

A high-magnification, blue-tinted electron micrograph of brain tissue, showing intricate cellular structures and organelles. The image is the background for the left side of the journal cover.

ADVANCES IN  
EXPERIMENTAL  
MEDICINE  
AND BIOLOGY

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Volume 671

# Frontiers in Brain Repair

Edited by  
Rahul Jandial

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# Frontiers in Brain Repair

Edited by

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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.

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# CONTENTS

## 1. IN VIVO IMAGING OF CELLULAR TRANSPLANTS ..... 1

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

Abstract.....	1
Introduction.....	1
Florescent Imaging.....	1
Quantum Dots .....	3
PET and SPECT.....	5
MRI .....	5
In Vivo Imaging and Tumors .....	6
In Vivo Imaging and Neurological Disease.....	8
Conclusion .....	10

## 2. CULTURE AND MANIPULATION OF NEURAL STEM CELLS ..... 13

Jennifer Katz, Bryan Keenan and Evan Y. Snyder

Abstract.....	13
Introduction.....	13
Neural Stem Cells.....	14
Genetic Modification of Neural Stem Cells .....	15
Maintaining Neural Stem Cells In Vitro .....	16
Materials and Methods.....	17
Conclusion .....	21

## 3. ANIMAL MODELS OF NEUROLOGICAL DISEASE ..... 23

Amol Shah, Tomas Garzon Muvdi, Rohit Mahajan, Vincent J. Duenas  
and Alfredo Quiñones Hinojosa

Abstract.....	23
Introduction.....	23
Parkinson's Disease.....	23
Cerebral Ischemia .....	29

**Huntington’s Disease ..... 32**  
**Alzheimer’s Disease ..... 33**  
**Conclusion ..... 35**

**4. STEM CELL TRANSPLANTATION METHODS..... 41**

Kimberly D. Tran, Allen L. Ho and Rahul Jandial

**Abstract..... 41**  
**Introduction..... 41**  
**Factors..... 43**  
**Choosing the Ideal Cell Source ..... 43**  
**Adult Neural Stem Cells..... 43**  
**Embryonic Stem Cells ..... 44**  
**Method of NSC Isolation ..... 45**  
**Preparing NSCs before Transplant ..... 45**  
**Choosing the Experimental Animal ..... 46**  
**Choosing the Surgical Procedure ..... 47**  
**Potential Routes of NSC Administration ..... 47**  
**Neonatal ..... 49**  
**Midgestational In Utero..... 49**  
**Adult..... 49**  
**Considerations during Surgery ..... 51**  
**Postoperative Care..... 52**  
**Optimization..... 52**  
**Anticipated Results and Methods of Detection ..... 53**  
**Conclusion ..... 54**

**5. STEM CELL ORIGIN OF BRAIN TUMORS..... 58**

Dawn Waters, Ben Newman and Michael L. Levy

**Abstract..... 58**  
**Introduction..... 58**  
**Reappraising the Prevailing Theory of Tumor Genesis..... 59**  
**Evidence for NSC as the Cell of Origin..... 60**  
**Conclusion ..... 64**

**6. THE TUMOR MICROENVIRONMENT ..... 67**

Lissa Baird and Alexey Terskikh

**Abstract..... 67**  
**Introduction..... 67**  
**Prevailing Theory of Tumor Initiation..... 68**  
**Cancer Stem Cells Discovery and Evidence of BTSC ..... 68**  
**Caveats to BTSC ..... 70**  
**The Tumor Microenvironment ..... 71**  
**Conclusion ..... 72**

**7. EXPLOITATION OF GENETICALLY MODIFIED NEURAL STEM CELLS FOR NEUROLOGICAL DISEASE ..... 74**

Allen L. Ho, Sassan Keshavarzi and Michael L. Levy

**Abstract..... 74**  
**Exploiting NSCs for Therapeutic Transplantation ..... 74**  
**Genetically Modified NSCs and Neurological Disease..... 76**  
**In Vivo Imaging of Transplanted NSCs ..... 86**  
**Conclusion ..... 89**

**8. BIOLOGICAL HORIZONS FOR TARGETING BRAIN MALIGNANCY ..... 93**

Samuel A. Hughes, Pragathi Achanta, Allen L. Ho, Vincent J. Duenas and Alfredo Quiñones Hinojosa

**Abstract..... 93**  
**Introduction..... 93**  
**Neural Stem Cells..... 94**  
**Exogenous and Endogenous NSCs Respond to Gliomas..... 95**  
**Mechanisms for NSC Homing to Gliomas..... 95**  
**Exploiting NSCs as Vehicles for Delivering Toxic Payloads..... 96**  
**Conclusion ..... 98**

**9. STEM CELLS IN THE TREATMENT OF STROKE ..... 105**

Klaudia Urbaniak Hunter, Chester Yarbrough and Joseph Ciacci

**Abstract..... 105**  
**Introduction..... 105**  
**Stem Cell Therapy ..... 106**  
**Stem Cell Biology In Vitro..... 106**  
**Stem Cell Biology and Animal Models..... 108**  
**Cellular Reconstitution of Stroke Lesions ..... 110**  
**Stroke Treatment Via Enhanced Trophic Factor Delivery..... 111**  
**The Potential of Cord Blood ..... 111**  
**Conclusion ..... 113**

**10. GENE- AND CELL-BASED APPROACHES FOR NEURODEGENERATIVE DISEASE ..... 117**

Klaudia Urbaniak Hunter, Chester Yarbrough and Joseph Ciacci

**Abstract..... 117**  
**Introduction..... 117**  
**Cellular and Molecular Pathophysiology of Alzheimer’s Disease ..... 118**  
**Cellular and Molecular Pathophysiology of Parkinson’s Disease ..... 119**



**Cellular and Molecular Pathophysiology of Huntington’s Disease ..... 121**  
**Stem Cell Therapy for Neurodegenerative Diseases..... 121**  
**Immunotherapy and Alzheimer’s Disease ..... 122**  
**Gene-Based Approaches to Therapy ..... 125**  
**Conclusion ..... 126**

**INDEX..... 131**

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# CHAPTER 1

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## In Vivo Imaging of Cellular Transplants

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

### Abstract

**W**e 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

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