Investigation of genes associated with maternal weaning weight in South African Bonsmara beef cattle

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Abstract

Maternal weaning weight (WW_{MAT}), the dam's genetic and permanent environmental components that contribute to the weaning weight of her calf, is a trait of economic importance in extensive beef production systems. Positive genetic correlations between milk yield and WW_{MAT} have been reported. In this study, a genome wide association was performed to search for genes associated with WW_{MAT}. A total of twenty-three significant single nucleotide polymorphisms (SNPs) was identified with a further 103 suggestive SNPs. These SNPs were collapsed into 12 quantitative trait loci (QTL) across eight autosomes with an additional QTL residing on the X-chromosome. Ten different genes were co-located with the detected QTL. Genes identified were either essential in protein ubiquination pathways or were related to mammary morphology and ability to respond to infection by the presence of bacterial species.

Introduction

Milk production in beef cattle is an essential component of calf growth (Mulliniks *et al.*, 2020), especially in extensive systems due to seasonal fluctuations in natural veld quality and low forage availability (Cortés-Lacruz *et al.*, 2017, Mulliniks *et al.*, 2020). Milk yield is influenced by both the calf, through its demand for milk in conjunction with nursing frequency, along with the nutritional, genetic and health status of the cow. Other maternal effects include the maternal ability of the cow to protect the calf, the gestational environment and the transfer of antibodies through colostrum which contribute to calf growth up to weaning (Mulliniks *et al.*, 2020).

Positive genetic correlations between milk yield and maternal weaning weight (WW_{MAT}) have been well documented (Nesengani *et al.*, 2018) and thus warrant investigation into the underlying genetic mechanisms of these traits (Meyer *et al.*, 1994). The majority of single nucleotide polymorphism (SNP) analyses in cattle have focused on traits such as measured milk production, growth and carcass characteristics. Fewer studies have attempted to locate genomic regions associated with WW_{MAT}. Significant SNPs on multiple autosomes were linked to WW_{MAT} in Brahman cattle (Martínez *et al.*, 2017), while Hay and Roberts, (2019) identified a region on *Bos taurus* autosome (BTA) 24 that contributed significantly to the genetic variance of WW_{MAT}.

The South African Bonsmara, classified as a Sanga type, is a composite breed of 5/8 Afrikaner and 3/8 exotic (Milk Shorthorn, Hereford) established through a well-documented crossbreeding program. The breed is the most numerous in South Africa (SA) and is farmed

under extensive production systems. In this study, a genome wide association was performed to search for genes associated with WW_{MAT}.

Materials & Methods

Ethical approval for the use of external data were granted by the Research/Ethics Committee (EC-180000127), Faculty of Natural and Agricultural Sciences, University of Pretoria.

Genetic evaluations for WW_{MAT} in SA are generated from a univariate model that includes the fixed effects of calf sex, if the dam was primiparous or multiparous, the age of the calf and the dam when the calf was weighed and the contemporary group in which the calf was weaned. Random effects included are Sire x Herd x Year (SHY), the permanent environmental effect of the dam as well as the direct genetic effect of both the animal and the dam. A total of 1,242,158 weaning weight records are used in the genetic evaluation with an average weaning weight of 216.82 kg. Direct and maternal heritability estimates used are 0.27 and 0.17, respectively.

Estimated breeding values (EBVs) of 3,253 genotyped animals for WW_{MAT} were available, which consisted of 1,498 males and 1,755 females. The genotypes originated from three genotype panels, namely, 1,932 animals on the GeneSeek Genomic Profiler (GGP) 150K (140,113 SNPs), 589 animals on the GGP 80K (76,883 SNPs) and 732 animals on the Irish Cattle Breeding Federation (ICBF) International Beef and Dairy (IDB, 55,445 SNPs) platforms. All SNP locations were based on the ARS-UCD1.2, INSDC Assembly (GCA_002263795.2, Low et al., 2019). Only autosomal and X-chromosomal SNPs with a known position and a call rate of ≥0.90 were retained. Non pseudo-autosomal SNPs on the X-chromosome were assumed homozygous for all male genotypes. All genotypes were subsequently imputed in FImpute v.3 to 134,421 SNPs.

Effective record contributions (ERCs) for each genotyped animal were generated using the reversed reliability approximation method in APaX99 (Lidauer *et al*., 2017). The estimated breeding values for WW_{MAT} were subsequently deregressed using the Secant method in MiX99 (Strande, 1999) with the generated ERC used as a weighting factor. Only animals with an ERC of ≥0.5 were retained, which resulted in 1,454 animals for WW_{MAT} (median ERC = 7.618) being available for the association analysis.

The weighted (by ERCs) deregressed WW_{MAT} EBVs were regressed on each SNP individually using a linear mixed model in WOMBAT (Meyer and Tier, 2012). An intercept term and the allele count per SNP were both included as fixed effects while relationships among animals was accounted using a genomic relationship matrix. The t-test statistic for all SNPs was obtained and SNPs with a $P \leq 1 \times 10^{-7}$ were considered to be genome-wide significant, while SNPs with a $P \leq 5 \times 10^{-6}$ were deemed to be suggestively significant.

The start and end of each quantitative trait loci (QTL) was defined by SNPs 0.5Mb up and downstream that had an $r^2 > 0.5$ with the significant SNP. Overlapping QTL were consolidated into one QTL. Identified QTL were then explored using ENSEMBL in order to detect candidate genes residing within and Panther (Mi *et al.*, 2017) was used to list the biological and metabolic functions and/or processes of possible genes.

Results & Discussion

Twenty-three significant SNPs were identified with a further 103 suggestive SNPs being identified. Fourteen of the significant SNPs were all located on BTA 8, with the remaining SNPs being on BTA 2, 6, 6, 9, 10, 16, 22 and *Bos taurus* X-chromosome (BTX). Eleven

different genes were co-located with the detected QTL (Table 1). The amalgamated QTL on BTA 8 contains nine significant SNPs that are in high linkage disequilibrium, with most of these being intron SNPs located in the *PCSK5* gene coding region.

DEGS1 was identified by Xu et al., (2018) to show differential gene expression in mammary tissue of dairy cattle after infection with *Escherichia coli* or *Streptococcus uberis*. *PCSK5* was reported by Hoac et al., (2018) to play a role in embryonic development, hormone regulation as well as bone mineralisation. *PCSK5* was associated with teat scores in Canadian Angus Cows (Devani *et al.*, 2021). These genes may play a role in the morphology of the udder as well as affect milk yield through mediating resistance to infection which would lead to mastitis.

Table 1. Detected quantitative trait loci with the most significant single nucleotide polymorphism and co-located genes.

BTA	Start	End	Distance (kbp)	SNPs in QTL	Genes
2	718140	882990	164.85	5	*HERC2*
6	374487838	37516229	28.39	3	*LCORL*
7	60414842	60452720	37.88	2	*SH3TC2*
8	51745358	51899568	154.21	5	
8	52180527	52333334	152.81	9	*PCSK5*
8	78145059	78145059	0	1	*NTRK2*
9	28257531	28257531	0	1	
9	56836009	56836009	0	1	*EPHA7*
10	2575344	2575344	0	1	
16	27298728	27407724	108.99		*FBXO28, DEGS1*
22	22033915	22033915		1	
X	59554341	59554341	0	1	DCX

Some of the detected genes (i.e., *DCX*, *EPHA7*, *FBXO28* and *SH3TC2)* have not been previously reported to be associated with any traits in beef cattle breeds. The number of genes linked to the posttranslational modification of proteins through ubiquination (i.e., *EPHA7*, *FBXO28* and *HERC2)* is interesting. This process essentially mediates the quantity and quality of various proteins that contribute to cellular homeostasis and influence life activities.

The *LCORL* gene has been identified as a candidate QTL for birth weight, growth and length in beef cattle breeds (McClure *et al.*, 2010; Lindholm-Perry *et al.*, 2011). Lindholm-Perry et al., (2013) reported 14 SNPs in the *LCORL* gene region to be associated with muscle and adipose tissue related *LCORL* transcript in crossbred beef cattle. In cows and heifers, an up-regulated expression of *LCORL* in adipose tissue is significantly correlated with average daily feed intake.

HERC2 is involved in protein modification through ubiquination and was only previously reported to be associated with back-fat thickness in the Hanwoo beef cattle breed (Naserkheil et al., 2020). *NTRK2* is a transmembrane signal receptor associated protein. A study on longevity indicated that *NTRK2* plays an important role in the development of reproductive tissues in both female and male beef cattle (Mészáros *et al.*, 2014). The occurrence of multiple adipose and reproductive tissue related genes indicates the complexity and polygenic effect of WW_{MAT}.

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