

Researchers uncover why the body can't defend against tuberculosis

November 14 2011

Tuberculosis, which kills over 2 million people each year, is caused primarily by infectious bacteria known as *Mycobacterium tuberculosis* – or *Mtb*. *Mtb* targets human immune cells as part of its strategy to avoid detection, effectively neutralizing the body's immune response.

Up until now, scientists had a general understanding of the process, but researchers in the Immunity and Infection Research Centre at Vancouver Coastal Health Research Institute and the University of British Columbia have shown *Mtb* produces a specific protein that allows it to defuse and bypass the body's security system. The results are published today in *The Proceedings of the National Academy of Sciences*, and provide a pathway for improved treatments against this disease.

"TB has been able to completely mislead our immune systems, convincing our body it isn't there, which is why it is such an effective killer," says Dr. Yossef Av-Gay, research scientist with the Immunity and Infection Research Centre at the Vancouver Coastal Research Institute and professor in the Division of Infectious Disease at UBC Faculty of Medicine. "We discovered that the cells in charge of targeting and destroying invading bacteria are being fooled by a special protein that blocks the immune cells ability to recognize and destroy it."

Here is how it works. Macrophages are dedicated human immune cells with the role of identifying and defeating dangerous microorganisms. Normally, macrophages engulf bacteria, or other infectious agents, and contain them in an enclosed secluded environment. Then, special

components of the cell (cellular organelles) move to the controlled area and release acid enzymes that dissolve the bacteria. The system works beautifully against most infectious agents. However, as Dr. Av-Gay's team found, *Mtb* operates in a stealth manner, turning off this immune response.

In the case of *Mtb*, once the bacteria become engulfed by macrophages, they secrete a protein named PtpA that disables the two separate mechanisms required for making the acidic environment that normally targets them. The end result is that *Mtb* lives comfortably in the [immune cells](#), like a Trojan horse, hidden from the rest of the immune system. The [bacteria](#) then multiply inside the macrophage, and when released, they attack the body.

"We have been engaged in studying the interaction between the TB bacterium and the human macrophage over the past decade," says Dr. Av-Gay. "We are delighted with this discovery. Through learning about the tricks it uses, we now have new targets, so that we can develop better drugs against this devastating disease."

TB is the leading cause of death among infectious diseases in the world today and is responsible for one in four adult preventable deaths, according to the World Health Organization (WHO). Every 20 seconds TB kills someone, with approximately 4400 people dying every day. The WHO estimates that one-third of the world's population is infected.

Provided by University of British Columbia

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