**Online links**

HtrA
http://us.expasy.org/uniprot/Q99XG9

SpeB
http://us.expasy.org/uniprot/P0C0J0

*Streptococcus pyogenes*
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj&cmd=Retrieve&dopt=Overview&list_uids=12327

BACTERIAL SECRETION

# Specialized ExPort

Gram-positive microorganisms face a unique challenge when it comes to protein folding and secretion. Although all microorganisms lack the endoplasmic reticulum (ER) found in eukaryotes, Gram-negatives have a periplasmic space where nascent polypeptides can be folded before secretion. This space is lacking in Gram-positives, and the mechanisms these organisms use to ensure that their vast quantities of secreted proteins are folded correctly have been largely unknown until recently.

In the streptococci, it was known that, although only the general secretory (Sec) pathway is present, secretion is a complex process that involves chaperones and accessory factors. In addition, the existence of a putative secretion microdomain in *Streptococcus pyogenes* was first revealed by Jason Rosch and Michael Caparon in *Science* last year. Then, immunogold electron microscopy showed that SpeB — a cysteine protease, and one of the most abundant *S. pyogenes* secreted proteins — was localized to a discrete location at the cell hemisphere. Given that they also detected a high concentration of Sec translocons in this area, Rosch and Caparon proposed that this location was a specialized microdomain for protein export, which they termed the ExPortal.

Now, in a paper available online in *Molecular Microbiology*, Rosch and Caparon have undertaken a more detailed analysis of the ExPortal, providing evidence to support their suggestion that it provides a specialized environment in which newly formed proteins can interact with chaperones and accessory proteins. Their recent experimental work has focused on HtrA (DegP), an extracellular serine protease also known to function as a chaperone for several *S. pyogenes* secreted proteins, including SpeB. Using immunoelectron microscopy, it was found that the distribution of HtrA on the streptococcal surface was similar to the distribution of the ExPortal — clustered at a single discrete location distal from both cell poles. Further work showed that HtrA co-localizes with SpeB, providing evidence that the ExPortal provides an environment in which chaperones and substrates can interact.

Previous work had shown that both the proteolytic and chaperone functions of HtrA can be involved in protein folding and maturation. Here, Rosch and Caparon found that the serine-protease activity of HtrA was crucial for SpeB maturation, although they did not show directly that HtrA acts on SpeB. It was also found that HtrA must be anchored in the membrane at the ExPortal to function in SpeB maturation.

Unlike Gram-negatives, which can contain up to five different secretion systems, the streptococci encode only the Sec system, and the discovery that the Sec apparatus was concentrated into a single location — the ExPortal — rather than being evenly distributed on the cell surface was perhaps contrary to expectations. However, Rosch and Caparon have now shown that the ExPortal might provide the streptococci with the functional equivalent of the periplasm or ER, allowing a subset of nascent polypeptides to mature and fold correctly before secretion.

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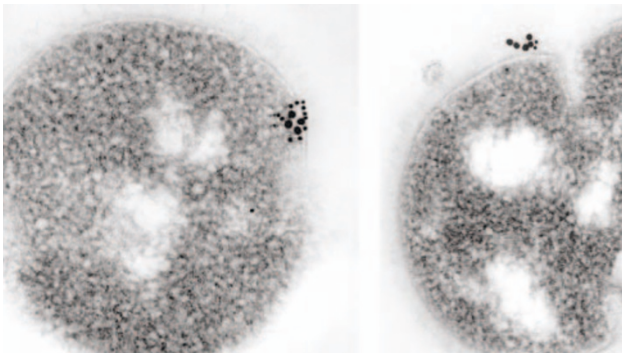

Immunogold electron micrographs showing the co-localization of HtrA tagged at the C terminus (18-nm beads) and SecA (12-nm beads). Reproduced with permission from *Molecular Microbiology* © (2005) Blackwell Publishing.

## References and links

**ORIGINAL RESEARCH PAPER** Rosch, J. W. & Caparon, M. G. The ExPortal: an organelle dedicated to the biogenesis of secreted proteins in *Streptococcus pyogenes*. *Mol. Microbiol.* Sep 2005 (doi:10.1111/j.1365-2958.2005.04887.x)
**FURTHER READING** Rosch, J. & Caparon, M. A microdomain for protein secretion in Gram-positive bacteria. *Science* **304**, 1513–1515 (2004) | Campo, N. *et al*. Subcellular sites for bacterial protein export. *Mol. Microbiol*. **53**, 1583–1599 (2004)