BACTERIAL PATHOGENICITY

A competent escape for *Listeria*

The facultative intracellular pathogen *Listeria monocytogenes* must escape from the phagosome into the host cell cytosol to complete the infectious cycle, and phagosomal escape is therefore an important component of virulence. Rabinovich *et al.* now reveal that the *L. monocytogenes* competence (Com) system has a key role in phagosomal escape and that activation of this system is controlled by a prophage excision event.

The term competence describes the physiological state in which bacteria can undergo transformation (the uptake of exogenous DNA). The genes of the Com system, including the late *comG*, *comE* and *comF* operons, and the main regulators have been characterized in *Bacillus subtilis*. Although *L. monocytogenes* contains homologues of most of the late *com* genes, it is not transformable, and the only known regulator in this species is a homologue of the key *B. subtilis* activator, ComK.

In several *L. monocytogenes* strains, the *comK* gene is disrupted by a temperate prophage; therefore, the impact of this insertion on virulence was investigated. In *L. monocytogenes* str. 10403S, *comK* is interrupted by the φ10403S prophage. Whole-genome transcriptomics of this strain growing in bone-marrow-derived macrophages, combined with analysis of the growth effects of in-frame *com* deletions, revealed that the *comG* and *comE* operons are required for intracellular growth. Further mutant analysis showed that only the membrane channel, encoded by *comEC*, and the pseudopilus, encoded by the *comG* operon, were required, suggesting that involvement of the Com system is independent of DNA uptake. The mutant analysis also revealed that the *comEC* and *comG* mutants were impaired in phagosomal escape, and this was confirmed by fluorescence microscopy.

How is the Com system regulated? The authors examined the promoters of the three *com* operons and identified a conserved binding site for the ComK activator. By monitoring the fate of *comK* during growth in liquid culture, they found that *comK* was disrupted in exponential phase but intact in stationary phase, suggesting that the φ10403S prophage had been excised. Similarly, during intracellular growth, *comK* was intact and an excised form of the phage genome could be detected. There was no evidence of bacterial cell lysis or progeny virion production, however, suggesting that phage propagation is blocked. Finally, by assessing the growth of a range of deletion mutants, the authors established that an intact *comK* gene (and, hence, prophage excision) is required for intracellular growth.

The authors propose that prophage excision during phagocytosis generates an intact *comK* gene, and the resultant functional ComK protein activates the Com system to induce phagosomal escape. Further work is required to determine what triggers prophage excision and the exact mechanism by which the Com pseudopilus and membrane channel promote phagosomal escape.

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