Searching for drugs in dirt, researchers call on citizen scientists

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Researchers, including postdoc Zach Charlop-Powers, are looking for antibiotics and other natural products by sequencing the genetic material found in soil.

(Phys.org) —Microbes are not only a rich source of disease, but also a rich source of medicines, and experts think many life-saving compounds produced by as-yet-unnamed bacteria are awaiting discovery. But they don't always give up their secrets easily. Researchers must know where to look to find promising bacteria, and how to get them to grow in the lab, the traditional route to identifying potentially valuable molecules they produce.

Researchers in Sean Brady's Laboratory of Genetically Encoded Small

Molecules are working on a way around these roadblocks. By using genomic sequencing technology, they can investigate the organisms that live in habitats like soil without having to grow the microbes in the lab. They are using this information to map out the location of gene clusters they believe may encode novel antibiotics, and, with help from citizen scientists around the country, they are hoping to process soil samples from areas they would never be able to visit on their own.

In a preliminary effort, Brady's lab has surveyed nearly 100 soil samples from two U.S. regions, looking for genetic sequences that encode certain molecule-making abilities. "We hope to expand to other regions of the country and the world, to incorporate many more samples in order to create maps of the biosynthetic diversity of soil microbes," says Zachary Charlop-Powers, a postdoc in the lab. "These maps could help guide drug discovery by identifying variants on known bacterial genes that might be part of a gene cluster encoding a new antibiotic."

Medicine already owes a major debt to microbes, particularly bacteria. These tiny organisms have produced or inspired many antibiotics, from tetracycline to vancomycin, as well as cancer-fighting drugs and immune system-suppressing therapies used for organ transplants. These bacterial natural products are part of the organisms' chemical defense system and these molecules have historically been isolated from the broth of bacteria grown in the laboratory.

"However, genetic evidence hints there are many, many more bacteria out there that we may not be able to grow," Brady says. "And they should be an equally rich source of useful natural products. We have been developing genetic tools to help us look for new chemistry by looking at the genes used to synthesize these natural products."

For the past five years, Brady's lab has been sequencing and shifting through DNA obtained directly from soil to identify potentially useful

genes, which the researchers then transplant into more-laboratory friendly bugs.

Charlop-Powers, Brady and colleagues recently published the first geographical survey intended to speed this discovery process in the Proceedings of the National Academy of Sciences. For this study, they focused on genes responsible for producing two important families of biologically active molecules: nonribosomal peptides and polyketides. These families include most of the therapeutic molecules isolated from cultured bacteria, but in spite of this diversity, the underlying genetic architecture remains constant. In these families, repetitive genetic domains generate molecules in an assembly line-like fashion that evolution has frequently retooled.

In DNA from 96 soil samples collected for the survey, the researchers looked at two of these domains to get a sense for the diversity and richness of microbes capable of producing compounds these families. They found a link between the type of soil and the sorts of molecules its resident microbes had the capacity to produce. "For reasons we don't understand, arid soils turned out to harbor microbes capable of producing a greater diversity of compounds," Charlop-Powers says. For this preliminary survey, Brady called on his family to send in samples from Arizona and New Mexico; another postdoc in his lab, Jeremy Owen, collected soil in New England.

The Brady Lab would like to extend this study and hopes to encourage citizen scientists to contribute to the effort. The lab has set up a website: www.drugsfromdirt.org and after signing up, citizen scientists will receive information about how to collect and ship samples. The process is simple, says Brady: "Take a sandwich bag, a spoon or a trowel, and dump a couple of spoonfuls in the bag and ship it to us."

More information: "Chemical-biogeographical survey of secondary

metabolism in soil." Zachary Charlop-Powers, Jeremy G. Owen, Boojala Vijay B. Reddy, Melinda A. Ternei, and Sean F. Brady. *Proceedings of the National Academy of Sciences* 111, 3757–3762. www.pnas.org/content/early/2014/02/13/1318021111

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