Preface

The crystalline lens, like the cornea, is one of the most transparent tissues dedicated to optical function. I, with my colleagues, have long been engaged in research on this remarkably unique tissue, in many diverse fields including embryology, physiology, pathology, and others. Disturbance of the optical nature of the crystalline lens by opacification caused by aging and/or other diseases directly impairs visual function. Treatment of the opacification of the tissue, primarily through cataract surgery, has developed into a very precise technique, along with continuous advances in medicine. Classical whole extraction of the opacified crystalline lens with an implantation of an iris-fixed intraocular lens (IOL) has long been replaced by the current modern procedure of extracapsular lens extraction, in association with a better understanding of the importance of the preservation of the lens capsule postoperatively. The design of IOLs has also progressively improved to suit this surgical procedure. After establishing the concept of phacoemulsification and aspiration of the cataractous lens, further innovation of surgical devices including the phaco machine, advanced microscopy, and improvement of biomaterials and the shape of IOLs encompass today's sophisticated cataract surgery. Modern phaco surgery has certainly achieved a dramatic recovery of patients' vision and provided an enormous contribution to healthy aging in humans.

Modern phaco cataract surgery involving IOL implantation is not yet free from complications, which still need to be addressed and overcome. Although postoperative infection or loss of accommodative vision occurs, one of the most common and to-be-prevented complications is posterior capsular opacification (PCO). PCO impairs the patient's vision and is associated with a requirement for further medical treatment, also disturbing the ability for ocular fundus examination by an ophthalmologist. Subsequent surgery or laser treatment of PCO also potentially increases the risk of rhegmatogenous retinal detachment of a "gloomy floater" and remnants of the PCO tissues.

The residual lens epithelial cells retained after extracapsular lens extraction are responsible for PCO. This cell is of ectodermal origin during embryonic development and lines the inner anterior surface of the lens capsule, the native basement membrane of the cell. The lens epithelial cell undergoes aberrant behavior post-phaco surgery. This epithelial cell can migrate posteriorly along the inner surface of the lens capsule, sometimes reaching the posterior lens pole in line with the optic portion of an IOL. The cells may then differentiate into lens-fiber-like tissues

or de-differentiate into a mesodermally derived fibroblastic-like cell, accompanied by aberrant deposition of extracellular matrix, all of which may contribute to the development of PCO.

It is timely that we present this publication dedicated to our current knowledge and understanding of lens epithelial cell biology and PCO, focusing on the key issues with respect to the basic and clinical sciences. I am so lucky to have friends who are leading experts in this field to edit the chapters with me: Frank and Liliana. With their extreme energy and efforts, it is fortunate that the book can deliver 25 specialist chapters by a number of internationally distinguished investigators leading the research in the basic science aspects of lens cells behavior, as well as the clinical problems of lens cells leading to PCO. This volume is edited not only as a series of review articles on cutting-edge findings from researchers, but also as a primer of basic and clinical research on the lens epithelium and PCO for young research investigators, residents, and clinicians alike.

We would like to express our deepest appreciation to Makie Kambara and Mariko Kubota, Springer Japan, as well as our sincerest thanks to the many external reviewers who kindly spent their invaluable time reviewing the chapters.

Wakayama, Wakayama, Japan Shizuya Saika

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Preface

This book provides invaluable and updated information on posterior capsular opacification. It approaches the problem in a very comprehensive manner, from basic science to clinical outcomes and surgical or intraocular device-related methods currently used to prevent it. I was very pleased and honored when Shizuya invited me to join him and Frank in this project, to help develop the clinical/surgical section of the book represented by Parts II to VI.

Cataract surgical removal with intraocular lens implantation evolved into an extremely successful procedure. Yet, despite considerable advances in basic science research, as well as surgical techniques and intraocular device manufacturing, posterior capsular opacification remains the most frequent long-term postoperative complication after cataract surgery. Prevention of any form of opacification within the capsular bag has actually become a primary research goal, particularly with the development of specialized intraocular lenses. For example, accommodating lenses, which are generally designed to move within the capsular bag or have shape alterations upon efforts for accommodation, could have their functionality impaired postoperatively by cellular proliferation and fibrosis. It is only through the prevention of this complication that we will be able to enjoy the full potential of these modern devices.

I would like to thank Shizuya and Frank again for this collaborative opportunity, as well as Makie Kambara and Mariko Kubota of Springer Japan, for their hard work in bringing this project to term. I also would like to thank our international friends and colleagues who contributed with outstanding chapters and who are also all considered leaders in their respective fields. We sincerely hope that this comprehensive report will set the basis for increasing research efforts in the near future towards the complete eradication of posterior capsular opacification. To my colleagues and fellows at the John A. Moran Eye Center, as well as my family, especially my parents, Heron and Nilma, thank you so much for your constant professional and personal support!

Salt Lake City, Utah, USA — Liliana Werner

Liliana Werner, M.D., Ph.D., is a tenured associate professor of ophthalmology and visual sciences and co-director of the Intermountain Ocular Research Center at the John A. Moran Eye Center, University of Utah, Salt Lake City, UT, USA. She has an M.D. degree from Brazil and a Ph.D. degree (biomaterials) from France. Dr. Werner's research is centered on the interaction between ocular tissues and different intraocular lens designs, materials, and surface modifications. These include intraocular lenses implanted after cataract surgery, and also phakic lenses for refractive surgery as well as ophthalmic implantable devices in general.

Preface

Since the turn of the last century, research on the ocular lens has flourished, with major advances in our understanding of its normal biology and pathology emerging, in particular over the last 30 years with the advent and development of powerful molecular tools. Although many candidate molecules have now been identified to play essential roles in the induction, growth, and maintenance of the ocular lens, much more needs to be understood in order to regulate many of the cellular processes that are essential for maintaining lens transparency and preventing cataract. Medical and surgical advances have also progressed with the years, and vision has been restored to many blind worldwide suffering from cataract, through what today seems to be a routine procedure of extracapsular extraction of the cataractous tissue and implantation of a prosthetic lens. This too, unfortunately, is not without its complications, one of the main being posterior capsular opacification (PCO). Much research on this secondary cataract has shown it to arise from lens epithelial cells remaining after surgery which undergo aberrant fiber cell differentiation and/or transformation into myofibroblast-like cells that form subcapsular plaques embedded in extracellular matrix. Although procedures have also been developed to deal with this secondary complication, much research has focused on its prevention. It is in this context of better understanding PCO and its cellular origins that this text was devoted specifically to the lens epithelium and PCO.

This text has allowed us to bring together, for the first time, an international panel of well-known lens cell biologists and clinicians currently working on research specifically related to lens induction, development, differentiation, growth, maintenance, pathology, and surgical practices. The first chapters provide a current view of basic research on the lens epithelium, serving as a foundation for the more clinical-based chapters that comprise the remainder of the text. These early chapters, where relevant, include discussions on lens pathology, such as processes leading to cataract and even PCO, to complement the basic lens research. From the establishment of the embryonic lens epithelium, its detailed morphology and association with its overlying basement membrane, the lens capsule, we cover the regulation of lens epithelial cell proliferation and their differentiation into fiber cells. From this we explore many of the key regulatory transcription factors implicated in congenital cataract before moving on to lens regeneration, a process unique to some lower vertebrates but with potential application to humans in the years to come. We conclude the basic science chapters highlighting different

models investigating the molecules and fibrotic changes to lens epithelia leading to cataract as well as fibrosis associated with lens wound healing. The remainder of the text is dedicated to clinical outcomes of PCO, with a heavy focus on the different modes of its prevention. By showcasing these clinical issues we hope to better educate and bring together our basic lens researchers who have the knowledge and expertise to potentially address some of the problems preventing the progression of this specialist field of research.

This text is unique in its unsurpassed depth of information specifically focused on the lens epithelium and PCO, written by many of the very people who lead the field. It is an invaluable resource for those interested in lens biology and pathology, providing an entry point into the primary research literature. I am privileged to have taken part in this endeavor initiated by Professor Saika, and we hope that graduate students, residents, postdoctoral fellows, principal investigators, and clinicians alike will all enjoy reading and using this book as much as we have enjoyed editing it.

On a final note, I would like to sincerely thank all of the contributing authors who made this work possible, as well as the many other lens researchers who have kindly offered feedback revising the chapters. Last but not least, it has been a great honor working with Professors Saika and Werner. Their professionalism and work ethic have made this exercise a most rewarding and pleasurable experience. To my three sons, Christopher, Alexander, and Matthew Lovicu, thank you for always keeping me grounded and for giving me the time to work on this project.

Sydney, New South Wales, Australia Frank J. Lovicu

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