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In Silico Analysis of Non-Synonymous Single Nucleotid Polymorphisms (nsSNPs) in Human *IL-6* Gene

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Abstract: *Introductio:* interleukin-6 (*IL-6*) Plays critical roles in immune responses, inflammation, and hematopoiesis and it has been proposed to be involved in development of multiple diseases, including susceptibility to diabetes mellitus, systemic juvenile rheumatoid arthritis, cancers, and coronary artery defects [1]. Several pathogenic single nucleotid polymorphisms in the *IL-6* gene have been identified that associated with numerous complex disorders, could destroy, modify, or create new protein coding sites. The structure and dynamics of proteins are an essential part of understanding the molecular foundations of complex biological processes and serve an important role in the field of computational biology [2]. PyMOL, a cross-platform molecular graphics tool, has been widely used for three-dimensional (3D) visualization of proteins, the new structure, nucleic acids, small molecules, electron densities, and surfaces. SIFT has been applied to human variant databases, considers the position at which the change occurred and the type of amino acid change, and calculates the probability that an amino acid at a position is tolerated conditional on the most frequent amino acid being tolerated [3].
Method: We identified four non-synonymous single nucleotide polymorphisms (nsSNPs) in the *IL-6* gene (rs11544633, rs56383910, rs148171375, and rs182812860) using dbSNP and then analyzed their effect on the protein structure using PyMOL software and SIFT database.
Results: Validation results showed that non-synonymous single nucleotid polymorphisms (nsSNPs) change the interaction patterns, polar groups, and length of hydrogen bonds. rs11544633 and rs56383910 lead to Leu119Pro and Ser136Gly, respectively. Both of SNPs caused to a hydrogen bond disappearing in protein structure. rs148171375 lead to a nonpolar and alphatic R group into an aromatic R group conversion, and two hydrogen bonds disappearing. rs182812860 caused to Q152H, that it just changes the length of hydrogen bonds and protein conformation. The results of the mutation in the SIFT predict scores less than 0.05 for all four mentioned SNPs.
Conclusions: These findings suggest that nucleotide changes in genomic sequences lead to changes in the amino acid sequence. As all SIFT scores are less than 0.05, this could modifiy the protein structure and may affect the protein function. Computational biology tools have advantages and disadvantages, and their results are predictions that require confirmation.

Keywords: *IL-6*; non-synonymous single nucleotid polymorphisms (nsSNPs); SNP structure prediction; SNP function prediction

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