Gene therapy: one-off treatment that cures diseases

Gene, RNA, and cell therapy are so-called genetic medicines. In this article, we describe how gene therapy works, its strengths and weaknesses, and give examples of medicines currently on the market. We conclude with a picture of future developments.

Innovative gene therapy addresses the cause of a disease. Many diseases are caused by genetic mutations either present since birth or later in life due to factors such as the sun, air pollution, alcohol, etc. Traditional medicines can usually treat the symptoms of a condition, but not remove the cause. In contrast, genetic medicines can treat the underlying cause. These medications have not only enabled the development of improved therapies but have also produced treatments for conditions for which there is currently no medication.

There are already 100 medicines based on these technologies on the market, treating conditions such as certain forms of ALS and cancer, as well as hemophilia and cardiovascular diseases.

What is gene therapy?
Gene therapy is a treatment that focuses on changing a gene within a patient's cells. Our genes are our body's blueprint; they contain the instructions for the development, growth and function of all our organs. When a mutation occurs in these genes, it can lead to disease.

In gene therapy, a gene (part of our DNA) is inserted into the body to repair a mutated (defective) gene or to deliver the correct gene into our cells. This enables the cell to function properly again and fights or even cures the disease. In principle, gene therapy only needs to be administered once. When this is done, the gene cannot be removed from the cell; the process is irreversible. Many gene therapies are currently under development for a wide range of diseases:

- Various cancers, such as leukemia and breast cancer.
- Hereditary diseases such as cystic fibrosis, Huntington's disease and sickle cell disease.
- Infectious diseases such as AIDS and malaria.
- Neurological diseases like ALS, Alzheimer's and Parkinson's.

How does gene therapy work?
Currently, there are 2 forms of gene therapy:

1. Gene therapy: adding the correct gene into the cell
2. Gene editing: replacing the incorrect gene with the right one

<u>1. Adding the correct gene:</u>
In diseases caused by a defective or missing gene, a medicine containing the correct gene can be delivered into the body's cells via an infusion.

An example of this technology is the medicine Zolgensma. This is being marketed by our portfolio company Novartis to treat the deadly childhood muscle disease called spinal muscular atrophy (SMA). Children who receive a single treatment with Zolgensma achieve all normal motor milestones,

including walking independently. Without the treatment and, these children need permanent ventilation. Without that, they would die at the age of 1 year.

2. Repair of errors in genes

Besides being able to deliver the correct gene into cells, an error in DNA can also be repaired with gene editing. For example, via the Nobel Prize-winning CRISPR/Cas9 technique. This technology removes a specific gene in the cell nucleus and replaces it with the correct gene. Two of our portfolio companies, Crispr Therapeutics & Intellia, use CRISPR technology. In December 2023, Crispr received FDA approval for Casgevy, the world's first gene-editing therapy for the treatment of sickle cell disease. Click here for a 2-minute video on CRISPR technology.

Pros and cons of gene therapy

Gene therapy is a one-off treatment that targets the cause of the disease. As it is a relatively new treatment modality, there is still limited information regarding possible long-term side effects. However, given that many clinical studies have been conducted for several years and the first gene therapy medicines are already on the market, this innovative therapy is a great asset, especially for addressing serious conditions. Gene therapies are also being developed for common conditions such as high cholesterol and macular degeneration in the eye.

Gene therapy (still) is quite expensive. This is primarily due to high development and production costs coupled with the fact that one infusion is often sufficient.

Furthermore, because the immune system perceives gene therapy as an unfamiliar invader, it may respond negatively to it. There are multiple ways to address this. For instance, it is occasionally feasible to predict which patients will have a significant immunological response, and corticosteroid medication can be administered before treatment, thereby reducing the immune response.