

Comparative analysis of web-based programs for single amino acid substitutions in proteins

ABSTRACT

Single amino-acid substitution in a protein affects its structure and function. These changes are the primary reasons for the advent of many complex diseases. Analyzing single point mutations in a protein is crucial to see their impact and to understand the disease mechanism. This has given many biophysical resources, including databases and web-based tools to explore the effects of mutations on the structure and function of human proteins. For a given mutation, each tool provides a score-based outcomes which indicates deleterious probability. In recent years, developments in existing programs and the introduction of new prediction algorithms have transformed the state-of-the-art protein mutation analysis. In this study, we have performed a systematic study of the most commonly used mutational analysis programs (10 sequence-based and 5 structure-based) to compare their prediction efficiency. We have carried out extensive mutational analyses using these tools for previously known pathogenic single point mutations of five different proteins. These analyses suggested that sequence-based tools, PolyPhen2, PROVEAN, and PMut, and structure-based web tool, mCSM have a better prediction accuracy. This study indicates that the employment of more than one program based on different approaches should significantly improve the prediction power of the available methods.