

# The Logic of Cell Division in the Life Cycle of Yeast

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The budding yeast *Saccharomyces cerevisiae* has evolved two different patterns of mitotic cell division (see figure) (1). Diploid cells possess the polar budding pattern in which the first few new buds emerge from the daughter on the side opposite the junction to her mother (1, 2). Haploid cells possess the axial budding pattern in which new buds emerge at the mother-daughter junction (1). Here we argue that these patterns have evolved as a mechanism to orient the cells for biological functions specific to each cell type.

Although *S. cerevisiae* can exist either as a diploid or haploid organism, the diploid is the predominant cell type found growing in nature (3). The diploid cell is designed to extract nutrients from its growth substrate. Under conditions of nutrient limitation, the diploid forms pseudohyphae, linear chains of elongated yeast cells in which the daughters remain attached to the mothers (see figure) (2, 4, 5). These chains are formed by a repeated pattern of polar cell divisions. Upon nutrient limitation, an ellipsoidal diploid cell gives rise to a long thin daughter, which in turn gives rise to another long thin daughter. The first bud of the cell at the end of the chain, a cell that has not yet budded, always gives rise to a bud opposite the junction to its mother (2). Although the elongated shape and failure of cell separation are important to pseudohyphal growth, the polar budding pattern is key to the formation of this structure. Diploid cells that have been genetically manipulated to divide in an axial or random pattern do not form pseudohyphae when starved (2).

Pseudohyphal growth is a form of movement; each successive polar division propels the linear chain of cells away from the initial ancestral cell into new territory. Pseudohyphal growth enables otherwise sessile cells to forage for nutrients at a distance from their point of colonization. The ability of the growing pseudohyphal strand to penetrate the substrate may provide an additional advantage in the search for nutrients.

Why do haploid cells have the axial pattern, since this mode of cell division precludes pseudohyphal growth and therefore foraging? We believe that the haploid cells are essentially gametes designed to fuse with a cell of opposite mating type to reform the diploid. When diploid cells heterozygous for the mat-

ing type locus (*MATa/MAT $\alpha$* ) are deprived of nutrients (as opposed to limited for them), they cease vegetative growth and undergo meiosis to produce the four haploid meiotic products bound together in a sac called the ascus (figure, lower left). As a consequence of Mendelian segregation, two of the haploid cells in the ascus are *MATa* cells and the other two are *MAT $\alpha$*  cells. The spores are arranged with a characteristic tetrahedral geometry inside the ascus (figure, lower left). This unique geometric arrangement of the four ascospores juxtaposes sister spores of opposite mating types and expedites their efficient conjugation (dark arrows equal mating). Even when yeast meiosis produces linear asci (6, 7), the spore alignment is controlled to juxtapose ascospores of opposite mating type. That is, there are more asci of the *aaaa*, *aaaa*, and *aaaa* classes than of the *aa $\alpha\alpha$*  type. When environmental conditions again favor vegetative growth, the adjacent cells of opposite mating type fuse to form two *MATa/MAT $\alpha$*  diploid cells (3, 8).

According to our model the axial growth pattern is part of a default pathway that ensures diploid formation even when a wayward spore has been separated from its mate in the ascus (dashed arrow). Most wild *S. cerevisiae* strains contain a remarkable mating type interconversion system that can switch the mating type during cell division (from *MAT $\alpha$*  to *MATa* in the lower right of the figure) and thereby generate cells of opposite mating type. The rules of mating type switching are that a

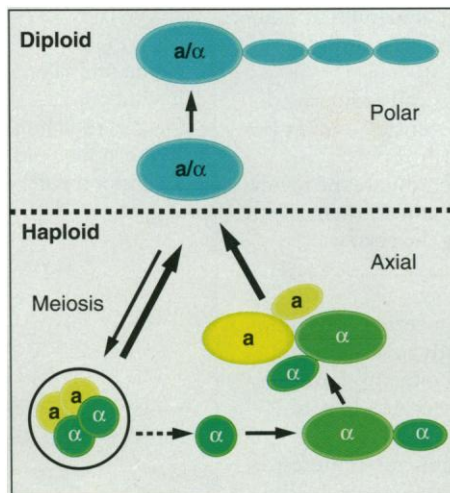
cell can switch only after it has divided once. A lone ascospore possessing this system germinates and undergoes two cell divisions to form a four-celled microcolony that includes two *MATa* cells and two *MAT $\alpha$*  cells (8). Because these cells are haploid they divide in the axial pattern, which, as first noted by Nasmyth (9), juxtaposes cells of opposite mating type. These cells, like those in the ascus, are geometrically positioned to fuse with each other to form two diploid cells (see figure). If the haploids divided in a polar pattern, some cells of opposite mating type would be spatially separated and therefore unable to mate. Thus, mating type switching and axial budding ensure that even an isolated haploid cell will generate diploid cells possessing the polar budding pattern that is optimal for vegetative growth.

Not every laboratory *S. cerevisiae* strain is capable of undergoing the dimorphic switch to pseudohyphal growth. Many strains in current laboratory use were selected to form smooth colonies that can be easily transferred from plate to plate (10). It is likely that the isolation of "good laboratory strains" led to the selection against the genes required for pseudohyphal growth. In agreement with this notion, we have found that the ability to form pseudohyphae is dominant to the inability (2).

The dimorphic transition from a unicellular to a filamentous form and from a filamentous to a unicellular form is a developmental switch characteristic of fungi from quite diverse taxonomic groups. Many of the fungi pathogenic to humans (for example, *Candida albicans*) or plants (for instance, *Ustilago maydis*) are dimorphic. Indeed, it has been proposed that pathogenicity is related to the ability to undergo the dimorphic switch. The finding of dimorphism in *S. cerevisiae* means that the genes controlling the switch can be obtained and analyzed with facility. Should these genes be conserved in pathogens, they will offer important insights into the mechanism and control of fungal disease.

## REFERENCES AND NOTES

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Roles of polarized cell division in the *S. cerevisiae* life cycle.

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