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Title:	In-silico Analysis of Damaging SNPs of Human DHFR Protein and Determining their Functional and Structural Consequences
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Abstract:	DHFR is an enzyme that is ubiquitous in all organisms. DHFR's main role is to maintain tetrahydrofolate at intracellular levels, which is required for certain cofactors to biosynthesize purine, pyrimidine, and several amino acids. As, it is the primary source of THF, it is vulnerable to quickly proliferating cells, which ends in making it a preferable target for many essential anticancer and antimicrobial drugs. With a set of SNPs data accessible via dbSNP, my thesis is planned to point out functional SNPs in DHFR by applying various in silico tools such as SIFT, PolyPhen2, PROVEAN, SNP&GO, PHD-SNP, Consurf, ModPred, MutPred, Tm-Align and lastly Project HOPE was used for estimating the impact of SNPs on a protein, functionally and structurally, PTM sites and energy minimization analysis. 241 SNPs found to be non-synonymous among 7967 DHFR SNP entries out of which SIFT estimated 64 nsSNPs as non-tolerable, while PolyPhen-2 estimated 60. An aggregate result was obtained by evaluating five tools with different perceptions where twenty-five nsSNPs were considered most likely to exert deleterious impact. To evaluate mutation's functional and structural impact on DHFR, Phyre2 was used to create 3D models of mutated proteins. Results from FoldX and Project HOPE reinforced the initial findings, as they predicted, upon mutation there will be significant structural and functional instability. To determine whether the mutations lies in any protein's functional domains. Considering these analyses, my study picked up 10 most damaging nsSNPs.
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