



ton, who also studies bacterial cell division (see p. 329) but was not a collaborator with Wirtz and Dajkovic. Nonetheless, he adds, antibiotics might be developed expressly to disrupt FtsZ bundling along with the higher-order structure of the Z ring. In other respects, the findings are “quite solid,” Margolin says. The use of quantitative rheology to measure the elastic modulus—stiffness—of FtsZ networks is novel and should be used in other studies of protein machines, he points out.

Scientists have known about bacterial FtsZ and the Z ring for about 20 years. Although FtsZ is structurally similar to tubulin, FtsZ in bacterial cells functions much as actin does in mammalian cells—squeezing a mother cell into two daughter cells. In contrast, bacterial molecules that are structurally similar to actin help to segregate DNA molecules, which is what tubulin does in mammalian cells, according to Wirtz. “It’s fascinating that clearly structurally similar counterparts [tubulin and actin] have switched functions in mammalian and bacterial cells,” he says.

Carol Potera

Versatile Metabolic Phenotyping Extending to More Cell Types, Situations

Broad-based phenotypic analysis is proving strikingly versatile for providing valuable insights into a range of microorganisms, including for fastidious pathogens that grow only in mammalian host cells, as well as for other microbes whose metabolic habits prove elusive when probed with other widely used analytic approaches. Moreover, because the repertoire of a popular commercial, metabolism-based phenotyping method is continuing to expand, its analytic versatility now encompasses anaerobic bacteria, fungi, and cultured mammalian cells.

With recent applications of that method as their focus, here are a few highlights from scientists from more than 20 countries who participated in the inaugural “Conference on Phenotype MicroArray Analysis of Microorganisms: the Environment, Agriculture and Human Health,” which was held last March in Florence, Italy.

Some bacterial pathogens such as *Coxiella burnetii*, the agent of Q-fever in humans, continue to thwart efforts to culture them in defined media but can be grown in mammalian host cells in vitro. Another such fastidious pathogen, *Legionella pneumophila*, which can give rise to severe pneumonia, undergoes dramatic changes while growing inside human alveolar macrophages—cycling between a transmissible form and a nonmotile, noninfectious replicative form. For both these pathogens, use of the metabolic-indicator technology, which was developed and commercialized by Biolog, Inc. of Hayward, Calif., is providing striking insights. The technology relies on a tetrazolium dye that changes color when microbial (or other) cells metabolize substances that promote respiration.

This technology, which now encompasses more than 2,000 distinct metabolic-based phenotypes, is prov-

ing useful for determining which nutrients, for example, *C. burnetii* depends on, according to Anders Omsland of the National Institute of Allergy and Infectious Diseases Rocky Mountain Laboratories in Hamilton, Mont. Ordinarily such cells grow only while sequestered within mammalian host cells, making it difficult to distinguish their metabolic activities from those of host cells. However, he and his collaborators lysed the phagocyte host cells, recovered the nongrowing but still-respiring bacterial cells, and then determined that their metabolism is maximal under acidic (pH 4.5) and microaerobic conditions of 2.5% oxygen. Based on that information, they developed a medium that sustains *C. burnetii* metabolic activity for 24 hours, permitting analyses of other activities such as protein synthesis.

Separately, the same kind of phenotyping analysis helped to reveal that short-chain fatty acids play a key role for *L. pneumophila* cells as they cycle between nonmotile and transmissible forms, according to Rachel Edwards and Michele Swanson at the University of Michigan, Ann Arbor. Further analysis is helping them to identify key bacterial genes that are involved in regulating this process.

Similarly, other investigators are

Cyanobacteria Metabolic Versatility Boosted

Transfer of cellulose synthesis genes from *Gluconacetobacter xylinus* strain ATCC 53582, which is a heterotrophic alpha proteobacterium, to the photosynthetic cyanobacterium *Synechococcus leopoliensis* strain UTCC 100, leads to the latter’s producing a distinct form of cellulose, according to R. Malcolm Brown Jr. and David Nobles Jr. of the University of Texas at Austin. “The non-crystalline nature of the cyanobacterial cellulose makes it an ideal potential feedstock for bio-fuel production,” they point out. “The cyanobacterium is potentially a very inexpensive source for sugars to use for ethanol and designer fuels,” Nobles adds. Moreover, it could be used for producing fuels without relying on arable lands that may otherwise be farmed for food. Details appear in the in the 12 April 2008 *Cellulose*, DOI 10.1007/s10570-008-9217-5.

looking at metabolic changes that are induced when bacterial pathogens interact at close range to—rather than within—host cells and tissues. Some of this analysis is directed at host tissues themselves, as in the case of Manal Abuoun from the U.K. Veterinary Laboratories Agency in Weybridge, United Kingdom, who is studying metabolic responses of a pig-derived jejunal cell line in terms of its nutrient requirements and sensitivity to ion stress, cytokines, hormones, and other effectors. These measurements will help to establish baseline values when she begins to look at how *Salmonella enterica* serovar Typhimurium interacts with these or similar mammalian cells. Similarly, Tyrrell Conway of the University of Oklahoma in Norman is examining how cells of *Escherichia coli* change metabolically when they encounter nutrient mixtures in mucus lining the mammalian colon.

These or similar pathogens of the gastrointestinal tract are also being analyzed metabolically to serve public health interests. Thus, for example, phenotypic profiles of *E. coli* O157:H7 and *S. enterica* are helping to identify strains responsible for foodborne disease outbreaks, including some that could not be differentiated by restriction enzyme-based subtyping, according to Thomas A. Cebula of the Food and Drug Administration and Jean Guard-Bouldin of the United States Department of Agriculture.

This same kind of metabolic analysis is being applied in yet other settings—for example, to address microbial morphologic changes. Thus, this phenotyping method is helping to analyze how light and other environmental conditions drive conidiation in two commercially important fungi, *Trichoderma* and *Fusarium*, according to Irina Druzhinina of the Vienna University of Technology in Vienna, Austria. And Alexander Boehm of Basel University in Basel, Switzerland, and his collaborators are using such

arrays to identify signals and metabolic changes and conditions that trigger *E. coli* cells to form biofilms.

Jeffrey L. Fox

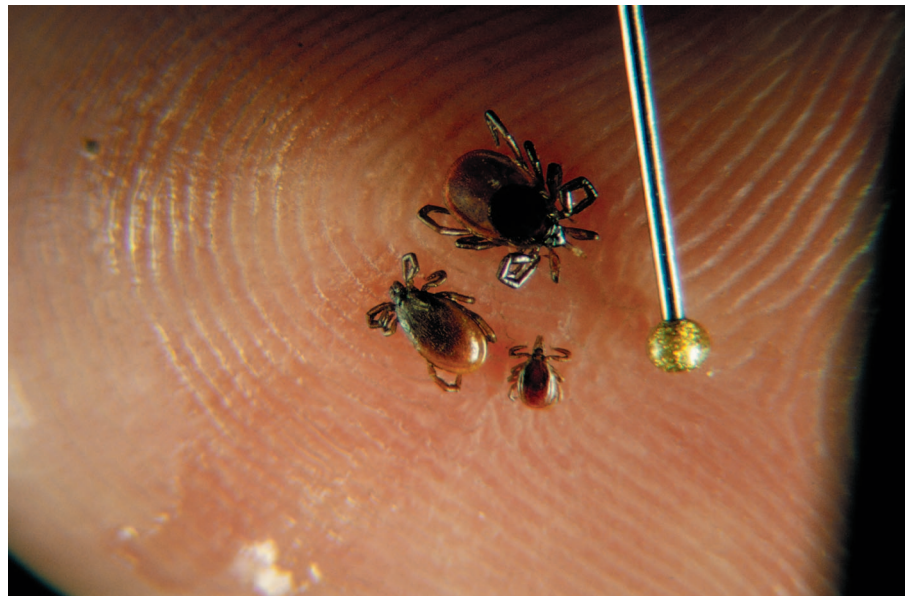
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Complexities in Gauging Climate Change Impact on Infectious Disease

Predicting how global climate change will affect infectious diseases is “not rocket science,” says Andrew Dobson of Princeton University in Princeton, N.J. “It’s much harder, and more important.” Indeed, in one example after another, the effects of climate change on infectious diseases appear ever more complex, particularly in those cases involving vector-borne diseases, as they fit into distinct geographic regions, according to several experts who spoke during the 58th annual meeting of the American Institute of Biological Sciences (AIBS), “Climate, Environment, and Infectious Diseases,” held last May in Arlington, Va.

Each disease seems to have its own peculiarities. In the case of vector-borne Lyme disease, for instance, “subtle influences are important,” says Durland Fish of Yale University in New Haven, Conn. *Borrelia burgdorferi*, a spirochete, causes this disease, which typically begins with a bulls-eye rash, leads to arthritis of the large joints, and often can be resolved with antibiotic treatment. The spirochete is carried into humans via bites from deer ticks that ordinarily live primarily on deer mice as well as other small mammals, such as chipmunks, squirrels, rabbits, and raccoons. As nymphs, those ticks feed for only two weeks in every two-year cycle, making them “very susceptible to environmental conditions,” during that gustatory interlude, he says.

To complicate matters, the pathogen carries “huge” genetic variability among its several distinct types, which differ in terms of symptoms they cause and in their relative fitness when circulating in nature, according to Fish. Those properties, thus, are at the mercy of the ticks carrying the microbes, the life stages of those ticks,



Deer tick (*Ixodes scapularis*) responsible for transmitting the spirochete *Borrelia burgdorferi*, the pathogen that causes Lyme disease, to humans in parts of the United States. Researchers are puzzling out how climate changes are affecting the range of this vector. (Photo © Scott Camazine/Photo Researchers, Inc.)