Editorial: Cytoskeleton Dynamics as Master Regulator of Organelle Reorganization and Intracellular Signaling for Cell-Cell Competition

Noa B. Martin-Cofreces1,2,3†, Francisco Sanchez-Madrid1,2,3† and Pedro Roda-Navarro4,5†

† These authors have contributed equally to this work

1 Department of Immunology, Hospital Universitario de la Princesa, Universidad Autónoma de Madrid, Instituto de Investigación Sanitaria Princesa (IIS-IP), Madrid, Spain, 2 Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain, 3 Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain, 4 Department of Immunology, Ophthalmology and ENT, School of Medicine, Universidad Complutense de Madrid, Madrid, Spain, 5 12 de Octubre Health Research Institute (Iamas12), Madrid, Spain

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Editorial on the Research Topic

Cytoskeleton Dynamics as Master Regulator of Organelle Reorganization and Intracellular Signaling for Cell-Cell Competition

The term cell-cell competition, meaning that cell growth and survival is affected by neighboring cells, was used to describe the consequences of this heterogeneous cell environment unveiled through the study of genetic mosaics of Drosophila melanogaster (Morata and Ripoll, 1975). In this regard, the organization of multicellular organisms relies on cell–cell interactions involving possible competition between individual somatic cells (Belardi et al., 2020). For example, many neurons compete for the same target to survive during the development of the nervous system (Buss et al., 2006) and the viability of thymocyte clones depends on the establishment of specific cell interactions for the engagement of the correct antigen (Kurd and Robey, 2016). Cell-cell competition may rely on regulators of cell signaling, gene expression or the cytoskeleton, such as vav1 (Tybulewicz et al., 2003), WASp and N-WASP (Cotta-de-Almeida et al., 2007). During the organization of the immunological synapse (IS), a proper regulation of actin and tubulin cytoskeletons is required to achieve full activation, thereby orchestrating the organization of the receptors and organelles essential for effector functions (Martin-Cófreces et al., 2011).

In this collection of articles (Figure 1), Lachowski et al. show that G-Protein-coupled Estrogen Receptor (GPER) activation down-regulates actin dynamics through RhoA phosphorylation at Ser188 and binding to Rho-GDI. The RhoA/mDia pathway is preferentially used by GPER, rather than ROCK/myosin-II, facilitating stress fiber and lamellipodia disorganization in fibroblasts. These data indicate that estrogens can regulate the actin cytoskeleton stiffness, modifying the cell shape and fitness, and point to differential regulation of cell adhesion and migration on different substrates depending on relative cell expression of GPER. Different receptors control actin organization and mechanotransduction in cells, which is now known to affect gene expression through factors such as MRTP/SRF (myocardin-related transcription factor/surface response factor) (Esnaul et al., 2014) and YAP/TAZ [Yes-associated protein (YAP) and its homolog transcriptional co-activator with PDZ-binding motif (TAZ, also called WWTR1)] (Dupont et al., 2011). In this regard, Antón and Wandosell review the role of WIP and YAP/TAZ in the connection of the actin cytoskeleton and the development of the nervous system. The role of nuclear vs. cytoplasmic actin...
is discussed in the context of the YAP transcriptional pathway regulation during neurite development and transformation of astrocytes into glioblastoma. Authors conclude that WIP regulates nuclear shuttling of MRTF/SRF and YAP/TAP through actin polymerization, and highlight some unclear aspects of the regulation of the YAP/TAZ pathway in neurons, astrocytes and leukocytes. The connection between the actin cytoskeleton and the nuclear envelope determines cell shape (Gruenbaum et al., 2015) and regulates cell ability to migrate through constrained spaces (Lomakin et al., 2020; Venturini et al., 2020).

Li et al. address the study of the protein nesprin-2 (Syne2b), which is an outer nuclear membrane protein that interacts with actin during Zebrafish development (Davidson and Cadot, 2021). Maternal Syne2b/nesprin-2 is required to preserve the epithelial
Primary cilia are indispensable for embryonic development and cell differentiation, which endows ciliopathies with great relevance (Reitter and Leroux, 2017). May et al. address phosphorylation and ubiquitylation of different components during cilia assembly and disassembly. K-63 linked α-tubulin poly-ubiquitylation—which takes place during microtubule de-polymerization (Wang et al., 2019), is used by IFT-A (intraflagellar transport complex A) for retrograde transport during cilia disassembly. Nolasco et al. study the effect of colchicine, a drug used to treat inflammatory diseases such as gouty arthritis and pericarditis. Tubulin binding cofactors (TBCs: TBCA, TBCB, and TBCE) are chaperones involved in the stabilization of the αβ-tubulin heterodimers. Here, authors observe that colchicine prevents the formation of β-tubulin/TBCA complexes by blocking the disassembly of TBCE/TBCB/αβ-tubulin complex. This system is key to regulate the critical concentration of αβ-tubulins needed to promote microtubule assembly. Therefore, colchicine would prevent microtubule dynamics by avoiding recycling of the αβ-tubulin heterodimers, which makes cells more dependent on new synthesis and possible metabolic constraints.

Altogether, this collection of articles summarizes part of the knowledge on cytoskeletal dynamics influencing cell-cell communication involved in sensing changes in the environment supporting development and cell responses. The underlying molecular mechanisms that account for the regulation of cell-cell competition are still barely understood. The diverse regulatory pathways exposed here support a unifying hypothesis postulating that the sensing of extracellular cues through membrane receptors stimulates changes in the cytoskeleton that eventually allow reorganizing other cellular components to adapt to the microenvironment, facilitating an accurate cell response and endurance.

**AUTHOR CONTRIBUTIONS**

NM-C: image composition. NM-C, PR-N, and FS-M: funding acquisition, conceptualization, and writing (original draft, review and editing). All authors contributed to the article and approved the submitted version.

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