How microtubules induce local membrane protrusion

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Microtubules play key roles in directional cell migration and neuron navigation, but the underlying mechanisms are extremely complex and poorly understood. We show that microtubules can regulate these processes by inducing assembly of branched actin networks at their tips and thereby driving local membrane protrusion. The key role in this mechanism in growth cones of cultured rat hippocampal neurons belongs to adenomatous polyposis coli (APC), a protein with both tumor suppressor and cytoskeletal functions. APC is localized at the interface between the microtubule and associated branched actin filaments. APC knockdown leads to severe depletion of branched actin filaments in growth cones and abrogates growth cone recovery after repellent-induced collapse. Overexpression of APC in non-neuronal cells induces elongated processes by a mechanism that depends on the N-terminus of APC. When dynamic APC-positive microtubule tips hit the cell edge in these cells, they often induce local actin- and cortactin-rich protrusions. Together, our data suggest a novel mechanism by which microtubules can navigate growth cone guidance and cell migration.