



# Microbes and Infectious Diseases

Journal homepage: <https://mid.journals.ekb.eg/>

## Editorial

# The new era for diagnostic microbiology laboratories: ‘All things are ready, if our mind be so’

**Ahmed Morad Asaad**

*Medical Microbiology and Immunology, Faculty of Medicine, Zagazig University, Microbes and Infectious Diseases Editor-In-Chief, Egypt*

### ARTICLE INFO

#### Article history:

Received 31 March 2020

Received in revised form 2 April 2020

Accepted 2 April 2020

#### Keywords:

PCR

MALDI TOF

NGS

Metagenomics

### ABSTRACT

Identification and characterization of micro-organisms that cause infections are crucial for successful management of patients. For several decades, routine clinical microbiological diagnostic laboratories have been equipped with a growing panel of culture-dependent and culture-independent methods to investigate the microbial etiology of infectious diseases. Considering the disadvantages of traditional methods, multiplex PCR techniques have been routinely endorsed in clinical microbiology laboratories as rapid and sensitive diagnostic and prognostic tool including many PCR panels routinely used in microbial diagnostics. The great advance in medical biotechnology has been associated with development of Matrix-Associated Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI TOF MS). The power of MALDI TOF MS correctly identified 93.2% of organisms to the species level and 5.3% to the genus level. Recently, the application of next-generation sequencing (NGS) technology and its various methodological variants makes it possible to detect different types of microorganisms present within a microbial sample simultaneously, using a culture-independent approach and in a single sequencing run. Over the next 5 to 10 years, although it is unlikely to see NGS completely replacing the conventional culture and susceptibility methods, a wealth of NGS applications will be acquired in the vast majority of diagnostic microbiology laboratories worldwide, providing enhanced diagnostic capabilities and improving the quality of patients care. In Egyptian diagnostic microbiology laboratories, we have to ask ourselves; are we ready to subsist this new era? Sure the answer is: ‘All things are ready, if our mind be so’.

### Introduction

Identification and characterization of micro-organisms that cause infections are crucial for successful management of patients. For several decades, routine clinical microbiological diagnostic laboratories have been equipped with a growing panel of culture-dependent and culture-

independent methods to investigate the microbial aetiology of infectious diseases. Considering the disadvantages of traditional methods, multiplex PCR techniques have been routinely endorsed in clinical microbiology laboratories as rapid and sensitive diagnostic and prognostic tool including many PCR panels routinely used in microbial diagnostics. The great advance in medical biotechnology has been associated with development of Matrix-Associated Laser

DOI: 10.21608/mid.2020.25905.1001

\* Corresponding author.

E-mail address: [ahmedmoradasaad@hotmail.com](mailto:ahmedmoradasaad@hotmail.com)

© 2020 The author (s). Published by Zagazig University. This is an open access article under the CC BY-NC-ND license (<https://creativecommons.org/licenses/by/4.0/>),

Desorption Ionization Time of Flight Mass Spectrometry (MALDI TOF MS). The power of MALDI TOF MS correctly identified 93.2% of organisms to the species level and 5.3% to the genus level. Recently, the application of next-generation sequencing (NGS) technology and its various methodological variants makes it possible to detect different types of microorganisms present within a microbial sample simultaneously, using a culture-independent approach and in a single sequencing run. Over the next 5 to 10 years, although it is unlikely to see NGS completely replacing the conventional culture and susceptibility methods, a wealth of NGS applications will be acquired in the vast majority of diagnostic microbiology laboratories worldwide, providing enhanced diagnostic capabilities and improving the quality of patients care. In Egyptian diagnostic microbiology laboratories, we have to ask ourselves; are we ready to subsist this new era? Sure the answer is: 'All things are ready, if our mind be so'.

**Key words:** PCR, MALDI TOF. NGS, metagenomics

Infectious diseases still remain a leading source of human morbidity and mortality. Of 57 million deaths per year reported worldwide, 14.9 million have been attributed to infectious diseases, representing more than 25% of all deaths [1].

Identification and characterization of microorganisms that cause infections are crucial for successful treatment, recovery and safety of patients. For several decades, routine clinical microbiological diagnostic laboratories have been equipped with a growing panel of culture-dependent and culture-independent methods to investigate the aetiology of microbial infections. However, the causative pathogens of many infections may not be detected using culture-dependent methods, as many microorganisms require specific growth conditions that cannot be easily provided within a laboratory environment. In addition, most culture-independent methods (e.g., serological ELISA and molecular PCR assays) require a previous knowledge of microorganisms that are suspected to be present within a clinical sample under investigation in

order to detect them [2].

In the last few years, multiplex PCR has been routinely endorsed in clinical microbiology laboratories as rapid and sensitive diagnostic and prognostic tool including respiratory PCR panel (FDA approved 2008), gastrointestinal panel (FDA approved 2012), blood culture panel (FDA approved 2014), and meningitis panel (FDA approved 2015). The great advance in medical biotechnology has been associated with development of Matrix-Associated Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI TOF MS). The findings of previous laboratory-evidence based studies have showed that the MALDI TOF MS correctly identified 93.2% of organisms to the species level and 5.3% to the genus level, while 1.5% remains unidentified [3]. Advantages and disadvantages of automated mass spectrometry microbial identification in clinical microbiology laboratories are listed in table 1.

**Table 1.** Automated mass spectrometry microbial identification system directly from clinical samples in clinical microbiological laboratories.

Technique	Advantages	Disadvantages
MALDI TOF	Fast Accurate Less expensive run cost per test than molecular and immunological methods Not technical complex	High initial cost of equipment Identification of new isolates depends on available database Does not identify resistance genes May require culture of organisms
Multiplex PCR	Culture is not required Sensitive, specific, rapid, and accurate Closed-tube system reduces risk of contamination Detect many organisms at the same time Detect fastidious and non-cultured pathogens	Highly-precise thermal cycler is required Highly-trained laboratory personnel are required Initial cost of equipment is less than MOLDI TOF, but the cost/run is more

Recently, the application of next-generation sequencing (NGS) technology and its various methodological variants makes it possible to detect different types of microorganisms present within a microbial sample simultaneously, using a culture-independent approach and in a single sequencing run. The 3 main applications of next-generation sequencing in

clinical microbiology laboratories include: (1) whole-genome sequencing (WGS), (2) targeted next-generation sequencing (tNGS), and (3) metagenomics next-generation sequencing [4].

The WGS is becoming commonplace in public health laboratories, helping in the rapid identification and tracking of infectious disease outbreaks alongside detection of emerging resistance and surveillance. The tNGS has been underutilized in clinical microbiology, however, the development of new enrichment methods will allow for

In conclusion, the world has witnessed a great momentum for the introduction of NGS applications in clinical microbiology laboratories in the last few years. Over the next 5 to 10 years, although it is unlikely to see NGS completely replacing the conventional culture and susceptibility methods, a wealth of NGS applications will be acquired in the vast majority of diagnostic microbiology laboratories worldwide, providing enhanced diagnostic capabilities and improving the quality of patients care. In Egyptian diagnostic microbiology laboratories, we have to ask ourselves; are we ready to subsist this new era? Sure the answer is: ‘All things are ready, if our mind be so’.

### Funding

Non declared

### Competing interests

Non declared

### Ethical approval

Not required

### References

- 1- World Health Organization. World Health Statistics Overview 2019. WHO, Switzerland, available at: <https://apps.who.int/iris/bitstream/handle/10665/311696/WHO-DAD-2019.1-eng.pdf>

broad pathogen detection combined with high sensitivity. The tNGS may become a more accessible assay in the future. Metagenomic next-generation sequencing has emerged as a promising single, universal pathogen detection method for infectious diseases diagnostics performed directly from clinical specimens. Laboratory-developed tests are now being offered as billable tests; understanding the limitations of these non standardized and expensive tests is imperative for appropriate test utilization and result interpretation [4-6].

- 2- Lagier JC, Hugon P, Khelaifia S, Fournies PE, La Scola B, Raoult D. The rebirth of culture in microbiology through the example of culturomics to study human gut microbiota. *Clin Microbiol Rev* 2015; 28: 237–64.
- 3- Tan KE, Ellis BC, Lee R, Stamper PD, Zhang SX, Carroll KC. Prospective evaluation of a matrix-assisted laser desorption ionization-time of flight mass spectrometry system in a hospital clinical microbiology laboratory for identification of bacteria and yeasts: a bench-by-bench study for assessing the impact on time to identification and cost-effectiveness. *J Clin Microbiol* 2012; 50:3301–8.
- 4- Bores SA, Jansen R, Hays JP. Understanding and overcoming the pitfalls and biases of next-generation sequencing (NGS) methods for use in the routine clinical microbiological diagnostic laboratory. *Eur J Clin Microbiol Infect Dis* 2019; 38 (6): 1059-70.
- 5- Simner PJ, Miller S, Carrol KC. Understanding the Promises and Hurdles of Metagenomic Next-Generation Sequencing as a Diagnostic Tool for Infectious Diseases. *Clin Infect Dis* 2018; 66 (1): 778-788.
- 6- Yu X, Jiang W, Shi Y, Ye H, Lin J. Applications of sequencing technology in clinical microbial Infection. *J Cell Mol Med* 2019; 23: 7143-50.