

# Reviews of microbial gene language published in special issue of *Trends in Microbiology*

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Ten articles describing how a universal language to describe genes is bringing benefits to the study of the microbial world have been published in a special issue of *Trends in Microbiology*, co-edited by Virginia Bioinformatics Institute professor Brett Tyler. The Gene Ontology is a powerful language that gives researchers a shared vocabulary to describe disease-related and beneficial interactions between a microbe and its host. By allowing scientists to link experimental results to a computer-readable language, the Gene Ontology provides scientists with an important bridge between specific experiments that characterize gene function and larger-scale, systems biology efforts to provide a global picture of host-microbe interactions.

The Gene Ontology was started in 1998 by a consortium of three databases for the organisms yeast, fruit fly, and mouse. The Plant-Associated Microbe Gene Ontology (PAMGO) Consortium joined the effort in 2004 to focus on microbe-plant associations, which include the many relationships of plants with bacteria, fungi, oomycetes, and nematodes. VBI researcher Trudy Torto-Alalibo, who coordinates the PAMGO project, remarked: "Advances in sequencing technologies have led to a remarkable increase in the number of sequenced microbial genomes. Analysis of these genomes has provided useful information about genes that may be important in microbe-host interactions. However related genes that have a common function can be missed in sequence comparisons if those genes arose from different evolutionary

paths. The Gene Ontology offers a way to overcome such limitations and can greatly facilitate the comparison of gene function across the different domains of life."

Candace Collmer of Wells College, who helped launch PAMGO in 2003, noted: "A crucial step at the beginning of the PAMGO project was the realization that plant pathogenesis is only one possible outcome along a continuum of broadly-defined, symbiotic microbial-host interactions ranging from detrimental to beneficial. Since all are types of intimate interactions, and because microbes initiating these different types have common needs in approaching a host, be it plant or animal, we initially crafted broad terms for describing "symbiont" [gene functions](#) in an attempt to highlight these similarities across a diverse set of microbes. For these and the more specific terms that followed, an important contribution of PAMGO to the Gene Ontology was the development of terms that describe the functions of gene products that are made by one organism, for example the microbe, but actually act in a different organism, namely the host."

The first review in the *Trends in Microbiology* publication describes how the PAMGO Consortium has developed more than 800 new Gene Ontology terms to assist in understanding how microbes interact with their hosts. The authors also point out that Gene Ontology terms will be of great benefit to metagenomics efforts - the sequencing of mixtures of multiple organisms from environmental samples - in helping define the functions of the many genes discovered by these initiatives. The Human Microbiome Project (HMP), for example, plans to extensively sequence the metagenomes of five human body sites and look for correlations between microbial communities and human health. Dr. Michelle Giglio, Assistant Professor at the Institute for Genome Sciences at the University of Maryland School of Medicine and a senior scientist on the PAMGO project, commented: "The surface has barely been scratched in the attempt to unravel the complex relationships between human health

and the microbes that inhabit us. Here at the Institute for Genome Sciences we are managing the Data Analysis and Coordination Center for the HMP. The application of standards such as the Gene Ontology, and particularly the PAMGO terms, will be essential to make sense of the massive amounts of metagenomic annotation that will be collected during this project."

Another paper in the series looks at how the Gene Ontology has been used to classify the function of genes in *Escherichia coli*, an organism that has long been the workhorse of the molecular biology laboratory. Gene Ontology terms are particularly well suited for classifying the similarities and differences in the function of gene products in *E.coli* as compared to their counterparts in other organisms. As the authors emphasize, linking other resources to Gene Ontology terms will also open up exciting new opportunities for biologists to explore gene function in the years ahead.

Four of the papers in the special issue look at how Gene Ontology can be used to dissect the complex interactions involved when pathogens invade their hosts and lead to disease. They include descriptions of bacterial effector proteins, virulence factors, effector protein delivery systems, and infection by filamentous pathogens. João Setubal, Associate Professor at the Virginia Bioinformatics Institute, remarked: "Symbiotic microbes have developed many ingenious ways to deliver effector molecules into their hosts to facilitate colonization. The biology behind this invasion of the host cell is rich and diverse and Gene Ontology terms help to reveal common themes in the delivery of effector molecules by different [microbes](#). Our understanding of the key steps in host-microbe interactions will be considerably enhanced by the further widespread use of Gene Ontology terms, which should in turn generate proposals for more terms."

Another review reveals how terms created by the PAMGO Consortium

have been used to assess the function of genes in *Candida albicans*, a type of yeast that can lead to disease in humans. The characterization of genes in *C. albicans* has also benefited from the transfer of Gene Ontology terms from the extensively studied yeast *Saccharomyces cerevisiae*. *S. cerevisiae* is another workhorse of the molecular biology laboratory and Gene Ontology terms have been instrumental in building a system-wide understanding of the biology of this organism. This type of work allows scientists to use Gene Ontology terms to identify common elements in both plant and animal disease.

One research area that has not received a lot of attention so far is the use of Gene Ontology terms to address viral infection, in part due to fundamental differences between the ways in which viruses and other pathogens infect their hosts. One article in the series outlines how viral pathogens can also be attributed Gene Ontology functions and reveals how scientists are in a position to apply Gene Ontology to the modeling of viral infections.

Brett Tyler, also the PAMGO project leader, remarked: "The research described in this series of articles summarizes both the many dimensions of the microbial world that have been revealed through using Gene Ontology terms as well as the benefits of adopting this shared language for gene function. We strongly encourage the authors of scientific papers to include their own Gene Ontology term assignments when publishing new experimental data about genes and we hope that scientific journals will assist in this process. This practice greatly facilitates the work of biologists interested in looking at organisms across kingdoms, from molecules all the way up to complex biological systems.

More information: The supplement is freely available on-line for one month via the cell.com web site at [www.cell.com/trends/microbiolo ...0966-842X\(09\)X0007-7](http://www.cell.com/trends/microbiolo...0966-842X(09)X0007-7)

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