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*Brucella*virulence

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Abstract

Investigation of transcriptional regulation of the *virB* operon has revealed clues to how *Brucella suis* survives within host cells

Significance and context

Successful infection by pathogenic bacteria often depends on their ability to survive and multiply within host cells. To do so, they alter or adapt to the host-cell environment. To these ends, pathogenic bacteria contain a variety of secretion systems, including type I, II and III secretion systems, which can export virulence factors to the environment or into the infected host cell. A type IV secretion system has also recently been identified, which is, for example, involved in the transfer of T-DNA from *Agrobacterium tumefaciens* into a host plant cell.

The VirB system of *B. suis* is an example of a type IV secretion system that is important in the virulence of medically important pathogenic bacteria. *B. suis* is a member of a genus of Gram-negative pathogenic bacteria that cause brucellosis in pigs, dogs and rodents, and Malta fever in humans. Relatively little is known about the genetics of *Brucella* virulence or about factors that facilitate bacterial survival and multiplication within host cells. The *virB* operon of *B. suis*, which encodes the VirB system, is essential for bacterial survival and multiplication in macrophages and epithelial cells. Boschiroli *et al*. studied the regulation of this operon and found that phagosome acidification is a key signal required for induction of *virB*-operon expression. This contributes to our understanding of how *B. suis* has adapted to and exploits an intracellular environment intended to destroy it.

Key results

The previously isolated *virB* region of *B. suis* strain 1330 contains 12 genes - *virB1* - *virB12*. Boschiroli *et al*. showed that transcription of all 12 genes is controlled by the same promoter, demonstrating that these genes are indeed part of the *virB* operon. No *vir* genes were found either immediately upstream of *virB1* or downstream of *virB12*. A mutation in *virB1* had an effect on the expression of the downstream *virB* genes, suggesting that no internal promoters were present. In contrast to mutations upstream of *virB1* and downstream of *virB12*, a mutation in *virB12* had a severe effect on survival and multiplication in macrophages and HeLa epithelial cells. To study *virB* promoter activity, a

plasmid carrying a transcriptional fusion between the putative *virB* promoter and a gene encoding green fluorescent protein (GFP) was introduced into *B. suis*. Using fluorescence-activated cell sorting, Boschiroli *et al.* showed that the *virB* promoter is not activated in free-living bacteria, but is specifically activated soon after infection of macrophage cell lines. One of the major induction stimuli was acidification for 3 hours to give a pH of 4. When phagosomal acidification was blocked, no activation of the *virB* promoter after infection could be observed. It has also recently been shown by other workers that phagosome acidification is required for intracellular multiplication of *B. suis*.

Links

Determination of the entire genome sequence of *B. suis* is in progress and can be followed at the NCBI Microbial Genomes page

Reporter's comments

Boschiroli *et al*. showed that the *virB* operon of *B. suis* is specifically activated shortly after infection in macrophages or epithelial cell lines and that this activation is dependent on the phagosomal acidification that occurs rapidly after infection. This is a convincing example of how *B. suis* adapts to the new environmental conditions within the host cell. As Boschiroli *et al*. indicate, the next step will be to identify the virulence factors secreted by the *virB* system. If the *virB* system of *B. suis* is involved in the secretion of particular proteins, comparative proteomics might be helpful to determine these virulence factors, now that the induction conditions for the *virB* operon are well described. Once the genome sequence of *B. suis* is available, microarray-based analysis can be used to discover other genes whose expression is induced by low pH. Characterization of virulence factors secreted by the *virB* system and proteins produced upon acidification of the environment will be a significant step towards unraveling how *B. suis* influences processes in the host cell and, consequently, to finding ways to block the early stages of infection.

Table of links

Proceedings of the National Academy of Sciences of the United States of America

NCBI Microbial Genomes

References

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