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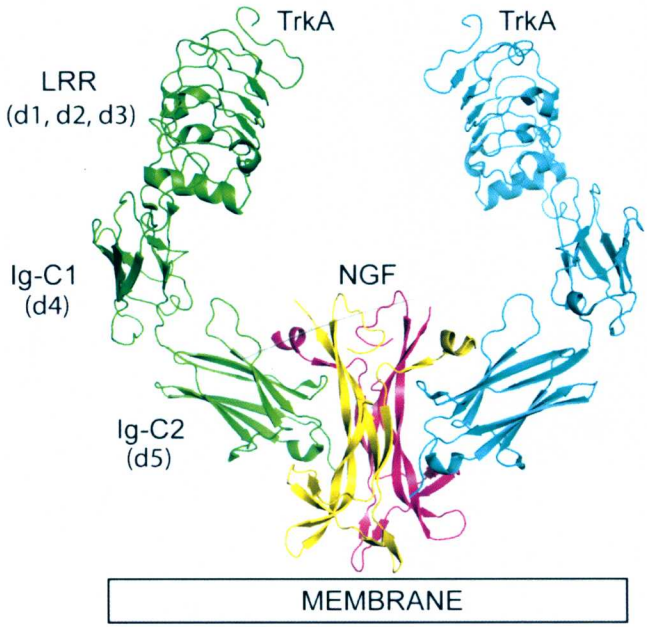

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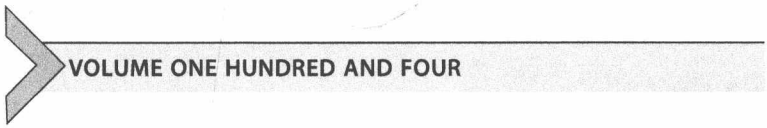

VITAMINS AND HORMONES

Neurotrophins

Series Editor

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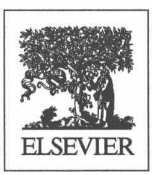

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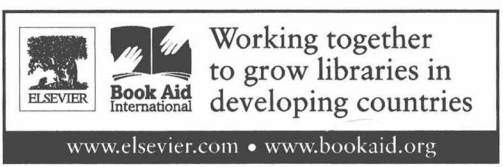

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Neurotrophins

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PREFACE

Neurotrophins were first discovered to be growth factors involved in neuronal development and functioning. Later on, they were shown to function in the immune system and reproductive system. These factors are first synthesized in the form of proneurotrophin precursors that become cleaved to generate the C-terminal mature neurotrophins. They bind and activate Trk (tropomyosin-related kinase) receptors and a p75 neurotrophin receptor ($p75^{NTR}$). The four family members of neurotrophins are comprised by the nerve growth factor (NGF), the brain-derived nerve growth factor (BDNF), neurotrophin-3 (NT-3), and neurotrophin 4/5 (NT-4/5). NGF and BDNF are prominent and have been most studied. NGF binds and activates the membrane Trk receptor leading to the activation of Ras-mitogen-activated protein kinase, phospholipase C, extracellular signal-regulated kinase, and phosphatidylinositol 3-kinase. BDNF activates the TrkB receptor that is involved in the development of the visual cortex, growth of neurons, and brain development. NT-3 activates TrkC (and to a lesser extent TrkB). NT-3 promotes neurite ganglion outgrowth. NT-4/5 activates TrkB and may be involved in bipolar disorder.

This volume is organized so that crystal structures and basic structural studies on neurotrophins and their receptors appear first. The following section focuses on neurotrophin functions and the final section concentrates on the biological actions of neurotrophins related to clinical conditions and disease.

To open with structural studies, T. Bertrand is the author of "Crystal structures of neurotrophin receptors kinase domain." This is followed by "BDNF pro-peptide: a novel modulator of synaptic plasticity" by M. Kojima and T. Mizui. Then, A. Travaglia and D. La Mendola report on "Zinc interactions with brain-derived neurotrophic factor and related peptide fragments." The "Structural characterization of p75 neurotrophin receptor: a stranger in the TNFR superfamily" is the subject of M. Vilar. Next, C. Sato reviews "Releasing mechanism of neurotrophic factors via polysialic acid." This is followed by M. Martorella, K. Barford, B. Winkler, and C.D. Deppmann who describe the "Emergent role of Coronin-1a in neuronal signaling." Finally, M. Budzinska, K.B. Wicher, and M. Terenzio report on the "Neuronal Roles of the Bicaudal D Family of Motor Adaptors."

Chapters on biological activities of neurotrophins open with "BDNF and hippocampal synaptic plasticity" by G. Leal, C.R. Bramham, and C.B. Duarte. K.E. Boschen and A.Y. Klintsova describe "Neurotrophins in the brain: interaction with alcohol exposure during development" and A.S. Sahay, D.P. Sundrani, and S.R. Joshi report on "Neurotrophins: role in placental growth and development."

In the final section devoted to clinical conditions, J. Janssens, D. Lu, B. Ni, W. Chadwick, S. Siddiqui, A. Azmi, H. Etienne, A. Jushaj, J. van Gastel, B. Martin, and S. Maudsley offer "Development of precision small-molecule pro-neurotrophic therapies for neurodegenerative diseases." "The role of neurotrophins in inflammation and allergy" is described by S. Manti, P. Brown, M.K. Perez, and G. Piedimonte. M. Dhobale reports on "Neurotrophic factors and maternal nutrition during pregnancy." "The role of neurotrophin signaling in gliomagenesis: a focus on the p75 neurotrophin receptor ($p75^{NTR}$/CD271)" is authored by M.M. Alshehri, S.M. Robbins, and D.L. Senger. S.I. Hodgetts and A.R. Harvey write on "Neurotrophic factors used to treat spinal cord injury." "Neurotrophins and migraine" is the topic of L.B. Martins, A.L. Teixeira, and R.B. Domingues. H. Geoffroy and F. Noble focus on "BNDF during withdrawal." In conclusion, N.F. Frydenlund and M. Mahalingam report on "Neurotrophin receptors and perineural invasion—analyses in select lineage-unrelated cutaneous malignancies with a propensity for perineural invasion."

The illustration on the cover is a reproduction of Fig. 1 in Chapter 1 by Thomas Bertrand: "Crystal structures of neurotrophin receptors kinase domain." The legend of this figure is: "Structure of the dimeric nerve growth factor complexed with the extracellular domain of TrkA (pnb code 2IFG). Both immunoglobulin-like domains (d5, d4) and the leucine-rich repeats (d3, d2, and d1) are labeled. The localization of the cell membrane is indicated by a *rectangular box*."

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