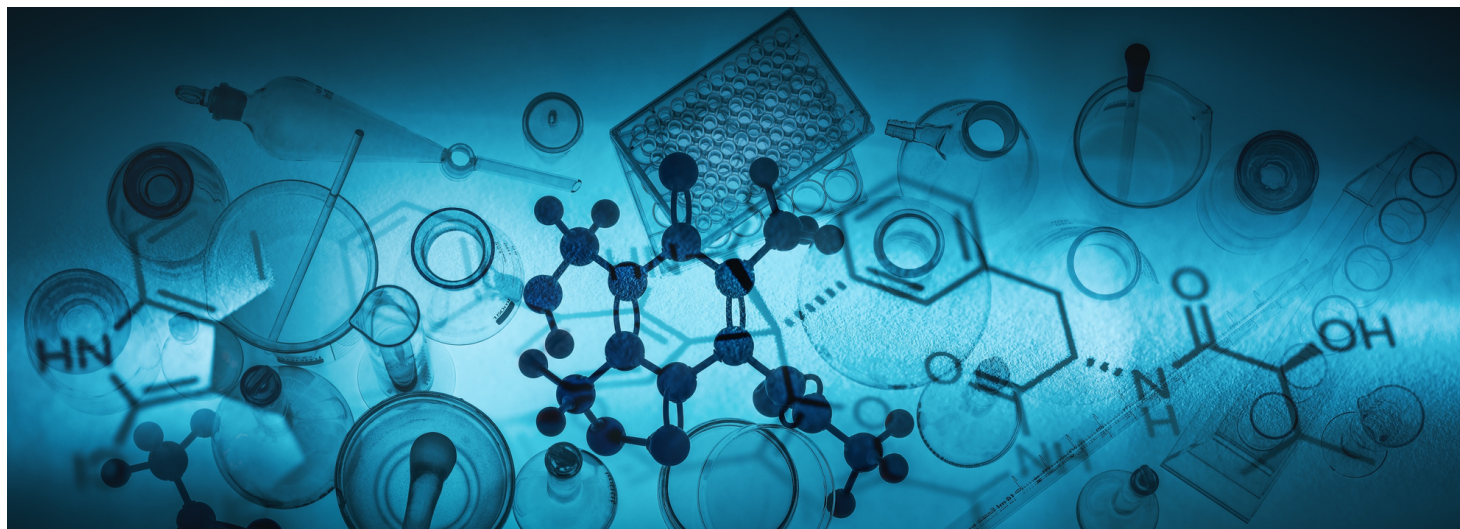


THE MONTHLY DOSE

Official Newsletter of The Mueller Health Foundation



WHAT'S NEW AT THE MUELLER HEALTH FOUNDATION:

At the Mueller Health Foundation, we remain committed to supporting innovative, person-centered approaches that extend beyond treatment completion and help improve long-term outcomes for people affected by tuberculosis.

As part of this effort, our partner REACH in India recently conducted a comprehensive post-treatment follow-up survey with 77 individuals who completed treatment for drug-resistant TB through our community-based program. The survey explores long-term health outcomes, persistent treatment-related side effects, functional status and daily limitations following treatment completion, as well as participants' experiences with the treatment and support services they received.

The findings will help identify opportunities to further strengthen person-centered care and improve our future program implementation. We are currently analyzing the results and look forward to sharing key insights and lessons learned in our next newsletter.

Stay tuned for more updates!

LATEST NEWS: SHOWCASING STORIES OF TB SURVIVORS

We at The Mueller Health Foundation remain deeply committed to sharing personal stories and giving a voice to TB patients, TB survivors, TB practitioners, and all the friends and family members affected by the disease. We are also proud to continue our support of our HeroRat Tamasha, who has been trained by APOPO, a charity focused on training rats to detect TB in sputum samples across Africa. APOPO has put together a wonderful collection of success stories, and this month, we would like to highlight Dr. Leah's story, who diagnoses and treats people for tuberculosis at a clinic in Dar es Salaam in Tanzania:

Dr. Leah Ndoveni serves as a physician at the DOTS clinic at Mbagala Rangi 3 Hospital in Dar es Salaam, Tanzania, one of APOPO's partner health facilities supporting tuberculosis diagnosis and treatment. Working in one of the country's highest TB-burden settings, she and her team care for approximately 100 patients each day. Patients provide sputum samples for both routine clinic testing and APOPO's second-line screening program, where trained HeroRATs help identify TB cases that may be missed by conventional smear microscopy. Over her decade of experience in the TB clinic, Dr. Leah has witnessed firsthand how APOPO's innovative detection program has enabled more patients to receive timely diagnoses and begin lifesaving treatment sooner. She has also observed that many patients delay seeking care because of limited awareness of TB symptoms, stigma, financial barriers, and reliance on traditional remedies before visiting a health facility. Dr. Leah emphasizes that partnerships between healthcare providers, APOPO, and community organizations are essential to improving case detection, supporting treatment adherence, reducing stigma, and preventing further transmission. She believes that expanding these collaborative, community-centered approaches will play a critical role in reducing the burden of tuberculosis and ensuring more people have access to the care they need. To read Dr. Leah's full story, please follow the link: <https://apopo.org/what-we-do/detecting-tuberculosis/success-stories/dr-leah/>

For more news, please also take a look at our top 3 picks for **July** in this newsletter, where we highlight novel research findings and news about the prevention and treatment of tuberculosis around the world.

MHF TOP PICKS FOR JULY

Every month, we at the Mueller Health Foundation like to showcase interesting news and updates in the field of tuberculosis (TB). Below are our top 3 picks for July:

1. Researchers Identify Mutation-Specific Vulnerabilities in Drug-Resistant TB

Researchers have identified previously unrecognized metabolic vulnerabilities associated with one of the most common mutations responsible for rifampicin resistance in *Mycobacterium tuberculosis*. The study found that the β S450L mutation in the *rpoB* gene not only prevents rifampicin from effectively binding to bacterial RNA polymerase but also alters the enzyme's transcriptional activity, disrupting key metabolic pathways. As a result, drug-resistant TB strains become increasingly dependent on pathways involved in the synthesis of branched-chain amino acids and vitamin B1 (thiamine). In laboratory experiments, these strains were significantly more susceptible to chlorflavonin, an experimental compound targeting the *IlvB1* enzyme, than other rifampicin-resistant strains. The findings demonstrate that resistance mutations can create distinct biological trade-offs that may be exploited therapeutically. Although this research remains in the preclinical stage, it provides important insight into the development of mutation-specific combination therapies that could improve treatment outcomes and help combat multidrug-resistant tuberculosis. To learn more, you can access the paper here: <https://www.nature.com/articles/s41564-026-02357-9>

2. AI-Powered Tool Accelerates the Search for New Tuberculosis Drugs

Researchers have developed two complementary technologies that could significantly accelerate the discovery of new drugs to treat tuberculosis. The first, called PAC-MAN (Peptidoglycan Accessibility Click-Mediated Assessment), rapidly screens thousands of chemical compounds to determine their ability to penetrate the protective outer membrane of *Mycobacterium tuberculosis*, a major barrier to effective drug development. The second, MycoPermeNet, is an artificial intelligence-based machine learning model trained on PAC-MAN data that predicts whether new compounds can cross the bacterial membrane based solely on their chemical structure. Together, these tools identified molecular characteristics associated with improved membrane permeability and demonstrated that compounds with these features were also more likely to exhibit anti-TB activity. Although further research is needed before new therapies emerge, these technologies have the potential to substantially streamline early-stage TB drug discovery by enabling researchers to identify promising drug candidates more efficiently. To learn more, you can access the paper here: <https://www.nature.com/articles/s41564-026-02412-5>

3. Study Identifies Genetic Mutation That Helped Tuberculosis Become a Global Pathogen

Researchers have identified a previously unknown genetic mutation that may have played a pivotal role in the evolution of *Mycobacterium tuberculosis* into one of the world's most successful human pathogens. The study found that the bacterium independently acquired mutations that disable a small gene called *Rv0080* across all major global TB lineages, suggesting this genetic change provided a strong evolutionary advantage. Laboratory experiments demonstrated that loss of *Rv0080* enhances bacterial survival under low-oxygen conditions by strengthening the bacterium's dormancy response, allowing it to persist within the body, evade the immune system, and reactivate months or even years after initial infection. These findings provide new insight into the evolutionary mechanisms underlying TB persistence and identify the dormancy pathway as a promising target for future drug development aimed at shortening treatment and preventing latent tuberculosis from progressing to active disease. You can read the paper here: <https://www.nature.com/articles/s41467-026-71566-x>

DID YOU KNOW?

When most people think of tuberculosis, they picture a disease that affects the lungs. While pulmonary TB is the most common form and the primary source of transmission, *Mycobacterium tuberculosis* can spread through the bloodstream or lymphatic system and infect almost any organ in the body. This form of the disease is known as extrapulmonary tuberculosis (EPTB). Some interesting facts about extrapulmonary TB include:

- Extrapulmonary TB accounts for approximately 15–20% of all TB cases worldwide, although it is much more common among people living with HIV and other individuals with weakened immune systems.
- The lymph nodes are the most frequently affected site of extrapulmonary TB, particularly those in the neck, resulting in painless swelling that may persist for weeks or months.
- TB can infect the bones and joints, especially the spine, causing a condition known as Pott disease, which can lead to chronic pain, spinal deformities, and, if left untreated, permanent neurological complications.
- Tuberculous meningitis, which affects the membranes surrounding the brain and spinal cord, is one of the most severe forms of TB. It is considered a medical emergency because delayed diagnosis and treatment can result in permanent disability or death.
- TB may also involve the kidneys, intestines, liver, pleura (lining around the lungs), heart, skin, and reproductive organs, producing symptoms that often resemble many other diseases.
- Unlike pulmonary TB, most forms of extrapulmonary TB are not contagious, as the bacteria are located outside the lungs and are generally not spread through coughing or sneezing.
- Diagnosing extrapulmonary TB can be particularly challenging because symptoms depend on the organ involved and may include swollen lymph nodes, back pain, abdominal pain, headaches, or urinary symptoms rather than the classic cough associated with pulmonary TB.
- Because bacteria are often present in very small numbers outside the lungs, diagnosis frequently requires specialized imaging, tissue biopsies, molecular testing, or culture in addition to routine laboratory evaluation.
- Prompt diagnosis and treatment are essential, as extrapulmonary TB can cause serious complications if left untreated. Fortunately, most cases respond well to standard anti-TB therapy when identified early.

Information Source:

WHO Global TB Report 2025: <https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2025>

Merck Manual: https://www.merckmanuals.com/professional/infectious-diseases/mycobacteria/extrapulmonary-tuberculosis-tb#Diagnosis_v11555591