

ADVANCES IN
EXPERIMENTAL
MEDICINE
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Volume 670

Therapeutic Applications of Cell Microencapsulation

Edited by
José Luis Pedraz
and Gorka Orive

Therapeutic Applications of Cell Microencapsulation

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Therapeutic Applications of Cell Microencapsulation

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DEDICATION

Gorka Orive dedicates the present book to his parents Araceli and Ramón, his wife Raquel and his brother Ibon.

José Luis Pedraz dedicates this book to his parents José Juan and Luisa, his wife Angela and his children Diana and Carlos.

FOREWORD

The advancement of science is ever more contingent upon the interaction of experts with different yet complementary sets of expertise. This is a natural consequence of the vast amount of scientific information being gathered every day that exceeds the ability of any one scientist to acquire. As an illustration of the frantic pace of scientific discovery, no single molecular biologist was able to keep up with all the available knowledge in the field by the 1980s, a mere two decades after its inception. This challenge is even more acute in the case of scientific fields at the interface of different and seemingly distant areas of study. Amidst these, the field of cell encapsulation brings together an array of diverse disciplines such as molecular biology and biopolymers, gene therapy and inorganic membranes, stem cell biology and physicochemistry, immunology and nanotechnology. Clearly, such range of topics is too broad for any individual scientist to cover with sufficient depth. The field is experiencing such a remarkable rate of growth that regular updates are necessary to keep abreast of the current knowledge. This book is aimed at providing the reader with a detailed and up-to-date account of the state-of-the-art in the field of cell encapsulation.

At the core of this technology, there is an interaction of physicochemical and biological elements forming three distinct layers of complexity. First, the chemistry of the biopolymer dictates the degree of protein adsorption, vascularization, toxicity and biocompatibility of the microcapsules. Advances in biopolymer science are providing solutions to overcome existing challenges and to improve microcapsules as delivery vehicles. Second, the choice of cells, and more precisely the plethora of metabolites they secrete, and how they interact with the polymer and the host, are key in determining the immune response elicited by the host to implanted microcapsules. Adequate cell viability is crucial to achieve long-term therapeutic delivery. Finally, most microcapsule applications are aimed at delivering a given therapeutic product that is missing or deficient in the host, and thus it is recognized as foreign by the immune system. In response to this insult, the host often generates a vigorous immune response that can seriously compromise the therapeutic delivery. This immune response is antigen-dependent, it is not necessarily identical for all transgenes, and thus must be considered independently for every medical application. Adding to this complexity, changes in one of the above-mentioned layers may also affect the other layers. As an

example, the choice of encapsulated cells may determine whether there is an immune response against the secretable transgene. Similarly, the purity of the polymer may influence the viability of the encapsulated cells. Therefore, it is imperative to consider and study the interaction of all three layers.

Type 1, or insulin dependent diabetes, was one of the first main applications of cell encapsulation. However, the initial promise of a treatment for this disease that imposes such a tremendous burden on both patients and health care system has not yet fully materialized. Despite these shortcomings, recent findings have provided us with a more detailed characterization of the immune responses against encapsulated islets, and in the process, new possibilities for more effective treatments are opening. Beyond diabetes, applications of cell encapsulation have been expanded to multiple human disorders. The initial exploration of intrathecal implantation of encapsulated cells into the CNS, have been followed by additional studies aimed at developing potential applications to very serious medical conditions, such as Parkinson, Alzheimer's, and stroke. Similarly, there are efforts to exploit cell encapsulation as a treatment for cancer, blood diseases and metabolic disorders. The maturity of the field is reflected in the various clinical trials that have explored the application of cell microencapsulation in medicine.

Recent developments in cell encapsulation have improved the outlook of this technology as a viable treatment for medical diseases. The knowledge resulting from the clinical trials, together with additional research on the basic physicochemical and biological characteristics of cell encapsulation will ultimately determine its feasibility.

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PREFACE

The main objective of this book has been to analyze in depth and discuss the different aspects related to the design and elaboration of cell-enclosing microcapsules, even the regulatory features and clinical trials under development. These improvements will lead to progression in this therapeutic approach which may become one day closer to a realistic proposal for clinical application.

The advances in drug delivery technology have enabled a new era of drug discovery and development. In this regard, cell microencapsulation is a technology that opens new venues and possibilities to the administration of new active principles and may be the key to solve several issues related to the correct administration of new therapeutic agents to finally success in the clinical setting.

The editors believe that this technology may have important applicability not only in the field of drug delivery (to treat diseases such as cancer, neurodegenerative disorders, metabolic diseases etc.) but also in cellular therapy and tissue regeneration among others.

Due to the organization of the chapters, this book can be read at different levels and readers may analyze from basic aspects of encapsulation, biomaterials, clinical applications and regulatory and industrial issues of this technology. This book is useful for both graduate and PhD students in the pharmaceutical, engineering and biomedical fields. Nevertheless, we hope that this book is also useful to expert researchers who may find information and new ideas about the cell microencapsulation area.

The general aspects of the technology are analyzed in Chapter 1. The main issues related to the use and selection of biomaterials employed in this type of technology are discussed in Chapter 2. The importance of microcapsule size and the possibility of reducing it through different approaches are discussed in Chapter 3.

In order to succeed in the clinical setting, it is of great importance to take into consideration all the regulatory aspects that may determine the therapeutic applicability of this technology. These issues are discussed in Chapter 4.

In the following chapters the broad spectrum of pathologies that may be treated using cell microencapsulation technology are discussed. Chapter 5 presents the advances achieved in the treatment of diabetes using microencapsulated islets of

Langerhans. The use of microencapsulated cells for the treatment of diseases related to the haematopoietic system are discussed in Chapter 6. Chapter 7 describes the latest advances achieved in the field of regenerative medicine and cell therapy using cell microencapsulation technology, which is nowadays gaining attention and being considered a very relevant and promising strategy for the area. Other pathologies discussed in the book (Chapter 8) deal with alterations and degenerative processes in the central nervous system and the approaches currently under study for the treatment of cancer (Chapter 9).

Chapters 10 and 11 examine the advances achieved in the field of inorganic nanoporous membranes and the aspects that will determine the future of this type of technology. Finally, Chapter 12 examines a very important issue related to the commercial applicability of cell microencapsulation.

Last but not least the editors would like to greatly thank all the participating authors for their dedicated contribution and help, which have been crucial to make the publication of this book possible.

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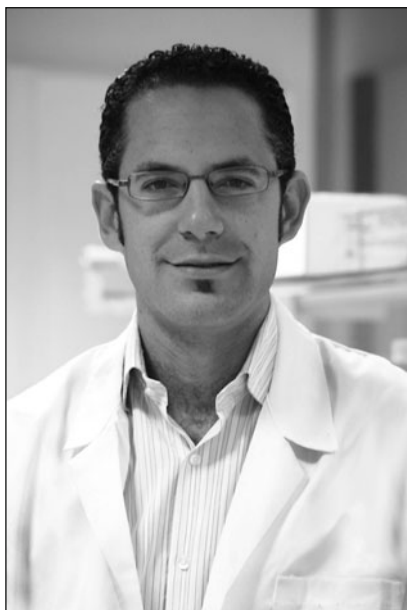
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CONTENTS

1. HIGHLIGHTS AND TRENDS IN CELL ENCAPSULATION 1

Gorka Orive and José Luis Pedraz

Abstract	1
Introduction	1
Pivotal Issues for the Progress in the Field	2
Therapeutic Applications of Cell Encapsulation Technology	3
Conclusion	4

2. BIOMATERIALS IN CELL MICROENCAPSULATION..... 5

Edorta Santos, Jon Zarate, Gorka Orive, Rosa M^a Hernández and José Luis Pedraz

Abstract	5
Introduction	5
Alginate	6
Other Polymers and Type of Biomaterials	14
Conclusion	16

3. DEVELOPMENT OF SUBSIEVE-SIZE CAPSULES AND APPLICATION TO CELL THERAPY 22

Shinji Sakai and Koei Kawakami

Abstract	22
Introduction	22
Narrow Dispersed Subsieve-Size Capsule Production Via the Jetting Process	23
Effect of Preparation Process on Mammalian Cells	26
Effect of Reduction in Microcapsule Diameter	27
Conclusion	28

4. REGULATORY CONSIDERATIONS IN APPLICATION OF ENCAPSULATED CELL THERAPIES 31

J. van Zanten and Paul de Vos

Abstract.....	31
Introduction.....	31
Background	32
Good Manufacturing Practice	32
Cell-Based Therapies	35
Conclusion	37

5. TREATMENT OF DIABETES WITH ENCAPSULATED ISLETS 38

Paul de Vos, Milica Spasojevic and Marijke M. Faas

Abstract.....	38
Introduction.....	38
Concepts of Encapsulation	39
Intravascular Designs	39
Extravascular Macrocapsules.....	41
Host Responses and Macroencapsulation.....	42
Extravascular Microcapsules.....	42
Biocompatibility and Microcapsule Composition.....	44
Biology of Encapsulated Cells.....	45
Conclusion	46

6. EPO DELIVERY BY GENETICALLY ENGINEERED C₂C₁₂ MYOBLASTS IMMOBILIZED IN MICROCAPSULES..... 54

Ainhua Murua, Gorka Orive, Rosa M^a Hernández and José Luis Pedraz

Abstract.....	54
Introduction.....	54
Therapeutic Applications Beyond Erythropoiesis	55
Novel Erythropoiesis Stimulating Strategies: Potential New Treatments for Anemia	55
Cell Encapsulation Technology as an Alternative to Frequent Dosing Schemes	57
Conclusion	63

7. ARTIFICIAL CELL MICROENCAPSULATED STEM CELLS IN REGENERATIVE MEDICINE, TISSUE ENGINEERING AND CELL THERAPY 68

Zun Chang Liu and Thomas Ming Swi Chang

Abstract.....	68
Introduction.....	68
Cell Encapsulation	69