Rab35 functions in axon elongation are regulated by P53-related protein kinase in a mechanism that involves Rab35 protein degradation and the microtubule-associated protein 1B

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© 2016 the authors. Rab35 is a key protein for cargo loading in the recycling endosome. In neuronal immortalized cells, Rab35 promotes neurite differentiation. Here we describe that Rab35 favors axon elongation in rat primary neurons in an activity-dependent manner. In addition, we show that the p53-related protein kinase (PRPK) negatively regulates axonal elongation by reducing Rab35 protein levels through the ubiquitin-proteasome degradation pathway. PRPK-induced Rab35 degradation is regulated by its interaction with microtubule-associated protein 1B (MAP1B), a microtubule stabilizing binding protein essential for axon elongation. Consistently, axon defects found in MAP1B knock-out neurons were reversed by Rab35 overexpression or PRPK inactivation suggesting an epistatic relationship among these proteins. These results define a novel mechanism to support axonal elongation, by which MAP1B prevents PRPK-induced Rab35 degradation. Such a mechanism allows Rab35-mediated axonal elongation