

REVIEW ARTICLE



# Role of cell membrane homeostasis in the pathogenicity of pathogenic filamentous fungi

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## ABSTRACT

The cell membrane forms a fundamental part of all living cells and participates in a variety of physiological processes, such as material exchange, stress response, cell recognition, signal transduction, cellular immunity, apoptosis, and pathogenicity. Here, we review the mechanisms and functions of the membrane structure (lipid components of the membrane and the biosynthesis of unsaturated fatty acids), membrane proteins (transmembrane proteins and proteins contributing to membrane curvature), transcriptional regulation, and cell wall components that influence the virulence and pathogenicity of filamentous fungi.

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## Introduction

The cell membrane not only determines the cell shape but also affects various cellular activities that are influenced by membrane homeostasis in terms of the structural and functional integrity and fluidity of the membrane [1,2]. Cell membranes are found in all living organisms [3] and are composed largely of lipids and proteins, with an amphiphilic lipid bilayer forming the overall framework of the membrane [4,5]. The cell membrane is responsible for both the physical and structural integrity of the cell [6].

Filamentous fungi undergo a complex development that includes conidial germination, polarized morphogenesis, and the differentiation of sexual and asexual structures [7,8]. The cell membrane represents a key barrier for resting conidia surviving in nature, and any damage to the membrane will lead to a loss of conidial viability [9]. Fungal cell membranes are responsible for the early recognition of nutrient availability, impending stress, or pathogen attack [10]. Although the mechanisms controlling cell membrane domains and the functional consequences of this organization, including membrane composition and the structure and functions of membrane components, have been reviewed in yeast [11], there has been little discussion of the role of cell membrane homeostasis in filamentous fungi. The overall influence of the morphology, integrity, permeability, and homeostasis of cell membranes on the growth and virulence of pathogenic filamentous fungi

has not been discussed and, to date, there is no review of how cell membrane homeostasis affects the pathogenicity of these fungi.

Here, we summarize the literatures on fungal cell membrane homeostasis and its roles in fungal pathogenicity by discussing the roles of the fungal transmembrane protein-lipid microdomains, cell wall-lipid microdomains, cytoskeleton-transmembrane protein microdomains, and membrane curvature.

## Effect of membrane structure on fungal pathogenicity

### Membrane lipid components and their biological roles

The rich and diverse lipid composition of the cell membrane affects the shape and structure of the membrane. There tends to be greater lipid diversity in eukaryotic membranes, indicating the complex role of membrane lipids in various cell functions [12]. Cell membrane lipids are usually arranged in bilayers and can participate directly in various cellular events as messengers or regulators of signal transduction [13,14]. Certain lipids, such as phosphatidylserine [15], phosphatidylcholine [16], ergosterol [17], C<sup>8</sup>-desaturated and C<sup>9</sup>-methylated glycosylceramide (GlcCer) [18], and ceramide [19] tend to accumulate in specific regions (domains) of the membrane forming membrane/lipid rafts (MLRs) [20], which

have evolutionarily conserved roles in the integrity and repair of the cell membrane.

Membrane lipids also play important roles in the regulation of asexual spore germination and mycelial growth. In *Pestalotiopsis microspora*, the absence of the *choC* or *choA* genes affects the conversion of phosphatidyl ethanolamine to phosphatidylcholine, which impedes the production of fungal spores or conidia and destroys the cell wall integrity [16]. Similarly, several choline precursors of membrane lipids also play important roles in the morphology of *Aspergillus nidulans* mycelia [21]. Ergosterol directly affects the growth and virulence of fungi and in treating fungal diseases caused by infection with *Aspergillus fumigatus* [17]. In *Aspergillus nidulans*, C<sup>8</sup>-desaturated and C<sup>9</sup>-methylated glycosylceramides (GlcCer), fungal-specific sphingolipids, influence both growth and virulence of the fungi [18]. Acyl-CoA-dependent ceramide synthetase (BarA) regulates cytoskeletal organization and mycelial morphogenesis by controlling ceramide synthesis to form specialized lipid microdomains [19]. In addition, some lipid-associated domains can recruit specific proteins regulating membrane-protein participation in important cellular functions such as signal transduction [13]. For example, spectrin, which forms filamentous networks on the cytoplasmic surface of the fungal cell membrane, participates in the structural integrity of the membrane and controls the lateral mobility of membrane proteins [22].

Membrane lipids also make important contributions to biological processes such as vegetative growth, morphological development, and host infection of pathogenic filamentous fungi [23,24]. Cell membrane homeostasis is not only closely related to membrane lipid but also depends on membrane proteins which thus modulate fungal pathogenicity. For example, the targeting of Scp2 by peroxisomes is essential for maintaining the virulent function of *Ustilago maydis*. Such conserved eukaryotic proteins can ensure the correct distribution of peroxisomes by fine-tuning the lipid composition of the membrane to maintain biotrophy during pathogen infection [25]. In *Magnaporthe oryzae*, *MoVps13* regulates fungal pathogenicity by contributing to impaired plasma membrane homeostasis through sphingolipid synthesis [26]. In addition, the lipid bilayer plays a central role in the physicochemical environment and shape of the membrane by influencing the arrangement and function of membrane proteins [27]. Lipids, especially membrane lipids, are important for the integrity of the cytoplasmic membrane. In addition, many fungal membrane lipid components, such as sphingolipids, ergosterol, and phospholipids, participate in signalling pathways,

which regulate the integrity of fungal cell walls [28]. Therefore, the lipid composition is a major factor influencing the homeostasis of the cell membrane and, in turn, the pathogenicity of filamentous fungi.

### Biosynthesis of unsaturated fatty acid

Studies have shown that UFAs (Unsaturated Fatty Acids) contribute to cell membrane integrity and thus influence the ability of cells to respond to various environmental stresses such as that induced by high salt [29]. The fatty acid synthetase  $\beta$ -subunit dehydrogenase (FAS1) enzyme in *Magnaporthe oryzae* is involved in the process of lipid synthesis, which may allow expansion for the oppressor to regulate the processes of fungal germination and host penetration [30]. In addition, in the pathogenic filamentous fungus *M. oryzae*, the hydrolysis of stored lipids to fatty acids and glycerol facilitates conidial germination, which is critical for fungal virulence [31]. In conclusion, the length and degree of saturation of fatty acid chains can provide reserve energy for pathogenic filamentous fungi by allowing greater signalling diversity on the one hand [32–34] while, on the other hand, UFAs provide turgor pressure for fungal growth, germ tube germination, and spore maturation, allowing the spore to contribute to the early stages of infection.

The proportion of unsaturated fatty acids (UFAs) in the membrane is a major determinant of membrane integrity and permeability in fungi, affecting both membrane homeostasis and pathogenicity. Higher proportions of UFAs increase the fluidity of the membrane, affecting the rotation and movement of functional proteins [35]. Most fungi contain both saturated (such as palmitic acid and stearic acid) and unsaturated (such as oleic acid, linoleic acid, and linolenic acid) fatty acids. The product of the delta 9-fatty acid desaturase gene (*Ole1*) introduces a double bond into saturated acyl-CoA to form a monounsaturated fatty acid [36,37]. The anabolic fatty acid biosynthesis pathway is conserved in filamentous fungi [38]. For example, the *Ole1* enzyme participates in the synthesis of ultra-long fatty acid chains and plays a crucial role in cytoplasmic membrane homeostasis [39,40].

The expression of *Ole1* is regulated by upstream transcription factors, such as the ER membrane proteins MGA2/SPT23 (yeast) [39,41,42] and HapX (*Beauveria bassiana*) [43], amongst others. In *Aspergillus flavus*, FarA (a Zn<sup>2+</sup>-Cys<sub>6</sub> transcription factor) positively regulates the expression of stearic acid desaturase genes required for oleic acid synthesis [44]. In addition, Ubx2p is a key upstream regulator of the essential fatty acid desaturase *Ole1p*. The absence of

Ubx2p affects the transcription of *Ole1*, causing fatty acid desaturation and abnormal nuclear membrane morphology [45]. In *Aspergillus giganteus*, 2-hydroxyfatty n-acyl- $\delta^3$ (E)-desaturase controls the level of saturation of fatty acid chains and interferes with cytoplasmic membrane integrity [46]. The absence of *BbSAY1* decreases the contents of oleic acid and membrane permeability, leading to a significant reduction in the fungal virulence of *Bassiana bassiana* [47].

## Effect of transmembrane proteins on cell membrane homeostasis in pathogenic filamentous fungi

### Transmembrane proteins and other essential components

Fungal transmembrane proteins, such as G protein-coupled receptors (GPCRs), glycosylphosphatidylinositol-anchored proteins (GPI-APs), GTPases, and Can1 membrane compartment as arginine/H<sup>+</sup> transporters (MCCs), form complex domains within the cell membrane, helping to regulate various physiological functions of the membrane [48,49]. *Magnaporthe grisea* GPCRs (PTH11) was shown to be an integral membrane protein required for pathogenicity [50]. GPCRs with the CFEM (common in fungal extracellular membrane) domain have also been shown to be important membrane proteins regulating fungal development and/or pathogenicity in entomopathogenic fungi, such as *Beauveria bassiana* [47] and *Metarhizium Robertsii* [51]. These proteins regulate membrane transport through interactions with lipid and cell wall components, as well as with intracellular cytoskeletal components, to maintain the homeostasis of the cell membrane.

Transmembrane proteins are present in almost all cells and they play important roles in development, cell adhesion, cell signalling, and development, as well as in the infection and evasion of the host defence in fungi [52]. The cell membrane, as a selective osmotic barrier for living cells, is essential for cell survival and function [53]. Transmembrane proteins are responsible for maintaining normal concentrations of various substances inside and outside the membrane, thus ensuring normal membrane functioning. GPCRs are known to be involved in a wide range of membrane transport activities and are capable of initiating or modulating signal transduction at multiple membrane sites [54]. GPI-APs are attached to the outer surface of the cell membrane through the GPI post-translational modification and play important roles in cell signalling, cell adhesion, cell wall metabolism, the immune response,

and cell membrane homeostasis [55]. Proteins of the *FgDnf* gene family mediate transmembrane transport of substances and are involved in vesicle budding, charge distribution, and intramembrane protein diffusion, and are critical for vegetative growth, development, and pathogenicity in *Fusarium graminearum* [56].

Various fungal membrane proteins interact with chitin, lipids, and actin, and are widely involved in the transport of different substances, thus playing important roles in cell function and structure. Fungal transmembrane proteins can form dynamic and stable structures with the cytoskeleton to maintain the homeostasis of the cell membrane. In fungi, two principal mechanisms, namely, turgor and the actin cytoskeleton, regulate cell membrane tension (PMTS) that modulates the connection between cell membrane and the cell wall. These systems function together with the cell membrane to facilitate adhesion to the cell wall. Depolymerization of F-actin leads to the rapid formation of endocytic pits while preventing their separation from the cell membrane [57]. Actin filaments can be organized into a variety of structures that are capable of exerting or resisting mechanical forces in the cellular environment [58]. In *Aspergillus fumigatus*, GTPases combine with septin (AspA-E), a cytoskeletal component, to regulate chitin deposition, separation, cytokinesis, and sporulation of the fungal cell wall, thus contributing to host invasion and virulence in mycogenic fungi [59,60].

The cytoskeleton not only helps stabilize the structure of the cell through the cell membrane but also regulates mycelium and spore formation to a certain extent. Phosphatidylinositol-(4,5)-bisphosphate (PI[4,5]P<sub>2</sub>) and septin in *Candida albicans* regulate the caspofungin response and the development of fungal mycelia in early fungal stages [61,62]. Septin also colocalizes with sterol-rich regions in the membrane and promotes the recruitment of cell-wall synthases during cell-wall remodelling [63]. In addition, a protein kinase associated with septin ring assembly, Gin4, is an important regulator of fungal cell membrane asymmetry [64]. Fungal membrane proteins maintain homeostasis of the cell membrane by forming dynamic and stable structures within the cell wall. The cell walls of filamentous fungi are mainly composed of chitin and glucan. Fungal chitin synthetases form a large protein family in filamentous fungi. These proteins contain transmembrane domains and are transported to the cell membrane by secretory vesicles where they participate in cell-wall synthesis [65]. In *Trichoderma atroviride*, the LysM domain protein TAL6 binds to certain forms of polymerized chitin, protecting the fungus from plant chitinases [66]. Furthermore, Sur7, one of the many

proteins that constitute the MCC, is involved in membrane-related cellular events and regulates fungal spore formation, cell wall integrity, stress tolerance, and virulence [67]. These data suggest that transmembrane proteins assist in cell wall synthesis through the transportation of cell wall components. Therefore, fungal membrane proteins may play crucial roles in cell wall homeostasis.

### Membrane curvature

Membrane curvature is a major factor essential for cell growth, division, and movement; and curvature and curvature-sensing proteins help vesicle budding and vesicle transport [68]. The shape of the cell membrane is a conserved phenotypic feature. The membrane shape/curvature has a significant effect on the biological function of the cell [69]. Certain intracellular proteins can bend lipid bilayers to generate the bent membrane required for substrate transport [70]. The cell membrane acts as a flexible barrier surrounding the cell and its compartments and its shape changes during cell locomotion and on receptor binding. Proteins are inserted into the membrane in a wedge-like manner, thus altering the curvature of the membrane [68]. For example, BAR-domain proteins assist in the recruitment of other proteins to specific locations where the membrane needs to be bent [71].

In fungi, membrane curvature is closely associated with both the cytoskeleton and the lipid content. Transmission electron microscopy of high-pressure frozen sections was used to evaluate the membrane structure during fungal infection. This showed that host cells infected by powdery mildew fungi form a haustorium in the outer membrane that is thicker than other cell membranes and is highly coiled, especially near the distal end of the haustorium neck [72]. Septin plays an important role as it promotes changes in the fungal cell shape and organizes the F-actin cytoskeleton to promote aggressive growth [73–75]. Septins in *Magnaporthe grisea* support F-actin via the ezrin-radixin-moesin protein Tea1 and interact with the phosphatidyl side of the appressorium membrane, providing cortical rigidity and membrane curvature to the appressorium. The fungi physically destroy the cuticle of the leaf to enter the plant tissue [76]. Studies in mice demonstrate that the E2-like enzyme, Atg3, facilitates LC3/GABARAP lipidation only on membranes exhibiting local lipid-packing defects. Atg3 is designed to work at highly curved membranes, perhaps including the limiting edge of the growing phagophore [77]. Among filamentous fungi, there are few reports on ATG3. *Beauveria bassiana* ATG3 is

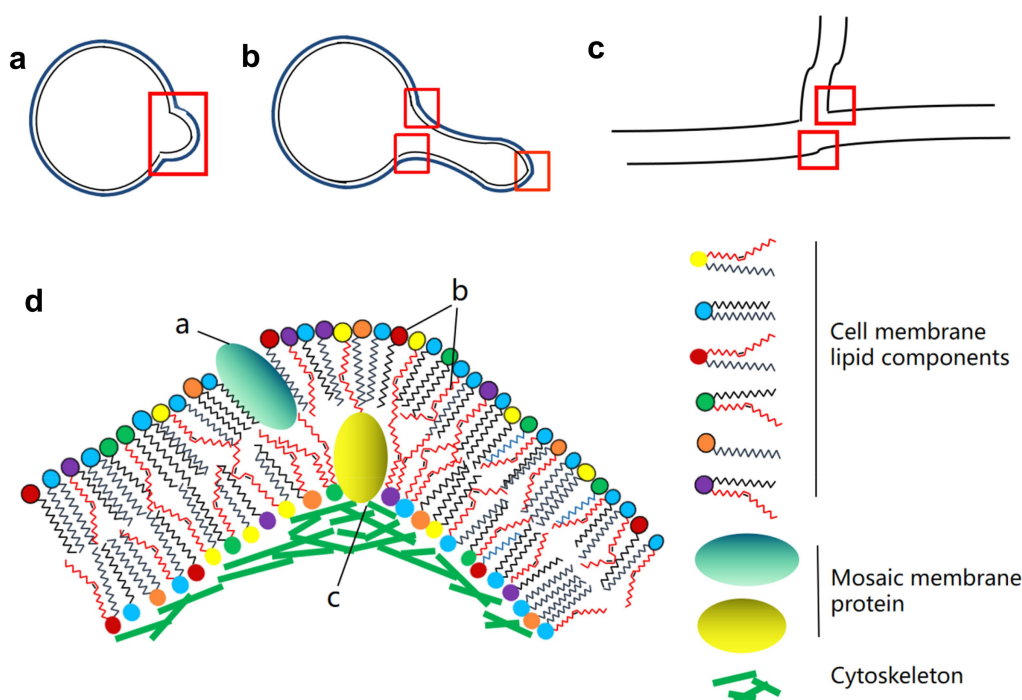
phosphorylated by ATG1 to participate in the autophagy process of fungi, thus regulating the development and pathogenicity of fungi [78]. Studies in human cells have shown that membrane curvature is an important parameter for defining the morphology of cells, organelles, and local membrane subdomains. The generation and maintenance of curvature is essential for maintaining traffic and cellular function. In addition to providing cell or organelle shape, local curvature can also affect processes such as membrane division and fusion, as well as protein concentrations and enzyme activation on the membrane [79]. In pathogenic filamentous fungi, the curvature of the cytoplasmic membrane not only promotes the formation of mycelia but also affects growth and spore formation. Overall, the curvature of the cell membrane contributes to fungal virulence (Figure 1).

### Cell wall components, regulation and modifications affecting cell membrane homeostasis in pathogenic filamentous fungi

Cell growth, membrane tension, and cell wall synthesis are interdependent. The interplay between membrane tension and cell wall mechanical stress enables cells to rapidly rectify mismatches between the rates of the membrane and cell wall synthesis during cell growth, thus ensuring balanced and normal growth [80]. Cell walls isolate cells from their surroundings and protect them from environmental stressors. Cell wall integrity is maintained by highly regulated processes of cell wall biosynthesis [81]. Maintenance of mutual structural integrity between the cell wall and membrane is one of the important conditions for cell wall homeostasis. Studies in *Candida albicans* showed that cell growth is regulated by two powerful complementary inducible forces, where membrane tension prevents cell wall expansion by inhibiting the synthesis of peptidoglycans, major components of the cells wall, while mechanical stress within the cell wall promotes the irreversible expansion of the cell wall. Only optimal membrane tension and cell wall stress ensure the balance between cell membrane and cell wall synthesis [80]. The sensor of cell wall mechanical stress, Wsc1 (MCW), participates in the regulation of homeostasis between the cell membrane and cells wall, as well as the apical growth of fungal cells and the protection of membrane domains under conditions of stress [82].

The components of the fungal cell wall provide mechanical protection against damage to the cell membrane. Filamentous fungi regulate the growth of both the cell wall and membrane as well as pathogenicity through endocytosis and exocytosis [83]. In





**Figure 1.** Formation of membrane curvature in pathogenic filamentous fungi. A. Morphology of fungi during early spore germination. B. The dividing or germinating germ tube in yeast cells infected with pathogenic fungus. C. Hypha of pathogenic filamentous fungi. The red boxes indicate the positions of potential membrane curvature at different developmental stages. D. Factors contributing to the formation of membrane curvature. a. Induction of curvature in the cell membrane by the insertion of mosaic membrane proteins. b. Effects of membrane curvature on the combination of polar fatty acid chains and various lipid components. c. Membrane bending caused by interaction between membrane proteins and cytoskeletal proteins.

*Beauveria bassiana*, BbLec1, which binds to chitosan and chitin in fungal cell walls, plays a wide range of physiological roles including defence responses and host-pathogen interactions [84]. A loss of *Bbmcm1* results in impaired cell integrity, distorted cell wall structure, altered cell wall composition, and delayed pathogenicity in insects [85]. *MoVps13*, an important virulence factor in *Magnaporthe oryzae*, plays an important role in cell wall integrity and cell membrane homeostasis by participating in cell wall and sphingolipid synthesis [26]. *Hex1* regulates osmotic stress and modulates the integrity of the cell wall and membrane, and has been shown to influence the colonization and pathogenicity of *Verticillium dahliae* [86]. Chitosan can inhibit conidial germination by destroying the integrity of the conidial membrane [87]. In *Fusarium* species, target of rapamycin (TOR), calcium/calcieneurin, and cell wall integrity pathways are important in responses to environmental signals [88].

Fungal cell wall components also affect the tension of the cell membrane and the mechanical tension of the cell wall, providing suitable turgor pressure for fungal germination and even host infection. In *Metarhizium acridum*, the absence of *MaPmt1* makes fungi more

sensitive to cell wall disruptors, with the cell wall becoming thinner with changes in its composition, thus reducing the pressure resulting from appressorium dilation and an inability to maintain the normal appressorium dilation pressure through the host cuticle [89].

### Transcriptional regulation of cell membrane and cell wall homeostasis in pathogenic filamentous fungi

Filamentous pathogenic fungi are widely distributed in nature and infect diverse host species, including higher animals, plants, and lower animals, necessitating extensive interactions between the fungus and the host [90]. Cell membrane homeostasis is closely related to the pathogenicity of fungi in both plant and animal hosts. In filamentous fungi, the involvement of transcriptional regulation of cell membrane homeostasis in fungal pathogenicity is rarely reported. For example, *Beauveria bassiana* HapX is an indispensable bZIP transcription factor in iron acquisition. It plays an important role in the early stage of fungal infection by regulating conidial oleic acid homeostasis and cell membrane function via initiation downstream gene *BbOle1* [84]. In *Aspergillus fumigatus*,  $\Delta$ *hacA* mutants

have increased sensitivity to antifungal agents that damage the membrane or cell wall, and decreased toxicity [91].

There have been many reports of involvement in fungal pathogenicity through regulation of cell wall component synthesis or cell wall integrity. Garcia-Rubio et al. reviewed recent studies on transcriptional regulation of the synthesis and integrity of cell wall components on fungal growth and development and pathogenicity in *Candida*, *Cryptococcus*, and *Aspergillus* Species [92]. In addition, there have been some reports of other filamentous pathogenic fungi. Such as, the loss of *Bbpmr1* resulted in a sharp decrease in the tolerance of *B. bassiana* to cell wall stressors and a loss of half of the virulence of the fungus [93]. *Rho2* regulates the response of *Fusarium oxysporum* to inhibitors of cell wall synthesis [94]. The transcription factors Con7p, Con7-1 and two identical Con7-2 encoded by *F. oxysporum* genes play an important role in the pathogenesis of fungi by regulating cell wall biogenesis [95]. *ChSat4* plays an important role in asexual development, cell wall integrity maintenance and pathogenicity of *Colletotrichum higginsianum* [96].

### **The cell membrane also requires the homeostasis of other membrane-enclosed organelles**

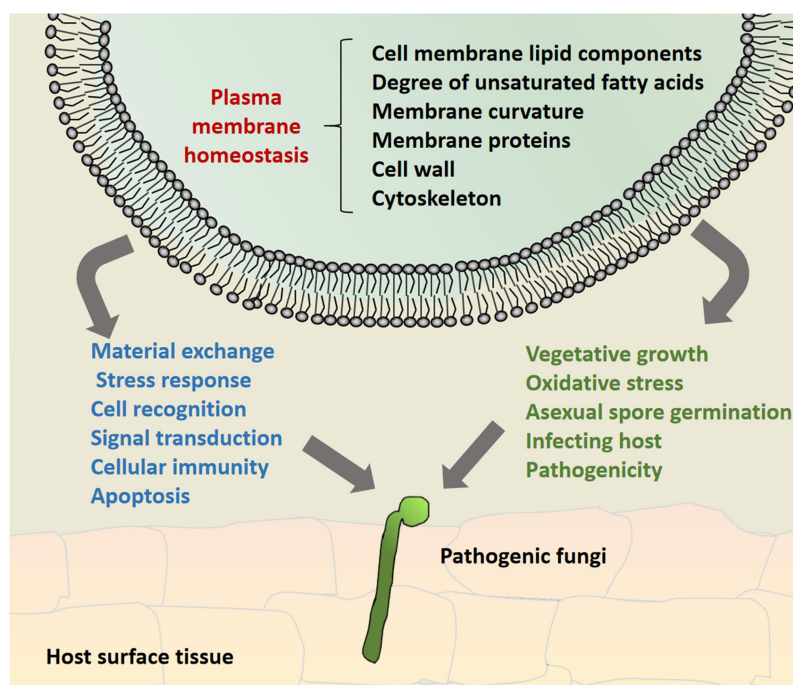
Several works show structurally and functionally dynamic contacts between mitochondria, the plasma membrane, the endoplasmic reticulum, and other subcellular organelles [97]. The cell membrane is a complex system that also requires the homeostasis of other membrane-enclosed organelles such as the endoplasmic reticulum [98,99], mitochondrion [100], and Golgi apparatus, as well as vacuolar membranes and the vesicular membrane system [101]. Endoplasmic reticulum homeostasis is very important for the growth and virulence of *Aspergillus fumigatus* [91]. In *B. bassiana*, vacuoles, as one of the membranous structures of cells, have also been shown to be involved in maintaining fungal pathogenicity [102]. Peroxisome genes (*AoPEX1* and *AoPEX6*) Are Required for Mycelial Growth, Conidiation, Stress Response, Fatty Acid Utilization, and Trap Formation in *Arthrobotrys oligospora* [103]. The succinate dehydrogenase gene *BbSdhC1* is critical for energy supply in the electron transport chain (ETC) by mediating the flow of electrons along the mitochondrial membrane, and disruption of this gene significantly reduces the virulence of the *B. bassiana* against the insect host [104].

However, here, we have only focused on the homeostasis of the cell membrane and its influence on fungal pathogenicity. In terms of composition, membrane lipids and transmembrane proteins are indispensable factors determining the complexity and diversity of all cellular organelles and membrane systems. While the contributions of transmembrane proteins and lipid components to cell membrane homeostasis have been widely reported, it is, however, not clear how membrane microdomains formed by transmembrane proteins and various lipid components contribute to cell membrane homeostasis and pathogenicity in fungi.

A further important factor affecting the homeostasis of the fungal cell membrane [105] is membrane curvature. Transmembrane proteins, the cytoskeleton, and microdomains formed by proteins all contribute to the degree of membrane curvature, which in turn affects the dimorphic transformation of filamentous fungi and the formation of invasive organs (such as appressoria) that contribute significantly to fungal virulence. However, most research on these topics has been performed by using biophysical simulation, with only a small amount of research focused on the mechanisms of host disease induction due to changes in the membrane curvature of fungi. There are still many unanswered questions surrounding pathogenic filamentous fungi. For instance, how do transmembrane proteins, membrane lipids, cell walls, and cytoskeletal components regulate interactions between the cell membrane and the cytoskeleton? How are the cell membrane and cell wall involved in conidial or blastospore (yeast cell) conversion to filamentous cells? How do they mediate fungal infection of the host? Nonetheless, unsaturated non-polar fatty acids also play important roles in determining fungal membrane curvature. Several genes suggested to influence the curvature of the fungal cell membrane have also been reported [106]. The effect of membrane curvature on the homeostasis and pathogenicity of fungal cytoplasmic membranes could be a promising research direction. In addition, the actin cytoskeleton exerts mechanical forces on the membrane and thereby regulates various cellular and subcellular morphogenetic processes such as cell migration, cytoplasmic division, and membrane transport [107]. This suggests that the cytoskeleton determines the homeostasis of fungal cell membranes. In all, the microdomains formed between membrane proteins, the cytoskeleton, the cell wall, and membrane lipid components are critical for the homeostasis of the cell membrane and the pathogenicity of fungal cells.

**Table 1.** Summarizes the substances involved in cell membrane homeostasis of filamentous fungi.

Member component	Substance name	Biological function	Reference
Membrane lipid components	Phosphatidylserine	Conidia and destroys the cell wall integrity	[15]
	Phosphatidylcholine	Conidia and destroys the cell wall integrity	[16]
	Ergosterol	Growth and virulence of fungi	[17]
	C8-desaturated and C9-methylated glycosylceramide (GlcCer)	Growth and virulence of the fungi	[18]
	Ceramide	Cytoskeletal organization and mycelial morphogenesis	[19]
unsaturated fatty acids	oleic acid	Fungal growth, germ tube germination and spore maturation	[84; 108].
Membrane curvature related proteins	BAR-domain proteins	Fungal growth and morphology, pathogenicity	[71]
Membrane protein	Septin	Fungal growth and morphology, pathogenicity	[59; 60,76].
	GPCRs	Fungal growth, development and pathogenicity	[50]
	CFEM domain proteins	Fungal growth, pathogenicity	[47; 51]
	GPI-APs	Fungal growth and development	[55]
	F-actin skeleton	Fungal growth and morphology, pathogenicity	[73; 74;] [75,76].
Cytoskeleton	chitosan and chitin	defense responses and host-pathogen interactions	[84]
Cell wall components			



**Figure 2.** Schematic diagram of the effects of cell membrane homeostasis on the growth and development of pathogenic filamentous fungi. This involves interactions between membrane lipid components, transmembrane proteins, cytoskeletal, and cell wall components, as well as the formation of membrane curvature, to maintain the integrity of the cell membrane assembly, structure, and function in pathogenic fungi at various stages of cell development, thus maintaining homeostasis of the cell membrane and contributing to fungal virulence. The blue and green notes respectively represent cell membrane homeostasis involved in the activity of filamentous fungi at the cytological level and microbial onto developmental level.

In conclusion, the contribution of cell membrane homeostasis to the pathogenicity of filamentous fungi is direct or indirect (Table 1, Figure 2). Membrane homeostasis is composed of membrane integrity, fluidity and permeability, and is closely related to membrane structure (membrane lipid type and saturation degree of non-polar fatty acid chains), transmembrane proteins and their transcriptional regulatory networks, membrane curvature, cell wall composition and cytoskeleton. These components and regulatory processes contribute to fungal virulence either by directly participating in the virulence of pathogenic fungi,

or by regulating cell growth and development, and even stress.

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## Data availability statement

Data availability is not applicable to this article as no new data were created or analysed in this study.

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