
Preface

It has become clear that tumors result from excessive cell proliferation and a corresponding reduction in cell death caused by the successive accumulation of mutations in key regulatory target genes over time. During the 1980s, a number of oncogenes were characterized, whereas from the 1990s to the present, the emphasis has shifted to tumor suppressor genes (TSGs). It has become clear that oncogenes and TSGs function in the same pathways, providing positive and negative growth regulatory activities. The signaling pathways controlled by these genes involve virtually every process in cell biology, including nuclear events, cell cycle, cell death, cytoskeletal, cell membrane, angiogenesis, and cell adhesion effects. Mutations in tumor suppressor genes have been identified in familial cancer syndromes, and the same genes in many cases have been found to be mutationally inactivated in sporadically occurring cancers. In their normal state, TSGs control cancer development and progression, as well as contribute to the sensitivity of cancers to a variety of therapeutics. Understanding the classes of TSGs, the biochemical pathways they function in, and how they are regulated provides an essential lesson in cancer biology. We cannot hope to advance our current knowledge and to develop new and more effective therapies without understanding the relevant pathways and how they influence the present approaches to therapy. Moreover, it is important to be able to access not only the powerful tools now available to discover these genes, but also their links to cell biology and growth control.

The scope of this two volume work, *Tumor Suppressor Genes, Volume 1: Pathways and Isolation Strategies* and *Volume 2: Regulation, Function, and Medicinal Applications*, is broad in the sense that it covers all the known tumor suppressor pathways and provides key information on the road to their discovery, analysis, and uses in cancer therapeutics. The aim of the first volume, *Pathways and Isolation Strategies*, is to educate the reader about known TSGs and the relevance of the biochemical pathways they regulate to human cancer. The reader has an opportunity in Volume 1 to access state-of-the-art protocols that have been successful in the identification of TSGs in the past, and that can be applied to isolate novel TSGs. With a novel TSG in hand, the reader has an opportunity in Volume 2, *Regulation, Function, and Medicinal Applications*, to explore the cell biology and biochemical function of the encoded protein, as well as its physiological role in vivo. Finally, in Volume 2, the reader is exposed to strategies for the use of information on TSGs to develop diagnostic and therapeutic strategies for cancer.

The two volumes of *Tumor Suppressor Genes* bring together many of the world's experts in the identification and characterization of TSGs. The work is thus intended to become the core reference and compilation of the emerging path-

ways and the growing number of molecules that suppress cancer. Importantly, it should also serve as a wide-ranging source of protocols useful in understanding and characterizing the function of TSGs. One of the challenges facing cancer researchers and clinicians is to bring forward and develop active therapeutics. This book, by example, puts forward highly useful paradigms for rational drug design, based on our dramatic new understanding of molecular pathogenesis.

Tumor Suppressor Genes thus lays down a firm and timely foundation for understanding cancer. In this age of expression profiling and proteomics, there has already been revealed a remarkable complexity and interrelatedness of seemingly diverse processes and signal transduction pathways. For the student, this book provides a reference to the basics concerning the identity of the major TSGs and the signaling pathways they use to inhibit tumors. For the investigator, it provides not only a critical update, but also an extremely useful compendium of newly assembled research protocols, including both classical methods and state-of-the-art techniques. For the translational scientist, the book provides fertile ground for the development of therapeutic strategies based on understanding the mechanisms of action and appreciating the existing preclinical data. One of the criticisms of an effort leading to such a book is that the field is moving very quickly and material is likely to be outdated. However, with many of the world's leading experts providing a comprehensive overview of all tumor suppressing pathways, along with their detailed protocols, we believe we have provided an invaluable resource for continued learning and discovery. Finally, *Tumor Suppressor Genes* provides a bridge to those interested in translational research by giving examples of the rationale for many of the most promising manipulations that may lead to novel therapeutic agents.

Tumor Suppressor Genes is targeted at a broad audience including medical and graduate students, postdoctoral fellows, physician scientists, academics, and principal investigators. The text provides the critical information needed to rapidly gain appreciation of important TSGs in human cancer, as well as modern methods for their discovery, analysis, and clinical application. The reader is enabled to learn the background and then access the literature in which studies designed to define the biology and biochemistry of known TSGs have been performed. Details of protocols with examples of their previous uses allow the researcher to apply current technologies to novel or known genes whose role has not yet been defined.

In summary, *Tumor Suppressor Genes* is a comprehensive compilation of the known tumor suppressing pathways, and the key molecular approaches to their discovery, analysis, and clinical applications. It should be of enduring value to students at all levels of experimental biology and medicine, as well as those clinicians who want to better understand the molecular biology of cancer.

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