File Type PDF Cancer In Drugs Peptide And Protein Of Delivery

If you ally infatuation such a referred **Cancer In Drugs Peptide And Protein Of Delivery** books that will give you worth, get the certainly best seller from us currently from several preferred authors. If you want to funny books, lots of novels, tale, jokes, and more fictions collections are plus launched, from best seller to one of the most current released.

You may not be perplexed to enjoy every ebook collections Cancer In Drugs Peptide And Protein Of Delivery that we will extremely offer. It is not on the order of the costs. Its more or less what you craving currently. This Cancer In Drugs Peptide And Protein Of Delivery, as one of the most in action sellers here will unquestionably be in the middle of the best options to review.

KEY=AND - NEAL MARKS

Delivery of Protein and Peptide Drugs in Cancer

World Scientific Written by leading scientists in the field of delivery of protein and peptide drugs to tumors for cancer therapy, this important book provides a broad introduction to the field, with discussion by key experts on the physiological barriers for protein and peptide drugs in tumors, and the different approaches to stabilization of these drugs in biological surroundings, as well as their enhanced delivery to tumors and inside cancer cells. This book can be used as an advanced textbook by graduate students and young scientists and clinicians at the early stages of their career. It is also suitable for non-experts from related areas of chemistry, biochemistry, molecular biology, physiology, experimental and clinical oncology and pharmaceutical sciences, who are interested in general problems of drug delivery and drug targeting as well as in a more specialized topics of using protein and peptide drugs for tumor therapy. Prof Torchilin is an expert in Nanomedicine and a recipient of numerous awards including the Lenin Prize in Science & Technology of the former USSR, membership in the European Academy of Sciences, and AAPS Research Achievement Award in Pharmaceutics and Drug Delivery. He served as an Associate Professor of Radiology at Harvard Medical School before joining Northeastern University as the Chairman of the Department of Pharmaceutical Sciences. Contents:Influence of Tumor Physiology on Delivery of Therapeutics (R B Campbell)Enhanced Permeability and Retention (EPR) Effect and Tumor-Selective Delivery of Anticancer Drugs (K Greish et al.)Basic Strategies for PEGylation of Peptide and Protein Drugs (G Pasut et al.)PEGylated Proteins as Cancer Therapeutics (M Morpurgo et al.)PEGylated Proteins in Immunotherapy of Cancer (J F

Eliason)Silencing Proteins: Nanotechnological Approaches to Deliver of siRNA for Cancer Therapy (R M Schiffelers et al.)Anti-Cancer Proteins and Peptides in Liposomes (V Torchilin)Folate-Mediated Delivery of Protein and Peptide Drugs into Tumors (J A Reddy et al.)Transferrin Receptor Mediated Delivery of Protein and Peptide Drugs into Tumors (J Fahrmeir & M Ogris)Transmembrane Delivery of Protein and Peptide Drugs into Cancer Cells (C C Saenz & S F Dowdy)Protein and Peptide Drugs to Suppress Tumor Angiogenesis (C Rüegg)Utilizing Lymphatic Transport in Enhancing the Delivery of Drugs, Including Proteins, and Peptides, to Metastatic Tumors (E K Wasan & K M Wasan)Delivery of Protein and Peptide Drugs to Brain Tumors (H B Newton)Protein and Peptide-Based Cancer Gene Therapy (S Chada & R Ramesh) Readership: Graduate students & academics from cancer therapy, protein & peptide drugs, drug delivery, & tumor targeting areas; non-experts interested in drug delivery to tumors. Key Features:Written by leading scientists such as Prof Veronese, Prof Maeda, Prof Dowdy, Prof Torchilin & Prof WasanDetailed explanation of physiological barriers for protein and peptide drugs in tumorsDifferent approaches to the stabilization of proteins and peptides in biological surroundings and their enhanced delivery into tumors and inside cancer cellsKeywords:Cancer;Protein & Peptide Drugs;Delivery;Tumor Physiology;Drug Carriers;Pegylation;Liposomes;Angiogenesis;Lymphatic Transport;Protein Transduction

Development of New Peptide Based Inhibitors of Protein Kinase B (PKB/Akt) as Potential Drugs for Cancer

Addition au factum des syndic et adjoints des maistres imprimeurs...

Identification of Novel Inhibitory Peptides of Protein-Protein Interactions Involved in DNA Repair

as Potential Drugs in Breast Cancer Treatment

Protein-protein interactions are critical to almost every cellular process. Disruption of these interactions would effectively interfere with the cell's functions and its ability to grow and divide normally. The Rad51 and Rad52 proteins are important proteins involved in DNA repair. Rad51 acts as a hexamer binding single-stranded DNA to drive strand exchange during homologous recombination. By blocking Rad51 from multimerization we can theoretically disrupt homologous recombination, and thus decrease the efficacy of DNA repair. Deficiency in DNA damage repair will sensitize cells to DNA damaging agents and thus such tumors can be effectively treated with a lower dose of chemotherapeutic agents/radiation. Short peptides of a few amino acids (5-10) have been shown to be enough to destabilize protein-protein interactions. Thus a library of random combinatorial peptides of sufficient complexity will in theory have an inhibitory molecule for any protein-protein interaction. This project attempts to isolate peptides that inhibit Rad 51 from multimerisation to be used as a chemosensitizing agent during chemo/radiotherapy using a modified Yeast two hybrid screen called the reverse two-hybrid system.

Protein and Peptide Nanoparticles for Drug Delivery

Academic Press Published continuously since 1944, the Advances in Protein Chemistry and Structural Biology series has been the essential resource for protein chemists. Each volume brings forth new information about protocols and analysis of proteins. Each thematically organized volume is guest edited by leading experts in a broad range of protein-related topics. Describes advances in application of powerful techniques in a wide bioscience area Chapters are written by authorities in their field Targeted to a wide audience of researchers, specialists, and students The information provided in the volume is well supported by a number of high quality illustrations, figures, and tables

Cyclized Helical Peptides

Synthesis, Properties and Therapeutic Applications

John Wiley & Sons An important and timely guide to the progress being made on constrained helical peptides Constraint helical peptides have emerged as a solution to target previously undruggable protein-protein interactions, which feature large

and complex surfaces. Cyclized Helical Peptides: Synthesis, Properties and Therapeutic Applications offers a review of the most current methodologies of constructing constrained helices. The authors noted experts on the topic include the information on the fundamental features of cyclized helical peptides and discuss their limitations. The book summarizes and explores the effects of chemical methods constructing helical peptides on helicity, binding affinity, cell penetration, and nonspecific toxicity. The book examines the therapeutic applications of the constraint helices and includes comparison with existing small molecule modulators or antibodies. Designed as a useful resource for both those outside and inside the field. Those new to the field will find a comprehensive introduction to cyclized helical peptide and those inside the field will find a deeper understanding of the topic. This important book: Offers a practical introduction to constrained helical peptides Includes all aspects of constrained helical peptides Includes information on the most recent methods that have emerged Presents a guide to help solve practical problems in the field Written for academics, pharmaceutical professional, Cyclized Helical Peptides is a comprehensive guide to the developments of constrained helical peptides.

Inflammation and Angiogenesis

Springer This book is focused on the analysis of the role played by immune cell components in the angiogenic process associated with inflammation and tumor growth. Both innate and adaptive immune cells are involved in the mechanisms of endothelial cell proliferation, migration and activation, through the production and release of a large spectrum of pro-angiogenic mediators. These may create the specific microenvironment that favors an increased rate of tissue vascularization. The link between chronic inflammation and tumorigenesis was first proposed by Rudolf Virchow in 1863 after the observation that infiltrating leukocytes are a hallmark of tumors and first established a causative connection between the lymph reticular infiltrate at sites of chronic inflammation and the development of cancer. Tumors were described as wounds that never heal and surgeons have long described the tendency of tumors to recur in healing resection margin and it has been reported that wound healing environment provides an opportunistic matrix for tumor growth. As angiogenesis is the result of a net balance between the activities exerted by positive and negative regulators, this book will also provide information on some anti-angiogenic properties of immune cells that may be utilized for a potential pharmacological use as anti-angiogenic agents in inflammation as well as in cancer. The work is written for researchers in the field and also for graduate students which approach this matter.

Peptides as Drugs

Discovery and Development

John Wiley & Sons By covering the full spectrum of topics relevant to peptidic drugs, this timely handbook serves as an introductory reference for both drug developers and biomedical researchers interested in pharmaceutically active peptides, presenting both the advantages and challenges associated with this molecular class. The first part discusses current approaches to developing pharmaceutically active peptides, including case studies of the use of peptidic drugs in cancer and AIDS therapy. The second part surveys strategies for the development and targeting of peptidic drugs. With its integration of biochemical, pharmaceutical and clinical research, this work reveals the full picture of modern peptide drug research in a single volume, making it an invaluable reference for medicinal chemists, biochemists, biotechnologists, and those in the pharmaceutical and biotechnological industries.

Targeting of Drugs 3

The Challenge of Peptides and Proteins

Springer Science & Business Media Proceedings of a NATO ASI held in Cape Sounion Beach, Greece, June 24-July 5, 1991

Novel Peptide/Protein Delivery System Targeting ErbB2-Overexpressing Breast Cancer Cells

It has been well recognized that the next frontier in molecular medicine is the delivery of therapeutics. Among the biological therapeutics, peptides/proteins are especially difficult and challenging to deliver. A peptide sequence localized within a 13-amino acid domain of Tat (named "penetratin"), when linked to other peptides or proteins, was able to carry attached peptide or protein into the cells when they were added to cell culture medium. We hypothesized that the unique property of "penetratin" can be utilized for delivery of therapeutic peptides/proteins. It should be noted that after the funding of this Idea Award, a report published in Science by Steven Dowdy's laboratory demonstrated that "penetratin" can deliver functional beta-galactosidase protein (120 kD) to all tissues in mice.

Drug Delivery

Principles and Applications

John Wiley & Sons Following its successful predecessor, this book covers the fundamentals, delivery routes and vehicles, and practical applications of drug delivery. In the 2nd edition, almost all chapters from the previous are retained and updated and several new chapters added to make a more complete resource and reference. • Helps readers understand progress in drug delivery research and applications • Updates and expands coverage to reflect advances in materials for delivery vehicles, drug delivery approaches, and therapeutics • Covers recent developments including transdermal and mucosal delivery, lymphatic system delivery, theranostics • Adds new chapters on nanoparticles, controlled drug release systems, theranostics, protein and peptide drugs, and biologics delivery

Peptide-Mediated Transduction of Proteins and Nucleic Acids to Prevent and Treat Experimental Prostate Cancer

Our goal in this project is to prevent the occurrence of bone metastasis in early experimental prostate cancer using protein transduction: the ability of small peptides to facilitate the entry of large biologically active fusion protein cargos into cells. The hypothesis to be tested is that protein transduction can deliver therapeutic proteins to skeletal tissues and bone marrow in such a manner that they may facilitate the apoptotic, or programmed cell death of cancerous cells and tissues of the bone. Prostate cancer is lethal and incurable once it has metastasized to the bone. We and others have previously shown that protein transduction can allow many proteins into organs previously unaccessible to other delivery methods (drugs, viral vectors etc). We have constructed unique protein-transduction domains (PTD5 and Lys8) which we have demonstrated efficiently facilitate the entry and activity of the pro-apoptotic peptide Smac34 into prostate cancer cell lines. Protein transduction may prove to be a useful drug delivery method of biologically active proteins in cancer.

Nanotechnology in Drug Delivery

Fundamentals, Design, and Applications

CRC Press This important new book provides the fundamental understanding of the peptide and protein drug delivery systems with a special focus on their nanotechnology applications. Addressing an increasing interest in peptide and protein drug delivery systems in both academic and industrial circles worldwide, this book fills the need for a comprehensive review and assessment of conventional and nonconventional routes of administration.

Proteins and Peptides

Pharmacokinetic, Pharmacodynamic, and Metabolic Outcomes

CRC Press Addressing the increased use of protein and peptide candidates as treatments for previously untreatable diseases, this comprehensive and progressive source provides the reader with a roadmap to an increased understanding of issues critical for successfully developing a protein or peptide therapeutic candidate. Proteins and Peptides is

Topics in Anti-Cancer Research

Bentham Science Publishers The fifth volume of the eBook series entitled "Topics in Anti-Cancer Research" is based on new contributions from scientists working in the field of cancer research and therapy. The topics presented in this eBook cover advances in cancer drug Development targeting carbonic anhydrase IX and XII. An overview of the patents and Anti-Cancer drug development analyzing regulatory policies in anticancer drugs in China is included. Approaches on cell based Anti-Cancer drug delivery systems and current developments in Anti-Cancer agents targeting heat shock proteins, besides the promising field of tumor homing peptides (THPs) in the treatment of cancer are also covered in this volume. We anticipate that these topics on new drug targets, drug delivery approaches and techniques in cancer research & therapy will attract the audience, researchers and scientists in the field of cancer and its treatment.

Zebrafish: A Model for Marine Peptide Based Drug Screening

Springer This book offers a comprehensive overview of toxicology, highlighting the significance of peptide-based toxins from marine environments. It discusses the principles of protein-carbohydrate and domain-domain interactions to increase our understanding of toxicology in zebrafish models, as well as drug interaction mechanisms and target definition in drug discovery. It also reviews the structure of marine peptides/toxins and the toxicology of peptide secreting cells and cells that respond to these enzymes, and describes the normal and abnormal toxicology of marine peptides in zebrafish models. Offering insights into the field of proteomics, particularly current practice and research models for solving its many riddles, the book also explains the analytical principles of marine protein-protein and protein-carbohydrate interaction in the context of teratogenicity in target identification in peptide- based drug discovery. Lastly, the book methodically examines the preclinical research on marine proteins/peptides.

Drug Delivery in Oncology

From Basic Research to Cancer Therapy

John Wiley & Sons In this first authoritative overview on modern cancer chemotherapy 121 international specialists have contributed their experience and recent data for what is likely to become the gold standard in the field. The authors summarize knowledge gained over the past decade, from basic concepts to successful applications in the clinic, covering active and passive targeting strategies as well as tissue-specific approaches. All current and future targeted delivery systems are discussed, from ligand-based to antibody-based polymer-based systems, right up to micro- and nanoparticulate systems. A special section covers the delivery of nucleic acid therapeutics, such as siRNA, miRNA and antisense nucleotides. In each case, a description of the basic technique is followed by a discussion of the latest preclinical and clinical developments in the field. By virtue of its clear and didactic structure, rich illustrative material and summary chapters, this handbook and ready reference enables the efficient transfer of knowledge between different disciplines, from basic research to the clinician and vice versa. It is equally well suited for professionals, researchers and students in medical oncology and cancer biology, and is also excellent for teaching medical students the foundations of 21st century cancer chemotherapy.

Delivery Technologies for Biopharmaceuticals

Peptides, Proteins, Nucleic Acids and Vaccines

John Wiley & Sons Advances in biotechnology have provided scientists with an increasing number of biopharmaceuticals such as novel peptide and protein drugs as well as nucleic acid based drugs for gene therapy. However, successful delivery of these biopharmaceuticals is a major challenge because their molecular properties lead to poor physical and chemical stability in the body and limited membrane permeability. Therefore researchers are developing a range of new delivery technologies and materials to enable these new drugs to be delivered intact to their target sites. Delivery Technologies for Biopharmaceuticals describes strategies to overcome the main barriers for successful delivery of therapeutic peptides, proteins, and nucleic acid-based drugs or vaccines related to the site of administration and the target site. Many of the approaches described are reported in formulations in current clinical trials as well as in marketed products. Contents include: challenges in delivery of biopharmaceuticals novel formulation approaches for peptide and protein injectables non-viral chemical vectors and viral technology for delivery of nucleic acid based drugs immune response, adjuvants and delivery systems for vaccines several examples of delivery systems for different biopharmaceuticals a critical assessment of delivery technologies for biopharmaceuticals Delivery Technologies for Biopharmaceuticals is an essential single-volume introduction to the technologies used by researchers to ensure efficient delivery of this exciting new class of drugs. It will be of value to researchers and students working in drug delivery, formulation, biopharmaceuticals, medicinal chemistry, and new materials development.

Peptide-based Drug Discovery

Challenges and New Therapeutics

Royal Society of Chemistry With potentially high specificity and low toxicity, biologicals offer promising alternatives to small-molecule drugs. Peptide therapeutics have again become the focus of innovative drug development efforts backed up by a resurgence of venture funds and small biotechnology companies. What does it take to develop a peptide-based medicine? What are the key challenges and how are they overcome? What are emerging therapeutics for peptide modalities? This book answers these questions with a holistic story from molecules to medicine, combining the themes of design, synthesis and clinical applications of peptide-based therapeutics and biomarkers. Chapters are written and edited by leaders in the field

from industry and academia and they cover the pharmacokinetics of peptide therapeutics, attributes necessary for commercially successful metabolic peptides, medicinal chemistry strategies for the design of peptidase-resistant peptide analogues, disease classes for which peptide therapeutic are most relevant, and regulatory issues and guidelines. The critical themes covered provide essential background information on what it takes to develop peptide-based medicine from a chemistry perspective and views on the future of peptide drugs. This book will be a valuable resource not only as a reference book for the researcher engaged in academic and pharmaceutical setting, from basic research to manufacturing and from organic chemistry to biotechnology, but also a valuable resource to graduate students to understand discovery and development process for peptide-based medicine.

Development of In-Tether Carbon Chiral Center-Induced Helical Peptide

Methodology and Applications

Springer Nature This book focuses on the development of stapled peptides, a novel molecular modality used to regulate aberrant intracellular protein–protein interactions (PPIs). The author designs and presents a novel helical peptide stabilization methodology by constructing a chiral cross-linker moiety, namely “chiral center induced peptide helicity (CIH)”. The book demonstrates that a precisely positioned carbon chiral center on tether can decisively determine the secondary structure of a peptide, and that the R-configured peptide is helical, while the S-configured peptide is non-helical. Further, it reports that helicity-enhanced R isomer peptides displayed significantly enhanced cell permeability and target binding affinity, as well as tumor inhibition efficiency, in comparison to S isomer peptides. The book will not only advance readers’ understanding of the basic principle of stapled peptides, but also accelerate the clinical transformation of stapled peptide drugs.

P53, Protein Kinases and Peptide Based Therapies in the Treatment of Cancer

Protein Analysis using Mass Spectrometry

Accelerating Protein Biotherapeutics from Lab to Patient

John Wiley & Sons Presents Practical Applications of Mass Spectrometry for Protein Analysis and Covers Their Impact on Accelerating Drug Discovery and Development Covers both qualitative and quantitative aspects of Mass Spectrometry protein analysis in drug discovery Principles, Instrumentation, Technologies topics include MS of peptides, proteins, and ADCs , instrumentation in protein analysis, nanospray technology in MS protein analysis, and automation in MS protein analysis Details emerging areas from drug monitoring to patient care such as Identification and validation of biomarkers for cancer, targeted MS approaches for biomarker validation, biomarker discovery, and regulatory perspectives Brings together the most current advances in the mass spectrometry technology and related method in protein analysis

Peptide-Based Drug Design

Humana Press Due to their high specificity and low toxicity profile, peptides have once again become central to the development of new drugs. In Peptide-Based Drug Design: Methods and Protocols, expert researchers provide a handbook which offers a selection of research and production tools suitable for transforming a promising protein fragment or stand-alone native peptide into a pharmaceutically acceptable composition. The volume delves into contemporary, cutting-edge subjects such as hit isolation and target validation, computer-aided design, sequence modifications to satisfy pharmacologists, in vivo stability and imaging, and the actual production of difficult sequences. Written in the highly successful Methods in Molecular BiologyTM series format, chapters include readily reproducible, step-by-step laboratory protocols, lists of materials, and the Notes section, which highlights tips on troubleshooting and avoiding known pitfalls. Comprehensive and up-to-date, Peptide-Based Drug Design: Methods and Protocols shows its subject to be an independent science on the rise, and provides scientists with a clear, concise guide for continuing this vital research.

Peptides Targeting Protein-Protein

Interactions: Methods and Applications

Frontiers Media SA

Novel Approaches for Targeted Delivery of Cancer Therapeutics to Nuclei of Malignant Cells

The primary goal of this project is to increase specific uptake of anti-cancer therapeutics by nuclei of cancer cells. A lot of research has been done to target therapeutics specifically across plasma membrane of malignant cells. However not much research has been done to deliver them to their target cellular compartment where the drug elicits its pharmacological response. In case of majority of anti-cancer drugs the target is usually nuclei of cancer cells. Hence nuclear delivery of therapeutics is the next frontier of pharmaceutics. In this dissertation work this issue has been investigated. Initially in the first strategy adopted, novel peptide prodrug of doxorubicin was developed which may evade over-expressed efflux pumps on breast cancer cells. This approach may lead to increased uptake and higher drug accumulation in nuclei of cancer cells. L-val-L-val doxorubicin prodrug was synthesized following standard f-moc chemistry. The prodrug was analyzed for stability, cellular and nuclear uptake and interaction with efflux and peptide transporters. Breast cancer cells (T-47D) were grown on polystyrene 12-well plates. The prodrug Val-Val-doxorubicin was found to be very stable in breast cancer cell homogenate. It was able to evade efflux pumps. The prodrug penetrated cytoplasm and nuclei of cancer cells by interacting with peptide transporters over-expressed on plasma and nuclear membrane of T-47D.Uptake of prodrug was found to be 10 fold higher than parent drug. Peptide prodrug derivatization of doxorubicin has potential to evade efflux pumps and increase availability and nuclear accumulation of doxorubcin in breast cancer cells. However due to its stability the prodrug did not biorevert to its parent drug in therapeutic concentration. Hence alternative approaches were investigated. As part of this alternate approach novel nuclear localization signal (NLS) peptide analogues have been designed that can carry therapeutic molecules specifically into nuclei of cancer cells. This strategy might be able to reduce toxicity to non-malignant cells by delivering anticancer drugs to subcellular organelle i.e. nucleus of cancer cells preferentially. Native NLS peptide-conjugated drugs can reach nucleus of any cell non-specifically. However the overarching challenge is to enhance drug uptake across plasma and nuclear membranes to enhance anticancer drug delivery in drug resistant cancer cells. Adenoviral fiber protein (AFP) that encodes for NLS has been known to penetrate both plasma and nuclear membrane nonspecifically. Therefore novel NLS peptide

analogues have been synthesized by substitutions of NLS sequence specific amino acids for targeting cancer cells primarily. Specific amino acids of native NLS have been substituted based on hydrophobic interactions between the peptides with plasma membrane and nucleo pore complex (NPC) that can influence cytoplasmic and nuclear transport. These peptides can carry therapeutics selectively to nuclei of cancer cells simultaneously evading normal cells. Five NLS peptides have been synthesized. These peptides were synthesized by AAPtech automated peptide synthesizer. Following synthesis, the peptides were purified by a shimadzu Preparative HPLC which was confirmed by HPLC-MSMS. Confocal and quantitative uptake studies with various cancer and corresponding non-cancerous human cell lines were performed. It was observed that two (NLS3 and NLS5) peptides are specific for targeting cancer cell nucleus. It has led to an unequivocal conclusion that these novel peptide analogues can selectively bind to plasma membranes of cancer cells and target NPC simultaneously. Following screening of peptides which can function as targeting moieties, nanoparticle formulation was developed to deliver anti-cancer drugs. One of the important parameters for nuclear drug delivery is size. The nucleopore complex has a diameter of 30 nm. Cargo with 30-40 nm can enter the NPC passively. However particles higher than 40 nm need to be actively transported across NPC. It has been reported that particles with 60-70 nm with anti cancer drugs can be delivered into nucleus with localization signals. This is the target size which has been achieved for doxorubicin loaded nanoparticle. PLGA-PEG-NH2 was used as polymer for preparation of doxorubicin loaded nanoparticles. This is because of availability of NH2 group at the end of PEG group for conjugation of peptide moiety for targeted delivery following optimization of size. Nanoparticles were prepared by nanoprecipitation method. Parameters like effect of solvent, polymer concentration, effect of aqueous phase volume, drug concentration were optimized to yield a nanoparticle of size range 60-70 nm as this size can be taken up by nucleus if actively aided by nuclear localization signal. Following preparation of nanoparticle of optimized size, screened peptides (NLS3 and NLS5) with maximum affinity for cancer cell nuclei with minimal entry into corresponding non-malignant cells were conjugated to nanoparticles. Targeted nanoparticles were investigated for its active targeting property in a 3D model of breast cancer. It was observed that nanoparticle with NLS conjugated to its surface delivered higher concentration of doxorubicin compared to unconjugated nanoparticle or free doxorubicin.

Heat Shock Protein Inhibitors Success Stories

Springer Medicinal chemistry is both science and art. The science of medicinal chemistry offers mankind one of its best hopes for improving the quality of life. The art of medicinal chemistry continues to challenge its practitioners with the need for both intuition and experience to discover new drugs. Hence sharing the experience of drug research is uniquely beneficial to the field of medicinal chemistry. Drug research requires interdisciplinary team-work at the interface between chemistry,

biology and medicine. Therefore, the topic-related series Topics in Medicinal Chemistry covers all relevant aspects of drug research, e.g. pathobiochemistry of diseases, identification and validation of (emerging) drug targets, structural biology, drugability of targets, drug design approaches, chemogenomics, synthetic chemistry including combinatorial methods, bioorganic chemistry, natural compounds, high-throughput screening, pharmacological in vitro and in vivo investigations, drug-receptor interactions on the molecular level, structure-activity relationships, drug absorption, distribution, metabolism, elimination, toxicology and pharmacogenomics. In general, special volumes are edited by well known guest editors.

Pharmaceutical Perspectives of Cancer Therapeutics

Springer Science & Business Media Pharmaceutical Perspectives of Cancer Therapeutics covers a wide variety of therapeutic approaches including gene therapy, immunological therapy; cancer vaccines; strategy for solid tumors as well as for hematological cancers; methods to suppress tumor angiogenesis and metastasis; development and utilization of relevant animal models; introduction of new concepts such as cancer stem cells and new technologies, such as DNA and tissue microarrays; and RNA interference. In addition, clinical application, the development of DNA diagnosis biomarkers and cancer prevention, as well as the utilization of imaging in cancer therapy are also discussed. The use of synthetic carriers, such as lipids, polymers, and peptides for delivery and targeting of small molecules, proteins, and nucleic acids to cancer cells in vivo are discussed. Pharmaceutical Perspectives of Cancer Therapeutics also includes cancer therapy modality in surgery, chemotherapy, and radiotherapy, as well as in combination or multi-modality, giving our book a more focused view of cancer therapy.

Cancer Proteomics

From Bench to Bedside

Springer Science & Business Media "Over the past 20 years, there have been tremendous advances in our understanding of how normal cells transform to cancer and the importance of signaling pathways in cancer initiation and progression. To keep pace, proteomics technologies must constantly be improved. In Cancer Proteomics, the authors collectively outline the current status of proteomics in cancer therapy and describe the existing technologies used in proteomics that allow for protein profiling and the identification of druggable targets in human samples. Mass spectrometry-based protein characterization and protein microarrays hold great promise for predicting response to specific drugs in cancer therapy. This book offers a broad perspective on topics related to the use of proteomic strategies in cancer therapy and addresses challenges that may arise from its application in daily practice."--Jacket.

Protein Tyrosine Kinases

From Inhibitors to Useful Drugs

Springer Science & Business Media Protein tyrosine kinases as targets for cancer and other indications / Mark Pearson, Carlos Garcia-Echeverria, Doriano Fabbro -- Inhibitors of signaling interfaces: targeting Src homology 2 domains in drug discovery / Carlos Garcia-Echeverria -- PI 3-kinase inhibition: a target for therapeutic intervention / Peter M. Finan, Stephen G. Ward -- Src as a target for pharmaceutical intervention: potential and limitations / Mira Susa ... [et al.] -- Activated FLT3 receptor tyrosine kinase as a therapeutic target in leukemia / Blanca Scheijen, James D. Griffin -- JAK kinases in leukemias/lymphomas and multiple myeloma / Renate Burger, Martin Gramatzki -- Glivec (Gleevec, Imatinib, STI571): a targeted therapy for CML / Elisabeth Buchdunger, Renaud Capedeville -- Platelet-derived growth factor: normal function, role in disease, and applications of PDGF antagonists / Tobias Sjoblom ... [et al.] -- Structural biology of protein tyrosine kinases / Sandra W. Cowan-Jacob ... [et al.] -- Testing of signal transduction inhibitors in animal models of cancer / Terence O'Reilly, Robert Cozens -- Phosphoproteomics in drug discovery and development / Michel F. Moran.

Self/Co-Assembling Peptide-based Nanocarriers for Anticancer Drug Delivery

Current diagnostic and therapeutic nanocarriers, including liposomes, micelles, and polymeric- and protein-based nanoparticles, are designed to have key functional properties such as: (i) longevity in the bloodstream, leading to accumulation of therapeutic cargos in neoplastic areas with leaky vasculatures; (ii) targeting of specific pathological sites through surface modification with targeting ligands; (iii) stimuli-responsive characteristics for controlled drug release under specific conditions. While some of these drug delivery systems have advanced into clinical stages, other nanocarriers remain under development to overcome issues with effective delivery such as lack of target-ability and fast clearance from circulation. Self-assembling peptides have recently shown great potential as nanocarrier materials for drug and gene delivery, owing to their safety, efficiency, and targeting capabilities. An amino acid pairing strategy enables us to design self/co-assembling peptides with multiple functionalities to fulfill drug delivery requirements. This thesis focuses on functionalization and characterization of self/co-assembling peptides as nanocarriers for hydrophobic anticancer drug delivery. Diethylene glycol (DEG) conjugation and protein binding are the two modification strategies used in this thesis to impart longevity and target-ability upon the peptide-based delivery system. The studies include: (i) characterization of self-assembling properties of the

diethylene glycol (DEG)-conjugated amino acid pairing peptide AAP8, (ii) investigation of the self/co-assembling features of a model ionic-complementary peptide (EAR8-II) in complex with the hydrophobic drug pirarubicin, and the anticancer activity of the complex, (iii) the interactions between peptide-drug complexes and serum proteins from the thermodynamic viewpoint, (iv) quantification of the effect of protein binding to the peptide-based delivery system on immune responses and biocompatibility, and (v) exploration of the targeting capability of albumin-bound peptide-drug complexes towards lung cancer cells. Uncontrollable aggregation of AAP8 was the first issue to address in order to develop a promising platform for the peptide-based delivery system. Diethylene glycol (DEG), a short segment of polyethylene glycol (PEG), was conjugated to AAP8 either at one or both terminals, and then self-assembling and drug encapsulation properties of both functionalized AAP8s were characterized to evaluate the effect of DEG-modification. The results illustrated a significant reduction in uncontrollable aggregation, and the formation of uniform fibular nanostructures. In addition, DEG conjugation provided the peptide with safer features towards immune cells by reducing cellular toxicity to macrophages. Moreover, DEG-functionalization improved hydrophobic drug stabilization, as demonstrated by sustained cytotoxic efficacy against lung carcinoma cells over a relatively long time compared to the non-functionalized AAP8. Protein binding strategy was the second approach to utilize the peptide-based delivery system with more biocompatibility and target-ability features. EAR8-II was studied as a model ionic-complementary peptide with high capability of pirarubicin encapsulation and anticancer activities against different cancer cells. Albumin as a most abundant protein in serum was selected to assess its binding affinity to the delivery system, and evaluate its binding effect on immune responses and anticancer activities. The results showed a central role of albumin in the in vitro delivery of peptide-drug complexes to target lung cancer cells based on the following characteristics: (a) Non-covalent binding of albumin to the complex through hydrogen bonding and Van der Waals interactions. The interaction was confirmed by physicochemical methods such as fluorescence quenching and isothermal titration calorimeter (ITC). (b) Shielding properties of albumin for the complex against macrophages and blood components (erythrocytes and complement protein C5b-9). In the presence of albumin, phagocytosis and cytokine expression level of macrophages and hemolytic activity of the peptide-drug complex reduced significantly due to the smaller particle size of the albumin-bound complexes compared to unprotected ones. (c) Targeting the lung cancer cells, possibly because of the inhibition of the albumin-binding protein SPARC (secreted protein, acidic and rich in cysteine). SPARC is a glycoprotein over expressed in lung cancer cells with high affinity to albumin. The results from in vitro SPARC expression in A549 cells, a type of human non-small cell lung carcinoma (NSCLC), showed a significant drop by the albumin-bound complex at the mRNA level evaluated by qRT-PCR. This effect can be explained by transporting the albumin-bound complex into the cell surface, binding to the SPARC proteins, and so inhibiting the SPARC expressions. This work lays out a foundation for modification and characterization of the self/co-assembly peptide-based nanocarriers for hydrophobic anticancer drug delivery, especially to improve longevity and target-ability properties.

Peptide Chemistry and Drug Design

John Wiley & Sons 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

Successful Drug Discovery

John Wiley & Sons Provides unique insider insight into the current drug development process, and what it takes to achieve success In this fourth volume in the series, inventors and primary developers of drugs that made it to the market continue telling the story of the drugs? discovery and development, and discuss the sometimes twisted route from the first drug candidate molecule to the final marketed one. Beginning with a general section addressing overarching topics for drug discovery, the book offers seven chapters that feature selected case studies describing recently introduced drugs or drug classes. These include small molecule drugs as well as biopharmaceuticals and range across different therapeutic fields. Together, they provide a representative cross-section of the present-day drug development effort. Successful Drug Discovery: Volume 4 covers trends in peptide-based drug discovery and the physicochemical properties of recently approved oral drugs. The section on drug class studies looks at antibody-drug conjugates and the discovery, evolution, and therapeutic potential of dopamine partial agonists. Featured case studies examine the discovery of Etelcalcetide for the treatment of secondary hyper-parathyroidism in patients with chronic kidney disease; the development of Lenvatinib Mesylate; the discovery and development of Venetoclax; and more. -Focuses on recently introduced drugs that have not been featured in any textbooks or general references, including Ocrelizumab, a new generation of anti-CD-20 mAb for the treatment of multiple sclerosis, and Venetoclax, a selective antagonist of BCL-2 -Features personal experiences of successful drug developers from industry and academia -Endorsed and supported by the International Union of Pure and Applied Chemistry (IUPAC) Successful Drug Discovery: Volume 4 provides a fascinating and informative look into the process of drug discovery and would be a great reference for those in the pharmaceutical industry, organic and pharmaceutical chemists, and lecturers in pharmacy.

Mid-size Drugs Based on Peptides

and Peptidomimetics

A New Drug Category

Springer This brief describes studies conducted by the authors on mid-size drugs utilizing peptides and peptidomimetics, and on the development of anti-HIV agents. Peptides are important biological molecules and have various physiological actions. Peptide-based drug discovery may help bring about the development of useful medicines that are highly safe and show potent pharmacological effects in small doses. Recently, it has been shown that there is an important drug-like space in the mid-sized region between low- and high-molecular-weight compounds. Thus, mid-size drugs such as peptide compounds are being focused on. To date, several peptidomimetics that mimic primary, secondary, and tertiary structures of peptides have been developed to maintain and improve biological activities and actions of peptides. In this book, the features and advantages of mid-size drugs are described in detail. In addition, the merits of utilizing peptidomimetics in the development of mid-size drugs are referred to. Understanding such peptide-derived mid-size drugs will lead to a comprehensive expansion of medicinal chemistry.

Protein Degradation

Ubiquitin and the Chemistry of Life

Wiley-VCH The first volume in a new series dedicated to protein degradation, this book lays the foundations of targeted protein breakdown via the ubiquitin pathway. The outstanding importance of the ubiquitin pathway has been recognized with the 2004 Nobel Prize in Chemistry for Aaaron Chiechanover, Avram Hershko, and Irwin Rose. Aaron Ciechanover is one of the editors of this series, and Avram Hershko has contributed to the opening chapter of the present volume. Drawing on the the expertise of two Nobel prize winners, this handy reference compiles information on the initial steps of the ubiquitin pathway. Starting out with a broad view of protein degradation and its functions in cellular regulation, it then goes on to examine the molecular mechanisms of ubiquitin conjugation and recycling in detail. All currently known classes of ubiquitin protein ligases are treated here, including latest structural data on these enzymes. Further volumes in the series cover the function of the proteasome, and the roles of the ubiquitin pathway in regulating key cellular processes, as well as its pathophysiological disease states. Required reading for molecular biologists, cell biologists and physiologists with an interest in protein degradation.

Polymerizable Peptide Monomers for the Targeted and Intracellular Delivery of Cancer Therapeutics

For the treatment of cancer, peptides hold great potential as both targeting and therapeutic agents. One particularly promising anti-cancer strategy is peptides derived from the third Bcl-2 homology domain (BH3), which antagonize pro-survival Bcl-2 proteins and induce apoptosis. Unfortunately, before the clinical potential of peptides can be realized, a number of drug delivery barriers must be overcome. Namely, peptides have short circulation half-lives, are susceptible to degradation by extracellular proteases, and are unable to cross cell membranes and access intracellular targets. An antibody-targeted, pH-responsive polymeric system was recently developed and implemented for the intracellular delivery of the pro-apoptotic BH3 peptide BIM1. Unfortunately, the delivery properties of this system were limited by the poor stability of the disulfide-linkage used for conjugating BIM to the polymeric carrier. It was the objective of this thesis to develop highly stable polymer-peptide conjugates for the targeted and intracellular delivery cancer drugs. Initially, steric hindrance was investigated for enhancing the stability and delivery properties of disulfide-linked polymer-BIM conjugates. Two methyl groups were introduced onto the peptide's disulfide-adjacent carbon by substituting BIM's C-terminal cysteine with pencillamine and conjugating the peptide to the polymeric carrier via disulfide exchange. In a murine xenograft model of B-cell lymphoma, steric hindrance significantly enhanced conjugate stability, peptide half-life and peptide deposition into tumors. However, benefits were relatively minor with much left to be desired. Next an enzyme-labile peptide linker was developed that is highly stable in human serum and efficiently cleaved in cancer cells to release active BIM peptide. A methacrylamido-peptide macromonomer containing BIM capped with a four amino acid (FKFL) cathepsin B substrate was synthesized and directly integrated into the polymeric delivery vehicle via RAFT polymerization. The resulting cathepsin-B cleavable BIM prodrug system demonstrated potent apoptotic activity in ovarian cell cultures and is currently being investigated for apoptotic activity and therapeutic efficacy in intraperitoneal ovarian cancer xenograft model. Lastly, peptide monomer technology was alternatively implemented for tumor-specific targeting. A peptide monomer containing the EGFR-targeting sequence GE112 was polymerized into a hydrophilic polymeric drug delivery system in combination with an ester-linked camptothecin prodrug monomer. GE11 was shown to enhance targeting and activity of the polymeric prodrug in ovarian cancer cell cultures. [1] Berguig GY, Convertine AJ, Frayo S, Kern HB, Procko E, Roy D, Srinivasan S, Margineantu DH, Booth G, Palanca-Wessels MC, Baker D, Hockenbery D, Press OW, Stayton PS. Intracellular delivery system for antibody-Peptide drug conjugates. Mol Ther. 2015 May;23(5):907-17. [2] Li Z, Zhao R, Wu X, Sun Y, Yao M, Li J, Xu Y, Gu J. Identification and characterization of a novel peptide ligand of epidermal growth factor receptor

for targeted delivery of therapeutics. FASEB J. 2005 Dec;19(14):1978-85.

Protein Surface Recognition Approaches for Drug Discovery

John Wiley & Sons A new perspective on the design of molecular therapeutics is emerging. This new strategy emphasizes the rational complementation of functionality along extended patches of a protein surface with the aim of inhibiting protein/protein interactions. The successful development of compounds able to inhibit these interactions offers a unique chance to selectively intervene in a large number of key cellular processes related to human disease. Protein Surface Recognition presents a detailed treatment of this strategy, with topics including: an extended survey of protein-protein interactions that are key players in human disease and biology and the potential for therapeutics derived from this new perspective the fundamental physical issues that surround protein-protein interactions that must be considered when designing ligands for protein surfaces examples of protein surface-small molecule interactions, including treatments of protein-natural product interactions, protein-interface peptides, and rational approaches to protein surface recognition from model to biological systems a survey of techniques that will be integral to the discovery of new small molecule protein surface binders, from high throughput synthesis and screening techniques to in silico and in vitro methods for the discovery of novel protein ligands. Protein Surface Recognition provides an intellectual “tool-kit” for investigators in medicinal and bioorganic chemistry looking to exploit this emerging paradigm in drug discovery.

Targets for Cancer Chemotherapy Transcription Factors and Other Nuclear Proteins

Springer Science & Business Media 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.

Advances in Cancer Research

Genomics in Cancer Drug Discovery and Development

Elsevier The Advances in Cancer Research series provides invaluable information on the exciting and fast-moving field of cancer research. This volume stands as the first ever thematic volume in the series, focusing on the topic of genomics in cancer drug development. The chapters included in this book represent the cutting-edge information in the field and span such topics as Mass Spectrometry: Uncovering the Cancer Proteome for Diagnostics; Biomarker Discovery in Epithelial Ovarian Cancer by Genomic Approaches; The Application of siRNA Technology to Cancer Biology Discovery; Ribozyme Technology for Cancer Gene Target Identification and Validation; Cancer Cell-Based Genomic and Small Molecule Screens; Tumour Antigens as Surrogate Markers and Targets for Therapy and Vaccines; Practices and Pitfalls of Mouse Cancer Models in Drug Discovery; Biomarker Assay Translation from Discovery to Clinical Studies in Cancer Drug Development – Quantification of Emerging Protein Biomarkers; Molecular Optical Imaging of Therapeutic Targets of Cancer; Cancer Drug Approval in the United States, Europe and Japan.

Heat Shock Proteins in Cancer

Springer Science & Business Media Heat shock proteins are emerging as important molecules in the development of cancer and as key targets in cancer therapy. These proteins enhance the growth of cancer cells and protect tumors from treatments such as drugs or surgery. However, new drugs have recently been developed particularly those targeting heat shock protein 90. As heat shock protein 90 functions to stabilize many of the oncogenes and growth promoting proteins in cancer cells, such drugs have broad specificity in many types of cancer cell and offer the possibility of evading the development of resistance through point mutation or use of compensatory pathways. Heat shock proteins have a further property that makes them tempting targets in cancer immunotherapy. These proteins have the ability to induce an inflammatory response when released in tumors and to carry tumor antigens to antigen presenting cells. They have thus become important components of anticancer vaccines. Overall, heat shock proteins are important new targets in molecular cancer therapy and can be approached in a number of contrasting approaches to therapy.

PEGylated Protein Drugs: Basic

Science and Clinical Applications

Springer Science & Business Media PEGylation technology and key applications are introduced by this topical volume. Basic physical and chemical properties of PEG as basis for altering/improving in vivo behaviour of PEG-conjugates such as increased stability, improved PK/PD, and decreased immunogenicity, are discussed. Furthermore, chemical and enzymatic strategies for the coupling and the conjugate characterization are reported. Following chapters describe approved and marketed PEG-proteins and PEG-oligonucleotides as well as conjugates in various stages of clinical development.