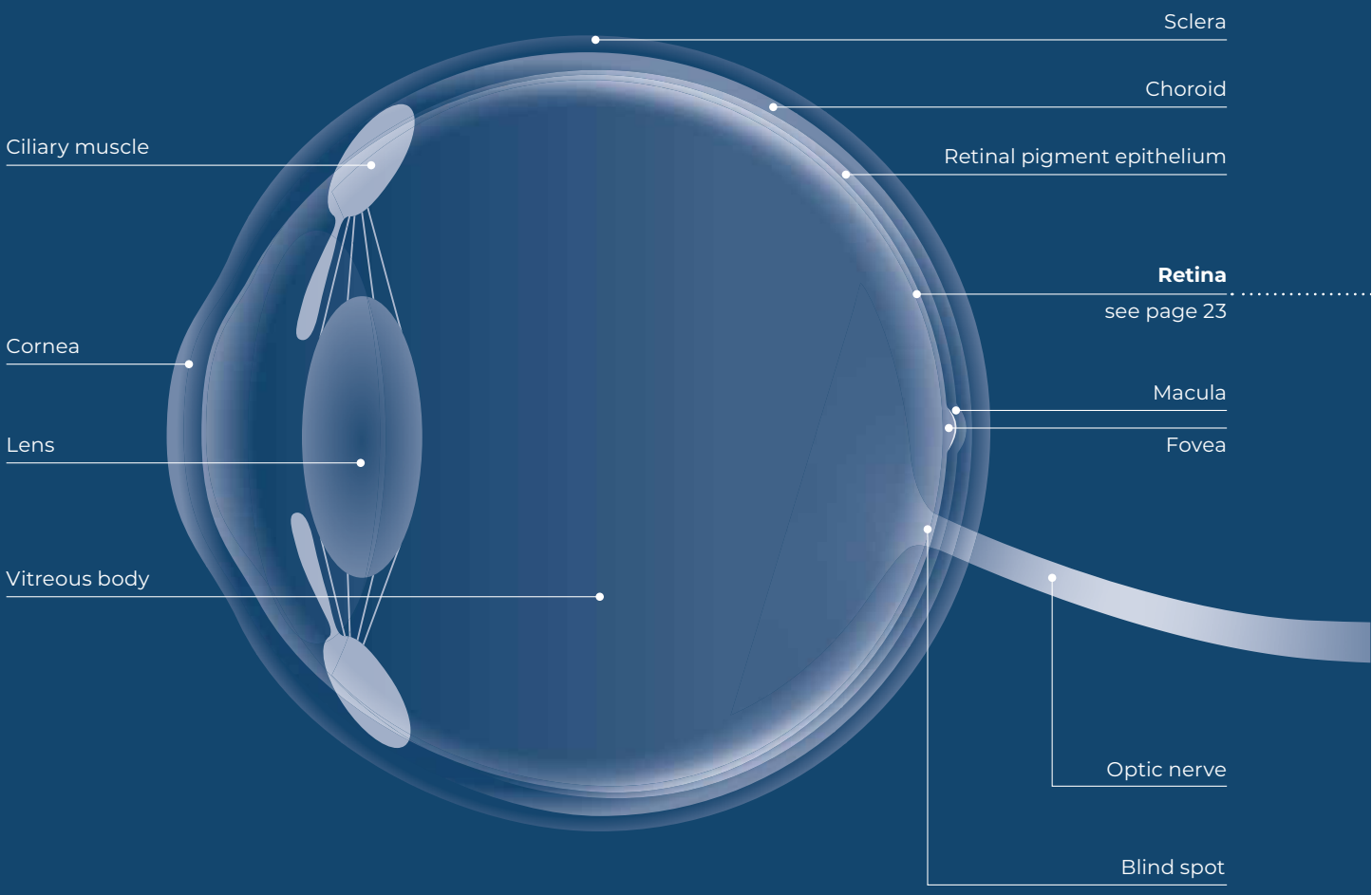
Institute of Molecular and Clinical Ophthalmology Basel

ANNUAL REPORT
2024

THE HUMAN EYE



Sclera Protects the eye from external influences
Choroid Supplies the retina with nutrients
Retinal pigment epithelium (RPE) Pigment layer of the retina, lies directly on the choroid
Retina Absorbs light and computes visual information
Macula Yellow spot on the retina where a particularly large number of cones are present
Fovea Depression located in the “center” of the yellow spot, site of the sharpest vision, consisting mainly of cones
Optic nerve Transmits electrical impulses from the eye to the brain
Blind spot Location where no sensory cells are present and the optic nerve meets the retina
Vitreous body Gel-like substance for stabilizing the eye structure
Lens Helps to focus the image onto the retina
Cornea Protective layer, helps to focus the image onto the retina
Ciliary muscle Helps to adjust the focus for near and far vision (accommodation)

Cover picture Retinitis pigmentosa, a genetic eye disorder, creates areas of vision loss (the dark spots on the apple). This disease, affecting over two million people worldwide, typically begins with night blindness in youth, then progresses to the loss of peripheral vision, and can lead to complete blindness. Currently incurable, it highlights the urgent need for advanced treatments in ophthalmology.

LETTER FROM THE CHAIRMAN OF THE BOARD OF TRUSTEES

Dear Reader,

Creating a world-class institute that merges the strength of basic research with real-world experience has been one of the declared goals of the Institute of Molecular and Clinical Ophthalmology Basel when it was created in 2017. Not even 10 years after its founding, the IOB is living up to its ambitious goal with new research insights that have the potential to change the course of ophthalmology.

Recent findings in myopia and mitochondria-related research have put the institute in the spotlight in 2024, making it one of its most productive years in its short history. The findings come hot on the heels of the institute's first spin-out, in which RhyGaze AG will develop a novel gene therapy that targets cone cells to restore vision in patients suffering from retinitis pigmentosa.

For an institute with around 130 scientists from all over the world, the dynamic at the IOB is exceptionally high. Partnerships with several dozen companies and research peers show that the work of the IOB is being recognized by the industry. Investors too are showing an interest in financing the top-notch research conducted under the operative leadership of Botond Roska and Charles Gubser.

The Board of Trustees, which will hand over stewardship to a new generation of leaders in 2025, is convinced that the IOB is set to thrive as its focus on translational science uniquely positions the institute within the global research ecosystem. And its efforts to attract world-class talent will continue as the IOB works on novel mechanisms of action that reflect unmet patient needs, giving hope to millions of patients suffering from vision loss.

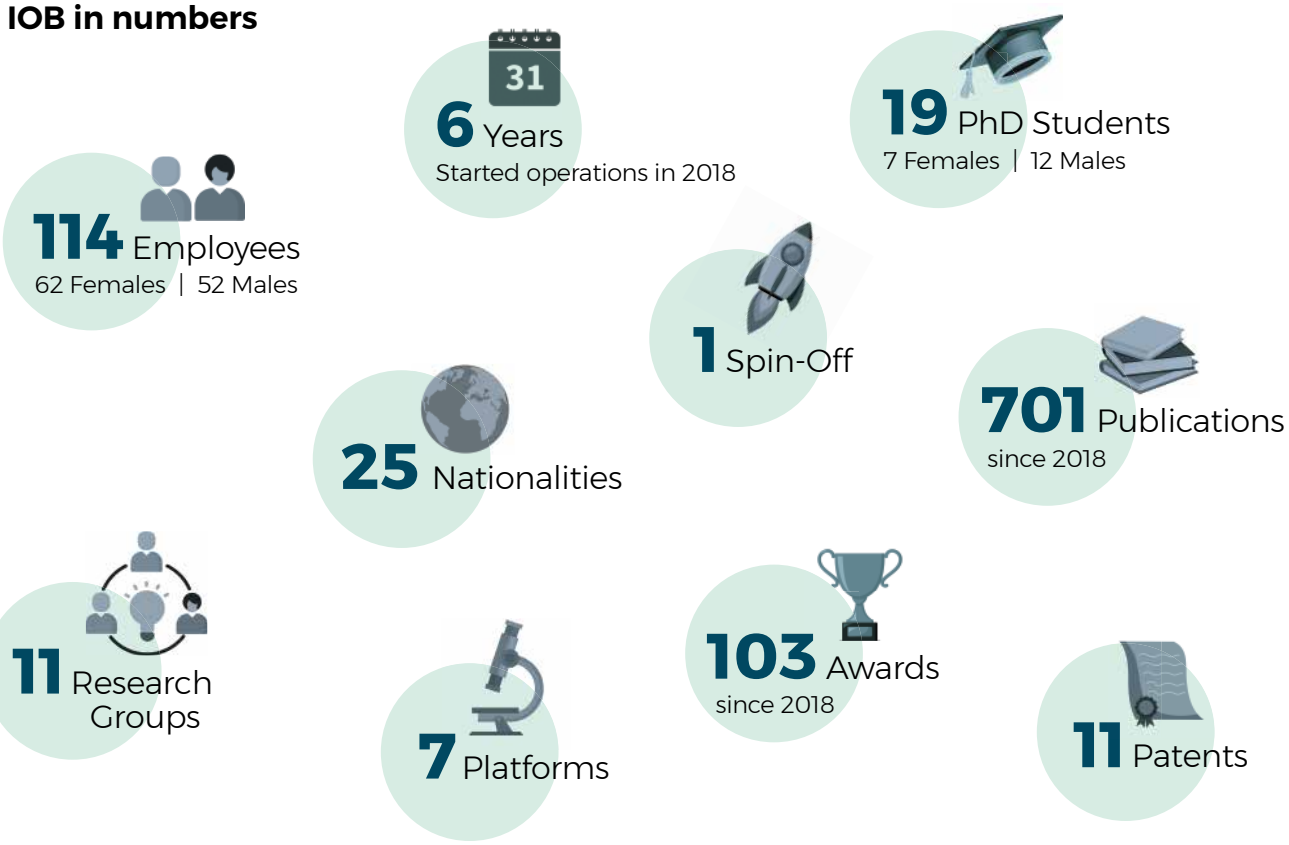
Sincerely,

Joerg Reinhardt

Chairman of the Board of Trustees

FACTS & FIGURES

IOB in numbers



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FROM BENCH TO BIOTECH – A NEW CHAPTER IN VISION RESTORATION AT IOB

Restoring vision remains one of the great unsolved challenges in medicine. Blindness is among the most feared conditions and represents a significant unmet medical need, as no effective therapies currently exist. At IOB, researchers and clinicians have joined forces to develop a novel approach to vision restoration based on optogenetics.

Optogenetic therapy uses light-sensitive proteins, primarily derived from algae, to restore light sensitivity in remaining retinal cells of the blind retina. While optogenetic therapies have already reached human patients, existing technologies do not yet enable high-resolution vision, which is necessary for critical functions like reading and identifying faces. IOB's approach is distinct, as it is predicted to restore high-resolution vision.

Over the past several years at IOB, human model systems have played a crucial role in the development of a gene therapy candidate that restores both light sensitivity and retinal processing in the blind human retina. In May 2024, following an initial 11 million USD investment from BioGeneration Ventures and Novartis Venture Fund, IOB launched its first spinout, the biotech company RhyGaze AG. The name RhyGaze originates from the Swiss-German word for the Rhine (Rhy), the river on whose banks IOB is located.

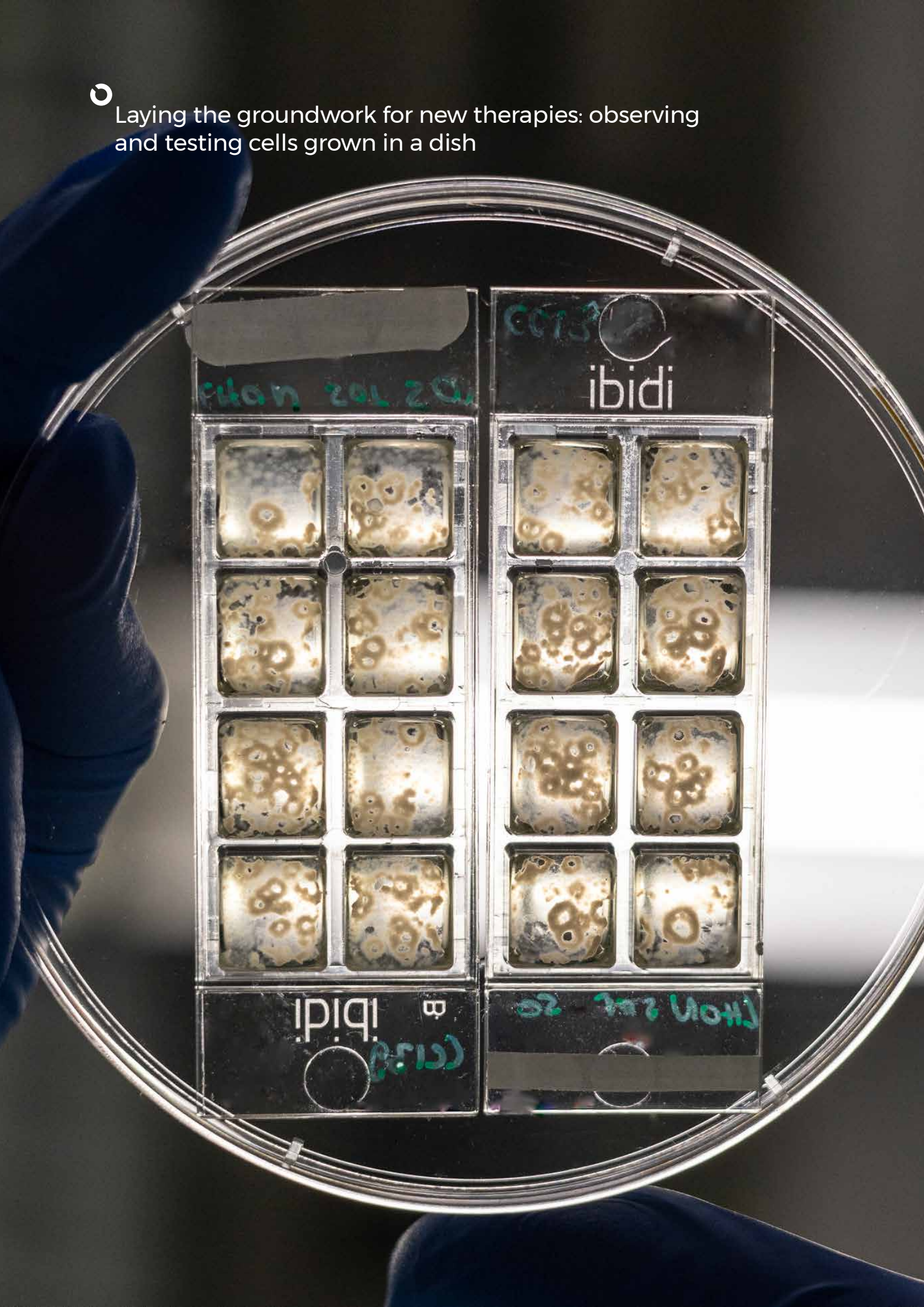
At IOB, researchers and clinicians have joined forces to develop a novel approach to vision restoration based on optogenetics.

Momentum quickly grew: By December 2024, RhyGaze secured 86 million USD additional funding from the Seed investors and leading U.S. investors, including Google Ventures (GV), ARCH Venture Partners, and F-Prime Capital. RhyGaze is led by Dr. Katherine High, a pioneer in gene therapy and former President and Head of Research and Development at Spark Therapeutics, a company which developed the first gene therapy, Luxturna, for the eye.

Operating between Basel, Switzerland, and Philadelphia, USA, RhyGaze is collaborating with IOB to bring IOB's optogenetic therapy to the clinic. The company's first priorities include establishing the manufacturing process for IOB's optogenetic gene therapy vector. With support from IOB researchers, RhyGaze will also conduct IND-enabling pharmacology and toxicology studies. Additionally, the company will launch a non-interventional observational study to assess potential clinical endpoints for eligible patients. These milestones are essential steps toward initiating a clinical trial to evaluate the therapy's safety, tolerability, and potential efficacy in blind patients.

At IOB, translation is no longer an abstract goal – it is part of our daily work

Laying the groundwork for new therapies: observing and testing cells grown in a dish



TARGETED MITOCHONDRIA DELIVERY FOR REPAIRING DISEASE-AFFECTED CELL TYPES OF THE BODY

Mitochondria are organelles within human cells, taking part in energy production, cell signaling, cell growth and death. When mitochondria malfunction, they can cause severe diseases that affect different organs in the body depending on the specific condition. Mitochondria are highly dynamic—they divide, fuse, and even transfer between cells. The transplantation of healthy mitochondria into damaged cells has emerged as a potential therapeutic approach for mitochondrial diseases, but current delivery methods remain inefficient and lack precision in targeting specific cell types.

In nature, viruses use specialized proteins on their surfaces to attach to and enter human cells. Inspired by this mechanism, IOB researchers developed a technology to efficiently and selectively deliver healthy mitochondria to specific target cells. By modifying the mitochondrial surface, this technique enables mitochondria to bind to and enter specific cells, mimicking viral infection. After attaching to cells, donor mitochondria penetrate the cellular membrane and integrate into the host cell, where they divide, fuse, and fulfill their metabolic functions.

IOB researchers developed a technology to efficiently and selectively deliver healthy mitochondria to specific target cells.

To demonstrate the versatility of this approach, IOB researchers engineered mitochondria with various targeting proteins, including nanobodies, synthetic binders, and full antibodies. The ability to use full antibodies is especially promising, as it allows for the utilization of already optimized antibodies to enhance targeted delivery. IOB researchers have successfully targeted mitochondria into multiple cell types commonly affected by mitochondrial diseases, including human neurons, photoreceptors, heart muscle cells, immune cells, and blood vessel cells.

In a patient-derived neuronal model of hereditary blindness caused by mitochondrial dysfunction, targeted mitochondrial delivery improved both the cells' energy production and their survival. Additionally, in a mouse model of optic nerve degeneration, cell-type-targeted mitochondrial delivery led to increased neuronal survival, demonstrating its potential for preventing vision loss.

Beyond the treatment of optic nerve disorders, cell-type-targeted mitochondria delivery holds broad therapeutic potential for diseases caused by mitochondrial dysfunction, including those affecting the heart, brain, and lungs.

MYOPIA: NEW THERAPEUTIC STRATEGIES FOR THE LEADING CAUSE OF BLINDNESS

Myopia, or near-sightedness, has emerged as a global health concern of epidemic proportions. Since the 1970s, the number of cases has risen steeply, reaching an all-time high. Currently affecting 30% of the world's population, myopia is projected to impact 50% by 2050 (nearly 5 billion people).

In its most common form, myopia results from excessive eye elongation, causing images to be out of focus and therefore perceived as blurred. In severe cases, called high myopia, excessive eye growth leads to stretching of the retina and other ocular structures, which can result in tearing and rupture. This induces pathologies in the eye, such as retinal detachments, macular degeneration, choroidal neovascularization, and glaucoma which can result in permanent vision loss. This is why myopia is expected to become the leading cause of blindness worldwide.

While eyeglasses and contact lenses correct blurred vision, they do not prevent the structural damage caused by myopia. Therapies to prevent myopia progression are limited because the mechanisms governing eye growth are not well understood.

IOB has made the understanding of myopia at the cellular and molecular levels one of its core research focuses, with the goal of developing new therapies.

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The highly collaborative research environment at IOB has recently enabled several major breakthroughs in this effort. By leveraging expertise in single-cell sequencing technologies and computational modeling, IOB researchers partnered with leading research groups in the US specializing in animal models of myopia. Together, the research teams built the largest to-date single-cell atlases of the eye during myopia formation, revealing the specific cell types, genes and pathways involved in the development of the disease.

Building on extensive experience in stem cell technologies, IOB researchers created the first organoid model of the human sclera. This model has led to the validation of key findings and served as a high-content screening tool for identifying new therapeutic targets.

The resources and biological insights generated through this research significantly accelerate progress toward developing effective treatments for pathologic myopia.

Collaboration lies at the heart of IOB's success.

Researchers from across the globe unite with diverse perspectives, shared curiosity, and a common purpose: advancing science and developing therapies through teamwork.

OPTOGENETIC THERAPY FOR RESTORING HIGH-ACUITY VISION: THE EYECONIC STUDY

Optogenetic therapies for vision restoration are currently being evaluated in human clinical trials. However, current technologies do not yet provide the high-resolution central vision required for daily activities, such as reading or recognizing faces. At IOB, researchers are developing a novel optogenetic therapy aimed at restoring high-acuity central vision in the macula. This innovative approach offers new hope for patients with severe vision loss.

To identify those who could benefit from IOB's high acuity optogenetic therapy, IOB researchers have developed a diagnostic screening method and launched the EyeConic Study. This initiative, in collaboration with 12 expert centers worldwide specialized in inherited retinal dystrophies, has led to the collection of extensive ocular imaging data from affected patients.

Findings from this study reveal that, despite profound vision loss, a large proportion of patients with inherited retinal dystrophy have preserved central retinal structure.

Findings from this study reveal that, despite profound vision loss, a large proportion of patients with inherited retinal dystrophy have preserved central retinal structure. Longitudinal data indicate that, despite significant progressive vision loss, cells in the macula remain stable for years and, in some cases, even decades. This contrasts sharply with conditions such as Stargardt disease, where progressive vision loss is accompanied by continuous degeneration of retinal tissue in the central macula. These insights suggest that in many blind patients, the central retina could be re-sensitized to light using optogenetic therapy.

Yet, the factors determining why some blind patients retain central retinal structure remain unclear. Current research suggests that genetic mutations only partially explain macular preservation, indicating the need for further investigation into additional contributing factors.

The presence of preserved retinal cells is a unique opportunity for IOB's novel vision restoration approach, which is now being developed by RhyGaze AG, IOB's first spinout based in Basel.

TRAINING THE NEXT GENERATION OF VISION SCIENTISTS: THE IOB PHD AND MD-PHD PROGRAM

The IOB PhD and MD-PhD Program in Translational Visual Neurosciences, launched in 2022, prepares young scientists to become leaders in vision research. The program has quickly gained global recognition for attracting top talent and fostering groundbreaking discoveries in understanding vision and its diseases, and the development of innovative therapies for blinding conditions.

IOB offers a comprehensive curriculum that combines lectures on vision science, hands-on training in advanced biomedical technologies, and interactions with clinicians and patients. Students also develop expertise in scientific writing, data analysis, and biomedical research, along with interpersonal and transferable skills, preparing them for careers in academia, medicine, and industry. The annual IOB Research Retreat provides a platform for presentations and new collaborations, while social events support student well-being and community building.

IOB celebrated the graduation of five PhD and MD-PhD students, whose research has been recognized with awards and high-impact publications.

Since 2022, the Sedinum Foundation has played a key role in supporting the IOB PhD program. By 2024, 36 young scientists, including 19 PhD & MD-PhD students, had received full or partial funding. The program's global reach is reflected in its international student body.

The program strengthens IOB's translational focus by fostering collaboration between basic and clinical research. Currently, five MD-PhD students bridge laboratory science and patient care, reflecting IOB's commitment to addressing unmet medical needs.

IOB's interdisciplinary research spans neuroscience, ophthalmology, genetics, molecular biology, protein engineering, cell biology, biomedical engineering, and computational biology. Students benefit from access to state-of-the-art platforms, including the Single Cell Genomics, Human Organoid, Protein Engineering, Complex Viruses, Scientific Computing, and Clinical Trial Center Platforms.

In 2024 and early 2025, IOB celebrated the graduation of five PhD and MD-PhD students, whose research earned awards and high-impact publications. One example is PhD student Alissa Müller, who described a base editing therapeutic approach for Stargardt disease, an inherited cause of blindness (Müller et al, *Nature Medicine*, 2025).

The program continues to attract outstanding candidates, with many applications from different continents. The yearly recruitment culminates in on-site interviews, where selected candidates engage with faculty, explore research facilities, and experience IOB's collaborative environment. A rigorous selection process evaluates the scientific excellence, critical thinking, and communication skills of the candidates.

With its strong interdisciplinary foundation, cutting-edge infrastructure, and translational focus, the IOB PhD and MD-PhD Program trains the next generation of vision scientists, advancing knowledge, innovation, and therapies for blinding diseases.

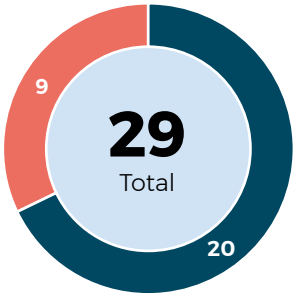
At the annual IOB Research Retreat (Valbella, October 2024), the entire institute came together for three days of in-depth scientific exchange. With plenary talks, flash presentations, and posters, the Retreat sparked collaborations across disciplines and strengthened IOB's community.

FINANCIAL SUMMARY

In mCHF

Income 2024

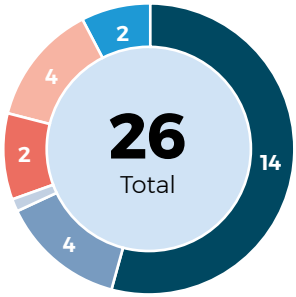
Since its inception, IOB has consistently diversified its funding sources, increasing third-party income from scientific grants, philanthropic donations, and industrial collaborations.
In 2024, this external funding represented 31% of IOB's total income.



- Contributions (Novartis, Canton Basel-Stadt, University Hospital Basel, University of Basel)
- Third parties (grants, donations, industrial collaborations)

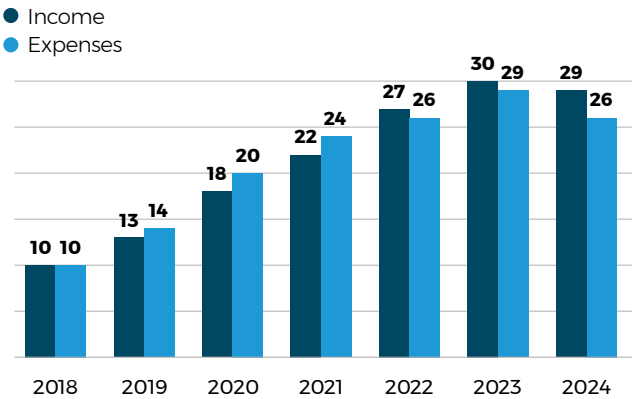
Expenses 2024

The personnel costs reflect the active recruitment and expansion of new groups and platforms in recent years. This growth phase has now stabilized at approximately 54% of total expenditures.

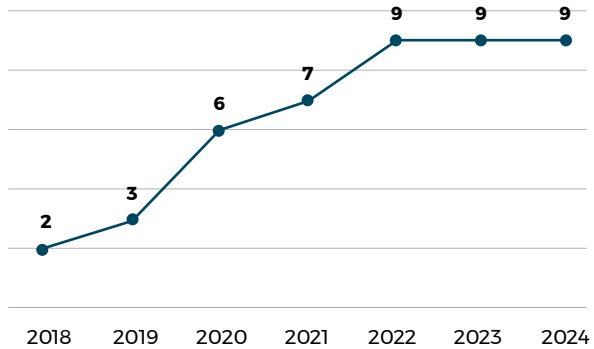


- Personnel expenses
- Research
- Maintenance: 0.4
- Rents and utilities
- Administrative expenses and IT
- Depreciation

Income/Expenses by year



Third-party income by year



Supervisory Authority BVG- and Stiftungsaufsicht beider Basel (BSABB)
Auditors PricewaterhouseCoopers AG, Basel
Accounting standard The financial statements of the Institute of Molecular and Clinical Ophthalmology Basel, with registered office in Basel, comply with the requirements of Swiss accounting legislation within the Swiss Code of Obligations (SCO).

BALANCE SHEET

In mCHF

Assets	31.12.2024	31.12.2023
Current Asset		
Cash and cash equivalents	3,722,685	2,616,545
Accounts receivable	2,588,712	1,333,044
from third parties	*1,081,025*	*797,401*
from affiliated parties	*1,507,687*	*535,643*
Other short-term receivables	61,157	20,431
from third parties	*61,157*	*20,431*
Prepaid expenses	1,055,068	712,631
Total current assets	**7,427,622**	**4,682,651**
Non-current assets		
Participations	208,000	–
Property, plant and equipment	5,827,244	7,299,427
Intangible assets	254,084	303,263
Total non-current assets	**6,289,328**	**7,602,690**
Total assets	13,716,950	12,285,341

Liabilities and equity

Short-term liabilities		
Accounts payable	-933,652	-692,268
from third parties	*-823,518*	*-541,284*
from affiliated parties	*-110,133*	*-150,984*
Other short-term payables	-276,938	-341,793
from third parties	*-276,938*	*-341,793*
Short-term interest-bearing liabilities	-1,000,000	-1,000,000
from third parties	*0*	*-1.000.000*
Accrued expense and deferred income	-1,546,479	-1,260,903
Restricted funds	-2,273,872	-1,754,947
Total short-term liabilities	**-6,030,941**	**-5,049,912**
Long-term liabilities		
Long-term interest-bearing liabilities	0	-4,000,000
from third parties	*0*	*0*
from affiliated parties	*0*	*-4,000,000*
Other long-term liabilities	-680,206	-557,460
from third parties	*-680,206*	*-557,460*
Total long-term liabilities	**-680,206**	**-4,557,460**
Total liabilities	**-6,711,147**	**-9,607,372**
Equity		
Foundation capital	-500,000	-500,000
Profit brought forward	154,276	1,737,327
Unrestricted funds	-3,659,270	-2,332,245
Net result for the period	-3,000,809	-1,583,051
Total equity	**-7,005,803**	**-2,677,969**
Total liabilities and equity	**-13,716,950**	**-12,285,341**

THANK YOU FOR SUPPORTING US IN 2024

We are deeply grateful to our founders, as well as to the private donors, public funding agencies, foundations, and industry partners for their generous support. These partnerships are essential to advancing our research and mission.

Founders

- Novartis
- University Hospital Basel
- University of Basel

We are very grateful for the generous financial support of the Canton Basel-Stadt.

Affiliations

IOB is proud to be affiliated with the University of Basel.

Major funders

We are truly thankful for the commitment of:

- **the Sedinum Foundation** supporting the interdisciplinary IOB PhD and MD-PhD Program in Translational Visual Neurosciences and the research program on age-related macular degeneration.
- **the Claudine und Hans-Heiner Zaeslin-Bustany-Foundation** supporting the myopia research program.

Further institutional and organisational funding

- Accentus Charitable Foundation
- European Molecular Biology Organization (EMBO)
- European Union (Horizon 2020)
- European Research Council (ERC)
- Fond Action
- Freiwillige Akademische Gesellschaft Basel
- Hedy Glor Meyer Stiftung
- National Institutes of Health (NIH)
- Plusoptix AG
- Simons Foundation
- Sloan Foundation
- Swiss Academy of Medical Sciences (SAMW-ASSM)
- Swiss National Science Foundation (SNSF)
- SVRG Swiss VitreoRetinal Group
- Teofilo Rossi di Montelera e di Premuda Foundation, advised by CARIGEST SA
- The Wellcome Trust
- University of Basel Research Fund

Private donors

We thank all individuals who generously supported IOB in 2024. Your commitment makes a meaningful difference in our efforts to understand and treat vision loss.

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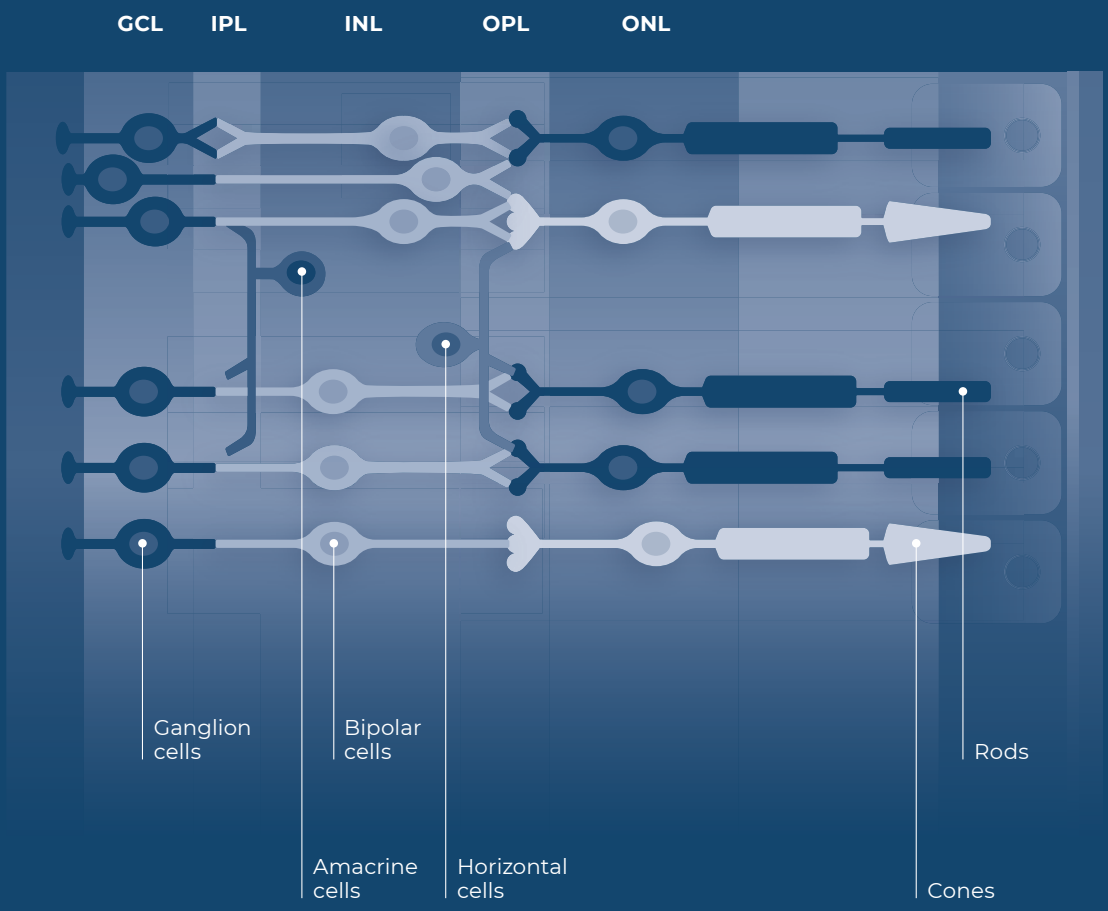
THE HUMAN RETINA



Ganglion cell layer (GCL) with ganglion cells

Inner plexiform layer (IPL) with the synapses between bipolar cells, amacrine cells and ganglion cells
Inner nuclear layer (INL) with bipolar and horizontal cells and amacrine cells

Outer plexiform layer (OPL) with the synapses of the rods and cones to the bipolar cells and horizontal cells
Outer nuclear layer (ONL) with the rods and cones (photoreceptors)

Researchers and Clinicians united
to restore vision.

IOB
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