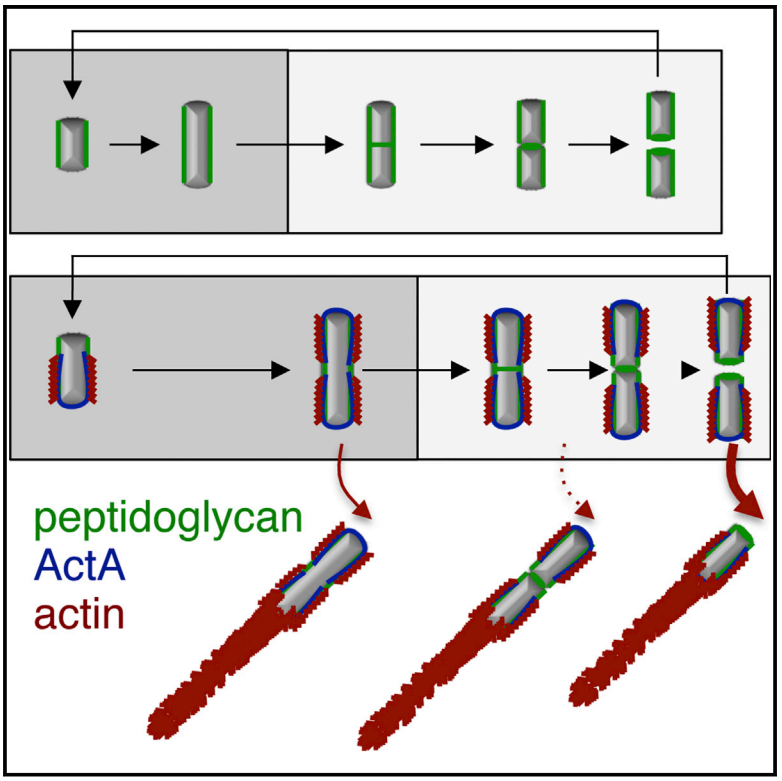
Cell Reports

Host Actin Polymerization Tunes the Cell Division Cycle of an Intracellular Pathogen

Graphical Abstract



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In Brief

Siegrist et al. use a chemical labeling strategy to show that host actin polymerization rebalances the cell division cycle of intracellular *Listeria monocytogenes* (*Lm*). This skews the bacterial population toward shorter cells that are more likely to form actin tails, which, in turn, are critical for motility and virulence.

Highlights

- Division is faster and non-dividing elongation is slower when *Lm* are intracellular
- Actin polymerization rebalances *Lm* cell division cycle
- Cell division cycle rebalancing increases *Lm* propensity to form actin tails

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Report

Host Actin Polymerization Tunes the Cell Division Cycle of an Intracellular Pathogen

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SUMMARY

Growth and division are two of the most fundamental capabilities of a bacterial cell. While they are well described for model organisms growing in broth culture, very little is known about the cell division cycle of bacteria replicating in more complex environments. Using a D-alanine reporter strategy, we found that intracellular *Listeria monocytogenes* (*Lm*) spend a smaller proportion of their cell cycle dividing compared to *Lm* growing in broth culture. This alteration to the cell division cycle is independent of bacterial doubling time. Instead, polymerization of host-derived actin at the bacterial cell surface extends the non-dividing elongation period and compresses the division period. By decreasing the relative proportion of dividing *Lm*, actin polymerization biases the population toward cells with the highest propensity to form actin tails. Thus, there is a positive-feedback loop between the *Lm* cell division cycle and a physical interaction with the host cytoskeleton.

INTRODUCTION

Growth and division are well defined for model bacteria replicating in broth culture. These organisms rely on proteins like the actin homolog MreB and tubulin homolog FtsZ to organize elongation and division, respectively (Bi and Lutkenhaus, 1991; Jones et al., 2001). One role of these proteins is to provide a scaffold for enzymes that synthesize, remodel, and degrade peptidoglycan (PG), a biopolymer that forms a protective meshwork around the cell (de Boer, 2010; White and Gober, 2012). The dimensions of rod-shaped bacteria such as *Escherichia coli* and *Bacillus subtilis* are initially determined by MreB, FtsZ, and other cytoskeletal proteins and fixed in place by the rigid cell wall (Typas et al., 2012; Young, 2010).

However, the vast majority of bacterial species are unlikely to fit this paradigm neatly because of differences in shape, mode of growth, or envelope structure. Moreover, growth and division have been primarily studied under defined conditions that may or may not recapitulate replication in the natural environment. There is increasing evidence that bacteria respond to the external milieu by adjusting their growth or division (Deghelt et al., 2014; Frirdich and Gaynor, 2013; Justice et al., 2008). Such alterations are often apparent in obvious changes to the size and shape of the cell, since inhibiting division can cause a bacterium to filament and inhibiting elongation can result in very short or even spherical cells (Young, 2006). Even for species that are not known to undergo clear morphological changes, transcriptional and mutant data suggest that the requirements for both cell wall-acting enzymes and cytoskeletal proteins change according to the environment (Boneca, 2005; Camejo et al., 2009; Frirdich and Gaynor, 2013).

Defining the impact of environmental perturbations on the bacterial cell division cycle is not straightforward. Alterations in growth and division may not necessarily manifest in changes to colony-forming units (CFUs), the most common measurement of bacterial replication outside of broth culture (Crimmins and Isberg, 2012; Helaine and Holden, 2013; Manina and McKinney, 2013). Enumeration of the total bacterial burden can undercount quiescent organisms as well as those that are growing but not dividing. The traditional standard for assessing whether bacteria are in the process of septating is electron microscopy, but this is laborious and poorly suited to screening a multiplicity of bacterial strains or conditions. Finally, fluorescent protein fusions can, in