Bovine Respiratory Disease (BRD) is the most common infectious disease in beef and dairy cattle. The objective of this study was to identify host loci associated with susceptibility to BRD in pre-weaned Holstein calves as a preliminary step towards reducing BRD prevalence. Thirty day old Holstein calves were monitored 4d/week for signs of BRD using established calf-health scoring criteria (McGuirk, 2008). BRD affected calves scored ≥5, and controls scored ≤5. Over 200,000 calves were screened to obtain 1,003 cases and 1,012 controls over 180 days. Blood samples and diagnostic swabs (mid-nasal and 2 deep pharyngeal) were obtained for each calf. Genome wide association analysis was performed using four different analytical approaches (GBLUP, EMMAX, SNP and Variation Suite 7 and PLINK). SNP were filtered for UMD3.1 chromosomal assignment, low minor allele frequency, genotype call rate, and Hardy-Weinberg disequilibrium. Animals were removed for genotype call rate <90%, heterozygosity >40% or if predicted to be Kleinfelter males. GBLUP SNP effects explained 20% of the variation in BRD incidence. All analytical approaches identified concordant single SNP associations on BTA3, BTA15 and BTA23. Twelve additional chromosomes provided evidence for association with two or more approaches. When chromosomal regions (rather than single SNPs) were compared, 29 regions on 13 chromosomes were associated with BRD including those identified in the single SNP association comparison. Twelve regions were identified by all analyses and seventeen by two of these. These results represent initial work to identify loci associated with BRD and select that are less susceptible to BRD.

Key words: bovine respiratory disease, genetics, association

INTRODUCTION

BRD causes annual losses of more than one million animals and $692 million. Despite extensive use of vaccines and antimicrobials, morbidity and mortality rates have actually increased in some feedlot cattle. Typically, cattle with BRD have clinical symptoms including fever, rapid breathing, repetitive coughing, nasal and/or eye discharge, diarrhea, dehydration, and appetite depression. Animals are more likely to be affected by BRD when stressed by sudden changes in feed, crowding, temperature, transportation, and when clean air is contaminated with ammonia, dust and pathogens. Although the environment plays a major role in BRD infection rates, there is increasing evidence that resistance to BRD is under genetic control. Differences in BRD resistance have been found between cattle breeds and sire lines, and a heritability estimate of 0.48 on an underlying continuous scale was reported in unweaned beef calves. This suggests that selecting for BRD resistant cattle could have a substantial impact on BRD prevalence. A limited number of quantitative trait loci related to bovine health, including susceptibility to BRD, have been reported.

OBJECTIVE

The objective of this study was to identify host loci associated with susceptibility to bovine respiratory disease in pre-weaned Holstein calves.

MATERIALS AND METHODS

Samples:
- 2015 animals were identified as either a case or a control between d 30 and d 73 of life at a single operation based on a calf-health scoring system
- Deep pharyngeal and mid-nasal diagnostic samples were taken for identification of bacteria and viruses common to BRD
- Blood samples were used for DNA extraction
- 2015 animals were genotyped with the Illumina HD BeadChip
- Genome wide association analysis was performed using GBLUP, EMMAX, SVS7 and PLINK
- Animals and SNPs were quality filtered

<table>
<thead>
<tr>
<th>ANIMALS</th>
<th>GBLUP</th>
<th>EMMAX</th>
<th>SVS7</th>
<th>PLINK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Call rate</td>
<td>&gt;95% (98)</td>
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<td>18%</td>
<td>9%</td>
<td>9%</td>
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</table>

Several loci have been identified as being associated with susceptibility to BRD by evaluation of single SNPs as well as chromosomal regions by 3 different approaches. Many associated SNPs and regions are concordant. Some differences in results between methods is likely due to differences in modeling assumptions (i.e. Additive effects). A region on BTA26, which has previously been identified as associated with BRD in beef cattle, showed moderate evidence for association in Holstein calves. These preliminary data will be validated in an independent population of Holstein calves and compared to ongoing studies in beef cattle. Loci associated with susceptibility to infection by specific BRD pathogens and with clinical scores as a continuous trait will also be investigated.

CONCLUSION

These results represent a preliminary analysis of ongoing work to identify loci associated with BRD and represents the first step in selection of cattle that are less susceptible to disease resulting in improved production and animal welfare, and increased profitability.