Major breakthrough could lead to new antibiotics for human use

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Gill tissue using bright-field microscopy. Photo © University of Bristol

(PhysOrg.com) -- The means to fully understand and exploit a type of fungus that could form the basis of a new class of antibiotics has been developed by researchers at the University of Bristol. With certain strains of bacteria becoming resistant to existing drugs, there is a growing need to find new sources of antibiotics.

The Bristol work focussed on the organism *Clitopilus passeckerianus* which produces a natural antibiotic called pleuromutilin.

In 2007, a derivative of pleuromutilin - called retapamulin - was approved for use in humans as a treatment for impetigo and infected wounds. However, despite its increasing importance, no molecular tools were available to fully understand and exploit this type of antibiotic - until now.

The group at the University of Bristol, led by Professor Gary Foster and Dr Andy Bailey, have developed all the necessary tools to transform, study, manipulate and enhance C. passeckerianus.

Professor Gary Foster said: “The emergence and spread of bacterial resistance to existing antibiotics is of major concern worldwide to animal and human health. Therefore, there is an urgent need to identify and exploit new classes of antibiotics, in order to circumvent the issue of bacterial resistance.

“The ability to transform and manipulate the host organisms that produce these new antibiotics, such as derivatives of pleuromutilin from Clitopilus, will be a vital tool for discovery and development of new antibiotic products.”

Professor Foster’s team successfully manipulated the genome of C. passeckerianus using two different techniques (Agrobacterium-mediated and PEG-mediated transformation).

Clitopilus fruiting bodies. Photo © University of Bristol

The researchers were able to switch-off individual genes, and target native and foreign promoter regions into the C. passeckerianus genome

to stimulate the production of fluorescent proteins which could be seen under the microscope.

These results demonstrate that the Bristol-based group is able to manipulate and control the C. passeckerianus genome. This provides a molecular toolbox which will make it possible to identify and manipulate individual genes of this fungus, and could lead to some major new drugs which are not compromised by antibiotic-resistant strains of bacteria.

The Bristol study, published online in *AEM (Applied and Environmental Microbiology)*, was carried out with financial support from GlaxoSmithKline (GSK).

The work builds on the success of the Basidio Molecular Toolkit developed through BBSRC funding that allows rapid transformation, gene analysis and manipulation within basidiomycete fungi such as Clitopilus passeckerianus.

More information: Establishing molecular tools for genetic manipulation of the pleuromutilin-producing fungus Clitopilus passeckeria by Sreedhar Kilaru, Catherine M. Collins, Amanda J. Hartley, Andy M. Bailey, and Gary D. Foster *Appl. Environ. Microbiol*. published ahead of print, doi:10.1128/AEM.01151-09

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