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Review

Proteomic databases and tools to decipher post-translational modifications

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ABSTRACT

Post-translational modifications (PTMs) are vital cellular control mechanism, which affect protein properties, including folding, conformation, activity and consequently, their functions. As a result they play a key role in various disease conditions, including cancer and diabetes. Proteomics as a rapidly growing field has witnessed tremendous advancement during the last decade, which has led to the generation of prodigious quantity of data for various organisms' proteome. PTMs being biologically and chemically dynamic process, pose greater challenges for its study. Amidst these complexities connecting the modifications with physiological and cellular cascade of events are still very challenging. Advancement in proteomic technologies such as mass spectrometry and microarray provides HT platform to study PTMs and help to decipher role of some of the very essential biological phenomenon. To enhance our understanding of various PTMs in different organisms, and to simplify the analysis of complex PTM data, many databases, software and tools have been developed. These PTM databases and tools contain crucial information and provide a valuable resource to the research community. This article intends to provide a comprehensive overview of various PTM databases, software tools, and analyze critical information available from these resources to study PTMs in various biological organisms.

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Contents

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1. Introduction

The completion of genome projects has accelerated the analysis of proteome; however, due to the complexity of proteins its study is more challenging than any other biomolecules. This complexity arises due to the biological phenomenon such as gene splicing to form different isoforms and various post-translational modifications (PTMs), which gives rise to enormous number of proteins, about three orders of magnitude higher than the total number of genes encoded in genome [1,2]. As the name indicates for PTMs, the process of protein modifications takes place after translation of mRNA into a protein. All proteins undergo appreciable amount of PTMs to make biologically active form, and this dynamic process occurs in various cell compartments to decide the function of modified protein. About 300 different types of PTMs have been reported till date and many more are still being reported [2]. PTMs, also designated as 'cellular switches', provide diverse role to proteins as per cellular requirements. For instance, ubiquitination is a predominant phenomenon, in which sequential, covalent attachment of ubiquitin on a protein leads to the degradation and decides the fate of protein. Several signaling pathways are majorly regulated through phosphorylation cascades. Hence it is impossible to judge on protein nature and function without having a precise idea about what PTM it undergoes in a given time span.

Initially PTM studies were carried out on selected candidates with mutational screens, western blotting, and tracking with radio labeling; however, recent advancements in mass spectrometry and microarray have enabled HT screening and quantification of PTMs, with sensitivity at subattomolar level [2]. Each run of such HT screening experiment generates large amount of data, which requires intense analysis and interpretation to provide clues for its biological significance.

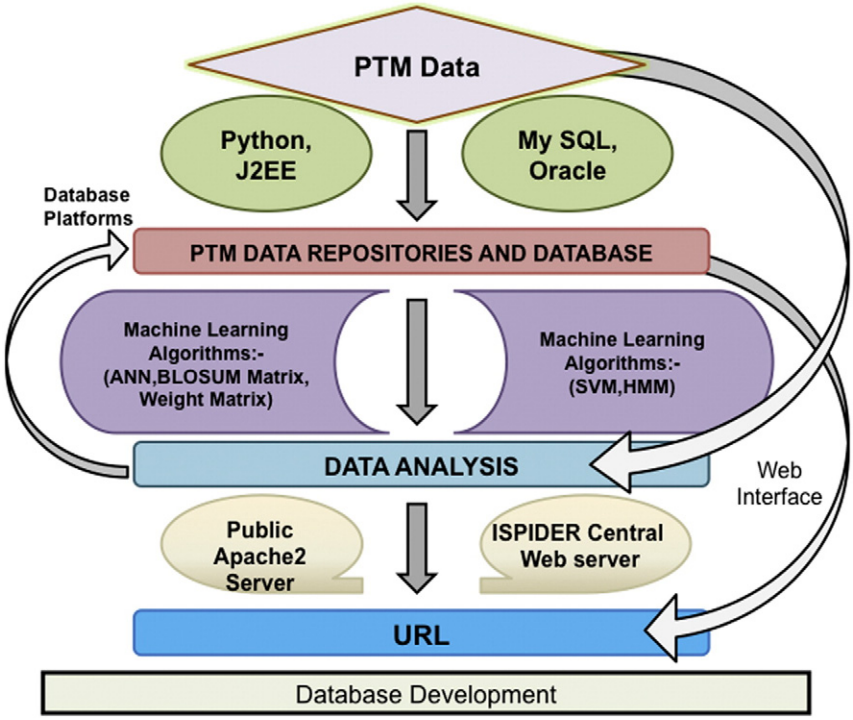

Fig. 1 – Creation of PTM databases and tools: The general scheme of creation of database using database building platforms. PTM data from various sources are continuously annotated in the databases. As a result the curated data are utilized to teach machine learning techniques thereby building a classifier, which mimics biological condition and predicts PTM in the input sequence. These tools and databases are made publically available over World Wide Web.

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