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Characterization and Associations of Haplotypes Containing PLAG1 in Cattle

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Summary and Implications

Genomic regions tend to be inherited in blocks known as haplotypes. The general region spanning *PLAG1* shows association with various traits in beef cattle. There are few haplotypes spanning *PLAG1*, and these are common across breeds but do not capture the true effect. Higher density 770K genotyping demonstrates greater diversity of haplotypes in this region. The tag SNP in Holstein and Jersey dairy cattle segregates in Hereford cattle who show no effect in this region. Collectively, these results show the 50K SNP chip has inadequate coverage in this region of the genome.

Introduction

Body weight is an economically important trait for livestock, therefore the genetic determinants of body weight has become the focus of numerous genetic studies. Karim et al (2011) reported a genomic interval on *Bos taurus* chromosome 14 (BTA14) with a major effect on stature and weight in dairy cattle, and then identified several tightly linked polymorphic markers as potential causative genetic elements. These variants influenced expression of the surrounding genes, including *PLAG1* whose knockout in mice causes dwarfism in the absence of other symptoms. Littlejohn et al (2011) confirmed this effect by demonstrating strong association between body weight and *PLAG1* genotype.

We previously identified the *PLAG1* region as having strong associations with body weights and calving ease in Gelbvieh and Simmental populations, and carcass weight in Brangus. It is not known whether other breeds such as Angus and Hereford that have no evidence of a QTL here are homozygous for the large or the small variant at this locus. It is also unclear if the same mutation is associated with body weights in Brangus, Gelbvieh and Simmental animals or whether different mutation(s) in *PLAG1* or nearby genes cause this variation. We plan to identify mutations in this region across a range of cattle breeds to improve genomic prediction. This GC-rich region is hard to sequence using Illumina technology and is better suited to PacBio sequencing technology that provides longer reads. First, we need to identify the most suitable animals to sequence.

Materials and Methods

The genotypes of over 60,000 cattle characterized with Illumina 50K or 770K beadchips were scrutinized in the interval from 24 to 26 Mb on BTA14. This interval is centered on the *PLAG1* location containing the mutation believed to be causal in Holstein and Jersey cattle. Haplotypes were formed for BTA14 using BEAGLE on about 30,000 of these cattle. Diplotypes and haplotypes were analyzed within and across breeds to determine the level of diversity. Analysis of 770K data included a tag SNP believed to be in perfect linkage disequilibrium with the causal mutation in Holstein and Jersey cattle. Growth and calving ease data were subjected to genome-wide association studies (GWAS) for subsets of the data in Gelbvieh, Simmental and Brangus for those animals carrying only the most common diplotypes or haplotypes.

Results and Discussion

Based on 50K SNP data and UMD3.1 assembly, two haplotypes spanning 24.4Mb to 25.5Mb were found to account for 75% individuals across all beef breeds. Animals carrying these two haplotypes were analyzed in Gelbvieh and Simmental but the haplotypes did not capture the QTL effect. Inspection of 770K haplotypes demonstrated more diversity than was apparent from 50K SNP. Hereford cattle segregating the tag SNP from Holstein and Jersey cattle showed no effect of that locus. Collectively these data suggest the 50K SNP chips provide inadequate coverage of this region.

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