Regulation of Rap2A by the Ubiquitin Ligase Nedd4-1 Controls Neurite Development

Summary

Nedd4-1 is a 'Neuronal Precursor Cell Expressed and Developmentally Downregulated Protein' and among the most abundant E3 ubiquitin ligases in mammalian neurons. In analyses of conventional and conditional Nedd4-1 deficient mice, we found that Nedd4-1 plays a critical role in dendrite formation. Nedd4-1, the serine/threonine kinase TNIK, and Rap2A form a complex that controls Nedd4-1-mediated ubiquitination of Rap2A. Ubiquitination by Nedd4-1 inhibits Rap2A function, which reduces the activity of Rap2 effector kinases of the TNIK family and promotes dendrite growth. We conclude that a Nedd4-1/Rap2A/TNIK signaling pathway regulates neurite growth and arborization in mammalian neurons.