Gene Therapy
Background and introduction

REMEDIUM

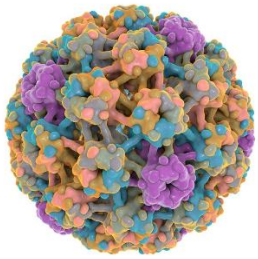
Remedium Bio, Jun 2021

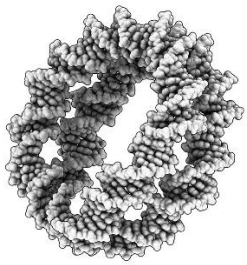
The genetic code of every living organism contains molecular instructions for making proteins, which are the functional element of biology. These instructions are written in a 4-letter molecular language of DNA and RNA, or generally – nucleic acids. In its simplest form, Gene Therapy is a medical treatment that delivers nucleic acids that encode molecular instructions for making proteins capable of preventing, managing, or curing disease.

Since the majority of the work in living cells is performed by proteins, they are quickly turned over and replaced in the general biological process of continuous self-renewal. RNA, which is an intermediary between the genetic code inscribed in DNA and the functional proteins, is also a relatively short-lived molecule. DNA, however, is generally either permanently integrated into the genome or resides in episomes (free genetic material) within the center of the cell called the nucleus. Even within episomes, DNA can persist within the cell nucleus for years or at times the entire lifetime of the cell.

In its most basic form, gene therapy includes a vector, or a vehicle to deliver the nucleic acid, and the nucleic acid itself. The vector can be a viral shell, which has been optimized by millions of years of evolution to efficiently deliver genetic material to the nucleus or a non-viral carrier such as a lipid nanoparticle. The nucleic acid sequence, typically DNA, contains the instructions for the therapeutic protein as well as other regulatory element that tell the cell when, where, and how much protein to produce.

Delivery vehicle or vector – a viral shell or non-viral lipid nanoparticle.



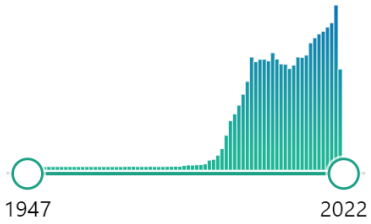


Nucleic acid – genetic instructions encoding the therapeutic protein.

Over 100 years passed between Friedrich Miescher's isolation of DNA in 1869 and Rudolf Jaenisch's creation of a genetically modified mouse in 1974. Yet from the day that Mendel's theory of inheritance was associated with human disease, in part due to the groundbreaking work of Theodor Boveri and Walter Sutton, humanity was focused on changing the balance of heritability in our favor. Since then, gene therapy has been the subject of over 60,000 research papers, and 1,000 registered clinical trials from around the globe – meticulous, steady progress, not without its setbacks.

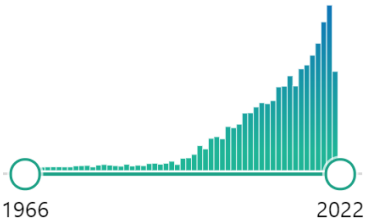
Gene Therapy

60k+ Scientific Publications on PubMed



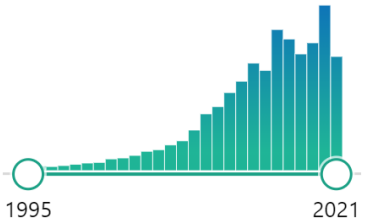
Adeno Associated Virus

9k+ Scientific Publications on PubMed



Lipid nanoparticles

4k Scientific Publications on PubMed



Having realized the significant therapeutic potential of gene therapy by the early 90's, the scientific community quickly began to probe the technology, its mechanisms, means of delivery, and regulation. Today, the most commonly utilized methods to deliver nucleic acids, the Adeno Associated Viral vectors and lipid nanoparticles, have been the subject of over 13,000 peer reviewed publications, of which over 100 are clinical trial reports with published results. Clinical gene therapy has made incredible progress in the last 20 years with nearly 1,000 registered clinical trials on ClinicalTrials.gov of which 142 are using the Adeno Associated Viral vector and 30 delivering its therapeutic cargo with lipid nanoparticles. With the recent US regulatory approvals for the treatment of Leber congenital amaurosis and spinal muscular atrophy, traditional gene therapy has now been administered to thousands of patients worldwide.

Yet, despite the decades of groundbreaking work, the most significant validation for gene therapy, as well as viral and non-viral delivery of nucleic acids, came within the last 2 years. Driven by the Covid pandemic, the brightest minds of the pharmaceutical industry proposed a novel approach for vaccination, the delivery of genetic material for expression of viral antigens in human cells – effectively a gene therapy vaccine. The approaches utilized messenger RNA encapsulated in lipid nanoparticles and DNA delivered via an Adenoviral vector. Hundreds of thousands of healthy volunteers participated in truly global-scale clinical trials for the Moderna, Pfizer/BioNTech, JNJ, Sputnik V, and AstraZeneca vaccines unequivocally confirming their exceptionally high safety and effectiveness profiles. Less than a year from the initiation of R&D activities, commercial supply chains were fully primed and operational. With breakneck speed, gene therapy was finally being validated on a global scale, across a number of platforms, developed by half a dozen companies from across the world.

For the first time in history, therapeutic delivery of nucleic acids to human cells was happening at a scale of multiple-million doses per day. According to OurWorldInData.org, as of the end of June, over 2.6 billion doses of Covid vaccines have been successfully administered in the world, of which over a billion were from the nucleic acid vaccine types containing DNA or messenger RNA. Via the largest trial by fire in human history, gene therapy received validation at an unprecedented global scale, proving not only the ability to quickly engineer nucleic acid therapeutics and delivery systems, but setting a new bar for safety, effectiveness, and affordability.

Remedium Bio, 2021

Remedium Bio is a Boston area gene therapy company focused on the development of highly innovative treatments for a broad range of diseases. The Remedium approach utilizes proven scientific fundamentals, in a novel way, to treat the most debilitating conditions. Starting with well-characterized pathophysiological principles, our scientists modularly apply proven technologies to quickly advance curative treatments through the R&D cycle. Today, our leading candidates include gene therapy treatments in the fields of Endocrinology, Cardiology, Hematology, and Rheumatology.