Novel Function of Paxillin in Modulating RNA Splicing During Early Neuron Development

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Paxillin is a known regulator of focal adhesions and actin cytoskeleton dynamics, crucial for cell migration. However, our study discovered a novel function of paxillin in neurons. We found that on the seventh day in vitro, neuronal paxillin is phosphorylated at Ser119 residue (p-paxillinS119) and translocated into the nucleus. This study aims to elucidate the importance of this phenomenon for neuron development. Using a neural differentiation model of N2a cells, we explored the molecular mechanism of p-paxillinS119 nuclear translocation. We found that inhibition of nucleocytoplasmic transport importin-b 2 activity blocked p-paxillinS119 nuclear translocation, and mutations of Ser119 and the PY-type nuclear localization signal peptides of paxillin reduced nuclear translocation. Co-immunofluorescence staining revealed that p-paxillinS119 punctate co-localizes with the RNA splicing factors on nuclear speckles. We confirmed that paxillin interacts with multiple RNA splicing regulators using co-immunoprecipitation. Our minigene splicing assay showed that paxillinS119 phosphorylation modulates RNA splicing activity. Additionally, we found that loss of paxillinS119 phosphorylation suppresses axon outgrowth. These findings suggest that nuclear p-paxillinS119 plays a crucial role in neuronal maturation.