

PREFACE

Glioblastoma is the most common and the most malignant variant in the wide spectrum of intrinsic glial brain tumors. Although it can affect children, its incidence increases with age. To date, no uniform etiology has been identified. The pathogenesis in genetic and epigenetic terms is gradually being unraveled. Unlike most aggressive malignancies, glioblastoma only seems to thrive in the exclusive microenvironment of the brain and as such, extracranial metastasis is rare. Nevertheless, individual glioblastoma cells display an unmatched capacity to invade surrounding brain areas and thus exert a locally destructive influence on brain tissue and function. This finding, together with the intrinsic and extrinsic heterogeneity of the tumor, and its environment, makes glioblastoma one of the most difficult cancers to treat. In spite of significant improvements in surgical techniques, radiation technology, and systemic therapies, glioblastoma continues to be an incurable disease causing an enormous individual and societal burden. Although a slow, incremental improvement in survival rates has been noticed in those patients who are fit enough to get an intense, multimodal treatment schedule, the medical need still is widely unmet. Therefore, physicians and basic scientists will have to join forces to create some long-awaited breakthroughs for patients with this devastating disease.

This book, aimed at students, basic scientists, and physicians dedicated to neuro-oncological research and care to its full extent, is divided into three sections, focusing on a better understanding of the disease biology, an inclusive diagnostic and therapeutic management of the disease in the clinic, and an outreach to upcoming new insights and technical innovations.

Section I gives a comprehensive overview on the molecular genetics, biological hallmarks, and the current state-of-the-art preclinical animal models in glioblastoma research. Chapter 1 guides us through the complicated story of glioblastoma genomics and discusses validated and upcoming biomarkers with a potential to improve diagnosis and treatment. In Chapter 2, the genetic identity of secondary glioblastomas, an important minority subgroup, is highlighted as an example of how molecular genetics directly impacts clinical decision-making. Chapter 3 introduces the reader to the fascinating world of epigenetics and its role in pathogenesis, therapy response, and prognosis. Glioma cancer stem cell as the niche for glioma initiation and therapy resistance is the central topic of Chapter 4. In Chapter 5, which discusses glioma cell motility, the most important driver of glioblastoma invasiveness in a healthy brain is being thoroughly discussed, and in Chapter 6, the regulatory role of both microRNAs and long non-coding RNA is being explained showing their steadily mounting importance in understanding glioblastoma biology. Finally in Chapter 7, a concise and clear overview is given of the most widely used small animal models for preclinical research in malignant glioma.

Section II deals with the many diagnostic, therapeutic, and prognostic management challenges physicians are facing every day. Chapter 8 nicely rehearses the epidemiological factors involved in disease and outcome. In Chapter 9, an extensive overview is given of PET imaging options that are increasingly being used in

the neuro-oncological field, and Chapter 10 further elaborates on the potential of different PET tracers as promising tools to assess therapy response versus disease progression, as a highly relevant item in the clinical arena since pseudo-progression and pseudo-responses are known to interrupt our classical decision-making based on MRI imaging and clinical performance of the patient. In Chapter 11, in a central position in the book, a bright and critical appraisal is being performed on the current standard-of-care in glioblastoma therapy, including both conventional radiotherapy and chemotherapy but also newer approaches based on medical evidence. After a comprehensive update on the surgical management of glioblastoma in Chapter 12, intraoperative cortical brain mapping is highlighted in Chapter 13. Challenges and considerations in the context of recurrent glioblastoma are described in Chapter 14 from a surgeon's point of view. The peculiar aspects of pediatric glioblastoma, as a separate disease entity, are dealt with in Chapter 15 to conclude this clinical section on glioblastoma.

Section III has six chapters that try to capture innovative approaches and techniques that might have the potential to gain impact in the field in the coming years. Chapter 16 elaborates on a comprehensive overview of the glioblastoma tumor microenvironment as an underexplored gateway to the tumor, lodging quite some new targets for therapy in the near future. In Chapter 17, combined targeting of cytotoxic compounds is described as a promising tool to maximize local access to therapeutic deliveries in glioblastoma. Chapter 18 elaborates on further improvements on the development of arborizing, multi-channel catheters for convection-enhanced delivery, and Chapter 19 introduces irreversible electroporation as a selective and powerful technique to destroy glioblastoma tumor cells. In Chapter 20, the authors discuss how to improve drug delivery by overcoming the blood–brain barrier, and in Chapter 21 the audience will discover how canine models can instruct us on the values of new therapeutic approaches.

We are confident that this book will enable students, scientists, and physicians to widen their understanding of glioblastoma as a complex brain cancer with an ongoing high medical need, and develop potential game-changing innovations in the field of neuro-oncology.

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