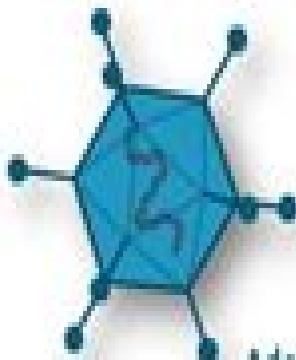


Viral vectors in approved gene therapies



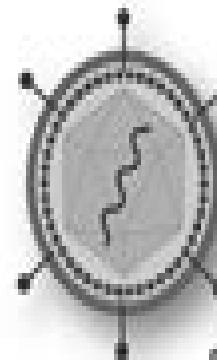
Adenovirus

- 36 kb genome size
- Non-integrating vector
- High immunogenicity
- Used in vaccines, oncolytic viral therapy, localized gene delivery



AAV

- 4.8 kb genome size
- Non-integrating vector
- Low immunogenicity
- Used in *in vivo* gene therapy
- Serotype varieties for tissue specificity



Retrovirus

- 8 kb genome size
- Integrating vector
- Risk for insertional mutagenesis
- Used in *ex vivo* cell-based gene therapies



Lentivirus

- 8 kb genome size
- Integrating vector
- Low immunogenicity
- Lower risk of mutagenesis
- Widely used in cell-based gene therapies



HSV

- 150 kb genome size
- Non-integrating vector
- Low immunogenicity
- Natural neuronal tropism

Nonviral Vectors For Gene Therapy

Sayyed Imran Shah

Nonviral Vectors For Gene Therapy:

Non-viral Vectors for Gene Therapy Leaf Huang,Mien-chie Hung,Ernst Wagner,2005 Annotation The field of non viral vector research has rapidly progressed since the publication of the first edition This new edition is expanded to two separate volumes that contain in depth discussions of different non viral approaches including cationic liposomes and polymers naked DNA and various physical methods of delivery as well as a comprehensive coverage of the molecular biological designs of the plasmid DNA for reduced toxicity prolonged expression and tissue or disease specific genes New developments such as the toxicity of the non viral vectors and recent advances in nucleic acid therapeutics are fully covered in these volumes

Nonviral Vectors for Gene Therapy, Part 2 Leaf Huang,Mien-Chie Hung,Ernst Wagner,2005-08-01 The field of non viral vector research has rapidly progressed since the publication of the first edition This new edition is expanded to two separate volumes that contain in depth discussions of different non viral approaches including cationic liposomes and polymers naked DNA and various physical methods of delivery as well as a comprehensive coverage of the molecular biological designs of the plasmid DNA for reduced toxicity prolonged expression and tissue or disease specific genes New developments such as the toxicity of the non viral vectors and recent advances in nucleic acid therapeutics are fully covered in these volumes

Nonviral Vectors for Gene Therapy Mark A. Findeis,2008-02-02 The purpose of this volume of Methods in Molecular Medicine is to set forth examples of the great variety of techniques and applications that are now emerging in the field of nonviral gene therapy The book emphasizes not only specific approaches to gene delivery but in particular the best current methods to prepare handle and characterize gene delivery agents These topics are of very broad importance since gene therapy evolves from its mostly academic based experimental and clinical research to the ever increasing number of industry driven programs directed toward commercial development Successful introduction of nonviral gene therapy agents into the clinic should be expected to require rigorous manufacturing and analytical methods that readily meet the regulatory guidelines under which new drug candidates are reviewed for marketing approval Exactly what those guidelines will prove to be certainly depends on the established guidelines for review of both biological and chemical therapeutics Additionally many new techniques are being devised and applied to gene therapy research these techniques will be instrumental in developing and characterizing successful gene delivery agents Nonviral Vectors for Gene Therapy Methods and Protocols has two main sections To start with there is a series of chapters on specific protocols for the synthesis characterization and application of gene delivery agents Several chapters address the topic of materials to bind with DNA to form the compact condensed phases that facilitate cellular delivery **Nonviral Vectors for Gene Therapy** ,2015-01-23 The field of genetics is rapidly evolving and new medical breakthroughs are occurring as a result of advances in our knowledge of genetics Advances in Genetics continually publishes important reviews of the broadest interest to geneticists and their colleagues in affiliated disciplines Includes methods for testing with ethical legal and social implications Critically analyzes future directions Written and edited

by recognized leaders in the field **Nonviral Vectors for Gene Therapy, Part 2** Leaf Huang,Mien-Chie Hung,Ernst Wagner,2005-07-07 The field of non viral vector research has rapidly progressed since the publication of the first edition This new edition is expanded to two separate volumes that contain in depth discussions of different non viral approaches including cationic liposomes and polymers naked DNA and various physical methods of delivery as well as a comprehensive coverage of the molecular biological designs of the plasmid DNA for reduced toxicity prolonged expression and tissue or disease specific genes New developments such as the toxicity of the non viral vectors and recent advances in nucleic acid therapeutics are fully covered in these volumes [Nonviral Vectors for Gene Therapy](#) ,2005 [Nonviral Vectors for Gene Therapy](#) ,2014-11-18 The field of genetics is rapidly evolving and new medical breakthroughs are occurring as a result of advances in our knowledge of genetics Advances in Genetics continually publishes important reviews of the broadest interest to geneticists and their colleagues in affiliated disciplines Includes methods for testing with ethical legal and social implications Critically analyzes future directions Written and edited by recognized leaders in the field [Non-viral Vectors for Gene Therapy: \(v. 53\). Recent advances in non-viral gene delivery](#) Leaf Huang,Mien-chie Hung,Ernst Wagner,2005 [Nonviral Vectors for Gene Therapy](#) Mien-Chie Hung,Leaf Huang,Ernst Wagner,1999-07-01 Gene transfer within humans has been an obstacle until about 10 years ago At that time it was found that viral vectors were effective carriers of healthy genes into patients cells The problem however was that viral vectors proved unnecessarily harmful to humans subjects experienced inflammatory activity and negative immunological responses to the genes Viral vectors were also unable to meet the needs of the pharmaceutical community they were not reproducible in large scale proportions in cost effective ways Thus research was undertaken to find a safer way to transfer genes to patients without jeopardizing the safety of the patient And so non viral vectors were discovered This volume presents the various non viral vectors currently under development Although not methodologically oriented it will provide the necessary details behind the development of the vectors This information will prove useful to both researchers and clinicians Key Features Presents state of the art developments of nonviral vectors as tools for modern molecular medicine Covers all types of nonviral vectors from molecular structure to therapeutic applicationProvides a comprehensive review of synthetic vectors Includes contributions from major investigators and leading experts in the field [Nonviral Vectors for Gene Therapy, Part 2](#) Leaf Huang,Mien-Chie Hung,Ernst Wagner,2005-07-07 The field of non viral vector research has rapidly progressed since the publication of the first edition This new edition is expanded to two separate volumes that contain in depth discussions of different non viral approaches including cationic liposomes and polymers naked DNA and various physical methods of delivery as well as a comprehensive coverage of the molecular biological designs of the plasmid DNA for reduced toxicity prolonged expression and tissue or disease specific genes New developments such as the toxicity of the non viral vectors and recent advances in nucleic acid therapeutics are fully covered in these volumes **Cancer Gene Therapy by Viral and Non-viral Vectors** Malcolm Brenner,Mien-Chie Hung,2014-02-25

Provides expert state of the art insight into the current progress of viral and non viral gene therapy Translational medicine has opened the gateway to the era of personalized or precision medicine No longer a one size fits all approach the treatment of cancer is now based on an understanding of underlying biologic mechanisms and is increasingly being tailored to the molecular specificity of a tumor This book provides a comprehensive overview of the pertinent molecular discoveries in the cancer field and explains how these are being used for gene based cancer therapies Designed as a volume in the Translational Oncology book series Cancer Gene Therapy by Viral and Non viral Vectors deals with the practice of gene therapy with reference to vectors for gene expression and gene transfer as well as viral therapy It covers the history and current and future applications of gene transfer in cancer and provides expert insight on the progress of viral and non viral gene therapy with regard to delivery system vector design potential therapeutic genes and principles and regulations for cancer gene therapy Presented in three parts Cancer Gene Therapy by Viral and Non viral Vectors covers Delivery Systems Translational Cancer Research Gene Therapy by Viral and Non viral Vectors Retroviruses for Cancer Therapy DNA Plasmids for Non viral Gene Therapy of Cancer Cancer Therapy with RNAi delivered by Non viral Membrane Core Nanoparticles Targeted Expression Cancer Gene Therapy by Tissue specific and Cancer targeting Promptors MicroRNAs as Drugs and Drug Targets in Cancer Principles of Clinical Trials in Gene Therapy Regulatory issues for Manufacturers of Viral Vectors and Vector transduced Cells for Phase I II Trials US Regulations Governing Clinical Trials in Gene Therapy Remaining Obstacles to the Success of Cancer Gene Therapy Focusing on speeding the process in clinical cancer care by bringing therapies as quickly as possible from bench to bedside Cancer Gene Therapy by Viral and Non viral Vectors is an absolutely vital book for physicians clinicians researchers and students involved in this area of medicine

Nonviral Vectors for Gene Therapy

Mark A. Findeis,2001 Mark A Findeis and a panel of active researchers present their best methods not only for preparing handling and characterizing gene delivery agents but also for gene delivery To help those preparing and characterizing gene transfer agents the contributors examine a broad range of compounds that bind with DNA to form the compact condensed phases that facilitate cellular delivery among them peptide conjugates synthetic polymers and lipids They also outline specific approaches to gene transfer in vivo including direct delivery by intratumoral injection and indirect delivery by cell specific targeting of DNA complexes and discuss in detail many spectroscopic techniques for characterizing nonviral gene delivery agents

Efficient Non-viral Vector for Gene Therapy Bansari Shah,2013 Gene therapy is a method with great potential for the treatment of heritable disorders One difficulty with this approach is that the vectors used in early trials were derived from viruses Viral genomes have several disadvantages as vectors for gene therapy including the interruption of cancer causing genes by random insertion into the genome and activation of the immune system The purpose of this project was to compare vectors that could serve as a foundation for gene therapy that avoids these difficulties The author used as a model the treatment of Hunter syndrome a lysosomal storage disease to compare efficiencies of non viral vectors in

delivering genes to cultured cells deficient in functional genes Mucopolysaccharidosis type II MPSII also known as Hunter syndrome is an x linked recessive disorder that occurs when the IDS gene located on the X chromosome becomes mutated The IDS gene is responsible for making the I2S enzyme The lack of I2S or reduced function of this enzyme causes a buildup of glycosaminoglycans GAGs within cells everywhere in the body Due to this accumulation many cells of the body become swollen which makes this disorder a progressive debilitating condition Currently enzyme replacement therapy ERT is the only FDA approved treatment option for affected individuals Unfortunately ERT does not treat or provide a cure for this disorder For a permanent therapy in the future gene therapy may be the solution In this study the author examines the effect of a non viral vector containing the IDS gene on MPSII fibroblasts The IDS gene was cloned into a non viral vector pIRES hrGFP 2a MPSII fibroblasts were transfected with the construct which encodes the I2S enzyme A 4 methylumbelliferyl sulfate 4 MUS assay was performed to test for secreted sulfatases in the conditioned media CM after transcription of the IDS gene was allowed to proceed Fluorescence indicated the release of a fluorophore when the sulfate group on the 4 MUS sulfate was cleaved by sulfatases The highest sulfatase activity was present in the CM post transfection indicating that the I2S enzyme was successfully produced and secreted The pIRES hrGFP IDS 2a construct yielded I2S enzyme up to 24 hours MPSII fibroblasts survived with the construct for up to 48 hours In this study the author shows how a non viral vector can be used to restore gene function and prolong the life of mutated cells This non viral construct with modifications can be used to cross the blood brain barrier to treat this disease in the central nervous system CNS which is not currently available for treatment because of the blood brain barrier BBB

The Development of Non-viral Vectors for Gene Therapy

Sheetal Patel, University of London, 2002

Non-viral Gene Therapy Kazunari Taira, Kazunori Kataoka, Takuro Nidome, 2006-03-20

Presents information on non viral gene delivery techniques covering a spectrum of disciplines that include chemistry molecular biology cell biology and pharmacokinetics This work is useful to researchers and engineers in genetic engineering molecular medicine biochemical engineering and biotechnology

Design and synthesis of non-viral vectors for gene therapy Sayyed Imran Shah, 2001

Nonviral Vectors for Gene Therapy, Part 1 Leaf Huang, Mien-Chie Hung, Ernst Wagner, 2005 The field of non viral vector research has rapidly progressed since the publication of the first edition This new edition is expanded to two separate volumes that contain in depth discussions of different non viral approaches including cationic liposomes and polymers naked DNA and various physical methods of delivery as well as a comprehensive coverage of the molecular biological designs of the plasmid DNA for reduced toxicity prolonged expression and tissue or disease specific genes New developments such as the toxicity of the non viral vectors and recent advances in nucleic acid therapeutics are fully covered in these volumes

Investigation of Barriers to Non-viral Gene Delivery and Design of Novel Polymer-based Gene Delivery Systems Akin Akinc, 2003 The safe and effective delivery of therapeutic genes is the most significant challenge facing gene therapy today Viral vectors remain the dominant approach for addressing the delivery problem however

concerns regarding the safety of viral vectors have resulted in an increasing interest in non viral vectors Non viral vectors offer the promise of improved safety but because they have yet to match the functional sophistication of viral vectors their transfection efficiencies have lagged those of viral vectors The rational design of functional non viral vectors requires a thorough understanding of both the cell's sophisticated machinery and the vector material's functional properties We have developed a novel flow cytometry based tool for investigating both the cellular uptake and lysosomal trafficking of non viral vectors two important barriers to efficient gene transfer Using this and other tools we investigated the gene transfer properties of polyethylenimine PEI a highly effective non viral vector material We demonstrated that the transfection efficiency of this polymer is due to its ability to avoid lysosomal degradation as a result of its buffering capacity providing quantitative validation of the proton sponge hypothesis By studying the gene transfer properties of a library of polymeric vectors we were able to elucidate new vector structure function relationships We also investigated the combined impact of non structural factors such as polymer molecular weight polymer chain end group and polymer DNA ratio on gene transfer The findings of these studies have lead to the development of non viral vectors with transfection efficiencies surpassing those of PEI and Lipofectamine 2000 two of the best commercially available non viral vectors Non-viral Vectors for Gene Therapy: (v. 54). The mechanism of naked DNA uptake and expression Leaf Huang,Mien-chie Hung,Ernst Wagner,2005

Gene Therapy: New Developments of Non-viral Vectors Iulian Oprea,2010

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