

Project title: Uncovering the function of animal septins

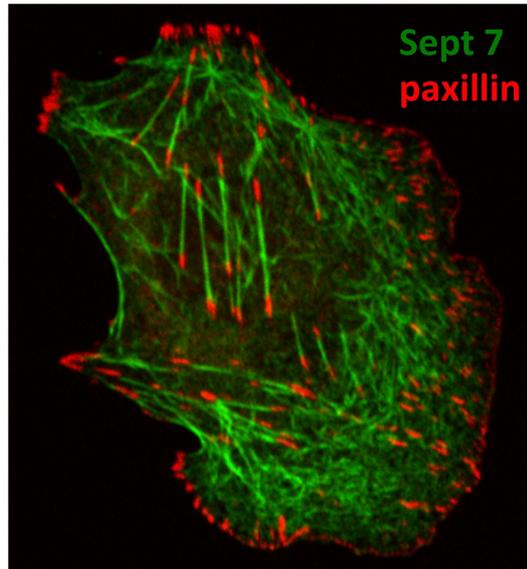
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Cell Morphogenesis Lab <https://sites.google.com/view/cell-morphogenesis-lab>

Concept and Objectives. Septins are ubiquitous GTP-binding cytoskeletal proteins with essential functions for cell and tissue physiology (1). Mutants in septins, or dysregulation of their expression levels are linked to a wide range of diseases, including neurodegeneration, tumorigenesis and infertility (2), however their precise organization and function in cells and tissues remains unknown. Purified septins have the capacity to associate with membranes, actin filaments and microtubules in vitro, but it is unclear if such direct interactions exist in vivo. Our recent work suggests that the actin filament cross-linking activity of human and *Drosophila* septins could contribute to septin function (3-5), but it remains to be shown whether direct actin-septin interactions are relevant in vivo and how such interactions interplay with membranes and microtubules. We have recently generated a series of candidate mutants that aim at identifying membrane-, actin- and microtubule-binding sites on septins. The M2 student will combine polarization-resolved fluorescence microscopy in living mammalian cells with immunostainings and pharmacological treatments to characterize the different septin mutants.



Human osteosarcoma cell stained for septins (green) and focal adhesions (red).

References

- 1) Mostowy and Cossart (2012) Septins: the fourth component of the cytoskeleton. *Nature Reviews Molecular Cell Biology* 13(3), 183-94
- 2) Dolat, Qicong and Spiliotis (2014) Septin functions in organ system physiology and pathology. *Biol. Chem.* 395(2), 123-141
- 3) Mavrakis, M., Azou-Gros, Y., Tsai, F.-C., Alvarado, J., Bertin, A., Iv, F., Kress, A., Brasselet, S., Koenderink, G.H. and T. Lecuit (2014) Septins promote F-actin ring formation by cross-linking actin filaments into curved bundles. *Nature Cell Biology* 16 (4), 322-334
- 4) Mavrakis, M. (2016) Visualizing septins in early *Drosophila* embryos. *Methods in Cell Biology*, Volume 136, 199-220
- 5) Mavrakis, M., Tsai, F.-C., and Koenderink, G.H. (2016) Purification of recombinant human and *Drosophila* septin hexamers for TIRF assays of actin-septin filament assembly. *Methods in Cell Biology*, Volume 136, 183-198