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## **Article Analysis: Ad5 Specific**

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Since its discovery in 1983, scientists and researchers have been working hard to neutralize the threat of HIV against humans . This advance has included many strategies. Researchers have tried counterattacking the virus while it still hibernates in monkeys, once it was concluded that is where HIV originated . Other strategies have included offsetting the virus after it becomes active in humans. Unfortunately, some of these vaccinations, such as the Ad5 vaccination, allowed the vaccine to progress further, as seen in human trials . Other vectors, such as CMV were used in order to correct Ad5, and to compare results.

Trials of Ad5, or the adenovirus 5-vectored HIV vaccine, were halted when efficacy of the drug not only ceased, but also threw some patients in a state of retrograde . The HIV vaccine recipients were seen to progress with the HIV infections more excessively than the control group that was not given the vaccination. No immunological basis for the outcome was given, nor was one found in later studies also involving the adenovirus 5. However, other studies did suggest that only specific T cells were susceptible to rapid progression of the virus. The primary study used phenotypes of human CD4 T cells impacted by Ad5 and CMV, two different, mildly successful HIV vaccine options. They also tested on patients with HIV, using 24 who did not have HIV as a control. The study showed that CD4 T cells that are Ad5 specific, whether naturally induced or exposed by recombinant Ad5 HIV, are more susceptible to HIV while under the influence of Ad5 . The results were conclusive with a similar study performed involving rhesus monkeys . The

cells themselves are often lost to the infection in most HIV infected individuals after the vaccination is administered .

CD4 T cells that were CMV specific were found to be more malleable than those that were Ad5 specific. They were not lost within the infected victim, and did not experience the damage experienced by Ad5 specific T cells found in HIV infected victims . Upon further investigation, researchers found that CD4 T cells with Ad5 specificity show a pro-inflammatory Th17-like phenotype, much like the one displayed in rhesus monkeys diagnosed with SIV . HIV infected humans showing the Th-17 phenotype expressed a macrophage protein 3a, as well as a  $\alpha 4\beta 7$  integrin . This information suggested the gut mucosa could be used for homing potential, as it was envisioned in vaccines that would not appear until the year 2020 for conditions such as malaria, tuberculosis, and HIV .

Analysis of the vaccine continued with the study of cytokine expression. Flow cytometry showed partisan infection in IL-2 producing, as well as IL-17, which are Ad5 specific T cells by HIV . The concluding data of the study suggested a potential apparatus that would explain the excess HIV infection in vaccine recipients after they had received rAd5-HIV. Even Rhesus monkeys in other studies appeared to have an excess of the infection after being vaccinated using the rAd5-HIV compared to the control group, suggesting there was a biological trigger in the susceptible T cells that would put them more at risk than other monkeys and, therefore, other humans. Some studies suggested it was the combination of CD8 and Ad5 vaccinated CD4 specific T cells that acted as a mechanism within the monkeys.

Researchers postulated a similar reaction could take place within human

victims .

Unfortunately, it was unwise of tests to continue because the vaccine itself weakened subjects. The exposure to the vaccine ensured they were more susceptible to the virus and, therefore, more susceptible to experiencing its progression sooner. Despite the failure of Ad5, as well as rAd5-HIV vaccine, not likely HIV vaccines were observed in the process. The study claims that earlier experiments suggested using Ad5 on autologous T cells resulted in in vitro Ad5 CD4 T cells; the cells were susceptible to HIV infection based on the comparison with resting CD4 cells. Researchers were concerned that any cell introduced in vitro would then become susceptible and then infected with HIV, causing the virus to spread at an alarming rate. This would have effectively made Ad5 a conduit, rather than a vaccination. However, it was found that only Ad5 specific cells were susceptible. CMV specific cells were still found to be resistant, a result which was found to be similar in rhesus monkeys . Non-dividing CD4 T cells were also found to be more susceptible to HIV, and the spread of HIV, regardless of if they were specific to Ad5 or CMV. Continuation of the study would have yielded few results beyond the fact that dividing CD4 T cells were also susceptible to the spread of the virus. The paper's only true con was its admission of guilt: continuing the experiment meant the endangerment of lives. Several subjects experienced a rapid decline in health due to the Ad5-HIV vaccination because that is what it was proven to do. Several answers were gleaned for the medical community's future concerning the HIV vaccine. However, it might be considered unethical that the imminent death of these individuals was sped up, even if in the name of science. Perhaps it would be more ethical if

researchers began dedicating more time to discovering antibodies that can fight the virus, rather than a vaccine that can prevent it. Research suggests that antibody persistence and gene manipulation are the two most promising fronts in HIV vaccination for humans .

In sum, the vaccination Ad5 or rAd5 was a failure. Neither humans or rhesus monkeys profited directly from the vaccinations, and the study only served to help researchers better see the direction in which they should avoid going. It helped researchers better understand the human body's response to the HIV infection, but it did not help protect the human body against the infection itself. In fact, the vaccination only allowed the CD4 T cells to spread the virus more voraciously. Researchers are now aware they must insert specific CD4 T cells into vaccination experiments concerning HIV vaccinations in order to test their response, as well as the cell's susceptibility to the virus after the vaccination is administered.

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