**Research / Discovery**

# Researchers launch novel investigation into tuberculosis transmission and infection

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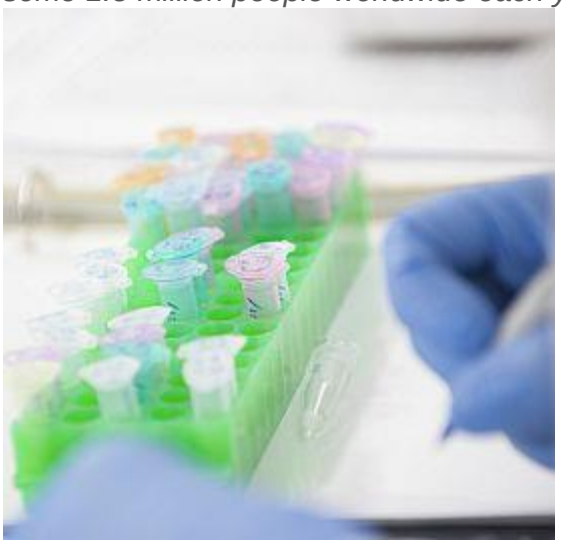
by Coleman Cornelius

*Researchers at Colorado State University are launching the most realistic study ever conducted into how transmission of the tuberculosis pathogen triggers infectious disease, an investigation expected to yield new insights into a disease that attacks the lungs and kills some 1.5 million people worldwide each year.*



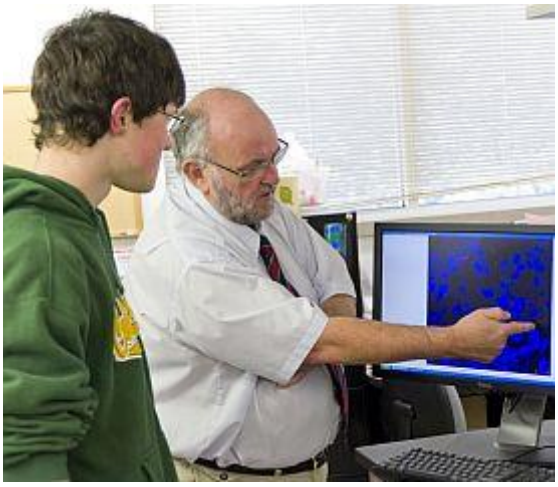
The Bill and Melinda Gates Foundation has supported the university's TB research with 10 grants totaling nearly $10 million in the past several years.

## Tuberculosis hot spot

The study is based at the Airborne Infection Research Facility, near Pretoria, South Africa, in one of the globe's tuberculosis hot spots. The investigation is starting as CSU hosts the first Front Range Mycobacteria Conference, focusing on tuberculosis and related infections, beginning June 18.

A grant of nearly $1 million from the Bill and Melinda Gates Foundation is funding the research, led by Diane Ordway, Randall Basaraba and Ian Orme, who are part of CSU's world-renownedMycobacteria Research Laboratories. The CSU team is working with colleague Edward Nardell at Harvard University.

In the next several weeks, infected patients coming to the Airborne Infection Research Facility for treatment will stay in a sealed tuberculosis ward. Air from the patient ward will be sucked through a specialized ventilation system and into an animal exposure room. Here, 360 guinea pigs – some vaccinated to protect against tuberculosis infection – will breathe air containing *Mycobacterium tuberculosis* from human patients.



University Distinguished Professor Ian Orme, right, is among CSU's standout tuberculosis researchers.

## Unique study

In this unique study setting, which replicates how the airborne tuberculosis pathogen is passed from person to person, it is certain that some of the guinea pigs will become infected, while others will have an immune response that effectively battles back. In examining outcomes at a genetic level, researchers will gain new understanding about exactly why some people become infected and develop disease, while others stave it off.

“Ethically, we would never expose people to*Mycobacterium tuberculosis* for a study, so this is the most realistic model for us to use as we try to establish novel vaccines and new therapeutic drugs for tuberculosis,” said Ordway, a faculty member in the CSU Department of Microbiology, Immunology and Pathology.

Two other study elements help mimic *M. tuberculosis* transmission in the real world: The guinea pig pulmonary system is similar to the human system, making the rodent an ideal model; and, like human infants throughout the developing world, some research animals have been inoculated with the only tuberculosis vaccine now available, called BCG, a vaccine whose protective properties inexplicably wane over time.

“This is the first study looking at human transmission of *Mycobacterium tuberculosis* to guinea pigs, and then looking at the immune response and at correlates of protective immunity,” Ordway said. “We are devising this study to further understand the genetic properties of the bacterium *M. tuberculosis* that enable it to transmit and cause disease in humans.”

Patrick Brennan, University Distinguished Professor and founder of the renowned CSU Mycobacteria Research Laboratories, helped mark World TB Day on campus in March.

## Developing effective vaccines

Those are the very insights needed to help develop effective vaccines and therapies for tuberculosis, a disease that has declined in the United States but remains an intractable health problem in the world's poorest countries, especially in sub-Saharan Africa. About one-third of the global population is infected with *M. tuberculosis,* and millions fall ill each year, according to the World Health Organization.

Worsening the epidemic is the alarming spread of multidrug-resistant tuberculosis, as well as the disproportionate impact of tuberculosis on people whose immune systems are weakened by HIV.

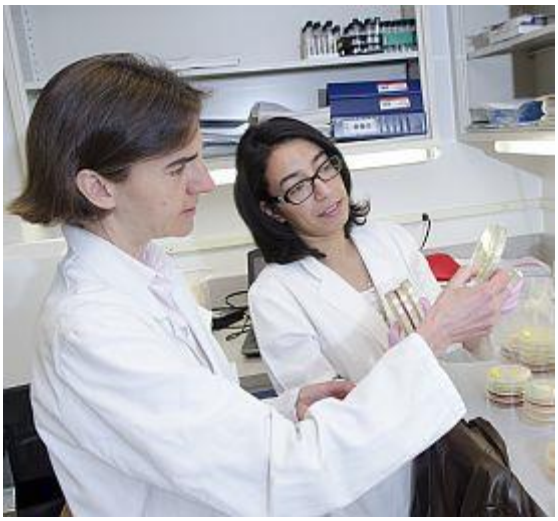
## Mycobacteria Conference

As the new Gates-funded study moves into full swing, the CSU Mycobacteria Research Laboratories hosted the first Front Range Mycobacteria Conference last week. The conference drew about 170 top mycobacteria scientists from nine countries for presentations and discussions.

These researchers are experts on the pathogens that cause tuberculosis, leprosy and nontuberculous mycobacterial infections. The visitors represented research institutions including the Harvard School of Public Health, Johns Hopkins University, the Global Alliance for TB Drug Discovery and National Jewish Health.

## World's foremost research

No surprise they came to Colorado State University, one of the world's foremost tuberculosis research universities, with a brain trust of about 170 experts in all aspects of the disease.



Mary Jackson, director of the CSU Mycobacteria Research Laboratories, studies the infamous waxy outer shell of the tuberculosis bacterium with colleagues in her lab.

“Colorado State University is proud to lead international scientific efforts to understand tuberculosis starting at the cellular level,” CSU President Tony Frank said. “Our tuberculosis expertise is a clear example of our mission to solve problems and help people both close to home and around the world.”

CSU tuberculosis research, housed in the Mycobacteria Research Laboratories, began in 1980 with arrival of University Distinguished Professor Patrick Brennan, who is transitioning into retirement. The program has grown along with Brennan’s own research into understanding the cell wall of *M. tuberculosis* and how it might be targeted with new drugs.

University Distinguished Professor Ian Orme is another standout who has helped boost CSU tuberculosis expertise. A partner on the new study based in South Africa, Orme researches how tuberculosis impacts immune response. His work focuses on developing drugs and vaccines, including a post-exposure tuberculosis vaccine.

The Front Range Mycobacteria Conference honored the work of these pioneering tuberculosis scientists.

“We celebrated many years of excellence at the Mycobacteria Research Laboratories, and we wanted to provide a platform to honor the insights and leadership of people who established the MRL,” Director Mary Jackson said. Her own studies seek discoveries to help pry open the drug-thwarting waxy shell of*M. tuberculosis*.

## Colorado's tie to tuberculosis

The state’s ties to tuberculosis date to the late 1800s, when droves of people afflicted with “consumption” arrived in Colorado for its therapeutic clean air, dry climate and sunshine. Colorado’s reputation as a tuberculosis mecca sparked a curious type of economic development: Sanatoriums sprang up across the state, as did businesses and tourist attractions – such as the Stanley Hotel in Estes Park – built by consumptives whose symptoms dramatically improved.

This connection has evolved with CSU's noted expertise in the science of tuberculosis and related infectious diseases.

CSU studies have attracted millions in funding from key sources, including the National Institutes of Health. During the past six years, the Bill and Melinda Gates Foundation alone has provided researchers with the CSU Mycobacteria Research Laboratories with 10 grants totaling nearly $10 million.

***More information about CSU tuberculosis research.***