

## GEPHE SUMMARY

CDKN2A ( <a +cdkn2a+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=">https://www.gephebase.org/search-criteria?/and+Gene+Gephebase="+CDKN2A+"#gephebase-summary-title</a> )	Gephebase Gene	GP00002162	GepheID
Published	Entry Status	Martin	Main curator

## PHENOTYPIC CHANGE

Morphology ( <a +morphology+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait+Category=">https://www.gephebase.org/search-criteria?/and+Trait+Category="+Morphology+"#gephebase-summary-title</a> )	Trait Category
Coloration (feathers ; sex-linked barring) ( <a +coloration+(feathers+;+sex-linked+barring)+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait=">https://www.gephebase.org/search-criteria?/and+Trait="+Coloration+(feathers+;+sex-linked+barring)+"#gephebase-summary-title</a> )	Trait
Gallus gallus	Trait State in Taxon A
B1 White Leghorn males with Sex-linked barring allele	Trait State in Taxon B
Taxon A	Ancestral State
Domesticated ( <a +domesticated+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=">https://www.gephebase.org/search-criteria?/and+Taxonomic+Status="+Domesticated+"#gephebase-summary-title</a> )	Taxonomic Status

Taxon A	Latin Name	Taxon B	Latin Name
Gallus gallus ( <a +gallus+gallus+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms="+Gallus+gallus+"#gephebase-summary-title</a> )	Gallus gallus ( <a +gallus+gallus+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms="+Gallus+gallus+"#gephebase-summary-title</a> )	Gallus gallus ( <a +gallus+gallus+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms="+Gallus+gallus+"#gephebase-summary-title</a> )	Gallus gallus ( <a +gallus+gallus+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms="+Gallus+gallus+"#gephebase-summary-title</a> )
chicken	Common Name	chicken	Common Name
Gallus gallus domesticus; chicken; bantam; chickens	Synonyms	Gallus gallus domesticus; chicken; bantam; chickens	Synonyms
species	Rank	species	Rank
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	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	Lineage
Gallus () - (Rank: genus) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9030">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9030</a> )	Parent	Gallus () - (Rank: genus) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9030">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9030</a> )	Parent
9031 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9031">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9031</a> )	NCBI Taxonomy ID	9031 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9031">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9031</a> )	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

## GENOTYPIC CHANGE

CDKN2A	Generic Gene Name	P42771 ( <a href="http://www.uniprot.org/uniprot/P42771">http://www.uniprot.org/uniprot/P42771</a> )	UniProtKB Homo sapiens
ARF; MLM; P14; P16; P19; CMM2; INK4; MTS1; TP16; CDK4; CDKN2; INK4A; MTS-1; P14ARF; P19ARF; P16INK4; P16INK4A; P16-INK4A	Synonyms	NP_001308484 ( <a href="https://www.ncbi.nlm.nih.gov/nuccore/NP_001308484">https://www.ncbi.nlm.nih.gov/nuccore/NP_001308484</a> )	GenebankID or UniProtKB
9606.ENSPP00000394932 ( <a href="http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPP00000394932">http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPP00000394932</a> )	String		
Belongs to the CDKN2 cyclin-dependent kinase inhibitor family.	Sequence Similarities		
GO:0003723 : RNA binding ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0003723">https://www.ebi.ac.uk/QuickGO/term/GO:0003723</a> )	GO - Molecular Function		
GO:0019901 : protein kinase binding ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0019901">https://www.ebi.ac.uk/QuickGO/term/GO:0019901</a> )			
GO:0004861 : cyclin-dependent protein serine/threonine kinase inhibitor activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0004861">https://www.ebi.ac.uk/QuickGO/term/GO:0004861</a> )			
GO:0051059 : NF-kappaB binding ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0051059">https://www.ebi.ac.uk/QuickGO/term/GO:0051059</a> )			

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](https://www.gephebase.org/search-criteria?/and+Presumptive Null=))

Presumptive Null

Cis-regulatory ([https://www.gephebase.org/search-criteria?/and+Molecular Type="Cis-regulatory"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular Type=))

Molecular Type

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

Aberration Type

12kb haplotype including 2 non-coding

Molecular Details of the Mutation

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

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; Håglund A; Fogelholm J; Wright D; Jemth P; Hallböök F; Bed'Hom B; Dorshorst 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](https://www.gephebase.org/search-criteria?/and+Presumptive Null=))

Presumptive Null

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

Molecular Type

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

Aberration Type

Nonsynonymous

SNP Coding Change

g.78636804 c.26T&gt;A p.V9D

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	Val	Asp	9

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

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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=~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/>