Analysis of the *SLC11A1* (NRAMP-1) gene and association with resistance to Bovine Tuberculosis

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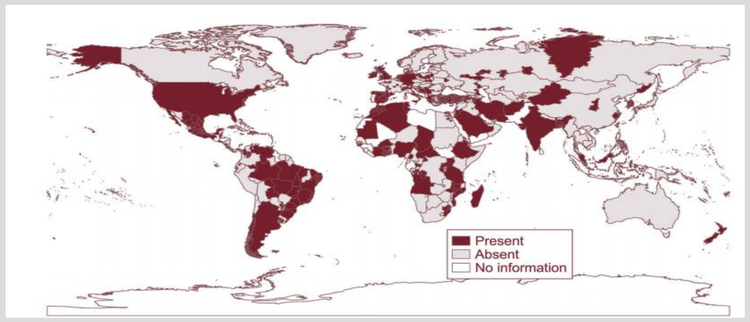
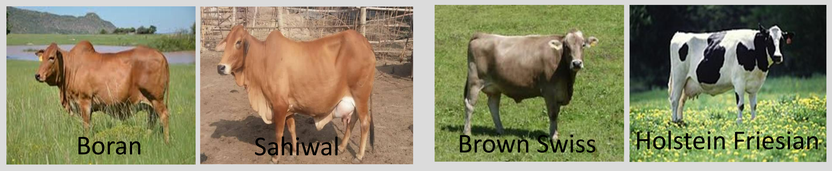
Background

Bovine Tuberculosis is a chronic, zoonotic, respiratory disease. To combat the disease, attention has turned to identifying a genotype for resistance [3]. The natural resistance-associated macrophage protein 1 (NRAMP1), encoded by the *SLC11A1* gene, plays a major role in controlling intracellular pathogens [2]. Thus, polymorphisms within its gene may play an important role in potential resistance to bTB. Different breeds of cattle have been described to be more resistant to *M. bovis* [1]. Therefore, the aim is to identify sub-species, as well as breed specific polymorphisms within the *SLC11A1* gene in association with potential resistance to *M. bovis.*

Bovine Tuberculosis global consensus



Bos Indicus ***Bos Taurus***



Resistant → Susceptible

Degree of resistance

Materials and Methods

cDNA from 48 healthy animals created. This was composed of:

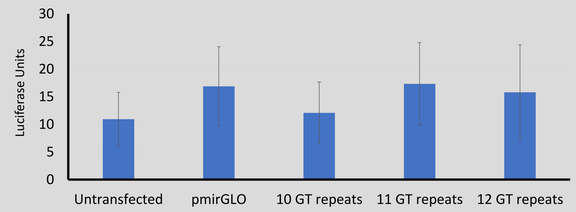
- 19 Holstein Friesian,
- 10 Brown Swiss
- 10 Boran
- 9 Saihwal

The coding region of the *SLC11A1* gene and two microsatellites within the 3'UTR of the *SLC11A1* gene were amplified, sequenced and analysed for breed specific polymorphic variations.
Subsequently, functioning studies were performed.

Results

10 GT repeat tended to show a lower luciferase activity.

Studies have shown that different microsatellite lengths within the 3'UTR of the *SLC11A1* gene are related to resistance / susceptibility to some intracellular pathogens. Three different length repeats for the first microsatellite were assessed for their influence over post-transcriptional gene expression, using a dual-GLO luciferase assay. Results are mean +/-SEM (n=3).



Key Aim:

To identify sub-species, as well as breed specific polymorphisms within the *SLC11A1* gene in association with potential genetic resistance to *M. bovis*.

Impact of polymorphisms on SLC11A1 protein model and ligand binding. I-Tasser results generated models to assess ligand binding differences between animals with minor and major alleles for SNP rs109453173.

A B

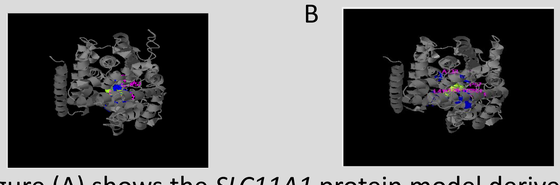
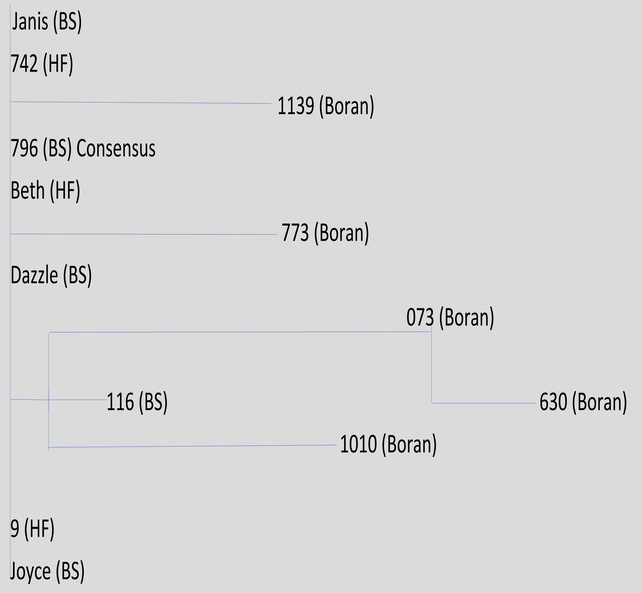


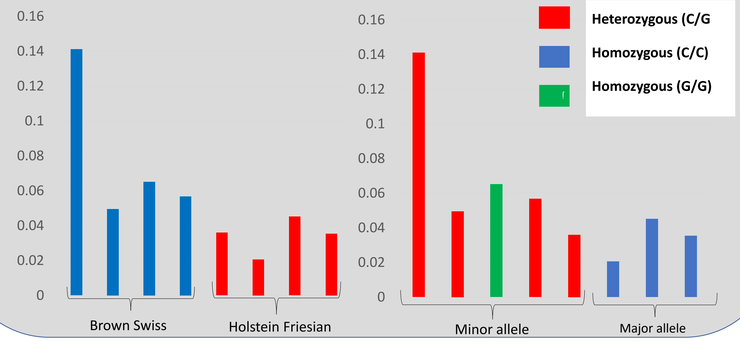
Figure (A) shows the *SLC11A1* protein model derived from the sequence generated from a homozygote for the major allele (C/C). Figure (B) shows the *SLC11A1* protein model derived from a homozygote for the minor allele (G/G).

Results

The sequence tree corresponds to the relatedness of the individual animals on the basis of variations they share within their *SLC11A1* gene.



Macrophages from Brown Swiss animals and animals possessing the minor allele of SNP rs109453173 have a tendency to produce more *SLC11A1*. Primary MØs were generated, stimulated with LPS and assessed for *SLC11A1* concentration by ELISA (ng/ml).



References

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