

Source of drug-tolerant tuberculosis possibly behind TB relapses, intensity of treatment

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University of Pittsburgh-led researchers discovered that the primary bacteria behind tuberculosis can grow on surfaces and that drug-tolerant strains flourish in these bacterial communities, the research team recently reported in *Molecular Microbiology*. The findings suggest a possible reason why human tuberculosis (TB) requires months of intensive antibiotic treatment and indicate a potential cause of the relapses that can nonetheless occur.

The researchers are the first to show that *Mycobacterium tuberculosis* can grow in surface-level bacteria clusters known as biofilms that are common in nature but never before shown for TB bacteria, explained the paper's senior author Graham Hatfull, chair and Eberly Family Professor of Biological Sciences in Pitt's School of Arts and Sciences. Hatfull collaborated and coauthored the paper with Professor William Jacobs Jr. of the Department of Microbiology and Immunology at the Albert Einstein College of Medicine in New York.

Hatfull, Jacobs, and their colleagues found that the biofilm bacteria are physiologically and genetically different from TB bacteria harvested in a lab—the type used in developing antibiotics. These variations result in a population of the bacteria that are "drug-tolerant and harbor persistent cells that survive high concentrations of anti-tuberculosis antibiotics," the team reports.

People with TB typically undergo six to nine months of treatment with multiple antibiotics and most of the bacteria generally die within the first

two weeks. Yet the disease can recur, presumably because of drug-tolerant bacteria that have escaped the antibiotic. The source and location of these persistent cells are unknown, but Hatfull and Jacobs' research reveals a possible biofilm origin, Jacobs said.

"The nature of persisting *M. tuberculosis* cells has been an enigma for the entire field," Jacobs said. "Clearly *M. tuberculosis* cells in biofilms represent at least one class of persistent cells, and we are testing their biological relevance."

It is not yet known whether the biofilm actually factors into human TB infections, Hatfull said. He added that the only similar research regarding biofilm in living creatures showed the presence of biofilm-like or biofilm-related bacteria in guinea pigs.

"While our data does not show conclusively that biofilm formation in people gives rise to a drug-tolerant population, the fact that biofilms do so in the lab makes this an interesting and testable hypothesis," Hatfull said.

Source: University of Pittsburgh

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