

GEPHE SUMMARY

IRF4 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase= [^] IRF4 [^] #gephebase-summary-title)	Gephebase Gene	GP00001364	GepheID
Published	Entry Status	Prigent	Main curator

PHENOTYPIC CHANGE

Morphology (https://www.gephebase.org/search-criteria?/and+Trait Category= [^] Morphology [^] #gephebase-summary-title)	Trait Category		
Coloration (skin) (https://www.gephebase.org/search-criteria?/and+Trait = [^] Coloration (skin) [^] #gephebase-summary-title)	Trait		
Human-dark pigmentation	Trait State in Taxon A		
human-light pigmentation and presence of freckles and brown hairs and high sensitivity of skin to sun exposure	Trait State in Taxon B		
Taxon A	Ancestral State		
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status= [^] Intraspecific [^] #gephebase-summary-title)	Taxonomic Status		
	Taxon A		Taxon B
	Latin Name		Latin Name
Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms= [^] Homo sapiens [^] #gephebase-summary-title)		Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms= [^] Homo sapiens [^] #gephebase-summary-title)	
	Common Name		Common Name
human		human	
	Synonyms		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		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		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; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo		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
Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9605)		Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9605)	
	NCBI Taxonomy ID		NCBI Taxonomy ID
9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9606)		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

IRF4	Generic Gene Name	Q15306 (http://www.uniprot.org/uniprot/Q15306)	UniProtKB Homo sapiens
MUM1; LSIRF; SHEP8; NF-EM5	Synonyms		GenebankID or UniProtKB
9606.ENSPO0000370343 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000370343)	String		
Belongs to the IRF family.	Sequence Similarities		
	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			

(<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>)

No (<https://www.gephebase.org/search-criteria?/and+Presumptive+Null=~No~#gephebase-summary-title>) Presumptive Null
Cis-regulatory (<https://www.gephebase.org/search-criteria?/and+Molecular+Type=~Cis-regulatory~#gephebase-summary-title>) Molecular Type
SNP (<https://www.gephebase.org/search-criteria?/and+Aberration+Type=~SNP~#gephebase-summary-title>) Aberration Type
a C>T substitution in intron4 located within an enhancer Molecular Details of the Mutation
Association Mapping (<https://www.gephebase.org/search-criteria?/and+Experimental+Evidence=~Association+Mapping~#gephebase-summary-title>) Experimental Evidence
A polymorphism in IRF4 affects human pigmentation through a tyrosinase-dependent MITF/TFAP2A pathway. (2013) (<https://pubmed.ncbi.nlm.nih.gov/24267888>) Main Reference

Authors

Praetorius C; Grill C; Stacey SN; Metcalf AM; Gorkin DU; Robinson KC; Van Otterloo E; Kim RS; Bergsteinsdottir K; Ogmundsdottir MH; Magnúsdóttir 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; Sobhiahshar U; Emre NC; Pavan WJ; Cornell R; Smith AG; McCallion AS; Fisher DE; Stefansson K; Sturm RA; Steingrímsson 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.

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