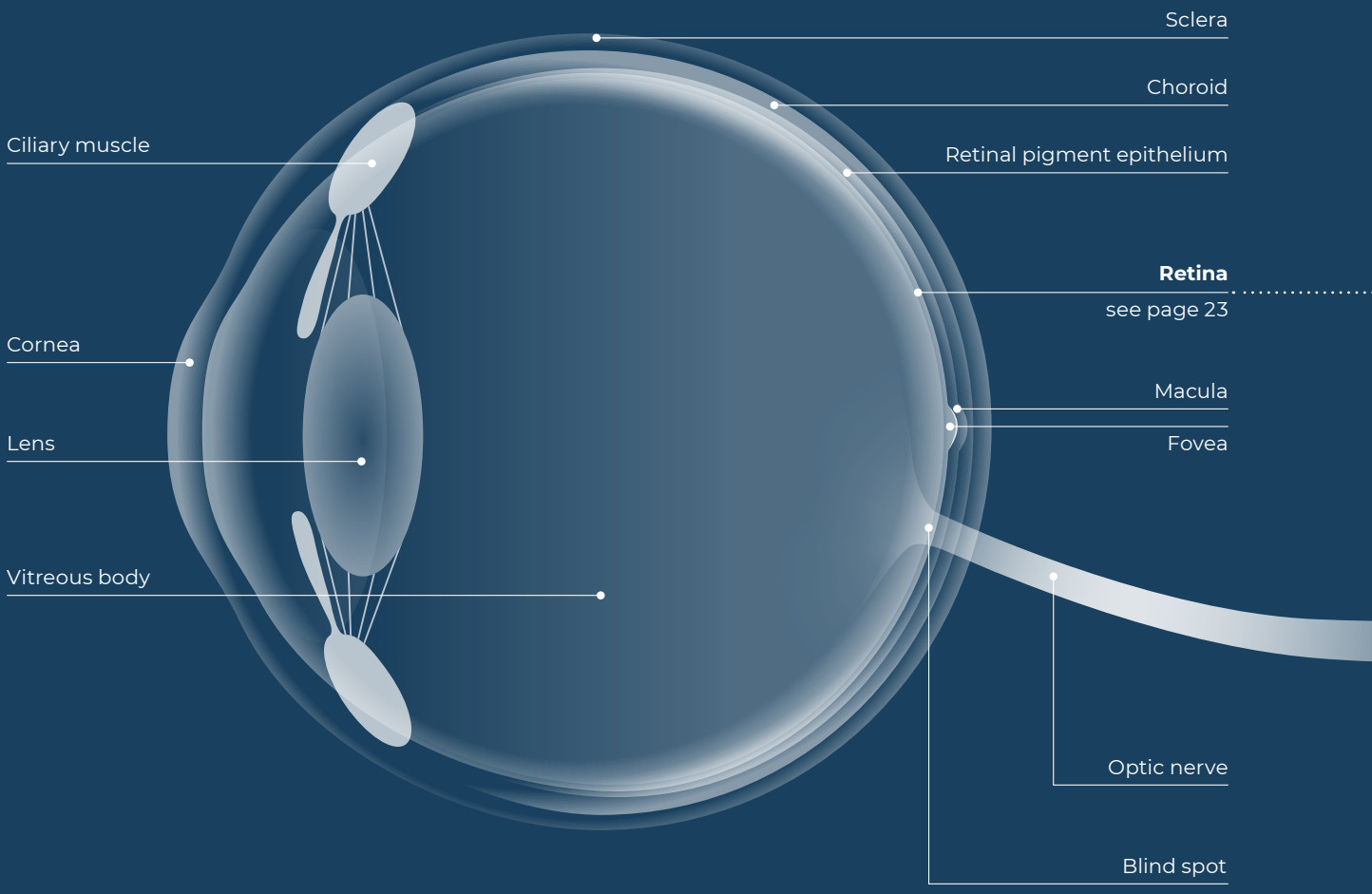
Institute of Molecular and Clinical Ophthalmology Basel

ANNUAL REPORT
2023

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 pear). This disease, affecting over five 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,

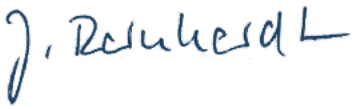
Since the inception of the Institute of Molecular and Clinical Ophthalmology Basel in 2017, we have come a long way. What started as a small venture in a back office has grown into a unique research organization that is able to attract top talents from all over the world, drive cutting-edge research and pave the way for a more intense collaboration with clinical experts to develop innovative and urgently needed therapies.

The ability to translate basic research findings into applicable treatments is why the University of Basel, the University Hospital Basel and Novartis founded the institute in the first place. We were convinced that the confluence of basic research insights, the emergence of new gene technology tools, and the increased need for innovative eye disease treatments justified the creation of such an institute that is focused on translational research.

We can safely say the results that have been produced so far have exceeded our expectations. The speed at which the teams are working to drive breakthrough insights and translate these findings into robust drug development protocols is astonishing, especially in view of the short time frame since the institute became operational. With crucial developments in areas such as optogenetics and myopia, to name two examples, the IOB has made impressive progress.

The Board of Trustees is convinced that the IOB is in a good position to continue along this path. It has a strong leadership that can guide the institute in its next phase, and it has the ability to attract leading talents in diverse fields of science who will be instrumental in accelerating translational insights. Given the huge medical need in ophthalmology as well as the institute's distinctive position between academia and industry, we believe the IOB can look forward to a successful future.

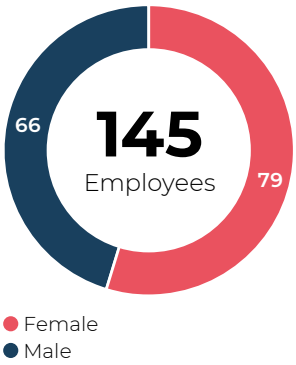
Sincerely,



Joerg Reinhardt
Chairman of the Board of Trustees

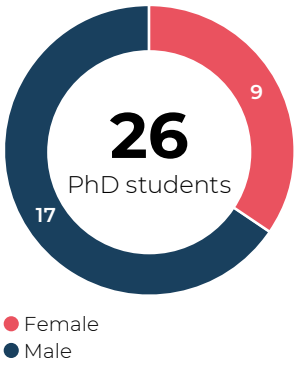
FACTS & FIGURES

IOB in numbers



618 Publications
since 2018

31 Nationalities



86 Awards
since 2018

11 Research Groups

7 Platforms

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RESTORING SIGHT: USING LIGHT-SENSITIVE GENES TO REACTIVATE EYE CELLS

Vision loss is a major health concern and one of the most feared conditions worldwide. Many causes of blindness start in the retina, the light-sensitive layer at the back of the eye. The central part of the retina, called the fovea, is especially important. It contains special cells called cones that allow us to see colors and fine details. When diseases affect the fovea, people lose their ability to read and recognize faces, which can be devastating.

Scientists at IOB have made an exciting discovery: They found that in about two-thirds of patients who are blind due to inherited eye diseases or age-related macular degeneration, the cone cells in the fovea are still present but not working. This finding opens up a new possibility for treatment.

IOB researchers have developed a method to "wake up" these dormant cone cells. They use a technique called optogenetics, which involves adding a light-sensitive protein to the cells. This protein acts like a tiny solar panel, allowing the cells to respond to light again.

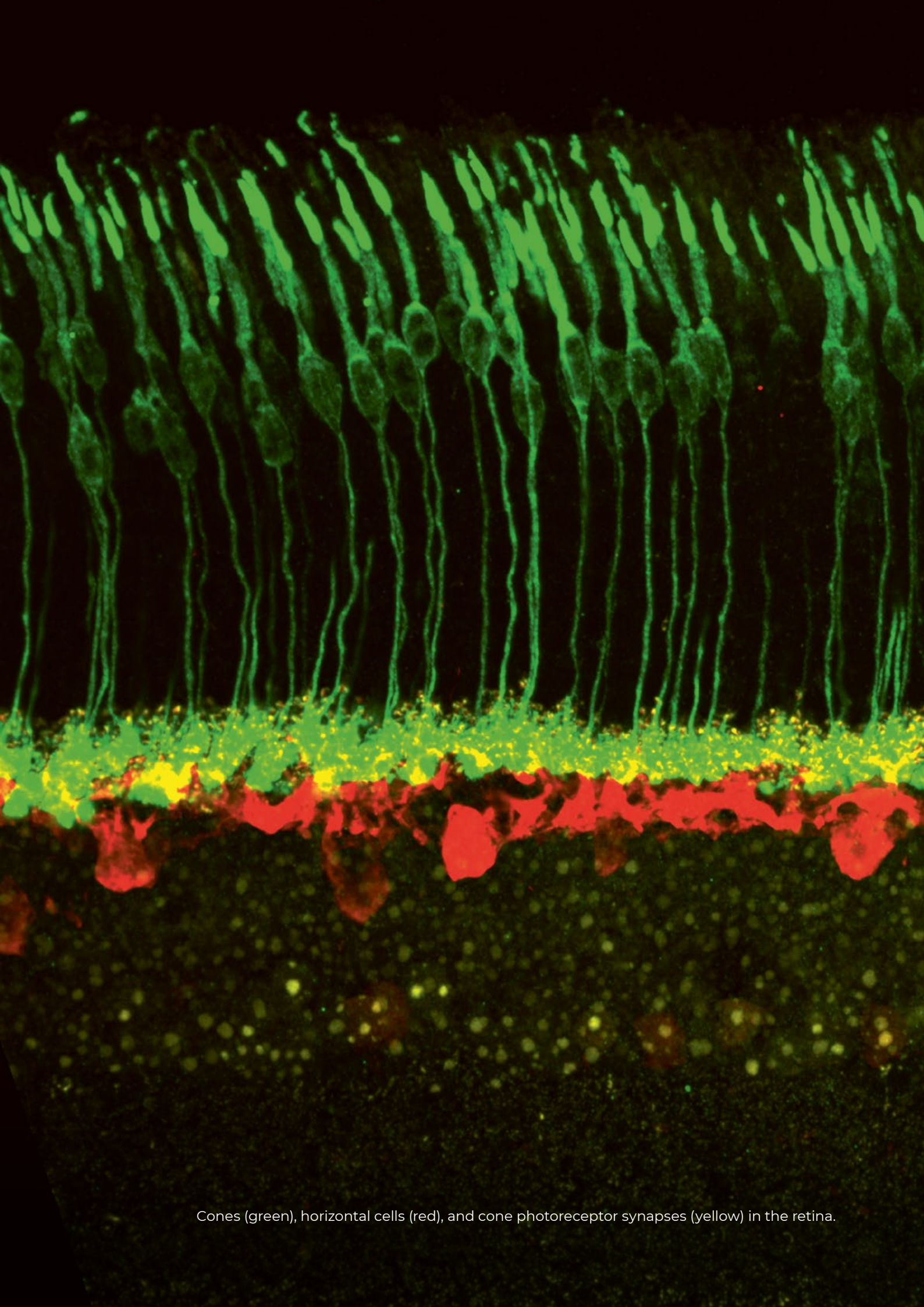
IOB researchers have developed a method to "wake up" these dormant cone cells.

To do this, IOB scientists created a special delivery system that targets only the cone cells. When they tested this approach on human retinal tissue in the lab, they saw impressive results: The cone cells became active again, and the retina started processing visual information almost as well as a healthy one.

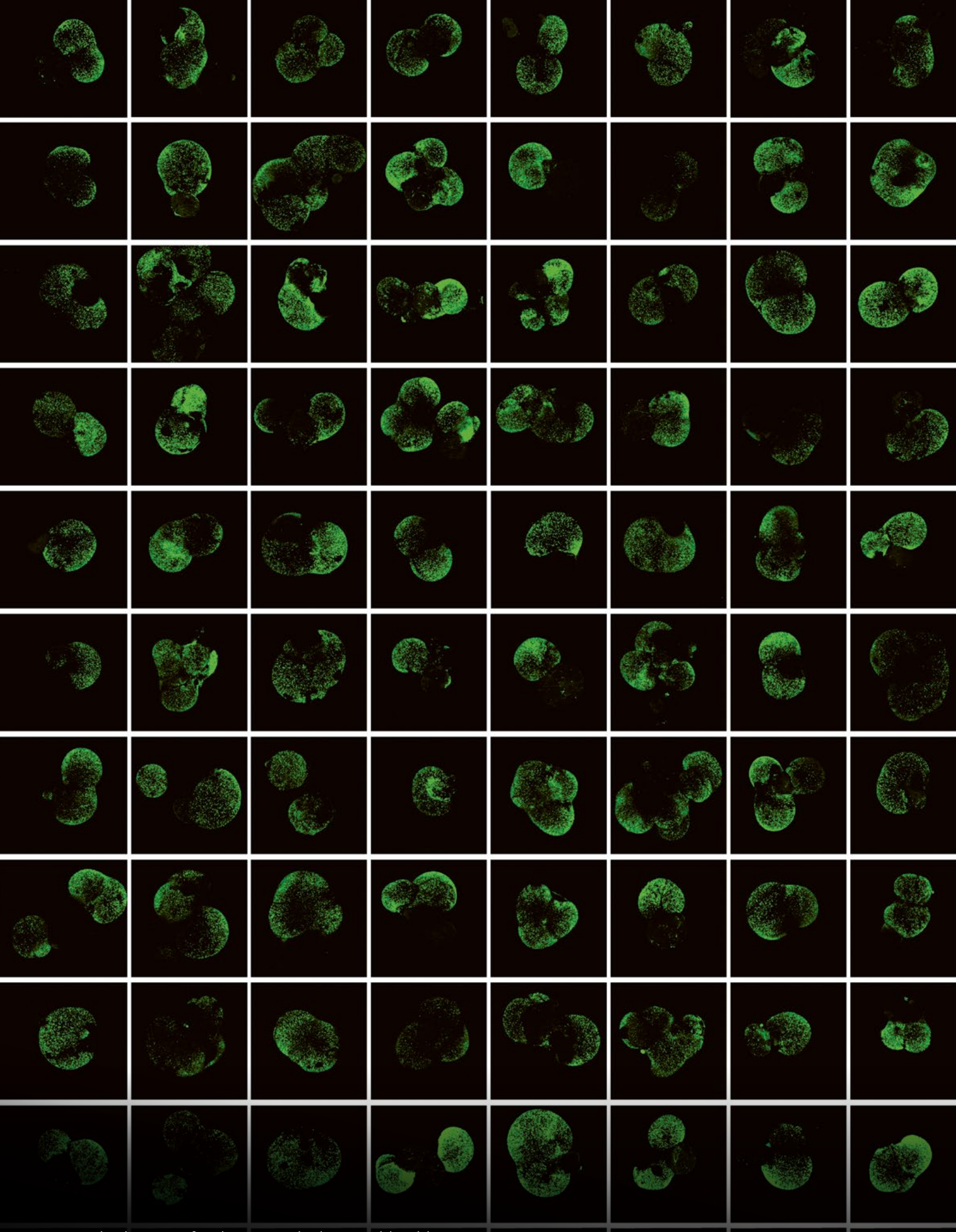
This method, called cone-targeted optogenetics, could potentially restore detailed vision in blind patients who still have cone cells in their fovea. It is particularly promising because it might bring back high-quality vision, not just the ability to see light and shadows.

The research at IOB builds on earlier work in optogenetics. Similar approaches targeting other types of retinal cells are already being tested in clinical trials and showing early signs of success.

While there is still more work to be done before this treatment can be used in patients, it is a significant step forward in the fight against blindness. For many people living with vision loss, this research offers new hope for regaining sight in the future.



Cones (green), horizontal cells (red), and cone photoreceptor synapses (yellow) in the retina.



Live images of 96 human retinal organoids with green fluorescent cone photoreceptors, each treated with a different compound.

USING HUMAN MINI-RETINAS TO FIND NEW TREATMENTS FOR EYE DISEASES

Scientists at IOB are using an innovative approach to search for new treatments for eye diseases. They have grown tiny versions of human retinas in the lab, called retinal organoids. These mini-retinas are like miniature artificial eyes that mimic the structure and cell types found in real human retinas. The team has created over 20,000 of these mini-retinas and focused on studying cone cells, which are the light-sensitive cells that allow us to see colors and fine details. These are the cells that let us read books and recognize faces.

To test potential new treatments, IOB scientists simulated an eye disease called macular degeneration. They did this by causing the cone cells in their mini-retinas to die off, mimicking what happens in the real disease.

Then, in collaboration with scientists at Novartis, they tested 2,707 different chemical compounds on these diseased mini-retinas, looking for any compounds that could prevent or slow down the death of the cone cells.

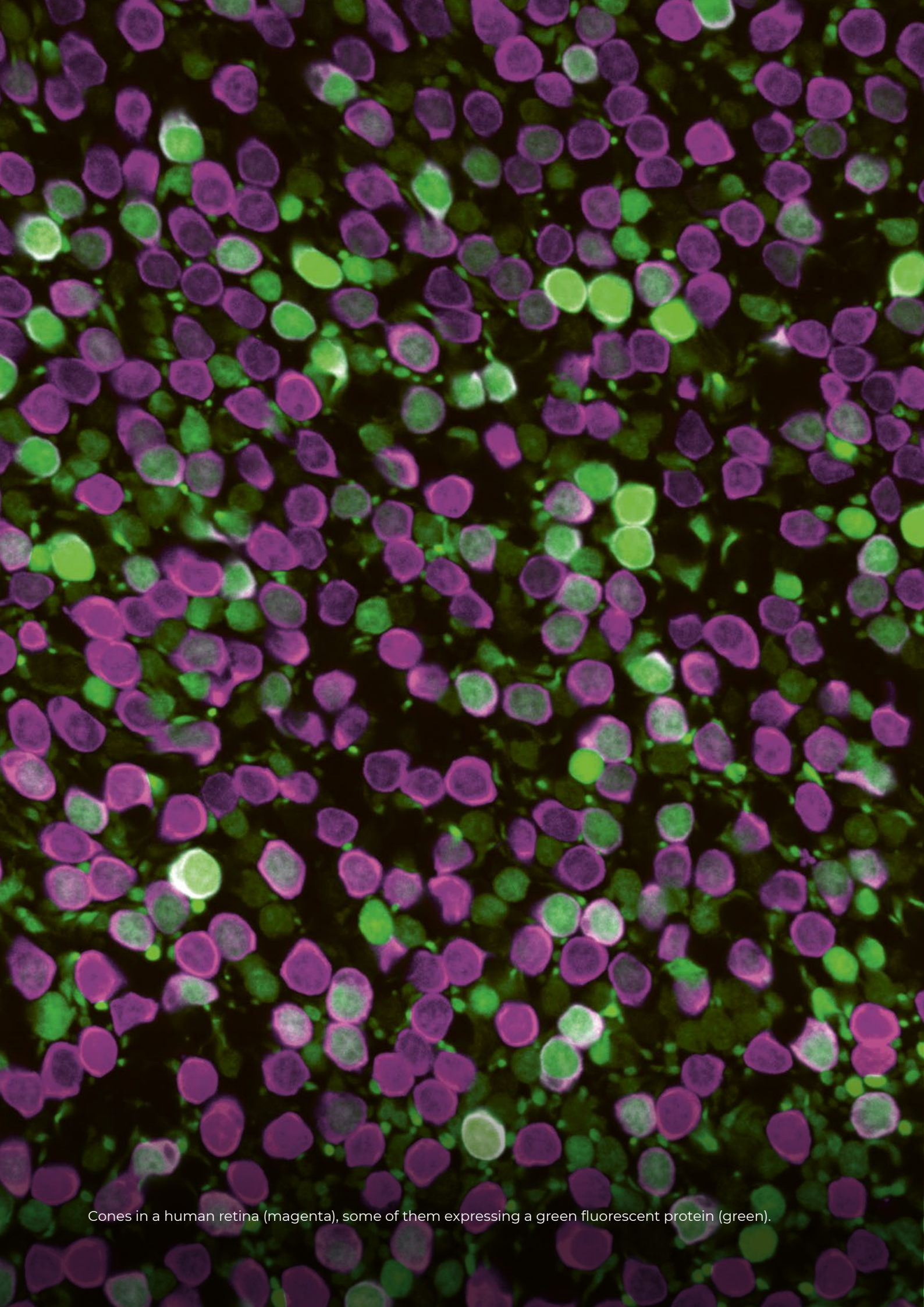
IOB researchers tested 2,707 different chemical compounds on these diseased mini-retinas.

The results were truly exciting. First they found a few compounds called kinase inhibitors that effectively protect the cone cells. These compounds work both immediately and over a longer period, which makes them promising candidates for future treatments for retinal degeneration.

Interestingly, they also discovered that some compounds currently used in cancer treatments can significantly harm cone cells. This is valuable information for protecting the vision of cancer patients.

Finally, the study has resulted in a comprehensive database of compounds that can either protect or harm cone cells. This information will be useful for developing new treatments to prevent or slow down diseases like macular degeneration.

This research demonstrates the power of using lab-grown mini-organs for medical research. By testing thousands of compounds on these mini-retinas, scientists can quickly identify potential new treatments and safety concerns, speeding up the process of developing new therapies for eye diseases. It is an important step forward in the fight against blindness and vision loss.



Cones in a human retina (magenta), some of them expressing a green fluorescent protein (green).

NEW HOPE FOR TREATING AN INHERITED EYE DISEASE

Scientists at IOB are making exciting progress in treating a common inherited eye condition called Stargardt disease. This condition affects the central part of the retina, causing patients to gradually lose their ability to read, drive, and recognize faces, eventually leading to blindness.

To understand this breakthrough, let us start with some background. In 2003, scientists completed mapping the human genome, allowing us to "read" our genetic information. More recently, a tool called CRISPR was developed, which allows scientists not just to read but also to edit genes. This opened up possibilities for treating genetic diseases at their root cause.

IOB researchers, working with scientists from BEAM Therapeutics in the USA, have developed a new approach using a safer version of gene editing called "base editing". This method aims to correct the specific genetic mutation that causes Stargardt disease.

The team tested their approach on lab-grown mini-retinas (called retinal organoids) carrying the disease-causing mutation. The researchers found that they could correct the mutation with high precision. They believe that correcting just 20% of the affected cells could significantly improve a patient's vision.

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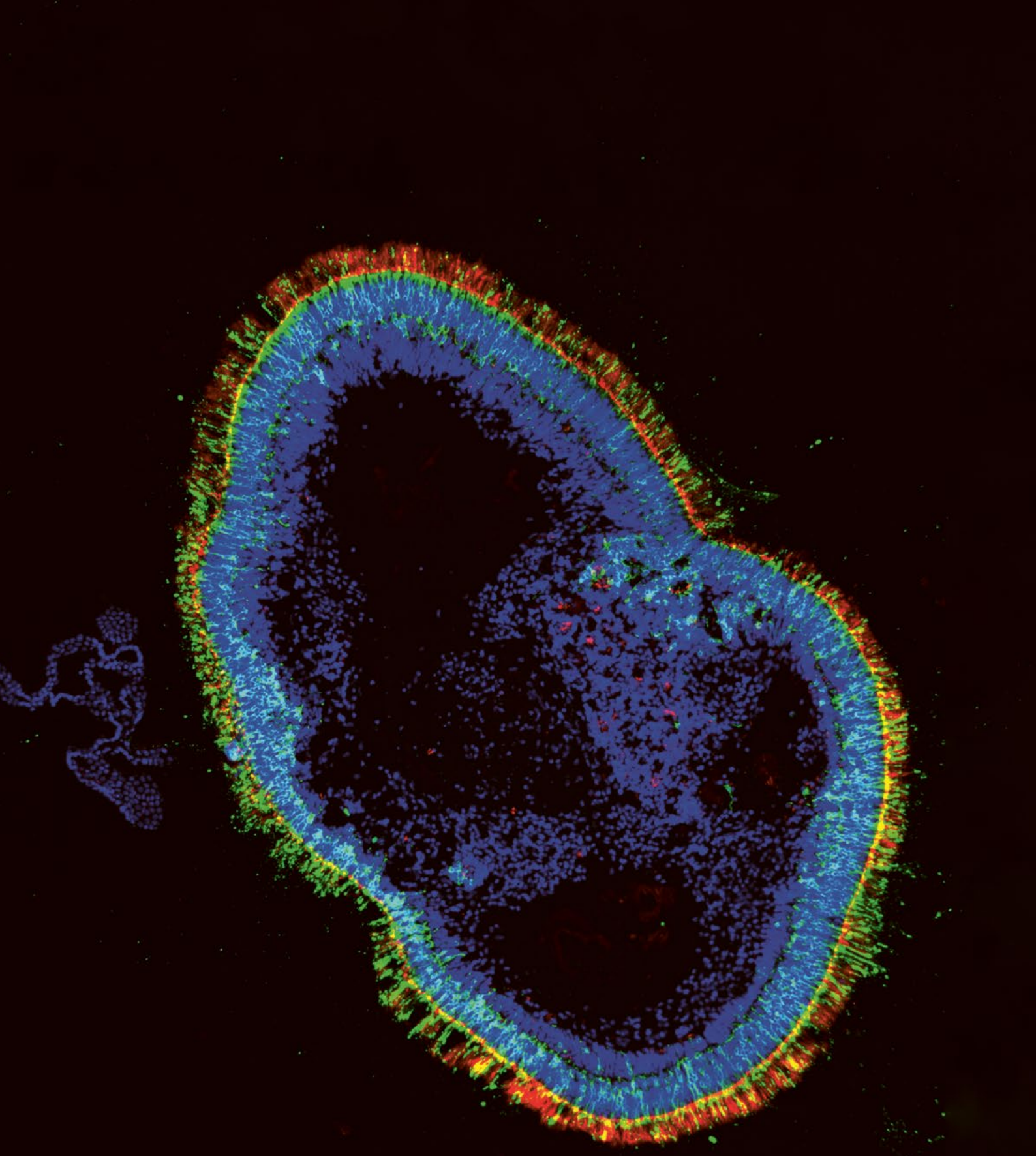
When they tested their method on human retinal tissue samples, the results were even better than expected. They were able to correct the genetic error in about 65% of the cone cells (the cells responsible for color vision and detailed sight) and 70% of retinal pigment epithelial cells.

Importantly, when the scientists checked for unintended effects elsewhere in the genome, they did not find any – suggesting this method is safe as well as effective.

This research brings hope not just for people with Stargardt disease, but potentially for other inherited eye conditions as well. It is a significant step forward in using genetic editing to treat diseases that were once considered incurable.

IOB is a research institute combining basic and clinical research. Its mission is to drive innovations in understanding vision and its diseases and to develop new therapies for vision loss.



Cross-section of a retinal organoid labeled with antibodies: rod photoreceptors (green), light-sensitive compartment of rod photoreceptors (red), cell nuclei (blue).

FLASH-SEQ: A NEW WAY TO READ GENETIC INFORMATION

IOB scientists have developed an innovative method called FLASH-seq to study genetic information in individual cells. This new approach addresses several problems with existing methods that were often time-consuming, expensive, and not very efficient.

FLASH-seq, introduced in 2022, is a quick and cost-effective way to prepare genetic material for analysis. It does not require any special commercial kits, and scientists can prepare samples for sequencing in just half a day. The method is also very efficient, using tiny amounts of materials to keep costs down.

IOB scientists first used FLASH-seq to study how different types of cells in human retinal organoids (lab-grown mini-organs that mimic the retina) use different versions of important developmental genes.

However, the original FLASH-seq method still had some limitations. It relied on breaking long pieces of genetic material into shorter fragments for analysis, which then had to be pieced back together by computers. This process could introduce errors and change the overall picture of the genetic information.

To overcome this issue, IOB scientists are now developing an improved version called FLASH-seq-ONT. This new method works with a technology that can read long pieces of genetic material directly, without breaking them up. This approach makes the process even faster and more accurate, allowing scientists to directly observe and count different versions of genes without the uncertainty of computer reconstruction.

IOB scientists believe FLASH-seq-ONT will become a go-to tool for researchers studying how cells use different versions of genes during development and specialization.

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This could lead to a deeper understanding of how cells change and grow, potentially opening new avenues for medical research and treatments.

HOW OUR BRAIN SYNCHRONIZES VISUAL INFORMATION

Our brain creates a consistent model of the world around us, but this is more complicated than it might seem. Different senses work at different speeds, and even within a single sense like vision, information from different parts of what we see can arrive at different times.

Let us focus on our eyes: The human eye is about an inch wide, and the retina (the light-sensitive part at the back of the eye) covers an area about the size of a postage stamp. When light hits the retina, it is processed by special cells called retinal ganglion cells. These cells send electrical signals through long fibers called axons to the brain.

Here is where it gets interesting: These axons do not all have the same length. Some are very short, while others can be over an inch long, depending on where they start in the retina.

You might think this would cause problems, with signals from different parts of our vision arriving at different times. But our body has a clever solution: IOB researchers found that longer axons are also thicker, which allows the signals to travel faster. This increased speed compensates for the extra distance, so all the signals arrive at the brain at roughly the same time.

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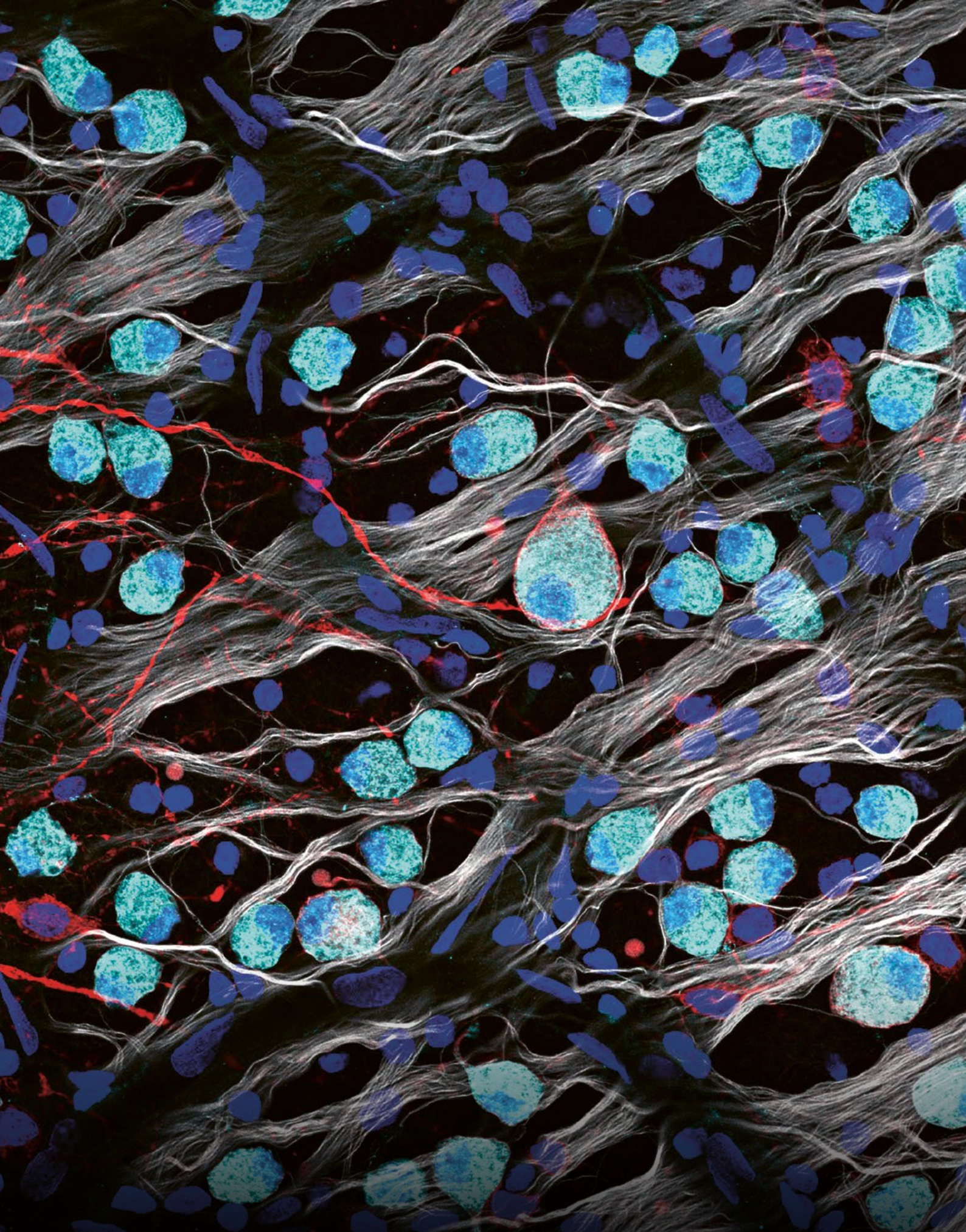
To discover this, IOB scientists used a variety of methods. They recorded electrical activity from retinas, measured how quickly people respond to visual cues, looked at the structure of axons under powerful microscopes, and used mathematical models to understand how signals travel through the eye.

This synchronization is crucial for our brain to create a coherent picture of the world. It ensures that what we see is processed as a unified whole, rather than a jumble of information arriving at different times. In essence, our eyes have developed a built-in "equalizer" that keeps visual information synchronized, helping us to perceive the world accurately and respond to it quickly.



The cell bodies of the retinal ganglion cells are shown in cyan, their extensions (axons) in white and the cell nuclei in dark blue. The red structures indicate some of the dendrites from retinal ganglion cells.

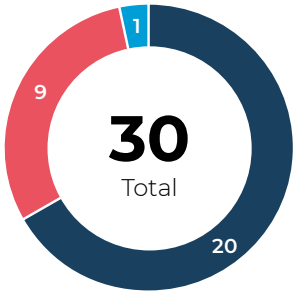
IOB research platforms develop cutting-edge technologies essential for understanding visual diseases and creating therapies to combat vision loss.

FINANCIAL SUMMARY

in mCHF

Income 2023

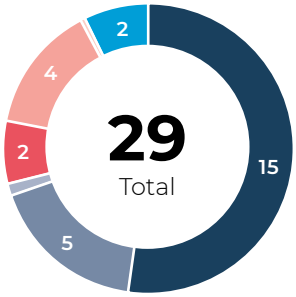
Since its inception, IOB has consistently diversified its funding sources, increasing third-party income from scientific grants, philanthropic donations, and industrial collaborations.
In 2023, this external funding represented nearly 30 % of IOB's total income.



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

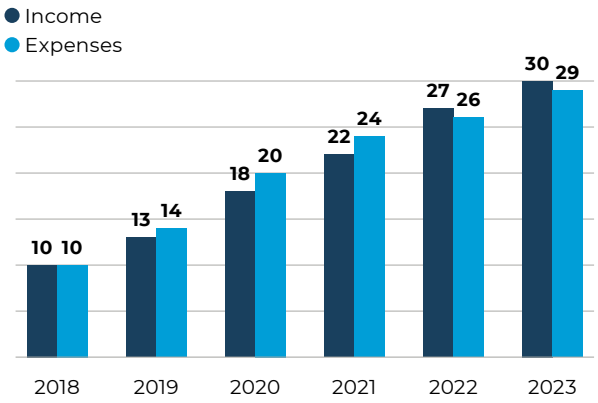
Expenses 2023

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 50 % of total expenditures.

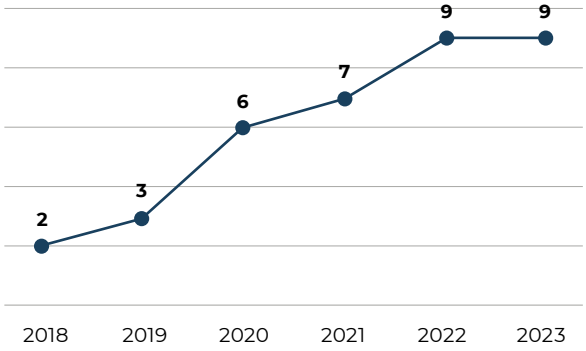


- Personnel expenses
- Research
- Maintenance: 0.4
- Rents and utilities
- Administrative expenses and IT
- Other expenses: 0.1
- Depreciation

Income/Expenses year by year



Third-party income year 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 Obligation (SCO).

BALANCE SHEET
in CHF

Assets	31.12.2023	31.12.2022
Current Assets		
Cash and cash equivalents	2,616,545	1,416,390
Accounts receivable	1,333,044	1,306,821
from third parties	*797,401*	*822,075*
from affiliated parties	*535,643*	*484,746*
Other short-term receivables	20,431	29,163
from third parties	*20,431*	*29,163*
Prepaid expenses	712,631	353,158
Total current assets	**4,682,651**	**3,105,532**
Non-current assets		
Property, plant and equipment	7,299,427	8,530,229
Intangible assets	303,263	352,442
Total non-current assets	**7,602,690**	**8,882,671**
Total assets	**12,285,341**	**11,988,202**

Liabilities and equity

Short-term liabilities		
Accounts payable	-692,268	-1,308,645
from third parties	*-541,284*	*-1,118,712*
from affiliated parties	*-150,984*	*-189,933*
Other short-term payables	-341,793	-310,013
from third parties	*-341,793*	*-310,013*
Short-term interest-bearing liabilities	-1,000,000	-1,000,000
from third parties	*-1,000,000*	*-1,000,000*
Accrued expense and deferred income	-1,260,903	-789,959
Restricted funds	-1,754,947	-2,137,362
Total short-term liabilities	**-5,049,912**	**-5,545,979**
Long-term liabilities		
Long-term interest-bearing liabilities	-4,000,000	-5,000,000
from third parties	*0*	*-1,000,000*
from affiliated parties	*-4,000,000*	*-4,000,000*
Other long-term liabilities	-557,460	-417,503
from third parties	*-557,460*	*-417,503*
Total long-term liabilities	**-4,557,460**	**-5,417,503**
Total liabilities	**-9,607,372**	**-10,963,482**
Equity		
Foundation capital	-500,000	-500,000
Profit brought forward	1,737,327	2,733,699
Unrestricted funds	-2,332,245	-2,262,047
Net result for the period	-1,583,051	-996,372
Total equity	**-2,677,969**	**-1,024,720**
Total liabilities and equity	**-12,285,341**	**-11,988,202**

THANK YOU FOR SUPPORTING US IN 2023

We are deeply grateful for the generous contributions and ongoing collaborations with private individuals, foundations, and institutions. These partnerships are vital to our research.

Swiss

- Accentus Charitable Foundation
- Alessia Martinetti
- Bandung Foundation
- Bertarelli Foundation
- Christian Ziesolleck
- City of Basel
- Ernst Göhner Stiftung
- Freiwillige Akademische Gesellschaft Basel
- Fond Action
- Georg H. Endress Stiftung
- Hedy Glor Meyer Stiftung
- Dr. Hubertus Ludwig
- Innosuisse
- MBF Foundation
- Novartis
- Palatin-Stiftung
- Plusoptix AG
- Pro Sanandis Oculis
- Swiss Life Jubiläumsstiftung
- Swiss National Science Foundation SNSF/ Theron Foundation
- University Hospital Basel
- Unversity of Basel
- University of Basel Research Fund

International

- European Molecular Biology Organization (EMBO)
- European Union (Horizon 2020)
- Human Frontier Science Program HFSP
- Simons Foundation
- Sloan Foundation
- Teofilo Rossi Foundation of Montelera and Premuda, advised by CARIGEST SA

Founders

- Novartis
- University Hospital Basel
- University of Basel

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Affiliations

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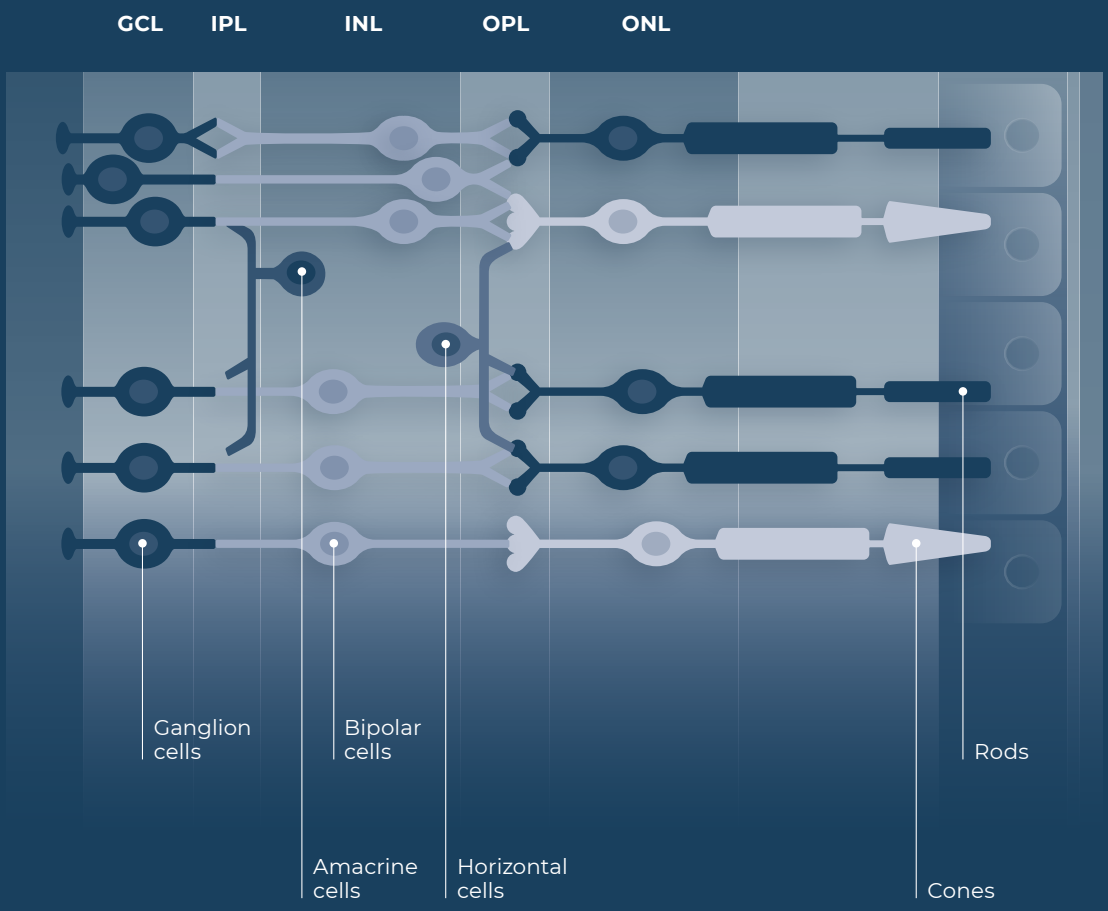
THE HUMAN RETINA



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
Institute of Molecular and Clinical Ophthalmology Basel
Mittlere Strasse 91 | 4031 Basel | Switzerland
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