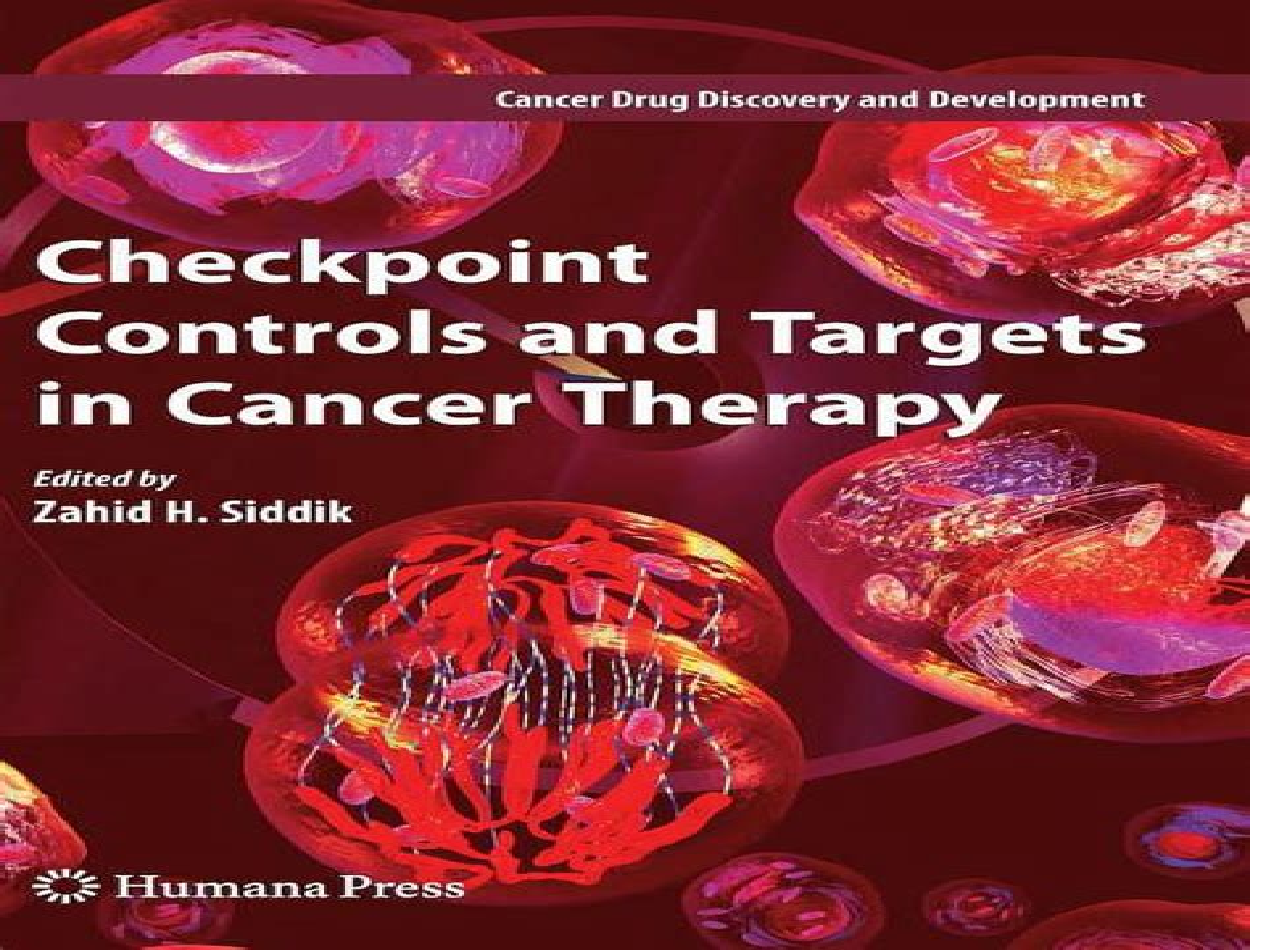




Cancer Drug Discovery and Development

Checkpoint Controls and Targets in Cancer Therapy

Edited by
Zahid H. Siddik

 **Humana Press**

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JE Gale



Checkpoint Controls And Targets In Cancer Therapy Cancer Drug Discovery And Development:

Checkpoint Controls and Targets in Cancer Therapy Zahid H. Siddik, 2010-03-12 Much work over the last two decades has firmly established that loss of cell cycle checkpoint regulation and resultant unabated cellular proliferation is an inherent characteristic of cancer. This loss may occur through aberration in any single component involved in signal transduction pathways that orchestrate checkpoint regulation which may manifest through either a failure to activate the checkpoint or a failure to respond to the activated checkpoint. In normal cells, checkpoint pathways are activated when genetic or cellular homeostasis is compromised and signals are then transduced to re-stabilize homeostasis and failing this to activate the apoptotic machinery to induce a cellular suicidal response. This implies that both survival and cell death pathways are induced following checkpoint activation and that the final decision is dependant on the net result of integrating the two sets of signals. It is intriguing that checkpoint pathways are also critical in cancer therapy to provide an apoptotic stimulus when cellular damage induced by the therapeutic agent is detected by the sensor system. Therefore, it is not surprising that failure in pro-survival checkpoint response will render tumor cells hypersensitive to cytotoxics and conversely failure in pro-apoptotic checkpoint response will induce genetic instability and/or therapeutic resistance. Understanding the intricacies of checkpoint response is therefore central to the design of therapeutic regimen that will enhance antitumor effects. Although early versions of this design entail combination of cytotoxic agents with cell cycle or checkpoint inhibitors, a greater understanding of the concepts could make such combinations clinically more effective. The contributions in this book will consolidate the current state of knowledge on checkpoint responses that may lay the foundation for hypothesis-driven rational approaches in advancing the management of cancer. The immediate attraction of the book to the scientific community is that it represents a timely opportunity to build upon existing concepts of checkpoints to expand our understanding of the inner workings of the critical checkpoint machinery. The present understanding has provided ample appreciation that response to checkpoint activation is manifested through coordinated inhibition of cyclin-dependent kinase (CDK) complexes in G1/S and/or the G2 phase in order to arrest the cell cycle. Kinase inhibition can occur through several mechanisms including inhibitory phosphorylation of CDK, destruction of the cognate cyclins, and recruitment of CDK inhibitors from the INK and WAF1/CIP1 families. However, the wealth of information from recent discoveries needs to be examined critically to consolidate our conceptual knowledge of checkpoints. At the same time, there is acute awareness in the diversity of checkpoint response between cytotoxic agents and this serves as a reminder of the magnitude of complexity that is inherent in checkpoint regulation. This volume is intended to bring the cancer research community closer toward an improved understanding of this regulation, how checkpoint abnormalities can impact negatively on cancer therapy, and emerging strategies to target checkpoint response as a therapeutic end point. *Checkpoint Responses in Cancer Therapy* Wei Dai, 2008-05-01 Extensive research has uncovered a set of molecular surveillance mechanisms commonly called

checkpoints which tightly monitor cell cycle processes Today s anticancer drug development has identified many of these cell cycle checkpoint molecules as effective targets Research now promises to uncover a new generation of anticancer drugs with improved therapeutic indices based on their ability to target emerging checkpoint components Checkpoint Responses in Cancer Therapy summarizes the advances made over the past 20 years identifying components of cell cycle checkpoints and their molecular regulation during checkpoint activation and validating the use of checkpoint proteins as targets for the development of anticancer drugs This book s distinguished panel of authors takes a close look at topics ranging from the major molecular players affecting DNA synthesis and the response to DNA damage to advances made in the identification of chemical compounds capable of inhibiting individual mitotic kinases Illuminating and authoritative Checkpoint Responses in Cancer Therapy offers a critical summary of findings for researchers in the pharmaceutical and biotechnology industries and a valuable resource for academic scientists in cancer research and the study of cell cycle regulation signal transduction and apoptosis

Targets for Cancer Chemotherapy Nicholas B. La Thangue, Lasantha R. Bandara, 2002-04-03 In *Targets for Cancer Chemotherapy Transcription Factors and Other Nuclear Proteins* a panel of leading basic researchers pharmaceutical scientists and clinical oncologists explain in detail the therapeutically relevant protein targets that contribute to cancer pathology and spell out their implications for cancer drug discovery and clinical application The authors identify and illuminate selected transcription factor oncoproteins and tumor suppressors together with nuclear proteins that are central to the phenotype of the tumor cell involved in chromatin control The emphasis is on new targets and approaches to cancer treatment derived from the cancer cell cycle gene control targets and angiogenesis

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Advances in DNA Repair in Cancer Therapy Lawrence Panasci,Raquel Aloyz,Moulay Alaoui-Jamali,2012-12-09 A comprehensive review of the recent developments in DNA repair research that have potential for translational applications The book explains in detail the various biological mechanisms by which cancer cells can circumvent anticancer therapy and limits its usefulness in patients They also review the impact of such novel inhibitors of DNA repair mechanisms as methylguanine DNA methyltransferase Also examined are inhibitors of other DNA repair enzymes such as PARP and DNA PK The book captures for both cancer researchers and oncologists dealing with hallmark relapse or drug resistance phenomena on a daily basis the many exciting new uses of DNA repair inhibitors either alone or in combination with anticancer therapies

Cancer Drug Design and Discovery Stephen Neidle,2013-09-30 Cancer Drug Design and Discovery Second Edition is an important reference on the underlying principles for the design and subsequent development of new anticancer small molecule agents New chapters have been added to this edition on areas of particular interest and therapeutic promise including cancer genomics and personalized medicine DNA targeted agents and more This book includes several sections on the basic and applied science of cancer drug discovery and features those drugs that are now approved for human use and are in the marketplace as well as those that are still under development By highlighting some of the general principles involved in taking molecules through basic science to clinical development this book offers a complete and authoritative reference on the design and discovery of anticancer drugs for translational scientists and clinicians involved in cancer research Provides a clinical perspective on the development of new molecularly targeted anticancer agents with the latest and most promising chemotherapeutic approaches Offers a broad view of where the field is going what tools drug discovery is using to produce new agents and how they are evaluated in the laboratory and clinic Features 6 new chapters devoted to advances in technology and successful anticancer therapies such as cancer genomics and personalized medicine DNA targeted agents B Raf inhibitors and more Each chapter includes extensive references to the primary and review literature as well as to relevant web based sources

Computational Methods in Drug Discovery and Repurposing for Cancer Therapy Ganji Purnachandra Nagaraju,Venkatesan Amouda,Ampasala Dinakara Rao,2023-03-22 Computational Methods in Drug Discovery and Repurposing for Cancer Therapy provides knowledge about ongoing research as well as computational approaches for drug discovery and repurposing for cancer therapy The book also provides detailed descriptions about target molecules pathways

and their inhibitors for easy understanding and applicability The book discusses tools and techniques such as integrated bioinformatics approaches systems biology tools molecular docking computational chemistry artificial intelligence machine learning structure based virtual screening biomarkers and transcriptome those are discussed in the context of different cancer types such as colon pancreatic glioblastoma endometrial and retinoblastoma among others This book is a valuable resource for researchers students and members of the biomedical and medical fields who want to learn more about the use of computational modeling to better tailor the treatment for cancer patients Discusses in silico remodeling of effective phytochemical compounds for discovering improved anticancer agents for substantial significant cancer therapy Covers potential tools of bioinformatics that are applied toward discovering new targets by drug repurposing and strategies to cure different types of cancers Demonstrates the significance of computational and artificial intelligence approaches in anticancer drug discovery Explores how these various advances can be integrated into a precision and personalized medicine approach that can eventually enhance patient care

[Index Medicus](#), 2001 Vols for 1963 include as pt 2 of the Jan issue Medical subject headings

Toxicogenomics-Based Cellular Models Jos Kleinjans, 2014-01-02 Toxicogenomics Based Cellular Models is a unique and valuable reference for all academic and professional researchers employing toxicogenomic methods with respect to animal testing for chemical safety This resource offers cutting edge information on the application of toxicogenomics to developing alternatives to current animal toxicity tests By illustrating the development of toxicogenomics based cellular models for critical endpoints of toxicity and providing real world examples for validation and data analysis this book provides an assessment of the current state of the field as well as opportunities and challenges for the future Written by renowned international toxicological experts this book explores omics technology for developing new assays for toxicity testing and safety assessment and provides the reader with a focused examination of alternative means to animal testing Describes the state of the art in developing toxicogenomics based cellular models for chemical induced carcinogenicity immunotoxicity developmental toxicity neurotoxicity and reproduction toxicity Illustrates how to validate toxicogenomics based alternative test models and provides an outlook to societal and economic implementation of these novel assays Includes an overview of current testing methods and risk assessment frameworks Provides a real world assessment by articulating the current development and challenges in toxicogenomics while suggesting ways to move this field forward

Targeted Cancer Therapy Razelle Kurzrock, Maurie Markman, 2008-03-07 Emerging technologies in target identification drug discovery molecular markers and imaging are rapidly changing the face of cancer This book provides a foundation of knowledge in targeted cancer therapeutics The treatment of cancer is increasingly being individualized based on an understanding of underlying biologic mechanisms Poised to change the landscape in oncology this volume provides a state of the art overview It will be valuable to practicing and academic physicians fellows residents and students as well as basic scientists interested in the cancer field

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