

GEPHE SUMMARY

Gephebase Gene
EPAS1

Entry Status
Published

GepheID
GP00002062

Main curator
Courtier

PHENOTYPIC CHANGE

Trait Category
Physiology

Trait
Hypoxia response

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

Taxon A

Latin Name

Peromyscus maniculatus

Common Name

North American deer mouse

Synonyms

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

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)

NCBI Taxonomy ID

10042

is Taxon A an Intraspecies?

No

Taxon B

Latin Name

Peromyscus maniculatus

Common Name

North American deer mouse

Synonyms

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

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)

NCBI Taxonomy ID

10042

is Taxon B an Intraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name
EPAS1

Synonyms

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

String

9606.ENSP00000263734

Sequence Similarities

-

GO - Molecular Function

GO:0046982 : protein heterodimerization activity

GO:0043565 : sequence-specific DNA binding

GO:0008134 : transcription factor binding

GO:0003677 : DNA binding

GO:0000981 : DNA-binding transcription factor activity, RNA polymerase II-specific

GO:0001077 : proximal promoter DNA-binding transcription activator activity, RNA polymerase II-specific

GO:0035035 : histone acetyltransferase binding

UniProtKB Homo sapiens
Q99814

GenebankID or UniProtKB

GO - Biological Process

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

GO - Cellular Component

GO:0005829 : cytosol
GO:0005654 : nucleoplasm
GO:0005634 : nucleus
GO:0005667 : transcription factor complex
GO:0016607 : nuclear speck

Presumptive Null

No

Molecular Type

Coding

Aberration Type

SNP

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

	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)

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-2 α , 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)

Related Haplotypes

No matches found.

COMMENTS