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Editorial overview: The molecular and cellular biology of septins

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This Septins Special Issue of Cytoskeleton addresses fundamental aspects of septin structure, assembly and function. The group of 18 articles has been inspired by the recent European Molecular Biology Organization (EMBO) Workshop entitled 'Molecular and Cellular Biology of Septins' held in Berlin, Germany, on October 8-11, 2017, furthe described in a recent meeting report (Caudron and Yadav, 2018). r

The septin cytoskeleton has a rich history. Septins were discovered by Nobel Laureate Leland Hartwell whilst screening for cell division cycle (*cdc*) mutants in the budding yeast *Saccharomyces cerevisiae*. Septin genes have since been found throughout fungi and higher eukaryotes, yet their number ranges from 2 in *Caenorhabditis elegans* to 13 in humans and 19 in zebrafish. Septins form hetero-oligomeric complexes, which assemble to form non-polarized filaments and higher-order structures. Septins are essential for various cellular process including cell division, vesicle trafficking, cytoskeletal organisation and membrane dynamics. Despite recent progress, the field is small and septins remain a relatively poorly understood component of the cytoskeleton as compared to actin or microtubules. This Special Issue, which includes both primary research articles and reviews, provides a forum for novel research on current themes dealing with the molecular and cellular biology of septins.

S. cerevisiae is an essential model organism to understand fundamental aspects of septin biology. Here, Marquardt et al. describe in detail the architecture, remodeling and functions of the *S. cerevisiae* septin cytoskeleton at the mother-bud neck of dividing cells (Marquardt et al., 2018). Perez and Thorner present their latest findings, describing how septin associated proteins traffic between the yeast bud neck and nucleus (Perez and Thorner 2018). As a resource to the community, Mela and Momany provide a comprehensive overview of known yeast septin mutations and phenotypes, and discover that a majority o them reside in the G1 motif of the conserved G-domain essential for septin-septin and septin-nucleotide interactions (Mela and Momany, 2018).

Fundamental septin biology- such as GTP-binding and hydrolysis, or the assembly of septin complexes into higher order structures- remain active areas of research. In this issue, Bau et al. report on nucleotide binding properties of recombinant purified yeast septins (Baur e al., 2018). In a mini-review, Abbey et al. debate the role of GTP binding and hydrolysis in septin assembly and function across species (Abbey et al., 2018). The assembly of septins into filamentous bundles is visualized and quantitatively analyzed by Keynote speaker Bil Trimble using single molecule localization-based superresolution microscopy (Vissa et al 2018). Banko et al. report the development of a genome-edited fibroblast cell line, in which a green fluorescent protein (GFP) is incorporated into the *SEPT2* gene in both alleles, providing an important tool for future quantitative microscopy studies (Banko et al.,). A crucial aspect of septin biology is the interaction of mammalian septins with other cytoskeleton components and phospholipids. To investigate septin-microtubule interactions Nakos et al. develop an *in vitro* assay and show that SEPT9 controls plus-end dynamics of microtubules (Nakos et al., 2018). To investigate septin-phospholipid interactions, an assay for the investigation of septin assembly on giant unilamellar vesicles containing $PI_{(4,5)}P_2$ is described by Beber et al. (Beber et al., 2018).

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In recent years, septins have been found to be involved in a number of processes essential for cellular homeostasis, including regulation of Ca^{2+} entry through Orai channels. In new work contributed by Deb and Hasan using *Drosophila* neurons, this process is discovered to require several septins (Deb and Hasan, 2018). An emerging role of septins in the regulation of mechanotransduction is reviewed by Lam and Calvo (Lam and Calvo, 2018). Septins have been suggested to be involved in nuclear import, and the Mabjeesh laboratory describe a role for SEPT9 in this process (Tazat et al., 2018).

Septins are associated with human diseases such as neoplasia, neurodegeneration, infertility and infection. In this issue, there are several contributions examining the role of septins in human disease. Neubauer et al. describe a family with duplications in an exon of the *SEPT9* gene, resulting in childhood onset Hereditary Neuralgic Amyotrophy (Neubauer et al., 2018a). A role for SEPT12 in male fertility is discussed by Lin et al. (Lin et al., 2018). In this case, mutations in the *SEPT12* gene can result in immotile sperm and a defective sperm annulus (a SEPT12 phosphomimetic knockin mouse displays similar defects), suggesting a role for SEPT12 phosphorylation in sperm maturation. Septins are highly expressed in kidneys, and two aspects of septin function in the kidney are addressed in this Special Issue. Neubauer et al. show using immunohistochemistry and RTPCR that septin expression is significantly upregulated in fibrotic kidney (Neubauer et al., 2018b). Moreover, Wasik et al. report that Sept7b knockdown in zebrafish results in damaged pronephros and defective cilia formation (Wasik et al., 2018). These two studies will hopefully lead to future studies concerning septin function in the kidney. Finally, a new role for septins during bacterial infection is revealed by the Mostowy laboratory (Lobato-Márquez et al., 2018), discovering a requirement for septins and the autophagy machinery in the proliferation of intracellular *Shigella*. These data suggest a new role for septins in cellular metabolism that may be exploited for infection control.

In conclusion, we thank all our colleagues for their contribution to this Special Issue of Cytoskeleton. We are excited to present this Special Issue to the community, and look forward to the next gathering of this growing field.

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