Functional and structural analysis of non-synonymous single nucleotide polymorphisms (nsSNPs) in the MYB oncoproteins associated with human cancer

ABSTRACT

MYB proteins are highly conserved DNA-binding domains (DBD) and mutations in MYB oncoproteins have been reported to cause aberrant and augmented cancer progression. Identification of MYB molecular biomarkers predictive of cancer progression can be used for improving cancer management. To address this, a biomarker discovery pipeline was employed in investigating deleterious non-synonymous single nucleotide polymorphisms (nsSNPs) in predicting damaging and potential alterations on the properties of proteins. The nsSNP of the MYB family; MYB, MYBL1, and MYBL2 was extracted from the NCBI database. Five in silico tools (PROVEAN, SIFT, PolyPhen-2, SNPs&GO and PhD-SNP) were utilized to investigate the outcomes of nsSNPs. A total of 45 nsSNPs were predicted as high-risk and damaging, and were subjected to PMut and I-Mutant 2.0 for protein stability analysis. This resulted in 32 nsSNPs with decreased stability with a DDG score lower than -0.5, indicating damaging effect. G111S, N183S, G122S, and S178C located within the helix-turn-helix (HTH) domain were predicted to be conserved, further posttranslational modifications and 3-D protein analysis indicated these nsSNPs to shift DNA-binding specificity of the protein thus altering the protein function. Findings from this study would help in the field of pharmacogenomic and cancer therapy towards better intervention and management of cancer.