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Pathologic angiogenesis is involved in cancer and several blinding conditions such as wet age-related macular degeneration, proliferative retinopathies and corneal neovascularization. In these diseases, the angiogenic triggers are hypoxia and inflammation, and both involve the main angiogenic mediator, which is Vascular Endothelial Growth Factor (VEGF). Among

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available treatments, anti-VEGF often shows limited or temporary efficacy, while steroids are potentially responsible for many side-effects. This thesis presents a series of linked studies aimed at elucidating the early pathologic changes leading to inflammation and corneal neovascularization, and how various treatments affect this process. In this thesis, anti-inflammatory and anti-angiogenic treatments are applied in corneal neovascularization models, to identify VEGF-independent pathways and other novel factors as future therapy targets, as well as to investigate the endogenous modulation of angiogenesis. A model of experimental neovascularization in the rat cornea was used as main

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model, where the neovascular response is triggered by a surgical suture placed into the cornea.

Investigational treatments (anti-Vegf, dexamethasone, IMD0354, Gap27, or control substances) were then given topically, with the exception of IMD0354, which was given systemically. The effects in the cornea were studied in vivo with slit lamp photography to assess and quantify macroscopic vessel growth and using in vivo confocal microscopy (IVCM) to study cell infiltration and limbal vessel dilation and detect microscopic vessel sprouts; these examinations were performed longitudinally. Genomic analysis with RNA microarray, selected gene expression with q-RT-PCR, and selected protein

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expression in tissue (immunohistochemistry, immunofluorescence, Western blot) were performed at different time-points. Moreover, other experiments on cell cultures (HUVEC and HCEC), organ cultures (human corneas), ex vivo models (aortic rings) and in vivo studies (zebrafish vasculogenesis) were performed. Dexamethasone suppressed limbal vasodilation and corneal neovascularization more than anti-Vegf, despite no difference in inflammatory cell infiltration into the cornea. Five-hundred eleven fewer genes were differentially expressed in dexamethasone-treated corneas relative to naïve corneas, compared to anti-Vegf. Among them, several major pro-angiogenic and pro-inflammatory factors

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and chemokines were suppressed only by dexamethasone and represent novel candidate factors to target in order to improve anti-VEGF treatment. On the other hand, selective inhibition of a single inflammatory pathway (NF- κ B), despite showing similar early effects as dexamethasone in suppressing tissue inflammation, was not effective enough to suppress new vessel growth. The same factors suppressed by dexamethasone are also inhibited in endogenous modulation of angiogenesis. Surprisingly, dexamethasone activated several complement factors, which could possibly be beneficial in the anti-angiogenic response. In a different therapeutic approach, promoting cell migration to accelerate

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epithelial wound closure similarly was not sufficient to avoid inflammation and angiogenesis in the cornea. In conclusion, new and more effective treatments are needed for corneal inflammation and neovascularization with fewer side-effects. In this thesis, several novel factors and mechanisms related to inflammation are identified, factors that are not addressed by anti-Vegf therapy, and therefore represent interesting objects for further study, as they have the potential to be targets for adjuvant therapy. Specific anti-inflammatory treatment as well as therapeutic activation of endogenous regulatory pathways, and potentially complement modulation, might represent new strategies to improve anti-

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angiogenic therapy, but when used alone they do not seem to avoid corneal neovascularization.

Part of the new series Gems of Ophthalmology, this book provides the latest information in the diagnosis and management of diseases of the cornea and sclera. Beginning with an overview of corneal topography, the following chapters compare LASIK and SMILE procedures for refractive surgery, and their potential complications. The remaining sections discuss numerous disorders, covering both common conditions and more complex, less common infections such as fungal keratitis and acanthamoeba keratitis. Corneal dystrophies and their latest classification and

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management are explained in depth, as is DALK (Deep Anterior Lamellar Keratoplasty). A chapter on corneal changes in contact lens wearers, is also included. This comprehensive text is further enhanced by clinical and surgical photographs. Other topics in the series include: Diseases of the Uvea, Glaucoma, and Retina. Key points Comprehensive guide to diagnosis and management of diseases of the cornea and sclera Part of the new Gems of Ophthalmology series Covers many common and more complex disorders and infections Other topics in the series include: Diseases of the Uvea, Glaucoma, and Retina

This book is a comprehensive guide to ocular

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pharmacology for trainees and practising ophthalmologists. Beginning with the basic physiological aspects of ocular pharmacology and ophthalmic drug administration, the following sections discuss different types of drugs used in the treatment of eye disease. The final sections examine contact lens care systems, nutritional supplements and adverse effects of systematically administered drugs into the eye. This useful, quick reference text is highly illustrated with more than 145 images and tables. Key points

Comprehensive guide to ocular pharmacology for trainees and practising ophthalmologists Covers different drugs for treatment of eye diseases Includes section on adverse effects of systematically

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administered drugs Highly illustrated with more than 145 images and tables

This book presents the fundamentals and the state of the art of the photophysics of molecular oxygen. The author examines optical transitions between the lowest-lying electronic states in molecular oxygen and how these transitions respond to perturbation, either from an organic molecule or from the plasmon field of a metal nanoparticle. We live on a planet filled with light and oxygen. The interaction between these two components forms the basis of excited state chemistry spanning the fields of synthetic organic chemistry, materials chemistry, molecular biology,

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and photodynamic treatment of cancer. Still, the fundamental ways in which oxygen is affected by light is an active subject of research and is continually being developed and rationalized. In this book, readers will learn that singlet oxygen, the excited state of oxygen that exhibits unique chemical reactivity, can be selectively made via direct optical excitation of oxygen in a sensitizer-free system. Readers will also discover that this approach can perturb living cells differently depending on the singlet oxygen “dose”.

Inflammation and angiogenesis, the growth of new blood vessels from pre-existing ones, are involved in

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tumor growth, ocular diseases and wound healing. In ocular angiogenesis, new pathological vessels grow into a specific eye tissue, leak fluid, and disrupt vision. The development of safe and effective therapies for ocular angiogenesis is of great importance for preventing blindness, given that current treatments have limited efficacy or are associated with undesirable side effects. The search for alternative treatment targets requires a deeper understanding of inflammation and how it can lead to angiogenesis in the eye in pathologic situations. This thesis provides new insights into the regulation of inflammation and angiogenesis, particularly at the gene expression and phenotypic levels, in different

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situations characterized by angiogenesis of the cornea, often called corneal neovascularization. For instance, specific genes and pathways are either endogenously activated or suppressed during active inflammation, wound healing, and during resolution of inflammation and angiogenesis, serving as potential targets to modulate the inflammatory and angiogenic response. In addition, as part of the healing response to restore corneal transparency, inflammation and angiogenesis subside with time in the cornea. In this context, LXR/RXR signaling was found to be activated in a time-dependent manner, to potentially regulate resolution of inflammation and angiogenesis. During regression of new angiogenic capillaries, ghost

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vessels and empty basement membrane sleeves are formed, which can persist in the cornea for a long time. Here, ghost vessels were found to facilitate subsequent revascularization of the cornea, while empty basement membrane sleeves did not revascularize. The revascularization response observed here was characterised by vasodilation, increased inflammatory cell infiltration and by sprouting at the front of the reperfused vessels. Importantly, reactive oxygen species and nitrous oxide signaling among other pro-inflammatory pathways were activated, and at the same time anti-inflammatory LXR/RXR signaling was inhibited. The interplay between activation and inhibition of these

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pathways highlights potential mechanisms that regulate corneal revascularization. When treating corneal neovascularization clinically, corticosteroids are in widespread use due to their effectiveness. To minimize the many undesirable side effects associated with corticosteroid use, however, identifying new and more selective agents is of great importance. Here, it was observed that corticosteroids not only suppressed pro-inflammatory chemokines and cytokines, but also activated the classical complement pathway. Classical complement may represent a candidate for further selective therapeutic manipulation to investigate its effect on treatment of corneal neovascularization. In summary, this thesis

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identifies genes, pathways, and phenotypic responses involved in sprouting and remodeling of corneal capillaries, highlights novel pathways and factors that may regulate inflammation and angiogenesis in the cornea, and provides insights into regulation of capillary regression and reactivation. Further investigation of these regulatory mechanisms may offer alternative and effective treatment targets for the treatment of corneal inflammation and angiogenesis.

Volume 1 of this edited book covers basics of endothelial keratoplasty and various surgical techniques currently in use. Chapters on DSAEK,

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DMEK, big bubble, air pump-assisted and endoilluminator assisted DMEK/PDEK, pre-Descemet's endothelial keratoplasty (PDEK), and Descemet's membrane endothelial transfer (DMET) complete the topics on various surgical procedures. Complex situations and complications have been covered in volume 2 of Mastering Endothelial Keratoplasty. Endothelial keratoplasty is a field of great interest to all corneal surgeons. It is an exciting and evolving field in corneal transplantation as the newer techniques of DSAEK, DMEK, E-DMEK and PDEK have inherent advantages that make them supersede the older techniques by far. Hence, in today's scenario with the clearly superior results that these techniques

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offer, it is imperative for all corneal surgeons to learn them and know everything about managing the patient from the pre-operative to the postoperative period. This two-volume book is a must-read for the beginner as well as the established ophthalmologist with interest in corneal transplantation. It is also a must-have for educational institutions, hospital-based libraries and for post-graduate students, fellows and residents who want to expand their knowledge.

This book, "Histopathology-An Update" is a comprehensive book that deals with the latest advances in the field of histopathology. This book will be of help to pathologists, clinicians and researchers

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in the latest update in histopathology of various organs.

Highly praised in its first three editions, Cornea has become a market-leading cornerstone text and the immediate go-to resource for anyone working in this hugely popular and evolving sub-specialty. Offered over two volumes and featuring the knowledge of over 200 experts worldwide, it presents state-of-the-art coverage of the expanding range of contemporary corneal surgery, new diagnostic technology, and medical management of corneal and external disease as well as ocular surface disease. This updated edition includes 20 brand-new chapters, while an enhanced

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focus on images provides key visual guidance in this challenging field. Exceptionally clear illustrations, diagnostic images, and step-by-step surgical photographs offer superb visual guidance. 20 brand-new chapters cover the latest advances in the field, such as DMEK, Ultra-Thin DSEK and DSAEK techniques; endothelial cell transplantation; keratoplasty and prosthokeratoplasty techniques; collagen cross-linking; and new refractive surgical techniques (presbyopic implants and SMILE surgery). Boasts over 170 chapters with unique, cutting-edge content, as well as 2,300 clear illustrations - 670 of which are new to this edition. Presents a detailed exposition of the growing number of techniques for

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lamellar keratoplasty, including outcomes. Includes new sections on the latest developments in the management of ocular surface disease. Key point overviews in each chapter offer easier access to crucial information.

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