Neuronal GAP Porf-2 transduces EphB1 signaling to brake axon growth

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Abstract

Axonal outgrowth and guidance require numerous extracellular cues and intracellular mediators that transduce signals in the growth cone to regulate cytoskeletal dynamics. However, the way in which cytoskeletal effectors respond to these signals remains elusive. Here, we demonstrate that Porf-2, a neuron-expressed RhoGTPase-activating protein, plays an essential role in the inhibition of initial axon growth by restricting the expansion of the growth cone in a cell-autonomous manner. Furthermore, the EphB1 receptor is identified as an upstream controller that binds and regulates Porf-2 specifically upon extracellular ephrin-B stimulation. The activated EphB forward signal deactivates Rac1 through the GAP domain of Porf-2, which inhibits growth cone formation and brakes axon growth. Our results therefore provide a novel GAP that regulates axon growth and braking sequentially through Eph receptor-independent and Eph receptor-dependent pathways.