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UNIVERSIDADE ESTADUAL PAULISTA – UNESP

CÂMPUS DE JABOTICABAL

SELECTION SIGNATURES IN SHEEP

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Julia Lisboa Rodrigues – born on January 08, 1998, in São Carlos - São Paulo, Brazil, daughter of Vilson André Rodrigues and Carmem Eunice Lisboa da Conceição. Started her bachelor's degree in Animal Science at São Paulo State University, Campus of Jaboticabal, in 2017. During her undergraduate studies, Julia was granted two scientific initiation scholarships from The São Paulo Research Foundation (FAPESP - process number 2018/04727-6 and 2019/27508-0) and one Research Internships Abroad (BEPE - process number 2018/20723-0) scholarship from FAPESP to intern at Massey University, New Zealand. In December 2021, she became a Bachelor of Animal Science and, in January 2022, started a Master's degree in Animal Science, focusing on Genetics and Animal Breeding at São Paulo State University, Jaboticabal, under the supervision of Prof. Dr. Danísio Prado Munari and Prof. Dr. Marcos Eli Buzanskas. During her master's degree, Julia was granted scholarships in Brazil from the National Council for Scientific and Technological Development (CNPq - process number 130045/2022-5) and FAPESP (process number 2022/13986-0) and one of Canada's government scholarship, Emerging Leaders in the Americas Program (ELAP), to intern at the University of Guelph, Canada.

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ASSINATURAS DE SELEÇÃO EM OVINOS

RESUMO – A pressão da seleção natural favorece animais mais adaptados a determinados ambientes. A seleção artificial visa atender necessidade econômicas de produção animal. Ambas afetam a diversidade genética e podem causar modificações genômicas nos animais. Os padrões identificados no genoma são denominados assinaturas de seleção. O objetivo do presente estudo foi mensurar a diversidade genética e detectar e caracterizar assinaturas de seleção em 9.498 animais de cinco raças comerciais ovinas (Belclare, Charollais, Suffolk, Texel e Vendéen), criadas na Irlanda. Análise de componentes principais (PCA) e de decaimento do desequilíbrio de ligação foram utilizadas para verificar a estrutura da população. A diversidade genética foi acessada por meio de seis métricas, incluindo diversidade de nucleotídeos, coeficiente de endogamia, heterozigosidade observada e esperada, frequência do alelo menor e distância genética média e dois métodos diferentes foram utilizados na detecção das assinaturas de seleção: escore de Haplótipo Integrado (iHS) e Tajimas'D em janelas não sobrepostas de 100 kb. A heterozigosidade média observada e esperada para todas as raças ovinas foi de 0,353 e 0,355, respectivamente. A raça Suffolk apresentou a menor variação genética e, juntamente com a Texel, teve um decaimento do desequilíbrio de ligação mais lento. Assinaturas de seleção foram identificadas em todas as raças, com algumas regiões se sobrepondo, formando assim segmentos mais longos de assinaturas de seleção. Belclare e Texel apresentaram várias regiões comuns sob seleção positiva. Vários genes foram detectados dentro das regiões de assinaturas de seleção, incluindo *ITGA4*, *TLR3* e *TGFB2* relacionados ao sistema imunológico contra endoparasitas, *DLG1*, *ROBO2*, *MXI1*, *MTMR2*, *CEP57* e *FAM78B* relacionados a características reprodutivas; *WDR70* relacionado a características de produção de leite; *SCHM1* e *MYH15* relacionados a características de produção de carne; e *TAS2R4*, *TAS2R39* e *TAS2R40* relacionados a características adaptativas. Em conclusão, nossos resultados demonstraram uma diversidade genética moderada entre as raças ovinas comerciais e as assinaturas de seleção foram caracterizadas por genes associados a características reprodutivas, produção de leite, produção de carne e características adaptativas, como resistência a endoparasitas.

Palavras-chave: Desequilíbrio de ligação, Espectro de frequência de sítios, Genômica, *Ovis aries*, Polimorfismo de nucleotídeo único, Varredura seletiva

SELECTION SIGNATURES IN SHEEP

ABSTRACT – Natural selection pressure favors animals that are better adapted to certain environments. Artificial selection aims to meet the economic needs of animal production. Both affect genetic diversity and can cause genomic modifications in animals. The patterns identified in the genome are called selection signatures. The present study aimed to measure genetic diversity and detect and characterize selection signatures in 9,498 animals of five commercial sheep breeds (Belclare, Charollais, Suffolk, Texel, and Vendéen) raised in Ireland. Principal component analysis (PCA) and decay of linkage disequilibrium were used to verify the population structure. Genetic diversity was assessed through six metrics, including nucleotide diversity, inbreeding coefficient, observed and expected heterozygosity, minor allele frequency, and average genetic distance. Two methods were used to detect selection signatures: Integrated Haplotype Score (iHS) and Tajimas'D in non-overlapping 100 kb windows. The mean observed and expected heterozygosity for all sheep breeds was 0.353 and 0.355, respectively. The Suffolk breed showed the lowest genetic variation and, together with Texel, had a slower decay of linkage disequilibrium. Selection signatures were identified in all breeds, with some regions overlapping, thus forming longer segments of selection signatures. Belclare and Texel presented several common regions under positive selection. Several genes were detected within the selection signature regions, including *ITGA4*, *TLR3* and *TGFB2* related to the immune system against endoparasites, *DLG1*, *ROBO2*, *MXI1*, *MTMR2*, *CEP57*, and *FAM78B* related to reproductive traits; *WDR70* related to milk production traits; *SCHM1* and *MYH15* related to meat production traits; and *TAS2R4*, *TAS2R39*, and *TAS2R40* related to adaptive traits. In conclusion, our results demonstrated moderate genetic diversity among commercial sheep breeds, and selection signatures were characterized by genes associated with reproductive traits, milk production, meat production, and adaptive traits such as resistance to endoparasites.

Keywords: Linkage disequilibrium, Site frequency spectrum, Genomics, *Ovis aries*, Single nucleotide polymorphism, Selective sweep

CHAPTER 1 – OVERALL CONSIDERATIONS

1. INTRODUCTION

The domestic sheep (*Ovis aries*) is a descendent of Asian mouflon (*Ovis orientalis*), one of the seven extant wild sheep relatives (*Ovis ammon*, *Ovis orientalis*, *Ovis musimon*, *Ovis vignei*, *Ovis canadensis*, *Ovis dalli*, and *Ovis nivicola*) (Zeder, 2012; Cao et al., 2020). The domestication occurred ~11,000 years ago in the Fertile Crescent region between the Middle East and northeastern Africa (Zeder, 2012). These animals acquired a worldwide distribution due to their capacity to endure diverse climates (e.g., cold and hot weather), geographic (e.g., flat and mountain land) (Wei et al., 2015), production systems, and socio-economic contexts (OECD and FAO, 2021).

Sheep can be economically raised by sheep farmers to produce meat, milk, wool, and pelt, with the main uses of sheep products varying by country (Morris, 2017). The main source of income for farmers until the end of the XIX century was wool (Thorne et al., 2021), and the economic exploitation of this trait considered the fiber diameter, fiber length, strength, uniformity, and color metrics to be the most economically valuable (Fang et al., 2014). However, with the increase of synthetic fibers in the XX century, natural fibers were devalued, and sheep farmers turned their attention to meat production (USDA, 2020).

The largest producers of sheep meat are China, India, Pakistan, Australia, United Kingdom, and New Zealand, while countries of the Asian, African, and European continents are the major consumers (OECD&FAO, 2023). The worldwide sheep meat consumption is projected to grow by 15%, reaching 19 thousand tons of carcass weight equivalent by 2032 (OECD&FAO, 2023). The worldwide sheep meat consumption per capita is 1.4 kg, which is lower than other animal-derived proteins such as beef and poultry (OECD&FAO, 2023). However, it remains an essential source of protein for many consumers who demands sheep meat from early maturing animals with high carcass yield, good body conformation, and marbling. A small number of breeds are responsible for meat production (Woolley et al., 2023), which

were selected over the years by breeding programs to improve efficiency and productivity.

Artificial and natural selection pressure are meant to align animals to meet the environment and the farmer's needs (Wanjala et al., 2023), affecting the genetic diversity and causing genomic modifications in regions that might control body conformation, production, and behaviour (Saravanan et al., 2020; Wanjala et al., 2023). These genomic modifications may occur due to the increased frequency of beneficial alleles related to adaptative or economic traits. The increased frequency of beneficial alleles might also increase the frequency of closely linked alleles, forming haplotypes, which reduces the genetic diversity up and downstream of the beneficial allele (Hermisson and Pennings, 2005). These regions in the animal's genome are called "selection signatures" (Eydivandi et al., 2021).

The detection of selection signatures and genetic diversity within and between sheep populations can be accessed by the use of single nucleotide polymorphisms (SNP) arrays (Wanjala et al., 2023). The development of bioinformatic and statistical analysis methods associated with SNP information allowed the detection of gene networks involved in phenotypic variation. Identifying the selection signatures can allow the comprehension of gene flow in the selection process and genetic evolution within populations, documenting the genetic responses to selective pressures for traits of interest (Saravanan et al., 2020). Besides that, it can be a tool to complement genome-wide association and genomic selection studies (Chen et al., 2016). Selection may reduce genomic diversity, which is a concern for breeding and conservation programs that works avoiding inbreeding and extinction of local sheep breeds.

Therefore, this study aimed to explore the genetic diversity and detect selection signatures within the Belclare, Charollais, Suffolk, Texel, and Vendéen sheep breeds. These commercial sheep breeds are raised in Ireland and included in the Irish breeding program focusing on meat production. Genes and QTL identified under selection were evaluated according to their biological functions by performing an enrichment analysis to provide insight into the genomic mechanisms related to these sheep breeds' economic and adaptative traits.

5. CONCLUSION

In conclusion, the study examined the genetic diversity and selection signatures in Belclare, Charollais, Suffolk, Texel and Vendeen sheep breeds. The results demonstrated that Suffolk had the least genetic diversity and, along with Texel, had the slowest rate of linkage disequilibrium decay among the studied breeds. We identified several common regions under selection across breeds and between methodologies. The genes detected within the selection signature regions, including *TLR3* and *TGFB2*, were related to the immune system against endoparasites; *DLG1*, *ROBO2*, *MXI1*, *MTMR2*, *CEP57*, and *FAM78B* related to reproductive traits; and *TAS2R4*, *TAS2R39*, and *TAS2R40* related to adaptive traits. In conclusion, our results demonstrated moderate genetic diversity in the commercial sheep breeds raised in Ireland. The detected selection signatures harbored genes associated with reproductive traits, milk production, meat production, and adaptive traits such as endoparasite resistance. Therefore, our study provided insights into the genomic mechanisms, enhancing our understanding of the genes involved in economic and adaptive traits.

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