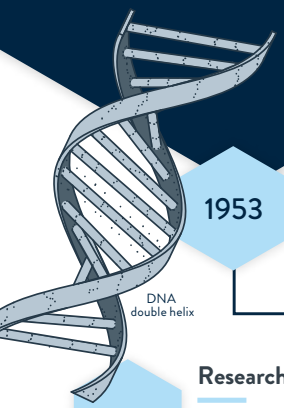
The EVOLUTION of GENE THERAPY

From the early days of gene therapy research, many researchers believed that treating inherited diseases at the genetic level would unlock a new potential for treatment. Over time, researchers have gained a better understanding of genetics and discovered techniques that have led us to the world of gene therapy today.[1]

Take a look at some key milestones in the evolution of genetic research and gene therapy



1953 Discovery of the structure of DNA

The structure of DNA is characterized by a double helix.[2]

1973 Engineering DNA

Researchers discover genetic engineering, which allows DNA or ribonucleic acid (RNA) to be replicated and expressed in another organism.[3]

1980 Concerns raised due to ethical violations

A researcher from the University of California at Los Angeles tests gene therapy in humans without permission from the university or the National Institutes of Health (NIH). The researcher loses multiple grants and the NIH warns others that human experimentation will not be tolerated.[4,5]

1990 First clinical trial using viral vector technology

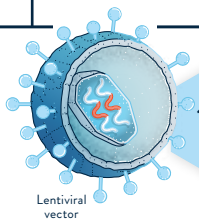
Two patients with a rare inherited pediatric disorder called severe combined immunodeficiency (SCID) receive treatment using novel gamma-retroviral vector technology.[6]

1999 Setbacks in research

The US Food and Drug Administration (FDA) and NIH create new programs in an effort to ensure the safety and transparency of gene therapy clinical trials following the death of Jesse Gelsinger, an 18-year-old patient, during a clinical trial using an adenoviral vector.[9]

2000 Research faces another setback

Scientists use gamma-retroviral vector-based gene therapy in 10 patients with SCID. Following treatment, 4 of the patients develop leukemia, raising concerns about the safety of gene insertion and highlighting the need to improve safety and reduce toxicity when using viral vectors.[10]



1996 Researchers create first lentiviral vectors

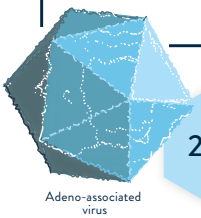
The first generation of lentiviral vectors (LVVs) based on the human immunodeficiency virus (HIV) are created.[7] Second- and third-generation LVVs follow.[8]

2003 First regulatory approval of a gene therapy product

The China Food and Drug Administration approves the world's first commercially available gene therapy to treat squamous cell carcinoma, a form of skin cancer.[11]

WHAT IS A VECTOR?

Vectors introduce genetic material into the nucleus of a cell. There are two types of vectors, viral and nonviral. **Viral vectors** deliver genetic material using the blueprint of a virus because of its natural ability to access the cells of the body.[15] When creating a viral vector, nonessential parts of the virus are never used. This is so that the viral material does not produce the infection that would be caused by the complete virus.[16] **Nonviral vectors**, which are not based on a virus, introduce genetic material to a cell either physically or chemically.[17]



2012 First gene therapy approval in the EU

The European Medicines Agency (EMA) approves the first adeno-associated virus (AAV)–based *in vivo* gene addition therapy for treatment of a rare inherited disorder, lipoprotein lipase deficiency (LPLD).[11-13]

Developments in gene editing

Scientists develop a gene-editing technique called CRISPR/Cas9 that has the potential to modify pieces of a specific DNA sequence.[14]

2018 First clinical trial using CRISPR/Cas9

Researchers investigate the use of CRISPR/Cas9 for gene disruption in patients with genetic β-hemoglobinopathies.[22]

2017 First gene therapy approval in the US

The FDA approves the first AAV-based *in vivo* gene addition therapy for a genetic eye disease that causes progressive vision loss.[20,21]

2016 First *ex vivo* gene therapy approval in the EU

The EMA approves the first gamma-retroviral vector-based gene addition therapy for the treatment of adenosine deaminase deficient severe combined immunodeficiency (ADA-SCID).[18,19]

TODAY

Today, the US FDA has received more than 900 applications to investigate gene therapy in clinical trials. Gene therapy continues to advance from research into potential approvals, with the ultimate goal of serving the patient populations who may benefit.[23]

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