Study sheds light on tuberculosis

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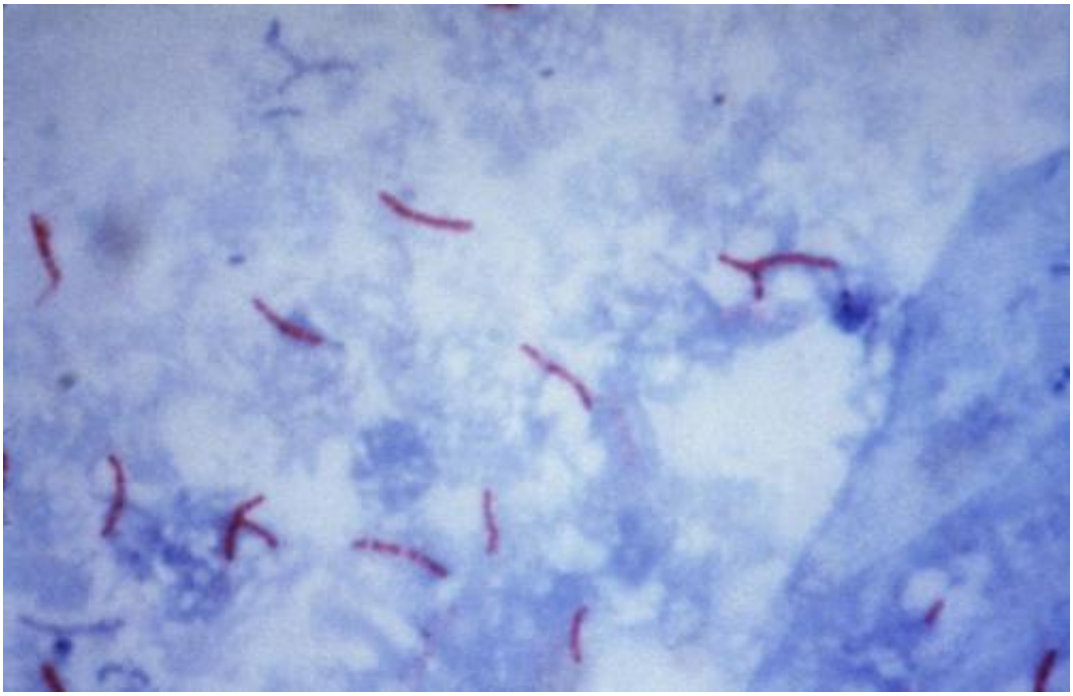

This photomicrograph reveals Mycobacterium tuberculosis bacteria using acid-fast Ziehl-Neelsen stain; Magnified 1000 X. The acid-fast stains depend on the ability of mycobacteria to retain dye when treated with mineral acid or an acid-alcohol solution such as the Ziehl-Neelsen, or the Kinyoun stains that are carbolfuchsin methods specific for M. tuberculosis. Credit: public domain

Each year the World Health Organization (WHO) recognizes World Health Day with the goal of spreading awareness for global health issues. The WHO names tuberculosis (TB) as one of the top 10 causes of death worldwide and over 95 percent of those deaths occur in low- and middle-income countries. To improve the global health community's

understanding of TB and provide information that could help treat it, Notre Dame researchers have developed a new strain of the bacteria along with a new method to better study this deadly disease.

TB is caused by the bacteria Mycobacterium tuberculosis, which grows within a body's cells. To explain more about how the bacteria causes TB, Matthew Champion, Research Associate Professor of Chemistry and Biochemistry in the Mass Spectrometry and Proteomics Facility in McCourtney Hall, said, "Mycobacteria, like all organisms, secrete proteins and these proteins are used for all life processes. Specific proteins secreted by the Mycobacteria enable it to cause disease, and EsxA – the one we studied – is one of these key proteins."

Despite the fact that the EsxA protein is crucial for the disease, the tools available to study it are limited. To overcome this obstacle, Matthew Champion and Patricia A. Champion, Associate Professor of Biological Sciences, together with their research team, have improved the analysis of the EsxA protein.

The study, which was funded by the National Institutes of Health, improved upon common mass spectrometry methods – analytical techniques that measure the mass of proteins. In doing so, the Notre Dame researchers developed a method that advanced proteomic analyses of the natural protein while retaining EsxA protein function. Before this development, the proteins were unsuitable when current analytical methods were applied, in turn holding back TB research. Therefore, this outcome helps scientists study the EsxA protein's functions more fully.

The ability to study the EsxA protein is an important step in being able to specifically target it, treat it, and potentially avoid the development of antibiotic-resistant treatments. To explain, Matthew Champion said, "Any time you create a medicine that kills bacteria, you're making a huge selective pressure change, driving the organism to attempt to evolve

so that it won't die, which leads to antibiotic-resistance. Instead, here at Notre Dame we are following the theory that if researchers can eliminate the bacteria's ability to cause disease – or in this case the EsxA protein – the organism will be less likely to feel any pressure to develop resistance."

The goal of the study was not only to improve proteomic detection, but also to build tools that can support the scientific community's effort to develop treatments that block the secretion of the EsxA protein. Any potential treatment that blocks this process could potentially mitigate a TB infection, and reduce the need for the bacterium to develop a resistance to antibiotics, which are currently used as a treatment.

This research is a collaboration with Cristal Reyna, a Biological Sciences Ph.D. candidate and Felix Mba Medie, a former post-doctoral fellow. Matthew Champion and Patricia Champion are also members of the Eck Institute for Global Health, which recognizes health as a fundamental human right and endeavors to promote research, training, and service to advance health standards for all people, especially people in low-and middle-income countries, who are disproportionately impacted by preventable diseases.

More information: Cristal Reyna et al. Rational engineering of a virulence gene from Mycobacterium tuberculosis facilitates proteomic analysis of a natural protein N-terminus, *Scientific Reports* (2016). DOI: 10.1038/srep33265

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