

Lung lesions of TB variable, independent whether infection is active or latent

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The lung lesions in an individual infected with tuberculosis (TB) are surprisingly variable and independent of each other, despite whether the patient has clinically active or latent disease, according to a new animal study led by researchers at the University of Pittsburgh School of Medicine. The findings, published online today in *Nature Medicine*, could point the way to new vaccines to prevent the hard-to-treat infection.

More than 30 percent of the world's population is infected with *Mycobacterium tuberculosis*, the bacterium that causes TB, yet only 5 to 10 percent of those infected develop active, contagious disease with symptoms of coughing, chest pain, night sweats and weight loss. Most have asymptomatic, or "latent," infections that are not contagious, but could become active years later.

When the lungs become infected with M. [tuberculosis](#), the body's immune system walls off the [bacteria](#) into lesions called granulomas, explained co-senior investigator JoAnne Flynn, Ph.D., professor of microbiology and molecular genetics, Pitt School of Medicine.

"It's long been thought that the patient with a weakened immune system or some other immune vulnerability was more likely to develop active disease," Dr. Flynn said. "But to our surprise, our study showed that every infected individual has a collection of granulomas, some containing live bacteria and some that are sterile because the immune system has killed all the bacteria. So in this sense, there's no such thing

as a latent or active granuloma."

For the study, the research team infected monkeys with TB and then carefully tracked the granulomas that developed in the lungs. They determined that each granuloma starts with only one bacterium, and that bacterial replication continued for about four weeks before the body counters with an adaptive [immune response](#) to kill off the invaders.

"This response was sufficient to kill all the bacteria and sterilize some granulomas, but bacteria persisted in others and spread to create new granulomas," Dr. Flynn said. "You need only one granuloma to 'go bad' in order to get active TB."

Even when an animal had a severe, active infection, some of their granulomas were sterile, indicating the immune system was capable of killing bacteria, the researchers found.

"We don't know yet why the immune response produced different results in different lesions," Dr. Flynn said. "When we develop a deeper understanding of why the immune response produced different results in different lesions, we will be closer to harnessing the right mechanisms to develop effective vaccines to prevent TB."

More information: Sterilization of granulomas is common in active and latent tuberculosis despite within-host variability in bacterial killing, [DOI: 10.1038/nm.3412](https://doi.org/10.1038/nm.3412)

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