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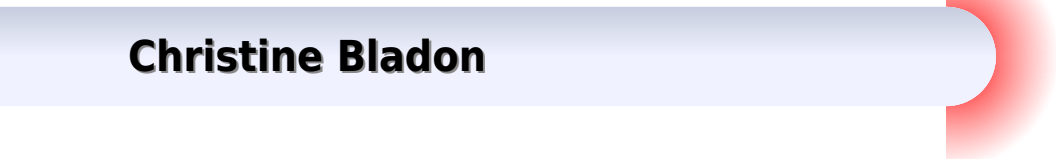
OLIGONUCLEOTIDES AS THERAPEUTIC AGENTS



Ciba Foundation

Oligonucleotides As Therapeutic Agents

Christine Bladon



Oligonucleotides As Therapeutic Agents:

Oligonucleotides as Therapeutic Agents Derek J. Chadwick, Gail Cardew, 2008-04-30 The use of oligonucleotides as therapeutic agents rests upon their ability to interfere in a sequence specific manner with the fundamental machinery of protein synthesis either by binding to the mRNAs transcribed from a gene or by binding directly to a target gene This approach can be used not only for inhibition of the synthesis of host proteins but also of those required by invading pathogens Potential therapeutic applications are enormous ranging over hypertension cardiovascular disease autoimmune disease viral and other parasitic infections especially HIV and cancer This book discusses the chemistry and pharmacokinetics of oligonucleotides and their analogues and surveys the results of structure activity studies and current clinical trials It also critically reviews the problems with antisense therapy such as the enzymatic destruction of oligonucleotides the doses required for a therapeutic response the difficulty in directing oligonucleotides to particular target tissues and cells the need for parenteral administration and doubts concerning the mechanism of action especially problems associated with non specific binding to proteins and long term effects

Oligonucleotide-Based Drugs and Therapeutics Nicolay Ferrari, Rosanne Seguin, 2018-06-06 A comprehensive review of contemporary antisense oligonucleotides drugs and therapeutic principles methods applications and research Oligonucleotide based drugs in particular antisense oligonucleotides are part of a growing number of pharmaceutical and biotech programs progressing to treat a wide range of indications including cancer cardiovascular neurodegenerative neuromuscular and respiratory diseases as well as other severe and rare diseases Reviewing fundamentals and offering guidelines for drug discovery and development this book is a practical guide covering all key aspects of this increasingly popular area of pharmacology and biotech and pharma research from the basic science behind antisense oligonucleotides chemistry toxicology manufacturing to safety assessments the design of therapeutic protocols to clinical experience Antisense oligonucleotides are single strands of DNA or RNA that are complementary to a chosen sequence While the idea of antisense oligonucleotides to target single genes dates back to the 1970 s most advances have taken place in recent years The increasing number of antisense oligonucleotide programs in clinical development is a testament to the progress and understanding of pharmacologic pharmacokinetic and toxicologic properties as well as improvement in the delivery of oligonucleotides This valuable book reviews the fundamentals of oligonucleotides with a focus on antisense oligonucleotide drugs and reports on the latest research underway worldwide Helps readers understand antisense molecules and their targets biochemistry and toxicity mechanisms roles in disease and applications for safety and therapeutics Examines the principles practices and tools for scientists in both pre clinical and clinical settings and how to apply them to antisense oligonucleotides Provides guidelines for scientists in drug design and discovery to help improve efficiency assessment and the success of drug candidates Includes interdisciplinary perspectives from academia industry regulatory and from the fields of pharmacology toxicology biology and

medicinal chemistry Oligonucleotide Based Drugs and Therapeutics belongs on the reference shelves of chemists pharmaceutical scientists chemical biologists toxicologists and other scientists working in the pharmaceutical and biotechnology industries It will also be a valuable resource for regulatory specialists and safety assessment professionals and an important reference for academic researchers and post graduates interested in therapeutics antisense therapy and oligonucleotides

Antisense Drug Technology Stanley T. Crooke, 2007-07-25 Extensively revised and updated Antisense Drug Technology Principles Strategies and Applications Second Edition reflects the logarithmic progress made in the past four years of oligonucleotide based therapies and in particular antisense therapeutics and research Interpreting lessons learned from the clinical trials of first generation drugs the book evaluates the technology as a whole and offers new directions and avenues of research and development Divided into five parts the book begins with a thorough introduction to the mechanism of antisense drug action including the RNase H mechanism small RNA silencing pathways and the potential therapeutics of splice switching oligonucleotides Leading researchers demonstrate the basics of oligonucleotide therapeutics in part two by delineating medicinal chemistry pharmacokinetics and delivery routes such as liposomal formulations for nucleic acid delivery Part three details hybridization based drugs and considers the dramatic advances represented by 2 methoxyethyl chimeric antisense inhibitors and duplex RNA drugs Other chemical classes of drugs and mechanisms of action are described in part four with further discussions on improving the second generation antisense drugs The final part delves deeply into therapeutic applications Contributing authors examine the potential of antisense drugs for the alleviation of cardiovascular diseases metabolic diseases inflammatory diseases cancer neurological disorders and immune modulation Presenting a highly detailed lucid discussion of the remarkable advances in the field Antisense Drug Technology Principles Strategies and Applications Second Edition provides the platform for researchers to continue to aggressively pursue the great opportunity represented by this exciting technology

Oligonucleotide-Based Drugs and Therapeutics Nicolay Ferrari, Rosanne Seguin, 2018-07-31 A comprehensive review of contemporary antisense oligonucleotides drugs and therapeutic principles methods applications and research Oligonucleotide based drugs in particular antisense oligonucleotides are part of a growing number of pharmaceutical and biotech programs progressing to treat a wide range of indications including cancer cardiovascular neurodegenerative neuromuscular and respiratory diseases as well as other severe and rare diseases Reviewing fundamentals and offering guidelines for drug discovery and development this book is a practical guide covering all key aspects of this increasingly popular area of pharmacology and biotech and pharma research from the basic science behind antisense oligonucleotides chemistry toxicology manufacturing to safety assessments the design of therapeutic protocols to clinical experience Antisense oligonucleotides are single strands of DNA or RNA that are complementary to a chosen sequence While the idea of antisense oligonucleotides to target single genes dates back to the 1970 s most advances have taken place in recent years The increasing number of antisense oligonucleotide programs in

clinical development is a testament to the progress and understanding of pharmacologic pharmacokinetic and toxicologic properties as well as improvement in the delivery of oligonucleotides This valuable book reviews the fundamentals of oligonucleotides with a focus on antisense oligonucleotide drugs and reports on the latest research underway worldwide Helps readers understand antisense molecules and their targets biochemistry and toxicity mechanisms roles in disease and applications for safety and therapeutics Examines the principles practices and tools for scientists in both pre clinical and clinical settings and how to apply them to antisense oligonucleotides Provides guidelines for scientists in drug design and discovery to help improve efficiency assessment and the success of drug candidates Includes interdisciplinary perspectives from academia industry regulatory and from the fields of pharmacology toxicology biology and medicinal chemistry Oligonucleotide Based Drugs and Therapeutics belongs on the reference shelves of chemists pharmaceutical scientists chemical biologists toxicologists and other scientists working in the pharmaceutical and biotechnology industries It will also be a valuable resource for regulatory specialists and safety assessment professionals and an important reference for academic researchers and post graduates interested in therapeutics antisense therapy and oligonucleotides

Transdermal and Intradermal Delivery of Therapeutic Agents Ajay K Banga, 2011-05-16 Skin once thought to be an impenetrable barrier is an extremely active organ capable of interacting with its environment Advancements in science combined with the need for diverse drug delivery modalities have introduced a variety of transdermal and intradermal products for existing drugs at a fraction of the cost of new drug development Interest in drug delivery systems is growing as the delivery of many drugs continues to be a problem due to safety stability and compliance issues This is especially true for the increased number of biologic medicines which include peptides proteins and nucleic acids Transdermal delivery is an important part of such systems and the use of physical enhancement methods to penetrate the skin barrier is where the field is headed This book reviews the strategies available for the delivery of compounds into and through the skin It also focuses on technological developments in the domain of nanotechnology that can be exploited to enhance the transdermal delivery of drugs

Pharmaceutical Perspectives of Nucleic Acid-Based Therapy Ram I. Mahato, Sung Wan Kim, 2002-06-27

Emphasizing its uses in cancer and cardiovascular and autoimmune diseases Pharmaceutical Perspectives of Nucleic Acid Based Therapy presents a comprehensive account of gene therapy from development in the laboratory to clinical applications Internationally acclaimed scientists discuss the potential use of lipids peptides and polymers for the in

Commercialization of Oligonucleotides as Therapeutic Agents Brian Minter, 1995 Gene Therapy Kam M. Hui, 1994 With advances in our understanding of the molecular biology of human diseases and the development of efficient gene transfer techniques the treatment of such diseases as cancer and infectious disease using gene therapy has progressed from a distant prospect to a distinct possibility in a very short time The development of gene transfer methods which are suitable for different forms of therapy has been a major topic of research over the past several years A common goal of this

research has been to achieve the efficient delivery of genes into cells. The successful implementation of gene transfer as a cure for diseases however will continue to require the translation of preclinical studies in gene therapy into effective clinical protocols. This volume outlines the latest developments in cancer treatment using various gene delivery systems which include cytokine gene transfer, the delivery of anti-ras DNA by retroviral vector and the injection of allogeneic HLA DNA via liposomes. Several of these molecular approaches have recently been approved by the US FDA as human clinical trial protocols in order to assess their therapeutic efficiency and safety for cancer treatment. Further developments in recombinant DNA technology within this field should ultimately lead to dramatic improvements in the practice of medicine.

Advanced Delivery and Therapeutic Applications of RNAi Kun Cheng, Ram I. Mahato, 2013-04-19 Commonly used by researchers to develop technologies for modifying and studying genetic process, RNA interference (RNAi) has many potential uses in medicine, biotechnology and functional genomics. This book covers all essential aspects involved in the development of RNAi therapeutics, providing detailed guidance on the challenges and opportunities of bringing RNAi technologies from bench to clinic. It explores the design and mechanism of RNAi molecules, delivery strategies and therapeutic applications in various diseases. Preclinical, regulatory, market and intellectual aspects of RNAi technologies are also covered. [Delivery Strategies for Antisense Oligonucleotide Therapeutics](#) Saghir Akhtar, 2017-07-28 With contributions from leading experts, this book is the first to focus solely on addressing the problems and reviewing the strategies currently being used to improve the delivery of antisense nucleic acids. Important delivery issues such as improving biological stability, improving cell specific targeting and cellular uptake, manipulating subcellular distribution and producing liposomal delivery systems for antisense agents are comprehensively covered in this volume. This book links review type articles with contributions that contain exciting, never before published data on the cellular delivery of oligonucleotides. It stimulates reading for both established researchers and newcomers to the antisense field. **Novel Anticancer Drug Protocols** John K. Buolamwini, Alex A. Adjei, 2008-02-01 We are in an exciting era in the war against cancer with real prospects for novel anticancer drugs that are cancer cell specific without the toxicities that have been the hallmark of conventional cytotoxic cancer chemotherapy. Advances in cancer cell biology, fueled by the molecular biology revolution, have resulted in the uncovering of many novel potential molecular targets for cancer therapy. New anticancer drug discovery and development is now largely focused on exploiting these new molecular targets which encompass oncogenes, tumor suppressor genes and their gene products as well as targets involved in tumor angiogenesis, metastasis, survival and longevity mechanisms. Exploitation of some of these targets has already yielded fruits and introduced new paradigms of molecularly targeted cancer therapy into the clinic, namely protein kinase inhibition by antibodies or small molecules exemplified by Herceptin (trastuzumab), a humanized antibody targeted against the HER2 growth factor receptor tyrosine kinase for the treatment of metastatic breast cancer, and Gleevec (imatinib), a small molecule bcr-abl kinase inhibitor for the treatment of chronic myelogenous leukemia. **Percutaneous Absorption**

Nina Dragičević, Howard Maibach, 2021-07-29 Updating and expanding the scope of topics covered in the previous edition **Percutaneous Absorption Drugs Cosmetics Mechanisms Methods Fifth Edition** supplies new chapters on topics currently impacting the field including cutaneous metabolism skin contamination exposure to protein allergens in vitro absorption methodology and the percutaneous absorption of chemical mixtures Complete with studies on the role of the skin as a key portal of entry for chemicals into the body this book serves as a detailed reference source for recent advances in the field as well as an experimental guide for laboratory personnel Key Features Details in vivo and in vitro methods for measuring absorption dermal decontamination mechanisms of transdermal delivery and the relationship of transepidermal water loss to percutaneous absorption Considers a range of mathematical models the safety evaluation of cosmetic ingredients the absorption of hair dyes nanoparticles for drug delivery and other novel methods of drug delivery Discusses topics including skin metabolism the skin reservoir and the effects of desquamation on absorption **Therapeutic Modulation of**

Cytokines M. W. Bodmer, Brian Henderson, 1996-01-23 Cytokines are peptide or protein cell to cell signaling molecules that play vital roles in normal cell and tissue homeostasis as well as in responses to infectious agents Because of their importance in virtually all forms of pathology the pharmaceutical industry is devoting great effort to develop methods for the control of cytokine synthesis or action This is the first volume to bring together experts from academia and the pharmaceutical industry to discuss problems and solutions in the therapeutic control of cytokines An introductory section reviews the biology physiology and pathology of cytokines Internationally recognized scientists then discuss the development of low molecular mass inhibitors including inhibitors of cytokine convertases and oligonucleotide drugs The potential use of natural inhibitors such as soluble receptors interleukin 1 receptor antagonists and anti cytokine antibodies is detailed This interesting book also covers intracellular signaling pathways induced by pro inflammatory cytokines and the bio modulatory activity of specific cytokines such as TGF Therapeutic Modulation of Cytokines will interest academic scientists in biochemistry cell biology pharmacology and molecular biology and biological scientists in the pharmaceutical and biopharmaceutical industries

Gene Therapy, 1997-08-12 Each volume of **Advances in Pharmacology** provides a rich collection of reviews on timely topics Emphasis is placed on the molecular bases of drug action both applied and experimental Volume 40 **Gene Therapy** features important new research on gene transfers and therapy in the herpes simplex virus anti tumor immunity steroid receptors cystic fibroses and more Key Features It provides an excellent overview on a series of topics on gene therapy for the serious investigator **Biotechnology And Safety Assessment** John A. Thomas, 1993-06-30 In this volume experts from academe industry and public health institutes discuss the issues involved in toxicology evaluation safety assessment and regulation of biotechnology derived drugs foods and plant products Coverage includes recombinant DNA agents monoclonal antibodies recombinant hormones and other proteins biotechnology derived drug delivery systems gene therapy for genetic diseases and genetically engineered plants and plant products Full consideration is given to key methodological issues in

product development and testing such as use of in vitro and in vivo toxicology tests choice of animal models and use of transgenic animal models and genetically altered species to study human diseases The book includes an appendix describing available animal models and a glossary of terms definitions and acronyms **Pharmaceutical Chemistry** Christine

Bladon,2002-04-03 Providing a broad introduction to the growing field this book explores the way in which peptides proteins nucleic acids and carbohydrates used therapeutically With help of numerous illustrations it covers both the compounds and how therapeutics exert their influence through an understanding of biological processes Includes the latest developments in the field Covers the various strategies behind the development and production of a range of key clinically useful compounds Focuses on the concepts and ideas of why compounds are developed as pharmaceuticals Provides many examples and problems Invaluable to all students of chemistry medicinal and pharmaceutical chemistry pharmacy and pharmacology Will also be of interest to researchers and professionals needing a concise up to date account of this subject **Cytotoxic**

Anticancer Drugs: Models and Concepts for Drug Discovery and Development Frederick A. Valeriote,Thomas H. Corbett,Laurence H. Baker,2012-12-06 The focus of the 22nd Annual Detroit Cancer Symposium was the presentation and discussion of cytotoxic agents with a significant portion of the symposium including the exciting frontiers of drug discovery being explored by the National Cooperative Drug Discovery Groups NCDDG Program The symposium brought together a large number of investigators from government universities and pharmaceutical companies involved in the discovery and development of new anticancer agents Exciting new leads were presented and the status of others presently under development was discussed Of particular significance has been the initiation of renewed efforts in the area of natural product drug discovery where the discovery of new cytotoxics is very promising at the moment A number of major changes have occurred during the last decade in research on drug discovery of cytotoxic agents Critical reviews of a number of the models and concepts underlying drug discovery represented a continuous thread throughout the meeting being constantly discussed in terms of their advantages disadvantages and capabilities of discovering solid tumor active anticancer agents A recent development which is to be much applauded and which portends to great discoveries is the new relationship formed between Government University of Industry The NCDDG mechanism which stimulates this interaction is an inexpensive manner to greatly magnify the drug discovery and development effort nationally Cytotoxic Anticancer Drugs Models and Concepts for Drug Discovery and Development represents a forum which will become the major mode for bringing together these three different components in the equation to regularly discuss new results and ideas **Novel Anticancer Agents** Alex A.

Adjei,John K. Buolamwini,2011-04-28 Novel Anticancer Agents offers pertinent basic science information on strategies used for the rational design and discovery of novel anticancer agents and in addition translational studies involving clinical trial design and execution with these novel mostly cytostatic agents This book covers basic science strategies that are being used in drug discovery and preclinical evaluation focused on novel molecular targets as well as clinical trial methodology including

clinical pharmacokinetics and imaging to address issues of efficacy evaluation of the new relatively non cytotoxic anticancer agents At present there is no book that provides such an integration of basic and clinical studies of novel anticancer agents covering both drug discovery and translational research extensively Addresses the critical issues involved in the development of novel agents for cancer therapy by experts in the field Presents drug discovery strategies Discusses regulatory issues surrounding drug development

Antisense Research and Applications Stanley T. Crooke, Bernard Lebleu, 1993-05-27 Antisense Research and Applications is a comprehensive review of oligonucleotide research covering molecular biological advances in this field the current status of antisense drug research and strategies for future research and therapeutic applications In bringing together the latest research from an array of authoritative scientists Antisense Research and Applications provides an integrated conceptual basis for considering oligonucleotide therapeutics Topics covered in the 32 chapters of this book include nucleic acid structure and function antisense RNA medicinal chemistry of oligonucleotides analogs pharmacokinetics and toxicology and activities of current antisense drugs This volume addresses advances in a broad range of disciplines and is an excellent resource for basic researchers and applied investigators in pharmaceutical laboratories and in such fields as biochemistry and molecular biology

Pharmaceutics Alekha Dash, Somnath Singh, 2023-09-13 Pharmaceutics Basic Principles and Application to Pharmacy Practice Second Edition is a valuable textbook covering the role and application of pharmaceutics within pharmacy practice This updated resource is geared toward meeting and incorporating the current curricular guidelines on pharmaceutics and laboratory skills mandated by the American Council for Pharmacy Education It includes a number of student friendly features including chapter objectives and summaries practical examples case studies numerous images and key concept text boxes Two new chapters are included as well as a new end of chapter section covering critical reflections and practice applications Divided into three sections Physical Principles and Properties of Pharmaceutics Practical Aspects of Pharmaceutics and Biological Applications of Pharmaceutics this new edition covers all aspects of pharmaceutics and providing a single and compelling source for students Facilitates an integrated and extensive coverage of the study of pharmaceutics due to the clear and engaging language used by the authors Includes chapter objectives and summaries to illustrate and reinforce key ideas Meets curricular guidelines for pharmaceutics and laboratory skills mandated by the Accreditation Council for Pharmacy Education ACPE Includes new practice questions answers and case studies for experiential learning

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