Zayas, G., Santos Rojas, C., Rodriguez, E., Matescu, R. (2026) Fine-mapping genomic regions contributing to thermotolerance in beef cattle, *Proceedings 13th World Congress on Genetics Applied to Livestock Production* 23499: https://doi.org/10.31274/wcgalp.23499
©2026 Zayas, et al. CC BY-NC-ND

Fine-mapping genomic regions contributing to thermotolerance in beef cattle

G.A. Zayas[1*], C. Santos Rojas[2], E.E. Rodriguez[2], and R.G. Matescu[2]

[1]*University of Wisconsin, Madison, WI, USA* [2]*University of Florida, Gainesville, FL, USA*
[*]*Corresponding author: zayas@wisc.edu*

Introduction

Approximately 65% of the world's cattle production occurs in tropical and subtropical environments, where chronic heat stress limits productivity, fertility, and animal welfare as stated by Burrow (2015). Heat stress disrupts metabolic homeostasis and impairs physiological functions, making thermotolerance a critical trait for sustainable beef production in these regions (Burrow, 2015). Thermotolerance refers to an animal's ability to maintain core body temperature and productive performance under thermal challenge. Previous studies have demonstrated low to moderate heritability for body temperature regulation (0.16–0.21), hair characteristics (0.27–0.41), and heat dissipation traits (0.27–0.46), indicating substantial potential for genetic improvement (Sarlo Davila *et al*., 2019; Hernandez *et al*., 2024). However, the underlying genomic architecture of these traits remains incompletely resolved, particularly with respect to causal variants. The objective of this study was to identify and fine-map genomic regions contributing to thermotolerance and heat dissipation in Angus–Brahman crossbred cattle using genome-wide association analyses followed by whole-genome sequencing of phenotypic extremes for fine-mapping and functional annotation.

Materials & Methods

The research protocol for this study was approved by the University of Florida Institutional Animal Care and Use Committee (IACUC #202200000019). The population in this study included a total of 3,962 heifers originating from Brangus commercial herds in Florida and Angus–Brahman crosses from the University of Florida's multibreed Angus–Brahman herd. Phenotypes were collected across multiple years during the summers of 2016-2023. Phenotypes were grouped into body temperature regulation traits (minimum, maximum, and difference in vaginal temperature, thermal stress slope, thermal stress burden), hair characteristics (coat score, long hair length, short hair length), epidermal morphology, and sweat gland morphology. Detailed phenotyping protocols and in-depth description of phenotypes can be found in previous studies (Sarlo Davila 2019; Nunez 2023; Hernandez 2024; Zayas 2025).

All animals were genotyped using the Bovine GGP F250 array (221,115 SNPs), which includes variants enriched for predicted functional effects. Genome-wide association analyses were conducted using a mixed linear model implemented in GCTA with a leave-one-chromosome-out approach to account for population structure and relatedness. Genome-wide significance was defined using a Bonferroni-corrected threshold ($\alpha = 0.1$), applied to prioritize loci for downstream fine-mapping rather than strict discovery control.

Whole-genome sequencing (WGS) was performed on 92 animals selected from phenotypic extremes for key traits, including thermal stress slope, hair length, and sweat gland morphology. Individuals were selected from the upper and lower quartiles of adjusted phenotypic distributions and included purebred Angus (n = 10), purebred Brahman (n = 10), and commercial Brangus cattle (n = 72). Sequence reads were aligned to the bovine reference genome, and variants were called using standard best-practice pipelines.

Fine-mapping analyses were conducted within significant GWAS regions using a forward-selection approach implemented with custom R scripts and the gaston R package. Candidate variants were prioritized based on association strength and local linkage disequilibrium structure. Functional annotation was performed using snpEff and publicly available genome browsers. Expression quantitative trait loci were evaluated using the cattle GTEx resource and an independent whole-blood RNA-seq–based eQTL dataset derived from a subset of this population.

Results & Discussion

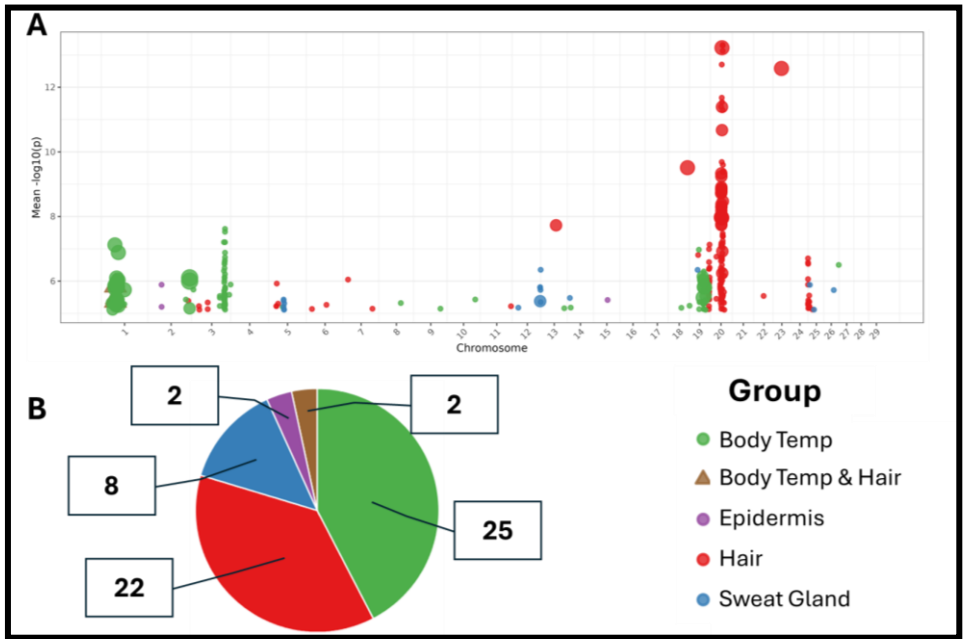

Figure 1. Summary of GWAS results for thermotolerance and heat dissipation traits.

Genome-wide association analyses identified 319 significant SNP–trait associations across 19 thermotolerance and heat dissipation traits, which clustered into 59 distinct QTL regions (Fig. 1). Traits were grouped into body temperature regulation (BT), hair characteristics (Hair), epidermal morphology (Epi), and sweat gland morphology (SG). In Fig. 1, each point represents a significant SNP–trait association, with color indicating trait group and point size reflecting the number of traits associated with each SNP. A locus on BTA1 showed pleiotropic effects across both BT and Hair traits and is highlighted separately.

Overall, significant loci were distributed across the genome but exhibited clear trait-group–specific patterns, indicating partially distinct genetic architectures underlying different physiological mechanisms of heat adaptation. BT traits were associated with multiple loci on BTA1, BTA2, BTA3, and BTA19, consistent with the polygenic control of thermal homeostasis. In contrast, Hair traits were dominated by a small number of major-effect QTLs, primarily on BTA20, BTA23, and BTA24. Epi traits exhibited the fewest significant loci, likely reflecting their lower heritability estimates reported previously by Nunez (2023).

Fine-mapping analyses within significant QTL regions prioritized candidate variants with large effect sizes and consistent association signals across related traits (Table 1). Several loci showed evidence of putative functional variation underlying major GWAS signals for thermotolerance and heat dissipation traits. Hair length traits were primarily associated with a major QTL on BTA20. A 9-bp insertion–deletion variant at 35,820,858 bp showed strong associations with both long and short hair length, with large standardized effects (1.33 SD and 1.21 SD, respectively). This variant is located downstream of *RICTOR*, a core component of the mTORC2 complex involved in hair follicle stem cell regulation, suggesting a plausible role

in coat growth and density. A second variant within the same QTL, a 7-bp deletion at 38,593,307 bp, was associated with long hair length (1.51 SD) and lies upstream of *PRLR*, a gene previously implicated in hair growth and thermoregulatory adaptation in cattle. Notably, while classical *PRLR* SLICK mutations have not been reported in Brahman cattle, this signal has been previously identified as being driven by Brahman ancestry within the crossbred population, suggesting the presence of novel variation influencing hair length in indicine-derived germplasm (Zayas *et al*., 2025).

Table 1. Putative candidate mutations for several thermotolerance and heat dissipation related traits.

Trait[1]	Chr[2]	Pos[2]	RSID[2]	Ref[2]	Alt[2]	p-value	SD[3]	Variant Type	Genes
LHL	20	35820858	rs534043980 7	ACACACACC	*	8.7E-12	1.29	downstream	*RICTOR, OSMR*
LHL	20	38593307	rs534045654 4	CTATATA	C	1.3E-06	1.51	upstream	*SPEF2, PRLR*
SGA	19	24622460	rs538171146 1	AT	A	1.0E-06	1.28	intron	*ZZEF1*
SHL	20	35820858	rs534043980 7	ACACACACC	*	6.4E-09	1.21	downstream	*RICTOR ,OSMR*
TSB	19	47351457	rs538224059 1	C	CAA	2.4E-07	1.62	intron	*ENSBTAG000 00070332*
TSS	1	59369285	rs437400062	G	C	7.2E-08	1.02	intron	*ZBTB20*
VT_{dif}	1	59369285	rs437400062	G	C	9.2E-08	1.01	intron	*ZBTB20*
VT_{max}	19	31214637	rs210062985	A	G	1.4E-08	1.49	intron	*ARHGAP44*
VT_{min}	19	44967275	rs381632699	C	A	3.7E-06	1.06	upstream	*MAP3K14*

[1] Trait of interest: Long hair length (LHL), Short hair length (SHL), Sweat gland area (SGA), Thermal stress slope (TSS), thermal stress burden (TSB), maximum vaginal temperature (VT_{max}), minimum vaginal temperature (VT_{min}), difference in vaginal temperature (VT_{dif}).

[2] Chr is chromosome, Pos is base pair position, RSID Is the Reference SNP ID, Ref is the reference allele, Alt is the alternative allele

[5] SD is the allele substitution effect divided by the standard deviation of the trait.

Several QTLs associated with body temperature regulation traits were prioritized for fine-mapping (Fig. 2). On BTA1 (Fig. 2A), a QTL associated with thermal stress slope and vaginal temperature difference was led by rs437400062, an intronic variant in *ZBTB20* with moderate standardized effects (approximately 1.02 SD). *ZBTB20* has been implicated in circadian regulation and NF-κB stress-response pathways, suggesting a potential role in coordinating thermal adaptation (Qu *et al*., 2016; Luo *et al*., 2024). On BTA19 , a QTL associated with minimum vaginal temperature (Fig. 2B) was led by rs381632699, located upstream of *MAP3K14*, a kinase involved in NF-κB signaling and cellular stress responses as described by Huang *et al.* (2022). A separate QTL on BTA19 associated with maximum vaginal temperature (Fig. 2C) was led by an intronic variant in *ARHGAP44* with a large effect (1.49 SD). This

variant was identified as a cis-eQTL for *ARHGAP44* and neighboring genes involved in mitochondrial function and cellular structure, implicating energy metabolism and epithelial integrity in tolerance to acute thermal load as described by Southwell *et al.* (2023). Finally, a QTL for thermal stress burden on BTA19 (Fig. 2D) mapped to an intronic variant within *ENSBTAG00000070332*, which was identified as a cis-eQTL for *TANC2*, a gene linked to mTOR-related stress signaling as described by Chou *et al.* (2012).

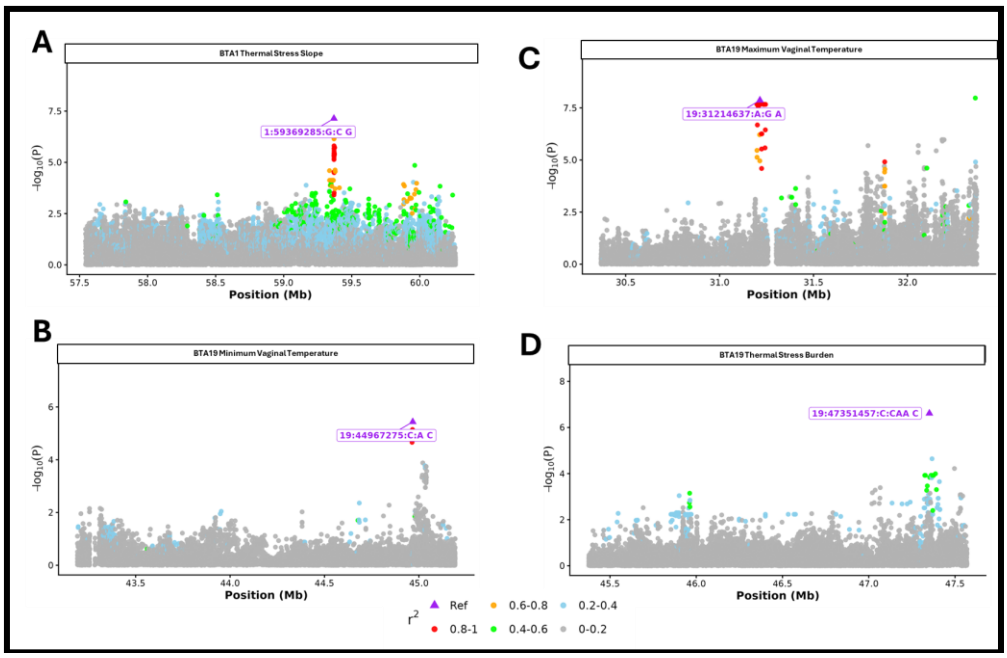

Figure 2. Fine-mapped QTLs for A) TSS on BTA1, B) VT_{min} on BTA19, C) VT_{max} on BTA19 and D) TSB on BTA19.

Conclusions

This study fine-mapped genomic regions and identified putative functional variants associated with thermotolerance and heat dissipation in Angus–Brahman cattle, providing high-resolution insight into the genetic architecture of heat resilience. This study highlighted biologically meaningful loci involved in hair growth, sweat gland morphology, cellular stress response, and energy metabolism. These fine-mapped variants represent candidates for incorporation as biologically informed markers within genomic selection frameworks, prioritizing functionally relevant loci may enhance the prediction of thermotolerance.

References

Burrow H. M. (2015) Genetic Aspects of Cattle Adaptation in the Tropics. In: Garrick D.J., and Ruvinsky A.,The Genetics of Cattle. CABI, Wallingford.

Chou S.-D., Prince T., Gong J., *et al*. (2012) PLoS One. 7:e39679. doi:10.1371/journal.pone.0039679.

Hernandez A. S., Zayas G. A., Rodriguez E. E., *et al*. (2024) Journal of Animal Science and Biotechnology. 15:66. doi:10.1186/s40104-024-01025-4.

Huang Q., Liu Y., Qiu M., *et al*. (2022) Front. Oncol. 12. doi:10.3389/fonc.2022.990160.

Luo Q.Q., Cheng L., Wang B., *et al*. (2024) Neurogastroenterology & Motility. 36:e14718. doi:10.1111/nmo.14718.

Nunez Andrade A. N (2023) Epidermis Properties and Thermotolerance in Beef Cattle. University of Florida, Gainesville, Fla.

Qu Z., Zhang H., Huang M., *et al*. (2016) eLife. 5:e17171. doi:10.7554/eLife.17171.

Sarlo Davila K. M., Hamblen H., Hansen P. J., *et al*. (2019) Journal of Animal Science. 97:3246–3252. doi:10.1093/jas/skz188.

Southwell N., Primiano G., Nadkarni V., *et al*. (2023) EMBO Mol Med. 15:EMMM202216951. doi:10.15252/emmm.202216951.

Zayas G. A., Santos Rojas C., Rodriguez E. E., *et al*. (2025) Front. Genet. 16. doi:10.3389/fgene.2025.1576966.