

NEUROTROPHINS: Roles in Neuronal Development and Function*

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■ Abstract Neurotrophins regulate development, maintenance, and function of vertebrate nervous systems. Neurotrophins activate two different classes of receptors, the Trk family of receptor tyrosine kinases and p75NTR, a member of the TNF receptor superfamily. Through these, neurotrophins activate many signaling pathways, including those mediated by ras and members of the cdc-42/ras/rho G protein families, and the MAP kinase, PI-3 kinase, and Jun kinase cascades. During development, limiting amounts of neurotrophins function as survival factors to ensure a match between the number of surviving neurons and the requirement for appropriate target innervation. They also regulate cell fate decisions, axon growth, dendrite pruning, the patterning of innervation and the expression of proteins crucial for normal neuronal function, such as neurotransmitters and ion channels. These proteins also regulate many aspects of neural function. In the mature nervous system, they control synaptic function and synaptic plasticity, while continuing to modulate neuronal survival.

INTRODUCTION

Neurotrophins are important regulators of neural survival, development, function, and plasticity (for reviews, see Korsching 1993, Eide et al 1993, Segal & Greenberg 1996, Lewin & Barde 1996, Reichardt & Fariñas 1997, McAllister et al 1999, Sofroniew et al 2001). As the central concept of the neurotrophic factor hypothesis, targets of innervation were postulated to secrete limiting amounts of survival factors that function to ensure a balance between the size of a target organ and the number of innervating neurons (reviewed in Purves 1988). Nerve growth factor (NGF), the first such factor to be characterized, was discovered during a

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