12. Modern use of molecular genetics in determining the origin of dogs and cats

Hello. The topic of this lecture is using of molecular genetics in determining the origin of dogs and cats. 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.

Plant and animal domestication are rightly considered to be the main human cultural innovations, ranking in importance alongside tool production, fire control, or the development of verbal language. Animal domestication has interested biologists since the time when Charles Darwin first pointed out the parallel between evolution through natural selection and the breeding of agricultural and social animals carried out by humans. Molecular genetics can be used to determine the origin of dogs and cats.

After the appearance of the domestic dog (Canis familiaris) in archaeological finds, the domestication of crops and livestock followed soon after, allowing humans to significantly expand the food they obtained through hunting and gathering. As a result, during the Neolithic transition - archaeologically documented transition from a hunter-gatherer mode of food production to plant cultivation and animal husbandry - increasingly sophisticated agricultural societies developed in many parts of Eurasia, northern Africa, and South and Central America. The figure shows timelines of the domestication of a range of animal species, along with corresponding information on key climatic events in the last 20,000 years, which likely influenced the emergence of agriculture. The domestication of dogs was proven to have occurred around 15,000 years ago, but they accompanied humans several thousand years earlier. On the other hand, the cat is one of the youngest animal species to be domesticated, about 5,000 years ago.

The origin of dogs has been analyzed using the variability of the ASIP gene for coat color. Distinctive coat color patterns are an integral part of their diversity. It is believed that differences in color arose through mutations and artificial selection during and after domestication from wolves, but there are significant gaps in understanding how these patterns evolved and how they are genetically controlled.

Specific coat color patterns are caused by differential regulation of the Agouti (ASIP) gene, which encodes a paracrine signaling molecule and antagonist of the melanocortin 1 receptor gene (MC1R), which causes hair follicle melanocytes to switch from producing eumelanin (black or brown pigment) to producing pheomelanin (yellow to nearly white pigment). The figure shows examples of five patterns caused by regulatory deviations of the ASIP gene. Dominant yellow (DY), shaded yellow (SY), agouti (AG), black saddle (BS), and black (BB).

The canine ASIP gene has three alternative promoters and 5' non-coding exons. Structural differences within 1.5-kb segments of promoters specific for ventral (VP) and hair cycle (HCP) explain the five different coat color patterns in dogs.

Schematically, two VP haplotypes and five HCP haplotypes are indicated. The star denotes the third promoter and non-coding exon not related to the ASIP pattern. At the bottom of the figure, we can see the five types of coloration and combinations of VP and HCP haplotypes.

Yellow dogs and white wolves share an ancient haplotype of ASIP.

In picture a), genotypes at 377 SNVs (columns) at the ASIP locus in gray wolves and dogs (rows) are shown, encoded for heterozygosity (light blue), homozygosity for the reference (yellow) or alternative (dark blue) allele, or as missing genotypes (white). Alternative first exons (arrows) and nearby structural variants associated with DY (SINE insertions, green; polynucleotide expansions, orange) are included for reference. Picture b) shows the phylogeny including seven extant canid species and the dog, from 48 and 16 kb before and after the haplotype of canine pigmentation (HCP), respectively. Phylogenetic clusters of the gray wolf and dog are emphasized by squares indicating relationships consistent (blue) or inconsistent (red) with the genome-wide phylogeny. In picture d), the phylogeny represents the distinct evolutionary history of HCP derived from genetic variation in extant canids. Structural variants and derived SNVs (cyan) differentiate haplotypes of Canids (blue), Ghost lineages (red), and basic canids (black).

The evolutionary origin of ASIP haplotypes was examined by constructing phylogenetic trees using the maximum likelihood method. All dogs and gray wolves form a single cluster corresponding to known species relationships. However, in the HCP tree, dominant yellow and shaded yellow dogs form a separate cluster with Arctic gray wolves; notably, this cluster is basal to the golden jackal and distinct from other canid species.

Distribution of ASIP alleles in ancient dogs and wolves and the evolutionary model for the acquisition of dominant yellow color. ASIP haplotypes in five ancient dogs (circles), two ancient wolves (squares), and 68 modern wolves (pie charts) occurring in the Holarctic. Picture b) presents a model for the origin of the dominant yellow haplotype and its transmission to dogs and arctic wolf canids, in which molecular changes in modular promoters were acquired by introgression (red, HCP1) or mutation in gray wolves (blue, VP1).

Phylogeny of canids for VP (48 kb) and HCP (16 kb) regions. Derived substitutions shared by gray wolves and dogs (blue). Ancestral alleles on DY/Arctic wolf haplotypes (red) or BB and DY/Arctic wolf haplotypes (orange), corresponding to derived substitutions within the canid lineage. In picture b), dashed lines delineate the HCP region (chr24:23,375,800–23,380,000). The solid line denotes the lower boundary for phylogenetic analysis. Solid green and orange lines indicate the location of SINEs and 24-bp insertion associated with DY/Arctic wolf haplotype, respectively.

Segments of ASIP haplotypes. Color (red or blue) of ASIP haplotype segments indicates ancestral origin inferred from phylogenetic analysis.

Relevant structural variants near ventral (VP) and hair cycle (HCP) promoters are shown as yellow triangles (polynucleotide expansions), green bars (SINE insertions), and white bars (deletions).
Altered promoter activity is marked by a cross (no activity) or additional arrow (enhanced expression) based on RNA-seq and/or fur color derivation.

The widespread distribution of dominant yellow color in modern dog breeds from various locations, as well as in the wild domesticated dog, the dingo, frequently found in Australia, suggests that the dog originated in Southeast Asia.

Another published study indicates that the hypothesis of self-domestication can finally be rigorously tested and evaluated using high-resolution comparative genomics.

Origin of cats. Wildcats (Felis silvestris) are distributed throughout the Old World. DNA analysis suggests that cats lived alongside humans for thousands of years before they were domesticated.
During that time, their genes changed little from those of wild cats, except for one recent change: the distinctive tabby markings of domestic cats.

Surprisingly, wild and domestic cats showed no major differences in genetic makeup, and one of the few available traits by which they could be distinguished was the tabby coat markings.

The early ancestors of today's domestic cats spread from southwest Asia to Europe as early as 4400 BCE. Cats likely began to frequent agricultural communities in the Fertile Crescent about 8000 years ago, where they settled into a mutually beneficial relationship as human rodent controllers. The second lineage, consisting of African cats that dominated in Egypt, spread to the Mediterranean and the rest of the Old World around 1500 BCE. These Egyptian cats likely exhibited behavior that made them attractive to humans, such as sociability and tameness. Modern genetic analysis of nuclear short tandem repeats (STRs) and 16% of the mitochondrial DNA (mtDNA) genome in living wild and domestic cats has revealed that only one of them, the North African/Southwest Asian Felis silvestris lybica, has been ultimately domesticated.

Spatial-temporal distribution of cat maternal genealogies. Map a) showing the current distribution of the Felis silvestris species with the geographic area of each subspecies. B) mtDNA tree of the observed lines in ancient samples and modern wild and domestic cats from literature. C) Spatial-temporal representation of ancient cat haplotypes, as depicted by symbols from the tree in point b.

Spatial-temporal representation of alleles determining the phenotypic variation of tabby patterns: mackerel (Ta^M) and spotted (Ta^b). We can see that the mackerel pattern is older, and the spotted pattern appeared only after the turn of the century. The picture shows a "cat under a chair" from an ancient Egyptian painting with a typical mackerel tabby pattern, characteristic for F. silvestris lybica cats.

The domestication of cats was a complex, long-term process with extensive translocations that allowed gene flow between geographically separated cat populations at different time periods. Cats became domesticated companions of humans without changing too much. Domestic cats look similar to wild cats, but they are not solitary and can get along with humans and other cats.

This differs from dogs, the first domesticated animals. Dogs were selectively bred for specific tasks - which never applied to cats - and this selection for specific traits led to the diversification of dogs into many modern breeds.

Conclusion: The first high-resolution studies of paleogenomes of domesticated animals suggest the future of archaeogenetics of domestic animals. They aim towards studies with high resolution in time and space that will reveal the genetic structure of animal domestication and the physiological and neurobiological changes that occur when domestic and social animals come under human control and undergo long-term reproductive management and artificial selection. It is likely that high-resolution studies of pre-domesticated and early animals' paleogenomes will provide new important information about interesting features of domesticated animals and the domestication process.

Thank you for your attention.