UNIVERSIDADE FEDERAL DE LAVRAS

KARINE DAENQUELE SILVA PINTO

SINGLE-STEP GENOME-WIDE ASSOCIATION STUDY FOR CARCASS QUALITY TRAITS IN ANGUS BEEF CATTLE

LAVRAS-MG
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Dissertação apresentada à Universidade Federal de Lavras, como parte das exigências do Programa de Pós-Graduação em Zootecnia, para obtenção do título de Mestre

Prof.(a) Dr.(a) Sarah Laguna Conceição Meirelles
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Ficha catalográfica elaborada pelo Sistema de Geração de Ficha Catalográfica da Biblioteca Universitária da UFLA, com dados informados pelo(a) próprio(a) autor(a).

Pinto, Karine Daenquele Silva.
Single-step genome-wide association study for carcass quality traits in Angus beef cattle / Karine Daenquele Silva Pinto. - 2024.
51 p.

Orientador(a): Sarah Laguna Conceição Meireles.

Dissertação (mestrado acadêmico) - Universidade Federal de Lavras, 2024.
Bibliografia.

1. Backfat thickness. 2. Marbling. 3. Ribeye area. I. Meirelles, Sarah Laguna Conceição. II. Título.

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SINGLE-STEP GENOME-WIDE ASSOCIATION STUDY FOR CARCASS QUALITY TRAITS IN ANGUS BEEF CATTLE

ASSOCIAÇÃO GENÔMICA AMPLA APLICADA À CARACTERISTICAS DE QUALIDADE DA CARCAÇA EM BOVINOS DA RAÇA ANGUS

Dissertação apresentada à Universidade Federal de Lavras, como parte das exigências do Programa de Pós-Graduação em Zootecnia, para obtenção do título de Mestre

APROVADA EM 27 DE MARÇO DE 2024.

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LAVRAS–MG
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À minha mãe Ediane e meu pai Geraldo pelo amor, compreensão e apoio incondicional. Obrigado por serem minha fonte constante de inspiração e motivação. A eles dedico todo meu amor.

AGRADECIMENTOS

Agradeço primeiramente à Deus, por me permitir chegar até aqui. Pela saúde e por me guiar e colocar pessoas especiais no meu caminho.

Aos meus pais, por todo apoio e por acreditarem sempre que sou capaz. Aos meus irmãos Karla e Marcos por dividirem a vida comigo, e ao meu sobrinho Enzo por tornar meus dias melhores. Aos amigos e família, que muito torceram por mim.

Agradeço também a minha orientadora, professora Sarah, por todos os ensinamentos e apoio. Também, ao GMAB, por dividirem tantas experiencias durante esse tempo do mestrado.

À Universidade Federal de Lavras por me receber tão bem e por se fazer também um lar.

À Coordenação de Aperfeiçoamento de Pessoal do Nivel superior (CAPES), pelo apoio financeiro.

E à Fazenda Casa Branca Agropastoril, por ceder os dados para realização desta pesquisa.

RESUMO

A identificação de regiões genômicas e genes que influenciam as características de qualidade da carcaça é importante para melhorar a seleção de bovinos de corte. Dentro deste contexto, o objetivo deste estudo foi identificar regiões genômicas e possíveis genes candidatos associados à área de olho de lombo (AOL), marmoreio (MARM), espessura de gordura subcutânea (EGS) e espessura de gordura na garupa (EGPS) em bovinos da raça Angus. O arquivo de pedigree continha dados de 2.446 animais sendo que um total de 1.391 animais foram genotipados com o GGP Bovine 150K (Illumina). O estudo de associação genômica ampla (ssGWAS) foi realizado para estimar os efeitos e variações dos SNPs contabilizados pelas janelas subjacentes de 10-SNPs. Foram identificadas 23, 23, 22 e 31 janelas genômicas que explicaram mais de 0,5% da variância genética aditiva para AOL, MARM, EGS e EGP8, respectivamente, o que confirma a natureza poligênica das características. Um total de 66, 56, 36 e 105 genes codificadores de proteínas foram encontrados em janelas associadas a AOL, MARM, EGS e EGP8, respectivamente. Vários genes codificadores de proteínas foram identificados nessas regiões genômicas, como *SIRT6, CREB3L3, HNRNPH1, RUFY, EEF2, NMRK2, FDS1, CTNNA2, MAMSTR, PCCB, GALNT13, CTNNA3, EPHB2, PLA2G4E, APOD, RPL9, AGAP1, MFSD2A, FAM13A, DDHD1, CAST, CISD1, PLA2G1B, DROSHA, CDH6, FAM83A, SPHK2* e *NEIL3*, os quais foram destacados de acordo com suas funções. A análise de enriquecimento funcional foi realizada com a ferramenta DAVID também revelou várias vias metabólicas KEGG significativas ($p<0,05$) e termos Ontologia Gênica, como a ligação específica à sequência da região reguladora da transcrição da RNA polimerase II (GO:0001228), processo catabólico de glicerofosfolipídeo (GO:0046475), processo catabólico de fosfolipídio (GO:0009395) e processo catabólico lipídico (GO:0016042). Estes resultados contribuem para melhorar o conhecimento da arquitetura genética das características de qualidade de carcaça em bovinos de corte Angus e podem contribuir para avaliações genéticas.

Palavras-chave: Área de olho de lombo; *Bos taurus taurus*; Espessura de gordura na garupa; Espessura de gordura subcutânea; GWAS; marmoreiro.

ABSTRACT

The identification of genomic regions and genes that influence carcass quality traits is important for improving beef cattle selection. Within this context, the objective of this study was to identify genomic regions and putative candidate genes associated with the ribeye area (REA), marbling (MARB), backfat thickness (BFT) and rump fat thickness (RFT) in Angus beef cattle. The pedigree file contained data for 2,446 animals and a total of 1,391 animals were genotyped with the GGP Bovine 150K (Illumina). The single-step approach for genome-wide association study (ssGWAS) was performed to estimate the SNP effects and variances accounted by 10-SNP sliding windows. Confirming the polygenic nature of the studied traits, 23, 23, 22, and 31 genomic windows that explained more than 0.5% of the additive genetic variance were identified for REA, MARB, BFT and RFT, respectively. A total of 66, 56, 36, and 105 protein-coding genes were found in windows associated with REA, MARB, BFT and RFT, respectively. Several protein-coding genes were identified within those genomic regions, such as *SIRT6, CREB3L3, HNRNPH1, RUFY, EEF2, NMRK2, FDS1, CTNNA2, MAMSTR, PCCB, GALNT13, CTNNA3, EPHB2, PLA2G4E, APOD, RPL9, AGAP1, MFSD2A, FAM13A, DDHD1, CAST, CISD1, PLA2G1B, DROSHA, CDH6, FAM83A, SPHK2*, and *NEIL3* gene, according to its function. Functional enrichment analysis by DAVID tool also revealed several significant ($p < 0.05$) KEGG pathways and Gene Ontology terms such as glycerophospholipid catabolic process (GO:0046475), phospholipid catabolic process (GO:0009395) and lipid catabolic process (GO:0016042). These results contribute to improving the knowledge of the genetic architecture of carcass quality traits in Angus beef cattle and may contribute to genetic evaluations.

Keywords: Backfat thickness; *Bos taurus taurus*; GWAS; Marbling; Ribeye area; Rump fat thickness.

IDICADORES DE IMPACTO

O estudo de associação genômica ampla (GWAS), de maneira geral, tem como objetivo identificar marcadores moleculares, regiões genômicas e consequentemente genes associados a características de interesse econômico. Além de disso, auxilia no entendimento da arquitetura genética das características e como são expressos os fenótipos. O GWAS para características de qualidade da carcaça em bovinos Angus promove impactos importantes para o desenvolvimento social, tecnológico, econômico e cultural. Pela perspectiva social, a utilização do GWAS pode auxiliar no desenvolvimento da pecuária ao possibilitar a seleção de animais geneticamente superiores de forma mais precisa e eficiente. Isso resulta em animais com características desejáveis, como melhor qualidade de carne e maior rendimento de carcaça. Para os produtores, isso possibilita um aumento na produtividade e, consequentemente, na lucratividade. Para os consumidores finais, pode permitir o acesso a carne de alta qualidade, que poderá estar cada vez mais disponivel. Além disso, animais superiores geneticamente podem favorecer sistemas de produções mais sustentáveis, uma vez que, animais mais eficientes reduz o impacto ambiental da produção, que tem sido grande preocupação global.Para a tecnologia, a genômica é uma área em grande desenvolvimento, e a sua utilização na pecuária possibilita avanços significativos na produção de carne, sendo que o Brasil possui grandes possibilidades de avanço, garantindo sua competitividade mundial. Sobre o impacto tecnológico, as tecnologias de sequenciamento de DNA e os métodos de análise de dados genômicos proporciona a identificação de marcadores genéticos associados a características da qualidade da carcaça em Angus, que poderão ser utilizados em programas de melhoramento genético nas avaliações genéticas e no entendimento de como as características estudadas são expressas pelos animais e, além de aperfeiçoar a seleção dos animais, a utilização do GWAS promove o desenvolvimento de biotecnologias e bioinformáticas na pecúaria. Economicamente, a seleção de bovinos utilizando em marcadores moleculares pode auxiliar na eficiência da produção, pois animais que crescem mais rapidamente e produzem mais carne e de melhor qualidade podem reduzir custos e aumentar a rentabilidade dos pecuaristas. Pois são bonificados ao entregarem carcaças de melhor qualidade aos frigoríficos. Além disso, a capacidade de selecionar animais antes mesmo do nascimento para características de interesse econômico pode reduzir o intervalo de geração e aumentar o ganho genético dos animais. Para o mercado, isso significa uma cadeia produtiva mais eficiente e produtos de melhor qualidade, beneficiando tanto os produtores quanto os consumidores finais. De maneira geral, culturalmente, o estudo pode permitir a maior disponibilidade de produtos de melhor qualidade em supermercados e açougues, provocando mudanças na percepção sobre a pecuária e melhorando o interesse por parte dos consumidores.

IMPACT INDICATORS

The single-step genome-wide association study (GWAS), in general, aims to identify molecular markers, genomic regions and consequently genes associated with characteristics of economic interest. Furthermore, it helps to understand the genetic architecture of characteristics and how phenotypes are expressed. GWAS for carcass quality traits in Angus cattle promotes important impacts on social, technological, economic and cultural development. From a social perspective, the use of GWAS can help in the development of livestock farming by enabling the selection of genetically superior animals in a more precise and efficient way. This results in animals with desirable characteristics, such as better meat quality and higher carcass yield. For producers, this enables an increase in productivity and, consequently, profitability. For end consumers, it can allow access to high quality meat, which may be increasingly available. Furthermore, genetically superior animals can favor more sustainable production systems, since more efficient animals reduce the environmental impact of production, which has been a major global concern. For technology, genomics is an area undergoing great development, and its use in livestock farming allows significant advances in meat production, with Brazil having great possibilities for advancement, guaranteeing its global competitiveness. Regarding technological impact, DNA sequencing technologies and genomic data analysis methods provide the identification of genetic markers associated with carcass quality characteristics in Angus, which can be used in genetic improvement programs in genetic evaluations and understanding of how the studied characteristics are expressed by animals and, in addition to improving animal selection, the use of GWAS promotes the development of biotechnology and bioinformatics in livestock farming. Economically, the selection of cattle using molecular markers can help with production efficiency, as animals that grow faster and produce more and better-quality meat can reduce costs and increase the profitability of livestock farmers. Because they receive bonuses when they deliver better quality carcasses to slaughterhouses. Furthermore, the ability to select animals even before birth for traits of economic interest can reduce the generation interval and increase the animals' genetic gain. Forthe market, this means a more efficient production chain and better-quality products, benefiting both producers and end consumers. In general, culturally, the study can allow for greater availability of better-quality products in supermarkets and butchers, causing changes in the perception of livestock farming and improving consumer interest.

SUMÁRIO

1. INTRODUÇÃO

O cenário mundial mostra destaque ao Brasil quanto a bovinocultura de corte, que apresenta sucessivos recordes. O país possui o segundo maior rebanho comercial do mundo com aproximadamente 203 milhões de cabeças, se tornando o maior exportador de carne bovina (ABIEC, 2023). Entretanto, para continuar a garantir sua competitividade, é necessário considerar também a qualidade do produto gerado e não somente a quantidade. Além do bem-estar animal, o mercado consumidor tem exigido condições relacionadas à qualidade de carcaça (LIU et al., 2022).

Para a avaliação da qualidade da carcaça bovina, são utilizadas algumas características que apresentam bons indicativos de qualidade como: área de olho de lombo (REA), marmoreio ou gordura intramuscular (MARB), espessura de gordura subcutânea (BFT) e espessura de gordura na garupa (RFT). Essas características são expressas de forma tardia no animal, e por isso, a busca por estudos relacionados com a associação genômica ampla (GWAS) possibilita a identificação de variantes genômicas associadas ao fenótipo e além disso, o entendimento sobre a arquitetura genética da característica (GRIGOLETTO et al., 2019).

Raças zebuínas (*Bos taurus indicus*) são mais utilizadas no rebanho nacional total, principalmente devido a sua rusticidade e adaptação ao clima tropical e subtropical, entretanto, as raças taurinas (*Bos taurus taurus*) possuem alta fertilidade, precocidade sexual e melhor qualidade de carcaça e carne (MAIA FILHO et al., 2015). A raça Angus, nos últimos anos, está entre as principais raças europeias utilizadas em cruzamentos no Brasil, uma vez que algumas características contidas na raça garantem excelentes resultados econômicos na bovinocultura de corte de forma geral. Dentre todas as vantagens das raças taurinas, a raça Angus é capaz de oferecer cortes com acabamento padronizado e alto índice de marmoreio (RAMOS et al., 2022).

Apesar dos programas de melhoramento genético já incluírem características de carcaça nos métodos de avaliação genética, é importante entender quais marcadores moleculares estão associados a estas características em animais puros da raça Angus criados no Brasil. Por esta razão, estudos moleculares se fazem necessários, com objetivo de aumentar a acurácia de predição e intensidade de seleção (SANTANA et al., 2015), além de subsidiar estudos de validação das associações genômicas, e participar da seleção genômica, auxiliando nas tomadas de decisão dos programas de melhoramento genético da raça.

2. REVISÃO DE LITERATURA

2.1 PRODUÇÃO DE CARNE BOVINA

O Brasil está em uma posição de liderança quando se trata de produção de carne bovina, sendo que desde 2017 o país atinge recordes de produção, sendo o segundo maior país produtor e o primeiro em exportação de carne bovina, chegando em 203 milhões de cabeças em 2023, o que gerou o faturamento de mais de R$ 135,79 bilhões de reais (MAPA, 2024).

Este destaque está relacionado aos estudos e investimentos em tecnologia voltados para a pecuária, onde a produção de carne bovina brasileira é cada vez mais competitiva, produtiva e com elevada qualidade. A necessidade de melhoria veio através das mudanças dos hábitos alimentares, pelo qual a indústria e o mercado consumidor buscam principalmente carcaças de alta qualidade (PAIXÃO; DE ALMEIDA, 2020). Estes têm encontrado diversas opções de produtos diferenciados, como variados cortes, preparos, embalagens e até mesmo a identificação da origem dos animais que estão relacionados ao sistema de criação e às raças (CHAMPREDONDE et al., 2014).

Dentre os fatores que influenciam a qualidade da carne, como o manejo, nutrição e sistema de produção, a genética está entre os principais, sendo que a escolha da raça ou do grupo genético é de suma importância para a caracterização dos aspectos desejados no produto final. O sistema de produção, bem como a genética, é capaz de influenciar no tipo da fibra, no tipo e qualidade do colágeno, marmoreio e atividade das proteínas que regulam a maciez e sabor da carne. Sendo que, as propriedades do músculo são conduzidas pela expressão de diferentes genes, tendo funções importantes nestes mecanismos (RAMALINGAM; HWANG, 2021).

2.2 A RAÇA ABERDEEN ANGUS

A raça Aberdeen Angus originou-se na Escócia por cruzamento de uma linhagem de bovinos mochos da região do condado de Aberdeen e outra linhagem de bovinos sem aspas, do condado de Angus, no qual seus primeiros registros são de 1862. Em 1906, os primeiros animais foram trazidos do Uruguai ao Brasil e deu-se início a criação da raça. No ano de 1963, quando o número de cabeças da raça chegou a 1362 animais, foi fundada a Associação Brasileira de Angus (ABA, 2017).

Os animais da raça Angus, são caracterizados pela precocidade sexual e de abate, além da alta fertilidade. As fêmeas apresentam boa habilidade materna, curto intervalo entre partos e são longevas. Já os machos, quando criados em pastagens com o manejo adequado, são abatidos em média com 24 meses. E quando criados em confinamento, podem ser abatidos até antes dos 18 meses (SCHULER, 2013).

Sobretudo o grande diferencial do Angus é a alta qualidade de carne. Esta característica conquistou o mercado interno e externo e fez com que a raça ganhasse lideranças em vendas. Os animais apresentam gordura entremeada na carne e que, simultaneamente à idade precoce ao abate e o acabamento de gordura de no mínimo de 3mm, proporciona maciez e sabor único aos cortes cárneos (ABA, 2017).

Entretanto, são menos adaptados ao clima brasileiro que as raças zebuínas, devido a adaptação do clima do país de origem. Possuem menos glândulas sudoríparas, com o diâmetro menor, estão mais distantes da superfície da pele, o que dificulta a troca de calor com o ambiente (NURSITA et al., 2020). Isso torna um desafio na criação de animais da raça Angus no Brasil, com clima predominantemente tropical, prevalecendo temperaturas mais altas durante o ano. Sendo que o estresse térmico está diretamente relacionado com o desempenho e a produtividade, que afeta desfavoravelmente a fisiologia, saúde e comportamento do animal (MISHRA, 2021).

Uma das estratégias usadas na pecuária de corte para contornar os desafios climáticos sofridos pela raça no país é a utilização de cruzamentos entre raças taurinas e zebuínas. As raças zebuínas são mais adaptadas ao clima tropical e desta forma, esse método é capaz de provocar maior vigor híbrido aos animais, que resulta no aumento da eficiência produtiva e melhora a qualidade de carne (MENDONÇA et al., 2021). Segundo a Associação Brasileira de Angus, este fato foi responsável pelo expressivo aumento desses animais no Brasil, além de se tornar a principal raça taurina na bovinocultura de corte (ABA, 2017).

2.3 CARACTERÍSTICAS DE QUALIDADE DE CARNE

As características utilizadas para avaliação da carcaça devem ser parâmetros mensuráveis e estão associados a seus aspectos qualitativos e quantitativos. São exigidas pelo mercado consumidor, sejam frigoríficos, a agroindústria ou o consumidor final (ARAÚJO et al., 2022). De acordo com Luchiari Filho (2000), a carcaça de boa qualidade e rendimento apresenta o máximo de músculo, o mínimo de ossos e quantidade de gordura adequada que garanta sua preservação e as condições desejadas para o consumo. O peso, o rendimento dos cortes cárneos, a gordura de cobertura e o marmoreio são fatores que influenciam na qualidade da carcaça e consequentemente implicam no seu valor comercial (CLINQUART et al., 2022).

No Brasil, é realizada avaliação visual ao abate para determinar o grau de acabamento das carcaças, de acordo com escores de acabamento que apresentam carnes de melhor qualidade, a fim de realizar melhores remunerações ao produtor (GOMES et al., 2022). Essa iniciativa de bonificação permite estimular os criadores a produzir carcaças com melhor qualidade (FELÍCIO, 2005). Diante disso, a mensuração de características como área de olho de lombo é utilizada como indicadora do desenvolvimento muscular, juntamente com medidas de espessura de gordura, são capazes de predizer informações quanto à qualidade da carcaça (PRADO et al., 2004).

Para mensuração dessas características, a utilização da ultrassonografia de carcaça apresenta diversas vantagens, sendo elas: a avaliação de animais vivos, diminuição do tempo e custos para avaliação genética; é considerada uma técnica não invasiva; podem ser utilizadas quando os animais começam a ganhar peso, apresentam boa acurácia e alta correlação com os dados mensurados na carcaça após o abate (SILVA et al., 2017). Os principais indicadores de medidas de carcaça existentes que possibilitam a coleta de informações via ultrassonografia são a espessura de gordura subcutânea e na garupa, área de olho de lombo e gordura de marmoreio, sendo assim, possível a determinação de ponto de abate (SUGUISAWA et al., 2003).

2.3.1 Área de olho de lombo (AOL)

A área de olho de lombo é a área em cm² da secção transversal do músculo *longissimus*, está localizada entre as 12ª e a 13º costela. É bastante utilizada como parâmetro de desenvolvimento muscular, pois é representativo do rendimento de carcaça, como grau de musculosidade e de composição de carcaça. Além disso, está correlacionada com o rendimento de cortes cárneos de alto valor (LUCHIARI FILHO, 2000; MEIRELLES et al., 2011).

2.3.2 Marmoreio (MARM)

O marmoreio ou gordura intramuscular refere a gordura entremeada que é caracterizada por manchas brancas ou estrias de tecido adiposo e não podem ser separadas da carne (NGUYEN et al.; 2021). Geralmente, é medida no músculo *longissimus* longitudinalmente e é avaliada de forma subjetiva através da inspeção visual de uma secção transversal do músculo, denominado escore de marmoreio, também pode ser avaliada por meio de análise química (CHENG et al., 2015) ou então por meio da ultrassonografia que obtém o percentual de gordura e como está distribuída (TAVEIRA et al., 2016).

A gordura intramuscular está associada positivamente à qualidade da carne, em virtude das características sensoriais que atribui a carne, como sabor, suculência e maciez. Isso colabora com o maior valor agregado e provoca maior interesse de alguns nichos pela compra desses produtos (HAUSMAN et al., 2014).

2.3.3 Espessura de gordura subcutânea (EGS)

A espessura de gordura subcutânea é representada pela gordura que fica localizada entre a 12ª e 13ª costela, sobre o músculo *longissimus* transversalmente, e a mensuração é obtida a ¾ da altura do músculo (SILVA et al., 2017). Essa espessura representa significativa importância na qualidade da carne, pois a indústria recomenda espessuras entre 3 e 6 mm de gordura subcutânea (PACHECO et al., 2023).

A gordura que envolve a carcaça possibilita proteção em baixas temperaturas, fundamental no processo de resfriamento da carcaça. Quando há uma pequena espessura de gordura pode ocorrer perdas significativas, como o encurtamento das fibras musculares pelo frio, que provoca o endurecimento da carne. Além disso, a pouca gordura permite a perda de água, que ocasiona a perda de peso e o escurecimento da carne. E como consequência, prejudica o peso e a qualidade dos cortes cárneos comerciais (MOURÃO et al, 2007).

Outro fator importante é que a maciez pode ser alterada pela gordura subcutânea, acarreta alterações na força de cisalhamento, que de acordo com Olmedo et al. (2011), há uma superioridade dos animais terminados em confinamento, por haver maiores espessuras de gordura e ainda, há uma relação com o rendimento de carcaça, que eleva a receita da carcaça ao abate. Em contrapartida, o excesso de gordura pode gerar prejuízos para a indústria, uma vez que há a necessidade de fazer a correção com a retirada dos excessos para a padronização dos cortes, que provoca uma menor eficiência da indústria (RODRIGUES et al., 2015).

2.3.4 Espessura de gordura na garupa (EGP8)

Devido a sua localização e a facilidade de mensuração, realizada entre os músculos *Glúteo médius* e *Bíceps femoris*, a avaliação da espessura de gordura na picanha ou garupa, surgiu como alternativa para a predição da composição da carcaça. Tal medida também é capaz de oferecer resultados satisfatórios, pois apresenta alta correlação com a composição da carcaça, assim como a espessura de gordura subcutânea (NETO et al., 2017). A vantagem dessa avaliação é que a deposição de gordura na garupa se inicia mais cedo que na costela, que possibilita a avaliação do animal ainda mais magro (WILLIANS, 2002).

2.4 ASSOCIAÇÃO GENÔMICA AMPLA

A associação genômica ampla é o estudo que associa regiões do genoma com fenótipos de interesse e, tem como objetivo identificar essas regiões e entender suas funções biológicas. A finalidade é compreender ainda mais como a genética influencia sobre o desempenho animal e como está relacionada a produtividade e a qualidade do produto gerado (ZHANG et al., 2012).

Através da utilização da genotipagem, é possível estimar os efeitos das regiões que contém marcadores moleculares, juntamente com as informações fenotípicas. A combinação das informações genotípicas e fenotípicas contribuem para a estimativas de valores genômicos, que explicam parte da variação genética de uma característica de interesse econômico (TAM et al., 2019).

Os marcadores moleculares são uma classe de marcadores genéticos que são utilizados para avaliar diferenças genéticas entre dois ou mais indivíduos. Essa diferença é conhecida como polimorfismo genético, que são alterações na sequência de nucleotídeos na molécula de DNA, tornando-se importante ao ser detectada e analisada com o propósito de compreender a base molecular dos mecanismos biológicos (SERROTE et al., 2020).

Dentre tantos tipos de marcadores, os mais utilizados são os SNPs (Polimorfismo de Nucleotídeo Único), responsáveis por diferenças em um único nucleotídeo, que pode ser uma substituição, deleção ou inserção de um nucleotídeo (AITKEN et al., 2004). Além disso, é o marcador molecular mais abundante no genoma, que permite distinguir polimorfismos com alto rendimento, e que possibilita a avaliação da diversidade genética com os estudos de associação genômica (YOU et al., 2018).

O desenvolvimento de painéis contendo um grande número de marcadores moleculares do tipo SNP foi possível com o sequenciamento do genoma bovino, que permite a identificação das variações genéticas para determinadas características de interesse. E ainda, foi possível realizar a identificação de QTLs (Quantitative Trait Loci), que são regiões do genoma envolvidas na expressão do fenótipo, através de estudos de GWAS para diferentes características (DWININGSIH et al., 2020).

Dessa forma, o estudo de GWAS tem o objetivo de detectar marcadores SNPs que estão relacionados com características de interesse e analisar regiões do genoma que estão localizados os marcadores moleculares, encontrando genes e QTLs ligados à expressão fenotípica das características (YANG et al., 2013). A utilização do GWAS torna-se um método importante para entender como a genética se comporta na expressão de características relacionadas à qualidade da carcaça, por meio da associação das informações genotípicas e fenotípicas.

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ARTICLE

Single-step genome-wide association study for carcass quality traits in Angus beef cattle

Formatted according to the guidelines of the periodical Revista Brasileira de Zootecnia

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Declarations of interest: none

ABSTRACT

The objective of this study was to identify genomic regions and putative candidate genes associated with the ribeye area (REA), marbling (MARB), backfat thickness (BFT) and rump fat thickness (RFT) in Angus beef cattle. The pedigree file contained data for 2,446 animals and a total of 1,391 animals were genotyped with the GGP Bovine 150K (Illumina). The single-step approach for genome-wide association study (ssGWAS) was performed to estimate the SNP effects and variances accounted by 10-SNP sliding windows. Confirming the polygenic nature of the studied traits, 23, 23, 22, and 31 genomic windows that explained more than 0.5% of the additive genetic variance were identified for REA, MARB, BFT and RFT, respectively. A total of 66, 56, 36, and 105 protein-coding genes were found in windows associated with REA, MARB, BFT and RFT, respectively. Several protein-coding genes were identified within those genomic regions, such as *SIRT6, CREB3L3, HNRNPH1, RUFY, EEF2, NMRK2, FDS1, CTNNA2, MAMSTR, PCCB, GALNT13, CTNNA3, EPHB2, PLA2G4E, APOD, RPL9, AGAP1, MFSD2A, FAM13A, DDHD1, CAST, CISD1, PLA2G1B, DROSHA, CDH6, FAM83A, SPHK2,* and *NEIL3* gene, according to its function. Functional enrichment analysis by DAVID tool also revealed several significant (p< 0.05) KEGG pathways and Gene Ontology terms such as RNA polymerase II transcription regulatory region sequence-specific binding (GO:0001228), glycerophospholipid catabolic process (GO:0046475), phospholipid catabolic process (GO:0009395) and lipid catabolic process (GO:0016042). These results contribute to improving the knowledge of the genetic architecture of carcass quality traits in Angus beef cattle and may contribute to genetic evaluations.

Keywords: Backfat thickness, *Bos taurus taurus*, GWAS, Marbling, Ribeye area, Rump fat thickness.

1. INTRODUCTION

Brazil is a leading producer of beef cattle worldwide, setting records for production in successive years. The country has the largest commercial herd in the world with approximately 203 million animals making it the largest exporter of beef (ABIEC, 2023). However, to continue ensuring competitiveness, it is necessary to also consider the quality of the product generated rather than only the quantity. Consumer demands encompass not only animal welfare but also carcass quality (MACHADO et al., 2019).

Several quality indicators, such as the ribeye area (REA), marbling or intramuscular fat (MARB), backfat thickness (BFT) and fat thickness (RFT) are used for evaluating beef carcass quality. These traits are expressed late in the animal, and therefore, the identification of superior animals allows to reduce the generation interval and, consequently, increasing genetic gain (GRIGOLETTO et al., 2019).

In recent years, the Angus breed has been among the main European breeds used in crosses in Brazil since some characteristics of this breed ensure excellent economic results in beef cattle production in general. Among the advantages of this taurine breed, Angus meat cuts exhibit a standardized finish and high marbling index (RUCHAY et al., 2022).

Although breeding programs already include carcass traits in genetic evaluation methods, little is known about the molecular markers associated with these traits in purebred Angus animals raised in Brazil. For this reason, molecular studies are necessary for increasing the accuracy of prediction and strength of selection (SANTANA et al., 2015). In addition, subsidize validation studies of genomic associations, thus being able to participate in carrying out genomic selection, assisting in decision-making in genetic breeding programs for the Angus.

Therefore, the objective of this study was to identify genomic regions and putative candidate genes associated with the ribeye area, marbling, backfat thickness and rump fat thickness in Angus cattle, which will help to understand the genetic architecture of the mechanisms that regulate carcass quality traits in this economically important breed.

2. MATERIALS AND METHODS

Data

The genotypic, phenotypic and pedigree data used in this project were provided by a Fazenda located in the municipality of Silvianópolis (latitude: 22°1′44″ S; longitude: 45°50′ 6″W), Minas Gerais, Brazil.

This company uses genetic material from the Angus breed from the United States and other countries, in addition to animals born in Brazil, which means that these evaluated animals have a high representation of the breed.

The pedigree file contained information for 2,446 animals; 529 Angus animals with a mean age of 529 days had phenotypic data concerning the REA, MARB, BFT and RFT. Rib eye area (REA) was measured in the longissimus muscle in cm^2, between the 12th and 13th ribs. Backfat thickness (BFT) was measured in mm at a point three-quarters of the transverse orientation over the REA. Marbling (MARB) was measured through the percentage of intramuscular fat in the longissimus muscle. Rump fat thickness (RFT) was also measured in mm, at the junction of the biceps femoris and gluteus medius between the ischium and ilium. All traits were evaluated by ultrasonography using an automatic real-time scanner (model—ECM ExaGo Veterinary scanner, with a 3.5 MHz linear transducer, IMV imaging, Meath, Ireland). The animals received water and feed *ad libitum* in a feedlot system.

A total of 1,391 animals were genotyped with the GGP Bovine 150K SNP array (Illumina). The genotype quality control excluded SNPs with minor allele frequency lower than 0.05, call rate lower than 0.90. Only SNPs located on autosomes according to ARS-UCD1.2 genome assembly (ROSEN et al., 2020) were considered in this study. Samples with a call rate greater than 0.90 were retained for further analysis. After quality control, 1,253 genotypes with 112,466 SNPs were available.

Statistical analyses

Contemporary groups (CGs) were formed according to the year of birth, performance test (PD), age class and sex. The CGs with fewer than three observations and observations that varied by ± 3 standard deviations from the mean of its group were excluded. The model used to estimate the variance components included the direct additive genetic random effect, the CG fixed effect and age as covariates.

The variance components and genetic parameters were estimated using the AIREMLF90 program, which belongs to the BLUPF90 family (MISZTAL et al., 2002). Genomic information was not used to estimate the variance components. The model used can be represented by the following matrix form:

$$y = X\beta + Za + e$$

where y is the vector of the observations, β is the fixed effect vector, a is the direct additive genetic effect vector, X is the known incidence matrix, Z is the incidence matrix of the random additive direct genetic effect (associates the vector a to vector y) and e is the vector of the residual effect.

Single-step genome-wide association study

The single-step genome-wide association study (ssGWAS) involves modifying the BLUP by replacing the numerator of the relationship matrix A^{-1} with H^{-1} (AGUILAR et al., 2010):

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

Where A is the numerator of the relationship matrix for all animals, A_{22} is the numerator of the relationship matrix for genotyped animals and G is the genomic relationship matrix, which was calculated as described by Vanraden et al. (2009):

$$G = ZDZ'q$$

where Z is the matrix containing fits for allele frequencies, D is a weight matrix for SNP (D==I), and q is a normalizing factor. According to Vitezica et al. (2011), such factors can be obtained by ensuring that the average diagonal in G is close to A_{22}.

The model that was used to estimate the variance components was also used to identify the genomic windows associated with the traits.

To calculate the effects and weights of the SNPs, the iterative process described by Wang et al. (2012) was followed, considering D to estimate the effects of the SNP:

1. $D = I$;
2. Calculate GEBVs for all animals in the dataset using ssGBLUP;
3. Convert GEBV to SNP effects (û): $\hat{u} = q\mathbf{DZ}' (\mathbf{ZDZ}' q)^{-1} \hat{a}$, where a is the GEBV of animals which were also genotyped;
4. To calculate the variance of each SNP, $d_i = \hat{u}_i^2 2p_i (1— p_i)$, where i is the i-th marker;
5. Normalize the values of the SNPs to keep the additive genetic variance constant;
6. To calculate the matrix G:
7. Exit or go back to step 2.

The effects of the markers were obtained by 2 iterations of steps 2 to 7, as shown by Wang et al. (2012). The percentage of genetic variance explained by the i-th region was calculated as described by Wang H et al. (2014):

$$\frac{var(a_i)}{\sigma_a^2} = x100\% = \frac{var(\sum_{j=1}^{10} Z_j \hat{u}_j)}{\sigma_a^2}\ x100\%$$

where $_i$ is the breeding value of the i-th region consisting of ten consecutive SNPs, $\sigma^2{}_a$ is the total genetic variance, Z_j is the content of the genetic vector of the j-th SNP for all individuals, and $\hat{u}_j$ is the j-th effect of the marker within the i-th region.

Thus, the GWAS results were represented as the proportion of variance explained by a genomic window of ten adjacent SNPs.

Functional analysis and gene prospection

Genomic windows that explained more than 0.5% of the additive genetic variance for each of the studied traits were investigated for their gene content using the Ensembl Biomart tool with the Genes 109 database and the ARS-UCD1.2 bovine genome annotation version (CUNNINGHAM et al., 2022). Significant ($p<0.05$) Gene Ontology terms (GO Biological process, GO Molecular function and GO Cellular component) and KEGG pathways (Kyoto Encyclopedia of Genes and Genomes) were identified with the Database for Annotation, Visualization and Integrated Discovery (DAVID) tool version 2021 (SHERMAN et al., 2022).

3. RESULTS

Descriptive statistics for ribeye area (REA), marbling (MARB), backfat thickness (SGB) and rump fat thickness (RFG8) traits are presented in Table 1. The heritability estimates were 0.40, 0.28, 0.29 and 0.22 for REA, MARB, BFT and RFT, respectively, which represent values of moderate and high magnitude.

For REA, 23 significant genomic regions were found, located in BTA7, BTA9, BTA11, BTA12, BTA13, BTA14, BTA 15, BTA18, BTA19, BTA20, BTA22 and BTA23. These regions together explained 48.15% of the additive genetic variance and represented 66 putative candidate genes (Figure 1 and Table 2).

For MARB, 23 genomic regions that explained 26.25% of the additive genetic variance were found in BTA1, BTA2, BTA3, BTA7, BTA8, BTA10, BTA11, BTA14, BTA15, BTA16, BTA18, BTA23, BTA28 AND BTA29. In these regions, 56 putative candidate genes were identified (Figure 2 and Table 3).

Regarding the BFT trait, 36 putative candidate genes were identified in 22 significant regions, located in BTA1, BTA3, BTA4, BTA6, BTA7, BTA8, BTA10, BTA14, BTA16, BTA17, BTA18, BTA26 and BTA28, representing 35.65% of the genetic variance (Figure 3 and Table 4).

For RFT, 31 genomic regions were considered, explaining 41.37% of the additive genetic variance. These strains were located in BTA1, BTA3, BTA6, BTA7, BTA8, BTA9, BTA10, BTA13, BTA17, BTA18, BTA20, BTA21, BTA23, BTA24, BTA25, BTA26, and BTA27 and harbored 105 putative genes (Figure 4 and Table 5).

The BTA7:19764739-20095446 bp and BTA18:55206784-55405042 bp genomic regions associated with REA and BTA7:19827759-20135059 bp and BTA18:55105023-55328352 bp regions associated with RFT are partially overlapping and share common genes.

The functional analysis revealed seven, eleven, 21 and eight significant GO terms for REA, MARB, BFT and RFT, respectively (Tables 6-9), among which those that may be related to carcass quality stand out, such as RNA polymerase II transcription regulatory region sequence-specific binding (GO:0001228), glycerophospholipid catabolic process (GO:0046475), phospholipid catabolic process (GO:0009395) and lipid catabolic process (GO:0016042). In addition, three, three, two and six KEGG pathways were identified as significant to REA, MARB, BFT and RFT, respectively (Tables 6-9).

4. DISCUSSION

Ribeye area (REA)

The REA trait is related to the amount of meat available in the carcass, an important quantity measure that affects the added value of the final product. This association is due to the relationship between the growth and deposition of muscle tissue. The heritability estimate for the ribeye area was 0.40, which was high, indicating good potential for response to selection.

Genes such as *HNRNPH1* and *RUFY* were identified in a genomic region (BTA7:1614973-1757821 bp) associated with REA. The *HNRNPH1* gene encodes proteins involved in the regulation of critical alternative splicing in skeletal muscle tissue, an important process of cell development and survival (SUN et al., 2012). In contrast, *RUFY* is not directly associated with the development of muscle tissue but has been described as involved in the capture of glucose in muscle tissue, which is used as fuel to feed muscle cells or is stored long term as glycogen, which is related to intramuscular fat (ALBUQUERQUE et al., 2021).

The genomic windows associated with REA (BTA7:19764739-20095446 bp and BTA18:55206784-55405042 bp) and RFT (BTA7:19827759-20135059 bp and BTA18: 55105023-55328352 bp) partially overlapped, where genes such as *SIRT6, CREB3L3, MAP2K2, ZBTB7A, PIAS4, EEF2, DAPK3, NMRK2, ATCAY, ANKRD24,* and *H3-3B* (BTA7) and *SULT2B1, FAM83E, SPACA4, RPL18, SPHK2, DBP, CA11, NTN5,* and *SEC1* (BTA18) were shared between both traits.

In particular, the *SIRT6* gene plays a central regulatory role in growth, modulating the structure of neural chromatin. It has been associated with reduced levels of growth hormone (SCHWER et al., 2010), and in addition, when the *SIRT6* gene is overexpressed, the expression of the *PPARγ* gene decreases, causing excessive fat deposition (GUI et al., 2018). It is also associated with preadipocyte differentiation and lipid synthesis (HONG et al., 2020) as well as carcass quality traits in beef cattle (RAZA et al., 2019).

The *CREB3L3* gene is related to the transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific binding molecular function term (GO:0001228) and was reported to be one of the main transcriptional regulators of the tenderness and quality of meat in the Limousine cattle breed (RAMAYO-CALDAS et al., 2016). The *CREB3L3* gene has been linked to triglyceride metabolism and to the acute inflammatory response (NAKAGAWA et al., 2021), which, in studies of the Angus breed, was associated with shear force in response to acute stress (ZHAO et al., 2012). It is also related to growth suppression in reindeer (WELDENEGODGUAR et al, 2021). In addition, the *CREB3L3* gene has been related to cell proliferation and carcass quality in pigs (YU et al., 2020).

The *EEF2* gene plays an important role in the mTOR pathway, which regulates cell proliferation, growth and survival (OSPINA-ROJAS et al., 2019). In pigs and humans, it has been reported that *EEF2* stimulate protein translation and synthesis, aiding in muscle protein metabolism (ROSE et al., 2005; HAMILL et al., 2012; STEINER et al., 2014). The *NMRK2* gene has been related to mature skeletal muscle fibers in cattle (CAI et al., 2023). In chickens, it has been reported that the NMRK2 gene encodes a striated muscle-specific kinase required to muscle cells, which when there is a deficiency, the muscle needs to reduce the energy required for contraction (ZHANG et al., 2022); similarly, in mice, *NMRK2* deficiency is associated with greater muscle dysfunction (DELOUX et al, 2018).

The *FDS1* gene encodes a protein that neutralizes ligands of the TGFβ superfamily, which bind to activin and myostatin. Myostatin is related to the control of cell growth, apoptosis, proliferation and differentiation of embryonic cells to mature cells. *FDS1* in humans can promote hyperplasia and hypertrophy, resulting in increased muscle mass and strength, demonstrating likely associations that contribute to the development of REA (SCHNEYER et al., 2008).

The *CTNNA2* gene encodes a protein that plays an important role in skeletal muscle development, such as in collagen metabolism, cell adhesion and myogenesis (MALIK et al., 2015). This protein functions as a binding channel between cadherin adhesion receptors and the cytoskeleton to establish cell adhesion and differentiation in the nervous system (SCHAFFER et al., 2018). In Piedmontese cattle, the *CTNNA2* gene has been associated with the replacement of myofibers by adipose tissue, known as lipomatous myopathy. This disease can cause changes in fiber size, areas of necrosis, and mononuclear cell infiltration and increase the amount of connective tissue (PELETTO et al., 2017; MIOLETTI et al., 2019).

The *MAMSTR* gene is involved in the transcriptional regulatory process of MyoD, a myogenic process that transforms mesoderm cells to myoblasts in mice and humans (MOKALLED et al., 2012; WANG J et al., 2022). Ma et al. (2023) associated this gene to the differentiation of muscle cells of the *Longissimus dorsi* muscle of yaks, which may be highly important for muscle development and, consequently, for the ribeye area.

Marbling (MARB)

Also known as intramuscular fat, the MARB trait has the potential to add commercial value to the product because it is associated with the juiciness, flavor and tenderness of the meat. The heritability estimated for marbling presented moderate magnitude (0.28), indicating a good response to selection.

According to Fassah et al. (2018), castration of male cattle is correlated with meat quality, especially with marbling, because it reduces testosterone levels and increases the transcriptional activity of the hepatic gluconeogenesis pathway from propionate in the process of activating *ACCS3* and *PCCB* gene expression. The availability of glucogenic precursors, such as propionate, is associated with lipogenesis in the adipose tissue of cattle. The *PCCB* gene was found in the present study on BTA1:132982345-133179328 bp and may be a good putative candidate gene for marbling, which has also been related to fat weight in swine (YANG et al., 2012) and intramuscular fat deposition in chickens (SAN et al., 2021).

Another promising gene for MARB trait is the *GALNT13*, which is associated with lipoprotein metabolism and intramuscular fat deposition (SCHJOLDAGER et al., 2010; SCHJOLDAGER et al., 2012). In humans, a study suggested that this gene is involved in energy pathways (WANG G et al., 2014). Located in BTA 28, the *CTNNA3* gene identified in this study was associated with the marbling of the German Rotes Höhenvieh cattle breed (HALLI et al., 2022) and of an Italian cattle breed from the Aosta Valley (STRILLACCI et al., 2020), suggesting its participation in the expression of the MARB trait.

Genes such as *EPHB2* and *PLA2G4E* are associated with lipid metabolism, the former being associated with the regulation of the lipogenic pathway in chickens (BOHANNON-STEWART et al., 2014) and in mice (MUTHULAKSHMI et al., 2015; SINGH et al., 2019) and the latter with fat metabolism in the milk of dairy cows (MU et al., 2022), insulin resistance and obesity in humans (CERVERA et al., 2021). The *PLA2G4E* gene is related to the glycerophospholipid catabolic process, phospholipid catabolic process (GO:0046475). The composition of lipid molecules in adipose tissue influences meat quality. Molecules such as glycerophospholipids and phospholipids are more common in intramuscular fat deposition (LI et al., 2022; WANG D et al., 2022; ZHANG et al., 2023).

Backfat thickness (BFT)

The backfat thickness is a crucial indicator of the degree of improvement or maturity of the beef, in addition to the quality of the product *postmortem*. Regarding the heritability estimate, a moderate magnitude value of 0.29 was obtained for backfat thickness, demonstrating the potential to improve this trait through genetic selection.

The *APOD* gene, located at BTA1:72061983-72075639 bp, is a putative candidate gene for this trait because it has been described as related to the conversion of high-density lipoprotein (HDL) to intermediate-density lipoprotein (LDL) and is associated with lipid metabolism in humans and pigs (PERDOMO; DONG, 2009; PIÓRKOWSKA et al., 2022).

The *RPL9* gene, in addition to being associated with cell proliferation and differentiation, plays an important role in the growth and development of animals (MEI et al., 2019) and it has been related to the regulation of fat deposition (ZHAO et al., 2003; LI et al, 2015). Other authors also reported the overexpression of this gene in adipose tissue and liver (BAI et al., 2017), and the liver is responsible for much of the gluconeogenesis process in ruminants, which is important for energy generation and adipose tissue formation (SAKAMAKI et al., 2012).

The *AGAP1* gene, reported in BTA3, is expressed in skeletal muscle, bone and adipose tissue and is involved in lipid metabolism, transport and use of fatty acids and cholesterol and energy metabolism (FEITOSA et al., 2017). Leal-Gutiérrez et al. (2020) suggested that the gene was involved in meat quality in a population of

Angus cattle. In addition, the *AGAP1* gene was also associated with feed efficiency in cattle of various breed compositions (SERÃO et al., 2013).

Another gene identified in this study that could improve carcass quality is *MFSD2A*. According to Lin et al. (2022), this gene promotes the proliferation and migration of chicken intramuscular preadipocytes, as well as differentiation and adipogenesis through the *PPARγ* signaling pathway. In addition, it was reported that *MFSD2A* gene is highly expressed in brown adipose tissue during adaptive cold-induced thermogenesis in mice (ANGERS et al., 2008).

The *FAM13A* gene has great functional impact on adipose tissue. According to studies conducted in humans and mice, this gene can regulate the differentiation of adipocytes and promote changes in the distribution of body fat (TANG et al., 2018; FATHZADEH et al., 2020). It was also associated with the proliferation of precursor adipocytes in Qinchuan cattle (LIANG et al., 2021). Likewise, it has been suggested that the *DDHD1* gene participates in the differentiation of abdominal preadipocytes into adipocytes in chickens (TIAN et al., 2022) and different livestock species (HU et al., 2022). These findings indicate the importance of these genes in the determination of backfat thickness.

Calpastatin (*CAST*), located on BTA7:96033978-96167151 bp, although related to backfat thickness in the present study, has been associated with meat tenderness *postmortem* in Australian cattle (BOLORMAA et al., 2011). This association among the traits in question can be attributed to tenderness being favored over carcass fat thickness during the meat cooling process (OLIVEIRA SILVA et al., 2017).

In a study on the association of the *CISD1* gene with adipogenesis in humans, Moreno-Navarrete et al. (2016) reported that the expression of this gene was correlated with the expression of adipogenic genes, increased lipid uptake, adiponectin levels and adipocyte hyperplasia.

The *PLA2G1B* gene is related to the lipid catabolic process (GO:0016042). It encodes a phospholipase A2 protein that is important for the biological functions of the metabolic and catabolic processes of lipids and may inhibit the absorption of lysophospholipids (PEÑA et al., 2016). It was shown to be associated with fat deposition in chickens (MOREIRA et al., 2018), pigs (FU et al. 2020) and humans (WILSON et al., 2006). Thus, this gene, found on chromosome 17, is a putative candidate gene for backfat thickness.

Rump fat thickness (RFT)

Like the backfat thickness, the fat thickness in the croup is also important for improving meat quality; however, it is an earlier characteristic that is noticed in younger animals. This helps to increase the genetic gain due to the decrease in the generation interval. The estimated moderate heritability for rump fat thickness was 0.22, indicating the importance of using this trait as a selection criterion.

Previous GWA studies on carcass traits in Nelore cattle (SILVA et al., 2019) and Montana (GRIGOLETTO et al., 2019) identified significant regions that partially overlapped with the regions found in this study, such as those in BTA7:102059346-102336341 bp, BTA13:47933594-48226871 bp and BTA18:60630911-60817273 bp. Genes common to the rump fat thickness trait were identified, such as *GIN1* and *PPIP5K2* in the first study and *SHLD1, CHGB, TRMT6, MCM8, CRLS1, LRRN4,* and *ZNF331* in the second study.

Edea et al. (2020), in comparing carcass quality traits between two Korean breeds, Chikso and Hanwoo, also identified genes in common this study, such as *TCTN2, GTF2H3, EIF2B1, DDX55, TMED2,* and *RILPL1*. The *DROSHA* and *CDH6* genes are associated with fat thickness in pigs (PIÓRKOWSKA et al., 2023; VAHEDI et al., 2022). In addition, several genes, such as *FAM83A*, *SPHK2,* and *NEIL3*, have been associated to adipogenesis and adipocyte differentiation (KOMAKULA et al., 2021; HUANG et al., 2022).

5. CONCLUSION

The meat quality traits studied showed moderate to high heritability, indicating that they can respond well to traditional selection. Several genomic regions influencing the REA, MARB, BFT and RFT traits were identified in this study, which demonstrates that these are complex characteristics, determined by many genes of small effect. The results found in the present study contribute to improving knowledge about the molecular mechanisms underlying carcass quality characteristics in Angus cattle and can be applied to develop new strategies aimed at improving these traits. Furthermore, relevant information about genomic regions that influence the traits in question can contribute to targeting candidate genes for further investigation of causal mutations and assist in future genomic studies in Angus cattle.

ACKNOWLEDGMENTS

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) - Finance Code 8887.682925/2022-00 and we thank to Universidade Federal de Lavras and Casa Branca Agropastoril, Ltd., to transfer the data.

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Tables

Table 1. Descriptive statistics, variance components and heritabilities for REA, MARB, BFT and RFT in Angus cattle.

Trait	N	Mean	Min.	Max.	SD	σ^2a	σ^2e	h^2±SD
REA	523	67,98	30,26	109,55	12,52	41,95	61,82	0,40 ± 0,13
MARB	477	2,87	1,27	9,55	1,00	0,14	0,35	0,28 ± 0,12
BFT	519	3,96	1,02	10,50	1,56	0,36	0,87	0,29 ± 0,12
RFT	522	4,67	1,02	15,67	2,22	0,59	2,00	0,22 ± 0,12

N: number of observations; SD: standard deviation; σ^2a: additive variance; σ^2e: residual variance; h^2: heritability.

Table 2. Genomic regions that explained at least 0.5% of the additive genetic variance (Var %) for ribeye area (REA) in Angus cattle and genes contained in these regions.

BTA	Genomic region	Var (%)	Protein-coding genes
7	1614973-1757821	0.51	*CANX, CBY3, HNRNPH1, RUFY1*
7	24667183-24833451	1.16	*ADAMTS19*
7	22438353-22460905	2.40	-
7	19764739-20095446	16.18	*FSD1, TMIGD2, SHD, YJU2, EBI3, SIRT6, CREB3L3, MAP2K2, ZBTB7A, PIAS4, EEF2, DAPK3, NMRK2, ATCAY, ANKRD24, H3-3B*
7	20110398-20236370	7.20	*ZFR2, MATK, RAX2, MRPL54, APBA3, TJP3*
9	36676457-36805797	0.63	-
11	55856779-55996334	0.98	*CTNNA2*
11	56016684-56608407	0.53	*REG3G*
11	64138749-64262677	1.36	-
12	8743364-8881730	0.53	-
13	60640460-60916858	0.62	*TRIB3, NRSN2, SOX12, ZCCHC3, C13H20orf96, DEFB129, DEFB127, DEFB128, DEFB126, DEFB125, DEFB115, ENSBTAG00000050556*
14	22024607-22093493	0.92	*POLR2K*
15	30853024-31071603	0.76	*POU2F3, TLCD5, ARHGEF12*
15	8316546-8505778	0.59	*ARHGAP42*
18	55206784-55405042	1.12	*SULT2B1, FAM83E, SPACA4, RPL18, SPHK2, DBP, CA11, NTN5, SEC1, FUT2, MAMSTR, RASIP1, IZUMO1, FUT1, FGF21*
19	2868721-3019557	2.47	-
19	703575-930115	3.47	*CA10*
20	4506736-4550514	0.66	*DUSP1*
20	4591851-4616313	0.58	*ERGIC1*
20	71518465-71920923	1.50	*CEP72, SLC9A3, EXOC3, PDCD6, SDHA, LRRC14B, CCDC127, AHRR, IGHG4*
22	19634920-19930860	0.51	-
23	14614884-14792349	0.52	-
23	14387143-14609575	2.44	*LRFN2*

BTA: *Bos taurus autosomal.*

Table 3. Genomic regions that explained at least 0.5% of the additive genetic variance (Var %) for marbling (MARB) in Angus cattle and genes contained in these regions.

BTA	Genomic region	Var (%)	Protein-coding genes
1	132982345-133179328	0.60	*PCCB, MSL2, PPP2R3A*
2	42237251-42342093	1.24	*GALNT13*
3	32761404-32800931	0.77	-
7	9688780-10055082	0.76	*OR7A102, OR7A77, OR7A88, ENSBTAG00000047589*
7	37768199-38019483	0.74	*COMMD10, ARL10, NOP16, HIGD2A, CLTB, FAF2, RNF44*
7	83928846-84154480	0.60	*EDIL3*
8	22901895-23313119	0.68	*IFNAG, IFNB3, IFNW1, ENSBTAG00000052859, IFNZ, IFNA6, ENSBTAG00000053413, IFNA3, IFNB1*
8	36355776-36506589	0.66	*PTPRD*
8	40747744-41225279	1.76	*RFX3*
8	40601218-40723975	1.95	*EPHB2*
8	41244408-41408601	1.72	-
10	68748290-68975386	0.68	-
10	37150354-37476784	2.04	*MGA, MAPKBP1, JMJD7, PLA2G4B, EHD4, PLA2G4E*
10	68164248-68265390	1.41	-
11	32518440-32707373	1.78	*NRXN1*
11	55937548-56414999	1.18	*CTNNA2*
14	20893054-21145473	0.77	*PCMTD1*
15	30853024-31071603	0.79	*POU2F3, TLCD5, ARHGEF12*
16	12987496-13142992	0.69	*RGS18*
18	13956006-14164337	3.19	*PIEZO1, CDT1, APRT, GALNS, TRAPPC2L, CBFA2T3, PABPN1L*
23	11275619-11468938	0.79	*RNF8, CMTR1, CCDC167, ENSBTAG00000050874*
28	23567245-23891372	0.60	*CTNNA3, LRRTM3, GFR*
29	17135246-17310700	0.85	*TENM4*

BTA: *Bos taurus autosomal.*

Table 4. Genomic regions that explained at least 0.5% of the additive genetic variance (Var %) for backfat thickness (BFT) in Angus cattle and genes contained in these regions.

BTA	Genomic region	Var (%)	Protein-coding genes
1	72032606-72130418	0.85	*APOD, PPP1R2, ENSBTAG00000050331*
1	71771340-72027628	1.31	*DLG1, BDH1, RPL9*
3	96329955-96610952	0.61	*AGBL4*
3	115053241-115259392	0.52	*AGAP1*
3	105941131-106171388	5.04	*RLF, PPT1, CAP1, MFSD2A*
4	3314200-3468466	0.67	-
6	35695827-35810085	12.25	*FAM13A*
6	17410283-17511768	1.48	*PAPSS1*
7	95785453-96038573	0.81	*PCSK1, CAST*
7	24741419-24892384	0.58	-
8	25885978-26091172	0.81	-
8	26097892-26307123	0.53	*CISD1*
10	65647253-65846768	0.92	*DDHD1*
10	72582933-73180235	0.52	*SIX6, SIX1, SIX4, MNAT1, TRMT5, SLC38A6*
14	2739183-2905699	0.61	*DENND3, PTK2*
16	78427163-78603871	0.80	-
17	62652366-62772720	0.82	*PLA2G1B, MSI1, COX6A1, TRIAP1, GATC, SRSF9*
17	37908034-38165637	2.96	-
18	41442606-41607038	0.69	-
26	24858278-25049092	0.74	*ITPRIP, CFAP58*
26	33801595-33990300	1.41	-
28	13522558-13672538	0.72	*CSGALNACT2, RASGEF1A*

BTA: *Bos taurus autosomal.*

Table 5. Genomic regions that explained at least 0.5% of the additive genetic variance (Var %) for rump fat thickness (RFT) in Angus cattle and genes contained in these regions.

BTA	Genomic region	Var (%)	Protein-coding genes
1	91091148-91290150	0.63	-
1	143311428-143558129	0.54	*CRYAA, SIK1*
3	26066448-26193830	0.83	*VTCN1, TRIM45, TTF2*
6	112012758-112361665	0.71	*LDB2*
6	43253706-43346886	0.51	-
6	112384073-112544785	3.08	-
7	2367786-2462933	0.58	*GRM6, ZNF454, RPL17*
7	820916-854147	0.52	
7	102059346-102336341	1.89	*PAM, GIN1, PPIP5K2, MACIR, ENSBTAG00000054049*
7	19827759-20135059	1.26	*SIRT6, CREB3L3, MAP2K2, ZBTB7A, PIAS4, EEF2, DAPK3, NMRK2, ATCAY, ZFR2, ENSBTAG00000052694, H3-3B*
8	40747744-41225279	0.95	*RFX3*
8	71317380-71527981	0.61	*ADAM28, RRAGA*
9	92441012-92607598	0.70	-
10	98656876-98771835	0.56	-
13	47933594-48226871	8.52	*SHLD1, CHGB, TRMT6, MCM8, CRLS1, LRRN4*
13	22135679-22466567	1.56	*NEBL, LASP1*
13	22505137-22671945	0.61	*RPS13, ENSBTAG00000050131*
17	51959414-52161664	1.52	*ATP6V0A2, TCTN2, GTF2H3, EIF2B1, DDX55, TMED2, RILPL1, SNRNP35*
18	60630911-60817273	0.71	*ZNF331, ENSBTAG00000033642, ZNF16, SLC7A11*
18	56136613-56301350	0.62	*AP2A1, FUZ, MED25, PTOV1, PNKP, AKT1S1, TBC1D17, IL4I1, NUP62, ATF5, VRK3, SIGLEC11*
18	55105023-55328352	1.71	*GRIN2D, GRWD1, KCNJ14, CYTH2, LMTK3, SULT2B1, FAM83E, SPACA4, RPL18, SPHK2, DBP, CA11, NTN5, SEC1*
20	42067151-42258136	0.50	*DROSHA, CDH6*
21	34622761-34896344	2.22	*PML, STOML1, LOXL1, GZMB, GZMH, CMA1, LOC505326, ENSBTAG00000050353, CTSG, LOC786126, LOC508858*
23	13850106-14045477	0.91	*MOCS1*
24	27583413-27608571	0.83	-
24	61796843-61961047	1.08	*SERPINB12, SERPINB13, SERPINB3, SERPINB4, SERPINB11*
24	61972912-62102444	0.79	*SERPINB7, SERPINB2, SERPINB10*
25	21830405-21982141	1.28	*PRKCB, CACNG3*
26	30197564-30383399	0.65	-
27	8299115-8469326	0.80	*NEIL3, EIF3C*
27	5353792-5515065	1.36	*MCPH1*

BTA: *Bos taurus autosomal.*

Table 6. GO terms and KEGG pathways (p<0.05) related to the ribeye area (REA) trait and the putative candidate genes.

Term	P-Value	Genes
Biological process		
GO:0045087~innate immune response	0.00179824	*DEFB127, DEFB125, DEFB128, DEFB126, DEFB115*
GO:0001936~regulation of endothelial cell proliferation	0.01846506	*FUT1, FUT2*
GO:0006351~transcription, DNA-templated	0.05342046	*ZBTB7A, MAMSTR, POLR2K*
Cellular component		
GO:0032580~Golgi cisterna membrane	0.00732407	*SEC1, FUT1, FUT2*
GO:0034751~aryl hydrocarbon complex receptor	0.03016867	*AHRR*
Molecular function		
GO:0001228~transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific binding	0.03218345	*POU2F3, RAX2, CREB3L3, SOX12, DBP*
GO:0004089~carbonate dehydratase activity	0.04986940	*CA10, CA11*
KEGG pathway		
bta00603:Glycosphingolipid biosynthesis - globo and isoglobo series	0.00113701	*SEC1, FUT1, FUT2*
bta00601:Glycosphingolipid biosynthesis - lacto and neolacto series	0.00355079	*SEC1, FUT1, FUT2*
bta04714:Thermogenesis	0.03382655	*CREB3L3, FGF21, SDHA, SIRT6*

Table 7. GO terms and KEGG pathways (p<0.05) related to the marbling trait (MARB) and the putative candidate genes.

Term	P-Value	Genes
GO Biological process		
GO:0002323~natural killer cell activation involved in immune response	0.00000140	*IFNB3, IFNAG, IFNW1, IFNZ, IFNA3, IFN1, IFNA6*
GO:0033141~positive regulation of peptidyl-serine phosphorylation of STAT protein	0.00000407	*IFNB3, IFNAG, IFNW1, IFNZ, IFNA3, IFN1, IFNA6*
GO:0002286~T-cell activation involved in immune response	0.00000006	*IFNB3, IFNAG, IFNW1, IFNZ, IFNA3, IFN1, IFNA6*
GO:0042100~B-cell proliferation	0.00017181	*IFNB3, IFNAG, IFNW1, IFNZ, IFNA3, IFN1, IFNA6*
GO:0043330~response to exogenous dsRNA	0.00002193	*IFNB3, IFNAG, IFNW1, IFNZ, IFNA3, IFN1, IFNA6*
GO:0006959~humoral immune response	0.00003520	*IFNB3, IFNAG, IFNW1, IFNZ, IFNA3, IFN1, IFNA6*
GO:0030183~B-cell differentiation	0.01753575	*IFNB3, IFNAG, IFNW1, IFNZ, IFNA3, IFN1, IFNA6*
GO:0046475~glycerophospholipid catabolic process	0.02234412	*PLA2G4E, PLA2G4B*
GO:0048208~COPII vesicle coating	0.02785335	*TRAPPC2L, GFR*
GO:0009395~phospholipid catabolic process	0.03878081	*PLA2G4E, PLA2G4B*
GO Molecular function		
GO:0005132~type I interferon receptor binding	0.00000152	*IFNB3, IFNAG, IFNA6*
KEGG pathway		

bta05320: Autoimmune thyroid disease	0.02269694	*IFNAG,*
bta05100: Bacterial invasion of epithelial cells	0.02446929	*CLTB, CTNNA2, CTNNA3*
bta05200:Pathways in cancer	0.02752093	*IFNAG, CTNNA2, ARHGEF12, CTNAA3, IFNA6, IFNA3*

Table 8. GO terms and KEGG pathways (p<0.05) related to the characteristic backfat thickness (BFT) and the putative candidate genes.

Term	**P-Value**	**Genes**
GO Biological process		
GO:0048699~generation of neurons	0.00335741	*SIX1, SIX4*
GO:0061197~fungiform papilla morphogenesis	0,00335741	*SIX1, SIX4*
GO:0030910~olfactory placode formation	0.00335741	*SIX1, SIX4*
GO:0008582~regulation of synaptic growth at neuromuscular junction	0.00503204	*SIX1, SIX4*
GO:0072095~regulation of branch elongation involved in ureteric bud branching	0.00503204	*SIX1, SIX4*
GO:0061055~myotome development	0.00503204	*SIX1, SIX4*
GO:0072107~positive regulation of ureteric bud formation	0.00670395	*SIX1, SIX4*
GO:0031579~membrane raft organization	0.00670395	*PPT1, DLG1*
GO:0061551~trigeminal ganglion development	0.00670395	*SIX1, SIX4*
GO:0072075~metanephric mesenchyme development	0.00670395	*SIX1, SIX4*
GO:0016042~lipid catabolic process	0.01016405	*PPT1, PLA2G1B, DDHD1*
GO:0043524~negative regulation of neuron apoptotic process	0.01171230	*PPT1, SIX1, SIX4*
GO:0044257~cellular protein catabolic process	0.01336456	*PPT1, DENND3*
GO:0051451~myoblast migration	0.01502297	*SIX1, SIX4*
GO:0050678~regulation of epithelial cell proliferation	0.01667869	*SIX1, SIX4*
GO:0060037~pharyngeal system development	0.02162977	*SIX1, SIX4*
GO:0090190~positive regulation of branching involved in ureteric bud morphogenesis	0.02162977	*SIX1, SIX4*
GO:0048701~embryonic cranial skeleton morphogenesis	0.04923502	*SIX1, SIX4*
GO:0043086~negative regulation of catalytic activity	0.04923502	*PPP1R2, ITPRIP*
GO Cellular component		
GO:0005667~transcription factor complex	0.02396613	*SIX1, SIX4, SIX6*
GO Molecular function		
GO:0051537~2 iron, 2 sulfur cluster binding	0.04490128	*CISD1*
KEGG pathway		
bta01100:Metabolic pathways	0.02569005	*PAPSS1, PPT1, PLA2G1B, BDH1, COX6A1, CSGALNACT, GATC*
bta05202: Transcriptional misregulation in cancer	0.03723025	*SIX1, PTK2, SIX4*

Table 9. GO terms and KEGG pathways (p<0.05) related to the characteristic rump fat thickness (RFT) and the putative candidate genes.

Term	P-Value	Genes
GO Biological process		
GO:1902173~negative regulation of keratinocyte apoptotic process	0.01041348	SERPINB13, SERPINB12
GO:0032206~positive regulation of telomere maintenance	0.04101503	PML, SIRT6
GO Cellular component		
GO:0005615~extracellular space	0.00193120	SERPINB2, SERPINB7, LOXL1, SERPINB3, SERPINB10 SERPINB12, SERPINB13, CHGB, SERPINB11, SERPINB4, CMA1, LOC540321, LOC5224799, LOC511695, LOC519132, LOC100139881
GO:0005654~nucleoplasm	0.00282748	PML, GRWD1, RILPL1, PRKCB, NUP62, VRK3, DDX55, SIRT6, SPHK2, CRYAA, NEIL3, PIAS4, ATF5, PNKP, MED25, DROSHA, TRIM45, PT0V1, LDB2, NMRK2, CDH6
GO:0005737~cytoplasm	0.03289304	GZMB, LOC505326, DAPK3, MACIR, NUP62, ZBTB7A, VRK3, AKT1S1, EEF2, SULT2B1, PIAS4, SERPINB10, FUZ, ATACAY, NMRK2, RILPL1, PRKCB, SIK1, GZMH, SPHK2, CRYAA, CYTH2, GZMB
GO:0035861~site of double-strand break	0.04241936	PNKP, ZBTB7A, SHLD1
GO:0001669~acrosomal vesicle	0.04355180	ATP6VOA2, IL4I1, SPACA4
GO Molecular function		
GO:0008270~zinc ion binding	0.02868074	NEIL3, PML, PIAS4, TTF2, CA11, PRKCB, ZFR2, TRIM45, PAM
KEGG pathway		
bta04210:Apoptosis	0.00110507	GZMB, LOC509958, LOC505326, MAP2K2, LOC786126
bta05146:Amoebiasis	0.00388324	SERPINB4, SERPINB10, PRKCB, SERPINB3, CTSG
bta04614:Renin-angiotensin system	0.00895634	PRKCB, LOC100139881, CTSG
bta04921:Oxytocin signaling pathway	0.00994277	PRKCB, CACNG3, KCNJ14, MAP2K2, EEF2
bta04370:VEGF signaling pathway	0.04073243	PRKCB, MAP2K2, SPHK2
bta04140:Autophagy - animal	0.04585432	DAPK3, AKT1S1, MAP2K2, RRAGA

Figures

Figure 1. Manhattan plot of the additive genetic variance explained by windows of 10 adjacent SNP distributed by chromosomes for rib eye area (REA). The dots above the red line indicates the 23 genomic regions explaining together 48.15% of the additive genetic variance for REA in Angus beef cattle.

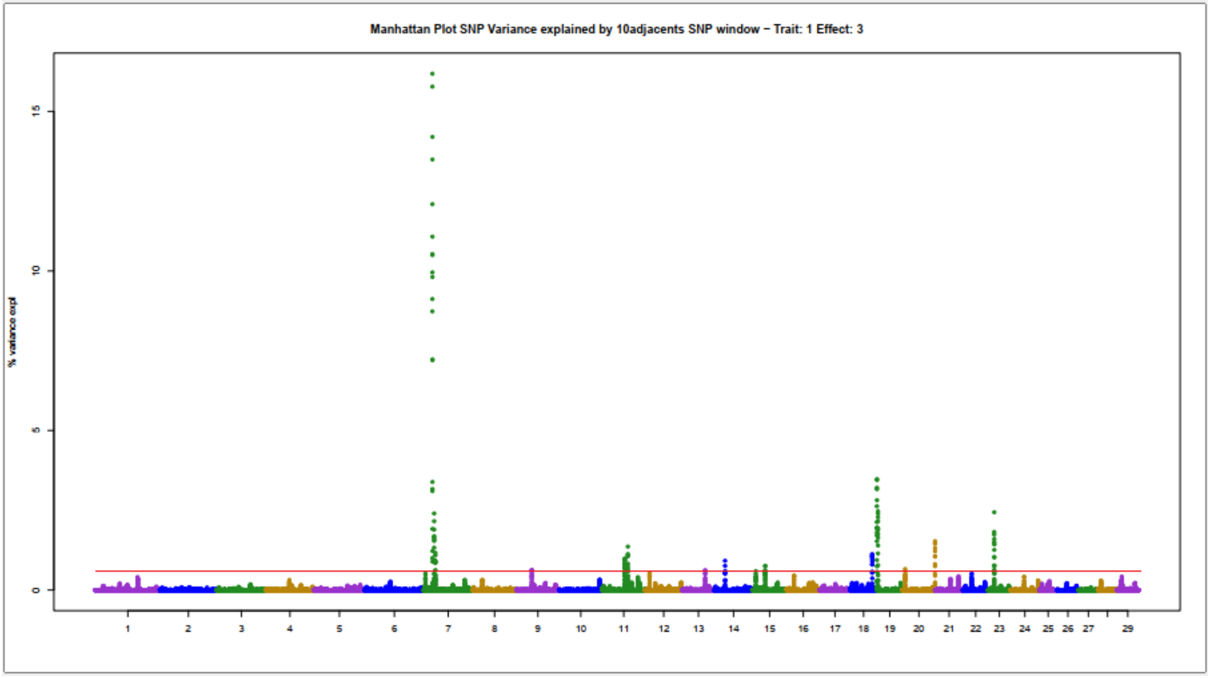

Figure 2. Manhattan plot of the additive genetic variance explained by windows of 10 adjacent SNP distributed by chromosomes for marbling (MARB). The dots above the red line indicates the 23 genomic regions explaining together 26.25% of the additive genetic variance for MARB in Angus beef cattle.

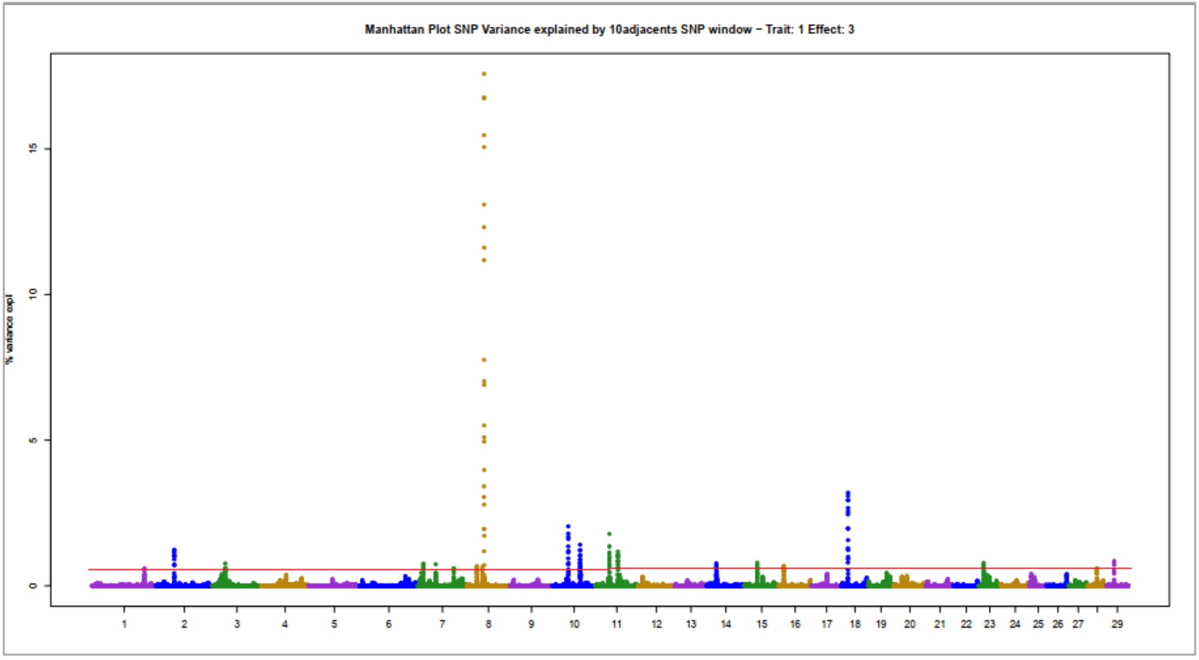

Figure 3. Manhattan plot of the additive genetic variance explained by windows of 10 adjacent SNP distributed by chromosomes for backfat thickness (BFT). The dots above the red line indicates the 22 genomic regions explaining together 35,65% of the additive genetic variance for BFT in Angus beef cattle.

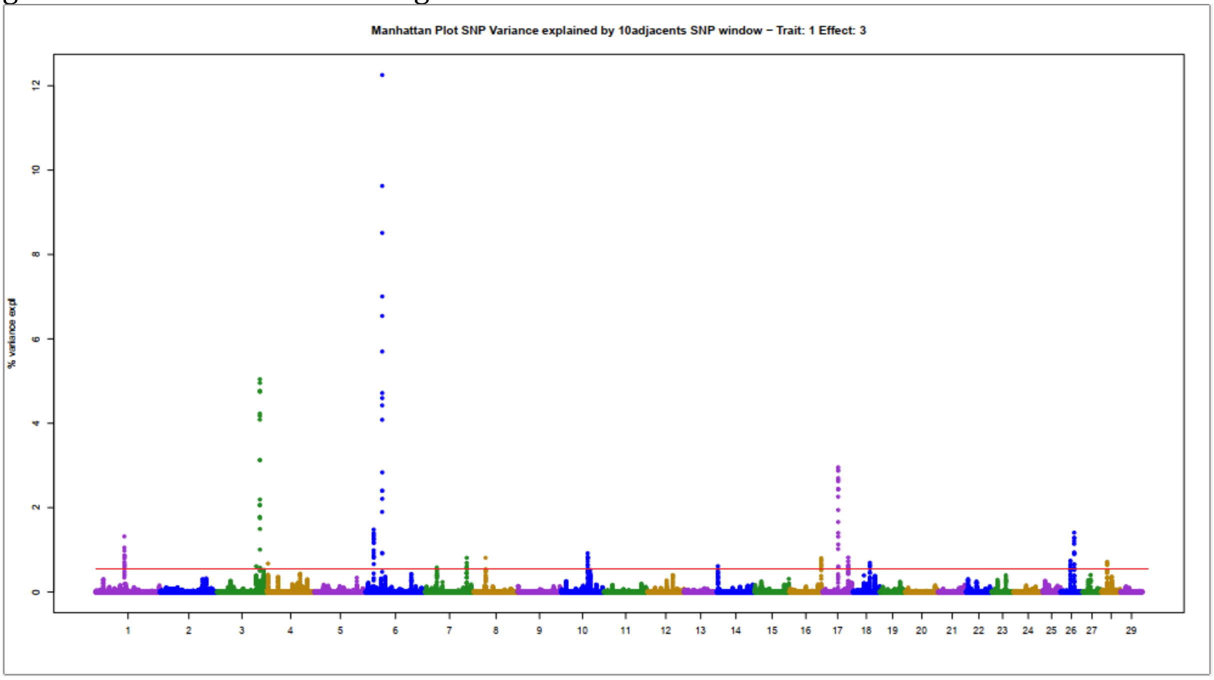

Figure 4. Manhattan plot of the additive genetic variance explained by windows of 10 adjacent SNP distributed by chromosomes for rump fat thickness (RFT). The dots above the red line indicates the 31 genomic regions explaining together 41.37% of the additive genetic variance for RFT in Angus beef cattle.