A genome-wide scan of positive selection signature using the ovine Infinium® HD SNP beadchip in two Romney lines, selected for resistance or resilience to nematodes

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Introduction

The advent of high-density (HD) single nucleotide polymorphism (SNP) microarray chips has facilitated detection of artificial selection signatures, based on patterns of linkage disequilibrium (LD) selection lines. This is based on the assumption that the frequency of a novel mutation, that confers an advantage, will increase more rapidly than that of a neutral mutation (Sabeti et al. 2002). Consequently, long LD blocks involving the mutant genes could exist in populations undergoing artificial selection since there would not be enough generations to break the LD through recombination (Slatkin 2008). Hence, a high frequency of an unusually long haplotype within a selected population is considered as a positive selection signature.

Objective

The objective of this study was to detect selection signatures in two Romney sheep lines selected for divergent approaches to cope with gastrointestinal nematode infections, that being either resistance or resilience.

Materials and methods

Ninety three Romney sheep belonging to two genetic lines (gastrointestinal nematode resistant, n = 42, and resilient, n = 51), that were selectively bred based on faecal egg count (FEC) for at least 24 years (1985-2009), were subjects of current investigation. Ear punches from the sheep were submitted to AgResearch, Mosgiel, New Zealand, for DNA extraction and SNP genotyping using the ovine Infinium® HD SNP beadchip.

The original SNP idat files were converted to PLINK format (PED/MAP) using GenomeStudio® (Illumina, San Diego CA, USA). Quality control was done using PLINK, v1.9 (Chang et al. 2015; Purcell et al. 2007). A within-individual call rate threshold of 99% was applied and individual SNPs with a call rate <95%, or a minor allele frequency <1%, or a p value of <10^{-6} for Hardy-Weinberg equilibrium were excluded. A total of 463,392 SNPs, located on the 26 autosomes in 93 animals were retained for further analysis. Haplotypes for each autosome were constructed using fastPHASE v1.4 (Scheet & Stephens 2006). Resultant haplotype data was used to detect selection signatures by calculating the allele-specific extended haplotype homozygosity (EHH) within population as well as the site specific extended haplotype homozygosity (EHHs) between populations, using an R package, REHH 2.0 (Gautier et al. 2017). For EHH, the test statistic was IHS (Gautier & Naves 2011), the standardized ratio of the integrated allele-specific EHH (IHH), while for EHHs, two separate test statistics were employed: xp-EHH (Sabeti et al. 2007) and Rsb (Tang et al. 2007). Significance of detected signatures of selection was determined based on the p values for IHS, xp-EHH and Rsb.

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Table 1. SNP markers detected by both the EHHs algorithms, XP-EHH and Rsb, suggesting evidence of positive selection signatures in lines of Romney sheep selected for resistance or resilience to gastrointestinal nematodes

<table>
<thead>
<tr>
<th>SNP</th>
<th>Chr</th>
<th>Position (Mb)</th>
<th>Gene</th>
<th>QTL symbol</th>
<th>QTL Trait</th>
<th>QTL ID</th>
<th>QTL Trait</th>
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<tr>
<td>oar3_OAR13_70853062</td>
<td>13</td>
<td>48327544</td>
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<td>FECGEN</td>
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<td>QTL:16028</td>
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<td>70820259</td>
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</tr>
</tbody>
</table>

None of the significant SNPs from EHHs analysis were common to those detected in EHH analysis. Figure 2 depicts the results for the Rsb and XP-EHH algorithms with respect to markers on chromosome 13.

Results

Within-population EHH testing revealed 62 and 85 SNPs to exhibit positive selection signatures (p<0.0001) in the nematode resistant and resilient groups, respectively. An iHS plot for OAR2 for the two lines, revealing the differences between the two populations is shown in Figure 1. Between-population EHH analysis revealed a total of 39 and 48 SNPs to exhibit positive selection signatures in xp-EHH and Rsb algorithms, respectively. Ten SNPs (Table 1) were common to the two algorithms and were found to be located within two previously identified QTLs, associated with nematode larval count and faecal egg count. Hence, these were considered, with high confidence, to be associated with nematode resistance or (and) resilience in sheep.

Conclusion

This study provided a genome-wide map of positive selection signatures in two Romney sheep lines selected for FEC. Several significant SNPs were identified and preliminary analysis of ten of the identified SNPs revealed that they were located within two previously detected QTLs associated with gastrointestinal nematodiasis in sheep.

Acknowledgements

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References

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