

GEPHE SUMMARY

	Gephebase Gene	GephelD
CDKN2A (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^CDKN2A^#gephebase-summary-title)	GP00000178	Main curator
Published	Entry Status	Martin

PHENOTYPIC CHANGE

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](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

CDKN2A

Generic Gene Name

UniProtKB Homo sapiens

Synonyms

GenebankID or UniProtKB

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

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

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>)

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

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
Complex Change (https://www.gephebase.org/search-criteria?/and+Aberration+Type=%Complex+Change%#gephebase-summary-title)	Aberration Type
Linkage Mapping (https://www.gephebase.org/search-criteria?/and+Experimental+Evidence=%Linkage+Mapping%#gephebase-summary-title)	Molecular Details of the Mutation
12kb haplotype including 2 non-coding mutations	Experimental Evidence
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)	Main Reference
Schwochow Thalmann D; Ring H; Sundström E; Cao X; Larsson M; Kerje S; Häggglund A; Fogelholm J; Wright D; Jemth P; Hallböök F; Bed'Hom B; Dorhorst B; Tixier-Boichard M; Andersson L	Authors
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.	Abstract
Sex-linked barring in chickens is controlled by the CDKN2A /B tumour suppressor locus. (2010) (https://pubmed.ncbi.nlm.nih.gov/20374521)	Additional References

Mutation #2

No (https://www.gephebase.org/search-criteria?/and+Presumptive+Null=%No%#gephebase-summary-title)	Presumptive Null
Coding (https://www.gephebase.org/search-criteria?/and+Molecular+Type=%Coding%#gephebase-summary-title)	Molecular Type
SNP (https://www.gephebase.org/search-criteria?/and+Aberration+Type=%SNP%#gephebase-summary-title)	Aberration Type
Nonsynonymous	SNP Coding Change

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

Experimental Evidence

Linkage Mapping ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence=%20Linkage%20Mapping%20#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental%20Evidence=%20Linkage%20Mapping%20#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; Sundström E; Cao X; Larsson M; Kerje S; Häggglund A; Fogelholm J; Wright D; Jemth P; Hallböök 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/>)

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=%209031%20/and+Trait=Coloration/and+groupHaplotypes=true#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Taxon%20ID=%209031%20/and+Trait=Coloration/and+groupHaplotypes=true#gephebase-summary-title))

Related Haplotypes

1 ([https://www.gephebase.org/search-criteria?/or+Gene Gephebase=%20CDKN2A%20/and+Taxon ID=%209031%20/and+Gene Gephebase=%20CDKN2A%20/and+Taxon ID=%209031%20#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene%20Gephebase=%20CDKN2A%20/and+Taxon%20ID=%209031%20/and+Gene%20Gephebase=%20CDKN2A%20/and+Taxon%20ID=%209031%20#gephebase-summary-title))

EXTERNAL LINKS

COMMENTS

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