November 2005 Power Machines N6 Question Papers

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Protein phosphorylation is one of the most abundant reversible post-translational modifications in eukaryotes. It is involved in virtually all cellular processes by regulating protein function, localization and stability and by mediating protein-protein interactions. Furthermore, aberrant protein phosphorylation is implicated in the onset and progression of human diseases such as cancer and neurodegenerative disorders. In the last years, tens of thousands of in vivo phosphorylation events have been identified by large-scale quantitative phospho-proteomics experiment suggesting that a large fraction of the proteome might be regulated by phosphorylation. This data explosion is increasingly enabling the development of computational approaches, often combined with experimental validation, aiming at prioritizing phosphosites and assessing their functional relevance. Some computational approaches also address the inference of specificity determinants of protein kinases/phosphatases and the identification of phosphoresidue recognition domains. In this context, several challenging issues are still open regarding phosphorylation, including a better understanding of the interplay between phosphorylation and allosteric regulation, agents and mechanisms disrupting or promoting abnormal phosphorylation in diseases, the identification and modulation of novel phosphorylation inhibitors, and so forth. Furthermore, the determinants of kinase and phosphatase recognition and binding specificity are still unknown in several cases, as well as the impact of disease mutations on phosphorylation-mediated signaling. The articles included in this Research Topic illustrate the very diverse aspects of phosphorylation, ranging from structural changes induced by phosphorylation to the peculiarities of phosphosite evolution. Some also provide a glimpse into the huge complexity of phosphorylation networks and pathways in health and disease, and underscore that a deeper knowledge of such processes is essential to identify disease biomarkers, on one hand, and design more effective therapeutic strategies, on the other.

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