Proceeding Paper

Genome-Wide Screening for SNPs Associated with Stature in Diverse Cattle Breeds [†]

Alexandra S. Abdelmanova [1,*], Alexander A. Sermyagin [1], Arsen V. Dotsev [1], Nikolay V. Bardukov [1], Margaret S. Fornara [1], Gottfried Brem [1,2] and Natalia A. Zinovieva [1]

[1] L.K. Ernst Federal Research Center for Animal Husbandry, Dubrovitsy, Podolsk Municipal District, Moscow Region, 142132 Podolsk, Russia; alex_sermyagin85@mail.ru (A.A.S.); asnd@mail.ru (A.V.D.); bardukv-nikolajj@mail.ru (N.V.B.); margaretfornara@gmail.com (M.S.F.); gottfried.brem@vetmeduni.ac.at (G.B.); n_zinovieva@mail.ru (N.A.Z.)

[2] Institute of Animal Breeding and Genetics, University of Veterinary Medicine (VMU), Veterinärplatz, A-1210 Vienna, Austria

[*] Correspondence: preevetic@mail.ru

[†] Presented at the 2nd International Electronic Conference on Diversity (IECD 2022)—New Insights into the Biodiversity of Plants, Animals and Microbes, 15–31 March 2022; Available online: https://sciforum.net/event/IECD2022.

Abstract: Cattle breeds used in industrial production tend to have a larger size compared to the local cattle, as the increased dairy and beef productivity is closely related to the stature. The aim of our work was to identify single nucleotide polymorphisms (SNPs), which are significantly associated with stature in diverse cattle breeds. Thirteen local and transboundary cattle breeds ($n = 670$) subjected to our study were divided in two groups according to the stature. The high-stature group included Angus, Ayrshire, Black-and-White, Holstein, Kholmogor, Yaroslavl, Tagil and Istoben breeds. The low-stature group comprised of Jersey, Kalmyk, Kyrgyz, Mongolian and Yakut cattle. The average height at withers was 136.3 ± 1.6 and 121.6 ± 2.8 cm in the high- and low-stature groups, respectively. The samples of 11 breeds were genotyped using high-density DNA arrays (Illumina Inc., USA). The genotypes of two remaining breeds were downloaded from the publicly available WIDDE database. Genome-wide association studies revealed four SNPs, which were strongly associated with the stature, including three SNPs at 77.3–77.8 cM on BTA4 (map53144-ss46525999, $p < 7.747 \times 10^{-101}$; BovineHD0400021479, $p < 1.173 \times 10^{-91}$; ARS-BFGL-NGS-116590, $p < 7.665 \times 10^{-105}$) and one SNPs at 25.2 cM on BTA14 (BovineHD1400007259, $p < 1.324 \times 10^{-109}$). Functional annotation showed the localization within identified regions of genes, which are responsible for growth, exterior characteristics, protein and lipid metabolism, and feed intake. Identified SNPs can be considered as useful DNA markers for marker-assistant cattle breeding aimed at increased stature. The study was funded by the Russian Ministry of Science and Higher Education No. 0445-2019-0024.

Keywords: local cattle; SNP; stature; allele frequency

1. Introduction

Animals' stature is closely related to the productivity. Many studies have been conducted, which revealed a large number of loci associated with body size in cattle [1,2]. The *PLAG1* gene, which is located on chromosome 14 was the one of the most frequently detected genes in such studies [3–5]. However, the most studies were carried out on commercial breeds of cattle that have been subjected to the strong artificial selection pressures. Although comprehensive genome-wide studies of Russian local cattle breeds were carried out [6–9], the genetic basis of stature in these breeds was not investigated until now. Local breeds usually have lower productivity compared to commercial breeds but exceed them in adaptability to climate condition. Thus, they can be useful as a reserve of genetic diversity in breeding programs.

The aim of our work was to identify single nucleotide polymorphisms (SNPs), which are significantly associated with stature in commercial and local cattle breeds bred in Russia.

2. Materials and Methods

A total of 670 samples of thirteen local and transboundary cattle breeds, including Aberdeen-Angus (ANG, *n* = 39), Ayrshire (AYR, *n* = 144), Black-and-White (BLW, *n* = 50), Holstein (HLS, *n* = 184), Istoben (IST, *n* = 22), Jersey (JRS, *n* = 32), Kalmyk (KLM, *n* = 27), Kholmogor (KHL, *n* = 26), Kyrgyz (KRG, *n* = 24), Mongolian (MNG, *n* = 26), Tagil (TAG, *n* = 26), Yakut (YKT, *n* = 29) and Yaroslavl (YRS, *n* = 41), were subjected to our study.

Domestic Animal Diversity Information System (DAD-IS) [http://www.fao.org/dad-is/en (accessed on 1 October 2021)] maintained and developed by FAO was used to obtain the mean values for height at withers for studied breeds. Each breed was assigned the average breed value for the height at withers.

The samples of 11 breeds were genotyped using high-density DNA arrays (Illumina Inc., USA) in the L.K. Ernst Federal Research Center for Animal Husbandry. The genotypes of two remaining breeds were downloaded from the publicly available WIDDE database [http://widde.toulouse.inra.fr/wide (accessed on 1 October 2021)].

To identify SNPs that are significantly associated with height at withers we performed across-breed genome-wide association studies using a multivariate linear-mixed model implemented in the program PLINK 1.9.

3. Results and Discussion

Cattle breeds were divided in two groups according to the stature. The high-stature group included Angus, Ayrshire, Black-and-White, Holstein, Kholmogor, Yaroslavl, Tagil and Istoben breeds. The mean values for height at withers for these breeds exceeded the mean values calculated for all the studied breeds. The low-stature group comprised of Jersey, Kalmyk, Kyrgyz, Mongolian and Yakut cattle revealing the less height at withers comparing to the mean value calculated for the entire data set of breeds. The mean values for height at withers in the high- and low-stature groups were 136.3 $\pm$ 1.6 and 121.6 $\pm$ 2.8 cm, respectively (Figure 1).

Almost all low stature breeds (except Jersey) are meat type productivity. They were bred for the centuries by nomadic tribes in the harsh climate of steppes and semi-deserts of Central Asia. These breeds are able to survive under poor forage conditions in short dry summers and cold winters and be quickly fattened up with improved feeding. For this reason, the above mentioned breeds are traditionally bred in regions with severe climates and unstable forage resources.

Genome-wide association studies (Figure 2) revealed four SNPs, which are strongly associated with the stature, including three SNPs at 77.3–77.8 cM on BTA4 (map53144-ss46525999, $p < 7.747 \times 10^{-101}$; BovineHD0400021479, $p < 1.173 \times 10^{-91}$; ARS-BFGL-NGS-116590, $p < 7.665 \times 10^{-105}$) and one SNPs at 25.2 cM on BTA14 (BovineHD1400007259, $p < 1.324 \times 10^{-109}$).
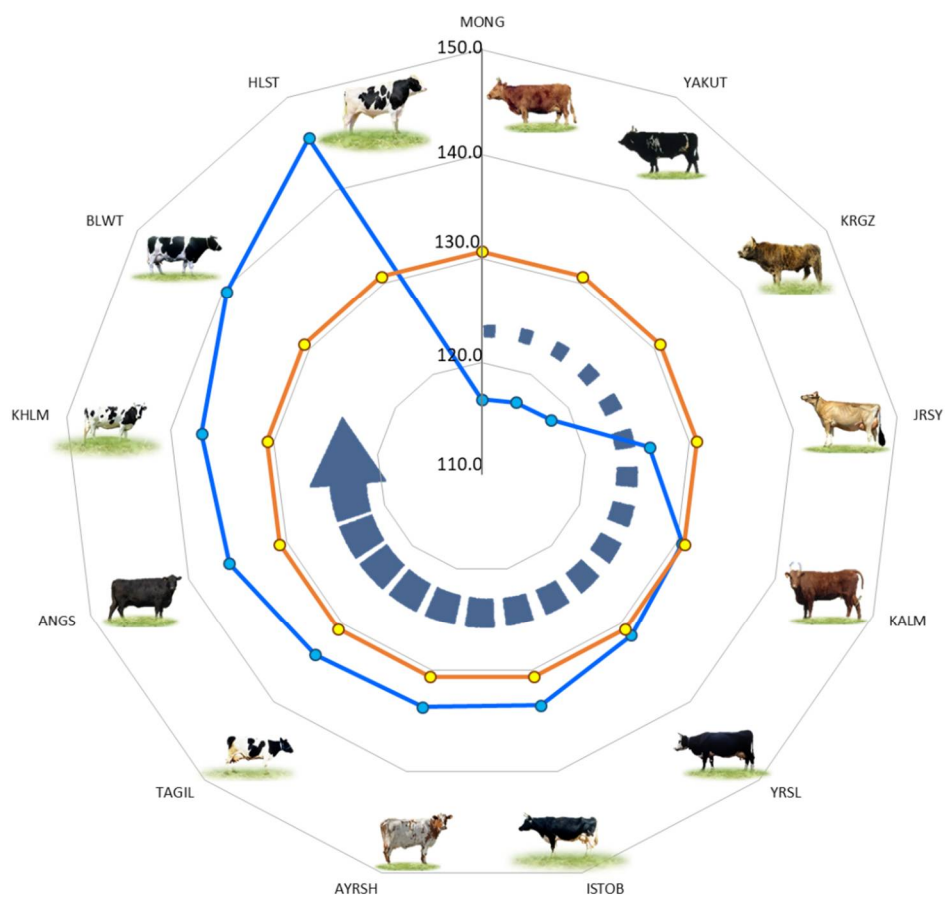
Figure 1. Distribution of cattle breeds according to the mean values for the height at withers. Blue line indicates the mean values calculated for each of the studied breeds; orange line indicates the mean value calculated for the entire data set; the breeds are located clockwise from the breed having the lowest stature (Mongolian cattle) the breed revealing the greatest stature (Holsteins) as it is indicated by an arrow; the breeds' abbreviations are deciphered in the Materials and Methods section.
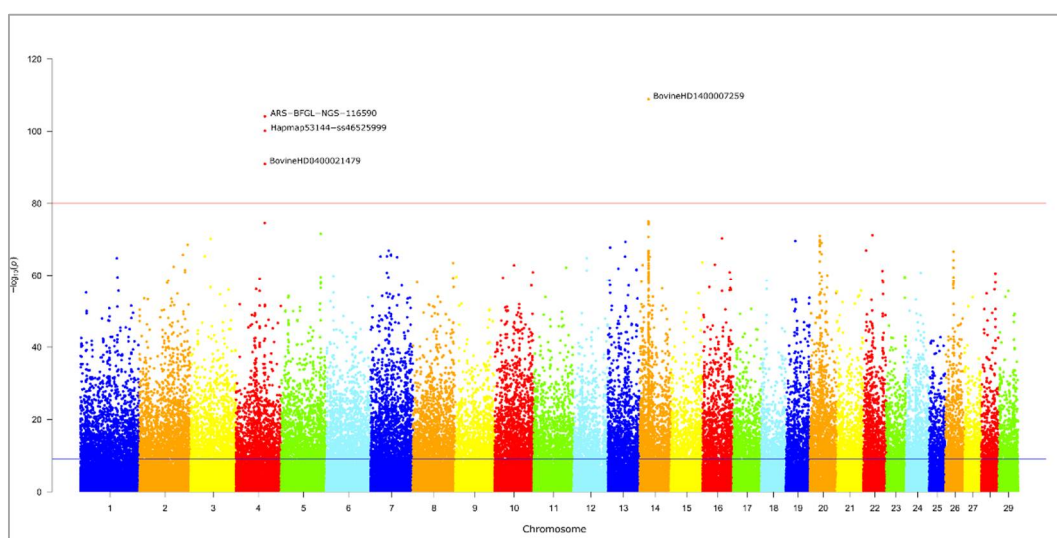

Figure 2. Genome-wide association studies for the height at withers for studied breeds.

The allele frequencies of significantly associated SNPs were calculated in each of two groups (Table 1).

Table 1. Frequencies of alternative alleles at the loci associated with the withers height.

Localization	SNP	Allele	Allele Frequencies	
			High-Stature Breeds	Low-Stature Breeds
Chr 4	ARS-BFGL-NGS-116590	T	0.204	0.349
		G [a]	0.796	0.651
		P [b]	***	***
	Hapmap53144-ss46525999	T [a]	0.795	0.082
		C	0.205	0.918
		p	***	**
	BovineHD0400021479	A	0.201	0.309
		G [a]	0.799	0.647
		p	***	***
Chr 14	BovineHD1400007259	T	0.090	0.959
		G [a]	0.910	0.041
		p	***	ns

a—alleles are associated with greater height at withers. b—** $p < 0.01$; *** $p < 0.001$; ns—not significant.

Our results agree with the previous studies, indicated that 24.8–25.2 Mb region on BTA 14 is strongly related to body size [1,5,10]. Additionally, we identified the 77.3–77.8 Mb region on BTA 4, which was not shown to be associated with stature in previous studies [3,11,12]. The structural and functional annotation revealed the presence of genes, which are associated with metabolism, milk composition and synthesis as well as the average daily gain.

4. Conclusions

Identified SNPs can be considered as useful DNA markers for marker-assistant cattle breeding aimed at increased stature in diverse cattle breeds bred in Russia.

References

1. Bouwman, A.C.; Daetwyler, H.D.; Chamberlain, A.J.; Ponce, C.H.; Sargolzaei, M.; Schenkel, F.S.; Sahana, G.; Govignon-Gion, A.; Boitard, S.; Dolezal, M.; et al. Meta-analysis of genome-wide association studies for cattle stature identifies common genes that regulate body size in mammals. *Nat. Genet.* **2018**, *50*, 362–367. [CrossRef] [PubMed]
2. Takasuga, A. PLAG1 and NCAPG-LCORL in livestock. *Anim. Sci. J.* **2016**, *87*, 159–167. [CrossRef] [PubMed]
3. Randhawa, I.A.S.; Khatkar, M.S.; Thomson, P.C.; Raadsma, H.W. Composite selection signals for complex traits exemplified through bovine stature using multibreed cohorts of European and African Bos taurus. *G3 Genes Genomes Genet.* **2015**, *5*, 1391–1401. [CrossRef] [PubMed]

4. Boitard, S.; Boussaha, M.; Capitan, A.; Rocha, D.; Servin, B. Uncovering adaptation from sequence data: Lessons from genome resequencing of four cattle breeds. *Genetics* **2016**, *203*, 433–450. [CrossRef] [PubMed]
5. Hou, J.; Qu, K.; Jia, P.; Hanif, Q.; Zhang, J.; Chen, N.; Dang, R.; Chen, H.; Huang, B.; Lei, C. A SNP in PLAG1 is associated with body height trait in Chinese cattle. *Anim. Genet.* **2020**, *51*, 87–90. [CrossRef]
6. Abdelmanova, A.S.; Kharzinova, V.R.; Volkova, V.V.; Mishina, A.I.; Dotsev, A.V.; Sermyagin, A.A.; Boronetskaya, O.I.; Petrikeeva, L.V.; Chinarov, R.Y.; Brem, G.; et al. Genetic diversity of historical and modern populations of russian cattle breeds revealed by microsatellite analysis. *Genes* **2020**, *11*, 940. [CrossRef] [PubMed]
7. Abdelmanova, A.S.; Kharzinova, V.R.; Volkova, V.V.; Dotsev, A.V.; Sermyagin, A.A.; Chinarov, R.Y.; Zinovieva, N.A.; Boronetskaya, O.I.; Lutshikhina, E.M.; Sölkner, J.; et al. Comparative study of the genetic diversity of local steppe cattle breeds from Russia, Kazakhstan and Kyrgyzstan by microsatellite analysis of museum and modern samples. *Diversity* **2021**, *13*, 351. [CrossRef]
8. Zinovieva, N.A.; Sermyagin, A.A.; Dotsev, A.V.; Boronetslaya, O.I.; Petrikeeva, L.V.; Abdelmanova, A.S.; Brem, G. Animal Genetic resources: Developing the research of allele pool of Russian cattle breeds—Minireview. *Sel'skokhozyaistvennaya Biol. Agric. Biol.* **2019**, *54*, 631–641. [CrossRef]
9. Sermyagin, A.A.; Dotsev, A.V.; Gladyr, E.A.; Traspov, A.A.; Deniskova, T.E.; Kostyunina, O.V.; Reyer, H.; Wimmers, K.; Barbato, M.; Paronyan, I.A.; et al. Whole-genome SNP analysis elucidates the genetic structure of Russian cattle and its relationship with Eurasian taurine breeds. *Genet. Sel. Evol.* **2018**, *50*, 37. [CrossRef] [PubMed]
10. Karim, L.; Takeda, H.; Lin, L.; Druet, T.; Arias, J.A.; Baurain, D.; Cambisano, N.; Davis, S.R.; Farnir, F.; Grisart, B.; et al. Variants modulating the expression of a chromosome domain encompassing PLAG1 influence bovine stature. *Nat. Genet.* **2011**, *43*, 405–413. [CrossRef] [PubMed]
11. Doyle, J.L.; Berry, D.P.; Veerkamp, R.F.; Carthy, T.R.; Walsh, S.W.; Evans, R.D.; Purfield, D.C. Genomic regions associated with skeletal type traits in beef and dairy cattle are common to regions associated with carcass traits, feed intake and calving difficulty. *Front. Genet.* **2020**, *11*, 20. [CrossRef] [PubMed]
12. Pryce, J.E.; Hayes, B.J.; Bolormaa, S.; Goddard, M.E. Polymorphic regions affecting human height also control stature in cattle. *Genetics* **2011**, *187*, 981–984. [CrossRef] [PubMed]