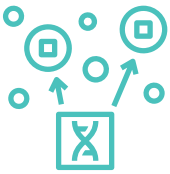
Understanding the Complexity of Gene Therapy Science & Manufacturing

IGT
Institute for Gene Therapies

Gene therapies have the potential to change the way we treat diseases

Gene therapies are potentially one-time treatments that aim to fix the underlying cause of genetic diseases at the DNA level. The effects are long-lasting – potentially life-long – and will prompt changes in how we think about the value of treatment, payment models and the like. Decades of research are beginning to yield FDA-approved gene therapies and hundreds more are working their way through clinical studies with FDA approval expected in the coming years.



The science underpinning gene therapies is highly complex

The development and manufacturing processes for gene therapies are built on a deep understanding of biologic medicines, e.g. vaccines, insulin, and monoclonal antibodies. While gene therapies and biologics share some characteristics, gene therapies are significantly more scientifically complex both in how they are designed for safety and efficacy and in how they are manufactured for scalability and capacity.

How gene therapies work

Gene therapies deliver a functional gene to affected cells throughout the body, so that tissues can begin to produce the protein that's missing due to the patient's disease. There are several types of gene therapies and gene therapy delivery mechanisms. The most advanced is called "gene transfer therapy" delivered to the cells via a non-disease-causing virus.

Three key components to gene transfer therapies:

1. **Transgene:** Healthy corrective gene
2. **Vector:** Usually a non-disease-causing virus that carries and delivers the transgene to the tissue
3. **Promoter**: Makes sure the transgene works once it's inside the patient and delivered to the intended tissue

Manufacturing a gene therapy requires a multi-step process that begins with a batch of virus cells and host cells grown in culture. The batch is repeatedly scaled to create much larger batches and the resulting cells are then harvested to obtain the viruses inside. Purification is necessary to remove cellular debris and isolate the vector.

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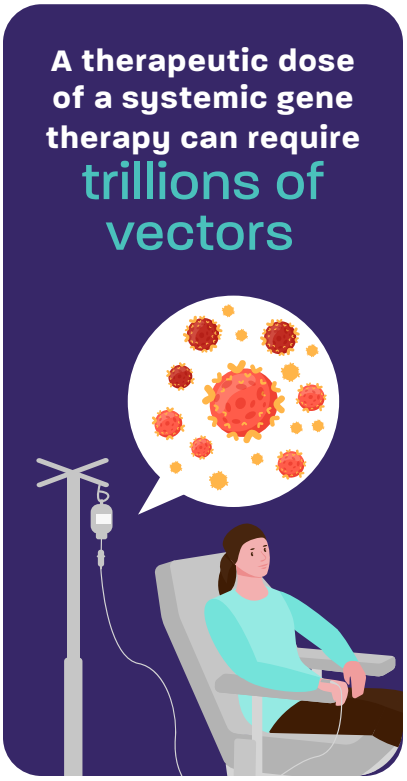
Scaling to meet the needs of systemic diseases

In the purification process, vast quantities of vector will get winnowed down to much smaller amounts. **In one example**, a 2,000-liter batch of virus will be reduced to just 20 liters before it has the purity level needed to be patient-ready. When manufacturing gene therapies for systemic diseases, like neuromuscular conditions or blood disorders, that affect many parts of the body, each patient requires a large, viral vector-rich dose of gene therapy that also does not cause harmful side effects. A therapeutic dose of a systemic gene therapy can require **trillions of vectors**.

Companies that are discovering, studying, and manufacturing gene therapies are investing heavily to build highly specialized facilities dedicated to gene therapy production. Yet manufacturing enough dosage to treat all patients, even for rare diseases, is an ongoing challenge.



Implications for the regulatory process

The Food and Drug Administration plays an important role in establishing the standards for evaluating safety and quality of all medicines, including gene therapies. Given the unique nature of gene therapy development and manufacturing, in recent years, the FDA has issued **a number of guidance documents** specific to gene therapies. Most recently, the FDA issued **draft guidance** that provides recommendations surrounding product design, manufacturing, testing, safety assessment, and clinical trial design, all of which make up the Investigational New Drug (IND) application that allows FDA to assess the safety and quality of the investigational gene therapy.

As the field evolves, the companies and institutions at the forefront of gene therapy science and medicine will continue exploring ways to advance the manufacturing capabilities and meet the needs of patients.

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