# New drugs from bugs

Scientists from the Universities of Bristol and Birmingham have discovered how marine bacteria join together two antibiotics they make independently to produce a potent chemical that can kill drug-resistant strains of the Methicillin-resistant Staphylococcus Aureus (MRSA) superbug.

Working with Japanese pharmaceutical company Daiichi-Sankyo, and funded by the UK Biotechnology and Biological Sciences Research Council (BBSRC), the researchers' work paves the way for the creation of new hybrid antibiotics that may help to solve the growing problem of bacterial infections that are resistant to essentially all antibiotics.

The research is published online in the journal PLoS ONE.

The team, comprising chemists from Bristol and microbial geneticists from Birmingham, determined the sequence of the complete DNA content of the marine bacterium that produces the new antibiotic, thiomarinol, owned by Daiichi-Sankyo. They then identified the genes responsible for making the antibiotic on the basis of their similarity to genes that make the related but less potent antibiotic, mupirocin, which is currently used to combat MRSA (methicillin resistant Staphylococcus aureus).

They found the genes are on a relatively small, separate DNA molecule called a plasmid, which is just big enough to carry the genes for making the antibiotic plus genes to allow the plasmid to replicate autonomously in the bacterium. The plasmid thus carries genes that make both the mupirocin-like antibiotic as well a second antibiotic, holomycin, and a gene responsible for joining both antibiotics together, forming a more potent molecule.

Tests showed that by joining the antibiotics together the resulting chemical is able to inhibit the growth of MRSA strains that have become resistant to mupirocin.

Professor Chris Thomas, lead researcher from the University of Birmingham, said: "This shows how mupirocin can be modified to make it more potent and suggests that related molecules could be used against the increasingly problematic

Enterobacteriacae like Escherichia coli and Klebsiella pneumoniae."

By using mutant strains that were unable to make either the mupirocin part or the holomycin part the team was able to feed alternative compounds to the bacteria - so-called mutasynthesis - so that a family of novel molecules was created, and tests showed some of these had biological activity.

Professor Tom Simpson from the University of Bristol's School of Chemistry, added: "This provides hope that the system will allow the production of new antibiotics that may help to combat the growing problem of antibiotic resistance in pathogenic bacteria."

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