GEPHE SUMMARY

Gephebase Gene

CDKN2A (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^CDKN2A^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00000178

Main curator

Martin

PHENOTYPIC CHANGE

Trait Category

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

Trait

Coloration (feathers ; sex-linked dilution) (https://www.gephebase.org/search-criteria?/and+Trait=^Coloration (feathers ; sex-linked dilution)^#gephebase-summary-title)

Trait State in Taxon A

Gallus gallus

Trait State in Taxon B

B0/B2 White Leghorn males with Sex-linked dilution allele

Ancestral State

Taxon A

Taxonomic Status

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

Taxon A

Latin Name

Gallus gallus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Gallus gallus^#gephebase-summary-title)

Common Name

chicken

Synonyms

Gallus gallus domesticus; chicken; bantam; chickens

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Archelosauria; Archosauria; Dinosauria; Saurischia; Theropoda; Coelurosauria; Aves; Neognathae; Galloanserae; Galliformes; Phasianidae; Phasianinae; Gallus

Parent

Gallus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9030)

NCBI Taxonomy ID

9031 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9031)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

Gallus gallus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Gallus gallus^#gephebase-summary-title)

Common Name

chicken

Synonyms

Gallus gallus domesticus; chicken; bantam; chickens

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Archelosauria; Archosauria; Dinosauria; Saurischia; Theropoda; Coelurosauria; Aves; Neognathae; Galloanserae; Galliformes; Phasianidae; Phasianinae; Gallus

Parent

Gallus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9030)

NCBI Taxonomy ID

9031 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9031)

is Taxon B an Infraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name

CDKN2A

Synonyms

ARF; MLM; P14; P16; P19; CMM2; INK4; MTS1; TP16; CDK4I; CDKN2; INK4A; MTS-1; P14ARF; P19ARF; P16INK4; P16INK4A; P16-INK4A

String

9606.ENSP00000394932 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000394932)

Sequence Similarities

Belongs to the CDKN2 cyclin-dependent kinase inhibitor family.

GO - Molecular Function

GO:0003723 : RNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003723)
GO:0019901 : protein kinase binding (https://www.ebi.ac.uk/QuickGO/term/GO:0019901)
GO:0004861 : cyclin-dependent protein serine/threonine kinase inhibitor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004861)
GO:0051059 : NF-kappaB binding (https://www.ebi.ac.uk/QuickGO/term/GO:0051059)

UniProtKB Homo sapiens

P42771 (http://www.uniprot.org/uniprot/P42771)

GenebankID or UniProtKB

NP_001308484 (https://www.ncbi.nlm.nih.gov/nuccore/NP_001308484)

GO - Biological Process

GO:0045892 : negative regulation of transcription, DNA-templated (https://www.ebi.ac.uk/QuickGO/term/GO:0045892)
GO:0008285 : negative regulation of cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0008285)
GO:0007050 : cell cycle arrest (https://www.ebi.ac.uk/QuickGO/term/GO:0007050)
GO:0090398 : cellular senescence (https://www.ebi.ac.uk/QuickGO/term/GO:0090398)
GO:0000082 : G1/S transition of mitotic cell cycle (https://www.ebi.ac.uk/QuickGO/term/GO:0000082)
GO:0030308 : negative regulation of cell growth (https://www.ebi.ac.uk/QuickGO/term/GO:0030308)
GO:0001953 : negative regulation of cell-matrix adhesion (https://www.ebi.ac.uk/QuickGO/term/GO:0001953)
GO:0045736 : negative regulation of cyclin-dependent protein serine/threonine kinase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0045736)
GO:0032088 : negative regulation of NF-kappaB transcription factor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0032088)
GO:0042326 : negative regulation of phosphorylation (https://www.ebi.ac.uk/QuickGO/term/GO:0042326)
GO:2000774 : positive regulation of cellular senescence (https://www.ebi.ac.uk/QuickGO/term/GO:2000774)
GO:2000111 : positive regulation of macrophage apoptotic process (https://www.ebi.ac.uk/QuickGO/term/GO:2000111)
GO:0034393 : positive regulation of smooth muscle cell apoptotic process (https://www.ebi.ac.uk/QuickGO/term/GO:0034393)
GO:0007265 : Ras protein signal transduction (https://www.ebi.ac.uk/QuickGO/term/GO:0007265)
GO:0090399 : replicative senescence (https://www.ebi.ac.uk/QuickGO/term/GO:0090399)
GO:0035986 : senescence-associated heterochromatin focus assembly (https://www.ebi.ac.uk/QuickGO/term/GO:0035986)

GO - Cellular Component

GO:0005737 : cytoplasm (https://www.ebi.ac.uk/QuickGO/term/GO:0005737)
GO:0005829 : cytosol (https://www.ebi.ac.uk/QuickGO/term/GO:0005829)
GO:0005634 : nucleus (https://www.ebi.ac.uk/QuickGO/term/GO:0005634)
GO:0035985 : senescence-associated heterochromatin focus (https://www.ebi.ac.uk/QuickGO/term/GO:0035985)

Mutation #1

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

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

Molecular Details of the Mutation

12kb haplotype including 2 non-coding mutations

Experimental Evidence

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

Main Reference

The evolution of Sex-linked barring alleles in chickens involves both regulatory and coding changes in CDKN2A. (2017) (https://pubmed.ncbi.nlm.nih.gov/28388616)

Authors

Schwochow Thalmann D; Ring H; SundstrÃ¶m E; Cao X; Larsson M; Kerje S; HÃ¶glund A; Fogelholm J; Wright D; Jemth P; HallbÃ¶Ã¶k F; Bed'Hom B; Dorshorst B; Tixier-Boichard M; Andersson L

Abstract

Sex-linked barring is a fascinating plumage pattern in chickens recently shown to be associated with two non-coding and two missense mutations affecting the ARF transcript at the CDKN2A tumor suppressor locus. It however remained a mystery whether all four mutations are indeed causative and how they contribute to the barring phenotype. Here, we show that Sex-linked barring is genetically heterogeneous, and that the mutations form three functionally different variant alleles. The B0 allele carries only the two non-coding changes and is associated with the most dilute barring pattern, whereas the B1 and B2 alleles carry both the two non-coding changes and one each of the two missense mutations causing the Sex-linked barring and Sex-linked dilution phenotypes, respectively. The data are consistent with evolution of alleles where the non-coding changes occurred first followed by the two missense mutations that resulted in a phenotype more appealing to humans. We show that one or both of the non-coding changes are cis-regulatory mutations causing a higher CDKN2A expression, whereas the missense mutations reduce the ability of ARF to interact with MDM2. Caspase assays for all genotypes revealed no apoptotic events and our results are consistent with a recent study indicating that the loss of melanocyte progenitors in Sex-linked barring in chicken is caused by premature differentiation and not apoptosis. Our results show that CDKN2A is a major locus driving the differentiation of avian melanocytes in a temporal and spatial manner.

Additional References

Sex-linked barring in chickens is controlled by the CDKN2A /B tumour suppressor locus. (2010) (https://pubmed.ncbi.nlm.nih.gov/20374521)

Mutation #2

Presumptive Null

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

Molecular Type

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

Aberration Type

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

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

g.78636802 c.28C>T p.R10C

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Arg	Cys	10

Main Reference

The evolution of Sex-linked barring alleles in chickens involves both regulatory and coding changes in CDKN2A. (2017) (https://pubmed.ncbi.nlm.nih.gov/28388616)

Authors

Schwochow Thalmann D; Ring H; SundstrÃ¶m E; Cao X; Larsson M; Kerje S; HÃ¶glund A; Fogelholm J; Wright D; Jemth P; HallbÃ¤Ã¤k F; Bed'Hom B; Dorshorst B; Tixier-Boichard M; Andersson L

Abstract

Sex-linked barring is a fascinating plumage pattern in chickens recently shown to be associated with two non-coding and two missense mutations affecting the ARF transcript at the CDKN2A tumor suppressor locus. It however remained a mystery whether all four mutations are indeed causative and how they contribute to the barring phenotype. Here, we show that Sex-linked barring is genetically heterogeneous, and that the mutations form three functionally different variant alleles. The B0 allele carries only the two non-coding changes and is associated with the most dilute barring pattern, whereas the B1 and B2 alleles carry both the two non-coding changes and one each of the two missense mutations causing the Sex-linked barring and Sex-linked dilution phenotypes, respectively. The data are consistent with evolution of alleles where the non-coding changes occurred first followed by the two missense mutations that resulted in a phenotype more appealing to humans. We show that one or both of the non-coding changes are cis-regulatory mutations causing a higher CDKN2A expression, whereas the missense mutations reduce the ability of ARF to interact with MDM2. Caspase assays for all genotypes revealed no apoptotic events and our results are consistent with a recent study indicating that the loss of melanocyte progenitors in Sex-linked barring in chicken is caused by premature differentiation and not apoptosis. Our results show that CDKN2A is a major locus driving the differentiation of avian melanocytes in a temporal and spatial manner.

Additional References

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RELATED GEPHE

Related Genes

14 (ABCA1, Agouti (ASIP), CYP19A1, EDN3, Endothelin receptor B2, GRAMD3, MC1R, Melanophilin (MLPH), PMEL17, SLC45A2=MATP, SLCO1B3, SOX10, tyrosinase (TYR), tyrosinase-related protein 1 (TYRP1)) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^9031^/and+Trait=Coloration/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

1 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^CDKN2A^/and+Taxon ID=^9031^/or+Gene Gephebase=^CDKN2A^/and+Taxon ID=^9031^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

@SexualTrait @ComplexAllele @AllelicSeries https://omia.org/OMIA000102/9031/