GEPHE SUMMARY

Gephebase Gene
MFSD12 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^MFSD12^#gephebase-summary-title)

GepheID
GP00002246

Entry Status
Published

Main curator
Martin

PHENOTYPIC CHANGE

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

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

Trait State in Taxon A
variation in melanization of skin melanocytes across the African continent and Afro-Asian populations

Trait State in Taxon B
variation in melanization of skin melanocytes across the African continent and Afro-Asian populations

Ancestral State
Taxon A

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

Taxon A

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

Common Name
human

Synonyms
human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens

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; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo

Parent
Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)

NCBI Taxonomy ID
9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)

is Taxon A an Infraspecies?
No

Taxon B

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

Common Name
human

Synonyms
human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens

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; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo

Parent
Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)

NCBI Taxonomy ID
9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
MFSD12

Synonyms
PP3501; C19orf28

String
9606.ENSP00000347583 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000347583)

Sequence Similarities
Belongs to the major facilitator superfamily.

GO - Molecular Function
GO:0015293 : symporter activity (https://www.ebi.ac.uk/QuickGO/term/GO:0015293)

GO - Biological Process

UniProtKB Homo sapiens
Q6NUT3 (http://www.uniprot.org/uniprot/Q6NUT3)

GenebankID or UniProtKB
()

GO:0048022 : negative regulation of melanin biosynthetic process (https://www.ebi.ac.uk/QuickGO/term/GO:0048022)
GO:0008643 : carbohydrate transport (https://www.ebi.ac.uk/QuickGO/term/GO:0008643)
GO:0071702 : organic substance transport (https://www.ebi.ac.uk/QuickGO/term/GO:0071702)

GO - Cellular Component

GO:0005887 : integral component of plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005887)
GO:0005765 : lysosomal membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005765)
GO:0005770 : late endosome (https://www.ebi.ac.uk/QuickGO/term/GO:0005770)

Presumptive Null

Yes (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^Yes^#gephebase-summary-title)

Molecular Type

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

Aberration Type

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

Molecular Details of the Mutation

eight potentially causal SNPs cluster in two regions: one within MFSD12 (intronic SNP and synonymous SNP in exon 9) and the other ~7600 to 9000 base pairs (bp) upstream of MFSD12 ; many SNPs are in predicted regulatory regions active in melanocytes and/or keratinocytes show enhancer activity in luciferase expression assays

Experimental Evidence

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

Main Reference

Loci associated with skin pigmentation identified in African populations. (2017) (https://pubmed.ncbi.nlm.nih.gov/29025994)

Authors

Crawford NG; Kelly DE; Hansen MEB; Beltrame MH; Fan S; Bowman SL; Jewett E; Ranciaro A; Thompson S; Lo Y; Pfeifer SP; Jensen JD; Campbell MC; Beggs W; Hormozdiari F; Mpoloka SW; Mokone GG; Nyambo T; Meskel DW; Belay G; Haut J; ; Rothschild H; Zon L; Zhou Y; Kovacs MA; Xu M; Zhang T; Bishop K; Sinclair J; Rivas C; Elliot E; Choi J; Li SA; Hicks B; Burgess S; Abnet C; Watkins-Chow DE; Oceana E; Song YS; Eskin E; Brown KM; Marks MS; Loftus SK; Pavan WJ; Yeager M; Chanock S; Tishkoff SA

Abstract

Despite the wide range of skin pigmentation in humans, little is known about its genetic basis in global populations. Examining ethnically diverse African genomes, we identify variants in or near SLC24A5, MFSD12, DDB1, TMEM138, OCA2, and HERC2 that are significantly associated with skin pigmentation. Genetic evidence indicates that the light pigmentation variant at SLC24A5 was introduced into East Africa by gene flow from non-Africans. At all other loci, variants associated with dark pigmentation in Africans are identical by descent in South Asian and Australo-Melanesian populations. Functional analyses indicate that MFSD12 encodes a lysosomal protein that affects melanogenesis in zebrafish and mice, and that mutations in melanocyte-specific regulatory regions near DDB1/TMEM138 correlate with expression of ultraviolet response genes under selection in Eurasians.

Additional References

RELATED GEPHE

Related Genes

14 (Agouti (ASIP), EGFR, EIF2S2, GSS (glutathione synthetase), IRF4, Kit ligand, MC1R, Oca2, OPRM1, SLC24A5 (NCKX5), SLC45A2=MATP, TPCN2, tyrosinase (TYR), tyrosinase-related protein 1 (TYRP1)) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^9606^/and+Trait=Coloration/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

1 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^MFSD12^/and+Taxon ID=^9606^/or+Gene Gephebase=^MFSD12^/and+Taxon ID=^9606^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

@Parallelism @AllelicSeries ; functional evidence for the function of this gene in skin melanocytes is presented in the reference