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MYC and the Pathway to Cancer

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Preface

THE DISCOVERY OF THE *MYC* ONCOGENE WAS a major milestone along the road leading to our current understanding of genetic alterations in cancer and how transcription contributes to tumorigenesis. The study of *MYC* began more than three decades ago and has now accumulated more than 26,000 publications listed in PubMed. With ramifications in almost every area of biological and medical sciences, the *MYC* field is poised for a book that captures not only key historical findings but also the latest advances and controversies. The immediate impetus for this volume came as the result of a Banbury Conference on *MYC* and cancer held in November 2011. Several things became apparent at this meeting. First, an immense amount of diverse information has been gathered on nearly every aspect of the regulation and activities of *MYC*. Second, exciting new experiments are continually forcing us to revise our picture of *MYC* and its functions. Third, there is still a great deal, much of it fundamental, to learn about the function of *MYC* in both normal and neoplastic cells.

MYC encodes a master transcription factor that dimerizes with MAX to control diverse biological processes that influence normal cell growth and proliferation. However, when deregulated, *MYC* becomes an oncogene that transforms cells in concert with other genetic alterations, including loss of tumor-suppressor checkpoints. Research on *MYC* over the past several decades has provided us with an understanding of how multiple cellular processes can be affected by a single transcriptional regulator and how the collective alterations of these processes result in cancer. The chapters in this volume have been arranged so that the topics move from a mechanistic focus on the *MYC* protein (regulation of expression, protein–protein interactions, genomic recognition, and transcriptional functions) through *MYC*'s biological activities in normal cellular processes (roles in pluripotency, vertebrate and invertebrate development, DNA replication, apoptosis, and metabolism) to the activities of *MYC* that render it a major driver of oncogenicity (regulatory mutations, induction of genomic instability, cell competition, and metabolic reprogramming). Other chapters examine specific examples of *MYC*'s diverse roles in human cancers (Burkitt lymphoma, medulloblastoma, and neuroblastoma) and consider approaches to attenuate *MYC* in tumors (synthetic lethal screens and targeted chemotherapy).

One fundamental area of research that receives considerable attention in this volume concerns the precise function of *MYC* as a regulator of gene expression. The generally accepted model that *MYC* acts as a transcriptional on/off switch has been challenged by the hypothesis that *MYC* functions solely to alleviate the widespread transcriptional pausing by RNA polymerases and thus amplifies the expression of genes that are already expressed in a given cellular context. The data supporting this “universal amplifier” model are described here in two chapters while these findings and their consequences are further considered and debated in several other chapters. We expect that the debate concerning *MYC*'s transcriptional functions will provide an impetus for further research focused on a deeper understanding of the mechanism(s) underlying the transforming potential of *MYC* oncogenes.

The editors thank Barbara Acosta, Richard Sever, and their colleagues at Cold Spring Harbor Laboratory Press for their help and excellent editorial efforts in assembling this book. We are indebted to all the authors, who have generously dedicated their time to contribute superb chapters that capture the essence and highlight important findings in their chosen topics. We dedicate this

Preface

book to Michael Potter, whose research and workshops on *MYC* and B-cell neoplasia over the years inspired many of us to pursue this enigmatic oncogene.

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