Published in final edited form as:
Traffic. 2013 December ; 14(12): . doi:10.1111/tra.12116.

Dynamin rings: not just for fission

Sanja Sever, **Joann Chang**, and **Changkyu Gu**
Massachusetts General Hospital, Nephrology Division, CNY 149 8.211, 149 13th Street, Charlestown, MA 02129

Abstract

The GTPase dynamin has captivated researchers for over two decades, even managing to establish its own research field. Dynamin's allure is partly due to its unusual biochemical properties as well as its essential role in multiple cellular processes, which include the regulation of clathrin-mediated endocytosis and of actin cytoskeleton. Based on the classic model, dynamin oligomerization into higher order oligomers such as rings and helices directly executes the final fission reaction in endocytosis, which results in the generation of clathrin-coated vesicles. Dynamin's role in the regulation of actin cytoskeleton is mostly explained by its interactions with a number of actin binding and regulating proteins; however, the molecular mechanism of dynamin's action continues to elude us. Recent insights into the mechanism and role of dynamin oligomerization in the regulation of actin polymerization point to a novel role for dynamin oligomerization in the cell.

Keywords

dynamin; actin; oligomerization; endocytosis; microtubules

Classical role of dynamin rings/helices: to directly execute fission

Dynamin was first isolated from a calf brain by Shpetner and Vallee in 1989. In their original manuscript, the authors showed that dynamin could induce microtubules to form hexagonally packed bundles (1). Specifically, Shpetner and Vallee noticed that in the presence of ATP and an activating fraction, microtubules appeared to slide. Together, these findings led the authors to suggest that there was a 100 kd mechanochemical enzyme (dynamin) that might mediate microtubule sliding *in vivo*. Cloning and sequencing of rat brain dynamin complementary DNA identified an N-terminal GTP-binding domain (2). The following year, the role of dynamin in endocytosis was established by identification of a dynamin homolog encoded by the Drosophila *shibire* gene (3). Subsequent insights then removed dynamin from the ATPase family and placed it into the GTPase family of enzymes essential for endocytosis, but the mechanochemical enzyme description survived the transition.

Biochemical analysis established that dynamin exists in an equilibrium between a homodimer (Dyn^{DIMER}) and a homotetramer (Dyn^{TETRA}) (4, 5), which can self assemble into higher order structures such as rings and helices (Dyn^{OLIGO}) (6). Oligomerization results in increased GTPase activity of dynamin (7). The widely accepted current model states that "GTPase dynamin catalyzes membrane fission by forming a collar around the necks of clathrin-coated pits" (8). Thus, based on the prevalent view, dynamin is a mechanochemical enzyme that uses GTP hydrolysis while in a helical structure to directly

Sanja Sever: ssever@partners.org.

execute the fission reaction at the plasma membrane. In the last twenty years, the dynamin field has focused on a major unanswered question regarding dynamin's role in the cell: "what specific structural interactions and conformational changes within dynamin collar around the necks of coated pits drive the fission reaction?" (8).

At present, there are several co-existing plausible molecular mechanisms by which Dyn^{OLIGO} executes the fission reaction, all of which have been extensively reviewed (9–11). We will mention only the cornerstones of this model. Dynamin's ability to form rings and helices around different lipid templates *in vitro* and clathrin-coated pits in cells has been comprehensively documented (12–15). Diverse biochemical assays in combination with structural studies demonstrated distinct conformational alterations within Dyn^{OLIGO} upon GTP hydrolysis (8, 13). The effects of these alterations on underlying lipid templates have been clearly demonstrated (10, 16) and supported by molecular modeling (16, 17). Use of total internal reflection fluorescence microscopy (TIRFM) further extended the *in vitro* observations by identifying a burst of dynamin fluorescence that coincides with the fission reaction (18). Since dynamin oligomerization is cooperative (7), it is logical to assign this burst in fluorescence to the formation of Dyn^{OLIGO}. Together, these studies provide compelling evidence for the role of Dyn^{OLIGO} in executing the fission reaction.

While Dyn^{OLIGO} is best known for its role in fission reaction, genetics (19), pharmacologics (20), live cell imaging studies (21) in conjunction with dynamin mutants (22, 23) clearly demonstrate that dynamin's GTPase activity regulates maturation of clathrin coated pits at the membrane. The GTPase activity of dynamin regulates its own oligomerization (7) and recruitment of endocytic proteins such as N-BAR proteins (18), endophilin and amphiphysin (24), chaperone machinery (25), actin (18), and actin binding proteins (18, 26) prior to the fission reaction. Therefore, the GTPase cycle of dynamin has been implicated at distinct steps during coated vesicle formation: formation of clathrin-coated pits (steps involved in maturation) and budding of coated pits from the membrane (final fission reaction) (22, 27, 28). Given the classical model, which states that dynamin oligomerization in endocytosis is membrane dependent, it was highly surprising that the actin-deploymerizating drug, Latrunculin B, dramatically abrogated the burst of dynamin fluorescence prior to fission as observed by TIRFM(18). This suggested for the first time that the observed pre-scission burst of dynamin fluorescence (which corresponds to formation of Dyn^{OLIGO}) might be dependent on actin dynamics. In addition, while acute inhibition of actin polymerization significantly decreased the incidence of scission, a significant amount of coated pits were still able to bud off in a dynamin-dependent manner in the absence of a burst of dynamin fluorescence (18). Consistent with this observation, the formation of clathrin-coated vesicles that originated from endosomes and the trans-Golgi network also proceeded without a burst of dynamin fluorescence prior to the fission reaction (29). It has been shown *in vitro* that the epsin N terminal homology (ENTH) domain caused extensive membrane vesiculation of liposomes, thus providing an alternative molecular mechanism for the fission reaction in the absence of dynamin oligomerization (30).

Dynamin as a regulator of actin cytoskeleton

Dynamin has been implicated in diverse actin driven processes such as lamellipodia (31), dorsal membrane ruffles (32), podosomes (33), invadopodia (34), comet tails (35, 36), and growth cones (37). Originally, dynamin's role in the regulation of actin cytoskeleton has been explained by its ability to alter endocytosis. Thus, dynamin has been shown to modulate localization of Rac, a canonical small GTPase that regulates actin cytoskeleton (31). Expression of a dominant negative form of dynamin, dyn^{K44A}, a mutant that cannot bind GTP and acts as a potent inhibitor of endocytosis, induced Rac mislocalization away from cell edges into abnormal dorsal ruffles, and resulted in increased total activity of Rac

(31). This alteration demonstrated that dynamin's GTPase activity had a role in the formation of lamellipodia and cell spreading, which was explained by dynamin's effect on localization and activity of Rac through its effect on endocytosis. Subsequent studies suggested an endocytosis-independent and GTPase-dependent mechanism by which dynamin regulates the actin cytoskeleton. Thus, expression of dyn^{K44A} significantly reduced formation of F-actin comets generated by either *Listeria* (36) or vesicles formed through overexpression of type I phosphatidylinositol 5-phosphate kinase (35). Neither process was dependent on endocytosis. Furthermore, when expressed in PtK1 cells, dyn^{K44A} decreased dynamics of the cortical actin followed by GFP-capping protein (GFP-CP) (38). GFP-CP, used as a probe for dynamic actin, labeled sites of actin assembly at foci within lamellae and at the periphery of PtK1 cells, locations also enriched in F-actin, Arp2/3 complex, and cortactin. Dynamin was found to partially co-localize with GFP-CP. Cells expressing dyn^{K44A} exhibited longer foci, suggesting impairment in actin disassembly, as well as local, transient burst of actin assembly at punctate structures, thus establishing the role of dynamin's GTPase activity in cycles of cortical actin polymerization and deplymerization in PtK1 cells.

Further expanding the role of the GTPase activity of dynamin in the regulation of actin cytoskeleton, it has been shown that expression of dyn^{K44A} decreased osteoclast resorption and migration (39). In contrast, overexpression of wild type dynamin increased these processes. Furthermore, dynamin's GTPase activity was implicated in the control of actin-driven remodeling at invadopodia (34). Invadopodia are specialized plasma membrane protrusions by which invasive cells make contact with the extracellular matrix, which induces its degradation by matrix metalloproteases. Expression of dyn^{K44A} resulted in drastically reduced extracellular matrix degradation at invadopodia by altering their morphology (34). In addition, depletion of dynamin in epithelial cells prevented establishment and maintenance of epithelial polarity (40). By comparison, expression of dyn^{K44A} resulted in dramatic apical constriction without disruption of polarity. Together, these compelling studies provided a distinct role for dynamin's GTPase cycle in the regulation of actin cytoskeleton at distinct sites in the cell that is independent from its role in endocytosis.

Since dynamin binds a number of actin-regulating and binding proteins, it has been suggested that GTPase activity of dynamin results in interactions with distinct effectors, which then differentially modulate actin cytoskeleton (40). Mooren and colleagues provided *in vitro* data supporting this model. They showed that in the presence of GTP, dynamin remodeled the actin filaments via its interactions with cortactin (actin binding protein) (41). Together, these data suggested a model in which GTP-hydrolysis induced conformational change within dynamin is transduced to cortactin, which in turn induces alterations in actin filaments. The main challenge to this molecular mechanism is the fact that interactions between dynamin's C-terminal proline, arginine-rich domain (PRD) and cortactin's Src homology 3 (SH3) domain (or any other SH3-domain containing protein) do not require GTP binding or hydrolysis of dynamin. In fact, they can occur with isolated dynamin and isolated SH3 domains of actin binding/regulatory proteins (42, 43). Thus, it is hard to envision how GTPase driven conformational changes within dynamin would affect actin binding/regulatory proteins. It has been well documented that PRD-SH3 interactions alter dynamin oligomerization *in vitro* and in cells. For example, cortactin and endophilin both promote dynamin oligomerization *in vitro* (41, 44) and it has been shown that endophilin A2 promotes dynamin assembly in cells (44). Thus, while it has been shown that SH3-domain containing proteins directly alter the dynamin oligomerization cycle, there are no data to suggest that dynamin oligomerization affects these interactions. It still remains to be answered how alterations in dynamin oligomerization cycle might regulate actin cytoskeleton.

Expanded role of dynamin rings: to regulate the actin cytoskeleton

In 2010, we reported direct interactions between dynamin and actin, which were mediated by conserved residues situated in the middle domain of dynamin (45). The affinity of dynamin for F-actin is ~ 0.4 μM, which is comparable to known actin-binding proteins such as α-actinin 4 or cortactin (46, 47). Dynamin's ability to bind actin filaments was independent of its oligomerization state or its ability to bind and hydrolyze GTP. One of our most surprising findings was the discovery that dynamin could remove actin capping protein gelsolin from the barbed ends, which allows for actin polymerization (45). The ability to remove gelsolin was dependent on dynamin oligomerization *in vitro*. Thus, dynamin was capable of removing gelsolin only if GTPγS, a non-hydrolysable analog of GTP, was present. In addition, oligomerized dynamin could remove gelsolin, but not CP (capping protein), suggesting specificity of dynamin's effect on actin capping proteins. While these *in vitro* data suggested that dynamin oligomerization might regulate actin polymerization in cells, our original study fell short of conclusively testing this hypothesis. However, by using dynamin mutants with altered actin binding affinities, we were able to show that direct dynamin-actin interactions are essential for global organization of the actin cytoskeleton in cultured podocytes (kidney cells that are involved in maintenance of the glomerular filter). Expression of a dynamin mutant with increased affinity for actin also resulted in an increased number of focal adhesions and stress fibers, consistent with dynamin's ability to stimulate actin polymerization *in vitro* (45).

While we focused on the role of dynamin-actin interactions in formation of focal adhesions and stress fibers, dynamin has also been implicated in the regulation of cortical actin cytoskeleton. Dorothy Schafer and John Cooper showed that dynamin influences actin nucleation by purified Arp2/3 complex and cortactin *in vitro* in a biphasic manner (38). Low concentrations of dynamin enhanced actin nucleation by Arp2/3 complex and cortactin, whereas high concentrations were inhibitory. Since dynamin oligomerization is concentration dependent and promoted by cortactin, these data indirectly implicate the role of dynamin oligomerization in the regulation of cortical actin nucleation.

We have suggested that dynamin releases gelsolin through dynamin's effect on the geometry/twist of actin filaments (45). A similar role by dynamin might be at work in Arp2/3 driven cortactin-dependent actin nucleation (38). Actin filaments have complex mechanical properties and internal motions (bending, twisting, and subunit dynamics), which occur on different time and length scales (48). Modulation of filament bending and twisting dynamics has been linked to regulatory actin-binding protein function, filament assembly, and overall cell motility. For example, binding of cofilin, an actin binding protein that disassembles actin filaments, to F-actin results in a change in filament twist, thus excluding binding of phalloidin, another actin-binding molecule (49). A similar effect has been shown for gelsolin, whose binding to filament ends results in phalloidin displacement (50).

The striking images of oligomerized dynamin wrapped around lipid templates provided insight into conformational changes in dynamin upon hydrolysis (8). They also suggest a distinct mechanism by which alterations in the conformation of oligomerized dynamin can influence the underlying membrane (16). New studies will tell us whether these insights also apply to the molecular mechanism by which dynamin alters filament geometry. By altering filament twist in an oligomerization dependent manner, dynamin might promote formation of a distinct population of actin filaments with unique conformations, which bind or release a specific set of actin binding and regulatory proteins. Modifying filament twist by an oligomerization dependent manner would provide an elegant molecular mechanism that could be used at multiple sites in cells depending on the cell type. Thus, the specificity and

effect of dynamin on diverse actin dynamics would depend on its interactions with actin binding and regulatory proteins via alterations of its oligomerization cycle (Summary figure).

Testing this model will require an array of novel experimental approaches in addition to the well-established dynamin assays. Biophysical assays and models developed to study actin filaments twisting and bending motions should be at the top of this list. Until now, dynamin oligomerization was only followed on the membrane, thus TIRFM was the technique of choice. Given that dynamin-actin interactions are most likely highly dynamic, single molecule TIRFM using recombinant proteins could also provide essential insights into real time dynamics of these interactions. Fluorescence lifetime imaging microscopy technique, which has been successful in studying the formation of oligomeric complexes in live cells (51), presents one of the possible new techniques to follow dynamin oligomerization in an actin-dependent manner in cells. Development of novel small molecules that promote and inhibit dynamin oligomerization will be essential tools to study the role of dynamin oligomerization cells. The role of dynamin oligomerization in endocytosis with a focus on its effects on actin dynamics is also worth revisiting. GTP hydrolysis of dynamin remodels actin filaments nucleated by Arp2/3 complex and cortactin that were associated with PIP2 containing lipid vesicles *in vitro* (38), suggesting a role of dynamin in regulating actin cytoskeleton associated with endocytic structures at the membrane. The actin cytoskeleton has been implicated in formation of endocytic membrane curvature formation either by providing pushing forces that help by drawing neck membranes closer together or providing pulling forces that keep the neck under tension, and actin dynamics have been shown to be essential for dynamin oligomerization prior to fission (18). Interestingly, the peak of dynamin fluorescence transiently overlaps with the beginning of actin depolymerization during fission (52). Since dynamin effect on actin nucleation by Arp2/3 complex and cortactin is biphasic (38), it is possible that dynamin plays a dual role in the regulation of actin polymerization in endocytosis: activating at low dynamin concentrations and inhibiting when present as dyn^{OLIGO}. Supporting this role of dyn^{OLIGO} in regulating actin cytoskeleton in clathrin-mediated endocytosis, cells lacking dynamin exhibited an abundance of clathrin-coated pits (CCPs) associated with the plasma membrane by long, narrow tubules (53). Formation of these long tubules, which harbor CCPs on their ends, was dependent on actin polymerization (53). These data suggest that while the actin polymerization that drives membrane dynamics in the vicinity of CCPs is dynamin independent, the process is dis-regulated and futile. Given dynamin's ability to bind a number of actin binding proteins implicated in endocytosis, such as SNX 9 (54), it seems highly likely that dyn^{OLIGO} is involved in spatial and temporal regulation of the actin assembly during endocytosis.

Is there a role for dynamin oligomerization in the regulation of microtubule dynamics?

Dynamin's role in the regulation of microtubule MT dynamics has been the least studied aspect of dynamin's role in cells. Although dynamin forms helices around MTs and the subsequent increase in the rate of GTP hydrolysis has been reported back in 1992 (55), these phenomenona have been mostly interpreted as *in vitro* artifacts. Yet, a growing body of evidence implicates dynamin in the regulation of microtubule-dependent cellular events such as cytokinesis (56), dynamic instability of microtubules (57), and centrosome cohesion (58). Dynamin was found to co-localize along microtubules at the spindle midzone (56), midbody (56), and cytoplasm (57). Recently, it has been observed that dynamin binds gamma tubulin via the middle domain of dynamin (58), the same domain we identified to bind actin filaments. Finally, it has been shown that dyn^{OLIGO} can induce formation of very

densely packed hexagonal bundles by wrapping around each adjacent microtubule (55), thus affecting MT higher-order organization.

The key insight that dynamin-MT interactions have an important role for MT organization in cells arose from studies of Charcot-Marie-Tooth (CMT) disease, a hereditary neuronal disorder. Dynamin 2 mutations found in CMT patients induced prominent decoration of microtubules with the mutant dynamin 2 protein and accompanied by a remarkable increase in microtubule acetylation, a marker of stable microtubules. Further supporting the role of dynamin in microtubule dynamics, depletion of endogenous dynamin 2 with a small interfering RNA in Cos 7 cells resulted in the accumulation of stable microtubules (57). In addition, formation of mature Golgi complexes, which depends on microtubule-dependent membrane transport, was also impaired in both dynamin 2 knockdown cells and cells expressing the dynamin 2 mutant. In contrast, dynamin 2 conditional knockdown mouse fibroblasts did not exhibit major alterations in morphology of mature Golgi complexes, though cells did exhibit increase in microtubule acetylation (59). Despite differences in phenotypes, which could be explained by the use of different cell types and experimental approaches, these data provide compelling support for dynamin's role in the regulation of microtubule dynamics. While the molecular mechanism by which dynamin regulates microtubule dynamics is still a mystery, it is seems reasonable to suggest that dyn^{OLIGO} might be involved, given dynamin's ability to form helices around microtubules.

Future outlook

The interaction between microtubules and actin is becoming a well accepted phenomenon that underlies many fundamental processes such as cell motility, cellular wound healing, cell division, and neuronal pathfinding (60). A growing number of proteins have been identified as candidates for mediating structural interactions between microtubules and actin. We propose dynamin and its oligomerization cycle as an ideal candidate that regulates the interplay between actin and microtubules. Given the fact that there are three dynamin isoforms and multiple dynamin binding partners, it is becoming increasingly evident that dynamin has multiple roles that must be investigated in physiological relevant contexts. Clearly, dynamin will continue to provide major challenges and to demand novel models in the future. What remains constant and essential in the dynamin field is to remain open minded and inquisitive.

Acknowledgments

This work was supported by the National Institutes of Health (R01 DK093773 to S.S.)

References

1. Shpetner HS, Vallee RB. Identification of dynamin, a novel mechanochemical enzyme that mediates interactions between microtubules. Cell. 1989; 59(3):421–432. [PubMed: 2529977]
2. Obar RA, Collins CA, Hammarback JA, Shpetner HS, Vallee RB. Molecular cloning of the microtubule-associated mechanochemical enzyme dynamin reveals homology with a new family of GTP-binding proteins. Nature. 1990; 347(6290):256–261. [PubMed: 2144893]
3. Van der Bliek AM, Meyerowitz EM. Dynamin-like protein encoded by the Drosophila shibire gene associated with vesicular traffic. Nature. 1991; 351(6325):411–414. [PubMed: 1674590]
4. Muhlberg AB, Warnock DE, Schmid SL. Domain structure and intramolecular regulation of dynamin GTPase. The EMBO journal. 1997; 16(22):6676–6683. [PubMed: 9362482]
5. Faelber K, Posor Y, Gao S, Held M, Roske Y, Schulze D, et al. Crystal structure of nucleotide-free dynamin. Nature. 2011; 477(7366):556–560. [PubMed: 21927000]
6. Hinshaw JE, Schmid SL. Dynamin self-assembles into rings suggesting a mechanism for coated vesicle budding. Nature. 1995; 374(6518):190–192. [PubMed: 7877694]

7. Warnock DE, Hinshaw JE, Schmid SL. Dynamin self-assembly stimulates its GTPase activity. The Journal of biological chemistry. 1996; 271(37):22310–22314. [PubMed: 8798389]
8. Chappie JS, Mears JA, Fang S, Leonard M, Schmid SL, Milligan RA, et al. A pseudoatomic model of the dynamin polymer identifies a hydrolysis-dependent powerstroke. Cell. 2011; 147(1):209–222. [PubMed: 21962517]
9. Ramachandran R. Vesicle scission: dynamin. Seminars in cell & developmental biology. 2011; 22(1):10–17. [PubMed: 20837154]
10. Schmid SL, Frolov VA. Dynamin: functional design of a membrane fission catalyst. Annual review of cell and developmental biology. 2011; 27:79–105.
11. Morlot S, Roux A. Mechanics of Dynamin-Mediated Membrane Fission. Annual review of biophysics. 2013
12. Hinshaw JE. Dynamin and its role in membrane fission. Annual review of cell and developmental biology. 2000; 16:483–519.
13. Marks B, Stowell MH, Vallis Y, Mills IG, Gibson A, Hopkins CR, et al. GTPase activity of dynamin and resulting conformation change are essential for endocytosis. Nature. 2001; 410(6825):231–235. [PubMed: 11242086]
14. Zhang P, Hinshaw JE. Three-dimensional reconstruction of dynamin in the constricted state. Nature cell biology. 2001; 3(10):922–926.
15. Praefcke GJ, McMahon HT. The dynamin superfamily: universal membrane tubulation and fission molecules? Nature reviews Molecular cell biology. 2004; 5(2):133–147.
16. Shnyrova AV, Bashkirov PV, Akimov SA, Pucadyil TJ, Zimmerberg J, Schmid SL, et al. Geometric catalysis of membrane fission driven by flexible dynamin rings. Science. 2013; 339(6126):1433–1436. [PubMed: 23520112]
17. Graham TR, Kozlov MM. Interplay of proteins and lipids in generating membrane curvature. Current opinion in cell biology. 2010; 22(4):430–436. [PubMed: 20605711]
18. Taylor MJ, Lampe M, Merrifield CJ. A feedback loop between dynamin and actin recruitment during clathrin-mediated endocytosis. PLoS biology. 2012; 10(4):e1001302. [PubMed: 22505844]
19. Narayanan R, Leonard M, Song BD, Schmid SL, Ramaswami M. An internal GAP domain negatively regulates presynaptic dynamin in vivo: a two-step model for dynamin function. The Journal of cell biology. 2005; 169(1):117–126. [PubMed: 15824135]
20. Macia E, Ehrlich M, Massol R, Boucrot E, Brunner C, Kirchhausen T. Dynasore, a cell-permeable inhibitor of dynamin. Developmental cell. 2006; 10(6):839–850. [PubMed: 16740485]
21. Loerke D, Mettlen M, Yarar D, Jaqaman K, Jaqaman H, Danuser G, et al. Cargo and dynamin regulate clathrin-coated pit maturation. PLoS biology. 2009; 7(3):e57. [PubMed: 19296720]
22. Sever S, Muhlberg AB, Schmid SL. Impairment of dynamin's GAP domain stimulates receptor-mediated endocytosis. Nature. 1999; 398(6727):481–486. [PubMed: 10206643]
23. Sever S, Damke H, Schmid SL. Dynamin:GTP controls the formation of constricted coated pits, the rate limiting step in clathrin-mediated endocytosis. The Journal of cell biology. 2000; 150(5): 1137–1148. [PubMed: 10974001]
24. Meinecke M, Boucrot E, Camdere G, Hon WC, Mittal R, McMahon HT. Cooperative recruitment of dynamin and BIN/amphiphysin/Rvs (BAR) domain-containing proteins leads to GTP-dependent membrane scission. The Journal of biological chemistry. 2013; 288(9):6651–6661. [PubMed: 23297414]
25. Sever S, Skoch J, Newmyer S, Ramachandran R, Ko D, McKee M, et al. Physical and functional connection between auxilin and dynamin during endocytosis. The EMBO journal. 2006; 25(18): 4163–4174. [PubMed: 16946707]
26. Yarar D, Waterman-Storer CM, Schmid SL. SNX9 couples actin assembly to phosphoinositide signals and is required for membrane remodeling during endocytosis. Developmental cell. 2007; 13(1):43–56. [PubMed: 17609109]
27. Sever S, Damke H, Schmid SL. Garrotes, springs, ratchets, and whips: putting dynamin models to the test. Traffic. 2000; 1(5):385–392. [PubMed: 11208124]
28. Liu YW, Mattila JP, Schmid SL. Dynamin-catalyzed membrane fission requires coordinated GTP hydrolysis. PloS one. 2013; 8(1):e55691. [PubMed: 23383266]

29. Kural C, Tacheva-Grigorova SK, Boulant S, Cocucci E, Baust T, Duarte D, et al. Dynamics of intracellular clathrin/AP1- and clathrin/AP3-containing carriers. Cell reports. 2012; 2(5):1111–1119. [PubMed: 23103167]
30. Boucrot E, Pick A, Camdere G, Liska N, Evergren E, McMahon HT, et al. Membrane fission is promoted by insertion of amphipathic helices and is restricted by crescent BAR domains. Cell. 2012; 149(1):124–136. [PubMed: 22464325]
31. Schlunck G, Damke H, Kiosses WB, Rusk N, Symons MH, Waterman-Storer CM, et al. Modulation of Rac localization and function by dynamin. Molecular biology of the cell. 2004; 15(1):256–267. [PubMed: 14617821]
32. Krueger EW, Orth JD, Cao H, McNiven MA. A dynamin-cortactin-Arp2/3 complex mediates actin reorganization in growth factor-stimulated cells. Molecular biology of the cell. 2003; 14(3):1085–1096. [PubMed: 12631725]
33. Ochoa GC, Slepnev VI, Neff L, Ringstad N, Takei K, Daniell L, et al. A functional link between dynamin and the actin cytoskeleton at podosomes. The Journal of cell biology. 2000; 150(2):377–389. [PubMed: 10908579]
34. Baldassarre M, Pompeo A, Beznoussenko G, Castaldi C, Cortellino S, McNiven MA, et al. Dynamin participates in focal extracellular matrix degradation by invasive cells. Molecular biology of the cell. 2003; 14(3):1074–1084. [PubMed: 12631724]
35. Orth JD, Krueger EW, Cao H, McNiven MA. The large GTPase dynamin regulates actin comet formation and movement in living cells. Proceedings of the National Academy of Sciences of the United States of America. 2002; 99(1):167–172. [PubMed: 11782546]
36. Lee E, De Camilli P. Dynamin at actin tails. Proceedings of the National Academy of Sciences of the United States of America. 2002; 99(1):161–166. [PubMed: 11782545]
37. Yamada H, Abe T, Satoh A, Okazaki N, Tago S, Kobayashi K, et al. Stabilization of actin bundles by a dynamin 1/cortactin ring complex is necessary for growth cone filopodia. The Journal of neuroscience : the official journal of the Society for Neuroscience. 2013; 33(10):4514–4526. [PubMed: 23467367]
38. Schafer DA, Weed SA, Binns D, Karginov AV, Parsons JT, Cooper JA. Dynamin2 and cortactin regulate actin assembly and filament organization. Current biology : CB. 2002; 12(21):1852–1857. [PubMed: 12419186]
39. Bruzzaniti A, Neff L, Sanjay A, Horne WC, De Camilli P, Baron R. Dynamin forms a Src kinase-sensitive complex with Cbl and regulates podosomes and osteoclast activity. Molecular biology of the cell. 2005; 16(7):3301–3313. [PubMed: 15872089]
40. Chua J, Rikhy R, Lippincott-Schwartz J. Dynamin 2 orchestrates the global actomyosin cytoskeleton for epithelial maintenance and apical constriction. Proceedings of the National Academy of Sciences of the United States of America. 2009; 106(49):20770–20775. [PubMed: 19948954]
41. Mooren OL, Kotova TI, Moore AJ, Schafer DA. Dynamin2 GTPase and cortactin remodel actin filaments. The Journal of biological chemistry. 2009; 284(36):23995–24005. [PubMed: 19605363]
42. Wunderlich L, Farago A, Buday L. Characterization of interactions of Nck with Sos and dynamin. Cellular signalling. 1999; 11(1):25–29. [PubMed: 10206341]
43. McNiven MA, Kim L, Krueger EW, Orth JD, Cao H, Wong TW. Regulated interactions between dynamin and the actin-binding protein cortactin modulate cell shape. The Journal of cell biology. 2000; 151(1):187–198. [PubMed: 11018064]
44. Ross JA, Chen Y, Muller J, Barylko B, Wang L, Banks HB, et al. Dimeric endophilin A2 stimulates assembly and GTPase activity of dynamin 2. Biophysical journal. 2011; 100(3):729–737. [PubMed: 21281588]
45. Gu C, Yaddanapudi S, Weins A, Osborn T, Reiser J, Pollak M, et al. Direct dynamin-actin interactions regulate the actin cytoskeleton. The EMBO journal. 2010; 29(21):3593–3606. [PubMed: 20935625]
46. Weins A, Kenlan P, Herbert S, Le TC, Villegas I, Kaplan BS, et al. Mutational and Biological Analysis of alpha-actinin-4 in focal segmental glomerulosclerosis. Journal of the American Society of Nephrology : JASN. 2005; 16(12):3694–3701. [PubMed: 16251236]

47. Van Rossum AG, de Graaf JH, Schuuring-Scholtes E, Kluin PM, Fan YX, Zhan X, et al. Alternative splicing of the actin binding domain of human cortactin affects cell migration. The Journal of biological chemistry. 2003; 278(46):45672–45679. [PubMed: 12952985]
48. De La Cruz EM, Roland J, McCullough BR, Blanchoin L, Martiel JL. Origin of twist-bend coupling in actin filaments. Biophysical journal. 2010; 99(6):1852–1860. [PubMed: 20858430]
49. McGough A, Pope B, Chiu W, Weeds A. Cofilin changes the twist of F-actin: implications for actin filament dynamics and cellular function. The Journal of cell biology. 1997; 138(4):771–781. [PubMed: 9265645]
50. Cooper JA, Bryan J, Schwab B 3rd, Frieden C, Loftus DJ, Elson EL. Microinjection of gelsolin into living cells. The Journal of cell biology. 1987; 104(3):491–501. [PubMed: 3029140]
51. Klucken J, Outeiro TF, Nguyen P, McLean PJ, Hyman BT. Detection of novel intracellular alpha-synuclein oligomeric species by fluorescence lifetime imaging. FASEB journal : official publication of the Federation of American Societies for Experimental Biology. 2006; 20(12): 2050–2057. [PubMed: 17012257]
52. Taylor MJ, Perrais D, Merrifield CJ. A high precision survey of the molecular dynamics of mammalian clathrin-mediated endocytosis. PLoS biology. 2011; 9(3):e1000604. [PubMed: 21445324]
53. Ferguson SM, Raimondi A, Paradise S, Shen H, Mesaki K, Ferguson A, et al. Coordinated actions of actin and BAR proteins upstream of dynamin at endocytic clathrin-coated pits. Developmental cell. 2009; 17(6):811–822. [PubMed: 20059951]
54. Soulet F, Yarar D, Leonard M, Schmid SL. SNX9 regulates dynamin assembly and is required for efficient clathrin-mediated endocytosis. Molecular biology of the cell. 2005; 16(4):2058–2067. [PubMed: 15703209]
55. Maeda K, Nakata T, Noda Y, Sato-Yoshitake R, Hirokawa N. Interaction of dynamin with microtubules: its structure and GTPase activity investigated by using highly purified dynamin. Molecular biology of the cell. 1992; 3(10):1181–1194. [PubMed: 1421574]
56. Thompson HM, Skop AR, Euteneuer U, Meyer BJ, McNiven MA. The large GTPase dynamin associates with the spindle midzone and is required for cytokinesis. Current biology : CB. 2002; 12(24):2111–2117. [PubMed: 12498685]
57. Tanabe K, Takei K. Dynamic instability of microtubules requires dynamin 2 and is impaired in a Charcot-Marie-Tooth mutant. The Journal of cell biology. 2009; 185(6):939–948. [PubMed: 19528294]
58. Thompson HM, Cao H, Chen J, Euteneuer U, McNiven MA. Dynamin 2 binds gamma-tubulin and participates in centrosome cohesion. Nature cell biology. 2004; 6(4):335–342.
59. Liu YW, Lukiyanchuk V, Schmid SL. Common membrane trafficking defects of disease-associated dynamin 2 mutations. Traffic. 2011; 12(11):1620–1633. [PubMed: 21762456]
60. Rodriguez OC, Schaefer AW, Mandato CA, Forscher P, Bement WM, Waterman-Storer CM. Conserved microtubule-actin interactions in cell movement and morphogenesis. Nature cell biology. 2003; 5(7):599–609.