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New Investigational HIV Therapeutic Vaccine Approach Helps Control SIV in Preclinical Studies

Silver Spring, Md. – Researchers have found that an investigational treatment combining a therapeutic vaccine and an immune stimulator improves virologic control and delays viral rebound following the discontinuation of antiretroviral therapy (ART) in non-human primates infected with SIV, the simian form of HIV.

The proof-of-concept study examined the combined effects of therapeutic vaccination with an adenovirus serotype 26 vector vaccine and an MVA vector vaccine (Ad26/MVA) and TLR-7 agonist stimulation in ART-suppressed, SIV-infected monkeys. Findings were published online today in *Nature*.

The study was a collaboration led by the Beth Israel Deaconess Medical Center (BIDMC) and the U.S. Military HIV Research Program (MHRP) of the Walter Reed Army Institute of Research (WRAIR), and includes scientists from Janssen Vaccines & Prevention B.V., one of the Janssen Pharmaceutical Companies of Johnson & Johnson, and Gilead Sciences, Inc.

All rhesus monkeys were started on suppressive ART seven days after infection with SIV. After 24 weeks, groups of animals then either received a placebo treatment, Ad26/MVA, TLR7 agonist or a combination intervention of Ad26/MVA and TLR-7. TLR7 agonist. At 72 weeks, ART was discontinued to test the ability of the investigational therapies to affect continued virological control.

“We found the combination of Ad26/MVA vaccination and TLR7 stimulation proved more effective than either component alone,” said Col. Nelson Michael, Director of MHRP, who helped design the preclinical study. “This was especially striking for viral load set-point, which impacts future disease.”

In the combination group, the mean viral load set-point was reduced by 100 fold in all animals. Researchers saw a 2.5-fold delay of viral rebound as compared with the other groups. TLR-7Stimulation of TLR7 alone did not impact viral load or rebound. The vaccine alone reduced viral load set-point by 10 fold and only marginally delayed rebound. Though all monkeys eventually experienced viral rebound following ART interruption, three of the monkeys in the combination intervention group showed effective virologic control to undetectable viral loads following ART discontinuation.

“Current antiretroviral drugs, although they’re lifesaving, do not cure HIV. They merely hold it in check. We are trying to develop strategies to achieve ART-free, long-term viral suppression,” said senior author Dan Barouch, MD, PhD, Director of the Center for Virology and Vaccine Research at BIDMC and Professor of Medicine at Harvard Medical School. “We reasoned that if we can activate the immune cells that might harbor the virus, then the vaccine-induced immune responses might perform better seeking them out and destroying them.”

A critical barrier to HIV cure is the viral reservoir that remains hidden and infects cells throughout the body, leading to viral rebound in the vast majority of HIV-infected individuals after they discontinue ART. According to Dr. Merlin Robb, Deputy Director for Clinical Research at MHRP, “the combination of Ad26/MVA vaccination and TLR7 stimulation resulted in decreased levels of viral DNA in both lymph nodes and peripheral blood. With further optimization this combination strategy may show promise to achieve a functional cure for HIV.”

Additionally, cellular immune breadth correlated inversely with set-point viral loads and correlated directly with time to viral rebound. According to Michael, “This gives us an immunologic correlate which can potentially be used to predict responses in humans, but this needs to be confirmed in human clinical studies.”

Ad26/MVA is a prime boost vaccine regimen. MHRP, in collaboration with Janssen, recently began evaluating this regimen as a therapeutic vaccine in HIV infected adults who initiated ART during acute HIV infection. That study is being conducted at the Thai Red Cross in Bangkok, and the protocol chair is Dr. Jintanat Ananworanich, MHRP’s Associate Director for Therapeutics.

The Ad26 vaccine was developed in partnership between the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), BIDMC and Janssen. MHRP developed the MVA vaccine in collaboration with the Laboratory of Viral Diseases at NIAID/NIH. The TLR7 agonist (GS-986) was developed by Gilead.

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