MEMBRANE TRAFFICKING

Squeezing and releasing

The GTPase *dynamain* forms helical structures around the necks of budding vesicles and has a key role in membrane fission. Two studies in *Cell* now show that dynamain assemblies squeeze the lipid bilayers and that GTP hydrolysis triggers disassembly. In the constant presence of GTP, dynamain undergoes multiple rounds of assembly and disassembly, leading to stochastic membrane fission events.

Using real-time microscopy, Pucadyil and Schmid observed that dynamain self-assembles on so-called SUPER templates (lipid bilayers that surround microbeads), which form long membrane tubules. The addition of GTP causes the disassembly of fluorescently labelled dynamain from the tubules, but not membrane fission. However, in the constant presence of GTP (which represents a more physiological condition), dynamain promotes the release of vesicles from SUPER templates. Further, fluctuations in fluorescence intensity of labelled dynamain collars that are assembled at the bud neck suggest that, in the presence of GTP, dynamain assembly is self-limited by cyclic rounds of assembly and disassembly.

Bashkirov *et al.* used electrophysiology techniques to measure the ionic permeability (conductance) of lipid nanotubes (NTs) that were pulled from membrane bilayers. As NT conductance decreases when NTs become thinner, the authors could monitor dynamain-induced changes of NT diameters in real time. In the absence of GTP, long dynamain assemblies coat the NTs and squeeze them to narrow radii. Upon squeezing, these assemblies stabilize the NT near the point of instability, so that NT constriction by dynamain assemblies does not

promote membrane fission. In the constant presence of GTP, however, periodic variations of NT conductance reveal the formation of short and transient dynamain assemblies on the NTs, and membrane fission occurs spontaneously during cycles of dynamain assembly and dis-

assembly. Thus, a short dynamain scaffold that brings a narrow membrane tubule close to the point of curvature instability is the key intermediate structure in membrane fission.

Furthermore, by varying the lipid composition of NTs to change the membrane rigidity, Bashkirov *et al.* found that dynamain-mediated squeezing and fission is lipid dependent.

Based on a mathematical model, Bashkirov *et al.* propose that “local narrowing of NT could induce cooperative lipid tilting, leading to self-merger of the inner monolayer of NT (hemifission)”. Indeed, simultaneously measuring the NT conductance and the ionic current through the NT membrane did not detect any leakage, thereby suggesting that membrane fission occurs through hemifission. It will be interesting to study whether this mechanism of membrane fission is unique to dynamain or is shared with other GTPases.

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ORIGINAL RESEARCH PAPERS Pucadyil, T. J. & Schmid, S. L. Real-time visualization of dynamain-catalyzed membrane fission and vesicle release. *Cell* **135**, 1263–1275 (2008) | Bashkirov, P. V. *et al.* GTPase cycle of dynamain is coupled to membrane squeeze and release, leading to spontaneous fission. *Cell* **135**, 1276–1286 (2008)

FURTHER READING Zimmerberg, J. & Kozlov, M. M. How proteins produce cellular membrane curvature. *Nature Rev. Mol. Cell Biol.* **7**, 9–19 (2006) | Martens, S. & McMahon, H. T. Mechanisms of membrane fusion: disparate players and common principles. *Nature Rev. Mol. Cell Biol.* **9**, 543–556 (2008)