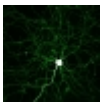
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Efforts to develop a vaccine against HIV in Puerto Rico [1]

Submitted by Manuel Delgado-Vélez [2] on 18 May 2016 - 6:32am

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A multisectorial effort in Puerto Rico is aiming to develop a vaccine against HIV. Learn about what Puerto Rican scientist have achieved and what they expect in the coming years.

Even before its discovery in the mid-80s, the human immunodeficiency virus (HIV) was already responsible for one of the most devastating pandemics in the history of humankind. Since then there have been significant advances, ranging from the approval by the FDA ("Food and Drug Administration") of the first antiretroviral drug, zidovudine (AZT) in 1987[1]; to the launch in 2015 by the World Health Organization (WHO) of the recommendation that all HIV-infected individuals should receive antiretroviral therapy immediately after being diagnosed.[2]

HIV is a retrovirus. That is, instead of using DNA as a template to replicate (transcribing it to RNA and later translating the code into proteins) like most viruses, HIV uses the mechanism of reverse transcription (RNA to DNA) to transmit its genetic information and replicate in the host cells, in this case, cells of the immune system.

Antiretroviral drug therapies were a breakthrough in the fight against HIV and still are of great value in the treatment of infected individuals. Nowadays, various combinations of antiretroviral drugs are used to increase the effectiveness of therapy. This pharmacological advance stabilizes the patient's' immune system to better fight the opportunistic infections that previously resulted in the death of many individuals. However, there's still more to be done.

Although in April 1984 the National Cancer Institute announced the development of a test to identify the virus and indicated that a vaccine would be developed over the next two years[3] this has not been possible to date. The closest attempt to a functional HIV vaccine was produced in a clinical trial called RV144 which was conducted in Thailand[4].

In this study, vaccination was effective for 31.2% of the individuals whose conduct represented a low to medium risk of contracting the virus. However, in individuals at high risk of acquiring the virus only 3.7% effectiveness was achieved.[4] Another aspect to note about this trial is that protection against HIV was of short duration.

There are significant challenges to developing an HIV vaccine. At the moment, there are three major obstacles to developing an effective vaccine, namely:

1. HIV destroys CD4+ T lymphocytes. These are a type of immune system cell that helps fight infection. For a vaccine to be effective, this cell type needs to be activated, which is a difficult task since these are the target of the virus and are destroyed by it. To make matters worse, those CD4+ cells that survive are already infected.

2. In an infected person, HIV mutates and recombines constantly creating new versions of the virus. Therefore, an effective vaccine must protect against a wide variety of versions of HIV.

3. Ideally, a functional vaccine should stimulate two types of immune responses: the first mediated by CD4 + T cells and another by antibody-producing B lymphocytes. Both types of cells are essential for eliminating the HIV infection. The former helps to identify the virus, and the latter contributes to destroying it. However, so far, scientists have failed to stimulate these two responses simultaneously. The vaccines that have been developed have only managed to stimulate weakly the response of T lymphocytes and promote a limited production of neutralizing antibodies by B lymphocytes.

Recently, a multisectoral effort to develop and manufacture a vaccine against HIV began at the Molecular Science and Research Center at the University of Puerto Rico[6]. This effort was possible thanks to the intervention of the Vice President of Science and Research at the University of Puerto Rico, Dr. José A. Lasalde-Dominicci, who brought together academia (University of Puerto Rico), biotechnology industries (CDI Laboratories [3], Eli Lilly and Amgen), Federal government (National Institute of Health) and State government (Puerto Rico Science, Technology, and Research Trust [4]) to support the research and development needed for the manufacture of a vaccine against HIV.

In addition to the support received by different entities, this initiative took advantage of a select group of scientists from different academic and professional backgrounds, which enables analysis of a problem as complex as the development of an HIV vaccine from various perspectives. The project's staff has expertise in areas such as biophysics, biochemistry, molecular biology, neuroimmunology, and aseptic manufacturing, among others.

In Puerto Rico, several HIV vaccine candidates have been tested, but none has effectively immunized individuals. This new study is using a different strategy, taking advantage of a phenomenon that occurs in 10-25% of infected individuals[7,8]: the presence of broadly neutralizing antibodies (bNAbs) against HIV.

The bNAbs are antibodies secreted by the immune system of infected individuals which effectively recognize the virus and neutralize it causing a dramatic decrease in the number of viruses in the individual. Using these bNAbs as a platform, a section of the virus (antigen) [5] that is recognized by bNAbs was determined. This made possible the design of a vaccine candidate that, in theory, should be similar to the HIV-presenting antigen.

This strategy generates an immunogen [6] (structure capable of producing a protective immune response) identical to presenting the virus in its native form. In this way, the immune system can generate a protective response to the virus before being infected by it, so that if one day the virus infects the individual, the immune system will already know how to identify, fight, and destroy the virus.

The first phase of the project finished successfully, fulfilling the main objective of increasing the levels of expression of the immunogen. The successful technology transfer necessary for manufacturing reproducibly at laboratory scale a high-quality immunogen was also accomplished. Additionally, the establishment of the Clinical Bioreagent Center at the Molecular Science and Research Center for the characterization of immunogens creates the opportunity to characterize other molecules with potential therapeutic value.

The next phase of this project includes the development of analytical tests required by the FDA to assure the safety and efficacy of the treatment and the establishment of manufacturing processes at a larger scale.

The author is the Project Manager for the Clinical Bioreagent Center at the University of Puerto Rico's Molecular Science Research Center.

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