AGRICULTURAL BIOLOGY,
2018, V. 53, № 4, pp. 659-672
(SEL'SKOKHOZYAISTVENNAYA BIOLOGIYA)

ISSN 2412-0324 (English ed. Online)
ISSN 0131-6397 (Russian ed. Print)
ISSN 2313-4836 (Russian ed. Online)

Reviews, challenges

UDC 636.012:575

doi: 10.15389/agrobiology.2018.4.659eng
doi: 10.15389/agrobiology.2018.4.659rus

GENE AND GENOMIC LEVELS OF DOMESTICATION SIGNATURE
(review)

V.I. GLAZKO

Timiryazev Russian State Agrarian University—Moscow Agrarian Academy, 49, ul. Timiryazevskaya, Moscow, 127550 Russia e-mail vigvalery@gmail.com (✉ corresponding author)
ORCID:
Glazko V.I. orcid.org/0000-0002-8566-8717
The author declares no conflict of interests
Received April 25, 2018

Abstract

Domestication is considered as a model of microevolution, problems and traits of domestication in animal species that distinguish them from closely related wild species are discussed. Data on different levels of "signature" of domestication, such as genomic, gene, protein, metabolomic, in the key genes of formation of economically valuable traits are presented. It is noted that the main differences of domesticated species from closely related wild ones are relatively high variability not only at the phenotypic level, manifested in large numbers of breeds and wide areas, but also in the population-genetic heterogenisity, as well as functional groups of genes involved in variability. The accumulated data suggest that there is a "subgenome", the increased variability of which is a source of genetic heterogeneity of domesticated animals, necessary for effective selection on economically valuable traits and adaptive potential. Literary data on the comparative analysis of the differences between SNP and CNV markers indicate that, mostly in genomic regions, in which are localized differentiating these species types the SNP and CNV markers, localized the genes which are associated with the development of the nervous and immune systems, as well as the characteristics of animal productivity in agricultural species, and involved in these processes specific genes varies depending on species, that is, similar phenotypic solutions are achieved with the involvement of different genetic systems (F.J. Alberto et al. 2018). It is known that almost half of mammalian genomes are engaged in retrotransposons (E.V. Koonin, 2016). The comparative analysis of domesticated and closely related wild species revealed differences in the relatively high density in the domesticated species the distribution of DNA fragments flanked by inverted sequences of tandem and dispersed repeats. It is proved that there is a certain contribution of transposing elements associated with a wide range of retroviral infections in the increased genetic variability of domesticated species, which can explain the unique genetic and phenotypic variability of domesticated animals.

Keywords: domestication, signature of domestication, microsatellites, dispersed repeats, endogenous retroviruses

Domestication of plants and animals is a key event in the formation of an agricultural civilization, which has almost completely forced out the civilization of hunters and foragers.

Domestication as a model of microevolution. The generally accepted definition of domestication implies a process of historic transformation of wild animals into domestic animals specifically adapted to satisfying human needs. In a negligibly short time the evolution in domestication conditions resulted in the biggest morpho-physiological changes in animals and created the species that could not have existed in nature. It is rather difficult to describe the domestication syndrome [phenotypic characteristics uniting taxonomically remote species and distinguishing them from closely related wild animals). The domestication syndrome was rather closely studied by S.N. Bogolyubskiy [1]. The weakened natural selection and introduction of human-defined parameters during selection (ethology, productivity, reproductivity) were essential during popu-

lation-specific and genetic adaptation to reproduction in the conditions of long-term domestication and breeding of different species under continued commercial selection. At the same time it is apparent that in terms of gene pool specifics, the domesticated species differ significantly from their closely related wild species. Essentially, the domesticated species are the life sustaining basis of modern civilization. All of this requires close focus on domesticated animals because only in-depth knowledge of their specific characteristics allows us to develop efficient methods of preserving and improving new genetic resources.

The genomic signatures of domestication. A series of studies (at molecular level from an organism to a population structure of a species) are dedicated to genomic differences of domesticated species from their closely related wild species ("domestication signature") of pigs [2], large and small ruminants [3, 4], horses and donkeys [5-7]. Not all domestic species have a complete set of these characteristics; however, each species has many to a certain extent. The combination of these characteristics was called the domestication syndrome.

The complexity of genomic makeup stipulates the diversification of elements selected for analysis of genomic distinction. Usually, molecular-genetic polymorphism markers of structural gene sections are used that encode the amino acid sequences of proteins (electrophoresis protein versions), non-coding sections of structural genes and various DNA sequences, the connection of which with structural genes is, as a rule, unknown. The studies analyze genomic distribution of short repeats (RAPD, ISSR, AFLP markers), microsatellite loci (tandem repeats 2-6 nucleotides long), use the data of whole-genome sequencing, compare single-nucleotide polymorphisms (SNP) and copy number variability (CNV).

Full genetic sequencing of the following species has already been performed: chicken *Gallus gallus domesticus* and ancestral species of *G. gallus* [8], pig and wild boars [9, 10], ancestral primitive bovine cattle and modern bovine cattle breeds [11], domesticated sheep and moufflon, goats and bezoar goats [4, 12], domesticated horse and Mongolian wild horse [13-15], domesticated and common rabbit [16, 17]. The basic conclusion is that most of SNP and CNV markers differentiating the domesticated and wild species fall within gene localization areas pertaining to the development of the nervous and immune systems and productivity of domesticated animals, and these genes vary depending on species, i.e., identical phenotypic effects are achieved with involvement of different genetic systems [12]. We will review some genomic domestication signature types below.

Domestication signature for milk proteins. We have analyzed the frequency of allele versions and genotypes based on genes encoding milk proteins (κ-casein, α-IS casein, β- lactoglobulin) and two key enzymes of lipid synthesis (acyl-CoA- diacylglycerol acyltransferase 1 and stearyl-CoA-desaturase 1) in dairy (black-and-white Holstein breed and Ayrshire breed) and beef (Aberdeen-Angus and Kalmyk breed) bovine cattle. In combination with analysis of literature these studies have shown that allele versions of candidate genes involved in metabolic pathways that determine the specifics of milk productivity formation in analyzed breeds do not allow reliably forecasting the quality of milk; however, allele versions of κ-casein и stearyl-CoA-desaturase 1 [18] can be used for quality forecast (micelle size and suitability for production of hard cheese, enrichment with desaturated fatty acids).

A mutation was identified in exon 4 of κ-casein gene in bovine cattle, which results in a small size of milk micelles, which is required for quality cheese production. The study of this exon in different species showed that the ratio between nonsynonymous and synonymous substitutions significantly varied both inside the family and among families [19]. In whole protein the quantity of

nonsynonymous substitutions is noticeably higher only for *Bovinae* species (0.045 versus 0.036), whereas in the other cases there were more synonymous substitutions, as is generally accepted for the evolution of protein-coding sequences [19]. At the family level, the differences in rate of divergence of this section are statistically valid only when making general comparisons for all studied *Bovinae* species and *Caprinae* species, which is indicative of a high rate of amino acid substitution in protein after divergence of these families. Its has also been found that amino acid sequence of κ-casein that corresponds to exon 4 is identical for closely related *Bos taurus* and *B. indicus* species that diverged less than 3 million years go (with the exception of 148 position substitution of *B. taurus*) and corresponds to the allele version bovine cattle B κ-casein preferable for cheese production [18, 19]. We can assume that domestication of zeboid cattle and bovine cattle emerged in different centers: the first occurred in India, the second occurred in the Mediterranean region [20, 21]. Consequently, the allele version of κ-casein B occurred after domestication of bovine cattle in the Mediterranean region and was preserved due to selection, which was more active in the European agricultural tradition than in the Indian tradition.

K-casein of C-end domain contains all sites of posttranslational phosphorylation and glycosylation [22]. The carboxyl groups are associated via glycoside O-link with threonine and serine residue of κ-casein, whereas 50% of C-domain contains residue of Thr and Ser, a part of which can also be phosphorylated. The physical properties (dimensions, solubility) and reactivity of micellar casein significantly depend on phosphorylation and glycosylation [22, 23]. During the process of *Bovinae* family formation the evolution is fastest in the gene segment corresponding to the C-end domain [19]. In *Bovinae* family, the total quantity of Thr and Ser residue in protein remains unchanged when their positions change, in other families both the quantity and position of residue remains. This can in some way explain the increase nonsynonymous and synonymous substitutions ratio in *Bovinae* cattle that we observed. By some accounts, uneven distribution of glycosylation in κ-casein C-domain can be accompanied by differences in its inhibiting *Helicobacter pylori* causing gastrointestinal diseases [23]. It can be expected that the observed fast evolution of amino acid sequence of this κ-casein section is attributable to adaptation of closely related *Bovinae* species to different pathogens. Therefore, positive selection (fast accumulation of nonsynonymous substitutions) is observed only for one section of κ-casein molecule, its C-domain, and only for *Bovinae* species in the course of their divergence during a relatively short period of time. This can possibly be attributable to breed differences in feeding that emerged after divergence (due to domestication of most researched family representatives), which triggered a need to adapt to different pathogens of the gastrointestinal tract [19].

Metabolomic domestication signatures. We have compared polymorphism for 30 loci of different protein groups in genetic pools of domesticated and closely related wild species from two orders: *Artiodactyla* (artiodactyles) and *Perissodactyla* (perissodactyle), including wild zoo species (biosphere reserves "Askania-Nova") and bovine cattle and horses from different households in Russia and Ukraine (26 species and interspecific groups, 12 species total) [24, 25]. The analysis was supplemented with population and genetic evaluation of differentiation of 18 species of soya bean (*Glycine max*) from different countries and 3 populations of wild Ussurian soybean from different regions of the Far East: *Soja ussuriensis* Moench (the presumed ancestral species of soybean). The average degree of polymorphism for analyzed loci was somewhat higher for domesticated animal species and plants. For domesticated animals this parameter varied from 0.036 (for pigs) to 0.171 (of bovine cattle), for closely related wild

species: from 0.017 (Grant's zebra *Equus quagga boehmi*) below 0.135 (*Taurotragus oryx* eland). The groups of species were distinctly differentiated in terms of contribution of different functional genetic and biochemical systems to polymorphism. For instance, the percentage of polymorphic loci in intracellular energy metabolism enzymes scaled to the number of species analyzed for domesticated representatives, was 0.179 for hollow-horned species, 0.629 for wild species, for metabolism enzymes of exogenous substrates: 0.464 and 0.193 respectively, for transport proteins: 0.357 and 0.178 [25], which means that universal difference of domesticated species from their closely related wild species lies in the increased enzyme polymorphism: for domesticated species of the substrate metabolism (associates the animal metabolome with environment substrates), for their closely related wild species: of intracellular energy metabolism (glycolysis, pentose-phosphate pathway, Krebs cycle) [26, 27]. In other words, in one case there was adaptation to broad substrate specificity, in the other case it was optimization of intracellular energy supply with a narrow substrate range.

By analyzing the biochemical markers of total metabolism in agricultural animals we may presume that there exists some connection between the intensity of form-building interspecific processes (the quantity of breeds can reflect it) and genetic genetic variability of a species. We have compared it for the "golden five" agricultural animals (goats, sheep, bovine cattle, pigs and horses). The lowest variability evaluated according to the percentage of polymorphic loci (P) and mean heterozygosity per locus per individual (H) (maximum values are listed further) were identified in goats and pigs (P is 0.03 and 0.02, respectively, H is 0.05 and 0.07), and the highest value was typical of bovine cattle (P = 0.52; H = 0.18), which corresponds to the highest number (1500 of bovine cattle breeds. For horses these parameters were somewhat lower (P = 0.4, H = 0.16). The accumulation of data is still insufficient to assert that there is a direct connection between the degree of genetic variability of biochemical markers of total metabolism key links and potential capacity of agricultural species to create new forms; however, a certain interconnection between these faxts is apparent.

Structural genes of dairy and beef productivity. The genetic pools of autochthonous displaced bovine cattle breeds are almost completely uninvestigated for commercially valuable allele versions of structural genes, which could be used directly in the modern practical selection. We have determined the occurrence rate and distribution of allele versions of six structural genes closely connected with productivity formation [18]. These are the following genes: growth hormone (GH), pituitary-specific transcription factor of growth hormones and some milk proteins (Pit-1), leptin lipid exchange hormone (LP), myostatin, the negative regulator of myogenesis and muscle tissue regeneration, for which "dual muscle system" mutations *nt821*(*del11*) of Belgian Blue cattle and *Q204X* of Piedmontese cattle were described, κ-casein (*CSN3*), the milk micelle protein, and β-lactoglobulin (*BLG*), the basic whey protein. Polymorphism of most genes was analyzed using PCR-RFLP method (amplification of structural gene fragments limited by matched pairs of flank primers with a restriction analysis of segments obtained). We arrived at a conclusion about presence of a mutation in myostatin gene by amplification product length without restrictions [26, 27]. We compared bovine cattle breeds in different breeding regions: Gray Ukrainian cattle (Kherson region, 34 animals; the Altai Territory, 32 animals); Red Polish cattle (Teropil region, 60 animals, Poland, 87 animals); White-Headed Ukrainian cattle (Sumy region, 35 animals); Brown Carpathian cattle (Ivano-Frankivsk region, 22 animals); Yakutian cattle (Novosibirsk region, 18 animals). Polymorphism of certain genes (specifically, myostatin) was studied on beef breeds (Herefords, Aberdeen-Angus, Charolais). The analysis also included wild representa-

tives of bovine subfamily (*Bovinae*): Ankole-Watusi (*Bos taurus macrocerons*), gayals (*Bibos gaurus frontalis*), aurochs (*Bison bonasus*), bisons (*Bison bison*), a representative of spiral-horned antelope subfamily (*Tragelaphinae*) canna (*Taurotragus oryx*), which are reproduced in Askania-Nova biosphere reserve [26, 27]. It turned out that allele versions associated with commercially valuable characteristics of domesticated forms almost never occur in closely related species (for instance, according to *CSN3*); moreover, as a rule, in indigenous species the rate of occurrence of such alleles is higher than in commercial breeds. At the same time, the highly productive breeds do not have complex genotypes for desirable alleles (in different genes) in spite of distinct differences between the breeds.

The analysis of interlocus associations demonstrated that linkage disequilibrium is a very irregular characteristic, which varies in different breeds and within intraspecific groups regardless of gene synteny (colocalization in the linkage group) [28]. Earlier, we have identified statistically-valid disequilibrium of locus linkage of transferrin and κ-casein (bovine cattle chromosomes 1 and 6) and lack of such disequilibrium in syntenic transferrin and ceruloplasmin (chromosome 1); disequilibrium in locus linkage of κ-casein and growth hormone in Brown Carpathian cattle (chromosomes 6 and 19), but its absence in Grey Ukrainian cattle [18]. This implies high variability of interlocus associations regardless of synteny for domestic species [29, 30]. As we have observed, in certain cases interlocus associations can be used as additional characteristic of genetic structure of species and intraspecific groups.

Genetic signature of artificial selection for variability of a complex of genomic segments (subgenome). It is still unclear whether genetic pool specifics of domestic animals (their capacity to create a great amount of genetic ensembles underlying stable morphofunctional types) are attributable to the fact that wild and domestic species differ in terms of polymorphism of different genetic systems. This assumption was made as far back as 30 years ago [24] and received a number of confirmation [31]. We analyzed the contribution made to polymorphism of a species by polymorphism of various functional protein groups [25]. For calculations we took mean heterozygosis of a species to be equal to 1 and evaluated its percentage created by polymorphism of each group. We studied primary genetic and biochemical systems used as markers of structural genes in more than 1000 animal and plant species analyzed so far [32]. These are three protein groups with different biochemical functions: the enzymes of intracellular energy metabolism, metabolism of exogenous substrates and transport proteins. By averaging the contribution of polymorphism of each group we discovered that wild and domestic animals differ by variability predominance of various genetic and biochemical systems (as is the case with morpho-physiological parameters). Which means that in case of artificial selection (unlike natural selection) the polymorphism of enzymes, associated with intracellular energy, declines, and polymorphism of enzymes that have broad specificity and metabolizing exogenous substrates increases. The varying contribution of functional protein groups in total polymorphism that we discovered in wild and domestic mammalian species correlates well with the assumptions about a link between formation of species with reorganization of cell energy supply mechanisms [24] and the factor that artificial selection (with the exception of cross-species hybridization) usually does not result in emergence of new species.

Apparently, natural selection facilitates the formation of species by supporting enzyme polymorphism of intracellular energy metabolism, and artificial selection facilitates the emergence of new forms with a high degree of adaptation to exogenous substrates. It is possible that the scope of phenotypic variation of domesticated species is connected with a variety of metabolic rates of exogenous

substrates. The latter allows us to assume that there is a subgenome, i.e. the genes encoding the systems involved in metabolism of these substrates. Its variability determines the involvement of a species in domestication and is important for broad phenotypic variety of domestic animals and is necessary for their directed breeding.

When analyzing enzyme system polymorphism of soybean breeds, populations of wild Ussurian soybean and five other species of wild soybean, all groups displayed monomorphism for 21 loci out of 42 [25]. The genetic and biochemical systems of plants were divided into two groups: enzymes involved in the creation of adenosine triphosphate in a cell (glycolysis, Krebs cycle), i.e. those involved in glucose metabolism (G), and the rest of the enzymes not involved in metabolism (NG). The analysis covered 21 enzyme loci of each group. Seven polimorphic loci were identified in the population of wild species, including one NG locus (ESTD-1) and 6 G loci. All in all 19 loci were identified for soybean breeds (11 for G, 8 fpr NG). Up to 86% polymorphic loci of wild soybean participate in controlling the intracellular energy metabolism, which is only 58% for domestic soybean; moreover, there were 3 times more (42%) of polymorphic loci non involved in glucose metabolism than for wild species (similar was observed for domestic animals). Consequently, we can assume that plants also have a subgenome involved in regulating the links between the internal and external biochemical environments via metabolism enzymes of exogenous substrates and transport protein.

The scope of genetic variability for *G. max* is larger than for *G. soja* (the percentage of polimorphic loci P is 45 and 17%), which means that a domesticated species is more polimorphic than its closely related wild species [25-27]. The interspecific genetic distances (DN) constituted from 0.059 to 0.129 and from 0.038 to 0.264 respectively. Consequently, for soybean the interspecific differentiation of breeds is comparable with the interspecific differentiation of populations of a closely related wild species.

Therefore, domesticated breeds have a higher protein variability that determines the metabolic link with the environment, and control of intracellular energy transformation is more stable. The comparison of electrophoretic protein (enzyme) versions allows us to accentuate the domestication characteristics related to a relatively high polymorphism of genetic and biochemical systems controlling the exogenous substrate metabolism (and transportation proteins for animals).

Genomic signature of artificial selection. The transition to polylocus genome genotyping and scanning (from analysis of several hundreds markers to complete sequencing) is the primary characteristic of modern population genomics [33].

The application of RAPD markers (randomly amplificated polymorphic DNA) is restricted to the ability of PCR-amplification of DNA segments flanked by inverted decanucleotid repeats [34]. Not every nucleotide sequence in inverted in a genome with high frequency and can be used as primer. For interspecies and intraspecies studies of *Equidae* family members, UBS-85 and UBS-126E primers are suggested [35]. With these primers we identified the largest similarity of domestic horse and bovine cattle (grouped in a separate dendrogram cluster) 7 wild and 2 domesticated species of artiodactyles and perissodactyles. These data can be construed as a confirmation of a certain similarity in genome variability of domesticated species [36, 37].

The ISSR analysis (inter-simple sequence repeat) allows increasing the accuracy of annealing. The products of ISSR-amplification contain an inverted microsatellite primer sequence on their flanks, and the resulting fingerprint is usually reproduced better than in RAPD [38-42], whereas the identified polymorphism is higher. The amplification is conducted with one or several primers of 15-24 nu-

cleotides in length [38] consisting of short tandem repeats (2-4 nucleotides) and one selective nucleotide at 3′-end. The microsatellite sequences surround many genes [38] and can be used for them as anchor sequences. Both RAPD and ISSR do not require preliminary cloning and sequencing for primer selection [38-42]. When using 3 dinucleotide and 12 trinucleotide ISSR-PCR primers, 310 amplicons [25-27] were identified for 11 domesticated and wild species, and short amplicons were reliably more frequent in domesticated species.

In IRAP-PCR (inter-retrotransposon amplified polymorphism) [38], a segment between the primers is amplified, which are complementary to two adjacent retrotransposons (typically these are segments of long terminal repeats of LTR endogenous retroviruses) in alternative DNA chains with REMAP-PCR (retrotransposon-microsatellite amplified polymorphism) located between the primers for LTR retrotransposon fragment and next to the located simple microsatellite repeat acting as an anchor (SSR-primer) [43, 44]. In REMAP and IRAP, the primers for 3′- and 5′-end LTR are used. Some retrotransposons (for instance, BARE-1) are distributed along the genome length relatively evenly [43, 44], some short retrotransposons, such as MITE, are rather often localized near coding sequences [45]. The REMAP markers can be useful when studying genomic singularity of domestication: they are flanked with a microsatellite sequence, therefore it is more probable that amplified fragments are evenly distributed in chromosomes and are not clustered in the areas of retrotransposon concentrations [46].

The retrotransposons are closely connected with microsatellites, for instance, in bovine cattle genome [47]. The endogenous retroviruses are very common in genomes of main domesticated species [48, 49]. Interestingly, retrotransposons resulted in significant intragenomic differentiation of laboratory murine lines with different sources (C57BL and BALB) during a relatively short period of time (a little more than 100 years) [50, 51]. The usage of one retrotransposon (Alu) was described (due to its wide occurrence) for human genome scanning [52, 53].

The study of species-specific ISSR-PCR marker formations using ancient Altai horse breed as an example has shown [46] that genomic fragment with the size of 416 nucleotide pairs flanked by an inverted repeat $(AG)_9C$ was formed as a result of recombination between ancient mobile elements (fish DNA transposon and LTR ERV3, which is typical for many mammals) and ERV1 endogenous retrovirus sequence specific for horse genome. In Altai horse DNA the segment with the size of 235 nucleotide pairs had homology only with domestic horse ERV1, which is indicative of its apparent later origin than, for instance, homology segment with LTR ERV3. The high correlation ($r = 0.9$) between integration frequency of endogenous retrovirus sequences with the size of 235 nucleotide pairs and chromosome length points to the fact that domestic horse undergoes further transpositions, recombination and evolution of endogenous retrovirus sequences. Similar correlations between integration frequency of segments of endogenous retrovirus sequences and chromosome length were observed in bovine cattle genome [54]. These integration regions are often depleted with CG sequences and enriched with AT [54]. The relatively even distribution over horse chromosome length is also described for segments homological to a fragment of long end repeated sequence of ERV3 beta1 endogenous retrovirus [55]. It was argued that spread of retrovirus end repeated sequence (in absence of more than one full-size copy of the latter) can occur according to the following pattern: at first the endogenous retrovirus integrates in the genome on a wide scale with subsequent exposure of most formed copies leaving traces of multiple iterations in the form of small terminal sequences [55]. Significant homology has been observed between EqERV beta1 of domestic horse and unclassified endogenous retrovirus in

bovine cattle genome and MMTV murine retrovirus – the phylogenetic ancestor of viruses of hoofed mammals; therefore, we can expect that both studied species were first infected with murine virus [55]. In the course of transposition and recombination the descendants of endogenous retroviruses can cause explosive outbreaks of mutational variability. Now therefore, the assumption that the genomic elements associated with such highly variable nucleotide sequences could particularly be involved in a wide-scale phenotypic variation characteristic of domesticated species seems only logical.

The nucleotide sequence of endogenous retrovirus make a significant contribution to the families of endogenous retrovirus, fragments of which and products of recombination of which with other mobile elements constitute an almost the main part of dispersed repeats of mammal genomes [49, 54, 56]. Detailed databases have been created containing full-size endogenous retrovirus available in genomes of primary domesticated mammals [49]. The horizontal transfer of some retrotransposones that unites the genomes of taxonomically remote species [57, 58] was described and its essential role in the evolution of vertebrates is being discussed [59]. The viruses and mobile genetic elements are thought of as drivers of evolution [60]. A close link between microsatellites and retrotransposones is known [61-63]. In our studies we have shown that in genomic DNA fragments flanked by inverted repeats of microsatellite loci segments both in horses and bovine cattle the frequency of recombination predominantly among retrotransposones is high [64, 65].

Now, therefore, it is apparent that in most cases the studied phenotypic characteristics and relevant gene systems are linked with species-specific commercially valuable characteristics. It was Charles Darwin who thought of domestication processes as accelerated evolution under the influence of artificial selection [66]; however, there is still no clear definition of what domestication really means and what are its genetic mechanisms. Some researchers suggest viewing domestication as a result of interactions stable in many generations, when one species significantly affects the reproduction and survival of the other [67]. One of the conditions of transformation of a wild animal in a domestic animal is reproduction under any conditions of maintenance, feeding, space constraints, reduced motor activity and adaptation to human presence. This is due to the change of animal behavior – one of the first and brightest domestication results. In fact, domestic animals differ from wild animals primarily by its reaction to humans. In other words, domestication is a coevolution process (in essence, symbiosis), when the population adapts to anthropogenic environment by combining genetic changes.

The modern concept of phenotypic variation describes the manifestation of characteristics as a result of interaction of a genotype and factors affecting the realization of genetic information (the maintenance and reproduction conditions, microbiome, pollutants and pathogens). This process is exercised at different interdependent levels (transcriptome, proteome, metabolome, microbiome) creating nonlinear links (for instance, singular changes in transcriptome can result in multiple changes in metabolome, and vice versa); moreover, direct impact of environmental factors is possible at each level [68, 69].

The varying impact of enzymes of intracellular energy metabolism observed by us, and exogenous substrate metabolism in total polymorphism of wild and domestic mammal species correlates well with the absence of formation of species during selection and its link with reorganization of energy supply of cells during evolution. By taking into account the specificity of selection and the choice of livestock population, the similarity of protein polymorphism of wild and domestic animals is unexpected, especially since allozyme divergence in

wild species is linked to formation of species, whereas in domestic animals it is linked solely to high morpho-physiological variability. Consequently, natural and artificial selection should have different impact on polymorphism of different genetic and biochemical systems and not on overall scope of genetic variability. We have confirmed this hypothesis by comparing the contribution of protein functional group polymorphism to the total genetic variability of wild and domestic species.

As it turns out, the domestic species are significantly more uniform than wild species in terms of polymorphism of certain biochemical markers, such as transferrin, esterase, diaphorase, acid phosphatase, catalase and albumin [24]. This also supports the hypothesis about dissimilar impact of natural and artificial selection on genetic variability due to impact on different metabolic links, which results in polymorphism of various biochemical markers.

Presumably the expansion of habitat of domesticated species migrating alongside humans increased the number of contacts with retroviruses and resulted in emergence of new transposable elements in the genome. By inhibiting recurrent infections they preserved in the course of natural selection and at the same time increased genetic variability (insertion mutagenesis, recombination processes) causing mutations essential for artificial selection. Please note that a link between the emergence of allele versions essential for selection distinguishing domesticated species from closely related wild species, as well as integration of mobile genetic elements in coding sequences [31] was observed in many studies. The involvement of transposable elements in genome divergence of closely related and wild species could explain some empirical data, for instance, the accelerated rate of evolution of a number of genetic elements in genomes of domesticated species [31] and higher frequency of occurrence of short fragments of genome DNA flanked by inverted repeats in domesticated cavicornians than in closely related wild species [27].

To summarize, the findings point to the fact that animal and plant species have characteristics of domestication that differ them from their closely related wild species not only at the level of complexes of phenotypic characteristics, but also in terms of polymorphism of structural genes encoding the proteins and enzymes, and in terms of occurrence of invested repeats of microsatellite loci, mobile genetic elements and segment duplications in the genome. We can anticipate that common retroviral infections can be one of the mechanisms behind such differences. In order to describe the common and specific genetic make-ups of domestication we need to identify the source of unique genetic variability of domesticated species that display increased variability of total metabolism (with identical scale of genetic and biochemical variance) defining the link between biochemical processes in internal and external environments, genetic systems of intracellular energy transformation control are more stable (glycolysis, Krebs cycle). We can expect that the systems involved in exogenous substrate metabolism are coded by the genes of "subgenome," the variability of which is linked to phenotypic flexibility and determines the possibility of involving a species in domestication.

REFERENCES

1. Bogolyubskii S.N. *Proiskhozhdenie i preobrazovanie domashnikh zhivotnykh* [The origin and transformation of domestic animals]. Moscow, 1959 (in Russ.).
2. Wang K., Wu P., Yang Q., Chen D., Zhou J., Jiang A., Ma J., Tang Q., Xiao W., Jiang Y., Zhu L., Li X., Tang G. Detection of selection signatures in Chinese Landrace and Yorkshire pigs based on genotyping-by-sequencing data. *Front. Genet.,* 2018, 9: 119 (doi: 10.3389/fgene.2018.00119).

3. Upadhyay M., da Silva V.H., Megens H.J., Visker M.H.P.W., Ajmone-Marsan P., Bâlteanu V.A., Dunner S., Garcia J.F., Ginja C., Kantanen J., Groenen M.A.M., Crooijmans R.P.M.A. Distribution and functionality of copy number variation across European cattle populations. *Front. Genet.*, 2017, 8: 108 (doi: 10.3389/fgene.2017.00108).
4. Alberto F.J., Boyer F., Orozco-terWengel P., Streeter I., Servin B., de Villemereuil P., Benjelloun B., Librado P., Biscarini F., Colli L., Barbato M., Zamani W., Alberti A., Engelen S., Stella A., Joost S., Ajmone-Marsan P., Negrini R., Orlando L., Rezaei H.R., Naderi S., Clarke L., Flicek P., Wincker P., Coissac E., Kijas J., Tosser-Klopp G., Chikhi A., Bruford M.W., Taberlet P., Pompanon F. Convergent genomic signatures of domestication in sheep and goats. *Nat. Commun.,* 2018, 9(1): 813 (doi: 10.1038/s41467-018-03206-y).
5. Renaud G., Petersen B., Seguin-Orlando A., Bertelsen M.F., Waller A., Newton R., Paillot R., Bryant N., Vaudin M., Librado P., Orlando L. Improved de novo genomic assembly for the domestic donkey. *Sci. Adv.*, 2018, 4(4): eaaq0392 (doi: 10.1126/sciadv.aaq0392).
6. Gaunitz C., Fages A., Hanghшj K., Albrechtsen A., Khan N., Schubert M., Seguin-Orlando A., Owens I.J., Felkel S., Bignon-Lau O., de Barros Damgaard P., Mittnik A., Mohaseb A.F., Davoudi H., Alquraishi S., Alfarhan A.H., Al-Rasheid K.A.S., Crubézy E., Benecke N., Olsen S., Brown D., Anthony D., Massy K., Pitulko V., Kasparov A., Brem G., Hofreiter M., Mukhtarova G., Baimukhanov N., Lxugas L., Onar V., Stockhammer P.W., Krause J., Boldgiv B., Undrakhbold S., Erdenebaatar D., Lepetz S., Mashkour M., Ludwig A., Wallner B., Merz V., Merz I., Zaibert V., Willerslev E., Librado P., Outram A.K., Orlando L. Ancient genomes revisit the ancestry of domestic and Przewalski's horses. *Science,* 2018, 360(6384): 111-114 (doi: 10.1126/science.aao3297).
7. Librado P., Gamba C., Gaunitz C., Der Sarkissian C., Pruvost M., Albrechtsen A., Fages A., Khan N., Schubert M., Jagannathan V., Serres-Armero A., Kuderna L.F.K., Povolotskaya I.S., Seguin-Orlando A., Lepetz S., Neuditschko M., Thèves C., Alquraishi S., Alfarhan A.H., Al-Rasheid K., Rieder S., Samashev Z., Francfort H.P., Benecke N., Hofreiter M., Ludwig A., Keyser C., Marques-Bonet T., Ludes B., Crubézy E., Leeb T., Willerslev E., Orlando L. Ancient genomic changes associated with domestication of the horse. *Science*, 2017, 356(6336): 442-445 (doi: 10.1126/science.aam5298).
8. Rubin C.J., Zody M.C., Eriksson J., Meadows J.R., Sherwood E., Webster M.T., Jiang L., Ingman M., Sharpe T., Ka S., Hallböök F., Besnier F., Carlborg O., Bed'hom B., Tixier-Boichard M., Jensen P., Siegel P., Lindblad-Toh K., Andersson L. Whole-genome resequencing reveals loci under selection during chicken domestication. *Nature*, 2010, 464(7288): 587-591 (doi: 10.1038/nature08832).
9. Frantz L.A., Schraiber J.G., Madsen O., Megens H.J., Cagan A., Bosse M. Paudel Y., Crooijmans R.P., Larson G., Groenen M.A. Evidence of long-term gene flow and selection during domestication from analyses of Eurasian wild and domestic pig genomes. *Nat. Genet.*, 2015, 47(10): 1141-1148 (doi: 10.1038/ng.3394).
10. Paudel Y., Madsen O., Megens H.J., Frantz L.A., Bosse M., Bastiaansen J.W., Crooijmans R.P., Groenen M.A. Evolutionary dynamics of copy number variation in pig genomes in the context of adaptation and domestication. *BMC Genomics*, 2013, 14: 449 (doi: 10.1186/1471-2164-14-449).
11. Park S.D., Magee D.A,. McGettigan P.A., Teasdale M.D., Edwards C.J., Lohan A.J., Murphy A., Braud M., Donoghue M.T., Liu Y., Chamberlain A.T., Rue-Albrecht K., Schroeder S., Spillane C., Tai S., Bradley D.G., Sonstegard T.S., Loftus B.J., MacHugh D.E. Genome sequencing of the extinct Eurasian wild aurochs, *Bos primigenius*, illuminates the phylogeography and evolution of cattle. *Genome Biol.*, 2015, 16: 234 (doi: 10.1186/s13059-015-0790-2).
12. Zamani W., Ghasempouri S.M., Rezaei H.R., Naderi S., Hesari A.R.E., Ouhrouch A. Comparing polymorphism of 86 candidate genes putatively involved in domestication of sheep, between wild and domestic Iranian sheep. *Meta Gene*, 2018, 17: 223-231 (doi: 10.1016/j.mgene.2018.06.015).
13. Der Sarkissian C., Ermini L., Schubert M., Yang M.A., Librado P., Fumagalli M., Jynsson H., Bar-Gal G.K., Albrechtsen A., Vieira F.G., Petersen B., Ginolhac A., Seguin-Orlando A., Magnussen K., Fages A., Gamba C., Lorente-Galdos B., Polani S., Steiner C., Neuditschko M., Jagannathan V., Feh C., Greenblatt C.L., Ludwig A., Abramson N.I., Zimmermann W., Schafberg R., Tikhonov A., Sicheritz-Ponten T., Willerslev E., Marques-Bonet T., Ryder O.A., McCue M., Rieder S., Leeb T., Slatkin M., Orlando L. Evolutionary genomics and conservation of the endangered Przewalski's horse. *Curr. Biol.*, 2015, 25(19): 2577-2583 (doi: 10.1016/j.cub.2015.08.032).
14. Librado P., Fages A., Gaunitz C., Leonardi M., Wagner S., Khan N., Hanghшj K., Alquraishi S.A., Alfarhan A.H., Al-Rasheid K.A., Der Sarkissian C., Schubert M., Orlando L. The evolutionary origin and genetic makeup of domestic horses. *Genetics*, 2016, 204(2): 423-434 (doi: 10.1534/genetics.116.194860).
15. Wutke S., Sandoval-Castellanos E., Benecke N., Döhle H.J., Friederich S., Gonzalez J., Hofreiter M., Lxugas L., Magnell O., Malaspinas A.S., Morales-Muciz A., Orlando L., Reissmann M., Trinks A., Ludwig A. Decline of genetic diversity in ancient domestic stallions in Europe. *Sci. Adv.*, 2018, 4(4): eaap9691 (doi: 10.1126/sciadv.aap9691).
16. Carneiro M., Rubin C.J., Di Palma F., Albert F.W., Alföldi J., Martinez Barrio A., Pielberg G.,

Rafati N., Sayyab S., Turner-Maier J., Younis S., Afonso S., Aken B., Alves J.M., Barrell D., Bolet G., Boucher S., Burbano H.A., Campos R., Chang J.L., Duranthon V., Fontanesi ., Garreau H., Heiman D., Johnson J., Mage R.G., Peng Z., Queney G., Rogel-Gaillard C., Ruffier M., Searle S., Villafuerte R., Xiong A., Young S., Forsberg-Nilsson K., Good J.M., Lander E.S., Ferrand N., Lindblad-Toh K., Andersson L. Rabbit genome analysis reveals a polygenic basis for phenotypic change during domestication. *Science*, 2014, 345(6200): 1074-1079 (doi: 10.1126/science.1253714).

17. Irving-Pease E.K., Frantz L.A.F., Sykes N., Callou C., Larson G. Rabbits and the specious origins of domestication. *Trends Ecol. Evol.*, 2018, 33(3): 149-152 (doi: 10.1016/j.tree.2017.12.009).
18. Glazko V.I., Andreichenko I.N., Kovalchuk S.N., Glazko T.T., Kosovsky G.Yu. Candidate genes for control of cattle milk production traits. *Russian Agricultural Sciences*, 2016, 42(6): 458-464 (doi: 10.3103/S1068367416060082).
19. Glazko V., Zybaylov B., Glazko T. Domestication and genome evolution. *International Journal of Genetics and Genomics,* 2014, 2(4): 47-56 (doi: 10.11648/j.ijgg.20140204.11).
20. Msalya G., Kim E.S., Laisser E.L., Kipanyula M.J., Karimuribo E.D., Kusiluka L.J., Chenyambuga S.W., Rothschild M.F. Determination of genetic structure and signatures of selection in three strains of Tanzania shorthorn zebu, boran and friesian cattle by genome-wide SNP analyses. *PLoS ONE*, 2017, 12(1): e0171088 (doi: 10.1371/journal.pone.0171088).
21. Upadhyay M.R., Chen W., Lenstra J.A., Goderie C.R., MacHugh D.E., Park S.D., Magee D.A., Matassino D., Ciani F., Megens H.J., van Arendonk J.A., Groenen M.A., European Cattle Genetic Diversity Consortium; RPMA Crooijmans. Genetic origin, admixture and population history of aurochs (*Bos primigenius*) and primitive European cattle. *Heredity* (Edinb), 2017, 118(2): 169-176 (doi: 10.1038/hdy.2016.79).
22. Khaldi N., Shields D.C. Shift in the isoelectric-point of milk proteins as a consequence of adaptive divergence between the milks of mammalian species. *Biology Direct*, 2011, 6(1): 40-49 (doi: 10.1186/1745-6150-6-40).
23. Strömqvist M., Falk P., Bergstrцm S., Hansson L., Lцnnerdal B., Normark S., Hernell O. Human milk kappa-casein and inhibition of Helicobacter pylori adhesion to human gastric mucosa. *J. Pediatr. Gastroenterol. Nutr.*, 1995, 21(3), 288-296.
24. Glazko V.I. An attempt at understanding the genetic basis of domestication. *Animal Science Papers and Reports,* 2003, 21(2): 109-120.
25. Glazko V.I., Glazko T.T. Domestication and N.I. Vavilov's law of homologous series in hereditary variability. *Russian Agricultural Sciences*, 2013, 39(1): 8-12 (doi: 10.3103/S1068367413010072).
26. Glazko V., Zybaylov B., Glazko T. Domestication and genome evolution. *International Journal of Genetics and Genomics*, 2014, 2(4): 47-56 (doi: 10.11648/j.ijgg.20140204.11).
27. Glazko V., Zybailov B., Glazko T. Asking the right question about the genetic basis of domestication: what is the source of genetic diversity of domesticated species? *Adv. Genet. Eng.*, 2015, 4: 2 (doi: 10.4172/2169-0111.1000125).
28. Aliloo H., Pryce J.E., González-Recio O., Cocks B.G., Hayes B.J., Validation of markers with non-additive effects on milk yield and fertility in Holstein and Jersey cows. *BMC Genet.,* 2015, 16: 89 (doi: 10.1186/s12863-015-0241-9).
29. Flori L., Fritz S., Jaffrézic F., Boussaha M., Gut I., Heath S., Foulley J.L., Gautier M. The genome response to artificial selection: a case study in dairy cattle. *PLoS ONE*, 2009, 4(8): e6595 (doi: 10.1371/journal.pone.0006595).
30. Zhao F., McParland S., Kearney F., Du L., Berry D.P. Detection of selection signatures in dairy and beef cattle using high-density genomic information. *Genet. Sel. Evol.*, 2015, 47: 49 (doi: 10.1186/s12711-015-0127-3).
31. Feng X., Jiang J., Padhi A., Ning C., Fu J., Wang A., Mrode R., Liu J.-F. Characterization of genome-wide segmental duplications reveals a common genomic feature of association with immunity among domestic animals. *BMC Genomics*, 2017, 18: 293 (doi: 10.1186/s12864-017-3690-x).
32. Nevo E. Evolution of genome-phenome diversity under environmental stress. *PNAS USA*, 2001, 98(11): 6233-6240 (doi: 10.1073/pnas.101109298).
33. Nosil P., Funk D.J., Ortiz-Barrientos D. Divergent selection and heterogeneous genomic divergence. *Mol. Ecol.*, 2009, 18: 375-402 (doi: 10.1111/j.1365-294X.2008.03946.x).
34. Owuor E.D., Fahima T., Beharav A., Korol A., Nevo E. RAPD divergence caused by microsite edaphic selection in wild barley. *Genetica*, 1999, 105(2): 177-192 (doi: 10.1023/A:1003781711908).
35. Bailey E., Lear T.L. Comparison of Thoroughbred and Arabian horses using RAPD markers. *Animal Genetics*, 1994, 25(Suppl. 1): 105-108 (doi: 10.1111/j.1365-2052.1994.tb00414.x).
36. Glazko V.I., Zelenaia L.B. Differentiation of domestic horse and Przewalski's horse using various DNA sequences. *Genetika,* 1998, 34(7): 996-999.
37. Glazko V.I., Dyman' T.N., Tarasiuk S.I., Dubin A.V. The polymorphism of proteins, RAPD-PCR and ISSR-PCR markers in European and American bison and cattle. *Cytol. Genet.*, 1999, 33(6): 30-39.
38. Zietkiewicz E., Rafalski A., Labuda D. Genome fingerprinting by simple sequence repeat (SSR)-anchored polymerase chain reaction amplification. *Genomics*, 1994, 20(2): 176-183 (doi:

10.1006/geno.1994.1151).
39. Rychlik W., Spencer W.J., Rhoads R.E. Optimization of the annealing temperature for DNA amplification in vitro. *Nucleic Acids Res.*, 1990, 18(21): 6409-6412
40. Shiue Y.L., Bickel L.A., Caetano A.R., Millon L.V., Clark R.S., Eggleston M.L., Michelmore R., Bailey E., Guérin G., Godard S., Mickelson J.R., Valberg S.J., Murray J.D., Bowling A.T. A synteny map of the horse genome comprised of 240 microsatellite and RAPD markers. *Animal Genetics*, 1999, 30(1): 1-9 (doi: 10.1046/j.1365-2052.1999.00377.x).
41. Sulima Iu.Iu., Kalendar' R.N., Sivolap Iu.M. The mapping of the barley genome by RAPD analysis using double haploid strains. *Cytol. Genet.*, 2000, 34(4): 41-49.
42. Owuor E.D., Fahima T., Beharav A., Korol A., Nevo E. RAPD divergence caused by microsite edaphic selection in wild barley. *Genetica*, 1999, 105(2):177-192.
43. Kalendar R., Schulman A.H. Transposon-based tagging: IRAP, REMAP, and iPBS. *Methods Mol. Biol.*, 2014, 1115: 233-255 (doi: 10.1007/978-1-62703-767-9_12).
44. Tomás D., Rodrigues J., Varela A., Veloso M.M., Viegas W., Silva M. Use of repetitive sequences for molecular and cytogenetic characterization of *Avena* species from Portugal. *Int. J. Mol. Sci.*, 2016, 17(2): E203 (doi: 10.3390/ijms17020203).
45. Shirasu K., Schulman A.H., Lahaye T., Schulze-Lefert P. A contiguous 66-kb barley DNA sequence provides evidence for reversible genome expansion. *Genome Res.*, 2000, 10(7): 908-915 (doi: 10.1101/gr.10.7.908).
46. Glazko V.I., Gladyr E.A., Feofilov A.V., Bardukov N.V., Glazko T.T. ISSR-PCR markers and mobile genetic elements in genomes of agricultural mammal species. *Agricultural Biology,* 2013, 2: 71-76 (doi: 10.15389/agrobiology.2013.2.71eng).
47. The Bovine Genome Sequencing and Analysis Consortium, Elsik C.G., Tellam R.L., Worley K.C. The genome sequence of taurine cattle: a window to ruminant biology and evolution. *Science,* 2009, 324(5926) 522-528 (doi: 10.1126/science.1169588).
48. Garcia-Etxebarria K., Jugo B.M. Evolutionary history of bovine endogenous retroviruses in the *Bovidae* family. *BMC Evolutionary Biology*, 2013, 13: 256 (doi: 10.1186/1471-2148-13-256).
49. Garcia-Etxebarria K., Sistiaga-Poveda M., Jugo B.M. Endogenous retroviruses in domestic animals. *Current Genomics,* 2014, 15(4): 256-265 (doi: 10.2174/1389202915666140520003503).
50. Zhang Y., Maksakova I.A., Gagnier L., van de Lagemaat L.N., Mager D.L. Genome-wide assessments reveal extremely high levels of polymorphism of two active families of mouse endogenous retroviral elements. *PLoS Genet.*, 2008, 4(2): e1000007 (doi: 10.1371/journal.pgen.1000007).
51. Nelleker C., Keane T.M., Yalcin B., Wong K., Agam A., Belgard T.G., Flint J., Adams D.J., Frankel W.N., Ponting C.P. The genomic landscape shaped by selection on transposable elements across 18 mouse strains. *Genome Biol.*, 2012, 13(6): R45 (doi: 10.1186/gb-2012-13-6-r45).
52. Mei L., Ding X., Tsang S.Y., Pun F.W., Ng S.K., Yang J., Zhao C., Li D., Wan W., Yu C.H., Tan T.C., Poon W.S., Leung G.K., Ng H.K., Zhang L., Xue H. AluScan: a method for genome-wide scanning of sequence and structure variations in the human genome. *BMC Genomics*, 2011, 12: 564 (doi: 10.1186/1471-2164-12-564).
53. Yang J.F., Ding X.F., Chen L., Mat W.K., Xu M.Z., Chen J.F., Wang J.M., Xu L., Poon W.S., Kwong A., Leung G.K., Tan T.C., Yu C.H., Ke Y.B., Xu X.Y., Ke X.Y., Ma R.C., Chan J.C., Wan W.Q., Zhang L.W., Kumar Y., Tsang S.Y., Li S., Wang H.Y., Xue H. Copy number variation analysis based on AluScan sequences. *Journal of Clinical Bioinformatics*, 2014, 4(1): 15 (doi: 10.1186/s13336-014-0015-z).
54. Garcia-Etxebarria K., Jugo B.M. Genome-wide detection and characterization of endogenous retroviruses in *Bos taurus*. *J. Virol.*, 2010, 84(20): 10852-10862 (doi: 10.1128/JVI.00106-10).
55. Van der Kuyl A.C. Characterization of a full-length endogenous beta-retrovirus, EqERV-Beta1, in the genome of the horse (*Equus caballus*). *Viruses,* 2011, 3(6): 620-628 (doi: 10.3390/v3060620).
56. Garcia-Etxebarria K., Jugo B.M. Genomic environment and digital expression of bovine endogenous retroviruses. *Gene*, 2014, 548(1): 14-21 (doi: 10.1016/j.gene.2014.06.048).
57. Oliveira S.G., Bao W., Martins C., Jurka J. Horizontal transfers of Mariner transposons between mammals and insects. *Mob DNA*, 2012, 3(1): 14 (doi: 10.1186/1759-8753-3-14).
58. Walsha A.M., Kortschaka R.D., Gardnerb M.G., Bertozzi T., Adelson D.L. Widespread horizontal transfer of retrotransposons. *PNAS USA*, 2013, 110(3): 1012-1016 (doi: 10.1073/pnas.1205856110).
59. Chalopin D., Naville M., Plard F., Galiana D., Volff J.N. Comparative analysis of transposable elements highlights mobilome diversity and evolution in Vertebrates. *Genome Biol. Evol.*, 2015, 7(2): 567-580 (doi: 10.1093/gbe/evv005).
60. Koonin E.V. Viruses and mobile elements as drivers of evolutionary transitions. *Phil. Trans. R. Soc. B*, 2016, 371(1701): 20150442 (doi: 10.1098/rstb.2015.0442).
61. Ahmed M., Liang P. Transposable elements are a significant contributor to tandem repeats in the human genome. *Comp. Funct. Genom.*, 2012, 2012: Article ID 947089 (doi: 10.1155/2012/947089).
62. Behura S.K., Severson D.W. Association of microsatellite pairs with segmental duplications in

insect genomes. *BMC Genomics*, 2013, 14: 907 (doi: 10.1186/1471-2164-14-907).
63. Sharma A., Wolfgruber T.K., Presting G.G. Tandem repeats derived from centromeric retrotransposons. *BMC Genomics*, 2013, 14: 142 (doi: 10.1186/1471-2164-14-142).
64. Bardukov N.V., Feofilov A.V., Glazko T.T., Glazko V.I. ISSR-PCR markers and mobile genetic elements in horse (*Equus caballus*) genome. *Agricultural Biology*, 2014, 4: 42-57 (doi: 10.15389/agrobiology.2014.4.42eng).
65. Glazko V., Kosovsky G., Glazko T. High density of transposable elements in sequenced sequences in cattle genomes, associated with AGC microsatellites. *Global Advanced Research Journal of Agricultural Science*, 2018, 7(2): 034-045.
66. Darvin Ch. *Izmeneniya domashnikh zhivotnykh i kul'turnykh rastenii. Tom 4* [Changes in domestic animals and cultivated plants. V. 4]. Moscow-Leningrad, 1951 (in Russ.).
67. Zeder M.A. Core questions in domestication research. *PNAS USA*, 2015, 112(11): 3191-3198 (doi: 10.1073/pnas.1501711112).
68. Ibeagha-Awemu E.M., Zhao X. Epigenetic marks: regulators of livestock phenotypes and conceivable sources of missing variation in livestock improvement programs. *Front. Genet.,* 2015, 6: 302 (doi: 10.3389/fgene.2015.00302).
69. Te Pas M.F.W., Madsen J., Calus M.P.L., Smits M.A. The importance of endophenotypes to evaluate the relationship between genotype and external phenotype. *Int. J. Mol. Sci.*, 2017, 18(2): 472 (doi: 10.3390/ijms18020472).