GEPHE SUMMARY

Gephebase Gene
Oca2

GephelD
GP00000747

Entry Status
Published

Main curator
Martin

PHENOTYPIC CHANGE

Trait Category
Morphology

Trait
Coloration (eyes; skin)

Trait State in Taxon A
Homo sapiens -Europe (also; see Cape Verde 2013 study)

Trait State in Taxon B
Homo sapiens -Europe (also; see Cape Verde 2013 study)

Ancestral State
Data not curated

Taxonomic Status
Intraspecific

Taxon A

Latin Name
Homo sapiens

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)

NCBI Taxonomy ID
9606

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Homo sapiens

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)

NCBI Taxonomy ID
9606

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
Oca2

Synonyms
p; D7Nic1; p<cas>; D7H15S12; D7Icr28RN; P

String
10090.ENSMUSP00000032633

Sequence Similarities
Belongs to the CitM (TC 2.A.11) transporter family.

GO - Molecular Function
-

GO - Biological Process
GO:0055085 : transmembrane transport
GO:0042438 : melanin biosynthetic process
GO:0043473 : pigmentation
GO:0008283 : cell proliferation
GO:0048066 : developmental pigmentation

UniProtKB Mus musculus
Q62052

GenebankID or UniProtKB
AAH12097

GO:0030318 : melanocyte differentiation
GO:0007286 : spermatid development

GO - Cellular Component
GO:0016021 : integral component of membrane
GO:0010008 : endosome membrane
GO:0005789 : endoplasmic reticulum membrane
GO:0005765 : lysosomal membrane
GO:0033162 : melanosome membrane

Presumptive Null
No

Molecular Type
Cis-regulatory

Aberration Type
SNP

Molecular Details of the Mutation
Causative SNP in enhancer localized in intron of neighbor gene

Experimental Evidence
Association Mapping

Main Reference
Blue eye color in humans may be caused by a perfectly associated founder mutation in a regulatory element located within the HERC2 gene inhibiting OCA2 expression. (2008)

Authors
Eiberg H; Troelsen J; Nielsen M; Mikkelsen A; Mengel-From J; Kjaer KW; Hansen L

Abstract
The human eye color is a quantitative trait displaying multifactorial inheritance. Several studies have shown that the OCA2 locus is the major contributor to the human eye color variation. By linkage analysis of a large Danish family, we finemapped the blue eye color locus to a 166 Kbp region within the HERC2 gene. By association analyses, we identified two SNPs within this region that were perfectly associated with the blue and brown eye colors: rs12913832 and rs1129038. Of these, rs12913832 is located 21.152 bp upstream from the OCA2 promoter in a highly conserved sequence in intron 86 of HERC2. The brown eye color allele of rs12913832 is highly conserved throughout a number of species. As shown by a Luciferase assays in cell cultures, the element significantly reduces the activity of the OCA2 promoter and electrophoretic mobility shift assays demonstrate that the two alleles bind different subsets of nuclear extracts. One single haplotype, represented by six polymorphic SNPs covering half of the 3′ end of the HERC2 gene, was found in 155 blue-eyed individuals from Denmark, and in 5 and 2 blue-eyed individuals from Turkey and Jordan, respectively. Hence, our data suggest a common founder mutation in an OCA2 inhibiting regulatory element as the cause of blue eye color in humans. In addition, an LOD score of Z = 4.21 between hair color and D14S72 was obtained in the large family, indicating that RABGGTA is a candidate gene for hair color.

Additional References
A genome-wide association study identifies novel alleles associated with hair color and skin pigmentation. (2008)

HERC2 rs12913832 modulates human pigmentation by attenuating chromatin-loop formation between a long-range enhancer and the OCA2 promoter. (2012)

Genetic architecture of skin and eye color in an African-European admixed population. (2013)

RELATED GEPHE

Related Genes
14 (Agouti (ASIP), EGFR, EIF2S2, GSS (glutathione synthetase), HERC2, IRF4, Kit ligand, MC1R, OPRM1, SLC24A5 (NCKX5), SLC45A2=MATP, TPCN2, tyrosinase (TYR), tyrosinase-related protein 1 (TYRP1))
Related Haplotypes
1

COMMENTS