EKFZ
Optogenetic Therapies

ANNUAL REPORT 2025

EKFZ.UNI-GOETTINGEN.DE

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ekfz.uni-goettingen.de/

TOBIAS MOSER

At the Göttingen Else Kröner Fresenius Center we strive to develop and clinically evaluate optogenetic therapies. We believe we can do this because we bring the required expertise, scientific rigor and collaborative spirit.

EMILIE MACÉ

Across the Teams and Platforms of our Center, we are united by a shared mission: to accelerate optogenetic therapies and help bring new treatments to patients as quickly and responsibly as possible. We pursue this goal by bringing together gene therapy, medical technology, and translational research.

TOBIAS BRÜGMANN

The academy focuses on the translation of new approaches into clinics and it's fascinating to see us all diving deep into norms, regulations, and new possibilities.

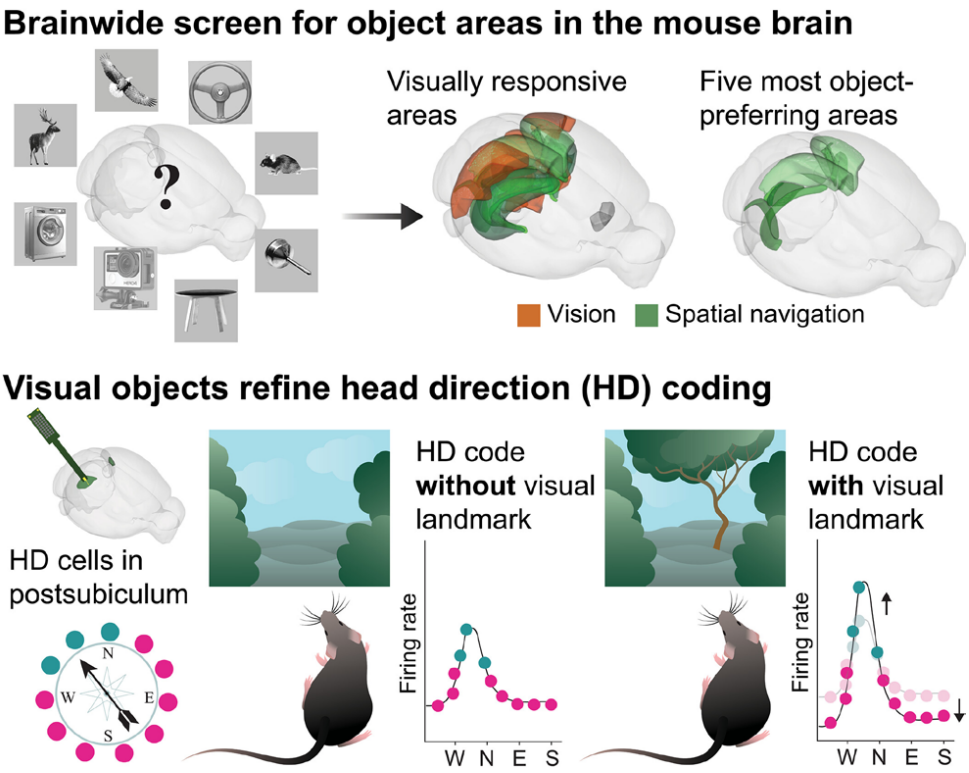
WELCOME

The spokespersons
for the EKFZ OT

We are pleased to present the 2025 Annual Report of the Else Kröner Fresenius Center for Optogenetic Therapies (EKFZ OT) at the University Medical Center Göttingen (UMG).

Since its start on April 1st, 2024, the EKFZ OT has been dedicated to advance the development of optogenetic therapies for restoring hearing and vision, as well as other innovative treatment approaches, at the Göttingen campus, and paving the way for the first clinical trials in humans.

Optogenetics opens up new possibilities for the targeted control of biological processes using light. Our goal is to provide therapeutic options for functional restoration for the first time or to significantly improve existing standards of clinical care. The innovative therapeutic approaches developed at the EKFZ OT offer particular promise for patients with deafness, blindness, gastroparesis, or movement disorders.



PUBLICATION IN SCIENCE

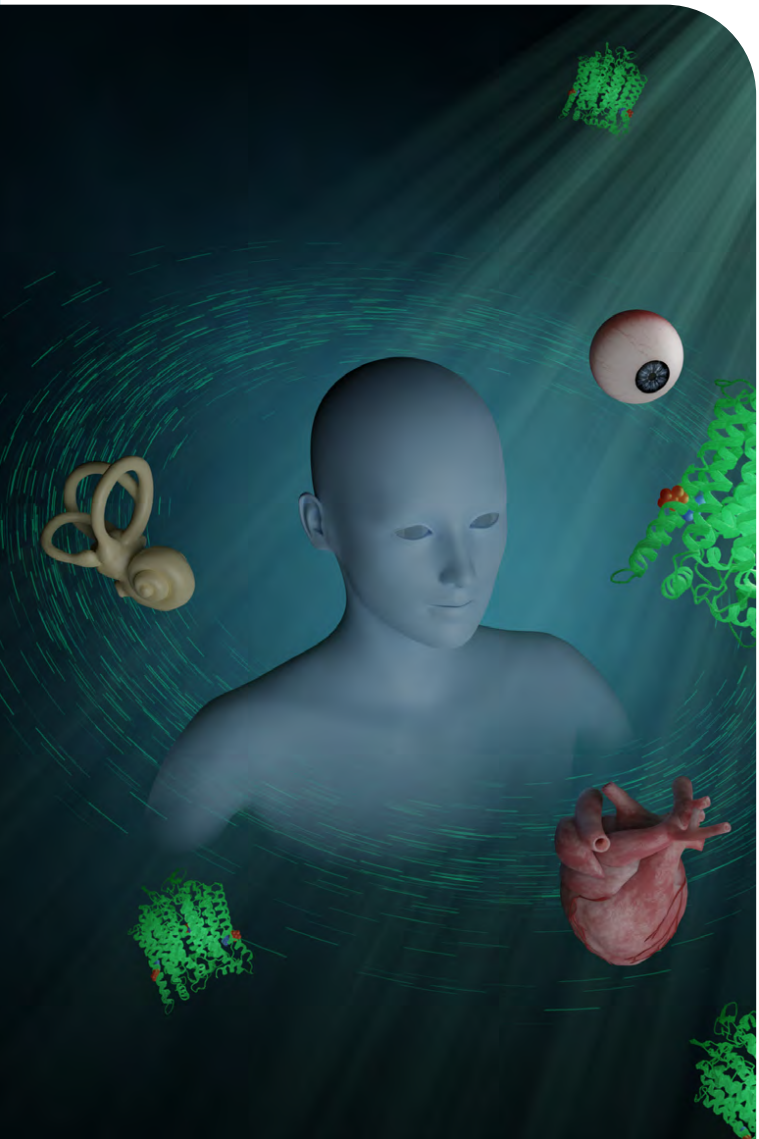
VISUAL OBJECTS REFINE HEAD DIRECTION CODING

Why do we orient ourselves better when visual landmarks are present? Researchers led by Prof. Dr. Emilie Macé, head of the "Brain-wide Networks" research group at the Department of Ophthalmology at UMG, addressed this question in a study published in Science. Using functional ultrasound imaging in mice, the team identified brain regions that respond particularly strongly to visual objects. Surprisingly, these responses were most prominent in the spatial navigation system rather than in the visual cortex. A key region was the postsubiculum, an area rich in head-direction cells – neurons that act as part of the brain's inner compass. Recordings in freely moving mice showed that visual objects boosted head-direction cells tuned to the object's direction, while cells representing other directions were suppressed. As a result, the object's direction was represented more precisely. These findings help explain how visual landmarks can sharpen the brain's inner compass and improve spatial orientation. This work also paves the way for efficacy studies on optogenetic vision restoration.

https://www.science.org/doi/10.1126/science.adu9828

PUBLICATION IN NATURE BIOMEDICAL ENGINEERING

EFFICIENT AND SUSTAINABLE OPTOGENETIC CONTROL OF SENSORY AND CARDIAC SYSTEMS



Reliable and gentle control of cellular activity using light: Researchers at the University of Göttingen's Cluster of Excellence in Multiscale Bioimaging and the EKFZ OT at the University Medical Center Göttingen (UMG) have developed a light-sensitive protein that can restore vision and hearing and regulate heart rhythm. What makes this special is that even very small amounts of light are sufficient to activate this "molecular light switch." By specifically modifying the structure of this light-activated protein and using analytical methods, some of which are robot-based, we have succeeded in significantly increasing the efficiency of optogenetic stimulation. All teams and several platforms contributed to evaluate the potential of the powerful new channelrhodopsin for auditory, cardiac, and visual systems which demonstrates the great synergies of EKFZ OT. This opens up new possibilities for the development of innovative therapies for the treatment of blindness, deafness and cardiac arrhythmias.

https://www.nature.com/articles/s41551-025-01461-1

ACCELERATING THE IDENTIFICATION OF SUITABLE VIRAL VECTORS FOR OPTOGENETIC THERAPY

Optogenetics is a method in which light-sensitive proteins are introduced into cells via gene therapy in order to specifically control their activity using light. A so-called “gene shuttle” is used as the vehicle for this gene therapy. These are reprogrammed, harmless adeno-associated viruses (AAVs). To identify the most efficient “gene delivery vehicles”, we conducted screens using AAV capsid libraries in gerbils and non-human primates through a particularly close, cross-site collaboration among all EKFZ OT Teams and the Platforms.

Researchers from the EKFZ OT in Göttingen and the Hannover Medical School synergistically utilized shared animal models and organ samples to identify optimal viral vectors for optogenetic therapy of the eye, ear, brain, and stomach. Our “EKFZ Spirit” enabled us to overcome the enormous workload, complex project logistics, elaborate surgical protocols, and technical challenges. This has significantly strengthened the collaboration and further consolidated the EKFZ’s joint gene therapy strategy.

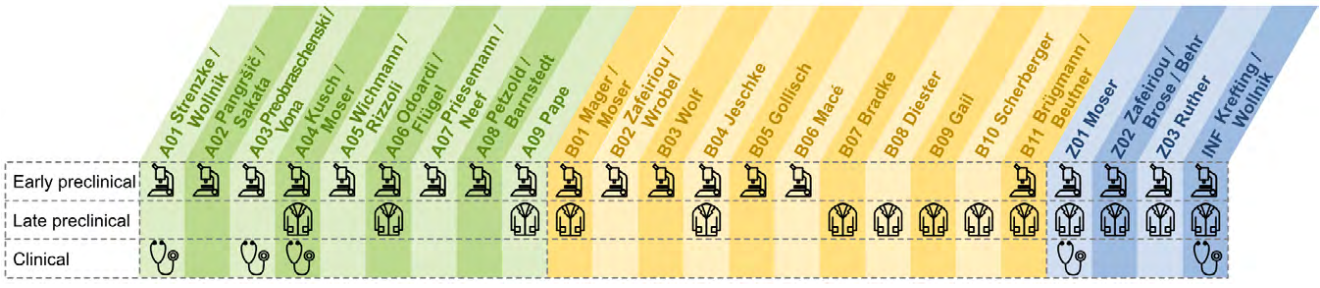
NEW COLLABORATIVE RESEARCH CENTRE 1690 AT THE UNIVERSITY MEDICAL CENTER GÖTTINGEN

SFB 1690

Disease Mechanisms & Functional Restoration of Sensory and Motor Systems

Since April 1, 2025, the German Research Foundation is funding Collaborative Research Centre 1690 (SFB 1690), titled "Disease Mechanisms and Functional Restoration of Sensory and Motor Systems". Similar to the EKFZ OT, SFB 1690 addresses the need for improved functional recovery of impaired sensory and motor systems. To achieve this goal, we need a better understanding of how the brain processes information in these two closely intertwined systems, as well as the mechanisms underlying these disorders at the molecular, cellular, and network levels.

Within the framework of SFB 1690, these disease mechanisms are examined and the potential of novel therapeutic approaches using innovative methods from basic research, such as multicolour optogenetics, is explored, which will also benefit the work at the EKFZ OT. For example, advanced coding mechanisms are being developed for the optogenetic control of the auditory system, with the aim of further improving the performance of optical cochlear implants in the future.



https://sfb1690.uni-goettingen.de

EKFZ ACADEMY

In May 2025, the EKFZ Academy was officially launched with an interactive seminar on ethical and legal challenges of optogenetic research, in collaboration with the NeurOPTICS research group at Martin Luther University Halle-Wittenberg.

The subsequent Academy workshops, which took place once a month, covered topics relevant to the early stages of clinical development, such as patent law and regulatory requirements. A highlight was the workshop on clinical trials, which included a guided tour at the Fraunhofer ITMP's Early Clinical Trial Unit.

https://ekfz.uni-goettingen.de/ueber-die-academy/

OPTOGENETICS MEETING 2025

The Optogenetics Meeting took place for the second time near Göttingen from October 9th to 11th, 2025. During these inspiring days, leading experts in the field of optogenetics gathered to present and discuss the latest research findings. This year's focus was on translation. International speakers presented not only the current state of research, particularly in the field of vision restoration, but also critically examined the major challenges and obstacles on the path to clinical application. The Optogenetics Meeting also serves as a platform for young researchers to present their work through short talks and posters. In total, over 100 people from Europe, America, China, and other regions attended. Prizes were awarded for the best poster presentation and the best talk. A follow-up event is planned for 2027.

THE AWARDS FOR BEST POSTER WENT TO:

Lennard Rohr, Ruhr University Bochum, Shreshth Shekhar, University Medical Center Göttingen, Department of Ophthalmology, Raluca Tifrea, Charité, University Medical Center Berlin, and Anna Vavakou, University Medical Center Göttingen, Institute for Auditory Neuroscience

Photo: Emilie Macé, Anna Vavakou, Lennard Rohr, Raluca Tifrea, Nils Witte, Shreshth Shekahar (from left to right)

JUNIOR FELLOW
DR. PATRICK JENDRITZA

NEW RESEARCH GROUPS

Dr. Patrick Jendritza of the Salk Institute for Biological Studies in the United States has been appointed to a "Junior Fellow Position" at the Else Kröner Fresenius Center for Optogenetic Therapies at the University Medical Center (UMG). Since January 1, 2026, the young scientist has been leading the "Visual Circuits & Interfaces" research group, which focuses on the development of light-controlled brain-computer interfaces to restore vision. The research group, based at the German Primate Center – Leibniz Institute for Primate Research, is funded by the Else Kröner Fresenius Foundation and the Lower Saxony Ministry of Science and Culture. In the coming years, he and his team will develop brain-computer interfaces to restore vision. The new method for treating blindness involves genetically modifying nerve cells in the brain so that they can be controlled by light. This technique, also known as optogenetics, allows for the targeted stimulation of specific areas in the visual cortex, the region of the brain responsible for processing visual information.

https://www.dpz.eu/auditorische-neurowissenschaften-optogenetik/forschung/visual-circuits-interfaces

Dr. Christiane Grimm has been appointed to a “Junior Fellow Position” at the EKFZ OT and is affiliated with the Institute for Auditory Neuroscience at the University Medical Center Göttingen. Understanding the principles that link mammalian behavior in real time to the underlying neural dynamics remains a fundamental challenge in neuroscience.

To address these questions, neuroscience requires methods that allow for the study and manipulation of neural activity on a large scale, yet with the precision of individual cells and individual action potentials. With these goals in mind, Dr. Grimm’s laboratory is working to develop fully optical approaches for studying and manipulating neural activity in the mammalian brain.

JUNIOR FELLOW
DR. CHRISTIANE GRIMM

CLINICIAN SCIENTIST

DR. MED. LENNART ROOS

CLINICIAN SCIENTIST

Even whilst I was studying medicine, I was fascinated by therapeutic approaches such as gene editing and gene replacement therapies, which correct diseases at a molecular level with surgical precision. This passion led me into research via my doctoral thesis and subsequently for the Institute for Auditory Neuroscience – where I now work alongside my specialist training at the ENT Clinic. As balancing clinical work with research presents particular challenges, clinician-scientist programmes, such as that offered by the EKFZ, are of particular importance: they enable one to focus entirely on research, build a scientific profile and ensure clinical rotations for the seamless continuation of specialist training.

Interdisciplinary networking, lecture series and workshops on translational research complement the programme in Göttingen. This allows one to develop in an internationally recognised environment under the best possible conditions – with strong support from both clinical practice and research. I am very grateful for this.

https://ekfz.uni-goettingen.de/en/clinician-scientists/

FACTS AND FIGURES

FOUNDED
on April 1st, 2024

5
EKFZ
Lectures

4
Else Kröner
Professorships
advertised

27
Academy
members

EKFZ
Optogenetic
Therapies

16
Publications

2
New appointed
Professorships

4
Patents

52
Principal and Associated
Investigators

3
Newsletters

4
Teams

5
Clinical trials / studies

5
Platforms

TEMPORARY ACCOMMODATION OF THE EKFZ OT

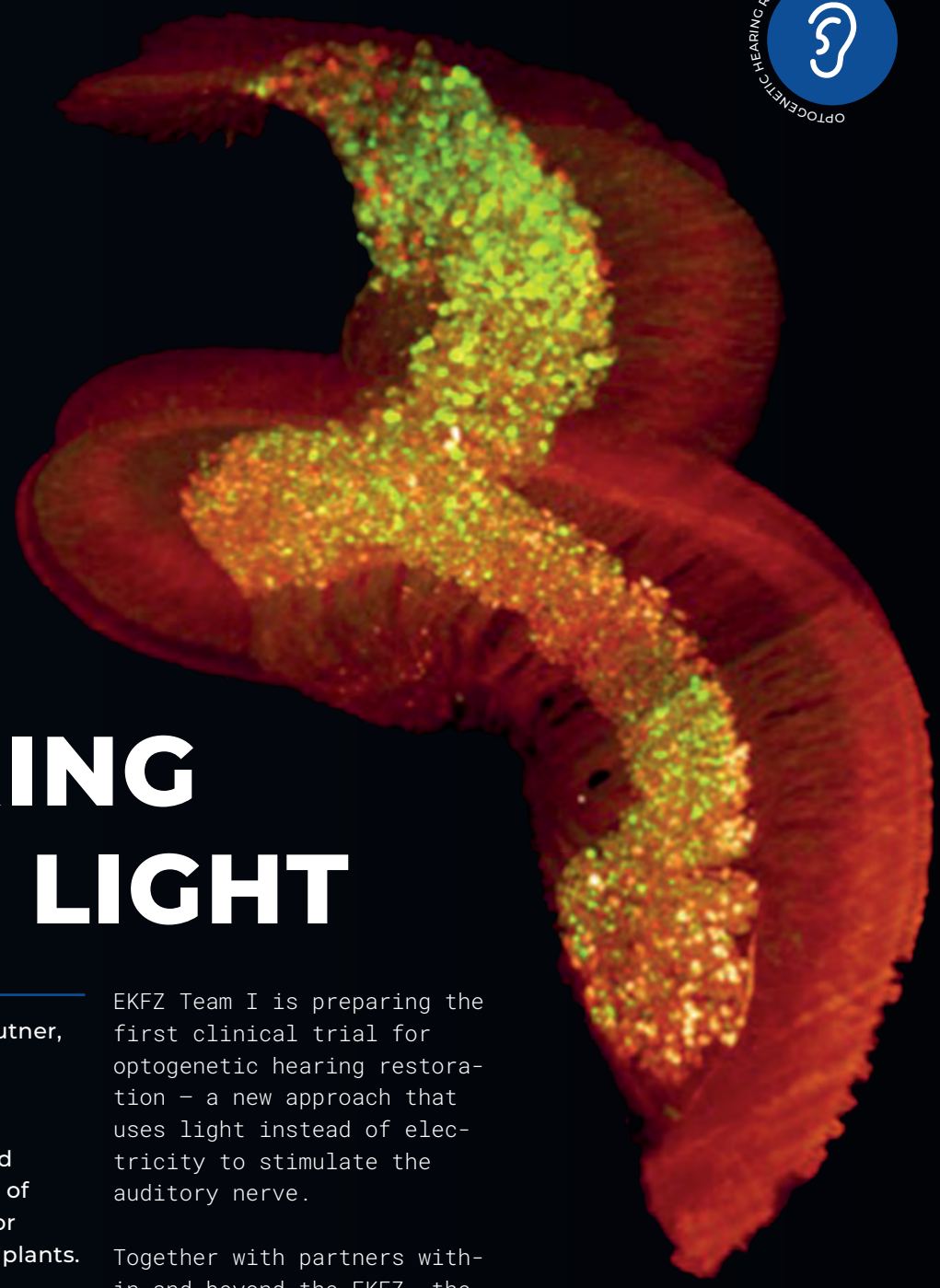
AT THE GERMAN PRIMATE CENTER – LEIBNIZ INSTITUTE FOR PRIMATE RESEARCH (DPZ)

UNIVERSITÄTSMEDIZIN GÖTTINGEN : UMG

DPZ Deutsches Primatenzentrum Leibniz-Institut für Primatenforschung

The state of Lower Saxony has included a new research building in its construction plans to meet the emerging need for laboratory and office space for the EKFZ OT. The building is currently expected to be completed by the end of 2028. The floor plan comprises approximately 1,600 m² of primary usable space. The following functions and types of space are planned: laboratories, some of which are designed for work with high-resolution microscopes; office space; seminar rooms; and a small animal facility with rooms for behavioral research.

UMG has signed a lease agreement with the German Primate Center – Leibniz Institute for Primate Research – that covers the construction phase until occupancy. Until then, several research groups will be housed at the DPZ.
The approximately 438 m² of additional space is adjacent to the existing research groups and, in addition to modern infrastructure, provides an ideal environment for tackling the tasks ahead.



TEAM I

HEARING WITH LIGHT

Moderators: Prof. Dirk Beutner, Prof. Tobias Moser

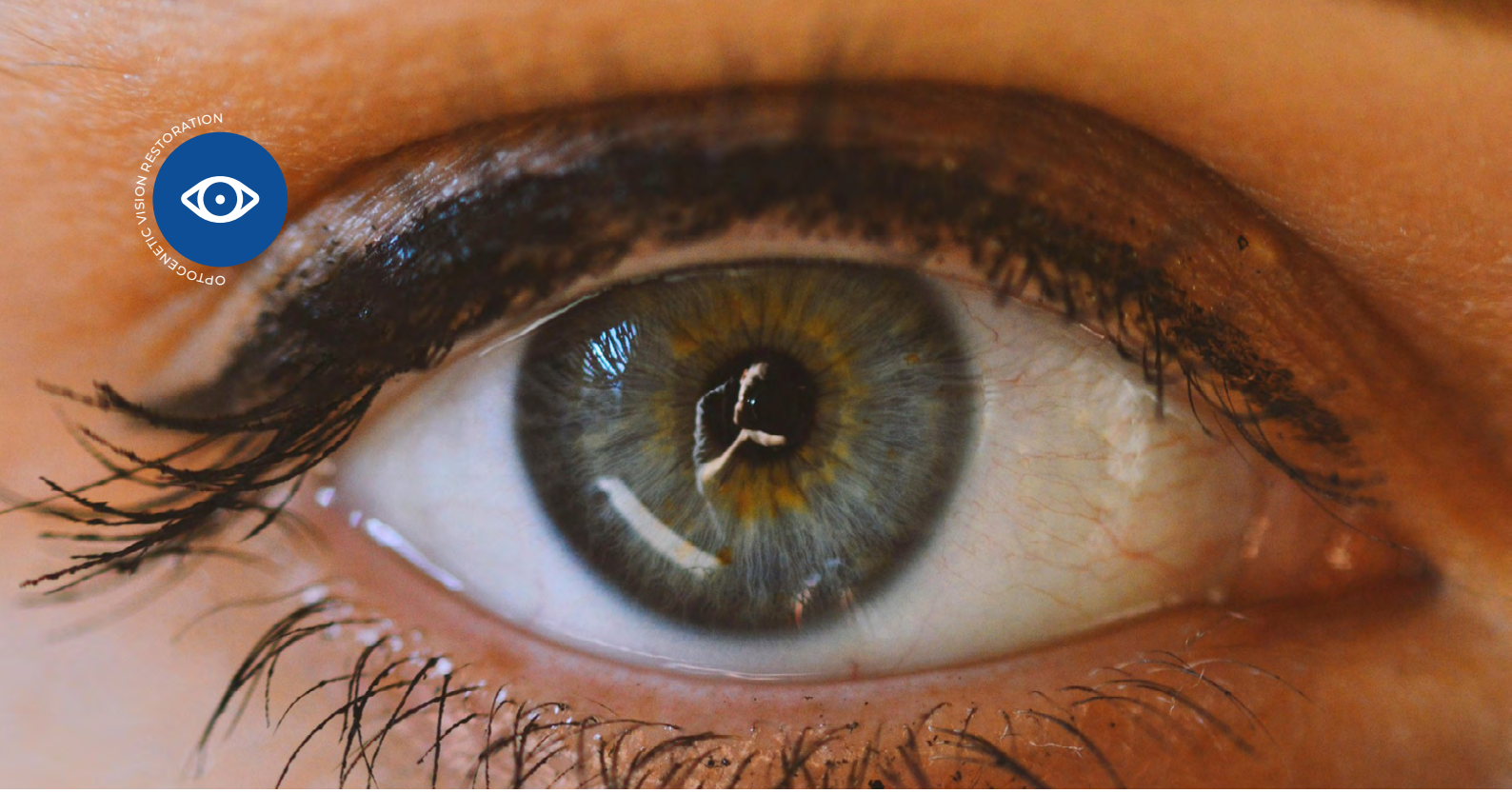
Selected publication:
Thirumalai et al., Improved optogenetic modification of spiral ganglion neurons for future optical cochlear implants. Theranostics 2025
https://www.thno.org/v15p4270.htm

https://ekfz.uni-goettingen.de/en/portfolio/team-i-optogenetic-hearing-restoration/

EKFZ Team I is preparing the first clinical trial for optogenetic hearing restoration – a new approach that uses light instead of electricity to stimulate the auditory nerve.

Together with partners within and beyond the EKFZ, the team advanced both the gene therapy and the optical cochlear implant (oCI) needed for this technology. We developed a minimally invasive catheter-based method for delivering gene therapy into the cochlea, tested new light-sensitive proteins for hearing restoration, and demonstrated in rodents that oCIs can achieve near-natural frequency resolution with sufficient temporal precision for hearing.

We introduced light-sheet microscopy to evaluate therapy. We coordinated collaborative research programs and prepared clinical translation by early interactions with regulatory authorities.



TEAM II

PROGRESS TOWARDS RESTORING VISION IN BLIND PATIENTS

Moderators: Prof. Emilie Macé, Prof. Hans Hoerauf

Team II is developing a new optogenetic therapy for people with severe retinal degeneration, including retinitis pigmentosa. The aim is to prepare a first clinical trial for an approach that makes surviving retinal cells sensitive to light again. In 2025, the team reached several important milestones. Preclinical studies showed that the Göttingen-developed light opsin ChReef can restore visual responses at light levels relevant for future clinical use. In parallel, Team II is working to select the optimal gene therapy vector for the planned clinical trial, a key step towards safe and effective delivery to the retina. A major patient study was launched to better understand disease progression and identify suitable candidates for future treatment.

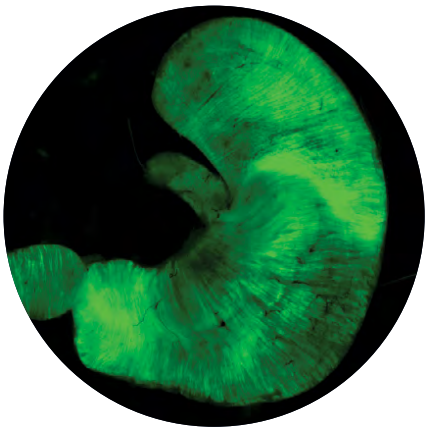
The team also developed new tools to improve retinal imaging and stimulation in blind patients, including automated image analysis and a novel fixation approach. Together, these advances bring optogenetic vision restoration closer to clinical application.

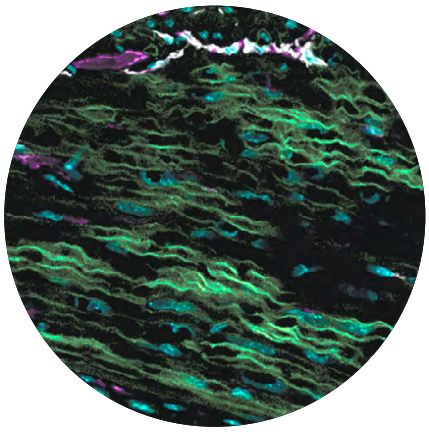
https://ekfz.uni-goettingen.de/en/portfolio/team-ii-optogenetic-vision-restoration/

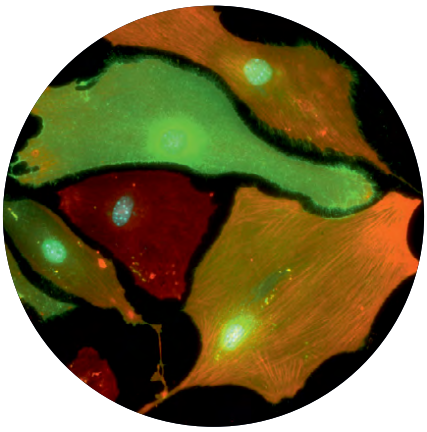
TEAM III

DEVELOPING THE FIRST CURATIVE TREATMENT FOR A DEVASTATING DISEASE

Moderator:
Prof. Tobias Brügmann





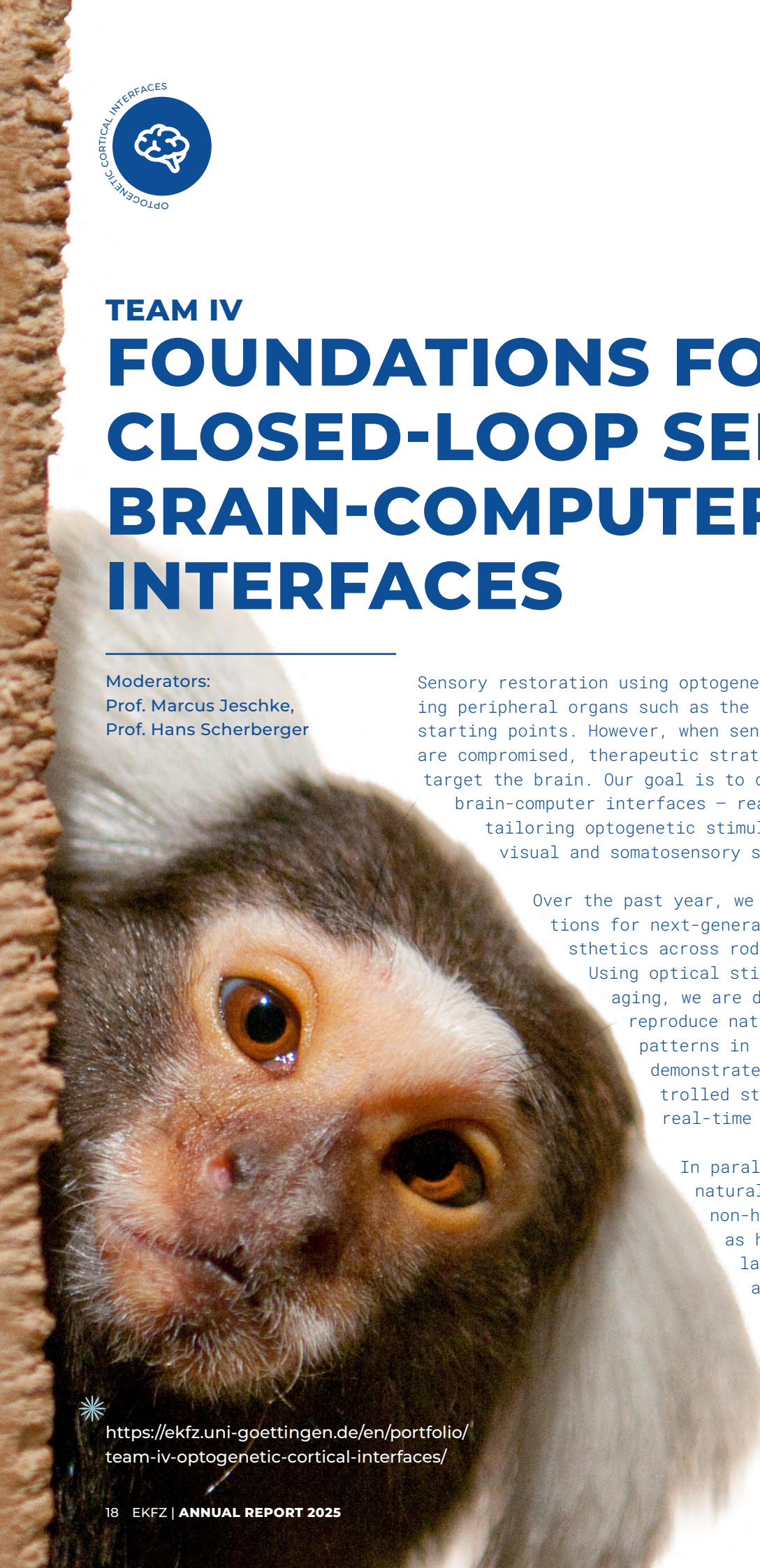


Optogenetic gastric pacemaking offers a promising strategy to restore gastric motility, which current therapies cannot achieve. We previously demonstrated optogenetic gastric pacing in intact stomachs of transgenic mice using channelrhodopsin-2 (ChR2) to directly stimulate smooth muscle cells.

We have now extended this concept using the optogenetic GPCR Neuropsin (OPN5), which selectively activates the Gq signaling cascade. In smooth muscle cells, this pathway induces contractions sufficient to increase intragastric pressure, even in an ex vivo gastroparesis model. We therefore established two complementary approaches: ChR-mediated membrane depolarization via Ca^{2+} channels and OPN5-mediated intracellular Ca^{2+} release through G_q signaling. We are currently comparing both systems directly.

In parallel, we are evaluating animal models, develop stimulation protocols to selectively activate the enteric nervous system, and establish and characterize patient-derived human gastric smooth muscle cells to optimize AAV delivery and translational applicability.

https://ekfz.uni-goettingen.de/en/portfolio/team-iii-optogenetic-gastric-pacemaking/



TEAM IV

FOUNDATIONS FOR CLOSED-LOOP SENSORY BRAIN-COMPUTER INTERFACES

Moderators:
Prof. Marcus Jeschke,
Prof. Hans Scherberger

Sensory restoration using optogenetic approaches targeting peripheral organs such as the eye and ear are natural starting points. However, when sensory pathways themselves are compromised, therapeutic strategies must directly target the brain. Our goal is to develop bidirectional brain-computer interfaces – reading neural activity and tailoring optogenetic stimulation accordingly for visual and somatosensory stimulation.

Over the past year, we established key foundations for next-generation sensory neuroprosthetics across rodent and primate models. Using optical stimulation and neural imaging, we are developing approaches to reproduce natural sensory activity patterns in the brain and want to demonstrate stable, spatially controlled stimulation compatible with real-time monitoring.

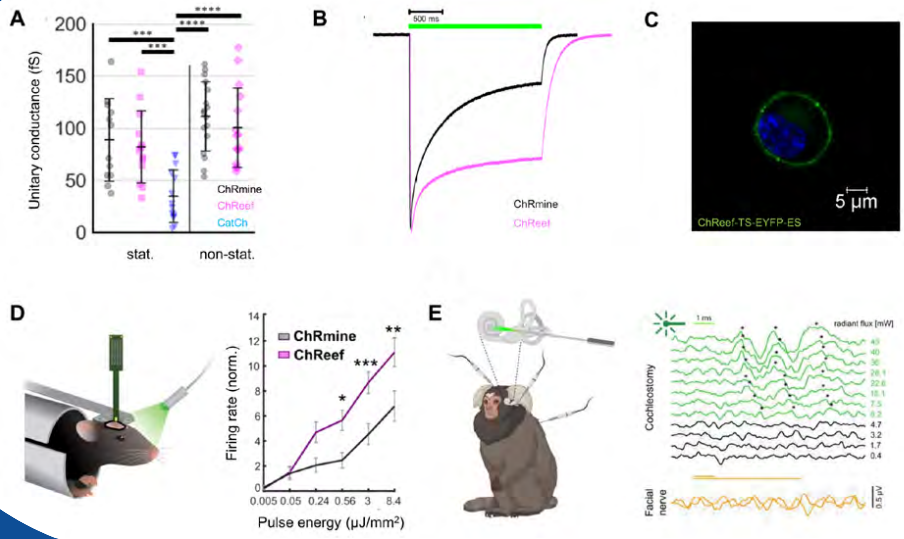
In parallel, we investigated natural grasping behavior in non-human primates as well as humans and explored the large-scale expression and safety of optogenetic tools in the primate brain. Together, these studies advance the development of closed-loop neurotechnologies for future sensory restoration therapies.

https://ekfz.uni-goettingen.de/en/portfolio/team-iv-optogenetic-cortical-interfaces/

PLATFORM 1

OPTIMIZATION OF OPSINS FOR OPTOGENETIC THERAPIES

Moderators:
Dr. Thomas Mager,
Prof. Emilie Macé



The Opsin Engineering Platform optimizes light-gated ion channels (Channelrhodopsins, ChRs) for optogenetic therapies. fChR2 TC enables rapid bluelight activation of spiral ganglion neurons (SGNs) at nearly physiological firing rates. The green light-activated variant ChReef generates exceptionally high photocurrents, therefore allowing for very efficient activation of neurons and myocytes.

To further expand the ChR toolkit the Opsin Engineering Platform performed in large parts automated characterizations of more than 100 previously uncharacterized ChRs. This led to the discovery of ChR variants with higher single channel conductance or redshifted action spectra, which show great potential for further efficiency improvements and risk reduction.

In 2026, the Opsin Engineering Platform, in cooperation with the EKFZ OT Teams and Platforms, plans a comprehensive biophysical characterization of these ChR variants, their further optimization through data-driven protein design and combinatorial mutagenesis, as well as their invivo assessment.

https://ekfz.uni-goettingen.de/en/portfolio/platform-1-optogenetic-actuators/

PLATFORM 2

DEVELOPMENT OF PRECISE AND SAFE OPTOGENETIC TREATMENTS WITH ADENO-ASSOCIATED VIRAL VECTORS

Moderators: Dr. Kathrin Kusch, Prof. Hildegard Büning

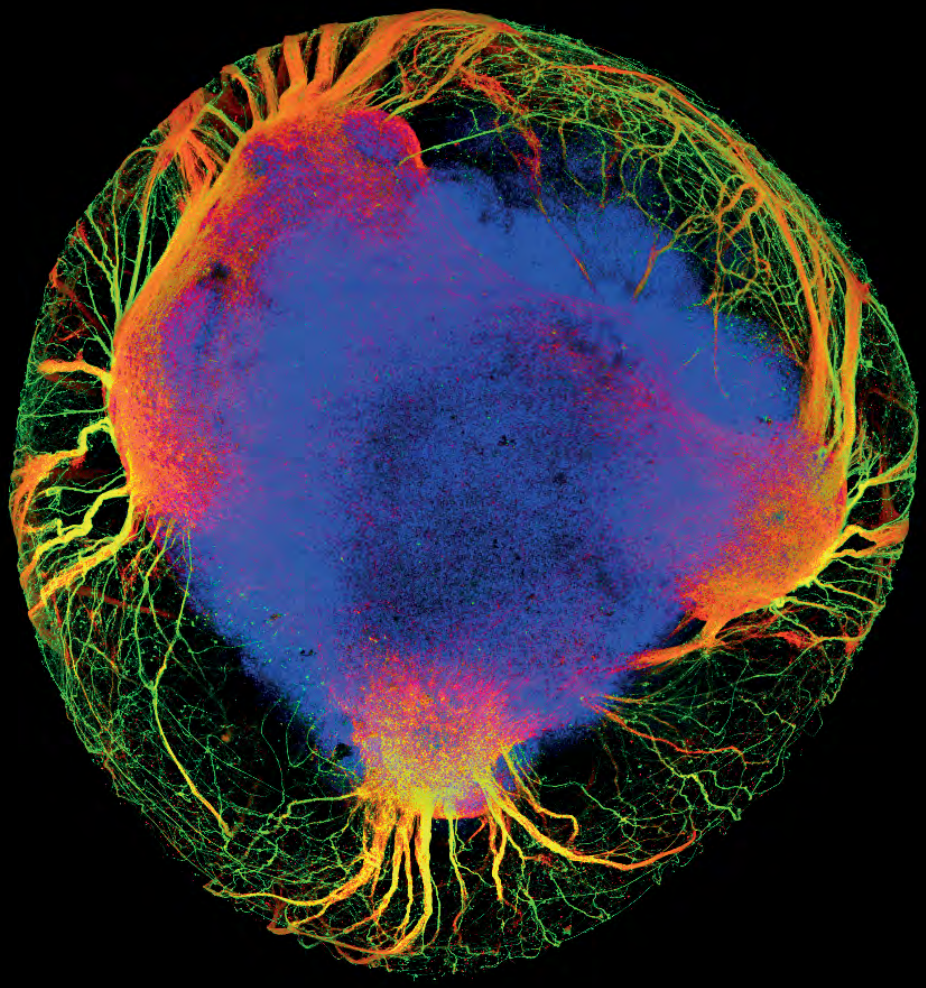
Platform 2 provides viral vectors for research application to all Teams and Platforms 1,3 and 4 tailored towards their specific needs. In addition, Platform 2 contributes to projects of all partners with molecular biological and analytical support. Together with all Teams and Platforms, viral vector library screening in two NPH species was initiated. The anticipated results of these screens will directly contribute to optimized opsin gene transfer for all four target organs. In close collaboration with Team I, a viral vector screening in deaf gerbils was further progressed and promotor variants for efficient opsin expression in spiral ganglion neurons were developed. A mastercell bank for GMP production of AAVs was produced at collaboration partner Fraunhofer IZI and passed all quality controls. The master cell bank will be released early in 2026. The same cell line in research grade was imported into the lab and method development for AAV production in suspension cells was initiated. Lab equipment for this process development was acquired and put into operation. Basic processes for upstream process and capture in downstream process were established. For analytics, cooperation with Fraunhofer IZI was extended to Mass photometry and additional analyses were established within Platform 2. Platform 2 furthermore contributed to the scientific advice meeting of Team I with PEI and BfArM and contacted various Contract Development and Manufacturing Organizations (CDMOs) to prepare process transfer for GMP-grade AAV productions.

https://ekfz.uni-goettingen.de/en/portfolio/platform-2-viral-vector-engineering/

PLATFORM 3

NEURONAL AND INNER-EAR ORGANOIDS DERIVED FROM HUMAN INDUCED PLURIPOTENT STEM CELLS

Moderators:
Prof. Zafeiriou, Prof. Jeschke



Platform 3 provides an integrated framework for experimental and computational disease modeling to support preclinical safety and efficacy assessment across the targeted optogenetic therapies. The platform combines complementary in silico, in vitro, and in vivo approaches to enable the systematic development, validation, and optimization of therapeutic strategies. Computational modeling activities generate mechanistic insight into optogenetic coding, network plasticity, and information processing, guiding the design of effective stimulation paradigms. Human iPSC-derived neural and inner ear organoids are employed as translational preclinical models for disease modeling and for the screening and validation of efficient, cell-type–specific gene delivery strategies. These studies are complemented by in vivo investigations in rodent and large animal models to evaluate therapeutic performance, safety, and robustness under physiological conditions. In silico, computational models and cochlear simulations showed that improved spectral selectivity can compensate for reduced temporal fidelity. In vivo, novel animal models including a non-human primate deafness model replicated human genetic hearing loss for realistic testing. In vitro, organoid systems identified a subset of effective viral vectors and promoters for targeted auditory neuron gene delivery.

https://ekfz.uni-goettingen.de/en/portfolio/platform-3-disease-modeling/

PLATFORM 4

CHARACTERIZING THE IMMUNE RESPONSE

OFTEN OVERLOOKED, BUT STILL SO IMPORTANT FOR TRANSLATION

Moderators:
Prof. Tobias Brügmann,
Prof. Philipp Ströbel

https://ekfz.uni-goettingen.de/en/portfolio/platform-4-immunomodulation-and-phenotyping/

Immune responses against AAV vectors and transgene products may impair viral transduction and long-term transgene expression, representing a major challenge for optogenetic therapies. Platform 4 therefore focuses on monitoring and modulating innate and adaptive immune responses in preclinical and clinical studies.

In 2025, we established assays to analyze tissue, blood, and serum samples from pigs and non-human primates (NHPs) following optogene transfer. After AAV injection into skeletal muscles, immunohistochemistry and flow cytometry revealed pronounced immune cell infiltration, while serum analyses identified high levels of neutralizing anti-AAV antibodies that may limit vector efficacy. These findings highlight the importance of immunomodulatory strategies, including hypoimmunogenic AAV vectors and optimized transgene variants, for the successful translation of optogenetic therapies.

PLATFORM 5

DEVELOPMENT OF NEW MEDICAL DEVICES TO IMPROVE HEARING

Moderators:
Dr. Christian Goßler,
Prof. Thomas Stieglitz

The medical device engineering team at the EKFZ OT builds multichannel optical modules that guide red light with high spatial precision for optogenetic stimulation. Compact laser diode arrays and micro-lenses couple light into flexible polymer waveguides fabricated at wafer scale and high index contrast and small bending radius make them suitable for implantation. In development, we map stray light to raise in- and outcoupling efficiency and minimize channel crosstalk.

In 2025, we demonstrated a tiny head-mounted module with five independent channels which now serves preclinical studies on efficacy of optogenetic hearing restoration with Team I. The scalable light-guiding platform is being adapted for brain interfaces and stomach activation, pointing to future therapies that help restore aspects of hearing, vision and muscle stimulation.

https://ekfz.uni-goettingen.de/en/portfolio/platform-5-medical-device-engineering/

6TH NIGHT OF SCIENCE

At the 6th Göttingen Night of Science, many scientific institutions once again opened their doors to the public to offer insights into their work. The EKFZ OT participated in this event for the first time since its founding.EKFZ OT Researchers engaged their audience with fascinating presentations. The titles „Wie Hören funktioniert, kaputtgeht und wiederhergestellt werden kann" and "Mit allen Sinneszellen sehen – ist Optogenetik die Antwort auf Erblindung?" sparked widespread curiosity and filled the lecture hall. Among the attendees were patients affected by these conditions, who took the opportunity after the presentations to learn about future treatment options and optogenetic therapies in general.

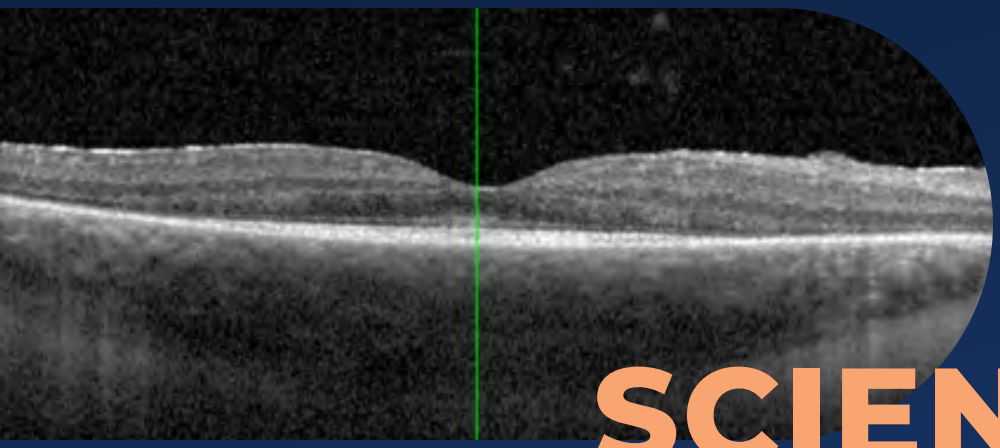
AUDIOVISUAL ART PROJECT LETS VIEWERS EXPERIENCE “HEARING WITH LIGHT”

KLANGLICHT – SOUND OF LIGHT

Researchers from the EKFZ OT, the Cluster of Excellence in Multiscale Bioimaging, and SFB 1690 have collaborated with audiologists and artists from the film and music industries to translate the auditory experience of an optogenetic cochlear implant into images and sound. The music video artistically conveys the restoration of “hearing with light,” a technology that promises an improved hearing experience compared to traditional cochlear implants. What does it sound like when someone hears again for the first time after years of severe hearing loss or deafness? The goal is to give viewers a tangible understanding of the current research in Göttingen on restoring “hearing with light.”

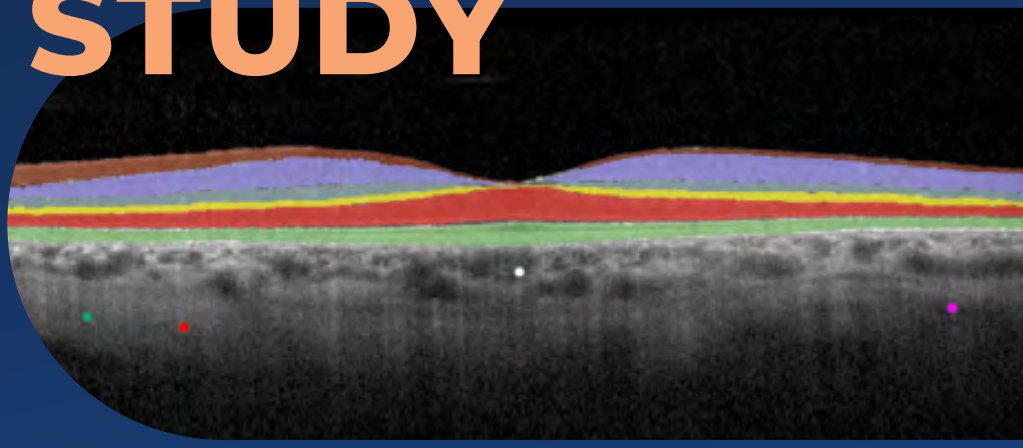
https://ekfz.uni-goettingen.de/en/mission/#licht

"LONGITUDINAL OBSERVATIONAL STUDY ON THE INTEGRITY OF INNER RETINAL LAYERS IN PATIENTS WITH RETINITIS PIGMENTOSA TO OPTIMIZE GANGLION CELL-BASED OPTOGENETIC THERAPY FOR VISUAL RECOVERY"



SCIENTIFIC STUDY

ClinicalTrials.gov ID: NCT07056738



In retinitis pigmentosa, the photoreceptors of the retina degenerate and cause blindness. However, downstream neuronal cells, like the ganglion cells, can survive for a very long time and provide a promising basis for optogenetic therapy. A large-scale observational study is investigating how long these ganglion cells survive in patients and which factors, such as genetic mutations, sex, or the age at diagnosis may contribute to their degeneration.

Clinical teams from the Department of Ophthalmology and the Institute of Human Genetics at the University of Göttingen are collaborating with researchers at the EKFZ. Computer scientists from the University of Göttingen are involved to help analyze the large amounts of imaging data that are being acquired.

We have already recruited more than 120 patients with retinitis pigmentosa from all over Germany and beyond. They will now be examined regularly over a period of at least 3 years.

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IMPRINT

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