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journal homepage: www.elsevier.com/locate/fbr

Review

Regulation of polarised growth in fungi

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Keywords:
Cdc42
Hyphae
Polarised secretion
Polarisome
Rho-type GTPases
Spitzenkörper

ABSTRACT

Polarised growth in fungi occurs through the delivery of secretory vesicles along tracks formed by cytoskeletal elements to specific sites on the cell surface where they dock with a multiprotein structure called the exocyst before fusing with the plasma membrane. The budding yeast, *Saccharomyces cerevisiae* has provided a useful model to investigate the mechanisms involved and their control. Cortical markers, provided by bud site selection pathways during budding, the septin ring during cytokinesis or the stimulation of the pheromone response receptors during mating, act through upstream signalling pathways to localise Cdc24p, the GEF for the rho family GTPase, Cdc42p. In its GTP-bound form, Cdc42p activates a multiprotein complex called the polarisome which nucleates actin cables along which the secretory vesicles are transported to the cell surface. Hyphae can elongate at a rate orders of magnitude faster than the extension of a yeast bud, so understanding hyphal growth will require substantial modification of the yeast paradigm. The rapid rate of hyphal growth is driven by a structure called the Spitzenkörper, located just behind the growing tip and which is rich in secretory vesicles. It is thought that secretory vesicles are delivered to the apical region where they accumulate in the Spitzenkörper. The Spitzenkörper then acts as vesicle supply centre, and it has been postulated that vesicles exit the Spitzenkörper in all directions, but because of its proximity, the tip receives a greater concentration of vesicles per unit area than subapical regions. There are no obvious equivalents to the bud site selection pathway to provide a spatial landmark for polarised growth in hyphae. However, an emerging model is the way that the site of polarised growth in the fission yeast, *Schizosaccharomyces pombe*, is marked by delivery of the kelch repeat protein, Tea1, along microtubules. The relationship of the Spitzenkörper to the polarisome and the mechanisms that promote its formation are key questions that form the focus of current research.

1. Introduction

Fungal hyphae grow almost exclusively from their tips. To do this, membranes and the raw materials and enzymes for the synthesis of new cell wall material are delivered to the tip in the form of secretory vesicles, which fuse with the plasma membrane at the tip. Research in the budding yeast *Saccharomyces cerevisiae*, has served as a model for the processes involved and their regulation. Sites of polarised growth are marked by cortical markers formed by the bud site selection pathways, the site of septation in vegetative cells or the site of pheromone stimulation in mating projections. At these sites a small GTPase, Cdc42p, is activated by its GEF, Cdc24p (Fig 1). Activated Cdc42p promotes the formation of

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1749-4613/$ – see front matter
doi:10.1016/j.fbr.2008.07.001

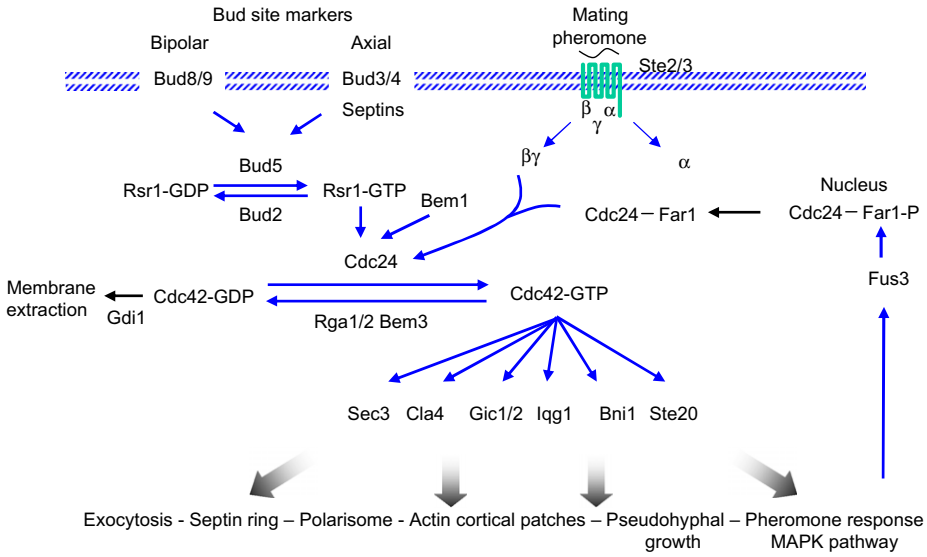

Fig. 1 – Cdc42p orchestrates morphogenesis in *Saccharomyces cerevisiae*. Cdc42p is activated by its GEF Cdc24p and returned to its GDP-bound state by its GAPs Rga1/2p and Bem3p. Cdc24p is activated by upstream bud site selection pathways and by the γβ G-protein dimer released from the tripartite G-protein complex when the cognate mating pheromone interacts with the mating pheromone receptors. Acting through its immediate effectors, activated Cdc42p stimulates polarised growth, activation of the pheromone response pathway, pseudohyphal growth and cytokinesis.

a multiprotein complex called the polarisome, which nucleates the formation of actin cables. Post-Golgi secretory vesicles are transported along these actin cables to dock with a second protein complex called the exocyst before fusion with the plasma membrane mediated by the interaction between v-SNARES on the vesicle and a t-SNARE complex on the membrane (Fig 2). Polarised growth in *S. cerevisiae* has been the subject of an excellent recent review to which the reader is referred to for details of these processes (Park and Bi, 2007).

The yeast model serves to highlight the different stages in this process where control over polarised growth can be exerted. First, polarised growth requires the establishment of the site, which may be subject to both temporal and spatial control. Second, once the site has been established, the actin or tubulin cytoskeletons must be polarised toward this site. This requires the formation of a structure such as the polarisome whose formation and activity may be controlled. Third, the formation and flow of post-Golgi secretory vesicles along the cytoskeletal tracks can be regulated. Fourth, the assembly of the exocyst and the docking of secretory vesicles with the exocyst may be controlled. Small GTPases, in particular Cdc42p and the closely related Rac GTPase, play a key role at many of these levels (Park and Bi, 2007).

This review takes the *S. cerevisiae* model as a base, but will seek to consider to what extent the yeast paradigm can be extended to fungi that grow in a hyphal rather than yeast form.

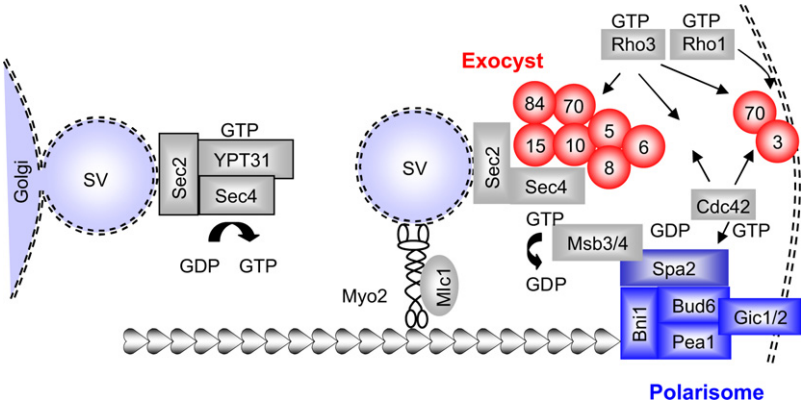

Fig. 2 – Polarised secretion in *Saccharomyces cerevisiae*. Secretory vesicles bleb off from the late Golgi compartments and travel along actin cables, nucleated by the polarisome, to fuse with the plasma membrane at sites of polarised growth. The process is controlled by the Rab GTPase Sec4p which is activated by its GEF Sec2p. Numerals enclosed in circles refer to exocyst components encoded by Sec genes (e.g. Sec15p, Sec6p, etc.). Encircled 70 and 84 refer to Exo70p and Exo84p. For details see text.