BACTERIAL PHYSIOLOGY

LPS IMPort

The mechanism by which lipopolysaccharide (LPS) is synthesized in the inner membrane of Gram-negative bacteria has long been understood. However, how it is transported to the outer membrane has remained unknown. Now, reporting in *Proceedings of the National Academy of Sciences*, Martine Bos and co-workers have identified an outer membrane protein, Imp (for increased membrane permeability), as responsible.

Previous work has shown that, unlike *Escherichia coli*, LPS is not an essential component of *Neisseria meningitidis* outer membranes, and for this reason, the authors used *N. meningitidis* to study the effects of Imp on LPS transport. Using the completed genome sequence of *N. meningitidis*, the authors identified the *N. meningitidis imp* gene and constructed an Imp-deficient mutant. SDS–PAGE analysis showed that, although the cellular content of LPS was reduced in these mutants relative to the wild type, the synthesized LPS was structurally unaltered.

The authors demonstrated that, when grown in the presence of CMP-NANA (which sialylates LPS) and treated with neuramidinase (which removes the sialic acid group), only a small fraction of the LPS of Imp-deficient cells is desialylated, indicating that LPS is not accessible on the surface of these mutants. This was further supported by expression in the mutant cells of the enzyme PagL, which covalently modifies LPS within the outer membrane; electrophoretic analysis of LPS showed that it had not been modified by this enzyme.

Although the authors have, as yet, been unable to identify the precise location of LPS in *imp* mutants, they have shown that it is not localized at the outer leaflet of the outer membrane, and they postulate that Imp is the transporter that mediates transport of LPS over the outer membrane.

Jane Saunders

References and links

ORIGINAL RESEARCH PAPER Bos, M. P. *et al.* Identification of an outer membrane protein required for the transport of lipopolysaccharide to the bacterial cell surface. *Proc. Natl Acad. Sci. USA* **101**, 9417–9422 (2004)

WEB SITE

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VIRAL PATHOGENESIS

Virulence beyond translation

New research published in the *Journal of Clinical Investigation* challenges a widely held opinion that poliovirus tropism for the brain, spinal cord and other tissues, and attenuation of the Sabin vaccine strain are mediated at the level of viral RNA translation.

Previous work has shown that poliovirus tropism and pathogenesis are determined by events that occur after the virus has entered a cell and that the cell-type-specific differences observed are linked to the virus internal ribosome entry site (IRES; a noncoding genomic element that allows the internal binding of ribosomes in a 5′ end and cap-independent manner). Indeed, analysis of attenuated and neurovirulent polioviruses has provided substantial evidence for the role of the IRES in poliovirus biology, leading to the interpretation that alterations in the IRES reduces viral RNA translation in attenuated poliovirus strains, and in host cells that are not neuronal in origin. In their study, Steven Kauder and Vincent Racaniello set out to formally test this hypothesis. Using bicistronic reporter genes, the authors were able to demonstrate that poliovirus IRES-dependent translation occurred in many organs, including those that do not normally support poliovirus replication. The authors were further able to show that in a transgenic mouse model of poliomyelitis, poliovirus containing the substituted IRES retained the wild-type tropism for the brain and spinal cord. Replication was also observed in these tissues even after the introduction of a single point mutation (C472U) into the IRES, which is a mutation thought to be an important determinant of poliovirus attenuation of neurovirulence. Interestingly, in polioviruses with this mutation, neurovirulence and paralysis were only observed in newborn mice.

In combination, these results clearly demonstrate that the tropism of wild-type and vaccine strains of poliovirus do not operate primarily at the level of IRES-mediated translation initiation but at a later, post-tanslational, stage of the intracellular virus life cycle. These conclusions differ from those derived from previous *in vitro* and *ex vivo* analyses which, as the authors point out, reinforce the concept that the ultimate outcome of any viral infection is the result of a complex interplay between virus and host.

David O'Connell

References and links

ORIGINAL RESEARCH PAPER Kauder S. E. & Racaniello V. R. Poliovirus tropism and attenuation are determined after internal ribosome entry. *J. Clin. Invest*. **113**, 1743–1753 (2004)

WEB SITE

Vincent Racaniello's laboratory: http://cumicro2.cpmc.columbia.edu/Micro_Files/Racaniello_Lab.html