IMPRS on Multiscale Biosystems

Project Title: Sculpting the membrane: control of membrane organization by septins

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Project description: Membrane remodeling is essential for cell division and other fundamental processes in animal cells. Septins are a poorly understood family of GTP-binding cytoskeletal proteins with evolutionarily conserved functions in cell division (panel A in figure). They are believed to provide scaffolds for recruiting other proteins and because they form filaments, they are considered to be part of the cytoskeleton. As such, they associate with cytoskeletal elements and the plasma membrane and can modulate the morphology of the latter. First discovered in a Nobel Prize winning cell division screen in yeast, they are now known to play important roles in a variety of processes from spermiogenesis to neuronal degeneration and several forms of cancer. However, fundamental principles of their important functions remain poorly understood.
The aim of this project is thus to understand the mechanism by which proteins from the septin family deform cellular membranes. We aim to engage a combination of purified components and *in vitro* reconstituted membrane systems (panel B in figure) mimicking the cellular environment. Live cell imaging and high-end microscopy techniques, including super-resolution microscopy and micro-manipulation approaches will be put to action to investigate how septins deform membranes, what forces are involved and which structural requirements of septins allow this to happen. The highly interdisciplinary project will involve biochemical and cell-biology work in the Ewers laboratory at FU Berlin and biophysical *in vitro* work (see link) in the Dimova lab at the MPI.

Your background: MSc in biochemistry, biophysics or physics. Strong interest in physics of biological systems, interest in interdisciplinary work; basic knowledge of membranes and microscopy experience will be advantageous.

Papers to read before the interview:

Cannon, K.S., Woods, B.L., Crutchley, J.M. and Gladfelter, A.S. (2019). An amphipathic helix enables septins to sense micrometer-scale membrane curvature. J. Cell Biol. doi: 10.1083/jcb.201807211
Beber, A., Taveneau, C., Nania, M., Tsai, F.C., Di Cicco, A.,... and Bertin, A. (2019). Membrane reshaping by micrometric curvature sensitive septin filaments. Nature Comm. doi: 10.1038/s41467-019-08344-5
R. Dimova, (2019). Giant vesicles and their use in assays for assessing membrane phase state, curvature, mechanics and electrical properties, Annu. Rev. Biophys. doi: 10.1146/annurev-biophys-052118-115342

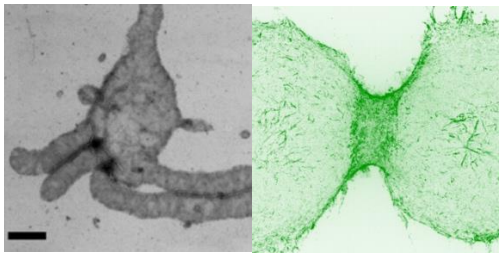
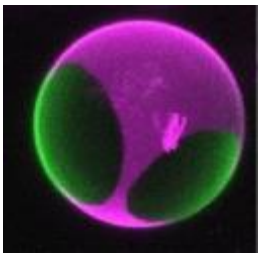
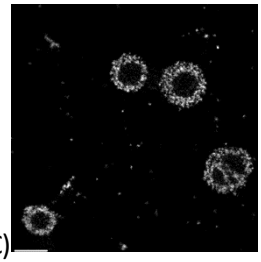
(A)  (B)  (C) 

Figure: (A) Left: Septin filaments polymerized on a vesicle deform it. Right: Septin filaments in the cleavage furrow of dividing cells. (B) A giant lipid vesicle (~25 microns in diameter) exhibiting lipid phase separation as visualized by fluorophores partitioning in the domains. (C) Superresolution microscopy of septin filaments in genome-edited cells polymerized into a ring structure. Every dot represents one septin molecule. Scale bar = 500 nm.

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