

RNA and Cancer

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1. Auflage 2013. Buch. XIII, 245 S. Hardcover

ISBN 978 3 642 31658 6

Format (B x L): 15,5 x 23,5 cm

Gewicht: 555 g

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Preface

In the last decade, it has become increasingly clear that RNA (ribonucleic acid) is not simply a messenger molecule (mRNA) directing protein synthesis. RNA has multiple versatile functional roles in cells, especially in mammalian gene regulation to influence almost every aspect of cellular life.

This volume reviews recent progresses in the selected areas of RNA processing, especially data related to cancer development and therapy. It is not our intention to cover comprehensively all areas of RNA processing. Instead, we have focused on several areas in which more information with cancer relevance has been obtained.

Cancer is a group of highly complex, multifactorial genetic diseases. In cancer, genetic defects may affect each step of gene expression: from transcription, splicing to translational regulation, mRNA stability control, and post-translational modifications. With the rapid development in technologies in gene expression profiling and sequencing, we now have much more comprehensive knowledge about the entire collection of different transcripts encoded by the human genome. The vast majority of human protein-coding genes use a mechanism known as alternative pre-mRNA splicing to generate more than one transcript from single genes. This alternative splicing process, in which different combinations of different regions of the primary gene transcript (pre-mRNA) are selected to form different mRNA species, is one of most robust mechanisms to achieve genetic diversity. Alternative splicing pattern changes have been detected in many types of cancer in genes critical for various aspects of tumor development and cancer metastasis. Such alternative splicing perturbations are being systematically investigated not only for the underlying mechanisms but also as potential biomarkers for diagnosis and therapeutic development.

In addition to protein coding genes, a large number of non-protein coding transcripts (ncRNAs) are produced by the human genome. This recent discovery has grown into a very active area of research. Evidence is accumulating that ncRNAs including microRNAs play important roles in regulating signal transduction pathways involved in cancer development and progression. In addition, small RNAs and oligonucleotides are becoming promising tools for cancer therapy development.

This book begins with the coupling between transcription and splicing. Three subsequent chapters describe in detail cancer-associated aberrant RNAs, new

methodology for their detection, and the functional impact on expression of important genes including oncogenes and tumor suppressor genes. The following chapter focuses on microRNAs in cancer. The possible involvement of particular subcellular compartment, such as perinucleolar compartment (PNC), in cancer is reviewed. Implications of mRNA stability regulation in cancer are also discussed. In addition to genes controlling cell proliferation, cell death genes are tightly regulated by alternative splicing. Splicing defects in regulation of cell death genes have been discovered in many types of cancer. Potentials of developing therapeutics using oligonucleotides to modulate cancer-associated RNA defects are then reviewed. Finally, clinical perspectives of studying RNA defects in cancer are discussed together with their relevance to cancer diagnosis, therapies, and treatment resistance.

The target readers of this book are primarily those interested in gene regulation and cancer biology, especially those who are not directly working on RNA biology, including clinicians and medical students.

We are very fortunate to have internationally renowned experts to contribute to this book. We hope that this book will stimulate further innovative research collaborations between RNA biologists and cancer researchers, improving cancer diagnosis and treatment in the future.

Chicago, USA, March 2012

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