Preface

Special issue on mitogen-activated protein kinases: New insights into regulation, function and role in human disease

The mitogen-activated protein kinase (MAPK) signaling pathways have been extensively studied for the past 20 years, establishing their key roles in numerous cellular functions and founding a model signaling pathway system. Of special significance was the early recognition of their involvement in various human cancers, prompting a concerted effort to identify inhibitors along the pathway as potential cancer therapeutics. Currently there are several lead compounds in clinical trials that target various MAPK pathways, predominantly Raf, MLK and MEK inhibitors. Although remarkable progress has been made in understanding various aspects of MAPK function and regulation, many other remain poorly understood. These aspects include among others the physiological effects of MAPKs under normal cell growth conditions, during development, in cell cycle regulation and with respect to distinct cell type functions. Other pressing questions relate to defining the exact molecular aspects of their regulation, defining the cross-talk relationships between the various MAPK pathways and better defining their downstream targets. Furthermore, the extensive incorporation of inhibitors of MAPK pathways in clinical trials and potentially in the near future in the clinic calls for ways to better evaluate the data coming from clinical trials to help in designing future targets and approaches to improving treatment efficacy. The aim of this MAPKs-dedicated special issue is to provide a comprehensive and up-to-date review of the field while underlining the remaining questions and gaps in our understanding. In addition, a special focus is given to the role of MAPKs in various pathologies and our perceptions regarding the targeting of these pathways for therapy.

The first part of this issue provides a historical overview of the field and introduces the classical Ras-Raf-MEK-ERK MAPK pathway, covering the pathway from the receptor level to ERKs and their targets. The second part focuses on aspects of MAPK regulation by phosphatases and through cross-talk mechanisms and addresses clinical aspects and other emerging novel concepts. The third part covers physiological aspects of MAPK function and also includes an overview of yeast MAPKs. The final part covers the so-called stress-activated MAPK pathways and includes a review of atypical MAPKs. Obviously, not all aspects of this diverse field could be addressed in one issue, and we extend our apologies to the many contributors to this field whose work was not covered.

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