Researchers chart path forward on developing mRNA vaccines for infections beyond COVID-19

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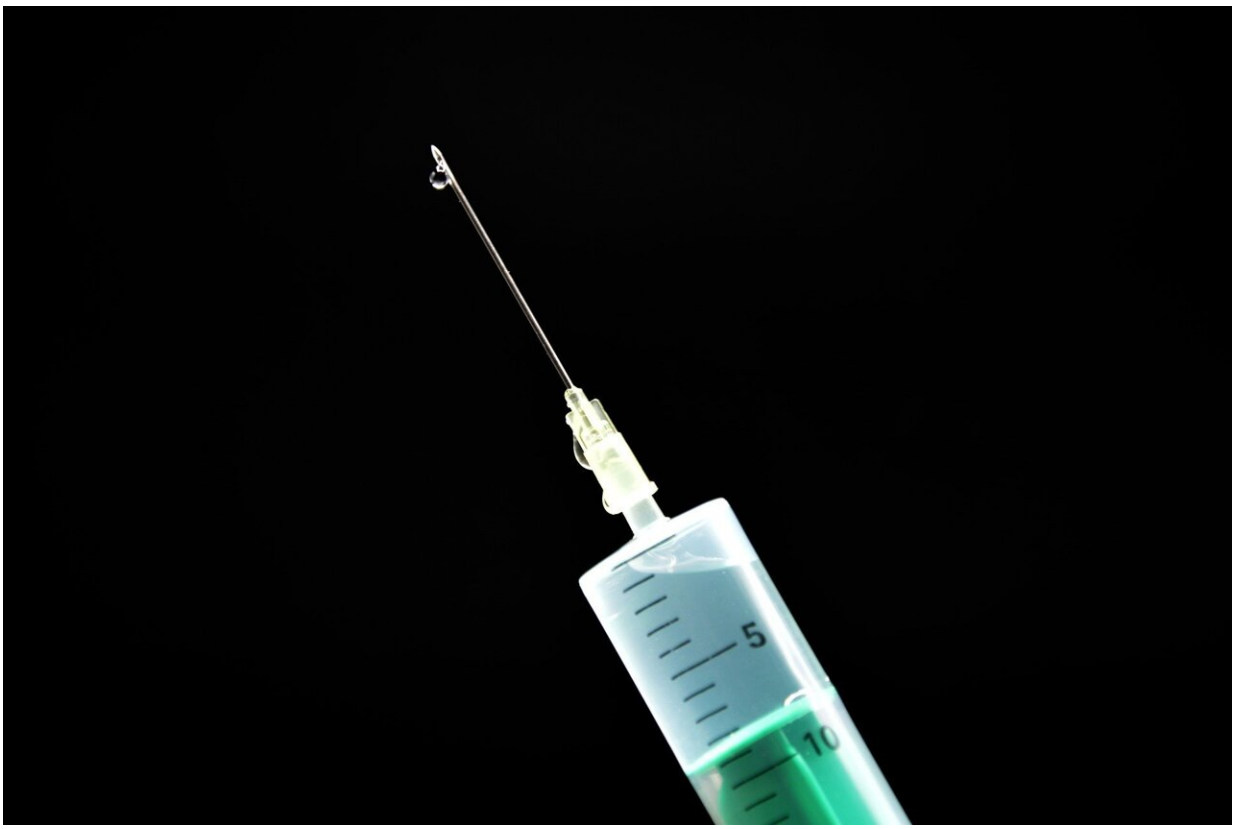

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After helping to develop and test new mRNA technologies for COVID-19 vaccines, University of Maryland School of Medicine

(UMSOM) researchers and scientists are turning their attention to utilizing this innovative technology to ward off other infectious diseases like malaria and influenza. Last month, UMSOM faculty in the Center for Vaccine Development and Global Health (CVD) launched a new clinical trial to investigate the use of mRNA technologies to create a vaccine against malaria.

CVD Director Kathleen M. Neuzil, MD, MPH, FIDSA also provided commentary in the *New England Journal of Medicine* on the feasibility of using mRNA to develop a universal influenza vaccine that could eliminate the need for seasonal shots.

The huge success of mRNA vaccines to combat COVID-19 has opened up a new era in vaccine development, offering the potential for faster, more efficient, and more effective vaccine production. In the editorial commenting on a new study published last week in the *New England Journal of Medicine* (*NEJM*), Dr. Neuzil, who is also the Myron M. Levine, MD, Professor in Vaccinology at UMSOM, wrote, "the application of mRNA technology to influenza vaccines would permit the design of vaccines that incorporate mRNAs matched to multiple influenza strains, a rapid adaptive response to virus evolution, and the manufacture of combination vaccines that include influenza and noninfluenza proteins, which would facilitate delivery to populations."

Dr. Neuzil pointed to more than 20 studies underway or in the planning stages to test novel influenza vaccines utilizing this technology. She commented on a recent animal study published in *Science*that tested an mRNA vaccine against all 20 known influenza virus subtypes. The study found that the single vaccine can provide protection against different strains of the influenza virus by simultaneously inducing antibodies against multiple antigens, which she said suggests that an mRNA vaccine against influenza is "feasible" but that "careful attention to safety evaluations will be critical."During the COVID-19 pandemic, Dr. Neuzil

led the team that launched the first clinical trial in the U.S. to test the Pfizer and BioNTech mRNA vaccine against COVID-19.

The recently launched phase 1, first-in-human clinical trial investigating an mRNA-based vaccine for malaria will aim to determine whether the vaccine is safe and its potential for efficacy against one of the world's most deadly parasitic illnesses.

"Many scientists who study malaria have long been invested in developing vaccines to prevent malaria deaths and disease, and the COVID-19 pandemic advanced the mRNA vaccine platform that can readily be adapted for other illnesses," said Matthew Laurens, MD, MPH, Professor of Pediatrics and Medicine at UMSOM's Center for Vaccine Development and Global Health (CVD) and Coordinating Investigator for the BioNTech mRNA malaria vaccine trial.

"As this is the first study to test this novel mRNA-based vaccine in humans, we are hopeful we'll see promising results that may be life changing for children who are at highest risk of death, severe disease, and inferior school performance due to malaria."

Study participants ages 18 to 55 will receive three total injections of a vaccine made by BioNTech SE, or a placebo, over six months. The study is expected to be completed in September 2024. Investigators will carefully track how well the participants tolerate the injection and monitor any reactions that might occur. Importantly, participant immune responses will be measured after vaccination.

There were 247 million malaria cases and 619,000 deaths reported worldwide in 2021 alone, which is a 9% increase from 2019 before the pandemic. Public health experts contend new strategies are urgently needed to achieve the United Nation's sustainable development goal of 90 percent reduction in malaria incidence and mortality by 2030.

Scientists have tried for decades to develop a highly effective malaria vaccine without much success.

The current study's mRNA approach—and other recent research investigating monoclonal antibodies for malaria—represent a promising advances to reduce malaria morbidity and mortality.

The first vaccine against malaria (RTS,S/AS01) was approved by the World Health Organization in October 2021, and it provides modest protection against malaria. Unfortunately, it is in short supply and thus additional vaccines are urgently needed.

In 2022, UMSOM researchers published findings from a study that showed a three-dose regimen of a whole-parasite vaccine against malaria—called Plasmodium falciparum sporozoite (PfSPZ) vaccine—demonstrated safety and efficacy when tested in adults living in Burkina Faso, West Africa, an area highly endemic for malaria.

"Instead of relying on inactivated microbes to trigger an immune response, mRNA vaccines use mRNA to teach our cells how to make a protein, or piece of a protein, that resembles a microbe's protein," said UMSOM Dean Mark Gladwin, MD, who is also Vice President for Medical Affairs, University of Maryland, Baltimore, and the John Z. and Akiko K. Bowers Distinguished Professor at UMSOM. "This foreign protein triggers a human immune response against the microbe. The mRNA vaccine platform has several advantages in terms of stimulating a more robust immune response and enabling quick adaptation and scalability to new strains or variants that emerge during pandemics."

More information: Kathleen M. Neuzil et al, An mRNA Influenza Vaccine—Could It Deliver?, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMcibr2215281

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