Meta-Analysis Reveals Patterns of Bacteria-Virus Infection Networks

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Bacteria are common sources of infection, but these microorganisms can themselves be infected by even smaller agents: viruses. A new analysis of the interactions between bacteria and viruses has revealed patterns that could help scientists working to understand which viruses infect which bacteria in the microbial world.

A meta-analysis of the interactions shows that the infection patterns exhibit a nested structure, with hard-to-infect bacteria infected by generalist viruses and easy-to-infect bacteria attacked by both generalist and specialist viruses.

"Although it is well known that individual viruses do not infect all bacteria, this study provides an understanding of possibly universal patterns or principles governing the set of viruses able to infect a given bacteria and the set of bacteria that a given virus can infect," said Joshua Weitz, an assistant professor in the School of Biology at the Georgia Institute of Technology.

Discovering this general pattern of nested bacteria-virus infection could improve predictions of microbial population dynamics and community assembly, which affect human health and global ecosystem function. Knowing the patterns of which bacteria are susceptible to which viruses could also provide insights into strategies for viral-based antimicrobial therapies.

The results of the meta-analysis were published June 27, 2011 in the early edition of the journal *Proceedings of the National Academy of Sciences*. The work was sponsored by the James S. McDonnell Foundation, the Defense Advanced Projects Research Agency and the Burroughs Wellcome Fund.

Georgia Tech physics graduate student Cesar Flores, Michigan State University zoology graduate student Justin Meyer, Georgia Tech biology undergraduate student Lauren Farr, and postdoctoral researcher Sergi Valverde from the University Pompeu Fabra in Barcelona, Spain also contributed to this study.

The research team compiled 38 laboratory studies of interactions between bacteria and phages, the viruses that infect them. The studies represented approximately 12,000 distinct experimental infection assays across a broad spectrum of diversity, habitat and mode of selection. The studies covered a 20-year period and included hundreds of different host and phage strains.

The researchers converted each study into a matrix with rows containing bacterial types, columns containing phage strains, and cells with zeros or ones to indicate whether a given pair yielded an infection. Then they applied a rigorous network

theory approach to examine whether the interaction networks exhibited a nonrandom structure, conformed to a characteristic shape, or behaved idiosyncratically -- making them hard to predict.

Of the 38 studies, the researchers found 27 that showed significant nestedness. Nestedness was measured by the extent to which phages that infected the most hosts tended to infect bacteria that were infected by the fewest phages. The researchers used statistical tests to rule out forms of bias. However, because the majority of the data consisted of closely related species, the researchers anticipate that more complex patterns of infection may form with species with more genetic diversity.

"Considering the large range of taxa, habitats and sampling techniques used to construct the matrices, the repeated sampling of a nested pattern of host-phage infections is salient, but the process driving the nestedness is not obvious. The pattern suggests a common mechanism or convergent set of mechanisms underlying microbial co-evolution and community assembly," explained Weitz.

The researchers examined three hypotheses to explain the nestedness pattern based on biochemical, ecological and evolutionary principles, but found that additional experiments will be required to determine why this pattern occurs so often.

This meta-analysis demonstrated the utility of network methods as a means for discovering novel interaction patterns. According to the researchers, viewing host-phage interaction networks through this type of unifying lens more often will likely unveil other hidden commonalities of microbial and viral communities that transcend species identity.

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