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Editorial overview: Growth and development: prokaryotes

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The field of microbial cell biology is a very broad one. It includes the fundamental aspects of how microbes become larger and divide; how individual cells sense their changing environment to execute different cellular responses; how cells coordinate different stages of their cell cycle and switch from binary fission to alternative developmental pathways; how the morphology of the cell surface, which interacts with the environment, is elaborated; and how individual cells begin to coordinate their activities to exert an orchestrated behavior at the community level. In this issue, we have sampled the diversity of this field and present eleven articles that review recent data and speculate on how specific pathways may impact how bacterial cells grow, develop, and behave in a community.

Well-studied rod-shaped model bacteria such as *E. coli* and *B. subtilis* are known to elongate by addition of peptidoglycan along the lateral side wall, before they divide in the center along their short axis into identical daughter cells. Correct placement of the division septum in *E. coli* is mediated by two negative regulatory systems (the well-studied “Min” system and nucleoid occlusion system) which together prevent the placement of the septum at incorrect locations. Cytokinesis itself is mediated by the divisome, a complex of approximately ten proteins that assemble at mid-cell and constrict with the division septum during cytokinesis. The core component of the divisome is FtsZ, a widely conserved bacterial homolog of tubulin, which has been previously proposed to provide the physical force required to remodel the membrane during cell division. Three papers in this issue offer alternative examples to these traditionally proposed mechanisms. Howell and Brown describe emerging mechanisms in taxonomically diverse species that grow by extending the cell wall at the poles, not along the lateral edges. Garcia et al. discuss a recently discovered system in *Streptococci*, in which placement of the division system is primarily mediated by positive regulation, not negative regulation as exemplified by the Min system. Finally, Goley and Xiao review recent evidence which suggests that FtsZ may not be the primary force-generating factor that remodels the membrane at mid-cell, and that its primary role is instead to orchestrate the recruitment of cell wall machinery components that are more directly involved in membrane remodeling during cytokinesis.

To properly grow and proceed through a developmental program, cells must constantly assess environmental signals and mount an appropriate cellular response. These responses are often mediated by signaling pathways that sense an extracellular cue, which then transmit a signal to initiate a transcriptional response to respond to the extracellular event. Recent years have witnessed the identification of several nucleotide-based intracellular “secondary” messengers that help coordinate how robust this response to an extracellular signal may be. Orr et al. discuss examples of second messenger nucleotides that not only

bind to multiple receptors that regulate unrelated pathways, but also peculiar examples in which the same nucleotide binds different receptors that actually regulate the same pathway. They propose that this process may produce a “sustained signaling” event in which a cell mounts a robust response to a cue that may then be subject to multiple levels of regulation. Sometimes, though, the physical nature of an extracellular signal is not entirely clear. Spore formation in *B. subtilis* is a developmental program in which a cell differentiates into a dormant endospore in response to nutrient-limiting growth conditions, but the physical cue that signals starvation conditions and causes a cell to trigger the sporulation program has remained elusive. Narula et al. propose a threshold concentration model of a master regulator of sporulation that allows the cell to monitor nutrient-limiting environmental conditions indirectly by measuring the cell’s own growth rate. This model, together with feedforward loops that activate transcriptional regulators permit the cell to decide between robustly committing to sporulation or to continue with normal growth.

Once the decision to commit to a particular growth program has been made, the cell must decide how to orchestrate cell growth with initiating replication of its genetic material in an attempt to maintain the correct ploidy of the organism. Murray reviews different strategies that diverse bacteria employ to coordinate the onset of DNA replication to different phases of growth, including an extreme example in which a *Synechococcus* species almost completely uncouples DNA replication and cell division. Vass et al. examine how *Caulobacter crescentus* proceeds through its growth cycle, from the perspective of how the regulated proteolysis of key cell cycle regulators and chromosome replication initiators is achieved at different stages of development.

A crucial event during cell growth is the biogenesis of the cell envelope, which helps defines the morphology of a particular cell. Ruiz examines how the mesh-like cell wall, composed of peptidoglycan, is built around Gram-negative bacteria, highlights how cell wall precursors are transported to the periplasm, and how cell wall assembly may be coordinated with cell division to permit normal growth. In contrast to the Gram-negative envelope, the Gram-positive cell surface is a platform that displays several distinct molecules. Siegel et al. describe how teichoic acids and cell wall-associated proteins are sorted and displayed on the surface of the Gram-positive cell, and how surface-displayed proteins may fold properly in the absence of a periplasm.

Finally, two articles in this section go beyond how single bacterial cells develop and examine how communities of similar bacteria collectively orchestrate their behavior. Arnaouteli et al. describe the production and secretion of a small hydrophobic self-assembling protein by *B. subtilis* that helps forms a hydrophobic “raincoat” that allows biofilm communities to resist wetting by water and biocides. Mercier and Mignot examine cooperative, multicellular motility in *M. xanthus* with an emphasis on how a central signaling pathway regulates the frequency at which individual cells switch direction.

In sum, the articles review recent advances in bacterial cell biology that investigate how bacteria grow and divide, sense their environment, orchestrate DNA replication with growth, attain their proper morphology, and interact with one another. Together with increasingly mechanistic understandings derived from examining well-studied model organisms, several

reviews showcase the emergence of discoveries that come from traditionally understudied organisms and highlight the diversity of mechanisms that drive bacterial growth and development.

Vitae

Kumaran Ramamurthi is a Senior Investigator in the Laboratory of Molecular Biology at the National Cancer Institute, National Institutes of Health in Bethesda, Maryland (USA). His lab studies how proteins localize and assemble during bacterial spore formation and cell division, with an emphasis on shape-sensing proteins that preferentially bind to differently curved membranes. Research in the Ramamurthi lab combines classical genetics and biochemistry with fluorescence microscopy and biophysical techniques to first understand how bacterial proteins recognize specific subcellular localization cues during morphogenesis and to ultimately reconstitute those events in vitro using defined components. Work in his lab is funded by the Intramural Research Program of the NIH, National Cancer Institute, Center for Cancer Research.