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The community ecology of microbial molecules

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Community ecology is the study of assemblages of organisms and the dynamics of those assemblages in time and space. In the last decade, microbial community ecology has greatly advanced by employing high-throughput approaches, such as 16S rDNA sequencing and metagenomics. This has enabled the analysis of polymicrobial communities (defined as assemblages of multiple to thousands of microbial species) in their natural habitats and enhanced our understanding of the structure of these communities and how they change during perturbations. Polymicrobial communities and the molecules they produce are invariably linked. Specialized metabolites have been shown to function as major mediators of the structure and function of microbial communities (Dorrestein et al. 2014). Despite this discovery, the metabolomics of microbial communities has not received as much attention, even though high-throughput approaches using mass spectrometry are similarly available and there are parallels between the data generated in these two approaches.

In microbial ecology, communities of microorganisms are studied on the level of ‘operational taxonomic units’ (OTUs), each representing a unit of evolutionary divergence, loosely associated with the term “species”. High-throughput nucleic acid sequencing methods produce data quantifying the abundances of hundreds to thousands of OTUs that, together, constitute a microbial community. Multiple methods are available for aligning DNA sequences for the comparison and quantification of individual OTUs and the genes they carry, such as BLAST (http://blast.ncbi.nlm.nih.gov/Blast.cgi) and sequence assembly algorithms. Untargeted mass spectrometry-based metabolomics is similar to sequencing based -omics in that the data comprise the abundances of thousands of variables, but in metabolomics, the variables are metabolites. However, algorithms analogous to assigning sequence similarity are limited for the analysis of metabolomics data. This has hindered progress compared with methods based on sequence alignments. Recently though, novel algorithms have been developed for scoring molecular similarity and building chemical relationships analogous to those of OTUs (Barupal et al. 2012, Watrous et al. 2012). Molecular networking, for example, can visualize molecular relatedness by computationally comparing individual MS/MS spectra to build relationship networks (Watrous et al. 2012). This approach is a novel means of identifying unique and related molecules in large data sets, and is similar to the bioinformatics tools used to identify sequence similarity. The nascent field of untargeted metabolomics could benefit greatly from combining decades-old

statistical approaches from community ecology and novel algorithms designed to identify unique and related molecules in MS data, an approach that has been highly successful in the field of microbial community ecology based on OTU population dynamics.

Ecological statistics, including measures such as the Shannon and Simpson indices of diversity and rarefaction curves, may be particularly useful in the analysis of chemical species. Applying these methods in metabolomics can help us to understand the diversity of molecular species and relate the microbial diversity in polymicrobial communities to the molecular diversity. Microbial communities are directly influenced by, and themselves directly influence, their environmental chemistry. Questions that can be addressed with ecological indices include: do the well-described drivers of microbial diversity affect molecular diversity? How does molecular diversity change for a disrupted community? Are particular molecules responsible for population changes in microbial communities, and do these molecules serve the same function under different conditions? These indices can be used to determine if fundamental concepts in ecology can be observed in chemical data, such as the concept of climax communities and ecological succession. There may be interesting similarities, and even more interesting differences, between the ecology of microorganisms and the ecology of their chemistry. For example, with the potential to produce multiple end-products of microbial metabolism in the same cell (e.g., among facultative anaerobes), a single well-described climax community of microbes may have multiple climax chemical communities.

Microbiome studies of microbial communities often find a decrease in diversity during times of disease, indicative of a disrupted ecological balance. Studying the metabolomics of these pathogenic communities may reveal similar changes during dysbioses, and has potential for the detection of molecular biomarkers of those diseased states. The influence of specialized metabolites in microbial community interactions indicates that changes in community diversity may be specifically due to changes in community chemistry. Studying specialized metabolites in the context of an entire metabolome may reveal how these molecules can drive dysbioses themselves, by detecting their presence, and then observing their effect on the molecular diversity in a longitudinal manner. Having the tools to identify, quantify, and interpret these molecules in a high-throughput manner will greatly aid our understanding of the causes and effects of changes in microbial community chemistry.

As recent microbiome studies, in particular the Human Microbiome Project (http://commonfund.nih.gov/hmp/index) have revealed, our microbial world is remarkably diverse, and the molecules produced may be even more so (Dorrestein et al. 2014). Untargeted metabolomics can improve our ability to assess the molecular diversity of microbial communities and monitor changes in both time and space. By utilizing novel methods of mass spectrometry data analysis and adapting statistical approaches developed in community ecology, ecological questions of chemical diversity are now approachable. This will allow for an exploration of the depth of chemical diversity and better understanding of the complex ecology of microbial communities.

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