

Endosomal transport of neurotrophins: Roles in signaling and neurodegenerative diseases

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Abstract

The internalization and retrograde axonal transport of neurotrophin receptors is important for their retrograde signal transduction supporting neuronal differentiation, plasticity, and survival. To influence transcription, neurotrophin signals initiated at synapses have to be conveyed retrogradely to the cell body. Signaling endosomes containing neurotrophin receptor signaling complexes mediate retrograde neurotrophin signaling from synapses to the nucleus. Interestingly, many neurodegenerative diseases, including Alzheimer's disease, Niemann Pick disease Type C, and Charcot-Marie-Tooth neuropathies, show alterations of vesicular transport, suggesting that traffic jams within neuronal processes may cause neurodegeneration. Although most of these diseases are complex and may be modulated by diverse pathways contributing to neuronal death, altered neurotrophin transport is emerging as a strong candidate influence on neurodegeneration. In this article, we review the mechanisms of internalization and endocytic trafficking of neurotrophin receptors, and discuss the potential roles of perturbations in neurotrophin trafficking in a number of neurodegenerative diseases.