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Guest Editorial

Highlight: The 5th International Workshop on Septin Biology

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Septins are guanosine triphosphate (GTP)-binding proteins that assemble into hetero-oligomeric complexes and form nonpolar filaments that associate with cellular membranes and the cytoskeleton (Mostowy and Cossart, 2012; Saarikangas and Barral, 2011). Septins function as scaffolds and diffusion barriers that control the spatial organization of cytoplasmic and membrane proteins (Kinoshita, 2006; Spiliotis and Gladfelter, 2012). Though septins have been linked to a variety of human diseases including cancer, infertility, bleeding and neurological disorders, their precise roles remain poorly understood.

Since 2005, biannual workshops have gathered researchers from all over the world to share their latest findings and discuss progress in the growing field of septin biology. The fifth workshop was held in Hefei, China on March 15-17, 2013. Meeting highlights included a novel mechanism for septin assembly and cellular morphogenesis in budding yeast (Okada *et al.*, 2013), new roles for septins in T-cell development (Lassen *et al.*, 2013) and the spreading of squamous cell carcinomas (Mizutani *et al.*, 2013), the use of zebrafish (*Danio rerio*) as a new model system to study septin biology *in vivo* (Mostowy *et al.*, 2013), and new insights into how mammalian septins interact with microtubules (Bai *et al.*, 2013). This Highlight Issue of Biological Chemistry features work presented during the meeting and reviews of current septin literature.

The biological function of septins depends on their ability to form higher order filamentous structures, yet the role of GTP-binding and hydrolysis for the assembly of septin filaments remains poorly understood. In this issue, Wittinghofer and Zent investigate the GTPase activity of different human septins, and conclude that GTP hydrolysis can stabilize septin polymers (Wittinghofer and Zent, 2014; this issue pp. ●●-●●). These data highlight that the GTP-GDP cycle is crucial in the dynamics of septin polymerisation, as it is in the actin and microtubule cytoskeleton networks. Once polymerized, septins act as scaffolds and diffusion barriers for the localization and sub-compartmentalization of cellular proteins (Caudron and Barral, 2009). Initial studies have suggested that septins function as diffusion barrier at the base of primary cilia, maintaining the localization of ciliary proteins (Hu *et al.*, 2010; Kim *et al.*, 2010). Fliegauf and coworkers have investigated the localization of septins in the motile cilia of airway epithelial cells (Fliegauf *et al.*, 2014; this issue pp. ●●-●●). In these cells, the distinct localization of septins at the ciliary base support their function as a sub-ciliary barrier and are in agreement with the septin cytoskeleton having essential roles in ciliated tissues. New work presented by Bill Trimble's laboratory during the

septin workshop confirmed a role for SEPT9 in controlling cilia length (Ghossoub *et al.*, 2013), and showed that a novel signalling pathway downstream of SEPT9 enables the growth of axonemal microtubules by stabilizing microtubule plus ends. The diversity of septin localizations and functions is reviewed by Dolat and colleagues, who provide a comprehensive account of septin functions in tissue and organ systems, and discuss how abnormal septin expression leads to the pathogenesis of tissue-specific diseases (Dolat *et al.*, 2014; this issue pp. ●●-●●). Numerous studies have shown that SEPT9 expression is altered in many cancers, suggesting that deregulation of SEPT9 expression contributes to tumorigenesis (Connolly *et al.*, 2011). Here, Connolly and coworkers analyze the expression of seven different isoforms of SEPT9 in peritumoral and tumor breast tissue, and show that SEPT9 is genomically amplified in breast carcinomas with severe clinical outcomes (Connolly *et al.*, 2014; this issue pp. ●●-●●). SEPT9 has also been linked to hereditary neuralgic amyotrophy (HNA), an autosomal dominant neuropathy characterized by shoulder-arm pain and atrophy (Kuhlenbaumer *et al.*, 2005). The abundance and localization of septins in myelin, a specialized plasma membrane of glial cells that electrically insulates axons to accelerate the transmission of information in the nervous system, can have critical consequences on several neurological processes. A mini-review by Patzig and colleagues provides an overview of septins in glial cells (Patzig *et al.*, 2014; this issue pp. ●●-●●).

In closing, the architecture and regulation of different septin higher–order structures (e.g. filaments, rings and hourglasses) requires further investigation. Understanding how post-translational modifications affect septin assembly is an area of intense interest (Hernández-Rodríguez and Momany, 2012), and new work presented by Xuebiao Yao's laboratory during the septin workshop has discovered that SEPT7 is acetylated by the acetyl-transferase TIP60, altering the assembly properties and dynamics of septin filaments in mitosis. How septins function as a unique component of the cytoskeleton, and how they interact with actin, microtubules and intermediate filaments, remains to be fully determined using both i*n vitro* and *in vivo* approaches, including new animal models. Septin knock-out mice currently and soon-to-be available include Sept2, Sept3, Sept4, Sept5, Sept6, Sept7, Sept8, Sept9, and Sept11. Alternatively, the zebrafish is genetically tractable and advantageous for *in vivo* imaging (Mostowy *et al.*, 2013).

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