The Future of mRNA Technology

Beyond Covid-19: The Versatility of mRNA in Health and Innovation

Vaccines against the coronavirus based on mRNA have become firmly established in medicine since the pandemic. Nevertheless, the technology is still at the beginning of its potential. Hundreds of clinical trials with corresponding active ingredients are now underway worldwide. Experts see a wide range of potential applications for this relatively new technology, particularly in infectious diseases and cancer.

Until the beginning of 2020, only experts were familiar with the term mRNA. But with the coronavirus pandemic and the feverish search for a vaccine, the term became part of the daily news within a few months. There was great hope that messenger RNA could be used to find a cure for the increasingly widespread pandemic. A hope that ultimately proved to be true: several biotech and pharmaceutical companies developed mRNA vaccines against Covid-19 in a comparatively short time and under high pressure of expectation.

Today, around four years later, the term mRNA has fallen somewhat out of the public eye, but scientists and developers are working hard to exploit the full potential of this technology. At the center of interest is the question: For which indications and against which diseases can mRNA-based therapies or vaccines be developed in the foreseeable future?

More than 700 Clinical Studies Worldwide

A look at the international database clinicaltrials.gov shows just how intensive research is in the world of mRNA. According to this digital library, which keeps records of clinical trials worldwide, the number of tests with mRNA agents has almost doubled in the past two years. In total, the document currently lists over 700 studies with mRNA agents worldwide. In addition, there are more than 1,200 completed studies.

Nobel Prize Winner Karikó Sees Wide Range of Applications

Katalin Karikó, Nobel Prize winner and one of the key pioneers of mRNA-based vaccines, also sees considerable potential in the technology. According to the researcher, in addition to coronavirus vaccines, it could potentially soon be used against a number of other diseases such as influenza, HIV or the herpes simplex virus (HSV). The biochemist, who works as an external consultant for the Mainz, Germany-based pharmaceutical company BioNTech, also sees good potential applications for the technology in cancer therapy.

John Cooke, Medical Director of the Center for RNA Therapy at Houston Methodist Hospital in the US, is also confident that in ten years' time there will be numerous mRNA drugs and vaccines on the market for diseases for which there are currently no effective therapies.

According to Carsten Watzl, Head of the Immunology Research Unit and Scientific Director of the Leibniz Institute for Occupational Research at TU Dortmund University, Germany and Secretary General of the German Society for Immunology, mRNA technology has two major advantages: Firstly, it ensures robust T-cell immunity to Covid-19 more than conventional inactivated vaccines. Secondly, mRNA can be used to specifically deliver various blueprints for the production of proteins into the cells. These proteins cause the creation of antibodies that help to fight the virus in the event of subsequent contact with it.

More Effective Cancer Therapy with mRNA

Scientists are making use of this property in mRNA cancer therapies, among other things. The aim is to teach the immune system to recognize and destroy its own tumour before it spreads by using an individually adapted mRNA.

Niels Halama, Head of the Translational Immunotherapy Department and Senior Physician and Head of the Adaptive Immunotherapy Research Group at the National Center for Tumor Diseases in Heidelberg, Germany, points out that precursors of cancer cells are created every day in every person, e.g., through mutations that occur during cell division. Normally, the immune system recognizes the altered cells as "foreign" and destroys them. However, some cancer cells manage to camouflage themselves or thwart the immune system's attack. The vaccination is intended to teach the immune system again that the tumor cells are "foreign" and must be fought.

Klaus Cichutek, who was President of the German Paul Ehrlich Institute (PEI) from 2009 to 2023, also points out in a podcast with Ärzte Zeitung that developments in cancer therapy are moving towards variable and individually tailored tumor vaccines. The corresponding RNAs would be mixed individually for patients and would

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enable a completely new approach to cancer therapy if clinical data confirms this. Cichutek: "This type of therapy is exactly what we need: as individual as the body is, we also need individually tailored active substances."

The now retired scientist even believes it is possible that mRNA could one day be produced in special printers, virtually at the patient's bedside.

However, the Heidelberg scientist Halamba points out that the development of active substances is still "in its infancy". Initial results would indicate that a vaccination against cancer could be effective. "We are therefore very confident," says Halamba. Ultimately, however, large clinical trials would have to show which patients would benefit from the vaccination — and which would not.

According to a report in the Deutsches Ärzteblatt, Nobel Prize winner Karikó sees another approach to fighting cancer in the intratumoral injection of mRNA. This principle has been successfully tested in animal models and studies with humans are currently underway.

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Vaccines Against Infectious Diseases

There is also a lot going on in the field of mRNA therapies against infectious diseases. Karikó points out that phase 3 studies are currently underway on the use of mRNA-based vaccines against respiratory syncytial virus (RSV) infections, for example. In addition, mRNA vaccines against influenza, HIV, HSV, Epstein-Barr virus (EBV) and cytomegalovirus (CMV) are being researched. Scientists are also working on a vaccine against the Nipah virus, which is particularly prevalent in Southeast Asia.

But viruses are not the only focus of mRNA vaccine research. Investigations into vaccines against tuberculosis and malaria have also begun. Furthermore, vaccines against borrelia are being evaluated in preclinical studies. According to Karikó, another interesting aspect is multivalent vaccines against tick bites.

The Companies' mRNA Projects

Long before the coronavirus pandemic, German company BioNTech was already researching a vaccine against cancer. The development pipeline currently has 21 cancer product candidates in clinical trials, eight of which are based on mRNA technology. BioNTech states: "Our cancer vaccine platforms Fixvac and Inest are set to revolutionize cancer treatment as we know it. They are designed to offer cancer patients a customized treatment approach that is specifically tailored to a particular tumor indication or even to their individual tumor."

In addition, the company's pipeline includes several mRNA projects in the field of infectious diseases, including influenza, tuberculosis, and malaria.

The pipeline of the US biotech company Moderna includes more than 40 mRNA projects that are in various clinical stages or close to market launch. These include vaccine candidates against influenza, Covid and RSV, as well as against HIV, norovirus and zika virus. Moderna is also working on cancer vaccines and therapeutics for various rare diseases. "We believe that our mRNA platform can tackle the world's biggest health challenges — from diseases that affect millions of people, to highly rare diseases that affect a few, to medicines that can be personalized to patients," Moderna quotes its CEO Stéphane Bancel on its website.

The product candidates of the Munich, Germany-based biotech company Ethris are at a comparatively early, preclinical stage. Development is focused on the treatment of respiratory viral infections and rare pulmonary diseases, as well as next-generation prophylactic vaccines that are mucosal, multivalent and mutation-agnostic.

The French pharmaceutical company Sanofi is also working on mRNA programs. These include product candidates for the treatment of RSV and influenza. The Tübingen, Germany-based biotech company CureVac, a self-proclaimed mRNA pioneer and one-time hopeful for a Covid-19 vaccine, is continuing to work on mRNA vaccines against influenza and Covid after its flop with the product candidate. The projects have not yet progressed beyond clinical phase 2, the former management has been almost completely replaced and the share price has plummeted. Although the company has been in existence for around 24 years, it has not managed to develop a drug to market maturity in this time.

In the fall of 2023, Darmstadt, Germany-based science and technology company Merck announced that it was the first provider to offer an integrated service for contract development, manufacturing and testing (CTDMO) of mRNA and related products. To this end, the company opened two new manufacturing facilities for mRNA active ingredients in Darmstadt and Hamburg.

Mode of Action of mRNA

Messenger RNAs (mRNA) are essential molecules in our cells that serve as the link between our DNA and all biological activities in our bodies. mRNA consists of four different building blocks, the nucleotides. An mRNA molecule is made up of many nucleotides that are strung together in a unique way. This is how the information for the production of the respective protein is transmitted in the cells. In therapy, mRNA can therefore be used as an information carrier.

The mRNA Knowledge of the Population

The acceptance of future mRNA vaccines and therapeutics depends not only on the quality of the products but also on the knowledge of the population. With this in mind, Moderna Germany conducted a survey by the market research institute Civey. According to the survey, 42% of respondents believe that mRNA technology will have a decisive influence on future medicine, and 8% even believe that it will revolutionize medicine. 68% see cancer treatment as a promising area of application for mRNA technology, followed by infectious diseases, autoimmune diseases, and rare diseases.

According to immunologist Watzl, who analyzes the results for Moderna, the continuous media coverage of mRNA technology during the coronavirus pandemic has borne fruit. Generation Z, born between 1995 and 2020, has the most mRNA technology know-how compared to older people. Overall, however, a lot of educational work is still needed to dispel misinformation.

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