Mycopathologia (2020) 185:87–101
https://doi.org/10.1007/s11046-019-00390-3

ORIGINAL PAPER

She Loves Me, She Loves Me Not: On the Dualistic Asexual/Sexual Nature of Dermatophyte Fungi

Banu Metin · **Joseph Heitman**

Received: 25 April 2019 / Accepted: 23 September 2019

Abstract Dermatophytes are ascomycetous fungi whose sexuality is greatly influenced by their ecology. Sexual reproduction is ubiquitous among soil-related geophiles and some animal-associated zoophiles. In contrast, anthropophiles are generally present as a single mating type in the population and appear to reproduce asexually. In this article, the current knowledge on the sexuality of dermatophytes including reproduction modes, mating conditions, mating type distributions and the mating type (*MAT*) locus is presented in the context of revised taxonomy and discussed from an evolutionary perspective.

Keywords Dermatophytes · Sexual reproduction · Mating · Mating type (*MAT*) locus

Introduction

Although costly, sexual reproduction is widespread throughout eukaryotes possible because of its counterbalancing benefits such as the selection of beneficial mutations from a deleterious background and accelerating adaptation in response to changing conditions [1, 2]. Asexuality might provide short-term advantages based on well-adapted genomic configurations, but due to the lack of a mechanism providing adaptation and because of the accumulation of deleterious mutations, asexual species are at an increased risk of extinction. Therefore, the few examples that appear to be asexual have been referred to as evolutionary scandals [3, 4].

Sexual reproduction is pervasive in the fungal kingdom, but approximately 20% of fungi have been referred to as asexual because they do not have a known sexual cycle [5]. Recent molecular evidence brings into question whether these species are indeed asexual based on the presence of mating- and meiosis-related genes in the genomes of these presumed "asexual fungi." In fact, direct or indirect evidence of sexual cycles has been discovered for many of these species. One of the most notable is *Candida albicans*, in which a parasexual cycle was identified involving the fusion of two diploid cells to produce a tetraploid cell, which morphs into a diploid/aneuploid state via concerted chromosome loss [6, 7]. Another example is *Aspergillus fumigatus*, a species that has long been

---

Handling editor: Sybren deHoog.

B. Metin (✉)
Department of Food Engineering, Faculty of Engineering and Natural Sciences, Istanbul Sabahattin Zaim University, Halkali Cad, No: 2, Halkali, Kucukcekmece, 34303 Istanbul, Turkey
e-mail: banu.metin@izu.edu.tr

J. Heitman
Department of Molecular Genetics and Microbiology, Duke University Medical Center, Durham, NC 27710, USA

regarded as asexual. *A. fumigatus* forms cleistothecia (fruiting bodies) on oatmeal agar after extended incubation time for up to 6 months [8]. The discovery of sexual reproduction in several other *Aspergillus* and *Penicillium* species followed these findings [5, 9].

Sexual reproduction in the Pezizomycotina subphylum of Ascomycota is governed by a single mating type (*MAT*) locus [10, 11]. There are two alleles of the *MAT* locus, termed idiomorphs, that are completely different in sequence and harbor key transcription factor genes [12]. One of the idiomorphs, *MAT1-1*, codes for an alpha-domain transcription factor, while the other, *MAT1-2*, encodes a high-mobility group (HMG) transcription factor. In heterothallic species, isolates harboring different idiomorphs are mating partners, while homothallic species bear both idiomorphs (linked or unlinked) in their genome, permitting self-fertility. However, there are also self-fertile species harboring only a single *MAT* idiomorph in their genome [13, 14]. This special type of homothallism is called unisexual reproduction and has been observed in a number of species including the pathogens *Cryptococcus neoformans* and *C. albicans*, as well as in certain species of *Neurospora*, *Stemphylium*, and *Huntiella* [15–19].

Dermatophytes belong to the family of Arthrodermataceae in Onygenales, an order that contains several pathogenic filamentous fungi [20]. Dermatophytes are keratinolytic fungi that live as saprobes in soil containing keratinaceous debris or as commensals on the hairy skin of animals, but these species can also cause infections in both humans and in animals [21]. They are classified into three groups based on their habitats: the soil-related geophiles, animal-associated zoophilic organisms, and human-associated anthropophiles [22]. Sexual reproduction is common in geophilic species and in zoophiles related to animals closely associated with soil [23]. Therefore, it has been hypothesized that the niche in which the sexual reproduction of dermatophytes occurs in nature is soil with keratin sources [24]. On the other hand, nonsoil-associated dermatophytes, such as anthropophiles and some zoophiles, seem to have lost the ability to sexually reproduce [24, 25]. In addition, some of the anthropophiles such as *Trichophyton rubrum* and *T. interdigitale* appear to be present as a single mating type in the population [23, 26–29]. However, recent genomic evidence shows that these species have the necessary mating- and meiosis-related genes in their genome compared to their sexually reproducing relatives [30, 31].

Sexual reproduction of dermatophytes can be observed in the laboratory by using a variety of media. The most common and oldest of these are hair and soil plates [32–34] resembling the niche of geophiles. Other media, such as DCM agar with powdered hair, dextrose agar with powdered hair [35], 2.5% malt extract agar [36], oatmeal salts agar [37], diluted Sabouraud dextrose agar with salts [38, 39], diluted Pablum cereal agar with salts [39], and niger seeds salt agar with yeast extract [40], have also successfully been used for different species as detailed later in the text. Because most sexually reproducing dermatophyte species are heterothallic, compatible mating partners, (+) and (−), or *A* and **a**, are inoculated on these media a couple of mm's apart [35, 36] and incubated mostly at room temperature to see the fruiting bodies [35]. These structures are called gymnothecia or cleistothecia bearing asci and ascospores enclosed by an interwoven network of peridial hyphae [36, 41]. Even the single mating type having species, for which sexual reproduction has not been seen, has been observed to demonstrate a positive response when co-cultured with compatible mating type isolates of tester strains of *T. simii* [26]. Before the molecular era, the “Stockdale test” had been very helpful in indicating the mating type of nonmating species.

The *MAT* locus structure is very similar among dermatophytes (Fig. 1) [23]. For the dermatophytes where both mating type sequences are available, such as *T. benhamiae* and *N. gypsea*, the *MAT* locus boundaries can be determined [42, 43]. In addition to harboring the key transcription factor gene (*MAT1-1-1* or *MAT1-2*-1), the *MAT* locus extends to include the 3′ end of the *MAT1-1-4* gene on the right and the 5′ end of a gene coding for a hypothetical protein (*HYP1*) on the left. In other Pezizomycotina members, generally, *SLA2* is located on the left of the *MAT* locus and *APN2* and *COX13* are located on the right [44]; however, all three genes are linked to the right-hand side of the *MAT* locus in dermatophytes.

In this review, we discuss the current knowledge on dermatophyte reproductive strategies, mating conditions, *MAT* loci and mating types based on the revised taxonomy, which defines the dermatophytes into nine genera: *Guarromyces*, *Ctenomyces*, *Arthroderma*,

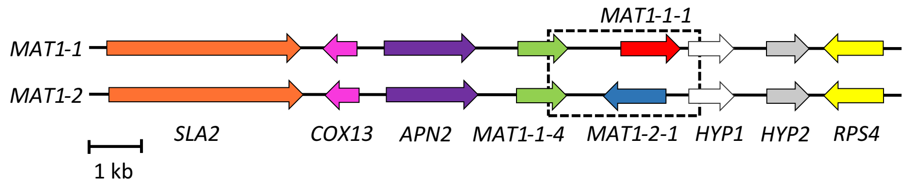

Fig. 1 Archetypal *MAT* locus structure of dermatophytes. The isolates harboring the *MAT1-1* locus are *T. benhamiae* CBS809.72 (GQ996965.1), *T. rubrum* CBS118892 (NW_003456427.1), *T. tonsurans* CBS112818 (GG698488.1), *M. canis* CBS113480 (DS995708.1), and *N. gypsea* CBS118893 (FJ798794.1). The *MAT1-2* locus-bearing isolates are *T. benhamiae* strain 2354 (ABSU01000008.1), *T. equinum* CBS127.97 (DS995742.1), *T. verrucosum* HKI 0517 (NW_003315532.1), *T. megninii* CBS735.88 (KK210299.1), *T. interdigitale* MR816 (AOKY01000593.1), and *N. gypsea* ATCC48982 (The available sequence (FJ798798.1) harbors *SLA2*, *COX13*, *APN2*, *MAT1-1-4*, *MAT1-2-1*, and *HYP1*.). The dashed line indicates the limits of the *MAT* locus for *T. benhamiae*

Lophophyton, *Microsporum*, *Epidermophyton*, *Paraphyton*, *Nannizzia*, and *Trichophyton* [20].

The Genera *Guarromyces*, *Ctenomyces*, and *Arthoderma*

Guarromyces and *Ctenomyces* are basal genera of dermatophytes [20] (Table 1). *Guarromyces* was defined recently in the new taxonomy and is represented by one species, *Guarromyces ceretanicus*, with the older name *Keratinomyces ceretanicus*, which is a soil fungus with no known sexual cycle [20, 45]. In the genus *Ctenomyces*, several species have been described. *Ctenomyces serratus* is the type species and is associated with soil and feathers [46]. It is the only species of *Ctenomyces* described with a sexual cycle. The ascomata of *C. serratus*, which can be observed on hair and soil plates, oatmeal salts agar (Medium E), and diluted Pablum cereal agar with added salts, are clearly different from those of the rest of the dermatophytes with distinct ctenoid appendages that resemble the teeth of a comb with tiny projections [46, 47]. The sexual cycle observed is heterothallic [48]. In a study analyzing the mating behavior of *C. serratus*, of the 19 isolates analyzed, seven were found to be (−) and 11 were of (+) mating type, while one isolate was sterile with the isolates tested [47]. Four new *Ctenomyces* species, *C. indicus*, *C. albus*, *C. obovatus*, *C. peltricolor*, isolated from soil have recently been described [49, 50]. In addition, *Ctenomyces vellereus*, previously proposed to be a synonym of *C. serratus* [51, 52], was suggested to be a separate species in these studies.

According to the new taxonomic scheme, the previous teleomorphic genus name *Arthroderma* was accepted as the genus name of the species of dermatophytes harboring mostly geophilic and sexually reproducing species [20]. The genus *Arthroderma* comprises 22 species, 16 of which have the ability to reproduce sexually (Table 1). Most of these species have heterothallic sexual cycles; the only exceptions are *A. ciferrii* and *A. curreyi*, which have been described as homothallic [23, 53–56].

Arthroderma species have mainly been isolated from decaying feathers in soil near burrows or from animal fur. For example, *A. cuniculi* and *A. multifidum* were isolated from the soil of rabbit burrows and from apparently normal live rabbits [57]. Other studies reported *A. gloriae*, *A. uncinatum*, *A. phaseoliforme*, and *A. insingulare* from soil samples [58–61], *A. ciferrii* from the soil of hog pens [55], *A. melis* from badger burrows [62], *A. eboreum* from the soil of badger and rabbit burrows [63], *A. tuberculatum* from bird-related environments such as the feathers of a robin and from an owl pellet and soil [64, 65], *A. flavescens* from birds [66], *A. amazonicum* and *A. redellii* from rats [67, 68], *A. vespertilii* from bats [69], *A. silverae* from arctic fox dung from arctic regions [70], and *A. thuringiensis* from small mammals and once from a human [71, 72].

Sexual reproduction is common in *Arthroderma* and can be induced using a variety of media, such as oatmeal agar, water agar, Takashio medium with hair [73], hair and soil plates [55, 57–60, 63, 68, 74], and oatmeal salts agar (Medium E) [37, 65, 75]. Only *A. onychocola* requires special conditions: low temperature (17 °C, instead of 25 °C) for gymnothecia formation [73]. Ascomata are similar between the

Table 1 Host preferences and mating characteristics of the species of the genera *Guarromyces*, *Ctenomyces*, and *Arthroderma*

Genera	Species	Host	Mating	References
Guarromyces	*G. ceretanicus*	Geophilic?	?	[20, 45]
Ctenomyces	*C. serratus*	Geophilic?	Heterothallic	[46–48]
	C. vellereus	?	?	[49–52]
	C. indicus	?	?	[49]
	C. albus	?	?	[50]
	C. obovatus	?	?	[50]
	C. peltricolor	?	?	[50]
Arthroderma	*A. amazonicum*	Zoophilic	Heterothallic	[54, 68]
	A. ciferrii	Geophilic	Homothallic	[54, 55]
	A. cuniculi	Geophilic	Heterothallic	[57]
	A. curreyi	Geophilic	Homothallic	[53, 56]
	A. chiloniense	?	?	[76]
	A. eboreum	Zoophilic	Heterothallic	[63]
	A. flavescens	Zoophilic	Heterothallic	[54, 66]
	A. gertleri	Geophilic	Heterothallic	[54, 77]
	A. gloriae	Geophilic	Heterothallic	[58]
	A. insingulare	Geophilic	Heterothallic	[54, 59]
	A. lenticulare	Geophilic	Heterothallic	[54, 74]
	A. melis	Geophilic	Heterothallic	[62]
	A. multifidum	Geophilic	Heterothallic	[57]
	A. onychocola	?	Heterothallic	[73]
	A. phaseoliforme	Geophilic	?	[61]
	A. redellii	Zoophilic	?	[67]
	A. silverae	?	?	[70]
	A. thuringiensis	Zoophilic?	?	[71–73]
	A. quadrifidum	Geophilic	Heterothallic	[34, 54]
	A. tuberculatum	Zoophilic	Heterothallic	[64, 65]
	A. uncinatum	Geophilic	Heterothallic	[34, 54]
	A. vespertilii	Zoophilic	?	[69]

Arthroderma species and have peridial walls formed by a network of interwoven hyphae composed of dumbbell-shaped cells, sometimes terminating with spiral appendages [68].

The structure of the *MAT* locus of *Arthroderma* species is not yet known. The only molecular study involved PCR amplification of *MAT1-2* from single isolates of *A. onychocola* and *A. thuringiensis*, a species with no known sexual cycle [73].

The Genera *Lophophyton*, *Microsporum*, *Paraphyton*, *Epidermophyton*, and *Nannizzia*

Lophophyton

Lophophyton gallinae is the only species of the *Lophophyton* genus [20]. It is a zoophilic species that has been isolated from a squirrel, a dog, a cat, humans, and soil (Table 2) [78–81]. The sexual cycle of *L. gallinae* is heterothallic and was observed on hair and soil plates, oatmeal salts agar, diluted Sabouraud dextrose agar with salts, and diluted Pablum cereal agar with salts [39, 78]. The ascomata resemble those of the *Arthroderma*, with interwoven, branched, septate peridial hyphae, and spiral appendages;

Table 2 Sexual reproductive patterns and host characteristics of the genera *Lophophyton*, *Microsporum*, *Paraphyton*, *Epidermophyton*, and *Nannizzia*

Genera	Species	Host	Mating	*MAT* idiomorph	References
Epidermophyton	*E. floccosum*	Anthropophilic	?	?	[26, 93]
Nannizzia	*N. aenigmatum*	?	?	*MAT1-2* (single isolate)	[73, 107]
	N. corniculata	Geophilic	Heterothallic	Not determined	[99]
	N. duboisii	?	?	?	[20]
	N. fulva	Geophilic	Heterothallic	*MAT1-1* and *MAT1-2*	[94, 98]
	N. gypsea	Geophilic	Heterothallic	*MAT1-1* and *MAT1-2*	[43, 94]
	N. incurvata	Geophilic	Heterothallic	*MAT1-1* and *MAT1-2*	[41, 43]
	N. nana	Zoophilic	Heterothallic	Not determined	[34]
	N. perplicata	?	?	?	[108]
	N. persicolor	Zoophilic	Heterothallic	Not determined	[101]
	N. praecox	Geophilic?	?	?	[109–111]
Paraphyton	*P. cookei*	Geophilic	Heterothallic	?	[89, 90]
	P. cookiellum	Geophilic	Heterothallic	?	[88]
	P. mirabile	Zoophilic	Heterothallic	?	[92]
Lophophyton	*L. gallinae*	Zoophilic	Heterothallic	?	[78, 79]
Microsporum	*M. canis*	Zoophilic	Heterothallic	Predominantly *MAT1-1*	[40, 84, 85]
	M. audouinii	Anthropophilic	?	*MAT1-2*	[87]
	M. ferrugineum	Anthropophilic	?	*MAT1-2*	[87]

however, the peridial cells have been described to be only gradually constricted at the center as opposed to the dumbbell-shaped cells of *Arthroderma* [78]. The *MAT* locus of *L. gallinae* has not been described, yet.

Microsporum

The *Microsporum* clade consists of three species: *M. canis*, which is zoophilic, and the anthropophilic species, *M. audouinii* and *M. ferrugineum*. Among these, only *M. canis* has a heterothallic sexual cycle that can be observed on hair and soil plates, oatmeal salts agar, and Niger seed salts agar with yeast extract (Table 2) [40, 82, 83]. Ascomata of *M. canis* consist of septate, echinulate (spiny), and usually curved peridial hyphae harboring dumbbell-shaped outer cells and spiral appendages [64]. However, almost all *M. canis* isolates are the (−) mating type [40, 84]. A total of 12 (+) mating type isolates, all from Japan, have been reported [40, 82, 83, 85]. The (+) and (−) mating type isolates currently used in phylogenetic studies, CBS495.96 (VUT-77054) and CBS496.86 (VUT-77055), respectively, are monoascospore cultures obtained from a cross of the strains VUT-73015 (+) and VUT-74001 (−), which were isolated from feline ringworm in Japan [20, 40, 82, 86]. The availability of the genome sequence of the clinical isolate CBS113480 has allowed characterization of the *M. canis MAT* locus, which is quite similar among the dermatophytes (Fig. 1). Based on the genomic sequence, the commonly observed (−) mating type is *MAT1-1* [23, 30, 43]. Recently, sequencing of the *MAT* PCR amplicons from the two monoascospore strains indicated that CBS496.86 (−) and CBS495,96 (+) harbor the *MAT1-1* and the *MAT1-2* idiomorphs, respectively [87]. Additionally, *8 M audouinii* isolates and 26 *M. ferrugineum* isolates harbor the *MAT1-2* idiomorph (Table 2) [87]. Interestingly, CBS495.96, the only (+) mating type (*MAT1-2*) *M. canis* isolate analyzed, is phylogenetically more closely related to *M. audouinii* than to *M. canis* [20, 86]. Analysis of the other (+) mating type isolates from Japan would be informative to study the phylogeny of these three species. It would also be interesting to cross a super-mater *M. canis* isolate (*MAT1-1*) with *M. ferrugineum* and *M. audouinii* (*MAT1-2*) in the search for a successful cross.

Paraphyton

The genus *Paraphyton* consists of three species: *P. cookei*, *P. cookiella*, and *P. mirabile* [20]. *P. cookei* and *P. cookiella* are geophilic species that have mainly been isolated from soil, but *P. cookei* also has been isolated from wild animals, dogs, sheep, rats, and humans [88–91]. *P. mirabile* has been isolated from a dog, an alpine chamois, and a human and is thought to be zoophilic [92]. All three species are heterothallic and reproduce sexually resulting in ascomata composed of interwoven, branched, peridial hyphae (Table 2) [88, 89, 92]. Sexual reproduction was observed on hair and soil plates and oatmeal salts agar for *P. cookei* [39, 89, 90], Niger seed salts agar for *P. cookiella* [88], and Niger seeds agar for *P. mirabile* [92]. Interspecies mating assays, such as *P. mirabile* x *P. cookiella* and *P. mirabile* x *P. cookei* crosses, result in pseudoascomatal structures either without asci or without ascospores [92]. These findings indicate that *Paraphyton* species are phylogenetically close enough to stimulate the sexual reproduction pathways but too distant to result in viable recombinant ascospores. Molecular studies have not been performed on *Paraphyton* species; therefore, their *MAT* locus structures are not known.

Epidermophyton

Epidermophyton flocossum, the only species of the genus *Epidermophyton*, is an anthropophile (Table 2) [20]. Although spiral hyphae that might represent degenerate peridial hyphae have been observed for certain isolates [93], a sexual cycle has not been described. *E. floccosum* isolates do not respond to *A. simii* tester strains, which is a useful method to determine the mating type of some dermatophytes [26]. Because its *MAT* locus has not been described and because the genome sequence is not known yet, the mating type of the isolates remains to be determined.

Nannizzia

Nannizzia harbors four geophilic and two zoophilic species with heterothallic sexual cycles and four species with unknown hosts and undefined sexual cycles (Table 2). Among the geophilic species, *N. incurvata*, *N. gypsea*, and *N. fulva* are commonly observed and cause occasional infections in humans and animals [94]. The heterothallic sexual reproduction of *N. incurvata* and *N. gypsea* can readily be observed on hair and soil plates, oatmeal salts agar, diluted Pablum cereal agar with salts, DCM agar with powdered hair, and dextrose agar with powdered hair [35, 37, 39, 94]. However, *N. fulva* forms ascomata poorly on oatmeal salts agar or on diluted Pablum cereal agar with salts [37, 39]. In addition, sterilization of the soil by autoclaving reduces the efficiency of ascomata formation suggesting either heat-labile components or other viable microbes that contribute to stimulate mating [94]. The ascomata of *Nannizzia* species are similar to *Lophophyton* and *Arthroderma*, but the peridial cells are not as constricted in the dumbbell-shaped cells and instead show only a slight central constriction [94]. Spiral appendages are also observed. The mating type distribution of *N. incurvata*, *N. gypsea*, and *N. fulva* was determined to be nearly equal [94–97]. Among *Nannizzia* species, only the *MAT* locus of *N. gypsea* has been characterized and was shown to have the typical dermatophyte *MAT* locus structure (Fig. 1) [43]. Other molecular studies have included the amplification of *MAT1-1* and *MAT1-2* sequences from *N. incurvata* [43] and *N. fulva* [98]. For *N. corniculata* (the other geophilic species), sexual reproduction was observed between soil-derived strains, one isolated in Somalia and the other in Guinea. The species was determined to be heterothallic after ascospore mating analysis, with ascomata production on Niger salts agar and Sabouraud 1/10 with salts agar [99].

Among the zoophilic species, *N. persicolor* has been isolated from soil, small mammals (especially rodents), and occasionally human infections [100–104]. Sexual reproduction was observed on hair and soil plates and determined to be heterothallic [101]. Interestingly, oatmeal salts agar was not successful for the induction of ascomata production [39]. *N. nana* is the other zoophilic species and is generally associated with pigs [105], but sometimes is observed in humans as well [106]. A sexual cycle is challenging to observe ascomata are not formed on hair and soil plates or on oatmeal salts agar [39], but could be induced on unsterilized soil with hair after a long incubation period (10–12 weeks) [34]. Mating assays with single-ascospore isolates indicate that *N. nana* is heterothallic [34].

Four *Nannizzia* species have no known sexual reproduction: *N. aenigmaticum*, of which only a single human isolate has been reported [107], *N. perplicata*, a recently described species isolated from a human tinea corporis case [108], *N. duboisii* [20], and *N. praecox*, which is likely a geophilic species and has been isolated from soil, horse hair, and humans in contact with horses [109–111].

The Genus *Trichophyton*

The *Trichophyton* genus contains the highest number of anthropophilic species of the dermatophytes. Sixteen defined *Trichophyton* species are recognized in five different series: *T. mentagrophytes*, *T. simii*, *T. benhamiae*, *T. bullosum*, and the *T. rubrum* complex (Table 3) [20].

T. mentagrophytes Series

T. mentagrophytes is a zoophilic species isolated from chinchillas, guinea pigs, cats, dogs, mice, horses, and humans [28, 112–115]. Ascomata are of the *Arthroderma*-type with constricted dumbbell-shaped peridial cells [116]. The heterothallic sexual cycle can be observed on Sabouraud 1/10 plus salts [112, 116], Niger seed agar [28], and Takashio medium [95, 117]. Mating type distribution is skewed in favor of the (+) mating type (*MAT1-2*) (80% to 95%) in different geographical locations, including Japan, India, and Germany [87, 95, 112, 118]. However, one study reported that 30% of ten Czechoslovakian isolates were of the (+) mating type [117].

Trichophyton interdigitale had been considered the anthropophilic counterpart of *T. mentagrophytes* [20, 28], but recent studies identified new genotypes of *T. mentagrophytes* as the causative agent of dermatophytosis [119–122]. Currently, ten ITS

Table 3 *Trichophyton* species: host preferences, reproductive patterns, and mating types

Series	Species	Host	Mating	Mating type	References
T. mentagrophytes	*T. tonsurans*	Anthropophilic	?	*MAT1-1*	[30, 87, 95, 128, 129]
	T. equinum	Zoophilic	?	*MAT1-2*	[26, 30, 87]
	T. interdigitale	Anthropophilic	?	*MAT1-2*	[28, 29, 112]
	T. mentagrophytes	Zoophilic	Heterothallic	*MAT1-1* and *MAT1-2*	[116]
T. simii	*T. schoenleinii*	Anthropophilic	?	*MAT1-2*	[87]
	T. simii	Zoophilic	Heterothallic	*MAT1-1* and *MAT1-2*	[36, 134]
	T. quinckeanum	Zoophilic	Heterothallic	*MAT1-1* only? *A* and *a*?	[87, 136]
T. benhamiae	*T. benhamiae*	Zoophilic	Heterothallic	*MAT1-1* and *MAT1-2*	[87, 117, 139, 143–147]
	T. concentricum	Anthropophilic	?	*MAT1-1*	[87]
	T. erinacei	Zoophilic	Heterothallic	*MAT1-2* (detected in four isolates) (+/*A*) and (−/**a**)	[26, 87, 148, 151, 152]
	T. verrucosum	Zoophilic	?	*MAT1-2*	[42, 87, 153]
	T. eriotrephon	Anthropophilic?	?	*MAT1-1* (a single isolate was studied)	[87]
T. bullosum	*T. bullosum*	Zoophilic	?	*MAT1-1* (a single isolate was studied)	[87, 156, 157]
T. rubrum	*T. rubrum*	Anthropophilic	?	*MAT1-1*	[26, 27, 31, 43, 56]
	Morphotype *megninii*	Anthropophilic	?	*MAT1-2*	[87, 160]
	T. soudanense	Anthropophilic	?	*MAT1-1*	[87]
	T. violaceum	Anthropophilic	?	*MAT1-1*	[87]

genotypes have been defined for *T. mentagrophytes* (eight genotypes) and *T. interdigitale* (two genotypes) [121]. The Indian genotype (VIII) has come to prominence over the past several years due to the highly increased number of cases in India and the resistance of the isolates to treatment [119–122]. The genome-wide phylogeny of 20 isolates shows that the Indian isolates form a distinct clade apart from the other *T. mentagrophytes* and *T. interdigitale* genotypes [123]. In addition, three of the isolates bear both an HMG and an alpha-box gene in their genomes, while the other 17 harbor only an HMG gene [123]. The presence of both idiomorphs might be indicative of hybridization events or an incomplete sexual cycle demonstrating the possibility of sexual reproduction, which could be important in spreading antifungal resistance properties [123]. The inflammatory nature of the isolates might be indicative of zoophilic ancestry; however, because zoophilic species are not expected to cause an epidemic like this, the Indian genotype could be in the process of evolving into an anthropophilic species. It would be interesting to test the sexual reproduction potential of these isolates with fertile *T. mentagrophytes* tester strains. Unlike the Indian genotype VIII, all known *T. interdigitale* isolates are of the (+) mating type (*MAT1-2*) [29, 112]. The genome sequence of *T. interdigitale* also indicates the *MAT1-2* locus structure [31]. The four Japanese isolates having the (−) mating type reported to be *T. interdigitale* by Anzawa and colleagues in 2011 with the GenBank accession numbers AB617768 and AB617769 [124] fall into other genotypes of *T. mentagrophytes* according to the ten-genotype scheme [121]. Therefore, *T. mentagrophytes* appears to be a mixture of different genotypes/species including *T. interdigitale*, and the populations of some are composed of only one mating type.

The other species in the *T. mentagrophytes* series are *T. equinum* and *T. tonsurans* [20]. While *T. tonsurans* is an anthropophilic species [125], *T. equinum* is zoophilic and mainly associated with horses, but it is sometimes observed in humans who interact with horses as well [126, 127]. Mating has not been observed in either species, but their mating types have been studied either by molecular analysis or by confrontation tests [26]. Sixty *T. tonsurans* isolates from Japan were reported to harbor the *MAT1-1* idiomorph implying that they all are of (−) the mating type [128]. A recent study screened eight isolates of *T. tonsurans* composed of reference strains and clinical isolates (from Germany and of unknown origin) and found that all were *MAT1-1* [87]. The sequenced isolate of *T. tonsurans* (CBS 112818) also harbors the *MAT1-1* idiomorph (Fig. 1) [30]. Other studies show that ten isolates from India [95], as well as 15 isolates from around the world [102 and references therein], all have the (−) mating type. The same study found that two isolates from Kenya have the (+) mating type, but questioned the identity of these strains [129]. On the other hand, studies on the mating type of *T. equinum* are limited. Three reference strains from horses [87] and the sequenced clinical isolate (CBS127.97) [30] harbor the *MAT1-2* idiomorph (Fig. 1) [(+) mating type]. Additionally, five isolates have been determined to be (+) mating type by confrontation assays [26]. Although their host preferences differ significantly, molecular methods have demonstrated surprisingly high similarity between *T. tonsurans* and *T. equinum* [30, 129, 130]. While there has been a debate for and against conspecificity of these species [130, 131], mating between *T. tonsurans* and *T. equinum* has not been observed.

Trichophyton simii Series

The *T. simii* series includes three species: *T. simii* and *T. quinckeanum*, which are zoophilic, and *T. schoenleinii*, which is anthropophilic [20]. *T. simii* has been isolated from monkeys, chickens, dogs, small mammals, humans, and soil [36, 132, 133]. It was reported to have a heterothallic mating system [36, 134] that can be observed on 2.5% malt extract agar, hair (horse) and soil plates, oatmeal agar, and glucose peptone agar, in addition to a variety of other media [36]. Ascomata have been observed to be the *Arthroderma* type, with interwoven, branched, peridial hyphae with cells constricted in the middle and spiral appendages [36].

The other zoophilic species in this series is *T. quinckeanum*, which is associated with small rodents and camels and is sometimes observed in horses, cats, dogs, and humans [135, 136]. Ajello et al. [136] reported the heterothallic sexual reproduction of two *T. quinckeanum* isolates [TQ10 (X804) and TQ13 (X808)] among a total of 17 strains on hair and soil plates. The progeny obtained from this cross successfully mated both with other isolates of *T. quinckeanum* and with *T. benhamiae* in a heterothallic mode on oatmeal agar. In this study, two of the isolates [TQ5 (X392) and TQ10] were found to be "*A*" mating type, while three were "**a**" mating type, the other isolates did not mate. Six isolates from this study and 13 new isolates of *T. quinckeanum* were evaluated in another study [137], involving mating assays with *T. simii* and *T. benhamiae*. In this study, all 19 isolates mated with *A. benhamiae* mating type *A*, indicating that all evaluated *T. quinckeanum* isolates were mating type **a**. In addition, some of the isolates also produced fertile ascomata with *T. simii* mating type *A*, but the ascospores had irregularities in germination or maturation resembling interspecific crosses. However, the study by Weitzman and Padhye [137] includes the isolate X392 (TQ5), previously found to be the *A* mating type [136]. The inconsistency might be due to incorrect isolate numbers and requires further clarification. In the previous study [136], a heterothallic sexual cycle was observed with an *A*/**a** ratio of 2/3; however, in the later study [137] all isolates were mating type **a** (inferred idiomorph: *MAT1-1*). In agreement with the study by Weitzman and Padhye [137], the *MAT1-1* idiomorph was detected in the two reference and three clinical isolates of *T. quinckeanum* [87]. Additional studies are needed to clarify the sexual reproduction properties of *T. quinckeanum*.

The only anthropophilic species in the *T. simii* series is *T. schoenleinii*, which is mainly involved in scalp infections [138]. The 16 *T. schoenleinii* isolates that have been analyzed were reported to harbor the *MAT1-2* idiomorph [87].

Trichophyton benhamiae Series

Trichophyton benhamiae is a zoophilic species that is generally associated with guinea pigs, but it has been isolated from other animals such as dogs, rabbits, cats, and humans [113, 114, 139–141]. Different genotypes/phenotypes have been defined for *T. benhamiae*, such as the African and American-European races [142], and the yellow and white phenotypes [143]. A recent study defined four ITS genotypes: genotype 1 group II (American-European race/yellow phenotype), a related genotype group I (American-European race/white phenotype), genotype 2 (the African race), and genotype 3 (a new genotype defined in the study) [144]. Compatibility is reduced when strains belonging to different genotypes/phenotypes are crossed [142], which might indicate the presence of a complex composed of closely related species. *T. benhamiae* mating has been observed on soil and hair plates [139], Sabouraud 1/10 with salts [142], and oatmeal salts agar [37] showing ascomata typical of the genus *Arthroderma* and with a reportedly heterothallic mating system [139]. The mating type distribution differs between genotypes. For example, Symoens and colleagues [143] reported the presence of both mating types, but 12 of the 14 group I (white phenotype) isolates were (+), whereas only (−) isolates were identified in the 13 genotype 1 (yellow phenotype) isolates. Similarly, ten clinical yellow phenotype isolates of German/Swiss origin were typed as *MAT1-1*, while white isolates harbored either the *MAT1-1* ($n = 5$) or the *MAT1-2* ($n = 8$) idiomorph [87]. In other studies, one (−) and 40 (+) among 41 Czechoslovakian isolates [117], seven (−) and five (+) among US and Canadian isolates [145], two (−) and five (+) among Russian isolates [146], and eight *MAT1-1* (−) and two *MAT1-2* (+) among Japanese isolates [144] were detected. The (−) and (+) mating type isolates were reported to harbor the idiomorphs *MAT1-1* and *MAT1-2*, respectively [147]. The sequenced clinical isolate, strain 2354 (LAU2354), unveiled a *MAT1-2* structure, and sequencing the *MAT* locus of its mating partner (CBS 809.72) showed the complete *MAT* locus of *T. benhamiae* (Fig. 1) [42].

T. erinacei is a zoophilic fungus mainly isolated from hedgehogs and hedgehog nests, but sometimes from humans as well [148–150]. Stimulation by *T. simii* tester strains showed that all 21 isolates of *T. erinacei* were mating type (+) (inferred idiomorph: *MAT1-2*) [26]. Similarly, Padhye and Ajello [151] found that 26 out of 27 *T. erinacei* isolates mated with the mating type **a** *A. benhamiae* tester strain on Pablum cereal with salts agar and on dilute Sabouraud dextrose agar with salts, which indicates that almost all isolates analyzed in this study were of mating type *A* (inferred idiomorph: *MAT1-2*). On the other hand, Takahashi et al. reported the presence of both mating types of *T. erinacei*, 12 (+/*A*) and six (−/**a**) and demonstrated complete fertility of two compatible isolates [152]. Of the six (−/**a**) isolates studied, five were from Kenya and one was from Japan. Overall, these results indicate that, although infrequent, the (−/**a**) mating type of *T. erinacei* is found in nature and the organism is able to reproduce sexually. In addition, *T. erinacei* mates with the African race of *T. benhamiae*, but the resulting ascomata are small, with a low number of asci, suggestive of interspecific crossing [152]. A recent study involving *T. erinacei* indicates the presence of the *MAT1-2* idiomorph in the four reference strains [87].

T. verrucosum, another zoophilic species in the *T. benhamiae* series, is mainly implicated in cattle dermatophytosis [20, 125]. Sexual reproduction has not been observed in *T. verrucosum*. In a study of four isolates from the Czech Republic and 18 from Japan, all were found to harbor the *MAT1-2* idiomorph [153]. Similarly, four reference strains and three clinical strains of unknown origin were also found to be *MAT1-2* [87]. Genome sequencing of *T. verrucosum* demonstrated the presence of the whole set of genes necessary for mating and meiosis, similar to *T. benhamiae* [42]. In addition, the *MAT* locus of the sequenced strain (which is of clinical origin) appears to have the typical dermatophyte *MAT1-2* locus structure (Fig. 1).

T. concentricum, an anthropophilic species in the *T. benhamiae*, series has been observed in Southeast Asia, Central and South America, and the South Pacific islands [20, 154]. The species is not known to reproduce sexually, and the only study focusing on the *MAT* locus indicated that all 13 analyzed isolates contained the *MAT1-1* idiomorph [87].

T. eriotrephon is a species in the *T. benhamiae* series that is closely related to the zoophilic species *T. verrucosum* and *T. erinacei* [20]. Very few clinical isolates of this species have been isolated [141, 155], and the only molecular study revealed the presence of *MAT1-1* in the reference strain CBS220.25 [87]. Rarity of clinical cases brings into question the presumed anthropophilic nature of the species, and it might have an as-yet-unknown habitat.

Trichophyton bullosum

Trichophyton bullosum is a rare, zoophilic dermatophyte that has been isolated from horses and donkeys and once from a human [156, 157]. No sexual cycle has been described for this species. A *MAT1-1* idiomorph sequence was amplified from the only studied isolate (CBS363.35) [87], and the potential for sexual reproduction is unknown in this species [157].

Trichophyton rubrum Complex

The *T. rubrum* species complex contains the most commonly observed anthropophilic dermatophyte, *T. rubrum* [158], and species closely related to it: *T. violaceum*, which causes scalp infections and *T. soudanense* [20]. A majority of *T. rubrum* isolates analyzed were of the (−) mating type (inferred mating type by *T. simii* stimulation assays) and harbored the *MAT1-1* idiomorph [26, 27, 31, 43, 56]. Eleven analyzed *T. violaceum* isolates and 12 analyzed *T. soudanense* isolates also harbored the *MAT1-1* idiomorph [87]. The *MAT1-1* locus of *T. rubrum* has the structure of the archetypal *MAT* locus of dermatophytes (Fig. 1) [43]. *T. rubrum* was shown to mate with a super-mater isolate of *T. simii*, producing one hybrid progeny on Takashio medium (1/10 Sabouraud plus salts) [159]. In addition, genome analysis showed that *T. rubrum* has the genes necessary for mating and meiosis [30]. These findings suggest that *T. rubrum* has the ability to sexually reproduce. The only (+) mating type species in the *T. rubrum* complex is the morphotype *T. megninii* [160], which harbors the *MAT1*-2 idiomorph (Fig. 1) [31, 87]. *T. megninii* was found to be very similar to *T. rubrum* with the highest-diversity region in the *MAT* locus [31], suggesting that mating could be possible between the two species. However, mating assays did not result in ascomata production between *T. rubrum* and *T. megninii* using Takashio medium or Medium E [31]. However, it is possible that *T. rubrum* requires other conditions for mating.

Conclusions

Dermatophytes are keratinophilic microorganisms that are associated with soil with keratinaceous materials (geophiles), with animals (zoophiles), or with humans (anthropophiles). Sexual reproduction is common among geophiles and some zoophiles, but has not been observed among the anthropophilic dermatophytes, which are mostly found as a single mating type. In terms of evolutionary concepts, it could be advantageous in the short term for dermatophyte pathogens to proliferate asexually once they have attained the genetic composition that allows successful host invasion. However, in the long term, asexual propagation would not be advantageous based on the Red Queen hypothesis, which necessitates continual adaptation of both the host and the pathogen, [161, 162]. What we know about other fungal pathogens is that they somehow reduce their sexual activity, and it is hypothesized that this is to avoid disrupting their well-functioning genomic order [163]. For example, the population of *C. neoformans* largely consists of a single mating type, but this species has retained the ability to sexually reproduce both in a heterothallic manner and through unisexual reproduction. Similarly, *C. albicans* requires specific conditions to undergo a parasexual cycle both in a heterothallic and in a unisexual form. Likewise, *A. fumigatus* requires stringent conditions for mating, and mating is not as ubiquitous as in its saprobic *Neosartorya* relatives [164]. It may be the case for dermatophytes that restricted mating has led to successful pathogens, but they are expected to retain some form of sexual activity. Sexual reproduction might occur between different mating types infrequently, such as between *T. rubrum* and *T. megninii* or between *T. tonsurans* and *T. equinum*, under conditions that have not yet been found. Another possibility is that the dermatophytes have developed other mechanisms that have not detected, yet, such as unisexual reproduction, which is observed in two of the three most common fungal pathogens (*C. neoformans* and *C. albicans*). Future studies will shed light on these concepts.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

1. Felsenstein J. The evolutionary advantage of recombination. Genetics. 1974;78:737–56.
2. McDonald MJ, Rice DP, Desai MM. Sex speeds adaptation by altering the dynamics of molecular evolution. Nature. 2016;531:233–6.
3. Maynard Smith J. Evolution: contemplating life without sex. Nature. 1986;324:300–1.
4. Judson OP, Normark BB. Ancient asexual scandals. Trends Ecol Evol. 1996;11:41–6.
5. Dyer PS, Kück U. Sex and the imperfect fungi. Microbiol Spectr. 2017;5:FUNK-0043-2017.
6. Hull CM, Raisner RM, Johnson AD. Evidence for mating of the "asexual" yeast *Candida albicans* in a mammalian host. Science. 2000;289:307–10.
7. Magee BB, Magee PT. Induction of mating in *Candida albicans* by construction of *MTL*a and *MTL*α strains. Science. 2000;289:310–3.
8. O'Gorman CM, Fuller HT, Dyer PS. Discovery of a sexual cycle in the opportunistic fungal pathogen *Aspergillus fumigatus*. Nature. 2009;457:471–4.
9. Dyer PS, O'Gorman CM. A fungal sexual revolution: *Aspergillus* and *Penicillium* show the way. Curr Opin Microbiol. 2011;14:649–54.
10. Bennett RJ, Turgeon BG. Fungal sex: the ascomycota. Microbiol Spectr. 2016;4:FUNK-0005-2016.
11. Fraser JA, Heitman J. Fungal mating-type loci. Curr Biol. 2003;13:R792–5.
12. Turgeon BG, Yoder OC. Proposed nomenclature for mating type genes of filamentous ascomycetes. Fungal Genet Biol. 2000;31:1–5.
13. Feretzaki M, Heitman J. Unisexual reproduction drives evolution of eukaryotic microbial pathogens. PLoS Pathog. 2013;9:e1003674.
14. Roach KC, Feretzaki M, Sun S, Heitman J. Unisexual reproduction. In: Friedmann T, Dunlap JC, Goodwin SF, editors. Advances in genetics. Cambridge: Academic Press; 2014. p. 255–305.
15. Lin X, Hull CM, Heitman J. Sexual reproduction between partners of the same mating type in *Cryptococcus neoformans*. Nature. 2005;434:1017–21.
16. Alby K, Schaefer D, Bennett RJ. Homothallic and heterothallic mating in the opportunistic pathogen *Candida albicans*. Nature. 2009;460:890–3.
17. Inderbitzin P, Harkness J, Turgeon BG, Berbee ML. Lateral transfer of mating system in *Stemphylium*. Proc Natl Acad Sci USA. 2005;102:11390–5.
18. Wilson AM, Godlonton T, van der Nest MA, Wilken PM, Wingfield MJ, Wingfield BD. Unisexual reproduction in *Huntiella monilifo*rmis. Fungal Genet Biol. 2015;80:1–9.
19. Nygren K, Strandberg R, Wallberg A, et al. A comprehensive phylogeny of *Neurospora* reveals a link between reproductive mode and molecular evolution in fungi. Mol Phylogenet Evol. 2011;59:649–63.
20. de Hoog GS, Dukik K, Monod M, et al. Toward a novel multilocus phylogenetic taxonomy for the dermatophytes. Mycopathologia. 2017;182:5–31.
21. Zhan P, Dukik K, Li D, et al. Phylogeny of dermatophytes with genomic character evaluation of clinically distinct T*richophyton rubrum* and *T. violaceum*. Stud Mycol. 2018;89:153–75.
22. White TC, Oliver BG, Gräser Y, Henn MR. Generating and testing molecular hypotheses in the dermatophytes. Eukaryot Cell. 2008;7:1238–45.
23. Metin B, Heitman J. Sexual reproduction in dermatophytes. Mycopathologia. 2017;182:45–55.
24. Summerbell RC. Form and function in the evolution of dermatophytes. In: Kushwaha RKS, Guarro J, editors. Biology of dermatophytes and other keratinophilic fungi.

Bilbao: Revista Iberoamericana de Micología; 2000. p. 30–43.

25. Summerbell R. What is the evolutionary and taxonomic status of asexual lineages in the dermatophytes? Stud Mycol. 2002;47:97–101.
26. Stockdale PM. Sexual stimulation between *Arthroderma simii* Stockd., Mackenzie & Austwick and related species. Sabouraudia. 1968;6:176–81.
27. Kano R, Isizuka M, Hiruma M, Mochizuki T, Kamata H, Hasegawa A. Mating type gene (*MAT1-1*) in Japanese isolates of *Trichophyton rubrum*. Mycopathologia. 2013;175:171–3.
28. Symoens F, Jousson O, Planard C, et al. Molecular analysis and mating behaviour of the *Trichophyton mentagrophytes* species complex. Int J Med Microbiol. 2011;301:260–6.
29. Kano R, Kawasaki M, Mochizuki T, Hiruma M, Hasegawa A. Mating genes of the *Trichophyton mentagrophytes* complex. Mycopathologia. 2012;173:103–12.
30. Martinez DA, Oliver BG, Gräser Y, et al. Comparative genome analysis of *Trichophyton rubrum* and related dermatophytes reveals candidate genes involved in infection. mBio. 2012;3:e00259-12.
31. Persinoti GF, Martinez DA, Li W, et al. Whole Genome analysis illustrates global clonal population structure of the ubiquitous dermatophyte pathogen *Trichophyton rubrum*. Genetics. 2018;208:1657–69.
32. Griffin DM. Perfect stage of *Microsporum gypseum*. Nature. 1960;186:94–5.
33. Szathmary S, Herpay Z. Perithecium-formation of *Microsporon gypseum* and its cognate, *Epidermophyton radiosulcatum* var. *flavum* Szathmary 1940 on soil. Mycopathol Mycol Appl. 1940;13:1–14.
34. Dawson CO, Gentles JC. The perfect states of *Keratinomyces ajelloi* Vanbreuseghem, *Trichophyton terrestre* Durie & Frey and *Microsporum nanum* Fuentes. Sabouraudia. 1961;1:49–57.
35. Weitzman I. Incompatibility in the *Microsporum gypseum* complex. Mycologia. 1964;56:425–35.
36. Stockdale PM, Mackenzie DWR, Austwick PKC. *Arthroderma simii* sp. nov., the perfect state of *Trichophyton simii* (Pinoy) comb. nov. Sabouraudia. 1965;4:112–23.
37. Weitzman I, Silva-Hutner M. Non-keratinous agar media as substrates for the ascigerous state in certain members of the gymnoascaceae pathogenic for man and animals. Sabouraudia. 1967;5:335–40.
38. Takashio M. Sexual reproduction of some *Arthroderma* and *Nannizzia* on diluted Sabouraud agar with or without salts. Mycoses. 1972;15:11–7.
39. Padhye AA, Sekhon AS, Carmichael JW. Ascocarp production by *Nannizzia* and *Arthroderma* on keratinous and non-keratinous media. Sabouraudia. 1973;11:109–14.
40. Hironaga M, Nozaki K, Watanabe S. Ascocarp production by *Nannizzia otae* on keratinous and non-keratinous agar media and mating behavior of *N. otae* and 123 Japanese isolates of *Microsporum canis*. Mycopathologia. 1980;72:135–41.
41. Stockdale PM. *Nannizzia incurvata* gen. nov., sp. nov., a perfect state of *Microsporum gypseum* (Bodin) Guiart et Grigorakis. Sabouraudia. 1962;1:41–8.
42. Burmester A, Shelest E, Glöckner G, et al. Comparative and functional genomics provide insights into the pathogenicity of dermatophytic fungi. Genome Biol. 2011;12:R7.
43. Li W, Metin B, White TC, Heitman J. Organization and evolutionary trajectory of the mating type (*MAT*) locus in dermatophyte and dimorphic fungal pathogens. Eukaryot Cell. 2010;9:46–58.
44. Butler G. The evolution of *MAT*: the ascomycetes. In: Heitman J, Kronstad JW, Taylor J, Casselton L, editors. Sex in fungi: molecular determination and evolutionary implications. Washington: ASM Press; 2007. p. 3–18.
45. Punsola L, Guarro J. *Keratinomyces ceretanicus* sp. nov., a psychrophilic dermatophyte from soil. Mycopathologia. 1984;85:185–90.
46. Orr GF, Kuehn HH. The genus *Ctenomyces* Eidam. Mycopathol Mycol Appl. 1963;21:321–3.
47. Sekhon AS, Padhye AA. Mating behaviour of *Ctenomyces serratus*. Mycopathologia. 1976;60:33–7.
48. Varsavsky E, Reca ME. Demonstration of heterothallism in *Ctenomyces serratus* Eidam 1880. Mycopathol Mycol Appl. 1964;24:119–20.
49. Sharma R, Shouche YS. Diversity of Onygenalean fungi in keratin-rich habitats of Maharashtra (India) and description of three novel taxa. Mycopathologia. 2019;1:1. https://doi.org/10.1007/s11046-019-00346-7.
50. Zhang Z, Han Y, Chen W, Liang Z. Phylogeny and taxonomy of three new *Ctenomyces* (Arthrodermataceae, Onygenales) species from China. MycoKeys. 2019;47:1–16.
51. Guarro J, Punsola L, Cano J. *Myceliophthora vellerea* (*Chrysosporium asperatum*) anamorph of *Ctenomyces serratus*. Mycotaxon. 1985;23:419–27.
52. van den Brink J, Samson RA, Hagen F, Boekhout T, de Vries RP. D Phylogeny of the industrial relevant, thermophilic genera *Myceliophthora* and *Corynascus*. Fungal Divers. 2012;52:197–207.
53. Udagawa S. Geographical distribution of the pleomorphic plectomycetes in Asia and their teleomorph-anamorph connections. In: Sugiyama J, editor. Pleomorphic fungi: the diversity and its taxonomic implications. Tokyo: Kodansha LTD and Elsevier Science Publishers B. V; 1987. p. 9–28.
54. Howard DH, Weitzman I, Padhye AA. Onygenales: Arthrodermataceae. In: Howard DH, editor. Pathogenic fungi in humans and animals. 2nd ed. New York: Marcel Dekker Inc; 2003. p. 141–95.
55. Varsavsky E, Ajello L. The perfect and imperfect forms of a new keratinophilic fungus *Arthroderma ciferrii* sp. nov.: *Trichophyton georgii* sp. nov. Riv Patol Veg. 1964;4:351–64.
56. Takashio M. Taxonomy of dermatophytes based on their sexual states. Mycologia. 1979;71:968–76.
57. Dawson CO. Two new species of *Arthroderma* isolated from soil from rabbit burrows. Sabouraudia. 1963;2(3):185–91.
58. Ajello L, Cheng S-LY. A new geophilic Trichophyton. Mycologia. 1967;59:255–63.
59. Padhye AA, Carmichael JW. *Arthroderma insingulare* sp. nov., another Gymnoascaceous state of the *Trichophyton terrestre* complex. Sabouraudia. 1972;10:47–51.

60. Padhye AA, Carmichael JW. Mating reactions of pigmented and non-pigmented isolates of *Arthroderma uncinatum*. Sabouraudia. 1970;8:112–5.
61. Alteraş I, Evolceanu R. *Trichophyton phaseoliforme* (Dante BoreIIi & Feo—1966) in Romanian soil. Mycoses. 1969;12:421–6.
62. Krivanec K, Janecková V, Otcenásek M. *Arthroderma melis* spec. nov.—a new dermatophyte species isolated from badger burrows in Czechoslovakia. Ceská Mykol. 1977;31:91–9.
63. Campbell CK, Borman AM, Linton CJ, Bridge PD, Johnson EM. *Arthroderma olidum*, sp. nov. A new addition to the *Trichophyton terrestre* complex. Med Mycol. 2006;44:451–9.
64. Kuehn HH. Observations on gymnoascaceae. VIII. A new species of *Arthroderma*. Mycopathol Mycol Appl. 1960;13:189–97.
65. Sekhon AS, Padhye AA, Carmichael JW. Mating reactions in *Arthroderma tuberculatum*. Sabouraudia. 1973;11:283–6.
66. Rees RG. *Arthroderma flavescens* sp. nov. Sabouraudia. 1967;5:206–8.
67. Lorch JM, Minnis AM, Meteyer CU, et al. The fungus *Trichophyton redellii* sp. nov. causes skin infections that resemble white-nose syndrome of hibernating bats. J Wildl Dis. 2015;51:36–48.
68. Moraes M, Padhye AA, Ajello L. The perfect state of *Microsporum amazonicum*. Mycologia. 1975;67:1109–13.
69. Vidal P, Guarro J, de Vroey C. Studies on keratinophilic fungi: VII. *Chrysosporium vespertilium* sp. nov. from Zaire. Mycotaxon. 1996;59:189–96.
70. Currah RS, Abbott SP, Sigler L. *Arthroderma silverae* sp. nov. and *Chrysosporium vallenarense*, keratinophilic fungi from arctic and montane habitats. Mycol Res. 1996;100:195–8.
71. Nenoff P, Winter I, Winter A, et al. *Trichophyton thuringiense* H.A. Koch 1969. A rare geophilic dermatophyte–now isolated for the first time from man. Hautarzt Z Dermatol Venerol Verwandte Geb. 2014;65:221–8.
72. Hoffmann R, Kolipp D, Koch HA. Die Bedeutung von Mäusen und anderen Kleinsäugern für die Verbreitung von Dermatophyten und anderen keratinophilen Pilzen. Mycoses. 1970;13:583–7.
73. Hubka V, Nissen CV, Jensen RH, et al. Discovery of a sexual stage in *Trichophyton onychocola*, a presumed geophilic dermatophyte isolated from toenails of patients with a history of *T. rubrum* onychomycosis. Med Mycol. 2015;53:798–809.
74. Pore RS, Tsao GC, Plunkett OA. A new species of *Arthroderma* established according to biological species concepts. Mycologia. 1965;57:969–73.
75. Weitzman I, Kozma I, Silva-Hutner M. Some observations on *Arthroderma uncinatum*. Sabouraudia. 1969;7:216–8.
76. Brasch J, Beck-Jendroschek V, Voss K, Yurkov A, Gräser Y. *Arthroderma chiloniense* sp. nov. isolated from human stratum corneum: description of a new *Arthroderma* species. Mycoses. 2019;62:73–80.
77. Böhme H. *Arthroderma gertleri* sp. nov., die perfekte form von *Trichophyton vanbreuseghemii* Rioux, Jarry et Juminer. Mycoses. 1967;10:247–52.
78. Georg LK, Ajello L, Friedman L, Brinkman SA. A new species of *Microsporum* pathogenic to man and animals. Sabouraudia. 1962;1:189–96.
79. Morganti L, Padhye AA, Ajello L. Recovery of *Nannizzia grubyia* from a stray Italian cat (*Felis catus*). Mycologia. 1975;67:434–6.
80. Sethi KK, Randhawa HS, Kurup PV, Ajello L. Isolation of *Microsporum vanbreuseghemii* from soil in India. Sabouraudia. 1968;6:81–2.
81. Naseri A, Fata A, Khosravi AR. Tinea capitis due to *Microsporum vanbreuseghemii*: report of two cases. Mycopathologia. 2012;174:77–80.
82. Hasegawa A, Usui K. *Nannizzia otae* sp. nov., the perfect state of *Microsporum canis* Bodin. Jpn J Med Mycol. 1975;16:148–53.
83. Takatori K, Hasegawa A. Mating experiment of *Microsporum canis* and *M. equinum* isolated from animals with *Nannizzia otae*. Mycopathologia. 1985;90:59–63.
84. Weitzman I, Padhye AA. Mating behaviour of *Nannizzia otae* (= *Microsporum canis*). Mycopathologia. 1978;64:17–22.
85. Kubo H, Iizuka H, Shibaki H. Mating behaviour of *Microsporum canis* from human ringworm cases in Hokkaido prefecture in Japan. J Dermatol. 1987;14:241–3.
86. Kaszubiak A, Klein S, de Hoog GS, Gräser Y. Population structure and evolutionary origins of *Microsporum canis*, *M. ferrugineum* and *M. audouinii*. Infect Genet Evol. 2004;4:179–86.
87. Kosanke S, Hamann L, Kupsch C, Moreno Garcia S, Chopra A, Gräser Y. Unequal distribution of the mating type (*MAT*) locus idiomorphs in dermatophyte species. Fungal Genet Biol. 2018;118:45–53.
88. De Clercq D. *Nannizzia cookiella*, a new species of dermatophyte. Mycotaxon. 1983;18:23–8.
89. Ajello L. The ascigerous state of *Microsporum cookei*. Sabouraudia. 1962;1:173–7.
90. Padhye AA, Carmichael JW. Incompatibility in *Microsporum cookei*. Sabouraudia. 1971;9:27–9.
91. Jeske J, Lupa S, Seneczko F, Głowacka A, Ochęcka-Szymańska A. Epidemiology of dermatomycoses of humans in Central Poland. Part V. Tinea corporis. Mycoses. 1999;42:661–3.
92. Choi JS, Gräser Y, Walther G, Peano A, Symoens F, de Hoog S. *Microsporum mirabile* and its teleomorph *Arthroderma mirabile*, a new dermatophyte species in the *M. cookei* clade. Med Mycol. 2012;50:161–9.
93. Guého E, Castro I, Badillet G. Existence of ornamentations on macroconidia and hyphae of *Epidermophyton floccosum*. Ann Inst Pasteur Microbiol. 1985;136:195–207.
94. Stockdale PM. The *Microsporum gypseum* complex (*Nannizzia incurvata* Stockd., *N. gypsea* (Nann.) comb. nov., *N. fulva* sp. nov.). Sabouraudia. 1964;3:114–26.
95. Ranganathan S, Balajee SAM, Menon T. Mating patterns of dermatophytes of diverse origin in India. Mycopathologia. 1996;136:91–4.
96. Hironaga M, Tanaka S, Watanabe S. Distribution of mating types among clinical isolates of the *Microsporum gypseum* complex. Mycopathologia. 1982;77:31–5.
97. Weitzman I, Gordon MA, Rosenthal SA. Determination of the perfect state, mating type and elastase activity in

clinical isolates of the *Microsporum gypseum* complex. J Invest Dermatol. 1971;57:278–82.

98. Fukutomi T, Kano R, Kamata H. First Isolation of *Arthroderma fulvum* in Japan. Med Mycol J. 2017;58:E115–8.
99. Takashio M, de Vroey C. *Nannizzia corniculata* sp. nov., the perfect state of *Microsporum boullardii*. Mycotaxon. 1982;14:383–9.
100. Padhye AA, Ajello L. Further observations on *Nannizzia persicolor* (= "*N. quinckeani*"). Sabouraudia. 1974;12:362–3.
101. Stockdale PM. *Nannizzia persicolor* sp. nov., the perfect state of *Trichophyton persicolor* Sabouraud. Sabouraudia. 1967;5:355–9.
102. Faure-Cognet O, Fricker-Hidalgo H, Pelloux H, Leccia MT. Superficial fungal infections in a French teaching hospital in Grenoble area: retrospective study on 5470 samples from 2001 to 2011. Mycopathologia. 2016;181:59–66.
103. Otcenasek M, Hubalek Z, Sixl W. Survey of dermatophytes in the hair of small mammals from Austria. Folia Parasitol. 1980;27:83–7.
104. Rajak RC, Sharma R, Presber W, Gräser Y. Molecular detection of *Microsporum persicolor* in soil suggesting widespread dispersal in central India. Med Mycol. 2008;46:67–73.
105. Roller JA, Westblom TU. *Microsporum nanum* infection in hog farmers. J Am Acad Dermatol. 1986;15:935–9.
106. Bonifaz A, Córdoba-García B, Simancas-Llanos T, Hernández MA, Martínez-Herrera E, Tirado-Sánchez A. Dermatophytosis caused by *Nannizzia nana* in two siblings. Rev Iberoam Micol. 2019;36:30–3.
107. Hubka V, Dobiáš R, Dobiášová S, Kolařík M. *Microsporum aenigmaticum* sp. nov. from *M. gypseum* complex, isolated as a cause of tinea corporis. Med Mycol. 2014;52:387–96.
108. Szekely A, Johnson EM, Fraser M, Borman AM, Lovegrove S. A novel dermatophyte relative, *Nannizzia perplicata* sp. nov., isolated from a case of tinea corporis in the United Kingdom. Med Mycol. 2018. https://doi.org/10.1093/mmy/myy099.
109. Alanio A, Romand S, Penso-Assathiany D, Foulet F, Botterel F. *Microsporum praecox*: molecular identification of a new case and review of the literature. Mycopathologia. 2011;171:61–5.
110. Uhrlaß S, Mayser P, Schwarz R, Koch D, Krüger C, Korfmann I, et al. Dermatomycoses due to *Nannizzia praecox* (formerly *Microsporum praecox*) in Germany: case reports and review of the literature. Mycopathologia. 2018;183:391–8.
111. Weitzman I, McMillen S. Isolation in the United States of a culture resembling *M. praecox*. Mycopathologia. 1980;70:181–6.
112. Hironaga M, Watanabe S. Mating behavior of 334 Japanese isolates of *Trichophyton mentagrophytes* in relation to their ecological status. Mycologia. 1980;72:1159–70.
113. Bartosch T, Frank A, Günther C, et al. *Trichophyton benhamiae* and *T. mentagrophytes* target guinea pigs in a mixed small animal stock. Med Mycol Case Rep. 2019;23:37–42.
114. Drouot S, Mignon B, Fratti M, Roosje P, Monod M. Pets as the main source of two zoonotic species of the *Trichophyton mentagrophytes* complex in Switzerland, *Arthroderma vanbreuseghemii* and *Arthroderma benhamiae*. Vet Dermatol. 2009;20:13–8.
115. Chollet A, Wespi B, Roosje P, Unger L, Venner M, Goepfert C, et al. An outbreak of *Arthroderma vanbreuseghemii* dermatophytosis at a veterinary school associated with an infected horse. Mycoses. 2015;58:233–8.
116. Takashio M. Une nouvelle forme sexuée du complexe *Trichophyton mentagrophytes*, *Arthroderma vanbreuseghemii* sp. nov. Ann Parasitol Hum Comp. 1973;48:713–32.
117. Hejtmánek M, Hejtmánková N. Hybridization and sexual stimulation in *Trichophyton mentagrophytes*. Folia Microbiol. 1989;34:77–9.
118. Hiruma J, Kano R, Kimura U, et al. Mating type gene for isolates of *Trichophyton mentagrophytes* from guinea pigs. J Dermatol. 2014;41:743–5.
119. Taraskina AE, Vasilyeva NV, Pchelin IM, et al. Species boundaries in the *Trichophyton mentagrophytes/T. interdigitale* species complex. Med Mycol. 2018. https://doi.org/10.1093/mmy/myy115.
120. Chowdhary A, Singh A, Singh PK, Khurana A, Meis JF. Perspectives on misidentification of *Trichophyton interdigitale/Trichophyton mentagrophytes* using internal transcribed spacer region sequencing: urgent need to update the sequence database. Mycoses. 2019;62:11–5.
121. Nenoff P, Verma SB, Uhrlaß S, Burmester A, Gräser Y. A clarion call for preventing taxonomical errors of dermatophytes using the example of the novel *Trichophyton mentagrophytes* genotype VIII uniformly isolated in the Indian epidemic of superficial dermatophytosis. Mycoses. 2019;62:6–10.
122. Nenoff P, Verma SB, Vasani R, et al. The current Indian epidemic of superficial dermatophytosis due to *Trichophyton mentagrophytes*—a molecular study. Mycoses. 2018;62:336–56.
123. Singh A, Masih A, Monroy-Nieto J, et al. A unique multidrug-resistant clonal *Trichophyton* population distinct from T*richophyton mentagrophytes/Trichophyton interdigitale* complex causing an ongoing alarming dermatophytosis outbreak in India: genomic insights and resistance profile. Fungal Genet Biol. 2019 (submitted).
124. Anzawa K, Kawasaki M, Hironaga M, Mochizuki T. Genetic relationship between *Trichophyton mentagrophytes* var. *interdigitale* and *Arthroderma vanbreuseghemii*. Med Mycol J. 2011;52:223–7.
125. Reiss E, Shadomy HJ, Lyon GM. Dermatophytosis. In: Reiss E, Shadomy HJ, Lyon GM, editors. Fundamental medical mycology. Hoboken: Wiley; 2012. p. 526–66.
126. Georg LK, Kaplan W, Camp LB. *Trichophyton equinum*—a re-evaluation of its taxonomic status. J Invest Dermatol. 1957;29:27–37.
127. Veraldi S, Genovese G, Peano A. Tinea corporis caused by *Trichophyton equinum* in a rider and review of the literature. Infection. 2018;46:135–7.
128. Hiruma J, Okubo M, Kano R, et al. Mating type gene (*MAT*) and itraconazole susceptibility of *Trichophyton*

tonsurans strains isolated in Japan. Mycopathologia. 2016;181:441–4.

129. Hayashi N, Takashio M. Mating type of *Trichophyton tonsurans*. Mycoses. 1984;27:377–9.
130. Gräser Y, Kuijpers AFA, Presber W, De Hoog GS. Molecular taxonomy of *Trichophyton mentagrophytes* and *T. tonsurans*. Med Mycol. 1999;37:315–30.
131. Woodgyer A. The curious adventures of *Trichophyton equinum* in the realm of molecular biology: a modern fairy tale. Med Mycol. 2004;42:397–403.
132. Beguin H, Goens K, Detandt M, Planard C, Stubbe D, Hendrickx M. Is *Trichophyton simii* endemic to the Indian subcontinent? Med Mycol. 2013;51:444–8.
133. Gugnani HC, Shrivastav JB, Gupta NP. Occurrence of *Arthroderma simii* in soil and on hair of small mammals. Sabouraudia. 1968;6:77–80.
134. Kwon-Chung KJ. Genetic study on the incompatibility system in *Arthroderma simii*. Sabouraudia. 1972;10:74–8.
135. Uhrlaß S, Schroedl W, Mehlhorn C, et al. Molecular epidemiology of *Trichophyton quinckeanum*—a zoophilic dermatophyte on the rise. J Dtsch Dermatol Ges. 2018;16:21–32.
136. Ajello L, Bostick L, Cheng S. The relationship of *Trichophyton quinckeanum* to *Trichophyton mentagrophytes*. Mycologia. 1968;60:1185–9.
137. Weitzman I, Padhye AA. Is *Arthroderma simii* the perfect state of *Trichophyton quinckeanum*? Sabouraudia. 1976;14:65–74.
138. Ilkit M. Favus of the scalp: an overview and update. Mycopathologia. 2010;170:143–54.
139. Ajello L, Cheng S. The perfect state of *Trichophyton mentagrophytes*. Sabouraudia. 1967;5:230–4.
140. Sieklucki U, Oh S-H, Hoyer LL. Frequent isolation of *Arthroderma benhamiae* from dogs with dermatophytosis. Vet Dermatol. 2014;25:39-e14.
141. Forouzanfar F, Candolfi E, Denis J, Letscher-Bru V, Sabou M, Boulanger N, et al. Molecular identification of *Trichophyton benhamiae* in Strasbourg, France: a 9-year retrospective study. Med Mycol. 2017;56:723–34.
142. Takashio M. Observations on African and European strains of *Arthroderma benhamiae*. Int J Dermatol. 1974;13:94–101.
143. Symoens F, Jousson O, Packeu A, et al. The dermatophyte species *Arthroderma benhamiae*, intraspecies variability and mating behaviour. J Med Microbiol. 2013;62:377–85.
144. Hiruma J, Kano R, Harada K, et al. Occurrence of *Arthroderma benhamiae* genotype in Japan. Mycopathologia. 2015;179:219–23.
145. Summerbell RC, Weitzman I, Padhye AA. The *Trichophyton mentagrophytes* complex: biological species and mating type prevalences of North American isolates, and a review of the worldwide distribution and host associations of species and mating types. Stud Mycol. 2002;47:75–86.
146. Vasilyev OD, Bogomolova TS. Tipy sparivaniya isovershennaya forma shtammov griba *Trichophyton mentagrophyte*s (Robin) Blanchard, vydelennykh ot bol'nikhdermatofitiyami. Mikol Fitopatol. 1985;19:309–17.
147. Kano R, Yamada T, Makimura K, et al. *Arthroderma benhamiae* (the teleomorph of *Trichophyton mentagrophytes*) mating type-specific genes. Mycopathologia. 2011;171:333–7.
148. Smith JMB, Marples MJ. *Trichophyton mentagrophytes* var. *erinacei*. Sabouraudia. 1964;3:1–10.
149. English MP, Morris P. *Trichophyton mentagrophytes* var. *erinacei* in hedgehog nests. Sabouraudia. 1969;7:118–21.
150. Kim J, Tsuchihashi H, Hiruma M, Kano R, Ikeda S. Tinea corporis due to *Trichophyton erinacei* probably transmitted from a hedgehog. Med Mycol J. 2018;59:E77–9.
151. Padhye AA, Ajello L. The taxonomic status of the hedgehog fungus *Trichophyton erinacei*. Sabouraudia. 1977;15:103–14.
152. Takahashi Y, Sano A, Takizawa K, Fukushima K, Miyaji M, Nishimura K. The epidemiology and mating behavior of *Arthroderma benhamiae* var. *erinacei* in household four-toed hedgehogs (*Atelerix albiventris*) in Japan. Nippon Ishinkin Gakkai Zasshi. 2003;44:31–8.
153. Kano R, Yoshida E, Yaguchi T, et al. Mating type gene (*MAT1-2*) of *Trichophyton verrucosum*. Mycopathologia. 2014;177:87–90.
154. Bonifaz A, Archer-Dubon C, Saúl A. Tinea imbricata or Tokelau. Int J Dermatol. 2004;43:506–10.
155. Rezaei-Matehkolaei A, Makimura K, de Hoog S, et al. Molecular epidemiology of dermatophytosis in Tehran, Iran, a clinical and microbial survey. Med Mycol. 2013;51:203–7.
156. Sitterle E, Fréalle E, Foulet F, Cabaret O, Cremer G, Guillot J, et al. *Trichophyton bullosum*: a new zoonotic dermatophyte species. Med Mycol. 2012;50:305–9.
157. Lyskova P, Hubka V, Petricakova A, Dobias R, Cmokova A, Kolarik M. Equine dermatophytosis due to *Trichophyton bullosum*, a poorly known zoophilic dermatophyte masquerading as *T. verrucosum*. Mycopathologia. 2015;180:407–19.
158. Achterman RR, White TC. Dermatophyte virulence factors: identifying and analyzing genes that may contribute to chronic or acute skin infections. Int J Microbiol. 2012;2012:358305.
159. Anzawa K, Kawasaki M, Mochizuki T, Ishizaki H. Successful mating of *Trichophyton rubrum* with *Arthroderma simii*. Med Mycol. 2010;48:629–34.
160. Sequeira H, Cabrita J, de Vroey C, Wuytack-Raes C. Contribution to our knowledge of *Trichophyton megninii*. J Med Vet Mycol. 1991;29:417–8.
161. Ene IV, Bennett RJ. The cryptic sexual strategies of human fungal pathogens. Nat Rev Microbiol. 2014;12:239–51.
162. Lively CM. A review of red queen models for the persistence of obligate sexual reproduction. J Hered. 2010;101:S13–20.
163. Heitman J. Evolution of eukaryotic microbial pathogens via covert sexual reproduction. Cell Host Microbe. 2010;8:86–99.
164. Kwon-Chung KJ, Sugui JA. Sexual reproduction in *Aspergillus* species of medical or economical importance: why so fastidious? Trends Microbiol. 2009;17:481–7.