

## Preface

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For many years, it was widely believed that the cell cycle in the central nervous system (CNS) was mostly of a prenatal, developmental nature. The concept of adult neurogenesis remained dormant until recently, while reports of an altered cell cycle in a damaged CNS gained strength. The discovery that the adult mammalian brain creates new neurons from pools of stem cells was a breakthrough in neuroscience. However, cell cycle regulation and disturbances are also a significant event in the life of other, nonneuronal cells of the brain (and spinal cord). *The Cell Cycle in the Central Nervous System* has been assembled with this in mind, and the authorship reflects these concepts.

There is still controversy over how to define a mitotic cell and how to study the relevance of neurogenesis in the CNS. Part I begins with an introduction to some of the tools that neuroscientists have used to determine mitotic propensity in neurons and other CNS cells (Dr. Prayson). The relevance of cell expansion and differentiation, with emphasis on both neuronal and glial cells, is outlined in the chapters by Drs. Taupin and Bradl. The development of blood vessels and their relevance during brain development is discussed in the chapter by Dr. Grant and myself, and Drs. Battaglia and Bassanini describe how impaired cell expansion results in postnatal malformations of cortical structures.

Neurons and glia, brain parenchyma, and cerebral vasculature are regarded today as an integrated system rather than an aggregate of different cell types. The concept of a neurovascular unit is clearly a centerpiece of modern neurobiology. Drs. Walker and Sikorska open Part II with an illustration of how mass screening of genes and gene products can be applied to neurogenesis, and Dr. Lo and colleagues describe how the development of new neurons is counterbalanced by cell death by apoptotic activation. The brief reviews by Drs. Arcangeli and Becchetti and the contributions by Dr. Bordey and colleagues, as well as Dr. Yu, introduce a new and provocative role for ion channels and neurotransmitters expressed in the CNS and apparently involved in the process of cell division and mitotic arrest. The renewal of stem cells in the mammalian brain is introduced by Dr. Arsenijevic.

Part III is devoted specifically to the regulation of cell cycle in glia and how its regulation may fail in pretumor conditions or following a nonneoplastic CNS response to injury (*see* Chapter 12 by Dr. Couldwell and colleagues, and Chapter 13 by Dr. Hallene and myself). In addition to ion channels (Part II, Chapter 8), evidence suggests that electrical field potentials are responsible for the relative quiescence of excitable cells or cells exposed to constant electrical activity (brain, heart, nerve, muscle). This is presented in the chapter by Dr. Dini and colleagues.

The therapeutic success of neurosurgical resections for the treatment of neurological disorders challenges the view that more is necessarily better (Part IV). The chapters by Drs. Taupin and Bengeiz show that brain injury often translates in cell cycle re-entry. Whether this may be beneficial, and to what extent, is discussed in a cerebrovascular

framework by Drs. Kobiler and Glod (Chapter 17), Stanimirovic et al. (Chapter 18), and Moons et al. (Chapter 19).

The possibility that cell cycle re-entry is actually detrimental is presented in Part V. Changes in postmitotic neurons in a variety of pathologies are presented by Drs. York et al., Gustaw et al., Gonzalez-Martinez et al., Eisch and Mandyam, and Casadesus et al. Dr. Cucullo's chapter expands this to the cerebral vasculature.

Cell cycle control fails during tumorigenesis and brain tumors are not an exception. Unfortunately, little progress has been made in the treatment of malignant brain tumors. Part VI focuses on recent advances in the biology and detection of gliomas (Drs. Spence et al., Aeder and Hussaini, Kapoor and O'Rourke, Zhang and Fine), as well as drug resistance (Drs. Teng and Piquette-Miller).

The promises of postnatal neurogenesis and the possible pathological significance of cell cycle re-entry in the central nervous system will greatly influence the neuroscience world in the next several years. There is much hype and controversy surrounding the issue of stem cell research, and also uncertainty concerning the moral and ethical correlates of what we as scientists can do with molecular manipulation of the human genome. In some respects, however, the future is already here, and attempts to treat neurological disorders by gene transfer (Chapter 33), electrical stimulation (Chapter 34), or stem cell introduction (Chapter 35) are presented in Part VII. Drs. DalToso and Bonisegna address the issue of stem cell rejection by the host in Chapter 32, and Chapter 36 by Dr. Aumayr and myself gives a brief overview of how epigenetic modifications may impact CNS development.

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