Septins recognize micron-scale membrane curvature

Damión Lobato-Márquez and Serge Mostowy

Section of Microbiology, Medical Research Council Centre for Molecular Bacteriology and Infection, Imperial College London, London SW7 2AZ, England, UK

How cells recognize membrane curvature is not fully understood. In this issue, Bridges et al. (2016. J. Cell Biol. http://dx.doi.org/10.1083/jcb.201512029) discover that septins, a component of the cytoskeleton, recognize membrane curvature at the micron scale, a common morphological hallmark of eukaryotic cellular processes.

Eukaryotic cells have dedicated proteins that sense membranes, depending on their curvature (Antonny, 2011). Sensors of membrane curvature are important because they organize a wide variety of cellular functions, including vesicle trafficking and organelle shaping (McMahon and Gallop, 2005). Curvature-sensing proteins, for example, the Bin-Amphiphysin-Rvs (BAR) domain–containing proteins, have been mostly described to work at the nanometer scale (Zimmerberg and Kozlov, 2006). In contrast, a clear mechanism of sensing membrane curvature at the micron scale in eukaryotic cells has not been described. In this issue, Bridges et al. discover that septins, a poorly understood component of the cytoskeleton, recognize plasma membrane curvature at the micron scale and serve as landmarks for eukaryotic cells to know their local shape.

Septins are an evolutionarily conserved family of GTP-binding proteins that assemble into nonpolar filaments and rings (John et al., 2007; Sirajuddin et al., 2007; Bertin et al., 2008). Septins have been implicated in diverse membrane organization events where micron-scale curvature takes place (Saarikangas and Barral, 2011; Mostowy and Cossart, 2012), including the cytoskeletal furrow, the annulus of spermatooza, the base of cellular protrusions (e.g., cilium and dendritic spines), and the phagocytic cup surrounding invasive bacterial pathogens (Fig. 1). However, the precise role of septin–membrane interactions remains elusive. It was first suggested in 1999 that the interaction of human septins with phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) is important for septin localization (Zhang et al., 1999). More recently, work using recombinant septins from budding yeast Saccharomyces cerevisiae assembled on PI(4,5)P2 lipid monolayers showed that septins interact with membrane to facilitate filament assembly (Bridges et al., 2014). Membrane-facilitated septin assembly has also been observed using phospholipid liposomes, and in this case septins were also shown to induce membrane tubulation (Tanaka-Takiguchi et al., 2009). Given that (a) septins can interact with membrane, (b) septin assembly is membrane facilitated, and (c) septin assemblies are associated with a variety of membrane organization events from yeast to mammals, Bridges et al. (2016) hypothesized that septins serve as a mechanism to recognize membrane curvature.

In their new work, Bridges et al. (2016) provide several lines of evidence to support the hypothesis that septins recognize micron-scale curvature. First, using the filamentous fungus Ashbya gossypii, they performed in vivo localization studies and showed that the fungal septin Cdc11a concentrates in regions of positive micron-scale curvature and that the degree of concentration is proportional to the degree of curvature. Moreover, septins localize to curved membranes that also recruit septin-interacting proteins (e.g., the signaling protein Hsl7). These findings indicate that, by acting as curvature-sensing proteins, septins can localize signaling platforms in the cell. To test if septins can differentiate among micron-scale curvatures, Bridges et al. (2016) developed an elegant model system for septin assembly in vitro. They decorated silica beads with anionic phospholipid bilayers and measured the interaction affinity between purified fungal septin complexes and beads of different curvatures. Interestingly, septins were maximally recruited to “intermediate” sized beads (1.0–3.0 µm in diameter), with little to no recruitment to either very large (5.0–6.5 µm in diameter) or very small (0.3 µm in diameter) beads. These results indicate that septin filaments preferentially localize to a curvature (κ) of 0.7–2.0 µm−1 in the absence of other cellular factors. To provide additional information on the mechanism of sensing, the authors purified mutant septin complexes that fail to polymerize into filaments and showed that the affinity of septins for micron-scale membrane curvature does not require filament formation per se. However, septins must polymerize into filaments for stable membrane association. Collectively, in vivo experiments using A. gossypii and in vitro experiments using silica beads highlight that septins have the intrinsic ability to recognize membrane curvature at the micron scale.

Finally, to study the recognition of micron-scale membrane curvature beyond fungi, Bridges et al. (2016) turn their attention to human septins. Using tissue culture cells, they observe that the abundance of septins is associated with the degree of membrane curvature. To confirm these observations in vitro, they purified human septins and analyzed their binding affinity to silica beads with phospholipid bilayers. As seen with A. gossypii septins, human septins also showed a preference for beads ~1.0 µm in diameter, strongly suggesting an evolutionarily conserved property of septins for sensing membrane curvature at the micron scale.

Based on their findings, Bridges et al. (2016) propose that septins provide eukaryotic cells with a mechanism to recognize curvature at the micron scale. This feature differentiates septins from other sensor proteins that strictly detect curvature at the...
Acknowledgments

Work in the S. Mostowy laboratory is supported by a Wellcome Trust Research Career Development Fellowship (WT097411MA) and the Lister Institute of Preventive Medicine.

The authors declare no competing financial interests.

Submitted: 17 March 2016
Accepted: 22 March 2016

References


