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) in 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.

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 EHHS 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.

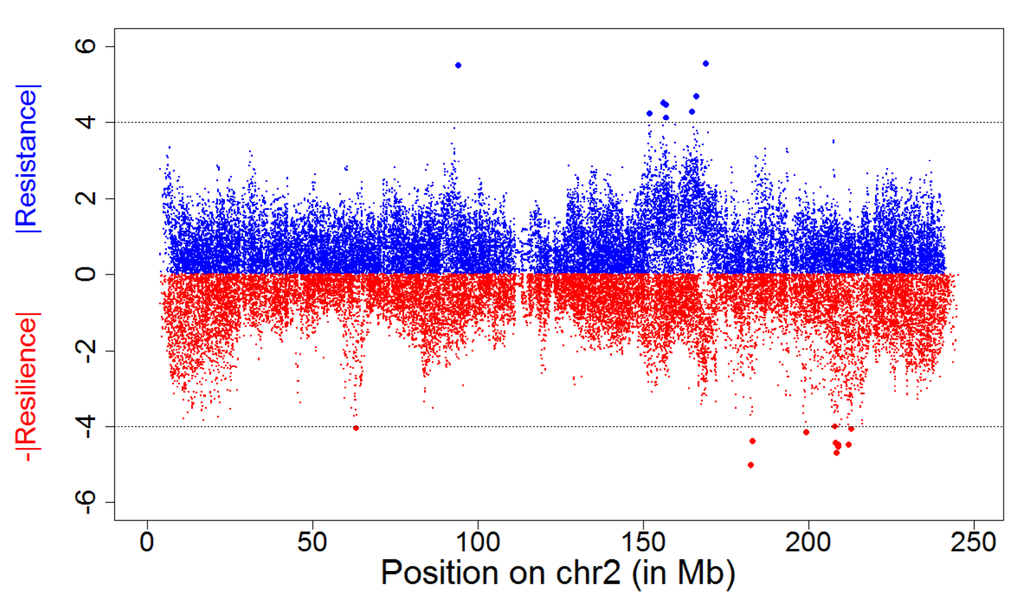

Figure 1. *iHS plot for markers on chromosome 2 in lines of Romney sheep selected for either resistance or resilience to gastrointestinal nematodes*

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 gastro-intestinal nematodes*

SNP	Chr	Position	Gene	QTL symbol	QTL ID	QTL Trait
oar3_OAR11_48327544	11	48327544	None	LATRICH_2	QTL:12901	Larva count
oar3_OAR13_70810243	13	70810243	PTPRT	FECGEN	QTL:16027	FEC
oar3_OAR13_70820259	13	70820259	PTPRT	FECGEN	QTL:16028	FEC
oar3_OAR13_70853062	13	70853062	PTPRT	FECGEN	QTL:16029	FEC
oar3_OAR13_70853714	13	70853714	PTPRT	FECGEN	QTL:16030	FEC
oar3_OAR13_70870621	13	70870621	PTPRT	FECGEN	QTL:16031	FEC
oar3_OAR13_70876794	13	70876794	PTPRT	FECGEN	QTL:16032	FEC
oar3_OAR13_70887333	13	70887333	PTPRT	FECGEN	QTL:16033	FEC
oar3_OAR13_70891326	13	70891326	PTPRT	FECGEN	QTL:16034	FEC
oar3_OAR13_70896117	13	70896117	PTPRT	FECGEN	QTL:16035	FEC

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.

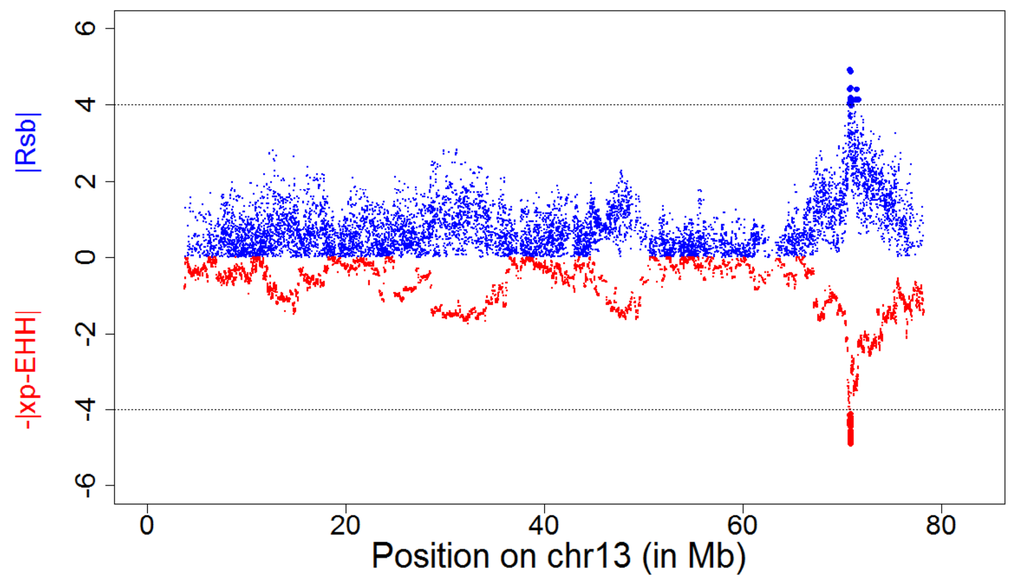

Figure 2. *XP-EHH and Rsb plots for markers on chromosome 13, from between-population EHHS analysis in divergent lines of Romney sheep, selected for resistance and resilience to gastrointestinal nematodes*

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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