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Comparative Evaluation of the Functionality of Non-Synonymous Substitutions in MHC DRB Gene of Nigerian Goats

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Abstract

The Major Histocompatibility Complex (MHC) contains highly variable multi-gene families, which play a key role in the adaptive immune response within vertebrates. Among the *Capra* MHC class II genes, the expressed DRB locus is highly polymorphic, particularly in exon 2, which encodes the antigen-binding site. Models of variable non-synonymous/synonymous rate ratios among sites may provide important insights into functional constraints at different amino acid sites and may be used to detect sites under positive selection. Many non-synonymous single nucleotide polymorphisms (nsSNPs) at the DRB locus in goats are suspected to impact protein function. This study, therefore, aimed at comparing the efficiency of three computational approaches to predict the likelihood of a particular non-synonymous (amino acid change) coding SNP to cause a functional impact on the protein. This involved the use of SNAP (screening for non-acceptable polymorphisms), PANTHER and PROVEAN bioinformatics analytical tools in detecting harmful and beneficial effects at H57G, Y89R, V104D and Y112I substitutions in the peptide binding region of the DRB gene of Nigerian goats. The results from PANTHER analysis revealed that H57G, Y89R and Y112I substitutions ($P_{deleterious}$ = 0.113, 0.204 and 0.472, respectively) were beneficial; while that of V104D was deleterious ($P_{deleterious}$ = 0.756), an indication that it was non-neutral. As regards the SNAP approach, H57G and Y89R substitutions were returned neutral with expected accuracy of 53 and 69%, respectively while V104D and Y112I substitutions were harmful. However, only H57G substitution was found to be beneficial under PROVEAN method. Although, the PANTHER and SNAP approaches appeared to be better, there is need for standardisation for easy comparison of the efficiency of the analytical tools employed to detect the functional effects of amino acid substitutions. The present information may be used in search of disease resistant genotypes at the DRB locus of Nigerian goats.

Keywords: Bioinformatics tools, DRB gene, goats, Nigeria, non-synonymous substitutions