

Tiny Talk on a Barnacles Back

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Scientists use new imaging technique to reveal complex microbial interactions

Even the merest of microbes must be able to talk, to be able to interact with its environment and with others to not just survive, but to thrive. This cellular chatter comes in the form of signaling molecules and exchanged metabolites (molecules involved in the process of metabolism or living) that can have effects far larger than the organism itself. Humans, for example, rely upon thousands of products derived from microbially produced molecules, everything from antibiotics and food supplements to ingredients used in toothpaste and paint.

Remarkably, most of what's known about how microbes communicate with each other is the result of indirect observation and measurements. There has been no general or informative technique for observing the manifold metabolic exchange and signaling interactions between microbes, their hosts and environments. Until now. In a paper published in the May 5 online issue of the journal *Angewandte Chemie*, researchers at UC San Diego and Scripps Institution of Oceanography report using a new form of imaging mass spectrometry to dramatically visualize multiplex microbial interactions.

"Being able to better see and understand the metabolic interplay between microbial communities and their surrounding biology means we can better detect and characterize the molecules involved and perhaps discover new and better therapeutic and commercially viable compounds," said Pieter C. Dorrestein, PhD, associate professor at the UCSD Skaggs School of Pharmacy and Pharmaceutical Sciences and the paper's senior author.

Dorrestein and colleagues used matrix-assisted laser desorption ionization (MALDI) mass spectrometry, a relatively new approach that creates two-dimensional, spatial images of microbes and biomolecules (proteins, peptides, sugars) too fragile to withstand other mass spectrometry techniques.

As their first subject, the scientists collected marine microbial assemblages scraped off the slimy surfaces of a barnacle attached to the Scripps Pier. The resulting images, produced after careful preparation, offered new revelations.



In this photo illustration, the Scripps Institution of Oceanography pier is shown with images generated using imaging mass spectrometry set between pilings. One of the molecules identified in metabolic exchange by the study is illustrated along the upper course of the pier. Barnacles and other marine organisms cling to one of the pier's pilings

"One of the things we see that we haven't with other techniques is that the dialog between microbes is multiplexed," said Dorrestein. "There are many conversations going on at the same time, many changes happening at the same time. We see competition for resources such as iron, but also that microbes secrete molecules that alter the phenotypes (sets of observable characteristics) of neighboring organisms."

Dorrestein said the ability to better visualize the vastly complex world of microbial communication is changing the ways scientists investigate how two or more microbes are studied and eventually engineered.

"Rather than enumerating which microbes are present, as in many metagenomic efforts, our current approach is anticipated to address the why, when and how questions of microbial interactions instead of just the who," Dorrestein said.

Co-authors of the paper are Yu-Liang Yang, Yuquan Xu, Michael J. Meehan, Bradley S. Moore, Nuno Bandeira, UCSD Skaggs School of Pharmacy and Pharmaceutical Sciences; Roland Kersten, Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, UCSD; Wei-Ting Liu, UCSD Department of Chemistry and Biochemistry.

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