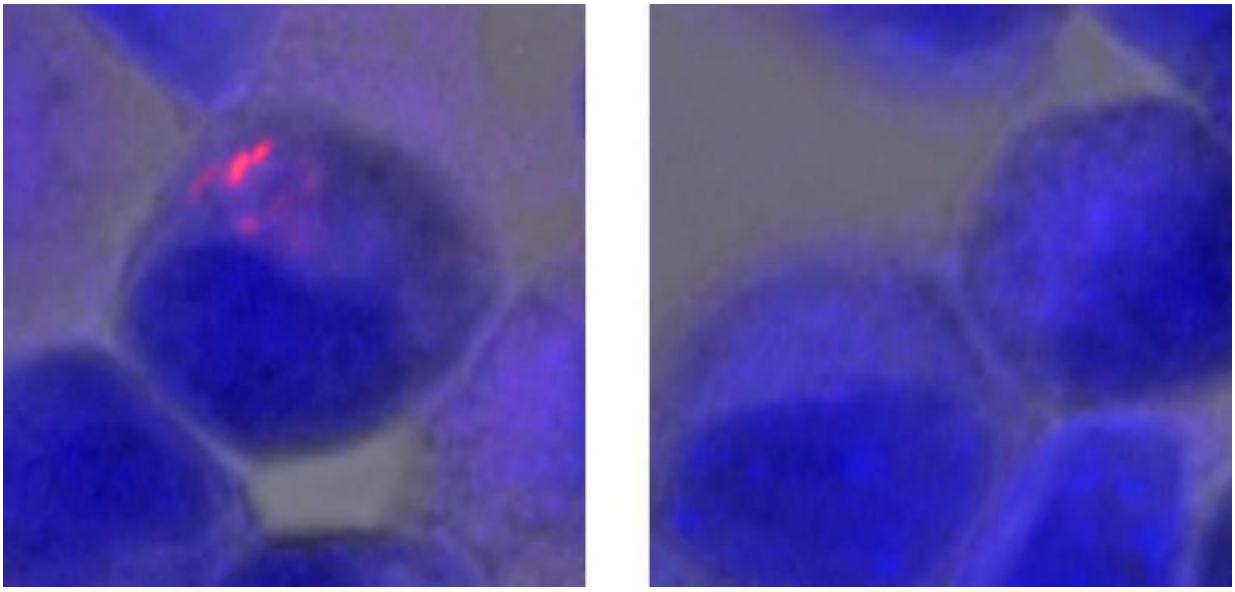
Powering off TB: New electron transport gene is a potential drug target

August 12 2015



Mycobacterium tuberculosis, shown in red, is known to propagate in macrophage cells (left), but loses that ability when MenJ is knocked out (right). Credit: American Chemical Society

The U.S. Food and Drug Administration recently approved the first new drug to fight tuberculosis (TB) in more than 40 years, but treatment still takes six months, 200 pills and leaves 40 percent of patients uncured. Thus, new targets are needed. Today in *ACS Central Science*, researchers report they have identified one such target—a gene that allows the disease to camp out in human immune cells, and is thus essential for the

organism's proliferation.

TB kills about 1.3 million people around the world every year. The microorganism that causes the disease, *Mycobacterium tuberculosis*, can hide from the immune system in the macrophage cells of the lungs and go undetected for years. Drugs that target *M. tuberculosis* generally target cell-wall and protein synthesis, like most antibiotics. However, since TB remains in a latent phase for many patients, and these treatments target growth processes, they are often ineffective at eliminating the bacteria. Other universal processes may provide better targets for rapid treatment of the disease. One such essential process is electron transport, which powers all life forms by shuttling electrons between key protein complexes. In bacteria, the only electron chauffeur is a molecule called menaquinone (MK) that has species-specific variations in its structure. Dean Crick and coworkers at Colorado State University set out to determine how MK might be involved in TB virulence.

First, the researchers compared genes in TB with those known to modify the electron shuttles for other organisms, leading them to a gene they called MenJ. This gene was shown to produce the specific form of MK unique to TB. To test MenJ's function, Crick and coworkers created a mutant strain of *M. tuberculosis* without the MenJ gene and found that while this deletion did not kill the bacteria outright, it lost its ability to infect human macrophage cells in less than four days. Crick says they have identified a novel virulence factor that could be ripe for drug development.

More information: *ACS Central Science*, pubs.acs.org/doi/full/10.1021/acscentsci.5b00212

Provided by American Chemical Society