

New discovery brings customized tuberculosis therapies based on genotype closer to reality

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Are you genetically predisposed to tuberculosis? Scientists may now be able to answer this question and doctors may be able to adjust their therapeutic approach based on what they learn. That's because new research presented in the *Journal of Leukocyte Biology* suggests that two frequent mutations in an immune system gene called TLR1 are responsible for cellular changes that ultimately make us less likely to resist the disease.

"The study may help to characterize individuals with increased susceptibility to [tuberculosis](#), which might result in faster and more effective recognition and therapy of this disease," said Lothar Rink, Ph.D., a researcher involved in the work from the Institute of Immunology at RWTH Aachen University Hospital in Aachen, Germany. "We hope that our results have implications for understanding the [pathogenesis](#) of mycobacterial infections associated with TLR1."

To make this discovery, scientists tested 71 healthy individuals and found that about half lacked the toll like receptor 1 (TLR1) proteins necessary for the immune system to adequately recognize *Mycobacterium tuberculosis*. Using specific TLR1 agonists, researchers found that cells without TLR1 (TLR-negative) showed a decreased functionality when compared to cells with TLR1 (TLR-positive). Sequencing and [genotyping](#) of TLR1-positive and TLR1-negative cells from healthy individuals revealed that lack of TLR1 surface expression

accompanied by impaired function was strongly associated with increased susceptibility to tuberculosis. Further studies are needed to confirm that a TLR1-negative genotype accounts for hyporesponsiveness to mycobacterial infections or for tuberculosis vaccination.

"Antibiotics have been helpful in managing tuberculosis in the developed world," said John Wherry, Ph.D., Deputy Editor of the [Journal of Leukocyte Biology](#), "but unfortunately, these treatments are expensive, take a long time and are becoming less effective against drug-resistant strains. Understanding why some people are more likely than others to become infected should help prioritize who should receive drug treatment in the developing world and lead to strategies for universal vaccines or therapeutics."

According to the U.S. Centers for Disease Control and Prevention, tuberculosis one-third of the world's population are infected with TB, with more than 9 million people around the world becoming sick with tuberculosis each year. Nearly 2 million people die from tuberculosis each year worldwide. In the United States, there were 11,545 tuberculosis cases reported in 2009. The bacteria that cause tuberculosis usually attack the lungs, but they can attack any part of the body such as the kidney, spine, and brain. If not treated properly, tuberculosis can be fatal. The disease is spread through the air from one person to another. The bacteria that cause the disease are put into the air when a person with active tuberculosis of the lungs or throat coughs, sneezes, speaks, or sings. People nearby may breathe in these bacteria and become infected.

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