Preface

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The development, progression, and maintenance of human cancer are polygenic in nature and involve dysregulation of multiple regulatory genes and molecular pathways and resulting cellular processes. While sub-sets of some cancers are driven by mutant versions of certain genes and/or are “addicted” to specific genes, the majority of cancer types are dependent on multiple genes for sustaining cancerous phenotypes. For the most part, these representative facts about the polygenomic basis of human cancer argue against the notion of cancer dependency on a single gene. Although the question about the orderly *versus* random dysregulation of regulatory pathways and resulting network activities during the natural history of human cancer remains to be fully resolved, it is expected to involve the principles of coordinated, compensatory, and orderly misregulation of core pathways. The propensity of focusing on a single-gene/protein approach might represent one of the barriers to gaining a full understanding of human cancer and in turn, our effort to combat cancer progression, for most, if not all, cancer types. Nevertheless, these approaches have been very fruitful and were somewhat essential to reaching the current stage of our knowledge of cancer medicine. Reductionist approaches will continue to be important for learning more about the nature and functions and/or diagnostic value of individual genes and proteins. However, it

is now clear that we must start viewing cancer as a process of coordinated dysregulation of molecules and pathways beyond the one gene approach. Considering the huge progress in understanding several prototypic molecules and/or families of regulatory genes that underscore the significance of the notion of coordinated dysregulation of pathways, the journal considered devoting a special issue of Cancer and Metastasis Reviews (CMR) to this theme. The guest editors of this issue of CMR, Rakesh Kumar, Robert Clarke, and Simak Ali, have recruited leading subject matter experts with original contributions to specific prototypic molecules of dysregulated pathways in the human cancer.

The editors believe the current special issue of CMR, with a focus on coordinated dysregulation of pathways and beyond the one-gene approach, will provide a timely update on a set of molecules that are at the interface of multiple indispensable processes of human cancer. When considered together, the articles in this collection will serve as an important guide for cancer researchers and biologists alike, and will also be of interest to the readership of CMR and Cancer Medicine.

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