225, respectively, positions the α2,6-linked sialic acid of a human receptor lower in the HA receptor-binding site then the α2,3-linked sialic acid of an avian receptor. This, in turn, allows Asp190 and Lys222 to form interactions with the receptor, forming a network of interactions between 1918HA residues and human receptors.

These analyses provide important insights into the interactions between HAs and human receptors, and reveal the residues that enable 1918HA to interact with human receptors. All human influenza viruses responsible for major epidemics — including the virus responsible for the 1918 influenza pandemic — are believed to be of avian origin. Although based on a now extinct influenza virus, these analyses could be used to design anti-influenza agents and vaccines to help prevent outbreaks of viral diseases such as avian influenza in humans.

Jane Saunders

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WEB SITES

Steve Gamblin's laboratory: http://www.nimr.mrc.ac.uk/protstruct/gamblin/

Ian Wilson's laboratory: http://www.scripps.edu/mb/wilson/

mature biofilms formed by *rhlR*/*lasR* mutant bacteria was very efficient. As the RhlR/LasR quorum-sensing systems are known to regulate the expression of several toxins, these findings indicate that quorum-sensing-mediated toxin production in mature biofilms is an effective mechanism that allows *P. aeruginosa* to resist protozoan feeding.

In conclusion, the authors have convincingly shown that the formation of microcolonies in the early stages of biofilm development, the production of toxins at later stages, and the regulation of these processes by cell-to-cell communication combine to promote resistance of *P. aeruginosa* to ingestion by protozoan predators. This protection mechanism might also partly explain the widespread presence of this microorganism, and its persistence in both natural and clinical environments.

David O'Connell

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WEB SITE

Centre for Marine Biofouling and Bio-Innovation, University of New South Wales: http://www.babs.unsw.edu.au

BACTERIAL VIRULENCE

Not quite as easy as ABC…

The development of direct genetic analysis techniques for *Borrelia burgdorferi* is now beginning to give researchers an insight into the specific functions of this spirochete's outer membrane proteins, as three recent publications have shown.

The life cycle of *B. burgdorferi*, the aetiological agent of Lyme disease in the United States, is divided between mammals and *Ixodes scapularis* ticks. The ticks ingest spirochetes from an infected mammalian host (commonly the white-footed mouse). *B. burgdorferi* colonizes the tick mid-gut and remains in a latent state until the tick matures and begins feeding. *B. burgdorferi* then migrates from the tick mid-gut to the salivary glands, from where it can be transmitted into a new host.

To survive in such different environments, *B. burgdorferi* has an extensive repertoire of cell-surface lipoproteins. Until recently, the paucity of direct genetic analysis techniques has hampered the investigation of the precise functions of these proteins. However, three groups have now used direct genetic analysis in *B. burgdorferi* and have recently reported their results.

Yang *et al*. targeted the *ospA/B* gene. Analysis of the infectivity of the resulting deletion mutant in mice and ticks showed that, although OspA/B is not essential for *B. burgdorferi* to colonize mice, it is essential for colonization of the tick mid-gut.

In a separate study, also a collaboration between Michael Norgard and Erol Fikrig's groups, the gene encoding another outer surface protein, OspC, was disrupted. In ticks, immunoelectron microscopy showed that an OspC deletion mutant was unable to bind to tick salivary glands, supporting earlier thinking that OspC is involved in the migration of *B. burgdorferi* from the mid-gut to the salivary glands. However, in a third study, this time from Patricia Rosa's group, in which *ospC* was also disrupted, although OspC was found to be essential for *B. burgdorferi* to infect mice, the opposite result was obtained for the analysis in ticks, with the OspC deletion mutant able to migrate to the salivary glands.

The different experimental designs could account for these different results. One major difference that is apparent between the two studies is the method used to artificially infect ticks with *B. burgdorferi* — Pal *et al*. used direct microinjection into the mid-gut, whereas Grimm *et al*. infected naive ticks by immersion in exponential-phase cultures of *B. burgdorferi*. Additionally, Pal *et al*. deleted the entire *ospC* gene, whereas in the work of Grimm *et al*., *ospC* was disrupted rather than deleted. Finally, migration to the salivary glands and transmisson to mice were assessed at different times post-tick infection.

The availability of techniques for the effective genetic manipulation of *B. burgdorferi* is an exciting development for the field. However, it is clear that, even once these techniques are available, teasing out the roles of specific proteins in the complex life cycle of this spirochete will be far from easy.

Sheilagh Clarkson

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