De Novo And Acquired Resistance To Immune Checkpoint

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Targeted Cancer Therapy Springer
This volume gives the latest developments in on the mechanisms of cancer cell resistance to apoptotic stimuli, which eventually result in cancer progression and metastasis. One of the main challenges in cancer research is to develop new therapies to combat resistant tumors. The development of new effective therapies will be dependent on delineating the biochemical, molecular, and genetic mechanisms that regulate tumor cell resistance to cytotoxic drug-induced apoptosis. These mechanisms should reveal gene products that directly regulate resistance in order to develop new drugs that target these resistance factors and such new drugs may either be selective or common to various cancers. If successful, new drugs may not be toxic and may be used effectively in combination with subtoxic conventional drugs to achieve synergy and to reverse tumor cell resistance. The research developments presented in this book can be translated to produce better clinical responses to resistant tumors.
Ridaforolimus (MK-8669) Synergizes with Dalotuzumab (MK-0646) in Hormone-Sensitive Breast Cancer Springer Science & Business Media
Stephen P. Ethier and a panel of leading investigators comprehensively analyze the cellular, molecular, and endocrine factors in the development of cancers of the breast, prostate, endometrium, and ovary. Concentrating on defining the most important unresolved issues in the field, the authors review how steroid hormones function to regulate normal mammary gland homeostasis in humans, with particular emphasis on the roles of estrogen, progesterone, and growth factors. Comprehensive and up-to-date, Endocrine Oncology offers both basic and clinical researchers not only the latest molecular and cellular findings on endocrine cancers, but also a powerful critical analysis that will prove invaluable to all endocrinologists and oncologists working in the area today.
Resistance to Aromatase Inhibitors in Breast Cancer Springer
Leading experts summarize and synthesize the latest discoveries concerning the changes that occur in tumor cells as they develop resistance to anticancer drugs, and suggest new approaches to preventing and overcoming it. The authors review physiological resistance based upon tumor architecture, cellular resistance based on drug transport, epigenetic changes that neutralize or bypass drug cytotoxicity, and genetic changes that alter drug target molecules by decreasing or eliminating drug binding and efficacy. Highlights include new insights into resistance to antiangiogenic therapies, oncogenes and tumor suppressor genes in therapeutic resistance, cancer stem cells, and the development of more effective therapies. There are also new findings on tumor immune escape mechanisms, gene amplification in drug resistance, the molecular determinants of multidrug resistance, and resistance to taxanes and Herceptin.
Genetics of Melanoma CRC Press
This edited volume brings together the expertise of numerous specialists on the topic of particles – their physical, chemical, pharmacological and toxicological characteristics – when they are a component of pharmaceutical products and formulations. The book discusses in detail properties such as the composition, size, shape, surface properties and porosity of particles with respect to how they impact the formulations and products in which they are used and the effective delivery of pharmaceutical active ingredients. It considers all dosage forms of pharmaceuticals involving particles, from powders to tablets, creams to ointments, and solutions to dry-powder inhalers, also including the latest nanomedicine products. Further, it discusses examples of particle toxicity, as well as the important subject of pharmaceutical industry regulations, guidelines and legislation. The book is of interest to researchers and practitioners who work on testing and developing pharmaceutical dosage and delivery systems.
Estrogens, Progestins, and Their Antagonists Springer Science & Business Media
Molecular Genetics of Drug Resistance forms a vital and timely review of the genetic processes behind drug resistance. Starting with an overview of the area, each chapter focuses on a particular target with important sections on drug resistance in malaria and in cancer.
DARPP-32 Expression in Acquired Resistance of Breast Cancer Cells to Trastuzumab CRC Press
This issue of Hematology/Oncology Clinics, guest edited by Dr. F. Stephen Hodi, is devoted to Melanoma. Articles in this issue include: The current state of Melanoma; Understanding the Biology of Melanoma Development and Therapeutic Implications; Surgical Management of Melanoma; Targeted Therapies for Cutaneous Melanoma; Treatments for Non-cutaneous Melanoma; Resistant Mechanisms and Therapeutic Implications; The Role of the Immune System in Melanoma Development and Treatment; Vaccines and Melanoma; IL-2, Interferon, and Cytokines; Immune Checkpoint Blockade; Adjuvant Treatments, Chance for Cure in Melanoma; and Combinatorial Approach to Treatment of Melanoma.
AACR 2019 Proceedings: Abstracts 2749-5314 John Wiley & Sons
Overcoming drug resistance requires identification of redundant survival signals. Even in the best case scenario of personalized medicine wherein cancer- specific genomic alterations are treated with molecular targeted therapeutics, increasing resistance predicates concurrent identification of compensatory mechanisms. For a lethal malignancy with limited treatment options such as pancreatic ductal adenocarcinoma (PDA), the development and clinical implementation of a novel targeted strategy i.e. PARP inhibitors was a major breakthrough. However, PARPi have not progressed as a frontline therapy for PDA patients despite being in the clinical trials pipeline for over a decade now. Identifying and combating de novo and acquired PARPi resistance mechanisms is a critical medical goal in oncology, and the focus of this study. Attempts to target the most frequent mutations in PDA patient samples, including KRAS (86%), TP53 (68%), CDKN2A (21%), SMAD4 (21%) and EGFR (7%) identified through multiple next-generation sequencing studies haven't yielded any considerable success. However, over 10% of PDA patients are associated with germline or sporadic loss of DNA repair and genome maintenance genes, specifically BRCA1 and BRCA2, which compromises repair of damaged DNA resulting in increased chromosomal instability (CIN). Paradoxically, while CIN promotes tumorigenesis, these genetic mutations become the tumor cells' "Achilles heel". These DDR- defective cells rely heavily on an alternative DNA repair pathway dictated by PARP1, and thus are particularly susceptible to PARP inhibitors and intra-strand crosslinkers such as mitomycin C, cisplatin, etc. Therefore, DNA damage repair (DDR), one of twelve core signaling pathways dysregulated in PDA, has provided a promising approach for treating selective patients with DNA repair-deficient tumors. Unfortunately, there is an unmet demand to understand how initially responsive patients develop resistance to PARPi. While genomic and proteomic alterations, such as BRCA reversion mutation or upregulation of a PARPi efflux pump respectively, have been widely explored as PARPi resistance mechanisms, rapid reprogramming of the RNA expression signature in response to PARPi exposure has been largely ignored. This is the first study to demonstrate that post-transcriptional gene regulation (PTGR) by an RNA- binding protein HuR upregulates expression of a novel resistance gene Poly-ADP Ribose Glycohydrolase (PARG) which supports DNA damage response and facilitates PARPi resistance. We have previously shown that HuR-mediated transcriptomic rewiring causes PDA cells to reprogram core cellular processes and enhance expression of several pro-survival factors such as DCK, WEE1 and PIM1 which, in turn, support acute chemoresistance and survival of PDA cells in a harsh tumor microenvironment. The ultimate clinical goal of this study relates to 1) optimizing and extending a proven synthetic lethal therapeutic strategy to all pancreatic cancer patients, regardless of their DNA-repair status, 2) recognizing PARG as a more suitable target over PARP1 due to its ability to be acutely induced in response to drug exposure and 3) inhibiting PARG and/or HuR as an effective therapeutic strategy to improve efficacy of not only PARP inhibitor therapy but other chemotherapy regimens in pancreatic cancer.
Role of NK Cells in the Efficacy of Anti-HER2 Therapeutic Antibodies in Breast Cancer Academic Press
Overexpression of ErbB2 is found in several types of human carcinomas. In breast tumors, ErbB2 overexpression is detected in up to 20% of patients. Breast cancers in with amplification of ErbB2 are characterized by rapid tumor growth, lower survival rate and increased disease progression. The molecular mechanisms underlying the oncogenic action of ErbB2 involve a complex signaling network that tightly regulates malignant cell migration and invasion and hence metastatic potential. Recent efforts have been made to identify gene expression signatures of ErbB2-positive invasive breast cancers that may represent important mediators of ErbB2-induced tumorigenesis and metastatic progression. In this chapter, we will discuss the canonical ErbB2 signaling pathways responsible for tumor growth and dissemination along with newly identified mediators such as adaptor protein p130Cas and miRNAs. From a therapeutic point of view, the treatment with anti-ErbB2 monoclonal antibody trastuzumab has greatly improved the outcomes of patients with ErbB2 aggressive cancer. Nevertheless, de novo and acquired resistance to trastuzumab therapy still represent a major clinical problem. In the second part of the chapter, we will provide an overview of the mechanisms so far implicated in the onset of resistance to targeted therapy and of the new strategies to overcome resistance.
The Epithelial-to-Mesenchymal Transition (EMT) in Cancer Springer Science & Business Media
This book provides a comprehensive overview of the fast-evolving subject of clinical application of cancer therapeutic biomarkers. The second edition captures significant progress of cancer immunotherapy and emphasizes the genetic basis for selective cancer treatment. It covers an in-depth insight on biomarkers across a broad area of cancer research and oncology with a wealth of integrated genetic and molecular information about specific therapies by a multidisciplinary team of internationally recognized experts. Each chapter focuses on a class of targeted, immunologic, or chemotherapy agents and their companion biomarkers that predict response, benefit or resistance, and severe adverse event. The book will serve as a handbook for health professionals and scientists on the current applicable biomarkers in the management of cancer. The vision into the systemic classification and statistical consideration of therapeutic biomarkers summarized by the book editors and chapter authors will help advance precision medicine—a precisely tailored cancer treatment strategy for cancer patient care.
Lung Cancer and Personalized Medicine: Novel Therapies and Clinical Management Springer Science & Business Media
This reference examines the biological factors and genetic and molecular pathways potentially responsible for the development and progression of breast cancer-analyzing the latest therapeutic strategies as well as breakthroughs in endocrine treatments, angiogenesis, and non-hormonal approaches to predict, control, and inhibit the formation and grow
Diagnostics and Therapy in Veterinary Dermatology Academic Press
This book is a printed edition of the Special Issue "The Epithelial-to-Mesenchymal Transition (EMT) in Cancer" that was published in Cancers
Drug Resistance in Breast Cancer – Mechanisms and Approaches to Overcome Chemoresistance Springer Science & Business Media
Cancer is the leading cause of death in most countries and its consequences result in huge economic, social and psychological burden. Breast cancer is the most frequently diagnosed cancer type and the leading cause of cancer death among females. In this book, we discussed various therapeutic modalities from signaling pathways through various anti-tumor compounds as well as herbal medicine for this deadly cancer. We hope that this book will contribute to the development of novel diagnostic as well as therapeutic approaches.
Cancer Drug Resistance Springer Science & Business Media
Cultured Cells—Advances in Research and Application: 2012 Edition is a ScholarlyBrief™ that delivers timely, authoritative, comprehensive, and specialized information about Cultured Cells in a

concise format. The editors have built Cultured Cells—Advances in Research and Application: 2012 Edition on the vast information databases of ScholarlyNews.™ You can expect the information about Cultured Cells in this eBook to be deeper than what you can access anywhere else, as well as consistently reliable, authoritative, informed, and relevant. The content of Cultured Cells—Advances in Research and Application: 2012 Edition has been produced by the world's leading scientists, engineers, analysts, research institutions, and companies. All of the content is from peer-reviewed sources, and all of it is written, assembled, and edited by the editors at ScholarlyEditions™ and available exclusively from us. You now have a source you can cite with authority, confidence, and credibility. More information is available at http://www.ScholarlyEditions.com/.

Regulation of the Opioid Growth Factor-Opioid Growth Factor Receptor Axis in the Progression of Triple Negative Breast Cancer and Its Potential as a Therapeutic Agent Cambridge University Press

This issue of Hematology/Oncology Clinics, Guest Edited by F. Stephen Hodi, is devoted to Melanoma. This issue is one of six selected each year by our series Consulting Editors, George P. Canellos and Edward J. Benz. Topics discussed in this important issue include: State of Melanoma, Biology of Melanoma, Epidemiology of Melanoma, Surgical Management of Melanoma, Melanoma Adjuvant Therapy, Targeted Therapies for Melanoma, Non-cutaneous Melanomas, Immune Checkpoint Therapies for Melanoma, Resistance Mechanisms to Current Therapies, Cellular Therapy and Cytokine Treatments for Melanoma, Combinatorial Approaches to the Treatment of Melanoma, and Melanoma Future Directions.

Companion and Complementary Diagnostics Springer

"Amplification of the receptor tyrosine kinase ErbB-2 has been linked to the proliferation of breast cancer cells.1,2 Trastuzumab targets the extracellular domain of ErbB-2, leading to growth inhibition of approximately 15% of the breast cancers with genomic amplification of the ERBB2 gene.3 Clinical studies have demonstrated its efficacy in both early4 and metastatic breast cancers. 5,6 However, many tumors with ERBB2 amplification are not responsive to treatment.7 Moreover, the ones that initially respond, eventually progress and acquire drug resistance.8 An in vitro model for this acquired resistance was established by Chan & al.9 The breast cancer cell line, BT474, containing amplified ERBB2, was grown in the presence of trastuzumab for several months until subclones outgrew. Gene expression profiling was performed on these clones to determine differentially expressed genes between the parental and resistant cells. DARPP-32 (Dopamine and cAMP regulated phosphoprotein of 32kDa) was, by far, the most overexpressed transcript. DARPP-32 is coamplified with ERBB2 on the same amplicon of chromosome 17.10 This protein has been mostly described in neurobiology, but DARPP-32 overexpression was recently reported in gastrointestinal, esophageal, prostate and breast cancer.11 Therefore, we suggest that overexpression of DARPP-32 can cause acquired resistance of breast cancer cells to trastuzumab. The in vitro knockout of DARPP-32, using stable shRNA transfection, abolishes the resistance to trastuzumab in the clones, while overexpression of DARPP-32 in the parental cells results in de novo resistance. Overall, our results suggest that DARPP-32 may be a potential therapeutic target in breast cancer patients who develop acquired trastuzumab resistance." --

ErbB2 Receptor in Breast Cancer: Implications in Cancer Cell Migration, Invasion and Resistance to Targeted Therapy BoD – Books on Demand

Aromatase Inhibitors (AIs) treat postmenopausal estrogen receptor positive tumours, which constitute the majority of breast cancer patients. This comprehensive volume brings together the current knowledge from different relevant areas, including molecular mechanisms and translational aspects of drug resistance in AIs. Topics covered include research, experimental , and clinical data specifically focused on AI resistance in breast cancer. The volume will include three sections. The first section covers general knowledge about aromatase inhibitors, including regulation of aromatase genes, and structure and function of aromatase protein. The second section provides the detailed mechanisms of resistance to AIs, while the third section explores prediction of resistance and potential strategies to overcome resistance. Breast cancer is the most common female cancer and AIs significantly improve treatments outcomes compatibly to previously used endocrine treatments. However 10-15% of post-operative patients develop a relapse during adjuvant treatment with AIs; about 25-50% of the patients do not respond to AIs in neo-adjuvant or metastatic setting, and the majority of metastatic patients who initially respond develop resistance within 3 years. There is an important need to understand these mechanisms of resistance in order to develop methods of preventing or overcoming the resistance to AIs, which will ensure a more successful outcome in treating breast cancer.

Advances in Clinical Chemistry Springer Science & Business Media

Companion and Complementary Diagnostics: From Biomarker Discovery to Clinical Implementation provides readers with in-depth insights into the individual steps in the development of companion diagnostic assays, from the early biomarker discovery phase straight through to final regulatory approval. Further, the clinical implementation of companion diagnostic testing in the clinic is also discussed. As the development of predictive or selective biomarker assays linked to specific drugs is substantially increasing, this book offers comprehensive information on this quickly-evolving area of biomedicine. It is an essential resource for those in academic institutions, hospitals and pharma, and biotech and diagnostic commercial companies. Covers all aspects, from biomarker discovery, to development and regulatory approval Explains the "how to" aspects of companion diagnostics Incorporates information on the entire process, allowing for easier and deeper understanding of the topic

Journal of the National Cancer Institute Springer Science & Business Media

Steroid Receptors—Advances in Research and Application: 2012 Edition is a ScholarlyEditions™ eBook that delivers timely, authoritative, and comprehensive information about Steroid Receptors. The editors have built Steroid Receptors—Advances in Research and Application: 2012 Edition on the vast information databases of ScholarlyNews.™ You can expect the information about Steroid Receptors in this eBook to be deeper than what you can access anywhere else, as well as consistently reliable, authoritative, informed, and relevant. The content of Steroid Receptors—Advances in Research and Application: 2012 Edition has been produced by the world's leading scientists, engineers, analysts, research institutions, and companies. All of the content is from peer-reviewed sources, and all of it is written, assembled, and edited by the editors at ScholarlyEditions™ and available exclusively from us. You now have a source you can cite with authority, confidence, and credibility. More information is available at http://www.ScholarlyEditions.com/.

Melanoma, An Issue of Hematology/Oncology Clinics of North America Springer

Diagnostics and Therapy in Veterinary Dermatology presents thorough coverage of the latest discoveries, drugs, and treatments for dermatologic conditions in animals. Chapters written by experts in each respective area of veterinary dermatology contain up-to-date information on new diagnostic tools and tests, autoimmune diseases, parasitic and fungal infections, medical management of acute and chronic conditions, alternative dermatologic therapies, and more. Offering practical solutions for both specialist and general practice veterinarians dealing with dermatology cases, this wide-ranging resource also addresses antibiotic resistance and misuse, the availability of foods for elimination diet trials, problems with generic drugs, emerging infectious diseases, and other important problems currently facing the profession. Throughout the text, veterinary practitioners are provided with real-world guidance on improving how they work up their dermatology cases and strengthening communication between the primary care veterinarian and the dermatologist. Edited by a leading board-certified dermatologist, this volume: Focuses on cats and dogs Includes numerous high-quality clinical photographs illustrating all key concepts Covers topics such as how to use your nursing staff to the fullest, the One Health movement, and how changing climate is increasing the spread of certain dermatologic diseases Discusses approaches for building a better working relationship between clients, primary care veterinarians and dermatologists Provides insights on the future of technology in the diagnosis and treatment of dermatologic diseases Covering the very latest developments in the field, Diagnostics and Therapy in Veterinary Dermatology is essential reading for veterinary dermatologists, veterinary students, and any veterinary general practitioner with a dermatology caseload.

Handbook of Therapeutic Biomarkers in Cancer Elsevier Health Sciences

De novo and acquired resistance to anti-estrogen therapy and aromatase inhibitors remains a challenge in the treatment of estrogen-receptor positive breast cancer. We employed a systems biology approach to identify survival determinants of estrogen independent breast cancer cells with varying sensitivities to hormonal therapeutics. An estrogen receptor-centered network was developed using bioinformatics databases to probe, with a network-targeted 631-element siRNA library, for essential genes involved in the proliferation and survival of estrogen independent breast cancer cells. We identified a unique subset of 25 genes that are essential for the proliferation of estrogen independent breast cancer cells, 15 of which also promote apoptosis.