New type of tuberculosis vaccine developed

Danish scientists have developed a new vaccine against tuberculosis. The vaccine was created in an entirely new way and may potentially save millions of lives, say the researchers.

Tuberculosis annually kills some 1.4 million people, making it one of the world’s deadliest diseases.

This may be about to change now, as Danish researchers have developed a vaccine which they say hits the bacteria “where it hurts the most”.

The vaccine has so far only been tested on mice, where it has shown early promise:

“We have developed a vaccine that teaches the immune system to recognise essential proteins in the tuberculosis bacterium. The vaccine makes it much more difficult for the bacterium to escape the body’s natural defences,” says Niels Peter H. Knudsen, of the Department of Infectious Disease Immunology at the Danish State Serum Institute, who is the lead author of the new study.

“The tuberculosis bacterium is incredibly well adapted to infecting and living inside humans without our immune system being able to do anything about it. That’s also what makes it so difficult to vaccinate against. But we hope that our vaccine can be the solution which will ultimately save millions of lives.”

Tuberculosis is a great threat

Doctors currently vaccinate against tuberculosis using the so-called BCG vaccine, which provides protection against the most acute forms of tuberculosis.

This protective effect, however, only lasts up to between 10 and 15 years and revaccination has no effect.

This has created a great need for better vaccines, says co-author Peter Lawætz Andersen, a professor at the University of Copenhagen and the vice president of Vaccine R&D at the State Serum Institute.

“’There is currently a great need for new vaccines against tuberculosis,” he says.

“These vaccines should be based specifically on proteins that are present throughout the course of the disease. And the vaccines should be given in order to provide lifelong immunity against the disease. That’s what we have done in our new vaccine.”

Vaccine targets essential proteins

Since the proteins that are the targets of the new vaccine play a central part in the infection process of tuberculosis, the bacterium cannot just dispose of the proteins in an effort to evade the immune system.

In other words, new vaccine differs from conventional vaccines in that the researchers did not design it to attack the bacterium as a whole, like the BCG vaccine does.
Instead, the new vaccine only 'teaches' the immune system to recognise and respond to the essential parts of the bacterium, thus making it impossible for the bacterium to escape the effect of the vaccine.

At the same time, the new vaccine is not based on only a single protein, but many. That makes the vaccine more robust:

"We have seen some examples where researchers have based the development of new vaccines on just a single protein. The effect of this has been that the bacteria merely start producing less of the protein and thus evade the vaccine," says Andersen.

"This has meant that some otherwise promising vaccines have become discarded at a late stage in the clinical trials. It is therefore important that new vaccines are based on multiple targets in the bacteria."

**Vaccine with six proteins fused into one**

To find the ideal targets for the new vaccine, the researchers studied a group of pumps on the surface of the tuberculosis bacterium.

These pumps, known as ESX systems, transport proteins that are known to play a key role in the survival of the bacterium and its ability to infect people. Unfortunately, these proteins are so small and scarce that the immune system does not automatically include them in its defence against tuberculosis.

The BCG vaccine does not build up an immune response to these proteins; however, by collecting a total of six of these essential proteins, the Danish researchers have created a fusion protein, which the immune system can recognise and build its defence against tuberculosis around.

"By fusing the proteins into one, we have created a potent target which the immune system can recognise," says Knudsen.

"Once the immune system has met the fusion protein, it will recognise it later and attack the individual proteins in a tuberculosis infection."

**Success in mouse trials**

The new vaccine has already shown its potential in mouse trials.

When mice had the new fusion protein injected into their bloodstream, they were subsequently well protected against tuberculosis.

This indicated to the researchers that they were on the right track with their vaccine.

"We have taught the immune system to recognise the essential proteins in the ESX systems. This is an entirely new way of making vaccines," says Knudsen.

"Our next task consists of refining the vaccine so that it can provide the best possible protection against the disease. And then there are all the clinical trials, so we may have to wait 10 to 15 years before the vaccine hits the market, but this is a good first step."

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Fact box

Tuberculosis is an extremely deadly infectious disease, which often affects the lungs. Symptoms include chronic cough, breathing difficulty, fever and weight loss.

Only some ten percent of people who are infected with tuberculosis develop the disease. Around half of untreated tuberculosis patients die.

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Tuberculosis vaccine with high predicted population coverage and compatibility with modern diagnostics, PNAS, doi: 10.1073/pnas.1314973111

Kristian Sjøgren

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