# Readily available antibiotic could help to curb lung damage from TB

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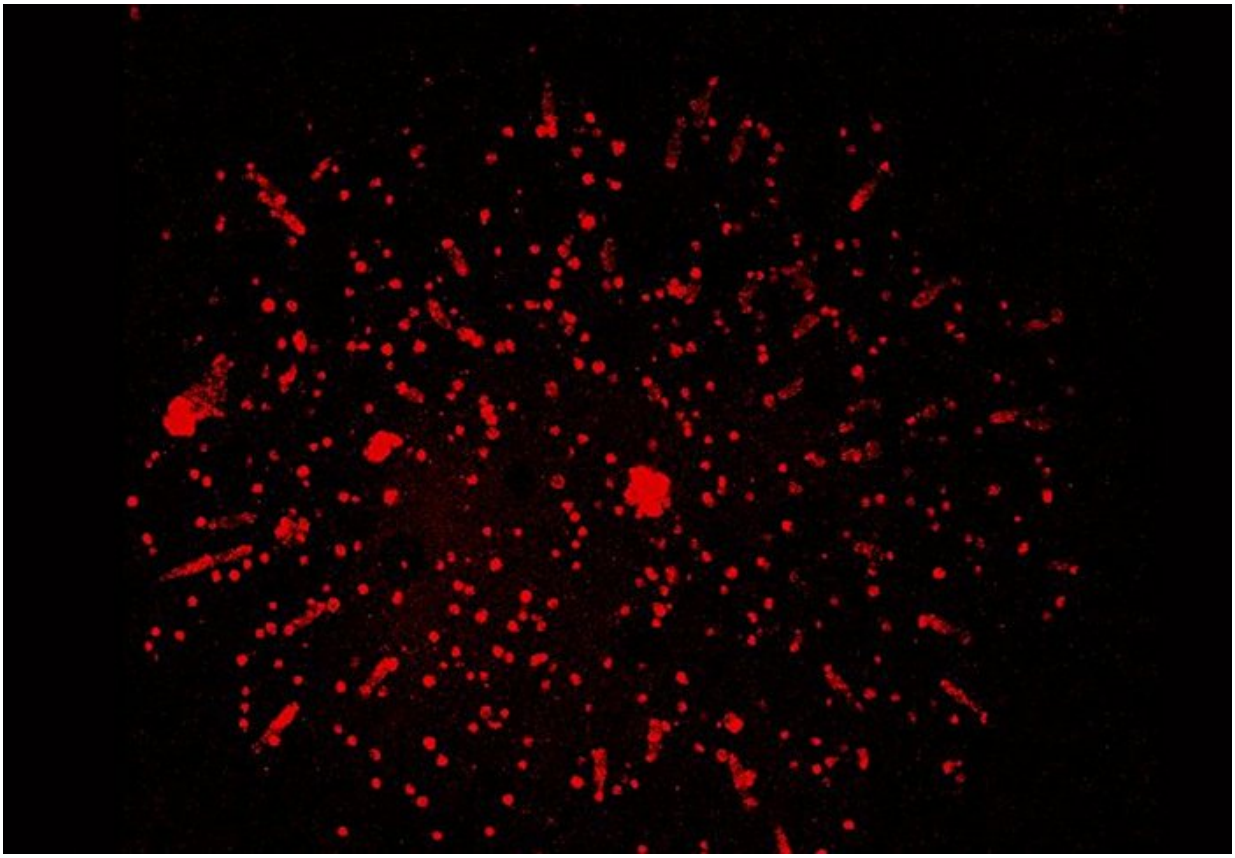

Fluorescent TB infection model mimicking human lung infection in the laboratory. Credit: Imperial College London

Imperial scientists have found how a common antibiotic could help reduce lung destruction in people with Tuberculosis (TB).

TB is a leading cause of mortality worldwide, causing 1.8 million deaths in 2015 and infecting one in three people globally, with or without symptoms.

Left untreated, the disease can cause massive tissue damage in the lungs, leading to a contagious cough and eventual death.

People with HIV, whose immune systems are suppressed, are at increased risk of infection, as are those with diabetes, poor nutrition, and alcoholism.

Although effective, current antibiotics for TB take at least six months to clear the infection. They can also interact with anti-retroviral drugs used to treat HIV, causing a condition known as TB-IRIS which over-activates the immune system, causing further lung damage.

Now, a group of researchers from Imperial College London, University of Cape Town, London School of Hygiene and Tropical Medicine (LSHTM) and University of Southampton, led by Dr Naomi Walker from LSHTM and Imperial's Department of Medicine, has found differences in immune responses between TB patients with and without HIV that could enable existing treatments to be used more effectively to treat TB.

They tested the phlegm, or sputum, of 210 patients in Cape Town, South Africa, for levels of enzymes called matrix metalloproteinases (MMPs), and found that the TB patients who were most infectious with worse lung damage tended to have the highest MMP levels, suggesting that MMP activity is linked to lung damage. HIV-infected TB patients, who tended to have milder lung damage and were less infectious, had lower MMP levels.

MMPs are known to digest collagen, a major structural protein in the

body which helps to keep lung's structure intact. However, a readily-available and relatively cheap antibiotic, called doxycycline, can inhibit the enzymes, which could help to reduce lung damage.

After creating a 3-D model of TB infection that mimicked human lung infection in the laboratory, the authors then investigated whether they could prevent lung destruction by reducing MMP activity using doxycycline. They found in the laboratory model that doxycycline did indeed reduce the level of destruction in TB infected lung tissue.

The authors say that this means the now-probable link between MMP activity and lung destruction could potentially be targeted by doxycycline in humans, and lead to more treatment options for treating TB in the future.

## Potential new treatments

Dr Walker said: "Our study paves the way for a clinical trial using doxycycline for TB. We have known for decades that, although TB patients with HIV do become very unwell, they don't tend to suffer lung destruction as often as TB patients without HIV. From researching the mechanisms behind this, we now have a new potential drug target and a widely available, relatively cheap drug with which to take this forward."

Dr Walker added: "Our findings may also help to diagnose those patients most at risk of lung damage for targeted treatment. However, although higher MMP levels and severe TB lung damage appear related at this stage, we have not proven that one causes the other. We also cannot say until it is tested on humans whether this will help to treat TB patients."

"We are at an exciting stage in our research where we can put our findings to the test and hopefully help to reduce TB's destructiveness in the future," she said.

**More information:** Naomi F. Walker et al. Matrix Degradation in Human Immunodeficiency Virus Type 1–Associated Tuberculosis and Tuberculosis Immune Reconstitution Inflammatory Syndrome: A Prospective Observational Study, *Clinical Infectious Diseases* (2017). DOI: 10.1093/cid/cix231