

First genetically-engineered malaria vaccine to enter human trials

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Professor Alan Cowman from the Walter and Eliza Hall Institute in Melbourne, Australia, has created the world's first genetically-modified strain of the malaria parasite that will be used as a live vaccine against the disease. The vaccine, developed in collaboration with researchers from the US, Japan and Canada, will be trialled in humans from early 2010. Credit: Walter and Eliza Hall Institute of Medical Research

Walter and Eliza Hall Institute scientists have created a weakened strain of the malaria parasite that will be used as a live vaccine against the disease. The vaccine, developed in collaboration with researchers from the US, Japan and Canada, will be trialled in humans from early next year.

Malaria kills more than one million people each year and destroys -

through premature death and disability - the equivalent of at least 35 million years of healthy, productive human life every year.

Professor Alan Cowman, head of the institute's Infection and Immunity division, said in developing the [vaccine](#) the research team had deleted two key genes in the *Plasmodium falciparum* parasite - which causes the form of [malaria](#) most deadly to humans. By removing the genes the [malaria parasite](#) is halted during its liver infection phase, preventing it from spreading to the blood stream where it can cause severe disease and death.

Their success in genetically modifying the parasite and thereby preventing its invasion of [red blood cells](#) is published in the current issue of the [Proceedings of the National Academy of Sciences](#) USA.

Professor Cowman said similar vaccines had been tested in mice and offered 100 per cent protection against malaria infection. He said it was hoped the vaccine would produce similar results in humans. "Although two genes have been deleted the parasite is still alive and able to stimulate the body's protective immune system to recognize and destroy incoming mosquito-transmitted deadly parasites," Professor Cowman said.

This approach to vaccine development - using a weakened form of the whole organism that causes a particular disease - has proven successful in eradicating smallpox and controlling diseases such as flu and polio.

Professor Cowman said the research team, which includes Dr Matthew O'Neill and Dr Alex Maier from the institute as well as scientists from the Seattle Biomedical Research Institute, the Walter Reed Army Institute for Research and the University of Maryland, had used knowledge from several decades ago - when scientists proved that irradiated malaria parasites provide protection against subsequent

malaria infection in animal models and humans - in developing the vaccine.

"Although vaccines are under development that use whole malaria parasites weakened by irradiation to protect against infection, their safety and effectiveness rely on a precise irradiation dose and trial results have been variable," Professor Cowman said. "We believe that our genetically attenuated parasite approach provides a safe and reproducible way of developing a whole organism malaria vaccine."

Professor Cowman said it was unlikely the weakened parasites used in the vaccine would regain their potency as the genes had been deleted from the genome and could not be recreated by the parasite. "In addition, the 'one-two punch' approach of deleting two essential genes make it extremely unlikely that the attenuated parasite vaccine could restore its capacity to multiply and lead to disease," he said.

The human trials of the vaccine will take place at the Walter Reed Army Institute of Research in Maryland, US. The genetically attenuated parasites to be used in the trial are being manufactured at the Walter and Eliza Hall Institute, which has the only facility worldwide capable of producing genetically-altered malaria parasites that comply with the good manufacturing practice guidelines required for human clinical trials.

Source: Walter and Eliza Hall Institute

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