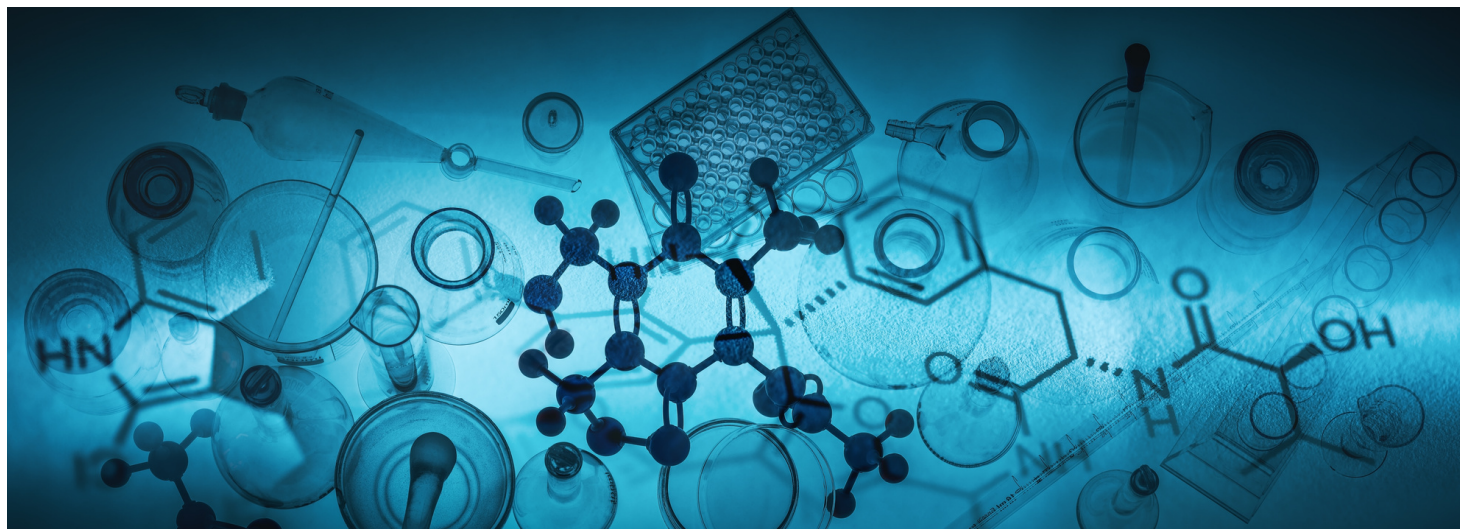


THE MONTHLY DOSE

Official Newsletter of The Mueller Health Foundation



WHAT'S NEW AT THE MUELLER HEALTH FOUNDATION:

We at the Mueller Health Foundation are excited to enter the fourth year of our collaboration with the David Russell Lab at Cornell University.

This partnership focuses on optimizing a novel platform for profiling anti-TB drugs and screening for synergistic drug/drug combinations. Additionally, we have conducted preliminary mouse infection studies exploring epigenetic modifiers in combination with frontline anti-TB compounds.

We are incredibly grateful for the team's outstanding work and look forward to another successful year of collaboration.

Stay tuned for more updates!

LATEST NEWS: SHOWCASING STORIES OF TB SURVIVORS

We at The Mueller Health Foundation continue to be deeply committed to sharing personal stories and giving a voice to TB patients, TB survivors, TB practitioners, and all the friends and family members of the people who have been affected by the disease. We are also proud to continue our support of our HeroRat Carolina 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 from TB survivors and this month we would like to highlight Naima's story:

Last year, Naima, a 10 year old girl living in Tanzania, began coughing and feeling tired all the time. Her mother thought the BCG vaccine Naima had as a baby would protect her. However, over the next few weeks, her cough worsened, and she lost weight. Her mother took her to their local clinic, where x-rays of her lungs indicated that she had TB. The clinic carried out a microscopy test using her sputum, but the results came back negative, so she could not start treatment. Naima continued coughing, could not eat properly, and began experiencing night sweats. She became very weak, and her mother grew increasingly worried. For three months, Naima remained sick and underwent two more TB tests, both of which were negative. Each time, she had to cough up sputum from her lungs, which was very difficult and painful. One day, the clinic called to inform her that an organization called APOPO had retested her sample, and it was positive for tuberculosis. APOPO uses giant rats to check samples that have already been tested by clinics like hers. The rats are so skilled at detecting TB that they often find cases missed by clinics. After the APOPO lab confirmed the results using advanced microscopy, Naima was soon put on treatment, and she now feels much better. She takes two pills a day and still experiences some stomach pain, but is improving. Her community has been very supportive, holding regular meetings where diseases like tuberculosis are openly discussed. This helps people who are worried to get support and know they are not alone. The key, Naima believes, is recognizing the symptoms and getting tested early, as tuberculosis is now a major topic of concern. To read her full story please follow the link here: <https://apopo.org/what-we-do/detecting-tuberculosis/success-stories/naima/>

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

MHF TOP PICKS FOR SEPTEMBER

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 **September**:

1. Pitt Study Suggests a New Vaccine Strategy for Tuberculosis: Focus on Anti-inflammatory Response

In using macaques, a new report from the University of Pittsburgh finds that the body's first line of defense against a primary tuberculosis infection or vaccination is driven by a broad epigenetic reprogramming of its innate immunity resulting in long-lasting protective responses against a subsequent *Mycobacterium tuberculosis* (Mtb) infection. This protective response is mostly CD4 T cell dependent which in this case trigger a variety immune cell responses that suppress lung inflammation instead of activating it. This is contrary to the immune system's typical, pro-inflammatory response to infection. Surprisingly, instead of observing that CD4 T lymphocytes secreted molecules that attract other infection-fighting cells to the sites of the Mtb invasion, CD4 cells instead contained the inflammation, making the infection site less hospitable to the bacteria. The team showed that this process is mediated in part by the effects of CD4 T cells on CD8 T cells— another subset of white blood immune cells whose main function is killing infected cells. They concluded that the interplay between CD4 and CD8 T cells creates an anti-inflammatory environment that is hostile to Mtb and, as a result, limits bacterial growth and disease severity. The expanded understanding of the role of CD4 T cells in preventing tuberculosis could provide new strategies for treatment and vaccine development. To learn more, you can access the full paper at: <https://www.sciencedirect.com/science/article/pii/S1074761324003753>

2. Drug Resistance and Genomic Variations among *Mycobacterium tuberculosis* Isolates from The Nile Delta in Egypt

Earlier reports suggested the emergence of high rates of drug resistant tuberculosis in Egypt. This study included 102 isolates of *Mycobacterium tuberculosis* collected from two reference laboratories in Cairo and Alexandria. Extracted genomic DNA was subjected to whole genome sequencing (WGS) using the Illumina platform. Isolates that belong to lineage 4 represented > 80%, while lineage 3 represented only 11% of the isolates. The percentage of drug resistance for the streptomycin, isoniazid, rifampicin and ethambutol were 31.0, 17.2, 19.5 and 20.7, respectively. Nearly 47.1% of the isolates were sensitive to the four anti-tuberculous drugs, while only one isolate was resistant to all four drugs. In addition, several new and known mutations were identified by WGS. Overall, high rates of drug resistance and new mutations were identified in the isolates and tuberculosis control measures should therefore focus on the spread of mono (S, I, R, E)- and double (S, E)-drug resistant strains present at higher rates throughout the whole Nile Delta in Egypt. To learn more, you can read about the research here: <https://www.nature.com/articles/s41598-024-70199-8>

3. Clinical Profiles and Related Factors in TB Patients with Positive Sputum Smear *Mycobacterium Tuberculosis* Tests

The aim of this study was to explore factors linked to the development and infectivity of tuberculosis by analyzing clinical data from 1612 recently hospitalized patients diagnosed with pulmonary tuberculosis in China. The study compared clinical characteristics between patients who tested positive on sputum Gene-Xpert tests and those who tested positive on sputum smear tests. In comparison to the GeneXpert positive group, the sputum smear positive group exhibited a higher proportion of elderly patients (aged 75–89) and individuals classified as underweight (BMI < 18.5 kg/m²). Furthermore, this group was more prone to experiencing symptoms such as weight loss, coughing and sputum production, hemoptysis, shortness of breath, and difficulty breathing. Moreover, this group is also more likely to develop extrapulmonary tuberculosis, such as tuberculous meningitis, tuberculous pleurisy, and tuberculous peritonitis. These clinical features, when present, not only increase the likelihood of a positive result in sputum smear tests but may also suggest a high infectivity of pulmonary tuberculosis. You can read the full paper here: <https://www.nature.com/articles/s41598-024-71403-5>

DID YOU KNOW?

The U.S. Agency for International Development (USAID) submits an annual report to Congress on the global status of tuberculosis (TB). Key facts from the 2023 report, include:

- 2023 saw the highest number of TB diagnoses and treatments since global monitoring began in 1995, following two years of COVID-19-related disruptions.
- Global case notifications rose to 7.5 million in 2022, a 16 percent increase from 2021 and a five percent increase from 2019.
- TB mortality decreased by seven percent in 2022 compared to 2021 and was two percent lower than in 2019.
- Despite advances in rapid molecular tests, only 63 percent of reported TB cases were bacteriologically confirmed in 2022, with 47 percent tested using WHO-recommended rapid molecular tests.
- TB variants cause one-third of all deaths due to antimicrobial resistance (AMR), and remain a global public health challenge in that they are more difficult and expensive to diagnose and treat. Of those with DR-TB, 175,650 people (43 percent) started on treatment in 2022, representing a 26 percent increase compared to 2021.
- TB disproportionately impacts impoverished populations, with individuals often paying over 20 percent of TB healthcare costs out-of-pocket. On average, households are losing 50 percent of their annual income due to the disease and its treatment, even when TB services are provided free-of-charge.

Information Source:
https://www.usaid.gov/sites/default/files/2024-01/USAID_TB_REPORT_2023_508_Final.pdf