Researchers find new chemical key that could unlock hundreds of new antibiotics

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(PhysOrg.com) -- Chemistry researchers at The University of Warwick and the John Innes Centre, have found a novel signalling molecule that could be a key that will open up hundreds of new antibiotics unlocking them from the DNA of the Streptomyces family of bacteria.

With bacterial resistance growing researchers are keen to uncover as many new antibiotics as possible. Some of the Streptomyces bacteria are already used industrially to produce current antibiotics and researchers have developed approaches to find and exploit new pathways for antibiotic production in the genome of the Streptomyces family. For many years it was thought that the relatively unstable butyrolactone compounds represented by "A-factor" were the only real signal for stimulating such pathways of possible antibiotic production but the Warwick and John Innes teams have now found a much more stable group of compounds that may have the potential to produce at least one new antibiotic compound from up to 50% of the 1000 or so known Streptomyces family of bacteria.

Colonies of bacteria such as Streptomyces naturally make antibiotics as a defence mechanism when those colonies are under stress and thus more susceptible to attack from other bacteria. The colonies need to produce a compound to spread a signal across the colony to start producing their natural antibiotic weapons.

The amounts of such signalling material produced are incredibly small. Only micrograms of these compounds can be isolated by Chemists and

usually the available instrumentation needs at least milligrams of material to make a useful analysis. However the Warwick team was able to make use of the University of Warwick's 700 MHz NMR machine to get a close look at just micrograms of 5 new possible signalling compounds identified as 2-alkyl-4-hydroxymethylfuran-3-carboxylic acids (or AHFCAs).

The researchers, led by Dr Christophe Corre, and Professor Greg Challis from the University of Warwick's Department of Chemistry were able to combine their new insight into these compounds with the relatively new full genetic sequences now available of some Streptomyces bacteria. They became convinced that the AHFCA group of compounds could play a role in stimulating the production of known and novel antibiotics. When they added AHFCAs to Streptomyces coelicolor W81 they were proved correct as it stimulated the production of methylenomycin antibiotics.

While the methylenomycins were already known as antibiotics, the researchers think it likely that novel pathways for antibiotic production are also under the control of AHFCAs. The AHFCAs should be relatively easy to make in significant quantity in a lab and could be used as a new tool for discovery of antibiotics. The researchers are now seeking funding to explore the AHFCAs and develop a novel approach for drug discovery. Introducing a variety of AHFCAs to various Streptomyces bacteria could activate hundreds of pathways for antibiotic production.

The lead researcher on the paper Dr Christophe Corre, from the University of Warwick's Department of Chemistry said:

"Early results also suggest that this approach could switch on novel antibiotic production pathways in up to 50% of Streptomyces bacteria. With thousands of known members of the Streptomyces family that

could mean that AHFCAs could unlock hundreds of new antibiotics to replenish our dwindling arsenal of effective antibiotic drugs."

Provided by University of Warwick