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To hunt for better malaria vaccines, researchers turn to machine learning

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Anti-malaria drugs have been a central component of a global public health effort that saw a 44% drop in the deadly mosquito-borne disease from 2000 to 2019, but progress has stalled as the parasites that cause malaria gain resistance to these drugs.

Now, computational biologists from the University of Maryland, College Park have partnered with researchers at the University of Maryland School of Medicine in Baltimore to pursue a malaria vaccine using machine learning—a subset of artificial intelligence that doesn't require direct programming.

They're using a novel approach called "reverse vaccinology" that employs powerful bioinformatic tools to delve into the genetic makeup of several parasites that cause malaria to target proteins, or antigens, associated with these pathogens for vaccine testing.

The team's initial study was recently published in *npj Systems Biology and Applications*.

The paper's lead author is Renee Ti Chou Ph.D. '23, a data scientist at Lexical Intelligence in Rockville, Md., with co-authors including Professor Michael Cummings, a professor of biology with an appointment in the University of Maryland Institute for Advanced Computer Studies, and Amed Ouattara, Matthew Adams, Andrea A. Berry and Shannon Takala Harrison, all from the medical school's Center for Vaccine Development and Global Health.

The researchers not only identified new potential vaccine targets, Cummings said, but also ranked them based on importance. To prioritize the most promising candidates, they looked at factors like gene essentiality and when the proteins are active in the parasite's life cycle.

"These findings offer a flexible framework for future vaccine research," said Cummings, who was Chou's academic adviser at UMD. "We can adjust our criteria and even apply this approach to other diseases beyond malaria. It's a big step forward in the quest for better vaccines."

More than 240 million people, mostly in Africa, contract malaria every year, according to the Centers for Disease Control and Prevention and Prevention. Current vaccines leave many who take them at risk of the disease; without a highly effective one, the researchers say, defeating the disease that killed an estimated 608,000 people in 2022 could be out of reach.

To do so, however, scientists must target different life cycle stages of the P. falciparum parasite, the deadliest species of the Plasmodium blood parasite that causes malaria.

This can be tricky, said Cummings, director of the Center for Bioinformatics and Computational Biology; not only does the parasite take on different forms during its life cycle, but its genetic proteins also change, making it difficult for the human immune system to counter. So far, most vaccine efforts have focused on a few proteins without looking at the whole picture of the P. falciparum parasite's genes.

The team analyzed thousands of proteins from the P. falciparum parasite, considering 272 different factors for each. They used a machine learning technique called positive-unlabeled learning to sort through this data, letting the system learn from what is already known about effective targets.

More information: Renee Ti Chou et al, Positive-unlabeled learning identifies vaccine candidate antigens in the malaria parasite Plasmodium falciparum, *npj Systems Biology and Applications* (2024). DOI: 10.1038/s41540-024-00365-1