Researchers develop new TB test that will dramatically cut diagnosis time

March 19 2009

Researchers from the Albert Einstein College of Medicine and The University of Pittsburgh have developed an onsite method to quickly diagnose tuberculosis (TB) and expose the deadly drug-resistant strains that can mingle undetected with treatable TB strains. This study will be published in *PLoS ONE*, a peer-reviewed online journal from the Public Library of Science.

The researchers engineered bacteriophages, tiny viruses that attack bacteria, with a green fluorescence protein (GFP) implanted in their genome. Bacteriophages spread by injecting their DNA into bacterial cells. In this case, the GFP gene accompanies the DNA of the phage into the *Mycobacterium* tuberculosis cell, the bacterium that causes TB, causing the cell to glow. A clinician could detect the glow with equipment available at many clinics.

"The development of these reporter flurophages allows us to bypass the existing method of diagnosing TB, which requires cultivating slow-growing bacteria in a biosafety level 3 environment, a time-consuming and costly process," says William R. Jacobs, Jr., Ph.D., one of the authors of the study. "By infecting live M. tuberculosis cells with a flurophage, a quick and highly sensitive visual reading can be done. We are optimistic that we can move the diagnostic process from several weeks to several days or even hours, which could have a significant impact on treatment."

"A report from South Africa showed that the extensively drug-resistant

TB strains can kill within 16 days, on average," says Graham Hatfull, Ph.D., the lead author and close collaborator of Dr. Jacobs. "In rural Africa, it takes too long to collect samples, send them off, do the test, and have the data sent back. Clinicians need rapid, relatively cheap, and simple methods for detecting TB and drug-resistant strains in the local clinic. This test provides a quick diagnosis so the patient can be isolated and treated."

Besides quick diagnosis, the test also could be used to distinguish treatable TB strains from those that are drug resistant (DR-TB) and extensively drug resistant (XDR-TB), which normally takes months. Researchers treated M. tuberculosis with antibiotics at the same time the bacteriophages were introduced; the TB strains that were sensitive to antibiotics died, but the drug-resistant cells survived and continued to glow.

The study, "Fluoromycobacteriophages for Rapid, Specific, and Sensitive Antibiotic Susceptibility Testing of Mycobacterium tuberculosis," will appear in the March 19, 2009 edition of PLoS ONE.

The group's research was funded as part of a major new research initiative from Howard Hughes Medical Institute (HHMI). HHMI announced on March 19 that it will partner with University of KwaZulu-Natal in South Africa to establish an international research center focused on the TB and HIV coepidemics, called KwaZulu-Natal Research Institute for TB-HIV (K-RITH). Dr. Jacobs will direct research into developing rapid and effective TB tests, one of the new institute's primary objectives. His work with Hatfull and postdoctoral fellow Mariana Piuri on the flurophage study was related to that effort.

Source: Albert Einstein College of Medicine