146 Genomics and Infectious Disease

Roby P. Bhattacharyya, Yonatan H. Grad,
Deborah T. Hung

Just as microscopy opened up the worlds of microbiology by providing a tool with which to visualize microorganisms, technological advances in genomics are now providing microbiologists with powerful new methods with which to characterize the genetic map underlying all microbes with unprecedented resolution, thereby illuminating their complex and dynamic interactions with one another, the environment, and human health. The field of infectious disease genomics encompasses a vast frontier of active research that has the potential to transform clinical practice in relation to infectious diseases. While genetics has long played a key role in elucidating the process of infection and managing clinical infectious diseases, the ability to extend our thinking and our approaches beyond the study of single genes to an examination of the sequence, structure, and function of entire genomes is identifying new possibilities for research and opportunities to change clinical practice. From the development of diagnostics with unprecedented sensitivity, specificity, and speed to the design of novel public health interventions, technical and statistical genomic innovations are reshaping our understanding of the influence of the microbial world on human health and providing us with new tools to combat infection. This chapter explores the application of genomics methods to microbial pathogens and the infections they cause **(Table 146-1)**. It discusses innovations that are driving the development of diagnostic approaches and the discovery of new pathogens; providing insight into novel therapeutic approaches and paradigms; and advancing methods in infectious disease epidemiology and the study of pathogen evolution that can inform infection control measures, public health responses to outbreaks, and vaccine development. We draw on examples in current practice and from the recent scientific literature as signposts that point toward the ways in which the insights from pathogen genomics may influence infectious diseases in the short and long terms. **Table 146-2** provides definitions for a selection of important terms used in genomics.

MICROBIAL DIAGNOSTICS

The basic goals of a clinical microbiology laboratory are to establish the presence of a pathogen in a clinical sample, to identify the pathogen, and, when possible, to provide other information that can help guide clinical management and even prognosis, such as antibiotic susceptibility profiles or the presence of virulence factors. To date, clinical microbiology laboratories have largely approached these goals phenotypically by growth-based assays and biochemical testing. Bacteria, for instance, are algorithmically grouped into species by their characteristic microscopic appearance, nutrient requirements for growth, and ability to catalyze certain reactions. Antibiotic susceptibility is determined in most cases by assessing growth in the presence of antibiotic.

With the sequencing revolution paving the way to easy access of complete pathogen genomes **(Fig. 146-1)**, we are now able to more systematically clarify the genetic basis of these observable phenotypes. Compared with traditional growth-based methods for bacterial diagnostics that dominate the clinical microbiology laboratory, nucleic