GEPHE SUMMARY

Gephebase Gene

hemoglobin; HBB-T1 and T2 paralogues (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^hemoglobin; HBB-T1 and T2 paralogues^#gephebase-summary-title)

Entry Status

Published

GephelD

GP00000476

Main curator

Martin

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

Peromyscus maniculatus -low elevation

Trait State in Taxon B

Peromyscus maniculatus - high elevation

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

HBB

Synonyms

ECYT6; CD113t-C; beta-globin

String

9606.ENSP00000333994 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000333994)

Sequence Similarities

Belongs to the globin family.

GO - Molecular Function

GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)
GO:0020037 : heme binding (https://www.ebi.ac.uk/QuickGO/term/GO:0020037)
GO:0005344 : oxygen carrier activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005344)
GO:0043177 : organic acid binding (https://www.ebi.ac.uk/QuickGO/term/GO:0043177)

UniProtKB Homo sapiens

P68871 (http://www.uniprot.org/uniprot/P68871)

GenebankID or UniProtKB

()

GO:0019825 : oxygen binding (https://www.ebi.ac.uk/QuickGO/term/GO:0019825)
GO:0031721 : hemoglobin alpha binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0031721)
GO:0030492 : hemoglobin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0030492)

GO - Biological Process

GO:0006898 : receptor-mediated endocytosis
(https://www.ebi.ac.uk/QuickGO/term/GO:0006898)
GO:0007596 : blood coagulation (https://www.ebi.ac.uk/QuickGO/term/GO:0007596)
GO:0008217 : regulation of blood pressure
(https://www.ebi.ac.uk/QuickGO/term/GO:0008217)
GO:0042542 : response to hydrogen peroxide
(https://www.ebi.ac.uk/QuickGO/term/GO:0042542)
GO:0043312 : neutrophil degranulation
(https://www.ebi.ac.uk/QuickGO/term/GO:0043312)
GO:0015701 : bicarbonate transport (https://www.ebi.ac.uk/QuickGO/term/GO:0015701)
GO:0098869 : cellular oxidant detoxification
(https://www.ebi.ac.uk/QuickGO/term/GO:0098869)
GO:0042744 : hydrogen peroxide catabolic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0042744)
GO:0015671 : oxygen transport (https://www.ebi.ac.uk/QuickGO/term/GO:0015671)
GO:0010942 : positive regulation of cell death
(https://www.ebi.ac.uk/QuickGO/term/GO:0010942)
GO:0051291 : protein heterooligomerization
(https://www.ebi.ac.uk/QuickGO/term/GO:0051291)
GO:0030185 : nitric oxide transport (https://www.ebi.ac.uk/QuickGO/term/GO:0030185)
GO:0070527 : platelet aggregation (https://www.ebi.ac.uk/QuickGO/term/GO:0070527)
GO:0045429 : positive regulation of nitric oxide biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0045429)
GO:0050880 : regulation of blood vessel size
(https://www.ebi.ac.uk/QuickGO/term/GO:0050880)
GO:0070293 : renal absorption (https://www.ebi.ac.uk/QuickGO/term/GO:0070293)

GO - Cellular Component

GO:0005829 : cytosol (https://www.ebi.ac.uk/QuickGO/term/GO:0005829)
GO:0070062 : extracellular exosome (https://www.ebi.ac.uk/QuickGO/term/GO:0070062)
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:0072562 : blood microparticle (https://www.ebi.ac.uk/QuickGO/term/GO:0072562)
GO:0071682 : endocytic vesicle lumen
(https://www.ebi.ac.uk/QuickGO/term/GO:0071682)
GO:0031838 : haptoglobin-hemoglobin complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0031838)
GO:0005833 : hemoglobin complex (https://www.ebi.ac.uk/QuickGO/term/GO:0005833)
GO:1904813 : ficolin-1-rich granule lumen
(https://www.ebi.ac.uk/QuickGO/term/GO:1904813)
GO:1904724 : tertiary granule lumen (https://www.ebi.ac.uk/QuickGO/term/GO:1904724)

Mutation #1

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

Nonsynonymous

Molecular Details of the Mutation

Ala62Gly; Gly72Ser; Ser128Ala; Ala135Ser

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Ala	Gly	62

Main Reference

Evolutionary and functional insights into the mechanism underlying high-altitude adaptation of deer mouse hemoglobin. (2009) (https://pubmed.ncbi.nlm.nih.gov/19667207)

Authors

Storz JF; Runck AM; Sabatino SJ; Kelly JK; Ferrand N; Moriyama H; Weber RE; Fago A

Abstract

Adaptive modifications of heteromeric proteins may involve genetically based changes in single subunit polypeptides or parallel changes in multiple genes that encode distinct, interacting subunits. Here we investigate these possibilities by conducting a combined evolutionary and functional analysis of duplicated globin genes in natural populations of deer mice (Peromyscus maniculatus) that are adapted to different elevational zones. A multilocus analysis of nucleotide polymorphism and linkage disequilibrium revealed that high-altitude adaptation of deer mouse hemoglobin involves parallel functional differentiation at multiple unlinked gene duplicates: two alpha-globin paralogs on chromosome 8 and two beta-globin paralogs on chromosome 1. Differences in O(2)-binding affinity of the alternative beta-chain hemoglobin isoforms were entirely attributable to allelic differences in sensitivity to 2,3-diphosphoglycerate (DPG), an allosteric cofactor that stabilizes the low-affinity, deoxygenated conformation of the hemoglobin tetramer. The two-locus beta-globin haplotype that

predominates at high altitude is associated with suppressed DPG-sensitivity (and hence, increased hemoglobin-O(2) affinity), which enhances pulmonary O(2) loading under hypoxia. The discovery that allelic differences in DPG-sensitivity contribute to adaptive variation in hemoglobin-O(2) affinity illustrates the value of integrating evolutionary analyses of sequence variation with mechanistic appraisals of protein function. Investigation into the functional significance of the deer mouse beta-globin polymorphism was motivated by the results of population genetic analyses which revealed evidence for a history of divergent selection between elevational zones. The experimental measures of O(2)-binding properties corroborated the tests of selection by demonstrating a functional difference between the products of alternative alleles.

Additional References

Epistasis among adaptive mutations in deer mouse hemoglobin. (2013) (https://pubmed.ncbi.nlm.nih.gov/23766324)

Mutation #2

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

Nonsynonymous

Molecular Details of the Mutation

Ala62Gly; Gly72Ser; Ser128Ala; Ala135Ser

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Gly	Ser	72

Main Reference

Evolutionary and functional insights into the mechanism underlying high-altitude adaptation of deer mouse hemoglobin. (2009) (https://pubmed.ncbi.nlm.nih.gov/19667207)

Authors

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Additional References

Epistasis among adaptive mutations in deer mouse hemoglobin. (2013) (https://pubmed.ncbi.nlm.nih.gov/23766324)

Mutation #3

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

Nonsynonymous

Molecular Details of the Mutation

Ala62Gly; Gly72Ser; Ser128Ala; Ala135Ser

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Ser	Ala	128

Main Reference

Evolutionary and functional insights into the mechanism underlying high-altitude adaptation of deer mouse hemoglobin. (2009) (https://pubmed.ncbi.nlm.nih.gov/19667207)

Authors

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Additional References

Epistasis among adaptive mutations in deer mouse hemoglobin. (2013) (https://pubmed.ncbi.nlm.nih.gov/23766324)

Mutation #4

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

Nonsynonymous

Molecular Details of the Mutation

Ala62Gly; Gly72Ser; Ser128Ala; Ala135Ser

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Ala	Ser	135

Main Reference

Evolutionary and functional insights into the mechanism underlying high-altitude adaptation of deer mouse hemoglobin. (2009) (https://pubmed.ncbi.nlm.nih.gov/19667207)

Authors

Storz JF; Runck AM; Sabatino SJ; Kelly JK; Ferrand N; Moriyama H; Weber RE; Fago A

Abstract

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Additional References

Epistasis among adaptive mutations in deer mouse hemoglobin. (2013) (https://pubmed.ncbi.nlm.nih.gov/23766324)

RELATED GEPHE

Related Genes

2 (EPAS1, hemoglobin; HBA-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

Needs curation @Epistasis @SeveralMutationsWithEffect