Chapter 5

Beyond Fifty Shades: The Genetics of Horse Colors

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Additional information is available at the end of the chapter

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Abstract

Since the dawn of horse domestication, coat colors have always fascinated humankind. In the last century, knowledge of genetics and development of scientific tools have become powerful enough so that the effects of many DNA mutations could be critically studied. Coat color nomenclature varies according to countries and breed associations; in addition, many factors can modify the color of the coat, such as sun exposure, age, sex, and nutritional status of the animal. Nevertheless, horses are capable of producing only two pigments. Several genes have been indicated as putative to coat color modification, altering the basic color by dilution, redistribution, or lacking of pigments.

Keywords: horse, genetics, coat color, alleles, DNA

1. Introduction

Nearly 6000 years ago, an extraordinary event would change the course of human history: the domestication of horse, which began in the region known today as Kazakhstan [1], in Central Asia. Initially looking for food and materials for making clothes and tools, the primitive man had also found an ally that would provide relatively fast transport, and later an important instrument of war, agriculture, and trade. Still later, this partnership would inaugurate a new concept in supportive therapy for people with special needs, limited physical abilities [2, 3], and scientific research.

The horse ancestor, *Hyracotherium* (also known as *Eohippus*), dates from the Eocene period [1] (about 55–35 million years BP=before present, for modern archaeologists) and lived in the

northern hemisphere; the genus *Equus* appeared later in North America and migrated to Asia in the Pleistocene [1] (about 2.6–0.12 million years BP). It is believed that the wild coat color (more frequently from occurring in nature; "general rule") of the first horses was a light brown body (ranging from yellowish to light brown) with dark mane, tail, and limbs plus a dominant dilution called dun (characteristic marks and dilution of the body color); this phenotype apparently provided satisfactory camouflage against predators. At the end of the Pleistocene and early Holocene, appaloosa and black coats were already existent [4] in primitive herds.

Throughout horse's history, appearances of different phenotypes were promoted by genetic mutations. Such different phenotypes became more frequent when equine populations faced climatic and geological events of major proportions. For example, appearance of black horses at the beginning of Holocene in Europe (eastern and central regions) and Siberia could mean that there was a postice age migration and subsequent selection due to increasing foresting of areas. Reducing the space occupied by a given population would have led to departing from Hardy-Weinberg equilibrium (principle of gene balance) [5, 6] and the chances of mating between individuals carrying mutations increased, providing the birth of homozygotes for features that were previously not expressed in the phenotypes. But it was only with domestication, and later, when horse breeding was established in primitive societies (confinement of an equine population in smaller spaces with restricted matings; slaughter of undesirable individuals, as male offsprings and other stallions) that an explosion of new colors began. Black and chestnut horses became more frequent in the Copper Age, and it was not until 3000 years BP, at the beginning of the Bronze Age, that today's most widespread-diluted coats appeared [4].

It is also important to mention that at the time the horse was the main means of transport by land, different colors draw the attention of people holding some kind of power (political, financial, or religious) such that many understood that riding striking-looking animals would also represent the power those people possessed. As the Australian poet Pamela "Pam" Brown wrote:

"The horse is the projection of people's dreams about themselves—strong, powerful, beautiful, and it has the capability of giving us escape from our mundane existence."

Thus, kings, tribal chiefs, senior military ranked officers, noblemen, emperors, and the great conquerors were generally seen mounting horses of exquisite colors, which distinguished them from the common people. Those powerful ones usually rode stallions, and so it becomes easy to understand the spread of these mutations in relatively reduced timespan: a mare produces, even considering the advances in reproductive biotechnologies of today, much less offspring per year than a single stallion can produce by the same time.

Nowadays, various breeds are known to have impressive looking animals (although aiming a performancer), either through changes in the hair structure (such as the magnificent metallic sheen of the Akhal-Teke or the curly hairs of the Curly breed), or through different meshes and patches scattered over the horse's body. Usually, the colors with greater visual appealing are those originating from the combination of several mutations that lead to the localized

absence of pigment producing cells, contrasting with areas of intense and darker colors. Some of these mutations deliver somewhat unpredictable effects but still have great visual appeal.

2. Basic concepts

Since the dawn of horse domestication, coat colors have always fascinated mankind. However, it was not before a century ago that the knowledge of genetics and the development of scientific tools have become powerful enough so that major changes could be identified and their effects better understood.

Much of the confusion arising when the purpose is naming a coat color refers to the fact that not always this classification is in accordance with the genetic origin of the color or colors in question. For example, a very dark stallion mistakenly registered as dark brown, could be, in fact, a very dark chestnut. Another extreme example would be the presumed occurrence of a third allele at the Extension locus (other candidate locus might be the beta defensin locus [7]), relatively rare, called dominant black (represented as E^D) [8]; considering expression of only Extension and Agouti loci, such allele, when present, would determine an entirely black phenotype, regardless of the existence of the dominant allele agouti (A^A) on the ASIP locus (which encodes a bay phenotype in eumelanic horses). The important information about dominant black here is, no matter the intensity of the black (some could display even a near-black brown) color on a dominant black horse, it completely overrules the ASIP locus expression.

Another example would be the genetic difference between roaned (sparse white hairs intermingled with the basic color) and the true roan (sparse white hairs intermingled with the basic color, while maintaining solid mane, tail, limbs, and head): While no specific locus (or loci) has yet been determined for the roaned trait—in fact, it may even be not an inheritable characteristic [9]—the true or genetic roan is clearly documented as a dominant mutation in the KIT (KIT^R) [10] gene.

Additional difficulties on identification arise when considering:

Different classifications according to each breed standard. Different nomenclatures for the same coat color are not rare, depending on different countries, or regions within the same country. For example *alazão sopa de leite* (Southeastern Brazil), *baio ruano* (Southern Brazil, Uruguay, Argentina, and other Spanish-speaking countries), and *palomino* (USA and other English-speaking countries) are different names standing for the same genotype, which in time codes for a yellowish coat color with lighter mane and tail.

Subjective perception of a particular shade—for example, mahogany bay, dark bay, light bay, blood chestnut, liver chestnut, chocolate palomino, and jet black.

In fact, for some colors the expression of many genes plus external influences and individual factors (such as animal's age, time of year, insolation, and nutritional status) can make it somewhat difficult to identify a horse's color. A classic example is a black horse kept outdoors

all summer long, which causes a "fading" effect on coat color, making it easily confounded with a dark brown horse to the eyes of an unaware observer.

To really understand the genetic basis of coat color in horses, it is necessary to first understand some basic precepts. Because of empirical observations and secular traditions, it is not always easy to accept some of these key concepts:

Even though a wide range of nuances are noticeable in coat colors, and even considering the different classifications according to racial standards and individual assessments, the melanocytes of the horses are able to produce only two types of pigments [11]: eumelanin (black pigment) and pheomelanin (reddish pigment). Melanocytes are cells with dendritic extensions, originated from the embryonic neural crest and in which melanogenesis takes place in specialized organelles called melanosomes [12]. From these two pigments and the influence of several other genes [13], all variations of colors observed in the horse coat color are produced. For melanogenesis to happen, specific enzymes are required in melanocytes, being tyrosinase the one responsible for the initial step in the melanogenesis process, converting the amino acid tyrosine into a compound called dopaquinone [11].

The important matter herein is the definition of "points" of a horse. These mean manes, tail, and lower part of limbs and to some scholars, the inner line of the ear. For the identification of coat color it is very important to understand the concept of "points," as this is the first step to identify the color genetics: horses may have black points or points of the same color of the rest of the body (in some cases there can be variation on shade, though the color is the same), in the case of a nonblack horse. By points of the same body color we mean they are usually yellowish or reddish, but may also be dark brown (if the horse is brown). Knowing the horse's points color will provide the differentiation between horses producing eumelanin (black, dark pigment) from those producing only pheomelanin (reddish pigment). That is, horses with black points, independent of the rest of the body color, have at least one dominant allele at the Extension locus: E^E. Animals with points of the same color as the rest of the body (except in cases of entirely white horses) have a double dose (homozygous) of the recessive allele at the Extension locus: E^eE^e, meaning it is impossible to them to produce the black pigment eumelanin [14, 15].

The white in the coat of a horse is always superimposed on the basic coat color. The horses are primarily colored, being capable of producing pigment all over the body, and any and every white in the equine species is derived from a genetic directive that prevents color development due to the absence of melanocytes in that part of the body [16], and not to the lack of pigment production by melanocytes. Whether it is the meshes of a tobiano, or the entirely white body of an extensive expression of a white spotted, this means that in these areas there are no melanocytes. The same goes for the common white marking seen on the face and lower portion of horse's limbs (e.g., markings commonly found on the head as "star," "stripe," and on the limbs as "socks"). Such common marking is also due to the absence of melanocytes in the white hairs regions and has polygenic origin influenced by other random factors [13].

Once understood these fundamental concepts, one may proceed to the study of the genetic basis of the several coat colors.

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3. The three basic colors

Three basic colors, built from the two pigments produced by horses, are derived from the interaction of two genes: melanocortin-1 receptor (MC1R) and agouti signaling protein (ASIP) [14]. These colors are *bay*, *black*, and *chestnut*. The influence of other genes (for example, dilution genes) determines the variations of each of the three basic colors [13].

-MC1R gene: The dominant allele (E^E) determines the production of eumelanin; the recessive allele (E^e) determines the production of pheomelanin. The MC1R gene encodes the production of a protein called melanocortin-1 receptor, which plays a pivotal role in the pigment production process. This receptor is located on the surface of melanocytes. When activated by melanocyte stimulating hormone (MSH), it triggers a series of chemical reactions within the melanocytes, leading to production of eumelanin. In fact, melanocytes are capable of producing both eumelanin and pheomelanin, but when the animal has the E^eE^e genotype, what happens is that the receptor is defective, making it unable to properly transmit the information passed by MSH, thus leading to production of pheomelanin only. The net result of the forms of this gene is therefore an animal with a black coat when there is at least one dominant allele (E^EE^E or E^EE^e), or a *chestnut* horse (reddish color) when homozygous to the recessive allele (E^eE^e). The recessive allele (E^e) is a mutation of the wild form (E^E), which occurred about 7000 years BP [1].

-ASIP gene: the dominant allele (A^A) encodes production of a protein called agouti signaling protein—hence the gene's name—which has the ability to block the melanocortin receptor 1 in existing melanocytes in the body (but not in the points) of the horse. When the receptor is blocked, there is no stimulus for the production of eumelanin (as explained above), and only pheomelanin synthesis occurs. Therefore, an eumelanic horse (E^EE^-) with a dominant allele at the Agouti locus (A^AA^-) yields a *bay* horse—a horse with a reddish to brownish body color and black points. About 8000 years BP [1], a recessive mutation occurred in the ASIP locus, yielding black color throughout the entire body of the horse. For this to happen; however, two doses (homozygosity) of the recessive allele are required: A^aA^a. An interesting fact is that the agouti signaling protein is effective only in eumelanin-producers horses (i.e., whose genotype is E^EE^E or E^EE^e). As in *chestnuts* (whose genotype is E^eE^e) melanocortin-1 receptor is defective, the protein has no effect.

As a net result of the interaction of MC1R and ASIP genes, we have:

Genotype E^EE^- A^aA^a = *black* horse. It is a very common color in the Percheron breed, and valued when having white markings in some other breeds. Some breeds, such as Friesian admit only black animals. Note that a superscript dash character (-) along with the locus letter (as in E^E E^-) does not mean "negative," this dash means that the allele occupying that locus is unimportant to the phenotype.

Genotype E^EE^- A^AA^- = *bay* horse, comprising all its variants regarding shades: *Light bay*, *dark bay*, *blood bay*, *mahogany bay*, etc.; in South American countries, a bright red bay is called *colorado*; a faded shade of colorado is called *douradilho*. There are two more alleles (so far) possible to exist at this locus: A^+ for *wild bay* (a bay where black on the limbs is restricted to the region below the fetlocks) and A^t, which would be responsible for the near black coat

color with conspicuous lighter regions. These lighter areas are tan or reddish, and should not be confused with the mealy modifier (Pa^+), a dominant trait that affects all the basic coats, causing paler areas around the eyes, muzzle, distal part of limbs, and underside the body. In Latin America countries, this variant is known as *zaino* (causing many mistakes by the time of breed registry); in English-speaking countries they are called *seal browns*.

Genotypes E^eE^e A^AA^- *or* E^eE^e A^aA^a = *chestnut* horse. This means that *bay* is, in fact, hypostatic to *chestnut*, that is, the dominant allele in the locus Agouti (A^A) is masked by the homocigosis of the recessive allele in the Extension locus (E^eE^e). In other words, E^eE^e results in chestnut horses regardless that alleles are present in the ASIP locus.

Although recessive homozygous alleles at the MC1R locus encode always pheomelanic animals, each country (and regions within the same country) has its own designation based solely on phenotypic shade of red in the coat. For example, in Spanish and Portuguese-speaking countries, there is the *alazán*, *tostado*, and *ruano,* each one becoming even more detailed when more variants are perceived on the basic shade. Examples: *Tostado negro, tostado requeimado*, *alazán sangre*, and *alazán tostado*. In some English-speaking countries, the term *chestnut* defines a darker red horse, while *sorrel* would be a lighter colored red horse. Some breed associations, such as the American Quarter Horse Association (AQHA) use this distinction as a rule. Some breeds, namely the Suffolk Punch and the Haflinger admit only chestnut or sorrel animals.

As for breeders of draft horses, *sorrel* would be applied to a chestnut horse carrying the mealy modifier.

Once determined which pigment(s) is (are) produced by the horse and understood the relationship between all possible alleles in genes MC1R and ASIP, it is possible to understand the effects that other alleles, at other loci, yield over the three basic colors.

4. Diluted colors

Occur when proteins encoded by specific genes alter amount of pigment or deposition of pigment in receiver structures (keratinocytes and hairs). The effect is a dilution in the intensity of the original color.

4.1. Dun

(*gateado*, in Latin American countries): This is perhaps the oldest dilution, better known by the so-called *primitive marks*. It is believed that it was present in the primitive herds, being an effective camouflage against predators (**Figures 1** and **2**). Thus, the genotype notation would be the wild-type D^+ D^-. It is a consistent coat color in the Tarpan (*Equus ferus ferus*), Przewalski (*Equus przewalski*), and breeds like Konik (only *grullos*, black animals with the dun dilution), Sorraia, Fjord, and Dülmen.

The first mutation encoding a nondun phenotype occurred about 45,000 years BP, that is, predating domestication of horse. This phenotype retains the primitive marks, though a little lighter than the wild type. Evidences suggest a second nondun mutation originating from a chromosome

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Figure 1. Dun (gateado, in Latin American countries): the oldest dilution factor.

carrying the first nondun mutation and that would have happened only a few thousand years ago; this is consistent with selection to colors with no camouflage at the time of domestication [17]. The dun effect over the basic colors—no matter how many dominant alleles are present—is a dilution of body color but not of head and points color, and the primitive marks, being the *dorsal stripe* the more consistent and best observed one. Primitive marks vary in extent and intensity. They are called so because are displayed in breeds considered primitive, though not limited to. They consist in darkening of coat on some body parts, forming recognizable patterns:

- C*ob webbing*: These are thin darker stripes on the horse's front. It has radial orientation, hence the name *cob webbing* or *spider webbing*. It is not visible in all duns, being more visible in *grullos* (black animal carrying the dun dilution).
- *Shoulder stripe*: A shadow or stripe of darker hairs running distally from (and over) the withers. It may vary in color intensity, shape, and extent.
- *Zebra stripes, stripped legs* or *leg bars*: Horizontal stripes appearing on the carpi and hocks, varying in number and color intensity. These are not always seen. In *grullos* they are usually black or very dark colored.
- *Dorsal stripe*: This is the most common mark on the dun dilution carriers. If a horse lacks the dorsal stripe, then it does not have the dun factor. It is a dark stripe clearly distinct from the rest of the coat, extending from the poll to the dock of the tail on the

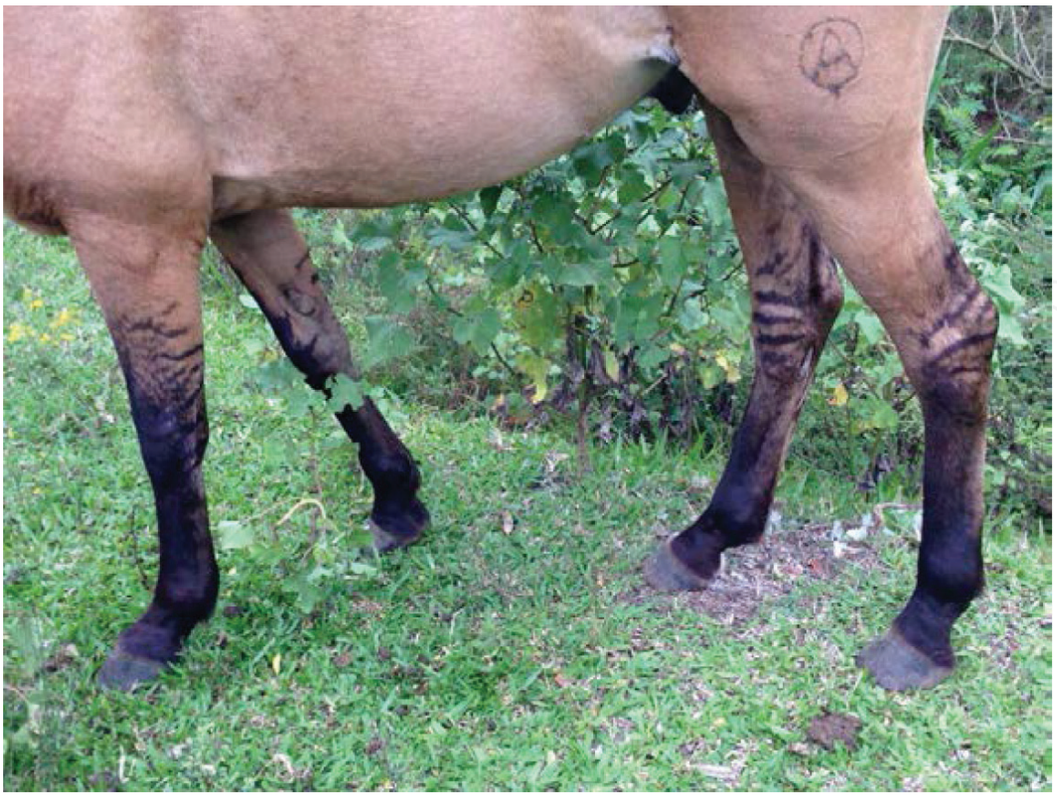

Figure 2. Dun markings as zebra and shoulder stripes are shown in more detail. *Source 1 and 2*: Mr. Jose Victor Isola.

dorsal line. Some horses not carrying the dun dilution may display a dorsal stripe, though this is less clear and lighter, and often subject of controversy. Whether this type of dorsal stripe is due to the first of mutations in wild-type allele [17], remains to be cleared by future researches.

- *Facial mask*: It is the undiluted color on the head coat. It varies in size, from a small band over the bridge of the nose or forehead to an entire undiluted head coat.
- *Guard hairs* (sometimes called *frosting*) are lighter colored hairs growing on the edges of the mane and at the tail base. A good example is the Fjord breed. Despite having different characteristics, care should be taken to not confuse guard hairs with those found on the tails of *roans* (genetic roans or not) and *rabicanos*.

There are some primitive marks that are not observed in all horses carrying dun, or slightly observed, or observed only during the first months of life. Such marks are not characteristic nor they attest the presence of the dun factor by themselves; often they are not even present in all duns. These appear as:

- *Dark bands* perpendicular to the dorsal stripe (barbs off the dorsal stripe) that may extend variably toward the ribs;
- *Shading on the neck (neck shadow)*, which can vary from a well-defined mark to only a shadowing;

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- Small dark marks (roughly the size of a pea) called *mottling*, on the stifle, legs, shoulders, and arms;
- *Dark bars on the ears*, occurring below a dark tip of the ears (upper third of the ear, caudal view), which are observed in most duns;
- *Zippers*, a thin longitudinal line of lighter hairs along the shins;
- *Bider marks*—a dark band or shadowing varying in shape and extent on the shoulder, identified so far only in some horses from Mongolia [18].

The nomenclature question when it comes to dun dilution colors, is somewhat complex due to different countries and breed registries where it is permitted. In Latin America countries these animals are called *gateados* preceded or succeeded by a term that identifies the underlying coat. In North America they are called *linebacked duns*, a clear reference to the typical dorsal stripe of the dun dilution. A wide range of terms is assigned to the various nuances caused by dun on basic coats and other dilutions. Interestingly, often two or more nuances, despite having different names, actually have the same genetic signature.

Until a few years ago, the gene responsible for the phenotype dun was unknown; it was known only about its autosomal mode of inheritance and complete dominance. Thus, it has been represented by the capital letter D, and the possible alleles as + (wild) and nd (mutant allele, not dun); with the recent release of the locus responsible for dun dilution, and possibly new genetic tests that will determine the type of mutation (nd1 or nd2) [17], this notation might be amended.

The net effects of dun on the basic coats are as follows:

- *Genotype* $E^{E}E^{-}$ $A^{a}A^{a}$ $D^{+}D^{-}$ That means a *black* horse with dun dilution becomes a *grullo* (female: *grulla*). *Grullos* are animals of yellow-grayish coat and black points and head. Like all carriers of this dilution, the primitive markings are present. In Latin countries they are called *lobuno*, a clear allusion to the wolf color ("lobo" is the Spanish and Portuguese word for wolf). This is one of the most susceptible to seasonal variations phenotypes: During winter months, when the coat is denser with longer hairs, the body presents an almost uniform and lighter cream color compared to summer months when the color can come to a grayish color similar to a mouse color. Obviously, cream and gray tones vary individually according to other genes in action, as well as the factors already mentioned, such as nutritional status and age. Thus, the lighter shades of this variant in North America are designated *silvery grullo*, *olive dun*, or *slate grullo*; the darker shades are called *wolf dun*.
- *Genotype* $E^{E}E^{-}$ $A^{A}A^{-}$ $D^{+}D^{-}$ This is a *bay* with dun dilution: In Latin America countries, it is called *gateado*; in North America nomenclature varies greatly, richly describing the intensity of the underlying color. Thus we have the *golden duns* and *silvery duns* (dun on *light bay*), *zebra dun* (dun on *medium bay*), *dark dun* (dun on *dark bay*), and *coyote dun* (dun on *sooty bay*); *dusty dun* (dun on lighter shades of *seal brown*), *shaded mealy grullo* (dun on intermediate shades of *seal brown*—note that *mealy* and *grullo* here are solely

phenotypic definitions, that hold no genetic match with the real (genetic) *mealy* and *grullo*), *shaded wolf dun* (dun on darker shades or sooty variant of *seal brown*). Sooty is the presence of very dark hairs spread over the coat, especially on the dorsal region. Many theories offer explanations for its origin and genetic mechanisms, but none has yet been adequately proven.

- *Genotype* E^eE^e A^-A^- D^+D^- *Chestnut* carrying dun: In Latin America countries it is called *gateado ruivo* (something like "auburn dun" or "ginger dun"). In North America, the dun on lighter *chestnuts* (and *sorrels*) is called *apricot dun* or *sooty apricot dun* (for sooty variant of *sorrel*), while dun on *tostado* (*chestnut*) ranges from *apricot dun* or *claybank dun* (lighter shades) to *red dun* for intermediary and sooty shades of *chestnut*.

4.2. Cream

Another widespread dilution; results from a dominant mutation in the membrane-associated transporter protein gene (MATP) [19]. The effect over the coat color depends on the allelic zygosity—what is called *incomplete dominance*. It means that homozygosity or heterozygosity of the dominant allele affect differently the phenotype. In the case of cream dilution, it happens that homozygosity of the dominant allele affects the phenotype more aggressively than heterozygosity. The MATP gene is represented by the C letter by convention; this comes from a time when it was thought that a "C" gene (with "C" standing for "color") was responsible for the color over the body, so that double-diluted cream horses lacked the "color gene" and were regarded as albinos. Obviously, the cream dilution had not yet been postulated at that time. Additionally, there are different effects of the cream dilution over feomelanic and eumelanic horses. Thus, the genotype $C^{Cr}C$ acting over pheomelanin will produce cream-colored hairs, varying from a very light cream color to a dark caramel, while genotype $C^{Cr}C^{Cr}$ will dilute hairs color to an off-white shade and will dilute also the skin color (which will become pinkish); the eyes will have a bluish color. On the other hand, the genotype $C^{Cr}C$ will have little (if much) effect over eumelanin (*black* horses with one copy of the mutated allele may display a faded black color or, in some cases, a very dark brown color), while homozygosity will produce a horse with off-white-colored hairs, pinkish skin, and bluish eyes. Therefore, we have the following net effect of cream dilution on the basic colors:

- One gene cream on *chestnut* = *Palomino*, a valued coat color especially when the body holds a golden sheen. The body is yellowish ranging from pale yellow/cream to dark caramel. Palominos can vary in shade, though manes and tails are usually lighter like the horse in the picture. The genetic representation is as follows:

  E^eE^e A^-A^- $C^{Cr}C$ Note that when the Extension locus presents both recessive alleles, any combination of alleles at the Agouti locus (A) will not produce any effect on the phenotype: *Chestnut* horses can only produce pheomelanin.

- Two genes cream on *chestnut* = *Cremello* (*cremello* is the definition given to the horse with very pale cream coat color, pink skin, and blue eyes). These animals usually have

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Figure 3. Palominos may vary in shade from a very light cream color like the horse in the picture. *Source*: Mrs. Albrecht.

eye and skin problems when not protected from continuous sun exposure (**Figure 3**). These horses are called *salgo* (because of the light-colored eyes) or *melado* in Spanish and Portuguese-speaking countries. The genetic representation is:

E^eE^e A^-A^- $C^{Cr}C^{Cr}$ Again, any combinations of alleles in the Agouti locus do not produce any effect on the phenotype, because E^eE^e horses are capable of producing only pheomelanin.

- One gene cream on *black* = *Smoky Black* (the coat color is usually faded black). In some Brazilian regions it is called *preto macaco*. The genetic representation is:

  E^EE^- A^aA^a $C^{Cr}C$ Note that in the Extension locus, only one of the alleles must be dominant to produce eumelanin. For the horse to display a black coat over the entire body (i.e., with melanocortin-1 receptors present and responsive to MSH in all melanocytes), it is necessary homozygosity of the mutant allele at the Agouti locus.

- Two genes cream on *black* = *Smoky Cream*, a very pale cream coat, with pinkish skin, and blue eyes; however, usually some areas still retain dark pigment—seen like dark hairs scattered over the entire body. The genetic representation is:

  E^EE^- A^aA^a $C^{Cr}C^{Cr}$ Note that, at the Extension locus, only one dominant allele is needed to produce eumelanin.

- One gene cream on *bay* = *Buckskin* is the name of the animal with black points and yellowish body, ranging from light cream to dark caramel. In Spanish and Portuguese-speaking countries it is called *baio*. The genetic representation is:

  $E^{E}E^{-}$ $A^{A}A^{-}$ $C^{Cr}C$ Note that, at the Extension locus, only one dominant allele is needed to produce the agouti signaling protein.

- Two genes cream on *bay* = *Perlino* (very pale cream coat with pinkish skin and blue eyes; some areas still retain dark pigment, mainly on the points. Also called melado and salgo in Spanish/Portuguese-speaking countries. The genetic representation is:

  $E^{E}E^{-}$ $A^{A}A^{-}$ $C^{Cr}C^{Cr}$ In Extension and Agouti loci, it is necessary only one dominant allele to produce eumelanin and agouti signaling protein, respectively.

Cream-diluted coats are highly valued by some breed associations, for example, the American Cream Draft Horse.

Because dun and cream loci operate separately, it is possible for a horse to carry both dilutions. In this case, the colors become even more diluted and an identification based solely on the visual aspect becomes more difficult and prone to mistakes.

4.3. Silver or silver dapple

It is a mutation at PMEL17 gene [20] (premelanosomal protein 17), which encodes a transmembrane protein involved in melanosomal production of eumelanin. The mutation produces a defective protein, causing a dilution effect on that pigment. Hence, the black color is diluted to shades of sepia or chocolate (called *silver chocolate* in some locations; in Australia it is known by *taffy*) and the manes, tails, eyelashes, and tactile hairs of face and muzzle show a grayish to whitish, sometimes silvered color. Limbs can be either whitish or near black colored. Usually the coat is dappled, and the more heavily dappled, the more valued it is. It is a dominant trait represented as Z^{Z}; the recessive allele (wild, normal, and nonsilver) is represented by Z^{+}. The variants are named according to the intensity of dilution; so we have the *blue silvers*, *black silvers*, *silvers chocolate*, *and silver dapples*. In the case of bay horses carrying the silver dilution, only eumelanic regions are affected, and so they are called *red* or *bay silvers* (in Rocky Mountain Horse breed, these are called *red chocolate*). It is a highly valued coat in some countries and quite common in breeds such as the Rocky Mountain Horse, Mountain Pleasure Horse, Kentucky Mountain Saddle Horse, and the Icelandic breed. It also appears in Quarter Horses, Morgans, and Miniatures. In horses homozygous for the condition it has been observed different combinations of symptoms affecting the anterior and posterior segments of the eye; such condition is known as multiple congenital ocular abnormalities (MCOA) [21–23].

In the same way, the cream and dun dilutions can act together, so when Z^{Z} Z^{-} occurs on a diluted coat color (by any other diluting gene) the degree of difficulty of color identification increases, and cases of mistaken registration due to several concurrent dilutions are not rare. For example, a *silver buckskins* can be easily confused with a *Palomino* due to the golden color

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of the body and pale points; *silver buckskins* usually have lighter skin, which can make them superficially similar to some *champagnes* (another dilution).

4.4. Champagne

A dominant mutation in the SLC36A1 gene (Solute Carrier 36 family A1) showing complete dominance [24]. It causes dilution of coat color, sometimes giving it a metallic sheen; it also makes the skin to dilute to a light brown color (with many small and darker splotches like freckles) and amber eyes. The dilution is represented as Ch^{Ch} (mutant allele) and Ch^{+} stands for the wild-type allele, nonchampagne. The net effect on the basic coat colors completely changes the original names. Sometimes very clear *champagnes* are confused with some cream-related coats colors due to a very light shade presented in some variants; however, the striking characteristics of skin and eyes colors should avoid confusion. Champagne dilution causes dilution of the coat color ranging from a very light yellowish to a light chocolate shade with varying points colors. The genetic representations are:

$E^{E}E^{-}$ $A^{a}A^{a}$ $Ch^{Ch}Ch^{+}$ it is called *classic champagne*. The color varies from dark beige to light chocolate, with points slightly darker than body.

$E^{E}E^{-}$ $A^{A}A^{-}$ $Ch^{Ch}Ch^{+}$ Champagne on a *bay* coat. It is called *amber champagne*. The body color is light tan brown or light yellowish brown and the points are usually light chocolate colored. Champagne on a *seal brown* coat ($E^{e}E^{e}$ $A^{t}A^{t/a}$ $C^{Ch}C^{+}$) or on darker shades of *bay* is called *sable champagne*.

$E^{e}E^{e}$ $A^{-}A^{-}$ $Ch^{Ch}Ch^{+}$ This is a *gold champagne*, often confused with *palominos* due to the golden glisten and lighter color. The combination of champagne with a cream allele causes an even lighter color, with greenish blue eyes with a hint of amber—these horses are called *ivory champagnes*.

4.5. Other dilutions

There are other dilutions found hitherto in some breeds (some not yet fully characterized from a genetic point of view). Examples are the *pearls* (dilution similar to champagne), *mushrooms* (dilution similar to silver, though it affects pheomelanin instead of eumelanin; so far found only in Miniatures). Some of these alleged dilutions/mutations have not yet been critically studied on a scientific basis. A dilution known as the lavender foal syndrome occurs in the Arabian breed and is due to a defective Myosin Va protein, coded by a recessive mutation in the gene MYO5A [25], causing severe neurological disorders and very light reddish, almost lilac hairs and skin in the neonate. These and other dilutions are an interesting and extensive subject, which could easily be the subject of an entire chapter.

5. Coat color modifiers

These genes impose areas of different colors on the basic coat color, modifying the original aspect.

5.1. Pangaré or mealy

This is a modifier whose genetic origin is unclear. It makes some areas paler than the rest of the body. These are around the eyes, muzzle, underside the body, flanks, and inner part of limbs [13]. The name pangaré derives from the observation made in horses of Spanish-speaking countries, and is translated into English as mealy. Apparently it is a dominant trait and is considered a wild trait, i.e., likely to be present in the original color of primitive horses. It is represented by the notation Pa^{+}, with the recessive mutation represented by Pa^{np} (standing for nonpangaré). It affects all coat colors, with its most dramatic effect seen on the *sorrel* coat color. Generally mealy *chestnuts* or *sorrels* (in Spanish and Portuguese, only *pangaré*) present a mane very lighter than the rest of the coat. The body color becomes slightly lighter, although pangaré is not considered a dilution factor. In *black* horses, it renders the coat to a slightly lighter or brownish color, easily leading to confusion with the *seal brown* color; it differs from the *seal brown* primarily due to the shade of the light areas: while in *seal brown* the lighter areas are tan and less extensive, in the *pangaré* those areas are more extensive and pale.

5.2. Rabicano

Its mechanism of action and genetic control are still unknown [13]. It causes the appearance of white hairs scattered on the coat over the rib cage (indeed following the direction of the bones), flanks, and tail base. It varies in intensity of expression and may appear as only a few white hairs on the base of the tail and sides of the rib cage, to a large amount of white hairs over these regions, in this case being easily confused with roaned or a true roan.

5.3. Flaxen

It is a recessive trait with variable expression; when homozygous determines a lighter shade (than the body) of the manes and tails (**Figure 4**). Acts only on chestnuts and sorrels. Its mechanism of action and genetic control are unclear, and it is even accepted to be of polygenic nature [13].

5.4. Brindle

Brindle is a very rare color, referred to as vertical dark stripes on any background color [13]. Usually, points and head are unaffected and may occur in any breed. It was suggested two causes for the brindle in horses [13]: either it is a reorganization of sootiness into vertical stripes instead of the usual sooty variant, or it is a chimera; in fact, some animals have been proven to be chimeras, resulting from the fusion of two embryos early during pregnancy.

6. The gray case

Gray is a dominant mutation in the gene STX17 [26], Syntaxin 17, represented by the capitalized letter G. It consists in a gradual and progressive whitening of all hairs on the horse's body, but the skin may remain dark for many years. In some cases, such as the Lipizzaners, the skin becomes gradually unpigmented as well. When this mutation is present, at every shedding time

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the original color of the horse will be replaced by white-colored hairs, even if the underlying coat is determined by dominant alleles. Thus, the gene that causes the graying of the coat is epistatic, which occurs when a gene at one locus masks the effect of another gene at another locus.

The dominant nature of the mutation implies that any gray horse is required to have at least one of its parents being a gray too. Gray horses, especially homozygotes (G^G G^G) tend to develop a type of tumor called the melanoma of the gray horse [27].

Animals are born colored (the color of the original coat) and graying starts around the eyes, already during the first months of life. However, total whitening can take years, ranging individually from horse to horse. This mutation leads to an excess of melanin production, and that is the reason why gray-carrying horses are born with vivid darker colors; such a characteristic is well observed in the foals whose coat is a jet black, unlike the black foals without the mutation, who are born a grayish color. This is the reason because some breeders say "blacks are born grays and grays are born blacks."

Many denominations are applied according to different stages of the graying process, varying by country: *Tordilho medalhado* or *apatacado* (*tordilho*/*tordillo* stands for gray in Portuguese and Spanish; respectively, the word is derived from "tordo," a bird whose plumage has a similar color) is the same of *dapple gray*; *branco*/*blanco porcelana* is the Portuguese/Spanish equivalent of *white porcelain*/*porcelain gray* (older grays with depigmented skin contrasting with the white hairs of body), *tordilho*/*tordillo vinagre* (*rose gray*), *tordilho*/*tordillo negro* (*iron gray*), and *tordilho*/*tordillo*

Figure 4. A cremello horse has pinkish skin, blue eyes, and a coat of a very light shade of cream. *Source*: Mrs. Albrecht.

pedrês (*fleabitten gray*). It is a widespread color between various breeds such as Thoroughbred, Purebred Arabian, Percheron, Andalusian, and it is the only color seen in Lipizzaners.

7. White patterns

Consist of white hairs mixed by or arranged in white spots overlapping the underlying coat; it has dominant or polygenic nature and arises from mutations in several genes. The phenotypic appearance can vary from one extreme to another, often being impossible to say how many and which mutant genes are present without genetic testing. These white patterns should not be confused with common white marks present on the face and the lower portion of limbs (white markings of small size, limiting white to small patches in the forehead, and white lower limbs not reaching carpi and hocks).

7.1. Overo

Overo frame is the name of a mutation in the gene EDNRB [28] (endothelin receptor B), represented by the letter O with superscript lw (lethal white). Much confusion has been caused due to this gene. Because it does not manifest phenotypically in all horses carrying the mutation, it was mistakenly understood as a recessive trait. For this reason, it is known as the "ninja gene" or "007 gene." What happens though, is that O^{lw} has highly variable expression, depending on the action of other genes, which makes confusing its mechanism of action—It can even crop out in a foal from parents with apparently solid-colored coats—in these case, hiding the gene ("ninja gene!"). What is known for sure is that it is a dominant mutation capable of amplifying the expression of other white patterns such as Splashed White and Sabino.

To breeders and horse enthusiasts, *overo* is the general empirical name given to animals showing many asymmetrical white spots of relatively reduced size and jagged edges distributed throughout the body (**Figure 5**); however, only with genetic testing one can be sure that the frame gene is present.

Usually limbs are solid (i.e., do not have any white marking) and the head is largely marked with white (sometimes called "baldface"). Irregular white spots appear on the sides of the body and neck (whence the name "frame"); many *overos* has the upper lip solid colored and blue eyes are common, even when the coat around the eyes is pigmented. *Overos* minimally marked can show only the baldface.

The problem with overo frame is that it is lethal when homozygous, causing the lethal white foal syndrome [28]. The medical condition is called ileocolonic aganglionosis and requires euthanasia of the foal by the first days of life for humanitarian reasons. It is a pleiotropic effect of the mutant gene EDNRB, resulting in faulty areas of intestinal innervation and a foal completely (or near so) white colored. Pleiotropy is a genetic condition in which a gene causes more than one effect [29]. That is why breeding programs discourage mating of two *overos*. Making use of the Punnet square, a tool that allows simple calculation of outcome probabilities out of a given mating, the possibility of obtaining a homozygous overo frame (O^{lw} O^{lw})—a

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Figure 5. Flaxen. *Source*: Mrs. Albrecht.

lethal white foal—from the mating of two *overos* is 25% which is an unacceptable risk both for ethical and economical issues.

7.2. Splashed White

At least two loci are identified as having mutant alleles for Splashed White [30]: microphtalmia transcription factor (MITF) and paired box-3 (PAX3). Three mutations have been identified hitherto, SW1 (dominant mutation in MITF gene), SW2, and SW3 (dominant mutations in the PAX3 gene). Splashed White causes white spots in a horizontal pattern on the horse's body coat, and these white spots always cross the ventral line. The head is extensively marked (the white mark on the forehead and muzzle is quite wide and round and the muzzle is usually all white; this is called a "blaze") and the limbs are white above carpi and hocks. In extreme-marked horses, the head may be entirely white and the body may keep color only on the dorsal line. The more copies of mutant genes, the greater the amount of white. Splashed Whites minimally marked can display only an extensively marked forehead, nose, and muzzle; limbs can have white only below shins, and usually in the forelimbs.

In Latin America countries, it is called *bragado* preceded by the name of the main coat (i.e., *colorado bragado*). In English-speaking countries, it is used *splash* after the name of the main coat, as in *bay splash*.

Splashed White is widespread among several breeds, including Welsh Pony, Icelandic, Finnish Draft, and Paints. It is present in some other breeds, although the respective stud books do not recognize and does not register it as a specific characteristic.

Accordingly to the extent of depigmentation on the animal's head, it may have blue eyes and/or congenital deafness. A problem of embryonic death occurs when both PAX3 alleles are mutated.

7.3. Roan

It is characterized by white and colored hairs intermingled over the coat in different proportions only on the horse's body, not affecting points and head. Sometimes when there is very little amount of white, it is confused with *roaned*, which does not have the same genetic origin of the true or genetic *roan*. Some confusion may also occur between *roans* and *rabicanos*. Roan is a dominant mutation in the KIT gene [10] (mast/stem cell growth factor receptor; v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog), represented by KIT^{R}. Contrary to what was once believed, homozygosity is possible in living animals and does not cause embryonic death. It can occur on any basic coat colors, diluted or modified. The nomenclature varies according to the country of origin: in Latin America countries, the word *rosilho* (*rosillo* in Spanish) is used with the name of the main coat, as in *rosilho gateado* (a roan dun horse), *rosilho prateado* (*chestnut* with large amount of white hairs intermingled with the basic color; does not means the presence of the silver dilution); *mouro* is the roan horse whose basic color is black. In English-speaking countries the word roan is used after the main color:

Figure 6. Overo. *Source*: Mr. Isola.

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red roan (a *chestnut* or *sorrel roan*), *blue roan* (the roan black), *bay roan*, *strawberry roan*, and so on (**Figure 6**).

7.4. Tobiano

Tobiano spotting is another mutation in the KIT gene [31], characterized by white spots in a vertical pattern crossing the dorsal line (unlike Splashed White, wherein the spots have a horizontal pattern and cross the ventral line). It has dominant nature and is represented by KIT^{To}. Usually the head is solid or has minimal white marking, the limbs have high socks (white mark that reaches the carpi and hocks), and the tail and manes are usually bicolored. The maximally marked *tobiano* may have the body almost completely white (especially if Splashed White is present), but keep solid-colored ears, what is called "Medicine Hat." On the other hand, minimally marked *tobianos* may display only high socks. In these cases, only a genetic test can demonstrate the presence of this mutant gene.

A frequent feature in homozygous *tobianos* (KIT^{To} KIT^{To}) is the so-called "paw prints," "cat tracks," "bear paws" (English), "marcas do perdigueiro" (Portuguese): colored small rounded spots arranged in small groups spread over white areas on the horse's body. Despite the presence of these marks be of great help when one wants a *tobiano* foal, the absence of these marks does not mean the *tobiano* parent is heterozygous.

Tobiano derives its name from Tobias, a Brazilian general who came to Argentina in the mid 1800s bringing with him soldiers mounted in very odd-spotted horses. The nomenclature varies according to country. Moreover, in Latin countries it varies also among countries' regions. *Tobiano* is used, in North and South America, including Southern Brazil, along with the main coat name: *tobiano colorado* (Portuguese and Spanish), *bay tobiano*, and *black tobiano* (English); in other regions of Brazil, *pampa de baio* (or other coat color) is used to designate a *buckskin tobiano* animal with large proportion of white spotting, or *baio pampa* (or other coat color) for the animal with little white spotting.

7.5. White spotted

Formerly known as Dominant White, it is another dominant mutation in the KIT gene [16] that holds extensive phenotypic variation. It is characterized by large amounts of sparse white hairs with no set pattern, overlapping the adjacent coat. The horses also have depigmented skin and dark eyes, and in extreme cases the animal can be completely white being easily confused with an older gray. When the eyes have colors other than dark brown, there is another gene (or genes) acting. White spotted is represented by the capitalized letter W followed by a number, which corresponds to the mutation variant [32] (for example, KIT^{W1} and KIT^{w19}). There are by now 20 known mutations, some of which are derived from spontaneous mutations in the gene. It occurs even in the Thoroughbred breed, and some countries such as Australia, New Zealand, and Japan recognize and do list these horses as authentic Thoroughbreds.

It has long been discussed the issue of lethal homozygosity (KIT^{W-} KIT^{W-}), taken as true for a long time. This is a debatable question considering that there are living animals whose genetic tests confirmed the presence of two alleles W [9, 33].

7.6. Sabino

Sabino is a common term originated from Spanish-speaking countries, to designate a coat speckled with white hairs that do not form a specific pattern [13]. This definition is based only on the phenotype and is generally used to define a white patterned coat that not necessarily has the genetic basis of the same name gene.

Sabino (genetic) occurs in two forms: a dominant mutation in the KIT gene named Sabino-1 (KIT^{Sb1} KIT^{-}) [34]. This variant, when homozygous, causes much more white on the body (incomplete dominance). The second form has a polygenic mode of inheritance [13] and results in horses completely white or near so. The eyes may be blue or dark brown. A typical sabino feature is the roaned edges of the white spots. White spots with these characteristics are common in the belly and intermandibular space. The appearance of *sabinos* may vary greatly from only common white marks on the limbs with roaned edges, to a whole white animal with very little pigmentation, whence it is called "the everything gene." This renders identification of the underlying coat color, whether or not there is expression of other white patterns, practically impossible without genetic testing or at least, extensive knowledge of the genealogy of the animal in question.

Usually the coat name is followed or preceded by the word "sabino:" *Colorada sabina* (Portuguese and Spanish); *bay sabino* (English).

An interesting fact about KIT mutations is that only two mutations can be presented in the KIT gene in a particular animal, since there are only two copies of the gene in every horse; that being understood, it becomes easy to see why we will never have one "white-spotted red roan tobiano" (it would require three KIT gene copies) or a homozygous tobiano roan.

7.7. Appaloosa

Characteristic coat color of the homonymous breed and frequent color in breeds like Knabstrupp, Miniatures, Noriker, and others. It is a white pattern with symmetric white patches. *Appaloosa* is the generic name of the leopard complex; "complex" because all patterns in this color are genetically related, and "leopard" because of the most distinctive feature observed: the round-colored spots on a white area, varying in extent over the animal's body. It is caused by a mutation in the gene TRPM1 (transient receptor potential cation channel, subfamily M, member 1) [35]. It shows incomplete dominance, represented by Lp^{Lp}. The most common appearance is a variable solid-colored anterior part of the body and the remainder covered by white (which is called *white cap blanket* or *snow cap blanket*), which may or may not display spots, depending on the genetic makeup (homozygous vs. heterozygous). The animals called "leopards," highly valued, present a white body (including the head) covered with white round spots (leopard spots). The leopard complex can be split into several patterns, and usually at least two of these patterns are expressed in the same animal. These patterns relate to quantity and arrangement of white areas on the animal's coat:

- *Frost* describes a roaning pattern that consists of scattered white hairs over the entire body of the horse.

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- *Varnish roan* is like frost, though areas over bony prominences are darker than the remainder of the coat.
- *Snowflake* occurs as small round patches of white hairs spread over the entire body. As well as frost and varnish roan, it is progressive from birth to maturity; that is why animals that have the leopard complex will present, year after year, an increasingly white-covered coat, although many horses end up stabilizing at some point in their lifes, contrary to what happens in the case of gray.
- *Speckled* describes a pattern of extensive roaning with numerous small dark spots are placed on a white background.
- *Blanket* is a white covering extending variably over the horse's body (**Figure 8**); it can be as small as only a few white patches on the hips, or extensive enough to cover the entire body. When the animal is heterozygous for Lp (Lp^{Lp} Lp) the blanket is covered by colored round spots that can vary in size (**Figure 7**). Homozygous (Lp^{Lp} Lp^{Lp}) horses show no spots, no matter the extent of the white blanket. In case of an extensive white blanket, the entire body will display white, while maintaining some color at the points and head and some very small-scattered spots on some regions of the body. These horses are called *few spots* (**Figure 8**).

The extent of the white blanket is a function of other loci, known to exert modifying action on the extent of white in the body [13, 35]. One of these modifiers is named Pattern-1, a domi-

Figure 7. Blue roan. *Source*: Mr. Isola.

Figure 8. A white blanket may vary in extension. *Source*: Mrs. Albrecht.

nant trait ($PATN^{P}$) that regulates the extent of the white blanket and acts when at least one copy of the leopard gene is present. Horses that do not have the dominant gene ($PATN^{+}$) can be solid-colored coats without white cover, displaying only the patterns of white hairs and depigmented skin described below.

Some characteristics occur independently of other manifestations of the leopard complex, being present in all animals carrying the mutation, whether they are homozygous or not. These characteristics are shown as small spots on the skin of the nose, genitalia, anus, mouth, and eyelids, called *mottled*; when the skin is dark these spots are pink and when it is clear, the spots are dark. Also there are changes in the sclera, which is white, resembling a human eye to many people.

The limbs may display the common white marks like in any other coat color. In leopard complex carriers lacking these common marks, a blend of white and dark regions may be presented on the lower limbs. These are called *lightning strikes* or *lightning marks*, and the coronary band is generally colored. The hooves can be striped. An interesting feature of the leopard complex are sparse manes and tails, often called "rat tailed" and more strongly expressed in dark-colored hairs.

A common problem found in homozygous horses (Lp^{Lp} Lp^{Lp}) is the congenital stationary night blindness (CSNB) [36].

The "appaloosa" mutation appeared about 25,000 years ago, according to drawings found in the Perch Merle caves in southwestern France. In the modern era, it was developed by Indians

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of the Nez Perce tribe, from horses brought by Europeans in the sixteenth and seventeenth centuries; these tribes lived in the northwestern United States, at the banks of the Palouse River, from where the name Appaloosa is originated and consequently the name by which the leopard complex became known worldwide.

8. Conclusion

The colors of horses are determined by genetic factors and influenced by factors such as insolation, season, nutritional status, age, sex, and health. The naming of colors varies according to individual perceptions of shades and colors, countries (regional classifications), and breed standards. A wide variety of colors appeared after the domestication of horse, with more impressive-looking phenotypes preferred since antiquity. The cells responsible for pigment production are the melanocytes, where melanogenesis takes place in specialized organelles called melanosomes. Two pigments are produced by horses (eumelanin and pheomelanin) and the interaction of the MC1R and ASIP genes determines the three basic colors of horses (bay, chestnut, and black). These pigments can be influenced by dilution genes and modifier genes, resulting in a variety of colors. Observing the color of a solid-colored horse's points, one can say which pigment is produced. Any white in the coat of a horse derives from the absence of melanocytes in the depigmented area. The exception is the process of graying, a depletion of pigment production, and leading to the gradual appearance of white hairs instead of colored hairs. Pleiotropic effects arise from the expression of some genes related to coat colors, affecting physiological systems of the horse and may even lead to death. Many colors have not been critically related to specific genes yet. Genetic tests are available to check the presence of many alleles, and without such testing is often difficult to pinpoint exactly that genes are at work to produce the color.

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The authors hereby declare, that all the pictures of horses in this chapter were taken by Mrs. Albrecht and Mr. Isola, especially on purpose to insert here, and the animals belong to them.

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Further reading

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