Scientists establish proof-of-concept for host-directed tuberculosis therapy

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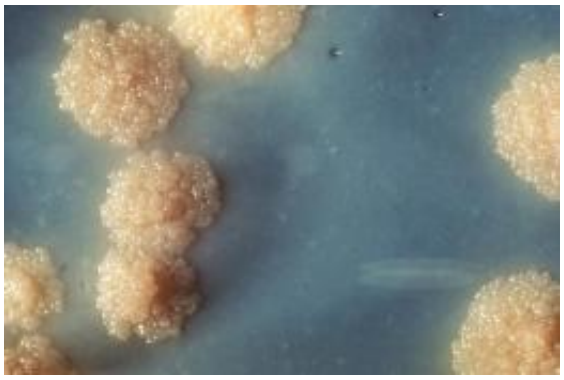

M. tuberculosis bacterial colonies. Credit: Centers for Disease Control and Prevention.

In a new study published in *Nature*, scientists describe a new type of tuberculosis (TB) treatment that involves manipulating the body's response to TB bacteria rather than targeting the bacteria themselves, a concept called host-directed therapy. TB remains a major cause of disability and death worldwide as an estimated 8.6 million people fell ill with TB and 1.3 million people died from the disease in 2012, according to the World Health Organization. Although TB is curable, adherence to therapy is difficult as treatment requires taking antibiotic drugs for at least six months and sometimes up to two years. Poor adherence to medication and other factors have resulted in drug-resistant strains, and currently no effective TB vaccine exists.

To address the need for alternative interventions, scientists from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, demonstrated proof-of-concept for a host-directed strategy to treat tuberculosis. They found that interleukin-1, a type of protein that regulates the body's immune response to infection, can help protect the body from TB infection. Their studies in cells and in mice and human patients infected with TB bacteria demonstrated that interleukin-1 induces a mediator, prostaglandin E2 (PGE2), that limits the production of type-I interferons, which are associated with increased TB disease severity.

The scientists found that host-directed immunotherapy using PGE2 and zileuton, a clinically-approved drug typically used to treat asthma, prevented death in TB-infected mice. This strategy could be of particular benefit to people infected with drug-resistant TB strains who have limited options for effective antibiotics because the treatment increased bacterial control and limited disease even in the absence of TB chemotherapy. In principle, this approach is compatible with standard antibiotic regimens, according to the authors. In future studies, NIAID scientists will test adjunct host-directed therapies in TB-infected individuals.

More information: KD Mayer-Barber et al. Host-directed therapy of tuberculosis based on interleukin-1 - type I interferon crosstalk. *Nature*. DOI: 10.1038/nature13489 (2014).

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