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GENOME-WIDE ASSOCIATION STUDY FOR MILK PRODUCTION AND MILK COMPOSITIONS TRAITS IN HOLSTEIN CATTLE

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Abstract: Genome-wide association studies (GWAS) have made possible the screening of several single nucleotide polymorphisms (SNPs) in genes associated with milk production and milk compositions traits in dairy cattle. In the present review, we focus on candidate genes that have been related with milk production and milk composition traits in Holstein cattle.

Key words: GWAS, Holstein, SNPs, Milk production, Milk compositions.

Introduction

The Holstein breed one of the most important dairy cattle breeds which originated in Europe. The major historical development of this breed occurred about 2000 years ago in the Netherlands. The intermingling of these animals evolved into an efficient, high-producing black-and-white dairy cow.

Milk production traits and milk compositions traits are important economic traits affecting profitability in dairy cattle. These traits are polygenic, affected by several genes and variants, each with small effects on the observed phenotype. Improvements in management and nutrition, along with intense genetic selection have increased milk production in recent decades (W. Snelling et al., 2013).

The improvement in these important economic traits by traditional methods in animal breeding became less useful today, so the modern technics plays a significant role to select and improve these traits in short time with high efficiency. Many quantitative regions and candidate genes related with milk production and milk compositions traits have been identified by GWAS (A. Reverter & M. Fortes., 2013).

The progress of genome sequencing and high-throughput genotyping technologies has made genome-wide association studies (GWAS) possible for identifying SNP associated with phenotypes of interest (L. Iung et al., 2019).

These studies are powerful tools for detecting genomic regions explaining variation in phenotype. GWAS has identified genetic variants linked to complex phenotypes including milk production and milk composition traits in dairy cattle (L. Iung et al., 2019). Several QTL regions and genes associated with milk yield, fat yield, protein yield, fat percentage and protein percentage have been reported in several studies, considering that the detection of QTLs associated with productive traits through GWAS is a preliminary step for the application of genomic selection. In the dairy industry, the most significant economic traits are milk production and milk compositions. Identifying pathways and genes that are linked with significant SNPs can give us a deeper biological vision into expression mechanisms of traits (W. Snelling et al., 2013).

Material and methods

The data were collected from several authentic sources, such as Web of Science, Scopus and Google Scholar, using SNPs, GWAS, Holstein, milk production traits and milk compositions traits as major keywords.

All the published studies that have discussed the polymorphisms in genes and their association with milk production and milk compositions traits in Holstein cattle were included in the current review.

The present review involved several polymorphisms in genes reported through GWAS or functional validation that were significantly related with milk production and milk compositions traits in Holstein cattle.

The traits under most of the studies in our review were: Milk production traits which included Milk yield (MY), Protein yield (PY) and Fat yield (FY). Also, Milk compositions traits which included Protein Percentage (PP) and Fat Percentage (PP). All traits were recorded, as well as the full pedigree file for all animals (cows and bulls). This step was followed by a quality control to discard the not adequate records

and to ensure a homogenous data set. For each cow, milk production traits were recorded using test-day approach from several number of lactations and milk composition traits was measured using MilkoScan.

- *Sample and genotype:*

The blood samples in several studies collected under sterile conditions by jugular vein puncture using 5-ml vacuum tubes of polypropylene containing EDTA. Genomic DNA extracted from blood samples using several protocols in the different studies such as the TIANamp Blood DNA Kit. After DNA extraction, using the Illumina BovineSNP150 BeadChip. Bos_taurus_UMD_3.1 as the genome reference the tested animals will be genotyped.

- *Genotype quality control, preparation and editing the genotype files:*

PLINK software (v1.07, http://pngu.mgh.harvard. edu/purcell/plink) to exclude individuals and remove SNPs from the genotyped individuals and SNPs. An individual was excluded if more than 10% of the genotype was missing, an error occurred in sex testing, or it was a duplicate sample.

- *The genetic evaluation of the animals:*

This step performed by estimating the breeding values using their phenotypic data set and the complete pedigree. The genetic evaluation of animals carried out using a univariate animal model using the BLUPF90 software. Estimated breeding values used as the phenotype as it only considers the genetic component of phenotypic variance.

- *Genome-wide association analysis:*

The association analyses performed using Bayesian procedures. A Multiple-Marker Regression performed under the Bayes B model. All GWAS performed using the GenSel software or the package JWAS of JULIA.

- *Bioinformatics analysis:*

The genome reference Bos_taurus_UMD_3.1 used to search for candidate genes. The online websites https://oct2018.archive.ensembl.org/Bos_taurus/Info/ Index https://www.ncbi.nlm.nih.gov/gene/,https://www.genome.jp/kegg/pathway.html, https://david.ncifcrf.gov/home.jsp used for functional analysis and pathway analysis of the candidate genes by GWAS.

- *Linkage disequilibrium analysis:*

The linkage disequilibrium (LD) in the most relevant extended regions to visualise the relationships between the SNPs will be studied. LD analyses were performed using plink software and LDheatmap function from R.

The table represents the different phases to detect candidate genes associated with milk production and milk compositions traits by using GWAS study in Holstein cattle (Table 1).

Table 1

Phase	Steps
Phase 1	• Preparation of phenotypic data files for milk production and milk compositions traits and the pedigree file as well.
Phase 2	• Blood sampling and DNA extraction.
Phase 3	• Genotyping of the tested cows.

	• Genetic evaluation of animals.
Phase 4	• Quality control and GWAS performing.
	• Gene annotation and Linkage Disequilibrium

Genome-wide association study for screening SNPs associated with milk production and milk compositions traits in Holstein cattle

Genome-wide association studies have been practiced screening the polymorphism in genes related with milk production and milk compositions traits in Holstein cattle. We presented the genes and their SNPs in table (2).

J. Jiang et al., (2019) reported that some genes (MAP3K1 and UGDH) associated with milk production traits milk yield (MY), fat yield (FY) and protein yield (PY) in Chinese Holstein cows through GWAS study. By using the GWAS study L. Liu et al., (2020) found that the genomic regions in DGAT1, EP400, EPHA6 and SLCO1A2 genes were associated with protein percentage (PP), fat yield (FY), fat percentage (FP) and protein yield (PY), respectively in Chinese Holstein cattle. Also, S. Yue et al., (2017) reported that EEF2K gene was related with milk yield (MY) in Chinese Holstein cattle. Finally, S. Kim et al., (2021) found several genes (PDE4B, ANO2, DGAT1) were related with some milk production traits (milk yield and fat yield) in Korean Holstein cattle (Table 2).

The table represents GWAS study for screening SNPs associated with milk production and milk compositions traits in Holstein cattle in several previous studies (*Table 2*).

Table 2

SNP	Traits	Country	Author
ss2019489562 (UGDH)	MY	China	J. Jiang et al., 2019
ss2137349058 (MAP3K1)	MY, FY and PY	China	J. Jiang et al., 2019
rs109421300 (DGAT1)	PP	China	L. Liu et al., 2020
rs109528658 (EP400)	FY		
rs42295213 (EPHA6)	FP		
rs134480235 (SLCO1A2)	PY		
BovineHD2500005573 (EEF2K)	MY	China	S. Yue et al., 2017
rs43454033 (ANO2)	MY and FY	Korea	S. Kim et al., 2021
rs41596885 (PDE4B), rs42314807 (PDE4B)	MY and FY	Korea	S. Kim et al., 2021
rs211223469 (DGAT1)	MY and FY	Korea	S. Kim et al., 2021

MY: Milk Yield; FY: Fat Yield: Protein Yield; FP: Fat Percentage; PP: Protein Percentage

Conclusion

In our review, we documented several genes associated with milk production and milk compositions traits in Holstein cattle. Also, many SNPs in candidate genes were documented in the review, which could be a useful addition to the genetic markers related to the genetic improvement for milk production and milk compositions traits in Holstein cattle. There are still many candidates genes association with milk production and milk compositions traits discovered through GWAS studies need more proof before selecting them as genetic markers in dairy cattle breeding.

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ПОЛИМОРФИЗМ ГЕНОВ GH И PRL КРУПНОГО РОГАТОГО СКОТА И ИХ СВЯЗЬ С МОЛОЧНОЙ ПРОДУКТИВНОСТЬЮ

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Аннотация: *В данной статье отображаются данные из литературы по генам, связанным с молочной продуктивностью, в частности по генам соматотропина и пролактина. Описаны наиболее ценные генотипы по удою, массовой доле жира и белка по холмогорской породе татарстанского типа, ярославской и белорусской чёрно-пёстрой породы коров.*

Ключевые слова: *Пролактин (PRL), соматотропин (GH), молочная продуктивность, полиморфизм, ген, корова.*