TYPE III SECRETION

MxiC: the gatekeeper

A recent paper in *Molecular Microbiology* sheds new light on the involvement of MxiC in the regulation of secretion through the *Shigella flexneri* type III secretion system (T3SS).

Bacterial T3SSs consist of a hollow needle that spans the bacterial inner and outer membranes and penetrates the host cell membrane following the formation of a translocator pore, and they are used to deliver secreted effectors directly into the eukaryotic host cell cytoplasm. Many of the details of the structure and assembly of T3SSs and the actions of their secreted effectors have been elucidated, but surprisingly little is known about the regulation of effector secretion. What is known is that, under the appropriate environmental conditions, a functional secretion device is built but effector secretion is blocked until the needle tip complex contacts the host cell membrane and an activation signal is detected.

Isabel Martinez-Argudo and Ariel Blocker were interested in what blocks *S. flexneri* effector secretion until detection of the activation signal. Previously, MxiC was identified as a *S. flexneri* 'gatekeeper' protein that negatively regulates T3SS activity. In agreement with previous results, the authors found that the absence of MxiC led to the constitutive secretion of effectors but, in contrast to earlier data, the secretion of the *S. flexneri* translocator proteins IpaB, IpaC and IpaD, which constitute the translocator pore, was impaired. MxiC therefore seems to be a negative regulator of effector secretion and a positive regulator of translocator release. A specific class of *S. flexneri* needle mutants can secrete translocators but not effectors. Analysis revealed that the effector secretion blockage in these mutants is due to a lack of MxiC secretion and that MxiC is released only after translocator secretion has been triggered. Further analysis of the secretion phenotypes of a range of double mutants demonstrated that the needle has a crucial role in transmitting a signal that controls MxiC release.

The authors propose a model for *S. flexneri* type III secretion regulation involving two activation signals. The first indicates that contact with the host cell membrane has occurred and stimulates translocator secretion, and the second releases MxiC, facilitating effector secretion. The identity of both signals is unknown and remains one of the key outstanding questions in T3SS research.

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ORIGINAL RESEARCH PAPER
Martinez-Argudo, I. & Blocker, A. J. The *Shigella* T3SS needle transmits a signal for MxiC release, which controls secretion of effectors. *Mol. Microbiol.* 11 Oct 2010 (doi: 10.1111/j.1365-2958.2010.07413.x)

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