

# Advancing NGS-Based, Pathogen-Detection Testing

Robert Schlberg, MD, Dr Med, MPH, has co-pioneered a new data-analysis technology for next-generation sequencing (NGS)-based, pathogen-detection testing that significantly advances laboratory diagnostic medicine. The Bill & Melinda Gates Foundation recently recognized him with a prestigious grant involving this technology.

This new technology, known as TaxonomerDx, can be used to diagnose infections in routine patient samples that are missed with standard methods. This analysis method extends the breadth of what can be detected—any known pathogen—and dramatically expedites data analysis down to seconds or minutes.

Schlberg is the medical director of Microbial Amplified Detection, Virology, and Fecal Chemistry laboratories and an assistant medical director of the Molecular Infectious Disease laboratory at ARUP, as well as an assistant professor of pathology at the University of Utah School of Medicine. He is also a co-founder of an ARUP spin-out company called IDbyDNA, which performs the data analysis for the test.

In the following Q & A, Schlberg discusses this new data-analysis technology for NGS-based, pathogen-detection testing, which ARUP will begin offering later this year.



## Expert Edge

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**Q: How does this new technology work to detect any known virus, bacteria, or fungus?**

**A:** This universal pathogen-detection test is based on unbiased (shotgun) next-generation sequencing of any DNA and RNA in a patient sample, also referred to as metagenomics and metatranscriptomics. Total DNA and RNA is extracted and converted to sequencing libraries, and millions of short DNA sequences are generated. The mix of patient cells, viruses, bacteria, and fungi in the sample determines the composition of DNA sequences.

The huge amount of sequence data is then analyzed with new software (TaxonomerDx) co-developed by ARUP and IDbyDNA. TaxonomerDx classifies each of the millions of short DNA sequences to detect any known virus, bacteria, or fungus and can also be used to discover new pathogens. Sequencing protocols and TaxonomerDx have been extensively studied with patient samples.

**Q: What are the advantages over current tests?**

**A:** Current testing strategies require knowledge of expected pathogens that are usually targeted with specific tests. In contrast, this new technology can detect expected and unexpected, common and rare, as well as easy to grow and fastidious, pathogens. In addition, it can detect micro-organisms that would not be cultivatable because patients had been given antibiotic therapy prior to sample collection or due to inappropriate sample transport or storage.

Universal pathogen detection is particularly advantageous in vulnerable patients such as the seriously ill,

immunocompromised, elderly, or young infants.

In addition to pathogen detection, sequencing results can also provide genotyping information and predict drug resistance. The relative abundance of different micro-organisms and their absolute quantities (comparable to bacterial colony forming units and viral genome copy counts) can be estimated based on the numbers of DNA sequences.

Importantly, recent advances in sequencing technology and bioinformatics tools, such as TaxonomerDx, have made it possible to generate test results within 24 hours of sample receipt in the laboratory, making this technology available for diagnostic testing in a clinically meaningful time.

**Q: What kind of pathogens will this testing detect?**

**A:** More than 200 viruses, bacteria, and fungi have been validated for this test based on their ability to cause respiratory tract infections. If additional, potentially relevant pathogens are detected, they will be reported after manual review.

**Q: Will it detect multiple pathogens?**

**A:** Yes, multiple pathogens can be detected. Their relative abundance can be measured.

**Q: Are there any disadvantages?**

**A:** In those particular cases where a specific pathogen is sought or strongly suspected, pathogen-specific tests may be faster and more cost effective. Intact DNA and RNA is required for successful pathogen detection. Sample collection, transport, and storage recommendations should be followed.