

מיפוי ואפיון אתרים כמותיים גנומיים הנמצאים בתאחיזה ליעילות ניצול מזון בפרות חלב מגזע הולשטיין.

Mapping and characterization of quantitative trait loci (QTLs) associated with feed efficiency in lactating Holstein cows.

Abstract

Optimizing the productivity of livestock animals represents a global challenge of utmost importance. The continuous population growth, competition for food between humans and livestock, and global climatic, demographic, and socio-economic changes necessitate a significant increase in the demand for animal-based products. Since feed costs constitute the primary expense in livestock production, improving feed efficiency has become a central focus of agricultural research in recent years.

In Israel, the national dairy herd comprises approximately 120,000 cows, with a daily feeding cost of about 25 ILS per cow. Improving feed efficiency by approximately 10% (equivalent to reducing daily consumption by about 0.9 kg) could save about 110 million ILS annually. However, collecting feed efficiency data in Israeli dairy farms is currently challenging due to the high costs and complexity involved in operating individualized feeding systems. Consequently, no practical tool for individual feed efficiency measurement exists in commercial dairy herds in Israel.

Genetic selection is an effective means of improving feed efficiency by utilizing genomic differences among animals with phenotypic variation. Recent advancements in high-throughput genotyping technologies have facilitated genetic selection through highly reliable and relatively low-cost methods.

In our preliminary work conducted several years ago, we mapped quantitative trait loci (QTLs) associated with feed efficiency, feeding behavior, and milk production traits in dairy cows from the Beit Dagan herd. This mapping was performed using a custom bovine SNP chip containing 777K genetic markers. DNA was analyzed from 19 of the most efficient and 20 of the least efficient cows based on residual feed intake (RFI) and feed conversion ratio (FCR) measures.

In the current research, funded by the Israeli Dairy Board, we aimed to further characterize existing and novel loci associated with feed efficiency traits in the Beit Dagan dairy herd (beyond the 19 most efficient and 20 least efficient cows previously mapped). For this purpose, we utilized the individual feed intake monitoring system available at Beit Dagan, equipped with 42 feeding stations, to conduct a genome-wide scan for markers associated with feed efficiency traits. The two primary feed efficiency measures are residual feed intake (RFI) and feed conversion ratio (FCR).

As part of the study, genotypes were determined using the 777K bovine SNP chip for dairy cows from the Beit Dagan herd (N=205). Feed efficiency traits (RFI and FCR) were characterized, and association tests identified a major QTL for RFI located on chromosome 14, near the Fatty Acid Binding Protein 4 (*FABP4*) gene. Given that RFI

is a complex trait in terms of both individual feed intake monitoring and genetic profiling, we sought to validate the reliability of our genotyping method for key polymorphisms in this gene.

Among several polymorphisms previously genotyped (Cohen-Zinder et al., 2019), we selected FABP4_4, located in exon 2 of the gene, which causes a missense mutation altering an amino acid at position 74 from isoleucine (*I*) to leucine (*L*). Another polymorphism, FABP4_5, located in the promoter region (at -373bp) and associated with transcription factors related to energy metabolism (allele A) or oxidative stress processes (allele G), was also examined. Genotypes for FABP4_4 and FABP4_5 were determined using high-resolution melting (HRM) and allelic discrimination assay, respectively.

To validate the accuracy of our results, we re-evaluated the genotypes using imputation based on genome sequencing data derived from the bovine SNP chip and whole genome sequencing (WGS). Imputation, which leverages observed haplotypes in reference populations, demonstrated significant advantages over other genotyping methods (Gershoni et al., 2022).

The results supported the view that RFI is a complex trait. Identifying causative sequence variations underlying RFI requires the development of advanced statistical methods capable of accounting for additive and epistatic interactions involving more than two loci. Using imputation, we identified discrepancies in genotypes for certain cows between the earlier methods (HRM and allelic discrimination) and the current imputation-based approach (Gershoni et al., 2022).

We also found that the genomic variants in *FABP4* associated with RFI in Holstein calves and cows had a lower effect size than initially estimated. A higher effect was observed using imputation for a polymorphism in the *ZHX2* gene, also located on chromosome 14, which harbors multiple QTLs associated with feed efficiency.

Our findings affirm that, in addition to being challenging to measure, RFI is genetically complex trait and is not governed by a single major gene, as observed in other traits like milk protein and fat content. Consequently, incorporating RFI into the breeding index should await the development of more advanced statistical-genomic methods for genotyping.