

# TUBERCULOSIS

## the search for a solution

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Photos Milagro Castro

It may be as old as humankind itself but tuberculosis (TB) is still a major cause of death worldwide. Now, the Foundation Institute of Colombian Immunology (FIDIC), in association with the School of Medicine and Health Sciences of the Universidad del Rosario, is working on finding a vaccine against the bacterium behind this disease.

**T**uberculosis is one of the ten biggest causes of death on the planet. In 2016 alone, the World Health Organization (WHO) reported that more than 10.4m people caught the disease, of which 1.7m died. These are disheartening results for an illness that was believed some years back to have been eradicated from certain countries. But it has returned with unexpected virulence.

The disease is produced by a bacterium called *Mycobacterium tuberculosis*, which is transmitted easily through the air and can infect anyone, regardless of their location, age, or sex. "People can pick up this bacterium anywhere, while travelling by bus or visiting a hospital or a prison. In fact the WHO estimates that one third of the world population carries the bacillus that starts it," comments Marisol Ocampo, professor at the School of Medicine and Health Sciences of the Universidad del Rosario and coordinator of the Tuberculosis Group of the Foundation Institute of Colombian Immunology (FIDIC).

Occasionally, those who acquire the bacterium have strong enough immune systems to control and eliminate it naturally. But it is common for those infected to conserve it in a latent state, whereby the immune system keeps it 'at bay', sometimes even for decades. "In this case, the person is completely healthy and does not transmit the tuberculosis in any circum-





← “The Universidad del Rosario, working jointly with the Foundation Institute of Colombian Immunology, is engaged on a project to develop a synthetic vaccine against tuberculosis, one that will improve quality of life for millions,” says Marisol Ocampo, professor of the School of Medicine and Health Sciences and coordinator of the FIDIC Tuberculosis Group.

stances. However, when they get old or their defences are low, the bacteria attack and the illness develops. This also happens if the subject acquires an infection that compromises the immune system, such as Human Immunodeficiency Virus (HIV),” Ocampo points out.

There are also people who pick up the bacterium and immediately develop the disease. They will experience the symptoms, which include fever, shivering, an intense cough for more than three weeks, chest pains, and mucus with blood in it. Only those who develop the illness can transmit it if they do not receive the right medical attention; they just need to cough in order to expel millions of bacteria into their surroundings.

Treatment for tuberculosis is intensive and supervised. In general, patients must stay in some kind of hospital center and take a ‘cocktail’ of five or six drugs at certain hours of the day. This routine runs for six months. “Since patients begin to feel better after two or three weeks of treatment, they often abandon it. This leads to major problems, since the bacteria mutate and acquire resistance to the drugs, bringing the greater complications of trying to treat relapsed patients,” adds the professor.

Faced by these facts, the School of Medicine and Health Sciences of the Universidad

del Rosario has joined forces with FIDIC to work on developing a synthetic vaccine against TB, one that might improve life for millions of people.

### A SYNTHETIC VACCINE

Traditionally, vaccines contain a complete pathogen of the disease they are designed to prevent, one that has been modified, through heat or radiation for example, to avoid causing infection and damage to the human organism.

In Colombia, the newborn are compulsorily given a BCG vaccine, one that aims at preventing several forms of TB. It contains *Mycobacterium bovis*, a bacterium originally from cattle but similar to that which produces the illness in humans. Nevertheless, according to the Colombian Ministry of Health and Social Protection, this vaccine has 50% effectiveness against pulmonary TB, and from 60 to 80% effectiveness against TB meningitis. On top of this, it only offers protection during the first ten years of life.

“We want a vaccine that does not use the entire pathogen, thus avoiding those parts that are not necessary and that can bring different responses to those expected. There are vaccines that employ the entire microorganism, and this sometimes ends up transmitting the illness it is aimed at preventing,” explains Ocampo.

This research project proposes the use of a model similar to that developed by the FIDIC team, led by Colombian scientist Manuel Elkin Patarroyo for a malaria vaccine. “The idea is to create vaccines in which we select the parts we wish to use, thus telling the person’s immune system to only attack pathogens that contain certain elements,” the professor continues.

Initially, the project will seek out the molecules on the surface of the microbacterium that help it to create infection. “We have to identify the ‘little hands’ that TB pathogens use to catch on to a cell it is going to infect. The immune system does not necessarily spot these ‘little hands’, and in fact, this is why people get ill; if it cannot see them, it cannot attack them,” she explains.

According to Ocampo, the genome offers around 4,000 different possibilities of proteins that may be involved, while smart bioinformatic tools can whittle this down to a quarter of that number. Then, each one of these proteins (chains of amino acids) is produced chemically in the laboratory in fragments of 20 amino acids. Each fragment is placed in front of the cell that might become infected, thus determining which ones latch on. A vaccine can then be designed to attack this pathogen.

Before this can be applied to humans, the likely fragments for the vaccine must be tested on animal models, as has been done with the malaria vaccine; but there is a snag, since this is not possible with TB. As it has a different form in animals, it must be tested directly on whoever has the bacteria, and this means a big challenge: those who have the bacterium in a latent state do not know they are infected, while those who have developed TB can easily infect others, not excluding the researchers themselves.

At this point in time, the FIDIC research at the Universidad del Rosario is at an initial stage, working out the first steps towards the development of a vaccine for an illness that is as old as the human being. ■

## TUBERCULOSIS - IN SEARCH OF A SOLUTION

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