Microtubule organization, movement and turnover in motile and non-motile cells

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Abstract

Microtubules are required for several cellular processes including vesicle transport, cytoplasmic organization, cell motility, maintenance of cellular polarity, and mitosis. The mechanisms by which microtubule arrays are established, maintained and remodeled are important for understanding these vital processes. I have used fluorescence analog chemistry and live cell imaging approaches in mammalian cells to address these questions. ^ I have documented the *de novo* formation of microtubules in peripheral regions of epithelial-like cells, at sites distant from the centrosome, challenging the traditional doctrine that microtubules are nucleated solely at microtubule organizing centers (MTOCs). Historically, the behavior of minus ends has been difficult to study *in vivo*, due to the high density of microtubules in central cellular regions; however, the peripheral position of the non-centrosomal microtubules allowed me to quantify the dynamic behavior of both microtubule ends. The results demonstrate that individual minus ends are remarkably stable, suggesting that their stability is either intrinsic to their structure or is the result of a molecular cap. ^ During cell motility, microtubules must populate the advancing lamella and be removed from retracting regions; however, the mechanisms that cells utilize to remodel microtubule arrays are complex and poorly defined. My experiments, using photoactivated fluorescent tubulin to mark the microtubule lattice, demonstrate that microtubules are transported in motile cells, and that transport is a two component process. The first component is the unidirectional transport of microtubules in the direction of the dominant actomyosin-generated contractile force; the second is the bidirectional movement of individual microtubules. In cells with numerous noncentrosomal microtubules, transport is likely to play a significant, and previously unrecognized, role in microtubule reorganization. ^ The mechanism of the bidirectional component was analyzed; inhibition of myosin II abolished microtubule movement, while inhibition of cytoplasmic dynein increased it. In addition, the absence of myosin function resulted in slower turnover of the microtubule array, which is the first direct evidence for myosin-generated forces modulating the kinetic behavior of microtubules. The results support a role for cytoplasmic dynein in tethering microtubules and resisting actomyosin-generated forces, suggesting that the antagonistic forces of these motors contribute to the organization of the microtubule array. ^

Subject Area

Cellular biology

Recommended Citation