Association Between *SLC11A1 (NRAMP1)* Polymorphisms and Susceptibility to Tuberculosis in Chinese Holstein Cattle

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Abstract: [Objective]: We investigated the associations between *SLC11A1 (NRAMP1)* polymorphisms and susceptibility to tuberculosis (TB) in Chinese Holstein cattle from the Yunnan Plateau. [Methods]: We performed a case-control study. The case group included 136 animals that had positive reactions to both the purified protein derivative test and the IFN-γ assay, as well as showing clinical symptoms of TB, and the control group included 96 animals that had negative reactions to both tests. Polymerase chain reaction (PCR) sequencing and the PCR-restriction fragment length polymorphism (RFLP) technique were used to detect and determine *SLC11A1 (NRAMP1)* polymorphisms. Next, association analysis was used to identify significant correlations between *SLC11A1 (NRAMP1)* polymorphisms and susceptibility/resistance to TB. In addition, two genetic markers for *NRAMP1* were established using the PCR-RFLP technique. [Results]: Sequence alignment of *SLC11A1 (NRAMP1)* revealed seven single-nucleotide polymorphisms (SNPs). This study is the first to report *MaeII* PCR-RFLP markers for the Nramp1-SNP3 site and *PstI* PCR-RFLP markers for the Nramp1-SNP5 and Nramp1-SNP6 sites of *NRAMP1* in Chinese Holstein cattle. With the exception of Nramp1-SNP3 and Nramp1-SNP7 in the control group, the polymorphism information content and heterozygosity of all SNPs in both groups were moderate. Furthermore, except for Nramp1-SNP2 in the case group and Nramp1-SNP6 in the control group, all SNPs in both groups were in Hardy–Weinberg equilibrium. Logistic regression analysis indicated that Nramp1-SNP1, Nramp1-SNP3, and Nramp1-SNP5 were significantly associated with susceptibility/resistance to TB, even after Bonferroni correction. Two genotypes of Nramp1-SNP3 were susceptible to TB, while one genotype of Nramp1-SNP1 and two genotypes of Nramp1-SNP5 were resistant to TB. Furthermore,
linkage disequilibrium analysis showed that nine haplotypes were potentially resistant to TB. After Bonferroni correction, three of the nine haplotypes remained significantly associated with TB resistance. **[Conclusion]**: *SLC11A1 (NRAMP1)* is a useful candidate gene related to TB in Chinese Holstein cattle.