

## Preface

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## PREFACE

The discovery of nerve growth factor (NGF) some four decades ago allowed new types of question to be asked about the nervous system. The same discovery, and subsequent ones, have also slowly revealed answers to some of those questions. Interest in the role of trophic factors in the development and maintenance of the nervous system has persisted unabated for four decades. Indeed it has steadily grown over this period. The impact of this field of study is reflected in the award of the Nobel prize for Medicine to Dr Levi-Montalcini and Dr Cohen for their work on NGF.

For 20 or 30 years after its discovery, the effects of NGF (and subsequently other neurotrophic factors) were of interest mainly to developmental neurobiologists. The principal tools available during this period were the protein itself and antibodies to it. These were used imaginatively in a wide variety of *in vivo* and *in vitro* studies. With only limited knowledge it was possible to make progress on important general questions. For instance, binding studies of labelled NGF revealed much about the nature and distribution of receptors long before they were identified.

Knowledge of what we now know as the low affinity neurotrophin receptor (the so-called p75 receptor), and particularly the identification of BDNF as the second member of the neurotrophin family, led to renewed vigour in the studies of neurotrophic factors in the 1980s. In the 1990s, interest has continued to grow, apparently at an explosive rate. For instance, over this 5 year period, submissions to the annual meeting of the American Society for Neuroscience meeting (always a good barometer of current trends) relating to trophic factors have increased from 195 (1990) to 493 (1995). There are undoubtedly a number of reasons for the enormous growth in the appeal of this field of study, some general and some specific. Particularly over the last decade it appears to me that there has been something of a decline in interest in the nervous system from the perspective of 'signal processing' and a corresponding increase in questions relating to long term regulation of neural connections.

Clearly, excitement about the neurotrophins has been fuelled by the discovery of a whole family of molecules, now stretching from NGF, BDNF, NT-3, NT4/5 to NT-6 (the latter in teleost fish only so far), and the simultaneous discovery of the *trk* family of high affinity receptors for the neurotrophins. Much of the early work on neurotrophic molecules was focused on their survival-promoting effects. An important recent change is the growing belief that many other aspects of neuronal function may be regulated by trophic factors, ranging from neurotransmitter production to neuronal morphology. One of the consequences of the increased interest in neurotrophic factors is that researchers from a wide range of disciplines are now actively considering the potential role of these molecules on a number of different levels. There are therefore many, other than developmental biologists, actively working on trophic factors, from biochemists working on signal transduction pathways to clinicians interested in the potential of these molecules as therapeutic agents. In fact, the popularity of the neurotrophins is reaching such a frenzied level that it seems likely that there will be a period of unbridled enthusiasm in which researchers will fling neurotrophins at their own model systems. We should be prepared for a few false positives.

This volume is also one of the consequences of burgeoning multidisciplinary interest in the neurotrophins. It consists of a series of chapters written by the speakers of a international meeting held at the Royal Society in London in September 1995. The meeting had the same title as this volume. It was organised around the theme of neurotrophins and sensory neurones because it struck us as organisers that many researchers used primary sensory neurones as the test system for their experiments. We also felt that this theme would allow an exchange of opinions by workers from very different disciplines.

This volume starts with an review on the fundamentals of neurotrophin actions on sensory neurones, and an overview of the major lines of investigation now being pursued. The following chapters are organised on a temporal theme, which consider in turn: (i) the role of

neurotrophins in neurogenesis and sensory neurone proliferation; (ii) their role in naturally occurring cell death and the neurotrophic hypothesis; (iii) influence on the postnatal maturation of sensory neurones; (iv) effects in adult animals and (v) clinical applications of neurotrophins in peripheral neuropathies. The final chapter is a thematic summary and retrospective review of the meeting.

The efforts of many have contributed to the rapid production of this volume. In particular the meeting organisers would like to thank the editorial staff of the Royal Society. We would also like to thank Genentech Inc, San Francisco for a grant aiding the production costs of this volume.

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