When researching human diseases, models allow for a better understanding of the disease process without the added risk of harming an actual human. Like other forms of medical research, ophthalmology and vision research focuses on the investigation of disease pathogenesis and the discovery of novel therapies through in vitro and in vivo methodology. The in vivo experiments employ animal models including vertebrates (zebrafish, rodents, rabbits, and primates) and invertebrates (fruit flies and nematodes) for drug screening. Development of suitable experimental models is critical in identifying risk factors for disease, elucidating fundamental molecular mechanisms in disease progression, and providing guidance as to whether or not a particular treatment could be safe and effective for humans. This book is disease-oriented and presents different animal models used for common ocular diseases, including herpetic keratitis, cataract, glaucoma, age-related macular degeneration, diabetic retinopathy, uveitis, Graves’ disease, and ocular tumors. In addition, world expert clinicians make critical comments on the clinical implications of each model.

Hendricks, Yun, Rowe, and Carroll compare some of the animal models of HSV-1 keratitis and their relation to human disease, and discuss some recent novel findings on the pathogenesis of HSV-1 keratitis in mice. Edward Holland states, “From a diagnostic and therapeutic perspective, HSV keratitis is one of the most challenging entities confronting the clinician.” and “Animal models of HSV are critical to the understanding of the pathophysiology and efficacy of new treatment.”

West-Mays describes the experimental animal models most commonly utilized for investigating the genetic and environmental risk factors known to contribute to cataract formation. The strengths and weaknesses of each of these models are highlighted, as well as many recent advances. Yizhi Liu commends: “Although animal models cannot fully represent the features of human cataracts, they are indispensable tools to explore the mechanism of cataractogenesis. Clinicians and researchers alike will find this chapter to be a guide for selecting proper cataract animal models according to different investigation purposes.”

Johnson and Tomarev review the most important rodent models of glaucoma, highlight recent progress in the development of new glaucoma models, and explore the strengths and weaknesses of these models for studying
human disease. John Morrison remarks “The rat and mouse both possess the essential cellular relationships that make the optic nerve head, the primary site of injury, unique. Coincident with the development of these models, modern cell biology methods are now available that allow us to study intraocular pressure-induced gene expression and protein changes in these small nerve heads.” and that “They [these models] will ultimately lead to effective neuroprotective strategies for our most vulnerable patients.”

Sennlaub discusses animal models of AMD risk factors that influence subretinal inflammation. He further outlines models as either “primary” due to genetic factors or “secondary” due to inflammatory responses. The use of these AMD models might help to understand the origin and role of the accumulation of subretinal mononuclear phagocytes in AMD; further, these models could help to identify drug targets able to inhibit the potentially pathogenic subretinal accumulation of these phagocytes or their neurotoxic and angiogenic mediators. Wai Wong affirms that the outlined concepts are helpful in putting the phenomenon of subretinal inflammation in the broad context of AMD pathogenesis. In fact, numerous AMD models have been developed both in vitro and in vivo. Animal AMD models have been reported in different species, mostly in the mouse.\cite{1,2} Recently, the application of new technology to manipulate gene expression such as CRISPR/Cas9 genome editing has effectively caused retinal pigment epithelial defect in zebrafish.\cite{3} Emily Chew states “Developing animal models to study human AMD is essential to our understanding of its pathogenesis and testing of potential therapies for this disease. Despite the lack of the macula in the mouse model and the inability to replicate all the characteristics of AMD in the mouse model, such as retinal pigment epithelial atrophy, the animal models will help us understand the basic processes involved in the pathobiology of AMD.”

Chen and Stiff reveal the wide range of animal models of diabetic retinopathy (DR). They believe the rodent diabetes models will remain the most popular animal models for research into DR. Noemi Lois praises the authors, as they provide us with a thorough review of the experimental animal models of DR available, pointing out both their advantages and their shortcomings. She suggests “Basic scientists and clinicians should work together in the search for improved in vivo models and endpoints for research into DR with the final goal of improving the quality of life of people with DR.”

Kieczewski and Caspi present the major animal models of non-infectious uveitis including the well-established and commonly used experimental autoimmune uveitis (EAU) as well as spontaneous genetic models and the humanized uveitis model. These models are important tools for vision researchers to unveil the complexities of ocular inflammation. On this, Robert Nussenblatt remarks “Clearly many experimental manipulations cannot be performed in patients, and animal models, which not perfect, provide the observer with the correct environment to observe and manipulate.” However, he also warns “Correlating the observations from an animal model to the human can be a daunting task.”
Chang focuses on mouse models of retinal degeneration and specifically, the use of the rd10 (Pde6b<sup>rd10</sup>) model as an example of how a retinitis pigmentosa (RP) model can be used to explore RP. The study of retinal physiology and pathophysiology in the rd10 model has already led to a strong understanding of retinal development, maintenance, and function on a molecular, cellular, and tissue-specific level. Paul Sieving comments, “The chapter provides an extensive review of the many ways that biological knowledge has been developed regarding the causes and cellular consequences of the abnormal Pde6b protein in the rd10 mouse… this chapter reviews the diverse biological strategies that have been employed to rescue vision by slowing or ameliorating the pathophysiology… Despite this, attempts at human therapy for RP remain extremely limited to date.”

Banga, Moshkelgosha, Berchner-Pfannschmidt, and Eckstein describe a mouse model of Graves’ orbitopathy (GO) that recapitulates orbital inflammation and adipogenesis by genetic immunization with human TSHR ectodomain with close field electroporation. Rebecca Bahn thinks this model of GO, and future animal models evolving from it, will facilitate novel experimental approaches and new discoveries regarding GO pathogenesis. These in vivo studies will no doubt lead to randomized clinical trials and ultimately to more effective approaches to the care of patients with Graves’ disease. Shivani Gupta and Raymond Douglas think although pathologic differences do exist between the animal model of Graves’ orbitopathy and human disease, this model provides considerable advances to further elucidate the complex mechanisms that underlie GO.

Jager, Cao, Yang, Carita, Kalirai, van der Ent, de Waard, Cassoux, Aronow, and Coupland summarize various models used for ocular malignancies including melanoma, retinoblastoma, and lymphoma, highlighting the different species that can be used. Arun Singh notes that animal models are useful for not only basic research but also therapeutic testing and patient management in oncology.

In summary, this book, written by international authorities in the field of ophthalmology and vision research, provides a comprehensive review on the most highly relevant animal models for the most common ocular diseases. World expert clinician scientists give positive critiques on the use of these animal models based on their clinical experience.

Finally, I wish to thank the National Eye Institute where I was trained and have been working for over 33 years. I also need to thank all the authors; most of them are my colleagues and friends, who contributed the chapters on these common ocular disease models or made insightful comments from their clinical and scientific experience and knowledge. I would like to also thank Nicholas Popp for his editing and discussion. Lastly, I save my most profound thanks to my family and friends, whose love and encouragement helped me immensely through the process of this book.

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