Genome-wide association study identifies variants associated with hair length in Brangus cattle


*Animal Sciences, University of Florida, 2250 Shealy Dr, Gainesville, FL 32608, USA. †Faculty of Animal Science, Bursa Uludag University, 16059 Nilufer, Bursa, Turkey.

Summary

Thermal stress limits beef cattle production owing to decreased animal performance including lower pregnancy rates and a reduction in feed intake and growth (Amundson et al. 2006; Renaudeau et al. 2012). In the USA alone this results in an economic loss of $369 million annually (St-Pierre et al. 2003). However, this is a global issue with over 65% of the world’s cattle (beef and dairy) residing in (sub)tropical areas known for hot, humid conditions (Burrow 2012). Hair coat is a key thermoregulatory adaptation. Cattle with a shorter-haired coat are able to lose heat more effectively through conductive, convective and radiative cooling at the hair–skin interface (Hansen 2004). Hair length has previously been demonstrated to have a major impact on body temperature (Hamblen et al. 2018) and has a high heritability (0.67 and 0.42 for undercoat and topcoat respectively) (Sarlo Davila et al. 2019), indicating that this trait is largely influenced by genetics. The objective of this study was to identify genetic variants associated with the length of the undercoat and topcoat of cattle.

The University of Florida Institutional Animal Care and Use Committee approved the research protocol used in this study (approval no. 201203578). This study utilized 1456 commercial Brangus heifers from the Seminole Tribe of Florida Inc. accumulated over two summers in 2016 and 2017. Hair samples were collected from the shoulder, 4 inches down from the spine and half-way along the horizontal axis of each animal. Hair samples were collected from eight groups of 200 animals: four groups over four consecutive weeks in 2016 (August 15–September 12) and four groups over four consecutive weeks in 2017 (July 31–August 28). Heifers within a year were from the same cohort and approximately the same age (about 2 years old). Hair samples were spread on white paper and photographed alongside a ruler to serve as a scale by which pixels could be converted in millimeters. IMAGEJ software (Schindelin et al. 2012) was used to measure hair length. The lengths of the undercoat (shorter coat closer to the body of the animal) and topcoat (longer coat that covers the undercoat) were evaluated for each individual by averaging the lengths of five short hairs and five long hairs respectively. DNA was extracted from blood samples and genotyped with the Bovine GGP F250 array (Illumina Inc.). Chromosomal assignments and positions of SNP were based on the ARS-UCD 1.2 B. taurus sequence assembly. Genotypes were filtered in PLINK (Purcell et al. 2007) to remove SNP with call rates <90% and MAFs <0.05. After quality control, 109 538 SNP were available for association analyses. Both hair length phenotypes were pre-adjusted for the fixed effect of year.
collection group using linear model procedures in R. The residuals from these models were used in GWASs using the univariate procedures of GEMMA (Zhou & Stephens 2012) that fitted a single, standardized, genomic relationship matrix to account for the genetic covariance among animals. The genomic relationship matrix was constructed in GEMMA using the 109,538 SNPs that remained after quality control. To correct for multiple tests, the Benjamini–Hochberg false discovery rate was constrained to 0.2. This false discovery threshold was utilized to reduce type II error.

Manhattan plots of the GWAS results for both hair phenotypes are shown in Fig. 1. The estimated genomic heritability for undercoat length in this population was 0.30 with a standard error of 0.05. We identified eight SNPs significantly associated with undercoat length within a 300 kb region on BTA 12. This region contains the gene PCCA. Seven of the significant SNPs were located within PCCA and one of the significant SNPs was an upstream variant (rs133787763). Of the seven intragenic SNPs there were two missense mutations (rs133791585, rs210751638), four intron variants (rs383191895, rs110703144, rs134127983, rs210217784) and one splice region variant (rs41679981). Propionyl-CoA carboxylase subunit alpha belongs to the biotin transport and metabolism pathway (Dakshinamurti 1988). PCCA can be measured in hair roots and low PCCA levels can be used to diagnose biotin deficiencies in human medicine (Wolf & Raetz 1983). Biotin deficiencies have been widely reported in multiple species to affect hair length, growth and texture and even to result in hair loss (Rauch 1952; Bryant et al. 1985; Dakshinamurti 1988; Campeau et al. 2001; Boccaletti et al. 2007). Much of the literature concerning the relationship between biotin and hair addresses nutritional deficiencies and strategies for supplementing biotin in the diet (Rauch 1952; Bryant et al. 1985). However, heritable genetic disorders in the biotin pathway that result in changes to the hair have been reported, such as familiar uncombable hair syndrome in humans (Boccaletti et al. 2007), where those affected have short, coarse hair. Whereas the association of PCCA with hair length in cattle is novel, it is biologically relevant and a candidate for future selection programs. Two SNPs (rs444824868, rs445292907) within a 46 kb region on BTA 10 were also significantly associated with undercoat length. This region contains the gene OR4F3, an olfactory receptor gene. The estimated genomic heritability for topcoat length was 0.34 with a standard error of 0.05. We identified four SNPs significantly associated with topcoat length within a 110 kb region on BTA 20. This region contains the genes PRLR, AGXT2 and DNAJC21. Two of the significant SNPs (rs377826688, rs383738120) were intergenic variants. Of the remaining SNPs, one was a splice region variant (rs134538752) in DNAJC21 and the other was a missense mutation (rs135164815) in PRLR. Each of the four significant SNPs was fitted one at a time as a fixed effect to determine if the same association signal was captured by these SNPs. The majority of the association signals was captured by the missense SNP in PRLR, rs135164815,
which explained 4.0% of the variation in topcoat length. Previously identified mutations in PRLR have been shown to have a major effect on hair length in cattle (Littlejohn et al. 2014; Porto-Neto et al. 2018). Mice with PRLR KO had significantly longer and coarser hair than wt mice, indicating that prolactin inhibits hair growth (Craven et al. 2001). The SLICK mutation in PRLR, originally identified in Senepol cattle, is a frameshift mutation that results in a truncated protein and a dramatically shorter hair coat (Olson et al. 2003; Littlejohn et al. 2014). Subsequently, two other mutations in PRLR have been associated with a slick hair coat in Limonero and Carora cattle that did not carry the previously identified Senepol mutation (Porto-Neto et al. 2018). All three of these previously identified SLICK mutations are truncation mutations in exons 10 or 11 of PRLR. In contrast, the PRLR SNP identified in this study is a missense mutation (A → G) in exon 2. This missense mutation identified in this study has not been previously associated with the slick phenotype but has been found to be associated with milk production in heat-stressed Holstein cattle (Hernández-Hernández-Cordero et al. 2017). The prolactin hormone has been demonstrated to regulate both milk production and hair length (Horseman & Gregerson 2013; Littlejohn et al. 2014). This association is of great interest as PRLR has not previously been associated with hair length in Brangus cattle. These results indicate that the prolactin pathway may regulate hair length across multiple breeds of cattle.

These genetic variants identified for both undercoat and topcoat are of great biological relevance. The variants have the potential to be used for selection in order to breed for animals with shorter hair, leading to greater thermostolerance and potentially increasing production in hot, humid climates. The current study is limited to the potential functional variants available on the GGP F250 array and should be followed up with WGS data to refine putative functional mutations.

Acknowledgements

This research was supported by USDA-NIFA grant no. 2017-67007-26143, The International Brangus Breeders Association, Seminole Tribe of Florida and UF ANS Hatch Project.

Data availability statement

Genotype data is available through OSF and can be accessed at https://osf.io/u3r6m/?view_only=1a1b43cb1b8473594d89ee8977eb8c

References


