MYCOLOGY ANSWERS

WHAT IS MEANT BY THE TERM DIMORPHISM AS APPLIED TO FUNGI AND IS IT AN IMPORTANT PHENOMENON?

Dimorphism literally means occurring in two forms. For fungi the term is sometimes applied to different types of mycelial growth e.g. aerial/submerged hyphae, diffuse/compact hyphal density and to the formation of spores. However, it is most usually used to describe the ability to exist as a filamentous (mycelial) form or as a cellular (yeast) form and to switch between these growth habits. In some cases a series of morphological forms can be recognised under different conditions e.g. for *Candida albicans* Berkh. yeast cells, intermediate forms occurring as chains of attached yeast cells sometimes termed pseudohyphae, and hyphae are seen. Species exhibiting dimorphism have attracted a great deal of research attention for several reasons. It is a relatively common property of fungi and is exhibited by members of the major groups, Zygomycota, Ascomycota, Basidiomycota and mitosporic fungi. Some dimorphic species are important and often virulent pathogens of man, animals, insects and plants, so that knowledge of their growth and development has been seen as a potential key to improving awareness and control of the conditions they cause. An understanding of the mechanisms which cause such a morphological switch, and endow such a level of morphological plasticity, might also provide information on spatial aspects and metabolic control of cell wall biosynthesis.

In general terms, mycelial fungi are usually regarded as invasive forms capable of penetration into and through substrates whereas yeast cells are considered as forms which are more easily dispersed and display more stress tolerance. There has therefore been a great deal of discussion concerning the significance of the morphological switch in relation to pathogenicity. This is an area of controversy and no definite correlation can be made. However, it is now clear that a range and combination of different factors influence the switch between the morphological forms and perhaps form-conversion plays some part in facilitating invasion into some hosts.

Several important dimorphic fungal pathogens of man usually enter the body by inhalation and through lung tissue initially causing "flu-like" symptoms quickly leading to infections of the lungs, blood and lymph nodes, e.g. *Histoplasma capsulatum* Darling, *Blastomyces dermatitidis* Cost. & Roll. and *Paracoccidioides brasiliensis* Almeida. These pathogens grow as mycelium at 25°C or below but convert to yeast cells near body temperature (37°C). However, for *Candida albicans*, also an important human pathogen (causing inflammation of mucous membranes) mycelial growth is encouraged at higher temperatures and low nutrient levels. *C. albicans* hyphae respond to surfaces and orientate their growth accordingly (i.e. display thigmotropism). This ability, combined with the production of proteases and other enzymes, may influence the penetrative ability of the organism and may aid the initial stages of infection. In humans, the degree of infection by such fungi is usually linked to the physiological state of the host and it is clear that immunocompromised and seriously ill patients succumb much more quickly to invasion whereas healthy individuals combat disease progression. Some insect pathogens also exhibit dimorphic growth, (e.g. *Beauveria bassiana* Vuill. and *Metarhizium anisopliae* Sorokin) adhering and penetrating through the host exoskeleton as mycelium but proliferating in the circulatory system as yeast cells competing for nutrients and releasing toxins, eventually leading to the demise of the host. Similarly, the plant pathogen *Ustilago maydis* (Pers.) Roussel causes corn smut disease of maize by mycelial form invasion; yeast form cells can be cultured independently of the host plant and are non-invasive.

Patterns of cell wall synthesis in growing fungi are related to the functioning of the cytoskeleton which directs vesicles carrying wall components and precursors to specific areas of synthesis for precisely controlled inclusion in wall structure. The cytoskeleton is essentially composed of microtubules and microfilaments built from proteins (mainly actin and tubulin with a range of other associated proteins). In hyphae wall extension occurs at apical regions which are rich in actin. In yeasts, site specific wall synthesis occurs at budding in similarly actin-rich regions but more generalised wall expansion follows as the cells round off.

Transitions between morphological forms are influenced by environmental conditions and are often accompanied by physiological changes in the fungi too. In addition, changes in the types of components incorporated into the wall may influence morphology. *Paracoccidioides brasiliensis* yeast form cell walls contain more α(1-3)-linked glucan, in contrast to mycelial forms which have very little α(1-3)-linked glucan and walls are composed mainly of β(1-3)-linked glucan, chitin, protein, galactomannan. There is more chitin (a structurally rigid β(1-4)-linked polymer of N-acetylglucosamine) in *Candida albicans* hyphal form walls than in the yeast form walls. In *Histoplasma capsulatum* changes in respiration rate occur after form conversion and alternative respiratory pathways are used which may alter levels of sulphydryl components in cells and affect wall composition and structure. Changes in carbon metabolism and the degree of aeration influence form conversion in the zygomycete *Mucor rouxii* Fresen. Anaerobic conditions favour growth of yeast form cells but low concentrations of oxygen promote mycelial form development. Research with *M. rouxii* has shown that cyclic AMP (cyclic adenosine monophosphate) may act as a regulator in the conversion between morphological forms. Cyclic AMP may activate protein kinases involved in wall synthesis, regulating precursor supply to sites of wall synthesis or by altering gene transcription.

Dimorphism is not an uncommon phenomenon among the fungi and it is quite clear that there is no universal regulatory mechanism. A wide range of environmental factors influence morphological development in these species and it seems likely that there are several signalling systems which operate independently to influence changes in gene expression, metabolism and cellular organisation. The extent to which this morphological plasticity is an advantage to these organisms is not yet clear.

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