# Potential new HIV drug may help patients not responding to treatment

March 31 2009

A potential treatment for HIV may one day help people who are not responding to Anti-Retroviral Therapy, suggests new research published tomorrow in The *Journal of Immunology*. Scientists looking at monkeys with the simian form of HIV were able to reduce the virus levels in the blood to undetectable levels, by treating the monkeys with a molecule called D-1mT alongside Anti-Retroviral Therapy (ART).

Simian Immunodeficiency Virus (SIV) is very similar to Human Immunodeficiency Virus (HIV) and it is used to study the condition in animal models. In both HIV and SIV, the level of virus in the blood, or 'viral load', is important because when the viral load is high, the disease progresses and it depletes the patient's immune system. This eventually leads to the onset of Acquired Immune Deficiency Syndrome (AIDS), where the patient cannot fight infections which would be innocuous in healthy individuals.

Currently, the 'gold standard' treatment for HIV is Highly Active Anti-Retroviral Therapy (HAART), a cocktail of drugs that reduces the viral load by stopping the virus from replicating. HAART can increase the life expectancy of an HIV-positive patient substantially if it works well. However, the treatment is not effective for around one in ten patients, partly because some develop resistance to the drugs used in HAART. The researchers, from Imperial College London, the National Cancer Institute, Bethesda, and Innsbruck Medical University, hope their study could ultimately lead to a new treatment that will help HAART to work more effectively in these people.

In the new study, researchers gave daily doses of a modified amino acid called D-1mT to 11 rhesus macaques infected with SIV. All of the macaques had been treated with ART for at least four months. Eight of the macaques had higher viral loads (reaching up to 100,000 copies of the virus per millilitre of blood), because they were not responding completely to the treatment. However, three had undetectable viral loads (fewer than 50 copies of the virus per millilitre of blood), because ART was working well.

The researchers took blood samples at six and 13 days. After six days, only three of the macaques had detectable SIV levels and after 13 days the virus could only be found in two of them, at very low levels (below 1,000 copies of the virus per millilitre of blood). The researchers repeated the research in eight macaques that were not being treated with ART but this time they found no change in viral load over 13 days.

Dr Adriano Boasso from Imperial College London said: "HIV can have a devastating effect on people's lives but with advances in Anti-Retroviral Therapy it is becoming a more chronic, manageable disease. Unfortunately, treatment does not work for everyone - some people develop resistance to the drugs and when that happens, we start to run out of options for treating them and delaying the onset of AIDS.

"Our early findings suggest that D-1mT could be used alongside antiretroviral therapy to stop the virus from replicating. The disease can only progress if the virus is replicating, so if we can slow replication down we can reduce the impact of the disease on the patient's life. We still need to figure out how D-1mT is working, then we can think about developing this as a potential treatment for HIV," added Dr Boasso.

The results of the new study surprised the researchers because D-1mT did not appear to work in the way they had expected. They had believed it might reactivate the immune system, because D-1mT is able to block

an enzyme called IDO, which HIV and SIV use to hold the immune system back. In healthy people, IDO prevents the immune system from attacking the body. HIV and SIV hijack the machinery that makes IDO and use it to stop the immune system from attacking them.

In the new study, the researchers could find no evidence that D-1mT reactivated the immune response against SIV, although they do not exclude this possibility. They are now keen to carry out further research to explore how D-1mT is working.

"The effect D-1mT seemed to have on viral load was really encouraging but it was a surprise to us - we didn't expect D-1mT to work only in macaques that were already being treated with ART. It seems that D-1mT synergises with ART and we would really like to find out how this works," said Dr Boasso.

In healthy people, the IDO enzyme controls allergic reactions and autoimmune diseases and it also stops the foetus from being rejected in pregnancy. As D-1mT blocks IDO, the researchers say that its effects may need to be tested in SIV-infected macaques over a longer time, to determine if taking the drug could increase the risk of these conditions.

D-1mT is currently in Phase I clinical trials to test its safety and potential efficacy as a treatment for cancer, which should indicate whether the drug is suitable for treating human patients. The researchers hope that if D-1mT proves safe in the initial trials for cancer and shows further promise for treating HIV, trials for using D-1mT as a treatment for HIV could begin as early as 5 years from now.

Source: Imperial College London (news : web)