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Identification of Selection Signatures for Milk Performance Traits among Indigenous Dairy Cattle Breeds using High Density Genomic Information

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ABSTRACT

Background: Selection process for milk performance traits has left remarkable selection signatures in the genome and their identification can guide to utilize under genomic breeding programs for improving productivity in dairy cattle.

Methods: This study utilizes genotype data of Sahiwal (19), Tharparkar (17) and Gir (16) to identify selection signatures in the genomes of Sahiwal-Gir (SW-GR), Sahiwal-Tharparkar (SW-TP) and Tharparkar-Gir (TP-GR) breed pairs by using F_{ST} approaches. The highest F_{ST} peaks (F_{ST} >0.25) were considered as selection signature region. The functional genes underlying signature regions controlling milk performance traits were also annotated.

Result: We identified 41, 29 and 60 selection signatures exhibiting footprints of positive selection among SW-GR, SW-TP and TP-GR breed pairs, respectively. The selection signals controlling milk performance traits were detected as ACADL, SLC26A2, PLCB1, SYT9 genes mapped on chromosome 2, 7, 13 and 15, respectively for SW-GR breed pair. Selection signature regions in the genome of SW-TP breed revealed genes ATPAF1, LEF1, PPARGC1B, EIF6 and ACSS3 for milk production. Furthermore, PLA2R1, SCP2, ATPAF1, CACNA2D1, LEF1 and SUMF1 genes were identified in TP-GR breed pair controlling metabolism and morphogenesis of mammary gland. Moreover, HSPB6, LTBP1, SLIT3, FSHR and ASIP genes were also found in association with thermo-tolerance, disease resistance, immunity, reproduction and coat colour in our indigenous dairy cattle breeds.

Key words: Bovine HD BeadChip, Fixation index, Indian dairy cattle, Milk performance traits, Selection signature.

INTRODUCTION

India has richly contributed to the world's total cattle genetic resources as it possesses 193.46 million cattle. Out of the total cattle population, indigenous descript and indigenous non-descript cattle population are 51.36 million and 142.11 million. It is also ranked as the top milk producing country in the world. The total milk production was 198.44 million tonnes in 2019-20 and cattle contribute about 51% to the total milk production (Anonumous, 2021-22). Sahiwal, Tharparkar and Gir are recognized as the best milch cattle breeds and their lactation milk yield were estimated as 1874±61 kg, 1903±77 kg and 2674±49 kg, respectively (Singh *et al.*, 2019). More recently, the process of strong artificial selection for improving milk performance traits have altered allele frequency spectrum due to which frequency of desirable alleles are increased in the genome. This may cause fixation of the allele at a locus. This fixation of allele not only acts on a single mutation, but also affects the linked loci and leads to a change in its allele frequency spectrum with a shift towards extreme frequencies and an excess of homozygous genotypes. This region is commonly called as selection signature.

In recent years, due to the availability of high-throughput genotyping and sequencing technologies, it is possible to apply genome-wide scan in order to detect selection signatures for economic traits in cattle (Makina *et al.,* 2015; Wang *et al.,* 2019). Saravanan *et al.* (2021) revealed 267 candidate genes under 231 selection signature regions related to adaptation, production traits and immune response in cattle. The fixation index (F_{ST}) approach was used to identify selection signatures based on differences in allelic frequencies between two populations (Dixit *et al.,* 2021). Flori *et al.* (2009) identified 13 highly significant regions subjected to strong positive selection by smoothing F_{ST} values over each chromosome. These regions harbour GHR gene for milk production and MC1R gene for body colour in cattle. The selection signature analysis in Italian cattle breeds revealed the highest F_{ST} peaks on chromosomes 6 and 13 containing ABCG2 (ATP-binding cassette, sub-family G2) responsible for milk yield and composition traits in cattle (Mancini *et al.,* 2014).

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There is dearth of literature with regards to identify selection signatures for milk performance traits among Indian dairy cattle breeds by using genome-wide SNP markers information. Therefore, the objective of the present study was to detect signatures of selection among dairy cattle using high density SNP genotyping data.

MATERIALS AND METHODS

Sample collection, genotyping and quality control

Blood samples from 52 unrelated individuals of three dairy cattle breeds *viz*., Sahiwal (n= 19), Tharparkar (n= 17) and Gir (n= 16) were collected from ICAR-NDRI, Karnal; Divya Jyoti Jagrati Sansthan, Jalandhar and RAJUVAS, Bikaner, respectively. Genomic DNA was extracted from whole blood using HiPurA™ SPP Blood DNA isolation kit according to the manufacturer's instructions. The quality and quantity of DNA were evaluated using agarose gel electrophoresis and Nanodrop Spectrophotometer.

Genotyping of all samples was performed at Sandor Life Sciences Pvt. Ltd., Hyderabad, India by using Illumina BovineHD BeadChip (Illumina, Inc. San Diego, CA, USA) according to the standard procedures of manufacturer. Genotypes were called and processed using GenomeStudio software (Illumina, Inc.). All the bioinformatic analyses were done at ICAR-NBAGR, Karnal during 2017-18. The samples with more than 10% missing genotypes (Sample call rate≤ 90%); SNPs not genotyped in more than 95% samples (SNP call rate≤95%); SNPs with minor allele frequency (MAF≤0.05) as well as SNPs not in HWE (P<0.001) were excluded using PLINK v1.07 software (Purcell *et al.,* 2007).

Selection signature analysis

The F_{ST} approach was applied to identify selection signature regions based on strong genetic differentiation among Sahiwal-Gir (SW-GR), Sahiwal-Tharparkar (SW-TP) and Tharparkar-Gir (TP-GR) by using the *HierFstat R package* (Goudet, 2005) with the unbiased estimator proposed by Weir and Cockerham (1984). The raw F_{ST} values were divided into 4 distance bins like 0-0.1, 0.1-0.2, 0.2-0.3 and 0.3-0.4 and the proportion of SNPs in each F_{ST} bin for each breed pair was computed. A sliding window of 5 consecutive SNPs was considered and the average F_{ST} values were evaluated for each window of 5 SNPs on each chromosome of a breed pair and for all the three breed pairs. The average F_{ST} value against the genomic position of middle SNP of each non-overlapping window for each chromosome was plotted in R software (R Development Core Team, 2008) and this plot was very commonly known as Manhattan plot.

Bioinformatics analysis

The genomic regions containing the significant SNPs (F_{ST}>0.25) showing strong differentiation among the population was declared as signature region (Makina *et al*., 2015; Dixit *et al.,* 2021). Furthermore, genes underlying in those regions were investigated through gene annotation process by exploiting the knowledge on UMD3.1 locations of genes from the National Centre for Biotechnology Information (NCBI) (*www.ncbi.nlm.nih.gov*) databases. The biological function of each annotated gene was searched by GeneCards (*www. genecards.org*), NCBI and QTL databases.

RESULTS AND DISCUSSION

Descriptive statistics

In the present study, 45 samples (Sahiwal: 13, Tharparkar: 17, Gir: 15) were considered after excluding 7 samples having less than 10% missing genotypes. Out of 777962 SNPs in the HD chip, 42669 unmapped, X, Y and MT SNPs were excluded. Approximately, 27765 and 278372 SNPs were also excluded owing to low SNP call rate (<95%) and MAF (<0.05) value. A total of 434519 SNPs were filtered to calculate locus wise F_{ST} values. After excluding the negative F_{ST} values from data set, SNPs that passed quality control were 236989, 229556 and 251653 for SW-GR, SW-TP and TP-GR breed pairs, respectively. Vineeth *et al.* (2020) identified 258231 genome-wide SNPs related to milk production and reproduction in Sahiwal cattle through sequence alignment to *Bos indicus* reference genome.

Genome-wide distribution of F_{ST} values for each SNP locus were evaluated among these three breed pairs (Fig 1). In total, 94.74%, 96.42% and 94.03% of SNPs in SW-GR, SW-TP and TP-GR breed pairs had very low F_{ST} value ranged from 0 to 0.1. Approximately 0.37%, 0.22% and 0.50% of SNPs showed high F_{ST} value ranged from 0.2 to 0.3, where as only a few SNPs (0.05%, 0.03% and 0.07%) had very high F_{ST} value ranged from 0.3 to 0.4 in these respective breed pairs. Similar to this study, Makina *et al.* (2015) also observed a less proportion of SNPs (31%) with F_{ST} ≤0.05 among South African cattle breeds.

SNP windows and Selection signatures

F_{ST} analysis identified 86419, 86452 and 86706 sliding windows after including 5 consecutive SNPs into a single window in order to identify the genome-wide selection signatures among the Indian cattle breeds. The average F_{ST} value in each SNP window was estimated and plotted as Manhattan plot for all the chromosomes in three breed pairs. The Manhattan plot identified 122, 81 and 191 SNP windows (F_{ST}>0.25) for SW-GR, SW-TP and TP-GR, respectively (Fig 2, 3 and 4). These most differentiated SNP windows with F_{ST}>0.25 represented the top 0.14%, 0.09% and 0.22% of the total SNP windows in these three respective breed pairs. Makina *et al.* (2015) reported the top 2% SNPs with the highest (F_{ST}<0.25) as the selection signature regions in South African cattle.

Functional annotation of selection signature regions

These genomic regions showing evidences of positive selection are further investigated to identify the underlying candidate genes and their association with milk performance traits in our indigenous cattle.

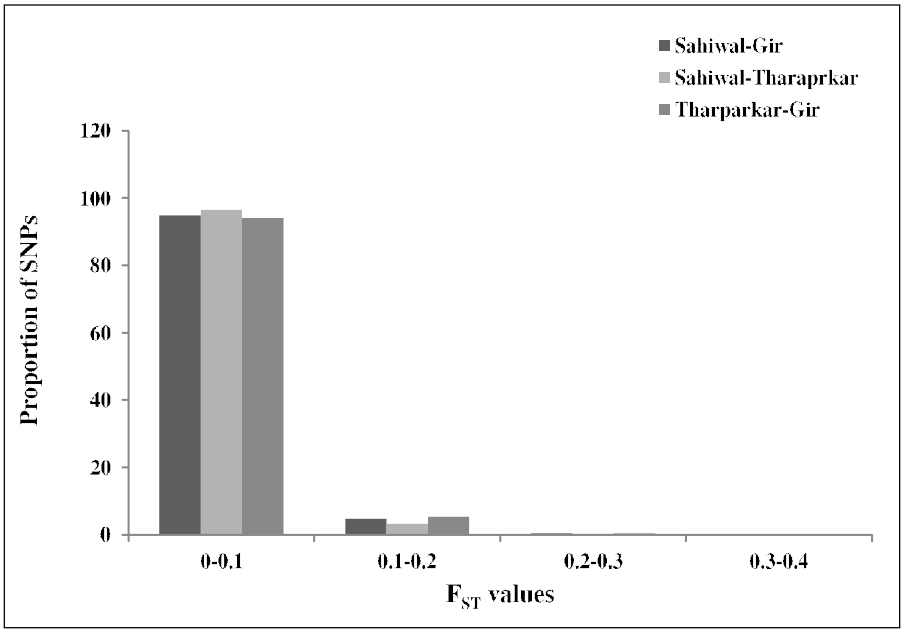

Fig 1: Distribution of F_{ST} values of SNPs among Sahiwal-Gir, Sahiwal-Tharparkar and Tharparkar-Gir pairs.

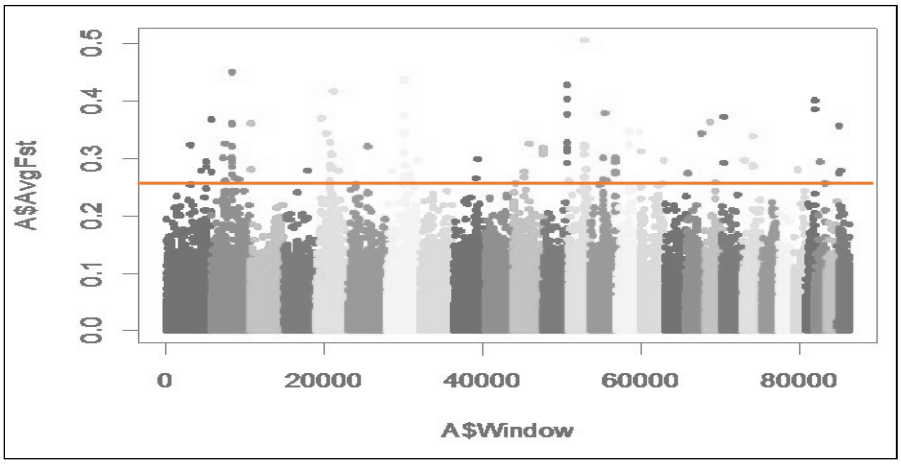

Fig 2: Genome scan for selection signatures among Sahiwal-Gir breed pair using Fst approach.

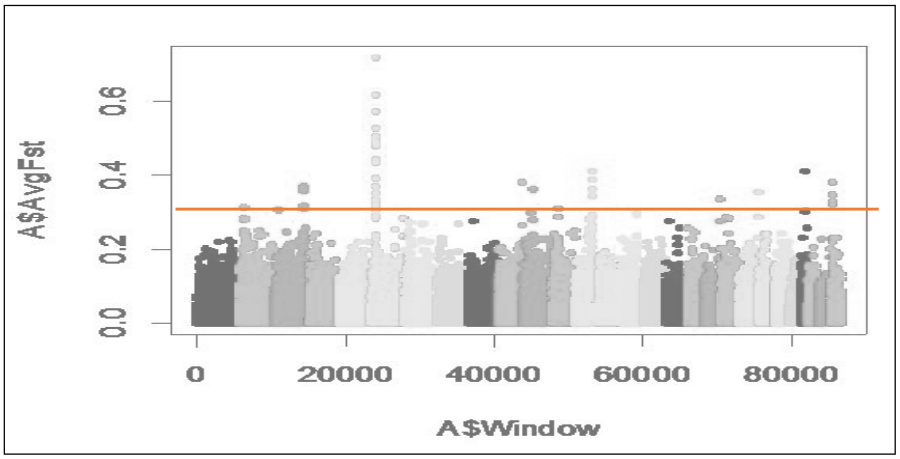

Fig 3: Genome scan for selection signatures among Sahiwal-Tharparkar breed pair using Fst approach.

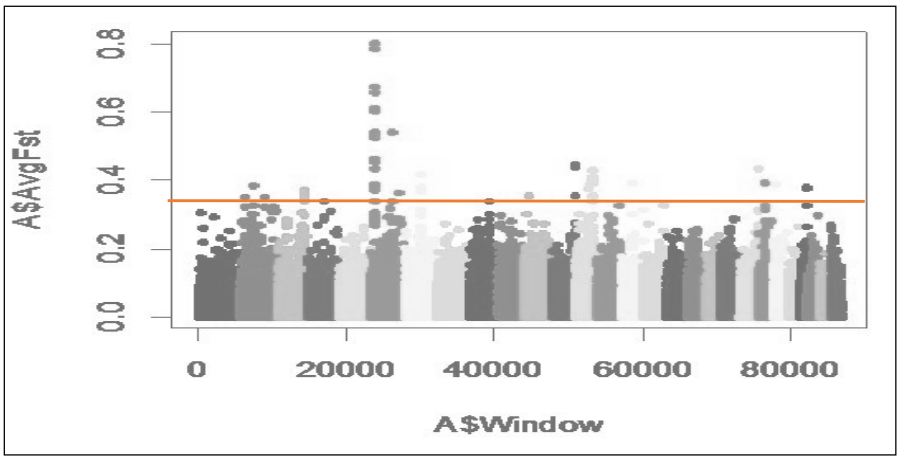

Fig 4: Genome scan for selection signatures among Tharparkar-Gir breed pair using Fst approach.

SW-GR pair

A total of 41 genome-wide selection signature regions were identified in SW-GR breed pair on F_{ST} statistics and these selection signatures contained 48 candidate genes. Notable candidate genes controlling milk performance traits were identified as ACADL, SLC26A2, PLCB1, SYT9 on chromosome 2, 7, 13 and 15, respectively (Table 1). Dias *et al.,* 2015 reported that Acyl-Coenzyme A dehydrogenase (ACADL) gene involved in metabolism of lipid and lipoproteins and plays a key role in the regulation of channeling of fatty acids towards copious milk fat synthesis in the mammary gland. Similarly, the putative selection signature region bearing solute carrier family 26-member 2 (SLC26A2) gene was responsible for carbohydrate metabolism and trans-membrane transport of sulfate like macronutrients in cell (Brenig *et al.,* 2003). Saravanan *et al.* (2021) revealed Phospholipase C beta 1 (PLCB1) gene related to milk production trait as a candidate gene among the indicine cattle breeds using F_{ST} method. Furthermore, chromosome 15 had a strong differentiating region (F_{ST}> 0.35) between 45986438-45998876 bp containing synaptotagmin 9 (SYT 9) gene, which was found in association with calcium binding and phospholipid binding in the present investigation (Table 1).

In addition to these candidate genes, a number of positively selected genes were associated with muscle and carcass traits (GAS2L3), amino acid and protein metabolism (TBC1D20), calcium binding and signal transduction (ATP2C1, GRM5) in the present study. A strong putative selection signature region on chromosome 7 includes TNFAIP8L1 gene which is involved in immune function and in the acute inflammatory response in cattle. Moreover, HSPB6 gene (Heat shock protein family B member 6) mapped on chromosome 18 suggests a strong selection signature in cattle which was associated with thermo-tolerance (Table 1). Kumar *et al.* (2015) reported the variants of HSPB6 gene in Sahiwal cattle for better thermo-tolerance capacity. Makina *et al.* (2015) detected one heat shock protein gene (HSPB9) under selection on BTA19 between 42.8-42.8 Mb, which was associated with adaptation to tropical environments in South African Zebu cattle.

SW-TP pair

We found 29 selection signatures for SW-TP breed pair based on F_{ST} analysis which are distributed over 423.93 kb region across 12 chromosomes. These selection signature regions had 30 candidate genes under positive selection, out of which five genes control the milk performance traits viz., ATPAF1, LEF1, PPARGC1B, EIF6 and ACSS3 mapped on chromosome 3, 6, 7, 13 and 20, respectively (Table 1). The ATPAF1 (ATP synthase mitochondrial F1 complex assembly factor 1) gene encodes an enzyme which involves in energy production through mitochondrial biogenesis in cell. Zhao *et al.* (2015) reported a selection signature region around the gene ATPAF1 on chromosome 3 in Angus cattle. The positively selected lymphoid enhancer-binding factor-1 (LEF1) gene is associated with Wnt signaling during the morphogenesis of the mammary gland during embryogenesis (Raven *et al.*, 2014). The chromosome 7 harbours a strong differentiation region among Tharparkar and Gir cattle containing peroxisome proliferator-activated receptor gamma coactivator 1 beta (PPARGC1B) gene which was associated with oxidation of lipid, energy homeostasis in cattle (Romao *et al.*, 2014). We found selection signatures for eukaryotic translation initiation factor 6 (EIF 6) gene and Acyl-Coenzyme A synthetase short-chain family member 3 (ACSS3) gene as a candidate gene for milk fat composition in cattle (Buitenhuis *et al.,* 2014).

In this study, a strongly selected CAPN5 gene was related with proteolytic activity in cell, marbling score and meat tenderness in cattle (Table 1). Wang *et al*. (2019) reported CAPN as a potential candidate gene for meat quality in Chinese Wagyu cattle. We detected a candidate region on chromosome 13 which harbours Agouti Signaling Protein (ASIP) gene influencing coat colour in cattle. Randhawa *et al.* (2014) reported a strong selection signature for coat colour around ASIP gene in cattle. Furthermore, SLIT3 encoded the inflammatory mediators such as IL-1β,

IL-6 and IL-8 and this gene was key regulator of pulmonary immune response during bovine respiratory disease complex in Holstein calves (Neibergs *et al.*, 2014). One selection signature region was found at TDRD9 which had an important role during spermatogenesis which is essential for germ line integrity in cattle (Table 1).

Table 1: Candidate genes with their functions within selection signature regions among dairy cattle breeds.

BTA	Position in UMD3.1	Smoothed F_{ST}	Candidate genes	Functions
			SW-GR	
1	140441380 - 140524195	0.31	ATP2C1	Calcium ion binding and signal transduction and ATP binding
2	98418803 - 98425203	0.26	ACADL	Fatty acid metabolism, Metabolism of lipids and lipoproteins and Beta-oxidation
5	64840446 - 64856596	0.42	GAS2L3	As growth modular for carcass trait in cattle
7	20688040 - 20715012	0.28	MYDGF	Angiogenesis, Endothelial cell proliferation and apoptotic process
			TNFAIP8L1	Association with immunity in cattle
7	63278956 - 63300781	0.39	SLC26A2	Metabolism of carbohydrates and trans-membrane transport of small molecules
13	1672104 - 1676337	0.26	PLCB1	Calcium signalling pathway, Carbohydrate metabolism and Phopholipase D signalling pathway
13	61128876 - 61141756	0.27	TBC1D20	Protein metabolism and GTPase activity
15	45986438 - 45998876	0.35	SYT9	Calcium and phospholipid binding
18	46644681 - 46657611	0.34	HSPB6	Adipocyte differentiation of bovine intramuscular fibroblast-like cells mRNA splicing *via* spliceosom Thermo-tolerance in Sahiwal cattle
29	6966128 - 6981860	0.32	GRM5	Calcium signalling pathway and Phospholipase D signalling pathway
			SW-TP	
3	100088096 – 100113162	0.36	ATPAF1	Mitochondrial biogenesis
6	18348426 -18382507	0.33	LEF1	Morphogenesis of mammary gland during embryogenesis
7	63139782 -63147200	0.27	PPARGC1B	Milk fat synthesis, Oxidation of lipid, Concentration of palmitic acid, stearic acid and cholesterol
13	64220819-64228423	0.40	ASIP	Coat colour (Type 3 Melanocortin receptor binding)
13	65209329	0.33	EIF6	Ribosome biosynthesis and regulation of fatty acid biosynthetic process
15	57262915 - 57267400	0.30	CAPN5	Proteolytic activity and meat tenderness
20	833408	0.46	ACSS3	Fatty acid metabolism and candidate gene for milk fat composition
20	861460	0.33	SLIT3	Inflammatory mediators such as IL-1β, Il-6 and IL-8, Angiogenesis and organogenesis
21	70159130 - 70193501	0.32	TDRD9	An important role during spermatogenesis which is essential for germ line integrity
			TP-GR	
2	17916659 - 17933165	0.32	CCDC141	Marbling in muscle and meat quality in cattle
2	36436710 - 36486642	0.28	PLA2R1	Phospholipase A2 Receptor activity and involved in proinflammatory cytokine productions during endotoxic shock
2	118237069 - 118243808	0.29	DNER	regulating puberty and associated with age at first calving (AFC) in cattle
3	93885498 - 93955184	0.28	SCP2	Lipid metabolism and Beta oxidation of fatty acid in cattle PPAR signaling pathway
3	100080472 - 100088096	0.37	ATPAF1	Assembly of mitochondrial F1-F0 complex and mitochondrial biogenesis
4	38539462 - 38544621	0.27	CACNA2D1	Association with milk somatic cell score and mastitis resistance in cattle
4	66045465 - 66089621	0.30	CRHR2	Fat accumulation and marbling in muscle, Associated with fat and organoleptic traits in cattle
6	18332881 - 18397886	0.32	LEF1	Morphogenesis of mammary gland during embryogenesis
11	31136597 - 31139229	0.27	FSHR	Follicle-stimulating hormone receptor activity and G-protein coupled peptide receptor activity
22	22004775 - 22007690	0.34	SUMF1	Metabolism of lipids and lipoproteins

TP-GR pair

There were 60 selection signature regions in TP-GR breed pair which were spread over 1541.12 kb genomic region across 19 chromosomes and they harbour 60 candidate genes. The candidate genes *viz*. PLA2R1, SCP2, ATPAF1, CACNA2D1, LEF1 and SUMF1 mapped on chromosome 2, 3, 4, 6 and 22 were found involving with lipid metabolism, carbohydrate metabolism and morphogenesis of mammary gland (Table 1). Devadasan *et al.* (2020) identified 2871 high quality genome-wide SNPs in 383 candidate genes related to milk production, fertility, carcass, adaptability and immune response of economically important traits in Tharparkar cattle.

Our analysis revealed Phospholipase A2 receptor 1 (PLA2R1) gene on chromosome 2 having a strong differentiation (F_{ST}> 0.28) between Tharparkar and Gir cattle was known to catalyze hydrolysis of phospholipids (Balsinde *et al.,* 2002) and involved in pro-inflammatory cytokine production in the mammary gland epithelial cells in cattle. Another gene sterol carrier protein 2 (SCP 2) on chromosome 3 was related with lipid metabolism and beta oxidation of fatty acid in cattle (Stolowich *et al.,* 2002). This gene was also significantly differentially expressed in Peroxisome Proliferator-Activated Receptors signaling pathway, which was activated by fatty acids and their derivatives. As described earlier, the ATP synthase mitochondrial F1 complex assembly factor 1 (ATPAF1) and lymphoid enhancer-binding factor-1 (LEF1) gene were identified as candidate gene under selection between Tharparkar and Gir cattle. The variants of CACNA2D1 gene were also found to be associated with somatic cell score (SCS) and mastitis resistance/susceptibility in Sahiwal cattle (Magotra *et al.,* 2016) of India. The sulfatase modifying factor 1 (SUMF1) gene on chromosome 22 was also found within the selection signature region and this gene is related with the metabolism of lipids and lipoproteins.

The genes within the selection signature region (CCDC141 and CRHR2) were associated with marbling in muscle meat quality traits in cattle. One selection signature region at DNER gene had an important role in regulating puberty and age at first calving, while another gene FSHR (Follicle Stimulating Hormone Receptor) on chromosome 11 controls the reproduction in cattle (Table 1). Cory *et al.* (2013) revealed seven SNPs in the coding region of the bovine FSHR gene and suggested that specific alleles of the bovine FSHR gene were associated with the embryo yield and number of unfertilized oocytes in cattle.

CONCLUSION

The present investigation provided a genome-wide map of selection footprints in association with milk performance traits among three indigenous dairy cattle breeds. Several candidate genes were also detected as putative targets for selection for thermo-tolerance, disease resistance, immunity, reproduction and coat colour. Moreover, a comprehensive understanding of how selection has acted on genome would provide an important conceptual framework with regard to evolution in our indigenous cattle. Therefore, this information may lead to better understand the mechanisms behind natural and artificial selection in domesticated cattle.

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REFERENCES

Balsinde, J., Winstead, M.V. and Dennis, E.A. (2002). Phospholipase A (2) regulation of arachidonic acid mobolization. FEBS Letters. 531: 2-6.

Brenig, B., Baumgartner, B.G., Kriegesmann, B., Habermann, F., Fries, R. and Swalve, H.H. (2003). Molecular cloning, mapping and functional analysis of the bovine sulfate transporter SLC26a2 gene. Gene. 319: 161-166.

Buitenhuis, B., Janss, L.L., Poulsen, N.A., Larsen, L.B., Larsen, M.K. and Sorensen, P. (2014). Genome-wide association and biological pathway analysis for milk-fat composition in Danish holstein and danish jersey cattle. BMC Genomics. 15: 1112.

Cory, A., Price, C., Lefebvre, R. and Palin, M. (2013). Identification of single nucleotide polymorphisms in the bovine follicle-stimulating hormone receptor and effects of genotypes on superovulatory response traits. Animal Genetics. 44(2): 197-201.

Devadasan, M.J., Kumar, D.R. *et al.* (2020). Reduced representation approach for identification of genome-wide SNPs and their annotation for economically important traits in Indian Tharparkar cattle. 3 Biotech. 10(7): 309.

Dias, M.M., Souza, F.R.P. *et al.* (2015). Study of lipid metabolism-related genes as candidate genes of sexual precocity in Nellore cattle. Genetics and Molecular Research. 14(1): 234-243.

Dixit, S.P., Singh, S., Ganguly, I., Bhatia, A.K., Sharma, A., Kumar, N.A., Dang, A.K. and Jayakumar, S. (2021). Genome-wide runs of Homozygosity revealed selection signatures in *Bos indicus*. Frontiers in Genetics. 11: 92.

Flori, L., Fritz, S., Jaffrezic, F., Boussaha, M., Gut, I., Heath, S., Foulley, J.L. and Gautier, M. (2009). The genome response to artificial selection: A case study in dairy cattle. PLoS ONE. 4(8): e6595.

Goudet, J. (2005). HierFstat, a package for R to compute and test variance components and F-statistics. Molecular Ecology Notes. 5: 184-186.

Kumar, R., Gupta, I.D., Verma, A., Verma, N., Magotra, A. and Vineeth, M.R. (2015). Molecular characterization and polymorphism detection in HSPB6 gene in Sahiwal cattle. Indian Journal of Animal Research. 49(5): 595-598.

Liao, X., Peng, F., Forni, S., McLaren, D., Plastow, G. and Stothard, P. (2013). Whole genome sequencing of gir cattle for identifying polymorphisms and loci under selection. Genome. 56(10): 592-598.

Magotra, A., Gupta, I.D., Verma, A., Alex, R. and Vineeth, M.R. (2016). Characterization and validation of SNPs in exon 19 of CACNA2D1 gene and its relationship with mastitis traits in Indigenous cattle. International Journal of Biotechnology and Biomedical Sciences. 2(2): 168.

Makina, S.O., Muchadeyi, F.C., van Marle-Koster, E., Taylor, J.F., Makgahlela, M.L. and Maiwashe, A. (2015). Genome-wide scan for selection signatures in six cattle breeds in South Africa. Genetics Selection Evolution. 47: 92.

Mancini, G., Gargani, M., Chillemi, G. *et al*. (2014). Signatures of selection in five Italian cattle breeds detected by a 54K SNP panel. Molecular Biology Reports. 41(2): 957-965.

Neibergs, H.L., Seabury, C.M. *et al*. (2014). Susceptibility loci revealed for bovine respiratory disease complex in pre-weaned Holstein calves. BMC Genomics. 15: 1164.

Purcell, S., Neale, B., Todd-Brown, K. *et al*. (2007). PLINK: A toolset for whole-genome association and population-based linkage analysis. American Journal of Human Genetics. 81: 559-575.

R. Development Core Team (2008). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

Randhawa, I.A.S., Khatkar, M.S., Thomson, P.C. and Raadsma, H.W. (2014). Composite selection signals can localize the trait specific genomic regions in multi-breed populations of cattle and sheep. BMC Genetics. 15: 34.

Raven, L.A., Cocks, B.G., Goddard, M.E., Pryce, J.E. and Hayes, B.J. (2014). Genetic variants in mammary development, prolactin signalling and involution pathways explain considerable variation in bovine milk production and milk composition. Genetics Selection Evolution. 46: 29.

Romao, J., Jin, W., He, M., Mcallister, T. and Guan, L. (2014). MicroRNAs in bovine adipogenesis: Genomic context, expression and function. BMC Genomics. 15: 137.

Saravanan, K.A., Panigrahi, M., *et al*. (2021). Genomic scans for selection signatures revealed candidate genes for adaptation and production traits in a variety of cattle breeds. Genomics. 113: 955-963.

Singh, A., Mehrotra, A., Gondro, C. *et al*. (2020). Signatures of selection in composite vrindavani cattle of India. Frontiers in Genetics. 11: 589496.

Singh, M., Mir, M., Gupta, A. and Gupta, I. (2019). Effect of non-genetic factors on milk yield and composition traits of sahiwal cattle at organized dairy farm. International Journal of Livestock Research. 9(12): 135-141.

Stolowich, N.J., Petrescu, A.D., Huang, H., Martin, G.G., Scott, A.I. and Schroeder, F. (2002). Sterol carrier protein-2: Structure reveals function. Cellular and Molecular Life Sciences. 59(2): 193-212.

Vineeth, M.R., Surya, T., Sivalingam, J. *et al*. (2020). Genome-wide discovery of SNPs in candidate genes related to production and fertility traits in Sahiwal cattle. Tropical Animal Health and Production. 52: 1707-1715.

Wang, Z., Ma, H., Xu, L., Zhu, B. *et al*. (2019). Genome-wide scan identifies selection signatures in chinese wagyu cattle using a high-density SNP array. Animals. 9(6): 296.

Weir, B.S. and Cockerham, C.C, (1984). Estimating F-statistics for the analysis of population structure. Evolution. 38: 1358-1370.

Zhao, F., McParland, S., Kearney, F., Du, L. and Berry, D. (2015). Detection of selection signatures in dairy and beef cattle using high-density genomic information. Genetics Selection Evolution. 47(1): 49.