

Malaria vaccine trials begin using 'chimpanzee virus'

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Trials are underway, funded by the Wellcome Trust, for a new vaccine to combat the most deadly form of malaria. For the first time ever, researchers will use a virus found in chimpanzees to boost the efficacy of the vaccine. The trials will take place at the University of Oxford's Jenner Institute, led by its Director, Professor Adrian Hill.

Malaria, caused by Plasmodium parasites, is one of the world's deadliest killers, killing over a million people each year, mainly women and young children in Africa and SE Asia. The most deadly species, *P. falciparum*, is responsible for 80% of malaria infections and 90% of deaths. As yet, there is no vaccine against malaria. This is because, for much of their life-cycle, the parasites responsible for infection live inside cells, where they cannot be reached by antibodies.

"We urgently need a vaccine to help in the fight against this deadly killer," says Professor Hill, a Wellcome Trust Principal Research Fellow. "Malaria parasites are able to outwit our immune system by hiding out in the body's cells, however. Finding a way to generate enough immune cells and antibodies to identify and destroy the parasites will be the key to preventing infection."

The vaccine being developed and trialled by Professor Hill's team in collaboration with Okairòs uses the company's genetically-modified chimpanzee adenovirus to produce the malaria antigen and to stimulate a response to the vaccine in the body. Adenoviruses appear to be particularly potent for increasing the immune response to the malaria

vaccine. However, because human adenoviruses, which cause diseases including the common cold and gastroenteritis, are widespread, most people have developed some immunity towards them. Using a chimpanzee adenovirus ensures that a recipient is unlikely to have resistance to this component of the vaccine.

"Chimpanzees have their own set of adenoviruses which rarely infect humans, so we have not built up immunity to them," explains virologist Dr Sarah Gilbert at the Jenner Institute. "This is why we have chosen such a virus to form the backbone of the new vaccine."

Professor Hill's team is currently recruiting for more volunteers for the first trials, which are to assess the safety of the vaccine. Because the active component of the adenovirus is removed, however, there is no danger of transmission to the human of the original chimpanzee virus.

The trial will also be measuring the response of the immune system. The team hopes to generate a response from CD8+ T-cells (sometimes known as killer cells) that should kill the parasites when they enter the liver, where they multiply undetected. However, if the T-cells do not kill all of the parasites, any that escape from liver into the bloodstream will still be able to enter red blood cells and cause illness.

The group plans to test a second vaccine which would then target the parasites in the bloodstream and red blood cells.

"Our ultimate goal is a combination product which targets the parasite at both the liver stage and the blood stage," says Professor Hill. "Few people still think that you can get really strong protection from malaria based on a single component."

Over a dozen vaccines have now been made by scientists at the University of Oxford and taken into clinical trials, but this is the first

vaccine to have also been manufactured within a UK university, according to Professor Hill.

Source: Wellcome Trust

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