EPIDEMIOLOGY

Promiscuous bacteria have staying power

Being able to take up DNA from their environment might allow pneumococcal bacteria to colonize the human nose and throat for longer periods of time.

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Streptococcus pneumoniae is a notorious bacterial pathogen hiding in plain sight. A common resident of the nose and throat, between 68% and 84% of young infants will carry this species at any given time (Turner et al., 2012). In most cases it causes no harm, yet the presence of pneumococci – as the bacteria are known – can predispose a person to life-threatening infections like pneumonia or meningitis. Indeed, pneumococci are responsible for around 10% of all deaths in young children around the world (O’Brien et al., 2009), with the vast majority of cases being in developing countries.

Research into S. pneumoniae is complicated because the species is a patchwork of distinctive strains and some of these strains remain in the nose and throat for longer than others. Now, in eLife, John Lees and Stephen Bentley – both at the Wellcome Trust Sanger Institute – and colleagues report that strains rendered impotent by a virus do not linger for as long as other strains (Lees et al., 2017).

Different pneumococci can be placed into groups called serotypes, based on the properties of their protective outer coating. Pneumococcal vaccines target the most harmful serotypes and vaccination reduces both the frequency of disease and symptomless colonization (Scott et al., 2012). People who are colonized often, or are colonized for long periods, have a greater risk of life-threatening infection (Simell et al., 2012). While the different serotypes were known to, on average, colonize people for different lengths of time (e.g. Abdullahi et al., 2012; Turner et al., 2012), it was not well understood how other factors such as the genetic background of the strain or its individual genes contributed to this variation in the duration of colonization.

Lees et al. focused on a high-risk population of infants from Maela, a camp near the Thailand-Myanmar border that provides refuge to more than 45,000 displaced people. Around one in four children in the camp developed bacterial pneumonia each year, with very severe pneumonia in around 8% of cases (Turner et al., 2013).

Using a combination of whole genome sequencing and sophisticated statistics, Lees et al. analyzed over 14,000 nose swab samples collected from almost 600 children in the camp over a two-year period (Figure 1). First, they removed noise from the epidemiological data to allow for the fact that the limited sensitivity of tests can make it appear that a continued episode of colonization is instead a series of shorter episodes. Second, they used statistics to determine how much a number of different variables – ranging from the age and infection history of
the child to the serotype and genetic background of the bacteria – could explain the observed variability in the length of time the children remained colonized. Finally, they searched the genomic data to look for any links between individual genetic elements in the bacteria and the duration of colonization.

The most striking finding reported by Lees et al., however, owes more to lateral thinking than state-of-the-art statistics. Faced with a difficult-to-interpret association between duration and a rare version of a housekeeping gene in the bacteria, they reassessed their data. The housekeeping gene in question is found in some phages (viruses that infect bacteria), so the researchers asked whether phage integration in general was associated with the duration of colonization. Others have also argued that bacterial promiscuity protects directly against phage infection itself (Croucher et al., 2016). But whatever the selective forces resulting in the association between the phage and prolonged duration of colonization, this work provides compelling evidence in support of the benefits of bacterial promiscuity.

Lees et al. – who are based at the Sanger Institute, Imperial College London, University College London, Oxford University and Mahidol University – also provide a timely example of the potential of genome wide association studies to uncover new links between genotypes and phenotypes in bacteria. This is particularly heartening in view of the challenges posed by clonal reproduction in bacteria, which normally makes it difficult to tease apart the effects of individual genes in this kind of observational study (Earle et al., 2016). With the arrival of studies into important traits related to human health and disease that are not readily studied in the laboratory (e.g. Recker et al., 2017), we are now entering a new era of discovery into the genomic basis of diverse bacterial traits.

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