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UCT researchers contribute to key finding to help fight TB

A team at the University of Cape Town has led research to pinpoint the transporter of vitamin B_{12} in *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis (TB).

The finding represents an important contribution to understanding the ability of the TB bacterium to cause disease – in particular, the possibility that it has the capacity to scavenge vitamin B_{12} from its human host.

A team of scientists from the Molecular Mycobacteriology Research Unit at UCT's Institute for Infectious Disease and Molecular Medicine led the research that was published in *Open Biology*, a new journal of the Royal Society.

The paper follows work done on a four-year project by a multidisciplinary team from research institutions in South Africa, Switzerland, Lithuania and the US.

A collaboration between UCT and the Swiss Federal Institute of Technology in Lausanne formed the core of the work. It was funded by the Switzerland-South Africa Joint Research Programme as part of a bilateral agreement between the Swiss and South African governments.

The new information is also expected to shape thinking in related areas of microbiological research. It turns out that the system used by the TB bacterium is quite distinct from previously known bacterial B_{12} transporters.

Humans and plants do not make their own supplies of vitamin B_{12}. It comes from a diet or food chain that includes contaminating micro-organisms, in other words, bacteria that can manufacture the vitamin.

But not all bacteria make B_{12}. Surprisingly, the TB bacterium is among those which can, yet it also comes armed with the ability to take it up from its host, possibly indicating the importance of vitamin B_{12} to the lifestyle of this major human pathogen.

Plotting this pathway should have been easy for the scientists. However, the TB bacterium's transport mechanism is nothing like those found in common bacteria such as *Escherichia coli*, or *Salmonella*. Instead, it is genetically related to human B_{12} transporters.

The uptake of vitamin B_{12} in the TB bacterium has long puzzled researchers working to prise open its defences. The protein, designated Rv1819c, provides new possibilities for interventions.

The UCT team of Dr Digby Warner and postdoctoral research fellow Dr Krishnamoorthy Gopinath applied a combination of innovative genetic and

molecular tools to identify the protein that transports vitamin B_{12} in the TB bacterium.

The findings are significant. TB is remarkably efficient; it passes from one infected human to infect another, surviving and growing rapidly, primarily in the lungs. South Africa bears a huge burden of TB, with approximately 1% of the population affected by the disease.

"In South Africa, we are in the eye of the storm, as HIV provides fertile soil for TB and other opportunistic pathogens," said Warner.

The researchers said the fact that the TB bacterium is able to take up a huge molecule like B_{12} is a big surprise. It is renowned for its tough, almost impenetrable cell wall, which resists most molecules, frustrating those who work in drug development.

The results also present a theoretical possibility: that biochemists can design TB drugs as conjugate molecules, in other words, antibiotics piggybacking on the B_{12} molecule or a chemical Trojan Horse at it were.

"We don't know yet, but we're revealing new capacity of this organism that we're hoping will take us somewhere," said Gopinath.

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