Is an AIDS Vaccine Possible?

iavi INFOsheet

DEVELOPMENT OF AIDS VACCINES

Overview

There are a number of indications in humans and in animals that the immune system can protect against HIV, which in turn implies that an AIDS vaccine is possible.

The most striking fact is that almost everyone who becomes infected with HIV manages to control the virus for many years, without drugs, before developing AIDS. There are even some clearly documented cases of individuals who have been infected with HIV for 25 years or more and remain healthy. This suggests a precariously balanced battle between the virus and the immune system; unfortunately, in the vast majority of cases, the virus eventually wins.

If we can improve on this natural immunological response and tip the balance in favor of the immune system, we will have a vaccine that can control HIV infection even better. A preventive vaccine would ensure that the body is primed to fight HIV before the individual is exposed to the virus.

Evidence from humans

In the normal course of HIV infection, most people have robust and long-lasting immune control of the virus.

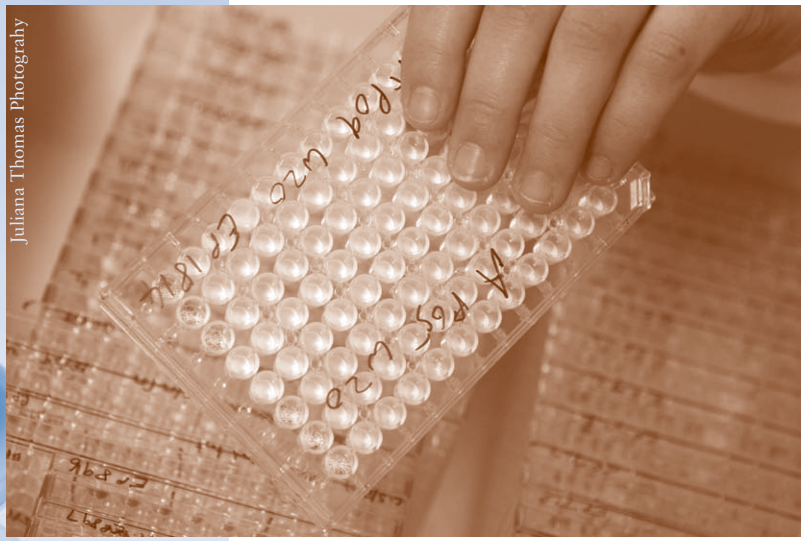
Most people's immune systems hold HIV in check for 8 to 10 years before they develop AIDS. UNAIDS recently estimated that, on average, people infected with HIV can survive without treatment for 11 years.

An outline of the clinical picture can help explain why. Initially, HIV-infected individuals have a high number of viruses circulating in their blood, but after about 5 to 6 weeks, the immune system deploys T cells against HIV that suppress the amount of virus. This new steady state is called the viral set-point. Antibodies against HIV are also generated early in infection, but these are not neutralizing (that is, they are not effective at neutralizing HIV). If we can develop a vaccine that strengthens the T cell responses and induces antibodies that are neutralizing, it should be effective against HIV.

Rare individuals can control their HIV infection indefinitely without recourse to antiretroviral therapy and apparently never develop AIDS.

At least some of these individuals, classified as either elite controllers or long-term non-progressors, control their HIV infection by means of their immune system. There are recorded cases of infected individuals who

AIDS vaccine researchers examine laboratory samples for evidence of an immune response.


Juliana Thomas Photograhy

have now successfully controlled their infection for 25 years and counting, without any symptoms of AIDS.

These individuals have long been studied in attempts to define the elusive "correlates of protection," which means the exact type of immune responses that protect people or other animals exposed to HIV from becoming HIV-infected, or if they become infected, from developing AIDS. T cells and antibodies are two types of immune response, but there are, for example, many types of T-cell responses, and there are other cell types that can assist in an immune response. If we can precisely work out the responses that protect the elite controllers, then the hope is that we can replicate those with a vaccine.

There are documented cases of individuals who have been repeatedly exposed to HIV but have not become infected.

These individuals, known as exposed seronegatives (or highly-exposed seronegatives), were first described among female sex workers in Nairobi, Kenya. These women remained free of HIV infection despite repeated exposure to HIV from infected sexual partners, suggesting they had a natural protective immunity to HIV. Some research has indicated that some of these exposed seronegatives have immune responses against HIV, implicating the immune system in their protection. Again, if we can define precisely how these individuals manage to be resistant to HIV infection, it might give us vital clues towards a vaccine.

Evidence from Non-Human Primates

Simian immunodeficiency virus (SIV) is in many respects the monkey equivalent of HIV. The best animal model we have of HIV infection in humans is SIV infection in rhesus macaques, a species of monkey.

Experimental vaccines can protect non-human primates from infection with immunodeficiency virus.

Many licensed vaccines use a crippled but live version of the targeted pathogen; these are called live-attenuated vaccines. A live-attenuated vaccine is not a viable option for an AIDS vaccine in humans because of concern that crippled HIV might revert to its disease-causing form. But live-attenuated SIV vaccines have proven effective in protecting rhesus macaques from infection with SIV. By studying the protection afforded by live-attenuated SIV vaccines in monkeys, researchers connected to IAVI's Live Attenuated SIV Consortium hope to learn what types of immune responses will be necessary to generate an effective HIV vaccine for humans.

Also, candidate vaccines that use viral vectors similar to those subsequently tested in humans have significantly lowered the amount of virus in the blood of and reduced disease severity in non-human primates, providing further evidence that it is possible to control immunodeficiency virus by priming the immune system with a vaccine.

Non-human primates injected with high doses of human antibodies against HIV are protected from infection.

A handful of human antibodies that

effectively neutralize HIV have been isolated from HIV-infected individuals over the years. When non-human primates are inoculated with large amounts of these neutralizing antibodies and then exposed to immunodeficiency virus (in this instance, SIV with some HIV genes), the non-human primates are completely protected from infection. This suggests that if a human vaccine is able to elicit neutralizing antibodies, it will protect from HIV infection. Researchers connected to IAVI's Neutralizing Antibody Consortium are studying these phenomena in an effort to construct a vaccine that elicits neutralizing antibodies.

Coda: The Power of Science

It is important to bear in mind that although devising a vaccine against HIV is a difficult challenge, history shows us that great obstacles can be overcome when the power of science is focused on a problem. For example, in 1983 when a virus was found to be the cause of AIDS, there were only a few licensed medicines for use against any virus, and scientists thought it implausible to develop any drugs against HIV. Today, we have more drugs to treat HIV than for all other viruses put together.

Conclusion

Taken together, the above suggests that control of HIV infection by the immune system can be improved and that a vaccine can be the means to that end if the right elements are put in the vaccine and they are delivered in the right way. Whether such protection can be turned into a practical, durable, safe, inexpensive vaccine can only be answered empirically through research.

Further reading

IAVI. "VAX Primer: Understanding Why an Effective AIDS Vaccine is Feasible."

Available at: http://www.iavireport.org/vax/primers/vaxprimer33.asp (accessed 2008).

AIDS vaccine researchers are working to develop preventive vaccines that would bolster a natural immunological response against HIV infection.

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About IAVI

IAVI's mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world. IAVI is a global not-for-profit, public-private partnership working to accelerate the development of a vaccine to prevent HIV infection and AIDS. Founded in 1996, IAVI researches and develops vaccine candidates, conducts policy analyses, and serves as an advocate for the field. IAVI supports a comprehensive approach to HIV/AIDS that balances the expansion and strengthening of existing HIV prevention and treatment programs with targeted investments in new AIDS prevention technologies. It also works to ensure a future vaccine will be accessible to all who need it.

IAVI is committed to promoting AIDS vaccine education worldwide, engaging communities in the trial process, and improving medical infrastructure in areas hardest hit by the epidemic. With five offices worldwide (New York, Amsterdam, New Delhi, Nairobi, and Johannesburg), IAVI collaborates with the public and private sectors in both industrialized and developing countries.

iavi International AIDS Vaccine Initiative

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