GEPHE SUMMARY

Gephebase Gene

EPAS1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^EPAS1^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00002062

Main curator

Courtier

PHENOTYPIC CHANGE

Trait Category

Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)

Trait

Hypoxia response (https://www.gephebase.org/search-criteria?/and+Trait=^Hypoxia response^#gephebase-summary-title)

Trait State in Taxon A

deer mice in lowlands

Trait State in Taxon B

deer mice native to the Rocky Mountain highlands

Ancestral State

Taxon A

Taxonomic Status

Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)

Taxon A

Latin Name

Peromyscus maniculatus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Peromyscus maniculatus^#gephebase-summary-title)

Common Name

North American deer mouse

Synonyms

North American deer mouse; Peromyscus maniculatus (Wagner, 1845); MSB Mamm 74965; MSB:collector:Mamm:74965; Peromyscus maniculatis

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; Glires; Rodentia; Myomorpha; Muroidea; Cricetidae; Neotominae; Peromyscus

Parent

Peromyscus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10040)

NCBI Taxonomy ID

10042 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10042)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

Peromyscus maniculatus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Peromyscus maniculatus^#gephebase-summary-title)

Common Name

North American deer mouse

Synonyms

North American deer mouse; Peromyscus maniculatus (Wagner, 1845); MSB Mamm 74965; MSB:collector:Mamm:74965; Peromyscus maniculatis

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; Glires; Rodentia; Myomorpha; Muroidea; Cricetidae; Neotominae; Peromyscus

Parent

Peromyscus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10040)

NCBI Taxonomy ID

10042 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10042)

is Taxon B an Infraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name

EPAS1

Synonyms

HLF; MOP2; ECYT4; HIF2A; PASD2; bHLHe73; BHLHE73

String

9606.ENSP00000263734 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 9606.ENSP00000263734)

Sequence Similarities

-

GO - Molecular Function

GO:0046982 : protein heterodimerization activity (https://www.ebi.ac.uk/QuickGO/term/GO:0046982)
GO:0043565 : sequence-specific DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0043565)
GO:0008134 : transcription factor binding

UniProtKB Homo sapiens

Q99814 (http://www.uniprot.org/uniprot/Q99814)

GenebankID or UniProtKB

()

(https://www.ebi.ac.uk/QuickGO/term/GO:0008134)
GO:0003677 : DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003677)
GO:0000981 : DNA-binding transcription factor activity, RNA polymerase II-specific (https://www.ebi.ac.uk/QuickGO/term/GO:0000981)
GO:0001077 : proximal promoter DNA-binding transcription activator activity, RNA polymerase II-specific (https://www.ebi.ac.uk/QuickGO/term/GO:0001077)
GO:0035035 : histone acetyltransferase binding (https://www.ebi.ac.uk/QuickGO/term/GO:0035035)

GO - Biological Process

GO:0007165 : signal transduction (https://www.ebi.ac.uk/QuickGO/term/GO:0007165)
GO:0045944 : positive regulation of transcription by RNA polymerase II (https://www.ebi.ac.uk/QuickGO/term/GO:0045944)
GO:0006357 : regulation of transcription by RNA polymerase II (https://www.ebi.ac.uk/QuickGO/term/GO:0006357)
GO:0043687 : post-translational protein modification (https://www.ebi.ac.uk/QuickGO/term/GO:0043687)
GO:0030324 : lung development (https://www.ebi.ac.uk/QuickGO/term/GO:0030324)
GO:0071456 : cellular response to hypoxia (https://www.ebi.ac.uk/QuickGO/term/GO:0071456)
GO:0061418 : regulation of transcription from RNA polymerase II promoter in response to hypoxia (https://www.ebi.ac.uk/QuickGO/term/GO:0061418)
GO:0001666 : response to hypoxia (https://www.ebi.ac.uk/QuickGO/term/GO:0001666)
GO:0001525 : angiogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0001525)
GO:0001974 : blood vessel remodeling (https://www.ebi.ac.uk/QuickGO/term/GO:0001974)
GO:0048469 : cell maturation (https://www.ebi.ac.uk/QuickGO/term/GO:0048469)
GO:0001892 : embryonic placenta development (https://www.ebi.ac.uk/QuickGO/term/GO:0001892)
GO:0030218 : erythrocyte differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0030218)
GO:0055072 : iron ion homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0055072)
GO:0007005 : mitochondrion organization (https://www.ebi.ac.uk/QuickGO/term/GO:0007005)
GO:0048625 : myoblast fate commitment (https://www.ebi.ac.uk/QuickGO/term/GO:0048625)
GO:0042415 : norepinephrine metabolic process (https://www.ebi.ac.uk/QuickGO/term/GO:0042415)
GO:0120162 : positive regulation of cold-induced thermogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0120162)
GO:0002027 : regulation of heart rate (https://www.ebi.ac.uk/QuickGO/term/GO:0002027)
GO:0043619 : regulation of transcription from RNA polymerase II promoter in response to oxidative stress (https://www.ebi.ac.uk/QuickGO/term/GO:0043619)
GO:0043129 : surfactant homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0043129)
GO:0006366 : transcription by RNA polymerase II (https://www.ebi.ac.uk/QuickGO/term/GO:0006366)
GO:0007601 : visual perception (https://www.ebi.ac.uk/QuickGO/term/GO:0007601)

GO - Cellular Component

GO:0005829 : cytosol (https://www.ebi.ac.uk/QuickGO/term/GO:0005829)
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:0005667 : transcription factor complex (https://www.ebi.ac.uk/QuickGO/term/GO:0005667)
GO:0016607 : nuclear speck (https://www.ebi.ac.uk/QuickGO/term/GO:0016607)

Presumptive Null

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

-

Molecular Details of the Mutation

non-synonymous polymorphism located at site 755 in the 14th exon that changes threonine to methionine Thr755Met

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	ACG	ATG	-
Amino-acid	Thr	Met	755

Main Reference

Physiological and genomic evidence that selection on the transcription factor Epas1 has altered cardiovascular function in high-altitude deer mice. (2019) (https://pubmed.ncbi.nlm.nih.gov/31697676)

Authors

Schweizer RM; Velotta JP; Ivy CM; Jones MR; Muir SM; Bradburd GS; Storz JF; Scott GR; Cheviron ZA

Abstract

Evolutionary adaptation to extreme environments often requires coordinated changes in multiple intersecting physiological pathways, but how such multi-trait adaptation occurs remains unresolved. Transcription factors, which regulate the expression of many genes and can simultaneously alter multiple phenotypes, may be common targets of selection if the benefits of induced changes outweigh the costs of negative pleiotropic effects. We combined complimentary population genetic analyses and physiological experiments in North American deer mice (Peromyscus maniculatus) to examine links between genetic variation in transcription factors that coordinate physiological responses to hypoxia (hypoxia-inducible factors, HIFs) and multiple physiological traits that potentially contribute to high-altitude adaptation. First, we sequenced the exomes of 100 mice sampled from different elevations and discovered that several SNPs in the gene Epas1, which encodes the oxygen sensitive subunit of HIF-2Î±, exhibited extreme allele frequency differences between highland and lowland populations. Broader geographic sampling confirmed that Epas1 genotype varied predictably with altitude throughout the western US. We then discovered that Epas1 genotype influences heart rate in hypoxia, and the transcriptomic responses to hypoxia (including HIF targets and genes involved in catecholamine signaling) in the heart and adrenal gland. Finally, we used a demographically-informed selection scan to show that Epas1 variants have experienced a history of spatially varying selection, suggesting that differences in cardiovascular function and gene regulation contribute to high-altitude adaptation. Our results suggest a mechanism by which Epas1 may aid long-term survival of high-altitude deer mice and provide general insights into the role that highly pleiotropic transcription factors may play in the process of environmental adaptation.

Additional References

RELATED GEPHE

Related Genes

2 (hemoglobin; HBA-T1 and T2 paralogues, hemoglobin; HBB-T1 and T2 paralogues) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^10042^/and+Trait=Hypoxia response/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS