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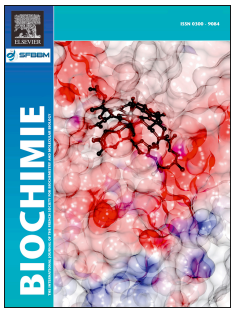

Sphingolipids from the human fungal pathogen *Aspergillus fumigatus*

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Sphingolipids from the human fungal pathogen *Aspergillus fumigatus*

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Summary
Sphingolipids (SPLs) are key components of the plasma membrane in yeast and filamentous fungi. These molecules are involved in a number of cellular processes, and particularly, SGLs are essential components of the highly polarized fungal growth where they are required for the formation of the polarisome organization at the hyphal apex. *Aspergillus fumigatus*, a human fungal pathogen, produce SGLs that are discriminated into neutral cerebrosides, glycosylinositolphosphoceramides (GIPCs) and glycosylphosphatidylinositol (GPI) anchors. In addition to complex hydrophilic head groups of GIPCs, *A. fumigatus* is, to date, the sole fungus that produces a GPI-anchored polysaccharide. These SPLs follow three different biosynthetic pathways. Genetics blockage leading to the inhibition of any SPL biosynthesis or to the alteration of the structure of SPL induces growth and virulence defects. The complete lipid moiety of SPLs is essential for the lipid microdomain organization and their biosynthetic pathways are potential antifungal targets but remains understudied.

1 Introduction

Aspergillus fumigatus is a saprotrophic filamentous fungus widely distributed in nature and is the most important airborne fungal pathogen in the world [1]. The continuous presence of conidia (asexual spores) in the air leads to their inhalation by humans and consecutively to allergic, pulmonary and invasive diseases [2]. The clinical presentation of *A. fumigatus* infection depends on the immune status of the host. Of the various pulmonary diseases, allergic bronchopulmonary aspergillosis (ABPA) and chronic pulmonary aspergillosis (CPA) generally occur in the immunocompetent individual while invasive pulmonary aspergillosis (IPA) manifests in the immunocompromised host [3]. Invasive aspergillosis (IA) remains the main cause of mortality in the patients undergoing allogeneic hematological stem cell transplantation [4,5].

Filamentous fungi are extremely polarized organisms, exhibiting continuous growth at their hyphal tip. Polarized growth requires an active vesicle trafficking to transport proteins and lipids required for the membrane extension and cell wall biosynthesis at the hyphal tip. The spitzenkorper is a vesicle structure and organizing center for hyphal growth [6]. Its integrity depends on microtubule, actin filament and also on the polarisome, a protein-ergosterol-sphingolipid complex localized at the plasma membrane of the apex. Ergosterol has been well studied as the main antifungal drug target. In contrast, the role of sphingolipids in fungal growth and as a putative antifungal target remains not well explored. Filamentous fungi are producing two types of sphingolipids, neutral and acidic. In this review, I will describe the knowledge on the structure and function of sphingolipids in *A. fumigatus* and discuss their putative importance during infection.

2 Neutral sphingolipids

Cerebrosides or monohexosylceramides are neutral glycosphingolipids produced by almost all eukaryotic organisms and also by few bacteria. In the fungal kingdom, cerebrosides have been described in many fungal species [7], with the exception of well-known yeasts such as *Saccharomyces cerevisiae, Schizosaccharomyces pombe* and *Candida glabrata* [8–10]. Their structures are conserved among fungal species studied so far. Fungal cerebrosides contain one glucose unit (GlcCer) or galactose unit (GalCer) covalently bound to the primary alcohol of an N-acyl sphingoid base through a