Hunting the 'perfect protein' for malaria mRNA vaccine

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A child and its mother being tested for malaria in Mozambique. Scientists are researching the safety and efficacy of mRNA-based malaria vaccines. Credit: Malaria Consortium

After the success of mRNA vaccines against COVID-19, scientists are cautiously optimistic that the same technology can be used to tackle other widespread diseases such as malaria. The technology is promising, say vaccine developers, but its success will depend on the results of initial tests currently underway.

A vaccine against all types of malaria has so far been elusive, due to the complexity of the parasite that causes the disease. Malaria remains a neglected disease, which means it has been overlooked by the research community.

"Neglected diseases affect poor populations," Carlos Zarate-Bladés, an immunologist at Brazil's Federal University of Santa Catarina, tells SciDev.Net. "Any industry that may generate a product will first look at the market. If the market isn't promising in financial terms, it won't even be tested."

Malaria is spread through the bites of Anopheles mosquitoes infected by Plasmodium parasites. In 2020, the disease caused roughly 627,000 deaths worldwide, among 241 million cases, according to the World Health Organization. In the same year, Africa registered 96 percent of malaria deaths. Children under five are the most affected, and accounted for an estimated 80 percent of all malaria deaths in Africa.

Malaria symptoms usually appear around ten to 15 days after infection and include fever, headache and chills. If left untreated, the disease can become severe and may cause kidney failure, seizures, coma and death. Groups at higher risk of developing severe disease include children under five, pregnant women, and people living with HIV/AIDS. The WHO says that malaria is "both a consequence and a cause of poverty and inequality."

First malaria vaccine

The first malaria vaccine was recommended by the WHO in October 2021 for broad use in children, an event which has been hailed as an historic moment. GlaxoSmithKline's Mosquirix, also called RTS,S, offers protection against Plasmodium falciparum, the malaria-causing parasite that is prevalent in Africa.

However, it is not effective against other types of Plasmodia, such as Plasmodium vivax, which is the dominant malaria parasite in most countries outside of Sub-Saharan Africa.

In Brazil, scientists are testing a recombinant protein-based vaccine against P. vivax, which causes 89 percent of malaria cases in the country. In this vaccine technology, a piece of DNA is taken from the pathogen and inserted into manufacturing cells that then become able to produce a protein from the virus—or in the case of malaria, the parasite—that can be used in the vaccine.

For the past two decades, Irene Soares, a microbiologist at the University of São Paulo, has been researching this potential malaria vaccine. Her team focuses on a P. vivax protein that has a similar function to the one that has been used in the vaccine approved for Africa. This protein attacks the parasite to prevent it getting to the blood and causing severe disease.

Tests in animalsshowed that the vaccine is safe and offers protection. "Now we are at the stage of preparing this formulation for the first phase of trials in human beings," Soares told SciDev.Net.

Global research

BioNTech, which developed a COVID-19 vaccine in partnership with Pfizer, plans to begin clinical trials with the first mRNA-based malaria vaccine by the end of 2022, the company informed investors and the press last year. The German company also aims to set up mRNA manufacturing facilities in Africa.

The WHO recently announced a global mRNA technology transfer hub, established to support manufacturers in low- and middle-income countries to produce their own vaccines. A South African consortium was selected to run the hub, and two regional "spokes" have been established in Brazil and Argentina.

Brazil's Immunobiological Technology Institute (Bio-Manguinhos/Fiocruz) was selected in September by the WHO for the development and production of vaccines using mRNA. The primary focus will be the COVID-19 pandemic, but this initiative is expected to allow the production and faster distribution of new vaccines, including one against malaria, in the future.

Fiocruz—a health research institute—is the largest vaccine producer in Latin America and was also developing a prototype for a coronavirus vaccine with a slightly different technology than mRNA, called self-amplifying RNA.

Patrícia Neves, a researcher at Bio-Manguinhos/Fiocruz tells SciDev.Net: "In addition to continuing the development of our [COVID-19] vaccine, we are also preparing our production area, quality control, and training professionals."

The search for a target

Even with a promising platform such as mRNA, the key for a malaria vaccine is finding the perfect target—the protein that will be presented to the human immune system.

The malaria parasite has a complex life cycle, with different forms and stages inside the host, and this makes it difficult to select a good target for a vaccine. Studies in the past have tested several proteins from various stages of the parasite, and most of them failed.

In addition, the genome of the parasite is more complex: viruses typically have dozens of genes, while malaria parasites have about 5,000 genes.

"If, on the one hand, there are more possible targets, on the other hand, it becomes more difficult to discover which of them are the parasite's biggest weaknesses," Daniel Bargieri, an immunologist and researcher at the University of São Paulo, tells SciDev.Net.

"And many gene collections fulfill the same function; so, if you attack one, it doesn't matter to the parasite, because it has other proteins that perform the same function."

To make matters worse, the parasites can mutate and have mechanisms to evade the immune system.

mRNA vs malaria

Bargieri and his team are looking for new antigens, or proteins, to identify a target among these 5,000 genes. They are exploring mRNA technology for a potential vaccine.

A protein can be a good target for a vaccine, but it is hard to produce in the lab. The mRNA vaccine circumvents that, as the mRNA itself, manufactured in a lab, will teach humans cells how to produce the protein—or part of it—that triggers an immune response.

"Even though this is a newer technology, it is sometimes easier to make mRNA than an antigen," says Bargieri. His team has just begun testing and results are not expected for a few years yet, he says.

Scientists are eagerly anticipating the first data on mRNA vaccines against parasites, protozoa or bacteria, which have a very different biology to viruses. Bargieri says that malaria vaccines are one of the most advanced, but trial results will determine if and when they become available.

If a new mRNA malaria vaccine eventually proves itself safe and effective, the challenge will be to deliver it to the most affected regions—developing countries in the global South.

During the pandemic, some regions have become better prepared to face this challenge. In some countries, including Brazil, scientific institutions secured the funding and technology to produce COVID-19 vaccines. "All this infrastructure that was set up will certainly help in the advance of other vaccines," says Soares.

For Zarate-Bladés, the only thing that Brazilian research institutes need is better funding: "There is no lack of knowledge or technique in Brazil. What is lacking is funding for research and product development."

Provided by SciDev.Net