Road mapping could be key to curing TB

February 5 2010

The complex chain of metabolic events in bacteria that lead to fatal diseases such as tuberculosis (TB) may be better understood using mathematical models, according to an article published in the February issue of *Microbiology Today*.

Scientists at the University of Surrey are using this new 'systems biology' approach to try and understand the metabolic changes that occur in the bacterium *Mycobacterium tuberculosis* which allow it to survive dormant in host cells for decades. A more complete knowledge of these changes could allow new drugs to be developed against such 'persistent' bacterial cells, which in turn would revolutionise TB control.

The classic approach to understanding biological functions in mammals and microbes alike has been based on the assumption that a single gene is primarily responsible for a single function - which can be inhibited by simply blocking the gene. This gene-centric approach has led to huge breakthroughs in scientific understanding of cellular processes, but is less useful for understanding complex functions such as metabolism. In this case, blocking a single gene does not impair function because other genes in the network are able to compensate to maintain that function. This suggests it may be more realistic to assume that many genes are likely to have minor roles in any number of functional pathways.

Professor Johnjoe McFadden who works on TB at the University of Surrey likens metabolic pathways in cells to Britain's road network. "For example, we may identify a particular road, say the A45, that takes goods from Birmingham to Coventry and call it the BtoC road - or BtoC

gene," he said. "Blocking the A45 might be expected to prevent goods from Birmingham reaching Coventry. But of course it doesn't because there are lots of other ways for the goods to get through. In truth, the 'road' (or gene) from BtoC isn't just the A45, but includes all those other routes."

A good starting point to study functional pathways is a mathematical model of the cell that takes into account the system properties of the whole network, rather than focussing on key control points. Professor McFadden explains how microbes are well suited to this systems-level approach. "Microbes have fewer genes to interact with each other making computational modelling simpler. Also, unlike multicellular organisms, microbes are able to precisely control their growth. This 'steady-state growth' is an important assumption that mathematical models are based on."

Provided by Society for General Microbiology