New malaria vaccine candidates identified

July 30 2014

Children and guardians present to a local dispensary for sampling for the detection of anti-malarial antibodies. Credit: Juliana Wambua

Researchers have discovered new vaccine targets that could help in the battle against malaria. Taking a new, large-scale approach to this search, researchers tested a library of proteins from the *Plasmodium falciparum* parasite with antibodies produced by the immune systems of a group of infected children.

The tests measured which proteins the children's immune systems responded to, revealing antigens that had not previously been identified as possible vaccine targets and new insights into the ways antigens could be used in combination to increase protection.

"Resistance to malaria drugs is an increasing problem so vaccines are desperately needed to battle the *Plasmodium falciparum* parasite before it has a chance to make people sick," says Dr Faith Osier, first author from the Kenya Medical Research Institute. "This study presents us with a large number of new vaccine candidates that offer real hope for the future."

A group of children infected with malaria were followed over a six-month period by scientists at the Kenya Medical Research Institute (KEMRI). While some patients became sick, others were protected by naturally occurring antibodies that stopped the malaria parasite from penetrating their red blood cells during the blood stage of the disease, which produces severe symptoms such as fever and anaemia. Researchers used samples taken from these children to identify combinations of antibodies that provided up to 100 per cent protection against clinical episodes of malaria.

The study used a library of parasite proteins that was generated using an approach developed at the Wellcome Trust Sanger Institute by Dr Gavin Wright and Dr Julian Rayner. These researchers had previously developed a new approach to express large panels of correctly folded, full-length proteins from the *Plasmodium falciparum* parasite, targeting proteins involved in the invasion of human red blood cells. In this study, Sanger Institute scientists collaborated with colleagues in Kenya to see which of them the children's immune systems had developed antibodies against.

"The use of these proteins by the Sanger Institute's Malaria Programme

is helping to zero in on and exploit the weakest point in the malaria parasite's life cycle," says Dr Julian Rayner, an author from the Sanger Institute. "Trials for vaccines in the past have focussed on one target at a time and have had limited success; with this approach, we can systematically test larger numbers of targets and identify targets that might work in combination."

The findings of this research add further weight to the theory that a successful blood-stage vaccine needs to target multiple antigens. The next step in this research will be to generate antibodies against all of the proteins in the library and test them in the laboratory in different combinations to see whether combinations that appear to protect individuals in the field are able to directly prevent parasite invasion. Such studies are now underway at the Sanger Institute. At KEMRI, Dr Faith Osier's team is working on validating these findings in other African countries.

"Each year, hundreds of thousands of people die from malaria; but hundreds of millions are infected, many of whom are protected from severe symptoms by their immune response," says Dr Kevin Marsh, Director of the KEMRI Wellcome Trust Research Programme at the Kenya Medical Research Institute. "Collaborating with our colleagues at the Sanger Institute helps to bring the latest technological advances to the field, which in this case has highlighted combinations of naturally occurring antibodies that could contribute to the design of new vaccines."

More information: *Science Translational Medicine*. DOI: 10.1126/scitranslmed.3008705

Provided by Wellcome Trust Sanger Institute