Editorial

Fungal Genotyping – Current Clinical Application

Azian Harun

Submitted: 19 Oct 2014
Accepted: 20 Oct 2014

Sub-Editor (Laboratory Base), Malaysian Journal of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kubang Kerian, Kelantan, Malaysia

Abstract

The emergence of fungal species as opportunistic pathogens has warranted further studies on their pathogenicity, epidemiology, and transmissibility. Fungal genotyping has been employed to study the genetic relatedness within the organism, in order to obtain answers to epidemiological questions (such as in outbreak confirmation) as well as to provide basis for the improvement for patients care. Various fungal genotyping methods have been previously published, which can be chosen depending on the intended use and the capability of individual laboratory.

Keywords: *fungi, genotyping, epidemiology*

Fungal pathogens cause a wide range of diseases ranging from mild, superficial infections to severe, life-threatening infections. The medical importance of fungi has been shown to be significantly increased, particularly in settings involving immunocompromised patients (1,2). Some fungal pathogens have been reported to be implicated in presumed outbreaks. Among medically-important fungi which have been implicated in severe fungal infections include *Candida, Cryptococcus,* and a number of filamentous fungi such as *Aspergillus*, *Scedosporium*, *Penicillium*, and *Fusarium* (1). Many of these fungal infections resulted in poor outcome despite administration of antifungal agents. Therefore, in order to improve outcomes, early interventions including preventative measures are warranted. Epidemiological studies to understand the course and evolution of these organisms in clinical settings require accurate species identification and genotyping.

Fungal genotyping is defined as genetic analysis of fungi (below species level) which is performed to determine strain specific fingerprints. Genotyping will generate molecular markers which enable comparison among strains and study their genetic relatedness. In the recent years, a number of molecular techniques have been applied for strain typing of fungal pathogens (2). Methods which have been used for fungal genotyping include multilocus enzyme electrophoresis (MLEE), random amplification of polymorphic DNA (RAPD), pulse field gel electrophoresis (PFGE), restriction fragment length polymorphism (RFLP) analysis, amplified fragment-length polymorphism (AFLP) analysis, variable number of short tandem repeats (VNTR) and DNA sequence-based method such as multilocus sequence typing (MLST) (2,3).

In medical mycology, genotyping techniques are employed to study the population dynamics and transmissibility of fungal pathogens in both clinical and environmental settings. Many opportunistic fungal pathogens are ubiquitous in nature and may pose as a significant threat to susceptible patients. Therefore, using data generated from genotyping methods, the relationship between isolates from environment and patients can be analysed, which subsequently enables determination of environmental source of infection. Similarly, in the presence of a cluster of fungal infections (presumed outbreak), the use of an accurate genotyping technique is crucial to prove or disprove outbreak situation. More importantly, analysis of genotyping data enables establishment of patient-to-patient transmission and the index patient serving as the source of the outbreak can be identified. Such exercise is crucial in an outbreak management, in which prompt and effective employment of infection control measures is mandatory (2,3).

Genotyping also enables further understanding of how a fungal pathogen behaves in a particular patient host. Multiple isolations of an organism may occur in a single patient host over a particular time frame. In many instances, the organism can either be present as transient colonisation or as persistent colonisation, which eventually may result in a genuine invasive infection. Genotyping enables differentiation

of these strains and the genotype associated with potential infection can be determined. In addition, associated factors leading to persistent colonisation and infection can be evaluated (3).

Fungal genotyping techniques differ in their discriminatory power, which consequently affect their applicability in differentiating fungal strains (2). Gel-based methods such as PFGE, RAPD, and AFLP have been frequently applied. Although these methods offer moderate to high discriminatory power, their interpretations and analyses are often difficult and subjected to person-to-person variability (operator-dependent). VNTR and MLST, on the other hand, provide easier interpretation due to their unambiguously generated data, which enables interlaboratory comparison with high reproducibility. However, these methods are generally more costly than the former methods (2,3). Therefore, each medical laboratory must identify its needs and capabilities before choosing the most appropriate genotyping methods for its clinical use.

Genotyping databases have been developed for a number of fungal species. These databases are publically accessible through specific websites e.g. *www.mlst.net*. Availability of MLST database for *Candida albicans* and *Cryptococcus neoformans* using standard consensus-generated protocols promotes sharing of data and enhances global collaboration among researchers in medical mycology.

Correspondence

Dr Azian Harun
MBBS (Malaya), M.Path (Microbiology) (USM), PhD (Sydney)
Malaysian Journal of Medical Sciences
Universiti Sains Malaysia Health Campus
16150 Kubang Kerian
Kelantan, Malaysia
Tel: +609-767 6972
Fax: +609-767 2359
Email: azian@usm.my

Reference

1. Alastruey-Izquierdo A, Mellado E, Pelaez T, Peman J, Zapico S, Alvarez M, et al. Population-based survey of filamentous fungi and antifungal resistance in Spain (FILPOP Study). *Antimicrob Agents Chemother*. 2013;**57(7)**:3380–3387.

2. Harun A, Perdomo H, Gilgado F, Chen SCA, Cano J, Guarro J, et al. Genotyping of Scedosporium species: a review of molecular approaches. *Med Mycol*. 2009; **47**:406–414.

3. Vanhee LME, Nelis HJ, Coenye T. What can be learned from genotyping of fungi? *Med Mycol*. 2010;**48(Suppl 1)**:S60–S69. doi: 10.3109/13693786.2010.484816.