Washington University in St. Louis
Office of Technology Management

TREATING TUBERCULOSIS WITH HOST-DIRECTED DRUG TARGETING

Chandra, Pallavi, Philips, Jennifer

Han, Nathan

T-017060

Background: Worldwide, there are over 10 million new cases of tuberculosis (TB) annually, resulting in 1.8 million deaths. This makes Mycobacterium tuberculosis (Mtb), the bacterium causing TB, the world's leading infectious disease killer. Even for drug susceptible TB, the treatment courses are long, complicated, and toxic. Multi-drug resistant (MDR) TB is increasing with over 500,000 cases reported globally in 2015, and extensively drug resistant (XDR) TB is already found in over 100 countries. Instead of targeting Mtb, scientists at Washington University in St. Louis have developed an approach in which the host cell is targeted. This approach aims to address the need for new effective TB therapies.

Technology Description: Mtb is phagocytosed by macrophages enabling its unchecked proliferation and thereby challenging TB treatment. The team headed by Dr. Philips has repurposed small molecule drugs that inhibit the growth of Mtb within macrophages by targeting a host process vital for the survival of Mtb. One of the drugs under investigation has shown to be highly effective at low concentrations in the prevention of colony forming units (CFU, see adjacent figure). The drug is approved for use in Europe and Australia, has a good safety profile, and outstanding pharmacokinetic properties. The drug concentration achieved in people exceeds the minimal inhibitory concentration of the compound against Mtb in macrophage by 40-fold. This approach opens up new treatment opportunities for MDR and XDR TB, and is prone to shorten the course of therapy for drug susceptible TB. Importantly, targeting the host circumvents development of drug resistance. Further studies that show efficacy in murine models are in progress.