Potential treatments from cryptic genes

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Big pharma gave up on soil bacteria as a source of antibiotics too soon, according to research published in the June issue of *Microbiology*. Scientists have been mining microbial genomes for new natural products that may have applications in the treatment of MRSA and cancer and have made some exciting discoveries.

"Over the last eight years we have been looking for new natural products in the DNA sequence of the antibiotic-producing bacterium Streptomyces coelicolor," said Professor Gregory Challis from the University of Warwick. "In the last 15 years it became accepted that no new natural products remained to be discovered from these bacteria. Our work shows this widely-held view to be incorrect."

In 1928 Alexander Fleming discovered penicillin, which was subsequently developed into a medicine by Florey and Chain in the 1940s. The antibiotic was hailed as a 'miracle cure' and a golden age of drug discovery followed. However, frequent rediscovery of known natural products and technical challenges forced pharmaceutical companies to retreat and stop looking for new molecules.

Currently the complete genetic sequences of more than 580 microbes are known. It is possible to identify pathways that produce new compounds by looking at the DNA sequences and many gene clusters likely to encode natural products have been analysed. 'Genome mining' has become a dynamic and rapidly advancing field.

Professor Challis and his colleagues have discovered the products of two

cryptic gene clusters. One of the clusters was found to produce several compounds that inhibit the proliferation of certain bacteria. Three of these compounds were new ones, named isogermicidin A, B and C. "This discovery was quite unexpected," said Professor Challis. "Our research provides important new methodology for the discovery of new natural products with applications in medicine, such as combating MRSA infections."

The other product they discovered is called coelichelin. Iron is essential for the growth of nearly all micro-organisms. Although it is the fourth most abundant element in the Earth's crust it often exists in a ferric form, which microbes are unable to use. "The gene cluster that directs production of coelicehlin was not known to be involved in the production of any known products," said Professor Challis. "Our research suggests that coelichelin helps S. coelicolor take up iron."

Many researchers have followed Professor Challis and his colleagues into the exciting field of genome mining. "In the near future, compounds with useful biological activities will be patented and progressed into clinical or agricultural trials, depending on their applications" said Professor Challis.

Source: Society for General Microbiology