GEPHE SUMMARY

Gephebase Gene

IRF4 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^IRF4^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00001364

Main curator

Prigent

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

Human-dark pigmentation

Trait State in Taxon B

human-light pigmentation and presence of freckles and brown hairs and high sensitivity of skin to sun exposure

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

IRF4

Synonyms

MUM1; LSIRF; SHEP8; NF-EM5

String

9606.ENSP00000370343 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 9606.ENSP00000370343)

Sequence Similarities

Belongs to the IRF family.

GO - Molecular Function

GO:0003700 : DNA-binding transcription factor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0003700)
GO:0043565 : sequence-specific DNA binding

UniProtKB Homo sapiens

Q15306 (http://www.uniprot.org/uniprot/Q15306)

GenebankID or UniProtKB

()

(https://www.ebi.ac.uk/QuickGO/term/GO:0043565)
GO:0008134 : transcription factor binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0008134)
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:0016279 : protein-lysine N-methyltransferase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0016279)

GO - Biological Process

GO:0045944 : positive regulation of transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0045944)
GO:0045893 : positive regulation of transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0045893)
GO:0019221 : cytokine-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0019221)
GO:0120162 : positive regulation of cold-induced thermogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0120162)
GO:0060333 : interferon-gamma-mediated signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0060333)
GO:0060337 : type I interferon signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0060337)
GO:0043011 : myeloid dendritic cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0043011)
GO:0042110 : T cell activation (https://www.ebi.ac.uk/QuickGO/term/GO:0042110)
GO:0043388 : positive regulation of DNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0043388)
GO:0042832 : defense response to protozoan
(https://www.ebi.ac.uk/QuickGO/term/GO:0042832)
GO:0043966 : histone H3 acetylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0043966)
GO:0043967 : histone H4 acetylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0043967)
GO:0034122 : negative regulation of toll-like receptor signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0034122)
GO:0045082 : positive regulation of interleukin-10 biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0045082)
GO:0045368 : positive regulation of interleukin-13 biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0045368)
GO:0045086 : positive regulation of interleukin-2 biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0045086)
GO:0045404 : positive regulation of interleukin-4 biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0045404)
GO:0045622 : regulation of T-helper cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0045622)
GO:0072540 : T-helper 17 cell lineage commitment
(https://www.ebi.ac.uk/QuickGO/term/GO:0072540)

GO - Cellular Component

GO:0005829 : cytosol (https://www.ebi.ac.uk/QuickGO/term/GO:0005829)
GO:0016020 : membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0016020)
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:0000788 : nuclear nucleosome (https://www.ebi.ac.uk/QuickGO/term/GO:0000788)

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

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

Molecular Details of the Mutation

a C>T substitution in intron4 located within an enhancer

Experimental Evidence

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

Main Reference

A polymorphism in IRF4 affects human pigmentation through a tyrosinase-dependent MITF/TFAP2A pathway. (2013) (https://pubmed.ncbi.nlm.nih.gov/24267888)

Authors

Praetorius C; Grill C; Stacey SN; Metcalf AM; Gorkin DU; Robinson KC; Van Otterloo E; Kim RS; Bergsteinsdottir K; Ogmundsdottir MH; Magnusdottir E; Mishra PJ; Davis SR; Guo T; Zaidi MR; Helgason AS; Sigurdsson MI; Meltzer PS; Merlino G; Petit V; Larue L; Loftus SK; Adams DR; Sobhiafshar U; Emre NC; Pavan WJ; Cornell R; Smith AG; McCallion AS; Fisher DE; Stefansson K; Sturm RA; Steingrimsson E

Abstract

Sequence polymorphisms linked to human diseases and phenotypes in genome-wide association studies often affect noncoding regions. A SNP within an intron of the gene encoding Interferon Regulatory Factor 4 (IRF4), a transcription factor with no known role in melanocyte biology, is strongly associated with sensitivity of skin to sun exposure, freckles, blue eyes, and brown hair color. Here, we demonstrate that this SNP lies within an enhancer of IRF4 transcription in melanocytes. The allele associated with this pigmentation phenotype impairs binding of the TFAP2A transcription factor that, together with the melanocyte master regulator MITF, regulates activity of the enhancer. Assays in zebrafish and mice reveal that IRF4 cooperates with MITF to activate expression of Tyrosinase (TYR), an essential enzyme in melanin synthesis. Our findings provide a clear example of a noncoding polymorphism that affects a phenotype by modulating a developmental gene regulatory network.

Additional References

Allele-specific transcriptional regulation of IRF4 in melanocytes is mediated by chromatin looping of the intronic rs12203592 enhancer to the IRF4 promoter. (2015) (https://pubmed.ncbi.nlm.nih.gov/25631878)

RELATED GEPHE

Related Genes

14 (Agouti (ASIP), EGFR, EIF2S2, GSS (glutathione synthetase), Kit ligand, MC1R, MFSD12, 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

No matches found.

EXTERNAL LINKS

COMMENTS