ONE STEP CLOSER to Eradicating HIV

by Lori Dajose

Caltech researchers have developed the first component of a possible HIV vaccine, a step that may mean the AIDS-causing virus could eventually be eradicated worldwide.

When exposed to an invading virus, the human immune system develops proteins called antibodies that become specialized to recognize and prevent infection by that particular virus. Generally, vaccines require a person to be injected with a piece of a virus, an amount insufficient to cause illness but enough to induce the body to create antibodies to the virus. Should a person later be exposed to that same virus again, the antibodies would recognize and fight it.

HIV, though, is particularly difficult to combat. HIV-1, the most common type of HIV, has thousands of variants that have been characterized, and each can mutate rapidly to evade antibodies. Because HIV mutates throughout the course of an infection, the viruses inside an infected person create a viral swarm of different HIV strains. When faced with a viral swarm, antibodies may successfully combat one or even several strains but ultimately fail to clear an infection. Although there are medications to manage the symptoms of HIV infection, an HIV vaccine would prevent infection in the first place.

The goal of any HIV vaccine or treatment is to prevent new infections by blocking the entry of the virus into the target cells. To do this, the human body makes antibodies that target the HIV envelope protein, the sole viral protein on the surface of HIV. Different strains of HIV all have similar envelope structures, and human antibodies are specialized to attack specific regions of the envelope. Antibodies that are effective against many different strains of HIV are called broadly neutralizing antibodies, or bNAbs, for their ability to quell a broad spectrum of HIV viruses.

In a study in collaboration with the Rockefeller University, Caltech scientists in the laboratory of Pamela Björkman, the David Baltimore Professor of Biology and Bioengineering, have developed the first component of a possible HIV vaccine.

Because antibody creation is a complex multistep process executed by the immune system, many vaccines must be administered in several doses known as boosts. The first step in an HIV vaccine must induce the immune system to create bNAb precursors, crucial younger versions of antibodies that will eventually mature into powerful bNAbs. An imprecise precursor will lead to an ineffective antibody.

The researchers aimed to develop an initial vaccine that would induce mice and nonhuman primates to produce bNAb precursors to target V3, a precise region on the HIV envelope. Certain features of V3 are found among a wide variety of HIV viruses, and thus it is a good target for robust bNAbs.

The team first engineered a piece of the HIV envelope to remove glycans, a sugar that HIV uses to shield vulnerable regions like V3 from antibodies. After exposing V3, the researchers then added glycans to other regions that are more variable between strains, covering them up in order to ensure that the test animals would produce antibodies specific to the V3 region. Then, the team placed approximately 70 of these identically engineered envelopes (that contain no viral genetic material) on a carrier particle and injected it into the animal models.

This engineered complex caused the animals to create the correct bNAb precursors specific to the V3 region on HIV. Furthermore, adding the engineered envelope to the carrier particle ensured a large response from the animals' immune systems. When exposed to an actual HIV virus, the precursor bNAbs developed by this initial inoculation were able to see past the virus's shielding glycans to target its vulnerable regions.

The team is now focused on the next step: a dose of the vaccine that would enable precursors to mature into bNAbs.

Read more about this research at
magazine.caltech.edu/post/eradicating-hiv