

# Department of Ophthalmology

## Chair of Ophthalmology

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### Director

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### Research focus

- Improvements in corneal transplantation
- Pharmacologic modulation of corneal endothelial regeneration
- Corneal stem cells and stem cell-based strategies for ocular surface reconstruction
- Erlangen Glaucoma Registry
- Biomorphometry of the optic nerve
- Minimally invasive glaucoma surgery
- Functional aspects of retinal neurodegeneration
- Retinal physiology
- Non-invasive electrophysiology in humans and animals
- Selective studies of photoreceptor types and postreceptoral pathways
- Autoimmunity and glaucoma
- Autoimmunity and Post-COVID-syndrome
- Pseudoexfoliation syndrome/glaucoma
- Clinico-pathological concepts in diagnosis and management of ocular diseases
- Circulation of the eye and the visual pathway, computer-aided-diagnosis

### Structure of the Department

Professorships: 8

Personnel: 176

- Doctors (of Medicine): 43
- Scientists: 13 (thereof funded externally: 7)
- Graduate students: 57

### Clinical focus areas

- Surgery of the frontal eye
- Cornea surgery
- Reconstructive surgery of the frontal eye
- Glaucoma seamless transconjunctival retinal vitreal surgery (23-gauge-vitreotomy)
- Minimal invasive glaucoma surgery employing implants
- Refractive surgery with the femtosecond laser
- Cataract surgery with innovative intraocular lenses
- Intraocular injections of compounds to treat age related macular degeneration (AMD)
- Special consultation
- Departments of optometry, fluorescence angiography, and laser
- Outpatients' department
- Cornea bank
- Laboratories

### Research

The Department of Ophthalmology belongs to the leading centers in the areas of lamellar corneal transplantation including structural biology of the cornea as well as diagnostics and pathophysiology of glaucomas at a national and international level. An interdisciplinary team of clinician and basic scientists conducts patient-oriented experimental and clinical research into corneal disorders, neurodegenerative diseases, such as glaucoma, and ocular tumors. The broad spectrum of methodologies applied includes molecular and cell biologic experiments, histology and electron microscopy, electrophysiology and visual psychophysics, and state-of-the-art imaging modalities, such as OCT angiography and magnetic resonance imaging. New medical devices for treatment of ocular diseases are being tested as part of multicenter studies. The major goal of the research efforts is to elucidate the pathophysiological causes underlying degenerative and vascular diseases of the eye and visual pathway on a molecular, cellular, and systemic level, to advance the microsurgical techniques, to secure the quality of treatments, and to promote the development of novel therapeutic concepts and treatment strategies.

### Development of new methods for lamellar corneal transplantation

PI: Prof. Dr. F.E. Kruse, PD Dr. T. Tourtas, PD Dr. J. Weller

The Department of Ophthalmology has an internationally leading position in the performance and advancement of new minimally invasive techniques of lamellar corneal transplantation, such as DMEK (Descemet Membrane Endothelial Keratoplasty), using grafts consisting of a single cell layer to replace the diseased corneal endothelium. The clinical research group focuses on the further development of pre-, intra-, and postoperative strategies and the analysis of clinical outcomes to continuously improve quality and reproducibility of the new surgical techniques.

### Pharmacologic modulation of corneal endothelial regeneration

PI: Prof. Dr. F.E. Kruse, PD Dr. T. Tourtas, PD Dr. J. Weller, Prof. Dr. U. Schlötzer-Schrehardt

Due to a worldwide shortage of donor corneas for transplantation, there is an increasing need for regenerative cell therapies for treatment of corneal endothelial disorders, such as Fuchs' corneal endothelial dystrophy. Rho kinases (ROCK) are involved in the regulation of multiple cell functions. The efficacy of selective ROCK inhibitors for functional regeneration of the corneal endothelium in early stages of disease is evaluated in clinical studies and accompanying experimental trials.

### Corneal stem cells and stem cell-based

### strategies for ocular surface reconstruction

PI: Prof. Dr. U. Schlötzer-Schrehardt, Prof. Dr. F.E. Kruse

Transplantation of cultivated limbal epithelial progenitor cell grafts has been used to restore epithelial defects of the human cornea in patients with limbal stem cell deficiency. This research project explores the molecular characteristics of corneal stem and progenitor cells together with their specific niche microenvironment and their utilization for improved stem cell based therapies on tunable biosynthetic matrices. The applicability of alternative autologous stem cell sources for corneal epithelial tissue engineering strategies is also investigated.

### Erlangen Glaucoma Registry

PI: Dr. Dr. B. Hohberger, Prof. Dr. R. Lämmer, Prof. Dr. C. Mardin

Due to the slow progression of glaucoma, a large study population and long-time observations are needed to gain insights into its long-term effects and progression rates. These data have been integrated into a unique patient registry, the Erlangen Glaucoma Registry, founded in 1991. It contains almost all available research data for registered glaucoma patients. This allows for cross-sectional and, in particular, for longitudinal observations and for evaluation of prognostic validity of diagnostic procedures. This database also serves for evaluation and optimization of personalized medical and surgical treatment procedures.

### Biomorphometry of the optic nerve

PI: Prof. Dr. C. Mardin, Prof. Dr. R. Lämmer, Dr. Dr. B. Hohberger

The main focus of this research project is the development and application of novel imaging methods for early detection of glaucoma and to quantify disease progression. Next to morphometric tests (e.g. OCT), OCT-angiography is implemented and improved. The findings are also applied to other diseases, like diabetic retinopathy and age-related macular degeneration.

### Minimally invasive glaucoma surgery

PI: Prof. Dr. R. Lämmer, Dr. Dr. B. Hohberger

As an alternative to traditional glaucoma surgery, minimally invasive glaucoma surgery (MIGS) has shown promise for the future management of glaucoma patients. It refers not to a single surgery, but rather to a group of distinct procedures and devices that aim to decrease intraocular pressure, the major risk factor of glaucoma. In this clinical study, the efficacy, safety, intraoperative complications and postoperative outcome of different procedures and devices will be comparatively evaluated, providing more reliable data for proper indications and personalized treatment strategies. The overall goal is to record all MIGS procedures in a registry and to identify risk factors for the surgical procedures and

clinical outcome. Individual and molecular targets, defining the clinical success, are investigated.

### **Functional aspects of retinal neurodegeneration**

PI: Prof. Dr. J. Kremers, PD Dr. C. Huchzermeyer

In this research project, new electrophysiological and psychophysical techniques are developed to study the functional aspects of retinal degeneration, especially of glaucoma and hereditary retinal degenerations. Electrophysiological tests are objective and allow a direct assessment of retinal pathophysiology. Psychophysical tests can be very sensitive and give an impression about perceptual changes in patients. Novel methods are developed to accurately study the responses that are elicited by single photoreceptor types or by different retinal pathways. Innovative developments in the multifocal stimulation technique and in perimetry are implemented to allow an early diagnosis of retinal degeneration.

### **Retinal physiology**

PI: Prof. Dr. J. Kremers

The goal of this working group is to study the function of the normal and diseased retina. To reach that goal, we record electrophysiological responses of the retina of rodent models of human diseases. In addition, we perform electrophysiological and psychophysical experiments with normal human test persons and patients to identify different signal pathways in the retina and the changes caused by a disease. The results of the animal and human experiments are related with each other so that the pathophysiological processes can be better understood.

### **Autoimmunity and glaucoma**

PI: Dr. Dr. B. Hohberger, Prof. Dr. C. Mardin

The pathomechanisms of glaucoma are complex and multifactorial. Apart from the most important risk factor, i.e. elevated intraocular pressure, autoimmune processes appear to be involved. In fact, there is increasing evidence from animal and human studies that glaucoma is an autoimmune disease, associated with alterations in autoantibody profiles. Clinical studies specifically investigate the role of agonistic autoantibodies against  $\beta_2$ -adrenergic receptors in glaucoma pathogenesis. The removal of  $\beta_2$ -autoantibodies as a novel therapeutic strategy for lowering intraocular pressure is also evaluated in this project.

### **Autoimmunity and Post-COVID syndrome**

Based on the experience in glaucoma research, studies on microcirculation and autoimmunity were done in patients after COVID-infection.

### **Pseudoexfoliation syndrome/glaucoma**

PI: Prof. Dr. U. Schlötzer-Schrehardt

Pseudoexfoliation (PEX) syndrome is worldwide a leading cause of chronic open-angle glaucoma. The focus of this research project is the molecular analysis of the underlying, genetically determined, fibrotic process through functional characterization of known PEX-associated coding and non-coding risk variants, functional analysis of rare genetic variants as well as the identification of novel PEX-associated genes through transcriptome analyses followed by pathway and gene

network analyses.

### **Clinicopathologic concepts in diagnosis and management of ocular diseases**

PI: PD Dr. J. Weller, Dr. R. Meiller, Prof. Dr. A. Bergua, Prof. Dr. G. Gusek-Schneider

Multidisciplinary diagnosis and management of orbital diseases and epibulbar lesions: The purpose of this study is to establish correlations between morphologic, biomicroscopic, histologic, and molecular genetic criteria and the long-term results of surgical excision and plastic reconstruction. Surgical management of periocular malignant tumors using frozen section control and plastic reconstruction: indications, methods, and results.

### **Circulation of the eye and the visual pathway, computer-aided diagnosis, and virtual education**

PI: Prof. Dr. G. Michelson

Ocular circulation of the eye and the visual pathway: The tissues and vessels of the eye reflect systemic diseases and are a perfect system for the visualization of physiologic processes of the body. Immunological processes, diabetes, and arterial hypertension can be evaluated quantitatively in the eye. Computer-aided-diagnosis and virtual education: Ophthalmology needs new methods for medical information processing to optimize diagnosis and therapy. Automated analysis of ophthalmic images combined with automated classification leads to a fast and bias-free evaluation, which is an important prerequisite for screening. Diffusion measurement of the visual pathway based on magnetic resonance images neurodegenerative eye diseases often involve the entire visual system. In some cases, they are induced by a cerebral macro- and microangiopathy with subsequent ischemic changes and degeneration of the visual pathway. The new non-invasive technique based on magnetic-resonance imaging provides information about the integrity and orientation of the visual pathway.

### **Teaching**

Results of research are directly implemented in medical student and postgraduate teaching. Owing to the extensive contacts with colleagues abroad, many foreign students come to the Department of Ophthalmology for at least a part of their study (graduate or post-graduate) and for further education.

### **Selected publications**

Schlötzer-Schrehardt U, Zenkel M, Strunz M, ..., Kruse FE. Potential Functional Restoration of Corneal Endothelial Cells in Fuchs Endothelial Corneal Dystrophy by ROCK Inhibitor (Ripasudil). *Am J Ophthalmol.* 2020; 224:185-199

Augustin VA, Weller JM, Kruse FE, Tourtas T. Influence of corneal guttae and nuclear cataract on contrast sensitivity. *Br J Ophthalmol.* 2020 Sep 9;bjophthalmol-2019-315206.

Huchzermeyer C, Fars J, Kremers J. Photoreceptor-Specific Loss of Perifoveal Temporal Contrast Sensitivity in Retinitis Pigmentosa. *Transl Vis Sci Technol.* 2020 May 27;9(6):27.

Deng SX, Kruse F, Gomes JAP, ...R, Tan D; and the International Limbal Stem Cell Deficiency Working

Group. Global Consensus on the Management of Limbal Stem Cell Deficiency. *Cornea.* 2020;39(10):1291-1302.

Deng SX, Borderie V, Chan CC, ..., Kruse FE; and The International Limbal Stem Cell Deficiency Working Group. Global Consensus on Definition, Classification, Diagnosis, and Staging of Limbal Stem Cell Deficiency. *Cornea.* 2019 Mar;38(3):364-375.

Polisetti N, Gießl A, Li S, Sorokin L, Kruse FE, Schlötzer-Schrehardt U. Laminin-511-E8 promotes efficient in vitro expansion of human limbal melanocytes. *Sci Rep.* 2020 Jul 6;10(1):11074.

Hohberger B, Kunze R, Wallukat G, ..., Herrmann M. Autoantibodies Activating the  $\beta_2$ -Adrenergic Receptor Characterize Patients With Primary and Secondary Glaucoma. *Front Immunol.* 2019;10:2112.

Hohberger B, Müller M, Hosari S, Mardin CY. OCT-Angiography: Mydriatic phenylephrine and tropicamide do not influence retinal microvasculature in macula and peripapillary region. *PLoS One.* 2019 Oct 17;14(10):e0221395.

Grau E, Horn F, Nixdorff U, Michelson G. OCT and IOP findings in a healthy worker cohort: results from a teleophthalmic study in occupational medicine. *Graefes Arch Clin Exp Ophthalmol.* 2019 Nov;257(11):2571-2578.

Berner D, Hoja U, Zenkel M, ..., Schlötzer-Schrehardt U. The protective variant rs7173049 at LOXL1 locus impacts on retinoic acid signaling pathway in pseudoexfoliation syndrome. *Hum Mol Genet.* 2019 Aug 1;28(15):2531-2548.

Michelson G, Forst T. Diabetic Macular Edema in Diabetological Practices. *Klin Monbl Augenheilkd.* 2020 Nov;237(11):1320-1325.

### **International cooperations**

Prof. Dr. M. Greiner, Department of Ophthalmology and Visual Sciences, University of Iowa Carver College of Medicine, Iowa: USA

Prof. Dr. S. Kinoshita, Department of Frontier Medical Science and Technology for Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto: Japan

Prof. Dr. N. Koizumi, Department of Biomedical Engineering, Faculty of Life and Medical Sciences, Doshisha University, Kyotanabe: Japan

Prof. Dr. T. Aung, Singapore Eye Research Institute, Singapore National Eye Centre: Singapore

Prof. Dr. S. Deng, Stein Eye Institute, University of California, Los Angeles: USA