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Molecular-genetic bases of plumage coloring in chicken

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The color of plumage in birds is an important feature, often determining descent to a particular species or breed. It serves as a key factor in the interaction of birds with each other due to their well-developed visual perception of the surrounding world. In poultry including chickens, the color of the plumage can be treated as a genetic marker, useful for identifying breeds, populations and breeding groups with their specific traits. The origin of diverse color plumage is the result of two interrelated physical processes, chemical and optical, due to which pigment and structural colors in the color are formed. The pigment melanin, which is presented in two forms, eumelanin and pheomelanin, is widely spread in birds. The basis for the formation of melanin is the aromatic amino acid tyrosine. The process of melano-genesis involves many loci, part of the complex expression of plumage color genes. In birds, the solid black color locus encodes the melanocortin 1 receptor (*MC1R*), mutations in which lead to a change in receptor activation and form different variants of the E locus. Using the GWAS analysis, possible genes affecting the formation of color in chickens were detected. The biosynthesis and types of melanin are affected by the activity of the enzyme tyrosine, and mutations in the tyrosinase gene (*TYR*) cause albinism in different species. The formation mechanism of brown, silver, gold, lavender and a number of other shades is determined by the influence on the work of the *MC1R* genes and *TYR* specific modifier genes. Thus, locus I currently associated with the *PMEL17* gene inhibits the expression of eumelanin, and the *MLPH* gene affects tyrosinase function. Research on the mechanisms of formation of the secondary coloring of plumage in chickens is being actively conducted nowadays. The formation of a marble feather pattern is associated with the mutation of the endothelin B2 receptor (*EDNRB2*), in the coding part of the gene of which a polymorphism is found associated with the mo locus. The molecular base that causes the feather banding (locus B and autosomal recessive banding) is identified. Today, only some genes that determine the color of the plumage of chickens are studied and described. Different genes can produce similar plumage patterns, and different phenotypes can be determined by the polymorphism of a single gene. Using molecular methods, you can more accurately identify these differences. This overview shows the nature of melanin coloration in birds using the example of chickens of various breeds and also attempts to systematize knowledge about the molecular-genetic mechanisms of the appearance of various types of coloration.
Key words: chickens; coloring plumage; genes; locus; expression; markers.

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Молекулярно-генетические основы формирования окраски оперения у кур

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Окраска оперения – важный признак у птиц, нередко определяющий принадлежность к тому или иному виду или породе. Окраска является результатом действия веществ, которые поглощают определенную длину волны и формируют так называемые пигментные цвета, и оптическим эффектом, обусловленным интерференцией света, отраженного биологическими микроструктурами пера. Основой для формирования окраски служит синтез меланина. Эумеланин ответственен за черные и коричневые оттенки, а феомеланин отвечает за красновато-коричневые оттенки. Молекулярно-генетический механизм появления того или иного типа окраски еще до конца не изучен, поскольку на один и тот же признак могут влиять несколько генов. Первичная пигментация оперения определяется взаимодействием полиморфных вариантов гена *MC1R* и генов, участвующих в регуляции меланогенеза. Гены-модификаторы вызывают изменение окраски любого генотипа по локусу E и могут как уменьшать или увеличивать экспрес-

сию эумеланина, так и разрушать меланоциты. Вторичная пигментация оперения определяется белыми пятнами или специфическим распределением эумеланина на отдельных перьях. Современные методы анализа ДНК, такие как секвенирование, полногеномный анализ с использованием чипов различной плотности, анализ экспрессии генов, позволяют получать новые данные о генах, определяющих окраску оперения.
Ключевые слова: *Gallus domesticus*; куры; окраска оперения; гены; локус; экспрессия; маркеры.

Introduction

Plumage color is an important feature in birds, often determining assignment to a particular species or breed. It was the color of the plumage that formed the basis for the development of such paradigms in biology as the theory of speciation. The color of the plumage largely determines how animals communicate with each other and plays an important role in adapting to environmental conditions (Cott, 1940). Birds have a variety of feather color patterns, which gave rise under the pressure of natural selection (Roulin, 2004; Roulin, Ducrest, 2013).

Plumage coloration is the result of two different but interrelated physical processes: (a) the chemical mechanism creates coloration as a result of substances that absorb a certain wavelength and form so-called pigment colors; and (b) the optical mechanism due to interference of light reflected by the biological microstructures of the feathers, which creates structural colors. The latter mechanism allows the creation of colors that cannot be generated only by pigments, but specialized microstructures often require the presence of pigments that absorb certain wavelengths to produce structural colors (D'Alba et al., 2012). Consequently, pigment and structural colors are not the result of two independent processes, but rather are the basis responsible for all the variety of color.

Birds are characterized by a wide variety of color plumage. This is due to the fact that they, unlike mammals and humans, in birds take place visual perception of relatives, interaction with them plays a leading role (Negro et al., 2016). The pigments responsible for this diversity are deposited not only in the feathers but also in the not feathered parts of the body such as the beak and legs. In birds, three groups of pigments that give variations in the color of the plumage are described: melanin, carotenoids and unusual colors (for example, porphyrin). Most of these pigments are present only in certain groups of birds птиц (Lopes et al., 2016; Brelsford et al., 2017; Cooke et al., 2017). The most widespread in birds are melanins and carotenoids. Melanins are usually more common, and in some species (e. g. swallows) melanin levels are an order of magnitude higher than carotenoid levels (McGraw et al., 2004).

In poultry, including chickens, plumage color can serve as a genetic marker, useful for the identification of breeds, populations and breeding groups with their characteristic features (Moiseyeva et al., 2012; Mitrofanova et al., 2017). The molecular genetic mechanism of the appearance of a particular type of color is not yet fully understood, since several genes can affect the same trait. Some genes cause primary effects of color, others play the role of modifiers and regulators that affect the zonal and regional distribution of the pigment, its distribution within individual feathers (banding, spotting, edging and other patterns) (Yurchenko et al., 2015). This division is conditional and the manifestation of the pigment may differ in the color of down, juvenile and adult plumage of chickens (Serebrovsky, 1926; Crawford, 1991; Yang et al., 2017).

In this review we consider the nature of melanin coloration in birds on the example of chickens of different breeds, as well as molecular genetic mechanisms of the appearance of different types of this color. As an example of different colors gene pool breeds from the Bioresource Collection "Genetic collection of rare and endangered breeds of chickens" (http://vniigen.ru/ckp-geneticheskaya-kollekciya-redkix-i-ischezayushhix-porod-kur/) is presented.

Biochemistry of melanin synthesis

The most common pigment in birds is melanin, which describes 2 types – eumelanin and pheomelanin. Eumelanin – a larger form responsible for black and brown shades, pheomelanin – is responsible for reddish-brown shades. These pigments are produced endogenously in peripheral tissues such as skin, in specialized melanocyte cells.

Melanocytes are most common in skin, hair, follicles of the feathers and in the eyes (Dupin, Le Douarin, 2003). They are also found in the inner ear, esophagus, thyroid gland, bones, heart and even brain, for example, neuromelanin (Zucca et al., 2014).

In mammals and poultry, melanin is produced in small organelles called melanosomes, which contain all the enzymes necessary for the pigmentation process. Depending on the structure and location of the melanosomes, the colour of the birds plumage may change (Maia et al., 2013; Nordén et al., 2018). Figure 1 shows the structure of the feather follicle during the rest and growth phases. Resting melanocyte progenitor cells are present at the base of the feather. If the feather is broken or lost as a result of molting, melanocyte progenitor cells activate and migrate up the growing stem of the feather, divide and differentiate into melanocytes producing the pigment.

Avian melanins are formed from the aromatic amino acid tyrosine (Lerner, Fitzpatrick, 1950). The enzyme tyrosinase catalyzes the initial oxidation of tyrosine to dopaquinone, which is an intermediate for the synthesis of both types of melanin. If additional enzymes TRP1 and TRP2/DCT are activated, the synthesis of black eumelanin will occur. In addition to genetic control, melanogenesis can be affected by environmental or physiological conditions, and the color will depend on the season, sex and shape of the cover. Melanin is influenced by 4 classes of hormones: androgens, estrogens, pituitary hormones (luteinizing hormone) and thyroid hormones. Melanin can interact with other pigments, giving a complex manifestation of the color of feathers. In addition, the colouring due to the feather structure is also applied (Rzepka et al., 2016).

Yellow pigment requires additional amino acid – cysteine. For example, high levels of cysteine in the environment

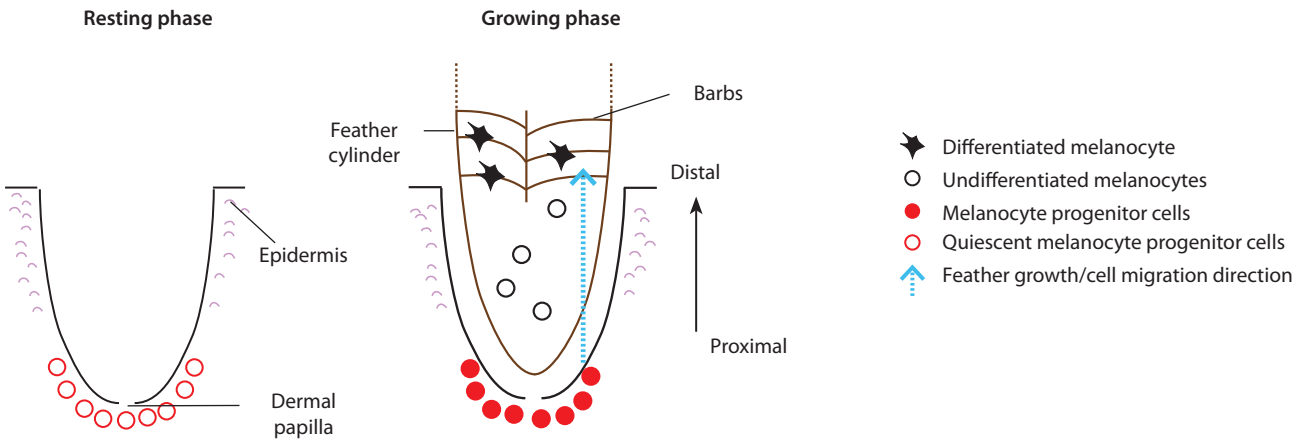

Fig. 1. Anatomy of the feather follicle during resting and growing phase (Schwochow-Thalmann, 2018).

may lead to increased synthesis of pheomelanin (Smit et al., 1997; Land, Riley, 2000). This situation will also be influenced by other factors (Ancans et al., 2001), or, for example, when *TYR* concentration or activity is low (Ozeki et al., 1997; Ito et al., 2000), when pathways that suppress eumelanin production are activated, for example, the agouti signal pathway (Takeuchi et al., 2000; Wolff, 2003). Higher expression of *TRP1* and *TRP2*/DCT correlates with dark pigmentation in several birds such as chickens, ducks, Chinese painted quails, pigeons, and geese (Galvan, Solano, 2016; Galvan et al., 2017). In addition, some hormones such as α-melanocytic stimulating hormone (αMSH) as well as steroid hormones (e. g. testosterone) affect melanogenesis, usually by increasing the production of eumelanin (Strasser, Schwabl, 2004; Eising et al., 2006) (Fig. 2).

Given the diversity of bird pigments and their functions, understanding the molecular basis of these processes remains poorly understood. Most of all, to date, knowledge about the synthesis of melanin has been accumulated.

The process of melanogenesis includes phases with multiple loci involved in the complex expression of the plumage color genes (Doucet et al., 2004; Baiao et al., 2007; Uy et al., 2009; Johnson et al., 2012). Molecular studies in mammals and birds have shown that the solid black locus encodes the melanocortin receptor 1 (*MC1R*) (Takeuchi et al., 1996; Mundy, 2005). This receptor is embedded in the melanocyte membrane and encoded by a small gene (less than 1000 bp). When

Fig. 2. The effect of testosterone level on sexual dimorphism of the color of Faverolles (*a*, *b*) and Leghorn Light Brown (Italian Partridge) (*c*, *d*).

In the photographs, gene pool breeds from the Bioresource Collection "Genetic collection of rare and endangered breeds of chickens". Authors of all the photos A. Sanganaeva, A.B. Vakhrameev.

Fig. 3. Reduction *MC1R* activity from eumelanin of completely black color (Pantsirevskay Black breed) – allele E (*a*), through birch color E^R (Uzbek Game) (*b*) to strengthening of feomelanin color at e^{Wh} (New Hampshire) (*c*) and e^y – buff (Buff Leghorn) (*d*).

linking with his antagonist αMSH there is a change in conformation of the receptor, activation of adenylylcyclase that causes the transition of ATP to form cyclic AMP. Increasing the level of cyclic AMP leads to activation of the *CREB* (cAMP response element-binding protein) and *MITF* (microphthalmia-associated transcription factor) trascription factors (Schiaffino, 2010). Higher *MC1R* activity usually results in darker pigmentation, while lower activity contributes to the production of pheomelanin (Garcia-Borron et al., 2005).

Primary pigmentation of plumage

The basic or zonal distribution of black eumelanin throughout the body of chickens is determined by mutations in the *MC1R* gene, leading to a change in receptor activation, which explains the color options for the locus E in chickens (Smyth, 1990; Sazanov et al., 1998; Kerje et al., 2003; Ling et al., 2003; Hoque et al., 2013). The locus E alleles includes: E – all black paint (Minorca, Black Australorp, Pantsirevskaya); E^R – birch colour (Yurlov crower breed); e^{Wh} – dominant wheaten (New Hampshire); e^+ – wild type colour (Italian Partridge, see Fig. 2, *c*, *d*); e^b – brown (Zagorsk salmon, Faverol; see Fig. 2, *a*, *b*); e^{bc} – Buttercup (Sicilian Buttercup); and e^y – recessive wheat (Rhode island) (Fig. 3). These alleles influence the distribution of melanin pigments (eumelanin and pheomelanin) in feathers (Serebrovsky, 1926; Somes et al., 1988; Davila et al., 2014).

Studies of Davila et al. (2014) showed that haplotypes of the gene *MC1R* explain the color changes of the *CSD* locus E of different breeds. Eleven haplotypes for 7 significant SNPs have been discovered. The association for the distribution of these haplotypes for alleles of locus E has been found. The greatest number of haplotypes known to breeds with a black, birch and blue colors of the plumage, whereas partridge and red breed was monomorphic. Davila et al. (2014) suggested that the Glu92Lys mutation may be responsible for activating the receptor for producing eumelanin, being a necessary but not always sufficient condition for maximum expression of the black phenotype. Another mutation Arg213Cys may be the cause of the loss or reduction of function of the receptor for the production eumelanin, and mutation Ala137Thr might be a candidate to mitigate Glu92Lys. The observed joint segregation of alleles and polymorphisms in E and *MC1R* confirms that E locus is equivalent to *MC1R*.

Recently, attempts have been made to conduct a genome-wide association search (GWAS) of black plumage with individual SNPs on chips of different densities. Park's general study with co-authors (2013) using the Illumina 60K chip revealed 12 significant color-associated SNPs. In the intron region of *AKT3*, SNP (rs14339964) was found, located on chromosome 3, and which is known to be one of the key genes in the formation of melanoma cells (Tsao et al., 2012). Thus, the authors conclude that *AKT3* mutations may be associated with pigmentation of the plumage. The other two SNPs (GGaluGA344987 and rs14641648 on chromosome 3 and 8, respectively) are located in the intergene region near the genes *KRT7* and *PAP2*, which are associated with pigmentation. *PAP2* (*LPPR5*) increases pigmentation (Shan et al., 2009), and *KRT7* is a member of the keratin gene family and is associated with melanocytic tumors (Blum et al., 2010). The detected polymorphism in the intron of the *DDX6* gene may also be associated with coloration, as it is an established gene causing vitiligo skin disease (Tang et al., 2012).

Yang and co-authors (2017) identified 13 significant SNPs in 10 genes using Affymetrix 600K HD chip. They found most likely affecting the synthesis eumelanin, candidate genes *SHH* and *NUAK*. Based on previous studies of model species, Yang and co-authors (2017) suggested that *NUAK 1* kinase genes and *SHH* signaling gene may

play a role in the development of melanoblast cells during the embryonic period, which also affects feathers pigmentation.

On the biosynthesis and types of melanin influences the activity of tyrosinase (Chang et al., 2006). It was found that the lack of its function leads to a complete loss of melanin in the skin, feather, retina and causes albinism in different species. Tyrosinase is an important enzyme in the biogenesis of melanin in pigment cells (Niwa et al., 2002). In studies of Liu et al. (2010), the tyrosinase (*TYR*) and melanocortin 1 (*MC1R*) genes were recognized as the main genes involved in pigmentation of chick plumage. Profiles change the color of the plumage and the gene expression levels of *TYR* and *MC1R* were observed from birth until the age of 112 days. The level of expression of *TYR* was maximum in 1-day age and then sharply decreased during the studied ages; the expression level of *MC1R* was higher on day 28 in comparison with other ages. *TYR* expression in chickens carrying E/E and E/e alleles at the *MC1R* locus was higher from birth to 28 days than in those carrying e/e alleles. These studies have shown that the mechanisms that affect the color of down in the 1-day age and those that regulate the color of the plumage at a later age are different. In addition, although the *TYR* gene in interaction with the *MC1R* gene are the determining factors for plumage coloration, different phenotypes did not correspond to different genotypic classes for both the *TYR* and *MC1R* genes, and the recessive white variation of the *TYR* gene could not completely block melanin synthesis until 28 days. Therefore, day-old chickens were colored according to the allele of locus E (Liu et al., 2010).

A study by Chang et al. (2006) showed the insertion of a full-size retrovirus inside the intron 4 of the *TYR* gene in recessive white chickens (Chang et al., 2006; Kuliawat, Santambrogio, 2009) resulting in impaired tyrosinase expression. Such recessive epistasis is typical for some white-colored breeds, for example, Silkie (Fig. 4). Deletion in the *TYR6* gene of nucleotides (-GACTGG) led to autosomal albinism (Tobita-Teramoto et al., 2000).

Genes *MC1R* and *TYR* are the molecular genetic basis for the formation of color plumage in chickens. Other genes are modifiers of their expression.

Genes-modifiers

A change in the color of any genotype at locus E can be induced by the dominant allele I, which inhibits the expression of eumelanin, destroying melanocytes. Locus I is associated with *PMEL17* gene, located on chromosome 33 in chickens, encodes protein specific to melanocytes which are important for the normal development of eumelanosomes (Keeling et al., 2004; Kerje et al., 2004; Natt et al., 2007). Locus I has 4 alleles: dominant white (I), Smoky (I^S), partially restores pigmentation and gives grayish phenotype, it is recessive for dominant white, but partially dominant for wild type allele (i), Dun (I^D) inhibits only eumelanin expression and gives brown color (Galeotti et al., 2003; Karlsson et al., 2010; Gaudet et al., 2011). Dominant white was found in White Leghorn and was associated with the insertion of 9 bp in exon 10 *PMEL17*, which led to the introduction of three amino acids into the transmembrane region. Similarly, there was a deletion of five amino acids in the transmembrane region in a protein encoded by Dun. Allele Smoky appeared already in White Leghorn and includes both 9-bp-insertion in exon 10 and deletion of 12 nucleotides in exon 6, excluding four amino acids from the protein.

Fig. 4. Silkie White breed of chickens. Recessive epistasis of the *TYR* gene.

Dark brown (Db) mutation in chickens reduces the expression of black eumelanin and increases the expression of red pheomelanin, but only in certain parts of the plumage. Gunnarsson with co-authors (2011) suggested association of the Db phenotype with 8.3 kb deletion located 14 kb above the *SOX10* gene on chromosome 1, which is an important transcription factor in melanocytes and some other cell types. The mechanism of action of this mutation suggests that deletion leads to a decrease in the expression of the *SOX10* gene, which in turn reduces the expression of key enzymes in the synthesis of pigments, such as tyrosinase. Further, tyrosinase leads to a shift towards more pheomelanin (reddish) colors of the plumage, which is characteristic of genotype *Db*. The dark brown allele is particularly interesting because it affects the nature of pigmentation rather than the presence or absence of pigmentation. A simple diagnostic test to determine the *Db* genotype will facilitate the study of other loci associated with feather color.

One more gene influencing the expression of the tyrosinase gene is *MLPH* (Vaez et al., 2008; Bed'hom et al., 2012; Xu et al., 2016). Vaez and co-authors (2008) studied the blue (LAV) coloration of chicken plumage based on orthology with the gene found in mice. They found a single-nucleotide polymorphism that weakens the color of gene E. Later, mutations in the *MLPH* gene leading to the formation of lavender color of the plumage were found in quails (Bed'hom et al., 2012). Xu and co-authors on the example of Ani chickens confirmed the connection of LAV color with mutations in this gene (Xu et al., 2016).

On chromosome Z in *Gallus gallus* there is a gene which determines golden and silver feathers (Gunnarsson et al., 2007). It forms a series of alleles S*S (silver), S*N (wild type/Golden) and S*AL (sex-related imperfect albinism) (Fig. 5).

In the orthologous locus AL, sex-related albinism (AL*A) was also found in the Japanese quail (*Coturnix japonica*). The determining color factor is the protein SLC45A2, which plays an important role in the sorting of vesicles in melanocytes. Mutation 106delT in allele S*AL chickens leads to a shift of the reading frame, formation of stop codons and degradation of the corresponding mRNA.

Fig. 5. Allele S – silver plumage color in Pervomayskaya breed (*a*, *b*) and allele s – Golden color in Poltavskaya clay breed (*c*, *d*).

Mutation in Japanese quail A-allele causes slippage of exon 4. Two independent missens mutations Tyr277Cys and Leu347Met were associated with silver allele in chickens. A special feature of the SLC45A2 variants is the specific inhibition of red pheomelanin in silver chickens (Gunnarsson et al., 2007). It remains unknown why mutations at this locus cause an almost complete absence of both eumelanin and pheomelanin, while some missens mutations are dominant and cause specific inhibition of pheomelanin production.

Oribe and co-authors (2012) studied the signal protein aguchi (ASIP), a paracrine factor that stimulates the synthesis of pheomelanin and inhibits the synthesis of eumelanin in follicular melanocytes. In mammals, the distal promoter of the *ASIP* gene acts exclusively on the ventral side of the body, creating a protective spotty color of pigmentation, stimulating the synthesis of pheomelanin on the abdominal side. ASIP produces spotting in chickens and adult females, similar to mammals. In addition, the promoter of class 1 of this gene plays an important role in creating estrogen-controlled sex differences.

Secondary color of plumage

Secondary pigmentation of the plumage is determined by white spots or specific distribution of eumelanin on individual feathers (Smyth, 1990). Molecular genetic studies have significantly expanded the field of knowledge of the genetic mechanisms of formation of such a color. In some breeds of chickens around the world there is a motley color of the plumage, where the tip of the plow is painted white. The formation of such a marble feather pattern is associated with a mutation of the endothelin receptor B2 *(EDNRB2)* located on chromosome 4 (Kinoshita et al., 2014). These studies found a polymorphism in the coding region of *EDNRB2*, leading to the replacement of Arg332His, which is associated with the locus *mo*.

Another G1008T mutation causes replacement of the amino acid Cys244Phe in exon 5 and provokes defective protein binding to endothelins. As a result of such replacement, the differentiation, proliferation and migration of melanocytes is changed. The plumage of mo^w/mo^w chickens is lightened to almost white color with several partially pigmented feathers. It is proved that such a phenotype is not associated with the tyrosinase gene and showed an autosomal recessive type of inheritance against the pigmented phenotype. Unlike albinos, mutant chickens mo^w/mo^w had painted the iris of the eyes and some pigmented spots on a whitish-yellow fluff. This mutation was also present in individuals of four Japanese breeds with white plumage. The results indicate that EDN3 (endothelin 3) – *EDNRB2* signaling is necessary for normal pigmentation in birds (Kinoshita et al., 2014).

Somes (1980) speaks of six phenotypes produced in different combinations of the gene *mo* with other color genes. In the Bioresource Collection "Genetic collection of rare and endangered breeds of chickens" there are several breeds containing allele *mo* in its genotype and having three different phenotypes (Fig. 6): black-and-white Australorp, mille fleur breed chickens, and Pushkin breed.

In modern breeds of chickens there is often a striped color of the plumage, coupled with the sex, which is characterized by a completely white stripe on the main background of the plumage and caused by the so-called barring effect. Weakening of the color is observed both in the plumage of an adult bird and in the fluff of day-old chickens (Campo, 1991; Alekseevich et al., 2000; Dorshorst, Ashwell, 2009).

Sex-linked banding is determined by the B-locus associated with the *CDKN2A* gene (Hellström et al., 2010, 2011). Locus B lightens the dermal pigment in

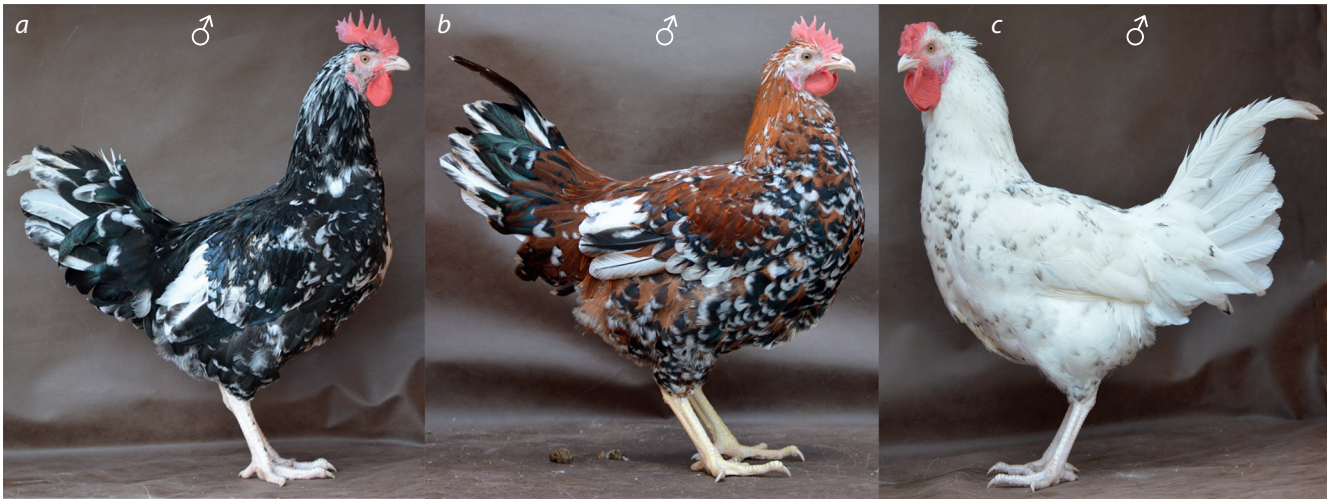

Fig. 6. Three different phenotypes in different combinations of the mo gene with other color genes: *a*, black-and-white color of plumage (Australorp black-and-white); *b*, mille fleur color of plumage (Leningradskaya Mille Fleur); *c*, white slightly-motley color of plumage (Pushkinskaya breed).

the shanks, beak and limits the spread of black pigment, creating a striped feather pattern (Jerome, 1939). Since the B gene is located in the Z chromosome, it can only be homozygous in roosters, and hemizygous in hens. The degree of pigmentation weakening depends on the homo- or heterozygous state of the allele (Kogan, 1979) (Fig. 7).

In studies by Schwochow Thalmann with co-authors (2017) it was found that the sex-linked striped pattern of plumage in chickens is associated with two non-coding and two coding mutations affecting the transcription of ARF in the locus of the *CDKN2A* tumor suppressor. These mutations form four functionally different alleles – BN, B1, B2 and B0. The last allelic variant is characterized by extreme dilution of melanin (Schwochow Thalmann et al., 2017). These allele variants were formed from four SNPs located in the 12 kb region, including exon 1 *CDKN2A*. Two of the SNPs were in non-coding regions, SNP1 in the promoter and SNP2 in intron 1. The other two SNPs are missense mutations. SNP3 causes valine to be replaced by aspartic acid (V9D), while SNP4 causes arginine to be replaced by cysteine (R10C). Haplotype B1 forms SNP1, SNP2, SNP3. Haplotype B2 includes SNP1, SNP2, SNP4 and B0 – SNP1, SNP2.

In addition to the striped color of the plumage linked to the sex, there is an autosomal striped pattern of the plumage in chickens. Black stripes on a white or red background, in this case,

Fig. 7. Plymouth Rock Barred. Lighter color of rooster plumage (B1/B1) compared to hen (B1/–).

are induced, perhaps, not by blocking, but by increasing melanogenesis against the background of recessive variants E. The molecular basis of such expression has not yet been sufficiently studied.

Change of the color type largely depends on changes in the number eumelanin and pheomelanin feather pigment (Guernsey et al., 2013), which creates a lot of different variations in the basic plumage. For example, the brown color in different breeds of chickens varies from dark brown (Rhode Island Red) to Golden or pale yellow (Brama pale yellow, experimental Tsarskoselskaya population).

Genes that regulate the variability in color, may have a pleiotropic effect and influence other economically useful traits of chickens. It is possible to use it as a marker of the intensity of growth and identification of certain diseases of the bird. For example, the endothelin receptor gene *EDNRB2* is associated with the ability of Tibetan chickens to hypoxic adaptation in mountain conditions (Zhang et al., 2017). Polymorphism in *TYR* tyrosinase gene promoter determines the black color of skin and bones in chickens, which is important in the selection of birds for breeding on these traits (Yu et al., 2017). Interactions between pigmentation genes and

Loci forming the basic types of plumage in chickens

Locus	Chromosome	Genotype	Color	Breed	Mutation type	References
MC1R	11	E	Black	Minorca, Australorp Black	Haplotype H1 (G274A)	Dávila et al., 2014
		E^R	Birchen	Yurlov Crower	Haplotypes H1, H4, H5, H6	
		e^{Wh}	Dominant wheaten	New Hampshire	Haplotype H7 (A427G)	
		e^+	Wild type	Leghorn Light Brown (Italian Partridge)	Haplotype H0 (reference sequence)	
		e^b	Brown	Zagorsk Salmon, Faverolles	Haplotype H9 (4SNP)	
		e^{bc}	Buttercup	Buttercup	Haplotypes H10, H7, H1	
		e^y	Recessive wheaten	Some lines of Rhode Island	Haplotype H11 (C637T)	
EDN3	20	FM	Intense black pigmentation of internal connective tissue and the exterior skin	Silkie White	Duplication and inversion of *EDN3*	Dorshorst et al., 2011
SOX10	1	Db	Dark brown	Friesian Fowl	8.3-kb deletion upstream of the SOX10 transcription start site	Gunnarsson et al., 2011
CDKN2A	Z	B0	White	Intercross between the red Junglefowl and the White Leghorn	A combination of three SNPs: two in a gene promoter, an SNP in an intron, a combination of two SNPs	Schwochow Thalmann et al., 2017
		B1	Sharp white and pigmented stripes	Plymouth Rock	A combination of three SNPs: one in a gene promoter, an SNP in an intron, a combination of two SNPs	
		B2	Light male chicken, Striped female chicken	Intercross between the red Junglefowl and the White Leghorn	A combination of three SNPs: one in a gene promoter, an SNP in an intron, a combination of two SNPs	
PMEL17	33	I (dominant white)	White with red/brown	White Leghorn	9-bp insertion in exon 10	Kerje et al., 2004
		D	Lighter than wild type	Dun	15-bp deletion	
		S	Smoky	Smoky	12-bp deletion in exon 6	
SLC45A2	Z	Al	White	Intercross between the red Junglefowl and the White Leghorn	A 1-bp deletion (106delT)	Gunnarsson et al., 2007
		S	Silver	Yurlov Crower	Two independent missense mutations (Tyr277Cys and Leu347Met)	
MLPH	7	LAV*L	Lavender	Orpington	C103T transition	Vaez et al., 2008
TYR	1	C*C	White	Silkie White	Insertion of a complete avian retroviral sequence of 7.7 kb in intron 4	Chang et al., 2006
		c^a	White	White Leghorn	Deletion of six nucleotides (–ΔGACTGG)	Tobita-Teramoto et al., 2000
EDNRB2	4	mo^w	Recessive White	Minohiki	G1008T substitution in exon 5	Kinoshita et al., 2014
		mo	Mottled	Cochin Dwarf, Australorp Black Speckled	C300T, A320G and G1272A	

the environment can contribute to the formation of melanoma and tumors (Gudbjartsson et al., 2008; Ibarrola-Villava et al., 2012). In quails, several mutations in the *MLPH* gene linked to the lavender color of the plumage lead to a decrease in live weight (Bed'hom et al., 2012).

The Table shows the characteristics of loci mapped on the chromosomes of chickens and determine the basic variants of plumage color, and also lists the main genes involved in the processes of pigmentation of plumage in chickens

The evolution of the *MC1R* gene

Melanocortin 1 receptor, which plays an important role in the formation of plumage color in chickens, is a representative of the whole family of G-protein-binding receptors, which are involved in a number of important functions of the body, including the regulation of energy balance.

Endogenous ligands-agonists in melanocortin system are α-melanocyte-stimulating hormone (α-MSH) and adrenocorticotropic hormone (ACTH). It is now known that five MCR subtypes mediate the action of these ligands (Schiöth, 2001). Apparently, all of them are found in most mammals, as well as in chickens (Takeuchi, Takahashi, 1998).

The melanocortin 1 receptor (*MC1R*) is primarily expressed in the skin and plays a role in skin, hair or fur pigmentation in most mammals, as shown in study of several mutations in this gene (Rees et al., 1999). In chickens, mutations in the gene *MC1R* are correlated with pigmentation of feathers (Takeuchi et al., 1996). This receptor also mediates the anti-inflammatory action of MSH peptides.

Little is known about the evolutionary origin of the melanocortin receptor gene family. Hen MCR is found in a much wider range of tissues compared to mammals, but their physiological effects are still unclear.

Schiöth and co-authors (2003) used available comparative cartographic information to determine the likely chromosome associated with the *MC1R* gene. *MC1R* in *Gallus domesticus* is located on *GGA11*, confirmation of this was obtained in two-color FISH experiments, which clearly showed consistent hybridization labeled with Biotin *MC1R* on the same chromosome, as labeled with digoxygenin ADL02232 and MCW0097. The latter are known to be present on *GGA11* (Schiöth et al., 2003).

The latest work also carried out phylogenetic analysis of the MCR family based on the method of maximum economy (MEGA2) using full-size amino acid sequences of each receptor. It was shown that the genes responsible for *MCR1* receptors form a separate cluster of genes, which probably arose during duplication.

Conclusion

The color of the plumage in birds is a trait that used as a key factor in the interaction of birds with each other due to their well-developed visual perception of the world. In poultry, including chickens, plumage color determines decorative qualities and is a marker for the identification of breeds, populations and breeding groups. The variety of plumage color is formed as a result of two interrelated physical processes – chemical and optical, through which pigment and structural colors are formed. The most common pigment in birds is melanin, for which 2 types are described – eumelanin and pheomelanin. Pigmentation of the plumage is caused by the distribution of black eumelanin throughout the body of chickens and is determined by mutations of the *MC1R* gene, which describes several haplotypes that explain changes in the color of chickens at the E locus in different breeds.

Melanogenesis can be influenced by hormones and enzymes. Genes *DN3E*, *SOX10*, *PMEL17*, *SLC45A2*, *MLPH* and *TYR* are molecular genetic modifiers in the formation of plumage color in chickens. Mutations in these genes alter the level of expression, which determines the biosynthesis and types of melanin. Some of them inhibit or reduce the formation of black eumelanin, others increase the amount of red pheomelanin. Variants of the specific distribution of pigments on individual feathers, forming a marble and striped pattern, which is associated with a mutation of the endothelin receptor B2 *(EDNRB2*) and mutations in the *CDKN2A* gene, are described. This review examines the nature of melanin coloration in birds on the example of chickens of different breeds, and also attempts to systematize knowledge about the molecular genetic mechanisms of the appearance of different types of coloration.

Despite the fact that the genome of chickens is well studied, not all genes affecting the color are described. Additional difficulties are associated with the fact that different genes sometimes produce the same pattern of plumage, and polymorphism of one gene can determine different phenotypes. The use of new modern methods of DNA analysis, such as sequencing, genomic analysis using chips of different densities, expression analysis on poultry from gene pool populations will provide new data on genes that determine the color of the plumage.

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