domain of Hia is not cleaved and remains attached to the translocator domain and, in contrast to the NalP structure, the HiaBD1 structure reveals a novel trimeric arrangement of individual HiaBD1 subunits, which has implications for the virulence of *H. influenzae* as it could enable multivalent interactions with the host cell. Sequence comparisons indicate that HiaBD1 is a member of a new subfamily of autotransporters in which both the passenger and translocator domains trimerize.

These studies provide clues as to the mechanisms and role of two autotransporters; however, further research is needed to determine not only if they do indeed represent two distinct classes of autotransporters, but also if the Omp85 complex is involved.

Jane Saunders

References and links

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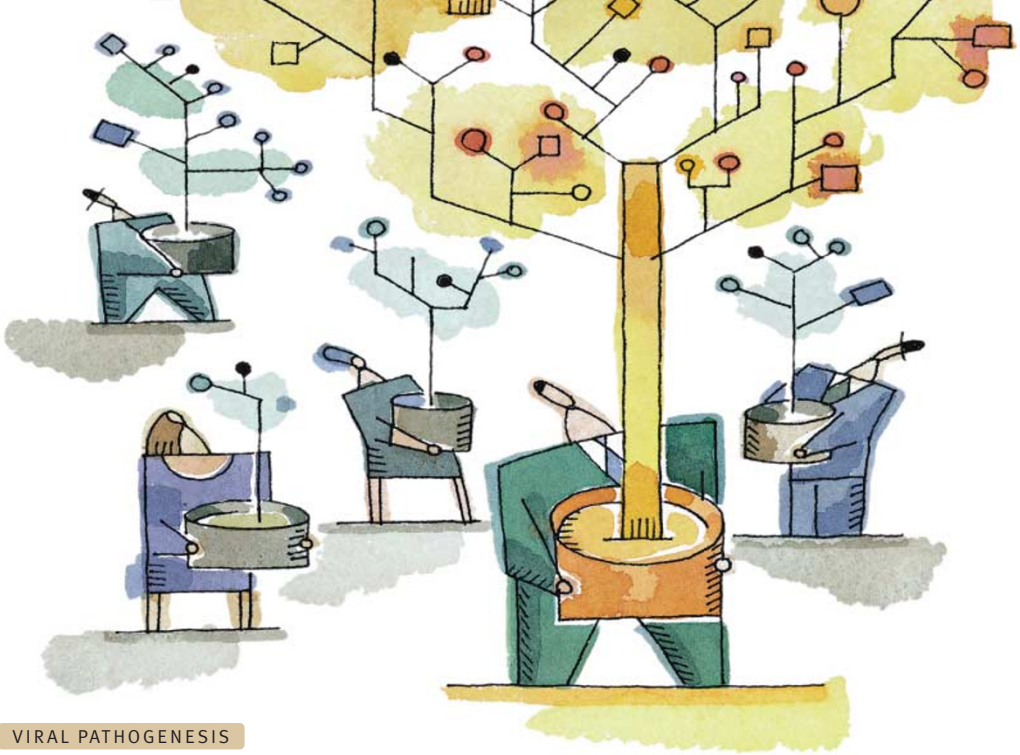

VIRAL PATHOGENESIS

Strategic comparisons

Studies of viral pathogenesis in model hosts, such as rodents, are often extrapolated to humans. But are the pathogenic strategies of viruses in different cell types really comparable? A study just published in the *Journal of Virology* tackles this question using a global transcriptome approach.

Pseudorabies virus (PRV) and herpes simplex virus type 1 (HSV-1) are α-herpesviruses, which, despite low overall sequence identity, have conserved genome organization, virion structure and replication cycles. PRV infects pigs and HSV-1 infects humans — in both cases only mild symptoms occur. PRV cannot infect humans, and HSV-1 cannot infect pigs, but both viruses infect rodents, with lethal effect. Because the replication cycles in human, porcine and rodent cells are similar, and because viral strains that are attenuated in the natural host are also attenuated in rodents, pathogenic mechanisms could be conserved.

Ray and Enquist used transcriptome studies of PRV and HSV-1 infection of rodent cells to ask a simple question. Do these viruses exploit the same cellular pathways to generate a productive infection? Surprisingly, of the ~1,500 transcripts affected following infection, only 32% were common to PRV and HSV-1. Key observations included changes in oxidative-stress gene transcription late in both PRV and HSV-1 infection — which could underline the important role of managing oxidation in a productive viral infection. Strikingly, heat-shock-stress genes were also affected late in infection. Perhaps the host cell sounds the alarm to galvanize the immune system into action to prevent virus spread. The P13K/Akt signalling pathways were both affected by PRV and HSV-1. These pathways encode proteins that can aid cell survival or activate apoptosis, and balancing their activity could fine-tune the outcome of virus infection. Surprisingly, while HSV-1 modulated the expression of interferon- and interleukin-regulated genes, PRV had no effect on the same pathways, which might be an important clue to help to delimit the pathogenic strategies of these viruses in rodents. One caveat is that the transcriptome only tells us about RNA levels, but both PRV and HSV-1 express proteins that regulate mRNA stability, transport and translation, which could affect protein production.

What about transcriptional responses to α-herpesvirus infection in other cell types? The rodent cell data for HSV-1 infection were compared with data gathered following infection of human cells with HSV-1 in a different study. A core set of 29 genes that were affected in both studies was defined. Of these, 12 genes were also regulated during PRV infection of rodent cells. Does this represent an α-herpesvirus host-cell signature?

Responses to viruses early in infection could prevent a productive infection from developing. But late responses might also be important. After all, the virus must spread to cause disease. This comparative study lays the foundation for an examination of α-herpesvirus-regulated genes, the differences between permissive and non-permissive hosts, and the role of late host responses in virus infection.

Susan Jones

References and links

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