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B cell-based vaccine effectively targets HIV

By FERNANDO VICENTE on April 7, 2016

Since the start of the human immunodeficiency virus (HIV) epidemic in the late 20th century, nearly 78 million people have been infected and 39 million people have died of HIV, according to the World Health Organization.

Every year there are about three new FDA-approved HIV medicines released to the public on average, as reported by AIDSinfo, which is released by the United States Department of Health and Human Services (HHS). These medicines, also called antiretroviral therapies (ARTs), are usually given in combinations of three ARTs, since a single ART can not comprehensively target the HIV infection.
Recent HIV research looks at immunotherapy — the use of our own immune system to combat disease — as a viable treatment. In particular, researchers are looking for B cells to aid the fight against HIV.

The reason for using B cells lies in their memory activation ability. That is, once activated by an antigen, B cells proliferate to generate B cells that are specialized to combat a specific disease.

The receptors on the surface of B cells function as a key-lock duo with molecules called immunogens, or antigens that produce an immune response, that originate from specific diseases or foreign substances in the host body. Hence, in order to fight HIV via this treatment, it is important to find immunogens that can effectively activate a large population of HIV-specific B cells.

A large problem with a disease like HIV, however, is its tremendous variability — HIV can continuously change and mutate so that few B cells are able to recognize it.

Prior clinical data demonstrated that HIV-infected people possessed HIV-specific B cells capable of secreting broadly neutralizing antibody (bnAbs). The bnABS target

relatively conserved patterns on HIV molecules. This discovery has inspired scientists to look for an immunogen couple to these rare cells.

The Scripps Research Institute (TSRI), the International AIDS Vaccine Initiative (IAVI) and the La Jolla Institute for Allergy and Immunology came together to engineer such an HIV immunogen. Through the use of library screening, coupled with next-generation sequencing, they improved on their hypothetical immunogen (eOD-GT6) to create another immunogen with superior affinity and breath of bindin.g: eOD-GT8.

The evolved immunogen had a geometric mean affinity 2,100 times greater than that of its precursor. Its disassociation constant also improved, this time by a factor of 5,900. Moreover, eOD-GT8 activated more germline-reverted Abs than eOD-GT8, thereby increasing its utility in a complex organism with a diverse repertoire of B cells.

To further demonstrate the extent of its application in humans, the scientists measured the frequency of B cells corresponding to the eOD-GT8 of 15 donors. The results confirmed that at least 2,700 cognate B cells present in all potential vaccine recipients. Additionally, the scientists also presented data suggesting that 96 percent of humans posses the necessary alleles for optimal treatment with the vaccine.

While the lymph nodes, which function as storage space for immune system cells, were calculated to host only around 15 HIV-specific B cells, the team remained optimistic due to the ability of proteins to selectively interact with their targets.

“The challenge for vaccine developers is to determine if an immunogen can present a particular viral surface in a way that distinct B cells can be activated, proliferate and be useful,” study co-author Shane Crotty, professor at the La Jolla Institute, said in a press release. “Using a new technique, we were able to show — well in advance of clinical trials — that most humans actually have the right B cells that will bind to this vaccine candidate. It is remarkable that protein design can be so specific as to ‘find’ one in a million cells, demonstrating the feasibility of this new vaccine strategy.”

Due to these positive results, researchers are planning a Phase I clinical trial using the “eOD-GT8 60mer,” a nanoparticle version of the lab-created HIV vaccine protein, which is expected to begin late next year.

“In the clinical trial that we’re planning, the goal will be to immunize humans and look in their memory B cells to see if this vaccine-protein activated those targets and cause them to mature a little bit in the right direction,” William Schief, lead author and director of the Vaccine Design of the IAVI Neutralizing Antibody Center at TSRI, said in a press release.