

GEPHE SUMMARY

	Gephebase Gene		GepheID
SMAD family member 2 (SMAD2) (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^SMAD family member 2 (SMAD2)^#gephebase-summary-title)		GP00001477	
	Entry Status	Prigent	Main curator
Published			

PHENOTYPIC CHANGE

	Trait Category		
Morphology (https://www.gephebase.org/search-criteria?/and+Trait+Category=^Morphology^#gephebase-summary-title)			
	Trait		
Body size (weight) (https://www.gephebase.org/search-criteria?/and+Trait=^Body size (weight)^#gephebase-summary-title)			
	Trait State in Taxon A		
Gray wolf of 38 to 66 kg			
	Trait State in Taxon B		
Dog of 5.5 kg on average			
	Ancestral State		
Taxon A			
	Taxonomic Status		
Domesticated (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=^Domesticated^#gephebase-summary-title)			
Taxon A		Taxon B	
	Latin Name		Latin Name
Canis lupus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Canis lupus^#gephebase-summary-title)		Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Homo sapiens^#gephebase-summary-title)	
	Common Name		Common Name
gray wolf		human	
	Synonyms		Synonyms
gray wolf; grey wolf; Canis lupus Linnaeus, 1758		human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sapiens; Homo sapeins; Homo sapien; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens	
	Rank		Rank
species		species	
	Lineage		Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Laurasiatheria; Carnivora; Caniformia; Canidae; Canis		cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo	
	Parent		Parent
Canis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9611)		Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9605)	
	NCBI Taxonomy ID		NCBI Taxonomy ID
9612 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9612)		9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9606)	
	is Taxon A an Intraspecies?		is Taxon B an Intraspecies?
No		No	

GENOTYPIC CHANGE

	Generic Gene Name		UniProtKB Canis lupus familiaris
SMAD2		E2RP23 (http://www.uniprot.org/uniprot/E2RP23)	
	Synonyms		GenebankID or UniProtKB
-		XM_005622830 (https://www.ncbi.nlm.nih.gov/nucore/XM_005622830)	
	String		
9615.ENSCAFP00000025899 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9615.ENSCAFP00000025899)			
	Sequence Similarities		
Belongs to the dwarfin/SMAD family.			
	GO - Molecular Function		
GO:0042803 : protein homodimerization activity (https://www.ebi.ac.uk/QuickGO/term/GO:0042803)			
GO:0046982 : protein heterodimerization activity (https://www.ebi.ac.uk/QuickGO/term/GO:0046982)			

GO:0048156 : tau protein binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0048156>)
GO:0003682 : chromatin binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0003682>)
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:0031625 : ubiquitin protein ligase binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0031625>)
GO:0019902 : phosphatase binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0019902>)
GO:0033613 : activating transcription factor binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0033613>)
GO:0070410 : co-SMAD binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0070410>)
GO:0097718 : disordered domain specific binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0097718>)
GO:0070411 : I-SMAD binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0070411>)
GO:0070878 : primary miRNA binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0070878>)
GO:0070412 : R-SMAD binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0070412>)
GO:0030618 : transforming growth factor beta receptor, pathway-specific cytoplasmic mediator activity (<https://www.ebi.ac.uk/QuickGO/term/GO:0030618>)
GO:0034713 : type I transforming growth factor beta receptor binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0034713>)

GO - Biological Process

GO:0009952 : anterior/posterior pattern specification (<https://www.ebi.ac.uk/QuickGO/term/GO:0009952>)
GO:0045892 : negative regulation of transcription, DNA-templated (<https://www.ebi.ac.uk/QuickGO/term/GO:0045892>)
GO:0010718 : positive regulation of epithelial to mesenchymal transition (<https://www.ebi.ac.uk/QuickGO/term/GO:0010718>)
GO:0001701 : in utero embryonic development (<https://www.ebi.ac.uk/QuickGO/term/GO:0001701>)
GO:0060395 : SMAD protein signal transduction (<https://www.ebi.ac.uk/QuickGO/term/GO:0060395>)
GO:0045165 : cell fate commitment (<https://www.ebi.ac.uk/QuickGO/term/GO:0045165>)
GO:0001707 : mesoderm formation (<https://www.ebi.ac.uk/QuickGO/term/GO:0001707>)
GO:0030513 : positive regulation of BMP signaling pathway (<https://www.ebi.ac.uk/QuickGO/term/GO:0030513>)
GO:0030324 : lung development (<https://www.ebi.ac.uk/QuickGO/term/GO:0030324>)
GO:0009791 : post-embryonic development (<https://www.ebi.ac.uk/QuickGO/term/GO:0009791>)
GO:0030073 : insulin secretion (<https://www.ebi.ac.uk/QuickGO/term/GO:0030073>)
GO:0001706 : endoderm formation (<https://www.ebi.ac.uk/QuickGO/term/GO:0001706>)
GO:0048701 : embryonic cranial skeleton morphogenesis (<https://www.ebi.ac.uk/QuickGO/term/GO:0048701>)
GO:0035265 : organ growth (<https://www.ebi.ac.uk/QuickGO/term/GO:0035265>)
GO:0001657 : ureteric bud development (<https://www.ebi.ac.uk/QuickGO/term/GO:0001657>)
GO:0007179 : transforming growth factor beta receptor signaling pathway (<https://www.ebi.ac.uk/QuickGO/term/GO:0007179>)
GO:0009749 : response to glucose (<https://www.ebi.ac.uk/QuickGO/term/GO:0009749>)
GO:0035556 : intracellular signal transduction (<https://www.ebi.ac.uk/QuickGO/term/GO:0035556>)
GO:0060039 : pericardium development (<https://www.ebi.ac.uk/QuickGO/term/GO:0060039>)
GO:0007182 : common-partner SMAD protein phosphorylation (<https://www.ebi.ac.uk/QuickGO/term/GO:0007182>)
GO:0048617 : embryonic foregut morphogenesis (<https://www.ebi.ac.uk/QuickGO/term/GO:0048617>)
GO:0038092 : nodal signaling pathway (<https://www.ebi.ac.uk/QuickGO/term/GO:0038092>)
GO:0031016 : pancreas development (<https://www.ebi.ac.uk/QuickGO/term/GO:0031016>)
GO:0048340 : paraxial mesoderm morphogenesis (<https://www.ebi.ac.uk/QuickGO/term/GO:0048340>)
GO:1900224 : positive regulation of nodal signaling pathway involved in determination of lateral mesoderm left/right asymmetry (<https://www.ebi.ac.uk/QuickGO/term/GO:1900224>)
GO:0051098 : regulation of binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0051098>)
GO:0017015 : regulation of transforming growth factor beta receptor signaling pathway (<https://www.ebi.ac.uk/QuickGO/term/GO:0017015>)
GO:0070723 : response to cholesterol (<https://www.ebi.ac.uk/QuickGO/term/GO:0070723>)
GO:0062009 : secondary palate development (<https://www.ebi.ac.uk/QuickGO/term/GO:0062009>)
GO:0007183 : SMAD protein complex assembly (<https://www.ebi.ac.uk/QuickGO/term/GO:0007183>)
GO:0007352 : zygotic specification of dorsal/ventral axis (<https://www.ebi.ac.uk/QuickGO/term/GO:0007352>)

GO - Cellular Component

GO:0005737 : cytoplasm (<https://www.ebi.ac.uk/QuickGO/term/GO:0005737>)
GO:0000790 : nuclear chromatin (<https://www.ebi.ac.uk/QuickGO/term/GO:0000790>)
GO:0032444 : activin responsive factor complex
(<https://www.ebi.ac.uk/QuickGO/term/GO:0032444>)
GO:0071144 : heteromeric SMAD protein complex
(<https://www.ebi.ac.uk/QuickGO/term/GO:0071144>)

Presumptive Null

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

Molecular Type

Cis-regulatory (<https://www.gephebase.org/search-criteria?/and+Molecular Type=~Cis-regulatory^#gephebase-summary-title>)

Aberration Type

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

Deletion Size

1-10 kb

Molecular Details of the Mutation

9.9 kb deletion 24-kb downstream from coding region

Experimental Evidence

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

Main Reference

Derived variants at six genes explain nearly half of size reduction in dog breeds. (2013) (<https://pubmed.ncbi.nlm.nih.gov/24026177>)

Authors

Rimbault M; Beale HC; Schoenebeck JJ; Hoopes BC; Allen JJ; Kilroy-Glynn P; Wayne RK; Sutter NB; Ostrander EA

Abstract

Selective breeding of dogs by humans has generated extraordinary diversity in body size. A number of multibreed analyses have been undertaken to identify the genetic basis of this diversity. We analyzed four loci discovered in a previous genome-wide association study that used 60,968 SNPs to identify size-associated genomic intervals, which were too large to assign causative roles to genes. First, we performed fine-mapping to define critical intervals that included the candidate genes GHR, HMGA2, SMAD2, and STC2, identifying five highly associated markers at the four loci. We hypothesize that three of the variants are likely to be causative. We then genotyped each marker, together with previously reported size-associated variants in the IGF1 and IGF1R genes, on a panel of 500 domestic dogs from 93 breeds, and identified the ancestral allele by genotyping the same markers on 30 wild canids. We observed that the derived alleles at all markers correlated with reduced body size, and smaller dogs are more likely to carry derived alleles at multiple markers. However, breeds are not generally fixed at all markers; multiple combinations of genotypes are found within most breeds. Finally, we show that 46%-52.5% of the variance in body size of dog breeds can be explained by seven markers in proximity to exceptional candidate genes. Among breeds with standard weights <41 kg (90 lb), the genotypes accounted for 64.3% of variance in weight. This work advances our understanding of mammalian growth by describing genetic contributions to canine size determination in non-giant dog breeds.

Additional References

RELATED GEPHE

Related Genes

5 (growth hormone receptor (GHR), HMGA2, Insulin-like growth factor 1 (IGF1), Insulin-like growth factor receptor 1 (IGF1R), stanniocalcin 2 (STC2))
(<https://www.gephebase.org/search-criteria?/or+Taxon ID=~9612^/and+Trait=Body size/or+Taxon ID=~9606^/and+Trait=Body size/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

each variant is potentially causal. Deletion could potentially affect transcription efficiency as predicted by the loss of a transcription factor binding site cluster