Nitrogen-fixing bacterial symbiont promises trove of natural products

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Soil-dwelling bacteria of the genus Frankia have the potential to produce a multitude of natural products, including antibiotics, herbicides, pigments, anticancer agents, and other useful products, according to Bradley S. Moore of the Scripps Oceanographic Institute, La Jolla, and his collaborators in an article in the June 2011 issue of the journal *Applied and Environmental Microbiology*.

The researchers found genetic structures in this bacterium that resemble those of various valuable natural product categories through bioinformatics and genome mining. “This tremendous biosynthetic capacity is reminiscent of many industrially important bacteria such as those belonging to the genus, Streptomyces that produce the majority of the natural antibiotics used as drugs,” says Moore.

“To see this capacity in a well-known microbe not previously exploited for its chemical richness was very rewarding from both an applied and basic science point of view,” says Moore. Frankia are nitrogen-fixing bacteria that live in symbiosis with actinorhizal plants (whose ranks include beech and cherry trees, and various gourd-producing plants). “Since the vast majority of the deduced [biosynthetic] pathways are unique to Frankia, it suggests that they employ a very complex and specialized communication with their plant host to establish and maintain their symbiosis. So lots to discover there.”

Frankia have not previously been exploited partly because these bacteria are difficult to grow in the lab. But new genetic methods make it easier to transplant genes for promising natural products from Frankia into "more user-friendly host bacteria for production," says Moore.

Moreover, genome mining, a recent technique that involves searching for genetic sequences, was critical to the results, and "complementary to the far more laborious traditional natural product drug discovery that has gone unchanged for decades," says Moore. A greater understanding of how complex organic molecules are synthesized in nature laid additional groundwork for this, and for "a new revolution in the discovery of natural chemicals that will fuel new research into what functions these chemicals play in nature, and how they can be used to benefit society," says Moore.

The project grew out of a graduate class that Moore and Daniel Udwary (then his post-doc, now at the University of Rhode Island) taught on "Microbial Genome Mining," says Moore. Each student in the class researched a group of biosynthetic gene clusters that Moore and Udwary preselected. The students—who are the majority of coauthors on the paper—annotated their genes and based on biosynthetic principles, and predicted pathways leading to putative natural products. They then worked with the laboratories of Pieter Dorrestein at the University of California, San Diego (a mass spec specialist) and Lou Tisa at the University of New Hampshire (a Frankia biologist) to conduct preliminary proteomic and metabolomic analyses to probe whether the predicted pathways were operative, and whether small molecule chemistry was evident.

More information: D.W. Udwary, et al., 2011. Significant natural product biosynthetic potential of actinorhizal symbionts of the genus Frankia, as revealed by comparative genomic and proteomic analyses." *Appl. Environ. Microbiol.* 77:3617-3625.

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