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Footrot resistance in sheep: Analysis of genetic associations in the host genome in presence of the infectious pathogen *D. nodosous* as additional option to control footrot

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Key words
Footrot, Lameness, sheep, *Dichelobacter nodosus*, Genome-wide association study, resistance, susceptibility

Aim of the study

The aim of this study was to identify genomic regions affecting susceptibility to footrot in Swiss White Alpine (WAS) sheep with known disease status based on high-density single nucleotide polymorphism (SNP) genotyping data. This breed was chosen as it is the most predominant in Switzerland. It has been demonstrated before that footrot resistance/susceptibility is a heritable trait and that some breeds or some individuals within breeds are more resistant to the disease than are others. The ultimate goal of using associated molecular markers is to reduce the impact of footrot on individual farms by creating more resilient stock that have less severe footrot.

Material and methods

A total of 373 Swiss White Alpine (WAS) sheep, which were collected from seven different flocks during a single Swiss alpine pasture season, were phenotyped using a clinical footrot scoring system, and classified into three groups: 154 healthy controls, 143 intermediate cases and 76 severe cases. In addition, interdigital skin swabs of all animals tested positive for the presence of the virulent *Dichelobacter nodosus* strain using a specific qPCR-test. All 373 sheep were genotyped using the Illumina ovine HD BeadChip for 503 411 SNP markers. Finally, a case–control genome-wide association study comparing the three groups of sheep was performed using a mixed linear model to account for population structure and relatedness between animals. Furthermore, the model also considered the fixed effect of the seven flocks to correct for flock-specific effects.

Results and significance

The DNA-based comparison of Swiss White Alpine (WAS) sheep with known clinical footrot status revealed a genome-wide significant association for markers on ovine chromosome 2. This study, revealing for the first time a genome-wide significant association for this trait using a moderate number of well-characterized animals, shows that significantly increasing the marker density might have increased the chances of identifying associated markers. Nonetheless, an increase of the number of genotyped sheep with known footrot status can be further expected to enhance the power to identify additional associated genome regions.

The three best associated SNP markers were located at the *MPDZ* gene, which codes for the multiple PDZ domain crumbs cell polarity complex component protein, also known as multi-PDZ domain protein 1 (MUPP1). This protein is possibly involved in maintaining the barrier function and integrity of tight junctions. Therefore, it could be speculated that individuals carrying *MPDZ* variants may differ in their footrot resistance/susceptibility due to modified horn and interdigital skin integrity.

In conclusion, the outcome of this study suggests that *MPDZ* might be a major gene responsible for this trait in sheep, at least in the Swiss White Alpine (WAS) breed. However, the precise function of the MUPP1/MPDZ protein is currently not well established and further research is needed to explore its role in footrot-affected sheep.

Furthermore, the identified genomic association needs to be validated using extended cohorts of thoroughly phenotyped Swiss White Alpine (WAS) sheep and/or cohorts of other breeds before before implementation into breeding practice.

Publications, posters and presentations

Niggeler, A. (2017) Moderhinke Resistenz / Empfänglichkeit beim Schweizer Weissen Alpenschaf (WAS). Fachtagung der nationalen Arbeitsgruppe Moderhinke. 25 October 2017 in Zürich.

Niggeler, A. (2017) A genome-wide significant association on chromosome 2 for footrot resistance/susceptibility in Swiss White Alpine sheep. Doctoral Dissertation, Vetsuisse faculty, University of Bern.

Niggeler, A.; Tetens, J.; Stäuble, A.; Steiner, A.; Drögemüller, C. (2017) A genome-wide significant association on chromosome 2 for footrot resistance/susceptibility in Swiss White Alpine sheep. Animal Genetics, Volume 48 (Issue 6), 5 October 2017, Pages 712-715. https://doi.org/10.1111/age.12614.

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