



Deoxynucleoside Analogs In Cancer Therapy Cancer Drug Discovery And Development

Pedro Merino



Deoxynucleoside Analogs In Cancer Therapy Cancer Drug Discovery And Development:

Deoxynucleoside Analogs in Cancer Therapy Godefridus J Peters, 2007-11-07 Successful cancer chemotherapy relies heavily on the application of various deoxynucleoside analogs. Since the very beginning of modern cancer chemotherapy a number of antimetabolites have been introduced into the clinic and subsequently applied widely for the treatment of many malignancies both solid tumors and hematological disorders. In the latter diseases cytarabine has been the mainstay of treatment of acute myeloid leukemia. Although many novel compounds were synthesized in the 1980s and 1990s no real improvement was made. However, novel technology is now capable of elucidating the molecular basis of several inborn errors as well as some specific malignancies. This has enabled the synthesis of several deoxynucleoside analogs that could be applied for specific malignancies such as pentostatin and subsequently chlorodeoxyadenosine cladribine for the treatment of hairy cell leukemia. Already in the early stage of deoxynucleoside analog development it was recognized that several of these compounds were very effective in the treatment of various viral infections such as for the treatment of herpes infections. This formed the basis initially for the design of azidothymidine and subsequently many other analogs which are currently successfully used for the treatment of HIV infections. As a spin off of these research lines some compounds not eligible for development as antiviral agents appeared to be very potent anticancer agents. The classical example is gemcitabine, now one of the most widely applied deoxynucleoside analogs used for the combination treatment of non-small cell lung cancer, pancreatic cancer, bladder cancer, and ovarian cancer.

Antiangiogenic Agents in Cancer Therapy Beverly A. Teicher, Lee M. Ellis, 2008-01-08 This volume represents a compendium of scientific findings and approaches to the study of angiogenesis in cancer. The second edition of *Antiangiogenic Agents in Cancer Therapy* is intended to give a current perspective on the state of the art of angiogenesis and therapy directed at this process. Antiangiogenesis is a dynamic and evolving field in oncology. New therapeutic targets continue to emerge followed by the rapid development of new therapeutic agents to be investigated in clinical trials. Optimizing the therapeutic potential of antiangiogenic agents in combination with the other therapies in the armamentarium to fight cancer will be an ongoing challenge.

Cancer Drug Resistance Beverly A. Teicher, 2007-11-09 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.

Transforming Growth Factor-Beta in

Cancer Therapy, Volume I Sonia B. Jakowlew, 2010-01-01 Transforming Growth Factor β in Cancer Therapy Volume I Basic and Clinical Biology The present volume brings together a wealth of information that is fundamental to understanding the role of TGF in the pathogenesis, prevention and treatment of cancer. It is not even 25 years since TGF was first isolated and characterized as a dimeric peptide from both human and bovine sources [1-3] but the entire field of TGF research has grown and expanded so that it is now a central theme in all of cell biology. There is almost no tissue or organ in the mammalian body in which TGF does not play a central role in embryonic differentiation or in adult function and furthermore malfunction of the normal physiology of TGF can have disastrous consequences in almost all of these sites. Therefore the present comprehensive review of so many aspects of TGF function is a most welcome attempt to bring together a huge body of experimental data that is of the utmost importance in the field of oncology.

Gene Therapy for Cancer Kelly K. Hunt, Stephan A. Vörburger, Stephen G. Swisher, 2007-10-26 The possibility of treating cancer, a disease defined by genetic defects by introducing genes targeting these very alterations has led to an immense interest in gene therapy for cancer. Although incremental successes have been realized, enthusiasm for gene therapy has declined due to an increasing number of obstacles. These obstacles include vector systems that do not reach systemic metastases, therapeutic genes with redundant mechanisms allowing for cellular resistance and toxicities in clinical trials leading to premature closure of these studies. Different tactics to overcome or circumvent these obstacles have catalyzed the development of a wide range of gene therapy approaches. Thus far almost two thirds of gene therapy trials have focused on cancer. This reflects the concept that gene therapy approaches for the treatment of cancer do not necessarily require long term expression of the gene as is necessary for the treatment of primary genetic defects like hemophilia or juvenile diabetes. Unlike the treatment of genetic defects where expression of the corrected gene needs to be strong, permanent and sometimes regulated, tactics to treat tumors can be based on temporary and locally limited effects. In addition cancer cells have different properties than normal cells and this allows for targeting gene therapy to specific cells, a major advantage over current antitumor therapies which are also toxic to normal cells and tissues.

Cancer Proteomics Sayed S. Daoud, 2008 This book covers current topics related to the use of proteomic strategies in cancer therapy as well as anticipated challenges that may arise from its application in daily practice. It details current technologies used in proteomics, examines the use of proteomics in cell signaling, presents clinical applications of proteomics in cancer therapy and looks at the role of the FDA in regulating the use of proteomics.

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

Genomics and Pharmacogenomics in Anticancer Drug Development and Clinical Response Federico Innocenti, 2008-10-30 Genomics and Pharmacogenomics in Anticancer Drug Development and Clinical Response provides the most comprehensive body of knowledge available on the role of genetic and genomic variation in the individualization of drug therapies in cancer patients As a consequence of the intrinsic chromosomal and genetic instability of the tumor genome it is generally believed that tailoring of chemotherapy in cancer patients might be achieved by molecular analysis of patient tumor DNA In addition to reduce the toxicity risk of patients the tumor DNA information should be integrated with the available data on polymorphic drug metabolizing enzyme and transporter genes mediating the exposure of patients to active drugs and/or their active metabolites The chapters of this book clearly show how DNA information from both the host germline and the tumor should be taken into account for rational selection of drug therapies in cancer patients an aspect that received little attention despite its importance The availability of new molecular approaches to the selection of drug therapy is an emerging need because the traditional approach based on the evaluation of patient and tumor characteristics is clearly far from optimal Many treated patients do not experience significant benefits from the treatment while they often experience moderate to severe toxicities In addition the development and clinical use of novel molecularly targeted agents alone or in combination with classical cytotoxic therapy requires the understanding of the molecular features of the tumors and the identification of tumor markers of response

Frontiers in Anti-Cancer Drug Discovery, Volume (1) Atta-ur- Rahman, M. Iqbal Choudhary, 2011-02-14 Frontiers in Anti Cancer Drug Discovery is an Ebook series devoted to publishing the latest and the most important advances in Anti Cancer drug design and discovery Eminent scientists write contributions on all areas of rational drug design and drug discovery

The Role of Microtubules in Cell Biology, Neurobiology, and Oncology Antonio Tito Fojo, 2009-01-14 This book presents the first comprehensive exploration of the dynamic potential of microtubules anti cancer targets Written by leading anti cancer researchers this groundbreaking volume collects the most current microtubule research available and investigates the potential of microtubules in cancer therapy

Research Awards Index, 1987 **EGFR Signaling Networks in Cancer Therapy** John D. Haley, William John Gullick, 2009-03-01 The epidermal growth factor EGF receptor and its downstream signal transduction networks have been implicated in the ontology and maintenance of tumor tissues which has motivated the

discovery and development of molecularly targeted anti EGF receptor therapies Over decades of study the EGF receptor structure its ligand binding domains the physical biochemistry underlying its intrinsic tyrosine kinase catalytic function and the modular interactions with SH2 PTB and SH3 domain containing signaling adaptor proteins required for signal transduction have been extensively dissected Not only is the EGF receptor the nexus of many streams of information but it also forms one part of a calculating device by forming dimers and oligomers with the other three receptors in its family in response to at least eleven ligands some of which are expressed in multiple forms with overlapping or quite distinct functions This phenomenon while recruiting to the inner surface of the cell membrane and activating multiple second messenger proteins also allows the possibility of cross talk between these systems permitting a further layer of information to be exchanged Less well described are the cross regulation of the EGF receptor and other anti apoptotic mitogenic and metabolic signaling systems The study of these systems has yielded new surprises One hurdle in these efforts has been that signal transduction pathways have frequently been defined in the generic absence of their tissue specific or cell interaction specific context *Biomedical Index to PHS-supported Research: pt. A. Subject access A-H* ,1992 *Biomedical Index to PHS-supported Research* ,1991

Nucleoside Analogs in Cancer Therapy Bruce D. Cheson, Michael J. Keating, William Plunkett, 2021-10-28 Offering the most current and complete coverage of nucleoside analog activity in oncology and hematology this single source volume includes topics from pharmacology to previously unpublished clinical findings on the pivotal role of fludarabine cladribine and pentostatin in the management of diseases such as chronic lymphocytic and hairy cell leukemia non Hodgkin s lymphoma membranous nephropathy and rheumatoid and psoriatic arthritis **Chemical Synthesis of Nucleoside Analogues** Pedro Merino, 2013-02-12 Compiles current tested and proven approaches to synthesize novel nucleoside analogues Featuring contributions from leading synthetic chemists from around the world this book brings together and describes tested and proven approaches for the chemical synthesis of common families of nucleoside analogues Readers will learn to create new nucleoside analogues with desired therapeutic properties by using a variety of methods to chemically modify natural nucleosides including Changes to the heterocyclic base Modification of substituents at the sugar ring Replacement of the furanose ring by a different carbo or heterocyclic ring Introduction of conformational restrictions Synthesis of enantiomers Preparation of hydrolytically stable C nucleosides Chemical Synthesis of Nucleoside Analogues covers all the major classes of nucleosides including pronucleotides C nucleosides carbanucleosides and PNA monomers which have shown great promise as starting points for the synthesis of nucleoside analogues The book also includes experimental procedures for key reactions related to the synthesis of nucleoside analogues providing a valuable tool for the preparation of a number of different compounds Throughout the book chemical schemes and figures help readers better understand the chemical structures of nucleoside analogues and the methods used to synthesize them Extensive references serve as a gateway to the growing body of original research studies and reviews in the field Synthetically modified nucleosides have proven their value as therapeutic

drugs in particular as antiviral and antitumor agents. However many of these nucleoside analogues have undesirable side effects. With Chemical Synthesis of Nucleoside Analogues as their guide researchers have a new tool for synthesizing a new generation of nucleoside analogues that can be used as therapeutic drugs with fewer unwanted side effects. *International Journal of Oncology* International Center for Cancer Research, 2009

Transforming Growth Factor-Beta in Cancer Therapy, Volume II Sonia B. Jakowlew, 2010-01-01 Transforming Growth Factor B in Cancer Therapy Volume II Cancer Treatment and Therapy The chapters in this volume confer an abundance of knowledge about the current state of our understanding of transforming growth factor B TGF B in cancer treatment and therapy. Unlike several more traditional positive polypeptide growth factors that stimulate cellular proliferation the prototypical TGF B is now known to inhibit the growth of most normal cell types including those of epithelial and mesenchymal origin. However there are examples of cell types that can be stimulated by TGF B under certain conditions. TGF B also induces the accumulation of matrix molecules by stimulating their synthesis as well as inhibiting their degradation. Moreover TGF B induces apoptosis of certain cell types thereby restricting their proliferation. Overactivity of TGF has been linked to several diseases. For instance the effect of TGF on matrix accumulation contributes to fibrotic conditions like glomerulonephritis lung fibrosis and liver cirrhosis. 1 TGF has a very complicated role in cancer that is only beginning to be understood.

Textbook of Biochemistry with Clinical Correlations Thomas M. Devlin, 2010-01-19 This book presents a clear and precise discussion of the biochemistry of eukaryotic cells particularly those of mammalian tissues. It relates biochemical events at a cellular level to the subsequent physiological processes in the whole animal and cites examples of abnormal biochemical processes in human disease. The organization and content are tied together to provide students with the complete picture of biochemistry and how it relates to human diseases.

Manual de Bioquímica Thomas M. Devlin, 2021-07-09 Manual de Bioquímica com Correções e Clônicas trata da bioquímica celular de eucariotos com ênfase em células e tecidos de mamíferos. As correções e clônicas são apresentadas em caixas separadas e dão ao aluno a dimensão de como a pesquisa bioquímica contribui ao entendimento das causas de muitas doenças. Nesta sétima edição todos os capítulos foram atualizados com inclusão de nova informação e condensação de outras. Algumas mudanças são: Discussão expandida sobre microRNAs. Profunda apresentação do complexo de proteínas da linha basal de motores moleculares morte celular programada e câncer. Exposição dos mecanismos de transporte de membrana em conformidade com a nomenclatura atual e orientações de pesquisa. Discussão sobre proteínas não estruturadas. Apresentação reorganizada sobre o metabolismo de aminoácidos que separa a síntese a degradação e as funções dos aminoácidos. Discussão sobre o metabolismo do heme incluída em aminoácidos o que a localiza o mais comum em programas de ensino. Apresentação abrangente da absorção e do transporte de ferro. Discussão inclusiva da função das vitaminas concentrada em um capítulo. Atualização das bibliografias dos capítulos com seleção de referências de fontes de fácil acesso. Muitas acessíveis na rede. Aproximadamente metade das questões e respostas anotadas são novas nesta edição e são semelhantes às de exames de admissão.

em cursos de pós graduação e profissionais e cada grupo de questões tem várias perguntas de solução de problemas. Além disso, em resposta às recomendações de revisores se as de muitos capítulos foram reorganizadas para um melhor fluxo de informação.

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