

**TABLE 146-1 CURRENT CLINICAL APPLICATIONS OF INFECTIOUS DISEASE GENOMICS**

Application	Technology	Notes/Examples
<b>Organism Identification</b>		
Viral detection	PCR	Identification of HIV, HBV, HCV, respiratory viruses including influenza, and others for diagnosis and response to therapy
TB detection	PCR	Amplification of the <i>rhoB</i> gene for species-specific identification of <i>Mycobacterium tuberculosis</i>
Bacterial detection	PCR, NAAT	Identification of <i>Chlamydia</i> , <i>Neisseria gonorrhoeae</i> , <i>Clostridium difficile</i> , <i>Ehrlichia</i> , <i>Anaplasma</i> , and others
Bacterial detection	16S ribosomal gene PCR	Targeting of highly conserved regions of the 16S rRNA gene for identification of suspected bacterial infections undiagnosed by conventional methods
<b>Pathogen Discovery</b>		
Bacterial pathogens	Sequencing, metagenomic assembly	Unbiased "shotgun" sequencing of isolated nucleic acid from patient samples to identify associated pathogens; proofs-of-concept: new <i>Bradyrhizobium</i> species associated with cord colitis, <i>Escherichia coli</i> O104:H4 from 2011 diarrheal outbreak in Germany; research use only at this time
Viral pathogens	Microarray, sequencing	Hybridization of clinical samples to microarrays from phylogenetically diverse known viruses identified the SARS coronavirus and others. Direct sequencing has identified West Nile virus and the MERS coronavirus, among others. Use is primarily in research.
<b>Antibiotic Resistance</b>		
MRSA detection	PCR	Detection of the <i>mecA</i> gene, the genotypic cause of methicillin resistance in <i>Staphylococcus aureus</i>
VRE detection	PCR	Detection of the <i>vanA</i> or <i>vanB</i> genes, the main genotypic causes of vancomycin resistance in <i>Enterococcus</i>
MDR-TB detection	PCR, NAAT	Detection of polymorphisms in the <i>rhoB</i> gene from <i>M. tuberculosis</i> , which account for 95% of rifampin resistance. Other probes available for <i>inhA</i> and <i>katG</i> genes can detect up to 85% of isoniazid resistance.
Carbapenemase detection	PCR	Detection of genes encoding one of two enzymes, NDM-1 or KPC, that hydrolyze carbapenems; use in United States currently restricted to CDC
HIV resistance detection	Targeted sequencing	Targeted sequencing of specific genes with known resistance-conferring mutations; now standard of care prior to initial therapy in United States and Europe
<b>Epidemiology</b>		
Outbreak and epidemic tracking	Sequencing	Application to tracking outbreaks and epidemics on local and international scales, including spread of carbapenemase-producing <i>Klebsiella</i> , <i>S. aureus</i> , <i>M. tuberculosis</i> , <i>E. coli</i> , <i>Vibrio cholerae</i> , and influenza virus
Evolution and spread of pathogens	Sequencing	Sequencing collections of pathogens to shed light on pathogen dissemination, virulence factors, and antibiotic resistance determinants

**Abbreviations:** CDC, Centers for Disease Control and Prevention; HBV, hepatitis B virus; HCV, hepatitis C virus; MDR, multidrug-resistant; MERS, Middle East respiratory syndrome; MRSA, methicillin-resistant *Staphylococcus aureus*; NAAT, nucleic acid amplification test; PCR, polymerase chain reaction; SARS, severe acute respiratory syndrome; TB, tuberculosis; VRE, vancomycin-resistant enterococci.

**TABLE 146-2 GLOSSARY OF SELECTED TERMS IN GENOMICS**

Term	Definition
Contig	A DNA sequence representing a continuous fragment of a genome, assembled from overlapping sequences; relevant for de novo assembly of sequence data that do not align to previously sequenced genomes
Genome	The entire set of heritable genetic material within an organism
Horizontal gene transfer	The transfer of genes between organisms through mechanisms other than by clonal descent, such as through transformation, conjugation, or transduction
Metagenomics	Analysis of genetic material from multiple species directly from primary samples without requiring prior culture steps
Microarray	A collection of DNA oligonucleotides ("oligos") spatially arranged on a solid surface and used to detect or quantify sequences in a sample of interest that are complementary (and therefore bind) to one or more of the arrayed oligos
Mobile genetic element	DNA elements that can move within a genome and can be transferred between genomes through horizontal gene transfer (e.g., plasmids, bacteriophages, and transposons)
Multilocus sequence typing	A methodology for typing organisms based on DNA sequence fragments from a prespecified set of genes
Next-generation sequencing	High-throughput sequencing using a parallelized sequencing process that produces millions of sequences concurrently, far beyond the capacity of prior dye-terminator methods
Nucleic acid amplification test (NAAT)	Biochemical assay that evaluates for the presence of a particular string of nucleic acids through amplification by one of several methods, including polymerase and ligase chain reactions
Polymerase chain reaction (PCR)	A subset of NAAT used to amplify a specific region of DNA with specific oligonucleotide primers and a DNA polymerase
Transcriptome	The catalog of the full set of messenger RNA (mRNA) transcripts from a cell or organism, which are typically measured by microarray or by next-generation sequencing of complementary DNA (cDNA) via a process called RNA-Seq
Whole-genome sequencing	A process that determines the full DNA sequence of an organism's genome; has been greatly facilitated by next-generation sequencing technology