Computational approaches for understanding mutational effects on protein structure and function: implications to diseases

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Proteins perform several functions in living organisms. These functions are dictated by their structures, which are influenced with contacts between amino acid residues, building blocks of proteins. The substitution of amino acid residues in a protein alters its structure, stability and function, and may lead to diseases (1,2). We have developed comprehensive databases for understanding protein structure and function (3,4), and annotating disease-causing mutations in globular and membrane proteins using experimental data reported in the literature. These databases provide a description of mutants, structural and functional features along with visualization, search, display, and download options. We have systematically analyzed the effect of these mutations at protein level on change in stability, binding affinity and disease-causing. Utilizing the information, we have developed computational methods for predicting the change in binding affinity upon mutation in protein-protein, protein-DNA and protein-carbohydrate complexes (5-7). Further, computational tools have been constructed for identifying the potential driver and passenger mutations at a large scale, which could be used for designing experiments (8-10). The salient features of the results will be discussed.

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