Ecological dynamics of *Malassezia* in the hair follicle homeostasis, dysbiosis, and disease

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Abstract:

The hair follicle serves as the foundation of a complex ecological system within the skin microbiome. Among its inhabitants, fungi contribute to maintaining a healthy microenvironment, helping prevent infections caused by pathogenic organisms such as keratinophilic fungi. However, excessive fungal growth can itself lead to inflammatory diseases. *Malassezia* is a lipophilic yeast that resides as a commensal organism within the hair follicle under homeostatic conditions. Its overgrowth is associated not only with a wide range of cutaneous disorders but has also been implicated in tumor progression and cancer onset. This review explores the multifaceted roles of *Malassezia*, including its colonization patterns, ecological niches, and disease associations. Given its dual nature—both protective and pathogenic—further research is needed to clarify its functions and to inform the development of targeted therapies for *Malassezia*-associated skin and hair disorders.

Keywords: Hair follicle, Fungi, *Malassezia* spp., Infection, Scalp microbiome

Introduction:

The skin is the largest organ of the human body. The skin surface, hair follicles, and sweat glands are inhabited by numerous bacterial, fungal, and mite microorganisms that constitute a complex ecosystem [1–3]. These microbial communities constitute a microbial barrier that, together with the host's epidermal barrier, maintains the homeostasis of our skin immune system [4,5]. And the scalp, as a specialized region of the skin, provides a unique environment for these microorganisms with its abundant follicular and sebaceous gland units [6,2,7].

An imbalance within the skin microbiome, known as dysbiosis, has been associated with a number of inflammatory skin diseases, including atopic dermatitis, acne, and psoriasis [1,2,7]. Fourteen well-established species of *Malassezia* and four additional species have been identified to date. Out of the 18 species, 10 species (*M. restricta, M. globosa, M. arunalokei, M. sympodialis, M. dermatis, M. slooffiae, M. furfur, M. obtusa, M. japonica, and M. yamatoensis*), were isolated mainly from human skin, whereas the others are normally isolated from animal skin [8]. In these skin disorders, *Malassezia* spp., similar to other commensal organisms, such as *Staphylococcus* spp. and *Propionibacterium acnes*, have gained increasing attention for their complex and sometimes contradictory roles [1,7]. Lipophilic *Malassezia* spp. are widely found on human skin and hair. Because they lack the ability to synthesize their own fatty acids, these organisms must rely on external sources for survival. Long-chain unsaturated fatty acids derived from sebum lipids, including triglycerides, wax esters, squalene, and free fatty acids, serve as their primary substrates [10–13] . Numerous human microbiome studies have identified *Malassezia* as the dominant component of the skin microbiome eukaryome across the majority of human sites [1,2,5,7,9]. Recent studies has increasingly focused on the mechanisms of action of *Malassezia* spp. in various skin diseases and its interaction with the host immune system [1–3,10]. Although *Malassezia* spp. are widely present on the human scalp and generally considered as commensals [1–3,5,7], certain physiological changes can disturb this balance. For example, during puberty, fluctuating hormone levels increased sebum secretion; because *Malassezia* depends on fatty acids for growth, this lipid-rich environment can promote abnormal proliferation or disrupt the microbial community structure. Such dysbiosis has been linked to a series of skin conditions, many of which directly or indirectly affect hair health [7,11–14] .

However, whether *Malassezia* truly constitutes an “enemy” or is simply an integral component of normal skin symbiosis remains a matter of debate [1]. Some argue that even low levels of *Malassezia* found in healthy individuals may carry potential, whereas others emphasize that clinical manifestations arise only when there is a disturbance in the local microenvironment [1,14]. Moverover, the intricate interactions between *Malassezia* and other members of microbiome, and the host immune system further blur the distinction between “friend” and “foe” [1–4,14,15]. Given these unresolved questions, this review aims to examine the complex and dynamic relationship between *Malassezia* and the hair follicle system, including

from its colonization pattern in the hair follicle system, dominant ecological niches, associated diseases, and paradoxical roles. Through a synthesis of current literature, we highlight the gaps in knowledge that must be addressed to clarify *Malassezia*'s dual nature and its implications for hair and skin health.

1. Fungi in hair follicle

The hair follicle system provides a unique and highly specialized environment for microbial community in the skin. Beyond anchoring the hair bulb, the deep tubular structure of the follicle extends into the dermis and associated with other accessory structures such as sebaceous glands, which produces sebum to lubricate the hair, and arrector pili muscle [16]. The different anatomical regions of the hair follicle exhibit distinct microenvironments and immune characteristics. The infundibulum (funnel part of the hair follicle) is the upper opening of the hair follicle that communicates directly with the skin surface and serves as the primary site of microbial colonization [17–19].

The traditional view is that the bulb and bulge are relatively sterile, immune-privileged region essential for maintaining the hair growth cycle [2,3]. However, recent studies have challenged this assumption. Analyses of plucked hair follicles have detected microbial DNA and antimicrobial peptides below the infundiblum, suggesting that microorganisms or their components may penetrate deeper into the follicle than previously thought. These interactions with the local immune system may influence both the hair growth cycle and follicle health [20]. Fungi that colonize or infect the skin surface and hair follicles [5] can be divided into two groups based on their substrate preferences and morphology: keratinophilic fungi (Dermatophytes) and yeasts, with *Malassezia* being an important representative [21].

Dermatophytes including *Microsporum*, *Trichophyton*, and *Epidermophyton* utilize keratin as a nutrient source and are the leading cause of tinea infections of the skin, hair, and nails [22–27]. Dermatophyte genera exhibit distinct scalp colonization tropism. *Microsporum* and *Trichophyton* species penetrate the hair follicle outer root sheath and invade the hair shaft (endothrix or ectothrix pattern), which defines tinea capitis. In contrast, *Epidermophyton* floccosum lacks the ability to invade hair follicles or shafts and is exclusively restricted to the stratum corneum of the scalp epidermis, and does not cause tinea capitis. All three genera colonize only keratinized structures and do not invade the deep follicular matrix or dermis [28–30]. The local host immune response is essential for clearing these infections but may also contribute to inflammation and tissue damage [31,22]. In contrast, yeast such as *Candida* spp. generally do not colonize hair follicles [32–34]. Although typically considered commensals inhabiting mucosal surfaces—including the oral cavity, intestines, and vagina—*Candida* can invade mucosal sites and skin folds when host immunity is compromised or the skin barrier is disrupted, causing candidiasis [35–37]. when host immunity is compromised or the skin barrier is disrupted, *Candida* spp. Notably, several case reports have documented that

Candida spp. can also involve hair follicles in regions such as the scalp, mustache and beard areas, trunk, and pubic region, leading to pustular or papular eruptions and the rare condition known as candidal folliculitis [38,39].

In contrast to keratin-avid fungi, lipophilic *Malassezia* colonize areas rich in sebaceous glands, such as the scalp, face, and upper trunk [40–44]. *Malassezia* is the most common fungal genus on the scalp, and its level of colonization is influenced by a variety of factors, including age, sex, geographic location, hygiene practices, and host physiology [45–48]. Its presence in these sebum rich area has been associated with variety of skin disorders, including dandruff, seborrheic dermatitis, pityriasis versicolor, and *Malassezia* folliculitis [7,9,13,24,44]. In those disorders directly affecting scalp and follicular health sometimes lead to hair loss [7,12,49].

Unlike dermatophytes, which are highly prevalent in prepubertal children, *Malassezia* dominates the adult scalp microbiome [45,50]. This shift is closely linked to the maturation of sebaceous glands and increased sebum secretion during puberty, which provides *Malassezia* with lipid-rich substrates that promote its growth and colonization [51]. As a major member of the scalp microbial community [7,17,51], alterations in both the abundance and species composition of *Malassezia* are associated with multiple scalp disorders [1,7,14]. The most common *Malassezia* species on the healthy adult scalp are *M. globosa* and *M. restricta*, typically present in yeast form [52,14,47,48]. However, the relative abundance of dominant species varies across populations and studies. For example, in an Indian cohort, *M. globosa* predominated in healthy controls, whereas *M. restricta* was more frequently detected in patients with seborrheic dermatitis or dandruff [48]. Similarly, an Ethiopian study identified *M. globosa*, *M. furfur*, and *M. restricta* as the main species in dandruff patients [47]. These findings suggest that different *Malassezia* species may play distinct roles in scalp health and disease, or that shifts in their relative abundance may reflect dysbiosis in the scalp microecology [52,14,47,48,53]. Taken together, fungi are an important component of the hair follicle microenvironment, and inflammatory disorders arising from overgrowth or ecological imbalance of yeasts such as *Malassezia* reflect a complex dialogue between microbes and the host immune system that ultimately influences hair health and disease.

2. *Malassezia* in hair follicle

2.1 Dominant ecological niches of *Malassezia* spp.

The scalp is one of the most sebaceous gland-rich regions of the body, secreting large amounts of sebum [52,45,46,54,55], which creates an ideal environment for the survival of *Malassezia* and makes it the predominant fungal inhabitant of healthy adult scalps [45,46,14]. Hair follicles—particularly the infundibulum, where the follicle connects to the sebaceous gland—further support *Malassezia* growth. Sebum drains into the follicular lumen and lubricates both the hair shaft and the skin

surface [2,3]. This region is not only rich in the fatty acids required by *Malassezia*, but also relatively moist, forming a favorable microenvironment for its proliferation. Studies have shown that *Malassezia* colonizes mainly in the funnel part of the hair follicle [2,56]. However, the detection of bacteria and their products deeper within the follicular structure [20] suggests that *Malassezia* or its metabolites may also penetrate beyond the infundibulum—an area of follicular biology that has likely been underestimated.

Hair follicles not only serve as a nutrient supply site for *Malassezia* but also provide a protective physical niche. *Malassezia* tends to aggregate within the funnel region of the follicle, where it forms biofilm-like structure [15]. These biofilms enhance microbial resistance, making the organisms more difficult to eliminate, and may facilitate their adhesion to and interaction with host cells [10,15]. The characteristics of the hair follicle microenvironment—including abundant lipids, a relatively anaerobic milieu in the deeper follicular compartments, and a unique immunological profile in the bulb and bulge regions [2,3], —together establish a dominant ecological niche for *Malassezia* within the follicular system.

Malassezia species composition differs significantly between the human scalp epidermis and hair follicles. The scalp surface is characterized by a mixed community dominated by *M. globosa* and *M. sympodialis*, with moderate fungal diversity. In contrast, hair follicles harbor a less diverse, specialized mycobiome where *M. restricta* is strongly enriched. *M. globosa* is present but less dominant in follicles, while *M. sympodialis* is scarce or absent in the hair follicles compartment. This spatial partitioning reflects niche adaptation: *M. restricta* is specialized for the sebaceous follicle environment, whereas *M. sympodialis* is restricted to the stratum corneum [57–59].

However, this seemingly stable symbiotic relationship is inherently dynamic and regulated by a combination of factors, including the host's physiological status, local microenvironmental parameters, as well as interactions with other commensal microorganisms. Perturbations in any of these factors can induce alterations in the abundance, species composition, or metabolic activity of *Malassezia*, thereby disrupting the microbial homeostasis and potentially predisposing the host to related diseases.

It is worth noting that different *Malassezia* species vary in their fatty acid requirements, spatial distribution on the scalp, and association with disease [14,52, 57,60-62,47,48]. The interactions with the host immune system may further influence their relative abundance across different scalp microenvironments or pathological states [52,53]. Although all *Malassezia* species depend on external lipids due to incomplete fatty acid synthesis pathways, their lipid utilization capacities differ. For example, *M. globosa* secretes a broader range of lipases and phospholipases than *M. restricta*, enabling it to proliferate extensively in sebum-rich environments and efficiently hydrolyze complex skin lipids. In contrast, *M. restricta* shows a stronger preference for simple lipids and contains fewer lipase genes;

nevertheless, it can dominate in certain scalp niches, potentially reflecting its metabolic specialization and reduced competitive pressure [63,64]. These metabolic and ecological differences help explain why specific *Malassezia* species preferentially dominate distinct regions of the human body.

Furthermore, different *Malassezia* species vary in their ability to activate keratinocytes and immune cells [61, 68–82] . For example, *M. globosa* tends to induce a stronger pro-inflammatory response due to its enzyme secretion and cell wall components. The expression of *Malassezia* allergens, such as Mala s 1, Mala s 6 and Mala s 11, also differs among various species, which may exert different effects on atopic dermatitis and other allergic reactions [66,68,70]. Key species-specific features of *Malassezia* species are summarized in **Table 1**.

Genotypic differences in specific *Malassezia* spp. or strains may also influence their colonization and pathogenicity. *M. restricta* with specific short sequence repeat (SSR) genotypes were more abundant on the scalp of patients with androgenetic alopecia (AGA), suggesting there may be a link between these genotypes with the onset or exacerbation of AGA [53,52,72]. Understanding these variations helps explain their role in related diseases [74,76,78].

2.2 *Malassezia*-related diseases

Malassezia is associated with a variety of skin diseases, many of which directly or indirectly affect the hair follicle system. The development of these diseases is usually associated with an abnormal increase in the population of *Malassezia*, dysbiosis, and an abnormal immune response of the host to *Malassezia* and its metabolites [1,7,11,12,14]. The most common *Malassezia*-associated diseases are dandruff and seborrheic dermatitis (SD) [7,12,14,47,48].

2.2.1 Seborrheic dermatitis

Seborrheic dermatitis presents clinically with erythema and greasy scales on sebaceous gland-rich areas of the scalp, face, and chest [12]. While *Malassezia* is a normal inhabitant of a healthy scalp, typically exhibit a significant increase in *Malassezia* load and alterations in species composition; in particular, *M. restricta* has been strongly associated with these conditions [14,48]. By hydrolyzing sebum lipids through secreted lipases, *Malassezia* releases free fatty acids—especially oleic acid—that can irritate keratinocytes, leading to inflammation and abnormal desquamation of the stratum corneum [10,80]. In addition, *Malassezia* induces the production of inflammatory cytokines in the host, further exacerbating the inflammatory process [80]. Chronic or severe dandruff and seborrheic dermatitis may result in itching, discomfort, and impairment of follicular function, which can be associated with hair shedding and reduced hair growth [12,48].

Antifungal therapies targeting *Malassezia*, such as ketoconazole-containing shampoos, are widely used and are generally effective in reducing symptoms [80,82,84]. Several natural extracts have also demonstrated inhibitory activity against *Malassezia* and have shown potential to improve scalp health and support

hair growth [12,80,86,88]. Increased hair shedding has been documented in individuals with dandruff, and moderate to severe dandruff is strongly correlated with hair loss and pruritus[48]. Therefore, controlling *Malassezia* overgrowth and inflammation in dandruff and seborrheic dermatitis is essential for maintaining scalp and hair health [7,12,84,54]**.**

2.2.2 Malassezia folliculitis

Malassezia folliculitis (MF) is an inflammatory disease caused by direct invasion of hair follicles by *Malassezia*[10,13,56]. Clinically, MF often presents as red papules and pustules on the chest, back, neck, and even face, and is easily confused with acne [10,13]. Diagnosis of MF requires the detection of large numbers of *Malassezia* yeast cells within the hair follicles by microscopic examination or histopathologic examination [10,13]. Studies indicate that the *Malassezia* species implicated in MF are typically resident skin commensals rather than invasive exogenous organisms [14]. This suggests that MF results from excessive proliferation of resident yeasts under specific conditions, followed by follicular invasion.

MF has significant differences in pathogenic species composition, including spatial, regional, and disease-specific variations. Spatially, hair follicle lesions mainly harbor *M. restricta, M. globosa,* and *M. sympodialis* [90]. Regionally, dominant species vary: *M. restricta* is prevalent in Japan and *M. globosa* in Turkey [92,94].

Although MF is primarily characterized by inflammation of the hair follicle, recurrent or chronic inflammation may exert long-term effects on follicular health. However, whether MF directly leads to irreversible hair loss remains unclear and requires further investigation.

2.2.3 Androgenetic alopecia

In addition to its direct involvement in the disorders discussed above, *Malassezia* has also been implicated in alopecia-related conditions. Androgenetic alopecia (AGA) is the most common form of hair loss and has a multifactorial pathogenesis involving genetic predisposition, androgen metabolism, and chronic follicular microinflammation [52,96,97]. *Malassezia* exhibits distinct spatial colonization patterns in the scalp of patients with AGA. It predominantly colonizes the scalp stratum corneum and preferentially accumulates in the infundibular region of hair follicles, rather than invading deep follicular compartments or the dermis. Significantly higher fungal loads and enrichment of *M. restricta* are observed in the vertex and frontal balding areas compared with the occipital non-balding scalp. This topographical distribution is closely associated with regional differences in sebaceous gland activity and sebum production [52,53,96]. Moreover, alterations in sebum composition have been described in AGA, such as elevated levels of triglycerides and palmitic acid—lipid substrates that *M. restricta* can efficiently utilize [52]. These changes may create a microenvironment more favorable to the

proliferation of particular *Malassezia* species.

Collectively, *Malassezia* may contribute to the onset or progression of AGA by modulating the lipid milieu of the follicular microenvironment or triggering local inflammatory responses [52,96,98]. Clinical observations provide indirect support for this hypothesis: shampoos containing ketoconazole have shown therapeutic benefit in AGA [99,84], and formulations containing caffeine and adenosine have been found to reduce *Malassezia* abundance and alter lipid fractions while improving hair loss [98].

2.2.4 Pityriasis versicolor

The typical clinical manifestation of pityriasis versicolor (PV) is the appearance of pigment-altered patches on the skin surface. The mycelial phase of *Malassezia* spp. is consistently detected within the lesions, making it the key causative agent of the disease [100]. From PV lesions, the most frequently isolated species was *M. furfur*, followed by *M. globosa* [101]. Regional differences are obvious: *M. globosa* is dominant in temperate regions, while *M. furfur* and *M. sympodialis* are more prevalent in hot and humid areas [102]. In addition, the species distribution of PV differs from that of healthy skin, *M. globosa* accounts of PV lesions, significantly higher than that in healthy individuals, while *M. sympodialis* is the dominant species on healthy skin [103]. Although PV primarily presents with pigmentary changes, one study reported that areas affected by PV may also show hair loss or thinning. Histopathological examination revealed features such as follicular degeneration, miniaturization, and atrophy, which appeared to be directly or indirectly related to the presence of *Malassezia* within hair follicles or in the stratum corneum [49]. These observations suggest that inflammation and metabolic products generated by *Malassezia* may exert toxic or inhibitory effects on hair follicles, potentially impairing normal hair growth.

2.2.5 Atopic dermatitis

Atopic dermatitis (AD) is a chronic recurrent inflammatory skin disease characterized by severe pruritus and skin barrier dysfunction. As a lipophilic commensal yeast on the skin, *Malassezia* mainly acts as an exacerbating factor in its pathogenesis, amplifying inflammation and accelerating disease progression. *Malassezia* is the most abundant fungal component in the skin mycobiome of both AD patients and healthy individuals, but significant differences exist in its species composition, abundance, and interaction with the host, which are closely related to the occurrence, development and severity of AD [104,105] .

There are regional and population differences in the pathogenic *Malassezia* species associated with AD, but the dominant species are relatively consistent globally: *M. globosa* and *M. restricta* are the most common, detected in approximately 90% of AD cases; *M. furfur* and *M. sympodialis* are the next, detected in about 40% of patients. The diversity of *Malassezia* species in AD patients is significantly higher than that in healthy individuals, and specific

genotypes of *M. globosa* are associated with AD exacerbation [106]. The positive rate of Malassezia-specific IgE in patients with head and neck AD is as high as 79.3%, further confirming the association between them [107].

The pathogenic mechanisms of *Malassezia* in AD mainly involve skin barrier damage, immune disorders and virulence factor release, forming a vicious cycle: it overproliferates by taking advantage of the damaged skin barrier in AD patients, and its metabolites further damage the barrier; it activates innate and adaptive immunity through Toll-like receptors, driving Th1/Th2/Th17 imbalance to amplify inflammation and pruritus; it secretes virulence factors such as lipases and phospholipases to aggravate skin damage, and can form biofilms to enhance drug resistance, promoting chronic recurrence of AD [105,108,109] .

2.2.6 Primary cicatricial alopecia

The relationship between *Malassezia* and hair disorders is not clear in some cases. A study of primary cicatricial alopecia including lichen planopilaris (LPP), fibrosing alopecia in a pattern distribution (FAPD), and frontal fibrosing alopecia (FFA) has shown that *Malassezia* and hair diseases are not always correlated. While *Malassezia* yeast was rarely detected on histopathologic examination in the lesions of FFA and FAPD, yeast cells were more abundant in seborrheic dermatitis-associated female pattern hair loss (FPHL) [110]. One of the characteristics of scarring alopecia is inflammation and fibrosis around the hair follicle (especially the funnel/isthmus) that will lead to sebaceous gland loss[111,112]. The researchers hypothesized that the absence of sebaceous glands may result in a local environment that is unsuitable for the survival of lipophilic *Malassezia*, and the absence of *Malassezia* thus could be a histological clue to scarring alopecia [110]. This finding highlights another perspective of the close association of *Malassezia* with the sebaceous gland and non-scarring follicular environment, where its presence may reflect the relative structural integrity of the hair follicle, i.e., *Malassezia* is unable to survive in an environment of severely damaged hair follicles and atrophied sebaceous glands. Its absence may be associated with follicular disruption and scarring.

In summary, *Malassezia* is closely associated with a wide spectrum of conditions involving the hair follicle system—from common seborrheic dermatitis, to *Malassezia* folliculitis, which directly affects hair follicles, to androgenetic alopecia, where it may act as a contributing factor. Moreover, its absence has been noted as a potential diagnostic clue in certain cases of scarring alopecia. Together, these diverse disease associations reflect the complex role of *Malassezia* within the hair follicle ecosystem, functioning either as a direct pathogen or as an indirect modulator by altering the local microenvironment or interacting synergistically with other factors.

2.3 Possible pathogenic mechanisms of *Malassezia* affecting hair follicle cycle

Malassezia cell wall components, such as β-glucans and mannans, are recognized by

scalp keratinocytes and follicular immune cells via pattern recognition receptors, especially Toll-like receptors (TLR2, TLR4) and C-type lectin receptors (Dectin-1). This triggers downstream NF-κB signaling, leading to the transcription of pro-inflammatory cytokines and CXCL8, that may inhibit the Wnt/β-catenin pathway, resulting in local inflammation and disruption of hair cycle homeostasis[113–115]. Furthermore, *Malassezia* secretes a variety of lipases and phospholipases, hydrolyzing host sebum triglycerides and phospholipids into free fatty acids. Certain byproducts can damage follicular keratinocytes, compromise barrier function, and activate inflammatory pathways. Altered lipid profiles also influence the microbiome and hair follicle stem cell niche[62]. *Malassezia* produces allergens that are processed by antigen-presenting cells and presented to T cells. These allergens induce Th2-skewed immune responses, contributing to atopic micro-inflammation and peri-follicular immune cell infiltration, which can disturb normal hair follicle cycling and promote telogen effluvium [113,40,116,117]. *Malassezia* forms biofilm structures on the scalp epithelial surface. Biofilm matrix protects yeast cells from antifungals and host immunity. Quorum sensing molecules may modulate gene expression in *Malassezia*, enhancing persistence and chronic inflammation which prolongs the telogen phase [118–120]. During its metabolic process, *Malassezia* generates reactive oxygen species (ROS), including superoxide and hydrogen peroxide. Excessive ROS can damage hair follicle stem cells and keratinocytes, and also promote the transition of hair follicles from the anagen phase to the catagen phase by activating the ASK1-MAPK pathway.[121–123]. In addition, *Malassezia* can outcompete beneficial scalp bacteria, leading to dysbiosis. This imbalance impairs local immune tolerance, upregulates follicular stress signals, and can indirectly affect stem cell quiescence and hair cycle progression [62,124,125].

3. Friend or foe? The paradoxical role of *Malassezia*

The relationship between *Malassezia* and the hair follicle system cannot be simply defined as beneficial or harmful. Rather, it represents a complex and dynamic equilibrium that depends heavily on the surrounding microenvironment and the host's physiological state. As mentioned earlier, *Malassezia* is the predominant commensal fungus on the scalp of healthy adults, and its presence alone does not imply disease [10,11,13]. once this equilibrium is disrupted, the same commensal organism can transition into an opportunistic pathogen capable of driving a spectrum of inflammatory conditions. It is precisely this dual identity—commensal under homeostasis yet pathogenic under dysbiosis—that reflects the paradoxical role of *Malassezia* within the hair follicle system, as illustrated in **Figure 1**.

3.1 An important component of the microbial barrier

Malassezia is a symbiotic microorganism that constitutes a normal component of the healthy skin microbiome [1–3,5,14]. In a healthy microecological balance, *Malassezia* coexists peacefully with the host as well as with other microorganisms,

and may be involved in the maintenance of skin homeostasis in a variety of ways. For example, the skin microbiome is thought to be in constant dialog with the host immune system, helping to regulate local immune responses and prevent pathogen invasion [109–112]. Its presence may act as a barrier by occupying ecological niches and competing for nutrients and space with other potential pathogens, such as certain bacteria or exotic fungi. For example, dominant colonization by *Malassezia* may be associated with the relative rarity of adult tinea capitis, although the exact mechanisms are not fully understood [23]. Although direct evidence suggests that the mechanism by which *Malassezia* is beneficial to the hair follicle system in a healthy state is unclear, its presence as a dominant bacterial population in itself constitutes part of the microecological balance. Several studies have suggested that healthy bacterial communities may maintain scalp health by synthesizing and metabolizing nutrients that are essential for hair growth, and that *Malassezia*, as a dominant member of the fungal group, may also be involved in some way in, or influence, the cycling or availability of such nutrients [14,14,126]. In addition, innate immune molecules such as antimicrobial peptides produced by the skin help to control microbial populations and maintain a symbiotic state [4,20,127,128]. *Malassezia,* as a commensal yeast, may have adapted to this immune environment and found survival strategies within it.

3.2 Inflammation inducer

However, when changes occur in the microenvironment, the quantity or community structure of *Malassezia* may become imbalanced, shifting from a commensal state to a pathogenic state. Factors such as increased sebum secretion, alterations in the host's immune function, and changes in other microbial communities can disrupt this balance(16,114,115). Consequently, interactions with bacteria may drive the transition to pathogenicity or exacerbate host inflammation [70,131].

Malassezia can sense environmental signals such as skin lipids, temperature, and host immune factors, and regulate gene expression accordingly. Transcriptomic studies have shown that during skin colonization and inflammation, *Malassezia* upregulates the expression of genes related to lipid metabolism, stress response, and immune evasion [132–136,40]. Meanwhile, some *Malassezia* species not only inhibit the production of inflammatory cytokines, including IL-8 and TNF-α but also induce the production of IL-10, thereby promoting regulatory T-cell responses and maintaining their commensal state [137,130,138]. In atopic individuals, however, *Malassezia* allergens can drive Th2-skewed immune responses and exacerbate chronic inflammation. *Malassezia* produces a variety of allergens, which can trigger IgE-mediated hypersensitivity reactions, particularly playing a role in atopic dermatitis [64,68,135].

Malassezia possesses a thick, lipid-rich cell wall and a biofilm matrix. This structure not only masks pathogen-associated molecular patterns (PAMPs) to reduce recognition by pattern recognition receptors but also protects *Malassezia* from

phagocytosis and antifungal drugs[40]. Furthermore, some *Malassezia* species, such as *M. furfur*can form biofilms on the skin surface and indwelling medical devices, enhancing their resistance to antifungal drugs and host defense mechanisms[8]. Additionally, heat shock proteins (HSPs) are upregulated under host temperature and immune stress, helping *Malassezia* survive—all of which undoubtedly enhance the invasive capacity of *Malassezia* [139].

In seborrheic dermatitis, increased *Malassezia* populations and dysbiosis lead to inflammation and flaking [12,14,47,140]. Lipases, phospholipases, and metabolites produced by *Malassezia* are considered to be major virulence factors that activate the host immune response and induce an inflammatory cascade [11,12,14]. *Malassezia* may also produce oxidative stressors that negatively affect scalp and hair health and even lead to premature hair loss [54]. In MF, *Malassezia* invades the hair follicle directly, causing inflammation and destruction of the follicle [56,141]. In PV-associated hair loss, the presence of *Malassezia* has also been associated with pathologic changes in the hair follicle [49]. Some studies have also suggested that *Malassezia* may be involved in androgenetic alopecia and PV-associated alopecia by inducing microinflammation around the hair follicle [52,49,96,98], but whether it is a direct or secondary cause of AGA still needs to be investigated in depth.

Animal models are crucial for understanding the pathogenic mechanisms, host responses, and therapeutic targets of fungal infections affecting hair. Several studies have attempted to explore the potential pathogenic mechanisms of *Malassezia* by establishing animal models of fungal infection.

Since dogs are naturally susceptible to *Malassezia* dermatitis—often presenting with greasy skin, desquamation, and patchy alopecia—stable induction of hair and skin lesions can be achieved by promoting the over proliferation of *Malassezia* , through inoculation or antibiotic-induced microbial dysbiosis [142]. In some studies, mild dermatitis, hyperkeratosis, and alopecia were induced in model mice via topical application or intradermal injection of *Malassezia*. It was found that the severity of skin lesions usually depends on the host's immune status and skin lipid content [136]. In immunosuppressed or genetically modified mice, those lacking the IL-17 signaling pathway, more severe symptoms of dermatitis, alopecia, and folliculitis were observed. Th17-driven inflammation plays a key role in controlling the over proliferation of *Malassezia* and infections associated with hair-related lesions; defects in Th17 function lead to more severe alopecia [144].Animal studies have shown that topical or systemic azole drugs, especially ketoconazole, can restore hair growth and reduce yeast load[146].Findings from animal models require cautious extrapolation to human disease.

Therefore, *Malassezia* may invade or tightly attach to hair follicles, causing local inflammation and abnormalities in the hair growth cycle. Additionally, it may alter the follicular microenvironment through enzyme activity, leading to hair shaft damage or shedding [136,144,148–151].

3.3 Paradoxical role of *Malassezia* within scalp microbiome

The paradoxical role of *Malassezia* can be reflected in its interactions with other microorganisms. The scalp microbiome is a complex community of multiple species and bacterial communities [137–139]. There are complex interactions between *Malassezia* and scalp bacteria, such as *Cutibacterium acnes* and *Staphylococcus epidermidis* that can be competitive or synergistic, and that collectively affect the balance of scalp microecology and host health [7,14,15,23,98,128]. For example, one study found that heat-inactivated *Lactobacillus paracasei* could co-aggregate with *M. furfur*, inhibit its biofilm formation, and modulate the scalp microbiome by increasing *M. globosa* abundance while decreasing *M. restricta* and *C. acnes* abundance, resulting in improved scalp health and hair growth [15]. Another study showed that a synthetic sandalwood-like odorant altered the hair follicle microbiome by activating olfactory receptors in the hair follicle and upregulating the expression of antimicrobial peptides, which favored the growth of *S. epidermidis* and *M. restricta* while inhibiting *S. aureus*, *M. globosa*, and *C. acnes*, suggesting that hosts can modulate the microbiome [128]. These studies suggest that the interactions between *S. marcescens* and other microorganisms as well as the host are dynamic and complex, and that its role in the hair follicle system depends on the state of the entire microcosm.

Studies have found significant differences in the structure of both bacterial and fungal communities between healthy and dandruff scalps, suggesting that an overall dysbiosis of the flora rather than alterations in a single microorganism is key to the disease [140,141] . The host immune system also plays a key role in maintaining this balance. Skin keratinocytes and immune cells recognize microbial components and produce antimicrobial peptides (AMPs) and inflammatory mediators that regulate the local microenvironment and microbial growth [142–144]. A study showed that the synthesis of sandalwood-like odorants could upregulate the expression of the anti-microbial peptide DCD by activating the olfactory receptor OR2AT4 in hair follicles, thereby affecting the follicular microbial community and favoring the growth of *S. epidermidis* and *M. restricta*, while inhibiting *S. aureus* and *M. globosa* and *C. acnes* [128]. This suggests that the host can actively shape the hair follicle microecology, including through the modulation of AMPs, to maintain a microbial composition conducive to health, including the relative abundance of specific *Malassezia* spp.

The choice of treatment strategy also reflects the paradoxical nature of the role of *Malassezia*. Treatments targeting *Malassezia* overgrowth can be effective in controlling dandruff and seborrheic dermatitis, improving scalp health and indirectly benefiting hair [154–156]. However, excessive or inappropriate antifungal treatments may disrupt the microecological balance of the scalp and generate drug resistance, instead creating new problems [157–159]. With growing concerns about drug resistance to traditional antifungal agents and increasing understanding of skin microecology, innovative therapeutic strategies have attracted widespread attention. Some novel therapeutic approaches—such as using probiotics/postbiotics or natural extracts to modulate the scalp microbiome, rather than simply

eliminating *Malassezia*—are showing potential[15,41,160,41,161,97,162].

Some novel therapies, such as the use of probiotics/postbiotics or natural extracts to modulate the scalp microbiome rather than simply killing *Malassezia*, are showing potential [15,80,86,88,98,128,140,163]. Prebiotics are substrates that selectively stimulate the growth and/or activity of beneficial skin microorganisms. By promoting the growth of commensal bacteria, prebiotics help maintain the balance of the skin microbiome and indirectly restrict the overproliferation of *Malassezia* [164–168]. Postbiotics refer to inactive bacterial products or metabolic by-products with health benefits, including short-chain fatty acids (SCFAs), bacteriocins, and other metabolites. Postbiotics can act through direct antifungal effects and/or modulating host immunity to reduce inflammation. [169,170,172,173,175,176]. In addition, approaches such as modulating sebum production and inhibiting biofilm formation also show potential and prospects for the future[178,180,182–188] . Major microbiome-targeted interventions are summarized in **Table 2**. It reflecting the recognition of *Malassezia* as a commensal, i.e., the goal is to restore homeostasis rather than to eliminate it completely.

It is worth noting that although the research field of microbial ecological intervention measures and alternative antifungal strategies targeting *Malassezia* has been explored, it still has obvious limitations in current clinical practice, and there is no sufficient basis to confirm its practical application value [189]. Currently, no topical probiotic preparation has been approved by regulatory authorities for the treatment of scalp fungal diseases. Ketoconazole remains first-line globally, with advanced delivery systems improving outcomes [84,155].

Furthermore, the absence of *Malassezia* in certain scarring alopecia lesions [110] is also worth pondering. This suggests that the presence of *Malassezia* is associated with a healthy follicular environment with an intact sebaceous gland structure. Its absence may not be the cause, but rather a consequence of the destruction of the hair follicle and the loss of sebaceous glands. However, this in turn suggests that a healthy follicular microenvironment may be required for normal colonization of *Malassezia* and that its presence itself is part of this healthy environment.

In summary, the role of *Malassezia* in the hair follicle system is paradoxical. While it constitutes an integral component of the healthy scalp microecology and may contribute to maintaining homeostasis, it can also shift into a pathogenic state under disrupted conditions, triggering inflammation, disease, and potentially impairing hair health. The outcome of its presence depends on multiple interacting factors, including the host's genetic background, immune status, sebum composition, coexisting microbiota, and the specific species or strain characteristics of *Malassezia* itself. Thus, categorizing *Malassezia* simply as either an enemy or a friend is overly reductive; rather, it exists in a complex, dynamic, and context-dependent relationship with the hair follicle system. Recognizing this ambivalent nature is essential for designing more precise and effective therapeutic strategies for hair and scalp disorders.

4. Current unresolved issues and prospects for the future

Despite substantial progress in understanding the relationship between *Malassezia* and the hair follicle system, several fundamental questions remain unanswered and require further investigation. Key unresolved issues include: (1) What triggers the transition of *Malassezia* from a commensal organism to a pathogenic state? (2) How do strain-specific genetic variations influence virulence, inflammatory potential, and disease associations? (3) To what extent does the shift toward the mycelial phase reflect pathogenic activity, and is this transition a reliable biomarker of disease severity? (4) How does the host hair follicle immune system interact with the local microbial community, and what signaling pathways mediate this crosstalk? (5) Does the presence of *Malassezia* or its metabolites in deeper follicular regions influence the hair growth cycle or follicular stem cell niche? (6) Can combined approaches—such as targeted microbiome modulation together with antifungal therapy—enhance treatment efficacy and reduce the risk of drug resistance?

5. Conclusion

Ultimately, a deeper understanding of the complex relationship between *Malassezia* and the hair follicle system will help develop more precise and effective diagnostic methods and therapeutic strategies. In the future, it is necessary to strengthen clinical observation and sample collection, and clarify the factors that trigger the transition of *Malassezia* from a commensal to a pathogenic state by combining in vivo and in vitro experiments; sequence clinically isolated strains, establish the correlation between genotypes and pathogenicity, and explore key virulence genes with the help of gene editing technology; analyze the interaction mechanism between host hair follicle immunity and local microbiota using multi-omics techniques and animal models; improve detection technologies and conduct clinical studies to evaluate the impact of *Malassezia* in the deep hair follicles on the hair growth cycle; design randomized controlled clinical trials to optimize the combined regimen of microecological intervention and traditional antifungal therapy.Thus, targeting species- or strain-specific pathways and integrating microbiome-based interventions represent promising avenues for future therapy.

Acknowledgment: Figure 1 was created using Figdraw (www.figdraw.com).

Source of funding: This work was supported in part by grants from the National Natural Science Foundation of China (NM 82272358).

Conflicts of interest: None declared.

Figure titles and legends: As a symbiotic microorganism, *Malassezia* is a normal component of the **healthy skin** microbiome **(A)**. Under the state of healthy microecological balance, *Malassezia* coexists harmoniously with the host and other microorganisms, and may participate in maintaining skin homeostasis through

various ways. *Malassezia* triggers the innate immune response by binding to Toll-like receptors (TLRs) on keratinocytes, leading to the secretion of antimicrobial peptides, which can quickly kill a variety of pathogenic microorganisms including fungi. Some *Malassezia* species not only inhibit the production of inflammatory cytokines, but also induce the generation of interleukin-10 (IL-10), thereby promoting regulatory T-cell responses and maintaining their own symbiotic state.

Malassezia can sense changes in environmental signals such as skin lipids, temperature, and host immune factors, leading to **pathogenesis (B)**. In this state, it exhibits an increase in quantity, conversion to the hyphal phase, and microbial dysbiosis. Byproducts generated during fatty acid metabolism—such as oleic acid, arachidonic acid, and indoles—are irritants that can promote the proliferation of keratinocytes and induce inflammation. Additionally, *Malassezia* produces a variety of allergens, which can trigger immunoglobulin E (IgE)-mediated hypersensitivity reactions.

Malassezia can form biofilm structures on the surface of scalp epithelium. The biofilm matrix protects yeast cells from the effects of antifungal drugs and clearance by the host immune system. *Malassezia* has a thick, lipid-rich cell wall and a biofilm matrix. This structure not only masks pathogen-associated molecular patterns (PAMPs) to reduce their recognition by pattern recognition receptors, but also protects *Malassezia* from phagocytosis and the impact of antifungal drugs, enhancing its ability to persistently colonize the scalp and trigger **chronic inflammation** (C). *Malassezia* may invade or tightly attach to hair follicles, causing local inflammation that may inhibit the Wnt/β-catenin pathway, leading to abnormalities in the hair growth cycle. It may also alter the hair follicle microenvironment through enzymatic activity, resulting in hair shaft damage or shedding. In addition, *Malassezia* produces reactive oxygen species (ROS); excessive ROS can damage hair follicle stem cells and keratinocytes, and also promote the transition of hair follicles from the anagen phase to the catagen phase by activating the ASK1-MAPK pathway

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