The Bench and Beyond

SAN DIEGO BIOMEDICAL RESEARCH INSTITUTE

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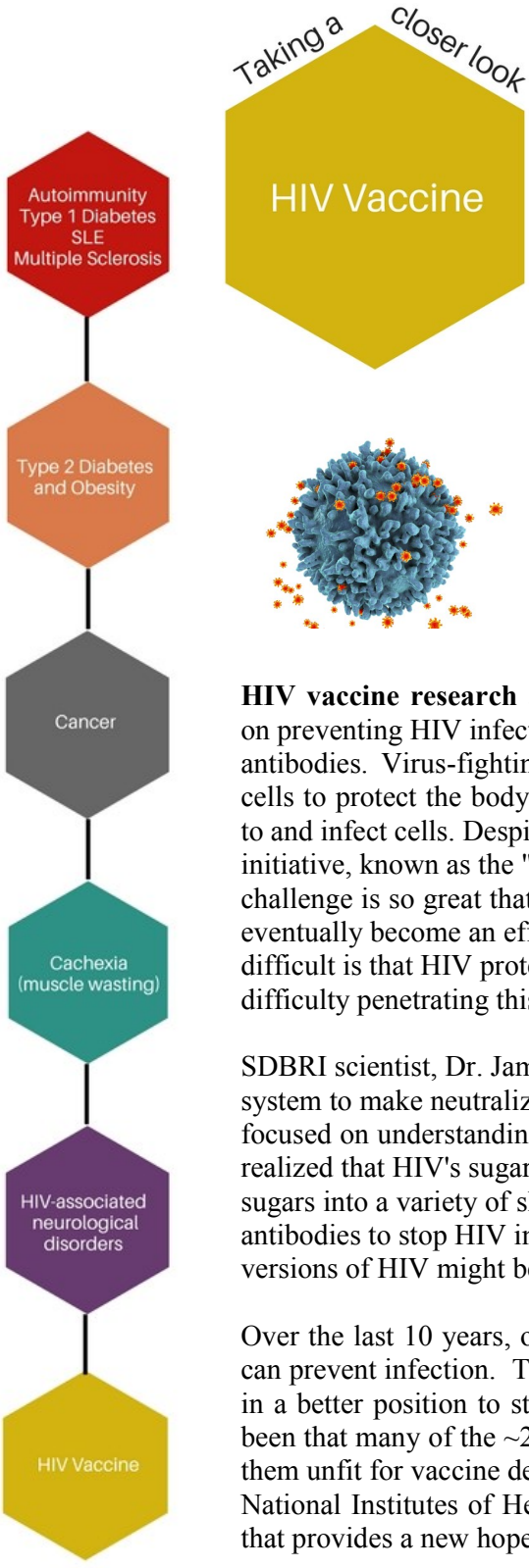
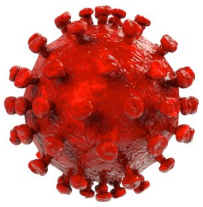


What is HIV and what is AIDS? HIV, or Human Immunodeficiency Virus, causes AIDS (Acquired Immune Deficiency Syndrome). When people are described as having HIV, it means that they are infected with the virus. Once inside the body, HIV attaches to and enters immune cells. Inside the cell, the virus inserts itself into the cell DNA and uses the cell machinery to replicate (make copies of itself). If the patient is left untreated, the virus kills the cells that they inhabit, releasing them to infect other immune cells. Over time, the immune cells are depleted and the immune system no longer functions properly. When this happens, patients with HIV become susceptible to "opportunistic" infections that healthy people can fight off - a hallmark of AIDS.

In the photo, the virus (orange) attaches to an immune cell called a CD4 T cell. Once attached, it moves into the cell (it infects the cell), copies itself, and kills the cell. If left untreated, the virus continues to kill other CD4 T cells until the immune system is so compromised that the patient has recurring opportunistic infections. This is AIDS.



HIV vaccine research at SDBRI Vaccine development at SDBRI is focused on preventing HIV infection by stimulating the production of proteins, called antibodies. Virus-fighting or "neutralizing" antibodies are made by immune cells to protect the body from infection by blocking the virus' ability to attach to and infect cells. Despite a huge 30 year long global HIV vaccine design initiative, known as the "Manhattan Project for AIDS", the scale of this challenge is so great that we are only now breaking real ground on what might eventually become an effective HIV vaccine. One of the reasons this challenge has been so difficult is that HIV proteins are protected by a "shield" of sugars - and antibodies have difficulty penetrating this shield.

SDBRI scientist, Dr. James Binley is working on a vaccine design to stimulate the immune system to make neutralizing antibodies that stop HIV from infecting cells. In one study, he is focused on understanding how HIV's surface sugars help it to avoid neutralizing antibodies. He realized that HIV's sugars can take on a variety of forms and recently was able to engineer these sugars into a variety of shapes and sizes. Some of these changes improved the ability of antibodies to stop HIV infection by 100-fold. This is exciting because these more vulnerable versions of HIV might be useful as vaccines.

Over the last 10 years, one mission has been to understand the myriad of ways that antibodies can prevent infection. The thinking is that if we are fully equipped with this knowledge, we are in a better position to stimulate similar antibodies with a vaccine. The problem until now has been that many of the ~200 antibodies discovered so far have highly unusual features that make them unfit for vaccine design. Dr. Binley and colleagues at the Vaccine Research Center at the National Institutes of Health recently discovered a new type of antibody with simpler features that provides a new hope for HIV vaccine development.

Frequently Asked Questions!

How many people are infected with HIV per year? The World Health Organization recently estimated that 36.7 million people live with HIV/AIDS worldwide with 1 million HIV-related deaths every year. New infections are estimated at an alarming 1.8 million worldwide. Despite the recent progress in creating new drugs to treat HIV infections, mostly in developed countries, these treatments are very costly, often have side effects and can also become ineffective with time as the virus finds ways around them. As a result, HIV/AIDS continues to be an enormous problem here in the US, where there are more than 39,000 newly infected people every year. According to a recent epidemiology report, the number of people living with HIV in San Diego is estimated to be over 15,000.

Why has it been so difficult to make an HIV vaccine? There is currently no vaccine that can prevent HIV infection. The main reasons for this are that the HIV virus has a number of characteristics that allow it to avoid the immune system, and it is extremely effective in changing the way it looks (mutating). As a result, it has been difficult to develop a vaccine that works against all the mutated forms of HIV. To put this point into perspective, HIV is much more variable than influenza for which a season vaccine is necessary. The challenge of vaccine development is therefore to find ways to target parts of the virus that do not change over time, just as researchers are trying to develop a pan-reactive flu vaccine. The ability of HIV to mutate allows it to stay one step ahead of the immune response, and the HIV vaccine field...although we are now making some headway.

How well does HIV therapy work? Except in very rare cases, people who are infected with HIV will be HIV positive for the rest of their lives, even if treated. The good news is that, if the virus fighting drugs (antiretroviral therapy, ART) are taken every day, the infection can be controlled, and some patients can live a near-normal life span. However, in many cases the side effects of ART can be debilitating and range from headaches, tiredness, and nausea to more serious long-term complications including cardiovascular disease, diabetes, HIV-associated neurological disorder (HART), and eventually, AIDS. Even if the HIV is controlled during clinical latency, people with HIV can infect others.

Will there ever be a successful HIV vaccine? A large HIV vaccine trial conducted over the past 10 years in Thailand showed some effectiveness, raising some hope. During that same time, lab research has yielded an enormous amount of new and exciting information and has resulted in a new generation of vaccine candidates, some of which are now in the preliminary stages of clinical testing. In contrast to 10 years ago, there is a great sense of excitement and belief that a vaccine may actually be possible in the reasonably near future, although much work remains to be done.

Next Issue:

Take a closer look at Breast Cancer

Location

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