

Introduction: Protein Phosphorylation and Signaling

Protein phosphorylation is an essential mechanism for enzymatic and cellular regulation, a field whose scope is enormous and rapidly expanding. In this thematic issue, we highlight reviews by investigators at the forefront of phosphorylation research, an area representing fertile territory for the integration of chemical principles with biological regulation. The excellent reviews in this issue emphasize themes at the chemistry–biology interface, ranging from a structural and mechanistic understanding of phosphorylation/dephosphorylation reactions and the enzymes involved in catalyzing these events to the control of diverse biological processes and the use of protein kinases and phosphatases as targets for clinical therapies.

We begin with an overview of how phosphorylation controls protein structure and authoritative treatises on the structure, dynamics, mechanism, and phylogeny of protein kinases and phosphatases, which catalyze phosphorylation and dephosphorylation reactions. Next, several reviews focus on specific classes of protein kinases and phosphatases, describing the unique properties and behaviors of individual enzyme subtypes within the kinase and phosphatase superfamilies. These provide detailed insight into how protein phosphorylation controls essential signaling processes within biological organisms, underlying the

modulation of processes as diverse as cell proliferation, development, and cell homeostasis. Finally, because phosphorylation is so fundamental to cell physiology, kinases and phosphatases have critical influence in diseases involving disruption of their regulation or function and thus represent important targets for pharmaceutical intervention. The targeting of kinases as therapeutic drug targets is an area of much progress and competition, as described in two articles which present case studies in the development of tyrosine kinase inhibitors.

Our goal in preparing this thematic issue has been to expand coverage by *Chemical Reviews* toward topics relevant to biochemistry and cellular regulation, to serve as a resource in research and teaching for readers in the chemical sciences. We are deeply grateful to the authors for their enormous effort in contributing reviews that provide important insight and perspectives on new discoveries in this field.

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