

A genomic approach to microbiology

This Focus issue highlights how high-throughput sequencing technologies have revolutionized the microbiology research field and their emerging impact on clinical practice.

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Since the publication of the first complete bacterial genomes almost a quarter of a century ago, genomics has transformed the field of microbiology. Accompanied by reductions in cost, technical advances in sequencing technologies and new computational developments have markedly increased the number of available microbial genomes. Genomic analyses are yielding unprecedented insights into microbial evolution and microbial diversity and are elucidating the extent and complexity of the genetic variation in both host and pathogens that underlies disease. The emerging application of genomic technologies in the clinic to combat infectious diseases is transforming clinical diagnostics and the detection and surveillance of outbreaks. The articles in this Focus issue on microbial genomics and its accompanying online collection highlight the role of high-throughput sequencing, also known as next-generation sequencing, in these and other areas.

Chiu and Miller¹ introduce metagenomic next-generation sequencing and emphasize how this technology is being leveraged for clinical purposes, from infectious disease diagnostics and human microbiome analyses, to host response analyses using RNA sequencing, and applications in oncology. Importantly, the authors critically discuss why, despite its potential and recent successes, clinical metagenomics applications are lagging behind research advances and propose steps that may overcome existing hurdles to successful implementation in the clinical laboratory.

Boolchandani, D'Souza and Dantas² focus on one particular area of clinical metagenomics: the identification and characterization of antimicrobial resistance from sequence data. Antimicrobial resistance poses a major threat to public health, and both individual-level patient care and global strategies to control infections will benefit from a greater understanding of the prevalence, mechanisms and spread of antimicrobial resistance. Focusing on sequence-based discovery, this Review discusses the strengths and weaknesses of different computational strategies and resources for resistance gene identification in genomic and metagenomic samples, including recent deep-learning approaches.

Providing an in-depth view of pathogen evolution, Spyrou et al.³ review recent advances in ancient pathogen genomics, including methodological improvements

in retrieving whole genomes from ancient remains and evolutionary analyses of ancient pathogens that remain relevant to public health today. With a focus on the evolutionary history of the plague pathogen *Yersinia pestis*, the authors emphasize the unique insights afforded by the study of ancient pathogen genomes.

The online collection that accompanies this Focus issue includes articles from past issues that address a number of other areas that have experienced the transformative effect of genomics, including public health microbiology, which has seen sequencing used for the surveillance and monitoring of infectious disease outbreaks. Next-generation sequencing technologies, particularly portable sequencers, have shown great potential in the field, enabling rapid in situ diagnostics and real-time tracking of emerging pathogens. In a recent Comment article, Johnson and Parker⁴ emphasize the ethical, legal and social issues arising from sequencing infectious disease pathogens in both clinical and public health settings. Importantly, genomic research in developing countries, which often suffer most from infectious disease outbreaks, remains limited, and the authors highlight the need to build local capacities and develop globally compatible surveillance systems to ensure a more equitable distribution of the benefits that genomics bring.

Additional Reviews online cover evolutionary perspectives afforded by comparative genomics of great ape microbiomes; phylogenomic analyses of virus genome sequence data; population genomics of bacterial host adaptation; the impact of host genetic variation on the microbiome in disease; and microbial genome-wide association studies (GWAS).

What emerges is that microbiology research has made great strides through the application of genomic technologies. What also becomes evident is that rapid, unrestricted access to genome sequence data is a prerequisite for microbial genomics to lead to successful, transformative change to global and public health worldwide.

1. Chiu, C. Y. & Miller, S. A. *Nat. Rev. Genet.* <https://doi.org/10.1038/s41576-019-0113-7> (2019).
2. Boolchandani, M., D'Souza, A. W. & Dantas, G. *Nat. Rev. Genet.* <https://doi.org/10.1038/s41576-019-0108-4> (2019).
3. Spyrou, M. A. et al. *Nat. Rev. Genet.* <https://doi.org/10.1038/s41576-019-0119-1> (2019).
4. Johnson, S. B. & Parker, M. *Nat. Rev. Genet.* <https://doi.org/10.1038/s41576-019-0109-3> (2019).