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Review

# Mechanisms of cytokinesis in basidiomycetous yeasts

*Sophie ALTAMIRANO, Srikripa CHANDRASEKARAN, Lukasz KOZUBOWSKI**

*Department of Genetics and Biochemistry, Clemson University, Clemson, SC, USA*

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ABSTRACT

While mechanisms of cytokinesis exhibit considerable plasticity, it is difficult to precisely define the level of conservation of this essential part of cell division in fungi, as majority of our knowledge is based on ascomycetous yeasts. However, in the last decade more details have been uncovered regarding cytokinesis in the second largest fungal phylum, basidiomycetes, specifically in two yeasts, *Cryptococcus neoformans* and *Ustilago maydis*. Based on these findings, and current sequenced genomes, we summarize cytokinesis in basidiomycetous yeasts, indicating features that may be unique to this phylum, species-specific characteristics, as well as mechanisms that may be common to all eukaryotes.



## 1. Introduction

Cytokinesis is the final step in the cell cycle that results in two physically separate cytoplasms of the dividing cells. The partition of cytoplasms is precisely coordinated with chromosomal segregation and subject to complex regulation, as its failure may result in aneuploidy (D'Avino *et al.*, 2015). In animal cells, the major force that drives the ingression of the plasma membrane during cytokinesis is the constriction of the cortex-associated ring consisting of filamentous F-actin and non-muscle myosin referred to as the actomyosin ring (AMR), otherwise known as contractile actomyosin ring. In fungi, in addition to the constriction of the AMR, a new cell wall is synthesized between the dividing cells in the form of septa. In yeasts, the physical separation of the daughter cells is triggered by septum hydrolysis.

Although fungi and animals have diverged about one billion years ago, major cytokinesis events are relatively well conserved between the two kingdoms (Pollard, 2010). In fact, largely what we know about animal cytokinesis has come from studying two classic models for eukaryotic biology, ascomycete yeasts, *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe* (model yeasts) (Pollard, 2010; Yanagida, 2014). On the other hand, mechanisms of events that accompany the assembly and the constriction of the AMR exhibit considerable plasticity across fungi and animals (Balasubramanian *et al.*,

Abbreviations AMR actomyosin ring; NE nuclear envelope; SPB spindle pole body; MEN mitotic exit network; SIN septation initiation network.

* *Corresponding author*. 190 Collings Street, Life Sciences Facility, 255A, Clemson, SC 29634, USA.
E-mail address: lkozubo@clemson.edu (L. Kozubowski).

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2004; Balasubramanian et al., 2012; Gu and Oliferenko, 2015). For instance, budding yeasts belonging to the second largest fungal phylum, Basidiomycota, undergo nuclear division through mechanisms significantly different from those described for ascomycete yeasts (Poon and Day, 1976; Mochizuki et al., 1987). Therefore, studying basidiomycetes may be critical for better understanding the evolution of the mechanisms of cytokinesis. While comparative genomics with other phyla may be informative, comparative cell biology of basidiomycete yeasts may provide functional insights beyond those obtained from studying model yeasts.

Ascomycota and Basidiomycota have diverged approximately 400 million years ago (Taylor and Berbee, 2006). Basidiomycetes are characterized by the production of basidiospores, via sexual reproduction, usually in a dimorphic manner (Lee et al., 2010). Both the sexual dimorphic and asexual yeast forms are common in all three main classes of Basidiomycota (Agaricomycotina, Pucciniomycotina, Ustilaginomycotina) (Fell et al., 2001; Morrow and Fraser, 2009). Most known basidiomycete yeasts undergo division by budding, while fission has not been well characterized in this phylum, except for limited studies on the *Trichosporon* species (Gueho et al., 1992).

Here we summarize current literature about cytokinesis in basidiomycetous yeasts, and analyze sequenced genomes to address the following questions: Is cytokinesis significantly different in basidiomycetes as compared to ascomycetes? Could elucidating cytokinesis in basidiomycetes improve our understanding of the evolution and mechanisms of this essential part of cell division?

This review focuses on two basidiomycetes that have been investigated relatively extensively, a representative of Ustilaginomycotina, corn smut, *Ustilago maydis* and a member of Agaricomycotina, pathogen of humans *Cryptococcus neoformans*. *U. maydis* exhibits two major morphologies, saprophytic yeast and filamentous hyphae that propagate within the plant host during infection. The yeast divides by budding and the bud grows mostly by tip extension resulting in an elongated, cigar shape morphology (Banuett, 1992; Steinberg and Perez-Martin, 2008; Vollmeister et al., 2012) (Fig. 1). *C. neoformans* yeast cells divide by budding, including the apical to isotropic switch, which results in a characteristic round shape similar to that of *S. cerevisiae* (Kozubowski and Heitman, 2012; Wang and Lin, 2015) (Fig. 1). In both *U. maydis* and *C. neoformans* the hyphae form as a result of mating. However, in *C. neoformans*, it is the yeast form that causes infection (Lin, 2009). *U. maydis* and *C. neoformans* belong to distinct classes of Basidiomycota. Therefore, our knowledge about cytokinesis in these yeasts may reflect mechanisms that are common to all basidiomycetes as well as pathways that are class- or species-specific.

Several excellent reviews have been published recently that describe cytokinesis in *S. cerevisiae* and *S. pombe*, and we refer the reader to these great resources for more information (Weiss, 2012; Wloka and Bi, 2012; Willet et al., 2015; Juanes and Piatti, 2016; Meitinger and Palani, 2016; Perez et al., 2016; Rincon and Paoletti, 2016). Here we provide a brief overview of the mechanisms in both model yeasts and focus mostly on studies describing cytokinesis in basidiomycetous yeasts.

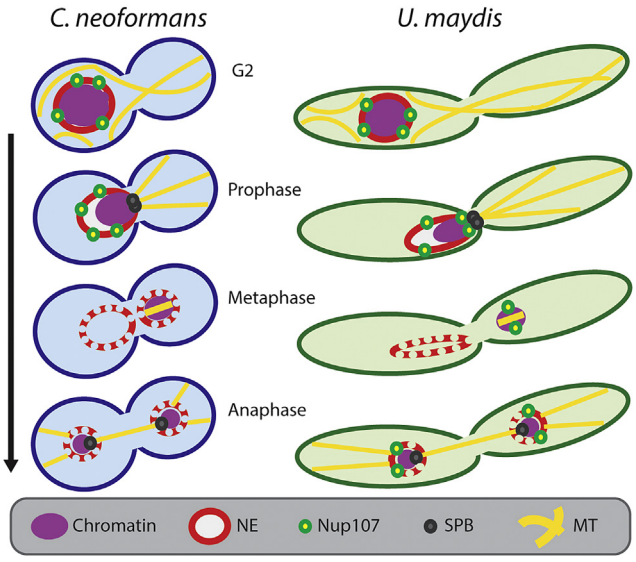


**Fig. 1 – Key events during mitosis in *C. neoformans* and *U. maydis*. In both yeasts, non-dividing cells (G2) contain a network of cytoplasmic microtubules (MT). In prophase cytoplasmic MT capture an outer plaque of the spindle pole bodies (SPBs) and pool the entire chromatin to the daughter cell. In metaphase, chromatin compacts and arranges around the spindle; at that time cytoplasmic MT disappear. In *C. neoformans* the nuclear envelope (NE) moves along with the chromatin to the daughter cell and partially breaks open. In *U. maydis* the NE stays in the mother cell and also disintegrates. Localization of the Nup107, which is the essential component of the Nuclear Pore Complexes (NPC), suggests that the NPCs disassemble from the NE during metaphase. In *U. maydis*, but not in *C. neoformans*, Nup107 is recruited subsequently to the chromatin. In late telophase, NE is rebuilt, NPCs re-assemble, and cytoplasmic microtubule network reappears (not shown).**

## 2. Mechanisms of entry into cytokinesis

The timing of cytokinesis has to be tightly controlled so that it always follows a successful chromosomal segregation. Mitotic cyclin-dependent kinase (Cdk) is the main regulator that prevents the onset of cytokinesis until the chromosomes are properly segregated and inactivation of Cdk allows the cytokinesis to proceed (Morgan, 1999).

In *S. cerevisiae*, the entry to cytokinesis is regulated through the signaling dependent on the Polo kinase and a network of proteins collectively known as the Mitotic Exit Network (MEN) (Lee et al., 2001a, 2001b; Petronczki et al., 2008; Meitinger et al., 2012). The MEN signaling initiates during late anaphase at the spindle pole body (SPB) where the GTPase, Tem1, stimulates the kinase, Cdc15, to activate the Mob1-Dbf2 kinase complex. Mob1-Dbf2 in turn promotes the release of the protein phosphatase, Cdc14, from the nucleolus. Cdc14 reverses phosphorylation of a number of Cdk1 targets leading to mitotic exit and cytokinesis (Jaspersen et al., 1998; Visintin et al., 1998) (Visintin et al., 1998; Shou et al., 1999; Visintin