New candidate vaccine neutralizes all tested strains of malaria parasite

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A new candidate malaria vaccine with the potential to neutralise all strains of the most deadly species of malaria parasite has been developed by a team led by scientists at the University of Oxford. The results of this new vaccine independently confirm the utility of a key discovery reported last month from scientists at the Wellcome Trust Sanger Institute who had identified this target within the parasite as a potential 'Achilles' heel' that could hold significant promise for vaccine development.

According to the *World Malaria Report 2010*, malaria killed an estimated 781,000 people in 2009, mainly young children and pregnant women. It is caused by parasites that are injected into the bloodstream by infected mosquitoes. The most deadly form, *Plasmodium* falciparum, is responsible for nine out of ten deaths from malaria. Vaccinating against malaria is likely to be the most cost-effective way of protecting populations against disease; however, no licensed vaccine is currently available. Another vaccine is achieving promising but incomplete levels of protection in clinical trials in Africa; scientists believe a new and more effective vaccine will be required to eradicate the disease.

In early November, research published in the journal *Nature* showed that the *P. falciparum* parasite relies on a single receptor, known as 'basigin', on the surface of red blood cells to invade the cell. The parasite attaches a protein – the antigen RH5 – to the receptor, in a sense 'unlocking' the doorway for the parasite to enter the red blood cell. Once there, it grows and replicates, causing potentially life-threatening disease.

Today, in a paper published in the journal *Nature Communications*, a team of scientists from the Jenner Institute at the University of Oxford led by Dr Simon Draper, working with colleagues from the Wellcome Trust Sanger Institute and the Kenyan Medical Research Institute-Wellcome Trust Programme in Kilifi, Kenya, demonstrate that a vaccine they have developed induces an antibody response in animal models capable of neutralising all the tested strains of the *P. falciparum* parasite.

"Our initial finding, reported last month, was unexpected and completely changed the way in which we view how the malaria parasite invades red blood cells," says Dr Gavin Wright from the Wellcome Trust Sanger Institute, a co-author on both studies. "It revealed what we think is the parasite's Achilles' heel in the way it invades our cells and provided a target for potential new vaccines."

Dr Sandy Douglas, a Wellcome Trust Clinical Research Training Fellow from the University of Oxford and first author on the new study, adds: "We have created a vaccine that confirms the recent discovery relating to the biology of RH5, given it can generate an immune response in animal models capable of neutralising many – and potentially all – strains of the *P. falciparum* parasite, the deadliest species of malaria parasite. This is an important step towards developing a much-needed vaccine against one of the world's major killers."

The antigens of the malaria parasite are often genetically very diverse as they are forced to evolve to stay one step ahead of the immune system and avoid recognition by antibodies. However, the RH5 antigen appears to have little genetic diversity. The researchers believe that this is because even people who have been naturally and repeatedly exposed to malaria have low or undetectable levels of antibodies that target this particular antigen; these very low levels of antibody would be insufficient to kill the parasites, and hence would not exert a selective pressure for the antigen to evolve variability.

Professor Adrian Hill, a Wellcome Trust Senior Investigator at the University of Oxford, says: "Vaccines against malaria are notoriously difficult to develop because the parasites' antigens – the target of vaccines – tend to be genetically so diverse. The RH5 antigen doesn't show this diversity, making it a particularly good target for a vaccine to exploit. Our next step will be to begin safety tests of this vaccine. If these prove successful, we could see clinical trials in patients beginning within the next two to three years."

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