

Genotype-phenotype correlations in rabbit coat color: an overview

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Abstract. This study provides an overview of genotype-phenotype correlations in rabbit coat color, a classical model for understanding the genetic basis of pigmentation in mammals. Recent advances in molecular genetics have enabled the identification of key genes underlying traditional coat color loci, including MC1R, ASIP, TYR, TYRP1, MLPH, KIT, and MITF. Specific mutations within these genes are strongly associated with distinct phenotypes such as albino, Himalayan, chinchilla, black, brown, yellow, dilute blue, and patterned coats. Evidence from genome-wide association studies and population genetics analyses demonstrates that coat color is governed by an oligogenic architecture, involving additive, recessive, and epistatic interactions among multiple loci. Furthermore, selective breeding has led to the fixation of characteristic allele combinations within breeds, reinforcing stable genotype-phenotype relationships. Functional studies also reveal the molecular mechanisms through which these genes regulate melanocyte activity, melanin production, and pigmentation patterns. Overall, rabbits represent a powerful model for dissecting the complex genetic architecture of visible traits and for advancing our understanding of genotype-phenotype relationships in mammalian biology.

Key Words: ASIP, epistasis, genetic variation, genotype-phenotype correlation, MC1R, melanogenesis, MLPH, pigmentation genetics, TYR.

Introduction. Coat color in rabbits is a classic system for linking specific DNA variants to visible pigmentation patterns and intensities. Recent molecular work has connected historical “color loci” to defined genes and mutations, allowing detailed genotype-phenotype correlations across many breeds.

The aim of this study is to synthesize current knowledge on the genetic mechanisms underlying coat color variation in rabbits and to highlight the relationships between specific gene variants and their corresponding phenotypic expressions.

Major Pigmentation Loci and Their Phenotypic Effects. Most coat color diversity is explained by variants in a core set of genes: MC1R (Extension locus), ASIP (Agouti), TYR (Albino C locus), TYRP1 (Brown), MLPH (Dilution), KIT, MITF and others (Fontanesi et al 2006; Fontanesi et al 2008; Fontanesi et al 2014; Utzeri et al 2014; Demars et al 2018; Letko et al 2019; Xiao et al 2019; Hu et al 2020; Fontanesi 2021; Utzeri et al 2021; Demars et al 2022; Ballan et al 2022; Zhang et al 2023; Chen et al 2025). Sequencing and genome wide scans in meat and fancy breeds repeatedly detect strong selection signals at these loci, tightly associated with specific coat colors and patterns (Letko et al 2019; Fontanesi 2021; Demars et al 2022; Ballan et al 2022; Ballan et al 2023; Zhang et al 2023; Chen et al 2025). Population studies confirm that breeds grouped by similar colors share common ancestry segments at these pigmentation genes (Ballan et al 2022; Ballan et al 2023) (Table 1).

Table 1

Representative genotype-phenotype links at major rabbit color loci

<i>Phenotype / pattern</i>	<i>Causative / major gene variant</i>	<i>Genotype-phenotype correlation</i>	<i>Citations</i>
Albino (white coat, red eyes)	TYR p.T373K	Defines albino C allele; fully white phenotype when homozygous (Figure 1)	Covrig et al 2013; Fontanesi 2021; Utzeri et al 2021
Himalayan, chinchilla	TYR p.E294G, p.T358I	Alleles reduce eumelanin/pheomelanin differently, giving temperature-sensitive (Figure 2) and grey phenotypes (Figure 3)	Botha et al 2011; Petrescu-Mag et al 2012; Botha et al 2013; Covrig et al 2013; Fontanesi 2021; Utzeri et al 2021
Uniform yellow/red (non-extension)	MC1R c.304_333del30 (e)	All red/fawn/yellow rabbits fixed for this deletion; loss of eumelanin	Fontanesi et al 2006; Fontanesi et al 2008; Fontanesi et al 2010; Xiao et al 2019; Fontanesi 2021
Dominant black / steel	MC1R c.280_285del6 (E ^D /E ^S)	Present in black-patterned but also albino lines; drives black pigment when visible	Fontanesi et al 2006; Fontanesi et al 2008; Fontanesi et al 2010; Xiao et al 2019; Fontanesi 2021
Japanese brindling (mosaic black–yellow)	MC1R c.[124G>A;125_130del6] (ei)	ei/ei rabbits show mixed black and yellow patches; expression appears epigenetically regulated	Fontanesi et al 2010; Xiao et al 2019; Oroian et al 2020; Fontanesi 2021
Non-agouti black	ASIP 1-bp insertion causing frameshift (a)	Insertion fixed in solid black breeds; removes banded agouti pattern	Fontanesi et al 2008; Fontanesi 2021
Black and tan pattern	ASIP 11 kb promoter–exon 1 deletion (a ^t)	Deletion in hair-cycle promoter; black dorsum with tan ventrum	Letko et al 2019; Fontanesi 2021
Brown (chocolate)	TYRP1 p.Trp190Ter	Premature stop; homozygotes only in brown Havana, abolishing black eumelanin	Utzeri et al 2014; Fontanesi 2021
Blue/grey (dilution of black and red)	MLPH c.585delG frameshift	Deletion perfectly cosegregates with dilute phenotypes; reduces MLPH transcript stability (Figure 4)	Fontanesi et al 2014; Demars et al 2018; Li et al 2020; Fontanesi 2021
Chinchilla-type dilution in Rex	MLPH missense haplotypes	Specific MLPH haplotypes associated with Chinchilla coat in Rex rabbits	Li et al 2020
Yellow body with distal white shading	ASIP intronic SNP + SNAI2 downstream SNP	ASIP g.23870943C>T linked to yellow, SNAI2 g.73725380A>G to pale extremities in Fujian yellow rabbits	Chen et al 2025



Figure 1. Red-eyed white rabbit (White Giant; author's original image).



Figure 2. Himalaya phenotype in Transylvanian Giant rabbit (author's original image).



Figure 3. Chinchilla phenotype in a giant variety (author's original image).



Figure 4. Blue coat phenotype (author's original image).

Polygenic Architecture and Epistasis. Genome wide association and epistasis analyses show that coat color is oligogenic rather than strictly monogenic, with additive and recessive effects from multiple loci (Demars et al 2021; Demars et al 2022; Demars & Iannuccelli 2022; Zhang et al 2023). In a Himalayan pattern population graded from white to dark brown, variants in ASIP, KIT, MC1R, TYR and ribosomal pseudogenes RPS20, RPS14 jointly determine continuous variation of extremity color (Demars et al 2021; Demars et al 2022). Specific gene–gene interactions modulate phenotype: ASIP:MC1R combinations influence light cream/beige shades, whereas KIT:RPS interactions are associated with darker chocolate/brown tones (Demars et al 2021; Demars et al 2022). Copy number variation in KIT underlies the English spotting pattern, fitting recessive inheritance (Demars et al 2021; Demars et al 2022). Functional work in Rex melanocytes shows that higher KIT expression increases TYR, MITF, PMEL, DCT expression, melanin content, and cell proliferation, directly linking KIT genotype to melanocyte behavior and coat darkness (Hu et al 2020).

Population Genetics and Selection on Color Genes. High density SNP studies in multiple rabbit breeds identify hundreds of selective sweep regions, with ASIP, MC1R, TYR, TYRP1, KIT, MITF, EDNRA, EDNRB, OCA2 and MLPH repeatedly under strong selection where coat colors are breed defining (Letko et al 2019; Fontanesi 2021; Ballan et al 2022; Ballan et al 2023; Zhang et al 2023). Breeds with similar color phenotypes show shared haplotypes at these loci, reflecting parallel selection on the same genotypes (Ballan et al 2022; Ballan et al 2023; Zhang et al 2023). Newly analyzed Chinese breeds with black, white, grey and yellow coats display distinct allele frequency patterns and low to moderate polymorphism at MC1R, MITF, TYR, TYRP1 and MLPH, further supporting stable genotype–phenotype correlations fixed within color breeds (Jia et al 2021; Zhang et al 2023; Chen et al 2025).

Conclusions. Across domestic rabbits, coat color is determined by a limited set of well characterized pigmentation genes, each with specific mutations that correlate tightly with recognizable phenotypes such as albino, Himalayan, black, brown, yellow, dilute blue, brindling and patterned coats. Genome wide and functional studies show that these loci act in combination, with additive, recessive and epistatic interactions refining shade, pattern and intensity. Strong selection during breed formation has fixed characteristic allele combinations, making rabbits a powerful model for dissecting genotype-phenotype relationships in mammalian pigmentation.

Conflict of Interest. The authors declare that there is no conflict of interest.

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