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Chapter 6: Structure and synthesis of fungal cell walls

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Chapter 6: Structure and synthesis of fungal cell walls

The fungal wall can justifiably be described as a sophisticated cell organelle because of the range of functions for which it is responsible and for its importance as a feature which is characteristic of the fungi.

In this Chapter we will discuss the fungal wall as a working organelle, and then consider the fundamental aspects of wall structure, function and wall architecture. We will describe each of the main components in detail; the chitin component, the glucan, and the glycoprotein. Wall synthesis and remodelling is also described, although you should already be aware of some of the mechanisms that may be involved (discussed in Section 5.15) and that the dynamic nature of the fungal cell wall is also mentioned during discussions of hyphal and spore differentiation (Section 9.3), hyphal branching (Section 4.11), septation (Sections 4.12 and 5.18) and hyphal anastomosis (Section 5.17).

In the final two Sections of this Chapter we give consideration to two aspects that are often overlooked: what happens on the outside of the wall is contemplated in the Section entitled *On the far side*; and finally we look, briefly, at the fungal wall as a clinical target (although antifungal agents that target the wall are dealt with in more detail in Chapter 18).

6.1 The fungal wall as a working organelle

The fungal cell wall is an important phylogenetic and taxonomic character, but it is a dynamic organelle, which, generally speaking, has four major functions:

- **maintenance of cell shape**. By so doing, the wall determines the morphology of the hypha or other fungal cell, like yeast cells and spores. The more spectacular multicellular fruit bodies of higher fungi are a striking example of how the cell wall contributes to morphogenesis;

- **stabilisation of the internal osmotic conditions** is an important outcome of maintaining cell shape. The wall is sturdy and elastic and creates a counteracting pressure, which stops excessive water influx;
- **the wall is also a protection against physical stress**, and functions as a protective coat. The combination of mechanical strength and high elasticity allows the wall to transmit and redistribute physical stresses, offering effective protection against mechanical damage ***and*** allowing the hypha to penetrate aggressively the substrata into which it grows (Money, 2004; 2008);
- **the cell wall is a scaffold for proteins**. Most of the mechanical strength of the wall is provided by its stress-bearing polysaccharides, but these also function as a scaffold to which an external layer of glycoproteins is attached. These glycoproteins function to limit the permeability of the wall (in both directions), create a microenvironment in the inner region of the wall adjacent to the plasma membrane which is under the control of the fungus. Negatively charged phosphate groups in their carbohydrate side-chains probably contribute to water retention, and proteins of this external layer allow recognition of mating partners, substrata, substrates and hosts, and subsequent adhesion and capture of any or all of these.

Cell wall construction is tightly controlled. The wall is the first part of the fungal cell to challenge the environment or potential host, so it is also the first to experience whatever demands the environment imposes or defensive inhibitors the host can produce. The wall is the target for environmental stress, natural plant and animal defences and for clinical pharmaceutical agents. Polysaccharide composition, structure and thickness of the wall all vary with environmental conditions and are coordinated with the cell cycle and developmental progress of the organism (Latgé, & Beauvais, 2014).

Formation and remodelling of the cell wall involve several biosynthetic pathways and the combined, and coordinated, actions of hundreds of gene products within the fungal cell. An indication of the significance of the cell wall in the cell biology of the fungal cell is that about 20% of the genome of *Saccharomyces cerevisiae* (i.e. approximately 1,200 genes) is devoted to the construction of the cell wall. Some provide substrates for the components of the wall; others are concerned with the delivery and assembly of wall materials; and many regulate the assembly and maintenance processes, as well as wall modifications in response to environmental challenges (Latgé, & Beauvais, 2014). The gene products include enzymes that create, modify or split glycosidic bonds, including multigene families of chitin and glucan synthases as well as enzymes such as glucanases and chitinases (glycohydrolases) and transglycosidases, which are concerned with remodelling the structure of the wall (Gow *et al*., 2017). Any disruption to the structure of the cell wall will have a profound effect on the growth and morphology of the fungal cell; ultimately making the cell vulnerable to lysis and death.

Although many of the building blocks of the cell wall are conserved in different fungal species, other aspects of wall composition vary between species (Coronado *et al*., 2007; Xie & Lipke, 2010). Many of the enzymes involved in wall construction and for cross-linking walls were strongly conserved; including glycosyl hydrolases and transferases, proteases, lipases, enzymes of the GPI-anchor synthesis pathway, and the chaperone proteins that assist polypeptide folding or unfolding and the assembly or disassembly of macromolecular structures. Indeed, many of these proteins are also conserved in other eukaryotes and are also associated with wall synthesis in plants. On the other hand the wall-resident proteins have diversified rapidly; these are the structural glycoproteins, adhesins and sexual agglutinins (in *Saccharomyces*). Coronado *et al*. (2007) suggest that fungal cell walls are assembled by the products of a conserved set of genes that is ancestral, like the basic architecture of the wall itself, to the evolutionary divergence of the ascomycete and basidiomycete clades. Xie & Lipke (2010) point out that the relatively fast sequence divergence of wall-resident proteins, together with their unusually high content of tandem and nontandem repeats, may have served as a driver for yeast speciation; enabling the yeast clade to adapt and exploit diverse environments.

Most of what we can describe here about the fungal wall has come from detailed molecular, genomic and proteomic analyses of model fungal systems, especially *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Candida albicans*, *Aspergillus fumigatus* and *Neurospora crassa*, and, in recent years, a growing number of pathogenic fungi, including human pathogens (Free, 2013). We will summarise information dealing with as wide a range of species as we can, but you should be aware that the story we can tell is still incomplete.

Structurally, the fungal wall is a **three-dimensional network of polysaccharides, glycoproteins and proteins**, many of which are unique to fungi. Typically, the walls contain **fibrillar polysaccharides** of high tensile strength embedded in a more gel-like matrix comprising a variety of polysaccharides, glycoproteins, and proteins with a range of minor components, including lipids, pigments, inorganic ions and salts.

The structural fibrillar material of the wall is largely inert, forming the main structural component, but the composition of the other materials changes with time and position as these components can serve as:

- nutrient reserves,
- in transport and translocation,
- for the metabolism of non-permeable substrates,
- for communication and interaction with the exterior,
- for protection from outside attack.

6.2 Fundamentals of wall structure and function

Most cell walls are layered, and the innermost layer (that is, the layer immediately surrounding the plasma membrane) is a relatively conserved structural skeletal layer and the outer layers are more varied between species and are dynamically tailored to needs of the organism as it develops and matures and in response to interactions with the environment. Proteins rarely make up more than 20% of the wall material, and most are glycoproteins. Some proteins have a structural role, but most contribute to the many other functions. Proteins at, or close to, the outer surface determine the surface properties of the wall; that is, whether it is **hydrophobic** or **hydrophilic** (= non-wettable or wettable), or **adhesive**, or **antigenic**. The low concentrations of lipids and waxes found in fungal walls usually serve to control water movement, especially to prevent desiccation.

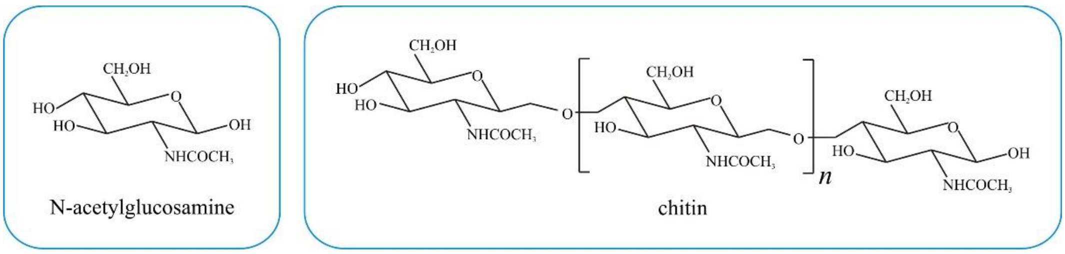

Fig. 6.1. Covalent structures of *N*-acetylglucosamine and its linear homopolymer, chitin, which is synthesised by the enzyme chitin synthase. Natural sources of chitin have molecular masses of a few million; extraction processes fragment the polymer and the molecular mass of commercial preparations of chitin can vary between 350,000 and 650,000.