



Guest Editor's Desk

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The ability of living organisms to respond to the environment is essential for their survival. The collection of molecular processes that regulate organismal as well as cellular responses to changes in their surroundings, is termed 'signal transduction'. The molecular base for these complex events has been, and continues to be, an area of intense scientific study. Since many diseases are associated with aberrant signaling, an understanding of the genes, proteins, and small molecules that participate in signaling events could provide novel approaches to therapy.

Critical to the efficient functioning of any signaling process is the requirement for precise spatial and temporal control of participating proteins and second messengers. The articles in this issue address a variety of mechanisms employed by living cells in regulating signaling events. They highlight not only the roles of various signaling intermediates within the cell, but also changes in their localization and concentration during a cellular response. For example, Nair et al. provide an overview of how canonical association of G-proteins with the plasma membrane is altered by specific stimuli, allowing these G proteins to function in intracellular niches and elicit distinct signaling outputs from those that happen at the cell surface. Pawar and Balasubramanian talk of the small GTPases and their role in integrin-mediated cell migration. There are multiple members in the family of small GTPases, and cross-talk amongst these proteins is also discussed in this article.

Post-translational modifications, such as phosphorylation or acetylation of signaling proteins, control their activities and cellular localization. Two articles in this issue deal with the reverse processes of dephosphorylation and deacetylation. Indeed, turning off a signaling event at an appropriate time is as critical as turning it on. Kumar and Maddika deal with phosphatases, while Deota et al. discuss the role of sirtuin deacetylases in coordinating organismal development.

Central to all events in a cell is metabolism. Laxman presents an interesting argument that

certain metabolites can act as signaling intermediates, and thereby modulate signaling outcomes. Autophagy, which is sensitive to the concentrations of intracellular metabolites, is an evolutionarily conserved process by which cells degrade unwanted proteins and organelles to survive. Chinchwadkar et al. review mechanisms of autophagy, and how this complex process is regulated by signaling events that impinge on diseases such as cancer, diabetes and neurodegeneration.

Signaling pathways are highly complex and often involve intermediates that act as second messengers. Shah et al. write on a relatively newly described signaling process, involving inositol pyrophosphates. These molecules are high energy compounds that modulate protein activity by binding to proteins, or by post-translational pyrophosphorylation. Sharma and Visweswariah describe methods to monitor the ancient second messengers, cAMP and cGMP, using modern approaches of fluorescence and bioluminescence energy transfer. These approaches allow one to study changes in concentrations in cAMP and cGMP with time, and at specific locations, in the cell.

How does one assimilate information on all these pathways that are occurring simultaneously in a cell? The new field of 'systems biology' attempts to do that, using computational methods to integrate knowledge obtained from experimental approaches, to predict signaling outcomes. Korla and Chandra present an overview of systems approaches to understanding signaling, with a focus on host-pathogen signaling events and cross-talk between the prokaryotic pathogen and the eukaryotic host.

It is hoped that these articles provide a glimpse of current research on diverse aspects of cellular signaling. The cover image is an artist's rendition of a cell, depicting findings described in various articles in this issue. The collage provides a challenge to the reader to correlate a picture in the image with an article in this issue!

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