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Peripheral mechanisms take central stage in microtubule dynamics: Commentary on "Signaling function of a-catenin in microtubule regulation" by Shtutman et al.

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Abstract

Although the centrosome is traditionally viewed as cell's principle microtubule organizing center (MTOC), regulation of microtubule dynamics at the cell cortex plays an equally important role in the formation of the steady-state microtubule network. Several recent studies, including one published in this issue, reveal that complex signaling mechanisms associated with adherence junctions influence both microtubule nucleation at the centrosome, and the stability of non-centrosomal microtubules.

In the mid 1980s Marc Kirschner and Timothy Mitchison proposed an elegant "search-and-capture" hypothesis that seemed to explain how cells manage to convert a simple radial array of microtubules produced by the centrosome into the complex and precisely regulated asymmetric network found in a typical polarized cell. The key to this mechanism was the selective stabilization of inherently dynamic microtubule plus ends at the certain parts of cell cortex.[4] Subsequently, it was shown that microtubule plus ends can in fact be captured and stabilized at diverse cortical loci including focal adhesions and adherence junctions. These observations provided direct support to the search-and-capture hypothesis. However, in recent years it became clear that role of cell cortex in the regulation of microtubule dynamics goes beyond simple stabilization of the plus ends. For example, there is evidence that integrin β1 is involved in the regulation of microtubule nucleation at the centrosome.[6] Further, in polarized epithelia, cell cortex serves as the dominant MTOC, effectively replacing the centrosome.[5] Thus, cell-cortex mechanisms affect microtubule dynamics both at their plus- and minus ends. The challenge now is to identify molecular pathways underlying this regulation.

A study in this issue of Cell Cycle (Shtutman et al.) suggests that α-catenin, a major component of adherence junctions is responsible for promoting microtubule nucleation and/or stability in a centrosome-independent fashion. Shtutman and coworkers used centrosome-free cytoplasts. The number of microtubules in these cytoplasts is low in the absence of cell-cell contacts but increases to near-normal levels in confluent cultures[3] or upon overexpression of cadherins[1] suggesting that adherence junctions somehow regulate microtubule dynamics. Shtutman and coworkers now demonstrate a similar increase in microtubule density can be induced by overexpression of a membrane-targeted α catenin. This is an exciting finding because α-catenin is also directly involved in the regulation of actin dynamics[2] and thus this molecule emerges as a central player in the global regulation of the cytoskeleton in response to extracellular interactions. Interestingly, expression of non-membrane-targeted α-catenin only mildly increased the density of microtubule network in centrosome-free cytoplasts suggesting that α-catenin needs to be engaged in an activation event at the cell cortex, perhaps within the adherence junction.

Although formation of cell-cell junctions clearly increases the density of microtubule network, microtubule nucleation appears to occur throughout the cytoplasm and not preferentially at

adherence junctions in these cells.[1] Thus, local interactions at adherence junctions ultimately result in the propagation of a certain factor(s) that influences global microtubule dynamics. The exact nature of this factor or even the general layout of the pathway that alters microtubule dynamics in response to cortical interactions remain unknown. However, the demonstration that α-catenin is one of the molecular players required for this pathway is an important towards the understanding the link between extracellular interactions and microtubule dynamics.

Further Reading

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