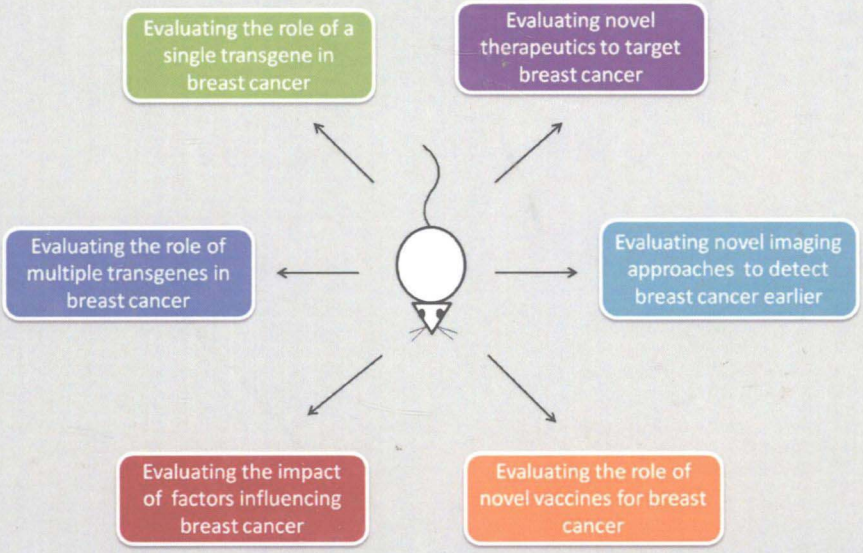
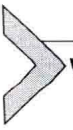
ADVANCES IN CANCER RESEARCH

VOLUME 121



Edited by
Kenneth D. Tew
Paul B. Fisher



VOLUME ONE HUNDRED AND TWENTY ONE

ADVANCES IN CANCER RESEARCH

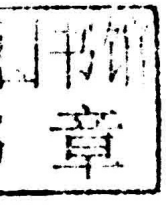
Edited by

KENNETH D. TEW

Professor and Chairman,
Department of Cell and Molecular Pharmacology,
John C. West Chair of Cancer Research,
Medical University of South Carolina,
Charleston, South Carolina, USA

PAUL B. FISHER

Professor and Chair,
Department of Human & Molecular Genetics,
Director, VCU Institute of Molecular Medicine,
Thelma Newmeyer Corman Chair in Cancer Research,
VCU Massey Cancer Center,
Virginia Commonwealth University, School of Medicine,
Richmond, Virginia, USA



ELSEVIER

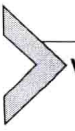
AMSTERDAM • BOSTON • HEIDELBERG • LONDON
NEW YORK • OXFORD • PARIS • SAN DIEGO
SAN FRANCISCO • SINGAPORE • SYDNEY • TOKYO

Academic Press is an imprint of Elsevier

Academic Press is an imprint of Elsevier
525 B Street, Suite 1800, San Diego, CA 92101-4495, USA
225 Wyman Street, Waltham, MA 02451, USA
32 Jamestown Road, London, NW1 7BY, UK
The Boulevard, Langford Lane, Kidlington, Oxford, OX5 1GB, UK
Radarweg 29, PO Box 211, 1000 AE Amsterdam, The Netherlands

First edition 2014

ISBN: 978-0-12-800249-0
ISSN: 0065-230X



VOLUME ONE HUNDRED AND TWENTY ONE

ADVANCES IN
CANCER RESEARCH

CONTRIBUTORS

Aiman Alhazmi
Department of Human and Molecular Genetics, VCU Institute of Molecular Medicine, Massey Cancer Center, Virginia Commonwealth University School of Medicine, Richmond, Virginia, USA

Albert S. Baldwin
Lineberger Comprehensive Cancer Center, University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA

Jennifer W. Bradford
Lineberger Comprehensive Cancer Center, University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA

Amy Lee Bredlau
Department of Pediatrics, and Department of Neurosciences, Medical University of South Carolina, Charleston, South Carolina, USA

Srikumar P. Chellappan
Department of Tumor Biology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, USA

Swadesh K. Das
Department of Human and Molecular Genetics, and VCU Institute of Molecular Medicine, Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA

Luni Emdad
Department of Human and Molecular Genetics; VCU Institute of Molecular Medicine, and VCU Massey Cancer Center, Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA

Benedetto Farsaci
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

Paul B. Fisher
Department of Human and Molecular Genetics; VCU Institute of Molecular Medicine, and VCU Massey Cancer Center, Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA

Daniel J. Foster
Department of Neurology; Department of Neurological Surgery and Brain Tumor Research Center, and Sandler Neurosciences Center, University of California, San Francisco, California, USA

Aaron Frantz
Department of Neurology; Department of Neurological Surgery and Brain Tumor Research Center, and Sandler Neurosciences Center, University of California, San Francisco, California, USA

John W. Greiner
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

James L. Gulley
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

Christopher R. Heery
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

James W. Hodge
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

Bin Hu
Department of Human and Molecular Genetics, Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA

Miller Huang
Department of Neurology, and Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, California, USA

Shirin Ilkanizadeh
Department of Neurology, and Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, California, USA

Caroline Jochems
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

Timothy P. Kegelman
Department of Human and Molecular Genetics, Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA

David N. Korones
Department of Pediatrics, and Department of Palliative Care, University of Rochester, Rochester, New York, USA

Joseph W. Landry
Department of Human and Molecular Genetics, VCU Institute of Molecular Medicine, Massey Cancer Center, Virginia Commonwealth University School of Medicine, Richmond, Virginia, USA

Jasmine Lau
Department of Neurology, and Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, California, USA

I. Levinger
Avram and Stella Goldstein-Goren Department of Biotechnology Engineering, Ben-Gurion University, Beer-Sheva, Israel

Ravi A. Madan
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

Kimberly Mayes
Department of Human and Molecular Genetics, VCU Institute of Molecular Medicine, Massey Cancer Center, Virginia Commonwealth University School of Medicine, Richmond, Virginia, USA

Mitchell E. Menezes
Department of Human and Molecular Genetics, Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA

Claudia Palena
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

Anders I. Persson
Department of Neurology; Department of Neurological Surgery and Brain Tumor Research Center, and Sandler Neurosciences Center, University of California, San Francisco, California, USA

Smitha Pillai
Department of Tumor Biology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, USA

Zhijun Qiu
Department of Human and Molecular Genetics, VCU Institute of Molecular Medicine, Massey Cancer Center, Virginia Commonwealth University School of Medicine, Richmond, Virginia, USA

Devanand Sarkar
Department of Human and Molecular Genetics; VCU Institute of Molecular Medicine, and VCU Massey Cancer Center, Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA

Courtney Schaal
Department of Tumor Biology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, USA

Jeffrey Schlom
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

Kwong-Yok Tsang
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

R. Vago
Avram and Stella Goldstein-Goren Department of Biotechnology Engineering, Ben-Gurion University, Beer-Sheva, Israel

Y. Ventura
Avram and Stella Goldstein-Goren Department of Biotechnology Engineering, Ben-Gurion University, Beer-Sheva, Israel

Susan Wang
Department of Neurology; Department of Neurological Surgery and Brain Tumor Research Center, and Sandler Neurosciences Center, University of California, San Francisco, California, USA

Xiang-Yang Wang
Department of Human and Molecular Genetics; VCU Institute of Molecular Medicine, and VCU Massey Cancer Center, Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA

William A. Weiss
Department of Neurology; Helen Diller Family Comprehensive Cancer Center, and Department of Neurological Surgery and Brain Tumor Research Center, University of California, San Francisco, California, USA

Jolene J. Windle
Department of Human and Molecular Genetics; VCU Institute of Molecular Medicine, and VCU Massey Cancer Center, Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA

Robyn Wong
Department of Neurology, and Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, California, USA

CONTENTS

CHAPTER ONE

Glial Progenitors as Targets for Transformation in Glioma

Shirin Ilkanizadeh[*,†], Jasmine Lau[*,†,1], Miller Huang[*,†,1], Daniel J. Foster[*,‡,§,1], Robyn Wong[*,†,1], Aaron Frantz[*,‡,§], Susan Wang[*,‡,§], William A. Weiss[*,†,‡,¶], Anders I. Persson[*,‡,§,2]

[*]Department of Neurology, University of California, San Francisco, California, USA
[†]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, California, USA
[‡]Department of Neurological Surgery and Brain Tumor Research Center, University of California, San Francisco, California, USA
[§]Sandler Neurosciences Center, University of California, San Francisco, California, USA
[¶]Department of Neurology, University of California, San Francisco, California, USA
[1]These authors have contributed equally.
[2]Corresponding author: e-mail address: anders.persson@ucsf.edu

Contents

Advances in Cancer Research, Volume 121
ISSN 0065-230X
http://dx.doi.org/10.1016/B978-0-12-800249-0.00001-9

Abstract

Glioma is the most common primary malignant brain tumor and arises throughout the central nervous system. Recent focus on stem-like glioma cells has implicated neural stem cells (NSCs), a minor precursor population restricted to germinal zones, as a potential source of gliomas. In this review, we focus on the relationship between oligodendrocyte progenitor cells (OPCs), the largest population of cycling glial progenitors in the postnatal brain, and gliomagenesis. OPCs can give rise to gliomas, with signaling pathways associated with NSCs also playing key roles during OPC lineage development. Gliomas can also undergo a switch from progenitor- to stem-like phenotype after therapy, consistent with an OPC-origin even for stem-like gliomas. Future in-depth studies of OPC biology may shed light on the etiology of OPC-derived gliomas and reveal new therapeutic avenues.

1. INTRODUCTION

Gliomas are the most common malignant primary brain tumor and associated with approximately 16,000 cancer-related deaths in United States per year (Louis et al., 2007). Recent advances in the molecular characterization of gliomas have defined subgroups of tumors that are genetically and epigenetically distinct (Noushmehr et al., 2010; Phillips et al., 2006; Sturm et al., 2012; Verhaak et al., 2010). The temporal and regional specificity of genetically distinct gliomas (Sturm et al., 2012), argue that either several discrete populations of precursor cells may be vulnerable to transformation, or that multiple glioma subgroups share a common cell of origin. Glial cells outnumber neurons by 10-fold in the human brain and are composed mainly of terminally differentiated cells and minor discrete precursor populations. Modeling of glioma in mice has demonstrated that cells at various differentiation stages throughout glial and neuronal lineages have the potential to generate gliomas. In this review, we present recent findings suggesting that the most wide-spread population of cycling cells in the pediatric and adult brain of mammalians, the oligodendrocyte progenitor cells (OPCs), represents a likely origin for large cohorts of gliomas. We propose that more in-depth studies of OPC biology will inform novel preventive measures and therapeutic interventions to reverse the fatal outcome of most glioma patients.

Gliomas can grossly be divided into astrocytic, oligodendrocytic, and ependymal phenotypes. Classification by the World Health Organization (WHO) distinguishes malignancy by grade (I–IV).

Based on histological appearance, gliomas of most grades and types are found in children and adults. Recent molecular profiling of grade IV glioblastoma (GBM) exemplifies that subsets of tumors in children, young adults, and adolescents, that are indistinguishable by histology, can be segregated based on genetic alterations, broad-scale gene expression, and methylation patterns. Here, we will present recent experimental advances on the understanding of why humans are diagnosed with a certain type of glioma and where it came from.

Gliomas show profound cellular heterogeneity and influences from the tumor microenvironment; with treatment-resistant tumor cells displaying a high degree of stemness. The failure to target glioma stem cells (GSCs) along with the inability to fully debulk tumors through surgical resection, radiation and chemotherapy, all contribute to poor survival of glioma patients (Huse & Holland, 2010). In this review, we will discuss ways to identify GSCs, their interactions with tumor microenvironment, and therapeutic advances to target GSCs. In 2012, Yanoko Nishiyama and John Gurdon were awarded the Novel Prize in Medicine for identifying factors that can reprogram somatic cells into pluripotent stem cells. Since these factors are also expressed in stem-like cancer cells, it is possible that they arose from more differentiated cells. In fact, viral transduction of oncogenes into mature neurons and astrocytes generate gliomas in mice (Friedmann-Morvinski et al., 2012). Similarly, it is plausible that OPCs also can give rise to more stem-like gliomas.

2. GLIAL CELL LINEAGES

The central nervous system (CNS) represents a mosaic organization of neural stem cells (NSCs) and astrocyte precursors, that generate neurons, astrocytes, and oligodendrocytes with a high degree of regional specificity (Merkle, Mirzadeh, & Alvarez-Buylla, 2007; Tsai et al., 2012). The positional identity is an organizing principle underlying cellular subtype diversification in the brain and is controlled by a homeodomain transcriptional code (Hochstim, Deneen, Lukaszewicz, Zhou, & Anderson, 2008). During embryonic development, expansion and cell fate determination of neural precursors is controlled by gradients of secreted molecules along rostrocaudal and dorsoventral axes. Radial glia and embryonic NSCs

generate neurons, glial cells, and ependymal cells during neural development (Rakic, 1990). As a remnant from fetal development, postnatal neurogenesis in mammalians is mainly restricted to the dentate gyrus of the hippocampus and the subventricular zone (SVZ) lining the lateral ventricles (Doetsch, 2003; Eriksson et al., 1998; Sanai et al., 2011), with NSCs also lining the third and fourth ventricles (Weiss et al., 1996; Xu et al., 2005). In the postnatal rodent cerebellum, Bergmann glia express markers associated with NSCs (Koirala & Corfas, 2010; Sottile, Li, & Scotting, 2006). In contrast to rodents, functional SVZ neurogenesis in humans ceases after 18 months, indicating that few SVZ NSCs are present in the aging human brain (Sanai et al., 2011). Given the extensive self-renewal capacity of NSCs, these cells have been suggested as the cell of origin for gliomas (Fig. 1.1). Considering the low abundance of NSCs and the wide distribution of gliomas throughout the human postnatal brain, it is puzzling how such a rare and anatomically restricted cell type could represent the origin of the most common primary malignant brain tumor.

A first wave of oligodendrocyte progenitors arises from the embryonic ventral forebrain, followed by a second wave originating from the lateral and caudal ganglionic eminences, and finally a third wave arises within

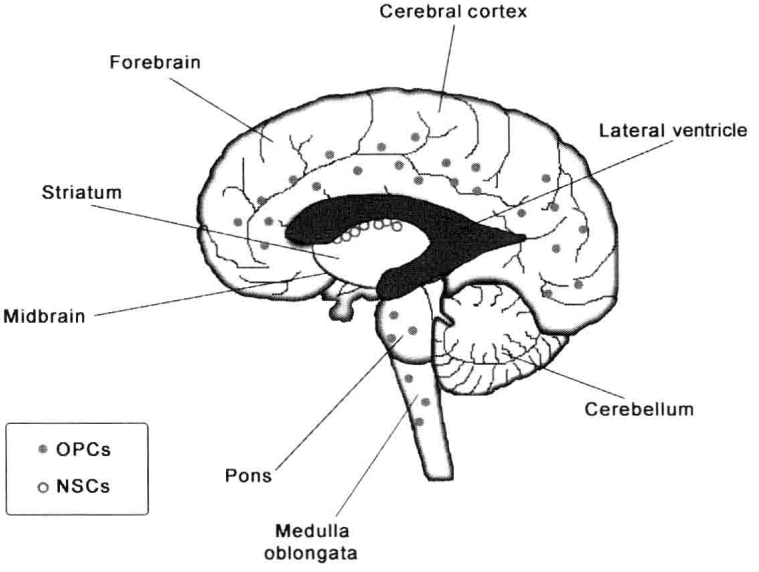


Figure 1.1 Distribution of neural precursor populations in the postnatal brain. OPCs are the most widely distributed population of cycling cells in forebrain and hindbrain regions. In contrast, a discrete population of NSCs is found in the SVZ lining the lateral ventricles. (See the color plate.)