11. Analysis of genetic diseases in rabbits and chinchillas

Hello. The topic of this lecture is genetic diseases in rabbits and chinchillas. The lecture is part of Module 4, **Precision Livestock Farming**. The creation of this presentation was supported by the ERASMUS+ KA2 grant within the project ISAGREED, Innovation of Content and Structure of Study Programs in the Field of Animal Genetic and Food Resources Management Using Digitalization.

What are genetic diseases? A genetic disease occurs when mutations affect the function of genes, resulting in physical or functional deviations from the normal state with a negative impact on vitality. There are many types of genetic diseases, including monogenic, multifactorial, and chromosomal disorders.

Causes of genetic diseases include mutations and their transmission to the next generation of offspring. Genetic diseases are divided into three groups: Monogenic diseases -> mutations in one gene (on one or both chromosomes) - for example, cystic fibrosis, sickle cell anemia (mainly metabolic disorders). Multifactorial inherited diseases -> a combination of variability in many genes and the environment (quantitative, complex diseases) - heart diseases, diabetes, most types of cancer, hip dysplasia in dogs. Chromosomal diseases -> increase or decrease in the number and functions of genes through changes in the number or structural changes of chromosomes.

Genetic nature of domestic rabbits The domestic rabbit (Oryctolagus cuniculus) is one of the most recently domesticated species (probably in the last 1,500 years) and is characterized by exceptionally high phenotypic diversity - there are more than 200 breeds known worldwide. Breeds differ significantly in weight, body structure, fur type, fur color, and ear length, and this visible morphological variability exceeds the phenotypic diversity of their wild counterparts.

Normal rabbits serve as a model for studying human diseases such as hyperlipidemia and related diseases, cancer and diabetes mellitus, tuberculosis, papillomavirus infection, atherosclerosis, obesity and type II diabetes, prion diseases, lung and airway morphometry. Rabbits are used as bioreactors for the production of pharmaceutical proteins - for example, recombinant human C1 inhibitor in milk.

Transgenic/gene-edited rabbits are widely used as model organisms for biomedical research. In the last decade, more than fifty rabbit models with gene knockouts or knock-ins have been described. Rabbits have a new role as specialized tools, especially as models for imaging organs and tissues in situ and in vivo.

The genome of a rabbit according to the OryCun2.0 assembly has a size of 2.7 Gbp and contains 20,613 protein coding genes. The rabbit genome was fully sequenced for the first time in 2009.

There is a database of Mendelian traits in animals - OMIA.org. Currently, there are a total of 125 traits recorded in rabbits, out of which 75 have a proven Mendelian trait or disease, and 16 have a determined gene and causal mutation.

Some of the autosomal recessive diseases in rabbits include:

Oculocutaneous albinism type I (OCA1), TYR-related: The TYR gene (tyrosinase) located on chromosome 1. The 1118C>A substitution leads to a missense mutation (Thr>Lys) at codon

373.
Abnormal gait, retinal dysplasia, cataracts: Disrupts saltatorial locomotion. The proven gene is RORB (RAR-related orphan receptor B) located on chromosome 1, with a mutation in the same allele - g.61103503G>A (in the 5' donor site of intron 9).

Adrenal hyperplasia: Results in death immediately after birth due to hypersecretion of adrenaline. The responsible gene is CYP11A1 (cytochrome P450, family 11, subfamily A, polypeptide 1), with an ah allele - a large deletion mutation.

Long hair: Regulates hair growth. The gene is FGF5 (fibroblast growth factor 5) located on chromosome 15. There is a missense mutation, c.571T>C, p.(L191S).

Autosomal incomplete dominance: Dwarfism with the HMGA2 gene (high mobility group AT-hook 2) on chromosome 4. The dw allele is a deletion, covering approximately 12.1 kb overlapping the promoter region and the first three exons of the HMGA2 gene, resulting in gene inactivation.

Chinchilla (Chinchilla lanigera): Chinchillas are rodents belonging to the family Chinchillidae and are closely related to guinea pigs and degus. There are two species of chinchillas, Chinchilla chinchilla (short-tailed chinchilla) and Chinchilla lanigera (long-tailed chinchilla). The chinchilla genome has a total sequence length of 2.39 Gbp, with a diploid chromosome number of 64. It contains 17809 protein–coding genes.

Fur chewing: Many captive chinchillas exhibit fur chewing behavior. This behavior not only affects the fur price but can also have negative physiological and productive consequences, impacting animal welfare. The estimated heritability is $h2 = 0.16$. To reduce the occurrence of this behavior, improvement in selection and management practices used in fur-bearing animal breeding should be implemented.

Urinary stones (Urolithiasis) occur in chinchillas: The formation of stones in the urinary tract or a condition associated with the presence of these stones. There is no direct evidence that this disorder is inherited in chinchillas. However, it was included because the same disorder is undoubtedly hereditary in other species, and there is no reason to believe that the same situation does not apply to chinchillas.

Skin diseases in chinchillas include:

Fur slip: Loss of fur often occurs when handling chinchillas roughly or when they are extremely stressed. The lost fur regrows but may take some time.

Fur ring: Fur rings commonly occur in male chinchillas. A ring of fur can wrap around the penis inside the prepuce. This ring needs to be removed before it constricts blood flow to the tip of the penis. Males, especially those in breeding colonies or housed with other chinchillas, should be regularly checked.

Ringworm: Ringworm caused by Trichophyton mentagrophytes can cause alopecia in chinchillas. The most commonly affected areas are the upper part of the nose and ear flaps. Treatment for this condition often involves adding an antifungal powder to a sand bath. These conditions are also considered to have a hereditary predisposition.

Infertility is another serious condition in chinchillas. Poor reproduction can be caused by several possible factors, including malnutrition, abnormal sperm, hormonal imbalance, infectious

diseases, lack of experience, and lethal genes from inappropriate crossbreeding. For example, mating between chinchillas with the same genes for white and velvet fur color should be avoided. Infectious and dietary factors and poor overall health can also cause infertility in both male and female chinchillas.

And thank you for your attention.