

## GEPHE SUMMARY

EPAS1 ( <a href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^EPAS1^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^EPAS1^#gephebase-summary-title</a> )	Gephebase Gene	GP00002062	GepheID
Published	Entry Status	Courtier	Main curator

## PHENOTYPIC CHANGE

Physiology ( <a href="https://www.gephebase.org/search-criteria?/and+Trait+Category=^Physiology^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Trait+Category=^Physiology^#gephebase-summary-title</a> )	Trait Category		
Hypoxia response ( <a href="https://www.gephebase.org/search-criteria?/and+Trait=^Hypoxia+response^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Trait=^Hypoxia+response^#gephebase-summary-title</a> )	Trait		
deer mice in lowlands	Trait State in Taxon A		
deer mice native to the Rocky Mountain highlands	Trait State in Taxon B		
	Ancestral State		
Taxon A	Taxonomic Status	Taxon B	
Intraspecific ( <a href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=^Intraspecific^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=^Intraspecific^#gephebase-summary-title</a> )			
	Latin Name		Latin Name
Peromyscus maniculatus ( <a href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Peromyscus+maniculatus^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Peromyscus+maniculatus^#gephebase-summary-title</a> )		Peromyscus maniculatus ( <a href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Peromyscus+maniculatus^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Peromyscus+maniculatus^#gephebase-summary-title</a> )	
North American deer mouse	Common Name	North American deer mouse	Common Name
	Synonyms		Synonyms
North American deer mouse; Peromyscus maniculatus (Wagner, 1845); MSB Mamm 74965; MSB:collector:Mamm:74965; Peromyscus maniculatus		North American deer mouse; Peromyscus maniculatus (Wagner, 1845); MSB Mamm 74965; MSB:collector:Mamm:74965; Peromyscus maniculatus	
species	Rank	species	Rank
	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; Glires; Rodentia; Myomorpha; Muroidea; Cricetidae; Neotominae; Peromyscus		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		Parent
Peromyscus () - (Rank: genus) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10040">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10040</a> )		Peromyscus () - (Rank: genus) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10040">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10040</a> )	
10042 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10042">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10042</a> )	NCBI Taxonomy ID	10042 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10042">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10042</a> )	NCBI Taxonomy ID
	is Taxon A an Intraspecies?		is Taxon B an Intraspecies?
No		No	

## GENOTYPIC CHANGE

EPAS1	Generic Gene Name	Q99814 ( <a href="http://www.uniprot.org/uniprot/Q99814">http://www.uniprot.org/uniprot/Q99814</a> )	UniProtKB Homo sapiens
HLF; MOP2; ECYT4; HIF2A; PASD2; bHLHe73; BHLHE73	Synonyms	()	GenebankID or UniProtKB
9606.ENSP00000263734 ( <a href="http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000263734">http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000263734</a> )	String		
-	Sequence Similarities		
	GO - Molecular Function		
GO:0046982 : protein heterodimerization activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0046982">https://www.ebi.ac.uk/QuickGO/term/GO:0046982</a> )			
GO:0043565 : sequence-specific DNA binding ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0043565">https://www.ebi.ac.uk/QuickGO/term/GO:0043565</a> )			
GO:0008134 : transcription factor binding			

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

Molecular Type

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

Aberration Type

SNP ([https://www.gephebase.org/search-criteria?/and+Aberration Type=^SNP^#gpebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration+Type+SNP+gpebase-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^#gpebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental+Evidence+Association+Mapping+gpebase-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

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 $\alpha$ , 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