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Review

Malassezia species in healthy skin and in dermatological conditions

Asja Prohic[1], MD, PhD, Tamara Jovovic Sadikovic[1], MD, MS, Mersiha Krupalija-Fazlic[1], MD, MS, and Suada Kuskunovic-Vlahovljak[2], MD, PhD

[1]Department of Dermatovenereology, University Clinical Center of Sarajevo, Sarajevo, Bosnia and Herzegovina, and [2]Institute of Pathology, Faculty of Medicine, University of Sarajevo, Sarajevo, Bosnia and Herzegovina

Correspondence
Asja Prohic, MD, PhD
Department of Dermatovenereology
University Clinical Center of Sarajevo
Bolnicka 25
71000 Sarajevo
Bosnia and Herzegovina
E-mail: asjaprohic@hotmail.com

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Abstract

The genus *Malassezia* comprises lipophilic species, the natural habitat of which is the skin of humans and other warm-blooded animals. However, these species have been associated with a diversity of dermatological disorders and even systemic infections. Pityriasis versicolor is the only cutaneous disease etiologically connected to *Malassezia* yeasts. In the other dermatoses, such as *Malassezia* folliculitis, seborrheic dermatitis, atopic dermatitis, and psoriasis, these yeasts have been suggested to play pathogenic roles either as direct agents of infection or as trigger factors because there is no evidence that the organisms invade the skin. *Malassezia* yeasts have been classified into at least 14 species, of which eight have been isolated from human skin, including *Malassezia furfur*, *Malassezia pachydermatis*, *Malassezia sympodialis*, *Malassezia slooffiae*, *Malassezia globosa*, *Malassezia obtusa*, *Malassezia restricta*, *Malassezia dermatis*, *Malassezia japonica*, and *Malassezia yamatoensis*. Distributions of *Malassezia* species in the healthy body and in skin diseases have been investigated using culture-based and molecular techniques, and variable results have been reported from different geographical regions. This article reviews and discusses the latest available data on the pathogenicity of *Malassezia* spp., their distributions in dermatological conditions and in healthy skin, discrepancies in the two methods of identification, and the susceptibility of *Malassezia* spp. to antifungals.

Introduction

Lipophilic yeasts of the genus *Malassezia* (formerly *Pityrosporum*) have been recognized for over a century as normally resident on human skin and also as agents of various skin and systemic diseases.[1] However, the pathogenic role of *Malassezia* yeasts remains subject to controversy. Both immunocompetent and immunosuppressed subjects may be affected by this type of infection. In immunologically competent hosts, *Malassezia* yeasts are known to be involved in the pathogeneses of various dermatological afflictions, including pityriasis versicolor (PV), *Malassezia* folliculitis (MF), and seborrheic dermatitis (SD). Recently, a growing number of reports have implicated *Malassezia* spp. in the development of atopic dermatitis (AD) and psoriasis.[2] Unlike in PV, in which *Malassezia* yeasts in the mycelial phase can be seen under the light microscope,[3] in all other cutaneous diseases, neither the number of yeasts nor their morphology seem to relate to skin lesions. However, most of the evidence on the roles of these yeasts comes from treatment studies, which show that antifungals are effective in the treatment of various diseases and that improvement of such conditions is associated with a reduction in *Malassezia* levels.[4,5] By contrast, in immunocompromised patients, including patients with acquired immune-deficiency syndrome (AIDS), immunohematological and oncological patients, and solid organ and bone marrow transplant recipients, these yeasts have been associated with catheter-related fungemia, sepsis, and a variety of deeply invasive infections.[6]

Since the designation of the genus *Malassezia* by Baillon in 1889, its taxonomy has been a matter of debate because yeasts are dimorphic, existing in both yeast and mycelial phases, depending on culture conditions. In 1996, Guého *et al.* reclassified the yeasts into seven species (*Malassezia furfur*, *Malassezia obtusa*, *Malassezia globosa*, *Malassezia slooffiae*, *Malassezia sympodialis*, *Malassezia restricta*, and *Malassezia pachydermatis*) based on their morphological, microscopic, physiological, and molecular biological characteristics.[7] Furthermore, in the last few years, some new species have been isolated from human (*Malassezia dermatis*, *Malassezia japonica*, and *Malassezia yamatoensis*)[8–10] and animal (*Malassezia*

nana, *Malassezia caprae*, *Malassezia equina*, and *Malassezia cuniculi*) skin.[11–13] At present, 14 species of *Malassezia* have been identified.

It seems that *M. globosa* and *M. restricta* are the species most commonly found on healthy and diseased human skin.[1–3] However, other species, such as *M. sympodialis* and *M. furfur*, have also been associated with various human skin disorders.[14] *Malassezia pachydermatis*, the only non-lipid-dependent species, is considered to be zoophilic and is frequently found on wild and domestic carnivores.[15]

In response to the taxonomic revision, a number of studies carried out worldwide have focused on the roles of the *Malassezia* in the pathogenicities and distributions of a range of different dermatoses. Results are not directly comparable between studies because the methodologies, isolation media, and identification procedures employed differ.

Malassezia as commensals

Malassezia yeasts are lipophilic and require specific lipids for growth. This property influences their distribution in sebum rich-areas of the skin such as the scalp, face, and trunk. Less frequently, they may be found on other areas of the body, including the arms, legs, and genitalia.[1,2]

A number of investigators have conducted studies of *Malassezia* colonization of healthy skin.[16–18] Such studies have demonstrated that these yeasts are unique in the fungal kingdom in that they represent the only species to be part of the normal human cutaneous commensal microbiota.

Colony formation begins immediately after birth and increases significantly with the age of the neonate. Skin colonization by *Malassezia* yeasts has been reported to amount to 5% at the first week and 30% at 2–4 weeks of life.[16] Using molecular analysis, Japanese investigators were able to detect *Malassezia* from 89 and 100% of neonate samples on days 0 and 1 after birth, respectively. Subsequently, the level of *Malassezia* colonization of the neonates increased with time, whereas that of the mothers did not change.[17] Early studies demonstrated that 97% of clinically healthy people carry fungus on the scalp, and 92% do so on the trunk. Some differences in carriage rates were noted between females and males, with higher population densities observed on the lower trunk and upper thigh in males.[18]

Studies examining the distribution of the new species of *Malassezia* on healthy human skin have reported variable results from different geographical regions (Table 1).[3,14,19–30]

Malassezia sympodialis emerges as the predominant species on healthy skin, especially on the trunk, from which it can be recovered in great numbers in more than 30% of individuals.[3,14,19,20,29,30] *Malassezia restricta* was found to be more prevalent on the scalp and forehead.[21,22,28,30] *Malassezia globosa* was found more frequently on the chest and arms than other areas,[23–25] whereas other species (*M. furfur*, *M. obtusa* and *M. slooffiae*) were less frequently recovered.

Significant differences were noted among age groups and species isolated. Lee *et al.*[22] recovered *M. restricta* more frequently in teenage subjects and young adults and found *M. globosa* to be the predominant species in subjects over 50 years of age. In a recent study, the present authors found *M. sympodialis* to be the predominant species on trunk skin in older subjects and *M. furfur* to be the most frequent in children.[30] These observations were contrary to those of Gupta *et al.*,[31] who cultured *M. globosa* more frequently on younger subjects and *M. sympodialis* on the skin of adolescents and adults.

Skin diseases associated with *Malassezia* spp.

In recent years, the genus *Malassezia* has come to be considered important in the etiologies of various skin diseases. In the yeast phase, the species reside on normal skin; once transformed into the mycelial phase, they can invade the stratum corneum, thereby inducing skin lesions. Pityriasis versicolor is the only human skin disease in which the causative role of lipophilic species is fully established; in other skin diseases, such as MF, SD, AD, and psoriasis, the pathogenic roles of these yeasts remain less clear, and the transition of yeast cells to their hyphal form cannot be clearly demonstrated.[1–3,14]

Pityriasis versicolor

Pityriasis versicolor is a common, benign, superficial noninflammatory cutaneous disorder, characterized by slightly scaly hyper- or hypopigmented lesions on the upper trunk.

The etiological role of *Malassezia* yeasts in PV is unquestioned; the organism found in the lesions is predominantly in its mycelial phase.[3,32] Several groups have published studies examining the mycology of PV. In particular, the species most commonly cultured was *M. globosa*, which was isolated from between 49 and 97% of cases (Table 1).[3,23–25,32–42] Recently, two further studies both reported *M. globosa* as the predominating species isolated from PV lesions. In the first study, from India, *M. globosa* was found in 52% of cases.[29] In the second study, conducted in Turkey, *M. globosa* was identified in 65% of cases.[42] *Malassezia sympodialis*, the second most common agent, has been isolated in frequencies of 4–13%.[23–25,33–35] However, other studies from North

Table 1 Summary of the different *Malassezia* species isolated from healthy and diseased skin, at different body sites and in different countries

Study ref.	Country	Condition	Patients, *n*	Site sampled	Sampling method	Culture medium/identification method	Predominant species (samples, %)
3	Spain	HS	75	Forehead and shoulder	Scraping	mDixons/culture-based	*M. sympodialis* (91.7)
14	Poland	HS	6	MS	Swabbing	mDixons/culture-based and molecular – PCR–RFLP and PCR sequencing	*M. sympodialis* (46)
19	Sweden	HS	31	Trunk	Contact plates	L–N/culture-based	*M. sympodialis* (69)
20	Canada	HS	20	MS	Contact plates	L–N/culture-based	*M. sympodialis* (47.2)
21	Japan	HS	18	Scalp and nape	Tape stripping	None (direct DNA extraction)/molecular – nested PCR	*M. restricta* (61.1)
22	South Korea	HS	120	MS	Scrub-wash	L–N/culture-based	*M. restricta* (31.6)
23	Japan	HS	105	MS	Swabbing	mDixons/culture-based	*M. globosa* (22)
24	Iran	HS	100	NS	Tape stripping	mDixons/culture-based	*M. globosa* (42)
25	Tunisia	HS	30	MS	Swabbing	mDixons/culture-based	*M. globosa* (7.8)
26	Iran	HS	123	Head	Tape stripping	L–N/molecular – PCR–RFLP	*M. globosa* (68.1)
27	Japan	HS	30	Face and neck	Tape stripping	None (direct DNA extraction)/molecular – nested PCR	*M. globosa* (86.7)
28	South Korea	HS	110	MS	Swabbing	L–N/molecular – nested PCR and RFLP	*M. restricta* (32)
29	India	HS	45	Trunk	Tape stripping	mDixons/culture-based	*M. sympodialis* (47.6)
30	B&H	HS	100	Trunk	Scraping	mDixons/culture-based	*M. sympodialis* (30)
			100	Scalp	Scraping	mDixons/culture-based	*M. restricta* (33)
3	Spain	PV	75	Lesional skin	Scraping	mDixons/culture-based	*M. globosa* (84)
20	Canada	PV	23	MS	Contact plates	L–N/culture-based	*M. sympodialis* (62.7)
23	Japan	PV	22	Trunk	Swabbing	mDixons/culture-based	*M. globosa* (55)
24	Iran	PV	94	NS	Scraping	mDixons/culture-based	*M. globosa* (53)
25	Tunisia	PV	100	MS	Swabbing	mDixons/culture-based	*M. globosa* (47)
29	India	PV	65	Lesional skin	Scraping	mDixons/culture-based	*M. globosa* (51.8)
32	Spain	PV	96	Lesional skin	Tape stripping	mDixons/culture-based	*M. globosa* (97)
33	Spain	PV	79	Trunk	Scraping	L–N/culture-based	*M. globosa* (90)
34	India	PV	427	Trunk	Scraping	L–N/culture-based	*M. globosa* (64)
35	Greece	PV	71	Lesional skin	Scraping	mDixons/molecular – PCR–SSCP	*M. globosa* (77)
36	Japan	PV	49	Lesional skin	Tape strip	None (direct DNA extraction)/molecular – nested PCR	*M. globosa*, *M. restricta* (93.9)
37	B&H	PV	90	Trunk	Scraping	mDixons/culture-based	*M. globosa* (63)
38	Tunisia	PV	58	NS	Scraping	mDixons/culture-based	*M. globosa* (76.2)
39	India	PV	139	NS	Scraping	mDixons/culture-based	*M. globosa* (50.3)
40	Italy	PV	74	Lesional skin	Scraping	mDixons/culture-based and molecular – PCR	*M. globosa* (60.3)
41	China	PV	24	Trunk	Transparent dressing	None (direct DNA extraction)/molecular – PCR	M. globosa (95.8)
42	Turkey	PV	146	MS	Scraping	mDixons/culture-based	*M. globosa* (65.1)
43	Canada	PV	129	MS	Scraping	L–N/culture-based	*M. sympodialis* (59.5)
44	Argentina	PV	218	MS	Scraping	mDixons/molecular – DNA extraction	*M. sympodialis* (37.7)
45	Brazil	PV	87	MS	Scraping	mDixons/culture-based	*M. sympodialis* (30)
46	Indonesia	PV	98	Lesional skin	Scraping	L–N/culture-based	*M. furfur* (42.9)
50	Turkey	MF	49	Lesional skin	Swabbing	None (direct DNA extraction)/rDNA ITSR internal transcribed spacer region	*M. globosa* (69.4)
51	Japan	MF	32	Lesional skin	Comedone extractor	L–N/culture-based None (direct DNA extraction)/molecular – PCR	*M. globosa* *M. restricta*
53	South Korea	MF	60	MS	Scrub-wash	L–N/molecular – PCR–RFLP	*M. restricta* (20.6)
19	Sweden	SD	16	Upper trunk	Contact plates	L–N/culture-based	*M. obtusa* (43) *M. sympodialis* (43)
3	Spain	SD	75	Lesional skin	Scraping	mDixons/culture-based	*M. restricta* (63.9)
20	Canada	SD	28	MS	Contact plates	L–N/culture-based	*M. globosa* (45)

Table 1 Continued

Study ref.	Country	Condition	Patients, *n*	Site sampled	Sampling method	Culture medium/identification method	Predominant species (samples, %)
23	Japan	SD	48	MS	Swabbing	mDixons/culture-based	*M. globosa* (21) *M. furfur* (21)
27	Japan	SD	31	Face	Tape stripping	None (direct DNA extraction)/molecular – nested PCR	*M. globosa* (93.5)
35	Greece	SD	38	Face	Scraping	mDixons/molecular – PCR–SSCP	*M. globosa* (39)
58	Serbia	SD	79	Forehead	Tape stripping	mDixons and L–N/culture-based	*M. globosa* (31.6)
59	B&H	SD	40	Scalp	Scraping	mDixons/culture-based	*M. restricta* (27.5)
63	South Korea	SD	40	Scalp	Swabbing	L–N/molecular – PCR–RFLP	*M. restricta* (47.5)
64	Iran	SD	100	MS	Scraping	mDixons/culture-based	*M. globosa* (55.8)
65	Iran	SD	110	Scalp	Scraping	mDixons/culture-based	*M. globosa* (11.4)
66	Argentina	SD	226	Lesional skin	Scraping	mDixons/molecular – nested PCR–RFLP	*M. globosa* (43.3)
67	China	SD	146	Lesional skin	Tape strip	None (direct DNA extraction)/molecular – nested PCR	*M. globosa* (87.0)
68	USA	SD	70	Scalp	Swabbing	None (direct DNA extraction)/molecular – FLPA	*M. restricta* (41.2)
14	Poland	AD	6	MS	Swabbing	mDixons/culture-based and molecular – PCR–RFLP and PCR sequencing	*M. sympodialis* (67)
19	Sweden	AD	124	Trunk	Contact plates	L–N/culture-based	*M. sympodialis* (46)
20	Canada	AD	31	MS	Contact plates	L–N/culture-based	*M. sympodialis* (51)
21	Japan	AD	32	MS	Tape stripping	None (direct DNA extraction)/molecular – nested PCR	*M. globosa* (93.8)
23	Japan	AD	28	Trunk	Swabbing	mDixons/culture-based	*M. furfur* (21)
27	Japan	AD	26	Face and neck	Tape stripping	None (direct DNA extraction)/molecular – nested PCR	*M. globosa* (100)
72	South Korea	AD	60	MS	Swabbing	L–N/molecular – PCR–RFLP	*M. sympodialis* (16.3)
14	Poland	Psoriasis	6	MS	Swabbing	mDixons/culture-based and molecular – PCR–RFLP and PCR sequencing	*M. furfur* (70) *M. sympodialis* (70)
20	Canada	Psoriasis	28	MS	Contact plates	L–N/culture-based	*M. globosa* (57)
26	Iran	Psoriasis	110	Head	Scraping	L–N/molecular – PCR–RFLP	*M. globosa* (47.2)
79	India	Psoriasis	50	Lesional skin	Tape stripping	None (direct DNA extraction)/molecular – PCR–RFLP	*M. furfur* (70.6)
84	B&H	Psoriasis	40	Scalp	Scraping	mDixons/culture-based	*M. globosa* (55)
85	Spain	Psoriasis	40	Scalp	Scraping	mDixons/culture-based	*M. globosa* (45)
86	Mexico	Psoriasis	20	MS	Scraping	mDixons/culture-based	*M. sympodialis* (38.2)
87	Japan	Psoriasis	22	Trunk	Tape stripping	None (direct DNA extraction)/molecular – nested PCR	*M. restricta* (96)
88	Japan	Psoriasis	20	MS	–	None (direct DNA extraction)/molecular – real-time PCR	*M. restricta* (92)

AD, atopic dermatitis; B&H, Bosnia and Herzegovina; FLPA, fragment length polymorphism analysis; ITSR internal transcribed spacer region; HS, healthy subjects; L–N, Leeming–Notman agar; mDixons, modified Dixon agar; MF, *Malassezia* folliculitis; MS, multiple sites; NS, not stated; PCR, polymerase chain reaction; PV, pityriasis versicolor; RFLP, restriction fragment length polymorphism; SD, seborrhoeic dermatitis; SSCP, single-strand conformation polymorphism.

and South America have reported *M. sympodialis* to be the predominant isolate and report frequencies of 59%, 38%, and 30%, respectively.[43–45] *Malassezia furfur*, by contrast, was isolated less frequently by many investigators, who reported it as the second or third species,[20,24,25,34,39,43] although an Indonesian, culture-based study described it as the first causative agent.[46]

The main role of *M. globosa* in the etiology of PV and its enhanced level of pathogenicity are supported by the fact that this species possesses the highest degree of lipase activity and capacity for hyphal growth.[33,47] The presence of this species in its yeast phase in diseased and even in healthy skin indicates that local factors (humidity, sweat, heat), together with some degree of idiosyncratic individual predisposition, are responsible for its transformation from the yeast to the mycelial form and hence for the development of clinical lesions.[24,32,43]

There is also evidence that *Malassezia* spp. are frequently isolated from non-lesional skin of patients with PV,[32,33,37,41] suggesting that the endogenous factors that

promote the development of PV in susceptible hosts do not necessarily favor the growth of some species over others.

Malassezia folliculitis

Malassezia folliculitis is an inflammatory skin disorder in which a chronic, pruritic, follicular, papulopustular eruption may occur on the upper trunk, neck, and upper arms. Predisposing factors include occlusion, sweating, and increases in temperature, as well as immunosuppression, diabetes mellitus, and the use of broad-spectrum antibiotics, which may be responsible for the imbalance between the *Malassezia* species and its host, predisposing towards disease occurrence.[48] Diagnosis is based on the clinical picture, microscopy, and a favorable response to antifungal therapy. Although the transformation of the yeast cells to their hyphal form is unique to PV, histological examination shows the colonization by budding yeasts of hair follicles, where they hydrolyze triglycerides, which are responsible for the inflammatory reaction in the follicle.[49] However, the colonization of hair follicles by *Malassezia* spp. may not be significant because these species can also be isolated from normal pilosebaceous follicles.[48]

To date, studies to determine which species of *Malassezia* may be involved in MF have yielded divergent results, with *M. globosa*,[50–52] *M. restricta*,[53] and *M. sympodialis*[50] all recovered from hair follicles (Table 1).

In a study conducted in Turkey, Durdu *et al.*[50] identified the most common species in lesional samples to be *M. globosa* (69.4%), followed by *M. sympodialis*, *M. restricta* and *M. furfur*. Using various identification methods, Akaza *et al.*[51] found the predominant species recovered from MF lesions to be *M. globosa* and *M. sympodialis* by culture method analysis and *M. restricta*, *M. globosa* and *M. sympodialis* by non-culture methods.

Although *M. restricta* was most commonly detected in MF patients, the high rate of recovery of *M. sympodialis* suggests that this species may possess a pathogenic potential. Findings of *M. sympodialis* on mycological examination of the folliculitis lesions of renal cell carcinoma patients have been reported, which further increases the possibility that this strain is pathogenic.[54]

Seborrheic dermatitis

There are now many studies indicating that *Malassezia* spp. play an important role in SD. The exact mechanisms by which these yeasts cause inflammation are still not fully understood. *Malassezia* spp. produce many enzymes (including lipases and phospholipases) that can initiate an inflammatory response by releasing unsaturated free fatty acids from the sebum lipids. Oleic acid has direct irritant and desquamative effects on keratinocytes, whereas arachidonic acid produces proinflammatory eicosanoides and leads to inflammation and damage to the stratum corneum.[55] In *Malassezia* spp., this modulation of the immune system appears to be mediated by the lipid-rich microfibrillar layer surrounding yeast cells. High quantities of lipid may prevent the yeast cell from inducing inflammation in a manner consistent with its commensal status. In SD, however, yeasts fail to show a lipid layer because of alterations in the availability of nutrients on the lipid surface, which may explain the inflammatory nature of the disease.[56,57]

Most of the studies published in recent years demonstrate geographical variations in the rates at which the various species are isolated, although a correlation between yeast density and severity of SD has been reported.[58] However, in some reports, the quantity of yeasts was found not to be correlated positively with the severity of disease.[59,60] In a culture-based study, Gupta *et al.*[20] showed a greater extent of *Malassezia* colonization at non-lesional sites than at lesional sites. However, a DNA-based study reported higher densities of *Malassezia* at lesional sites than at non-lesional sites.[27] It has been suggested that an overgrowth of *Malassezia* organisms is important only in those individuals who are immunologically predisposed towards the development of SD.[61] The possibility that *Malassezia* might locally modify the immune response, coupled with host susceptibility, may represent another explanation for the development of a clinical condition.[62] Arsic Arsenijevic *et al.*[58] and Lee *et al.*[63] reported high rates of recovery of *Malassezia* yeasts, at 87% and 85%, respectively. However, a study conducted in southern Iran reported a very low rate of recovery from SD patients of 24.5%, probably because the climate in the region is very dry.[64]

To date, the two species most commonly isolated from SD patients are *M. globosa*[20,23,27,35,58,64–67] and *M. restricta* (Table 1).[3,59,63,68] However, in Sweden[19] and in Eastern Europe,[60] skin lesions are more frequently colonized with *M. obtusa*, a species that was sporadically identified in previous studies from diseased[19,20,24,27,29,30,42,45,46] and healthy[19,27,29] skin.

It is worth noting the sporadic isolation of *M. pachydermatis* obtained from SD lesions. This species is considered to be zoophilic and is frequently found on wild and domestic carnivores.[15] The presence of this species on human skin is rare and transient and occurs possibly by transmission from pet animals and environmental sources.[38,66] However, in a study performed by Zarei-Mahmoudabadi *et al.*,[65] *M. pachydermatis* was the second most frequently isolated species and was recovered from 22% of cases.

Atopic dermatitis

Atopic dermatitis is a multifactorial disease in which microbial products from bacteria and yeasts play various roles in triggering disease. *Malassezia* spp. have been implicated as aggravating factors in AD, especially in a subset of patients with head and neck AD.[69] Because the yeasts are part of the normal cutaneous microbiota, it has been hypothesized that they act as allergens in patients who are susceptible, rather than as infectious agents.[1] Two lines of evidence support the role of *Malassezia* spp. in the development of inflammation and exacerbation associated with AD. Firstly, both topical and systemic antifungal treatments reduce the severity of skin symptoms in yeast-sensitized AD patients,[70] and, secondly, patients with AD react more frequently to *Malassezia* extract and recombinant *Malassezia* antigens than healthy controls.[71]

The rate of recovery of *Malassezia* spp. from the lesional skin of AD patients was found to be lower than those obtained from patients with other dermatoses (PV, SD, psoriasis) and from healthy subjects.[19,20,72] One reason for this may refer to the disruption of skin barrier function in AD patients, which reduces the amount of lipid available to support the growth of yeasts.[73] Another explanation for the low positive rate of isolated cultures may refer to the antifungal activity of the mediators and/or inflammatory cells present in AD lesions.[20] In addition, the prevalence of positive *Malassezia* cultures has been found not to correlate with the severity of AD.[72]

Multiple *Malassezia* spp. have been associated with AD and, again, results have differed among studies (Table 1).[14,19–21,23,27,72] However, one of the most frequently isolated species is *M. sympodialis*,[14,19,20,72] which has been considered to be associated with AD. One of the clearest indications to support this association is the fact that sensitization to *M. sympodialis* is specific for the skin manifestations of the disease and does not occur in AD patients with other allergic diseases.[74] Conversely, studies using culture-independent methods found *M. globosa* and *M. furfur* to be the predominant species among Japanese subjects.[21,23,27,75] These species were detected at frequencies ranging from 87.5 to 100%, whereas *M. sympodialis* was the third most frequently isolated species, at 40.6 and 58.3%.[21,27]

The implication of *Malassezia* yeasts in AD is currently under intense investigation, and further studies are required to elucidate the exact roles of these organisms in the course and exacerbation of disease. In order to determine the distribution and character of *Malassezia* yeasts on the skin of AD patients, further case–control studies and quantitative molecular biological analyses should be conducted in specific types of AD patients.

Psoriasis

Although psoriasis is considered to be a T cell-mediated autoimmune disease, increasing evidence suggests that both genetic and environmental factors play important roles in its initiation and exacerbation.[76] Fungal organisms, including *Malassezia* spp., have also been suggested to represent external triggers that release factors which serve as superantigens and stimulate T cells to initiate the pathogenic features of psoriasis.[77]

In recent years, many authors have reported a significant correlation between the presence of *Malassezia* yeasts and the severity of skin irritation in psoriasis patients.[78,79] Patients with psoriasis, but not healthy individuals, have been reported to show serum antibodies to *Malassezia* proteins and *Malassezia*-induced Th1-related cytokines in peripheral blood mononuclear cells.[80] Furthermore, *Malassezia* spp. can invade cultured human keratinocytes, modulate proinflammatory and immunomodulatory cytokine synthesis, and affect the expression of cutaneous proteins, especially those related to cell migration and proliferation, potentially enhancing inflammation.[81] The efficacy of antifungal drugs, both topical and systemic, in the treatment of the disease, supports only a secondary role for *Malassezia* yeast in psoriasis, possibly that of an exacerbating factor,[82,83] and it remains unclear whether these yeasts are able to initiate the development of psoriasis lesions.

Among very few reports on the prevalence and species composition of *Malassezia* yeasts in psoriasis patients, some authors have stated that *M. globosa* predominates,[20,26,84,85] whereas others have found *M. furfur*[79] or *M. sympodialis*[86] to be the most common species in scalp lesions of psoriasis (Table 1). The frequencies of the major isolate varied between 38 and 71%. However, in culture-independent studies, *M. restricta* was reported as the main species in psoriasis patients and was isolated in high frequencies of 96% and 92%, respectively.[87,88]

A very recent study performed in Poland, using both culture-dependent and molecular methods, identified only two species, both of which were equally abundant, namely, *M. sympodialis* and *M. furfur*.[14]

Other dermatological disorders

Malassezia spp. have been associated with a wide range of other superficial diseases, including onycomycosis,[89,90] confluent and reticulated papillomatosis,[91] and acne.[92] However, the evidence linking *Malassezia* spp. to these conditions is speculative and is largely reliant on the

clinical efficacy of antifungal drugs, and thus a definite causal relationship cannot be assumed.

Discrepancies in the identification of *Malassezia* spp.

Most studies have shown some discrepancies between traditional culture-based and molecular-based identifications of *Malassezia*. Molecular techniques are considered as fast, reliable, and more accurate methods of identifying *Malassezia* spp.[93] They also provide the possibility of identifying yeasts directly from skin samples without the need for culture.[94] However, some discrepancies are observed when such results are compared with data obtained using culture-dependent techniques. Using culturing methods, *M. globosa* was found to be the most prevalent species on the skin of healthy subjects[23–25,27] and patients with PV[3,23–25,29,33–35,37–39,42] and psoriasis,[20,84,85] whereas *M. restricta* was isolated only sporadically. By contrast with these findings, a higher detection rate of *M. restricta* was observed using molecular methods in healthy individuals,[21,28] and in patients with PV,[21,28] MF,[53] and SD,[63,68] although the samples were collected from multiple body sites.

In another study, the respective results of culture-based and molecular identification showed a rate of agreement of 66%, with the discordance reflecting the presence of multiple species in a single culture (co-colonization) rather than misidentification.[14] The co-isolation of two or more *Malassezia* spp. from the same specimen was recorded in many studies at frequencies ranging from 11 to 40%.[14,32,35,36,63] Furthermore, in a third of discrepant cases, molecular methods did not invalidate the presence of a species identified by conventional culture-based methods but only uncovered another, co-occurring *Malassezia* species.[14]

The discordance between these two identification methods may also relate to differences in growth rates between species. Fast-growing species in a culture medium, such as *M. sympodialis*, usually outgrow and obscure slow-growing species such as *M. restricta* and *M. globosa*. In particular, *M. restricta* does not survive well in culture and cannot be detected with high reliability using phenotypic identification methods.[68] *Malassezia globosa* present in a primary culture has been found to disappear from subsequent passages, with the result that only *M. sympodialis* remained in culture.[23]

Susceptibility of *Malassezia* spp. to antifungals

Malassezia spp. are susceptible to a wide range of topical antifungal therapies and several effective oral agents. The results of *in vitro* susceptibility studies have shown variations in the susceptibility of *Malassezia* spp. to various antifungal agents. Strains of *M. furfur*, *M. globosa*, and *M. obtusa* have been found to be more tolerant to terbinafine than other *Malassezia* spp., whereas *M. sympodialis* was highly susceptible.[95] Fluconazole was found to be very active against *M. sympodialis* and *M. slooffiae*, although to a lesser extent, but inactive against *M. globosa* and *M. restricta*. Meanwhile, itraconazole had high activity against *M. globosa*.[96] Hammer *et al.*[97] found ketoconazole to be more active against *M. furfur* strains isolated from systemic infection than econazole and miconazole but reported that investigations in other species showed all of these agents to have similar efficacies.

The variability identified in results from different laboratories stems from the lack of a standardized protocol for *Malassezia* susceptibility testing. The variety of susceptibility tests include urea broth microdilution methods,[98] a liquid medium using a colorimetric indicator for metabolic activity,[99] and a modified broth and solid Roswell Park Memorial Institute (RPMI) 1640 (Sigma-Aldrich Corp., St Louis, MO, USA) media.[100] Although *in vitro* susceptibility testing is not yet standardized for *Malassezia* spp., an adaptation of the Clinical and Laboratory Standards Institute (CLSI) broth microdilution protocol, in which the media, time of incubation, and inocula were modified, showed itraconazole, ketoconazole, and posaconazole to be the most effective drugs.[100,101]

These results suggest that correct identification of *Malassezia* spp. may be important for the selection of sensitive drugs in the clinic.

Conclusions

The distribution of *Malassezia* spp. on healthy and diseased skin shows significant variation. Although our knowledge of *Malassezia* yeasts has increased tremendously during the last two decades, their pathological roles remain ambiguous, and there is currently no conclusive evidence that any given species is responsible for a specific disease.

The identification of *Malassezia* yeasts to species level is of no diagnostic value in skin diseases because the same species form an integral part of normal cutaneous microbiota in humans. However, it is extremely important to determine which species are implicated in certain skin diseases and whether the distribution of the yeasts varies in line with clinical data, body site, and the origin of the population, among other factors. Moreover, the identification of pathogenic species is helpful in selecting appropriate antifungal therapy.

The differences among studies in the distributions of *Malassezia* spp. may be attributed to the use of different

sampling techniques (scraping/contact plates), different culture media (modified Dixon agar/Leeming–Notman agar), and perhaps ethnic and geographic factors.

Moreover, inadequate determination of the relative proportion of species on the skin, or the ability of the fungus to grow in any particular medium, may also have impact on the range of species recovered. The geographic and ethnic origins, clinical and demographic characteristics, and even the lifestyle habits of the subjects under study may contribute to the differences observed in the prevalences and species composition of *Malassezia* colonies.

References

1 Ashbee HR. Update on the genus *Malassezia*. *Med Mycol* 2007; **45**: 287–303.
2 Difonzo EM, Faggi E, Bassi A, *et al.* *Malassezia* skin diseases in humans. *G Ital Dermatol Venereol* 2013; **148**: 609–619.
3 Crespo Erchiga V, Ojeda Martos AA, Vera Casaño A, *et al.* Isolation and identification of *Malassezia* spp. in pityriasis versicolor, seborrheic dermatitis and healthy skin. *Rev Iberoam Micol* 1999; **16**: 16–21.
4 Heng MC, Henderson CL, Barker DC, *et al.* Correlation of *Pityosporum ovale* density with clinical severity of seborrheic dermatitis as assessed by a simplified technique. *J Am Acad Dermatol* 1990; **23**: 82–86.
5 Gündüz K, Inanir I, Sacar H. Efficacy of terbinafine 1% cream on seborrhoeic dermatitis. *J Dermatol* 2005; **32**: 22–25.
6 Tragiannidis A, Bisping G, Koehler G, *et al.* Mini review: *Malassezia* infections in immunocompromised patients. *Mycoses* 2010; **53**: 187–195.
7 Guého E, Midgley G, Guillot J. The genus *Malassezia* with description of four new species. *Antonie Van Leeuwenhoek* 1996; **69**: 337–355.
8 Sugita T, Takashima M, Shinoda T, *et al.* New yeast species, *Malassezia dermatis*, isolated from a patient with atopic dermatitis. *J Clin Microbiol* 2002; **40**: 1363–1367.
9 Sugita T, Takashima M, Kodama M, *et al.* Description of a new species *Malassezia japonica* and its detection in patients with atopic dermatitis and healthy subjects. *J Clin Microbiol* 2003; **41**: 4695–4699.
10 Sugita T, Tajima M, Takashima M, *et al.* A new yeast, *Malassezia yamatoensis*, isolated from a patient with seborrheic dermatitis, and its distribution in patients and healthy subjects. *Microbiol Immunol* 2004; **48**: 579–583.
11 Hirai A, Kano R, Makimura K, *et al.* *Malassezia nana* sp. nov., a novel lipid-dependent yeast species isolated from animals. *Int J Syst Evol Microbiol* 2004; **54**: 623–627.
12 Cabañes FJ, Theelen B, Castellá G, *et al.* Two new lipid-dependent *Malassezia* species from domestic animals. *FEMS Yeast Res* 2007; **7**: 1064–1076.
13 Cabañes FJ, Vega S, Castellá G. *Malassezia cuniculi* sp. nov., a novel yeast species isolated from rabbit skin. *Med Mycol* 2011; **49**: 40–48.
14 Jagielski T, Rup E, Ziółkowska A, *et al.* Distribution of *Malassezia* species on the skin of patients with atopic dermatitis, psoriasis, and healthy volunteers assessed by conventional and molecular identification methods. *BMC Dermatol* 2014; **14**: 3.
15 Guillot J, Bond R. *Malassezia pachydermatis:* a review. *Med Mycol* 1999; **37**: 295–306.
16 Ayhan M, Sancak B, Karaduman A, *et al.* Colonization of neonate skin by *Malassezia* species: relationship with neonatal cephalic pustulosis. *J Am Acad Dermatol* 2007; **57**: 1012–1018.
17 Nagata R, Nagano H, Ogishima D, *et al.* Transmission of the major skin microbiota, *Malassezia*, from mother to neonate. *Pediatr Int* 2012; **54**: 350–355.
18 Roberts SOB. *Pityrosporum orbiculare*: incidence and distribution on clinically normal skin. *Br J Dermatol* 1969; **81**: 265–269.
19 Sandström Falk MH, Tengvall Linder M, Johansson C, *et al.* The prevalence of *Malassezia* yeasts in patients with atopic dermatitis, seborrhoeic dermatitis and healthy controls. *Acta Derm Venereol* 2005; **85**: 17–23.
20 Gupta AK, Kohli Y, Summerbell RC, *et al.* Quantitative culture of *Malassezia* species from different body sites of individuals with and without dermatoses. *Med Mycol* 2001; **38**: 243–351.
21 Sugita T, Suto H, Unno T, *et al.* Molecular analysis of *Malassezia* microflora on the skin of atopic dermatitis patients and healthy subjects. *J Clin Microbiol* 2001; **39**: 3486–3490.
22 Lee YW, Yim SM, Lim SH, *et al.* Quantitative investigation on the distribution of *Malassezia* species on healthy human skin in Korea. *Mycoses* 2006; **49**: 405–410.
23 Nakabayashi A, Sei Y, Guillot J. Identification of *Malassezia* species isolated from patients with seborrhoeic dermatitis, atopic dermatitis, pityriasis versicolor and normal subjects. *Med Mycol* 2000; **38**: 337–341.
24 Tarazooie B, Kordbacheh P, Zaini F, *et al.* Study of the distribution of *Malassezia* species in patients with pityriasis versicolor and healthy individuals in Tehran, Iran. *BMC Dermatol* 2004; **4**: 5.
25 Ben Salah S, Makni F, Marrakchi S, *et al.* Identification of *Malassezia* species from Tunisian patients with pityriasis versicolor and normal subjects. *Mycoses* 2005; **48**: 242–245.
26 Zomorodian K, Mirhendi H, Tarazooie B, *et al.* Distribution of *Malassezia* species in patients with psoriasis and healthy individuals in Tehran, Iran. *J Cutan Pathol* 2008; **35**: 1027–1031.
27 Tajima M, Sugita T, Nishikawa A, *et al.* Molecular analysis of *Malassezia* microflora in seborrheic

dermatitis patients: comparison with other diseases and healthy subjects. *J Invest Dermatol* 2008; **128**: 345–351.
28 Oh BH, Song YC, Lee YW, *et al.* Comparison of nested PCR and RFLP for identification and classification of *Malassezia* yeasts from healthy human skin. *Ann Dermatol* 2009; **21**: 352–357.
29 Kaur M, Narang T, Bala M, *et al.* Study of the distribution of *Malassezia* species in patients with pityriasis versicolor and healthy individuals in Tertiary Care Hospital, Punjab. *Indian J Med Microbiol* 2013; **31**: 270–274.
30 Prohic A, Simic D, Jovovic Sadikovic T, *et al.* Distribution of *Malassezia* species on healthy human skin in Bosnia and Herzegovina: correlation with body part, age and gender. *Iran J Microbiol* 2014; **6**: 253–262.
31 Gupta AK, Kohli Y. Prevalence of *Malassezia* species on various body sites in clinically healthy subjects representing different age groups. *Med Mycol* 2004; **42**: 35–42.
32 Crespo Erchiga V, Ojeda Martos A, Vera Casano A, *et al. Malassezia globosa* as the causative agent of pityriasis versicolor. *Br J Dermatol* 2000; **143**: 799–803.
33 Aspiroz C, Ara M, Varea M, *et al.* Isolation of *M. globosa* and *M. sympodialis* from patients with pityriasis versicolor in Spain. *Mycopathologia* 2001; **154**: 11–17.
34 Dutta S, Bajaj AK, Basu S, *et al.* Pityriasis versicolor: socioeconomic and clinico-mycologic study in India. *Int J Dermatol* 2002; **41**: 823–824.
35 Gaitanis G, Velegraki A, Alexopoulos EC, *et al.* Distribution of *Malassezia* species in pityriasis versicolor and seborrhoeic dermatitis in Greece. Typing of the major pityriasis versicolor isolate *M. globosa*. *Br J Dermatol* 2006; **154**: 854–859.
36 Morishita N, Sei Y, Sugita T. Molecular analysis of *Malassezia* microflora from patients with pityriasis versicolor. *Mycopathologia* 2006; **161**: 61–65.
37 Prohic A, Ozegovic L. *Malassezia* species isolated from lesional and non-lesional skin in patients with pityriasis versicolor. *Mycoses* 2007; **50**: 58–63.
38 Trabelsi S, Oueslati J, Fekih N, *et al.* Identification of *Malassezia* species from Tunisian patients with pityriasis versicolor. *Tunis Med* 2010; **88**: 85–87.
39 Shah A, Koticha A, Ubale M, *et al.* Identification and speciation of *Malassezia* in patients clinically suspected of having pityriasis versicolor. *Indian J Dermatol* 2013; **58**: 239.
40 Romano C, Mancianti F, Nardoni S, *et al.* Identification of *Malassezia* species isolated from patients with extensive forms of pityriasis versicolor in Siena, Italy. *Rev Iberoam Micol* 2013; **30**: 231–234.
41 Xie Z, Ran Y, Zhang H, *et al.* An analysis of the *Malassezia* species distribution in the skin of patients with pityriasis versicolor in Chengdu, China. *ScientificWorldJournal* 2014; **2014**: 182596.
42 Rodoplu G, Saracli MA, Gümral R, *et al.* Distribution of *Malassezia* species in patients with pityriasis versicolor in Turkey. *J Mycol Med* 2014; **24**: 117–123.
43 Gupta AK, Kohli Y, Faergemann J, *et al.* Epidemiology of *Malassezia* yeasts associated with pityriasis versicolor in Ontario, Canada. *Med Mycol* 2001; **39**: 199–206.
44 Giusiano G, Sosa Mde L, Rojas F, *et al.* Prevalence of *Malassezia* species in pityriasis versicolor lesions in northeast Argentina. *Rev Iberoam Micol* 2010; **27**: 71–74.
45 Petry V, Tanhausen F, Weiss L, *et al.* Identification of *Malassezia* yeast species isolated from patients with pityriasis versicolor. *An Bras Dermatol* 2011; **86**: 803–806.
46 Krisanty RI, Bramono K, Made Wisnu I. Identification of *Malassezia* species from pityriasis versicolor in Indonesia and its relationship with clinical characteristics. *Mycoses* 2009; **52**: 257–262.
47 Juntachai W, Oura T, Murayama SY, *et al.* The lipolytic enzymes activities of *Malassezia* species. *Med Mycol* 2009; **47**: 477–484.
48 Rubenstein RM, Malerich SA. *Malassezia* (*Pityrosporum*) folliculitis. *J Clin Aesthet Dermatol* 2014; **7**: 937–941.
49 Ayers K, Sweeney SM, Wiss K. *Pityrosporum* folliculitis: diagnosis and management in 6 female adolescents with acne vulgaris. *Arch Pediatr Adolesc Med* 2005; **159**: 64–67.
50 Durdu M, Güran M, Ilkit M. Epidemiological characteristics of *Malassezia* folliculitis and use of the May–Grünwald–Giemsa stain to diagnose the infection. *Diagn Microbiol Infect Dis* 2013; **76**: 450–457.
51 Akaza N, Akamatsu H, Sasaki Y, *et al. Malassezia* folliculitis is caused by cutaneous resident *Malassezia* species. *Med Mycol* 2009; **47**: 618–624.
52 Anane S, Chtourou O, Bodemer C, *et al. Malassezia* folliculitis in an infant. *Med Mycol Case Rep* 2013; **2**: 72–74.
53 Ko JH, Lee YW, Choe YB, *et al.* Epidemiologic study of *Malassezia* yeasts in patients with *Malassezia* folliculitis by 26S rDNA PCR-RFLP analysis. *Ann Dermatol* 2011; **23**: 177–184.
54 Cuétara MS, Aguilar A, Martin L, *et al.* Erlotinib associated with rosacea-like folliculitis and *Malassezia sympodialis*. *Br J Dermatol* 2006; **155**: 477–479.
55 Lee YW, Lee SY, Lee Y, *et al.* Evaluation of expression of lipases and phospholipases of *Malassezia restricta* in patients with seborrheic dermatitis. *Ann Dermatol* 2013; **25**: 310–314.
56 Kesavan S, Holland KT, Ingham E. The effects of lipid extraction on the immunomodulatory activity of *Malassezia* species *in vitro*. *Med Mycol* 2000; **38**: 239–247.
57 Thomas DS, Ingham E, Bojar RA, *et al. In vitro* modulation of human keratinocyte pro- and anti-inflammatory cytokine production by the capsule of *Malassezia* species. *FEMS Immunol Med Microbiol* 2008; **54**: 203–214.

58 Arsic Arsenijevic VS, Milobratovic D, Barac AM, *et al.* A laboratory-based study on patients with Parkinsons disease and seborrheic dermatitis: the presence and density of *Malassezia* yeasts, their different species and enzymes production. *BMC Dermatol* 2014; **14**: 5.
59 Prohic A. Distribution of *Malassezia* species in seborrhoeic dermatitis: correlation with patients cellular immune status. *Mycoses* 2009; **53**: 344–349.
60 Zisova LG. *Malassezia* species and seborrheic dermatitis. *Folia Med (Plovdiv)* 2009; **51**: 23–33.
61 Bergbrant IM, Johansson S, Robbins D, *et al.* An immunological study in patients with seborrhoeic dermatitis. *Clin Exp Dermatol* 1991; **16**: 331–338.
62 Lally A, Casabonne D, Newton R, *et al.* Seborrheic dermatitis among Oxford renal transplant recipients. *J Eur Acad Dermatol Venereol* 2010; **24**: 561–564.
63 Lee YW, Byun HJ, Kim BJ, *et al.* Distribution of *Malassezia* species on the scalp in Korean seborrheic dermatitis patients. *Ann Dermatol* 2011; **23**: 156–161.
64 Hedayati MT, Hajheydari Z, Hajjar F, *et al.* Identification of *Malassezia* species isolated from Iranian seborrhoeic dermatitis patients. *Eur Rev Med Pharmacol Sci* 2010; **14**: 63–68.
65 Zarei-Mahmoudabadi A, Zarrin M, Mehdinezhad F. Seborrheic dermatitis due to *Malassezia* species in Ahvaz, Iran. *Iran J Microbiol* 2013; **5**: 268–271.
66 Sosa Mde L, Rojas F, Mangiaterra M, *et al.* Prevalence of *Malassezia* species associated with seborrheic dermatitis lesions in patients in Argentina. *Rev Iberoam Micol* 2013; **30**: 239–242.
67 Zhang H, Ran Y, Xie Z, *et al.* Identification of *Malassezia* species in patients with seborrheic dermatitis in China. *Mycopathologia* 2013; **175**: 83–89.
68 Gemmer CM, DeAngelis YM, Theelen B, *et al.* Fast, noninvasive method for molecular detection and differentiation of *Malassezia* yeast species on human skin and application of the method to dandruff microbiology. *J Clin Microbiol* 2002; **40**: 3350–3357.
69 Brodská P, Panzner P, Pizinger K, *et al.* IgE-mediated sensitization to *Malassezia* in atopic dermatitis: more common in male patients and in head and neck type. *Dermatitis* 2014; **25**: 120–126.
70 Svejgaard E, Larsen PÄ, Deleuran M, *et al.* Treatment of head and neck dermatitis comparing itraconazole 200 mg and 400 mg daily for 1 week with placebo. *J Eur Acad Dermatol Venereol* 2004; **18**: 445–449.
71 Sonesson A, Bartosik J, Christiansen J, *et al.* Sensitization to skin-associated microorganisms in adult patients with atopic dermatitis is of importance for disease severity. *Acta Derm Venereol* 2013; **93**: 340–345.
72 Yim SM, Kim JY, Ko JH, *et al.* Molecular analysis of *Malassezia* microflora on the skin of the patients with atopic dermatitis. *Ann Dermatol* 2010; **22**: 41–47.
73 Pilgram GS, Vissers DC, van der Meulen H, *et al.* Aberrant lipid organization in stratum corneum of patients with atopic dermatitis and lamellar ichthyosis. *J Invest Dermatol* 2001; **117**: 710–717.
74 Casagrande BF, Flückiger S, Linder MT, *et al.* Sensitization to the yeast *Malassezia sympodialis* is specific for extrinsic and intrinsic atopic eczema. *J Invest Dermatol* 2006; **126**: 2414–2421.
75 Kaga M, Sugita T, Nishikawa A, *et al.* Molecular analysis of the cutaneous *Malassezia* microbiota from the skin of patients with atopic dermatitis of different severities. *Mycoses* 2011; **54**: 24–28.
76 Nestle FO, Kaplan DH, Barker J. Mechanisms of disease: psoriasis. *N Engl J Med* 2009; **361**: 444–509.
77 Fry L, Baker BS, Powles AV, *et al.* Is chronic plaque psoriasis triggered by microbiota in the skin? *Br J Dermatol* 2013; **169**: 47–52.
78 Faergemann J, Diehl U, Bergfelt L, *et al.* Scalp psoriasis: synergy between the *Malassezia* yeasts and skin irritation due to calcipotriol. *Acta Derm Venereol* 2003; **83**: 438–441.
79 Rudramurthy SM, Honnavar P, Chakrabarti A, *et al.* Association of *Malassezia* species with psoriatic lesions. *Mycoses* 2014; **57**: 483–488.
80 Kanda N, Tani K, Enomoto U, *et al.* The skin fungus-induced Th1- and Th2-related cytokine, chemokine and prostaglandin E2 production in peripheral blood mononuclear cells from patients with atopic dermatitis and psoriasis vulgaris. *Clin Exp Allergy* 2002; **32**: 1243–1250.
81 Baroni A, Paoletti I, Ruocco E, *et al.* Possible role of *Malassezia* furfur in psoriasis: modulation of TGF-β1, integrin, and HSP70 expression in human keratinocytes and in the skin of psoriasis-affected patients. *J Cutan Pathol* 2004; **31**: 35–42.
82 Farr PM, Krause LB, Marks JM, *et al.* Response of scalp psoriasis to oral ketoconazole. *Lancet* 1985; **26**: 921–922.
83 Rosenberg EW, Belew PW. Improvement of psoriasis of the scalp with ketoconazole. *Arch Dermatol* 1982; **118**: 370–371.
84 Prohic A. Identification of *Malassezia* species isolated from scalp skin of patients with psoriasis and healthy subjects. *Acta Dermatovenerol Croat* 2003; **11**: 10–16.
85 Gomez-Moyano E, Crespo-Erchiga V, Martínez-Pilar L, *et al.* Do *Malassezia* species play a role in exacerbation of scalp psoriasis? *J Mycol Med* 2014; **24**: 87–92.
86 Hernández Hernández F, Méndez Tovar LJ, Bazán Mora E, *et al.* Species of *Malassezia* associated with various dermatoses and healthy skin in the Mexican population. *Rev Iberoam Micol* 2003; **20**: 141–144.
87 Amaya M, Tajima M, Okubo Y, *et al.* Molecular analysis of *Malassezia* microflora in the lesional skin of psoriasis patients. *J Dermatol* 2007; **34**: 619–624.
88 Takahata Y, Sugita T, Hiruma M, *et al.* Quantitative analysis of *Malassezia* in the scale of patients with psoriasis using a real-time polymerase chain reaction assay. *Br J Dermatol* 2007; **157**: 670–673.

89 Chowdhary A, Randhawa HS, Sharma S, *et al.* *Malassezia furfur* in a case of onychomycosis: colonizer or etiologic agent? *Med Mycol* 2005; **43**: 87–90.
90 Silva V, Moreno GA, Zaror L, *et al.* Isolation of *Malassezia furfur* from patients with onychomycosis. *J Med Vet Mycol* 1997; **35**: 73–74.
91 Tamraz H, Raffoul M, Kurban M, *et al.* Confluent and reticulated papillomatosis: clinical and histopathological study of 10 cases from Lebanon. *J Eur Acad Dermatol Venereol* 2013; **27**: 119–123.
92 Numata S, Akamatsu H, Akaza N, *et al.* Analysis of facial skin-resident microbiota in Japanese acne patients. *Dermatology* 2014; **228**: 86–92.
93 Cafarchia C, Gasser RB, Figueredo LA, *et al.* Advances in the identification of *Malassezia*. *Mol Cell Probes* 2011; **25**: 1–7.
94 Lecerf P, Hay R. A new approach to the diagnosis and study of *Malassezia* infections. *Br J Dermatol* 2014; **170**: 234.
95 Gupta AK, Kohli Y, Li A, *et al.* *In vitro* susceptibility of the seven *Malassezia* species to ketoconazole, voriconazole, itraconazole and terbinafine. *Br J Dermatol* 2000; **142**: 758–765.
96 Rojas FD, Sosa Mde L, Fernández MS, *et al.* Antifungal susceptibility of *Malassezia furfur*, *Malassezia sympodialis*, and *Malassezia globosa* to azole drugs and amphotericin B evaluated using a broth microdilution method. *Med Mycol* 2014; **52**: 641–646.
97 Hammer KA, Carson CF, Riley TV. *In vitro* activities of ketoconazole, econazole, miconazole, and *Melaleuca alternifolia* (tea tree) oil against *Malassezia* species. *Antimicrob Agents Chemother* 2000; **44**: 467–469.
98 Murai T, Nakamura Y, Kano R, *et al.* Susceptibility testing of *Malassezia pachydermatis* using the urea broth microdilution method. *Mycoses* 2002; **45**: 84–87.
99 Garau M, Pereiro M Jr, del Palacio A. *In vitro* susceptibilities of *Malassezia* species to a new triazole, albaconazole (UR-9825), and other antifungal compounds. *Antimicrob Agents Chemother* 2003; **47**: 2342–2344.
100 Velegraki A, Alexopoulos EC, Kritikou S, *et al.* Use of fatty acid RPMI 1640 media for testing susceptibilities of eight *Malassezia* species to the new triazole posaconazole and to six established antifungal agents by a modified NCCLS M27-A2 microdilution method and Etest. *J Clin Microbiol* 2004; **42**: 3589–3593.
101 Cafarchia C, Figueredo LA, Iatta R, *et al.* *In vitro* evaluation of *Malassezia pachydermatis* susceptibility to azole compounds using E-test and CLSI microdilution methods. *Med Mycol* 2012; **50**: 795–801.

