

Genomics empowers vaccine makers to tackle shapeshifting bacteria

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A pioneering genomic surveillance study has provided the clearest picture yet of the arms race between *Streptococcus pneumoniae*, the bacterium responsible for a range of illnesses such as pneumonia and meningitis, and the vaccines designed to protect against the most dominant types. A strain called GPSC10 was found to be a particular threat, due to its increased virulence, ability to transform its structure to

evade vaccines and its resistance to several common antibiotics.

The study, published today (16 August) in *Lancet Microbe*, was led by the Wellcome Sanger Institute, National Reference Center for Pneumococci, France, and Hospital Sant Joan de Deu, Spain, as part of the Global Pneumococcal Sequencing (GPS) project. The findings demonstrate the value of genomic surveillance to inform [vaccine design](#) and highlight the challenge posed by 'shapeshifting' strains like GPSC10.

Streptococcus pneumoniae, also known as the [pneumococcus](#), is a bacterial pathogen that causes diseases ranging from ear infections through to pneumonia, septicaemia and meningitis. It is responsible for around nine million global infections annually, with elderly adults and children particularly susceptible. More than 300,000 children die from pneumococcal infection each year, mainly in low- and [middle-income countries](#) (LMICs).

Since 2000, a series of pneumococcal conjugate vaccines (PCVs) have been deployed that have targeted *S. pneumoniae* serotypes responsible for most disease cases in infants, resulting in a reduction in disease worldwide. Currently, PCV-13 targets 13 serotypes and PCVs targeting up to 25 serotypes are in development. However, there are more than 100 distinct serotypes, and they can affect children and adults in different ways. Knowing which serotypes to target with the PCVs, and what the likely impact will be on disease and the wider pneumococcal population, is vitally important when designing effective global vaccination strategies.

Through the work of the GPS project since 2011, a picture of the *S. pneumoniae* serotypes in circulation has been built up that allows trends in the bacterial population to be identified. One [serotype](#), 24F, has been on the rise, as documented by the National Reference Center for Pneumococci, France and many other countries such as Canada,

Denmark, Germany, Israel, Italy, Japan, Lebanon, Norway, Spain, and UK.

In this new study, scientists from the Wellcome Sanger Institute performed [whole-genome sequencing](#) on 419 samples of *S. pneumoniae* serotype 24F, collected from individuals in France between 2003 and 2018 by the National Reference Center for Pneumococci (NRCP) and Association Clinique et Therapeutique Infantile du Val-de-Marne (ACTIV), and on 91 pneumococcal serotype 24F isolates collected from individuals in Spain by the Hospital Sant Joan de Deu. To provide a global comparison, an international collection of other *S. pneumoniae* genomes were added from the Global Pneumococcal Sequencing (GPS) project database.

Dr. Stephanie Lo, first author of the study from the Wellcome Sanger Institute, said: "In a microbiology lab, classifying strains and testing for drug resistance are time consuming and resource intensive. Whole genome sequencing can now reliably infer serotype and antibiotic resistance profiles, identify where outbreaks might be occurring and track which strains mediate serotype replacement. So it's one test that can answer a lot of different questions."

Analysis showed that 24F was present in many countries largely due to the spread of three strains: GPSC10, GPSC16 and GPSC206. One strain in particular, GPSC10, was responsible for the rapid increase in 24F in France around four years following the introduction of PCV-13. It was found to have high disease potential and be resistant to multiple antibiotic treatments.

These findings support recent research that showed that GPSC10 drove the increase in 24F after the introduction of PCV-13 in Spain, and that 24F is one of the most frequent causes of pneumococcal disease in children in different countries. In India, the country estimated to have

the largest burden of pneumococcal disease, researchers have predicted that GPSC10 has the potential to evade PCV-13. These and other studies from GPS partners across the globe are collected in an issue of *Microbial Genomics*.

Perhaps the biggest concern arising from the study was GPSC10's ability to express 17 different serotypes, only six of which are included in current PCV vaccines.

Dr. Emmanuelle Varon, a senior author of the study from the National Reference Center for Pneumococci, Centre Hospitalier Intercommunal de Créteil, France, said: "The *Streptococcus pneumoniae* strain GPSC10 is something of a shapeshifter, able to express a wide range of serotypes and multidrug resistance patterns. Surveillance on pneumococcal disease, such as that implemented in France since 2001, is our best tool to evaluate the impact of vaccine policies and will allow us to detect the emergence of other non-vaccine serotypes."

To some extent, the evolutionary [arms race](#) between pathogens and vaccine makers is inevitable. If one strain dies out because it has been targeted by a vaccine, other strains may rise to take its place. A strain may also evolve sufficiently that vaccines cease to be effective against it. The important thing is that [vaccine](#) makers and public health organisations have the best information with which to keep pace and, ultimately, to save lives.

Professor Stephen Bentley, a senior author of the study from the Wellcome Sanger Institute, said: "It's exciting that genomic surveillance now allows us to have a real impact on improving pneumococcal vaccines and, most importantly, helping to reduce the number of children who die from related illnesses in low- and middle-income countries. The whole Global Pneumococcal Survey consortium should also be proud of the huge collaborative effort that has gone into

generating these data."

More information: Emergence of a multidrug-resistant and virulent *Streptococcus pneumoniae* lineage mediates serotype replacement after PCV13: an international whole-genome sequencing study, *The Lancet Microbe* (2022). [DOI: 10.1016/S2666-5247\(22\)00158-6](https://doi.org/10.1016/S2666-5247(22)00158-6)

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