Taxonomy and evolution of Aspergillus, Penicillium and Talaromyces in the omics era – Past, present and future

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Abstract

Aspergillus, Penicillium and Talaromyces are diverse genera encompassing species important to the environment, economy, biotechnology and medicine, causing significant social impacts. Taxonomic studies on these fungi are essential since they could provide invaluable information on their evolutionary relationships and define criteria for species recognition. With the advancement of various biological, biochemical and computational technologies, different approaches have been adopted for the taxonomy of Aspergillus, Penicillium and Talaromyces; for example, from traditional morphotyping, phenotyping to chemotyping and/or phylotyping. Since different taxonomic approaches focus on different sets of characters of the organisms, various classification and identification schemes would result. In view of this, the consolidated species concept, which takes into account different types of characters, is recently accepted for taxonomic purposes and, together with the lately implemented ‘One Fungus – One Name’ policy, is expected to bring a more stable taxonomy for Aspergillus, Penicillium and Talaromyces, which could facilitate their evolutionary studies. The most significant taxonomic change for the three genera was the transfer of Penicillium subgenus Biverticillium to Talaromyces (e.g. the medically important thermally dimorphic ‘P. marneffei’ endemic in Southeast Asia is now named T. marneffei), leaving both Penicillium and Talaromyces as monophyletic genera. Several distant related Aspergillus-like fungi were also segregated from Aspergillus, making this genus, containing members of both sexual and asexual morphs, monophyletic as well. In the current omics era, application of various state-of-the-art omics technologies is likely to provide comprehensive information on the evolution of Aspergillus, Penicillium and Talaromyces and a stable taxonomy will hopefully be achieved.

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1. Introduction

Aspergillus, Penicillium and Talaromyces are diverse genera belonging to the Order Eurotiales and contain a large number of species possessing a worldwide distribution and a huge range of ecological habitats. They are ubiquitous and can be found in the air, soil, vegetation and indoor environments [1,2]. Some members are able to grow in extreme environments such as those with high/low temperatures, high salt/sugar concentrations, low acidities or low oxygen levels [3,4]. Species of the three genera are mainly environmental saprobes [3,4] and the primary contribution of these microorganisms to nature is the decomposition of organic materials [1].

Many Aspergillus, Penicillium and Talaromyces species are economically, biotechnologically and medically important with huge social impacts. For example, these species are vital to the food industry and quite a number of them are exploited to produce fermented food such as cheeses (e.g. P. roqueforti), sausages (e.g. P. nalgiovense) and soy sauce (e.g. A. oryzae and A. sojae). These fungi are also important biotechnologically for their strong degradative abilities which have been utilised for the production of enzymes [5,6]. In addition, they are robust producers of a diverse spectrum of secondary metabolites (or extrolites) some of which could be used as drugs and antibiotics or as the lead compounds of potential drug candidates with pharmaceutical or biological activities [7]. On the other hand, many of these species, such as A. chevalieri, A. flavipes, P. citreorugrum and T. macrosporus, are food spoiling decomposers which cause pre- and post-harvest devastation of food crops; and many of these food-spoiling species are also mycotoxin-producers [8]. Even worse, some of them are infectious agents and cause diseases in humans and animals. The most notorious
pathogenic species on a global sense is *A. fumigatus* [9], which is the aetiological agent for the majority of aspergillosis cases [10]. Other commonly encountered pathogenic *Aspergillus* species include *A. flavus, A. nidulans, A. niger* and *A. terrus*. Although *Penicillium* and *Talaromyces* species are less commonly associated with human or veterinary infections, the thermally dimorphic fungus *T. marneffei*, previously known as *P. marneffei*, is an exception. This notorious fungus is endemic in Southeast Asia and it is able to cause systemic infections particularly in immunocompromised individuals such as HIV-positive patients [11] or patients with impaired cell-mediated immunity [12].

*Aspergillus, Penicillium* and *Talaromyces* were traditionally classified according to their morphologies. As technologies capable of characterising biological macromolecules advanced, various approaches focusing on the profiles of different cellular constituents such as lipids, proteins and exometabolites have emerged to supplement the taxonomy of these fungi. The availability of DNA sequencing technology in the past two-to-three decades has generated an enormous amount of DNA sequence data, allowing fungal taxonomy through phylogenetics, including genealogical concordance. The currently accepted consolidated species concept [13], or informally known as the ‘polythetic taxonomic approach’, has revolutionised fungal taxonomy, and the classification scheme for a vast number of fungi has been revised. In particular, significant changes have been made to reclassify *Aspergillus, Penicillium* and *Talaromyces* species in the past seven years. Such revision on the classification of these fungi results in redefined species concepts for *Aspergillus, Penicillium* and *Talaromyces*, providing new insights on the evolution of these important filamentous fungi. In this article, the development of various taxonomic approaches as well as species recognition and identification schemes for *Aspergillus, Penicillium* and *Talaromyces* is reviewed. These include the traditional morphological/phenotypic approach, the supplementary lipidomic, proteomic and metabolomic approaches, as well as the currently widely used phylogenetic/consolidated approach. The clinical implications of this evolving taxonomy are also discussed.

2. Classification and nomenclature: a brief history and recent development

The name *Aspergillus* was first introduced by Micheli in 1729 to describe asexual fungi whose conidiophores resembled an aspergillum, a device used to sprinkle holy water [14] (Fig. 1a–f). Later in 1768 von Haller validated the genus [15] and in 1832 Fries sanctioned the generic name [16]. Similarly, the genus *Penicillium* was erected by Link in 1809 [17] to accommodate asexual fungi which bore penicillum (painter’s brush)-like fruiting bodies (Fig. 1g–i).

Although both *Aspergillus* and *Penicillium* were originally described as anamorphic (asexual), some species of the two genera were subsequently found to be ascacarp-forming (Fig. 1c, f and l). For example, the sexual genus *Eurotium* was first firmly connected to *Aspergillus* by de Bary in 1854 [18] whereas the ascomycetous genus *Eupenicillium* has been used to describe *Penicillium* species capable of producing sclerotoid cleistothecia from as early as 1892 [19]. Since the discovery of the various sexual states of *Aspergillus* and *Penicillium* species, it has been controversial as to whether separate sexual generic names should be used to describe species able to produce ascocarps. In spite of the fact that several sexual genera had already been established to accommodate the sexual morphs of some *Aspergillus* and *Penicillium* species, Thom, Church, Raper and Fennell, in their monographic masterpieces on the taxonomics of these two genera, neglected the use of sexual names. This was because, in their opinions, this would cause unnecessary nomenclatural confusion, especially for strains which were in sexual stages at first and then lost their ascospore-forming ability under laboratory maintenance. In addition, this would also lead to the fragmentation of the large and obviously cohesive *Aspergillus/Penicillium* groups [20–25]. Nevertheless, in order to abide by the then International Code of Botanical Nomenclature (Stockholm Code), where the first valid names of the 'perfect states' (sexual morphs) of fungi took precedence [26], Benjamin assigned *Aspergillus* species which possess sexual life cycles into the sexual genera *Eurotium, Emericella* and *Sartorya* [27]. In addition, he transferred *Penicillium* species with sexual life cycles to the ascomycetous genus *Carpenteles* (later synonym of *Eupenicillium*) [27,28]. During his assignment, Benjamin also established the novel genus *Talaromyces* to describe *Penicillium* species which, in their sexual life cycles, possessed soft ascocarps exhibiting indeterminate growth and whose walls were composed of interwoven hyphae [27] (Fig. 1m–o).

As the number of species of the genera *Aspergillus, Penicillium* and *Talaromyces* increased, closely related species were grouped into subgroups [29–32]. Such infrageneric classification system underwent vigorous changes since different authors focused on different morphological features when establishing their subgrouping schemes (Table 1). For example, Blochwitz as well as Thom and his co-workers were the first to divide *Aspergillus* species into seven and 18 subgeneric ‘groups’, respectively, based on their phenotypes [21,24,30,31].
subgrouping by Thom and associates formed the foundation of Aspergillus subgeneric classification which had been largely followed by other mycologists working on this genus in the last century. However, since these subgeneric ‘groups’ did not possess any nomenclatural status, Gams et al., in 1986, established six subgenera and 18 sections to accommodate these ‘groups’, formalising the subgeneric classification of Aspergillus species [33] (Table 1a). As for Penicillium, Dierckx and Bourge firstly subdivided the genus into the subgenera Biverticillium and Bulliardium (synonym: Monoverticillium) as well as Eupenicillium, which was further separated into sections Biverticillum and Bulliardium (synonym: Asymmetrica) [29,34]. Subsequently, Thom and his co-workers did not follow Dierckx's and Bourge's grouping and proposed a new subgeneric classification scheme for Penicillium composed of four main divisions/sections, where species were grouped according to features of their colonies and branching patterns of their conidiophores [20,22]. The system established by Thom and associates for Penicillium was adopted by other mycologists for the next 30 years until Pitt as well as Stolk and Samson separated into sections Biverticillium and Bulliardium (synonym: Asymmetrica) [29,34].

Similarly, Talaromyces species were also split into four sections based on the structures of their conidial states [32] (Table 1c).

As the species concept for fungi migrates from morphological, physiological, or phenotypic to genetic, phylogenetic (including genealogical concordance) and even consolidated, changes have been made to the infrageneric classification of Aspergillus, Penicillium and Talaromyces (Table 1). The adoption of the consolidated species concept, with reduced emphasis on morphological properties, in classifying species of these genera resulted in the fact that fungi with aspergilliun-shaped conidiophores no longer necessarily are Aspergillus species, while fungi with penicilliun-shaped conidiophores no longer necessarily are Penicillium species [37]. One notable change in relation to these genera, also as a result of the recent implementation of the single-naming system ('One Fungus – One Name' [1F1N] principle) [38–40], was the transfer of fungi belonging to Penicillium subgenus Biverticillum to the genus Talaromyces [41], whose close chemotaxonomic relationship [42] and phylogenetic connection [43–45] have been recognised since the 1990s, leaving both the genera Penicillium and Talaromyces as monophyletic clades [41] (Fig. 2). Interestingly, during this transfer the species P. aureocephalus (synonym for sexual morph: Lasioderma flavovirens) [46] was also accommodated in the Talaromyces clade.

Table 1a
Overview of major subgeneric classifications of Aspergillus species.

| Blochman et al. [31] | Thom & Church [30], Thom & Raper [21], Raper & Fennell [24] | Gams et al. [33] | Peterson [168] | Peterson et al. [169] | Houbraken & Samson [3] | Houbraken et al. [4] | Jurjevá et al. [170], Koschube et al. [60], Sklenář et al. [171] |
|---------------------|----------------------------------------------------------|----------------|----------------|------------------|----------------|----------------|----------------|
| **Euglobosi**       | Group A. candidus                                        | Subgenus Aspergillus | Subgenus Aspergillus | Subgenus Aspergillus | Subgenus Aspergillus | Subgenus Aspergillus | Subgenus Aspergillus |
|                     | Group A. cervinus                                        | Section Aspergillus | Section Aspergillus | Section Aspergillus | Section Aspergillus | Section Aspergillus | Section Aspergillus |
|                     | Group A. flavipes                                        | Section Circumdati | Section Circumdati | Section Circumdati | Section Circumdati | Section Circumdati | Section Circumdati |
| **Nigroides**       | Group A. flavius                                         | Section Candidi | Section Candidi | Section Candidi | Section Candidi | Section Candidi | Section Candidi |
|                     | Group A. fumigatus                                       | Section Crematii | Section Crematii | Section Crematii | Section Crematii | Section Crematii | Section Crematii |
|                     | Group A. gamsiacus                                       | Section Flavi    | Section Flavi    | Section Flavi    | Section Flavi    | Section Flavi    | Section Flavi    |
|                     | Group A. hilicrus                                        | Section Nigri    | Section Nigri    | Section Nigri    | Section Nigri    | Section Nigri    | Section Nigri    |
|                     | Group A. horbicans                                       | Section Sparisi  | Section Sparisi  | Section Sparisi  | Section Sparisi  | Section Sparisi  | Section Sparisi  |
| **Phaei**           | Group A. ochraceus                                       | Subgenus Circumdati | Subgenus Circumdati | Subgenus Circumdati | Subgenus Circumdati | Subgenus Circumdati | Subgenus Circumdati |
|                     | Group A. ornatans                                        | Subgenus Crematii | Subgenus Crematii | Subgenus Crematii | Subgenus Crematii | Subgenus Crematii | Subgenus Crematii |
|                     | Group A. restrictans                                     | Subgenus Flavi   | Subgenus Flavi   | Subgenus Flavi   | Subgenus Flavi   | Subgenus Flavi   | Subgenus Flavi   |
|                     | Group A. sparsus                                         | Subgenus Nigri   | Subgenus Nigri   | Subgenus Nigri   | Subgenus Nigri   | Subgenus Nigri   | Subgenus Nigri   |
|                     | Group A. terraeus                                        | Subgenus Sparisi | Subgenus Sparisi | Subgenus Sparisi | Subgenus Sparisi | Subgenus Sparisi | Subgenus Sparisi |
| **Nidulantes**      | Group A. versicolor                                      | Subgenus Nigri   | Subgenus Nigri   | Subgenus Nigri   | Subgenus Nigri   | Subgenus Nigri   | Subgenus Nigri   |
|                     | Group A. wentii                                          | Subgenus Sparisi | Subgenus Sparisi | Subgenus Sparisi | Subgenus Sparisi | Subgenus Sparisi | Subgenus Sparisi |

a Transferred to genus Sclerotella and excluded from Aspergillus [3,53]
b Merged with section Nidulantes [168]
c Merged with section Crematii [172]
d Transferred to genus Wuriapella and excluded from Aspergillus [3,53]
e Transferred to genus Penicilliosis and excluded from Aspergillus [3,60]
f Sexual synonym = Eurotium [4]
g Sexual synonym = Neopetromyces [4]
h Sexual synonym = Petromyces [4]
i Sexual synonym = Fennellia [4]
j Sexual synonym = Chaetosartorya [4]
k Sexual synonym = Dicotomomyces and Neocarpenteles [4]
l Sexual synonym = Neosartorya [4]
m Sexual synonym = Emericella [4]
| Subgenus Aspergilloides | Dierckx [29] | Biourge [34] | Thom [20] | Raper et al. [22] | Pitt [35] | Stolk & Samson [36] | Houbraken & Samson [3], Houbraken et al. [173] |
|-------------------------|-------------|-------------|-----------|------------------|----------|-------------------|-----------------------------------------------|
| Subgenus Eupenicillium | Division Asymmetrica | Section Asymmetrica | Subgenus Aspergilloides | Section Aspergilloides | Subgenus Aspergilloides | Subgenus Aspergilloides |
| Section Biverticillium | Section Brevicompacta | Section Biverticillata-symmetrica | Section Aspergilloides | Section Exilicaulis | Section Coremigenum | Section Brevicompacta |
| Section Fasciculata | Section Funiculosa | Section Monoverticillata | Section Polyverticillata-symmetrica | Section Eladia | Section Eosmithia | Section Eosmithia |
| Section Funiculosa | Section Fuscata | Section Monoverticillata-stricta | Section Cylindrosporum | Section Inordinate | Section Ramsalmona | Section Ochrusalmona |
| Section Lanata-divaricata | Section Monoverticillata | Section Monoverticillata-Ramigena | Section Penicillum | Section Torulomyces | Section Torulomyces | Section Thysanophora |
| Section Luteo-virida | Division Monoverticillata | Polyverticillata-symmetrica | Division | Torulomyces | Sclerotiora | Section Moldesahora |
| Section Miscellanea | Division Monoverticillata | Polyverticillata-symmetrica | Torulomyces | Stolkia | Section Turbata | Section Fracta |
| Section Monoverticillata-stricta | Division | Polyverticillata-symmetrica | Torulomyces | Section Torulomyces | Section Torulomyces | Section Torulomyces |
| Section Monoverticillata-Ramigena | Division | Polyverticillata-symmetrica | Torulomyces | Section Torulomyces | Section Torulomyces | Section Torulomyces |
| Subgenus Penicillium | Division | Polyverticillata-symmetrica | Torulomyces | Section Torulomyces | Section Torulomyces | Section Torulomyces |

* Not referring to the sexual genus *Eupenicillium* Ludwig

b Transferred to genus *Talaromyces* and excluded from *Penicillium*
hand, the main problem for the narrow Aspergillus concept rests in the retypification by conservation of the genus. This is because under the narrow Aspergillus concept, the type of the genus Aspergillus, A. glaucus of subgenus Aspergillus, would fall in the genus Eurotium instead. Since taxonomic properties of the type and related species determine the circumscription of the genus, if the name Aspergillus is to be applied to subgenus Circumdati, the type of the genus has to be changed to one of the species within this subgenus, for example, A. niger as suggested by Pitt and Taylor because of its more frequent use in literatures and databases [58]. However, in the eyes of the wide Aspergillus concept advocates, such generic retypification is debatable since the new type of choice would depend on the interest of different fields. For instance, A. flavus would be the type of choice for food mycology and mycotoxicology, A. fumigatus for medical mycology, whereas A. nidulans for fungal molecular genetics [2]. Recently, regarding the narrow Aspergillus proposal which considers Aspergillus to be non-monophyletic and recommends to apply the name Aspergillus only to members of the subgenus Circumdati through retypification by conservation while maintaining the sexual names for other supported clades [58,59], Kocubé et al., supporters of the wide Aspergillus concept, demonstrated in their phylogenetic analyses, based on six and nine genetic markers using both maximum likelihood and Bayesian approaches as well as extrolite profiling, that Aspergillus represents a well-supported monophyletic clade sister to the monophyletic Penicillium clade (Fig. 2) [60], rejecting Pitt et al.’s hypotheses and proposal. They also established the subgenus Polypaecilum to encompass species previously assigned to the genera Phialosimplex and Polypaecilum (Fig. 2), whereas the species A. clavatafavaus and A. zonatus, which are actually phylogenetically distantly related to Aspergillus, were transferred to the novel genera Asperrygillago as Asperrygillago clavatafavaus and Penicilltopsis as Penicilltopsis zonata, respectively [60]. Nevertheless, Pitt and Taylor have submitted a formal proposal to the NCF to retypify Aspergillus with A. niger to redefine the genus to members of subgenus Circumdati only, with sexual names taken up to replace other subgeneric names of Aspergillus [61]. In response to Pitt and Taylor, Samson et al. urged the NCF to reject the conservation proposal based on their arguments that Aspergillus is monophyletic as well as clearly-defined by phenotypic synapomorphies and secondary metabolite chemistry; that the size of the genus Aspergil-
us is irrelevant; and that conservation with a different generic type (A. niger) would lead to unpredictable name changes and would not result in a more stable nomenclature [62]. Recently, voting was held by the NCF and the proposal by Pitt and Taylor could not obtain a 60% majority for the ‘yes’ vote after two rounds of ballots. Although the ‘no’ vote was also one vote short of reaching 60%, it was in the majority. Since there is no definite recommendation from the NCF, this proposal will be referred to the General Committee on Nomenclature for final decision (Dr Tom May, personal communication).

3. Species recognition/identification and current advances

Since the establishment of Aspergillus, Penicillium and Talaromyces, species in these genera had been recognised by their morphological features until the dawn of molecular systematics. In particular, morphology of conidial structures, especially their branching patterns as discussed above, has played an important role in species recognition and identification. Other important morphological properties useful for diagnosing a species include cleistothecium and ascus/ascospore (when present) characters [1,2]. Macroscopically, characteristics of the colony, such as texture, growth rate, degree of sporation, conidial and mycelial colours, as well as production of diffusing pigments, exudates, acids and other secondary metabolites, are also used for species differentiation [1,2,63]. The need for standardisation of culture media and incubation condition for reproducible species identification was recognised as early as Bouger’s and Dierckx’s time [64]. This is because variations in the immediate cultural environment, such as nutrient availability, temperature, light intensity (including ultraviolet light), water activity,

Table 1c
Overview of major subgeneric classifications of Talaromyces species

| Stolk & Samson [32] | Yaguchi et al. [174] | Yilmaz et al. [63] |
|---------------------|---------------------|---------------------|
| Section Emersonii  | Section Emersonii   | Section Bacillispori |
| Section Purpurea    | Section Purpurea    | Section Helicis     |
| Section Talaromyces | Section Talaromyces | Section Islandici   |
| Section Thermophilae| Section Thermophilae| Section Purpurei    |
|                     | Section Trachyspermus| Section Talaromyces  |
|                     | Section Trachyspermus| Section Subfluifl    |
| a Transferred to genus Rasamsonia and excluded from Talaromyces [175] |
| b Transferred to genus Thermomyces and excluded from Talaromyces [4] |

Inclusion of this species, which is also the type and only species of the genus Lasioderma [47], necessitated the renaming of the Talaromyces clade as Lasioderma, since this is an older sexual name with nomenclatural priority [48]. However, such renaming would require many name changes (from Talaromyces species to Lasioderma species) and several species are better scientifically and economically well-known with their Talaromyces names. Also, even though using identical names for botanical/mycological and zoological genera is not forbidden by the Melbourne Code, the name Lasioderma [Ascomycota] is a later homonym to Lasioderma [Arthropoda] currently in use for one of the beetle genera and this might cause confusion to non-taxonomists. Hence, it was proposed to conserve the generic name Talaromyces over Lasioderma (Ascomycota) [49]. Recently, this proposal was approved by both the Nomenclature Committee for Fungi (NCF) [50] and General Committee for Nomenclature [51] of the International Association for Plant Taxonomy, retaining the generic name Talaromyces.

Despite the fact that the taxonomy of Penicillium and Talaromyces seems straightforward now since both of them clearly represent two separate monophyletic groups [41], the scenario for Aspergillus is much more complicated, involving two opposing generic concepts, namely the wide and narrow Aspergillus concepts. Early work by Benjamín summarised the links between Aspergillus and the sexual genera Emericella, Eurotium and Neosartorya (erroneously as Sartorya) by Benjamín which was later found that the original description of Sartorya was based on a contaminant in an A. fumigatus culture receiving radium radiation [24,27,52]. Following other subsequent changes in Aspergillus classification, seven additional sexual genera, including Chaetosartorya [53], Cristaspora [2], Dictotomomyces [2,54], Fennellia [55], Neocarpentes [56], Neopetromyces [57] and Petromyces [52], are further connected to Aspergillus. Remarkably, each of these sexual genera only associates with a particular Aspergillus subgenus or section (Table 1a).

Subsequent to the adoption of 1F1N, there have been disputes as to whether the generic name Aspergillus should be retained for the large monophyletic clade, although weakly supported (~50–70% bootstrap only) by maximum likelihood analyses [3,4], of classical Aspergillus species (broad/wide Aspergillus concept) [2]; or to adopt sexual names for those well-supported clades containing both pleomorphic species and asexual species with Aspergillus morphologies (narrow Aspergillus concept; i.e. subgenus Aspergillus = Eurotium, subgenus Cremei = Chaetosartorya, subgenus Fumigati = Neosartorya and subgenus Nidulantes = Emericella), leaving the weakly supported (~<50% bootstrap) [3] subgenus Circumdati as Aspergillus sensu stricto, even though this group does include several less-well-known sexual genera (Fennellia, Neopetromyces and Petromyces) [58]. The latter proposal was advocated based on the fact that the sexual genera Chaetosartorya, Emericella, Eurotium and Neosartorya differ significantly in their morphologies, physiologies, enzymologies, as well as toxicologies [59]. Also, Pitt, Taylor and Göker, proposers of the narrow Aspergillus concept, found in their phylogenetic analyses that classical Aspergillus was paraphyletic, encompassing the monophyletic Penicillium clade. As a result, according to Pitt et al. if the wide Aspergillus concept is to be adopted then Penicillium would also need to be synonymised under Aspergillus to make the whole clade monophyletic [58,59]. On the other
humidity and/or other environmental factors, regardless how subtle these discrepancies are, could change the appearance of the organism since morphology is one of the way in which an organism adapts to and survives in its environment [1]. The effects of these changes in incubation condition have been exemplified by the work by Okura et al. [65,66]. As such, standardised working techniques for morphological characterisation have been recommended for Aspergillus and Penicillium species [1,2]. Although no standard is proposed for Talaromyces, these methods should also be applicable to this genus since by tradition quite a number of Talaromyces species were considered and characterised as Penicillium species.

With the availability of newer techniques, such as gas–liquid chromatography and electrophoresis, for the characterisation of biomolecules in the 20th century, chemotaxonomy has gained popularity in Aspergillus, Penicillium and Talaromyces taxonomy, especially since the 1980s. One of the approaches for chemotaxonomy is zymogram profiling, where species are differentiated based on the polyacrylamide gel-electrophoretic patterns of certain isoenzymes [67].
been demonstrated to be highly successful in differentiating species of *Penicillium* subgenus *Penicillium*, where the isozyme patterns showed a high correlation with morphological species [68,69]. However, when species from other *Penicillium* subgenera were also included in the analysis it was found that correlation between zymogram grouping and morphological species only existed in some cases [70], rendering the utility of this technique for the identification of *Penicillium* species questionable. On the other hand, zymogram profiling has also been applied to *Aspergillus* species and this identification method was found to be practical especially for members of the subgenera *Circumdati*, *Fumigati* and *Nidulantes* [71–73], in spite of the fact that some closely related species, such as the wild type *A. flavus* and the domesticated counterpart *A. oryzae* or the wild type *A. parasiticus* and the domesticated *A. sojae*, produced very similar isoenzyme patterns and could not be well differentiated [71]. Nonetheless, fingerprinting of isozymes has not been widely employed as a practical identification system since the enzyme profiles for the vast majority of *Aspergillus*, *Penicillium* and *Talaromyces* species remained uncharacterised. Also, there is no consensus as to which isoenzymes should be used for comparison.

Another approach for chemotaxonomy is extrolite profiling. The extometabolome reflects the physiology of an organism in response to its biotic and abiotic environment [74] and profiling of the extometabolome is particularly useful for the chemotaxonomy of *Aspergillus*, *Penicillium* and *Talaromyces* species since these genera are the best known extometabolite producers, having the most diverse spectra of extometabolites amongst 26 different groups of ascomycetes [80] best known exometabolite producers, having the most diverse spectra of exometabolites amongst 26 different groups of ascomycetes [80]. On this view, *Aspergillus* species and this identification method was found to be practical especially for members of the subgenera *Circumdati*, *Fumigati* and *Nidulantes* [71–73], in spite of the fact that some closely related species, such as the wild type *A. flavus* and the domesticated counterpart *A. oryzae* or the wild type *A. parasiticus* and the domesticated *A. sojae*, produced very similar isoenzyme patterns and could not be well differentiated [71]. Nonetheless, fingerprinting of isozymes has not been widely employed as a practical identification system since the enzyme profiles for the vast majority of *Aspergillus*, *Penicillium* and *Talaromyces* species remained uncharacterised. Also, there is no consensus as to which isoenzymes should be used for comparison.

In view of this, an *Aspergillus* Secondary Metabolites Database (AZMDB) was established last year [90]. Recently, metabolic fingerprinting has also been demonstrated as a potentially successful tool for differentiating closely related *Aspergillus* species, without the need of investigating the actual identities of the metabolites. For example, utilising this technique Tam et al. showed that *A. nomius* and *A. tamarii* could be distinguished from their morphologically similar sibling *A. flavus* [91]. In addition, hierarchical cluster analysis by Tsang et al. also showed that except for *A. australis*, the metabolic fingerprints of species in the same *Aspergillus* section clustered together and those of infraspecific strains also formed smaller clusters [92].

Fatty acid profiling is another increasingly used method in diagnosing filamentous fungal species. Although characterisation of fatty acid composition and relative concentration has long been utilised for bacterial and yeast chemotaxonomy [93,94] and there is even a commercial fatty acid methyl ester (FAME)-based bacterial/yeast identification system containing profiles from more than 1,500 different species developed [95], there are only a few studies making use of this technique to characterise the chemotaxonomy of filamentous fungi [96]. This is because filamentous fungi do not produce fatty acids in the quantity and diversity that bacteria do [97] and therefore, traditionally fatty acid profiling had been regarded to have little taxonomic value for filamentous fungi [98]. Blomquist et al. [99] first examined the utility of this technique on the identification of filamentous fungi. They characterised the fatty acid contents of conidia and found that fatty acid profiling, even though performed at different times, could potentially be used to identify *Aspergillus* and *Penicillium* species in a reproducible way [99]. In 1996, Stahl and Klug performed a large-scale study to characterise the composition and relative concentration of fatty acids in the mycelia of a number of filamentous fungi from across different phyla [98]. Seven species of *Penicillium* and one of *Aspergillus* were included in their study. It was revealed that four fatty acids, namely palmitic acid (*C16:0*), stearic acid (*C18:0*), oleic acid (*C18:1Δ9[^[cis]]*[^[cis]]* and linoleic acid (*C18:2Δ9,12[^[cis]]*[^[cis]]*), represented more than 95% of the total cellular fatty acid content. These four fatty acids were also common to all the filamentous fungi characterised. In spite of this, discriminant analysis showed that the fatty acid profiles for these species are significantly different. Notably, all the seven *Penicillium* species characterised were found to possess unique fatty acid profiles [98]. Later in 1998, Da Silva et al. expanded the characterisation to 18 *Penicillium* species [100]; and they found that different *Penicillium* subgenera could be readily differentiated by fatty acid profiling. Moreover, in some cases, species of the same subgenus such as *Fuscum* could be separated based on their fatty acid profiles, which mainly differed in the relative concentration rather than the composition of fatty acids; although difficulties existed for the subgenus *Penicillium* [100]. The fact that the species differentiation power relied on the variation in fatty acid relative concentration was observed by Mahmoud et al. as well [101]. Fatty acid profiling has also been successfully used to differentiate *Aspergillus* species [102,103].

A recent chemotaxonomic approach for rapid identification of *Aspergillus*, *Penicillium* and *Talaromyces* is matrix-assisted laser desorption/ionisation–time-of-flight (MALDI–TOF) MS. The technology compares the cellular protein profiles of different organisms to achieve identification at the species level [104]. The advantage of this technique is that the methodology is simple, rapid and inexpensive, requiring a specialised bench-top MALDI–TOF mass spectrometer only. Also, since the majority of proteins analysed by MALDI–TOF MS are constitutively expressed...
Table 2

Novel Aspergillus, Penicillium and Talaromyces species/taxonomic entities described during January, 2013 to December, 2017 sampled from human or non-human vertebrate specimens

| Species Synonym(s) | Associated human infections or clinical specimensa | Associated non-human vertebrates | Molecular markersb | Year of valid publication | Reference(s) |
|--------------------|---------------------------------------------------|--------------------------------|-------------------|--------------------------|--------------|
| Aspergillus A. aurantiopurpureus Novel species | Kangaroo rat cheek pouch | ITS, bna, cmdA and rpb2 | 2016 | [86] |
| A. caninus ≡ Phialosimplex caninus | Bone marrow aspirate of a dog | rpb2 | 2014 | [2,176,177] |
| A. capsici ≡ Scopulariopsis capsica = Leuconeurospora capsica | Fur and skin of hibernating bat | | 2014 | [2,178] |
| A. chlamydosporus ≡ Phialosimplex chlamydosporus | Disseminated infection in a dog | rpb2 | 2014 | [2,176,179,180] |
| A. citrinoterreus Novel species | Nails, various respiratory specimen, wound and biopsy | bna and cmdA | 2015 | [181] |
| A. contaminans Novel species | Fingernail (probably as a contaminant) | ITS, bna, cmdA and rpb2 | 2017 | [182] |
| A. europaeus Novel species | Toenail | ITS, bna and cmdA | 2017 | [183] |
| A. felis Novel species | Chronic invasive pulmonary aspergillosis and onychomycosis; BAL, oropharyngeal exudate and sputum Invasive fungal rhinosinusitis in domestic cats and disseminated invasive aspergillosis in a dog | ITS, bna and cmdA | 2013 | [184–187] |
| A. hongkongensis Novel species | Onychomycosis | | 2016 | [92] |
| A. insolitus ≡ Polypaecilum insolitum | Onychomycosis; ear | cc8, rpb2 and tsr1 | 2014 | [2,188] |
| A. keratitidis ≡ Sagenomella keratitidis | Keratitis | ITS and 28S nrDNA | 2017 | [189,190] |
| A. latilabiatus Novel species | Sheep dung | ITS, bna, cmdA and rpb2 | 2016 | [86] |
| A. latus ≡ Aspergillus nidulans var. latus = Aspergillus montenegroi = Aspergillus sublatus = Emericella montenegroi = Emericella nidulans var. lata = Emericella sublata | Invasive pulmonary aspergillosis | ITS, bna, cmdA and rpb2 | 2016 | [53,86,191–195] |
| A. magnivesiculatus Novel species | Child carriers | ITS, bna, cmdA and rpb2 | 2017 | [171] |
| A. mallochii Novel species | Pack rat dung | bna, cmdA and rpb2 | 2017 | [196] |
| A. microperforatus Novel species | Lymph node and toenail | ITS, bna, cmdA and rpb2 | 2017 | [151] |
| A. pallidofulvus ≡ Aspergillus sulphureus var. minimus | Invasive pulmonary aspergillosis and disseminated aspergillosis | ITS, bna, cmdA | 2014 | [122,197] |
| A. parafelis Novel species | Invasive aspergillosis; oropharyngeal exudate and sputum Cats | bna, cmdA, rpb2, mcm7 and tsr1 | 2014 | [198,199] |
| A. pragensis Aspergillus section Candidi | Onychomycosis | ITS, bna and cmdA | 2014 | [200] |
| A. pseudofelis Novel species | Invasive aspergillosis; sputum and nail | bna, cmdA, rpb2, mcm7 and tsr1 | 2014 | [198] |
| A. pseudogracilis Novel species | Child carrier | ITS, bna, cmdA and rpb2 | 2017 | [171] |
| A. pseudosclerotiorum pseudoviridinutans Novel species | BAL, lung and sputum | ITS, bna, cmdA and rpb2 | 2017 | [149] |
| A. reticulatus Novel species | Invasive aspergillosis; mediastinal lymph node | bna, cmdA, rpb2, mcm7 and tsr1 | 2014 | [198] |
| A. sclerotialis * Sagenomella sclerotialis = Phialosimplex sclerotialis | Lung biopsy, child carrier | ITS, bna, cmdA and rpb2 | 2017 | [171] |
| A. spinulosporus ≡ Aspergillus nidulans | Recurrent prosthetic valve endocarditis | ITS, bna, cmdA | 2016 | [2,202–208] |
ribosomal proteins, microorganisms can be successfully identified even though varying culture media and incubation conditions are used [104,105]. More importantly, databases consisting of protein mass spectra from over 2,400 microbial species are commercially available [106,107], making the identification of a wide range of microorganisms possible. Given its numerous advantages, MALDI–TOF MS has been gaining popularity for identification of pathogenic microorganisms, including bacteria [108,109], yeasts [108–115] and even filamentous fungi [109,116–118], in clinical microbiology laboratories. The potential of this technology in diagnosing Aspergillus, Penicillium and Talaromyces species has also been evaluated by numerous studies. In general, MALDI–TOF MS is successful in identifying the more commonly found aspergilli/penicillia, such as A. flavus, A. fumigatus, A. nidulans, A. niger, A. sydowii, A. unguis, P. chrysogenum, P. aurantiogriseum and P. purpurogenum, with correct identification rates of ≥78% [117–121]. Yet, for other rare species misidentification is often encountered. Notably, these uncommon species could usually be identified to the sectional level. For example, A. tritici (section Candidi) was misidentified as A. candidus; A. oryzae (section Flavi) as A. flavus; A. fischeri (section Fumigati) as A. fumigatus; A. tubingensis and A. welwitschiae (section Nigr) as A. niger; A. hortai and A. niveus (section Terrei) as A. terreus; as well as A. sydowii (formerly section Versicolo) as A. versicolor [92,122]. A probable reason for this is that the mass spectra for many of these rare species are lacking in the commercial libraries. It should be noted that the Bruker MBT MSP 6903 Library, Bruker MBT Filamentous Fungi Library and Vitex MS V3.0 Knowledge Base only include reference mass spectra for 42, 127 and 82 filamentous fungal species, respectively [106,117,123]. Of these, only up to 22 Aspergillus, 21 Penicillium and 6 Talaromyces, which are still named with their previous Penicillium synonyms, species are included [107,123]. However, the numbers of accepted Aspergillus, Penicillium and Talaromyces species greatly outnumber those included in the MALDI–TOF MS databases, with both Aspergillus and Penicillium having approximately 350 species [1,2,60] and Talaromyces having more than 100 species [63,89]. Despite this, MALDI–TOF MS has still been demonstrated as a potential tool to differentiate members of the three genera by hierarchical cluster analysis of the mass spectra of various species [91,124,125]. As a result, theoretically if more reference mass spectra for different species, especially the rare ones, are generated for inclusion in the databases the species diagnosis power of MALDI–TOF MS would be greatly enhanced and it has already been exemplified by previous studies that the correct identification rates could be improved by the expansion of reference libraries.

| Table 2 (continued) |
|---------------------|-----------------|-----------------|-----------------|-----------------|
| Species             | Synonym(s)      | Associated human infections or clinical specimens* | Associated non-human vertebrates | Molecular markers* | Year of valid publication | Reference(s) |
| Emericella echinulata var. echinulatus = Aspergillus delacroixi (Samson, Visagie & Houbraken) | ribosomal proteins, microorganisms can be successfully identified even though varying culture media and incubation conditions are used [104,105]. More importantly, databases consisting of protein mass spectra from over 2,400 microbial species are commercially available [106,107], making the identification of a wide range of microorganisms possible. Given its numerous advantages, MALDI–TOF MS has been gaining popularity for identification of pathogenic microorganisms, including bacteria [108,109], yeasts [108–115] and even filamentous fungi [109,116–118], in clinical microbiology laboratories. The potential of this technology in diagnosing Aspergillus, Penicillium and Talaromyces species has also been evaluated by numerous studies. In general, MALDI–TOF MS is successful in identifying the more commonly found aspergilli/penicillia, such as A. flavus, A. fumigatus, A. nidulans, A. niger, A. sydowii, A. unguis, P. chrysogenum, P. aurantiogriseum and P. purpurogenum, with correct identification rates of ≥78% [117–121]. Yet, for other rare species misidentification is often encountered. Notably, these uncommon species could usually be identified to the sectional level. For example, A. tritici (section Candidi) was misidentified as A. candidus; A. oryzae (section Flavi) as A. flavus; A. fischeri (section Fumigati) as A. fumigatus; A. tubingensis and A. welwitschiae (section Nigr) as A. niger; A. hortai and A. niveus (section Terrei) as A. terreus; as well as A. sydowii (formerly section Versicolo) as A. versicolor [92,122]. A probable reason for this is that the mass spectra for many of these rare species are lacking in the commercial libraries. It should be noted that the Bruker MBT MSP 6903 Library, Bruker MBT Filamentous Fungi Library and Vitex MS V3.0 Knowledge Base only include reference mass spectra for 42, 127 and 82 filamentous fungal species, respectively [106,117,123]. Of these, only up to 22 Aspergillus, 21 Penicillium and 6 Talaromyces, which are still named with their previous Penicillium synonyms, species are included [107,123]. However, the numbers of accepted Aspergillus, Penicillium and Talaromyces species greatly outnumber those included in the MALDI–TOF MS databases, with both Aspergillus and Penicillium having approximately 350 species [1,2,60] and Talaromyces having more than 100 species [63,89]. Despite this, MALDI–TOF MS has still been demonstrated as a potential tool to differentiate members of the three genera by hierarchical cluster analysis of the mass spectra of various species [91,124,125]. As a result, theoretically if more reference mass spectra for different species, especially the rare ones, are generated for inclusion in the databases the species diagnosis power of MALDI–TOF MS would be greatly enhanced and it has already been exemplified by previous studies that the correct identification rates could be improved by the expansion of reference libraries. |

| = Aspergillus echinulatus | Aspergillus delacroixi (Samson, Visagie & Houbraken) | and invasive pulmonary aspergillosis | and rpb2 | 2016 | [86] |
| A. candidus | Novelia species | Lizard (Uromastix acanthinurus) | ITS, bnaA, cmdA and rpb2 | 2014 | [134,209] |
| A. fumigatus | Novelia species | Bone lesion of spayed Rhodesian ridgeback dog with osteomyelitis | ITS, bnaA and cmdA | 2014 | [210] |
| A. oryzae (section Flavi) | Novelia species | Mouse dung | ITS, bnaA, cmdA and rpb2 | 2016 | [173] |
| P. aurantiogriseum | Novelia species | Dung of dog and opossum | ITS, bnaA, cmdA and rpb2 | 2014 | [1,202,211,212] |
| T. alveolaris | Novel species | BAL | ITS, bnaA, cmdA and rpb2 | 2016 | [173] |
| T. atroroseus | Novel species | Mouse dung | ITS, bnaA, cmdA and rpb2 | 2017 | [150] |
| T. columbinus | Novel species | Fungaemia and pulmonary nodule and adjacent rib osteomyelitis | ITS, bnaA, cmdA, rpb1, rpb2, mcm7 and tsr1 | 2013 | [214–216] |
| T. Dịchgiensis | Novel species | Animal joint fluid | ITS, bnaA and rpb2 | 2017 | [150] |
| T. kalandensis | Novel species | BAL | ITS, bnaA, cmdA and rpb2 | 2016 | [150,217] |
| T. minnesotensis | Novel species | Ear | ITS, bnaA, cmdA and rpb2 | 2017 | [150] |
| T. rapidus | Novel species | BAL | ITS, bnaA, cmdA and rpb2 | 2017 | [150] |
| T. siglerae | Novel species | Tinea capitis | ITS, bnaA, cmdA and rpb2 | 2017 | [218] |

* BAL, bronchoalveolar lavage |

** a, b bnaA, β-tubulin gene; cmdA, chaperonin-containing T-complex protein 1 subunit theta gene; cmdA, calmodulin gene; ITS, internal transcribed spacer; mcm7, mini-chromosome maintenance complex component 7 gene; mDNA, nuclear ribosomal rDNA gene; rpb1, RNA polymerase II largest subunit gene; rpb2, RNA polymerase II second largest subunit gene; tsr1, ribosome maturation factor for 20S rRNA accumulation gene
using inhouse generated mass spectra [118,122,125]. To overcome the limitation of small reference data volume of the commercial databases, several organisations have self-established online supplementary databases. For example, the Spectra database (freely available at https://spectra.folkhalsomyndigheten.se/spectra/) by the Public Health Agency of Sweden (Folkhälsomyndigheten) is a platform for MALDI–TOF MS users to deposit and exchange user-generated mass spectra which are curated and continuously updated. Another such complementary database is the MSi Platform which serves as a webtool for MALDI–TOF MS-based fungal identification. This platform contains more than 11,800 reference mass spectra of more than 900 fungal species, aiming at supplementing the insufficient spectral diversity of the commercial databases so as to improve species identification [126].

With the current adoption of consolidated species recognition where molecular characters play a predominant role, DNA sequencing and phylogenetic analysis have become the gold standard for accurate fungal identification. As in other fungi, early molecular work on *Aspergillus*, *Penicillium* and *Talaromyces* involved the comparison of large and small subunit ribosomal nucleic acid (mitochondrial and/or nuclear) as well as internal transcribed spacer (ITS) sequences [43–45,127]. However, subsequent analysis showed that ribosomal genes are too conserved to separate these groups of fungi [128,129]. In addition, although ITS is now accepted as the official DNA barcode for fungi [130], it has also been recognised as an extremely conserved region for *Aspergillus*, *Penicillium* and *Talaromyces* [1,2,63]. Despite the fact that its sequence variability could be used to distinguish species belonging to different sections or series [128], very often it is not useful for the differentiation of species within the same section or series. In view of this and also to better reflect the genealogy of this group of organisms, sequencing of multiple genetic markers, in particular the β-tubulin (*benA*) and calmodulin (*cmdA* or CaM) genes, to define species boundaries has been advocated [131]. The exons of these genes are highly conserved and are therefore good locations for primer binding, whereas introns in between the exons act as the major source of sequence variation. As a result, sequences of these genes containing both exons and introns are able to provide variations at different levels for species delimitation [131]. With the majority of *Aspergillus*, *Penicillium* and *Talaromyces* species clearly defined nowadays, sequencing of *benA* and/or *cmdA* can be utilised to identify most of these species. In fact, *benA* and *cmdA* have been proposed as the secondary identification markers for *Penicillium* and *Aspergillus* species, respectively [1,2]. This is because there are universal primers available for these two genes and both of them are easy to amplify. In the case of *Aspergillus*, although *benA* could be easily amplified, the presence of paralogous genes (e.g. *tubC*) in some species which could also be amplified by the universal primers could be confusing and complicate species identification [132,133]. In contrast, although a similar problem has also been noted for *cmdA*, amplification of a pseudogene only occurred for one *Aspergillus* strain [134]. Moreover, *cmdA* is also easy to amplify and its sequence is available for nearly all accepted species. Therefore, *cmdA* was chosen over *benA* as secondary identification marker for *Aspergillus* [2]. On the other hand, as for *Penicillium*, amplification of *benA* paralogues has not been reported and since a complete *cmdA* sequence database is lacking, *benA* became the secondary identification marker of choice [1]. Although a third option, RNA polymerase II second-largest subunit gene (*rpb2*), also exists and its lack of introns allows robust and easy alignment for phylogenetic analysis, it was not selected over *benA* or *cmdA* because *rpb2* is sometimes difficult to amplify and a database with sufficient volume is lacking [1,2]. Nonetheless, when resources are available it is recommended to sequence all the four genetic markers (ITS, *benA*, *cmdA* and *rpb2*) to aid identification, especially when new species are diagnosed [1,2]. Although a recommendation of identification markers has not been put forward for *Talaromyces* species, they generally follow those for *Aspergillus* and *Penicillium* species [63]. In order to achieve accurate identification, sequences from reliable databases should be compared against. Despite the fact that the International Nucleotide Sequence Database Collaboration (INSDC) [135] contains a vast number of sequences, the reliability of the sequence annotation is questionable [136,137]. Notably, ≥10% of the fungal ITS sequences in these databases were found to be misannotated [136]. As such, the Fun- gal ITS ReSeq Targeted Loci Project has been initiated by the National Center for Biotechnology Information (NCBI) to improve the quality and accuracy of the sequences deposited to INSDC [138,139]. Similarly, the UNITe database was developed to include high-quality type or representative sequences for fungi or fungal species hypothesis with correct or up-to-date taxonomic annotations [140]. The International Society for Human and Animal Mycology (ISHAM) ITS database, specialised in the ITS-based identification of medical fungi, has also been recently established [141] and it contains quite a number of high-quality ITS sequences for *Aspergillus*, *Penicillium* and *Talaromyces* species, which are commonly encountered in the clinical settings. While curated databases for *benA*, *cmdA* and *rpb2* have not been created, reliable sequences for all the ex-type strains of *Aspergillus*, *Penicillium* and *Talaromyces* accepted species have been listed in the recent monographs on the three genera [1,2,63] or online at http://www.aspergilluspenicillium.org/. In addition to nuclear genes, attempts have also been made to understand the evolution (and thus species recognition) of *Aspergillus*, *Penicillium* and *Talaromyces* by sequencing of mitogenomes [142–145]. Yet, only a handful of mitogenomes are available for these groups of fungi currently and the utility of mitogenomes for species diagnosis awaits further examination.

## 4. Clinical perspectives

A stable taxonomy is important to the study of *Aspergillus*, *Penicillium* and *Talaromyces* in every aspect including medical mycology. First of all, the nomenclature of pathogenic fungi should be steady over time, without frequent vigorous name changes. The recently implemented 1F1N scheme, where one fungus shall only possess one name, drastically simplified fungal nomenclature. The accepted use of *Aspergillus* and *Penicillium* names over their respective ‘sexual names’ is particularly important to the medical community. This is because most clinical fungi are isolated in the asexual forms and these fungi are traditionally named with their asexual names. Use of the ‘sexual names’ would confuse clinicians since they would not be aware of what *Eupenicillium*, *Neosartorya* and *Emericella* are, thus hindering treatment and patient care. This could be exemplified by the recent transfer of *P. marneffei* to *T. marneffei*, where the well-known disease name ‘penicillosis’ also has to be changed to the unfamiliar ‘talaromycosis’. A stable taxonomy also clearly defines species and their identification methods. Therefore, the clinical spectrum of pathogenic species could also be better studied. In particular, rare and new aetiological agents could be revealed (Table 2) [92,146–151]. Accurate identification of the causative pathogen is crucial to epidemiological studies. Correct species diagnosis could also help predict antifungal susceptibility, which varies across different species and this could significantly affect patient treatment, disease management and prognosis. For example, it has been shown that *A. tubingensis* and *A. urginis* possessed elevated minimum inhibitory concentrations (MICs) to itraconazole [92]. The fact that triazole agents exhibit various activities against different *Aspergillus* species has also been demonstrated by other studies [148,149,151]. Also, although triazoles showed moderate activities against *Penicillium* species, their effectiveness against some *Talaromyces* species are poor [147].

## 5. Summary and outlook

With a consistent taxonomy, understanding on the epidemiology and clinical spectrum of diseases caused by *Aspergillus*, *Penicillium* and *Talaromyces* could be enhanced. This in turn facilitates laboratory diagnosis of these important mycotic pathogens and establishment of patient treatment strategies. The transition from morphological/
phenotypic to chemotaxonomic, genetic/phylogenetic, or consolidated species recognition results in the reclassification of these groups of fungi and enables sexual-asexual connection. In the current omics era, advancement in different omics technologies makes characterisation of the complete set of a particular group of characters possible, allowing more thorough analyses and therefore, a more stable taxonomy. For example, comparison of mitogenomes supported the transfer of *P. marneffei* to *Talaromyces* and demonstrated that *Aspergillus* and *Penicillium* are more closely related to each other than to *Talaromyces* [142,144,145]. The availability of contemporary advanced techniques, such as MALDI–TOF MS as well as UHPLC/HPLC–DAD–MS, significantly improves proteomic and metabolic fingerprinting of fungi, respectively, thus aiding chemotaxonomy. As the cost for second-generation sequencing is getting lower and the emerging third–generation sequencing is becoming more widely accessible, more and more complete/almost complete fungal genomes become available. These genome sequences could advance our knowledge on these fungi, such as *T. marneffei* [144,152–158], and taxonomy on them could thus be facilitated. With such additional novel data, further reclassification on *Aspergillus*, *Penicillium* and *Talaromyces* is expected. Application of all these state–of-the-art omics technologies is likely to provide comprehensive information on the evolution of the three related genera, and a more stable taxonomy for them will hopefully be achieved. Yet, it should be noted that even though these advanced methodologies are becoming more readily available for the identification and classification of fungi, it is equally important for mycologists to apply standard or best practices when studying fungal taxonomic relationships. In particular, fungal taxonomists should always keep themselves up–to-date with recent trends, tools, standards, recommendations and practices in the field, especially when describing new species [159–163]. When depositing DNA sequence data to public databases, the sequences should be well checked for authenticity as well as reliability [164], and they should be richly annotated as far as possible [165]. Also, multiple genetic markers and proper analytical tools should be used for the inference of phylogenetic relationships [166]. As nowadays taxonomy has entered a deep crisis where descriptive taxonomic studies are not encouraged, it is important for taxonomists to keep the pace for re–growth, to participate actively and to form a good ‘taxonomic culture’ so that the scientific community would value taxonomic work higher [167]. This could also help attract more research funding for more expensive technology or equipment for more detailed taxonomic characterisation. All these efforts could help speed up taxonomic and molecular ecology progress on *Aspergillus*, *Penicillium* and *Talaromyces* significantly.

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Conflict of interest

Patrick C.Y. Woo has provided scientific advisory/laboratory services for Gilead Sciences, Incorporated; International Health Management Associates, Incorporated; Merck & Corporation, Incorporated and Pfizer, Incorporated. The other authors report no conflicts of interest. The funding sources had no role in study design, data collection, analysis, interpretation or writing of the report. The authors alone are responsible for the content and the writing of the manuscript.

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Aspergillus fumigatus

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