
Essentials in Ophthalmology

Series Editor

Arun D. Singh

More information about this series at <http://www.springer.com/series/5332>

Jorge L. Alió

Jorge L. Alió del Barrio
Francisco Arnalich-Montiel
Editors

Corneal Regeneration

Therapy and Surgery

 Springer

Editors

Prof. Jorge L. Alió MD, PhD, FEBO
Professor and Chairman of Ophthalmology
University Miguel Hernandez
Vissum-Instituto Oftalmologico de Alicante
Alicante
Spain

Jorge L. Alió del Barrio
University Miguel Hernandez
Vissum-Instituto Oftalmologico
de Alicante
Alicante
Spain

Francisco Arnalich-Montiel
Vissum Corporation
Madrid
Spain

ISSN 1612-3212

ISSN 2196-890X (electronic)

Essentials in Ophthalmology

ISBN 978-3-030-01303-5

ISBN 978-3-030-01304-2 (eBook)

<https://doi.org/10.1007/978-3-030-01304-2>

Library of Congress Control Number: 2018963751

© Springer Nature Switzerland AG 2019

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors, and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

This book is dedicated to our families and our patients, who are those who enlighten our daily life with happiness and ideas and who make our lives useful.

Acknowledgement

Prof. Jorge L. Alió would like to thank his supporting co-editors Jorge L. Alió del Barrio, and Francisco Arnalich-Montiel for their contributions to this work.

Alicante, Spain

Prof. Jorge L. Alió

Preface

Corneal Regeneration, the Present and the Future of an Emerging Surgical Solution for Corneal Disease

Regeneration of human tissue is one of the most challenging and promising topics in surgery and indeed in the whole of medicine. Eye care today, based mainly on surgical options and medication, is finding the way to provide better care for our patients affected by ocular disease using biological methods of therapy, including tissue bioengineering which offers a new alternative that may lead to a totally different perspective in the way in which we consider the treatment of eye disease today.

Eye disease severely affects our quality of life. The possibility of successfully treating many ocular diseases which lead to visual impairment with methods which are today the standards of care that do not involve surgical options based on tissue substitution (transplantation), use of long-term therapy or even mutilation caused by the elimination of diseased tissue and replacement by new tissue (like in pseudophakia) is indeed extremely attractive. When accomplished, well-developed tissue regeneration therapy will be considered as one of the major steps forward in human medicine.

This alternative is now being pursued by researchers and innovative clinicians and surgeons finding a way to obtain new methods that are more anatomical and customized than those that we have today, even though these are successful.

The cornea is a privileged tissue for studies on tissue regeneration. It is the forefront of the eye, and due to its transparency, it provides the first step for vision. Corneal blindness is one of the leading causes of blindness in the world and can be cured only by tissue substitution, which is not always possible or even available. Corneal transplantation has been evolving over the last 20 years into different modalities which include lamellar grafts of the anterior and posterior surfaces that are, in fact, today, the most popular ways to treat corneal disease. However, we are all aware of the limitations of corneal grafting based on the availability of tissue and the biological hazard always associated to these procedures.

The cornea, due to its accessibility, is where the most important advances in corneal regeneration therapy and surgery are currently being developed. In this book, the reader will find the most advanced and promising authors, offering the alternative step that corneal regeneration may provide to clinical

practice today. From animal models to real applications based on data obtained in clinical human studies, corneal regeneration is taking a great step ahead towards an application that will change corneal surgery, creating a new revolution. From ocular surface regeneration, corneal stroma regeneration and corneal endothelial cell therapy, we may consider that there is an immediate future in which not only shall we be able to regenerate these three parts of the cornea (surface, stroma and endothelium), but, considered altogether, we could regenerate the whole cornea based on autologous or cell bank tissue. This is in part recreation and involves many challenges, from biological, ethical, organizational and probably financial costs. Of all these, the fundamental use of autologous stem cells for these purposes harbours huge benefits in terms of ethics and availability although we can already imagine the emerging role that cell therapy banks can offer in the future.

We welcome the reader to this book which is the first of its type on this topic and the first to offer in a systematic and improved way the developments that we have obtained today in corneal regeneration. We hope that this will open and stimulate the imagination of the reader and researchers in order to go further and faster in this new and most promising way and stage of eye surgery.

Just to finish this preface, I would like to thank all the participants, authors and investigators of different origins who have participated directly or indirectly in this book. Without their generous contribution, their ideas and their hard work over many years in the background, something like this would not have been possible. They have enlightened the future and this book aims to be the platform to support all this light that will take our practice to a higher level for the benefit of our corneal diseased patients.

Alicante, Spain

Prof. Jorge L. Alió

Perspectives on Regenerative Medicine

It is now widely recognized that regenerative medicine is sure to open novel treatment pathways deep into the twenty-first century, as it follows along the line of organ and tissue transplantation, as well as stem cell-related translational research [1]. In regard to the former, it is set to replace organ replacement therapies, such as heart, liver and kidney transplantations, via the use of sophisticated cell therapies and/or tissues and organs created by tissue engineering procedures [2, 3]. In regard to the latter, specific haematopoietic stem cell transplantation, mesenchymal stem cell transplantation, cultured skin sheets, corneal epithelial stem cell sheets, etc., can now be observed. In regard to the cells used for regenerative medicine, there are two different strategies. The first involves the direct use of stem cells in culture, while the second involves the use of tissue-specific well-differentiated cells in culture. In today's regenerative medicine, two different concepts and strategies exist: one is the direct transfer of cells and/or tissues that, expectedly, possess normal cell functions, while the other aims at releasing miracle substances, including some cytokines, from the transferred cultured cells to the recipient damaged/diseased organ, an example of which can now be seen in the heart-related field of regenerative medicine.

In the corneal field, upcoming medical advancements include superior methods of donor corneal graft preparation prior to surgery. Previous cornea-related surgical procedures, such as keratophakia or epikeratophakia, as well as more modern corneal endothelial grafting techniques, such as DSAEK and DMEK, are prime examples [4]. From the aspect of pioneering corneal regenerative medicine techniques, autologous cultured corneal epithelial [5, 6] and oral mucosal epithelial cell sheets [7, 8], as well as synthetic artificial corneal grafts [9], have all been used in the clinical setting. Moreover, mesenchymal stem cells have recently been applied for the reduction of corneal scarring and restoration of corneal transparency, as have autologous adipose-derived adult stem cells for the treatment of keratoconus [10, 11], a disorder that results in a progressive thinning of the cornea. In addition, a novel cultured corneal endothelial cell injection therapy for the treatment of bullous keratopathy [12] has recently been introduced. Some of these are truly 'stem cell-specific' therapies, while others are regenerative medicine-oriented treatments that involve the use of cultured well-differentiated cells.

It is widely known that there are extremely important issues that must firmly be addressed when considering the introduction of regenerative medicine products to the clinical stage worldwide. This is clearly illustrated by the

fact that although an impressive number of novel and significant academic research findings have been published in the field of corneal regenerative medicine, very few cell products have been officially approved by government agencies. In many countries worldwide, the approved medical products are categorized into three large groups, including pharmaceutical agents, medical devices and regenerative medicine products. Of those, regenerative medicine products fall into the newest category and are strictly regulated by laws and/or guidelines set by each government. The primary point of government laws and guidelines is to eliminate vague and/or false regenerative medicine products as well as to strictly control the products from the aspect of safety and efficacy. While it is true that academic research scientists tend to focus on the efficacy, regulatory authorities place the most importance on safety, which is a vital perspective of regulatory science. Since most regenerative medicine products deal directly with in vitro human cells, the possibility exists that recipients risk adverse events via dangerous unexpected chemicals and/or viruses, thus illustrating why strict government regulation is vitally important. With that aside, it remains undeniable that product efficacy is a primary aspect [13, 14]. To reach that goal, the applied concept of ‘quality by design’ [15] assures equal quality and flawless repeatability of the products, which is essential. To verify efficacy and safety in a clinical trial, one must set the primary endpoint from not only the viewpoint of clinicians and researchers but also via a general consensus of our society, which is the restoration of visual function. Moreover, the concept of a well-organized surrogate endpoint is important. In some ways, there are several important points that slightly differ between the process of research and development and the product development. Cutting-edge medical products originating from embryonic stem cells, induced pluripotent stem cells and direct conversion cells will assuredly emerge, as they may be key to unlocking the door to future treatment pathways, thus once again illustrating the importance of regulatory science, especially in regenerative medicine.

Shigeru Kinoshita
Department of Frontier Medical Science and Technology for
Ophthalmology
Kyoto Prefectural University of Medicine
Kyoto, Japan

References

1. Editorial. Advancing regenerative medicine. *Nature Med.* 2014;20(8):795.
2. Langer R, Vacanti JP. Tissue engineering. *Science.* 1993;260(5110):920-6.
3. Dimmeler S, Ding S, Rando TA, Trounson A. Translational strategies and challenges in regenerative medicine. *Nature Med.* 2014;20(8):814-21.
4. Tan DT, Dart JK, Holland EJ, Kinoshita S. Corneal transplantation. *Lancet.* 2012;379(9827):1749-61.
5. Pellegrini G1, Traverso CE, Franz AT, Zingirian M, Cancedda R, De Luca M. Long-term restoration of damaged corneal surfaces with autologous cultivated corneal epithelium. *Lancet.* 1997;349(9057):990-3.

6. Rama P, Matuska S, Paganoni G, Spinelli A, De Luca M, Pellegrini G. Limbal stem-cell therapy and long-term corneal regeneration. *N Engl J Med*. 2010;363(2):147-55.
7. Nishida K, Yamato M, Hayashida Y, et al. Corneal reconstruction with tissue-engineered cell sheets composed of autologous oral mucosal epithelium. *N Engl J Med*. 2004;351(12):1187-96.
8. Sotozono C, Inatomi T, Nakamura T, et al. Visual improvement after cultivated oral mucosal epithelial transplantation. *Ophthalmology*. 2013;120:193-200.
9. Fagerholm P, Lagali NS, Merrett K, et al. A biosynthetic alternative to human donor tissue for inducing corneal regeneration: 24-month follow-up of a phase 1 clinical study. *Sci Transl Med*. 2010;2(46):46-61.
10. Alio Del Barrio JL, El Zarif M, de Miguel MP, et al. Cellular therapy with human autologous adipose-derived adult stem cells for advanced keratoconus. *Cornea*. 2017;36(8):952-60.
11. Alio Del Barrio JL, El Zarif M, Azzar A, et al. Corneal stroma enhancement with decellularized stromal laminas with or without stem cell recellularization for advanced keratoconus. *Am J Ophthalmol*. 2018;186:47-58.
12. Kinoshita S, Koizumi N, Ueno M, et al. Injection of cultured cells with a ROCK inhibitor for bullous keratopathy. *N Engl J Med*. 2018;378:995-1003.
13. Charo RA, Sipp D. Rejuvenating regenerative medicine regulation. *N Engl J Med*. 2018;378(6):504-5.
14. Marks P, Gottlieb S. Balancing safety and innovation for cell-based regenerative medicine. *N Engl J Med*. 2018;378(10):954-9.
15. Lipsitz YY, Timmins NE, Zandstra PW. Quality cell therapy manufacturing by design. *Nat Biotech*. 2016;34:393-400.

Contents

Part I Corneal Regeneration: The Concept, the Facts, the Potential

- 1 Corneal Anatomy** 3
Miguel Gonzalez-Andrades, Pablo Argüeso, and Ilene Gipson
- 2 Corneal Healing** 13
Veronica Vargas, Francisco Arnalich-Montiel,
and Jorge L. Alió del Barrio
- 3 Corneal Tissue Engineering** 23
Mohammad Mirazul Islam, Roholah Sharifi,
and Miguel Gonzalez-Andrades

Part II The Stem Cell

- 4 Stem Cells: Concept, Properties, and Characterization** 41
Natalia Escacena-Acosta, Javier Lopez-Beas,
Christian Claude Lachaud, Mehrdad Vakilian,
Juan Rigoberto Tejedo, Vivian Capilla-González,
Francisco Javier Bedoya, Franz Martin, Abdelkrim Hmadcha,
and Bernat Soria
- 5 Corneal Stem Cells: Identification and Methods of Ex Vivo
Expansion** 57
Christian Claude Lachaud, Abdelkrim Hmadcha,
and Bernat Soria
- 6 Corneal Epithelial Stem Cells: Methods for Ex Vivo
Expansion** 77
Gustavo S. Figueiredo, Hardeep Singh Mudhar,
Majlinda Lako, and Francisco C. Figueiredo
- 7 Corneal Stromal Stem Cell: Methods for Ex Vivo Expansion** ... 99
Olena Al-Shymali, Jorge L. Alió del Barrio,
and James L. Funderburgh
- 8 Corneal Endothelial Cells: Methods for Ex Vivo Expansion** ... 109
Stephen Wahlig, Matthew Lovatt, Gary Swee-Lim Peh,
and Jodhbir S. Mehta

9	Corneal Regeneration: Use of Extracorneal Stem Cells	123
	Christian Claude Lachaud, Abdelkrim Hmadcha, and Bernat Soria	
10	One Cell, Two Phenotypes: Capturing Pluripotency for Corneal Regeneration	145
	Trevor Sherwin, Carol Ann Greene, Colin R. Green, and Kushant R. Kapadia	
11	Corneal Stem Cell-Based Therapies	155
	Yuzuru Sasamoto, Yoshinori Oie, and Kohji Nishida	
Part III Regenerative Surgery and Therapy of the Ocular Surface Epithelium		
12	Ocular Surface Epithelium: Applied Anatomy	175
	Harminder Singh Dua and Dalia G. Said	
13	Classical Techniques for Limbal Transplantation	191
	Rafael I. Barraquer and Juan Alvarez de Toledo	
14	Simple Limbal Epithelial Transplantation: An Update.	213
	Nandini Venkateswaran and Guillermo Amescua	
15	Cell Therapy Using Ex Vivo Cultured Limbal Cells: CLET and Equivalent.	221
	Paolo Rama and Giulio Ferrari	
16	Cell Therapy Using Cultivated Oral Mucosal Epithelial Transplant (COMET).	225
	Roberto Fernández Buenaga and Sajjad Ahmad	
17	Cell Therapy Using Extraocular Mesenchymal Stem Cells	231
	Teresa Nieto-Miguel, Sara Galindo, Marina López-Paniagua, Inmaculada Pérez, José M. Herreras, and Margarita Calonge	
18	Cell-based Therapy Using Induced Pluripotent Stem Cell	263
	Ricardo Pedro Casaroli-Marano	
19	Cultivated Limbal Stem Cell Transplantation: Indications and Technique	277
	Joséphine Behaegel, Sorcha Ní Dhubhghail, and Marie-José Tassignon	
20	Optimizing the Ocular Surface for Regenerative Surgery: What Is Important and What Is Essential for the Outcome. . . .	291
	Kai B. Kang and Ali R. D'jalilian	
21	Stem Cell Spheres for Corneal Regeneration.	299
	Salim Ismail, Jennifer J. McGhee, Ye Li, Jeremy John Mathan, Jinny Jung Yoon, Himanshu Wadhwa, Stephanie U-Shane Huang, and Trevor Sherwin	
22	Eye Platelet-Rich Plasma (E-PRP) for Corneal Regeneration . .	317
	Alejandra E. Rodríguez and Jorge L. Alió	

Part IV Regenerative Surgery of the Corneal Stroma

- 23 Applied Anatomy of the Corneal Stroma** 349
Harminder Singh Dua and Dalia G. Said
- 24 Confocal Microscopy of the Cornea in a Clinical Model of Corneal Stromal Expansion Using Adipose Stem Cells and Corneal Decellularized Laminas in Patients with Keratoconus** 363
Mona El Zarif, Karim Abdul Jawad, and Jorge L. Alió
- 25 Limbal Stromal Stem Cells in Corneal Wound Healing: Current Perspectives and Future Applications** 387
Noopur Mitragotri, Mukesh Damala, Vivek Singh, and Sayan Basu
- 26 Cell Therapy of the Corneal Stroma Using Ex Vivo Cultured Extraocular Cells** 403
Jorge L. Alió del Barrio

Part V Regenerative Surgery of the Corneal Endothelium

- 27 Corneal Endothelium: Applied Anatomy** 419
Francisco Arnalich-Montiel
- 28 Corneal Endothelium: Isolation and Cultivation Methods** 425
David Mingo-Botín, Marie Joan Therese D. Balgos, and Francisco Arnalich-Montiel
- 29 Corneal Endothelial Cell Transplantation: Animal Models** 437
Brad P. Barnett and Albert S. Jun
- 30 Cell Based Therapy for Corneal Endothelial Regeneration** 455
Noriko Koizumi and Naoki Okumura
- 31 Corneal Endothelium Regeneration: Future Prospects** 463
Wei-Ting Ho, Hsin-Yu Liu, Fung-Rong Hu, and I-Jong Wang

Part VI Bioengineering Cornea Surgery

- 32 Umbilical Cord Stem Cells in the Treatment of Corneal Diseases** 477
Mohammed Ziaei, Jie Zhang, Dipika V. Patel, and Charles N. J. McGhee
- 33 Dysfunctional Corneal Endothelium: Delivery of Cell Therapy** 485
Stephen Wahlig, Gary Swee-Lim Peh, Matthew Lovatt, and Jodhbir S. Mehta
- Index** 499

Contributors

Sajjad Ahmad, MB, BS, FRCOphth, PhD Cornea and External Diseases Department, Moorfields Eye Hospital, London, UK

Jorge L. Alió, MD, PhD, FEBO Professor and Chairman of Ophthalmology, University Miguel Hernandez, Vissum-Instituto Oftalmologico de Alicante, Alicante, Spain

Jorge L. Alió del Barrio, MD, PhD, FEBOS-CR University Miguel Hernandez, Vissum-Instituto Oftalmologico de Alicante, Alicante, Spain

Olena Al-Shymali, MD Vissum Corporation, Alicante, Spain

Juan Alvarez de Toledo, MD, PhD, FEBO-CR Centro de Oftalmología Barraquer, Anterior Segment, Department, Barcelona, Spain

Institut Universitari Barraquer, Universitat Autònoma de Barcelona, Barcelona, Spain

Guillermo Amescua, MD Bascom Palmer Eye Institute, University of Miami, Department of Ophthalmology, Miami, FL, USA

Pablo Argüeso, PhD Massachusetts Eye and Ear and Schepens Eye Research Institute, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA

Francisco Arnalich-Montiel, MD, PhD, FEBOS-CR Vissum Corporation, Madrid, Spain

Marie Joan Therese D. Balgos, MD Research and Development Department, Cornea, Cataract and Refractive Surgery Department, Vissum Alicante, Alicante, Spain

Brad P. Barnett, MD, PhD Wilmer Eye Institute at Johns Hopkins, Department of Ophthalmology, Baltimore, MD, USA

Rafael I. Barraquer, MD, PhD Centro de Oftalmología Barraquer, Anterior Segment Department, Barcelona, Spain

Sayan Basu, MBBS, MS Center for Ocular Regeneration (CORE), LV Prasad Eye Institute, Banajara Hills, Hyderabad, Telangana, India

Francisco Javier Bedoya, PhD, MD Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Andalusia, Spain

Joséphine Behaegel, MD Faculty of Medicine and Health Sciences, Department of Ophthalmology, Visual Optics and Visual Rehabilitation, University of Antwerp, Campus Drie Eiken, Antwerp, Belgium

Department of Ophthalmology, Antwerp University Hospital, Edegem, Belgium
Center for Cell Therapy and Regenerative Medicine, Antwerp University Hospital, CCRG-Oogheelkunde, Edegem, Belgium

Department of Ophthalmology, Brussels University Hospital, Jette, Belgium

Roberto Fernández Buenaga, MD, PhD Cornea, Cataract and Refractive Surgery Department, Visum Madrid, Madrid, Spain

Margarita Calonge, MD, PhD CIBER-BBN (Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine), Carlos III National Institute of Health, Valladolid, Spain

IOBA (Institute of Applied Ophthalmobiology), University of Valladolid, Valladolid, Spain

Vivian Capilla-González, PhD Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Andalusia, Spain

Ricardo Pedro Casaroli-Marano, MD, MSc, PhD Department of Surgery, School of Medicine and Hospital Clinic de Barcelona, University of Barcelona, Barcelona, Spain

Institute of Biomedical Research (IIB-Sant Pau) and Barcelona Tissue Bank, Banc de Sang i Teixits, Barcelona, Spain

Mukesh Damala, MSc Biochemistry Center to Ocular Regeneration (CORE); and Brien Holden Eye Research Center, LV Prasad Eye Institute, Hyderabad, Telangana, India

School of Life Sciences, University of Hyderabad, Hyderabad, Telangana, India

Harminder Singh Dua, MBBS, DO, MS, MD, PhD Academic Section of Ophthalmology, Division of Clinical Neuroscience, University of Nottingham, Nottingham, UK

Department of Ophthalmology, Queens Medical Centre, University Hospitals NHS Trust, Nottingham, UK

Mona El Zarif, Master in Optometry, OD Optica General Sarl, Department of Optometry and contactology, Saida, Lebanon

Visum Instituto Oftalmologico de Alicante, Alicante, Spain

Natalia Escacena-Acosta, PhD Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Andalusia, Spain

Giulio Ferrari, MD, PhD San Raffaele Hospital, Department of Ophthalmology—Cornea and Ocular Surface, Milan, Italy

Francisco C. Figueiredo Newcastle University, Institute of Genetic Medicine, International Centre for Life, Newcastle upon Tyne, Tyne and Wear, UK

Royal Victoria Infirmary, Newcastle upon Tyne, UK

Gustavo S. Figueiredo, MB, ChB, PhD Newcastle University, Institute of Genetic Medicine, International Centre for Life, Newcastle upon Tyne, Tyne and Wear, UK

James L. Funderburgh, PhD University of Pittsburgh, Department of Ophthalmology, Pittsburgh, PA, USA

Sara Galindo, PhD CIBER-BBN (Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine) Carlos III National Institute of Health, Madrid, Spain

IOBA (Institute of Applied Ophthalmobiology), University of Valladolid, Valladolid, Spain

Ilene Gipson, PhD Massachusetts Eye and Ear and Schepens Eye Research Institute, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA

Ali R. D'jalilian, MD University of Illinois at Chicago, Department of Ophthalmology and Visual Sciences, Chicago, IL, USA

Miguel Gonzalez-Andrades, MD, PhD Massachusetts Eye and Ear and Schepens Eye Research Institute, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA

Carol Ann Greene, PhD Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Colin R. Green, BSc, MSc, PhD, DSc Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

José M. Herreras, MD, PhD CIBER-BBN (Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine) Carlos III National Institute of Health, Valladolid, Spain

IOBA (Institute of Applied Ophthalmobiology), University of Valladolid, Valladolid, Spain

Department of Ophthalmology, Clinic University Hospital, Valladolid, Spain

Abdelkrim Hmadcha, PhD Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Andalusia, Spain

Wei-Ting Ho, MD Department of Ophthalmology, Far Eastern Memorial Hospital, New Taipei City, Taiwan

Fung-Rong Hu, MD Department of Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan
College of Medicine, National Taiwan University, Taipei, Taiwan

Stephanie U-Shane Huang, Bachelor of Science (Hons) Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Mohammad Mirazul Islam, MSc, PhD Massachusetts Eye and Ear and Schepens Eye Research Institute, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA

Salim Ismail, BSc, MSc (1st Class Hons) Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Karim Abdul Jawad, Bachelor of Science Optica General Sarl, Department of Optometry and Contactology, Saida, Lebanon
University of Nicosia, Department of Life and Health Sciences, Nicosia, Cyprus

Albert S. Jun, MD, PhD Wilmer Eye Institute at Johns Hopkins, Department of Ophthalmology, Baltimore, MD, USA
Division of Cornea, Cataract and External Eye Diseases, Baltimore, MD, USA

Kushant R. Kapadia, BSc, PGDipSci, MSc Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Christian Claude Lachaud, PhD Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Andalusia, Spain

Majlinda Lako, PhD, MSc, BSc Newcastle University, Institute of Genetic Medicine, International Centre for Life, Newcastle upon Tyne, Tyne and Wear, UK

Javier Lopez-Beas, PhD Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Andalusia, Spain

Kai B. Kang, MD University of Illinois at Chicago, Department of Ophthalmology and Visual Sciences, Chicago, IL, USA

Noriko Koizumi, MD, PhD Department of Biomedical Engineering, Faculty of Life and Medical Sciences, Doshisha University, Kyotanabe, Kyoto, Japan

Ye Li, MBBS (Student) Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Hsin-Yu Liu, MD Department of Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan

Marina López-Paniagua, PhD CIBER-BBN (Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine) Carlos III National Institute of Health, Valladolid, Spain

IOBA (Institute of Applied Ophthalmobiology), University of Valladolid, Valladolid, Spain

Matthew Lovatt, PhD Tissue Engineering and Stem Cell Group, The Academia, Singapore Eye Research Institute, Singapore, Singapore

Franz Martin, PhD, MD Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Andalusia, Spain

Jeremy John Mathan, BMedSc (Hons), MBChB Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Charles N. J. McGhee, DSc, FRCOphth Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Jennifer J. McGhee, BSc Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Jodhbir S. Mehta, BSc, MBBS, FRCSCed Singapore National Eye Centre, Department of Cornea and External Disease, Singapore, Singapore

David Mingo-Botín, MD, PhD Cornea Unit, Department of Ophthalmology, Hospital Universitario Ramón y Cajal, Madrid, Spain

Noopur Mitragotri, MSc Biochemistry Center to Ocular Regeneration (CORE); and Brien Holden Eye Research Center, LV Prasad Eye Institute, Hyderabad, Telangana, India

Hardeep Singh Mudhar, BSc, PhD, MBBChir, FRCPath Royal Hallamshire Hospital, Department of Histopathology, Sheffield, South Yorkshire, UK

Sorcha Ní Dhubhghaill, MD, PhD Faculty of Medicine and Health Sciences, Department of Ophthalmology, Visual Optics and Visual Rehabilitation, University of Antwerp, Campus Drie Eiken, Antwerp, Belgium

Department of Ophthalmology, Antwerp University Hospital, Edegem, Belgium
Center for Cell Therapy and Regenerative Medicine, Antwerp University Hospital, CCRG-Oogheelkunde, Edegem, Belgium

Teresa Nieto-Miguel, PhD CIBER-BBN (Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine), Carlos III National Institute of Health, Valladolid, Spain

IOBA (Institute of Applied Ophthalmobiology), University of Valladolid, Valladolid, Spain

Kohji Nishida, MD, PhD Department of Ophthalmology, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

Yoshinori Oie, MD, PhD Department of Ophthalmology, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

Naoki Okumura, MD, PhD Department of Biomedical Engineering, Faculty of Life and Medical Sciences, Doshisha University, Kyotanabe, Kyoto, Japan

Dipika V. Patel, PhD, MRCOphth Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Gary Swee-Lim Peh, PhD Tissue Engineering and Stem Cell Group, The Academia, Singapore Eye Research Institute, Singapore, Singapore

Inmaculada Pérez, PhD IOBA (Institute of Applied Ophthalmobiology), University of Valladolid, Valladolid, Spain

Paolo Rama, MD San Raffaele Hospital, Department of Ophthalmology—Cornea and Ocular Surface, Milan, Italy

Alejandra E. Rodríguez, PhD Laboratory of the Research, Development and Innovation Department, Vissum Innovation, Alicante, Spain

Dalia G. Said, MB, BCh, MSc, MD, FRCS Academic Section of Ophthalmology, Division of Clinical Neuroscience, University of Nottingham, Nottingham, UK

Department of Ophthalmology, Queens Medical Centre, University Hospitals NHS Trust, Nottingham, UK

Research Institute of Ophthalmology (RIO), Cairo, Egypt

Yuzuru Sasamoto, MD, PhD Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA

Roholah Sharifi, PhD Massachusetts Eye and Ear and Schepens Eye Research Institute, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA

Trevor Sherwin, BSc (Hons), PhD Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Vivek Singh, MSc, PhD Center to Ocular Regeneration (CORE); and Brien Holden Eye Research Center, LV Prasad Eye Institute, Hyderabad, Telangana, India

Bernat Soria, MD, PhD, FRCP Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Andalusia, Spain

Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Madrid, Spain

Marie-José Tassignon, MD, PhD Faculty of Medicine and Health Sciences, Department of Ophthalmology, Visual Optics and Visual Rehabilitation, University of Antwerp, Campus Drie Eiken, Antwerp, Belgium

Department of Ophthalmology, Antwerp University Hospital, Edegem, Belgium

Juan Rigoberto Tejedo, PhD Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Seville, Andalusia, Spain

Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Madrid, Spain University Pablo de Olavide, Seville, Spain

Mehrdad Vakilian, PhD Student Department of Cell Regeneration and Advanced Therapies, Andalusian Center of Molecular Biology and Regenerative Medicine-CABIMER, Junta de Andalucía-University of Pablo Olavide-University of Seville-CSIC, Seville, Andalusia, Spain

Veronica Vargas, MD Vissum Instituto Oftalmológico de Alicante, Alicante, Spain

Nandini Venkateswaran, MD Bascom Palmer Eye Institute, University of Miami, Department of Ophthalmology, Miami, FL, USA

Himanshu Wadhwa, MBChB, BMedSc (Hons) Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Stephen Wahlig, BSc Tissue Engineering and Stem Cell Group, The Academia, Singapore Eye Research Institute, Singapore, Singapore

I-Jong Wang, MD, PhD Department of Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan

College of Medicine, National Taiwan University, Taipei, Taiwan

Jinny Jung Yoon, PhD, MBChB Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Jie Zhang, PhD Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand

Mohammed Ziaei, FRCOphth Department of Ophthalmology, New Zealand National Eye Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand