Scientific breakthrough harnesses mRNA technology to develop powerful malaria vaccine

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Scientist using instruments wearing PPE in laboratory. Credit: Doherty Institute

Victoria University of Wellington's Ferrier Research Institute and the Malaghan Institute of Medical Research in New Zealand, and the Peter Doherty Institute for Infection and Immunity in Australia have developed an mRNA-based vaccine that can effectively target and

stimulate protective immune cell responses against the malaria-causing parasite Plasmodium in preclinical models. This research was published in *Nature Immunology*.

Ferrier Research Institute's Professor Gavin Painter says the approach is distinctive, as the team leveraged years of prior research from the University of Melbourne's Professor Bill Heath at the Doherty Institute and Professor Ian Hermans from the Malaghan Institute.

"Thanks to this synergy, we were able to design and validate an example of an mRNA vaccine that works by generating resident memory cells in the liver in a malaria model," says Prof Painter.

"It demonstrates the huge potential of RNA technology in solving some of the world's biggest health problems and the growing capability and expertise in mRNA vaccine development here in New Zealand and Australia."

The focus of the collaborative research investigating a novel target for malaria was originally on peptide-based vaccines. However, in 2018, the team shifted their approach and started investigating RNA-based vaccines—a decision that, so far, seems to have paid off with the recent success of RNA technology in vaccine development.

"While our successful peptide-based vaccines targeting malaria only contain small protein fragments of a malaria protein, mRNA vaccines encode an entire malaria protein," says the University of Melbourne's Dr. Lauren Holz, Research Officer at the Doherty Institute and co-author of the paper.

"This is a real strength because it means we can generate a broader and hopefully more protective immune response."

To pack an extra protective punch, the mRNA vaccine has been combined with an adjuvant—originally developed at the Malaghan and Ferrier Institutes for cancer immunotherapies—which targets and stimulates liver-specific immune cells. This additional ingredient helps localize the RNA vaccine response to the liver, a key site in preventing the parasite from developing and maturing in the body.

"When the parasite first enters the bloodstream, it travels to the liver where it develops and matures before going on to infect blood cells, which is when disease symptoms occur," says Dr. Mitch Ganley, Postdoctoral Research Fellow at the Ferrier Research Institute, and co-author of the study.

"Unlike the COVID-19 vaccine that works by neutralizing antibodies, our unique approach relies on T-cells which play a critical role in immunity. Specifically, a type of T-cell called a tissue-resident memory T-cell, that halts malaria infection in the liver to completely stop the spread of infection."

Dr. Holz says the key advantage of this vaccine is that it isn't affected by previous exposure to malaria.

"A lot of malaria vaccines undergoing trials have worked really well in animal models or when they're given to people who haven't had malaria before, but they don't work well when given to people living in malaria-endemic regions. In contrast, our vaccine is still capable of generating protective liver-specific immune cells and providing protection even when the animal models have been pre-exposed to the disease," says Dr. Holz.

The research team is now working towards taking the vaccine into human clinical trials, which they expect to take several years.

More information: mRNA vaccine against malaria tailored for liver-resident memory T cells, *Nature Immunology* (2023). DOI: 10.1038/s41590-023-01562-6