

SHORT TANDEM REPEATS (STR) IN CATTLE GENOMICS AND BREEDING

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Review paper

Abstract: Molecular markers are essential tool for determining the specific genetic makeup of an individual and are valuable approach for genetic improvement of farm animals. In cattle breeding their application is useful for improvement of breeding programs for desired traits, better productivity and high quality products. These markers provide more accurate genetic information and better knowledge of the animal genetic resources. In this review we attempt to make a brief summary on the application of one of more advanced DNA-based molecular markers in cattle breeding, namely short tandem repeat (STR, microsatellites).

Keywords: molecular markers, STR, microsatellites, genome, polymorphism, breeding, cattle

Introduction

In the middle of the last century the use of blood groups and enzymes were beneficial for studying the animal genetics. The first molecular markers used in livestock were the protein polymorphisms. Later the proteins such as hemoglobin and transferrin were involved in all studies. Most of the conducted studies for genetic variation were based on allozyme protein markers. During the 1970's a large number of studies have been documented to be useful tool in characterization of blood group and allozyme systems in livestock (*Hanotte and Janlin, 2005*). At the University of Wisconsin, Irwin and co-workers used blood group antigens for parentage verifications in the Holstein Friesians (*Hines, 1999*). Stormont studied

the blood group systems in cattle in the 1950's (*Hines, 1999*) and concluded that the blood groups are powerful tool in the recognition of incorrect parentage (*Brenig and Schütz, 2016*). Later due to intensive inbreeding and a lot of mistakes in pedigree information and incorrect relationships between the animal blood groups and proteins become uninformative (*Adamov et al., 2011*). The errors in cattle pedigrees were different in European countries: 5 – 15% in Denmark (*Christensen et al., 1982*), 4 – 23% in Germany (*Geldermann et al., 1986*), 8 – 20% in Ireland (*Beechinor and Kelly, 1987*), 12% in Netherlands (*Bovenhuis and Van Arendonk, 1991*), 2,9 – 5,2% (*Ron et al., 1996*) or 11,7% (*Weller et al., 2004*) in Israel, 10% in dairy cattle in the United Kingdom (*Visser et al., 2002*) and 10,7% in the Czech Republic (*Řehout et al., 2006*). The use of these markers was limited because they are products of the gene expression (*Drinkwater and Hetzel, 1991*). The level of polymorphism observed in proteins is often low which has reduced the general application of protein-typing in the studies of diversity.

In the last decades, molecular biology created valuable new means for studying cattle livestock genetics and breeding techniques - the DNA based molecular markers that are based on the mutations of the nucleotide sequence within the individual's genome. They are the most informative markers available so far (*Yang et al., 2013*). In this way the selection according to genotype has become possible in the breeding of farm animals.

The simple technique discovered in 1993 by Kary Mullis that revolutionized the molecular biology was polymerase chain reaction (PCR) (*Nicholas, 1996; Van Marle-Köster and Nel, 2003*). PCR is a fast, sensitive and reliable method and became an essential tool in molecular biology and plays a main role in "in vitro" techniques that are now applicable to the analysis of genomes. After discovery of this major scientific development blood group typing and protein biochemical proteins in animal populations were replaced by the use of molecular DNA markers.

In this review we attempt to highlight the application of short tandem repeats (STR) or microsatellites in cattle genomics and breeding.

Molecular marker

Genetic markers are two types—protein and DNA (molecular) markers. Molecular markers can be categorized into two classes, nuclear DNA and mitochondrial DNA (mtDNA) markers, based on their transmission and evolutionary dynamics (*Hanotte et al., 2003*). Nuclear DNA markers are usually bi-parently inherited. Mitochondrial DNA markers are maternally inherited, express high rates of mutation, and are non-recombining such that they have one-quarter of the genetic effective population size (N_e) of nuclear markers (*Hanotte et al., 2003*).

Molecular marker or genetic marker is a fragment of DNA sequence that is associated to a certain region of the genome (*Wakchaure et al., 2015*). Molecular markers are classified on the basis of techniques used for discovery of polymorphism. There are several types of markers used today: hybridization-based markers such as RFLP (Restriction Fragment Length Polymorphism) and PCR-based markers e.g. Random Amplified Polymorphic DNA (RAPD), Amplified Fragment Length Polymorphism (AFLP), Short Tandem Repeat (STR) or Microsatellites, Minisatellite, Single Nucleotide Polymorphism (SNP) and Single Strand Conformational Polymorphism (SSCP) (*Van Marle-Köster and Nel, 2003*).

In the animal genetic studies, the molecular markers revealing polymorphism at the DNA level play an important role. The term "Smart Breeding" is used to describe marker supported breeding strategies (*Firas et al., 2015*).

To studying the genetic variation in cattle breeds polymorphic DNA markers are usually used: D-loop and cytochrome B mitochondrial DNA (mtDNA) sequences for maternal inheritance, Y chromosome specific single nucleotide polymorphism (SNP) and STR (microsatellites) for paternal inheritance and autosomal microsatellite for bi-parental inheritance (*Avise, 1994*). DNA sequences as a new class of genetic markers were described in 1989 (*Machugh et al., 1997*). The number of repeats (Thymine, Adenine, Guanine or Cytosine) are variable in any DNA of the same population and within the alleles of every individual and can be characterized by using PCR (*Weber and May, 1989; Wang et al., 1998*).

Among the most polymorphic DNA markers that are contained in a large proportion of the eukaryotic genomes are the short tandem repeat (STR's) or microsatellites (SSR) and sequence tagged microsatellite repeats (STMR's).

STR are di-, tri-, or tetra nucleotide tandem repeats in tandemly repeated DNA sequences that are present in variable copy numbers at each locus and throughout the genome (*Ashley and Dow, 1994; Forbes et al., 1995; Bruford et al., 1996; Ellegren et al., 1997; Montaldo and Meza-Herrera, 1998; Schlötterer, 1998; Schmid et al., 1999; Toth et al., 2000; Beuzen et al., 2000; Teneva, 2009; Teneva and Petrovic 2010; Teneva et al., 2013; Gündüz et al., 2016*). PCR-amplified microsatellite repeats in the alleles can be detected using fragment analysis and other methods.

STR are located in the noncoding intronic regions of the bovine genome. They are most valuable and informative markers for genetic studies in cattle parentage verifications, genetic variability, genome mapping, relationships of individuals and populations, evaluation of inbreeding levels (F_{IS}), the genetic structure of subpopulations and populations, assessment of effective population size (N_e) and the gene flow between populations. They are used as markers for certain cattle disease in cattle diagnosis because several microsatellite alleles are associated with mutations in coding regions of the DNA that can cause a variety of medical disorders and variation in productive traits (*Selkoe and Toonen, 2006*).

The advantages of PCR- based microsatellite analysis for cattle studies are as follows:

- Locus-specific;
- Co-dominant (heterozygotes could be distinguished from homozygotes);
- Highly polymorphic ("hypervariable");
- Allow obtaining of rapid results in 48 hours or less;
- Useful at a range of scales from individual ID to fine-scale phylogenies;
- Easy to standardize and automate, results are very reproducible

The genotyping of microsatellite markers is performed automatically and with a low cost due to the use of multiplex technique, that allows the analysis of more microsatellites in one reaction.

Autosomal microsatellite loci in cattle are often used for genetic identification of individual and parentage analysis for the successful implementation and monitoring of ex-situ conservation programs, population diversity, differentiation of populations, genetic distances and genetic relationships. Microsatellite loci are highly sensitive to genetic bottlenecks and they are commonly used for inbreeding determination in cattle populations (*Hanotte and Janlin, 2005*). They are still the “gold standart” for many genetic population and identification purposes (*Brenig and Schütz, 2016*).

Parentage control and cattle identification

In 1993, with the development of a high density map of the bovine genome, many microsatellites became available (*Steffen et al., 1993; Fries et al., 1993*). In that year initial steps in using microsatellites in cattle identification and parentage control were performed (*Trommelen et al., 1993*). Parentage testing using DNA based markers yields much higher exclusion probability (> 90%) than the testing with blood groups (70–90%) or other biochemical markers (40–60%) (*Wakchaure et al., 2015*).

Further studies were performed to establish an internationally comparable panel of molecular markers (*Machugh et al. 1994; Glowatzki-Mullis et al., 1995; Heyen et al., 1997; Kemp et al., 1995; Peelman et al., 1998; Ma et al., 1996, Moazami-Goudarzi et al., 1997; Loftus et al., 1999; Kantanen et al., 2000; Canon et al., 2001; Hanotte et al., 2003; Beja-Perira et al., 2003; Gargani et al., 2015*). In many investigations FAO list of microsatellites in large number of cattle breeds were implemented (*Ajmone- Marsan and The GLOBALDIV Consortium, 2010*).

Microsatellite markers were widely used in cattle paternity analysis studies in different continents (*Bruford et al., 1996; Montaldo and Meza-Herrera, 1998;*

Beuzen et al., 2000; Schlötterer, 2004; Visscher et al., 2002; Hansen et al., 2002; Ibeagha-Awemu and Erhardt, 2005).

In Busha cattle in Serbia *Stevanov-Pavlović et al. (2015)* evaluated 12 microsatellite markers (TGLA227, BM2113, TGLA53, ETH10, SPS115, TGLA126, TGLA122, INRA23, BM1818, ETH3, ETH225, BM1824) recommended by International Society of Animal Genetics (ISAG) for paternity testing. The authors found high PIC (Polymorphism Information Content) values ranging from 0.513 to 0.905. The results showed that the 12 marker's set recommended by ISAG can be used with high confidence for forensic purposes in Busha cattle.

Genetic diversity analysis

The inbreeding process and various crossbreeding systems may lead to the loss of genetic variation within breeds. In this reason a lot of breeds may become extinct. The scientific community alarmed the necessity for the conservation of livestock resources. In 1992 the Food and Agricultural Organization (FAO) launched a program for the Global Management of Farm Animal Genetic Resources, with the main objective being to identify conservation activities and create an awareness of possible losses of genetic resources on an international basis (*Gandini and Oldenbroek, 1999*).

A global program was initiated directed towards genetic characterization of all farm animal species using DNA markers (*Groeneveld et al., 2010*). Microsatellite markers have been widely used for studying the genetic diversity in cattle (*MacHugh et al., 1997*). Genetic variability within and among populations is often of importance and may contribute to the selection and preservation of genetic resources (*Groeneveld et al., 2010*).

Microsatellite markers were considered as a marker of choice for diversity assessment in breeds (*FAO, 2004*). A list of microsatellite markers for genetic characterization of cattle breeds have been approved by Food and Agriculture Organization (FAO) (*Navani et al., 2002*). The 12 selected markers (BM1814, BM1818, BM2113, ETH3, ETH10, ETH225, INRA023, SPS115, TGLA53, TGLA122, TGLA126, TGLA227) were included in an International comparison test of ISAG.

Based on microsatellites as a marker of choice a lot of investigations have been performed to estimate both the relationships among the breeds and the genetic diversity within and between populations (*Ashwell et al., 2004; Sun et al., 2007*). Genotyping data of 30 microsatellite loci in 69 European breeds were used to determining the main criteria for conservation of breeds (*Lenstra et al., 2006*). The selected breeds showed high degree of molecular diversity, that is an apparent

reason for their conservation. The Busa and Anatolian breeds were considered to be valuable genetic resources on the basis of their high genetic diversity (Medugorac et al., 2009). Conservation priorities of Nordic cattle based on genetic diversity were outlined by Bennewitz et al. (2006) and Tapio et al. (2006).

Many other authors used common microsatellite markers to assess genetic diversity within breeds and the inbreeding in different cattle breeds (Teneva et al., 2005; 2007; Garcia et al., 2006; Tapio et al., 2006; Ginja et al., 2009a; Li and Kantanen, 2009; Qi et al., 2009). Several studies have been conducted in European and Eurasian cattle (*Bos taurus*) in which microsatellites were used to assess genetic variability and differentiation (Canon et al., 2001; European Cattle Genetic Diversity Consortium, 2006; Tapio et al., 2006; Li and Kantanen, 2009). For Creole breeds, several microsatellite-based studies were reported (Martinez et al., 2005; Armstrong et al., 2006; Quiroz-Valiente et al., 2006; Aquino et al., 2008; Ulloa-Arvizu et al., 2008; Martinez- Correal et al., 2009). Later, Delgado et al. (2011) using 19 microsatellites assessed the genetic diversity and relationships among 26 Creole cattle breeds from 10 American countries representing North, Central, South America and the Caribbean Islands. Creole cattle populations showed high level of genetic diversity comparing to the breeds subjected to intensive breeding. Regardless of the detected high genetic diversity, a significant inbreeding was also detected. Creole cattle breeds represent great reservoirs of cattle genetic diversity but measures to avoid inbreeding and uncontrolled crossbreeding is highly necessitated (Delgado et al., 2011).

In Indian zebu cattle (*Bos indicus*) Chaudhari et al. (2009) reported 25 microsatellite loci with a high PIC value (> 0.5) in 145 purebred cattle originating from unrelated Kenkatha and Gaolao cattle breeds which is an indication that these markers are highly informative and appropriate for characterization of both cattle populations. The authors estimated 21.21% and 22.48% heterozygotes in Gaolao and Kenkatha populations, respectively. However, the additional analyses based on a number of fluorescent labeled microsatellite markers used to characterize the same cattle breeds showed a little genetic differentiation between them (Alex et al., 2013). Numerous factors such as inbreeding, genetic hitchhiking, null alleles (non-amplified alleles) and occurrence of population substructures have been established as reasons of heterozygote deficit in the studied populations.

Several microsatellite markers have also been used in conservation studies concerning certain other important cattle breeds (Frankham et al., 2002; Navani et al., 2002).

Meta-analysis of different microsatellite loci revealed patterns of diversity and taurine–zebu admixture over Europe, South-West Asia and Africa (Freeman et al., 2006). The mixed origin of Indonesian zebras using microsatellites was confirmed in the diversity study of Mohamad et al. (2009). In contradiction, the microsatellite analysis showed that the Indonesian Bali cattle is a pure breed (*Bos javanicus*) (Groeneveld et al., 2010).

Most of the microsatellite data indicated a separate position of Mediterranean cattle, but divide the Transalpine cattle into two different clusters of breeds: Central-European and Northern European (*Lenstra et al., 2006*). Conservation priorities for Nordic cattle were reported by *Bennewitz et al. (2006)* and *Tapio et al. (2006)*.

Jersey is a common and unique cattle breed originating from the UK Channel Island of Jersey. A Jersey Island cattle was isolated from other UK and European cattle populations for approximately 50 generations. The genetic diversity of this breed was described for the first time by *Chikhi et al. (2004)* on the base of 12 microsatellite markers: HAUT27, HEL5, BM1314, BM1818, BM2113, INRA005, INRA063, ILSTS006, ETH10, ETH225, TGLA122, and TGLA227. This study showed that the average number of alleles per locus and the expected heterozygosity were comparatively higher with respect to that observed in a number of continental breeds. The authors reported absence of a loss of genetic diversity and inbreeding. They concluded that it is unnecessary to import unrelated animals for management purposes despite of the fact that no imports have taken place to the island since 1789.

Egito et al. (2007) also reported a significant amount of genetic variation in Brazilian local cattle populations on the base of the observed microsatellite variation in 22 STR loci. These data showed that Brazilian Creole breed constitutes an important and diverse source of genetic diversity for bovine breeding and conservation.

Recently, *Sharma et al. (2015)* investigated genetic diversity and relationship among 11 Indian cattle breeds using 21 microsatellite markers, and concluded that the Southern breed “Ongole” is distinct from the breeds of Northern/Central India. The results provide basic information about the genetic diversity and structure of Indian cattle which should have implications in the management and conservation of cattle diversity.

Several studies have been conducted in European and Eurasian cattle (*Bos taurus*) in which microsatellites were used to assess genetic diversity and differentiation (*Canon et al., 2001; Tapio et al., 2006; European Cattle Genetic Diversity Consortium 2006; Li and Kantanen, 2009*).

Allelic variation in sixteen microsatellite loci (CSSM 66, ETH 10, ETH 152, ETH 225, ETH 3, HEL 1, HEL 5, HEL 9, ILSTS 005, INRA 023, INRA 032, INRA 035, INRA 037, INRA 005, INRA 063, and TGLA 44) was studied in 10 Spanish, 5 Portuguese and 3 French cattle breeds. A total of 173 alleles were detected across the 16 loci analysed (*Canon et al., 2001*). Observed and expected heterozygosities per breed ranged from 0.54 to 0.72. The level of breed differentiation was considerable indicating that 93% is due to the differences among individuals while the remaining 7% corresponds to the differences between breeds. The authors concluded that the microsatellites provides reasonable statistical power for breed

assignment and allow future management of the breeds to be based on better knowledge of their genetic structure and relationships between populations.

In Romania, the genetic diversity among Romanian Grey, Brown, Spotted and Black and White cattle breeds was evaluated at 11 microsatellite loci focusing on the endangered Romanian Grey breed (Ilie *et al.*, 2015). High level of genetic diversity was established in the endangered Romanian Grey cattle population. The results confirmed that the breed's genetic diversity is preserved correctly using the current conservation program directed to reduction of the genetic loss.

Genetic markers with PIC values higher than 0.5 are normally considered as informative in a population (Botstein *et al.*, 1980). Higher PIC values were also observed in the taurine and indicus breeds using microsatellite markers (Bradley *et al.*, 1994; Canon *et al.*, 2001; Maudet *et al.*, 2002; Kumar *et al.*, 2003; Metta *et al.*, 2004; Mukesh *et al.*, 2004; Pandey *et al.*, 2006; Sodhi *et al.*, 2006; Chaudhari *et al.*, 2009).

Molecular characterization of Indian breed Hallikar, the native cattle breed of Karnataka was performed using 19 cattle specific microsatellite markers recommended by FAO. The study proved that the cattle specific microsatellite markers used were highly polymorphic and highly informative for genetic characterization of cattle breeds (Kumar *et al.*, 2003).

In comparison with other European and Balkan countries, in Bulgaria there is a big gap in molecular characterization of cattle based on microsatellites and other molecular markers. Teneva *et al.* (2005; 2007) studied local Bulgarian Grey and Bulgarian Shorthorn cattle breeds through microsatellite markers. They established a high PIC value (>0.5) and high heterozygosity based on 11 STRs.

Genome mapping

Molecular markers provide researchers with tools to develop genetic linkage maps. The maps show the position of markers and genes on a chromosome and the distance between genes. The genetic maps have been used to select markers that are distributed across the whole genome. The markers are used in QTL mapping studies to follow the inheritance of specific regions of chromosomes through generations. Microsatellite markers are particularly appropriate for linkage mapping (Wakchaure *et al.*, 2015). The efforts to map the cattle genome is progressing. The bovine genetic map contains over 2 200 microsatellites (Van Marle-Köster and Nel, 2003). The microsatellite-based genetic map is a fundamental tool for linkage mapping of monogenic as well as polygenic traits of interest. A high-density bovine microsatellite-based genetic map has been constructed in 2004 by Ihara *et al.* and it consists of 3960 markers including 3802 polymorphic ones (Ihara *et al.*, 2004). This map is a powerful tool for mapping of

QTLs and is a genetic basis for the development of well-annotated gene maps in cattle (Ihara *et al.*, 2004).

Association of microsatellites with productive traits and disease

During the past decades, the development in molecular genetics have led to the identification of multiple genes or genetic markers linked to genes that affect quantitative traits. This provided an opportunity to enhance the selection for traits that are difficult to be improved by conventional breeding due to their low heritability.

Usually, microsatellites should be neutral DNA markers maintaining their characteristics relatively constant (Mariani and Bekkevold, 2014; Brenig and Schütz, 2016). However, several of the microsatellites in the ISAG parentage control panel are under artificial selection and hence are not completely neutral. ETH10 on bovine chromosome 5, for example, is associated with growth and carcass traits in Angus, Brangus, and other cattle breeds (DeAtley *et al.*, 2011; Meirelles *et al.*, 2011). The ETH10 locus was also associated with coat colour in Brown Swiss cattle (Gutierrez-Gil *et al.*, 2007; Drogemuller *et al.*, 2009). BM1818 was proven to be associated with somatic cell score (SCS) and specific alleles of this locus are favorable or unfavorable for mastitis resistance (Chu *et al.*, 2005). In another study, significant differences in allelic frequencies for BM1824, ETH10, INRA023, SPS115 and TGLA53 alleles were described in Japanese Black cattle depending on selection of sires for intramuscular fat (Smith *et al.*, 2001).

After Brenig and Schütz (2016) most of the 12 microsatellite markers which were included in ISAG/FAO panel BM1814, BM1818, BM2113, ETH3, ETH10, ETH225, INRA023, SPS115, TGLA53, TGLA122, TGLA126, TGLA227 are associated with economical important traits. The authors concluded that microsatellite markers recommended for parentage control in cattle are influenced by selective breeding and are DNA markers related to adaptiveness. At least 40 different QTLs have been described flanking the microsatellite chromosomal positions and the most frequent traits included milk protein yield, milk fat yield, somatic cell score, milk fat percentage, body weight at birth and body weight at weaning (Hu *et al.*, 2013).

The application of microsatellite markers in QTL analysis has been found to be prolific in determining the effect of specific molecular markers on milk quality (Deb *et al.*, 2013; Olsen *et al.*, 2004). Several microsatellite markers have been developed for identification of the specific region of BTA6 with effect on milk fat and milk protein (Kuhn *et al.*, 1999).

Singh et al. (2013) reported that molecular markers have a great contribution to the better production performance and disease resistance in livestock.

Using microsatellite markers and identification of the particular biomarkers associated with various diseases and economically significant clinical conditions (such as mastitis) has helped to increase the specificity and accuracy of disease resistant breeding and to enhance productivity (*Deb et al., 2013*).

The results of *Hanotte et al. (2003)* from mapping the quantitative trait loci controlling the trypanotolerance revealed that the selection for trypanotolerance within an F_2 cross between N'Dama and Kenya Boran cattle could produce a synthetic breed with higher trypanotolerance levels than the currently existing in the parental breeds. In this QTL mapping the authors genotyped a cattle group at 477 microsatellite loci, distributed among the 29 cattle autosomes for 16 phenotypic traits.

Statistical methods used in microsatellite analysis

The average number of alleles (MNA), observed (H_o) and expected (H_e) heterozygosity and estimation of polymorphism information content (PIC), are the most commonly calculated population genetic parameters for assessing the diversity within cattle breeds (*Mburu and Hanotte, 2005; Hanotte and Janlin, 2005*). PIC values indicate the informativeness of the studied microsatellite loci. Hardy-Weinberg equilibrium test is always used to predict whether the population is stable or not. The observed genotypes are compared with the expected genotypes in a χ^2 -test for likeness of fit. The high heterozygosity values observed in the studies indicate the presence of large number of polymorphic loci. The most simple parameters for evaluating the distribution of diversity between breeds using genetic markers are the genetic differentiation or fixation indices e.g. F_{st} , G_{st} , R_{st} . They reveal the variation among populations. The most widely used is F_{st} , which measures the degree of genetic variation between subpopulations through the calculation of the standardized variances of allele frequencies amongst populations (*Weir and Basten, 1990; Mburu et al., 2003*). The genetic distances can also be analyzed in terms of genetic diversity and individual breed contributions to the total diversity of the breeds.

The most commonly used approach so far is the method proposed by Weitzman (*Weitzman, 1993; Hanotte and Janlin, 2005*). It involves calculation of a matrix of genetic distances and construction of dendrograms. Individual breed contributions are calculated by comparing the total length of the dendrogram including all breeds. Priority breeds for conservation would be the breeds contributing most to the diversity of the set. The Weitzman approach applied in 49 African cattle breeds (*Reist-Marti et al., 2003*) allowed their separation into two groups, the 'taurine' and 'indicine'.

The main cattle microsatellite genetic parameters like observed number of alleles, allele frequency, FIS, observed and expected heterozygosity, the presence of null alleles, the neutrality of the microsatellites, genetic distances, Analysis of molecular variance (AMOVA) usually are analysed by a number of commonly used population genetic computer programs for genetic microsatellite statistical analysis: GENEPOP, ARLEQUIN, POPGENE, MICROSAT, PHYLIP, STRUCTURE MICROSATELLITE ANALYZER (MSA), MICROCHECKER (Mburu and Hanotte, 2005).

Conclusion

The development of polymorphic microsatellite markers in advanced genetics and biotechnology gives the opportunity for the selection, improvement of cattle health and production. The microsatellite technology with its advantages and disadvantages has a huge variety of applications in cattle breeds. Microsatellite markers for improving milk production and other main productive traits as well as their association with disease in cattle breeds are useful for breeders. They may also be efficiently applied in conservation decisions. The employment of microsatellite markers in determining the resistance to economically important diseases such as mastitis and other cattle diseases is helpful to test the leak of animals and their productivity. Consequently, this genomic technology provides a valuable information for cattle genetics and breeding today and in the future.

Kratki tandemski ponovci (Short tandem repeats - STR) u genomici i odgajivanju goveda

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Rezime

Molekularni markeri su suštinsko sredstvo za određivanje specifičnog genetičkog sastava pojedinca i predstavljaju dragoceni pristup genetičkom oplemenjivanju farmskih životinja. U stočarstvu njihova primena je korisna za poboljšanje programa odgajivanja za željene osobine, veću produktivnost i proizvode visokog kvaliteta. Ovi markeri pružaju preciznije genetske informacije i bolje poznavanje genetičkih resursa životinja. U ovom preglednom radu pokušavamo da napravimo kratak pregled o primeni jednog naprednijeg molekularnog markera zasnovanog na DNK u stočarstvu, a to su kratki tandemski ponovci (STR, mikrosateliti).

Ključne reči: molekularni markeri, STR, mikrosateliti, genom, polimorfizam, uzgoj, stoka

References

- ADAMOV N., MICKOV L., PETKOV V., ADAMOV M. (2011): Microsatellite markers for pedigree verification in cattle. *Macedonian Journal of Animal Science*, 1, 1, 9–15.
- AJMONE-MARSAN, P. AND THE GLOBAL DIVERSITY CONSORTIUM. (2010): A global view of livestock biodiversity and conservation—global diversity. *Animal Genetics*, 41, 1–5.
- ALEX R., SINGH U., ALYETHODI RR., ET AL. (2013): A review on draught animal research in India: constraints and future thrust areas. *Advances in Animal and Veterinary Sciences*, 1, (6), 178–182.
- AQUINO Y.N., VELI E.A., RIVAS SEOANE E., RIVAS PALMA V. & ESTRADA R. (2008): Genetic variability of Criollo cattle of Peru using microsatellite markers. *Archivos de Zootecnia*, 57, 337–40.
- ARMSTRONG E., POSTIGLIONI A., MARTINEZ A., RINCON G. & VEGA-PLA J.L. (2006): Microsatellite analysis of a sample of Uruguayan Creole bulls (*Bos taurus*). *Genetics and Molecular Biology*, 29, 267–72.
- ASHLEY M.V., DOW B.D. (1994): The use of microsatellite analysis in population biology: Background, methods and potential applications. *EXS* 69, 185–201.
- ASHWELL M. S., HEYEN D. W., SONSTEGARD T. S., VAN TASSELL C. P., DAY, VANRADEN P. M., RON M. J., WELLER I., LEWIN H. A. (2004): Detection of quantitative trait loci affecting milk production, health, and reproductive traits in Holstein cattle. *Journal of Dairy Science*, 87(2), 468–475.
- AVISE J. C. (1994): *Molecular markers, natural history and evolution*. Chapman and Hall, New York, pp767.
- BEJA-PEREIRA A., ALEXANDRINO P., BESSA I. , CARRETERO Y., DUNNER S., FERRAND N., JORDANA J., LALOE D., MOAZAMI-GOUDARZI K., SANCHEZ A. (2003): Genetic Characterization of Southwestern European Bovine Breeds: A Historical and Biogeographical Reassessment With a Set of 16 Microsatellites. *Journal of Heredity*, 94, 3, 243–250.
- BEECHINOR J. G., KELLY E. P. (1987): Errors of identification amongst cattle presented as progeny of some bulls used in the artificial insemination service in Ireland. *Ireland Veterinary Journal*, 41, 348–352.
- BENNEWITZ J., KANTANEN J., TAPIO I. ET AL. (2006): Estimation of breed contributions to present and future genetic diversity of 44 North Eurasian cattle breeds using core set diversity measures. *Genetics Selection Evolution* 38, 201–20.

- BEUZEN N.D., STEAR M.J., CHANG K.C. (2000): Molecular markers and their use in animal breeding. *The Veterinary Journal*, 160, 42-52.
- BOTSTEIN D., WHITE R. L., SKOLNICK M., DAVIS R. W. (1980): Construction of a genetic linkage map in man using restriction fragment length polymorphism. *American Journal of Human Genetics*, 32 (3), 314–331.
- BOVENHUIS H., VAN ARENDONK A. M. (1991): Estimation of milk protein gene frequencies in crossbred cattle with maximum likelihood. *Journal of Dairy Science*, 74, 2728–2736.
- BRADLEY D. G., MACHUGH D. G., LOFTUS R. T., SOW R. S., HOSTE C. H., CUNNINGHAM E. P. (1994): Zebu–taurine variation in Y chromosome DNA: a sensitive assay for introgression in West African trypanotolerant cattle populations. *Animal Genetics*, 25, 7–12.
- BRENIG B., SCHÜTZ E. (2016): Recent development of allele frequencies and exclusion probabilities of microsatellites used for parentage control in the German Holstein Friesian cattle population. *BMC Genetics*, 8, 17:18.
- BRUFORD M.W., CHEESMAN D.J., COOTE T., GREEN H.A.A., HAINES S.A., O'RYAN C., WILLIAMS T.R. (1996): Microsatellites and their application to conservation genetics. In: Smith, Thomas B. and Wayne, Robert K. eds. *Molecular Genetic Approaches in Conservation*, New York: Oxford University Press, 278-297.
- CANON J., ALEXANDRINO P., BESSA I., CARLEOS C., CARRETERO Y., DUNNER S.(2001): Genetic diversity measures of local European beef cattle breeds for conservation purposes. *Genetics Selection Evolution*, 33, 311–332.
- CHAUDHARI M. V., PARMAR S.N.S., JOSHI C. G., BHONG C. D., FATIMA S., THAKUR M. S., THAKUR S. S. (2009): Molecular characterization of Kenkatha and Gaolao (*Bos indicus*) cattle breeds using microsatellite markers. *Animal Biodiversity and Conservation*, 32, 2, 71–76.
- CHIKHI L., GOOSSENS B., TREANOR A., BRUFORD M. (2004): Population genetic structure of and inbreeding in an insular cattle breed, the Jersey, and its implications for genetic resource management. *Heredity*, 92(5), 396–401.
- CHRISTENSEN L.G., MADSEN P., PETERSEN J. (1982): The influence of incorrect sire identification on the estimates of genetic parameters and breeding values. In: *Proceeding 2nd World Congress on Genetics Applied to Livestock Production*, Madrid, Spain, 7, 200–208.
- CHU M.X., ZHOU G.L., JIN H.G., SHI W.H., CAO F.C., FANG L., ET AL. (2005): Study on relationships between seven microsatellite loci and somatic cell score in Beijing Holstein cows. *Yi Chuan Xue Bao*. 32(5), 471-5.
- DEATLEY K.L., RINCON G., FARBER C.R., MEDRANO J.F., LUNA-NEVAREZ P., ENNS R.M., VANLEEUEWEN D.M., SILVER G.A., THOMAS M.G. (2011): Genetic analyses involving microsatellite ETH10 genotypes on bovine chromosome 5 and performance trait measures in Angus and Brahman influenced cattle. *Journal of Animal Science*, 89(7), 2031–41.

- DEB R., KUMAR A., CHAKRABORTY S., ET AL. (2013): Trends in diagnosis and control of bovine mastitis: a review. *Pak Journal of Biology Science*, 16(23), 1653-61.
- DELGADO J.V., MARTÍNEZ A.M., ACOSTA A., ALVAREZ L.A., ARMSTRONG E., CAMACHO E., CAÑÓN J., CORTÉS O., DUNNER S., LANDI V., MARQUES J.R., MARTÍN-BURRIEL I., MARTÍNEZ O.R., MARTÍNEZ R.D., MELUCCI L., MUÑOZ J.E., PENEDO M.C., POSTIGLIONI A., QUIRÓZ J., RODELLAR C., SPONENBERG P., UFFO O., ULLOA-ARVIZU R., VEGA-PLA J.L., VILLALOBOS A., ZAMBRANO D., ZARAGOZA P., GAMA L.T., GINJA C. (2011): Genetic characterization of Latin-American Creole cattle using microsatellite markers. *Animal Genetics*, 43(1), 2–10.
- DRINKWATER R.D., HETZEL D.J.S. (1991): Application of molecular biology to understanding genotype-environment interactions in livestock production. *Proceedings of an International Symposium on Nuclear Techniques in Animal Production and Health*. Vienna: IAEA, FAO; 437–452.
- DROGEMULLER C., ROSSI M., GENTILE A., TESTONI S., JORG H., STRANZINGER G., ET AL. (2009): Arachnomelia in Brown Swiss cattle maps to chromosome 5. *Mammalian Genome*, 20(1), 53–9.
- EGITO A.A., PAIVA S.R., MARIA D.O., SOCORRO M. A.E., ARTHUR S. M., ALMEIDA L.D., CASTRO S.R., GRATAPAGLIA D. (2007): Microsatellite based genetic diversity and relationships among ten Creole and commercial cattle breeds raised in Brazil. *BMC Genetics*, 7; 8, 83.
- ELLEGREN H., MOORE S., ROBINSON N., BYRNE K., WARD W., SHELDON BC. (1997): Microsatellite evolution - a reciprocal study of repeated lengths at homologous loci in cattle and sheep. *Molecular Biology of Evolution*, 14(8), 854-60.
- EUROPEAN CATTLE GENETIC DIVERSITY CONSORTIUM (2006): Marker assisted conservation of European cattle breeds: an evaluation. *Animal Genetics*, 37(5), 475–81.
- FAO, 2004: Secondary guidelines for development of national farm animal genetic resources management plans for global management of cattle genetic resources using reference Microsatellites global projects for the maintenance of domestic animal genetic diversity (MoDaD).
- FIRAS R., AL-SAMARAI, ABDULKAREEM A. AL-KAZAZ. (2015): Molecular Markers and Its Applications in Animal Breeding: A review. *American Journal of Applied Scientific Research*, 1, 1, 1-5.
- FORBES S.H., HOCC J.T., BUCHANAN F.C, CRAWFORD A.M., ALLENDORF F.W. (1995): Microsatellite evolution in congeneric mammals: domestic and bighorn sheep. *Molecular Biology and Evolution* 12, 1106-1113.
- FRANKHAM R., BALLOU J. D., BRISCOE D. A. (2002): *Introduction to Conservation Genetics*. New York: Cambridge University Press; 2002.

- FREEMAN A. R., BRADLEY D. G, NAGDA S., GIBSON J. P., HANOTTE O. (2006): Combination of multiple microsatellite data sets to investigate genetic diversity and admixture of domestic cattle. *Animal Genetics*, 37, 1, 1–9.
- FRIES R., A. EGGEN Y.E., WOMACK J. (1993): The bovine genome map. *Mammalian Genome*. 4, 405.
- GANDINI G.C., OLDENBROEK J.K. (1999): Choosing the onservation strategy in genebanks and the conservation of farm animal genetic resources. Ed. Oldenbroek, J.K., DLO Institute for Animal Science and Health, The Netherlands. 45-47.
- GARCIA D., MARTINEZ A., DUNNER S., VEGA-PLA J.L., FERNANDEZ C., DELGADO J.V., CANON J. (2006). Estimation of the genetic admixture composition of Iberian dry-cured ham samples using DNA multilocus genotypes. *Meat Science*, 72(3), 560–6.
- GARGANI M., PARISSET L., LENSTRA J. A., DE MINICIS E., VALENTINI A., EUROPEAN CATTLE GENETIC DIVERSITY CONSORTIUM, HOLM L-E. (2015): Microsatellite genotyping of medieval cattle from central Italy suggests an old origin of Chianina and Romagnola cattle. *Frontiers in Genetics*, 6, 1-6.
- GELDERMANN H., PIEPER U., WEBER W. E. (1986): Effect of misidentification on the estimation of breeding value and heritability in cattle. *Journal of Animal Science*, 63(6), 1759–68.
- GINJA C., TELO DA GAMA L., PENEDO M.C. (2009a): Analysis of STR markers reveals high genetic structure in Portuguese native cattle. *Journal of Heredity*, 101(2), 201–10.
- GLOWATZKI-MULLIS M.L., GAILLARD C., WIGGER G., FRIES R. (1995): Microsatellite-based parentage control in cattle. *Animal Genetics*, 26(1), 7-12.
- GROENEVELD L.F. LENSTRA J. A., EDING H., TORO M.A., SCHERF B., PILLING D., NEGRINI R., FINLAY E.K., JIANLIN H., GROENEVELD E., WEIGENDAND THE GLOBALDIV CONSORTIUM (2010): Genetic diversity in farm animals – a review. *Animal Genetics*, 41 Suppl 1, 6-31.
- GÜNDÜZ Z., YILMAZ O., CEMAL I., BİÇER O. (2016): A Comparison of Old and Modern Type DNA Marker Technologies and Their Impact on Animal Breeding Programs. *Iğdır University Journal of the Institute of Science and Technology*, 6(2), 175-180.
- GUTIERREZ-GIL B., WIENER P., WILLIAMS J.L. (2007): Genetic effects on coat colour in cattle: dilution of eumelanin and phaeomelanin pigments in an F2-Backcross Charolais x Holstein population. *BMC Genetics*, 16, 8, 56.
- HANOTTE O., RONIN Y., AGABA M., NILSSON P., GELHAUS A., HORSTMANN R., SUGIMOTO Y., KEMP S., GIBSON J., KOROL A., SOLLER M., TEALE A. (2003): Mapping of quantitative trait loci controlling trypanotolerance in a cross of tolerant West African N'Dama and susceptible East African Boran cattle. In: *Proceedings of the National Academy of Sciences*, 100, 13, 7443-8.

- HANOTTE O., JIANLIN H. (2005): Genetic characterization of livestock populations and its use in conservation decision-making. The role of biotechnology, Villa Gualino, Turin, Italy – 5-7 March.
- HANSEN C., SHRESTHA J.N., PARKER R.J., CROW G.H., MCALPINE P.J., DERR J.N. (2002): Genetic diversity among Canadienne, Brown Swiss, Holstein, and Jersey cattle of Canada based on 15 bovine microsatellite markers. *Genome*, 45(5), 897-904.
- HEYEN D.W., BEEVER J.E., DA Y., EVERT R.E., GREEN C., BATES S.R., ZIEGLE J.S., LEWIN H.A. (1997): Exclusion probabilities of 22 bovine microsatellite markers in fluorescent multiplexes for semiautomated parentage testing. *Animal Genetics*, 28(1), 21–7.
- HINES H.C. 1999. Blood groups and biological polymorphisms. In: *Genetics of cattle*. (Ed. R. Fries and A. Ruvinsky), CABI Publishing.
- HU Z.L., PARK C.A., WU X.L., REECY J.M. (2013): Animal QTLdb: an improved database tool for livestock animal QTL/association data dissemination in the postgenome era. *Nucleic Acids Research*, 41(Database issue): D871–9.
- IBEAGHA-AWEMU E.M., ERHARDT G. (2005): Genetic structure and differentiation of 12 African *Bos indicus* and *Bos taurus* cattle breeds, inferred from protein and microsatellite polymorphisms. *Journal of Animal Breed Genetics*, 122(1), 12-20.
- IHARA N., TAKASUGA A., MIZOSHITA K., TAKEDA H., SUGIMOTO M., MIZOGUCHI Y., HIRANO T., ITOH T., WATANABE T., KENT M. REED, SNELLING WARREN M., KAPPES STEVEN M., BEATTIE CRAIG W., BENNETT GARY L., SUGIMOTO Y. (2004): *Genome research*, 14,1987-1998.
- ILIE D., CEAN A., CZISZTER L., GAVOJDIAN D., IVAN AL., KUSZA S. (2015): Microsatellite and Mitochondrial DNA Study of Native Eastern European Cattle Populations: The Case of the Romanian Grey. *PLoS ONE* 10(9), 1-18.
- KANTANEN J., OLSAKER I., HOLM L-E., LIEN S., VILKKI J., BRUSGAARD K., EYTHORSDDOTTIR E., DANIEL B., ADALSTEINSSON S. (2000): Genetic diversity and population structure of 20 north European cattle breeds. *Journal of Heredity*, 91, 6, 446–457.
- KEMP S.J., HISHIDA O., WAMBUGU J., RINK A., LONGERI M.L., MA R.Z., DA Y., LEWIN H.A., BARENDSE W., TEALE A.J. (1995): A panel of polymorphic bovine, ovine and caprine microsatellite markers. *Animal Genetics*, 26(5), 299–306.
- KÜHN C., FREYER G., WEIKARD R., GOLDAMMER T., SCHWERIN M. (1999): Detection of QTL for milk production traits in cattle by application of a specifically developed marker map of BTA6. *Animal Genetics*, 30(5), 3330-340.
- KUMAR P., FREEMAN A. R., LOFTUS R. T., GALLARD C., FULLER D. Q. BRADLEY D. G. (2003): Admixture analysis of South Asian cattle. *Heredity*, 91(1), 43–50.

- LENSTRA J.A., AJMONE MARSAN P., EUROPEAN CATTLE GENETIC DIVERSITY CONSORTIUM, ECONOGENE CONSORTIUM (2006): Microsatellites and Y-chromosomal haplotypes of European and Middle-Eastern cattle, sheep and goats. Geographic clines, clusters, male introgression, conflicting views on diversity. In: 30th International Congress on Animal Genetics, Porto Seguro. Available at: http://www.isag.org.uk/Docs/2006ISAG_Proceedings.pdf
- LI M.H., KANTANEN J. (2009): Genetic structure of Eurasian cattle (*Bos taurus*) based on microsatellites: clarification for their breed classification. *Animal Genetics*, 41(2), 150-8.
- LOFTUS R.T., MACHUGH D.E., BRADLEY D.G., SHARP P.M., CUNNINGHAM P. (1994): Evidence for two independent domestications of cattle. *Proceedings of the National Academy of Science of the United States*, 91, 2757-2761.
- MA R.Z., RUSS I., PARK C., HEYEN D.W., BEEVER J.E., GREEN C.A., LEWIN H.A. (1996): Isolation and characterization of 45 polymorphic microsatellites from the bovine genome. *Animal Genetics*, 27(1), 43-7.
- MACHUGH D.E., LOFTUS R., BRADLEY D., SHARP P., CUNNINGHAM P. (1994): *Proceedings of the Royal Society of London*, 256, 25-31.
- MACHUGH D.E., SHRIVER M.D., LOFTUS R.T., CUNNINGHAM P., BRADLEY D.G. (1997): Microsatellite DNA variation and the evolution, domestication and phylogeography of Taurine and Zebu cattle (*Bos taurus* and *Bos indicus*). *Genetics*, 146(3), 1071-1086.
- MARIANI S., BEKKEVOLD D. (2014): The nuclear genome: Neutral and adaptive markers in fisheries science. Cadrin SX., Kerr LA., Mariani S., editors. In *Stock Identification Methods: Applications in Fishery Science*. 2. ed. Amsterdam: Academic Press. 297-328.
- MARTINEZ R.D., FERNANDEZ E.N., BROCCOLI A.M., MARTINEZ A., DELGADO J.V. (2005): Genetic variability in the Argentinian Creole Cattle of Patagonic origin. *Archivos de Zootecnia*, 54, 415-21.
- MARTINEZ-CORREAL G., ALVAREZ L.A., MARTINEZ G.C. (2009): Conservacion, Caracterizacion y Utilizacion de los bovinos Criollos en Colombia. In: *X Simposio Iberoamericano sobre Conservacion y Utilizacion de Recursos Zoogeneticos* (Ed. by L.A. Alvarez), 1695-7504.
- MAUDET C., LUIKART G., TABERLET P. (2002): Genetic diversity and assignment test among seven French cattle breeds based on microsatellite DNA analysis. *Journal of Animal Science*, 80, 942-950.
- MBURU D HANOTTE O. (2005): A practical approach to microsatellite genotyping with special reference to livestock population. *Genetics*. pp. 82.
- MEDUGORAC I., MEDUGORAC A., RUSS I., VEIT-KENSCH C.E., TABERLET P., LUNTZ B., MIX H.M., FORSTER M. (2009): Genetic diversity of European cattle breeds highlights the conservation value of traditional

unselected breeds with high effective population size. *Molecular Ecology*, 18, 3394–410.

MEIRELLES SL., GOUVEIA GV., GASPARIN G., ALENCAR M.M., GOUVEIA J.J., REGITANO L.C. (2011): Candidate gene region for control of rib eye area in Canchim beef cattle. *Genetic Molecular Research*, 10(2), 1220–6.

METTA M., KANGINAKUDRU S., GUDISEVA N., NAGARAJU J. (2004): Genetic characterization of the Indian cattle breeds, Ongole and Deoni (*Bos indicus*), using microsatellite markers - a preliminary study. *BMC Genetics*, 18; 5, 16.

MOAZAMI-GOUDARZI K., LALOE D., FURET J.P., GROSCLAUDE F. (1997): Analysis of genetic relationships between 10 cattle breeds with 17 microsatellites. *Anim Genetics* 28, 338-345.

MOHAMAD K., OLSSON M., VAN TOL H. T. A., MIKKO S., VLAMINGS BART H., ANDERSSON G., RODRÍGUEZ-MARTÍNEZ H., PURWANTARA B., PALING R.W., COLENBRANDER B., LENSTRA J. A. (2009): On the Origin of Indonesian Cattle. *PLOS ONE* 4(5),10. <https://doi.org/10.1371/annotation/e674f274-4378-47f1-97e1-f95a2>

MONTALDO H.H., MEZA-HERRERA C.A. (1998): Use of molecular markers and major genes in the genetic improvement of livestock. *Electronic Journal of Biotechnology*, 1(2), 83-89.

MUKESH M., SODHI M., BHATIA S., MISHRA B.P. (2004): Genetic diversity of Indian native cattle breeds as analyzed with 20 microsatellites. *Journal of Animal Breeding and Genetics*, 121, 416–424.

NAVANI N., JAIN P.K., GUPTA S., SISODIA B.S., KUMAR S. (2002): A set of cattle microsatellite DNA markers for genome analysis of riverine buffalo (*Bubalus bubalis*). *Animal Genetics*, 33(2), 149-154.

NICHOLAS F.W. (1996): Introduction to veterinary genetics. Oxford University Press. 317pp.

OLSEN H.G., LIEN S., SVENDSEN M., NILSEN H., ROSETH A., AASLAND OPSAL M., MEUWISSEN T.H. (2004): Fine mapping of milk production QTL on BTA6 by combined linkage and linkage disequilibrium analysis. *Journal of Dairy Science*, 87(3), 690-8.

PANDEY A.K., SHARMA R., SINGH Y., PRAKASH B. B., AHLAWAT S.P.S. (2006): Genetic diversity studies of Kherigarh cattle based on microsatellite markers. *Journal of Genetics*, 85(2), 117–122.

PEELMAN LJ., MORTIAUX F., VAN ZEVEREN A., DANSERCOER A., MOMMENS G., COOPMAN F., ET AL. (1998): Evaluation of the genetic variability of 23 bovine microsatellite markers in four Belgian cattle breeds. *Animal Genetics*, 29(3), 161–7.

QI X.B., JIANLIN H., WANG G., REGE J.E.O., HANOTTE O. (2009): Assessment of cattle genetic introgression into domestic yak populations using mitochondrial and microsatellite DNA markers. *Animal Genetics*, 41, 242–52.

- QUIROZ-VALIENTE J., MARTINEZ A., ULLOA R., VEGA-PLA J.L. (2006): Caracterización Genética de las Poblaciones Bovinas Criollas de México. In: VII Simposio Iberoamericano sobre conservación y Utilización de Recursos Zoogenéticos (Ed. by A. Stemmer), 220–222.
- ŘEHOUT V., HRADECKÁ E., CITEK J. (2006): Evaluation of parentage testing in the Czech population of Holstein cattle. Czech Journal of Animal Science, 51 (12), 503–509.
- REIST-MARTI S.B., SIMIANER H., GIBSON J., HANOTTE O., REGE J.E.O. (2003): Weitzman's approach and conservation of breed diversity: an application to African cattle breeds. Conservation Biology, 17, 1299–1311.
- RON M., BLANC Y., BAND M., EZRA E., WELLER J.I. (1996): Misidentification rate in the Israeli dairy cattle population and its implications for genetic improvement. Journal of Dairy Science, 79 (4), 676–681.
- SCHLÖTTERER C. (1998): Genome evolution: Are microsatellites really simple sequences? Current Biology, 8, 132–134.
- SCHLÖTTERER C. (2004): The evolution of molecular markers just a matter of fashion. Nature Reviews Genetics, 5, 63–69.
- SCHMID M., SAITBEKOVA N., GAILLARD C., DOLF G. (1999): Genetic diversity in Swiss cattle breeds. Journal of Animal Breeding and Genetics, 116(1), 1–8.
- SHARMA R., KISHORE A., MUKESH M., AHLAWAT S., MAITRA M., KUMAR A.PANDEY AND TANTIA MADHU SUDAN. (2015): Genetic diversity and relationship of Indian cattle inferred from microsatellite and mitochondrial DNA markers. BMC Genetics, 16:73.
- SELKOE K.A., TOONEN R.J. (2006): Microsatellites for ecologists: a practical guide to using and evaluating microsatellite markers. V. 9, 5, 615–629.
- SINGH U., KUMAR S., KUMAR A., ET AL. (2013): Advances in Cattle Research. New Delhi: Satish Serial Publishing; ISBN 13: 9789381226421
- SMITH S.B., ZEMBAYASHI M., LUNT D.K., SANDERS J.O., GILBERT C.D. (2001): Carcass traits and microsatellite distributions in offspring of sires from three geographical regions of Japan. Journal of Animal Science, 79(12), 3041–51.
- SODHI M., MUKESH M., PRAKASH B., AHLAWAT S.P.S., SOBTI R.C. (2006): Microsatellite DNA typing for assessment of genetic variability in Tharparkar breed of Indian zebu (*Bos indicus*) cattle, a major breed of Rajasthan. Journal of Genetics, 85, 165–170.
- STEFFEN P., EGGEN A., STRANZINGER G., FRIES R., DIETZ A.B., WOMACK Y.E. (1993): Isolation and mapping of polymorphic microsatellites in cattle. Animal Genetics, 24, 2, 121–124.
- STEVANOV-PAVLOVIĆ M., DIMITRIJEVIĆ V., MARIĆ S., RADOVIĆ D., STEVANOVIĆ J., STANIMIROVIC Z. (2015): Applicability assessment of a standardized microsatellite marker set in endangered Busha cattle. Slovenian Veterinary Research, 52 (3), 133–9.

- SUN W.B., CHEN H., LEI C.Z., LEI X.Q., ZHANG Y.H. (2007): Study on population genetic characteristics of Qinchuan cows using microsatellite markers. *Journal of Genetics and Genomics*, 34, 17–25.
- TAPIO I., VARV S., BENNEWITZ J. ET AL. (2006): Prioritization for conservation of northern European cattle breeds based on analysis of microsatellite data. *Conservation Biology*, 20, 1768–79.
- TENEVA A., TODOROVSKA E., TYUFEKCHIEV N., KOZELOV L., ATANASSOV A., FOTEVA S., RALCHEVA S., ZLATAREV S. (2005): Molecular characterization of Bulgarian livestock genetic resources. I. Genetic diversity in Bulgarian Grey cattle as revealed by microsatellite markers. *Bulgarian Journal of Agricultural Science*, 11, 3, 363–372.
- TENEVA A., TODOROVSKA E., TYUFEKCHIEV N., STELLA A., BOETTCHER P., DIMITROVA I. (2007): Molecular characterization of Bulgarian livestock genetic resources. II. Microsatellite variation within and among Bulgarian cattle breeds. *Biotechnology in Animal Husbandry*, 23, 5–6, 227–242.
- TENEVA A. (2009): Molecular markers in animal genome analysis. *Biotechnology in Animal Husbandry*, 25, 5–6, 1267–1285.
- TENEVA A., PETROVIC M. (2010): Application of molecular markers in livestock improvement. *Biotechnology in Animal Husbandry*, 26, 3–4, 135–154.
- TENEVA A., DIMITROV K., PETROVIC V., PETROVIC M., DIMITROVA I., TYUFEKCHIEV N., PETROV N. (2013): Molecular genetics and ssr markers as a new practice in farm animal genomic analysis for breeding and control of disease disorders. *Biotechnology in Animal Husbandry*, 29 (3), p 405–429.
- TOTH G., GASPARI Z., JURKA J. (2000): Microsatellites in different eukaryotic genomes: Survey and Analysis. *Genome Research*, 10(7), 967–81.
- TROMMELEN G.J., DEN DAAS JH., VIJG J., UITTERLINDEN A.G. (1993): DNA profiling of cattle using micro- and minisatellite core probes. *Animal Genetics*, 24(4), 235–41.
- ULLOA-ARVIZU R., GAYOSSO-VAZQUEZ A., RAMOS-KURI M., ESTRADA F.J., MONTANO M., ALONSO R.A. (2008): Genetic analysis of Mexican Criollo cattle populations. *Journal of Animal Breeding and Genetics*, 125, 351–9.
- VAN MARLE-KÖSTER E., NEL L.H. (2003): Genetic markers and their application in livestock breeding in South Africa: A review. *South African J. Anim. Sci.* 33, 1–10.
- VISSCHER P.M, WOOLLIAMS J.A, SMITH D., WILLIAMS J.L. (2002): Estimation of pedigree errors in the UK dairy population using microsatellite markers and the impact on selection. *Journal of Dairy Science*, 85, 2368–75.
- WAKCHAURE R., GANGULY S., PARVEEZ A. PARA., PRAVEEN K., QADRI K. (2015): Molecular markers and their applications in farm animals: a review. *International Journal of Recent Biotechnology*, 85(9), 2368–75.

- WANG D. G., FAN J. B., SIAO C., BERNO A., YOUNG P., SAPOLSKY R., GHANDOUR G., PERKINS N., WINCHESTER E., SPENCER J., KRUGLYAK L., STEIN L., HSIE L., TOPALOGLOU T., HUBBELL E., ROBINSON E., MITTMANN M., MORRIS M. S., SHEN N., KILBURN D., RIOUX J., NUSBAUM C., ROZEN S., HUDSON T. J., LANDER E. S. (1998): Large-scale identification, mapping, and genotyping of single nucleotide polymorphisms in the human genome. *Science*, 280, 1077–1082.
- WEBER J. L., MAY P. E. (1989): Abundant class of DNA polymorphisms which can be typed using the polymerase chain reaction. *American Journal of Human Genetics*, 44, 388–396.
- WEIR B. S., BASTEN C. J. (1990): Sampling strategies for distances between DNA sequences. *Biometrics*, 46, 551–582.
- WEITZMAN M.L. (1993): What to preserve? An application of diversity theory to crane conservation. *Quarterly Journal of Economics*, 108, 157–183.
- WELLER J.I., FELDMESSER E., GOLIK M., TAGER-COHEN I., DOMOCHOWKY R., ALUS O., EZRA E., RON M. (2004): Factors affecting incorrect paternity assignment in the Israeli Holstein population. *Journal of Dairy Science*, 87(8), 2627–40.
- YANG W., KANG X., YANG Q., LIN Y., FANG M. (2013): Review on the development of genotyping methods for assessing farm animal diversity. *Journal of Animal Science Biotechnology*, 4(1), 2–6.