Editorial

Progress towards understanding the pathology of the pneumococcus

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Despite the introduction of the childhood pneumococcal vaccines in 2000 and their next-generation successors in 2010, pneumonia remains the leading infectious cause of death in children less than 5 years of age. Similarly, pneumococcal infections in the elderly and immunocompromised continue to represent a significant healthcare burden; abatement is unlikely given expanding elderly populations, particularly in Western countries.

The 12th European Meeting on the Molecular Biology of the Pneumococcus (EuroPneumo) held in July 2015 in Oxford was attended by 174 scientists from 20 countries and provided an excellent forum for consideration of these and other issues relating to pneumococcal disease. The conference covered the whole range of *Streptococcus pneumoniae* biology, ranging through basic bacterial processes (e.g. cell wall synthesis), structural biology, antibiotic resistance and novel treatment approaches, understanding host–pathogen interactions during carriage and disease, the use of "–omics" technologies to characterise pneumococcal diversity, molecular epidemiology, immunology and novel vaccine development. The conference abstracts published in this issue support the continued research focus around *S. pneumoniae* to inform improved treatment and management of pneumococcal disease in at risk populations.

As an encapsulated diplococcus, the nearly 100 identified *S. pneumoniae* serotypes represent a considerable source of antigen diversity that remains a challenge in vaccine development. While pneumococcal disease has been attributed to a limited number of dominant serotypes, patterns of carriage and serotype replacement post-vaccination continue to be documented, particularly in developing nations and geographically isolated populations. Ongoing characterisation of serotype switching remains important for further vaccine evolution and presented data revealed options to pursue further in this context. Of particular interest were the data relating to serotype-independent whole-cell vaccines [1,2] and the development of an experimental pneumococcal human colonisation model for assessing vaccine efficacy [3], which also offers promise in the assessment of host–pathogen interaction.

The role of the polysaccharide capsule as a major virulence factor of *S. pneumoniae* underpins ongoing efforts to better understand regulation of capsule synthesis. However, non-encapsulated pneumococcal infection can cause mucosal infection, and data presented at the conference suggested the virulence of these strains is dependent on protein adhesins [4]. Other determinants of streptococcal virulence also continue to receive attention, including an elegant characterisation of the molecular interactions between microbial pili and the host extracellular matrix using atomic force microscopy [5]. The biological relevance of the substantial amount of genome variation between *S. pneumoniae* strains remains unclear; hence characterisation of phage-mediated genomic alterations in *S. pneumoniae* [6,7] was of particular interest and perhaps an important component driving *S. pneumoniae* evolution over time and associated variation in pathogenicity between strains.

Further insights into pneumococcal virulence may also be garnered from consideration of the host–pathogen interaction in both stable carriage and

overt pneumococcal disease. Increasing data demonstrate an important role of the respiratory microbiome in shaping local immune responses to *S. pneumoniae* at the mucosal surfaces [8], and these effects are likely to have wide-reaching consequences during carriage and disease development. The importance of the interplay between both bacterial and host factors in determining virulence was nicely demonstrated through the reported use of the less pathogenic *S. mitis* to assess host response in comparison to *S. pneumoniae* [9]. Likewise, the potential for the *S. pneumoniae* toxin pneumolysin to subvert the early host inflammatory response [10,11] and cause direct cardiac damage [12] confirms that bacterial-mediated disruption of host cells can also be a key determinant in the pathogenesis of infection.

After a conference with such varied content, what can we conclude about future directions for research into *S. pneumoniae*? Firstly, *S. pneumoniae* biology remains a highly energetic and innovative field with an increasing rate of novel and exciting discoveries. Secondly, and perhaps paradoxically, the more we learn about *S. pneumoniae* the more apparent it becomes how much more we need to know. For example, genome sequencing has identified much larger genetic variation between strains than expected [13], and the effects of the microbiome has added an additional layer of complexity to assessing host immunological responses to *S. pneumoniae* [8]. Considerably more research will be required if we are to state with confidence why *S. pneumoniae* is a highly successful pathogen and before we learn how to prevent it from causing such a huge level of morbidity and mortality across the globe.

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