Designer proteins—the new generation of HIV vaccines being put to the test

November 30 2017, by Penny Moore And Lynn Morris

Credit: SHVETS production from Pexels

South Africa has made tremendous advances in providing lifesaving antiretroviral therapy for HIV infected people. The country has the largest treatment programme in the world.

Despite this, the HIV epidemic continues to ravage key populations, especially young women. In 2016 there were more than 270,000 new infections in South Africa – a figure which has been fairly consistent in recent years.

This continued spread of the disease suggests that treatment will not ultimately end this epidemic. An HIV vaccine remains an urgent need.

Many HIV vaccines have already been tested, using approaches that have led to effective vaccines for other infectious diseases. A trial in Thailand in 2009 was the first HIV vaccine to show some protective effect. But the 31% protection it offered was too low to warrant a wider roll out.

Follow-up trials to try and confirm the results in the Thai trial are now underway, including a large scale study of 5 400 volunteers in South Africa.

While the world waits for the outcomes of these trials, researchers have turned to new strategies based on lessons learnt from studying the immune system of HIV-infected people. For example, researchers now know, in extraordinary detail, how the immune system of some HIV-infected people is able to make rare antibodies, called broadly neutralising antibodies.

When tested in the laboratory these antibodies are able to block various strains of HIV from across the world. These are precisely the types of antibodies that a vaccine should ideally elicit. And scientists are using their findings as a roadmap to develop the next generation of HIV vaccines.

Three new vaccine concepts, all based on cutting edge protein engineering, will shortly, or have already entered human trials and have the potential to revolutionise the HIV vaccine field.

Kickstarting the immune system

All humans have millions of B cells in their bodies that produce antibodies and protect them from an infection. But only a small number of these B cells have the potential to produce the broadly neutralising antibodies that fight the HIV virus.

In the first new concept, high-tech nanoprotein engineering has enabled scientists to develop a designer protein called eOD-GT8. The protein is specifically engineered to trigger these rare B cells, and turn them into the broadly neutralising antibodies.

In studies in mice, this "designer" protein was able to kickstart the process and set the immune system down the right pathway to fight the virus.

Over the next year eOD-GT8 will be tested in small-scale trials in humans to determine whether targeting these rare B cells is an effective way to generate the right kind of HIV antibodies.

Making a good mimic of HIV

A second challenge in HIV vaccine design has been to make a good mimic of the HIV proteins that broadly neutralising antibodies recognise.

This approach, of presenting the immune system with a close mimic of viral proteins, has been the basis of most vaccines, including the polio and hepatitis vaccines.

But the challenge with the HIV protein that is targeted by broadly neutralising antibodies is that it rapidly falls apart when it is produced in

a laboratory. As a result, it is not a good mimic. For the past 10 years, scientists have tried to come up with new ways of preserving the complex structure of this HIV protein.

Only recently, using an African virus isolated many years ago, vaccine researchers have finally learned how to biologically "glue" this envelope protein together using chemical bonds, resulting in a good mimic of the protein as it exists on the virus.

This stable protein, called BG505.SOSIP has shown promise in vaccine studies in monkeys, where we now see better antibodies than with previous proteins.

BG505.SOSIP will also soon be tested in small-scale trials in Africa and the US to see whether humans also recognise this protein, and make antibodies that would be able to block virus infection.

Training the immune system

The third new approach is based on how antibodies and HIV change over time in infected people. Research in South Africa and in the US has shown that antibodies become "broader" over many years, through an "arms race" between the virus and the immune system. As antibodies attempt to stop the virus, it mutates to escape and changes its coat.

Newly emerging antibodies learn to recognise the different coats the virus has tried. In doing so, some antibodies become experts at recognising every form of HIV. Eventually this leads to antibodies able to recognise viruses from across the world, the broadly neutralising antibodies that vaccines aim to elicit.

In a trial that started in August, scientists in the US are using this knowledge to vaccinate volunteers with four different coat proteins

representing viral changes, in the same order seen in an HIV infected person. The hope is that this will train the immune system to recognise many different viruses, so that in the event of a future virus exposure, these antibodies will provide broad protection against HIV infection.

Towards an AIDS-free future

The next two years will therefore be a critical phase for HIV vaccines. Not only will we learn whether more traditional approaches, such as the Thai vaccine, can be improved enough to roll out.

We will also learn whether these three entirely new concepts, the result of years of research by scientists across the world, can reshape the HIV prevention landscape and, hopefully, take us closer to ending the HIV pandemic.

This article was originally published on The Conversation. Read the original article.

Provided by The Conversation

Citation: Designer proteins—the new generation of HIV vaccines being put to the test (2017, November 30) retrieved 5 May 2024 from https://medicalxpress.com/news/2017-11-proteinsthe-hiv-vaccines.html