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### Brief Review

## The feasibility of molecular markers in animal production

Angela Adamski da Silva Reis<sup>1,3\*</sup>, Ana Lúcia Coutinho Teixeira<sup>1,2</sup>, Joice Aguiar Barbosa<sup>1,2</sup>, Laura Raniere Borges dos Anjos<sup>1</sup>, Rodrigo da Silva Santos<sup>1,4\*</sup>

1. Laboratory of Molecular Pathology, Institute of Biological Sciences (ICB II), Federal University of Goiás (UFG), Goiânia, GO, Brazil.

2. Veterinary and Zootechny School, Federal University of Goiás (UFG), Goiânia, GO, Brazil.

3. Department of Biochemistry and Molecular Biology, Institute of Biological Sciences (ICB II), Federal University of Goiás (UFG), Goiânia, GO, Brazil.

4. Department of Nature Sciences (LEdoC), Special Academic Unit of Human Sciences, Federal University of Goiás (UFG), Goiás, GO, Brazil.

\*Autores para correspondência: A.A.S.R (angeladamski@gmail.com); R.S.S (rdssantos@gmail.com).

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### ABSTRACT

In animal breeding programs, molecular markers can be used to select individuals with better phenotypes. The perspectives for the enhancement of the production indexes are associated with the use of genotyping through molecular biology methods. Furthermore, the advances in statistics and bioinformatics promoted significant progress in the quality of the animal productive chain. Molecular markers are important tools to identify the genetic variation between individuals. In addition, these methods may be used to detect the genetic variation of a trait of interest. In this way, the use of DNA markers permits the identification of the genetic potential of an animal before its expression as a phenotype.

### 1. General considerations

Nowadays, the molecular biology is an essential tool for animal phenotype and genotype investigation. New strategies of management, combined with the employment of efficient genetic methods in cattle genetic improvement programs, allowed increased genetic gains that maximized the decision-making processes. In this way, these techniques influence the breedings and focus on the development of the animal production (Singh et al., 2014).

The genomic information of cattle has a high predictive value because it enables the identification of animals with better productive potential. In this sense, the data obtained from molecular markers stand out with important information about the selection programs and genetic improvement, being commonly referenced as molecular markers assisted selection (Teneva, 2006).

Additionally, the search for molecular markers promotes a significant advance in the genetic improvement of commercial species destined to the animal production, in particular by the increase in the prediction accuracy of genetic value for the superior animal selection. Populational-genetic parameters (allele and genotype frequency estimation) permit the comparison of rates between populations and show differences in their genetic compositions, in which they contribute to the phenotypic variation (Pereira et al., 2015).

On the other hand, some studies have shown the possibility to map genes and their groups that may influence quantitative traits (Quantitative Trait Loci – QTL). The QTLs

are identified by detecting genes that are directly related to production characteristics, called candidate genes. Additionally, the QTLs are identified by random markers in the development of saturated genetic maps. These markers correlate with the traits of economic interest and describe the chromosomal regions with a locus that influences the QTLs (Alencar, 2004).

In cattle, the genetic polymorphisms have been associated with many characteristics of economic interest, such as weight gain in a particular age of the animal, fat content in milk, carcass quality, meat softness, lactation, and feeding conversion. The genetic polymorphisms can be microsatellites, insertion-deletion (INDEL), copy number variation (CNV) and the most recently described, the single nucleotide polymorphism (SNP), which represents the most important source of genetic variability in the genome (Gibson & Muse, 2004; Caetano, 2009; Yang et al., 2013).

Some factors influence the crescent interest in the use of the SNPs as markers for genetic analysis. SNPs are abundant in the genome and, because of this, are considered as a useful tool for the program of cattle selection, paternity tests, and association with the animals' phenotypes. Moreover, SNPs are localized in codifying and regulatory regions that may affect the expression of mutant proteins. As described, SNPs are directly responsible for the variations between individuals with traits of interest for zootechnicians (Maeda et al., 1989).

Additionally, the Genome Wide Association Studies (GWAS) and Genomic Selection (GS) evaluate alleles that might be associated with particular genomic regions. Furthermore, GWAS and GS can predict the phenotypes observed and promote the comprehension of the biological and physiological mechanisms of genes (WTCCC, 2007; Huson et al., 2014).

The high density genotyping chips enabled the use of new applications that promote large advances for the examination and animal improvement programs. The GWAS have an innovative character because they allow the identification of statistical associations between hundreds of genomic loci and complex traits, in a way that the knowledge of molecular and biological pathways are increased (Huson et al., 2014).

Due to the large number of SNPs in the genome and the facility of genotyping promoted by GWAS, SNPs are the chosen markers and are used in most associative studies. In this way, GWAS is a complete method for the investigation of SNPs and candidate genes (WTCCC, 2007).

GWAS evaluates the high coverage of the genome with markers (1 marker per 50.000 base pairs) and permits the evaluation of 100% of the additive genetic variability of one characteristic by all the genome. In this way, this method allows the estimation of the substitution value of an allele for each locus involved with the trait. With this, the genetic value of an individual can be estimated based on the genotypes of all markers that are associated with the characteristic (Meuwissen et al., 2001).

In the GS, the improved population is investigated, and the SNPs are used as tools for the prediction of accurate Progeny Expected Difference (PED), which promotes a more efficient genomic selection. Moreover, the primary objective of the GS is to predict the genetic value of the individual without determining the specific genes in the phenotype expression. Additionally, PEDs are associated with the genetic progress for the selection (Huson et al., 2014).

The use of molecular markers in the dairy cattle culture aims to identify the genetic profile of animals for the traits of interest, such as the milk fat content, which is very relevant for the production of milk-derived products. The milk composition is altered once the differences between the genotypes may modify the primary structure of the proteins, resulting in differences in the physical-chemical properties of the milk (Botaro et al., 2007). The DGAT1 gene, located on chromosome 20, is responsible for the expression of the diacylglycerol acetyltransferase enzyme, which plays a significant role in the synthesis of triacylglycerols. The SNP in the exon 8 of DGAT1 promotes the substitution of lysine by alanine, altering the enzyme to SNP K232A. This mutant enzyme increases the percentage of protein, fat, and total solids of the milk. In contrast, the presence of lysine in the wild-type enzyme determines the reduction of the total fat and protein production within the lactation. In this sense, the identification of genotypes associated with SNP K232A is efficient to select animals for the animal genetic improvement programs (Smaragdov, 2011).

The genetic polymorphism of the beta-lactoglobulin (Beta-Lg) is another example of a molecular marker associated with the composition of milk (Oner & Elmaci, 2006). The A allele of Beta-Lg increases milk production, protein content and reduces the casein concentration. The B allele, otherwise, is associated with the increase of casein and the efficiency of milk production. In this way, the selection criteria should be analyzed according to the output profile of the producer's aim, associating the cost for the maintenance of a particular genotype of the herd by the animal improvement program (Goes & Simonelli, 2009).

The molecular markers can predict the increase of the production performance and the reproductive rates, as well as the improvement of the efficiency of the carcass quality, health and animal well-being. The reproduction and sanity are fundamental within a production system, and the molecular methods can predict the selection of the best genotypes according to the needs of the producer (Silva et al., 2003). Regarding meat production, molecular markers can be used for the selection of animals that present the double musculature phenotype and produce leaner meat due to muscular hypertrophy (Teixeira et al., 2006).

The double musculature phenotype refers to the enhancement of the muscle mass as a result of the hypertrophy of the muscle fibers. In addition, this phenotype promotes the reduction of bone weight, resulting in a better carcass quality in comparison with animals without the syndrome, which exhibits meat with less fat due to myogenesis regulation (Teixeira et al., 2006). Moreover, the animals that have the double musculature show better carcass productivity and profitability, because they have generated meat cuts with better cost-effectivity. In this context, the syndromic animals are classified as superiors and considered as excellent by the European Common Community (ECC), being used for the exportation. Literature data associates this effect to the knockout of the exon 3 of GDF8 gene that promotes the inhibition of GDF8 protein expression. The mutation is detected through molecular methods and, consequently, will be selected to compose the herd of superior animals from the improvement programs (Teixeira et al., 2006; Fiems, 2012). The cattle races Belgian Blue, Piemontesa, Asturiana de los Valles, Maine Anjou, Charolesa, Limousin, Parthenaise and Rubea Gallega carry a mutation in the myostatin gene. These animals, when compared to those without the mutations, are considered superiors because they display increased meat production, a larger proportion of noble cuts and leaner and smooth meat (Teixeira et al., 2006).

The polymorphism of the halothane gene in swines is associated with increased meat deposition in the carcass. However, these animals tend to produce more pale, soft and exudative (PSE) meat (Bridi et al., 2006). The n allele of the halothane gene, which is responsible for the susceptibility to the genetic stress, can be detected through the HAL-1843TM test developed by Fujii and colleagues in 1991. However, the n allele homozygotic animals present more lean meat percentage and better carcass shape when compared to the dominant homozygote animals NN (Silva et al., 2003). Through QTL scans, regions that may be associated with characteristics of economic interest were described in many chromosomes. These areas are also studied, such as the fine mapping and comparative analysis of candidate genes. Currently, the swine industry investigates many markers that are related to the meat quality, such as the halothane gene, acid meat gene and the gene that impacts the intramuscular fat, as well as the fur color gene (Silva et al., 2003).

The advances in molecular genetics have contributed to the growth of the genome mapping of breeding animals. In pigs, the development of linkage maps and physical maps, as well as the possibility of success in the discovery of new genes and markers, show that their use in selection programs will certainly be amplified and efficient to improve the breeding animal quality. In front of the innovations and applications of the molecular markers, we can identify the evidence in the scope of the livestock production, in the quality of the products through the animal selection by genotypic profile, as well as the sustainability of the animal improvement system. In this way, these markers can predict innovations and decision making in the animal of reproduction programs (Silva et al., 2003).

Introgression is the process of applying markers and is initiated by obtaining the F1 population that from the breeding between the donor population (DP) and the receptor population (RP), and backcrossing with RP, for many generations. During this process, the markers are used to identify the allele that is introgressed. After many generations, individuals of the backcrossed population are crossed. Therefore, the progenies will be homozygotes for the introgressed allele. At the end of the process, the genetic background of the remaining lineage will be the same as the RP, but with the favorable genes for the trait of interest, existing and set in the DP (Silva et al., 2003).

Once these genes are mapped, they can be used in genetic improvement programs, including the marker-assisted introgression (MAI), marker-assisted selection (MAS), and positional cloning. However, in MAI and MAS, some aspects should be pointed out on the impact of mistakes during the process, such as the presence of false positives, incorrect estimation effects, the position of QTL, and the risk of the loss of the allele of interest (Visscher & Haley, 1995). The strategy used to avoid these losses is the selection of early males, based on the markers for the litter size that will be utilized for performance tests and disease resistant females (Silva et al., 2003).

In addition, the domestication and race formation permitted that the domestic animals would undergo natural and artificial selection. These selection pressures promoted the increase of the frequency of some mutations in specific regions of the genome that turned the individuals more adapted or conferred favorable traits. In the same way, other polymorphisms underwent the reduction of the frequency or complete elimination (Pereira et al., 2015).

The main variations that occur in the DNA molecule are the repeated regions (micro and minisatellites), insertions and deletions (INDEL) and single nucleotide polymorphism (SNPs) (Pereira et al., 2015). In this way, before transferring markers from the populations that they were investigated and set for commercialization, it is of extreme importance to confirm its effect on a characteristic of interest, considering the different races and the environment in a process known as validation (Pereira et al., 2015).

The genomic selection based exclusively on markers present many advantages, such as the no requirement of QTL discovery, high selective accuracy, avoidance of biased estimates of gene effect, and QTL individuals. These methods compute all variation due to small locus effects, completes the low heritability trait, and allows the use of prediction models to all families of the improvement program (Coutinho & Rosário, 2010).

New possibilities of genetic progress, in particular for the traits, in which the classical methods cannot demonstrate the expected aim. Through the selection made by genetic markers, the prediction of the results can be assigned, once the technology applied the use of DNA samples permits the investigation right after the birth or even during the preimplantation embryonic phase (Goes & Simonelli, 2009). According to Miller and colleagues (2010), the opportunities to increment the genetic progress include the increase of the selection accuracy, the reduction of the generation interval and the increase of the selection intensity. In addition, these opportunities improve the capacity of the measurement of certain traits, such as the individual feeding, and opportunities for changes in new characteristics.

The implementation of a low-density commercial panel should enable the decision-making process in a more informative manner, considering the genetic potential in all levels of the productive chain. This panel should include predictive SNPs based on efforts of QTL mapping, combined with additional SNP to allow the imputation of genotypes of a

high-density SNP panel. The use of the genomics will generate opportunities for the reproductive technologies, as the transference of embryos, once the identification of elite females is more precise. The potential changes in the industry structure of animal genetic improvement will be discussed, including the opportunities for cost reduction to obtain superior ox, variations in the phenotypic measurement and development of new meat products (Miller, 2010).

## 2. Conclusion

Molecular genetics will be definitively incorporated into Brazilian beef improvement programs after the implementation of studies on the association between molecular markers and production traits, in order to establish marker-assisted selection strategies. The information provided by genetic markers will be included to genetic evaluation programs within races or multibreed and breeding biotechnologies that may contribute to increase the intensity of selection. The molecular biology technologies associated to animal improvement focus on the variability of the markers with phenotypes of interest, and their applications display advantages in comparison with traits of difficult measurement. In this context, we can conclude that the use of molecular markers in animal production assists the selection effectiveness in breeding programs, predicting and selecting superior animals and consequently contributing to quality in animal production.

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