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## Preface

Neurotrophic factors can be broadly understood as any secreted factor that has nourishing or sustaining effect on neurons. The archetypical neurotrophic factor is nerve growth factor (NGF) which was first discovered in series of elegant embryological and biochemical experiments carried out by Rita Levi-Montalcini and her colleagues. In the 1980s and 1990s, the work of Hans Thoenen, Yves-Alain Barde, and others paved the way for the discovery of new members of this family BDNF, NT-3, and NT-4. This family of neurotrophic factors became known as the neurotrophins. In parallel to these discoveries, other neurotrophic factors were discovered, notably the glial-derived neurotrophic factor (GDNF) which also belongs to a small sub-family of factors which includes neuritin, artemin, and persephin. Our knowledge on the biology of neurotrophic factors has exploded in the last 15 years and it has become apparent that members of the neurotrophin family play important roles, not just in the development of the nervous system, but in the normal physiology and pathophysiology of the brain. For this reason we have chosen to largely restrict the focus of this new handbook of pharmacology volume on neurotrophic factors to the biology of the neurotrophins NGF, BDNF, NT-3, and NT-4. Research on the neurotrophins in the 1990s provided much hope that these factors would show therapeutic potential in a wide variety of neurodegenerative diseases from Alzheimer's to Parkinson's disease. It is probably fair to say that the research emphasis has moved away from pursuing a role for neurotrophins in neuroprotection. Nevertheless the last 15 years has witnessed outstanding progress in understanding the functional roles of these neurotrophic factors and their receptors in normal development and adult physiology, their mechanisms of action, as well as their role in the pathophysiology of disease. This book provides critical reviews of the role of neurotrophins and their receptors in a wide variety of diseases including neurodegenerative diseases like Huntington's, cognitive dysfunction, psychiatric disorders such as clinical depression, Rett syndrome, motor neurone disease, spinal cord injury, pain, metabolic disease, and cardiovascular disease. The book also contains contributions from leaders in the field dealing with the basic biology, transcriptional and post-translational regulation of the neurotrophins, and their receptors. The last decade has witnessed a radical change in the view of neurotrophins and their receptors, because of the discovery that the pro-peptide forms of NGF and BDNF, in particular, have distinct biological effects mediated by novel receptor constellations, including that of the VPS10p family transmembrane

receptor sortilin and the low-affinity neurotrophin receptor p75NTR. Thus there are more molecular targets for manipulating neurotrophins available and more validated disease processes in which neurotrophins play a relevant and powerful role. Pharmaceuticals tailored to interfere with neurotrophin function have not only been developed, but even show clinical efficacy in late stage clinical trials for the treatment of pain. This book will review all recent areas of progress in the study of neurotrophins and their biological roles. Importantly, world-renowned experts explain the detailed and complex biology of these factors in the context of disease, revealing future perspectives for new therapies based on neurotrophin signalling and their downstream targets.

We are very excited about this book as it contains contributions from the leading scientists in the field who bring a unique combination of expertise on the detailed molecular mechanisms by which neurotrophins signal as well as perspectives on their disease relevance. During the final stages of the production of this book, two pioneers in the field of neurotrophin research, Rita Levi-Montalcini and Hans Thoenen, sadly passed away. We both had the honour and the luck to benefit from close scientific contact with Hans Thoenen in the formative years of our research careers. We would like to dedicate this volume to the memory of these two wonderful scientists, Rita Levi-Montalcini and Hans Thoenen.

Berlin, Germany  
Nashville, TN

Gary R. Lewin  
Bruce D. Carter

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Lewin, G.; Carter, B.D. (Eds.)

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