**Small Things Considered**

**Flights of Discovery**
http://schaechter.asmblog.org/schaechter/2014/05/flights-of-discovery.html
by Mizuho Ota

The biosynthetic and metabolic capacity of microbes has evaded us for years due to their astounding range and variability under different growth conditions. Yet, its study has rich potential not only to reveal more about microbial communication, sensing, and signal transduction, but also to lead to the discovery of novel microbial compounds that may be useful in human applications.

Microbial production and secretion of secondary metabolites is thought to give the producers a competitive advantage in their native environments through more efficient foraging, suppressing growth of neighboring species, killing competitors, or other allelopathic mechanisms. Not surprisingly, a bacterial group rich in such compounds are the soil-dwelling Actinobacteria that live within highly diverse microbial ecosystems. When grown in pure culture without the stimulation of a neighbor species, they may not sense a need to synthesize their full range of bioactive metabolites.

In 2013, the Dorrestein and Kolter groups asked experimentally if the metabolome of a model actinomycete, *Streptomyces coelicolor*, grown on agar would change in the presence of five other Actinobacteria strains. They needed to detect metabolites in situ, attribute production to the correct organism, and observe temporal interactions. For this they developed a two-pronged, mass spectrometry-based approach to sample the excreted metabolome non-invasively. Nanospray desorption electrospray ionization (NanoDESI) combined with tandem mass spectroscopy can identify secreted compounds, but not their source. For that, add matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) that uses a laser beam to vaporize compounds from a small, precisely localized area. Repeated pinpoint sampling "scans" the sample surface yielding a spatial heat map for the compound.

This approach showed that species-species interactions widened the actinomycete metabolome dramatically, adding 629 compounds not found in single colony controls. Of these, 227 were produced only by *S. coelicolor*, the rest by the interacting species ("initiators") or both. Assembling their results into a visual network based on structural relatedness revealed that many of these new compounds were similar to known chemicals made by *S. coelicolor*. A large portion of the *S. coelicolor* metabolic repertoire is structurally related to desferrioxamine (DFO) B, a known siderophore. Identified here were 12 acyl-DFO analogs with varying fatty acid chain lengths. Generally, the identified compounds were differentially stimulated by all five initiators, both in the degree of response and in time. The specificity of metabolite production was evident in that the majority of these compounds were present only when *S. coelicolor* was grown in the presence of one of the five initiators. Thus not only does the *S. coelicolor* metabolome dramatically diverge from that when in single culture, but the chemical responses of *S. coelicolor* seem tailored to the interacting species.

This work also demonstrates that coupling the mass spectrometry methods NanoDESI and MALDI-TOF is a powerful way to assess secondary metabolites in microbes. This can facilitate drug discovery by enabling the detection and identification of compounds produced in small amounts and exclusively during interaction between two or more species. With the increased ease in surveying the metabolic landscape of the microbial world, it may be time to adopt the term suggested earlier by Mark Martin and Julian Davies for these small secreted bioactive molecules: the parvome. Surely it is time to begin to explore the mechanisms triggering their production and their role in microbial social life.

**Talmudic Question of the Month***
by Ramy Aziz

Is there anything microbes cannot do?

Answers? Add a comment online to Talmudic Question #69, December 9, 2010.

*We use this term to denote questions whose answers cannot be found by a Google search.*

Mizuho Ota is a graduate student at the University of California at San Diego.