

CANCER DRUG DISCOVERY AND DEVELOPMENT

Matrix Metalloproteinase Inhibitors in Cancer Therapy

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Matrix Metalloproteinase Inhibitors In Cancer Therapy

Sajal Chakraborti



Matrix Metalloproteinase Inhibitors In Cancer Therapy:

Matrix Metalloproteinase Inhibitors in Cancer Therapy Neil J. Clendeninn, Krzysztof Appelt, 2000-09-17 Cutting edge investigators review the current status of the entire field from the biology of MMPs through the current clinical studies The authors include many leading scientists from pharmaceutical companies who present all the latest concepts and results on the preferred design strategies for MMP inhibitors their molecular mechanisms and their substrates In addition they fully describe their personal research on specific MMP inhibitors detailing vanguard design strategies their in vitro activity the outcome of animal model studies and where available their toxicology safety efficacy in human clinical trials Comprehensive and state of the art *Matrix Metalloproteinase Inhibitors in Cancer Therapy* offers basic and clinical investigators alike a richly informative summary of all the latest research on these powerful new drugs and their high promise as emerging cancer therapeutics

Matrix Metalloproteinase Inhibitors Satya Prakash Gupta, 2012-04-07 Matrix metalloproteinases MMPs are proteolytic enzymes that are involved in many physiological and pathological processes The field of MMP research is very important due to the implications of the distinct paralogs in both human physiology and pathology Over activation of these enzymes results in tissue degradation producing a wide array of disease processes such as rheumatoid arthritis osteoarthritis tumor growth and metastasis multiple sclerosis congestive heart failure and others Thus MMP inhibitors are candidates for therapeutic agents to combat a number of diseases The present book discusses the design and development of different classes of inhibitors of important classes of MMPs such as gelatinases and collagenases The articles focus specifically on structure activity relationships of all classes of compounds and on their modes of action and specificity of binding with the receptors based on experimental and theoretical studies These studies constitute a valuable asset for all those involved in drug development

Camptothecins in Cancer Therapy Val R. Adams, 2007-10-27 A critical review our current understanding of camptothecins their shortcomings and of the possibilities for improving their clinical performance The authors discuss new camptothecin analog development drug delivery issues for optimizing their anticancer activity and their potential use in a variety of different cancers Additional chapters describe what is known about the biochemistry the pharmacology and the chemistry of the camptothecins including the mechanism of topoisomerase and how camptothecins poison this enzyme the use of animal models in defining the anticancer potential of camptothecins and the question of camptothecin resistance

Nanotechnology for Cancer Therapy Mansoor M. Amiji, 2006-12-19 While simultaneous breakthroughs occurring in molecular biology and nanoscience technology will ultimately revolutionize all of medicine it is with our efforts to prevent diagnose and treat cancer that many of the most dramatic advances will occur In support of this potential the U S National Cancer Institute NCI established the Alliance for

Radiolabeled Matrix Metalloproteinase Inhibitors for Breast Cancer Therapy, 2002 Matrix Metalloproteinases MMPs a family of over 20 types of enzymes collectively are capable of degrading all the components of the extracellular matrix MMP 2 and MMP 9 also known as

gelatinases are specifically thought to play critical roles in tumor cell invasion and are frequently co expressed in breast cancer Cyclic peptides containing the sequence HWGF have been described as selective inhibitors of MMP 2 and MMP 9 We tested the hypothesis that gelatinase expression may provide a target for in vivo tumor imaging using a radiolabeled gelatinase inhibitor The peptide DOTA CTTHWGF¹TLC DOTA CTT was labeled with Cu 64 T 1 2 1 2% 12 7 h % which has a decay scheme suitable for both PET imaging and cancer therapy This conjugate maintained MMP 2 inhibitory activity comparable to %Ilomastat a broad range inhibitor of MMPs An increase in the MMP 2 9 activity of human metastatic breast cancer MDA MB 435 tumors in nude mice was observed from 4 to 10 weeks post implantation MicroPET images of Cu 64 DOTA CTT in the tumor bearing nude mice showed tumor uptake at 8 wk post implantation however the same mouse with 5 wk palpable tumors showed no uptake of the tracer suggesting that the MMP 2 and MMP 9 activity is related to the stage of tumor growth These data suggest the potential of radiolabeled gelatinase inhibitors as markers for imaging the metastatic capability of human breast cancer

Therapeutics of Natural and Synthetic Compounds in Protease-Induced Cancer

Sajal Chakraborti, 2025-06-07 Therapeutics of Natural and Synthetic Compounds in Protease Induced Cancer presents a detailed discussion on the role of therapeutic and synthetic compounds in proteases and how they have been utilized to develop anticancer drugs covering both their structure and functions In addition the book explores the experimental and theoretical aspects of natural and synthetic compound design based on proteases Sections bridge the gap between fundamental and translational research with applications in the biomedical and pharmaceutical industry making it a thought provoking read for basic and applied scientists engaged in biomedical research In 23 chapters this book gives both insights on the general aspects of the role of natural and synthetic compounds in cancer therapeutics in cancer development treatment and their use in clinical trails Given the breadth and depth of information covered in the respective contributions the book will be immensely useful for researchers in oncology and for those working to identify targets for drug development Discusses natural and synthetics compounds as promising targets for future research since they play a pivotal role in cancer progression and response to chemotherapy treatment Provides insights into the multifaceted role of natural and synthetic compounds in regulating many important cell processes including cell proliferation apoptosis and autophagy Discusses the key role of compounds in cancer progression focusing on the status of natural chemically modified and synthetic inhibitors in various types of malignancies

Immunotherapy of Cancer

Mary L. Disis, 2007-10-28 Expert bench and clinical scientists join forces to concurrently review both the state of the art in tumor immunology and its clinical translation into promising practical treatments The authors explain in each chapter the scientific basis behind such therapeutic agents as monoclonal antibodies cytokines vaccines and T cells and illustrate their clinical manipulation to combat cancer Additional chapters address statistical analysis both of clinical trials and assay evaluations methods for the discovery of antigens adoptive T cell therapy and adaptive and innate immunity The challenges in clinical trial design the need for biomarkers of response such as

novel imaging techniques and immunologic monitoring and the new advances and directions in cancer immunotherapy are also fully examined

Therapeutic Targets in Airway Inflammation N. Tony Eissa, David P. Huston, 2003-05-13 This reference examines the cellular molecular and genetic mechanisms involved in airway inflammation as well as the pathophysiology epidemiology and aetiology of asthma It explores strategies to prevent cellular injury and oxidative tissue damage inhibit key inflammatory pathways and identify disease specific targets to reduce the induction

Hydroxamic Acids Satya P. Gupta, 2013-09-30 Satya P Gupta's Hydroxamic Acids is the first book to compile invited articles written by international experts on the class of compounds hydroxamic acids Found to possess a wide spectrum of biological activities the hydroxamic acids are of interest to theoretical and experimental chemists who can study and make use of them in drug design and development Chapters in this book provide a diverse and comprehensive coverage of this compound class and consequently this publication is a valuable resource for researchers in chemical pharmaceutical and biological sciences

Cell Invasion Jyrki Heino, 2002-08-01 Provides an overview of cell invasion Topics include information on the cellular matrix cell surface integrins matrix metalloproteinases and proteinases and the interplay between protein families

Antiangiogenic Cancer Therapy Darren W. Davis, Roy S. Herbst, James L. Abbruzzese, 2007-07-25 Top Investigators Explore the Complexities of Angiogenesis Cancer Research The targeting of tumor angiogenesis has evolved into one of the most widely pursued therapeutic strategies However as of yet no antiangiogenic agent used as a monotherapy has demonstrated a survival benefit in a randomized Phase III trial The combination of bev

Histone Deacetylases Eric Verdin, 2007-11-06 A panel of leading investigators summarizes and synthesizes the new discoveries in the rapidly evolving field of histone acetylation as a key regulatory mechanism for gene expression The authors describe what has been learned about these proteins including the identification of the enzymes the elucidation of the enzymatic mechanisms of action and the identification of their substrates and their partners They also review the structures that have been solved for a number of enzymes both alone and in complex with small molecule inhibitors and the biological roles of the several histone deacetylases HDAC genes that have been knocked out in mice

Matrix Metalloproteinase Biology Irit Sagi, Jean Gaffney, 2015-08-03 Discussing recent advances in the field of matrix metalloproteinase MMP research from a multidisciplinary perspective Matrix Metalloproteinase Biology is a collection of chapters written by leaders in the field of MMPs The book focuses on the challenges of understanding the mechanisms substrate degradation by MMPs as well as how these enzymes are able to degrade large highly ordered substrates such as collagen All topics addressed are considered in relation to disease progression including roles in cancer metastasis rheumatoid arthritis and other inflammatory diseases The text first provides an overview of MMPs focusing on the history the development and failures of small molecule inhibitors in clinical trials and work with TIMPS the endogenous inhibitors of MMPs These introductory chapters establish the foundation for later discussion of the recent progress on the design of different types of inhibitors including novel antibody based therapeutics

The following section emphasizes research using novel methods to further the study of the MMPs. The third and final section focuses on in vivo research particularly with respect to cancer models, degradation of the extracellular matrix and MMP involvement in other disease states. Written and edited by leaders in the field, *Matrix Metalloproteinase Biology* addresses the rapidly growing MMP research and will be an invaluable resource to advanced students and researchers studying cell and molecular biology. Cancer Chemoprevention Gary J. Kelloff, Ernest T. Hawk, Caroline C. Sigman, 2008-08-17. Despite significant advances in cancer treatment and measures of neoplastic progression, drug effect or early detection, overall cancer incidence has increased. Pharmacodynamic markers and markers that measure cancer-associated morbidity are considerable and overall prognosis as well as predict responses to specific therapy. Cancer survival has remained relatively flat over the past. All these biomarkers have the potential to greatly augment several decades. However, new technology, the development of successful chemoprevention therapies allowing exploration of signal transduction pathways, but two specific types of biomarkers will have the most identification of cancer-associated genes and imaging of immediate impact on successful chemopreventive drug, tissue architecture and molecular and cellular function is development. Those that measure the risk of developing, increasing our understanding of carcinogenesis and cancer-invasive life-threatening disease and those whose progression. This knowledge is moving the focus of cancer. Lation can reasonably predict clinical benefit and therapeutics including cancer preventive treatments to therefore serve as surrogate endpoints for later occurring drugs that take advantage of cellular control mechanisms. Clinical disease. Thus far, the biomarker that best measures to selectively suppress cancer progression, these two phenomena is intraepithelial neoplasia (IEN). Carcinogenesis is now visualized as a multifocal because it is a near-obligate precursor to cancer. **Journal of the National Cancer Institute**, 2002. Each issue is packed with extensive news about important cancer-related science, policy, politics and people. Plus there are editorials and reviews by experts in the field, book reviews and commentary on timely topics. *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

Enzyme Inhibition and Bioapplications Rakesh Sharma,2012-05-09 Enzyme Inhibition and Bioapplications is a concise book on applied methods of enzymes used in drug testing The present volume will serve the purpose of applied drug evaluation methods in research projects as well as relatively experienced enzyme scientists who might wish to develop their experiments further Chapters are arranged in the order of basic concepts of enzyme inhibition and physiological basis of cytochromes followed by new concepts of applied drug therapy reliability analysis and new enzyme applications from mechanistic point of view

Peptide Chemistry and Drug Design Ben M. Dunn,2015-02-02 This book focuses on peptides as drugs a growing area of pharmaceutical research and development It helps readers solve problems of discovering developing producing and delivering peptide based drugs Identifies promising new areas in peptide drug discovery Includes chapters on discovery from natural sources metabolic modification and drug delivery Overviews separation methods and techniques for analysis bond formation and purification Offers readers both a professional reference and a text or resource for graduate level students

Proteases in Gastrointestinal Tissues Uwe Lendeckel,Nigel M. Hooper,2006-05-09 This the fifth volume in the Proteases in Biology and Disease series is devoted to Proteases in Gastrointestinal Tissues Of course proteases play an important role in the digestion and utilization of ingested proteins but besides that they elicit a wide range of physiological and pathological effects Proteases have been recognized as essential regulators acting both locally and systemically of normal development growth and functioning Dysregulation of protease expression and or enzymatic activity is often associated with the onset or progression of disease and thus proteases represent interesting targets for the pharmacological therapy of e g cancer chronic inflammation graft rejection fibrosis diabetes vascular disease and viral or bacterial infections In addition changes in the localization abundance or activity of proteases may serve as informative diagnostic or prognostic markers This volume focuses on stomach gut pancreas and liver and highlights the role of proteases in normal physiology and disease processes involving these tissues The first chapter by Nigel W Bunnett and Graeme S Cottrell reviews the current knowledge about the protease activated receptors PARs in gastrointestinal tissues Starting with the mechanisms of activation signal transduction and regulation of PAR their role in controlling gastrointestinal functions and the possible involvement in gastrointestinal diseases are summarized In Chapter 2 Nikhil I Khushalani and Nithya Ramnath review the role of matrix metalloproteases MMPs and their natural inhibitors TIMPs in different types of gastric cancer

Extracellular Matrix: Pathobiology and Signaling Nikos Karamanos,2012-08-31 Over the last decades cell biology and biological chemistry have increasingly turned their attention to the space between cells and revealed an elaborate network of macromolecules essential for structural support cell adhesion and signaling This comprehensive handbook of the

extracellular matrix will give an overview of the current state of knowledge of matrix components structure and function their role in health and disease matrix pathobiology and new aspects related to pharmacological targeting It will provide an introduction to the extracellular matrix and detailed sections and chapters on Importance of extracellular matrix in health and disease Matrix proteoglycans aggrecan versican perlecan SLRPs syndecans glypicans serglycin Matrix proteinases remodeling wound healing regulatory roles in health and disease metalloproteinases cysteine proteases plasmin and plasminogen activator system Glycobiology hyaluronan and sulfated glycosaminoglycans in cancer inflammation and metabolic control Collagens supramolecular assembly proteins binding collagen scaffolds bacterial and mutated collagens procollagen proteinases Cell surface receptors integrins syndecans mechanical strain and TGF β CD44 and DDR Biotechnological and pharmacological outlook matrix regulation by growth factors hyaluronidases pathobiology disease targeting delivery systems EMT and proteomics The book Extracellular Matrix Pathobiology and Signaling provides a comprehensive and up to date collection of very relevant topics for understanding the various facets of extracellular matrix and its interactions with cells in normal tissue as well as in disease It represents the current front line and will serve as a reference for extracellular matrix and posttranslational modifications Dick Heinegård Department of Clinical Sciences Lund Section Rheumatology Lund University Sweden

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