RNA therapy: the future of medicine

RNA, gene and cell therapies are so-called genetic medicines. These innovative therapies treat the cause of diseases caused by:

- mutations found in genes from birth or,
- mutations caused by factors such as the sun, air pollution, alcohol, etc.

Traditional medicines can sometimes treat the symptoms of these diseases but are not able to 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 for example certain forms of ALS and cancer, as well as hemophilia and cardiovascular diseases.

This article provides an overview of cell therapy's benefits and drawbacks as well as some examples of available treatments. It concludes with an overview of future developments.

What is the function of DNA and RNA?
The DNA in our cells determines every characteristic of human beings. Height, eye color, bone structure, speed of metabolism, etc. Moreover, DNA determines what type and number of proteins a cell must create at any given time for the body to function properly. Proteins are responsible for almost every function performed in our body.

RNA (ribonucleic acid) transmits instructions from DNA to the mechanism responsible for making proteins in our cells. DNA and RNA are made up of different building blocks. The main difference is that RNA has only one strand instead of two. This makes the genetic code in RNA more accessible and easier for the cell to translate. The image below is a representation of this process.

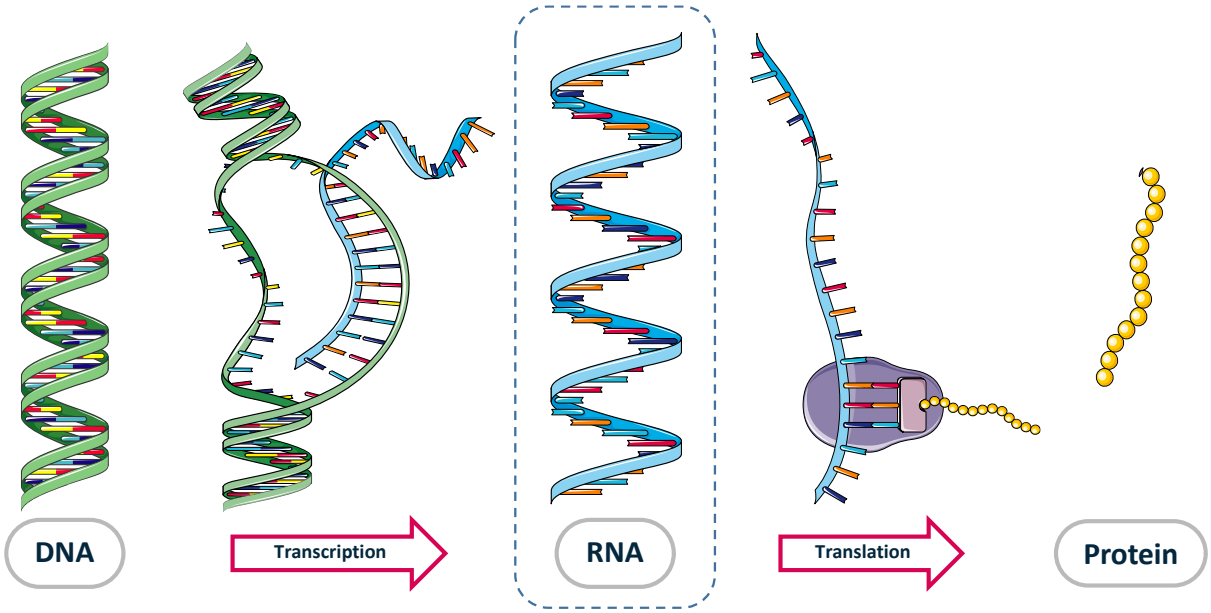

Figure 1. From DNA via RNA to protein: illustration of transcription and translation

This is how RNA can cure diseases

When DNA contains errors, either from birth or due to one or more mutations during life, the processes described above can produce non-functional or harmful proteins. As a result, diseases can arise. For decades, medical science could only address the symptoms of a very limited number of genetic disorders. However, with RNA therapies, we can cure an increasing number of these conditions.

RNA is formed over and over again in cells. To have a lasting effect, RNA medicines therefore need to be administered repeatedly, for example once a quarter. The advantage of this dosing regimen is that if side effects occur, they usually disappear as soon as the therapy is stopped. This is in contrast to gene therapy, which you can learn more about in this specific article.

4 forms of RNA therapy

There are 4 different forms of RNA therapy, each with its own scope, advantages and disadvantages. They offer promising possibilities for the treatment of various diseases, ranging from genetic disorders to infectious diseases and cancer. New developments are constantly taking place.

1. RNA Interference (RNAi): This causes the **degradation** of the specific RNA responsible for the production of a 'faulty' protein that causes a disease. An example is Onpattro, which was developed by Aescap portfolio company Alnylam Pharmaceuticals to treat polyneuropathy (a disease that causes damage to peripheral nerves due to hereditary accumulation of defective proteins that causes weakness, numbness and pain in the arms and legs).
   In summer 2022, Alnylam also successfully completed a final phase study for Onpattro for the treatment of cardiovascular disease caused by accumulation of a defective protein. This is currently under review by the FDA.
2. Antisense Oligonucleotide (AONs): This involves a medicine that **binds** to the malfunctioning RNA **and inactivates** it. An example is Spinraza from Aescap portfolio company Ionis, used to treat spinal muscular atrophy (SMA). SMA is a genetic muscle disease that, without the use of medication, often leads to patients not surviving beyond two years of age.
3. mRNA: This therapy gives instructions to cells to **produce proteins** that would otherwise not be produced in our bodies. mRNA is recognizable from its role in the Covid-19 vaccines developed by BioNTech and Moderna.
4. ADAR: This therapy is still at an early stage of development and is being used by Aescap portfolio company ProQR. It is a technology that uses the **body's own repair mechanism** to repair RNA. This video explains more about ADAR.

Pros and cons of RNA therapy

By not only treating the symptoms, but by removing the cause of the disease, RNA therapy has the potential to cure patients This is the main advantage of RNA therapy. In addition, this method can fix specific errors in genes without altering the entire gene.

Naturally, there also are drawbacks to RNA therapy. Our immune system is set up to attack and remove genetic material that is not our own. As a result, delivering RNA medicines to the targeted cells without them being destroyed is a challenge.

The future: from rare to common diseases

The first RNA medicines mainly treated rare, genetically well-characterized diseases. It is now clear that their potential is not limited to these diseases. For example, Leqvio, an RNAi medicine from portfolio company Novartis, lowers LDL cholesterol and could therefore be used by millions of people.

In addition, a lot of work is being done to develop RNA vaccines that can boost immunity to treat cancer. Cancer is the result of mutations in our genes that are congenital or arise spontaneously over the course of our lives due to, for instance, alcohol, smoking, chemicals, etc. Aescap portfolio companies Moderna in collaboration with cancer medicine leader Merck & Co. showed good research results of an mRNA vaccine to treat melanoma (a dangerous form of skin cancer) in patients in whom the primary tumor had been removed. The combination of the two medicines reduced both the risk of recurrence or death by 49% and also the risk of metastasis or death by 62%, compared with the use of Mercks' medicine Keytruda alone.

The number of patients that can be treated with RNA technology will only increase. With continued innovation and further investment in the companies developing these medicines, this technology is going to have an even greater positive impact on the lives of many patients and transform healthcare.