BioAgilytix

The History & Future of Gene Therapy

How Past Events are Informing New Breakthroughs

Gene therapy has experienced both setbacks and successes in its short history, all of which have shaped the therapeutic field into what it is today: one with great potential. In fact, by 2025, the US FDA predicts it will be approving 10 to 20 cell and gene therapy products a year.[1]

But to continue to progress this promising class of therapeutics, it is important to understand the key principles and events in gene therapy's history, so that we are aware of known challenges and can innovate new techniques that sidestep them – ultimately ensuring safe, effective products for patients.

Landmarks in Gene Therapy History

CRITICAL EVENTS | **CRITICAL BREAKTHROUGHS**

1972

Friedmann and Robin[2] **first suggest gene therapy as a treatment** for genetic diseases. But, they also...

...advise against gene therapy in humans until more data is gleaned.

1984

Planning for The Human Genome Project, an international scientific research project coordinated by the USA, commences.[3]

The goal of the project was to **determine the sequence of the human genome and identify the genes that it contains.**

1990

The first experimental gene therapy treatment is conducted in the USA on 4-year-old Ashanti DeSilva, who had severe combined immunodeficiency (SCID) called adenosine deaminase (ADA) deficiency.[4]

This was an example of **human *ex vivo* gene therapy.**

DeSilva's ADA deficiency was cured with a retroviral vector containing the functional ADA gene.

1999

Serious adverse events (SAEs) occur following gene therapy administration, resulting in a tragic death.

Jesse Gelsinger, a patient with ornithine transcarbamylase (OTC), is **the first publicly identified patient to die from gene therapy complications.[5]**

His death resulted within 4 days of receiving a **recombinant adenoviral vector that contained a corrective OTC gene.**

2003

The Human Genome Project is completed.

3 billion DNA letters in the human genome are mapped.[3]

2009

Intensive research is conducted to increase vector safety.

Gamma-retroviral and lentiviral vectors are modified to reduce the risk of activating host genes adjacent to their integration site.

Self-inactivating (SIN) vectors containing insulator sequences are generated to prevent vectors from activating oncogenes from their host cells.

SIN vectors also **demonstrate less genotoxicity and reductions** in the potential for recombination.

The first gene therapy is **approved in China:**

Recombinant human p53 adenovirus (Gendicine) for the treatment of head and neck squamous cell carcinoma (HNSCC).[6]

2012

The first gene therapy is **approved in Europe:**

Alipogene tiparvovec (Glybera) for a rare blood disorder, lipoprotein lipase deficiency.[7]

2017

The first gene therapy is **approved in the United States:**

Voretigene neparvovec-rzyl (Luxturna) for Leber congenital amaurosis, an inherited form of vision loss.[8]

2019

Gene therapies brought to market this year include Zolgensma[9] for spinal muscular atrophy (SMA) **and Zynteglo**[10] for transfusion-dependent β-thalassemia (TDT).

More regulatory approvals are anticipated.

Looking Ahead

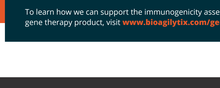
Unbound Promise

With these latest approvals and positive scientific momentum behind it, **gene therapy development is surging.** In fact, the FDA calls it "a turning point in the development of these technologies and their application to human health"[11] to cure previously intractable diseases.

By 2020, the FDA anticipates to receive **MORE THAN 200 gene and cell therapy** investigational new drug (IND) applications.[1]

If past experience tells us anything, it is that patient safety must be at the forefront of gene therapy development, and therefore **immunogenicity testing will remain a critical component of future programs.**

Each part of multicomponent drug modalities can trigger a distinct immune response.

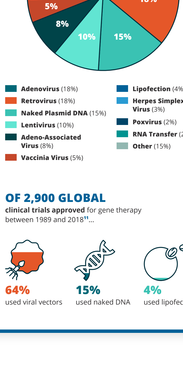


Tailored assessments are needed to gain a full understanding of a gene therapy's immunogenic profile.

A Major Turning Point

Increased Focus on Safety

The advent of safe and effective vectors for the delivery of gene therapy products was a **significant milestone that allowed the first gene therapy approvals to come to fruition.[11]**



OF 2,900 GLOBAL

clinical trials approved for gene therapy between 1989 and 2018[11]...

64% used viral vectors

15% used naked DNA

4% used lipofection

BioAgilytix

Expert Immunogenicity Testing for Gene Therapies

BioAgilytix's scientists worked on some of the very first cases of immunogenicity and **our team is comprised of experts in the assessment of cell-mediated and antibody-mediated immune responses to gene therapies** and their viral and non-viral vectors, including modified and novel vehicles.

We're ready to help write the next chapters of gene therapy history, which we anticipate to be rich in therapeutic breakthroughs and lives saved.

To learn how we can support the immunogenicity assessment needs for your gene therapy product, visit **www.bioagilytix.com/gene-therapy today.**

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Sources

1. https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics
2. https://ucsdnews.ucsd.edu/feature/friedmann_recognized_for_pioneering_gene_therapy_research
3. https://www.genome.gov/25520329/online-education-kit-1990-launch-of-the-human-genome-project
4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1083855/
5. https://www.genome.gov/human-genome-project/results
6. https://www.ncbi.nlm.nih.gov/pubmed/29338444
7. https://www.ema.europa.eu/en/medicines/human/EPAR/glybera#overview-section
8. https://www.npr.org/sections/health-shots/2017/12/19/571962226/first-gene-therapy-for-inherited-disease-gets-fda-approval
9. https://www.fda.gov/news-events/press-announcements/fda-approves-innovative-gene-therapy-treat-pediatric-patients-spinal-muscular-atrophy-rare-disease
10. https://www.ema.europa.eu/en/medicines/human/EPAR/zynteglo
11. http://www.abedia.com/wiley/vectors.php