GEPHE SUMMARY

Gephebase Gene
HMGA2 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^HMGA2^#gephebase-summary-title)

GepheID
GP00001675

Entry Status
Published

Main curator
Prigent

PHENOTYPIC CHANGE

Trait #1

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

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

Trait State in Taxon A
WT

Trait State in Taxon B
Dwarf breed

Trait #2

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

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

Trait State in Taxon A
-

Trait State in Taxon B
-

Ancestral State
Taxon A

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

Taxon A

Latin Name
Oryctolagus cuniculus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Oryctolagus cuniculus^#gephebase-summary-title)

Common Name
rabbit

Synonyms
Lepus cuniculus; rabbit; European rabbit; Japanese white rabbit; domestic rabbit; rabbits

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; Lagomorpha; Leporidae; Oryctolagus

Parent
Oryctolagus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9984)

NCBI Taxonomy ID
9986 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9986)

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Oryctolagus cuniculus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Oryctolagus cuniculus^#gephebase-summary-title)

Common Name
rabbit

Synonyms
Lepus cuniculus; rabbit; European rabbit; Japanese white rabbit; domestic rabbit; rabbits

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; Lagomorpha; Leporidae; Oryctolagus

Parent
Oryctolagus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9984)

NCBI Taxonomy ID
9986 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9986)

is Taxon B an Infraspecies?
Yes

Taxon B Description
Netherland dwarf breed

GENOTYPIC CHANGE

Generic Gene Name

HMGA2

Synonyms

BABL; LIPO; HMGIC; HMGI-C; STQTL9

String

9606.ENSP00000384026
(http://string-db.org/newstring_cgi/show_network_section.pl?identifier=
9606.ENSP00000384026)

Sequence Similarities

Belongs to the HMGA family.

GO - Molecular Function

GO:0008134 : transcription factor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0008134)
GO:0044212 : transcription regulatory region DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0044212)
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:0000978 : RNA polymerase II proximal promoter sequence-specific DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0000978)
GO:0003680 : AT DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003680)
GO:0001078 : proximal promoter DNA-binding transcription repressor activity, RNA
polymerase II-specific (https://www.ebi.ac.uk/QuickGO/term/GO:0001078)
GO:0003712 : transcription coregulator activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0003712)
GO:0051575 : 5'-deoxyribose-5-phosphate lyase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0051575)
GO:0070742 : C2H2 zinc finger domain binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0070742)
GO:0035497 : cAMP response element binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0035497)
GO:0008301 : DNA binding, bending
(https://www.ebi.ac.uk/QuickGO/term/GO:0008301)
GO:0003906 : DNA-(apurinic or apyrimidinic site) endonuclease activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0003906)
GO:0004677 : DNA-dependent protein kinase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0004677)
GO:0035501 : MH1 domain binding (https://www.ebi.ac.uk/QuickGO/term/GO:0035501)
GO:0035500 : MH2 domain binding (https://www.ebi.ac.uk/QuickGO/term/GO:0035500)
GO:0031492 : nucleosomal DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0031492)
GO:0046332 : SMAD binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046332)

GO - Biological Process

GO:0007275 : multicellular organism development
(https://www.ebi.ac.uk/QuickGO/term/GO:0007275)
GO:0009615 : response to virus (https://www.ebi.ac.uk/QuickGO/term/GO:0009615)
GO:0043066 : negative regulation of apoptotic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0043066)
GO:0045944 : positive regulation of transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0045944)
GO:0006355 : regulation of transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0006355)
GO:0000122 : negative regulation of transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0000122)
GO:0045892 : negative regulation of transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0045892)
GO:0045893 : positive regulation of transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0045893)
GO:0051301 : cell division (https://www.ebi.ac.uk/QuickGO/term/GO:0051301)
GO:0010628 : positive regulation of gene expression
(https://www.ebi.ac.uk/QuickGO/term/GO:0010628)
GO:2000774 : positive regulation of cellular senescence
(https://www.ebi.ac.uk/QuickGO/term/GO:2000774)
GO:0035986 : senescence-associated heterochromatin focus assembly
(https://www.ebi.ac.uk/QuickGO/term/GO:0035986)
GO:0006325 : chromatin organization
(https://www.ebi.ac.uk/QuickGO/term/GO:0006325)
GO:0048863 : stem cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0048863)
GO:0001837 : epithelial to mesenchymal transition
(https://www.ebi.ac.uk/QuickGO/term/GO:0001837)
GO:0048762 : mesenchymal cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0048762)
GO:0048333 : mesodermal cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0048333)

UniProtKB Homo sapiens

P52926 (http://www.uniprot.org/uniprot/P52926)

GenebankID or UniProtKB

()

GO:2000648 : positive regulation of stem cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:2000648)
GO:0043065 : positive regulation of apoptotic process (https://www.ebi.ac.uk/QuickGO/term/GO:0043065)
GO:0002062 : chondrocyte differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0002062)
GO:0045444 : fat cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0045444)
GO:0040008 : regulation of growth (https://www.ebi.ac.uk/QuickGO/term/GO:0040008)
GO:0006284 : base-excision repair (https://www.ebi.ac.uk/QuickGO/term/GO:0006284)
GO:0035988 : chondrocyte proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0035988)
GO:0031052 : chromosome breakage (https://www.ebi.ac.uk/QuickGO/term/GO:0031052)
GO:0030261 : chromosome condensation (https://www.ebi.ac.uk/QuickGO/term/GO:0030261)
GO:0042769 : DNA damage response, detection of DNA damage (https://www.ebi.ac.uk/QuickGO/term/GO:0042769)
GO:0035987 : endodermal cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0035987)
GO:0031507 : heterochromatin assembly (https://www.ebi.ac.uk/QuickGO/term/GO:0031507)
GO:0035978 : histone H2A-S139 phosphorylation (https://www.ebi.ac.uk/QuickGO/term/GO:0035978)
GO:0003131 : mesodermal-endodermal cell signaling (https://www.ebi.ac.uk/QuickGO/term/GO:0003131)
GO:0007095 : mitotic G2 DNA damage checkpoint (https://www.ebi.ac.uk/QuickGO/term/GO:0007095)
GO:0043922 : negative regulation by host of viral transcription (https://www.ebi.ac.uk/QuickGO/term/GO:0043922)
GO:2000773 : negative regulation of cellular senescence (https://www.ebi.ac.uk/QuickGO/term/GO:2000773)
GO:0043392 : negative regulation of DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0043392)
GO:2001033 : negative regulation of double-strand break repair via nonhomologous end joining (https://www.ebi.ac.uk/QuickGO/term/GO:2001033)
GO:0045869 : negative regulation of single stranded viral RNA replication via double stranded DNA intermediate (https://www.ebi.ac.uk/QuickGO/term/GO:0045869)
GO:0090402 : oncogene-induced cell senescence (https://www.ebi.ac.uk/QuickGO/term/GO:0090402)
GO:0045766 : positive regulation of angiogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0045766)
GO:0071158 : positive regulation of cell cycle arrest (https://www.ebi.ac.uk/QuickGO/term/GO:0071158)
GO:0071864 : positive regulation of cell proliferation in bone marrow (https://www.ebi.ac.uk/QuickGO/term/GO:0071864)
GO:2000685 : positive regulation of cellular response to X-ray (https://www.ebi.ac.uk/QuickGO/term/GO:2000685)
GO:2001022 : positive regulation of response to DNA damage stimulus (https://www.ebi.ac.uk/QuickGO/term/GO:2001022)
GO:2000679 : positive regulation of transcription regulatory region DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:2000679)
GO:0010564 : regulation of cell cycle process (https://www.ebi.ac.uk/QuickGO/term/GO:0010564)
GO:2001038 : regulation of cellular response to drug (https://www.ebi.ac.uk/QuickGO/term/GO:2001038)
GO:2000036 : regulation of stem cell population maintenance (https://www.ebi.ac.uk/QuickGO/term/GO:2000036)

GO - Cellular Component

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:0035985 : senescence-associated heterochromatin focus (https://www.ebi.ac.uk/QuickGO/term/GO:0035985)
GO:0000228 : nuclear chromosome (https://www.ebi.ac.uk/QuickGO/term/GO:0000228)
GO:0032993 : protein-DNA complex (https://www.ebi.ac.uk/QuickGO/term/GO:0032993)
GO:0071141 : SMAD protein complex (https://www.ebi.ac.uk/QuickGO/term/GO:0071141)

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

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

Deletion Size

10-100 kb

Molecular Details of the Mutation

deletion of 12.1 kb overlapping the promoter region and first three exons leading to inactivation of the gene. The 5′-end of this deletion overlaps a CSINE2 element

Experimental Evidence

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

Main Reference

Dwarfism and Altered Craniofacial Development in Rabbits Is Caused by a 12.1 kb Deletion at the HMGA2 Locus. (2017) (https://pubmed.ncbi.nlm.nih.gov/27986804)

Authors

Carneiro M; Hu D; Archer J; Feng C; Afonso S; Chen C; Blanco-Aguiar JA; Garreau H; Boucher S; Ferreira PG; Ferrand N; Rubin CJ; Andersson L

Abstract

The dwarf phenotype characterizes the smallest of rabbit breeds and is governed largely by the effects of a single dwarfing allele with an incompletely dominant effect on growth. Dwarf rabbits typically weigh under 1 kg and have altered craniofacial morphology. The dwarf allele is recessive lethal and dwarf homozygotes die within a few days of birth. The dwarf phenotype is expressed in heterozygous individuals and rabbits from dwarf breeds homozygous for the wild-type allele are normal, although smaller when compared to other breeds. Here, we show that the dwarf allele constitutes a â¼412.1 kb deletion overlapping the promoter region and first three exons of the HMGA2 gene leading to inactivation of this gene. HMGA2 has been frequently associated with variation in body size across species. Homozygotes for null alleles are viable in mice but not in rabbits and probably not in humans. RNA-sequencing analysis of rabbit embryos showed that very few genes (4-29 genes) were differentially expressed among the three HMGA2/dwarf genotypes, suggesting that dwarfism and inviability in rabbits are caused by modest changes in gene expression. Our results show that HMGA2 is critical for normal expression of IGF2BP2, which encodes an RNA-binding protein. Finally, we report a catalog of regions of elevated genetic differentiation between dwarf and normal-size rabbits, including LCORL-NCAPG, STC2, HOXD cluster, and IGF2BP2 Levels and patterns of genetic diversity at the LCORL-NCAPG locus further suggest that small size in dwarf breeds was enhanced by crosses with wild rabbits. Overall, our results imply that small size in dwarf rabbits results from a large effect, loss-of-function (LOF) mutation in HMGA2 combined with polygenic selection.

Additional References

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

Null mutation. Homozygotes die within a few days of birth (Autosomal Recessive Lethal) ; @HeterozygoteAdvantage ; https://omia.org/OMIA000299/9986/