MedicalXpress

Key milestone towards the development of a new clinically useful antibiotic

July 12 2010

Scientists have identified the genes necessary for making a highly potent and clinically unexploited antibiotic in the fight against multi-resistant pathogens.

"Lantibiotics are antibiotic molecules produced by soil bacteria, and we are studying probably the most potent one known, microbisporicin, which is active against many different pathogens," said Professor Mervyn Bibb from the John Innes Centre, co-author on the paper to be published in *PNAS*.

"Our study has allowed us to understand how the antibiotic is made by a bacterium that was first isolated from Indonesian soil. Now we can engineer the bacterium to make similar but better molecules, and lots of them."

"For example, we can take rational approaches to improve its pharmacological properties, such as its stability in the blood stream and how it distributes into tissues."

The producing bacterium, Microbispora corallina, is difficult to work with. It grows very slowly and no tools existed for its genetic manipulation. PhD student Lucy Foulston developed the tools herself. She then took advantage of new developments in genome sequencing to identify and then isolate the M. corallina gene cluster responsible for microbisporicin production.

This allowed her to analyse how the bacterium makes the molecule and the functions of the genes involved. Notably, she was able to identify the genes responsible for giving microbisporicin some of its unique features.

The antibiotic molecule binds to a well established target in the pathogenic bacteria it kills, and as yet there are no signs of resistance towards it.

Microbisporicin is very effective at killing disease-causing bacteria, including *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant pathogens.

"This molecule is already in late preclinical-phase trials and in animal models has shown to be more effective than the current drugs of last resort, linezolid and vancomycin," said Professor Bibb.

"We believe that this study will make a major contribution to the future clinical development of this exciting antibiotic, and the derivatives that can be made using the knowledge and technology that we have developed."

Provided by Norwich BioScience Institutes