Energy-saving bacteria resist antibiotics

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Bacteria save energy by producing proteins that moonlight, having different roles at different times, which may also protect the microbes from being killed. The moonlighting activity of one enzyme from the tuberculosis bacterium makes it partially resistant to a family of broad-spectrum antibiotics, according to a paper published in the September issue of the journal *Microbiology*.

"Glutamate racemase, or MurI, is an enzyme that bacteria use to make the building blocks of cell walls," said Professor Valakunja Nagaraja from the Indian Institute of Science in Bangalore, India. "MurI from Mycobacterium tuberculosis also stops the enzyme DNA gyrase from working, which in turn stops DNA replication and cell division."

The researchers found that the two different functions work independently of one another – the enzyme's ability to make cell wall components does not affect its ability to inhibit DNA gyrase and vice versa.

DNA gyrase is involved in DNA replication, which happens when bacteria reproduce. A family of antibiotics called fluoroquinolones target this enzyme, killing the bacteria that cause infections such as cholera, anthrax, gonorrhoea, meningitis, E. coli and MRSA. The researchers found that when MurI binds to DNA gyrase, it takes gyrase away from substrate DNA. Because of this, antibiotics cannot bind and stop it from working, so the bacteria become resistant to treatment.

"Our findings suggest that MurI has a role in safeguarding DNA gyrase

from attack by antibiotics," said Professor Nagaraja. "The moonlighting activity of MurI seems to have evolved more recently to protect and control DNA gyrase."

MurI is not alone in its moonlighting activities; other bacterial enzymes and proteins also carry out different functions. But why has this ability evolved? "Multifunctional proteins are mostly common enzymes that have acquired different roles over the long period of their existence," said Professor Nagaraja. "As long as these additional roles do not interfere with the original function of the protein, they could benefit the cell by providing a competitive advantage during evolution."

By having multifunctional enzymes, a cell has fewer proteins to build, therefore less DNA to replicate. This means they save a great deal of energy in growth and reproduction. Moonlighting proteins can also control cellular activities, such as DNA replication in the case of MurI.

"An alarming increase in the emergence of multi-drug resistant strains of M. tuberculosis has led to an active search for novel drug targets," said Professor Nagaraja. "Our results may help us to discover molecules to target MurI, to prevent bacteria from making cell walls and develop a successful treatment for a wide range of bacterial infections."

Source: Society for General Microbiology