Medical Xpress

Study opens new avenue in quest to develop tuberculosis vaccine

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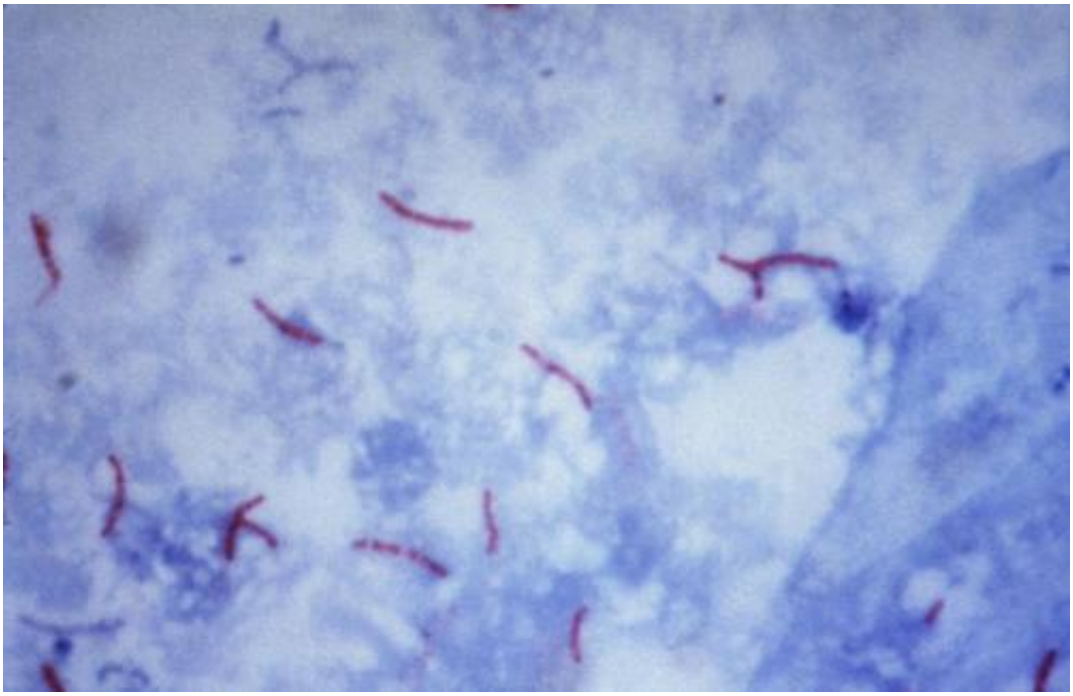

This photomicrograph reveals Mycobacterium tuberculosis bacteria using acid-fast Ziehl-Neelsen stain; Magnified 1000 X. The acid-fast stains depend on the ability of mycobacteria to retain dye when treated with mineral acid or an acid-alcohol solution such as the Ziehl-Neelsen, or the Kinyoun stains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

A team of scientists led by the University of Southampton has taken an important step forward in research efforts that could one day lead to an effective vaccine against the world's deadliest infectious disease.

Tuberculosis (TB) kills more people than any other infection, with an estimated 1.7 million people worldwide dying from it every year. The airborne disease is becoming increasingly resistant to antibiotics, but despite 20 years of intense global efforts no effective vaccine has been developed.

Recent efforts have focused on the response of conventional human T cells (a type of white blood cell essential to fighting off infection) to protein fragments found in Mycobacterium tuberculosis (Mtb), the bacteria that causes TB.

Now researchers from the universities of Southampton and Bangor, in partnership with Public Health England (PHE) Porton, have shown that certain lipids (fatty substances essential to cell structure that are found in abundance in Mtb) could trigger an immune response from other, 'unconventional', types of T cells.

In a new study published in the *Proceedings of the National Academy of Sciences*, the team showed that a group of lipids called mycolic acids - a major component of the Mtb cellular envelope - could be key to determining an immune response.

The study showed that the geometry, chemical make-up and movement of the mycolic acids' long lipid 'tails' when they are embedded in a type of human protein called CD1b determines the response of the body's unconventional T cells.

Lead author Dr Salah Mansour, of the University of Southampton, said: "This is an exciting discovery with potential therapeutic implications for TB patients. We have shown that synthetic lipids related to those in the cell wall of Mtb are selectively targeted by T-cells.

"Our findings could help drive advances in vaccine development through

the intelligent design of the lipid components of future TB vaccines."

The study combined cellular immunology with synthetic and computational chemistry, and used synthetic lipids developed at Bangor University's School of Chemistry.

Dr Juma'a Al Dulayymi, of Bangor University, added: "This is a very exciting result of a collaboration between organic chemists and immunologists which could provide a real opportunity for improved protection against TB."

The work is the fruit of a collaboration between a Southampton team consisting of immunologists, computational chemists and infection specialists, researchers from Bangor University led by Professor Mark Baird, and scientists from PHE Porton led by Dr Sally Sharpe.

More information: Andrew Chancellor et al. CD1b-restricted GEM T cell responses are modulated byMycobacterium tuberculosismycolic acid meromycolate chains, *Proceedings of the National Academy of Sciences* (2017). DOI: 10.1073/pnas.1708252114

Provided by University of Southampton