Disentangling the Microtubule Network in Differentiating Neurons: Learning from Mitosis

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Organization of microtubules into ordered arrays is best understood in mitotic systems, but remains poorly characterized in post-mitotic cells. In recent years various cases of recycling of so-called mitotic microtubule regulators in post-mitotic cells have been revealed. In this context I will present work from our lab describing how the microtubule nucleation machinery, which is key to microtubule network organization and remodeling, is contributing to cell morphogenesis during the transition from proliferation to differentiation. Recently, to identify microtubule regulators with roles in post-mitotic cells, we have analyzed the microtubule cytoskeleton proteome previously identified in cycling cells through expression profiling and targeted RNAi screening in cultured neurons. This led to the identification of the “mitotic” kinase NEK7 as regulator of dendrite morphogenesis in vitro and in vivo. NEK7 regulates dendrite growth and branching as well as formation and shaping of spines in part through phosphorylation of the kinesin Eg5/KIF11, promoting its accumulation on microtubules in distal dendrites. Here Eg5 limits retrograde microtubule polymerization, which is inhibitory to dendrite growth and branching. Eg5 exerts this effect through microtubule stabilization, independent of its motor activity. This work establishes NEK7 as a general regulator of the microtubule cytoskeleton, controlling essential processes during cell proliferation as well as differentiation.