		Rank
species		species	
	Lineage		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		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		Parent
Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)		Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)	
	NCBI Taxonomy ID		NCBI Taxonomy ID
9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)		9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)	
	is Taxon A an Intraspecies?		is Taxon B an Intraspecies?
No		No	

GENOTYPIC CHANGE

	Generic Gene Name	UniProtKB Homo sapiens
GHR		P10912 (http://www.uniprot.org/uniprot/P10912)
	Synonyms	GenebankID or UniProtKB
GHP; GHIP		
	String	
9606.ENSPP00000230882 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPP00000230882)		
	Sequence Similarities	
Belongs to the type I cytokine receptor family. Type 1 subfamily.		
	GO - Molecular Function	
GO:0042802 : identical protein binding (https://www.ebi.ac.uk/QuickGO/term/GO:0042802)		
GO:0042803 : protein homodimerization activity (https://www.ebi.ac.uk/QuickGO/term/GO:0042803)		

GO:0019901 : protein kinase binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0019901>)
GO:0017046 : peptide hormone binding
(<https://www.ebi.ac.uk/QuickGO/term/GO:0017046>)
GO:0019955 : cytokine binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0019955>)
GO:0004896 : cytokine receptor activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:0004896>)
GO:0019838 : growth factor binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0019838>)
GO:0004903 : growth hormone receptor activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:0004903>)
GO:0070064 : proline-rich region binding
(<https://www.ebi.ac.uk/QuickGO/term/GO:0070064>)

GO - Biological Process

GO:0050731 : positive regulation of peptidyl-tyrosine phosphorylation
(<https://www.ebi.ac.uk/QuickGO/term/GO:0050731>)
GO:0032870 : cellular response to hormone stimulus
(<https://www.ebi.ac.uk/QuickGO/term/GO:0032870>)
GO:0032355 : response to estradiol (<https://www.ebi.ac.uk/QuickGO/term/GO:0032355>)
GO:0040014 : regulation of multicellular organism growth
(<https://www.ebi.ac.uk/QuickGO/term/GO:0040014>)
GO:0006897 : endocytosis (<https://www.ebi.ac.uk/QuickGO/term/GO:0006897>)
GO:0048009 : insulin-like growth factor receptor signaling pathway
(<https://www.ebi.ac.uk/QuickGO/term/GO:0048009>)
GO:0006631 : fatty acid metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006631>)
GO:0040018 : positive regulation of multicellular organism growth
(<https://www.ebi.ac.uk/QuickGO/term/GO:0040018>)
GO:0006103 : 2-oxoglutarate metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006103>)
GO:0042976 : activation of Janus kinase activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:0042976>)
GO:0000187 : activation of MAPK activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:0000187>)
GO:0000255 : allantoin metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0000255>)
GO:0006101 : citrate metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006101>)
GO:0006600 : creatine metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006600>)
GO:0046449 : creatinine metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0046449>)
GO:0060396 : growth hormone receptor signaling pathway
(<https://www.ebi.ac.uk/QuickGO/term/GO:0060396>)
GO:0042445 : hormone metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0042445>)
GO:0006549 : isoleucine metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006549>)
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:0006107 : oxaloacetate metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006107>)
GO:0046427 : positive regulation of JAK-STAT cascade
(<https://www.ebi.ac.uk/QuickGO/term/GO:0046427>)
GO:0042531 : positive regulation of tyrosine phosphorylation of STAT protein
(<https://www.ebi.ac.uk/QuickGO/term/GO:0042531>)
GO:0031623 : receptor internalization (<https://www.ebi.ac.uk/QuickGO/term/GO:0031623>)
GO:0046898 : response to cycloheximide
(<https://www.ebi.ac.uk/QuickGO/term/GO:0046898>)
GO:0006105 : succinate metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006105>)
GO:0019530 : taurine metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0019530>)
GO:0006573 : valine metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006573>)

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:0005829 : cytosol (<https://www.ebi.ac.uk/QuickGO/term/GO:0005829>)
GO:0005887 : integral component of plasma membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0005887>)
GO:0043235 : receptor complex (<https://www.ebi.ac.uk/QuickGO/term/GO:0043235>)
GO:0005576 : extracellular region (<https://www.ebi.ac.uk/QuickGO/term/GO:0005576>)
GO:0005615 : extracellular space (<https://www.ebi.ac.uk/QuickGO/term/GO:0005615>)
GO:0009986 : cell surface (<https://www.ebi.ac.uk/QuickGO/term/GO:0009986>)
GO:0036464 : cytoplasmic ribonucleoprotein granule
(<https://www.ebi.ac.uk/QuickGO/term/GO:0036464>)
GO:0009897 : external side of plasma membrane

(<https://www.ebi.ac.uk/QuickGO/term/GO:0009897>)
GO:0070195 : growth hormone receptor complex
(<https://www.ebi.ac.uk/QuickGO/term/GO:0070195>)

Presumptive Null

Yes (<https://www.gephebase.org/search-criteria?/and+Presumptive Null=~Yes^#gephebase-summary-title>)

Molecular Type

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

Aberration Type

SNP (<https://www.gephebase.org/search-criteria?/and+Aberration Type=~SNP^#gephebase-summary-title>)

SNP Coding Change

Nonsense

Molecular Details of the Mutation

Arg61*

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Arg	STP	61

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 Vecchio 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, HMGA2, Insulin-like growth factor receptor 1 (IGF1R), JAZF1, KCNQ1, 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

Stop codon variant relatively frequent in Sardinia (0.87% versus <0.01% elsewhere) and can cause Laron-type dwarfism at the homozygous state