Preface

Characterized by the spontaneous appearance of seizures that are unpredictable in frequency and severity, epilepsy is a common neurological disorder that affects people of all ages and ethnicities. Onset most often occurs in infancy and childhood; this is followed by a second steep rise in older adulthood. More than 2.2 million people in the United States and more than 65 million people worldwide have epilepsy, and 150,000 new cases of epilepsy are diagnosed in the United States annually. Remarkably, 1 in 26 people in the United States will develop epilepsy at some point in their lifetime.

Epilepsy represents a spectrum of neuronal synchronization disorders arising in different brain regions because of a remarkable number of biological defects of neurons and glia, including genetic, vascular, metabolic, autoimmune, neoplastic, and traumatic brain injuries. These are associated with a wide range of clinical features, widely differing seizure types and underlying causes, and varying impacts on individuals and their families. Although episodic in nature, seizures are also associated with a broad range of devastating comorbidities, including depression, autism, anxiety, migraines, and cognitive difficulties. Individuals with epilepsy are also at substantial added risk for premature death, and sudden unexpected death in epilepsy (SUDEP) is the most frequent cause of this mortality. Nearly 7000 individuals in the United States and Europe die each year of SUDEP, which is the second most common cause, after stroke, of number of adult life years lost due to neurological disease.

The treatment of epilepsy centers on finding medication that eradicates or lowers the number of seizures, yet this is often ineffective. Although more than 40 drugs have been used to treat epilepsy, approximately one-third of individuals continue to have seizures or develop intolerable side effects to the medical regimen. Although epilepsy surgery can be curative in highly selected individuals, the number of people who benefit from surgery is miniscule compared with the number of individuals with medically intractable epilepsy.

For decades, epilepsy research remained markedly underfunded by federal funding agencies relative to its incidence in the general population compared to other chronic neurological disorders such as multiple sclerosis and Parkinson's disease. The growing recognition of the prevalence of epilepsy and the social burden of its comorbidities, along with the revolution in advanced genetic, molecular, and imaging tools, has resulted in renewed interest in understanding the cellular mechanisms of epilepsy and its accompanying comorbidities and developing new approaches to prevention and treatment.

New momentum and strategic direction of epilepsy research were spurred by the National Institute of Neurological Disorders and Stroke (NINDS) Benchmarks for Epilepsy, which were developed following scientific conferences held in the Natcher Center at the National Institutes of Health and published in 2007 and 2014 (http://www.ninds.nih.gov/research/epilepsyweb/2007_benchmarks.htm; http://www.ninds.nih.gov/research/epilepsyweb/2014benchmarks.htm). In 2007, these benchmarks, among many others, focused on identifying the underlying biological mechanisms of epilepsy and ictogenesis (seizure generation) that would lead to the development of cures. In 2014, the NINDS enlarged these goals, recommending that research be done to understand the causes not only of epilepsy, but of epilepsy-related neurologic, psychiatric, and somatic conditions, and to develop strategies to prevent epilepsy and its progression.

In response, remarkable strides have been made toward understanding the causes of epilepsy and epileptogenesis, developing new and improved treatments, and delineating factors that contribute to

comorbidities associated with epilepsy. In this volume we have invited an outstanding group of international investigators to review a number of these advances, emphasizing the biological underpinnings, clinical correlations, and emerging treatments of this remarkably heterogeneous group of disorders.

This is an exciting time in the long history of epilepsy research. Chapters in this text will take the reader from the genetics and molecular biology of epilepsy to network abnormalities responsible for seizures. Tremendous advances in delineating the epilepsy phenome/genome and functional consequences of genetic abnormalities have led to intriguing new ideas on the treatment of epilepsy comorbidities as well.

Our major goal in editing this book was to provide neuroscientists with a concise entry point and authoritative review of current "hot" topics in the biology of epilepsy and its comorbidities. Although we hope that clinicians interested in epilepsy will find the book helpful, our primary target audience is neuroscientists, to whom we hope to show the flavor of the innovative research currently being done in epilepsy. If we can entice investigators not currently involved in the study of seizures to investigate the biology of epilepsy, we will consider this volume a success.

We thank Barbara Acosta, Richard Sever, and their colleagues at Cold Spring Harbor Laboratory Press for their outstanding editorial and compositional efforts in completing this book. Their ability to deal effectively with the inevitable delays and minor crises that occurred during this project was greatly appreciated. Finally, we are indebted to individuals with epilepsy and their families who deal with seizures and associated comorbidities on a daily basis and who serve as a powerful reminder to investigators of the importance of understanding the biology of this spectrum disorder. It is only through such investigations that cures for epilepsy will be achieved.

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