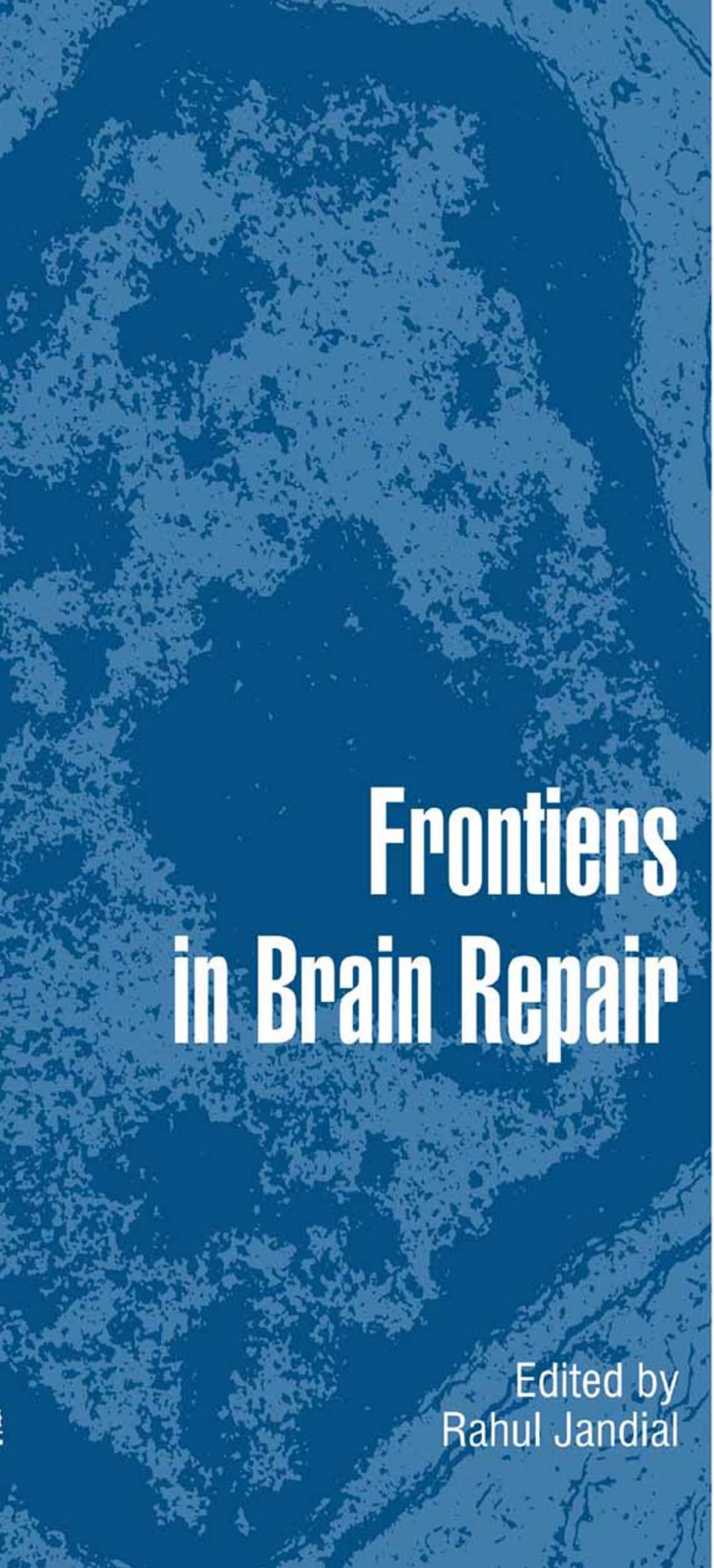

Frontiers in Brain Repair

Edited by
Rahul Jandial

ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

Volume 671

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Rahul Jandial, MD, PhD
Division of Neurosurgery
City of Hope Comprehensive Cancer Center & Beckman Research Institute
Duarte, California, USA

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DEDICATION

Once again and always, to my sons Ronak, Kai and Zain

PREFACE

In the rapidly-evolving landscape of neurosciences, it is not an easy task to select a limited array of topics to present in a text such as this. The purpose of this volume is to provide a representative survey of the current science of brain repair for those seeking to establish a foundation in the field or to replenish a prior knowledge base that may have lapsed in its currency. It also hopes to offer insights into what remains elusive to our collective investigations, defining the "frontiers" of brain repair for those that are currently immersed in the exciting intersection of biological advances and neuroscientific discoveries.

In Chapter 1 the fundamentals of imaging transplanted cells is discussed with emphasis on animal models as well as the horizon for clinical trials. Then, detailed methods on the culture of neural stem cells is reviewed as a foundation for approaching therapeutic goals. Chapter 3 presents the broad scope of animal models that serve as the basis for developmental and pre-clinical investigation, with mention of recent genetically engineered mouse models that represent the best models for studying disease development and treatment. Chapter 4 provides background on the delivery techniques to animals and patients that are available, providing vital information on the subtleties of technique necessary for optimal cellular grafting. Chapters 5 and 6 discuss new and evolving information on the origins of brain tumors and the indelible role of stromal and microenvironmental influences on oncogenesis and tumor progression. Subsequently, the utility of neural stem cells as cellular vehicles to deliver chemotherapeutics to broad neuropathology is reviewed. In Chapter 8 the scope of treating brain tumors is expanded beyond stem cells, to present the best biological interventions to improve upon current treatment options for brain

malignancy. The last two chapters present a comprehensive review on stem cell and gene therapy options for treating cerebrovascular and neurovascular pathology.

In amassing this collection, my intention has been to provide the reader with a broad introduction into molecular imaging, stem cell biology, cell therapy, animal models, central nervous system malignancies, stroke, and neurodegeneration. My hope is that *Frontiers of Brain Repair* will be the intellectual soil from which a deeply rooted and well-nourished vintage of neuroscience will arise.

Rahul Jandial, MD, PhD
Division of Neurosurgery
City of Hope Comprehensive Cancer Center and Beckman Research Institute
Duarte, California, USA

ABOUT THE EDITOR...

RAHUL JANDIAL, MD, PhD, is an Assistant Professor in the Division of Neurosurgery, Department of Surgery at City of Hope Comprehensive Cancer Center and the Beckman Research Institute in Los Angeles, California. His clinical practice focuses on the surgical and medical care of patients with brain and spine tumors. In the laboratory his team investigates the intersection of stem cell biology and neuro oncology, specifically identifying the cells from which brain tumors arise and whether treatment resistant cells can be selectively targeted to help patients live longer. A prolific author, Jandial has authored/edited seven books and over 35 papers. He lives with his wife Danielle and their three sons Zain, Kai, and Ronak.

PARTICIPANTS

Pragathi Achanta
Department of Neurosurgery
Johns Hopkins University School of Medicine
Baltimore, Maryland
USA

Lissa Baird
Division of Neurosurgery
UCSD Medical Center
San Diego, California
USA

Justin Chan
UCSD School of Medicine
San Diego, California
USA

Joseph Ciacci
Division of Neurosurgery
UCSD Medical Center
San Diego, California
USA

Vincent J. Duenas
Del E. Webb Neuroscience, Aging and Stem Cell Research Center
Burnham Institute for Regenerative Medicine
La Jolla, California
USA

Tomas Garzon Muvdi
Department of Neurosurgery
Johns Hopkins University School of Medicine
Baltimore, Maryland
USA

Allen L. Ho
Harvard Medical School
Boston, Massachusetts
USA

Samuel A. Hughes
Department of Neurological Surgery
Oregon Health and Sciences University
Portland, Oregon
USA

Rahul Jandial
Division of Neurosurgery
City of Hope Comprehensive Cancer Center & Beckman Research Institute
Duarte, California,
USA

Jennifer Katz
Del E. Webb Neuroscience, Aging and Stem Cell Research Center
Burnham Institute for Regenerative Medicine
La Jolla, California
USA

Bryan Keenan
Del E. Webb Neuroscience, Aging and Stem Cell Research Center
Burnham Institute for Regenerative Medicine
La Jolla, California
USA

Sassan Keshavarzi
Division of Neurosurgery
UCSD Medical Center
San Diego, California
USA

Michael L. Levy
Pediatric Neurosurgery
Rady Children's Hospital
San Diego, California
USA

Rohit Mahajan
College of Medicine
University of Toledo
Toledo, Ohio
USA

Jayant P. Menon
Division of Neurosurgery
UCSD Medical Center
San Diego, California
and
UCSD Jacobs School of Engineering
La Jolla, California
USA

Ben Newman
Division of Neurosurgery
UCSD Medical Center
San Diego, California
USA

Alfredo Quiñones Hinojosa
Neuroscience and Cellular and Molecular Medicine
Johns Hopkins University
Department of Neurosurgery
Baltimore, Maryland
USA

Amol Shah
UCSD School of Medicine
San Diego, California
USA

Evan Y. Snyder
Del E. Webb Neuroscience, Aging and Stem Cell Research Center
Burnham Institute for Regenerative Medicine
La Jolla, California
USA

Alexey Terskikh
Del E. Webb Neuroscience, Aging and Stem Cell Research Center
Burnham Institute for Regenerative Medicine
La Jolla, California
USA

Kimberly D. Tran
UCSD School of Medicine
San Diego, California
USA

Klaudia Urbaniak Hunter
University of Michigan
Department of Radiation Oncology
Ann Arbor, Michigan
USA

Dawn Waters
Division of Neurosurgery
UCSD Medical Center
San Diego, California
USA

Chester Yarbrough
Department of Neurological Surgery
Barnes Jewish Hospital
Washington University School of Medicine
St Louis, Missouri
USA

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Chapter 1

In Vivo Imaging of Cellular Transplants

Justin Chan, Jayant P. Menon, Rohit Mahajan and Rahul Jandial*

Abstract

We will talk about the techniques of in vivo imaging currently used in today's research and biomedical field, giving a general view of how each technique works and examples of practical applications of each technique. We will cover fluorescent (BL/CL), PET, SPECT and quantum dot imaging. Afterwards, we will cover how in vivo imaging is used in a biomedical sense; more specifically we will see how researchers studying cancer and neurodegenerative disease employ in vivo imaging.

Introduction

Imaging has always been an important part of medical science and research. It has always been important to study samples under microscope with high resolution and contrast. Unfortunately, because of the nature of microscope imaging, the only way to image cells and tissues of animals and humans has been to study the sample ex vivo, outside of the living body in an artificial bath, or from a dead sample. The body has several dynamic functions that clearly can not be studied with static, post mortem samples. This is where in vivo imaging comes in.

In vivo imaging allows researchers to study the movement and nature of target cells, tissue, molecules, etc. within a living organism. In vivo imaging requires a tag in order to make a contrast of the target tissue from the background and a method of imaging and recording the reporter tag. Though in vivo imaging is a simple idea it consists of vastly different routes; tags can consist of gene mutations leading to special protein synthesis, to a literal attachment onto a cell, to use of metal oxides to create a magnetic contrast. The possibilities are endless.

Fluorescent Imaging

In vivo cellular imaging allows researchers to study cell motility in a living organism, as opposed to studying artificial samples or placing dead tissue in an artificial environment. Previously, one had to resort to time-lapse static images from animal models or analyze dead tissue to track and research dynamic events. However now with the use of such noninvasive techniques such as fluorescence, magnetic resonance imaging, positron emission and the ability to capture in vivo trackings in picture and in video, there are now several better ways to study cell motility. In vivo imaging of cellular motility has an infinite amount of uses, from imaging cell in animal models to better understand its physiology to cell-based therapy of disease.

Fluorescent imaging uses reporter technologies, in which the cell or molecule of interest is tagged in vivo and then studied based on its presence. There are two types of fluorescent imaging: direct and indirect.

Direct fluorescence imaging involves an actual engineered probe which tags target cells by targeting a specific receptor or enzyme. Active direct probes are characterized by the fact that

*Corresponding Author: Rahul Jandial—Division of Neurosurgery, City of Hope Comprehensive Cancer Center & Beckman Research Institute Duarte, California, USA
Email: rahuljandial@hotmail.com

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