Genetic mechanisms of heartwater resistance in goats from endemic & non-endemic regions of South Africa investigated using Illumina Goat SNP65k genotypes

X. Nuse[1,2]*, M.A. Van Der Nest[3], E.F. Dzomba[1], H.C. Steyn[4] and F.C. Muchadeyi[2]

[1]Discipline of Genetics, School of Life Sciences, University of KwaZulu-Natal, South Africa
[2]Agricultural Research Council - Biotechnology Platform, Onderstepoort, Pretoria, South Africa
[3]Department of Biochemistry, Genetics and Microbiology, University of Pretoria, Pretoria, South Africa
[4]Molecular Biology, Agricultural Research Council – Onderstepoort Veterinary Institute, Pretoria, South Africa

Email: NuseX@arc.agric.za

INTRODUCTION

Food production in developing countries relies comprehensively on the utilisation of locally adapted animal species that are of agricultural, cultural and economic importance to humans (1). However, tick-borne diseases represent a significant constraint to ruminant production due to high mortality and decreased productivity. Heartwater disease poses an economic threat to goat production in endemic areas infested by *Amblyomma hebraeum* ticks that transmit the pathogen, *Ehrlichia ruminantium* (2). It is believed that genetic factors play an important role in the etiology of common diseases and traits.

The necessity for identifying and promoting use of genetically resistant breeds has been recommended as a practical alternative to the control of heartwater. GWAS allow for the identification of genetic variation that predisposes to complex disorders (3, 4). Identifying genomic regions associated with disease resistance could be used in animal breeding programs. The aim of this study was therefore to use a GWAS approach to identify genes and genomic regions associated with resistance to heartwater disease in South African indigenous goats from endemic and non-endemic regions.

MATERIALS & METHODS

Samples were collected from 368 indigenous goats in heartwater endemic and non-endemic regions in South Africa → Genomic DNA was extracted from whole blood (200 µl) and tissue samples → Determined titre test and heartwater endemicity status → DNA samples were genotyped using Illumina Goat 65K SNP BeadChips → SNPs that passed quality control (QC) were used for downstream analyses → Association testing using SVS Golden Helix v8.9.1 (MLMM model)

RESULTS AND DISCUSSION

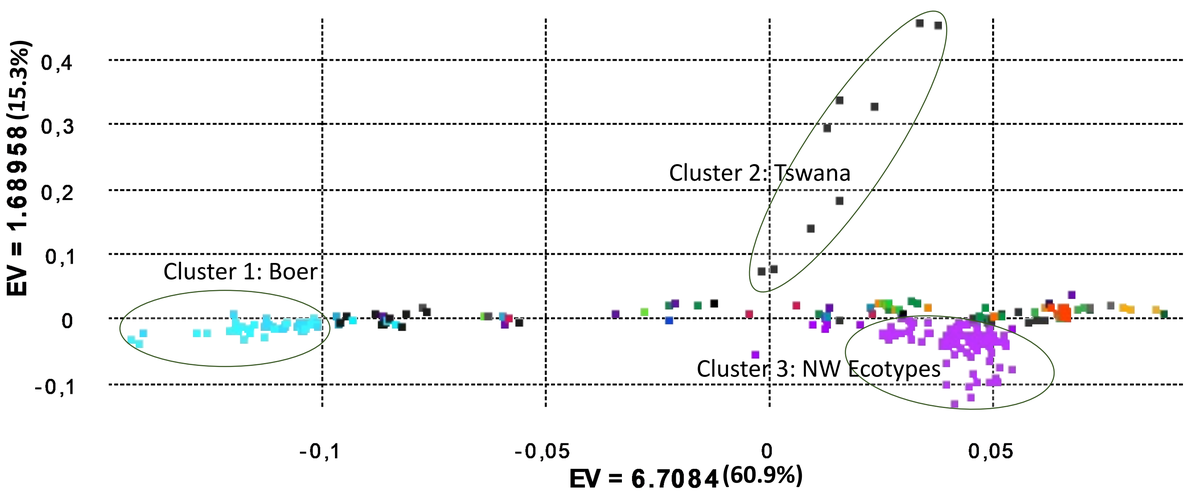

Figure 1. To correct our GWAS analysis for the presence of population structure, we performed a principal component analysis (PCA) using SVS Golden Helix software v8.9.1 on the 11 indigenous goat populations. The figure reveals clear population structures as samples from the same population cluster together. The first two principal components (PCs) separated clusters 1, 2 and 3. However, in each cluster, the were few individuals that were found clustering together with other populations.

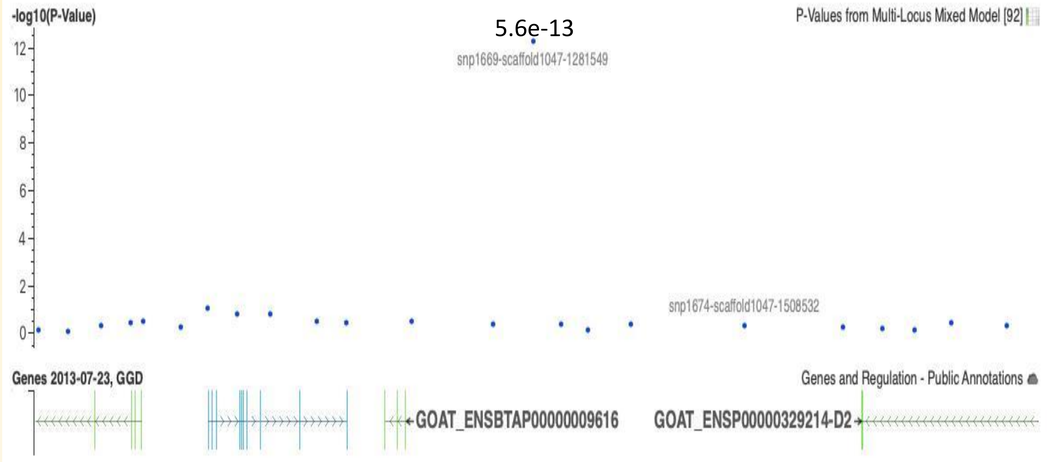

Figure 3. The SNP (snp1669-scaffold1047) on Chromosome 3, position 1281549 was significantly associated with the titre and heartwater endemic status (FDR-value = 5.6e-13) was localized near two genes (ENSBTAP00000009616 and ENSP00000329214-D2). This gene encodes the D2 subtype of dopamine receptor. This G-protein coupled receptor inhibits adenylyl cyclase activity. A missense mutation in this gene causes neurological hyperkinetic movement disorder; other mutations have been associated with severe mental diseases.

Figure 2. Manhattan plot of 54 832 filtered SNPs mapped to the 29 genome scaffolds. Each data point represents one SNP at which inheritance was tested for association with titre (immunity) across the 11 indigenous goat populations from endemic and non-endemic regions. The x-axis reports SNP positions on each scaffold and the y-axis reports the –log10 (P-Value). Multi-locus Mixed Model Analyses identified several genes and genomic regions of interest for various traits. Six SNPs (located on chromosomes 1, 3, 14, 22, 27 and 28) were identified at a false discovery rate (FDR) cut-off threshold (P < 0.05). Deviation from the expectation under the null hypothesis (threshold line) indicates the presence of either true causal effects or insufficiently corrected population stratification.

CONCLUSIONS

- Genetic studies of complex disease may inform the clinical application of remedies.
- GWAS allowed for the identification of genomic regions and genes that are significantly associated with heartwater susceptibility or resistance in indigenous goats from endemic regions (Figure 2).
- The chromosomal regions identified here as harbouring QTL underlying variation in antibodies/ titre form the best basis for further analysis to identify specific candidate genes related to goat heartwater resistance and provide the potential for marker-assisted selection in goats.
- Future work will involve characterizing these SNPs at the genomic-level as to infer the processes and pathways in which the corresponding genes are involved. Their role in virulence and pathogenicity will also be determined with mutational studies.

REFERENCES

1. Nyamushamba et al., 2017. A review.
2. Steyn and Pretorius, 2020. Onderstepoort Journal of Veterinary Research, 87(1): 1741.
3. Claussnitzer et al., 2020. Nature, 577(7789): 179-189.
4. Kullo et al., 2022. Nature Reviews Genetics, 23(9): 524-532.

ACKNOWLEDGEMENTS

National Research Foundation
Faculty of Natural and Agricultural Sciences
science & innovation
Department: Science and Innovation
REPUBLIC OF SOUTH AFRICA