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COLLEGE OF ANIMAL SCIENCE AND FOOD ENGINEERING

FELIPE EGUTI DE CARVALHO

Genome-wide association study and predictive ability for growth traits in Nellore cattle

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Master's thesis presented to the College of Animal Science and Food Engineering of the University of São Paulo, requirements as part to obtain a master's degree in sciences from the postgraduate program in Animal Science.

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DEDICATION

Everything I do I surrender to the hand of God, then I dedicate to him.

To my father, Leordino, for all support and to be my base. Writing would not be enough to show my gratitude.

To my grandfather Jair Kazuo Eguti, who was my inspiration to choose my profession. *In memoriam*

My grandmother Terezinha Candida Lamy, for all support and wisdom passed on, eternal gratitude. *In memoriam*

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To Prof. Dr. Fernando Sebastián Baldi Rey.

EPIGRAPH

“*War not make one great*…”

(Sun Tzu)

“Resilience ever”

RESUMO

Carvalho, F. E. **Estudo de associação genômica ampla e habilidade de predição para características de crescimento em bovinos da raça Nelore.** 2019. 67 f. Dissertação (Mestrado) – Faculdade de Zootecnia e Engenharia de Alimentos, Universidade de São Paulo, Pirassununga, 2019.

Este estudo teve como objetivo identificar regiões genômicas que influenciam características de crescimento em bovinos da raça Nelore e avaliar a capacidade preditiva de cada característica com base nos resultados obtidos a partir da metodologia single-step Genome-Wide Association Studies (ssGWAS) considerando diferentes densidades de marcadores do tipo SNP. A Associação Nacional de Criadores e Pesquisadores disponibilizou o conjunto de dados de dezoito rebanhos bovinos participantes do programa de melhoramento brasileiro da raça Nelore (Nelore Brasil). Foram consideradas as características peso ao nascer (PN), peso ajustado aos 210 (W210) e aos 450 (W450) dias de idade e peso adulto da vaca (PCA). Um total de 963 animais, genotipados utilizando o Illumina BovineHD BeadChip, foram utilizados como população de referência para imputar genótipos de 7.689 animais, genotipados em painel de baixa densidade. A imputação dos genótipos foi realizada utilizando o software FImpute 2.2.. Na análise de enriquecimento funcional, vários genes foram relacionados ao desenvolvimento e metabolismo de músculo e tecido adiposo, eficiência alimentar, composição do leite e comportamento materno. A habilidade de predição (HP)variou de baixa (0,10) a moderada (0,68). Os valores de viés e HP para ambos os painéis foram semelhantes para todas as características. Os resultados encontrados neste estudo devem melhorar a compreensão do mecanismo genético e fisiológico associado às características de crescimento. No entanto, associação desses resultados com outras abordagens, como informações biológicas do sistema e outras informações ômicas, devem melhorar a identificação de variantes genéticas causadoras de características de crescimento em bovinos zebuínos.

Palavras-chave: Bovinos de corte. Genômica. GWAS. SNP.

ABSTRACT

Carvalho, F. E. **Genome-wide association study and predictive ability for growth traits in Nellore cattle.** 2019. 67 f. Dissertação (Mestrado) – Faculdade de Zootecnia e Engenharia de Alimentos, Universidade de São Paulo, Pirassununga, 2019.

This study aimed to identify genomic regions influencing growth traits in Nellore cattle and evaluate the predictive ability of each trait based on results obtained from single-step Genome-Wide Association Studies (ssGWAS) considering different SNP markesr densities. The National Association of Breeders and Researchers provided the dataset from eighteen Nellore herds participating of the Nellore Brazil breeding program. The traits birth weight (BW), adjusted weight at 210 (W210) and at 450 (W450) days of age and adult cow weight (ACW) were considered. A total of 963 animals, genotyped using the Illumina BovineHD BeadChip, were used as a reference population to impute genotypes of 7,689 animals, genotyped in low-density panel. Genotype imputation was performed using the FImpute 2.2 software. Several genes in enrichment analysis were related to muscle and adipose tissue development and metabolism, feed efficiency, milk composition and maternal behavior. The predictive ability varied from low (0.10) to moderate (0.68). The predictive ability and bias for both panels were similar for all traits. The results found in this study should improve the understanding of genetic and physiologic mechanism associated with growth traits. However, the association of these results with other approaches, like system biologic and other omics information should improve the identification of causative genetic variants in growth traits in indicine cattle.

Keywords: Beef Catle. Genomic. ssGWAS. SNP.

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1. INTRODUCTION

In beef cattle, growth traits are considered the most important selection criteria due to their association with beef production (ABREU SILVA et al., 2018). Growth traits are easily assessed and displayed moderate to high heritability estimates, showing favorable genetic association with others productive and reproductive traits (BALDI; ALBUQUERQUE; ALENCAR, 2010). Beside the selection advantages of growth traits, the progeny-test is a common practice in beef cattle breeding programs to improve the expected breeding value (EBV) reliability of unproven sires. Thus, earlier reliable genetic evaluations of unproven sires are appealing in order to increase the genetic response for growth traits.

Genome-wide association studies (GWAS) have identified thousands of genetic variants associated with growth traits in several beef cattle breeds (JAHUEY-MARTÍNEZ et al., 2016; MATIKA et al., 2016; ZHOU et al., 2016). Studies were performed using crossbred and taurine breeds under temperate conditions (BUZANSKAS et al., 2014; SEABURY et al., 2017). However, there are few studies with *Bos indicus* breeds under tropical and subtropical conditions (UTSUNOMIYA et al., 2013; TERAKADO et al., 2017). Some methods were proposed to perform GWAS analysis using the concept of variable selection, such as BayesB (MEUWISSEN; HAYES; GODDARD, 2001; OLIVEIRA JÚNIOR et al., 2017), BayesC (HABIER et al., 2010; LU et al., 2016) Bayesian Lasso (GODDARD; HAYES, 2009; LI et al., 2011; WALDMANN et al., 2013) and BayesCπ (HABIER et al., 2010). An alternative GWAS approach called iterative single-step Genome-wide association studies (ssGWAS), proposed by Wang et al. (2012), considers the phenotypic records from both genotyped and non-genotyped animals, increasing the power to detect quantitative trait loci (QTLs) associated with complex traits (FRAGOMENI et al., 2017).

Beef farmers used to adopt new technologies at lower intensity than dairy farmers, probably due to the strait business margin of beef cattle production (BERRY; GARCIA; GARRICK, 2016). In this sense, reduce the genotyping cost through single nucleotide polymorphisms (SNP) panel density reduction, including the most informative markers for key traits, is a lower cost strategy to apply genomic selection in large scale. Recently, Silva et al. (2017) in a GWAS

for beef tenderness in Nellore cattle reported higher prediction ability when considered the most informative markers (5K SNP) compared to a high-density array (376K SNP). This result suggests that including non-informative SNP markers could impair the prediction ability, and SNP array reduction is a cheaper alternative for genomic selection in beef cattle.

Additional genomic studies in indicine cattle are necessary, since this cattle subspecies is prevalent in beef cattle herds under tropical and subtropical conditions. In this sense, the search for candidate and regulate genes underlying the genetic variation for growth traits resulted in potential chromosomal regions for further investigations (UTSUNOMIYA et al., 2013; TERAKADO et al., 2017), meanwhile substantial amount of the underlying genetic and physiological mechanisms remains mostly unaddressed.

2. OBJECTIVES

2.1. General objectives

This study aimed to identify genomic regions influencing growth traits at different ages in Nellore cattle using the single-step genomic best linear unbiased prediction method applied for association studies (ssGWAS) and evaluate the predictive ability for growth traits based on results obtained from ssGWAS analysis considering different SNP densities of preselected markers.

3. LITERATURE REVIEW

3.1. Growth traits

Cattle breeding in Brazil is predominantly based on grazing conditions and the use of more productive animals is paramount to produce beef cattle. The Brazilian herd is mostly composed of Zebu breeds, since zebu breeds are more adapted to tropical regions, edaphoclimatic conditions, hostile environments and resistance to endo and ectoparasites (SILVA et al., 2010; IBELLI et al., 2012). The Nellore breed (*Bos Taurus indicus*) stands out because of its ability to combine adaptability and productivity in tropical environments, so today it is the most used breed in Brazil and several studies in research centers, breeding programs, select and more accurately predict productive values.

In breeding programs, the use of animals with genetic values for traits that bring greater economic returns, are fundamental in meat production. Breeders seek to more reliably and rapidly identify animals with greater genetic potential for growth, in order to increase growth speed, identify and select the early animals (FARIA et al., 2017). Thus, selection for growth traits, directly impacts on the production systems economic efficiency, due to its high association with the final objective of beef cattle production, meat production. Growth traits are moderate to high heritability (SILVEIRA et al., 2018), indicating genetic progress when used for selection. Also, present genetic correlations between moderate to high magnitude, indicating that selection to any age should increase growth at other ages (BOLIGON et al., 2009, 2010; BALDI; ALBUQUERQUE; ALENCAR, 2010; ARAÚJO et al., 2014).

In this context, knowing the different stages of animal growth is of great relevance for the selection of animals (REZENDE et al., 2014). Regarding traits at young ages, such as birth weight and weaning weight, are economically important for beef cattle, since they exhibit enough genetic variability to respond to selection in different breeds, with a heritability ranging from 0.25 to 0.33 (BOURDON; BRINKS, 1982; MEYER, 1995; ALBUQUERQUE; MEYER, 2001; NOBRE et al., 2003; ERIKSSON et al., 2004; BOLIGON et al., 2010; FERREIRA et al., 2014;). In addition, they are excellent production indicators, since they

present association with other traits related to growth, yearling weight and carcass weight, as well could be used as selection criteria to improve calving easy (SCHMIDT et al., 2018).

Monitoring and controlling weights at the early stages could lead to reproductive problems lower, such dystocia calving and calf mortality, and could influence directly on weights at other ages (ROCHA et al., 2005). The birth weight is a trait could be difficult of measured, the necessity of daily appealed over the birth season, as well as proper equipment to perform the weighing. Also, is a difficult trait to select due to the low availability of reliable phenotypic records in genetic breeding programs, which allow the prediction of accurate genetic values for this trait.

In Brazil, it is still usual for breeders to select animals for higher weight at young ages which could lead to a large frame size on other age (BALDI; ALBUQUERQUE; ALENCAR, 2010; BOLIGON et al., 2011), and an undesired increase nutritional requirement of the herd, resulting in economic losses, due to higher food costs, since in times of food shortage there is an unfavorable relationship between the cow adult size and the reproductive and physiological efficiency (OWENS; DUBESKI; HANSONT, 1993; JENKINS; FERRELL, 1994; SILVEIRA et al., 2004).

Selection for cow mature weight presents some difficulties, such as the fact that it is a trait lately measured in animal life, (5 to 6 years), which makes it difficult to identify and select young bulls with reliable genetic values for this trait. However, it is an important measure to be incorporated into genetic assessments because it has considerable importance in bioeconomic indices (JORGE JÚNIOR; CARDOSO; ALBUQUERQUE, 2006; BRUMATTI et al., 2011). In addition, it presents heritability estimates ranging from moderate to high in breeds and present high magnitude of correlations with weight at young ages, such as birth weight, weaning and postweaning (SILVEIRA et al., 2004; MERCADANTE et al., 2004; CASTRO-PEREIRA; ALENCAR; BARBOSA, 2007; BALDI et al., 2008; BOLIGON et al., 2011).

The young animal selection for growth traits should be performed in a careful way, as it may result in late maturing animals and higher adult cow weight being unfavorable under grazing conditions (PEREIRA et al., 2010). In relation to the growth in the post-weaning phase, it presents an individual genetic potential

direct evaluation which demonstrates great economic importance, due to the high-performance relation in this period with carcass yield, and consequently the meat production (ASSAN; NYONI, 2009; BOLIGON et al., 2009).

3.2. Genome-wide association study (GWAS)

Genotyping processes, due to biotechnological advances, have been carried out on a large scale. Among these, the high-density panels (SNP markers – Single Nucleotide Polymorphisms) could be highlighted. The SNPs panels currently available have different densities of markers for genomic studies, which can harbor information on the possible regions that influence productive traits and may be used as potential predictors of production, aiming at complementing the accuracy of genetic values (MARTÍNEZ et al., 2017).

GWAS allow us to explore the available technology using molecular markers to identify genomic regions associated with interested phenotypes, such as the growth traits that require more time to measure all weights throughout the animal life, in order to obtain complete records of these phenotypic data (LU et al., 2013). These studies are carried out through SNPs from panels of different densities, to detect QTL to understand biology and genetic architecture. Such markers are useful to understanding the genetic structure of a particular trait for future applications in genomic selection (PETERS et al., 2012). In this way, to know more the genetic bases of evaluated breeds, with greater reliability, and to identify as soon as possible young animals with high genetic value (SNELLING et al., 2010).

An alternative GWAS approach has recently been proposed by Wang et al. (2012), where all genotypes, phenotypes and pedigree information are considered in a single- step (ssGBLUP), allowing the use of all kinship relationships simultaneously. This approach allows in a single-step that all SNPs are considered together with genotyped and non-genotyped animal phenotypes. This tool is potentially useful when the population contains a large number of phenotypes and few genotype data, especially when multiple-traits evaluations are simple and rapid to implement and the models of analysis are complex (MISZTAL; WANG, 2014; WANG et al., 2014).

3.2.1. GWAS for growth traits

Some studies of GWAS for growth traits in zebu cattle were carried out in recent years. Utsunomiya et al. (2013) in study with 654 genotyped progenies of Nellore bulls using a high-density SNP panel with 777,962 SNP's (*Illumina® BovineHD Genotyping BeadChip*), identified five SNPs on BTA14 (*Bos taurus chromosome*) associated with birth weight. Other association studies corroborate this region of QTLs, showing that they contain variables and many genes that affect the traits that are related to growth in cattle (MALTECCA et al., 2009; MCCLURE et al., 2010; PRYCE et al., 2011).

In a recent study, Terakado et al. (2017) evaluated 5,064 Nellore, using a high-density panel with 777,962 SNP's (Illumina® BovineHD Genotyping BeadChip), through the single-step methodology for GWAS with growth traits. In this study reported above, genes associated growth regulation were found, and regions with SNPs above 1.5% of additive genetic variance, were associated with BW in BTA14, weaning at BTA5, 8 and 29 and yearling at BTA11.

GWAS are being carried out in order to known the genetic architecture of Taurine breeds for growth traits. Jahuey-Martínez et al. (2016) worked with 823 Charolais cattle, genotyped with high density panel (76.883 SNP - GeneSeek Genomic Profiler Bovine HD), in association with birth weight, weaning and yearling, using the GWAS procedure and detected new QTLs associated with growth traits and possibly associated 5 positional and functional candidate genes potentially involved in the variations analyzed traits that may contribute to the knowledge basis genetic of growth. Snelling et al. (2010) evaluated crossbreed animals of Taurine breeds, and performed genomic associations for BW, at weaning and at approximately 12 months, mainly located in BTA 6 and 11. Other QTL studies with genomic associations in BTA6 for birth weight (GUTIÉRREZ-GIL et al., 2009), weight gain during and post-weaning (KNEELAND et al., 2004) and weight at 365 days (CASAS et al., 2000) have been reported. In a work with dairy cattle Schrooten et al. (2005) described a 19 to 31% increase in genetic progress when compared to the progeny test, with 50% of the genetic variance being explained by molecular markers.

Therefore, GWAS could be used as a tool in order to better understand the genetic architecture for productive traits of both Zebu and Taurine breeds. Thus, to enable information to elucidate the genetic mechanism of hard-to-measure or late-expressed traits, applying them to the selection of beef cattle through the use of genetic variations distributed throughout the genome to estimate genetic values, improving the genetic gain (HAMIDI HAY; ROBERTS, 2017).

3.3. Genomic Selection

Genomic selection refers to selection decisions based on genomic breeding values (GEBV), which are calculated as the effects sum of genetic markers scattered throughout the genome, potentially capturing the possible locus of quantitative traits (QTL), which possibly contribute to the variation of a traits (GODDARD, 2017; SCHAEFFER, 2006). The effects of QTL are first estimated in a large reference population with phenotypic information and in subsequent generations only marker information is required to calculate the GEBV (HAYES et al., 2009; HAYES; LEWIN; GODDARD, 2013).

The genomic selection is an innovation that in a short time can lower costs and accelerate genetic progress (GODDARD, 2017). In addition, when compared to the traditional progeny test selection system in dairy cattle, genetic gains with the use of genomic selection can be twice as high and costs can be reduced by up to 92% (SCHAEFFER, 2006; ZHANG; ZHANG; DING, 2011). Thus, it is fundamental to the breeding programs of beef cattle to monitor and select phenotypic traits of economic interest, in order to incorporate genomic data information in the prediction of genetic values to increase the selection accuracy of young animals (WIGGANS et al., 2017).

In dairy cows genomic selection is constantly advancing as it can be reduced to 2 years in the generation interval, potentially resulting in a 60 to 120% increase in the rate of genetic gain. The development and evaluation of genomic selection in beef cattle show slower advances when compared to dairy cattle, due to the larger number of animals and breeds. However further studies are needed on the use of markers in predictions (BERRY; GARCIA; GARRICK, 2016).

3.4. Prediction ability

The availability of genomic data can be used to improve the genetic prediction values by increasing the selection accuracy in traits difficult to measure or that are lately measured in the animal life (COLE et al., 2011; DIAS et al., 2006; MAGALHÃES et al., 2016; MORIGUCHI et al., 2012; NOBRE et al., 2003). Lourenco et al. (2015) working with Angus cattle obtained the ability to predict genomic value using the ssGBLUP method for BW, WW and post-weaning gain, using 51,883 animals genotyped with the *Bovine* SNP50k v2 *BeadChip* panel (*Illumina Inc., San Diego, CA*), and obtained greater gains in accuracy in the genomic prediction, in relation to the BLUP model. But these gains are dependent on the size and composition of population reference, since the ssGBLUP procedure algorithm allows the incorporation of large numbers of animals genotyped to low computational cost, without compromising predictive capacity and allowing for faster genomic predictions.

In a study with Nellore cattle, using genomic information for growth traits and different evaluation methodologies, Neves et al. (2014) reported prediction accuracies ranging from 0.24 to 0.53 for the GBLUP method and 0.30 to 0.50 for the BayesC and BLASSO methods. Silva et al. (2016) worked with feed efficiency trait, residual feed intake, using 761 genotyped Nellore cattle with high density panel (*BovineHD BeadChip assay 700k, Illumina Inc., San Diego, CA.*) in order to compare different models of genomic evaluation in different validation scenarios with the traditional BLUP, genomic BLUP, single step genomic BLUP (ssGBLUP), Bayesian regression methods (BayesCπ) and using 3 approaches, with sets of training and testing was based on the year of birth after 2010 (YOUNG), 3 less related subsets and the validation was done on each subset at a time (UNREL) and randomly divided into 4 subsets (considering the GCs) and validation was done in each RANDOM, obtained gains in predictions ranging from 0.10 to 0.58 using BLUP, from 0.09 to 0.48 using GBLUP, from 0.06 to 0.49 using BayesC and from 0.22 to 0.49 using ssGBLUP, considered that the ssGBLUP methods are more appropriate for genomic predictions.

In addition to the methods of analysis, genomic predictions must be related with the population reference structure as well as to the genotyping panels used in various genomic scenarios, consequently obtaining more genetic gains than the traditional progeny test (RAOUL; SWAN; ELSEN, 2017). Reliability in genomic predictions can be provided by validation in a group of animals that are not included in the training population. Close relationships between animals in training and validation populations tend to carry better predictive capacity than when groups are more distantly related (HABIER et al., 2010).

Regarding the use of low dense markers panels, aiming at a better cost /benefit between accuracy of prediction and amount spent for genotyping, high density panels are used to identify genomic regions highest effect on phenotypes of interest. Once such regions are identified, the panels can now be reduced, containing only the most interesting markers so that the complexity equations prediction is reduced, which impacts on the panel cost and, consequently, on the total cost of each percentage of achieved accuracy. Based on this procedure, a well-structured reference population is formed and the genotyping of new animals occurs only for the regions with the greatest effect, with low density panels (GARRICK, 2011; VANRADEN et al., 2011).

Considering the aforementioned, Silva et al. (2017) in a study of genomic selection for a trait of economic interest, as beef tenderness, carried out with 609 Nelore animals, 61 genotypes in 700K (BovineHD BeadChip, Illumina Inc., San Diego, CA.) and 548 genotypes in 80K (GeneSeek Genomic Profiler HD BeadChip), reported an accuracy gain of 285.71% after considering only informational regions (5K SNPs) when compared to the high-density panel (376K SNPs). Such a result would suggest that the inclusion of non-informative markers tends to impair the ability of prediction models as it makes them not very parsimonious therefore panel reduction should be considered for routine application in animal breeding programs.

4. MATERIAL AND METHODS

4.1. Data

The phenotypic and genotypic information belongs to the National Association of Breeders and Researchers (ANCP, Ribeirão Preto-SP, Brazil). The dataset contained information from eighteen Nellore herds distributed in the Southeast and Mid-West regions of Brazil, which participate in the Nellore Brazilian Breeding Program. Animals were raised in pasture-based production systems, with or without the use of creep feeding and supplementation. The traits birth weight (BW), adjusted weight at 210 (W210), 450 (W450) days of age, and adult cow weight (ACW) were considered. For W210, W450 and ACW, weights ranging from 165 to 255, 405 to 495 days of age and from 2 to 16 years of age were considered, respectively. The data structure and descriptive statistics for studied traits are presented in Table 1.

Table 1 - Descriptive statistics for growth traits in Nellore cattle for single-step genome-wide association (ssGWAS).

Trait[1]	N	Mean	SD	Minimum	Maximum	NCG[2]
BW (kg)	49,475	34.03	4.57	17.0	57.0	491
W210 (kg)	38,389	201.7	28.64	81.0	326.0	1,040
W455 (kg)	26,601	305.5	54.04	124.0	622.0	846
ACW (kg)	15,744	490.2	73.32	266.0	835.0	270

[1]BW= Birth weight; W210= Weaning weight; W450= Yearling weight; ACW= Adult cow weight; [2]NCG: Number of contemporary groups.
Source: Own authorship

The pedigree contained information from 192,483 animals (11,035 sires and 107,219 dams) distributed over nine generations. Contemporary groups (CG) were defined as farm, year and season of birth for trimestre, sex, and management group (lot group). Records within ± 3.5 standard deviations from the CG mean, and CG that had at least five animals were considered in the analysis.

4.2. Genomic information

A total of 963 animals were genotyped using the Illumina BovineHD BeadChip (Illumina Inc., San Diego, CA, USA), which contains 777,962 SNP markers. These animals were used as a reference population to impute genotypes of 7,689 animals, previously genotyped with a low-density panel (Clarifide Nelore 2.0) encompassing over 22,000 SNP markers. Genotype

imputation (with pedigree) was performed using the FImpute 2.2 software (SARGOLZAEI; CHESNAIS; SCHENKEL, 2014). The quality control criteria were performed by BLUPF90 software package (AGUILAR et al., 2014), removing animals and markers with call rate < 0.90 and minor allele frequency (MAF) < 0.05. Monomorphic SNPs with redundant position and those located in non-autosome chromosomes were removed. Additionally, animals and SNPs with Mendelian conflicts were excluded. After quality control, 8,545 genotyped animals and 460,838 SNPs remained for analyses.

4.3. Genetic parameter estimates

Variance components and genetic parameters estimates were obtained through an animal model including the direct additive genetic and residual effects as random effects, and the fixed effects of CG and the age of the animal as a covariable. For BW and W210, the maternal genetic and maternal permanent environment effects were included as random effects and the dam age at calving as covariable. The genetic covariance between the direct additive genetic and maternal genetic effects was set to be zero. The variance components and genetic parameters were estimated through the restricted maximum likelihood (REML) method, using the AIREMLF90 software (AGUILAR et al., 2010; MISZTAL, 2008; MISZTAL et al., 2002).

The analyses were conducted using the single-step genomic BLUP method (ssGBLUP), where the $\boldsymbol{A^{-1}}$ matrix is replaced by the $\boldsymbol{H^{-1}}$ matrix (AGUILAR et al., 2010):

$$\boldsymbol{H^{-1}} = \boldsymbol{A^{-1}} + \begin{bmatrix} 0 & 0 \\ 0 & \boldsymbol{G^{-1}} - \boldsymbol{A_{22}^{-1}} \end{bmatrix}$$

where $\mathbf{A_{22}}$ is a numerator relationship matrix for genotyped animals and **G**, a genomic relationship matrix. The genomic matrix by VanRaden et al. (2009) was built as follows:

$$\boldsymbol{G} = \boldsymbol{ZDZ'}q$$

where, ***Z*** is the matrix containing adjustments for allelic frequencies; ***D*** is the matrix with the effect of SNP (***D = I***); and *q* is a weighting/normalization factor. According to (VITEZICA et al., 2011), such factors can be obtained by ensuring that the mean diagonal in ***G*** is close to $\boldsymbol{A_{22}}$.

The model for genomic analysis is represented by the following matrix equation:

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{Z_1}a + \boldsymbol{Z_2}m + \boldsymbol{Z_3}c + e,$$

where: ***y*** is the vector of observations*; β* is the fixed effects vector; *a* is the vector of direct additive genetic effects; *m* is the vector of maternal additive genetic effects and ***c*** is the vector of maternal permanent environment effects, for traits BW and W210, ***X*** is known as the incidence matrix of fixed effects; $\boldsymbol{Z_1}$, $\boldsymbol{Z_2}$, and $\boldsymbol{Z_3}$ are the incidence matrices of direct additive genetic random effects, maternal additive genetic effects, and maternal permanent environment effects, respectively; *e* is the residual effect vector. However, for W450 and ACW is not include on model the $\boldsymbol{Z_2}$m and $\boldsymbol{Z_3}$c.

It was assumed that the vectors *a, m, c,* and *e* follow a normal distribution with zero mean, where var (*a*) **=** $\boldsymbol{H\sigma^2_a}$, var *(m)* **=** $\boldsymbol{H\sigma^2_m}$, var (*c*) **=** $\boldsymbol{I}\ \sigma^2_c$ and var (*e*) **=** $\boldsymbol{I}\ \sigma^2_e$ where ***H*** is the relationship matrix obtained from pedigree and genomic information relationship. $\boldsymbol{\sigma^2_a}$, $\boldsymbol{\sigma^2_m}$, $\boldsymbol{\sigma^2_c}$, and $\boldsymbol{\sigma^2_e}$ are the variances of the genetic effect, maternal genetic effect, permanent maternal environment, and residual effect variances.

4.4. Single step genomic wide association (ssGWAS)

The GWAS were performed using the ssGWAS methodology considering the same linear animal model used to estimate the variance components described above. The direct genetic additive (1) and genetic maternal (2) effects were decomposed into genotyped animals (a_g and m_g) and non-genotyped animals (a_n and m_n) as described below (WANG et al., 2012):

$$a_g = \boldsymbol{Z_1}\ u_d\ (1)$$

$$m_g = \boldsymbol{Z_2}\, u_m \text{ (2)}$$

where $\boldsymbol{Z}$ is a matrix that relates genotypes to each locus and u_d and u_m are the vector of SNPs effects for direct genetic additive and maternal genetic additive effect, respectively. Moreover, the variance of direct genetic additive and maternal genetic effects was assumed as:

$$Var(a_g) = Var(\boldsymbol{Z_1} u_d) = \boldsymbol{Z_1 D_1 Z_1'} \sigma^2_{u_d} = \boldsymbol{G_1^*} \sigma^2_a \text{ (1)}$$

$$Var(m_g) = Var(\boldsymbol{Z_2} u_m) = \boldsymbol{Z_2 D_2 Z_2'} \sigma^2_{u_m} = \boldsymbol{G_2^*} \sigma^2_m \text{ (2)}$$

where $\boldsymbol{D_1}$ and $\boldsymbol{D_2}$ are the weights matrix diagonal for variances of markers for direct genetic additive and maternal genetic additive effect, respectively ($\boldsymbol{D} = \boldsymbol{I}$ for GBLUP), $\sigma^2_{u_d}$ and $\sigma^2_{u_m}$ are the genetic and maternal additive variance captured by each SNP marker when there are no weights and $\boldsymbol{G_1^*}$ (direct genetic additive) and $\boldsymbol{G_2^*}$ (maternal genetic effects) are the weighted genomic relation matrix.

The (co) variance of genetic direct effects (a_g) and SNPs (u_d) is:

$$Var \begin{bmatrix} \mathbf{a_g} \\ \boldsymbol{u_d} \end{bmatrix} = \begin{bmatrix} \boldsymbol{Z_1 D_1 Z_1'} & \boldsymbol{Z_1 D_1'} \\ \boldsymbol{D_1 Z_1'} & \boldsymbol{D_1} \end{bmatrix} \sigma^2_{u_d} \text{ (1)}$$

The (co) variance of genetic maternal effects (m_g) and SNPs (u_m) is:

$$Var \begin{bmatrix} \boldsymbol{m_g} \\ \boldsymbol{u_m} \end{bmatrix} = \begin{bmatrix} \boldsymbol{Z_2 D_2 Z_2'} & \boldsymbol{Z_2 D_2'} \\ \boldsymbol{D_2 Z_2'} & \boldsymbol{D_2} \end{bmatrix} \sigma^2_{u_m} \text{ (2)}$$

Sequentially:

$$\boldsymbol{G_1^*} = \frac{Var(\boldsymbol{a_g})}{\sigma^2_a} = \frac{Var(\boldsymbol{Z_{u_d}})}{\sigma^2_a} = \boldsymbol{Z_1 D_1 Z_1'} \lambda_1 \text{ (1)}$$

$$\boldsymbol{G_2^*} = \frac{Var(\boldsymbol{m_g})}{\sigma^2_m} = \frac{Var(\boldsymbol{Z_{u_m}})}{\sigma^2_m} = \boldsymbol{Z_2 D_2 Z_2'} \lambda_2 \text{ (2)}$$

where λ_1 (direct genetic additive) and λ_2 (maternal genetic effects) are a variance ratio or normalization constant. According to (VANRADEN et al., 2009), in the same way for maternal:

$$\lambda_1 = \frac{\sigma^2_{u_d}}{\sigma^2_a} = \frac{1}{\sum_{i-1}^{M_d} 2p_i(1-p_i)} \text{ (1)}$$

$$\lambda_2 = \frac{\sigma^2_{u_m}}{\sigma^2_m} = \frac{1}{\sum_{i-1}^{M_m} 2p_i(1-p_i)} \quad (2)$$

where $\boldsymbol{M}$ is the number of SNP and p_i is the allele frequency of the second i[th] SNP allele. According to Stradén; Garrick (2009), the effect of markers can be described by:

$$\widehat{\boldsymbol{u}}_{\boldsymbol{d}} = \frac{\sigma^2_{u_d}}{\sigma^2_a} \boldsymbol{D_1 Z'_1 G_1^{*-1}} \hat{a}_g = \boldsymbol{D_1 Z'_1 [Z_1 D_1 Z'_1]^{-1}} \hat{a}_g \quad (1)$$

$$\widehat{\boldsymbol{u}}_{\boldsymbol{m}} = \frac{\sigma^2_{u_m}}{\sigma^2_m} \boldsymbol{D_2 Z'_2 G_2^{*-1}} \hat{m}_g = \boldsymbol{D_2 Z'_2 [Z_2 D_2 Z'_2]^{-1}} \hat{m}_g \quad (2)$$

SNP effects estimates can be used to estimate the individual variance of each SNP effect and apply different weighting for each marker (ZHANG et al., 2010):

$$\hat{\sigma}^2_{u_d,i} = \widehat{\boldsymbol{u}}_{\boldsymbol{d_i}}^{\boldsymbol{2}} 2p_i(1-p_i) \quad (1)$$

$$\hat{\sigma}^2_{u_m,i} = \widehat{\boldsymbol{u}}_{\boldsymbol{m_i}}^{\boldsymbol{2}} 2p_i(1-p_i) \quad (2)$$

The iterative procedure used in this study was described by WANG et al. (2012), considering $\boldsymbol{D_1}$ and $\boldsymbol{D_2}$ to estimate SNP effects:

1. **D** = **I**;
2. To calculate the matrix $\boldsymbol{G_1} = \boldsymbol{Z_1 D_1 Z'_1} q$ (1); $\boldsymbol{G_2} = \boldsymbol{Z_2 D_2 Z'_2} q$ (2)
3. To calculate GEBVs (predicted genomic value) for all animals in the dataset using ssGBLUP;
4. To calculate the effect of SNP: $\widehat{\boldsymbol{u}}_{\boldsymbol{d}} = \lambda_1 \boldsymbol{D_1 Z'_1 G_1^{*-1}} \hat{\boldsymbol{a}}_g$ (1); $\widehat{\boldsymbol{u}}_{\boldsymbol{m}} = \boldsymbol{\lambda_2 D_2 Z'_2 G_2^{*-1}} \hat{m}_g$ (2)
5. To calculate the variance of each SNP: $d_i = \hat{u}_i^2 2p_i(1-p_i)$, where *I* is the *i[th]* maker, with $i = \hat{u}_d$ or $\hat{u}_m$
6. To normalize the SNPs values to keep the additive genetic variance constant;
7. Back to step 2.

In order to obtain the effects and weights for the SNPs, three iterations from step 2 to 7 were performed. The percentage of genetic variance explained

by the i[th] region was calculated for direct and maternal effect (2) as described by (WANG et al., 2014):

$$\frac{Var(a_i)}{\sigma_a^2} = \times 100 = \frac{Var\left(\sum_{j=1}^{10} Z_j \hat{u}_{d_j}\right)}{\sigma_a^2} \times 100, (1)$$

$$\frac{Var(m_i)}{\sigma_m^2} = \times 100 = \frac{Var(\sum_{j=1}^{10} Z_j \hat{u}_{m_j})}{\sigma_m^2} \times 100, (2)$$

where a_i and m_i are the genetic value of the i[th] region consisting of contiguous 10 consecutive SNPs, σ_a^2 and σ_m^2 are the total genetic variance, $\boldsymbol{Z_j}$ is a genetic vector content of the j[th] SNP for all individuals and $\hat{u}_j$ are j[th] marker effect within the i[th] region.

The analyzes were performed using software from the BLUPF90 family (MISZTAL et al., 2002) modified to include genomic information (AGUILAR et al., 2010). The results were presented by the proportion of variance explained by each window of 10 SNPs.

4.5. Search for genes

The genomic windows of 10 consecutive SNPs that explained more than 1.0% of the direct or maternal additive genetic variance were selected to explore and determine possible QTL. To search possible candidate genes, 500 kb pairs that surround the genomic window ahead and behind as a confidence margin was considered. The Map Viewer of the bovine genome was used for the identification of genes, available at the National Center for Biotechnology Information (NCBI - http://www.ncbi.nlm.nih.gov) in the UMD3.1 bovine genome and Ensembl Genome Browser (ZERBINO et al., 2018). The classification of genes for biological function, identification of metabolic pathways, and gene enrichment were performed on the website "The Database for Annotation, Visualization and Integrated Discovery (DAVID) v. 6.8" (http://david.abcc.ncifcrf.gov/) (HUANG; SHERMAN; LEMPICKI, 2009) and GeneCards (http://www.genecards.org/). Also, the *Cytoscape* program was used to characterize the relationship among genes, gene ontology categories, and metabolic pathways (SHANNON et al., 2003).

4.6. Prediction ability

To calculate the prediction ability (PA), the dataset was split into training (772 animals) and validation (7885 animals) subsets. The validation subset consisted of genotyped young animals without progeny records and the training was composed by genotyped sires and dams. Phenotypic and genomic information from validation animals were omitted in the training set. Direct genomic values (DGV) was estimated inside the validation subset and corresponds to the predictive ability of the genetic evaluation. Posteriorly, the Pearson correlation between the EBV (obtained using the complete data set) and DGV was calculated.

For the ssGBLUP method, SNP effects were calculated using all available data, except validation animal records. DGV for young animals were obtained by multiplying all SNPs content by the estimated SNP effect (LOURENCO et al., 2015). The aforementioned procedures were applied for all traits and considering different density panels: HD (735,044 SNPs), 30k (26,576 SNPs) and custom panels assembled through previous ssGWAS and composed by those SNPs who explained more than 1% and 0.5% of the additive genetic variance. SNP effects for the direct genetic additive animal (1) and genetic maternal (2) effects, using the training population data were calculated as follows:

$$\hat{\boldsymbol{u}}_{\boldsymbol{d}} = \boldsymbol{D}_1 \boldsymbol{Z}_1' \boldsymbol{G}_1^{-1} \textit{(DGV)}, \quad (1)$$

$$\hat{\boldsymbol{u}}_{\boldsymbol{m}} = \boldsymbol{D}_2 \boldsymbol{Z}_2' \boldsymbol{G}_2^{-1} \textit{(DGV)}, \quad (2)$$

where $\hat{\boldsymbol{u}}$ is the estimated SNP vector for direct genetic additive or maternal effects, ***D*** *i*s the diagonal matrix of weights (standardized variances) for SNP (an identity matrix in this case), and ***Z*** is the matrix of genotypes centered for each animal (VANRADEN et al., 2009). The similar approach using GEBV instead of DGV to calculate the SNP effects was proposed by Wang et al. (2012).

The prediction equations obtained were used to predict the DGV in the validation population (genotyped young animals), which will be obtained based on the SNP effects, for the direct genetic additive animal (1) and genetic maternal (2) effects:

$$\boldsymbol{DGV_1} = \boldsymbol{Z}_{1y} \hat{\boldsymbol{u}}_{\boldsymbol{d}} \quad (1)$$

$$\mathbf{DGV_2} = \boldsymbol{Z_{2y}\hat{u}_m} \quad (2)$$

Where DGV_1 and DGV_2 are the direct and maternal genomic values and $\boldsymbol{Z_{1y}}$ and $\boldsymbol{Z_{2y}}$ are an array of genotypes centered for young animals not included in the ssGBLUP evaluation.

5. RESULTS AND DISCUSSION

5.1. Genetic Parameter Estimates

The heritability estimates for direct effect BW and W210 were moderate from 0.23 and 0.22, respectively. Low maternal heritability estimates for BW (0.05) and W210 (0.09) were found. Similar results for BW and W210 were observed in the literature for direct heritability, ranging from 0.23 to 0.37 and from 0.25 to 0.36, and for maternal heritability from 0.02 to 0.11 and 0.05 to 0.21,

respectively, in Nellore cattle (ARAÚJO et al., 2014; BOLIGON et al., 2009, 2011).

Direct heritability estimates for W450 and ACW were moderate,0.34 and 0.32, respectively. Results reported in the literature ranged from 0.30 to 0.67 and from 0.40 to 0.44 for W450 and ACW, respectively (BOLIGON; CARVALHEIRO; ALBUQUERQUE, 2012; MAGNABOSCO; LÔBO; FAMULA, 2000; REGATIERI et al., 2012; SCHMIDT et al., 2018). Our results show that heritability estimates for growth traits indicated that genetic progress for these traits is feasible and it would respond favorably to selection.

Table 2 - Variance components, heritability estimates (± SD) for direct and maternal effect and maternal environmental variance as proportion effects for growth trait in Nellore Cattle.

Traits	Parameters						
	σ^2_a	σ^2_m	σ^2_c	σ^2_e	h^2_a±SD	h^2_m±SD	c^2±SD
BW	2.750	0.590	0.490	7.990	0.23 ± 0.001	0.05 ± 0.006	0.04 ± 0.007
W210	100.930	40.740	55.120	261.510	0.22 ± 0.016	0.09 ± 0.010	0.12 ± 0.011
W450	268.010	-	-	520.400	0.34 ± 0.002	-	-
ACW	985.300	-	-	2050.900	0.32 ± 0.000	-	-

[1]BW= Birth weight; W210= Weaning weight; W450= Yearling weight; ACW= Adult cow weight; heritability genetic (h^2_a) and maternal (h^2_m); Components of variance genetic (σ^2_a), maternal (σ^2_m), maternal permanent environment (σ^2_c) and phenotypic (σ^2_e); Maternal environmental variance as proportion ($c^2=\frac{\sigma^2_c}{(\sigma^2_a+\sigma^2_m+\sigma^2_c+\sigma^2_e)}$). Source: Own authorship

5.2. Genomic Regions

5.2.1.Birth weight (BW)

5.2.1.1. Additive direct genetic effect

A total of 67 genes were identified within the genomic regions of the additive direct genetic variance for BW, 35 of them had described biological functions and 32 were uncharacterized genes (Table 3 and Figure 1).

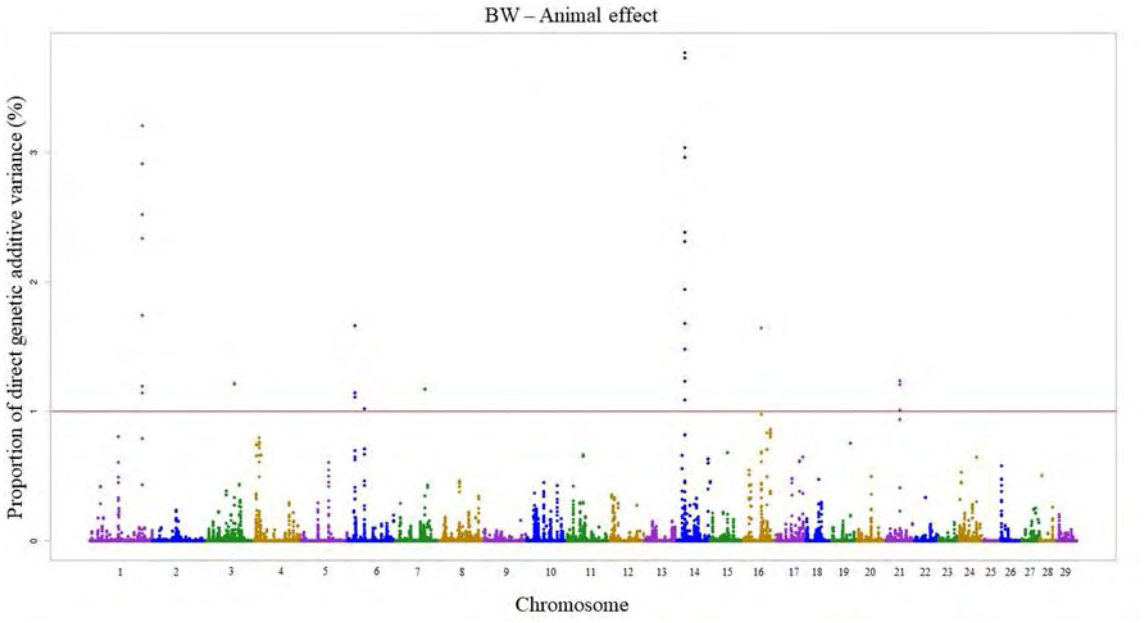
Table 3 - Genomic regions associated with birth weight, percentage of additive direct genetic effect and found genes.

Chromosome: position (bp)	Found genes*	% Variance explained by SNPs windows

BTA1: 135986929-137024183	*AMOTL2; RYK; LOC101902360; LOC781215; TRNAG-CCC; SLCO2A1; RAB6B; SRPRB; TF; LOC525947; LOC104971055; TOPBP1; APC13; CDV3*	3.206
BTA3: 72137558-73203960	*LOC101907235; LOC785254; NEGR1*	1.217
BTA6: 19806000-20831754	*LOC104972684; LOC104972685; GIMD1; AIMP1; TBCK; LOC104972686 LOC101904481; NPNT; GSTCD; INTS12; ARHGEF38*	1.662
BTA6: 43620875-44630560	*LOC101904854; GBA3; LOC100300713; LOC104972733*	1.021
BTA7: 74852007-75897003	*GABRB2; GABRA6; GABRA1; GABRG2*	1.174
BTA14: 19112165-20129540	*LOC100139328; LOC522769; HAS2; LOC515601*	3.771
BTA16: 47946915-48960993	*GPR153; HES3; ICMT; RNF207; RPL22; CHD5; KCNAB2; NPHP4; LOC104974452*	1.646
BTA21: 35148261-36162904	*LOC788565; LOC505658; LOC104969340; LOC509956; LOC617313; LOC786126; LOC788612; LOC508858; LOC788601; LOC618420; LOC508646; LOC104975377; STXBP6; LOC104975378; LOC104975379; LOC101905307; MIR2888-1; GZMB*	1.237

*NCBI Symbol (Assembly UMD3.1, annotation release 103; NCBI, annotation release 104).
Source: Own authorship

Figure 1 - Direct genetic additive effect explained by windows of 10 adjacent SNPs for birth weight.



Source: Own authorship

The *AMOTL2, SLCO2A1, SRPRB* and *TF* genes were related to muscle growth physiology and metabolism. Hultin et al. (2017) reported that the *AMOTL2* gene decodes a protein related to actin filaments building. The *SLCO2A1* gene function was related to muscle growth metabolism in broilers (COUDERT et al., 2018). The *SRPRB* gene was associated with transferrin, an iron signal recognition (SR) subunit receptor particle in organs, which is encoded by the *TF* gene, being fundamental in muscle metabolism acting over growth, and cellular differentiation (ORINO, 2016; SAITO et al., 2018).

The genes *AIMP1, TBCK, NPNT, INTS12, HAS2* and *ICMT*, could be related to muscle development, cellular and organs growth. The *AIMP1* gene and *TBCK*, act potentially over the muscle tissues and cartilage development (AHN et al., 2016; ZHU et al., 2009), and in the actin organization, cell growth, and proliferation (LIU et al., 2013), respectively. The *NPNT* and *INTS12* genes could be related to organs growth and regulation during gestation until birth (OBEIDAT et al., 2013; SUN et al., 2018). The *HAS2* gene displays a function related to the epidermal growth factor and fibroblasts production in humans (SAAVALAINEN et al., 2005). The *ICMT* gene acts in fibroblast growth function and is related to growth due to collagen and elastin production (BERGO et al., 2004; IBRAHIM et al., 2013).

5.2.1.2. Maternal genetic effect

A total of 152 genes were identified within the genomic regions of the maternal genetic variance for BW, 69 had described biological functions and 83 were uncharacterized genes (Table 4 and Figure 2).

Table 4 - Genomic regions associated with birth weight of maternal genetic effect and found genes.

Chromosome: position (bp)	Found genes*	% Variance explained by SNPs windows
BTA3: 6919551-70229867	*ASB17; MSH4; RABGGTB; ACADM; LOC100335176; SLC44A5; LHX8; TYW3;*	1.016
BTA4: 99992438-101040623	*CNOT4; NUP205; STMP1; RPL15P; SLC13A4; FAM180A; LOC104972218; LUZP6; MTPN; TRNAQ-CUG;*	1.011

	LOC104972219; LOC104972220; LOC104972221; TRNAR-GCG; LOC786173	
BTA6: 18333338-19363972	*LEF1; LOC104972679; HADH; CYP2U1; TRNAG-CCC; SGMS2; TRNASTOP-CUA; LOC101904032; PAPSS1; LOC104972682*	3.726
BTA6: 43620875-44630560	*LOC101904854; GBA3; LOC100300713; LOC104972733*	1.350
BTA6: 102008503-103030315	*LOC101909963; ARHGAP24; LOC104968922; TRNAC-GCA; MAPK10*	1.165
BTA10: 21907141-22907141	*LOC615014; LOC619067; LOC615040; LOC785963; LOC100337215; LOC786614; ABHD4; DAD1; LOC101908015; LOC104973085; LOC104969841; LOC104969842; LOC100295645; BVD1.23; LOC100299557; LOC506959; LOC407201; LOC616138; OR6J1; TRDC;*	1.143
BTA12: 2941384-3958969	*LOC101903418; LOC104973531; LOC101903827*	1.088
BTA13: 6942754-7987062	*SPTLC3; ISM1; TASP1; ESF1; NDUFAF5; SEL1L2; LOC104973699; MACROD2*	1.092
BTA14: 30928273-31951392	*LOC104974031; BHLHE22; CYP7B1; ARMC1; LOC104974039; LOC104974035; MTFR1; LOC104974034; LOC101902754; PDE7A; LOC101902020*	1.949
BTA14: 48999435-50032453	*SLC30A8; LOC104974077; LOC100847957; LOC101904715; AARD; LOC104974078; LOC781253; RAD21; UTP23; LOC104974079; EIF3H; LOC104974080*	3.025

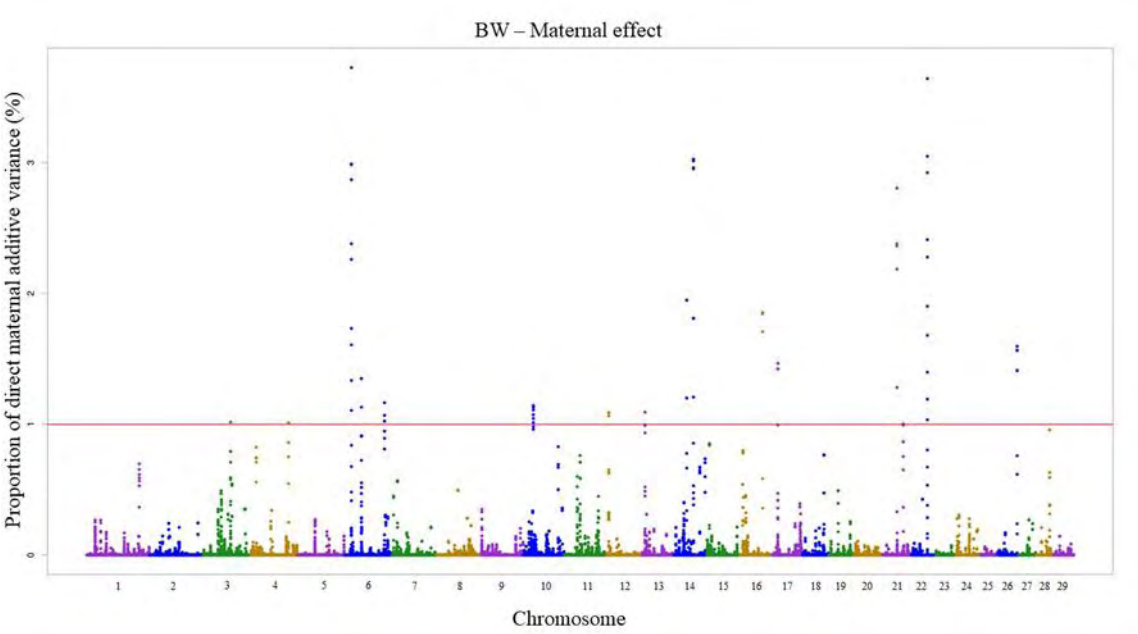
Table 4 (Continuation) - Genomic regions associated with birth weight of maternal genetic effect and found genes.

Chromosome: position (bp)	Found genes*	% Variance explained by SNPs windows
BTA16: 58490432-59002419	*COP1; LOC101902053; LOC100848409; RFWD2*	1.853
BTA17: 11805338-12832620	*POU4F2; SLC10A7; LOC101906679; LOC101907788; LSM6; ZNF827; LOC104974574; C17H4orf51; MMAA*	1.465
BTA21: 35150229- 36150229	*LOC788565; LOC505658; LOC104969340; LOC509956; LOC617313; LOC786126; LOC788612; LOC508858; LOC788601; LOC618420; LOC508646; LOC104975377; STXBP6; LOC104975378; LOC104975379; LOC101905307; MIR2888-1; GZMB*	2.805
BTA21: 52070871-52590367	*LOC104975418; LRFN5; LOC104975419; LOC104972837; LOC104975421*	1.002
BTA22: 41275365-42282514	*FHIT*	3.641

BTA26: 47325114-48343067	*NPS; FOXI2; TRNAC-GCA; CLRN3; LOC101902864; LOC104976006; LOC104976007; PTPRE; LOC101902915; MKI67; LOC101903141; LOC104976008; LOC104976009*	1.596

*NCBI Symbol (Assembly UMD3.1, annotation release 103; NCBI, annotation release 104).
Source: Own authorship

Figure 2 - Maternal genetic additive effect explained by windows of 10 adjacent SNPs for birth weight.



Source: Own authorship

The *ACADM* gene plays an important role in conversion of fatty acids into energy and to promote important energy reserve sources during fasting extended periods (HAN et al., 2016; SONG; TAN, 2018; WANG et al., 2017). The *SLC44A5* gene was associated with fat, protein and milk production at 305 days, which is related in a GWAS study with dairy buffalo (VENTURINI et al., 2014). This gene may exert some influence on birth weight, as reported by Sugimoto, Watanabe and Sugimoto (2012) in Holstein's calves. *SLC13A4* gene express a protein that acts as sulfate carrier to the fetus during pregnancy (ZHANG et al., 2017), affecting the sulfate demand in circulation, which increases due to fetal need to growth and development (BARNES et al., 2017). The *GBA3* gene was associated to hydrolyze beta-galactose and beta-glucose (DEKKER et al., 2011), and may be related with milk production, which influences calf weight after birth, since lactose represents 5% of milk composition and are a protein source for animal growth, coming from galactose (JENKINS, 1998).

5.2.2. Weaning weight (W210)

5.2.2.1. Additive Direct genetic effect

For W210, a total of 113 genes were identified of the additive direct genetic variance, 62 of them had described biological functions and 71 were uncharacterized genes (Table 5 and Figure 3).

Table 5 - Genomic regions associated with weaning weight of additive direct genetic effect and found genes.

Chromosome: position (bp)	Found genes	% Variance explained by SNPs windows
BTA1:134643214-135682483	*LOC104971047; LOC104971048; EPHB1; LOC104971049*	1.095
BTA3: 5877951-6889174	*NUF2; LOC104970589; LOC104970606; RGS4; RGS5; LOC104970616; LOC104970648; CCDC190; LOC101907096; HSD17B7; LOC104970668; DDR2*	1.161
BTA6: 18676059-19688516	*TRNASTOP-CUA; LOC101904032; PAPSS1; LOC104972682; LOC100848567; DKK2; LOC104972681*	4.203
BTA8: 66957724-67979763	*LOC101903343; LOC101903598; LOC104972914; LOC104972916; LOC104972915; LOC100298923; LPL; SLC18A1; ATP6V1B2; LZTS1; LOC101903443; LOC12343598*	1.187

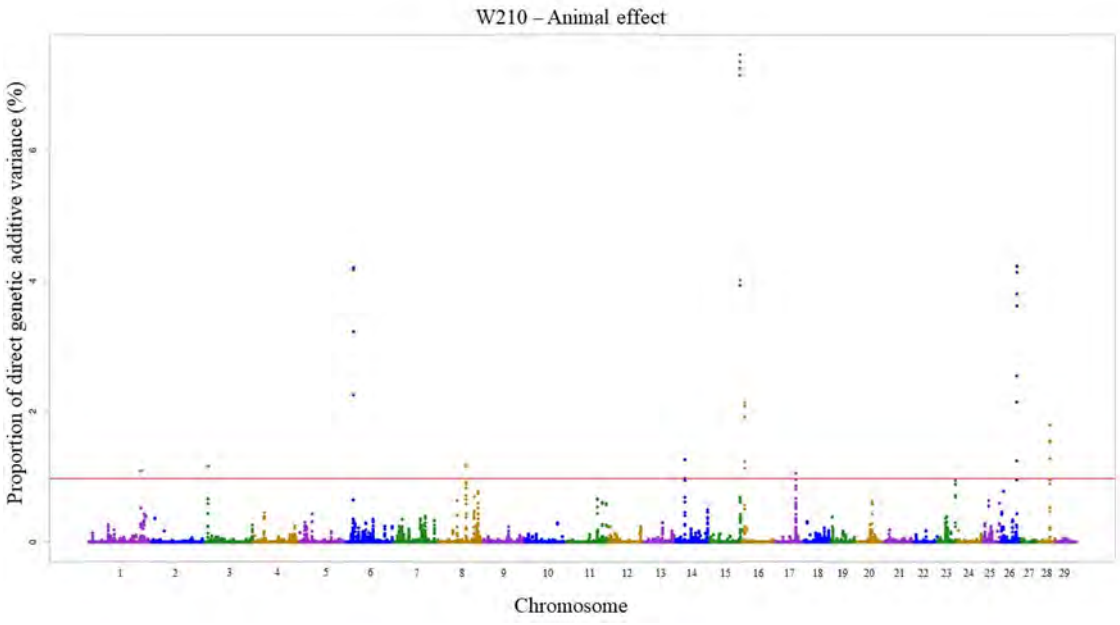
Table 5 (Continuation) - Genomic regions associated with weaning weight of additive direct genetic effect and found genes.

Chromosome: position (bp)	Found genes*	% Variance explained by SNPs windows
BTA14: 21629446-22646343	*LOC511847; LOC101905910; LOC104974015; LOC100139887; SNTG1; LOC614437; LOC104974016*	1.265
BTA15: 78658479-79669931	*AGBL2; FNBP4; NUP160; PTPRJ; LOC509884; LOC514818; LOC506121; OR4X1; OR4S1; LOC510901; LOC526335; OR4C3; OR4C12; OR4C46; LOC100848076; OR4C13; LOC785969;*	7.466
BTA16: 5361334-6453988	*CR1L; LOC786152; LOC100336868; LOC789312; LOC104974373; LOC514121; LOC790886; LOC101905630; LOC781004; LOC790886; CFH; KCNT2*	2.135
BTA17: 53549150-54567858	*LOC104968594; NCOR2; FAM101A; LOC104974632; MIR2322;*	1.050

	LOC104974633; LOC100847522; TRNAF-AAA; LOC101907789; ZNF664; LOC101904642; CCDC92; DNAH10; MIR1721; ATP6V0A2; TCTN2; GTF2H3; EIF2B1; DDX55; TMED2; LOC101901945; RILPL1; SNRNP35; RILPL2; KMT5A; LOC104974634; SBNO1; CDK2AP1	
BTA26: 43013115-44030499	*LOC617705; LOC100295742; LOC510536; FAM24A; C26H10orf88; PSTK; IKZF5; LOC104970824; LOC539705; ACADSB; HMX3; HMX2; BUB3; LOC104970825; LOC104970826; GPR26; LOC100138608; CPXM2*	4.226
BTA28: 32907742-33914298	*LRMDA; LOC101907319; KCNMA1; LOC104969723; LOC101907374; DLG5; POLR3A*	1.790

*NCBI Symbol (Assembly UMD3.1, annotation release 103; NCBI, annotation release 104).
Source: Own authorship

Figure 3 - Direct genetic additive effect explained by windows of 10 adjacent SNPs for weaning weight.



Source: Own authorship

The *RGS4* gene acts as a G-protein signaling regulator, GTPase activators, associated with adipogenesis and osteogenesis regulation, which controls the muscles, adipose tissue, bones and cartilage growth (MADRIGAL; TAN; ZHAO, 2017; SCHWARZ, 2018). The *DDR2* gene acts in processes related to the fibroblast's development, which may be associated with body growth (MAJKOWSKA et al., 2017; MIHAI et al., 2006). It is important to highlight these last two genes because they have functions related to muscle regulation, skeletal and adipose growth after birth.

In a study with experimental rat population, the *DKK2* gene was related with postnatal development and growth (Bodine et al., 2004). Zhan et al. (2015), also associated the expression of this gene with skeletal growth traits as well as meat quality traits in Qinchuan cattle.

The *LPL* gene may be related with muscle growth and development, this gene hydrolyzes triglycerides, allowing the metabolism absorption of free fatty acids available to the muscle tissues development (LEVAK-FRANK et al., 1995). The *LPL* gene was also identified by Hayashi, Kido and Hodate (2018) associated with muscle lipid deposition in Japanese Black cattle.

The *CDK2AP1* gene has a role in growth regulation of keratinocytes (ALSAYEGH et al., 2015; BUAJEEB et al., 2004; KIM et al., 2009). The *ACADSB* gene is associated with acyl-CoA dehydrogenase, involved in fatty acid

metabolism in deposition of expressed fat directly into adipose tissue, muscle tissue and rumen of bovine (FANG et al., 2017; JIANG et al., 2018; MEI et al., 2018). The *IKZF5* gene was described by (DAVIS et al., 2015) acting on fibroblasts in bovines and by Jakhesara et al. (2012) showing a possible regulating function on the muscle fibers growth in buffalo. Genes such as the *KCNMA1* and *DLG5* were related with muscle growth (BLOCH et al., 2007), and with epithelial tissues increases (STOLL et al., 2004).

5.2.2.2. Maternal genetic effect

For W210, a total of 139 genes were identified within the genomic regions of the maternal genetic variance, being 71 of them had described biological functions and 68 were uncharacterized genes (Table 6 and Figure 4).

Table 6 - Genomic regions associated with weaning weight of maternal genetic effect and found genes.

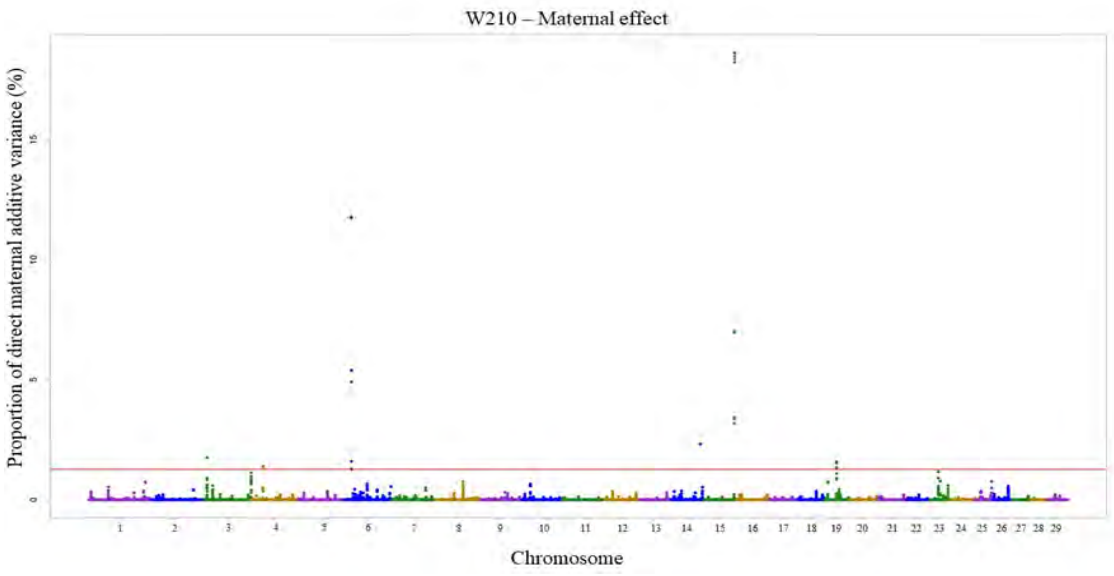
Chromosome: position (bp)	Found genes*	% Variance explained by SNPs windows
BTA3: 5877951-6889174	*NUF2; LOC104970589; LOC104970606; RGS4; RGS5; LOC104970616; LOC104970648; CCDC190; LOC101907096; HSD17B7; LOC104970668; DDR2*	1.752
BTA3: 119310508-120327826	*HDAC4; LOC101907383; LOC100336606; LOC100336476; LOC104971899; LOC789064; NDUFA10; NADH; LOC101908107; LOC613418; LOC782152; LOC782114; LOC615009; LOC100141012; LOC782255; LOC789457; LOC530175; LOC617467; LOC526047; COPS9; OTOS; LOC782275; ANKMY1; LOC101902184; LOC787244;*	1.133
BTA4: 30501570-31515917	*LOC104971985; DNAH11; TRNAC-GCA; LOC101907567; LOC101907305; LOC497208; LOC104971989; CDCA7L; RAPGEF5; LOC101907914; LOC100138586; LOC101907978; ANKMY1*	1.415

Table 6 (Continuation) - Genomic regions associated with weaning weight of maternal genetic effect and found genes.

Chromosome: position (bp)	Found genes*	% Variance explained by SNPs windows
BTA6: 18666708-19684636	*TRNASTOP-CUA; LOC101904032; PAPSS1; LOC104972682; LOC100848567; DKK2; LOC104972681*	11.785
BTA14: 75235614-76275553	*DGAT1; CYC1; CYP11B1; PTK2; TG; MYC; PLAG1; PENK; ASPH; CRH; FABP5; PMP2; FABP4; ANGPT1; NCALD; YWHAZ; PDP1; CA2; IMPA1; SLC26A7; LRRC69; OTUD6B; PIP4P2; TMEM64; CALB1; DECR1; NBN; OSGIN2; RIPK2*	2.322
BTA15: 78658479-79669931	*AGBL2; FNBP4; NUP160; PTPRJ; LOC540128; OR4X1; OR4S1; LOC510901; LOC526335; OR4C3; OR4C12; OR4C46; LOC100848076; OR4C13; LOC785969; LOC790154; LOC790152; LOC532479; LOC789193; LOC531097; LOC100294956; LOC521645; LOC523060; LOC618675; LOC100337063; LOC521252*	18.624
BTA19: 30282138-31292353	*SCO1; ADPRM; TMEM220; LOC101905715; PIRT; SHISA6; LOC101905806; LOC104975035; DNAH9; LOC104975036; ZNF18; MAP2K4*	1.582
BTA23: 21023302-22039674	*PTCHD4; LOC785693; MUT; CENPQ; GLYATL3*	1.163

*NCBI Symbol (Assembly UMD3.1, annotation release 103; NCBI, annotation release 104).
Source: Own authorship

Figure 4 - Maternal genetic additive effect explained by windows of 10 adjacent SNPs for weaning weight.



Source: Own authorship

Genes associated with a higher fat percentage (*CDCA7L* and *DKK2*); in milk production reported by a GWAS in Holstein cattle (LI et al., 2010; PIMENTEL et al., 2010). These genes probably influence the growth traits through the maternal effect. The *DKK2* gene was also associated with the direct genetic effect.

In a GWAS study with Jersey and Holstein cattle by Raven et al. (2014) the gene *PTK2* was associated with milk production, fat percentage, proteins and solids. The gene *FABP4*, regarding milk fat and composition, could be related by regulating fatty acids during lactation (BIONAZ; LOOR, 2008). Grisart et al. (2001) evidenced that the *DGAT1* gene would be causal for production and composition of milk in cattle, as it underlies the QTL mapped in this phenotype. Studies demonstrated breeds that have acting of *DGAT1* likely to produce more milk and higher quality and, consequently, wean heavier calves (KARIM et al., 2004; KAUPE et al., 2004; SPELMAN et al., 2002).

5.2.3. Yearling weight (W450)

A total of 72 genes were identified within the genomic regions of the additive direct genetic variance, 43 had described biological functions and 29 were uncharacterized genes (Table 7 and Figure 5).

Table 7 - Genomic regions associated with yearling weight, percentage of additive direct genetic effect and found genes.

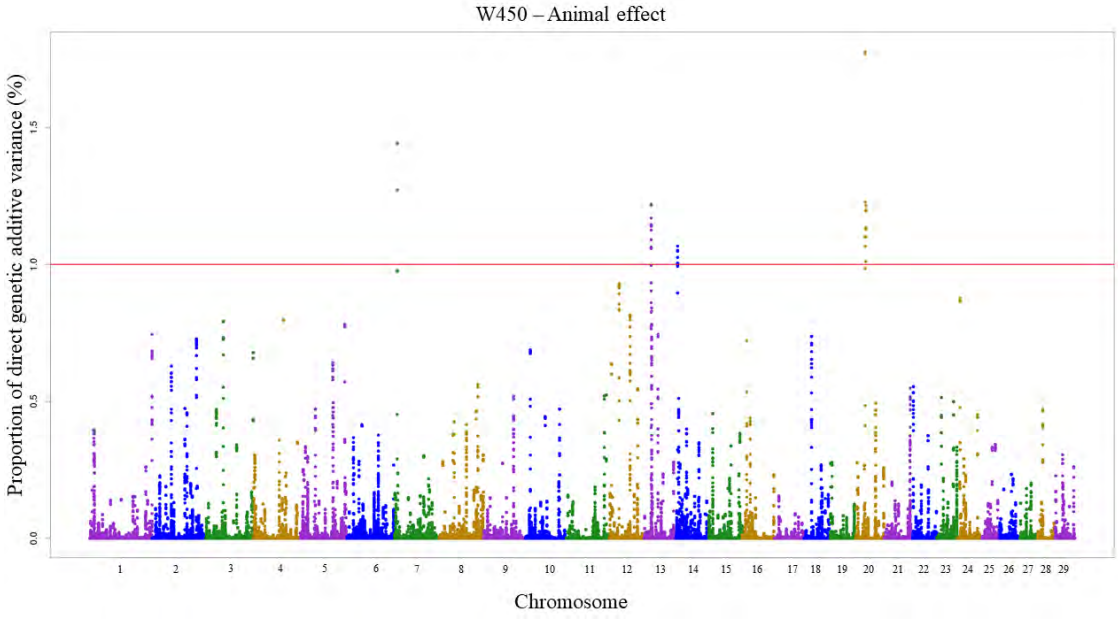
Chromosome: position (bp)	Found Genes*	% Variance explained by SNPs windows
BTA7: 5878944-6878944	*MYO9B; LOC104969051; HAUS8; LOC104972787; CPAMD8; MIR8550; F2RL3; SIN3B; NWD1; TMEM38A; SMIM7; MED26; SLC35E1; CHERP; C7H19orf44; LOC786929; CALR3; TRNAR-CCU; EPS15L1; KLF2; LOC101905667;*	1.444
BTA12: 23235862-24263161	*PROSER1; STOML3; FREM2; UFM1; TRPC4; PSTN; NHLRC3*	1.162
BTA13: 18197774-19262878	*PDSS1; APBB1IP; CCNY; LOC104973723; CREM; CUL2; TRNAG-UCC; PARD3*	1.221

Table 7 (Continuation) - Genomic regions associated with yearling weight in Nellore cattle, percentage of additive direct genetic effect and found genes

Chromosome: position (bp)	Found Genes*	% Variance explained by SNPs windows
BTA14: 5082271-6144742	*LOC104973977; COL22A1; LOC104973976; LOC104973975; FAM135B; LOC104973978*	1.067
BTA20: 21924887-2299451	*LOC539789; GPBP1; LOC104975245; LOC104975240; LOC524269; LOC101904908; MIER3; SETD9; LOC104975241; MAP3K1; LOC104975242; LOC104975243*	1.779
BTA20: 24061645-2512850	*GZMK; ESM1; LOC104975247; LOC530348; LOC101908144; LOC783202; SNX18; LOC104975248; HSPB3; LOC104975249; ARL15; COX8A*	1.215

*NCBI Symbol (Assembly UMD3.1, annotation release 103; NCBI, annotation release 104).
Source: Own authorship

Figure 5 - Direct genetic additive effect explained by windows of 10 adjacent SNPs for yearling weight.



Source: Own authorship

The *TMEM38A* and *F2RL3* genes were associated to muscle development and regeneration of new cells (JAFFERALI et al., 2017; ROBSON et al., 2016), with energy metabolism and lipids storage (KAJIMOTO et al., 2012). *COL22A1* gene was previously associated with synthesis and regulation of

collagen (NAGAI, 2015; WIBOWO, 2008), which has vital importance in muscle growth and deposition of intramuscular fat (DUARTE et al., 2018).

The *CREM* gene was related with nutrient and energy maintenance, physiological regulation and feed efficiency, also contributing to weight gain, since recent transcriptomic studies in Holstein cattle suggested that this gene acts in the metabolic adaptation interact of energy homeostasis (HA et al., 2017). The *ARL15* and *COX8A* genes could be related to subcutaneous fat deposition and feed efficiency, respectively. *ARL15* plays a role in the differentiation and secretion of adipocytes, and adiponectin, being responsible for the formation and regulation of adipose tissue (RICHARDS et al., 2009; ROCHA et al., 2017) and *COX8A* was associated with oxidative phosphorylation and better use of food (KONG et al., 2016).

5.2.4. Adult cow weight (ACW)

A total of 139 genes were identified within the genomic regions of the additive direct genetic variance, 92 had described biological functions and 47 were uncharacterized genes (Table 8 and Figure 6).

Table 8 - Genomic regions associated with adult cow weight in Nellore cattle, percentage of direct genetic additive effect and found genes.

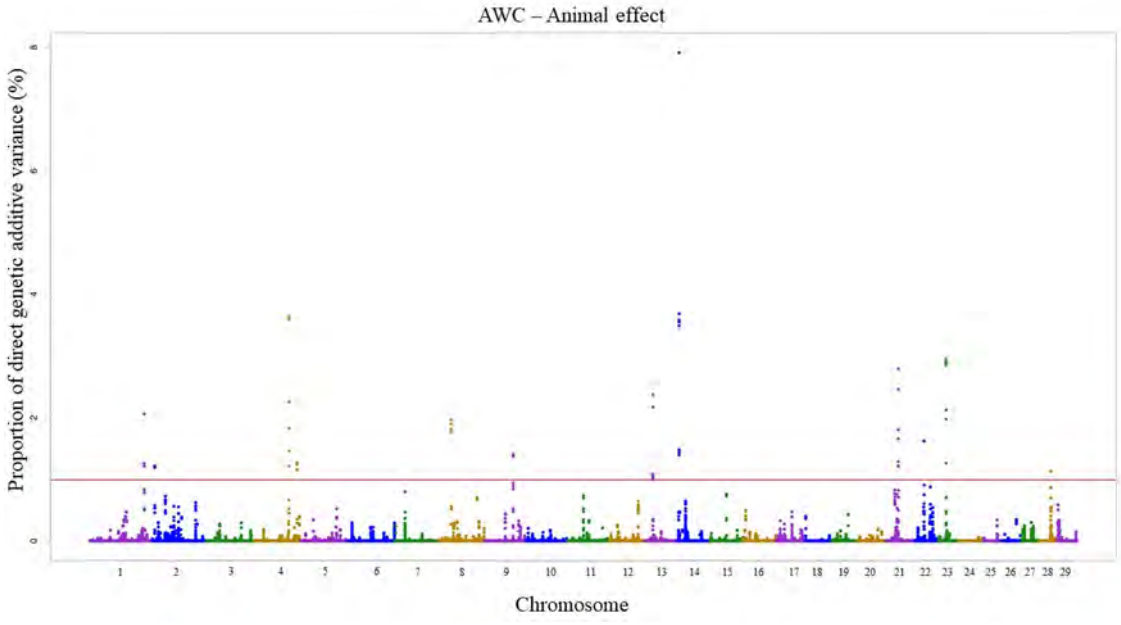
Chromosome: position (bp)	Found genes*	% Variance explained by SNPs windows
BTA1: 140921178-141946226	*SETMAR; LOC534913; WRB; LCA5L; SH3BGR; B3GALT5; LOC101905982; L17; IGSF5; PCP4; DSCAM*	2.064
BTA2: 5249223-6261420	*CYP27C1; BIN1; MIR2350; NAB1; NEMP2; MFSD6; INPP1; HIBCH; LOC104971104; LOC104971103; LOC104971102; C2H2orf88; MSTN*	1.211
BTA4: 92756562-93767464	*SND1; LRRC4; LOC104972189; LOC104972191; MIR129-1; LEP; RBM28; PRRT4; IMPDH1; HILPDA; FAM71F2; FAM71F1; CALU; OPN1SW; TRNAP-AGG; CCDC136; MIR2422; FLNC; ATP6V1F; IRF5; TNPO3*	3.636
BTA4: 112176107-113196612	*CNTNAP2; LOC104972283; CUL1; EZH2; PDIA4; LOC506408; ZNF398; ZNF282; ZNF212; ZNF783; TRNAC-GCA*	1.270

Table 8 (Continuation) - Genomic regions associated with adult cow weight, percentage of direct genetic additive effect and found genes.

Chromosome: position (bp)	Found genes*	% Variance explained by SNPs windows
BTA8: 27855182-28879279	*BNC2; LOC104969311; LOC616199; LOC100847480; CCDC171; PSIP1*	1.962
BTA9: 75095082-76104541	*PDE7B; MTFR2; BCLAF1; LOC100140614; MAP7; TRNAG-CCC; MAP3K5; PEX7; SLC35D3; IL20RA; IL22RA2; IFNGR1*	1.405
BTA13: 19164058-20195812	*PARD3; LOC104973724; LOC101904425; LOC104973725; LOC104973726; LOC104973727; NRP1; LOC104973728; LOC104973730*	2.368
BTA14: 5926125-6953636	*LOC104973979*	7.913
BTA21: 31390986-32412723	*IREB2; HYKK; PSMA4; CHRNA5; CHRNA3; CHRNB4; UBE2Q2; FBXO22; NRG4; LOC100295282; LOC616763; LOC101907528; TMEM266; ETFA; LOC100294924; ISL2; SCAPER*	2.786
BTA22: 24631847-25649014	*CNTN6; LOC516682; LOC104975530*	1.619
BTA23: 19774596-20803596	*CYP39A1; SLC25A27; TDRD6; PLA2G7; ANKRD66; MEP1A; ADGRF5; ADGRF1; LOC100296156; TNFRSF21; CD2AP; ADGRF2; ADGRF4; OPN5*	2.942
BTA28: 32354461-33386291	*LOC530965; LRMDA; LOC101907319; KCNMA1*	1.131

*NCBI Symbol (Assembly UMD3.1, annotation release 103; NCBI, annotation release 104).
Source: Own authorship

Figure 6 - Direct genetic additive effect explained by windows of 10 adjacent SNPs for adult cow weight.



Source: Own authorship

The *MSTN* gene is considered a growth factor member of growth transformer-β factor superfamily (MCPHERRON; LAWLER; LEE, 1997) Expression of *MSTN* mutations causes double musculature in cattle, a phenotype that is characterized by a substantial increase in skeletal muscle mass (GROBET et al., 1997; THOMAS et al., 2000). Gill et al. (2008) studied the *MSTN* gene mutation in Angus cattle in association with carcass quality and they observed this mutation effects on carcass traits of economic interest, significantly increasing carcass weight and quality.

The substitution of the *A* allele for a copy of the *T* base (*A252T*) of the *LEP* gene encodes the Leptin hormone, was associated with metabolism for milk production (BANOS et al., 2008). Lagonigro et al. (2003) showed the leptin function in cattle was associated with feed intake, carcass composition, marbling, and subcutaneous fat composition, energy balance and reproduction (GEARY et al., 2003; LIEFERS et al., 2004).

The *PLA2G7* gene may be associated with lipid metabolism, lower residual feed intake, and higher feed efficiency (SALLEH et al., 2017). *PSIP1*, *MAP3K5* and *MAP7* genes was related with feed efficiency, residual feed intake and growth biological function (OLIVIERI et al., 2016; TAYE et al., 2017), also reported *PEX7* gene related with meat qualitative aspects (SANTANA et al., 2014). Lemos et al. (2016) identified the *PEX7* gene in association with beef fatty acid profile in Nellore cattle.

5.3. Functional and biological analysis

The functional analyses revealed several significant gene ontology (GO) terms and KEGG pathways from the set of genes previously identified within the significant Windows (Tables 9 and 10), such as detection of chemical stimulus involved in sensory perception (GO:0050907), olfactory receptor activity and, acetylcholine receptor activity (GO:0015464), acetylcholine binding (GO:0042166), acetylcholine-activated cation-selective channel activity (GO:0004889) and acetylcholine-gated channel complex (GO:0005892).

Table 9 - DAVID Functional Annotation for gene category and pathway enrichment analysis for Direct Genetic Additive effect.

Gene Ontology	Terms	N. Genes[1]	Ann. Genes[2]	P-value	FDR (%)
GO:0005886	Plasma membrane	28	*NRP1, C2H2ORF88, GABRB2, OR4S1, ATP6V1B2, CD2AP, OR4C3, SLCO2A1, OR4C13, RILPL1, CCNY, IFNGR1, KCNMA1, GABRG2, LPL, RYK, GABRA6, EIF2B1, IGSF5, OR4X1, STXBP6, IL20RA, BNC2, RGS4, RGS5, ATP6V0A2, OR4C46, IL22RA2*	0.005	6.531
GO:0004930	G-protein coupled receptor activity	12	*ADGRF2, ADGRF1, ADGRF4, ADGRF5, OR4S1, OR4C3, OR4C13, GPR26, GPR153, OPN5, OR4X1, OR4C46*	0.000	0.178
GO:0007186	G-protein coupled receptor signaling pathway	7	*OR4S1, OPN1SW, OR4C3, OPN5, OR4C13, OR4X1, OR4C46*	0.001	1.290
GO:0004984	Olfactory receptor activity	5	*OR4S1, OR4C3, OR4C13, OR4X1, OR4C46*	0.006	7.810
GO:0050907	Detection of chemical stimulus involved in sensory perception	5	*OR4S1, OR4C3, OR4C13, OR4X1, OR4C46*	0.000	0.000
GO:0004888	Transmembrane signaling receptor activity	5	*OR4S1, OR4C3, OR4C13, OR4X1, OR4C46*	0.000	0.000
GO:0045211	Postsynaptic membrane	8	*KCNMA1,LRRC4, GABRG2,GABRA1, GABRB2,CHRNB4, CHRNA5,CHRNA3*	0.000	0.293
GO:0030054	Cell junction	8	*GABRG2,GABRA1, KCNAB2,GABRB2, GABRA6,CHRNB4, CHRNA5,*	0.016	17.538

Table 9 (Continuation) - DAVID Functional Annotation for gene category and pathway enrichment analysis for Direct Genetic Additive effect.

GO:0016485	Protein processing	1	*GZMB*	0.006	8.931
GO:1902711	GABA-A receptor complex	4	*GABRG2*, *GABRA1*, *GABRB2*, *GABRA6*	0.001	1.319
GO:0004890	GABA-A receptor activity	4	*GABRG2*, *GABRA1*, *GABRB2*, *GABRA6*	0.001	1.552
GO:0005230	Extracellular ligand-gated ion channel activity	4	*GABRG2*, *GABRA1*, *GABRB2*, *GABRA6*	0.002	2.811
GO:0035095	Behavioral response to nicotine	3	*CHRNB4*, *CHRNA5*, *CHRNA3*	0.002	3.181
GO:0005892	Acetylcholine-gated channel complex	3	*CHRNB4*, *CHRNA5*, *CHRNA3*	0.016	17.955
GO:0015464	Acetylcholine receptor activity	3	*CHRNB4*, *CHRNA5*, *CHRNA3*	0.010	12.298
GO:0042166	Acetylcholine binding	3	*CHRNB4*, *CHRNA5*, *CHRNA3*	0.012	14.102
GO:0004889	Acetylcholine-activated cation-selective channel activity	3	*CHRNB4*, *CHRNA5*, *CHRNA3*	0.016	17.935
KEGG Pathway					
bta04080	Neuroactive ligand-receptor interaction	10	*LEP*, *F2RL3*, *GABRG2*, *PARD3*, *GABRA1*, *GABRB2*, *GABRA6*, *CHRNB4*, *CHRNA5*, *CHRNA3*	0.005	5.324

Source: Own authorship.

Table 10 - DAVID Functional Annotation for gene category and pathway enrichment analysis for Maternal Genetic Additive effect.

Gene Ontology	Terms	N. Genes[1]	Ann. Genes[2]	P-value	FDR
GO:0050907	Detection of chemical stimulus involved in sensory perception	5	*OR4S1*, *OR4C3*, *OR4C13*, *OR4X1*, *OR4C46*	0.000	0.000

GO:0007186	G-protein coupled receptor signaling pathway	5	*OR4S1, OR4C3, OR4C13, OR4X1, OR4C46*	0.000	0.000
GO:0016485	Proteinprocessing	1	*GZMB*	0.001	2.112

Table 10 (Continuation) - DAVID Functional Annotation for gene category and pathway enrichment analysis for Maternal Genetic Additive effect.

GO:0005886	Plasma membrane	14	*OR4S1, OR4C3, MTFR1, OR4C13, ANGPT1, PTPRE, PIRT, OR4X1, PENK, STXBP6, RGS4, RGS5, CA2, OR4C46*	0.000	0.020
GO:0016021	Integral component of membrane	23	*CYP2U1, SLC44A5, CYC1, PTCHD4, OR4S1, DDR2, OR4C3, TMEM64, OR4C13, DAD1, ASPH, HSD17B7, CLRN3, PIRT, PTPRE, SEL1L2, SLC10A7, CYP7B1, OR4X1, DGAT1, STXBP6, TMEM220, OR4C46*	0.011	11.665
GO:0043231	Intracellular membrane-bounded organelle	1	*GZMB*	0.019	19.005
GO:0004888	Transmembrane signaling receptor activity	5	*OR4S1, OR4C3, OR4C13, OR4X1, OR4C46*	0.000	0.000
GO:0004984	Olfactory receptor activity	5	*OR4S1, OR4C3, OR4C13, OR4X1, OR4C46*	0.000	0.000
GO:0004930	Protein coupled receptor activity	5	*OR4S1, OR4C3, OR4C13, OR4X1, OR4C46*	0.000	0.000
KEGG Pathway					
bta04740	Olfactory transduction	5	*OR4S1, OR4C3, OR4C13, OR4C12, OR4X1, OR4C46*	0.000	0.000

Source: Own authorship.

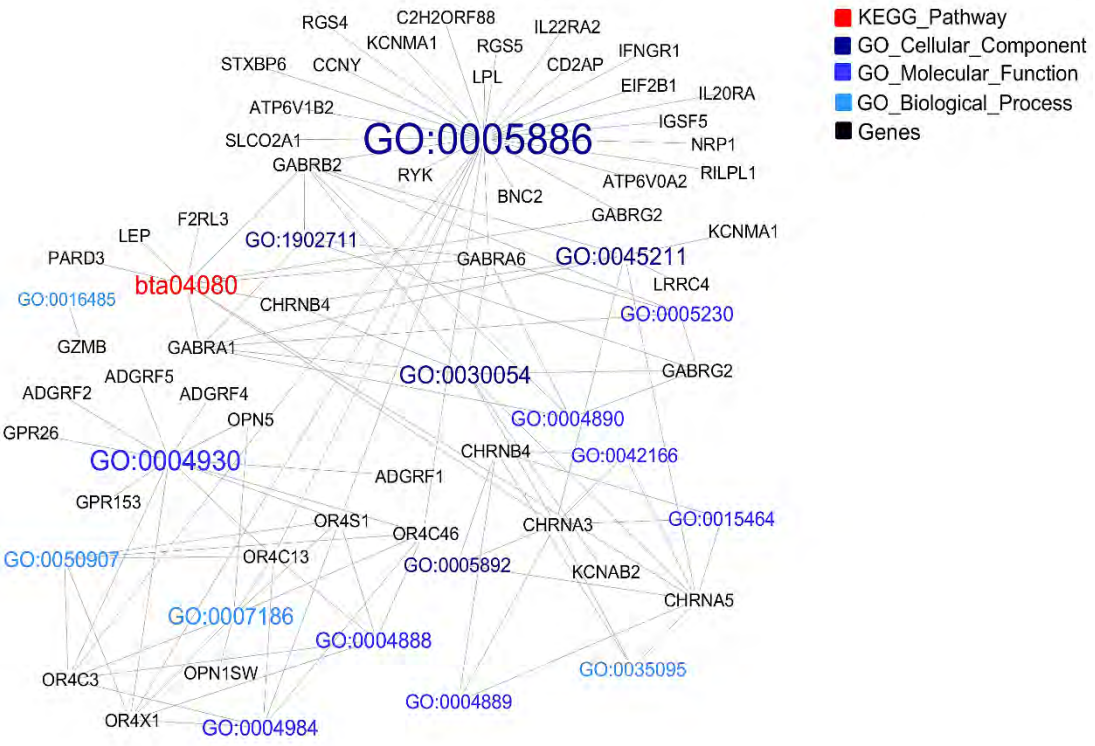
The detection of the chemical stimulus involved in sensory perception (GO: 0050907), significant for direct maternal and additive genetic effects (P <0.05), is defined as a series of events in which a chemical stimulus is received

and converted into a signal as part of sensory perception. This genetic ontology encompasses many olfactory receptor genes, responsible for triggering the perception of smell, as well as being related to feed intake and feed efficiency in Nellore cattle, factors that may be promote better growth (OLIVIERI et al., 2016).

Four gene ontology related to acetylcholine can be highlighted, they follow: (GO:0015464; GO:0042166; GO:0004889; GO:0005892). These gene ontologies act in response to chemical or mechanical signals which enables the transmembrane transfer of a cation by a channel that opens upon binding acetylcholine. In order to promote muscle cells growth, skeletal muscle cells rely on chemical signals in order to generate electrical signals, which are responsible for cell contraction and consequently may influence muscle development.

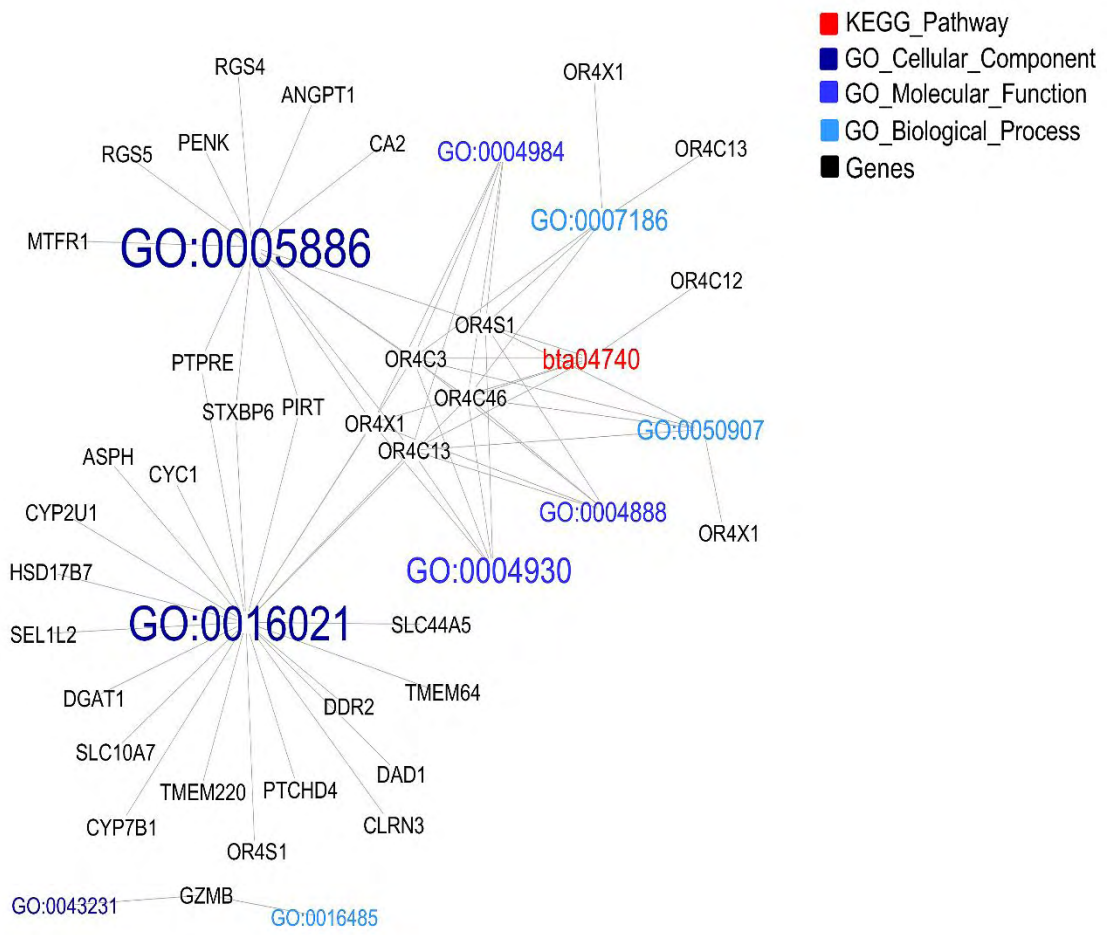
Several highlighted genes *AMOTL2, AIMP1, HAS2, DKK2, LPL, CREM, COX8A, MSTN, PLA2G7, LEP* and *PSIP1* were related to growth, muscle and adipose tissue metabolism and development, subcutaneous fat deposition, feed efficiency, while *SLC44A5, RABGGTB, DKK2*, and *DGAT1* genes were related to homeostasis, composition and production of milk and ability to produce heavier calves. The enrichment analysis also evidenced that the same gene could interact in different biological processes and pathways, as the *OR4* gene-family, acting in the same pathways/GO on direct and maternal effects, which influences the animal growth and development (Figure 7 and 8).

Figure 7 - Interaction between genes, gene ontology categories, and pathways of the functional analysis of all traits for additive direct genetic effect. Size pathways/GO letters are according to the number of interactions (GOs and pathways description is presented on table 9).



Source: Own authorship.

Figure 8 - Interaction between genes, gene ontology categories, and pathways of the functional analysis for additive maternal genetic effect for BW and W210. Size pathways/GO letters are according to the number of interactions (GOs and pathways description is presented on table 10).



Source: Own authorship.

5.4. Prediction Ability

Correlation values (EBV x DGV) of predictive abilities ranged from low (0.10) to moderate (0.68) values in the traits on different panels studied (Table 11). Lourenco et al. (2015) worked with growth traits in Angus cattle applying the ssGBLUP method and reported predictive abilities for DGV ranging from 0.13 to 0.39.

Table 11 - Prediction ability (PA) of direct genomic value (DGV) and bias in growth traits on Nellore cattle.

EBV x DGV	Traits

		BW_d	BW_m	$W210_d$	$W210_m$	W450	ACW
PA	HD	0.30**	0.54**	0.51**	0.68**	0.52**	0.11**
	30k	0.28**	0.50**	0.46**	0.66**	0.47**	0.10**
	0.5%	0.26**	0.33**	0.33**	0.36**	0.28**	0.25**
	1%	0.20**	0.25**	0.23**	0.31**	0.23**	0.18**
Bias	HD	0.14**	0.44**	0.64**	0.85**	0.66**	-0.14**
	30k	0.12**	0.36**	0.67**	0.80**	0.70**	-0.12**
	0.5%	0.12**	0.27**	0.45**	0.28**	0.46**	0.03
	1%	0.10*	0.21**	0.22**	0.24**	0.54**	-0.02

[1]BW_d= Birth weight direct effect; BW_m= Birth weight maternal effect; $W210_d$= Weaning weight direct effect; $W210_m$= Weaning weight maternal effect; W450= Yearling weight; ACW= Adult cow weight; Animals on validation set: 7,885; **P-value <0.001; *P-value < 0.01.
Source: Own authorship.

The 30K panel presented PA similar to those obtained with HD. Differences between panels of, approximately, 7, 8, 10, 3, 10 and 10% for BWd, BWm, W210d, W210m, W450 ACW, respectively. In this sense, genotyping with low/medium density markers may be an alternative contributing to the reduction of the time to processing analyzes, computational and genotyping costs (DASSONNEVILLE et al., 2012; VANRADEN et al., 2011).

PA for ACW (HD and 30k) were low, which may be explained by the training set structure. This dataset was composed of bulls and genotyped cows, in which the cows presented in the training set do not have phenotypic records for ACW (Table 12). Considering the aforementioned, we may highlight that for better genomic predictions, besides phenotypic information, genotyping panels and methods of analysis, a good relationship structure between the training and validation population sets need to be taken into account (HABIER et al., 2010; RAOUL; SWAN; ELSEN, 2017).

Table 12 - Descriptive statistics of animal phenotypes for validation and training set (ability prediction analysis).

Trait[1]	Validation					Training				
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max
BW	3,669	33.48	4.48	15.00	65.00	283	35.60	4.83	27.00	50.00

Table 12 (Continuation) - Descriptive statistics of animal phenotypes for validation and training set (ability prediction analysis).

Trait[1]	Validation					Training				
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max
W210	4,734	187.00	31.55	65.00	389.00	410	244.30	31.53	160.00	364.00
W450	4,711	272.00	56.33	82.00	698.00	397	393.90	86.00	205.00	698.00
ACW	144	466.60	75.00	230.00	1005.00	0.00	0.00	0.00	0.00	0.00

[1]BW= Birth weight; W210= Weaning weight; W450= Yearling weight; ACW= Adult cow weight.
Source: Own authorship.

Results for panels containing only SNPs that accounted for more than 0.5% of the additive (direct and maternal) genetic variance were an average of 30.40% higher, compared to the panel of SNPs that accounted for 1% of the additive genetic variance. However, PA for reduced panels (0.5% and 1%) was lower when compared to HD and 30k. This may be related to the number of SNPs in each panel (Table 13), where, the panels 0.5% and 1% even having markers with highest effects showed low values of PA, probably due to the reduction in the number of SNPs, criteria for SNP selection and lack of proper genome coverage, induced the possible non-capture of effects by ssGWAS. Thus, the prediction with more restrictive panels with lower numbers of markers may be surrounded equalized by limitations on the nature of the polygenic traits and/or the genetic architecture (MOSER et al., 2010).

Table 13 - Number of markers present on the custom chips from single-step genome-wide association analysis (ssGWAS) considering SNPs that explained of 0.5 and 1% of additive genetic variance.

Trait[1]	Number of SNPs	
	0.5%	1%
BW_d	431	54
BW_m	441	106
$W210_d$	332	63
$W210_m$	322	62
W450	151	52
ACW	229	99

[1]BW_d= Birth weight direct effect; BW_m= Birth weight maternal effect; $W210_d$= Weaning weight direct effect; $W210_m$= Weaning weight maternal effect; W450= Yearling weight; ACW= Adult cow weight.
Source: Own authorship.

The bias was overestimation (<1.0) for PA estimates over all traits and panels considered. PA was more overestimated with restrictive panels when

compared with HD and 30k. According to Calus et al. (2008); Meuwissen et al. (2001); Meuwissen (2009) and Muir (2007) who worked with genomic prediction using simulation data, markers should be in sufficient linkage disequilibrium (LD) with QTL for improvements in terms of prediction power and keep bias close to one.

In a panel reduction approach similar to that of the present study and using the SNPs associated with genes with known biological functions, Abdollahi-arpanahi, Morota, and Peñagaricano (2017), highlighted that gains in prediction ability did not overcome the prediction with the use of 55K SNPs.

6. CONCLUSION

The identification and description of regions of the genome, genes and biological processes that affect productive traits are important, since this can be used in future studies of fine mapping, whose primary function is the search for informative causative mutations. The results of the present study suggest that the identification of candidate and regulatory genes may influence future investigations in genetic architecture studies of growth traits, to assist in the discovery of underlying genetic and physiological mechanisms.

HD and 30K panels could be equally recommended for the implementation of genomic selection for the growth traits in Nellore cattle. However, in this study application of reduced panels (0.5% and 1% explain of the additive genetic variation) is not a better approach for prediction ability implementation.

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