

Pathogen genomics leading to vaccines

In the field of infectious diseases, genomics can be a useful tool for guiding vaccine development. Given the inevitability and increasing prevalence of antibiotic resistance, vaccines against pathogenic microbes can be even more valuable than antibiotics as a strategy to prevent serious or deadly infectious diseases. Genomic resources from global analysis of large numbers of clinical isolates can serve as a basis for identifying appropriate candidates for vaccine antigens, and we encourage continued efforts in the generation of pan-genome sequences for bacterial or viral pathogens.

Vaccines are one of the most amazing advances in public-health improvement in human history and have revolutionized how we experience childhood and infectious diseases. There are generations of people who have never known another person to have particular diseases, such as polio. With the complexities of the immune system and the rapid evolution of bacterial or viral agents, the successful development and implementation of vaccination for a particular pathogen is a remarkable accomplishment. Global collection and genome sequence analyses of large numbers of clinical isolates have been increasingly realized, and genomics can serve as an informed guideline for selecting vaccine candidates with the highest likelihood of success. We are excited for the utilization of large-scale pathogen genomics and infectious-disease pan-genome analysis in vaccine development strategies.

Encouragingly, in this issue, [Davies et al.](#) analyzed more than 2,000 group A *Streptococcus* (*Streptococcus pyogenes*) genomes, examined the variation in identified vaccine antigen candidates and identified new potential candidate genes encoding putative vaccine antigens. Strong vaccine candidates would be ubiquitous across strains and have low levels of

variation. The authors found that 13 out of 28 antigens were carried in almost all strains and had only low sequence diversity. Taking advantage of the pan-genome approach, the authors were also able to identify novel candidate vaccine antigens through analysis of conserved core genes. Group A *Streptococcus* is a particularly illustrative example of the potential for genomics to aid in vaccine development. Currently, there is no commercial vaccine for this prevalent bacterial pathogen, which causes more than 700 million infections per year, more than 600,000 of which are serious invasive infections. Additionally, immune reaction can lead to acute rheumatic fever or glomerulonephritis, and globally, group A *Streptococcus* is among the top ten causes of death from infectious disease. This particular pathogen has been recalcitrant to vaccine development, owing to antigen variation, strain diversity and challenges stemming from immunologically related consequences of infection. In this case, because of the global genetic diversity of *S. pyogenes* strains, a large-scale genomics approach was needed to analyze both the presence and the absence of putative vaccine candidates, as well as the sequence variation of the antigens. Thus, only by taking this global, pan-genome approach to the analysis were the authors able to

refine the list of potentially successful vaccine candidates.

Genomic analysis, of course, is only an early initial screening step to identify factors that are sufficiently present across strains and conserved at the genetic level to be appropriate for further characterization. Much further work is required to test and validate the safety and efficacy of infectious-disease vaccines in animal models and clinical trials. Even so, global genomic approaches to screen for potential vaccine candidates can be a powerful way to increase the chance of success, particularly for pathogens for which vaccines do not exist.

Although the public-health burden of infectious diseases in general has been mediated by both vaccine implementation and antibiotic treatment, rising threats, such as the development of resistance or the emergence of new strains, should temper any complacency and ensure vigilance. Genomics methods can be harnessed as a powerful weapon to keep humanity on the winning side of the infectious-disease battle, and we are encouraged to see analyses of pathogens on a truly worldwide scale being increasingly pursued. □

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