Topic 3: Coat color genetics in farm animals

Lecture

The topic of today's lecture is **Coat color genetics in farm animals.** The lecture is part of Module 2: Animal genetics, that is a part of the ISAGREED project. This presentation was supported by Erasmus+ KA2 Cooperation Partnerships Grant "Innovation of the content and structure of study programmes in the field of management of animal genetic and food resources using digitalization".

As part of the lecture we will first talk about the importance of coat color and changes in coloration related to domestication. Then I will briefly explain pigment systhesis. We will list the main genes involved in coat coloration in mammals and explain their action using the example of cattle. At the end of the lecture, I will mention pleiotropic effect of selected genes.

There are several important functions of pigment synthesis.

- Coat color is of importance for mating, for protection against predators, and as an adaptation to the environment.
- In fur animals, the coat color is an important production trait.
- In other species such as cattle and sheep, the coat color is an important breed characteristic.

In contrast to their wild ancestors, domesticated species are often characterized by a substantial allelic variability of coat-color-associated genes.

Recent studies demonstrate that the selection for coat-color phenotypes started at the beginning of domestication.

Characteristic of modern domesticated animals is their large phenotypic variation, which is not found in any of their wild ancestors.

Wild species are usually uniform in phenotype and show species-specific colors and patterns. By contrast, domesticated species are highly variable in both colors and color patterns.

Although to date more than 300 genetic loci and more than 150 identified coat-color-associated genes have been discovered, which influence pigmentation in various ways. Some of them are listed at the right side of this slide.

In connection with pigmentation, across mammal species, the first two are mainly mentioned, the gene for agouti signaling protein (ASIP), and the gene for melanocotin 1 receptor (MC1R). These two genes are related to the type of pigment produced and its subsequent distribution on the animal body. Several mutations of the KIT gene, which are related to the activity of tyrosinase, the important enzyme in the process of pigment formation, are often mentioned in connection with the white color, which is often referred to as the "color of domestication". It will be discussed later.

The process of pigment cell development is crucial for the determination of mammalian coat coloration. The pigmentation progress is subdivided into three major stages: melanocyte development; pigment production; and pigment distribution.

Melanocytes can produce the two different pigments - eumelanin (dark brownish to black) and pheomelanin (yellowish to reddish).

This picture shows the process of the formation of pigment cells.

During vertebrate embryogenesis, neural crest cells arise along the dorsal neural tube, and some differentiate into melanoblasts (precursors of melanocytes), which migrate ventrally along the body.

Melanoblasts typically enter the epidermis, where some remain, while others localize to the hair follicles and differentiate into melanocytes.

These melanocytes produce pigment.

Once pigment is produced, it is packaged into melanosomes and transferred to keratinocytes of developing hair (or epidermal cells).

Melanocytes can produce the two different pigments:

eumelanin (dark brownish to black) and **pheomelanin** (yellowish to reddish).

Tyrosinase is the rate-limiting enzyme in melanogenesis. There are over 100 alleles of tyrosinase that have been characterized, ranging from null alleles, resulting in the complete absence of pigmentation (**albinism**), to alleles with reduced function that limit the melanin production (seen for example in cremello horses).

Regarding the possible colour phenotypes we distinguish two basic categories. On the one hand the so called solid colour, which covers all forms from fully pigmented to white. The second group include patterned phenotypes – for example dorso-ventral pigmentation, white spotting or markings in varying extents or other special patterns as leopard complex.

The basic coat color in both categories is given by the ratio between the two types of pigment - eumelanin and pheomelanin. This ratio is primarily determined by the agouti signaling protein (ASIP) and melanocortin 1 receptor (MC1R) genes mentioned earlier.

As an example, we will now explain the determination of the formation of two different types of pigment and the determination of spotting in cattle.

In this case, the genotype at two loci, namely EXTENSION and SPOTTING, is important.

At the EXTENSION locus, three basic alleles have been described in cattle, denoted in the genetic notation as usual by uppercase and lowercase letters, and since it is an allelic series, we also use the so-called index notation. The order of dominance in this series is in the order in which the alleles are listed, therefore from dominant to recessive form.

The EXTENSION gene determines the pigment color of an animal. The dominant allele E is responsible for the production of eumelanin in coat cells of black animals and the recessive allele e for phaeomelanin responsible for the red color in animals. A third allele is responsible for the wild phenotype (red or red-brown, sometimes with a light backline).

It follows from the hierarchy of the alleles that homozygous recessive individuals at the EXTENSION locus are red, individuals with at least one dominant allele will be black, and carriers of the E+ allele represent the so-called "wild type" phenotype. The representation of individual alleles in the population is breed-specific. Not all breeds necessarily carry all the listed alleles. This also determines what colors we find in the given breed. There are breeds uniform in coat color, but also breeds where different color phenotypes are presented.

The second important locus for coat color in cattle is the SPOTTING locus.

A total of four alleles are known at this locus. The intra-allelic interaction are a bit more complicated resulting in different spotting pattern occuring in cattle.

There are four alleles recognized at the SPOTTING locus. S^+ for non-spotting phenotype, S^H for Hereford pattern, S^p is responsible for lined back-pattern seen Pinzgauers and reccessive allele makes up irregular white spotting seen in breeds like Holstein.

As a result of pleiotropy (the situation when one gene influences two or more seemingly unrelated phenotypic traits), some of the color phenotypes may be associated with the occurrence of defects or diseases.

For example:

Oculocutaneous albinism is often connected with vision disorders.

In horses, in connection with one of the spotting patterns (referred as frame overo), the so-called overo lethal white syndrome can appear, which is associated with a homozygous dominant genotype at the OVERO locus. Affected foals are born after the full 11-month gestation and externally appear normal, though they have all-white or nearly all-white coats and blue eyes. However, internally, these foals have a nonfunctioning colon. Within a few hours, signs of colic appear; affected foals die within a few days. Because the death is often painful, such foals are often euthanized once identified. In order to prevent the breeding of such an affected foal, it is recommended not to mate two carriers of the causative mutation in endothelin receptor type B gene.

Another disease associated with appaloosa or leopard spotting is night blindness, which is more prevalent in homozygous individuals.

In one of the types of pigment dilution (namely silver one), the occurence of multiple congenital ocular anomalies) was described.

Grey horses are proven to be more susceptible to melanoma's occurrence. The positive fact is that these horses usually only develop melanoma at an older age, the progression is slower compared to tumors in solid-colored horses, and many horses can live with melanoma for a relatively long time without any health complications.

The merle phenotype is problematic in dogs, where homozygotes (so-called double merle) are often deaf and infertile. In this context, the International Cynological Federation FCI prohibits the mating of two Merle individuals. In this case, the problem may be the so-called cryptic merle, which may not show up in the phenotype.

Furthermore, some mutations in the KIT gene can negatively affect fertility (e.g. in mice or cattle), or may even be lethal (e.g. in horses or hamsters).

Another manifestation of pleiotropy can be, for example, differences in behavior associated with certain coat color.

- Although the link between tame behavior and coat coloration is not well understood, mutations affecting receptor functions could be directly linked to both traits.
- Domestication studies on foxes, rats and minks strongly supported a close relationship between the selection for tameness and a manifestation of novel color variants.
- There is a speculated correlation between pale coat color and lower aggressiveness related to the common synthesis pathway of adrenalin and dopaquinone from DOPA.

There are several examples highlighting the correlation between coat color and temperament:

- albinos are less robust,
- horses with the cream allele are gentle and tame,
- piebald cattle, white sheep and swine are more sensitive to certain herbs,
- red Cocker Spaniels are much more nervous than other phenotypes of this breed.

To conclude this presentation:

- Artificial selection is the main factor responsible for the large phenotypic variation observed in domesticated animals.
- Selection for color phenotypes started at the beginning of domestication resulting in a significant increase of polymorphism in coat-color associated loci.
- The production and ratio of eumelanin/pheomelanin is mainly regulated by the MC1R and ASIP genes.
- Some coat-color phenotypes are associated with or linked to disorders.

At this moment I would like to thank you for your attention. If you have any questions, you can use the email listed here.