Effect of *IGF-1* and *LEP/ob* SNPs on growth parameters of Blanco Orejinegro cattle

Efecto de SNPs de *IGF-1 y LEP/ob* sobre parámetros de crecimiento del ganado Blanco Orejinegro

Efeito dos SNPs de *IGF-1* e *LEP/ob* nos parâmetros de crescimento do gado Blanco Orejinegro

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Abstract

The aim of this work was to identify the effect of some SNPs of the *IGF-1* and *LEP/ob* genes, on the growth in animals of the Blanco Orejinegro creole breed (BON) and to evaluate the relationship of age at first calving (AFC) with the curve trajectory. For this, 1217 phenotypic and 439 genomic records of pure BON bovines were used. The Gompertz, Logistic, Von Bertalanffy and Brody models were evaluated. The individual growth curve parameters were estimated and the effect of SNPs of the *IGF-1* and *LEP/ob* genes on the curve parameters was estimated through a linear model. Finally, the association of the curve parameters and the AFC was analyzed trough a linear model. The model that represented the best fit to the growth trajectory was Brody's. On average, the BON animals presented an adult weight (β_0) of 479.9±7.4 kg and a growth rate expressing the daily weight gain as a proportion of the total weight (β_2) of 0.002±0.00004. The SNPs rs110654613 (nucleotide change A/G) and rs110959643 (A/G), within the *IGF-1* gene, showed a significant effect ($p<0.05$) on the parameters of the BON cattle growth curve. There were no associations of *LEP/ob* gene SNPs on the parameters of the BON cattle growth curve. AFC was significantly associated ($p<0.05$) with the parameters β_0 and β_2. It is concluded that the use of genomic information for the *IGF-1* gene can lead to higher growth rates and earlier AFC.

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Resumen

El objetivo de este trabajo fue identificar el efecto de algunos SNPs de los genes de *IGF-1* y *LEP/ob*, sobre el crecimiento de animales de la raza criolla Blanco Orejinegro (BON) y evaluar la relación de la edad al primer parto (EPP) con la trayectoria de la curva. Para ello se utilizaron 1.217 registros fenotípicos y 439 registros genómicos de bovinos puros BON. Los modelos de Gompertz, Logístico, Von Bertalanffy y Brody fueron evaluados y se estimaron los parámetros individuales de la curva de crecimiento. Se estimó el efecto de SNPs en los genes *IGF-1* y *LEP/ob* sobre los parámetros de la curva, a través de un modelo lineal. Finalmente, se analizó la asociación de los parámetros de la curva y su trayectoria con la EPP, mediante un modelo lineal. El modelo que representó un mejor ajuste a la trayectoria de crecimiento fue el de Brody. En promedio los animales BON presentaron un peso adulto (β_0) de 479,9±7,4 kg y una tasa de crecimiento expresando la ganancia diaria de peso como proporción del peso total (β_2) de 0,002±0,00004. Los SNP rs110654613 (cambio nucleotídico A/G) y rs110959643 (A/G), dentro del gen *IGF-1,* mostraron efecto significativo sobre los parámetros de la curva de crecimiento de ganado BON. No hubo asociaciones de SNPs del gen *LEP/ob* con la curva de crecimiento de ganado BON. La EPP estuvo asociada significativamente ($p<0,05$) con los parámetros β_0 y β_2. Se concluye que el uso de información genómica para el gen *IGF-1* puede llevar a mayores tasas de crecimiento y EPP más tempranos.

Palabras clave: bovino criollo, marcadores moleculares, precocidad, productividad, recurso zoogenético.

Resumo

O objetivo deste trabalho foi identificar os efeitos de alguns SNPs dos genes *IGF-1* e *LEP/ob*, sobre a curva de crescimento de animais da raça Blanco Orejinegro (BON) e avaliar a relação da idade ao primeiro parto (IPP) com a trajetória da curva. Para isso, foram utilizados 1.217 registros fenotípicos e 439 registros genômicos de bovinos BON puros. Foram avaliados os modelos de Gompertz, Logístico, Von Bertalanffy e Brody. Os parâmetros individuais da curva de crescimento foram estimados e o efeito dos SNPs dos genes *IGF-1* e *LEP/ob* sobre os parâmetros da curva foi estimado por meio de um modelo linear. Finalmente, a associação dos parâmetros da curva e sua trajetória com a IPP foi analisada por meio de um modelo linear. O modelo que mais se adequou à trajetória de crescimento foi o de Brody. Em média, os animais BON apresentaram peso adulto (β_0) de 479,9±7,4 kg e uma taxa de crescimento expressando o ganho de peso diário em proporção ao peso total (β_2) de 0,002±0,00004. Os SNPs rs110654613 (mudança de nucleotídeo A/G) e rs110959643 (A/G), dentro do gene *IGF-1*, mostraram um efeito significativo ($p<0,05$) nos parâmetros da curva de crescimento de bovinos BON. Não houve associações com SNPs do gene *LEP/ob* com os parâmetros da curva de crescimento de gado BON. A IPP foi significativamente associada ($p<0,05$) aos parâmetros β_0 e β_2. Conclui-se que o uso de informações genômicas para o gene *IGF-1* pode levar a maiores taxas de crescimento e IPP mais precoce.

Palavras-chave: polimorfismos, precocidade, produtividade, raça crioula, recurso zoogenético.

Introduction

Growth is defined as the increase in weight of animals from birth to its stabilization in adulthood (Ramírez *et al*., 2009), where both biological and environmental aspects interfere (Rincón and Quintero, 2015). Some of the biological aspects are hormonal that regulate various productive and reproductive characteristics in the body. For example, insulin-like growth factor 1 (*IGF-1*), which is a protein hormone that plays an important role in various metabolic and physiological processes and in growth with anabolic effects (Castrelln *et al*., 2010). The bovine *IGF-1* gene is located on chromosome 5 (*Bos taurus* autosome – BTA5) and has been proposed as a candidate gene for growth traits in cattle (Rogberg-Muñoz *et al*., 2013). Another important hormone involved in energy metabolism is leptin (Saleem, 2015), a protein that regulates appetite and metabolism (Lusk, 2007) and has been used as a biological marker that reflects the degree of fat in the body. Leptin is encoded by the *LEP/ob* gene, which in bovines is located on chromosome 4 (BTA4).

In cattle, multiple genetic variants have been reported within the *IGF-1* gene, many of them single nucleotide polymorphisms (SNPs), some significantly associated with phenotypic variation and breeding values in the early growth phase (Andrade *et al*., 2008; Castrelln *et al*., 2010). It has also been proposed that the *LEP/ob* gene is associated with parameters of the growth curve and backfat in cattle (Lusk, 2007), and that variations in the SNP UASMS2 (C/T) of this gene have been significantly influential in the variability found for parameters of the growth curve (Lusk, 2007). However, the study of the association of markers of some genes with parameters of the growth curve has not been carried out in any of the Colombian Creole breeds, not even in the Blanco Orejinegro (BON), one of the most widely reported.

The BON is a breed that has undergone a process of natural selection close to 500 years in the conditions of the Colombian tropics (López-Herrera *et al*., 2001), belongs to the *Bos taurus* species (Rincón and Quintero, 2015) and is characterized phenotypically due to its white fur, black ears, skin and nose (López-Herrera *et al*. 2001). Its economic importance lies in its rusticity, ability to efficiently take advantage of low-quality forages and to be in steep terrain, ability to reproduce, survive, be long-lived and because it is a triple-purpose animal (milk, meat and work) (Bedoya *et al*., 2001; López-Herrera *et al*., 2001).

In cattle studies, Inoue *et al*. (2020) reported a negative genetic association between the adult weight of Japanese Black cattle and the age at first calving (AFC), where females with a lower adult weight would show a higher AFC. Likewise, these authors found a positive but low association between the maturation rate and AFC. In Holstein cattle in Brazil, Coelho *et al*. (2009) found positive, but not significant, correlations between AFC and adult weight; and negative and significant between AFC and the maturation rate, suggesting that cows with higher maturation rates have a better productive efficiency. In BON cattle, there is no type of study associating AFC with growth curve parameters, and the information available on BON growth at the molecular level is scarce (Caivio-Nasner *et al*., 2021; Cañas *et al*. , 2008; Londoño-Gil *et al*., 2021), so it is important to study the allelic variants of certain genes or regions of the genome that are related to growth variation in this breed and, in turn, to AFC (productive ability and reproductive). Therefore, the objective of this work was to identify the effect of some SNPs of the *IGF-1* and *LEP/ob* genes on the growth curve of animals of the Creole breed Blanco Orejinegro (BON) and to evaluate the relationship between age at first calving (AFC) with the trajectory of the curve.

Materials and methods

Data and animals of the BON breed

To model the growth of the animals, phenotypic and genotypic information was used from a BON cattle database belonging to 7 Colombian herds located in the departments of Antioquia, Caldas, Meta, Risaralda and Tolima. Management and environmental conditions varied according to the herd and its location. Historical production data from 1993 to 2018 were used. The information was analyzed and refined in the R program (R Core Team, 2020), taking into account the weight at birth as a starting point for modeling the growth curve, guaranteeing a minimum of 4 weighings per animal and that the last weight measurement had been recorded at least at 800 days (26.31 months) of age. After purification, the information from 11,140 consecutive weighings in the life of 1,217 animals (9.15 weighings per animal) was used to estimate the parameters of the growth curves.

Growth curve fitting models

To estimate the curve that best fit the data, the models were used: Gompertz (1825) $Y_{ij} = \beta_0 e^{-\beta 1 e^{-\beta 2t}}$; Logistical (Verhulst, 1838): $Y_{ij} = \beta_0 + (1 - e^{-\beta 1t})^{-1}$; Von Bertalanffy (1938): $Y_{ij} = \beta_0(1 - \beta_1 e^{-\beta 2t})^3$ and Brody (1945): $Y_{ij} = \beta_0 + (1 - \beta_1 e^{-\beta 2t})$; where: Y_{ij} : corresponds to the *j*-th weight of the *i*-th animal at time "*t*", β_0: corresponds to the asymptotic weight when "*t*" tends to infinity and is commonly interpreted as the adult weight, β_1: corresponds to a parameter of fit when $Y \neq 0$ and when $t \neq 0$, and indicates the proportion of asymptotic mature weight that is gained after birth, β_2: corresponds to the maturity index represented as a percentage proportion of maximum growth with respect to the adult weight of the animal; t_{ij} is the age in days at the *j*-th weighing of the *i*-th animal (Dominguez-Viveros *et al.*, 2017). The fit of the models to the data was determined by the criteria of lowest sums of squares of the error (SQE), Akaike information criterion (AIC), Bayesian information criterion (BIC), and highest percentages of convergence (%C) and coefficient of determination (R^2). Finally, the individual parameters of the growth curve of each of the animals were estimated.

SNPs within *LEP/ob* and *IGF-1* genes

Genotype information was obtained for 439 individuals, each with genotype information for 118,116 SNPs, which were part of the BON cattle data bank. These genotypes were coded as 0: homozygous for the first allele, 1: heterozygous, and 2: homozygous for the second allele. From the GenBank assembly ARS-UCD1.2 (https://www.ncbi.nlm.nih.gov/assembly/GCA_002263795.2; GenBank accession number NKLS00000000.2), where mapped SNPs located within *IGF-1* genes (AC_000162.1; 66523798…66604881) and *LEP/ob* (AC_000161.1; 93249803…93266625), located in BTAs 5 and 4, respectively. Five SNPs were identified within the *IGF-1* gene: rs133675145 change (A/G), rs110654613 (A/G), rs110959643 (A/G), rs109297640 (A/G) and rs109148720 (T/G); and two within the *LEP/ob* gene: rs136588988 (T/C) and rs110559656 (A/G).

Association of SNPs with the variation of the growth curve format

Once the parameters of the curve were estimated, individuals that presented a value for the parameter β_0 (adult weight) between 300 and 600 kg were kept, considering them biologically possible in the breed; records of animals that were well represented by herd (minimum 6 individuals per herd), sex, season (summer 1: January, February, March; summer 2: July, August, September; winter 1: April, May, June; and winter 2: October, November, December), year (from 2009 to 2017, minimum 3 observations per year) and also had a genotype. Finally, 90 animals (69 females and 21 males) had consistent phenotypic (growth curves) and genotypic information. The linear model used to evaluate the effect of the variations of the SNPs on the parameters of the growth curve of these animals was:

$$\mathrm{Y_{ijklmn}} = \mu + Herd_{\mathrm{j}} + EN_{\mathrm{k}} + Year_{\mathrm{l}} + \mathrm{Sex}_m + \mathrm{SNP}_n + \varepsilon_{\mathrm{ijklmn}}$$

Where, $\mathrm{Y_{ijklm}}$ is the parameter evaluated for growth in animal i; μ is the general mean of the evaluated traits, and $Herd_{\mathrm{j}}$, EN_{k}, $Year_{\mathrm{l}}$, Sex_m are the fixed effects of herd, season of birth, year of birth and sex of the individuals, respectively. SNP_n is the effect of the marker variant of the individually evaluated SNPs and $\varepsilon_{\mathrm{ijklmn}}$ is the random error associated with each observation (Cardona *et al.*, 2015). The lm function was used and the means of the genotypes were compared using the lsmeans package (Lenth, 2016), through the Tukey test in the R software (R Core Team, 2020). The curves of the animals with significant SNPs were plotted in the R software, to visually observe the differences in the growth curves according to the genotype.

Association of growth curve parameters with AFC

To make this association, information from 140 females that had sufficient and consistent information on growth curve parameters and AFC was used. The linear model used was:

$$\mathrm{Y_{ijk}} = \mu + Herd_{\mathrm{j}}\ \mathrm{Year} + \beta_0 + \beta_1 + \beta_2 + \varepsilon_{\mathrm{ijk}}$$

Where, $\mathrm{Y_{ijk}}$ is the AFC in animal i; μ is the overall mean of the AFC, and $Herd_{\mathrm{j}}$ and $Year_k$ are the fixed effects of herd and year of birth, respectively; β_0, β_1 and β_2 are the curve parameters of the model that was chosen as the best and $\varepsilon_{\mathrm{ijk}}$ is the random error associated with each observation. This analysis was performed using the lm function and the means of significant effects were compared by Tukey's test using the lsmeans package using R software (R Core Team, 2020).

Results and discussion

Table 1 shows the results of the fit evaluation of the models used and the means of the parameters obtained for each model.

The model that presented a better fit for the description of the growth curve of BON animals was the Brody model, with the lowest AIC, BIC and SQE, while obtaining the highest R^2. This model has been widely used to describe the growth curve in cattle, since it usually presents the best fits (Agudelo *et al.*, 2008: Ramírez *et al.*, 2009; Rincón and Quintero, 2015), especially at ages after 6 months, since for first months of life it tends to underestimate the weight (Agudelo *et al.*, 2008). However, for authors such as Dominguez-Viveros *et al.* (2017) the model with the best performance for grazing zebu cattle was the logistic one.

The average parameters with biological interpretation in the Brody model were: β_0: 479.9 ± 7.4 kg (adult weight) and β_2: 0.002 ± 0.00004 (maturity index or growth rate expressing the daily gain of weight as a proportion of the total weight), large numbers in this index indicate an early maturation of the animals (Hojjati and Hossein-Zadeh, 2018). These results are consistent with those previously reported in the BON breed by Rincón and Quintero (2015), under the Brody model, the data fit better, with higher adult weights (590 kg) and a maturity

Table 1. Evaluation of fit of non-linear models used in the description of the growth curve of animals of the Blanco Orejinegro (BON) breed from Colombia and estimated mean parameters.

Model	AIC	BIC	SQE	R^2	% C	β_0	β_1	β_2
Bertalanfy	119238.2	119267.5	29014728	0.79	50.53	389.4	0.5155	0.003
Logistic	119944.2	119973.5	30912991	0.78	84.96	347.0	4.95	0.006
Brody	118939.9	118969.2	28248116	0.80	76.83	474.9	0.924	0.002
Gompertz	119414.9	119444.1	29478432	0.79	85.30	372.0	2.042	0.004

AIC: Akaike Information Criterion, BIC: Bayesian Information Criterion, SQE: Error Sum of Squares, R^2: Determination Coefficient, %C: Convergence Percentage.

index of 0.00153. The small differences may be due to the fact that the parameters of the growth curves are probably influenced either by the genetic component of the animals studied, by management, by their ability to adapt to their environment (Rincón and Quintero, 2015), or because in the previous BON study information from a single herd was used, so there was probably greater homogeneity.

Association of the SNPs with the variation of the growth curve format

Of the 7 SNPs under study (2 within the *LEP/ob* gene and 5 SNPs within the *IGF-1* gene), only 2, within the *IGF-1* gene, showed a significant association with the growth curve parameters (table 2), corresponding to markers rs110654613 (β_2) and rs110959643 (β_1 and β_0).

In table 2, it is observed that the herd and the year of birth influence all the parameters of the curve, thus affecting the complete growth curve of the BON animals. This is important, since differences are generated in the growth of the animals that can be attributed to changes in forage availability, selection and management processes in the different herds, as well as climatic variations between years (Martins *et al*., 2000). Similarly, in studies of growth traits in BON cattle, Martínez *et al*. (2012) found that herd, year of birth and sex were important sources of variation. On the other hand, the SNP rs110959643 seems to be almost fixed in this population sample, since of the 90 animals under study, 85 animals presented genotype 0, five 1 and none 2 (0: homozygous for the first allele - GG, 1: heterozygous - GA, 2: homozygous for the second allele - AA). This situation may be because the animals in the population have been selected, naturally or artificially, towards genotype 0 (GG), due to the effects of drift, increased inbreeding, structuring or imbalance in the model, which could generate a spurious association and affect the robustness of the result. Gui *et al*. (2018) in a study evaluating the influence of *IGF-1* gene polymorphisms on growth traits, showed that the low sample number can lead to certain genotypes not being observed. However, in the present study, the individuals included came from a database where there were several selection criteria for genotyping, such as being the most representative of the population, having several phenotypic records, among others, which does not allow the sample was not representative.

Table 2. SNPs and factors associated with each of the parameters of the growth curve under the Brody model in a population of Blanco Orejinegro (BON) cattle from Colombia.

Parameter	SNP	Year	Sex	Herd	Season	R^2
β_0	rs110959643*	**	**	**	NS	0.45
β_1	rs110959643**	**	NS	**	NS	0.45
β_2	rs110654613*	**	NS	**	NS	0,48

**$p<0{,}01$, *$p<0{,}05$, NS $p>0{,}05$. rs110959643 y rs110654613: Intronic variants of the *IGF-1* gene. R^2: Coefficient of determination.

The mean difference for each of the parameters of the growth curve according to the genotype of the SNPs is shown in table 3. For the parameter β_0, related to the asymptotic adult weight, the animals with genotype 1 (heterozygous - GA) for SNP rs110959643 will have a lighter adult weight (427 kg) compared to the homozygous genotype 0 (GG - 534 kg), which is consistent with what has been previously reported in other beef cattle breeds.

Table 3. Adjusted means of the parameters of the growth curve (β_0, β_1 y β_2) according to the genotype of the associated SNPs in a population of BON cattle from Colombia.

SNP/Genotype	0	1	2
rs110959643 - β_0	534 ± 20.3^b	427 ± 48.3^a	
rs110959643 - β_1	0.937 ± 0.004^b	0.906 ± 0.010^a	
rs110654613 - β_2	0.0015 ± .0001^b	0.0015 ± .0001^b	0.0009 ± 0.0002^a

rs110959643 and rs110654613: Intronic variants of the IGF-1 gene. Same letters on the same line do not differ statistically. For rs110959643, 0 = GG, 1 = GA, 2 = AA; for rs110654613 0 = GG, 1 = GA, 2 = AA.

Rogberg-Muñoz *et al*. (2011) found that the SNP rs110959643 has important implications in the productivity of animals, since this gene has been reported to have a role in the growth and development of bovines and its polymorphisms have been associated with growth traits (weight at birth, daily weight gain, adult weight and other body weights) and development of mammals. The effect of these SNPs on the growth curve of BON animals can be verified graphically in figure 1.

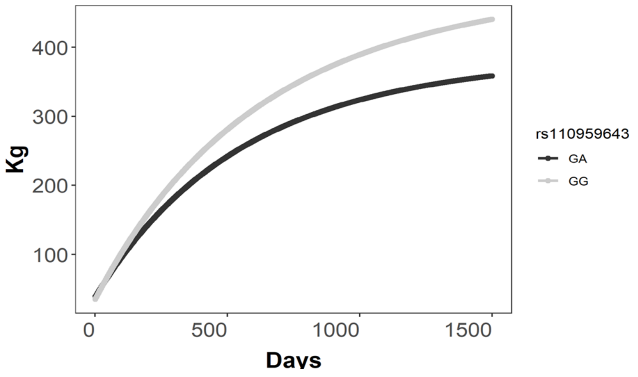

Figure 1. Average growth curve according to the genotype of the SNP rs110959643 associated with the parameters β0 and β1 of the Brody model.

Regarding the parameter β_2, associated with the maturity index, in table 3 a dominance effect is observed for the SNP rs110654613 (*IGF-1* SNP), where animals with genotypes 0 (GG) or 1 (GA) (i.e., homozygous for the first allele or heterozygotes) will have a higher maturity index and therefore will reach maturity earlier than homozygous 2 (AA) (0.001567, 0.001564 and 0.000942, respectively) (figure 2). These results disagree with reported in Brahman cattle from Brazil by Crispim *et al*. (2015), who found that for the maturity index (β_2) the most significant SNP was found in BTA 20 and was rs42482169. For this SNP the mean of the homozygous dominant genotype was 0.0063, for the heterozygous 0.0064 and for the homozygous recessive 0.0068.

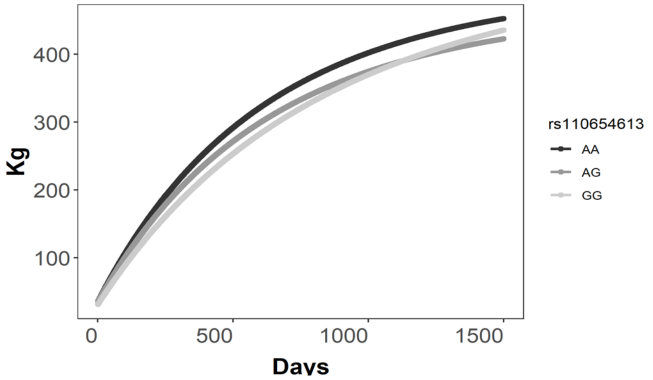

Figure 2. Average growth curve according to the genotype of the SNP rs110654613 associated with the parameter β_2 of the Brody model (1945).

The SNPs rs110959643 (5:66228391) and rs110654613 (5:66224046), important for the growth curve of Colombian Creole cattle BON, are located within introns of the *IGF-1* gene, with a difference of 4345 bp between each other and with a high degree of linkage with the possible causal variant, given the linkage disequilibrium that exists in the BON breed, of 0.39 at distances less than 25 Kb (Caivio-Nasner *et al*., 2021). The *IGF-1* gene has previously been related to myogenic factors directly involved in growth and sexual precocity, due to the effect of this gene on different metabolic and endocrine pathways, which have shown a connection between growth and the beginning of reproductive life (Mota *et al*., 2020). This has been shown in Nelore females from Brazil, where the higher concentration of the hormone *IGF-1* in the blood has been associated with greater growth and, therefore, a lower age at puberty and a lower AFC (Ferraz *et al*., 2018) and in Canchim animals (Gui *et al*., 2018), where its importance in growth traits has been demonstrated. This gene is important in the modulation of a variety of physiological activities such as cell development, differentiation and proliferation, leading to increased muscle growth (Gui *et al*., 2018); therefore, by finding an association of SNPs of the *IGF-1* gene with the parameters of the growth curve in this study, it can be inferred that it can be used as a candidate gene for early selection of BON animals for future work.

Finally, the SNPs within the *LEP/ob* gene did not show a significant association with growth or AFC. Previously, the *LEP/ob* gene has been associated with parameters of the growth curve and backfat of cattle (Lusk, 2007) and it has been reported that the variations in the SNP UASMS2 of this gene have been significant for the body weight growth curve ($p<0.001$). This is in contrast to what was reported by Ferraz *et al*. (2018), who stated that this gene has no implications for age at puberty, and that hormone secretion after 18 months was very low, which would help to understand why in the present study the *LEP/ob* gene had no significant effect.

Association of the growth curve parameters with AFC

In this study, the mean AFC for the BON females analyzed was found to be 1,044.04 ± 177.04 days or 34.23 ± 5.80 months. This AFC is lower than that reported by M-Rocha *et al*. (2012) in 22 populations of BON cattle, of 1,104 ± 141 days (36.8 months).

The AFC under study was significantly associated with the parameters β_0 ($p = 0.0124$), β_2 ($p = 0.0117$) and with the herd of origin ($p = 0.0010$), which can be evidenced in the table 4, but not with the year of birth ($P = 0.0654$), nor the parameter β_1 ($p = 0.2414$) (data not shown). These findings differ from those reported by M-Rocha *et al*., (2012), who found no effect of herd or year on AFC ($p>0.05$).

Table 4. Adjusted means of AFC according to the birth herd of BON females from Colombia.

Herd	PPE adjusted mean
1	830 ± 91.7^{a}
2	978 ± 35.6^{ab}
3	991± 31.8^{ab}
4	1029 ± 54.6^{ab}
5	1061 ± 38.9^{ab}
6	1140 ± 47.3^{bc}
7	1308 ± 77.3c

$^{a, b, c}$Means with different letters differ significantly ($p<0.05$) from each other.

The parameter β_0, associated with adult age, showed that for each kg more of weight at adult age in BON cattle, the AFC of BON females decreased by an average of 0.538 ± 0.212 days. In addition, for one unit of change in the parameter β_2, the AFC decreases by an average of 0.000719 ± 0.0003 days in BON females from Colombia; showing that animals that grow faster and have a higher adult weight, will be those that possibly have an earlier AFC. These animals will continue to grow after the first service and will end up with a considerable adult weight. These results differ from those found by Bayram *et al*. (2004), in Brown Swiss cattle using the Richards model, who reported a positive correlation between age at first calving and estimated adult weight (β_0). For these authors, an increase in weight at the age at first calving meant an increase in adult weight.

Similarly, Gaviolli *et al*. (2012), reported positive phenotypic correlations between AFC and the parameters β_0 and β_2, indicating that animals with higher adult weight and higher growth rate will have a higher AFC, which is not desirable from the productive point of view. The difference may be due to the differential management given to BON females in each herd and effects of the breed. According to the information provided by the producers of their herds, they often prefer to wait for a specific age to serve their animals, instead of doing it by weight, so animals that present a high growth rate can be served late in his life. In each herd, a different handling of the rearing of these BON females is carried out, and this should be taken into consideration in future works because the present results show that it is necessary to try to standardize the AFC according to the weight, ensuring that this traits do not vary significantly. Likewise, given that the genotype for genes such as *IGF-1* has an impact on the growth rate of animals, it is important to take it into consideration as a candidate gene within the improvement and management plans of BON herds to select animals. more efficient both productively and reproductively.

Conclusions

Of the methods evaluated in this research, Brody's method yielded the best estimate of the parameters studied, which makes it a practical tool to evaluate the growth curves of BON animals in Colombia, which presented an adequate adult weight and growth rate, which allows them to be economically and environmentally profitable. In this study, it was found that two SNPs in the *IGF-1* gene influenced the growth of BON cattle; however, no association was found between the growth curve parameters and the *LEP/ob* gene. In addition, the growth parameters, according to the Brody model, are associated with the age at first calving in the BON breed. This will allow studies to be carried out and the *IGF-1* gene to be applied as a candidate gene for growth in the selection of these animals, which in turn will allow improving AFC.

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Literature cited

Agudelo, D., Cerón, M., y Restrepo, L. (2008). Modelación de las funciones de crecimiento aplicadas a la producción animal. *Revista Colombiana de Ciencias Pecuarias*, *21*(1), 39–58. https://doi.org/10.17533/udea.rccp

Andrade, P. C., Grossi, D. A., Paz, C. C. P., Alencar, M. M., Regitano, L. C. A., & Munari, D. P. (2008). Association of an insulin-like growth factor 1 gene microsatellite with phenotypic variation and estimated breeding values of growth traits in Canchim cattle. *Animal Genetics*, *39*(5), 480–485. https://doi.org/10.1111/j.1365-2052.2008.01755.x

Bayram, B., Yanar, M., & Akbulut, Ö. (2004). Relationships among richards growth curve parameters, reproductive and milk production traits in brown swiss cattle sag feisfcfoh. *Journal of Applied Animal Research*, *26*(1), 29–32. https://doi.org/10.1080/09712119.2004.9706500

Bedoya, G., Carvajal, L. G., Moreno, F. L., Davies, S., Derr, J., Ossa, J., y Ruiz, A. (2001). Estructura molecular y poblacional del ganado criollo Colombiano (GCC). *Revista Colombiana de Ciencias Pecuarias*, *14*(2), 109–120. https://doi.org/10.17533/udea.rccp

Brody, S. (1945). *Bioenergetics and growth with special reference to the efficiency in domestic animals*. Hafner Publishing Company, INC. 1033 p. https://onesearch.library.rice.edu

Caivio-Nasner, S., López-Herrera, A., González-Herrera, L. G., & Rincón, J. C. (2021). Diversity analysis, runs of homozygosity and genomic inbreeding reveal recent selection in Blanco Orejinegro cattle. *Journal of Animal Breeding and Genetics*, *138*(5), 613–627. https://doi.org/10.1111/jbg.12549

Cañas, J. J., Ramírez, J., Arboleda, O., Ochoa, J., Vergara, O., y Cerón, M. (2008). Estimación de parámetros genéticos para peso al destete en ganado blanco orejinegro (BON) en el noroccidente colombiano. *Revista MVZ Córdoba*, *13*(1), 1138–1145. https://doi.org/10.21897/RMVZ.405

Cardona, S. J. C., Álvarez, J. D. C., Sarmento, J. L. R., Herrera, L. G. G., y Cadavid, H. C. (2015). Associação de SNPs nos genes para κ-caseína e β-lactoglobulina com curvas de lactação em cabras leiteiras. *Pesquisa Agropecuaria Brasileira*, *50*(3), 224–232. https://doi.org/10.1590/S0100-204X2015000300006

Castrelln, V. V., Vera, W. A., Bracamonte, M. P., Rincn, A. M. S., Montoya, H. M., & De la Rosa Reyna, X. F. (2010). Polymorphisms in the IGF1 gene and their effect on growth traits in Mexican beef cattle. *Genetics and Molecular Research*, *9*(2), 875–883. https://doi.org/10.4238/vol9-2gmr745

Coelho, J. G., Barbosa, P. F., Tonhati, H., & Freitas, M. A. R. de. (2009). Análise das relações da curva de crescimento e eficiência produtiva de vacas da raça Holandesa. *Revista Brasileira de Zootecnia*, 38(12), 2346–2353. https://doi.org/10.1590/S1516-35982009001200008

Crispim, A. C., Kelly, M. J., Guimarães, S. E. F., e Silva, F. F., Fortes, M. R. S., Wenceslau, R. R., & Moore, S. (2015). Multi-Trait GWAS and New Candidate Genes Annotation for Growth Curve Parameters in Brahman Cattle. *PLOS ONE*, *10*(10), 1–19. https://doi.org/10.1371/journal.pone.0139906

Dominguez-Viveros, J., Urbina-Valenzuela, A. R., Palacios-Espinoza, A., Callejas-Juárez, N., Ortega-Gutiérrez, J. Á., Espinoza-Villavicencio, J. L., Padrón-Quintero, Y., y Rodríguez-Castro, M. (2017). Caracterización del crecimiento de bovinos cebú en pruebas de comportamiento en pastoreo. *Ecosistemas y Recursos Agropecuarios*, *4*(11), 341–348. https://doi.org/10.19136/era.a4n11.1149

Ferraz, M. V. C., Pires, A. V., Santos, M. H., Silva, R. G., Oliveira, G. B., D. M., Polizel, D. M., Biehl, M. V., Sartori, R., & Nogueira, G. P. (2018). A combination of nutrition and genetics is able to reduce age at puberty in Nelore heifers to below 18 months. *Animal*, *12*(3), 569–574. https://doi.org/10.1017/S1751731117002464

Gaviolli, V. R. N., Buzanskas, M. E., Cruz, V. A. R., Savegnago, R. P., Munari, D. P., Freitas, A. R., & Alencar, M. M. (2012). Genetic associations between weight at maturity and maturation rate with ages and weights at first and second calving in Canchim beef cattle. *Journal of Applied Genetics*, *53*(3), 331–335. https://doi.org/10.1007/s13353-012-0100-6

Gompertz, B. (1825). On the nature of the function expressive of the law of human mortality, and on a new mode of determining the value of life Contingencies. *Philosophical Transactions ofthe Royal Society of London*, *115*, 513–583. http://www.jstor.org/journals/rsl.html

Gui, L., Wang, Z., Jia, J., Zhang, C., Chen, Y., & Hou, S. (2018). IGF-1 Gen Polimorfizmi Çin Qinchuan Sığırında Büyüme Özelliklerini Etkiler. *Kafkas Universitesi Veteriner Fakultesi Dergisi*, *24*(3), 387–392. https://doi.org/10.9775/kvfd.2017.19036

Hojjati, F., & Hossein-Zadeh, N. G. (2018). Comparison of non-linear growth models to describe the growth curve of Mehraban sheep. *Journal of Applied Animal Research*, *46*(1), 499–504. https://doi.org/10.1080/09712119.2017.1348949

Inoue, K., Hosono, M., Oyama, H., & Hirooka, H. (2020). Genetic associations between reproductive traits for first calving and growth curve characteristics of Japanese Black cattle. *Animal Science Journal*, *91*(1), 1–8. https://doi.org/10.1111/asj.13467

Lenth, R. V. (2016). Least-Squares Means: The R Package lsmeans. *Journal of Statistical Software*, *69*(1), 1–33. https://doi.org/10.18637/jss.v069.i01

López-Herrera, A., Saldarriaga, O. A., Arango, A. E., Fabio, N., Olivera, M., Bedoya, G., y Ossa, J. E. (2001). Ganado Blanco Orejinegro (BON): Una alternativa para la producción en Colombia. *Revista Colombiana de Ciencias Pecuarias*, *14*(2), 121–128. https://doi.org/10.17533/udea.rccp

Londoño-Gil, M., Rincón Flórez, J. C., Lopez-Herrera, A., y Gonzalez-Herrera, L. G. (2021). Genome-wide association study for growth traits in Blanco Orejinero (BON) cattle from Colombia. *Livestock Science*, *243*(104366), 104366. https://doi.org/10.1016/j.livsci.2020.104366

Lusk, J. L. (2007). Association of single nucleotide polymorphisms in the leptin gene with body weight and backfat growth curve parameters for beef cattle 1. *American Society of Animal Science*, *85*, 1865–1872. https://doi.org/10.2527/jas.2006-665

M-Rocha, J. F., Gallego, J. L., Vásquez, R. F., Pedraza, J. A., Echeverri, J., Cerón-Muñoz, M. F., y Martínez, R. (2012). Estimación de parámetros genéticos para edad al primer parto e intervalo entre partos en poblaciones bovinas de la raza Blanco Orejinegro (BON) en Colombia. *Revista Colombiana de Ciencias Pecuarias*, *25*, 220–228. https://doi.org/10.17533/udea.rccp

Martínez, R., Vásquez, R., y Gallego, J. L. (2012). Eficiencia productiva de la raza BON en el trópico colombiano. En *Corpoica* (Primera ed, Vol. 1). © Corporación Colombiana de Investigación Agropecuaria, Corpoica. 215 p.

Martins, G. A., Martins Filho, R., Lima, F. de A. M., y Lôbo, R. N. B. (2000). Influência de fatores genéticos e de meio sobre o crescimento de bovinos da raça Nelore no Estado do Maranhão. *Revista Brasileira de Zootecnia*, *29*(1), 103–107. https://doi.org/10.1590/S1516-35982000000100014

Mota, L. F. M., Lopes, F. B., Fernandes Júnior, G. A., Rosa, G. J. M., Magalhães, A. F. B., Carvalheiro, R., y Albuquerque, L. G. (2020). Genome-wide scan highlights the role of candidate genes on phenotypic plasticity for age at first calving in Nellore heifers. *Scientific Reports*, *10*(1), 6481. https://doi.org/10.1038/s41598-020-63516-4

R Core Team. (2020). *R: A Language and Environment for Statistical Computing* (4.0.0). R Foundation for Statistical Computing. https://www.r-project.org

Ramírez, E., Cerón-Muñoz, M., Herrera, A. C., Vergara, O. D., Arboleda, E. M., y Restrepo, L. F. (2009). Crecimiento de hembras cruzadas en el trópico colombiano. *Revista Colombiana de Ciencias Pecuarias*, *22*, 642–647. https://doi.org/10.17533/udea.rccp

Rincón, J., y Quintero, J. (2015). Comparación de modelos no lineales para describir el crecimiento en ganado Blanco Orejinegro (BON). *Revista CES Medicina Veterinaria y Zootecnia*, *10*(1), 31–37. https://doi.org/10.21615/cesmvz

Rogberg-Muñoz, A., Melucci, L., Prando, A., Villegas-Castagnasso, E. E., Ripoli, M. V., Peral-García, P., Baldo, A., Añon, M. C., & Giovambattista, G. (2011). Association of bovine chromosome 5 markers with birth and weaning weight in Hereford cattle raised under extensive conditions. *Livestock Science*, *135*(2–3), 124–130. https://doi.org/10.1016/j.livsci.2010.06.160

Rogberg-Mu**ñoz,** A., Cantet, R. J. C., Elena, M., Pedro, J., Prando, A., Nélida, A., Verónica, M., y Giovambattista, G. (2013). Longitudinal analysis of the effects of IGF1 - SnaBI genotypes on the growth curve of Angus bull calves. *Livestock Science*, *154*(1–3), 55–59. https://doi.org/10.1016/j.livsci.2013.03.016

Saleem, A. H. (2015). Role of Leptin in Growth, Reproduction and Milk Production in Farm Animals: A Review. *Advances in Animal and Veterinary Sciences*, *3*(5), 302–307. https://doi.org/10.14737/journal.aavs/2015/3.5.302.307

Verhulst, P. (1838). Notice sur la loi que la population pursuit dans son accroissement. *Correspondance Mathématique et Physique*, 10,113-121. http://www.neo-classical-physics.info/uploads/3/4/3/6/34363841/verhulst_-_law_of_population.pdf

Von Bertalanffy, L. (1938). A quantitative theory of organic growth (inquires on growth laws. *Human Biology*, *10*(2), 181–213. https://doi.org/10.2307/41447359