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Multiple Marker Effects of Single Nucleotide Polymorphisms in Two Genes, *NCAPG* and *PLAG1*, for Carcass Weight in Japanese Black Cattle

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Abstract

Carcass weight is an economically important trait for beef cattle breeding and markets. The previous studies detected two single nucleotide polymorphisms (SNPs) associated with carcass weight of Japanese Black: *c.1326T>G* in *NCAPG* gene and *FJX_250879* in *PLAG1* gene. Here, I carried out multiple marker association analysis for the two SNPs in Japanese Black population of 218 animals. The multiple marker analysis with the model including the main effects of the two SNPs and their interaction detected significant main effects of *c.1326T>G* and *FJX_250879* and a significant interaction between the two SNPs, for carcass weight. These findings suggest the presence of inter-allelic interactions among genes affecting the variation of carcass weight. For effective marker-assisted selection for beef production, interaction between the two markers needs to be considered.

Keywords

Association, Beef Cattle, Carcass Weight, Interaction, SNP

1. Introduction

Carcass weight is one of economically important traits for beef cattle [1]. The detection of genes affecting carcass weight and the establishment of an effective marker-assisted selection technique based on the genomic information are an important goal for the genetic improvement of beef production.

Setoguchi *et al.* [2] identified the *c.1326T>G* single nucleotide polymorphism (SNP) in the *non-SMC condensin I complex, subunit G* (*NCAPG*) gene, which

changes the amino acid Ile442 to Met442 in the encoded protein, as a candidate causative variation for a bovine carcass weight quantitative trait locus (QTL) on chromosome 6. In addition, Karim *et al.* [3] identified the stature quantitative trait nucleotide (QTN) in the *pleiomorphic adenoma gene* 1 (*PLAG1*)-*coiled-coil-helix-coiled-coil-helix domain containing* 7 (*CHCHD7*) intergenic region, as the causative variation for another carcass weight QTL on chromosome 14. Recently, Hoshiba *et al.* [4] compared the effects on growth-related traits of the *c.1326T>G* SNP and the *FJX_250879* SNP that was approximately 50-kb centromeric from the stature QTN and nearly linkage disequilibrium with the QTN on chromosome 14, using Japanese Black steers. As a result, they detected a genetic interaction between the *c.1326T>G* and *FJX_250879* SNPs for body and rump lengths.

Because the two SNPs have relatively large effects on carcass weight, it is important to examine whether a genetic interaction for carcass weight is present between them. Thus, I performed multiple marker analysis for association with carcass weight, using the model including the main effects of the two SNPs and their interaction in Japanese Black beef cattle.

2. Materials and Methods

2.1. Samples and Data

Two hundred eighteen paternal half-sib Japanese Black steers were produced from 53 sires (1 - 16 steers per sire) in Niigata prefecture. Hair root specimens of the progeny steers were provided from Niigata Agricultural Research Institute Livestock Research Center, and were used for genotyping the SNPs. DNA samples were prepared from the materials using DNeasy Blood & Tissue kit (Qiagen, Hilden, Germany), according to the manufacturer's instructions. The carcass weight was measured according to the Japanese meat grading system by certified graders from the Japan Meat Grading Association (Tokyo, Japan) [1]. The records of carcass weight for the progeny steers were obtained from the Niigata Prefectural Headquarters, National Federation of Agricultural Cooperative Association (Niigata, Japan).

2.2. SNP Genotyping

The *c.1326T>G* SNP was genotyped by the PCR-restriction fragment length polymorphism method as described previously [5]. The *FJX_250879* SNP was genotyped by direct sequencing of the PCR products according to Nishimura *et al.* [6]. Primers used in this study were shown in **Table 1**. In the Japanese Black population, the *C*-allele of *FJX_250879* increases carcass weight and corresponds to the *Q* (superior) allele of the stature QTN [6].

2.3. Association Analysis

I performed association analysis with multiple marker model of the two SNPs, *c.1326T>G* and *FJX_250879*, in which carcass weight records were used as the

Table 1. PCR primers used in this study.

SNP	Sequences
c.1326T>G	5'-ATT TAG GAA ACG ACT ACT GG-3'
	5'-ATT TGT ATT CTC TTA TTA TCA TC-3'
FJX_250879	5'-ATG GGA TCA CCA CAG ACC AT-3'
	5'-TGC ACA GAA TCA GTG TGT CTT TT-3'

dependent variable. The model included the two SNPs and their gene to gene (inter-allelic) interaction effect between the SNPs, slaughter years and months, and fattening farms as the fixed effects, and the sires as the random effect. The slaughter age of the animals was included as a covariate in linear regression. The analysis was performed by the MIXED procedure of the SAS program (SAS Institute, Inc., Cary, NC).

3. Results and Discussion

Using the multiple marker association analysis, I analyzed the main effects of the two SNPs, *c.1326T>G* and *FJX_250879*, and their gene to gene interaction effect for carcass weight. The main effects of *c.1326T>G* and *FJX_250879* were statistically significant (P = 0.0272 for *c.1326T>G* and P = 0.0235 for *FJX_250879*) (**Table 2**). The least-squares mean of the *GG* homozygote of *c.1326T>G* was significantly higher than the mean of the *TT* homozygote, and the mean of the heterozygote was intermediate. The mean of the *CC* homozygote of *FJX_250879* was significantly higher than that of the *GG*, and the mean of the heterozygote was intermediate. These results correspond with the previous studies [2] [6] where it was concluded that the favorable alleles for carcass weight were *G* at *c.1326T>G* and *C* at *FJX_250879*. The interaction between *c.1326T>G* and *FJX_250879* was statistically significant for carcass weight (P = 0.0147) (**Table 2**). The combination of *TT* at *c.1326T>G* and *GG* at *FJX_250879* gave a marked decrease.

In the multiple marker analysis of this study, *c.1326T>G* and *FJX_250879* had significant main effects on carcass weight with the same favorable tendency of alleles as previous studies [2] [6]. Further, I detected a significant epistatic interaction between *c.1326T>G* and *FJX_250879* for carcass weight. These findings suggest that *c.1326T>G* and *FJX_250879*, respectively, affect carcass weight both directly and through its interaction with *FJX_250879* and *c.1326T>G*.

The maximum difference between the largest and smallest combined genotypic effects of the two SNPs was expected as 101.96 in carcass weight scale (= 33.10 − [−68.86]; see below) based on **Table 2**. The largest effect came from the combination of *GG* at *c.1326T>G* (5.40) and *CC* at *FJX_250879* (10.72), and the interaction between *GG* at *c.1326T>G* and *CC* at *FJX_250879* (16.98) (*i.e.* 5.40 + 10.72 + 16.98 = 33.10). The smallest effect came from the respective combination of *TT* (−7.45) and *GG* (−14.78), and the interaction between *TT* at *c.1326T>G* and *GG* at *FJX_250879* (−46.63) (*i.e.* [−7.45] + [−14.78] + [−46.63] = [−68.86]).

Table 2. Main and interaction effects of the two single nucleotide polymorphisms (SNPs) for carcass weight in the multiple marker analysis using 218 animals.

SNP	Genotype	n^1	LSM[2]
c.1326T>G	*TT*	102	−7.45 ± 4.13[a]
(*P* = 0.0272)	*TG*	98	2.05 ± 2.91[b]
	GG	18	5.40 ± 2.12[c]
FJX_250879	*GG*	63	−14.78 ± 3.75[a]
(*P* = 0.0235)	*GC*	106	4.07 ± 3.07[b]
	CC	49	10.72 ± 4.21[c]
c.1326T>G & *FJX_250879*	*TT* & *GG*	26	−46.63 ± 30.70[a]
(*P* = 0.0147)	*TT* & *GC*	51	12.52 ± 7.68[b]
	TT & *CC*	25	19.54 ± 17.73[b]
	TG & *GG*	32	−8.13 ± 15.70[ab]
	TG & *GC*	46	12.65 ± 7.04[b]
	TG & *CC*	20	18.21 ± 12.34[b]
	GG & *GG*	5	27.77 ± 15.35[b]
	GG & *GC*	9	11.17 ± 8.21[b]
	GG & *CC*	4	16.98 ± 11.56[b]

[1]Number of genotyped animals. [2]Least-squares mean (LSM) ± SE of carcass weight. LSMs are shown as the deviation from the general mean of carcass weight. [a,b,c]Statistically significant among means with different superscripts ($P < 0.05$). *p* value was shown in the parentheses.

An epistatic interaction is measured as the departure of the combined effects of two or more genes from the sum of their individual effects [7]. This phenomenon is thought to play a significant role in evolution [8] [9]. Matsuhashi *et al.* [10] recently clarified multiple marker effects of four gene polymorphisms on the fatty acid composition and several carcass traits in Japanese Black cattle, but detected no epistatic interactions. However, I detected a possible epistatic interaction for carcass weight between *NCAPG* (*c.1326T>G*) and *PLAG1* (*FJX_250879*), the strongest candidate gene for the carcass weight QTL on chromosome 14. Although the functional relevance of such an interaction is still unknown, *NCAPG* is involved in arginine metabolism [11] and *PLAG1* in regulation of the expression of growth factors, including insulin-like growth factor 2 [12]. An interaction between them could play an important role in the variation of carcass weight in beef cattle. For confirmation of the presence of the interaction, other replication studies are recommended using other Japanese Black populations. In addition, a further investigation on detection of an epistatic interaction among three or more genes affecting the variation of carcass weight would be required for effective marker-assisted selection.

4. Conclusion

In conclusion, I have demonstrated significant associations and interaction of

two SNPs, referred to as *c.1326T>G* and *FJX_250879*, for carcass weight in Japanese Black population. For the effective genetic improvement of beef production in Wagyu population, the role of interactions among SNP markers under marker-assisted selection should be considered.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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