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ENDOCYTOSIS

# Bending around the BAR

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The process of clathrin-mediated endocytosis (CME) is driven by the collective effort of proteins that cause membrane invagination and those that cause membrane scission. Shimada *et al.* now report the structure of the F-BAR (Bin–amphiphysin–Rvs) protein domain, which provides insight into how these crescent-shaped modules drive membrane remodelling during endocytosis.

CME occurs in three steps. First, clathrin assembles on flat membranes and captures endocytic cargo to form hemispherical clathrin-coated pits. Second, the pit slowly invaginates with a narrowing neck region, and actin polymerizes around the nascent vesicle. Finally, scission proteins such as dynamin are recruited to the neck region where they sever the membrane. The neck region is shaped by the recruitment of N-BAR domain proteins, such as amphiphysins and endophilins, which self-organize into banana-shaped dimers and exert this shape onto membranes. However, these proteins are recruited at a late stage of CME and it is unclear what drives the initial invagination of the small clathrin-coated pit.

Shimada *et al.* determined the structures of the related F-BAR domains from formin-binding protein-17 (FBP17) and Cdc42-interacting protein-4 (CIP4). Compared with the N-BAR domain, the F-BAR domain also forms a dimer and has a similar crescent-shaped architecture; however, the F-BAR domain has longer α-helices and shallower curvature. Both N-BAR and F-BAR domains caused spherical lipid vesicles to tubulate, although F-BAR domains were found to bind preferentially to larger liposomes and generated tubules of a larger diameter. F-BAR domains therefore both 'sense' and induce less membrane curvature than the related N-BAR domain.

The authors show that, as well as enforcing their curved shape onto membranes, F-BAR domains oligomerize into filaments that wind around the membrane to induce curvature. Three pieces of evidence support this: F-BAR domains are arranged in filaments in the crystal lattice, striations of F-BAR protein decorate tubulated liposomes, and point mutations that block the formation of filaments also impair membrane tubulation. Furthermore, F-BAR domain proteins also appear to harness the membrane-deforming capabilities of actin filaments — the recruitment of FBP17 to clathrin pits was associated with activation of the actin-nucleating machinery and actin polymerization.

The authors propose that F-BAR and N-BAR proteins are recruited at different time points during CME. F-BAR domains recognize the shallow curvature of clathrin-coated pits to drive membrane invagination, whereas N-BAR domains are recruited to regions of already high curvature, where they further constrict the membrane in preparation for scission.

*James Pickett*

**ORIGINAL RESEARCH PAPER** Shimada, A. *et al.* Curved EFC/F-BAR-domain dimers are joined end to end into a filament for membrane invagination in endocytosis. *Cell* **129**, 761–772 (2007)
**FURTHER READING** Zimmerberg, J. & Kozlov, M. M. How proteins produce cellular membrane curvature. *Nature Rev. Mol. Cell Biol.* **7**, 9–19 (2006) | Kaksonen M. *et al.* Harnessing clathrin dynamics for clathrin-mediated endocytosis. *Nature Rev. Mol. Cell Biol.* **7**, 404–414 (2006)


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