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Making the Final Cut – The Role of Endosomes During Mitotic Cell Division

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1. Introduction

The last step of cell division is the physical separation of two daughter cells via a process known as cytokinesis (Barr and Gruneberg, 2007; Prekeris and Gould, 2008). After replication of the genetic material, the mother cell divides by the formation of a cleavage furrow that constricts the cytoplasm, thus leaving two daughter cells connected by a thin intracellular bridge (ICB). The resolution of this bridge, abscission, results in a physical separation of the two daughter cells and usually occurs on either, or both, sides of the midbody within the ICB. This abscission event occurs on either or both sides of the midbody within the intracellular bridge (ICB). While earlier studies thought this abscission event was simply a continuation of the constriction placed on the cleavage furrow by the actomyosin contractile ring, it was later discovered that abscission is a highly complex and organized event consisting of much more than a simple actin and non-muscle myosin constricting ring. Endocytic membrane transport, ESCRT protein complex function, and cytoskeletal reorganization were all shown to contribute to cytokinesis and abscission (Barr and Gruneberg, 2007; Prekeris and Gould, 2008). The goal of this review is provide an overview the newest advances in our understanding about the dynamics and roles of endosomal transport during cytoskeletal re-arrangements and ESCRT complex assembly throughout cytokinesis.

2. Post-Golgi transport is required for the completion of cytokinesis

Classically, cytokinesis in animal cells was thought to be mediated by the formation and contraction of the actomyosin contractile ring, which assembles at the equator of the dividing cells and is regulated by a variety of molecules, including the recruitment and activation of a RhoA GTPase-dependent signaling cascade (Glotzer, 2005). In contrast, plant cytokinesis was demonstrated to depend on the transport of post-Golgi organelles, which assemble and fuse to form an organelle, known as a phragmoplast (Jurgens, 2005). This organelle ultimately fuses with the plasma membrane, bisecting the plant cell into two daughter cells. These mechanisms in animal and plant cell division were thought to have differentially evolved due to the fact that plant cells have a rigid cell wall, while animal cells only need to separate a very dynamic and "bendable" plasma membrane. Interestingly, during recent years, multiple studies have challenged this dogma and suggested that animal cell cytokinesis may not be entirely different from plant cell cytokinesis. The first clues, that

membrane transport may play a role in animal cytokinesis, came from the observations that in large embryonic cells, such as amphibian eggs, the addition of endo-membranes is required for expanding the plasma membrane during the formation and ingression of the cleavage furrow (Bluemink and de Laat, 1973). Later studies have shown that similar membrane addition is required during cellularization of *Drosophila melanogaster* embryos (Albertson et al., 2008; Hickson et al., 2003). In addition, multiple genetics and proteomics screens in *Caenorhabditis elegans* and *Drosophila melanogaster* have identified many known endocytic membrane trafficking proteins, such as dynamin, SNAREs and Rab GTPases as factors required for the successful completion of cytokinesis (Low et al., 2003; Pelissier et al., 2003; Riggs et al., 2003). Based on this work, it has become widely accepted that endosomes are specifically targeted to the forming cleavage furrow, and appear to mediate the late step(s) of cell division. Finally, recent studies have suggested that these endosomes are not a homogeneous pool of endocytic membranes, but in fact consist of several post-Golgi organelles with different transport dynamics and distinct functions (Dambournet et al., 2011; Nezis et al., 2010; Schiel et al., 2011).

2.1 TGN-derived secretory vesicles

Some of the first organelles that were shown to be targeted to the forming cleavage furrow were trans-Golgi Network (TGN)-derived secretory organelles. Elegant work from Steve Doxsey and colleagues has demonstrated that secretory organelles can be targeted to the midbody of the cleavage furrow by binding to the centriolin-exocyst protein complex (Gromley et al., 2005). Centriolin was originally described as a protein that associates with the mother centriole. However, during late cytokinesis, centriolin also associates with a novel structure in the midbody, known as the midbody ring. This midbody-associated centriolin was shown to act as a scaffolding factor by binding to and recruiting the Exocyst protein complex to the midbody (Gromley et al., 2005). The exocyst complex was originally described as a tethering factor for secretory vesicles in budding yeast (TerBush et al., 1996), and later was shown to play a similar role in mammalian cells (Hsu et al., 1999). The exocyst is a multi-protein complex that is comprised of Sec3, Sec5, Sec6, Sec8, Sec10, Sec15, Exo70 and Exo84 subunits (Hurley, 2010). The exocyst complex was already shown to localize to the neck of the bud in budding yeast and to the midbody of the dividing animal cells (TerBush et al., 1996). As the result, these data provided a tantalizing possibility that the centriolin-exocyst complex may serve as a tethering factor for the targeting of secretory vesicles to the forming cleavage furrow. Indeed, the knock-down of various exocyst subunits leads to defects in late cytokinesis (Fielding et al., 2005; Gromley et al., 2005). In addition to the exocyst complex, centriolin was also shown to bind and recruit a SNARE-associated protein, SNAPIN (Gromley et al., 2005), thus providing another link between centriolin and membrane transport/fusion. Consistent with these data, SNAPIN also appears to be required for the successful completion of cytokinesis (Gromley et al., 2005). Taken together, it was proposed that the compound fusion of these secretory vesicles with each other and with the furrow plasma membrane may lead to the final scission of the intracellular bridge (ICB) connecting daughter cells. Since this model was introduced, high-resolution microscopy and tomography studies have questioned whether compound secretory vesicle fusion can mediate abscission (Elia et al., 2011; Schiel et al., 2011). It is clear that secretory vesicles are delivered to the forming cleavage furrow during early-to-mid telophase, the function of these secretory vesicles remains unknown.

2.2 Rab11-endosomes

In addition to secretory vesicles, recycling endosomes also have emerged as important players in mediating abscission. Several reports have demonstrated that pronounced changes occur in endocytic recycling during mitosis, and that these changes are required for the successful completion of cytokinesis (Boucrot and Kirchhausen, 2007). Additionally, VAMP8, a known endocytic SNARE, also was shown to be present in the cleavage furrow and is required for mitotic cell division (Schiel et al., 2011). Originally it was proposed that recycling endosomes, just like secretory vesicles, initiate abscission by fusing with each other and the plasma membrane, thus building a separating membrane in a manner similar to the formation of a phragmoplast in plant cells. However, recent data indicates that fusion of recycling endosomes instead mediates formation of the "secondary ingression" (Figure 2, Endosome fusion model), although it remains unclear how these recycling endosomes mechanistically induce this secondary ingression (Schiel et al., 2011). Rab11 is a small monomeric GTPase that plays a major role in the trafficking of recycling endosomes during interphase (Prekeris, 2003). As the result, it was proposed that Rab11 may play a role in targeting recycling endosomes to the cleavage furrow during mitosis. Indeed, work in several model organisms, such as *Caenorhabditis elegans* and *Drosophila mellanogaster* have shown that Rab11 is required for cytokinesis (Hickson et al., 2003; Pelissier et al., 2003; Skop et al., 2001). Similarly, recent work from several laboratories has shown that Rab11 also mediates late cytokinesis in mammalian cells (Hickson et al., 2003; Horgan et al., 2004; Wilson et al., 2004). Rab GTPases work by binding and recruiting distinct effector proteins to membranes. Because of the ability of the Rabs to bind multiple effector proteins, considerable effort within the last decade has been dedicated to the identification and characterization of Rab effector proteins and their roles in various cellular pathways. Work from several laboratories has identified Rab11-FIPs (**Rab11 F**amily **I**nteracting **P**roteins) as Rab11 effector proteins that serve as "targeting complexes" in specific recycling endosome transport pathways (Hales et al., 2001; Prekeris et al., 2001). Rab11-FIPs (henceforth referred to as FIPs) consists of five members, which bind to Rab11 with a very high affinity (~100-200nM) (Junutula et al., 2004). All FIPs contain a highly conserved C-terminally located Rab11-binding domain (RBD) (Prekeris, 2003). Recently solved crystal structures of FIP3/Rab11 and FIP2/Rab11 complexes have shown that FIPs form a parallel coiled-coil homo-dimer and bind to two Rab11-GTP molecules via Rab11-switch regions (Eathiraj et al., 2006; Jagoe et al., 2006). Interestingly, FIP binding induces a conformational change in Rab11, perhaps explaining the very high affinity of Rab11 and FIP binding (Eathiraj et al., 2006). Based on their structure and sequence similarity, the FIPs are divided into two classes (Figure 1). Class I FIPs (FIP1, FIP2 and FIP5) contain a N-terminally located phospholipid binding C2 domain and were shown to regulate endocytic recycling during interphase (Prekeris, 2003). Class II FIPs (FIP3 and FIP4) lack a C2 domain, but contain a N-terminally located proline-rich domain (PRD) and two calcium binding EF hands (Prekeris, 2003), although the functions of these domains remain unclear. FIP3, a Class II FIP, has emerged as a key regulator of recycling endosome targeting to the cleavage furrow during cytokinesis. In mammalian cells, knock-down of FIP3 results in failed cytokinesis, leading to the formation of bi-nucleate or multi-nucleate cells (Wilson et al., 2004). Similarly, nuclear fallout protein (nuf), a *Drosophila* orthologue of FIP3, is required for the cellularization of *Drosophila* embryos (Riggs et al., 2007). FIP3 also makes an excellent marker of furrow-associated recycling endosomes, because during cytokinesis FIP3 is present exclusively at this site in the cell (Schiel et al., 2011; Simon et al., 2008).

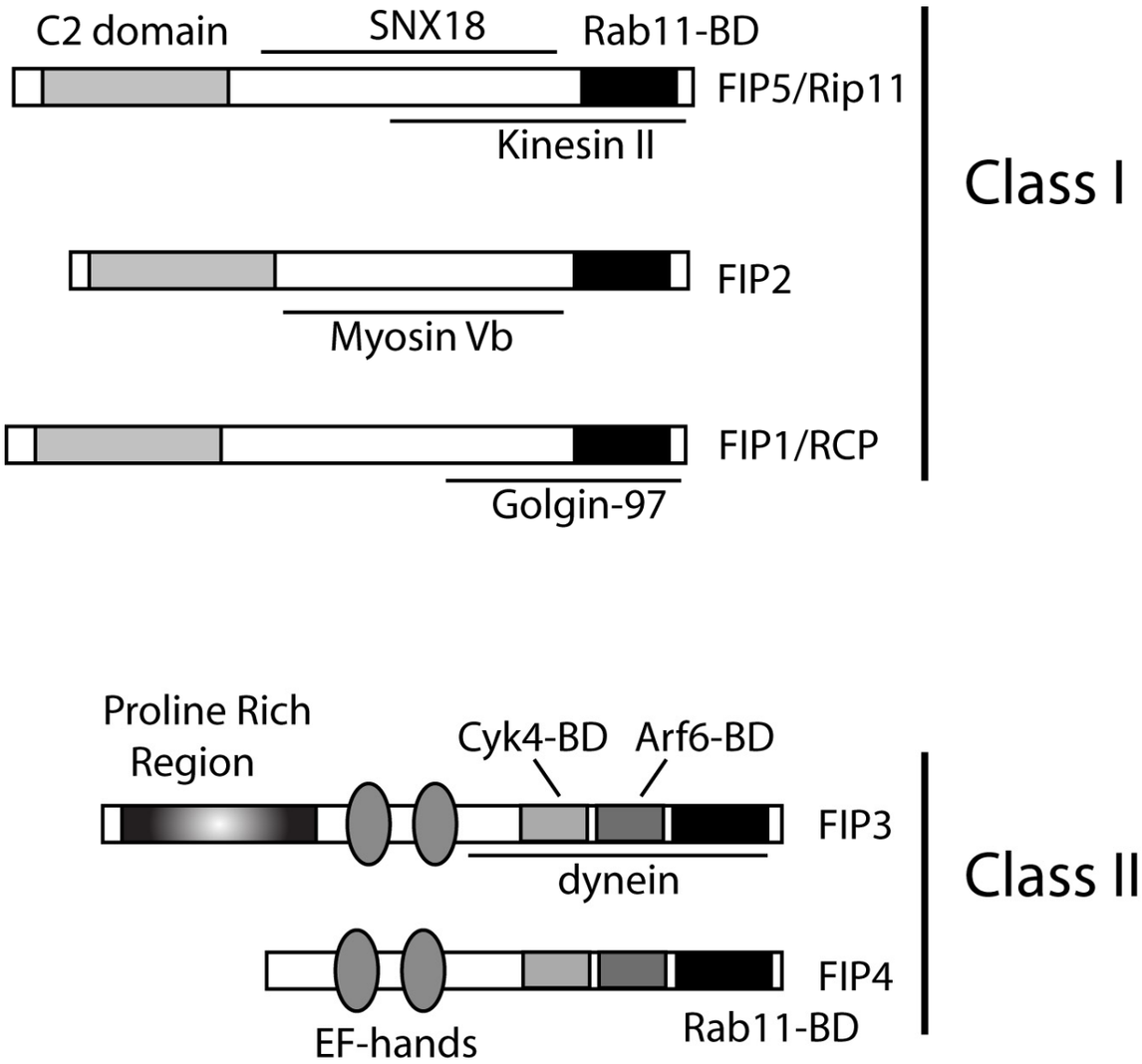

Fig. 1. The schematic representation of mammalian Rab11-FIP family members. Rab11-BD stands for Rab11-binding domain. Lines indicate binding domains mediating interactions with various FIP-binding proteins.

As a result, recycling endosomes enriched at the cleavage furrow, are often referred to as FIP3-endosomes (Schiel et al., 2011). Recent work from many laboratories on FIP3-endosome dynamics during cell division has identified the machinery that allows the targeting and accumulation of FIP3-endosomes close to the midbody of the dividing cells. It was shown that FIP3-endosomes are delivered to the cleavage furrow along central spindle microtubules in a kinesin-dependent manner. An elegant study by Dr. Chavrier and colleagues showed that the directionality of recycling endosome transport along central spindle microtubules depends on the differential association of endosomes with either the Kinesin I or dynein molecular motors (Montagnac et al., 2009). Interestingly, some evidence suggests that FIP3 may directly bind to dynein via an association with the dynein light intermediate chain 2 (Horgan et al., 2010). Once delivered to the cleavage furrow, FIP3-endosomes accumulate at close proximity to the midbody, a step that is required for the

completion of cytokinesis (Wilson et al., 2004). This accumulation depends on two distinct tethering mechanisms. It was indicated that FIP3 can directly bind to Cyk4/MgcRacGAP, and that this interaction is required for the efficient targeting of FIP3-endosomes (Simon et al., 2008). Cyk4 is a subunit of the Centralspindlin complex that is localized at the midbody during cytokinesis (Glotzer, 2005). In addition, FIP3 also was shown to bind Arf6 GTPase, an endocytic protein that is known to be required for cytokinesis (Hickson et al., 2003; Schonteich et al., 2007). Interestingly, Arf6 also binds the Sec10 subunit of the exocyst complex (Prigent et al., 2003). Rab11 was also shown to bind the exocyst complex via its Sec15 subunit (Wu et al., 2005). Thus Rab11/FIP3-containing endosomes can interact with the Exocyst tethering complex in at least two distinct binding interfaces. Why do FIP3-endosomes need a multiple protein-protein interactions to be targeted to the midbody? One possibility is that all of these targeting proteins work as the 'belt and braces' to ensure the fidelity of FIP3-endosome transport and targeting.

2.3 Rab35-endosomes

In addition to Rab11, Rab35 also recently emerged as a potential regulator of endosomes during mitotic cell division. The possible involvement of Rab35 in regulating cytokinesis was first uncovered during a non-biased Rab siRNA library screen for cell division defects in *Drosophila* tissue culture cells, and later was confirmed to also be required for cytokinesis in mammalian cells as well (Kouranti et al., 2006). Just like Rab11, Rab35 appears to act during the late stages of cytokinesis, since cells expressing the dominant-negative Rab35 mutant can still form and ingress a cleavage furrow, but fail to undergo abscission (Kouranti et al., 2006). The function of Rab35 still remains to be fully understood, mostly due to the fact that Rab35 effector proteins are only beginning to be identified. Rab35 has been implicated in regulating endocytic transport during interphase as it is localized to the plasma membranes, clathrin coated pits and endosomes (Chesneau et al., 2012). Consequently, Rab35 was shown to bind EHD1 and regulate fast endocytic recycling of MHC class I and II, components of the immunological synapse, and some synaptic proteins (Allaire et al., 2010; Walseng et al., 2008). Rab35 was also shown to bind fascin, a known actin cross-linking protein (Zhang et al., 2009). Consistent with this finding, Rab35 was suggested to regulate actin polymerization/bundling during neurite outgrowth, phagocytosis and cell motility (Chevallier et al., 2009; Egami et al., 2011; Kanno et al., 2010). The exact function of Rab35 during cytokinesis remains to be fully understood, however, it was proposed that it also may regulate the actin cytockeleton within the cleavage furrow (see below) (Dambournet et al., 2011; Kouranti et al., 2006).

3. The role of endosomes in regulating PI3P, PI(4,5)P2 and the actin cytoskeleton during cell division

Phosphoinositides (PIs) are well-established regulators of cytokinesis. It has been demonstrated by work in many laboratories that phosphoinositide 4-5 bisphosphate (PI(4,5)P2) is enriched at the ingressing cleavage furrow (Field et al., 2005). Inhibition of PI(4,5)P2 production by overexpressing a kinase-dead PI4P5-kinase leads to an increase in multinucleation, an indication of failed cytokinesis (Emoto and Umeda, 2000; Field et al., 2005). Two enzymes, phosphatase and tensin homologue on chromosome 10 (PTEN) and PI3-kinase, which regulate PI(4,5)P2 and PI(3,4,5)P3 levels, are required for cytokinesis

(Janetopoulos and Devreotes, 2006; Nezis et al., 2010). Interestingly, endosomes have recently emerged as important modulators of PI(4,5)P2 during cell division. For example, Vps34 (PI3-kinase C3) is delivered to the cleavage furrow by associating with Rab11-containing endosomes (Nezis et al., 2010). Several PI3K-III accessory proteins, such as Becklin 1, Vps15, UVRAG and BIF1 were all shown to be associated with endosomes and required for cytokinesis (Nezis et al., 2010). PI4P5-kinase was also shown to bind and be activated by Arf6, a protein which is targeted to the midbody by binding to the exocyst complex and FIP3/Rab11 (Hickson et al., 2003; Schonteich et al., 2007). Finally, Rab35 was shown to bind and recruit to the furrow a protein called phosphoinositide 5-phosphatase OCRL, that is responsible for a genetic disease oculocerebral syndrome of Lowe (Dambournet et al., 2011). This evidence clearly demonstrates that the cellular levels of PIs at the furrow are tightly regulated, and relay on several independent pathways that must coordinate with each other during mitotic progression. The actin cytoskeleton is one of the key players during cytokinesis. Classically, cytokinesis is defined as occurring through the formation and contraction of the actomyosin contractile ring at the equator of the cell. Initial actomyosin ring assembly and activation is regulated by RhoA GTPase and appears to be independent of endocytic transport, since the inhibition of either Rab11 or Rab35-dependent membrane delivery does not prevent the initial cleavage furrow ingression (Dambournet et al., 2011; Wilson et al., 2004). In late cytokinesis, the role of the actin cytoskeleton is less clearly defined. Actin appears to be required for the initial stabilization of the intracellular bridge, presumably by binding to a septin network via anillin adaptor proteins (Piekny and Maddox, 2010). Actin filaments also associate with the plasma membrane at the furrow by binding to the ezrin/radixin/moesin family of proteins, which bind directly with the plasma membrane (Kunda et al., 2008; Kunda et al., 2011). Finally, it is generally accepted that the actin cytoskeleton needs to be disassembled for the final abscission step to take place, however the machinery that regulates this final disassembly remains unclear. Interestingly, Rab35 appears to mediate the delivery of OCRL to the furrow only during late cytokinesis (Dambournet et al., 2011). Thus, it was postulated that OCRL may be responsible for the final disassembly of the actin cytoskeleon by depleting PI(4,5)P2 levels at the furrow. Consistent with this, it was demonstrated that a delay in abscission resulting from the depletion of OCRL or Rab35 can be rescued by incubating dividing cells with low concentrations of the actin depolymerizing agent, latrunculin-A (Dambournet et al., 2011). In addition to Rab35, Rab11 and FIP3 also appear to play a role in regulating the actin cytoskeleton during cytokinesis. Inhibition of *Drosophila* homologue of FIP3, nuclear fallout protein (Nuf), resulted in a very dramatic reorganization of the actin cytoskeleton within cleavage furrows (Riggs et al., 2007; Riggs et al., 2003). While the mechanisms that mediate Rab11 and FIP3 effects on actin remains to be determined, new data suggest that FIP3-containing endosomes deliver p50RhoGAP to the cleavage furrow (unpublished data). Since p50RhoGAP inactivates RhoA GTPase (Barrett et al., 1997; Sirokmany et al., 2006; Zhou et al., 2010), it is tempting to speculate that the targeting of FIP3 endosomes to the furrow may result in the inactivation of RhoA, and the subsequent depolymerization of the actin cytoskeleton.

4. ESCRTs and cytokinesis

Recently work from several laboratories has implicated the endosomal sorting complex required for transport (ESCRT) proteins in mediating the abscission step of cytokinesis. The

ESCRT proteins were originally identified as proteins involved in protein sorting to the lysosomes and in the formation of intraluminal vesicles during the maturation of multivesicular bodies. The ESCRT complex consists of four different protein complexes: ESCRT-0, ESCRT-I, ESCRT-II and ESCRT-III. While ESCRT-0 and ESCRT-I are involved in cargo recognition and sorting, ESCRT-II and ESCRT-III seem to play a role in initial vesicle formation (Wollert and Hurley, 2010). Finally, ESCRT-III appears to mediate the final scission of intraluminal vesicles (Wollert and Hurley, 2010). Since intraluminal vesicle scission is topologically similar to the scission of the intracellular bridge during cytokinesis, it was proposed that ESCRT proteins may mediate the abscission step of cytokinesis (Carlton et al., 2008; Carlton and Martin-Serrano, 2007).

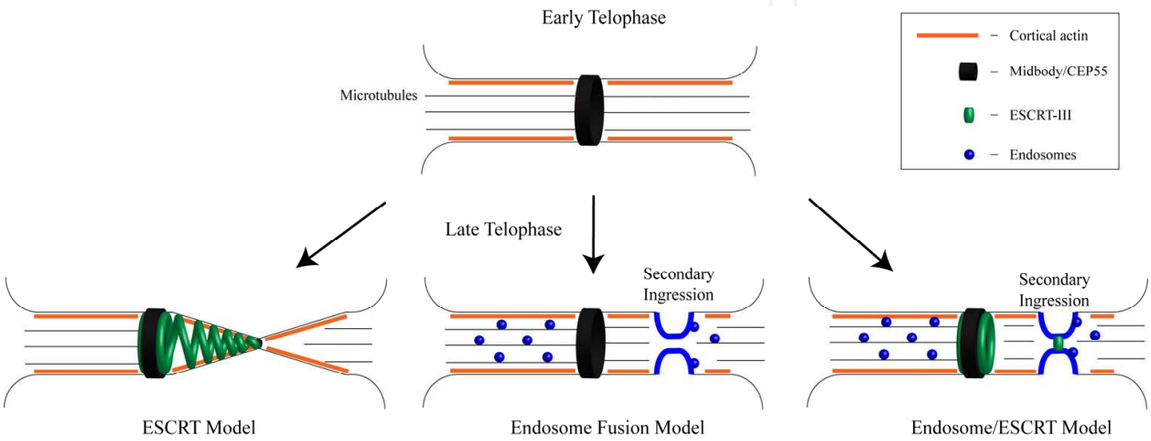

Fig. 2. Models for ESCRT and endosome roles during abscission.

Indeed, knock-down of various ESCRT-II and ESCRT-III members result in the inhibition of abscission, while having no effect on initial cleavage furrow ingression (Caballe and Martin-Serrano, 2011). Interestingly, ESCRT-dependent abscission does not require ESCRT-0 and ESCRT-I complexes (Hurley, 2010; Samson et al., 2008). Instead, ESCRT-III is recruited to the midbody of the cleavage furrow by binding to ALIX or Tsg101 proteins, which accumulate at the midbody by interacting with well-established midbody protein CEP55 (Caballe and Martin-Serrano, 2011). The actual scission step is mediated by the ESCRT-III complex subunit CHMP4. CHMP4 has the ability to form ~5 nm filaments and tubulate liposomes *in vitro* (Ghazi-Tabatabai et al., 2008; Lata et al., 2008). Since abscission usually occurs outside the midbody, it was postulated that CHMP4 is recruited to the midbody, where it polymerizes to form continuous spiral filaments that induces a gradual decrease in the diameter of the ICB and eventually leads to the scission of the membranes (Elia et al., 2011; Guizetti et al., 2011) (Figure 2, ESCRT model). While the discovery of ESCRT involvement in abscission does provide the novel conceptual framework for the mechanism of abscission, many questions remain to be answered. ESCRT complexes usually mediate scission of the membrane tubes that are about 24-50 nm in diameter. Consistent with this, it was shown that the ESCRT-III complex associate with the high-curvature (>100 nm) membranes (Fyfe et al., 2011). Thus, it remains unclear how the ESCRT-III polymers can form and contract intracellular bridges that are 2-3 mm in size (Schiel et al., 2011). Furthermore, the stability of the ICB is maintained by a complex cortical network consisting of actin and septin filaments, which are cross-linked to each other and to the plasma membrane by anillin. How the

ESCRT-III "spirals" are formed in the presence of these cytoskeletal elements remains a mystery. Some of these questions may be explained by recent findings that endosome delivery and fusion with the plasma membrane of the intracellular bridge may induce the disassembly of the actin cytoskeleton and lead to the secondary ingression that decreases the diameter of the intracellular bridge to ~100-200 nm (Dambournet et al., 2011; Schiel et al., 2011). Perhaps this endosome-dependent secondary ingression initiates the "de novo" recruitment of activated ESCRT-III to the abscission site by removing the actin cytoskeleton and narrowing the ICB to a smaller size (Figure 2, Endosome/ESCRT model) (Schiel and Prekeris, 2011). Indeed, while accumulation of the ESCRT-III at the abscission site can be readily detected, most recent studies have failed to observe an ESCRT "spiral" emanating from the midbody and continuing to the abscission site (Elia et al., 2011; Schiel et al., 2011).

5. Conclusions and future objectives

Work from multiple laboratories in the last few years has significantly advanced our understanding about the core machinery of the abscission step of cytokinesis. All these data have demonstrated that cell abscission is an immensely complicated event that involves coordinated changes in membrane transport, microtubules, the actin cytoskeleton, septin filaments and the ESCRT complexes. How all these components are regulated, and what the mechanisms of the cross-talk between them may be, remain completely unknown and will be the focus of future studies. One of the biggest problems in studying the spatiotemporal dynamics of various cellular components during cell division has been the inability to visualize the individual organelles or cytoskeletal elements within the intracellular bridge, due to the resolution limits of the light microscopy. The emergence of novel super-resolution imaging techniques, such as photo-activated localization microscopy (PALM), stimulated emission depletion microscopy (STED) and correlation high-resolution tomography will allow us to begin addressing some of these questions and testing/combining multiple competing abscission models.

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7. References

Albertson, R., Cao, J., Hsieh, T.S., and Sullivan, W. (2008). Vesicles and actin are targeted to the cleavage furrow via furrow microtubules and the central spindle. J Cell Biol 181, 777-790.

Allaire, P.D., Marat, A.L., Dall'Armi, C., Di Paolo, G., McPherson, P.S., and Ritter, B. (2010). The Connecdenn DENN domain: a GEF for Rab35 mediating cargo-specific exit from early endosomes. Mol Cell 37, 370-382.

Barr, F.A., and Gruneberg, U. (2007). Cytokinesis: placing and making the final cut. Cell 131, 847-860.

Barrett, T., Xiao, B., Dodson, E.J., Dodson, G., Ludbrook, S.B., Nurmahomed, K., Gamblin, S.J., Musacchio, A., Smerdon, S.J., and Eccleston, J.F. (1997). The structure of the GTPase-activating domain from p50rhoGAP. Nature 385, 458-461.

Bluemink, J.G., and de Laat, S.W. (1973). New membrane formation during cytokinesis in normal and cytochalasin B-treated eggs of Xenopus laevis. I. Electron microscope observations. J Cell Biol 59, 89-108.

Boucrot, E., and Kirchhausen, T. (2007). Endosomal recycling controls plasma membrane area during mitosis. Proc Natl Acad Sci U S A 104, 7939-7944.

Caballe, A., and Martin-Serrano, J. (2011). ESCRT machinery and cytokinesis: the road to daughter cell separation. Traffic 12, 1318-1326.

Carlton, J.G., Agromayor, M., and Martin-Serrano, J. (2008). Differential requirements for Alix and ESCRT-III in cytokinesis and HIV-1 release. Proc Natl Acad Sci U S A 105, 10541-10546.

Carlton, J.G., and Martin-Serrano, J. (2007). Parallels between cytokinesis and retroviral budding: a role for the ESCRT machinery. Science 316, 1908-1912.

Chesneau, L., Dambournet, D., Machicoane, M., Kouranti, I., Fukuda, M., Goud, B., and Echard, A. (2012). An ARF6/Rab35 GTPase Cascade for Endocytic Recycling and Successful Cytokinesis. Curr Biol.

Chevallier, J., Koop, C., Srivastava, A., Petrie, R.J., Lamarche-Vane, N., and Presley, J.F. (2009). Rab35 regulates neurite outgrowth and cell shape. FEBS Lett 583, 1096-1101.

Dambournet, D., Machicoane, M., Chesneau, L., Sachse, M., Rocancourt, M., El Marjou, A., Formstecher, E., Salomon, R., Goud, B., and Echard, A. (2011). Rab35 GTPase and OCRL phosphatase remodel lipids and F-actin for successful cytokinesis. Nat Cell Biol 13, 981-988.

Eathiraj, S., Mishra, A., Prekeris, R., and Lambright, D.G. (2006). Structural Basis for Rab11-mediated Recruitment of FIP3 to Recycling Endosomes. J Mol Biol 364, 121-135.

Egami, Y., Fukuda, M., and Araki, N. (2011). Rab35 regulates phagosome formation through recruitment of ACAP2 in macrophages during FcgammaR-mediated phagocytosis. J Cell Sci 124, 3557-3567.

Elia, N., Sougrat, R., Spurlin, T.A., Hurley, J.H., and Lippincott-Schwartz, J. (2011). Dynamics of endosomal sorting complex required for transport (ESCRT) machinery during cytokinesis and its role in abscission. Proc Natl Acad Sci U S A 108, 4846-4851.

Emoto, K., and Umeda, M. (2000). An essential role for a membrane lipid in cytokinesis. Regulation of contractile ring disassembly by redistribution of phosphatidylethanolamine. J Cell Biol 149, 1215-1224.

Field, S.J., Madson, N., Kerr, M.L., Galbraith, K.A., Kennedy, C.E., Tahiliani, M., Wilkins, A., and Cantley, L.C. (2005). PtdIns(4,5)P2 functions at the cleavage furrow during cytokinesis. Curr Biol 15, 1407-1412.

Fielding, A.B., Schonteich, E., Matheson, J., Wilson, G., Yu, X., Hickson, G.R., Srivastava, S., Baldwin, S.A., Prekeris, R., and Gould, G.W. (2005). Rab11-FIP3 and FIP4 interact with Arf6 and the exocyst to control membrane traffic in cytokinesis. Embo J 24, 3389-3399.

Fyfe, I., Schuh, A.L., Edwardson, J.M., and Audhya, A. (2011). Association of the endosomal sorting complex ESCRT-II with the Vps20 subunit of ESCRT-III generates a

curvature-sensitive complex capable of nucleating ESCRT-III filaments. J Biol Chem 286, 34262-34270.

Ghazi-Tabatabai, S., Saksena, S., Short, J.M., Pobbati, A.V., Veprintsev, D.B., Crowther, R.A., Emr, S.D., Egelman, E.H., and Williams, R.L. (2008). Structure and disassembly of filaments formed by the ESCRT-III subunit Vps24. Structure 16, 1345-1356.

Glotzer, M. (2005). The molecular requirements for cytokinesis. Science 307, 1735-1739.

Gromley, A., Yeaman, C., Rosa, J., Redick, S., Chen, C.T., Mirabelle, S., Guha, M., Sillibourne, J., and Doxsey, S.J. (2005). Centriolin anchoring of exocyst and SNARE complexes at the midbody is required for secretory-vesicle-mediated abscission. Cell 123, 75-87.

Guizetti, J., Schermelleh, L., Mantler, J., Maar, S., Poser, I., Leonhardt, H., Muller-Reichert, T., and Gerlich, D.W. (2011). Cortical constriction during abscission involves helices of ESCRT-III-dependent filaments. Science 331, 1616-1620.

Hales, C.M., Griner, R., Hobdy-Henderson, K.C., Dorn, M.C., Hardy, D., Kumar, R., Navarre, J., Chan, E.K., Lapierre, L.A., and Goldenring, J.R. (2001). Identification and characterization of a family of Rab11-interacting proteins. J Biol Chem 276, 39067-39075.

Hickson, G.R.X., Matheson, J., Riggs, B., Maier, V.H., Fielding, A.B., Prekeris, R., Sullivan, W., Barr, F.A., and Gould, G.W. (2003). Arfophilins are dual Arf/Rab11 binding proteins that regulate recycling endosome distribution and are related to Drosophila nuclear fallout. Molecular Biology of the Cell 14, 2908-2920.

Horgan, C.P., Hanscom, S.R., Jolly, R.S., Futter, C.E., and McCaffrey, M.W. (2010). Rab11-FIP3 links the Rab11 GTPase and cytoplasmic dynein to mediate transport to the endosomal-recycling compartment. J Cell Sci 123, 181-191.

Horgan, C.P., Walsh, M., Zurawski, T.H., and McCaffrey, M.W. (2004). Rab11-FIP3 localises to a Rab11-positive pericentrosomal compartment during interphase and to the cleavage furrow during cytokinesis. Biochem Biophys Res Commun 319, 83-94.

Hsu, S.C., Hazuka, C.D., Foletti, D.L., and Scheller, R.H. (1999). Targeting vesicles to specific sites on the plasma membrane: the role of the sec6/8 complex. Trends Cell Biol 9, 150-153.

Hurley, J.H. (2010). The ESCRT complexes. Crit Rev Biochem Mol Biol 45, 463-487.

Jagoe, W.N., Lindsay, A.J., Read, R.J., McCoy, A.J., McCaffrey, M.W., and Khan, A.R. (2006). Crystal structure of rab11 in complex with rab11 family interacting protein 2. Structure 14, 1273-1283.

Janetopoulos, C., and Devreotes, P. (2006). Phosphoinositide signaling plays a key role in cytokinesis. J Cell Biol 174, 485-490.

Junutula, J.R., Schonteich, E., Wilson, G.M., Peden, A.A., Scheller, R.H., and Prekeris, R. (2004). Molecular characterization of Rab11 interactions with members of the family of Rab11-interacting proteins. J Biol Chem 279, 33430-33437.

Jurgens, G. (2005). Plant cytokinesis: fission by fusion. Trends Cell Biol 15, 277-283.

Kanno, E., Ishibashi, K., Kobayashi, H., Matsui, T., Ohbayashi, N., and Fukuda, M. (2010). Comprehensive screening for novel rab-binding proteins by GST pull-down assay using 60 different mammalian Rabs. Traffic 11, 491-507.

Kouranti, I., Sachse, M., Arouche, N., Goud, B., and Echard, A. (2006). Rab35 regulates an endocytic recycling pathway essential for the terminal steps of cytokinesis. Curr Biol 16, 1719-1725.

Kunda, P., Pelling, A.E., Liu, T., and Baum, B. (2008). Moesin controls cortical rigidity, cell rounding, and spindle morphogenesis during mitosis. Curr Biol 18, 91-101.

Kunda, P., Rodrigues, N.T., Moeendarbary, E., Liu, T., Ivetic, A., Charras, G., and Baum, B. (2011). PP1-Mediated Moesin Dephosphorylation Couples Polar Relaxation to Mitotic Exit. Curr Biol.

Lata, S., Schoehn, G., Jain, A., Pires, R., Piehler, J., Gottlinger, H.G., and Weissenhorn, W. (2008). Helical structures of ESCRT-III are disassembled by VPS4. Science 321, 1354-1357.

Low, S.H., Li, X., Miura, M., Kudo, N., Quinones, B., and Weimbs, T. (2003). Syntaxin 2 and endobrevin are required for the terminal step of cytokinesis in mammalian cells. Dev Cell 4, 753-759.

Montagnac, G., Sibarita, J.B., Loubery, S., Daviet, L., Romao, M., Raposo, G., and Chavrier, P. (2009). ARF6 Interacts with JIP4 to control a motor switch mechanism regulating endosome traffic in cytokinesis. Curr Biol 19, 184-195.

Nezis, I.P., Sagona, A.P., Schink, K.O., and Stenmark, H. (2010). Divide and ProsPer: the emerging role of PtdIns3P in cytokinesis. Trends Cell Biol 20, 642-649.

Pelissier, A., Chauvin, J.P., and Lecuit, T. (2003). Trafficking through Rab11 endosomes is required for cellularization during Drosophila embryogenesis. Curr Biol 13, 1848-1857.

Piekny, A.J., and Maddox, A.S. (2010). The myriad roles of Anillin during cytokinesis. Semin Cell Dev Biol 21, 881-891.

Prekeris, R. (2003). Rabs, Rips, FIPs, and Endocytic Membrane Traffic. ScientificWorldJournal 3, 870-880.

Prekeris, R., and Gould, G.W. (2008). Breaking up is hard to do - membrane traffic in cytokinesis. J Cell Sci 121, 1569-1576.

Prekeris, R., Davies, J.M., and Scheller, R.H. (2001). Identification of a novel Rab11/25 binding domain present in Eferin and Rip proteins. J Biol Chem 276, 38966-38970.

Prigent, M., Dubois, T., Raposo, G., Derrien, V., Tenza, D., Rosse, C., Camonis, J., and Chavrier, P. (2003). ARF6 controls post-endocytic recycling through its downstream exocyst complex effector. J Cell Biol 163, 1111-1121.

Riggs, B., Fasulo, B., Royou, A., Mische, S., Cao, J., Hays, T.S., and Sullivan, W. (2007). The concentration of Nuf, a Rab11 effector, at the microtubule-organizing center is cell cycle regulated, dynein-dependent, and coincides with furrow formation. Mol Biol Cell 18, 3313-3322.

Riggs, B., Rothwell, W., Mische, S., Hickson, G.R., Matheson, J., Hays, T.S., Gould, G.W., and Sullivan, W. (2003). Actin cytoskeleton remodeling during early Drosophila furrow formation requires recycling endosomal components Nuclear-fallout and Rab11. J Cell Biol 163, 143-154.

Samson, R.Y., Obita, T., Freund, S.M., Williams, R.L., and Bell, S.D. (2008). A role for the ESCRT system in cell division in archaea. Science 322, 1710-1713.

Schiel, J.A., and Prekeris, R. (2011). ESCRT or endosomes?: Tales of the separation of two daughter cells. Commun Integr Biol 4, 606-608.

Schiel, J.A., Park, K., Morphew, M.K., Reid, E., Hoenger, A., and Prekeris, R. (2011). Endocytic membrane fusion and buckling-induced microtubule severing mediate cell abscission. J Cell Sci 124, 1411-1424.

Schonteich, E., Pilli, M., Simon, G.C., Matern, H.T., Junutula, J.R., Sentz, D., Holmes, R.K., and Prekeris, R. (2007). Molecular characterization of Rab11-FIP3 binding to ARF GTPases. Eur J Cell Biol 86, 417-431.

Simon, G.C., Schonteich, E., Wu, C.C., Piekny, A., Ekiert, D., Yu, X., Gould, G.W., Glotzer, M., and Prekeris, R. (2008). Sequential Cyk-4 binding to ECT2 and FIP3 regulates cleavage furrow ingression and abscission during cytokinesis. Embo J.

Sirokmany, G., Szidonya, L., Kaldi, K., Gaborik, Z., Ligeti, E., and Geiszt, M. (2006). Sec14 homology domain targets p50RhoGAP to endosomes and provides a link between Rab and Rho GTPases. J Biol Chem 281, 6096-6105.

Skop, A.R., Bergmann, D., Mohler, W.A., and White, J.G. (2001). Completion of cytokinesis in C. elegans requires a brefeldin A-sensitive membrane accumulation at the cleavage furrow apex. Curr Biol 11, 735-746.

TerBush, D.R., Maurice, T., Roth, D., and Novick, P. (1996). The Exocyst is a multiprotein complex required for exocytosis in Saccharomyces cerevisiae. Embo J 15, 6483-6494.

Walseng, E., Bakke, O., and Roche, P.A. (2008). Major histocompatibility complex class II-peptide complexes internalize using a clathrin- and dynamin-independent endocytosis pathway. J Biol Chem 283, 14717-14727.

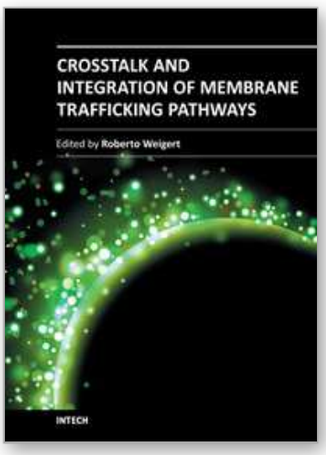
Wilson, G.M., Fielding, A.B., Simon, G.C., Yu, X., Andrews, P.D., Peden, A.A., Gould, G.W., and Prekeris, R. (2004). The FIP3-Rab11 Protein Complex Regulates Recycling Endosome Targeting to the Cleavage Furrow during Late Cytokinesis. Mol Biol Cell.

Wollert, T., and Hurley, J.H. (2010). Molecular mechanism of multivesicular body biogenesis by ESCRT complexes. Nature 464, 864-869.

Wu, S., Mehta, S.Q., Pichaud, F., Bellen, H.J., and Quiocho, F.A. (2005). Sec15 interacts with Rab11 via a novel domain and affects Rab11 localization in vivo. Nat Struct Mol Biol 12, 879-885.

Zhang, J., Fonovic, M., Suyama, K., Bogyo, M., and Scott, M.P. (2009). Rab35 controls actin bundling by recruiting fascin as an effector protein. Science 325, 1250-1254.

Zhou, Y.T., Chew, L.L., Lin, S.C., and Low, B.C. (2010). The BNIP-2 and Cdc42GAP homology (BCH) domain of p50RhoGAP/Cdc42GAP sequesters RhoA from inactivation by the adjacent GTPase-activating protein domain. Mol Biol Cell 21, 3232-3246.



Crosstalk and Integration of Membrane Trafficking Pathways
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Membrane traffic is a broad field that studies the complex exchange of membranes that occurs inside the cell. Protein, lipids and other molecules traffic among intracellular organelles, and are delivered to, or transported from the cell surface by virtue of membranous carriers generally referred as "transport intermediates". These carriers have different shapes and sizes, and their biogenesis, modality of transport, and delivery to the final destination are regulated by a multitude of very complex molecular machineries. A concept that has clearly emerged in the last decade is that each membrane pathway does not represent a close system, but is fully integrated with all the other trafficking pathways. The aim of this book is to provide a general overview of the extent of this crosstalk.

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