

# Preface

As long as our brain is a mystery, the universe, the reflection of the structure of the brain, will also be a mystery. —Santiago Ramón y Cajal

Over a century has passed since Santiago Ramón y Cajal, the father of modern neuroscience, was awarded the Nobel Prize for Physiology or Medicine. Yet the brain, like the universe, remains a mystery. But as is true in astrophysics, discoveries in neuroscience continue to astound us. We stand in awe of both these outer and inner worlds. Designation of the 1990s as “The Decade of the Brain” by President George H.W. Bush and the recent launching of the BRAIN (Brain Research through Advancing Innovative Technologies) Initiative by President Barack Obama reflect a universal curiosity about the workings of the nervous system.

The story behind this book, however, begins in the early years of the 1980s—what one might consider the end of the Dark Ages of neuroimmunology. At that time, two highly interdisciplinary scientific fields—psychoneuroimmunology and neuroimmunopharmacology—were just beginning to emerge. In contrast to the prevailing view that the nervous system and the immune system functioned more or less autonomously, research in these fields clearly demonstrated that these two systems are connected. The nervous system, via stress-responsive hormones and neuropeptides, impacted on the immune system. And cells and mediators of the immune system could profoundly affect the brain.

Fast forward to the chapters in this book: state-of-the-art reviews of the neuroimmunological mechanisms underlying some of the most crippling and challenging diseases of the twenty-first century, including Alzheimer’s disease, Parkinson’s disease, multiple sclerosis, Huntington’s disease, stroke, cerebral malaria, neuro-AIDS, meningitis, encephalitis, and substance abuse. The reader will find that the authors of these chapters and of the introductory chapters on mechanisms of brain defense and neuropathogenesis are talking the same language. This language—activated brain endothelial cells, microglia, and astrocytes and their mediators (cytokines/chemokines and free radicals)—did not exist in the Dark Ages. In that unenlightened era, the brain was regarded simply as an “immunologically privileged” organ.

Now, as you will read, cells of the peripheral immune system (neutrophils, monocytes, and T and B lymphocytes) are not only known to provide critical defense of the nervous system but also implicated in neuroinflammation-induced neurodegeneration.

A concept shared by many of the contributors to this book is that the healthful relationship of the cells of the nervous system and immune system is harmonious. It is when the yin-yang balance is tipped that neurodegenerative processes ensue. Having worked in the field of neuroimmunopharmacology, both before and after the Dark Ages, our main purpose in pulling this book together was to foster communication between neuroscientists, immunologists, and pharmacologists who are dedicated to discovering more about the yin-yang relationship of the nervous and immune systems. But our ultimate goal, which is shared by all the contributors, is to find better treatments and prevention strategies for the diseases highlighted in the book. Several chapters deal with such innovative approaches.

The number of stars in the universe is mind-boggling—current estimate of about one septillion ( $10^{24}$ ). But so too with the brain, which contains just shy of 100 billion neurons and ten times as many glial cells (totaling over one trillion cells). And when one considers an estimated 100 trillion synapses of neurons and a countless number of neuronal and glial cell receptors and signals, the brain is an incomprehensible organ. While enormous scientific progress has been made in the past quarter century, we remain at the threshold of understanding of how the brain functions and of how the immune system affects both neurophysiological and neuropathological processes. We hope that the readers of this book, like the editors, will share the same sense of awe inspired by the authors of the chapters in this book.

Somewhere, something is waiting to be known. —Carl Sagan

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