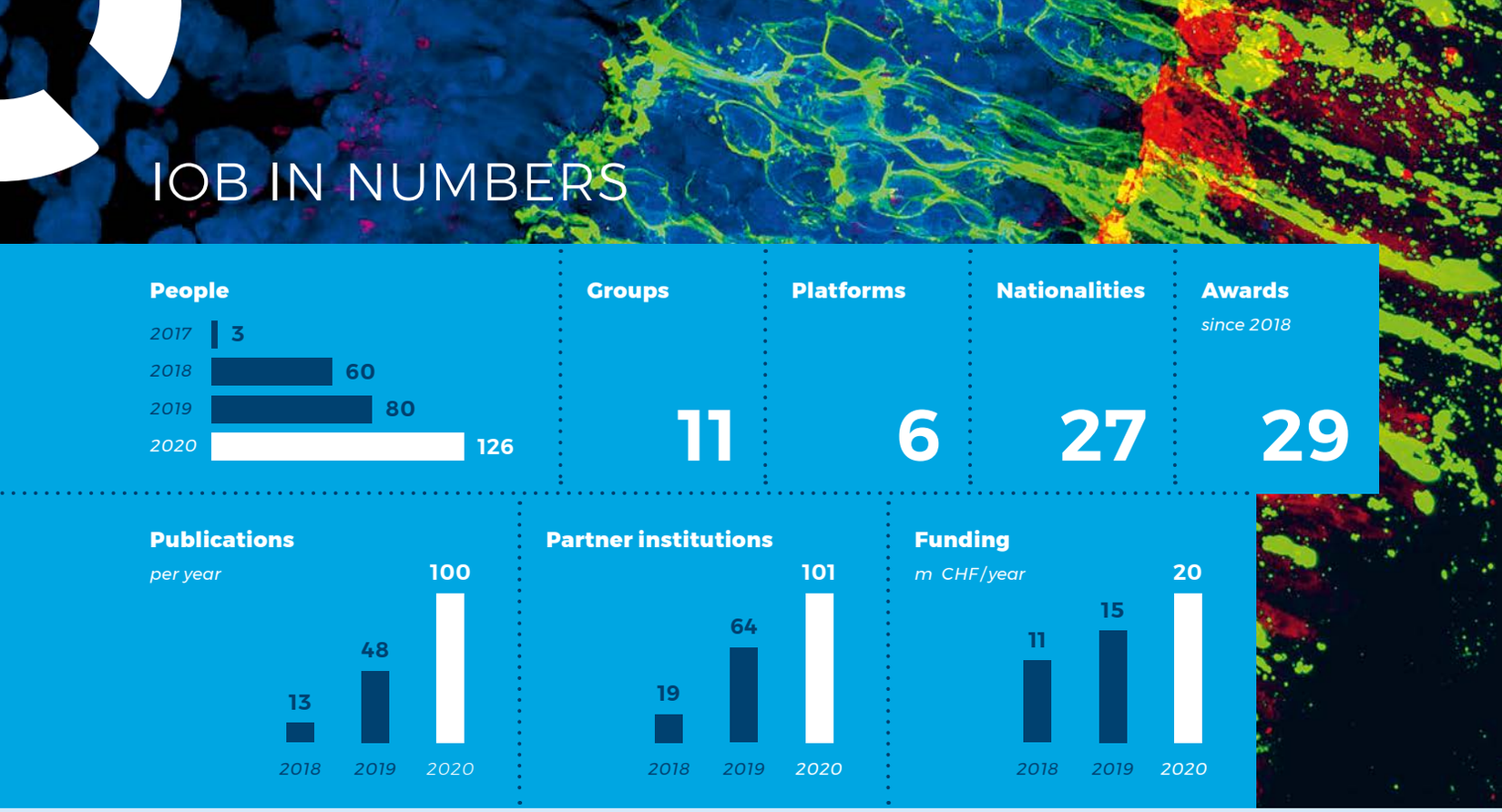
IOB Institute of Molecular and Clinical Ophthalmology Basel

ANNUAL REPORT 2020



IOB IN NUMBERS

People

Groups

11

Platforms

6

Nationalities

27

Awards

since 2018

29

Publications

per year

Partner institutions

Funding

m CHF/year

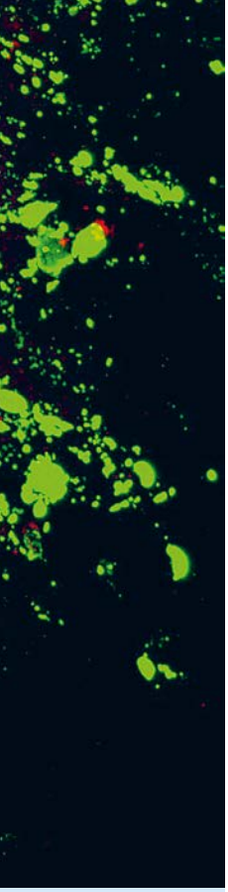
IOB MISSION

We advance the understanding of vision and human eye diseases and develop new therapies for vision loss.

GROUPS AND PLATFORMS AT IOB

	MOLECULAR	+	CLINICAL
11 Groups	› Central Visual Circuits Group › Human Retinal Circuits Group › Theoretical & Computational Neuroscience Group › Human Retina & Organoid Development Group › Quantitative Visual Physiology Group › Visual Cortex Plasticity Group*		› Ophthalmic Genetics Group › Ophthalmic Imaging & OCT Group › Ophthalmic Translational Research Group › Myopia Research Group › Genetic Epidemiology of Ophthalmic Diseases Group
6 Platforms	› Human Organoid Platform › Complex Viruses Platform › Single Cell Genomics Platform › Scientific Computing Platform		› Clinical Trial Center Platform › Visual Neurophysiology Platform

** new in 2021*



DIRECTORS' LETTER

Dear reader,

When 2020 began, none of us could have imagined that the year would end with a surging global pandemic. Despite the unprecedented challenge of COVID-19, people at IOB have worked hard towards a shared goal: restoring vision.

We are proud of the progress IOB made in its third year of operations. Thanks to careful planning and to the commitment of our researchers and staff, the institute has continued to grow: we recruited outstanding scientists, built and expanded high-performing technology platforms, and created a knowledgeable administrative team to support our investigators. Furthermore, we succeeded in bringing most of our people together under one roof: a dedicated, nine-floor building for wet-lab research.

In 2020, IOB scientists published breaking discoveries in top-tier journals and were recognized internationally through prestigious awards and highly competitive research grants. The constant interaction between basic researchers and clinicians has generated new insights into the human retina and contributed to innovations including organoid technology, gene therapy, genetic diagnosis and improved imaging of the eye, which bring us much closer to developing therapies for untreatable eye diseases.

We are grateful to our founders, our partners, and the many institutions that provided generous financial support. These resources will go a long way in helping us to champion scientific discovery in ophthalmology and develop life-changing treatments for patients.

As we look ahead to the rest of 2021, we are energized to continue leading IOB and fostering a culture of excellence and cross-disciplinary collaboration, because the research we do is critical to the future of millions of people affected by eye diseases and vision loss.

Sincerely,

Botond Roska
Director
Molecular Research

Hendrik Scholl
Director
Clinical Research

Norbert Spirig
Director
of Operations

A COFFEE WITH THE IOB DIRECTORS

A vision for success

The three directors offer insights into what makes IOB unique and share their thoughts on the "recipe" for the institute's growing success.

Understanding vision and developing new treatments for vision loss are incredibly ambitious goals. What's your approach to reaching them and what makes IOB stand out from other institutions active in vision research?

Hendrik Scholl: At IOB, there's a constant dialogue between basic researchers and people who are on the frontline working with patients every day. Basic researchers learn from clinicians what the unmet medical needs are, and clinicians learn from basic researchers which technologies are already available in the lab that have the potential to be developed into therapies for patients.

Botond Roska: It's extraordinary that such discussions between basic scientists and clinicians regularly take place. This rarely happens at other institutes.

Norbert Spirig: We always have interdisciplinary discussions, because nobody has all the knowledge. We bring people together through seminars, topic-related discussions and informal events.

IOB is one of the few institutes worldwide covering vision science from molecules to treatments. How does the institute make that possible?

Botond: At IOB, we have several research groups and technology platforms. When people from these groups get excited about a particular translational program, they assemble into a new unit that works along the development chain towards the clinical trial. Once the project is completed, they disassemble and may reassemble for a new project. This is a new concept, and we hope it will be successful. Certainly, none of this can be achieved in a basic science institute, because there are no clinicians. Also, in a purely clinical domain, this can't be achieved because there's no technology development.

IOB started operations in 2018. Looking back at the past years and 2020 in particular, what are you most proud of?

Norbert: In 2020, we moved into our laboratory building in the Klybeck area and brought together about 90% of IOB members. I'm proud that we accomplished this in one year. The second thing I'm proud of is that we implemented all sorts of groups that support scientists – from human resources to facility management to IT – so that researchers can concentrate on science. The phase of building up from scratch is now complete. In 2020, we, as an institute, reached maturity.

Botond: I'm proud to see that young people at IOB, especially young women, are being very successful. For example, Dasha Nelidova, who developed a technology that aids people with incomplete blindness, won eight international scientific awards in eight months: she's certainly one of the rising stars of Switzerland's research community. I'm also proud of a collaborative study with Hendrik and his colleagues in which we described the first large-scale disease map for the human retina at single-cell resolution. Any medical doctor – be they in South America or China – can look up this atlas, take our tools and start to build on them. This goes beyond IOB: we work on several major projects that are for the world, so that anyone can take our resources and act locally, developing treatments for patients.

In 2020 alone IOB hired 46 people, going from 80 to 126 employees. What makes the institute so attractive?

Hendrik: We can tell a story and it's a convincing one: we want to make blind people see again. And we are actively pursuing it. Here, people have the resources and lab space and technologies that they can use to really accomplish this goal in the future.

Botond: Now, we are in a position to hire world-renowned group leaders. Soon we'll have some openings and we are ready for the absolute best: if they join, they will be served in a way that no other institute in this field can provide.

From a clinical and a molecular point of view, what have been the highlights of 2020?

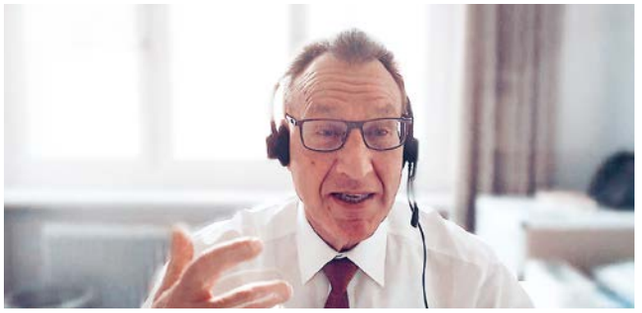
Botond: From the molecular side, we developed several technologies: one, published in *Cell,* allows us to grow tens of thousands of functional human retinas in a dish. This technology can help us to better understand eye diseases and develop new therapies. In *Science,* we also detailed a new way of restoring vision in people with incomplete blindness using near-infrared nanosensors, which interfere minimally with any healthy photoreceptors.

Hendrik: In the clinical center, innovations have been both diagnostic and therapeutic. We have imaging technologies that allow us to look at the retina in a patient in real time, and even track individual cells over time. This helps us to determine the efficacy of a therapy in ways that were not possible before. We also work on the surgical front to provide the best possible surgery. For example, last year we were certified as the only center in Switzerland to surgically administer the first commercially available gene therapy for vision loss.

In 2020, people at IOB were awarded prizes, received millions in research funding, and published several high-impact research articles. What's your recipe for success?

Botond: Excitement and extremely hard work: all of us work morning to night.

Norbert: IOB would not fly without Botond and Hendrik and all the people that we hired for the research groups, for the technology platforms, and for support functions.



The past 12 months have been challenging for everyone. Despite the coronavirus pandemic, IOB has continued to do cutting-edge research. How did you manage that?

Norbert: I'd like to claim that we did it by magic, but it's not true. It all comes down to good planning, and we were lucky that we had plenty of space in the building. This meant that people could keep physical distance and did not have to stay home if it wasn't mandatory.

Hendrik: It sounds strange, but 2020 was a very successful year for IOB. We may have been fortunate, but of course, there was a lot of effort that went into this success.

Looking ahead, what are the milestones that IOB hopes to achieve in 2021?

Botond: We want to build new tools for ophthalmology that could serve translation. We would also like to push forward our 2020 signature project – cone-based optogenetics – and select the final candidate optogenetic sensor that is ready to go to the clinic. Third, we would like to establish more collaborations with companies, because we believe they help us to distribute the tools that will end up in applied patient care.

Norbert: I'd like to finalize the planning of a new joint building for IOB and the Eye Clinic, which we'll start constructing sometime in 2023. One major reason why we want to change home is that the farther away people are from each other, the less they work together. So, we want to bring everyone together in the same building: physicians, nurses, administrators and, of course, scientists.

Hendrik: It will be a complex building, combining state-of-the-art medical care and cutting edge research. Operating theaters, day clinic, exam rooms, research labs, you name it – everything will be in the same building. We'd also like to have rooms where people can meet and talk. On the clinical side, we would like to bring therapies to patients: this means we'll prepare for the clinical trials of our signature projects, which will start in early 2023. But this is a scientific institute, which also means the future is largely unpredictable. But then again, I would like to predict that we will overcome the COVID-19 crisis in 2021. •

SCIENTIFIC ACHIEVEMENTS 2020

A new wave of research in ophthalmology

IOB has led advances in technologies that promise to bring exciting changes to the field of ophthalmology. These innovations include mini-retinas grown in a lab dish, known as **retinal organoids,** the development of **gene therapy vectors** for restoring vision, improved **imaging technologies** that offer an unprecedented view of the eye, and the optimization of **subretinal delivery of gene therapies.**

from MOLECULE to TREATMENT

PLATFORM LEADER:
Simone Picelli

SINGLE CELL GENOMICS PLATFORM

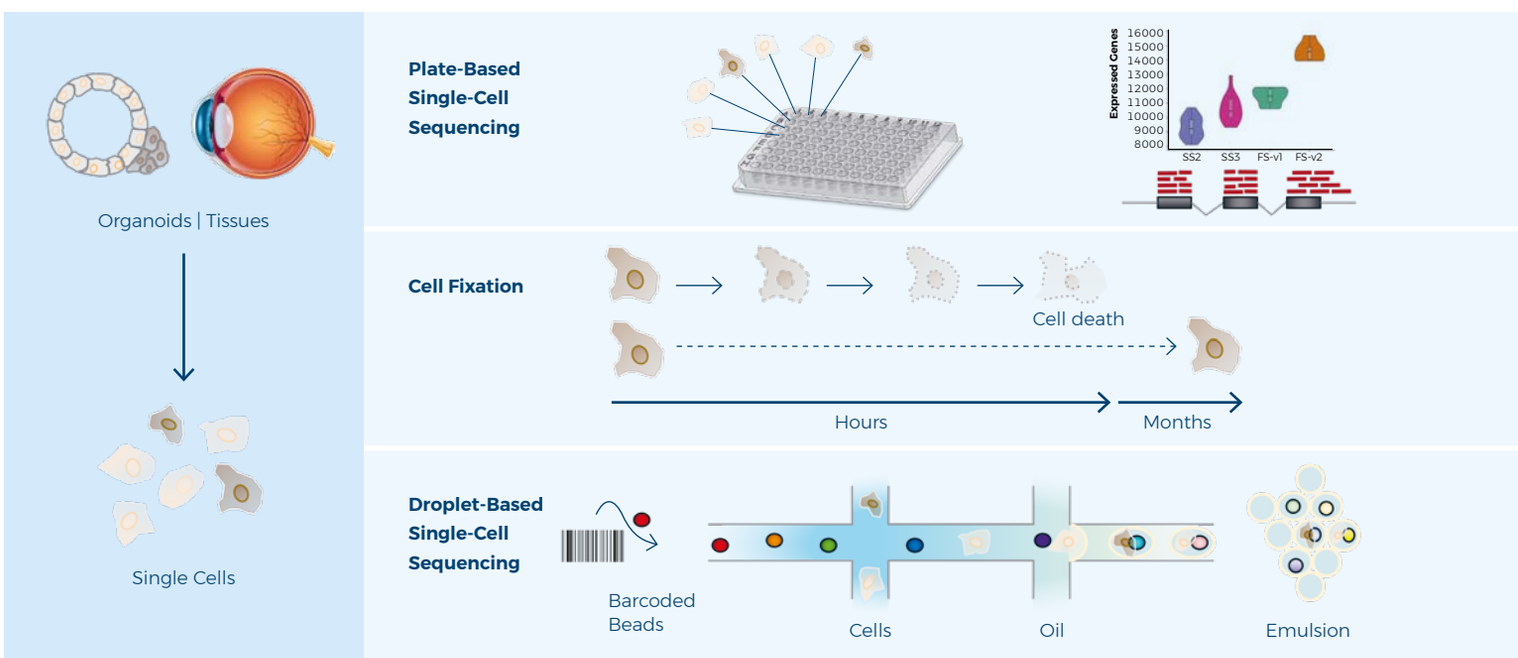
Single cells are the fundamental and structural units of life, reproduction, metabolism, and heredity. Cells differ in gene expression levels, an essential aspect that plays a key role in health and disease.

Understanding which combinations of genes are expressed in each cell type can help us obtain a comprehensive picture of both the physiological and pathological states, infer the biological mechanisms leading to disease and, ultimately, develop patient-tailored therapies.

We are generating a Human Eye Cell Atlas integrating multi-modal data from RNA, protein and epigenetic signatures from hundreds of thousands of cells in multiple tissues. This will shed light on the underlying molecular mechanisms leading to degenerative diseases like glaucoma and macular degeneration.

We are also working on new cutting-edge technologies. In collaboration with the company seqWell, we have recently developed a new single-cell RNA-seq method (scRapid), which is fast, economical and allows the retrieval of a lot more information from each cell compared to what was possible until now.

Finally, we are exploring new ways to preserve cell integrity for long periods of time, overcoming limitations imposed by logistics or lack of specialized equipment. De-coupling sample collection and sample processing is crucial for future single-cell studies.



A new method to scale up retinal organoid generation

HUMAN ORGANOID PLATFORM

Retinal organoids are a new model system to study the human retina in a cell culture dish. As starting material we use induced pluripotent stem cells that are reprogrammed from skin fibroblasts.

Published methods to generate retinal organoids are labor intense and the yield of organoids is low and variable. To scale up organoid production we developed AMASS (Agarose Microwell Array Seeding and Scraping), a new method for the generation of thousands of retinal organoids.

We thoroughly compared retinal organoids to adult human retina by single-cell RNA sequencing and immunohistochemistry. Retinal organoids are 5-layered like the human retina and contain all major retinal cell types. Furthermore, organoid photoreceptors are light-sensitive and contain functional synapses.

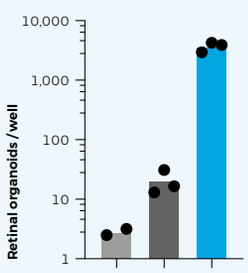
Retinal organoids can be used to model human retinal disease and to develop new therapies. Using AMASS to generate 20 000 organoids in combination with cell-type specific fluorescent labeling in live organoids allows us to perform a compound screen on retinal organoids. Screening can help to better understand disease mechanisms and to find new compounds to treat retinal disease.

PLATFORM LEADER:
Magdalena Renner

Scaling up retinal organoid generation

AMASS method compared to previous retinal organoid generation methods

- *Unregulated EB size + microdissection*
- *Unregulated EB size + checkerboard scraping*
- *AMASS: Regulated EB size + checkerboard scraping*



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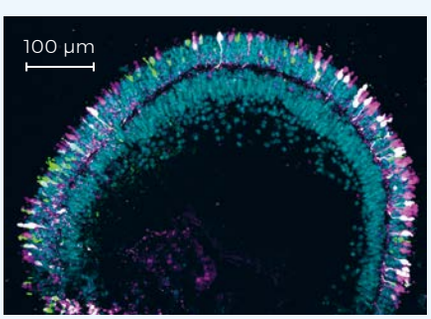
Cell-type specific fluorescent labelling in live organoids



- *AAV-mediated labeling of cone photoreceptors*
- *AAV-mediated labeling of both rod- and cone photoreceptors*
- *Hoechst (nuclei)*

Organoid compound screen on 20 000 retinal organoids

Targeting cell types with gene therapy vectors

COMPLEX VIRUSES PLATFORM

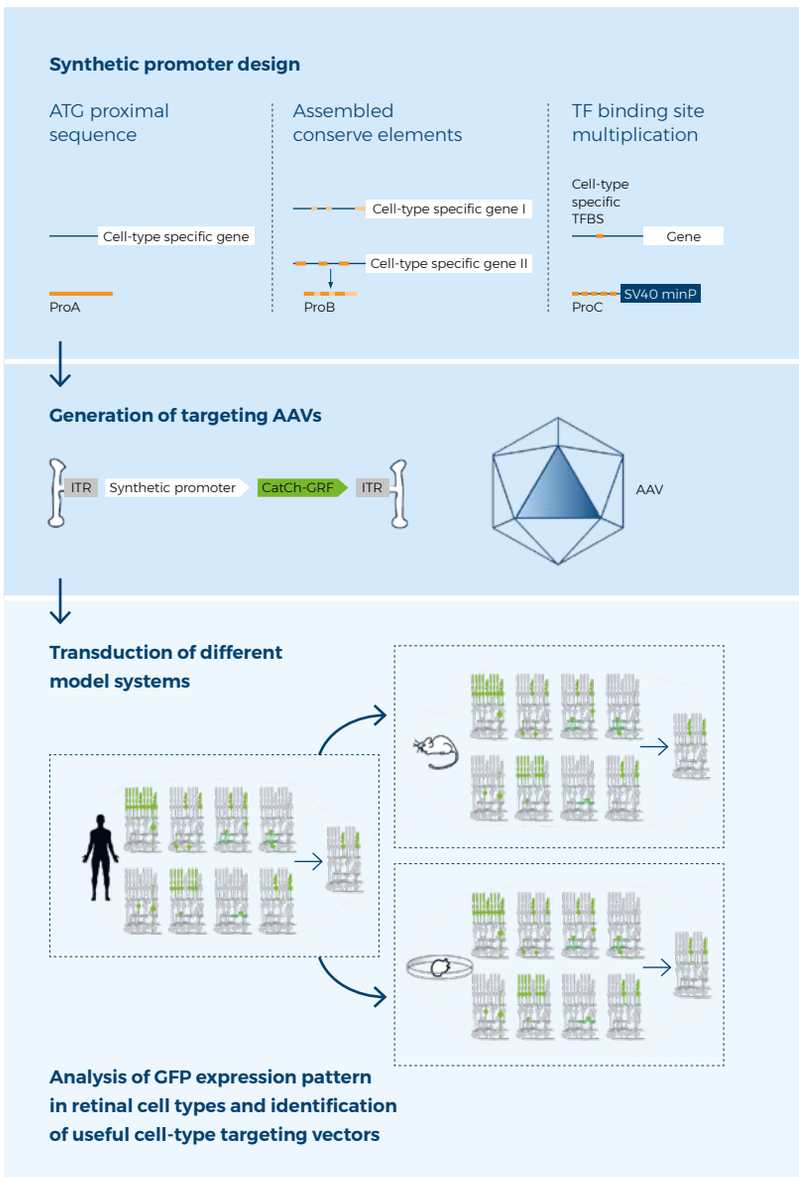
Targeting genes to specific cell types is valuable both for understanding and for repairing neuronal circuits. Adeno-associated viruses (AAVs) are frequently used for gene delivery into the retina, but targeting gene expression to specific cell types remains a challenge.

IOB's strategy is based on a synthetic DNA element – a promoter – which, when embedded into the AAV genome, drives transgene expression in a cell-type-specific manner.

We developed a pipeline to identify cell-type-specific promoters that starts with the design of unique synthetic promoters using three distinct strategies based on the transcriptomic identities of cell types in the human retina. As a proof of concept, AAVs are produced in which the synthetic promoter drives an optogenetic tool fused to green fluorescent protein (GFP). We previously found promoter activity and specificity to vary unpredictably between species. Since the ultimate goal is to use these vectors for gene therapy in humans, AAVs carrying the synthetic promoters are first tested in human post-mortem retinal explants by evaluating the GFP expression pattern. AAVs with useful expression profiles are then evaluated in mouse retina and retinal organoids. AAVs that induce reproducible cell-type-specific expression are shared with IOB researchers.

Our toolkit of targeting AAVs will accelerate translation of research in model systems like mice and organoids to gene therapy in humans. ●

PLATFORM LEADER:
Josephine Jüttner



Analysis of GFP expression pattern in retinal cell types and identification of useful cell-type targeting vectors

HUMAN RETINA & ORGANOID DEVELOPMENT GROUP

Human organoid models of the central nervous system, including the neural retina, are providing unprecedented opportunities to explore human neurodevelopment and neurodegeneration in controlled culture environments.

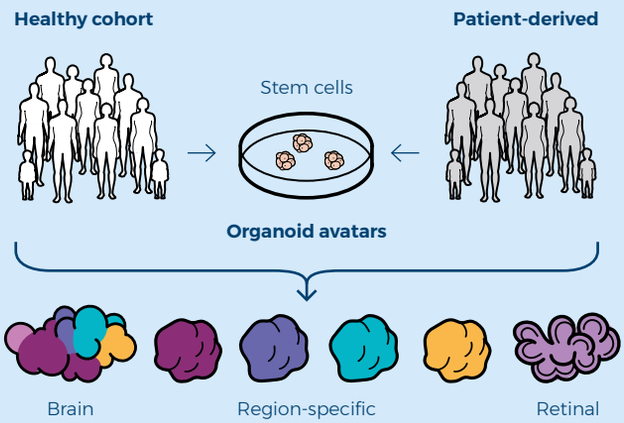
Giovanna Brancati and Gray Camp of the Human Retina and Organoid Development Group provided their perspective on how the single-cell multi-omic toolkit can be deployed to study congenital brain malformations and vision disorders in organoids (Brancati et al. Neuron 2020).

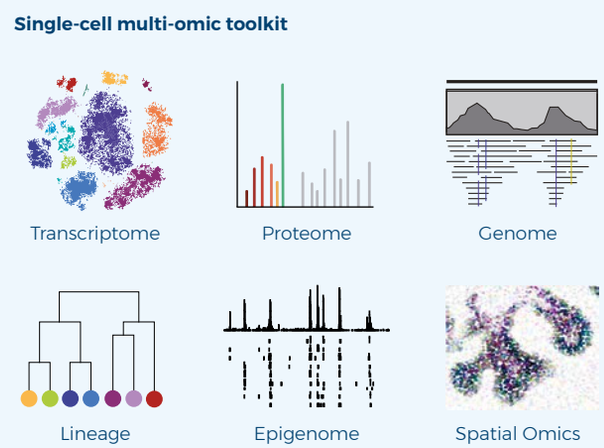
The toolkit contains exciting new technologies to study the status of individual cells within complex tissues. The molecular building blocks of each cell including DNA, RNA, and proteins can all be measured with high sensitivity for thousands of cells at a time. Even the history of a cell can be recorded in its DNA as it develops over months in culture.

Researchers at IOB are using these tools to understand how the human retina forms from stem cells, and how congenital mutations found in patients can disrupt the process and lead to blindness. ●

GROUP LEADER:
Gray Camp

Single-cell technologies and organoid avatars to understand neurodevelopmental disorders





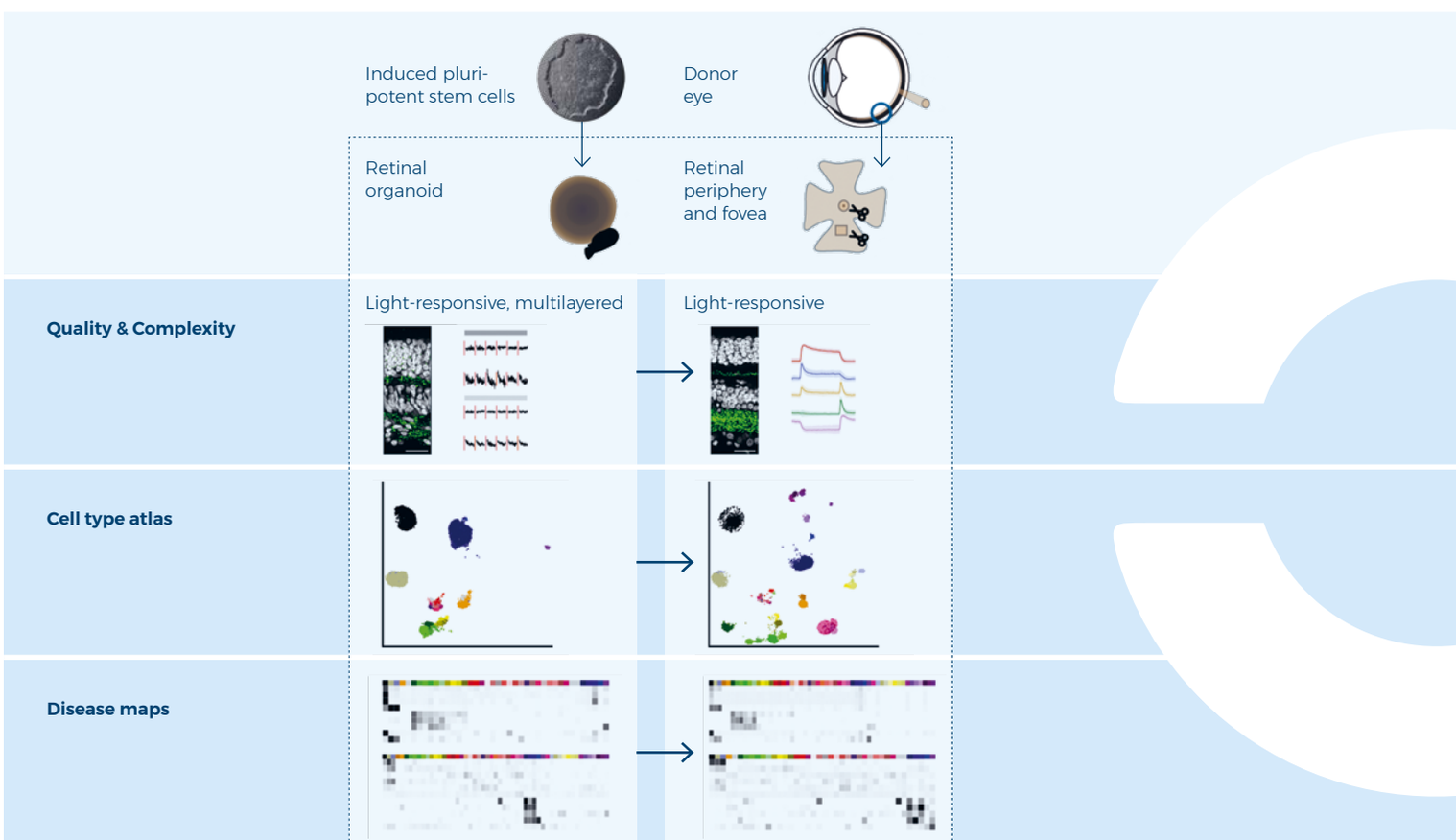
PLATFORM LEADER:
Cameron Cowan

SCIENTIFIC COMPUTING PLATFORM

Founded in 2020, the Scientific Computing Platform works with experimentalists to answer basic and translational research questions by combining quantitative methods with detailed domain knowledge.

A good demonstration of our work is the atlas of cell types in the human retina and retinal organoids recently published in *Cell*. Researchers and clinicians can use this atlas to distinguish cell types, determine where they express disease-associated genes, and ask whether organoids are sufficiently good reproductions that they can be used to model a disease.

Looking forward to 2021, we are developing an increasingly comprehensive catalogue of cell types in the eye and exploring how they combine to form tissues. These improvements complement our work to understand diseases and disorders by providing a more complete account of what a healthy human eye looks like.



From the retina to eye movements

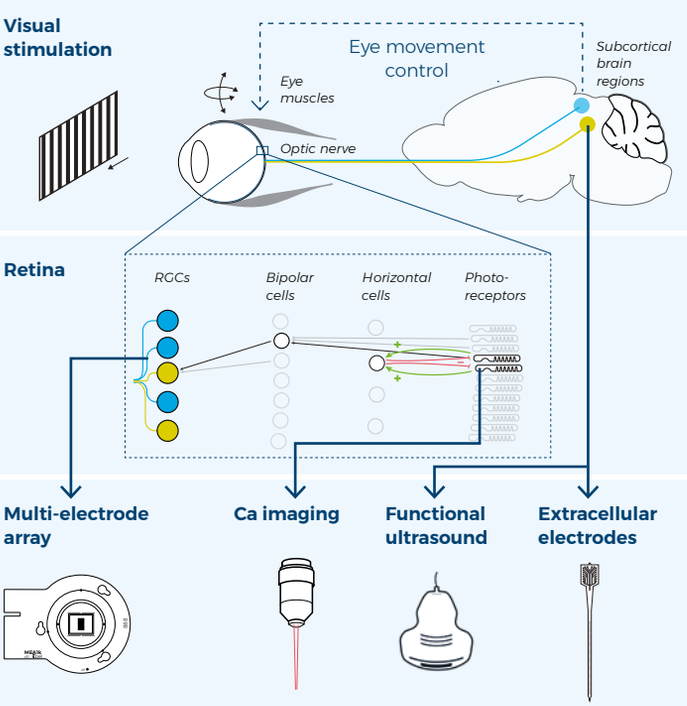
GROUP LEADER:
Felix Franke

QUANTITATIVE VISUAL PHYSIOLOGY GROUP

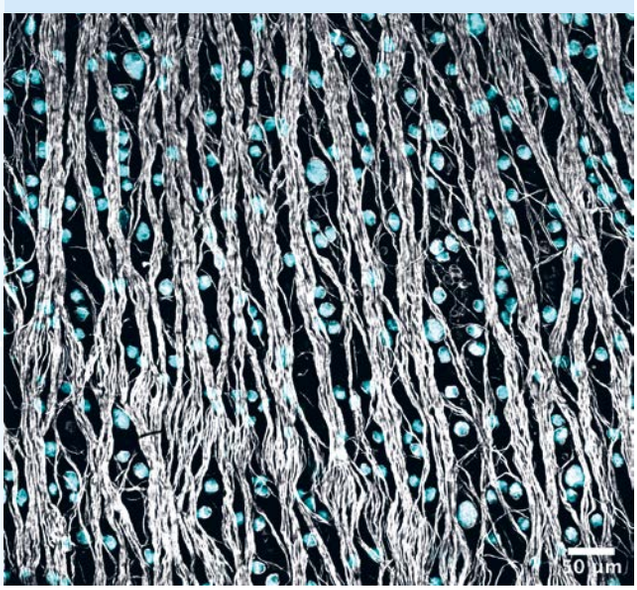
The eye is a remarkable sensory organ that converts light into the electrical activity of neurons. This activity carries all the information about the visual world that our brain can access.

The quantitative visual physiology group has two central questions: How do neurons in our eyes encode the information about what we see, and what do the downstream neurons in the brain do with this information?

We use methods from neurophysiology, ranging from microelectrode arrays to functional ultrasound imaging, to measure the activity of retinal and midbrain neurons when we stimulate the retina with specific light stimuli. Neurons in the retina and central nervous system come in a variety of different types, which can be identified using genetic, morphological, and functional characteristics. In the retina, different cell types encode different information about the visual world and send this information to different projection targets in the brain. Vision is active and we constantly move our eyes to scan the world. Specific cell types encode movement-related information from the light stimulus. One central problem we are addressing is the role played by these cell types in coordinating or even eliciting eye movements as well as in eye movement disorders.



Immunostaining of human retinal ganglion cells in blue and their axons in white



Restoring light sensitivity using tunable near-infrared sensors

HUMAN RETINAL CIRCUITS GROUP

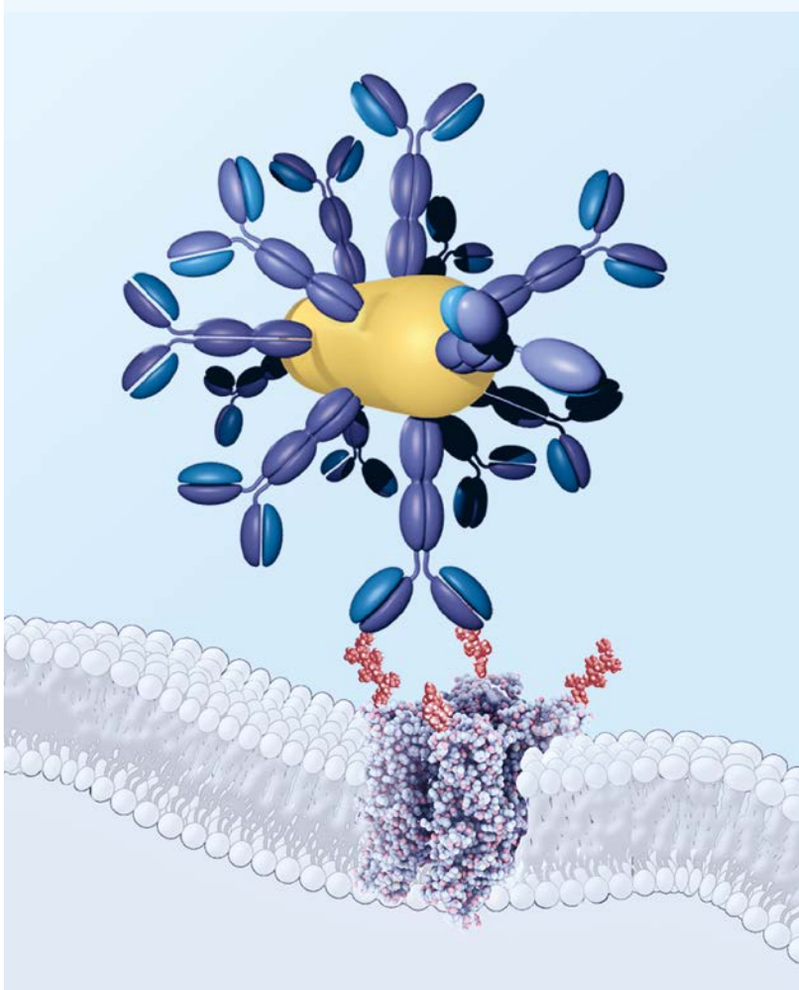
Photoreceptor degeneration, including age-related macular degeneration and retinitis pigmentosa, is the leading cause of blindness in industrialized countries.

In most cases, degeneration is incomplete and the remaining light-sensitive regions limit the utility of optogenetic therapies because these technologies require bright, visible light. Therefore, we induced near-infrared light sensitivity using gold nanorods bound to temperature-sensitive TRP channels. We expressed TRP channels in light-insensitive cones in a mouse model of retinal degeneration (Nelidova et al, 2020, Science). Near-infrared stimulation increased activity in cones, ganglion cell layer neurons and cortical neurons, and enabled mice to perform a learned, light-driven behavior. We tuned responses to different wavelengths by using nanorods of different lengths, and to different radiant powers by using engineered channels with different temperature thresholds. Finally, we targeted TRP channels to human retinas, which allowed the activation of different cell types by near-infrared light, post-mortem.

This combined nano-bio therapy provides a new therapeutic approach in photoreceptor-based blindness.

GROUP LEADER:
Botond Roska

Near infrared tunable sensor:
Gold nanorod is bound to a TRP channel in the membrane via a nanorod-attached antibody

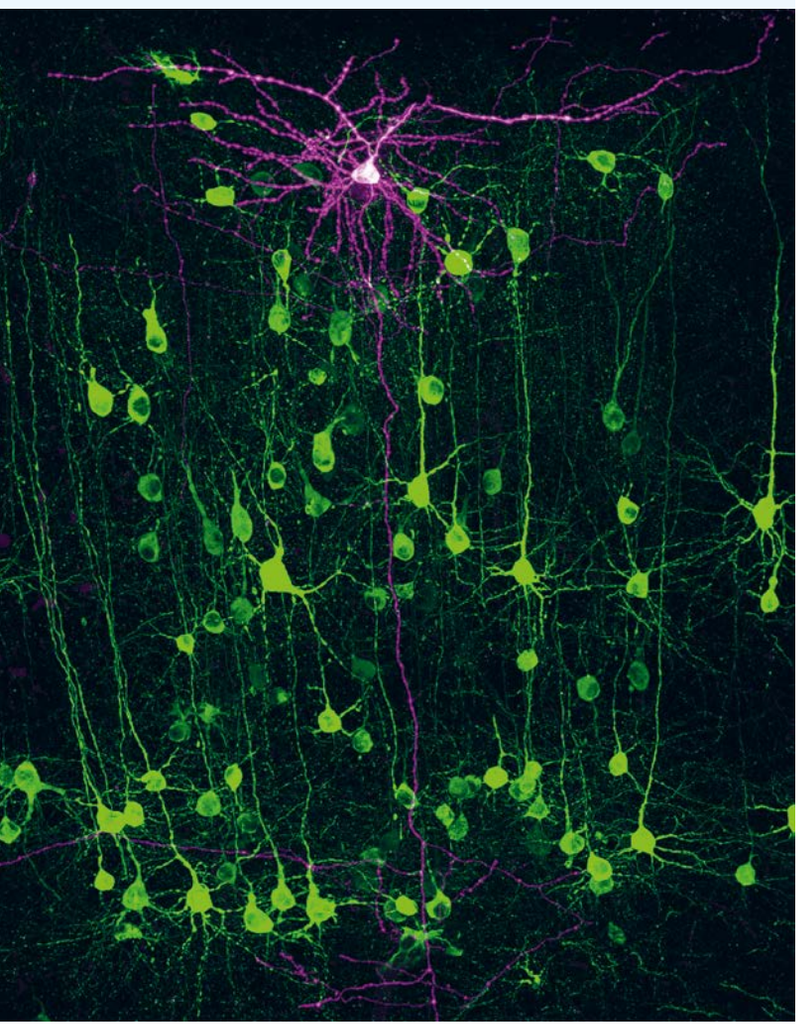


CENTRAL VISUAL CIRCUITS GROUP

GROUP LEADER:
Botond Roska

While the retina is the area of the brain where most visual diseases originate and therapies for blindness are currently focused on the retina, visual processing occurs across many brain areas, including the thalamus and the cortex.

A neuronal circuit in the mouse visual cortex highlighted using single cell initiated monosynaptic rabies tracing



Understanding visual processing in these higher brain areas is crucial for designing rehabilitation strategies following retinal vision restoration and for designing central vision restoration strategies for conditions in which the optic nerve is damaged. In the retina and early stations of the visual pathway, visual information is encoded in retinotopic coordinates. In order for visual perception to guide behavior, this has to be transformed into a representation of visual space that remains stable independent of eye, head, and body position; a representation of the visual world in "real-world", or spatiotopic, coordinates.

A key goal of our group is to understand the circuit mechanism of how retinotopic information is transformed into a spatiotopic representation.

THEORETICAL & COMPUTATIONAL NEUROSCIENCE GROUP

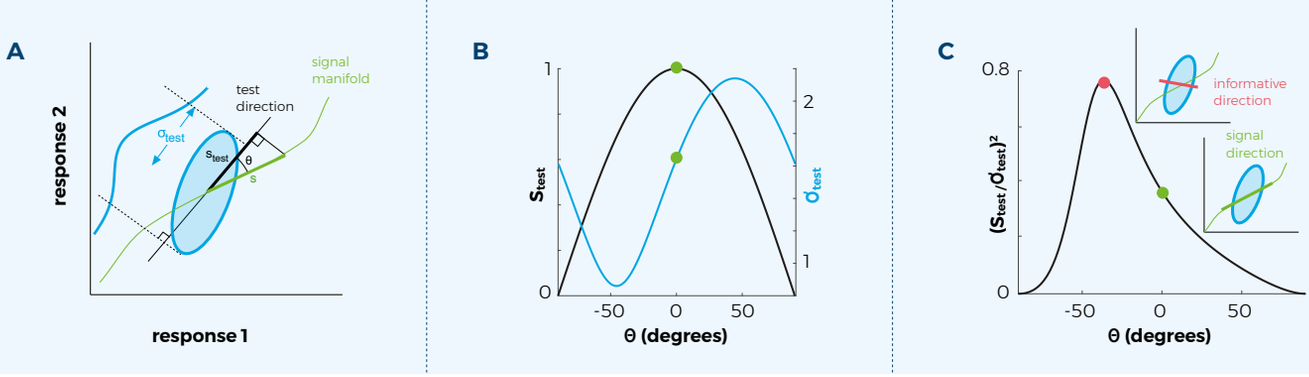
The visual world is represented by, and indeed accessible to us only through the activity of our nerve cells.

GROUP LEADER:
Rava Azeredo da Silveira

But this activity is unreliable: it is subjected to neural noise which, in the absence of adequate strategies employed by the brain, threatens to impair the representation of information. Over the past 20 years, a rich vein of literature has emerged on this issue.

The Silveira lab has provided a new, general, geometric understanding of the way in which different aspects of the activity in populations of neurons can conspire to preserve visual information in the face of neural noise.

The visual world is exceedingly rich: an enormous amount of information is absorbed by our eyes at any instant, and unfolds over time. The brain compresses this information in such a way as to extract the main features useful to behavior. In particular, we ceaselessly plan movements and make decisions on the basis of compressed, "internal models" derived from our visual input. The Silveira lab is studying the nature of this process of compression and of our internal models. With a combination of behavioral experiments, data analysis, and modeling, it has identified specific mechanisms with which internal models, that enable predictive behavior, emerge from the visual input. ●



Signal and noise interact in the representation of visual stimuli by neurons

A *A two-neuron illustration: the thin green line illustrates how the signal in the neural representation changes as the stimulus is varied; the blue ellipse illustrates the neural noise. Along any direction in the space of neural activity ("test direction", thin black line), the projection (thick black line) of the signal (thick green line) and the projection of the noise (blue curve) yield a value of the signal-to-noise ratio along that direction.*

B *The signal (black curve) and the noise (blue curve) vary differently as a function of the test direction; the green circles occur when the test direction coincides with the signal direction.*

C *The signal-to-noise ratio (black curve) varies non-trivially with the test direction. The insets show the signal direction (green) and the optimal direction (red): the direction that maximizes the signal-to-noise ratio depends on both structures of signal and noise.*


Canon

Mapping progressive vision loss in Stargardt disease

PLATFORM LEADER:
Hendrik Scholl

VISUAL NEURO-PHYSIOLOGY PLATFORM

The international multi-center Progression of Atrophy Secondary to Stargardt Disease (ProgStar) Study is a collaboration of nine centers in the US and Europe to characterize the natural history of Stargardt disease.

We are developing outcome measures and clinical endpoints for interventional trials for Stargardt disease that are acceptable by regulatory agencies. The main technology to map light sensitivity of the central retina over time is microperimetry, which allows the retina to be continuously imaged during examination while compensating for eye movements during visual field testing with an eye tracker. We could show that the mean sensitivity and the retinal locations with complete loss of light sensitivity increase significantly within only 12 months. Location specific visual field analysis showed that this effect was largest in areas near but outside the foveal center and around the area of severe visual loss ("scotoma edge").

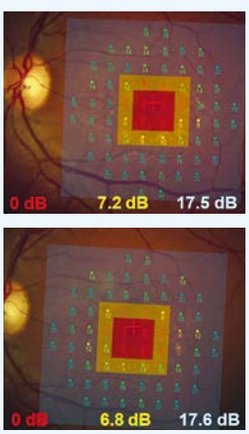
We have started to implement the so-called "Hill of Vision" analysis (VFMA), a topographic display of light sensitivity, which can be generated by interpolating between data points of any visual field-testing grid. This method allows the visual function to be expressed as a volume and the sensitivity to be condensed in one variable that the US Food and Drug Administration (FDA) has recommended as an approvable endpoint for clinical trials. We applied the technology to the ProgStar dataset and could show significant visual loss in Stargardt disease.

In 2021, we will apply this new technique for a novel detailed structure-function correlation analysis.

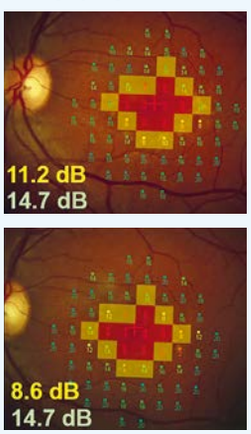
Microperimetry allows the light sensitivity of the central retina to be mapped. Applying this method to a prospective clinical dataset derived from patients suffering from Stargardt disease showed that retinal locations with complete loss of light sensitivity increase significantly within only 12 months. The effect was largest in areas near but outside the foveal center in a location-specific visual field analysis and around the area of severe visual loss ("scotoma edge"). Furthermore, "Hill of Vision" analysis (VFMA) revealed significant visual loss in Stargardt disease over time.

MICROPERIMETRY:

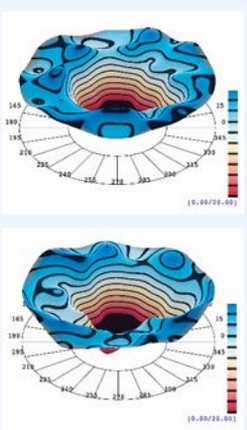
1. Location-specific visual field analysis



2. Scotoma edge progression



3. Hill of Vision analysis (VFMA)



← **Baseline**

← **Month 12**

OPHTHALMIC GENETICS GROUP

GROUP LEADER:
Carlo Rivolta

Our Ophthalmic Genetics group is involved in the study of the molecular bases of ocular diseases, and in particular of hereditary retinal dystrophies, which are invariantly caused by DNA mutations.

In 2020, we characterized numerous genes and mutations associated with hereditary vision impairment. This research has taken advantage not only of genetic expertise but also of computer-driven analysis of large sets of genomic information from hundreds of patients.

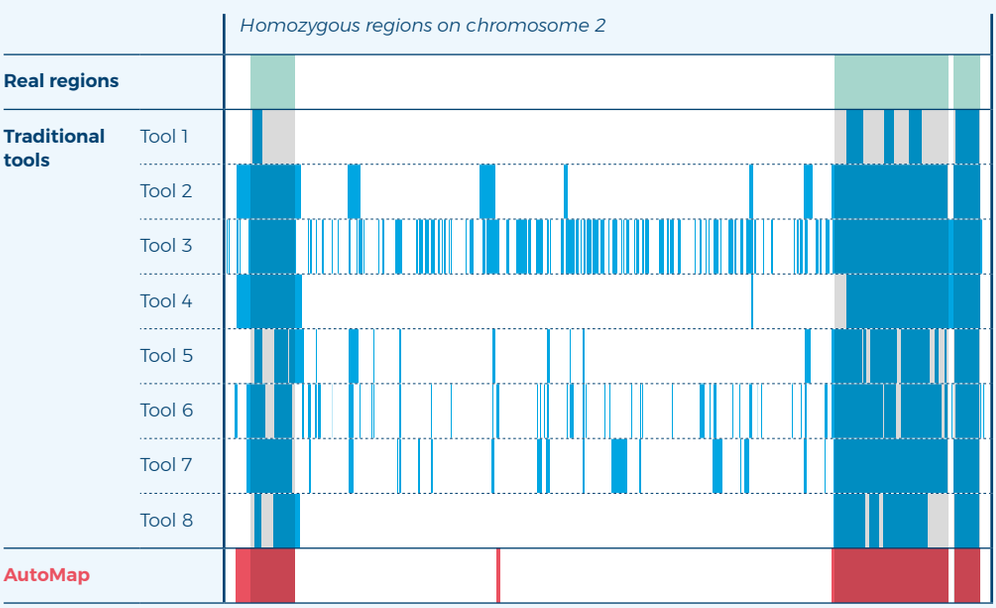
In particular, we have developed a new, powerful software, AutoMap, that facilitates the detection of mutations in patients with hereditary blindness as well as other inherited conditions. Information about the new AutoMap tool was published in *Nature Communication*.

This tool is now freely accessible and is both web-based and downloadable.

In more technical terms, AutoMap allows for enhanced homozygosity mapping, an essential procedure for identifying mutations in patients with a recessive disease (i.e. having healthy parents), especially in consanguineous families or in homogeneous populations.

Our research will be useful to patients all over the world and will contribute to the advancement of our understanding of hereditary visual loss. ●

Autozygous regions of the human genome are likely to harbor mutations responsible for recessive genetic diseases, including the majority of hereditary retinal dystrophies. In this image, real autozygous regions from a patient's genome are depicted in green, whereas blue bands represent the output of various algorithms aiming at identifying them. Compared to eight other tools, AutoMap displays the best performance in detecting such regions.



GENETIC EPIDEMIOLOGY OF OPHTHALMIC DISEASES GROUP

This research unit is a collaborative effort between IOB, University of Basel, Erasmus Medical Center and Radboudumc in the Netherlands. The research focuses on common complex eye disorders and uses Big Data from thousands of people.

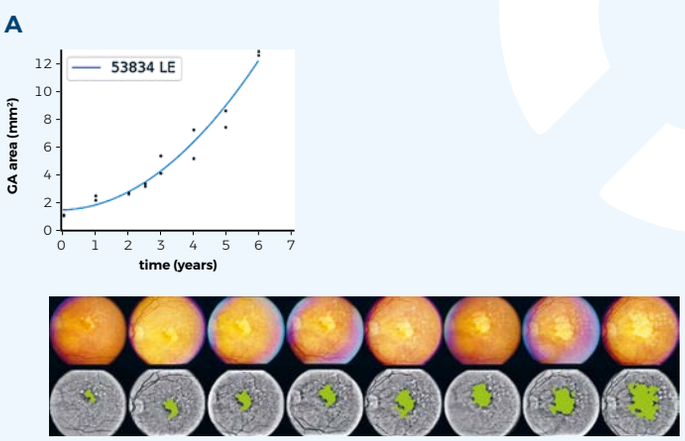
Based on our abundant data from many epidemiologic studies, we can figure out the risk profile for development of common eye diseases and progression rate. For age-related macular degeneration, we have defined the rate of progression of dry AMD as well as the time point when blindness occurs. We were able to predict the course of vision after the first diagnosis (Figures A–C).

In our studies on glaucoma, the comparison of data from African and European patients revealed an earlier disease onset in the African population, which is associated with higher intra-ocular pressures, faster progression, and significantly higher blindness rates.

For myopia, we found that not only high myopia may lead to severe ocular complications, but also that mild myopic refractive errors already increase the risk of retinal detachment, glaucoma, and myopic macular degeneration. In line with the growing myopia prevalence, ocular surgeons reported that retinal detachments had risen in frequency by 44% in the years 2009–2016.

The public needs to be aware that with the rising number of patients with these disorders, blindness will become a more common fate. ●

GROUP LEADER:
Caroline Klaver



Progression and burden of dry AMD (geographic atrophy)

A *Example of increase of the atrophic AMD lesion over 7 years.*

B *Most lesions increase exponentially up to 12 mm², and slow down thereafter.*

C *The average life expectancy after first diagnosis is 5.6 years, but this varies considerably among patients.*

OPHTHALMIC TRANSLATIONAL RESEARCH GROUP

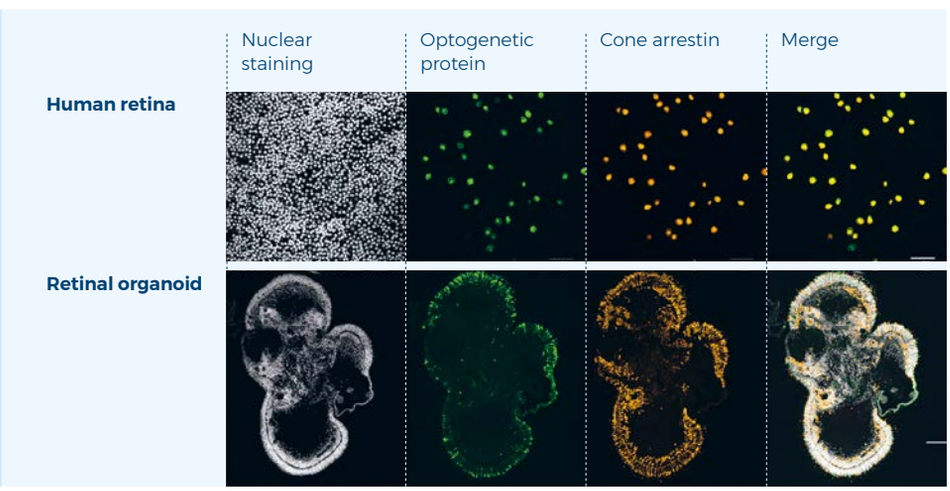
The Ophthalmic Translational Research Group is located at the interface of IOB's Molecular and Clinical Research Center. Our team is working on developing and bringing novel classes of medicines to the clinic.

Currently, our group is running three main preclinical programs: (1) cone-based optogenetic vision restoration, (2) adenine base editing for Stargardt disease to correct the most common mutation, and (3) precision gene correction for Usher syndrome type 2 using prime editing.

In 2020, our group grew significantly and currently has 14 members. One major scientific achievement is the development of an initial lead candidate gene therapy vector that expresses an optogenetic protein across all model systems (Fig.). To translate this strategy to the clinic we are already running a natural history and retinal imaging study on low vision patients. This clinical study will pave the way towards the first-in-human clinical trial aiming to restore vision in the blind. Furthermore, in 2020 our group officially established a research collaboration with a Cambridge MA-based company, Beam Therapeutics Inc., to bring our Stargardt disease base-editing program to patients.

We created mutation-carrying retinal organoids which are being used to model Stargardt disease. We are using dual adeno-associated virus (AAV) vectors to bring in the base editor machinery to photoreceptors and retinal pigment epithelial cells. Base correction is expected to slow down or stop the degeneration in patients suffering from this devastating disease.

GROUP LEADER:
Bence György



Targeting human cone photoreceptors in retinal explants (collaboration with Arnold Szabo, Semmelweis University, Budapest) and human retinal organoids with a therapeutic optogenetic construct (green).

Cells are labeled with nuclear staining (gray) and cones are labeled with cone arrestin (yellow).

Emmetropic but not myopic human eyes distinguish positive defocus from calculated blur

MYOPIA RESEARCH GROUP

GROUP LEADER:
Frank Schaeffel

It is largely unknown which visual cues stimulate juvenile eyes to grow longer than needed.

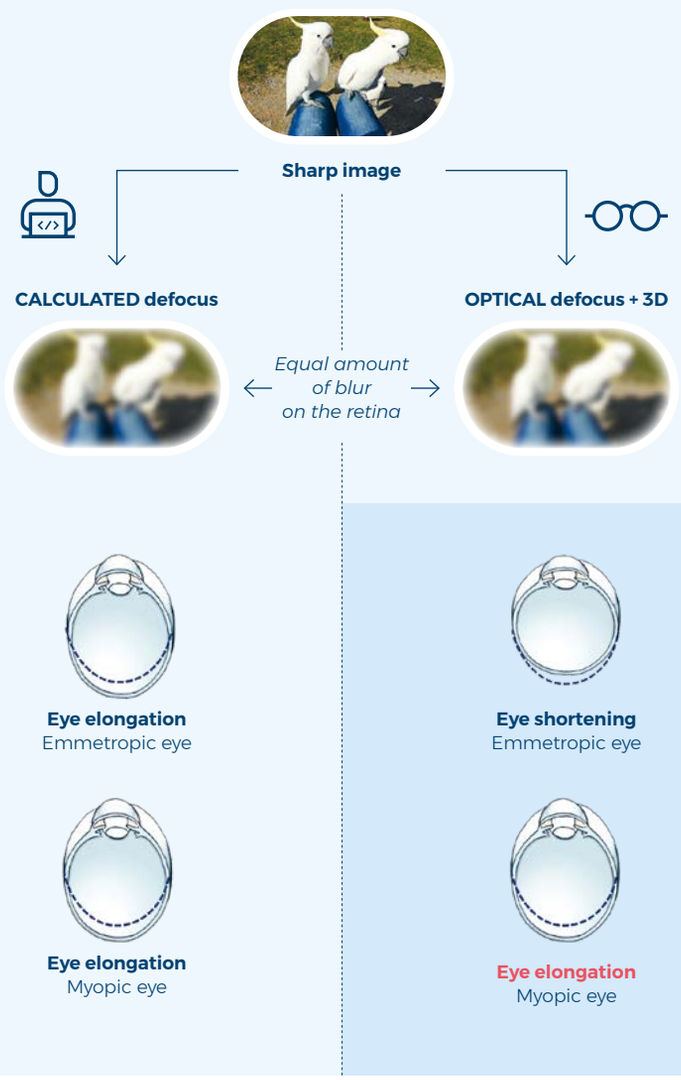
Previous studies demonstrated that the retina is able to distinguish positive defocus from negative defocus by driving bidirectional changes in the eye length. Defocus of the retinal image imposed by a positive lens placed in front of the eye causes its shortening (hyperopia development), while a negative lens causes eye elongation (myopia development). Moreover, it has been shown that eye elongation can also be caused by exposure to a blurred image. Together with Barbara Swiatczak, we studied the effect of the positive optical defocus and calculated defocus on changes in axial length of the eye in young emmetropic and myopic subjects.

Strikingly, eyes of normal-sighted people became shorter with the +3D lenses but longer with calculated blur. The most striking result, however, was that the eyes of myopic people became longer with either stimulus. Apparently, the retina had lost the ability to inhibit eye growth, even though the myopic subjects had normal vision. The question is now: what has changed in the myopic retina? Can this function be recovered or replaced?

Our work suggests that the retina in a myopic eye has reduced ability to detect positive defocus and inhibit eye growth. ●

It is a key question why the eye of myopic people grows longer than necessary – has the retina lost the capability to inhibit its growth?

To find this out, young human subjects watched a movie at 2 m distance with normal vision, or with a +3 diopter lens in front of both eyes, or the movie was "low pass filtered", causing "calculated blur". After 30 minutes, miniature changes in eye length were determined with "low coherence interferometry" (the Lenstar LS 900, Haag-Streit).



OPHTHALMIC IMAGING & OCT GROUP

Three-dimensional (3D) virtual reality (VR) extends the realm of 2D image visualization and enables an immersive VR experience with unimpeded spatial interaction by the user.

In close collaboration with Prof. Philippe Cattin, we transferred volumetric CT data and rendered them into a VR environment. Subsequently, seven graders performed repeated and blinded diameter measurements. The intergrader variability of the measurements in VR was much lower compared to measurements in the physical world, and measurements were reasonably consistent with their corresponding elements in the real context. This study attests the ability of VR to provide similar quantitative data alongside the added benefit of VR interfaces.

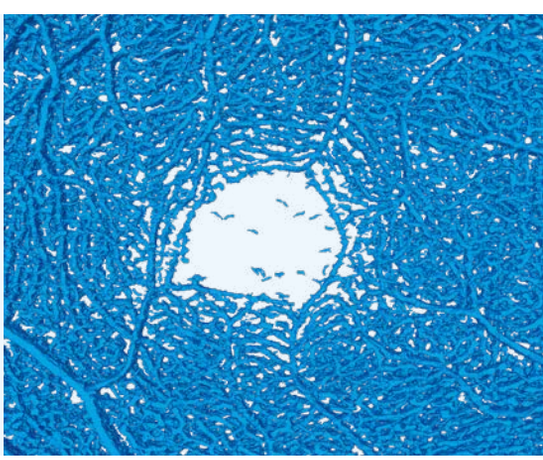
The Imaging lab was also successful in terms of OCT development. An OCT machine was equipped with two different scanning laser colors and allowed to provide evidence for the feasibility and safety of a coaxial dual-wavelength OCT imaging method under real-life conditions. The novel Hydra-OCT imaging device may offer the possibility of gaining additional insights into the pathology of retinal and choroidal diseases.

In so-called central serous chorioretinopathy (CSR), a common retinal disease with accumulation of pathological fluid beneath the retina, a specially developed 3D imaging technique was successfully applied. IOB, together with its collaboration partner University of Freiburg (Germany), was the first institute worldwide to characterize neovascularizations in CSR, which do not originate from the choroid, but directly from the retina.

GROUP LEADER:
Peter Maloca

Noncontact three-dimensional segmentation of pathologic vessels of the retina. A vascular convolute (white arrow) is connected to the retinal circulation by a vascular cord (black arrow).

Patient-friendly and gentle three-dimensional visualization of healthy macular vessels. As the site of sharpest vision, the macula shows a central vascular gap to allow light to reach the photoreceptors undisturbed.



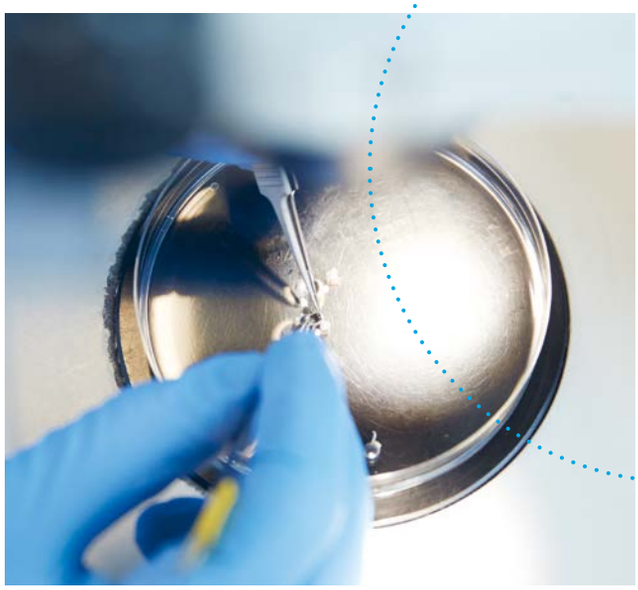
The first and only gene therapy center in Switzerland

PLATFORM LEADER:
Christian Prünte

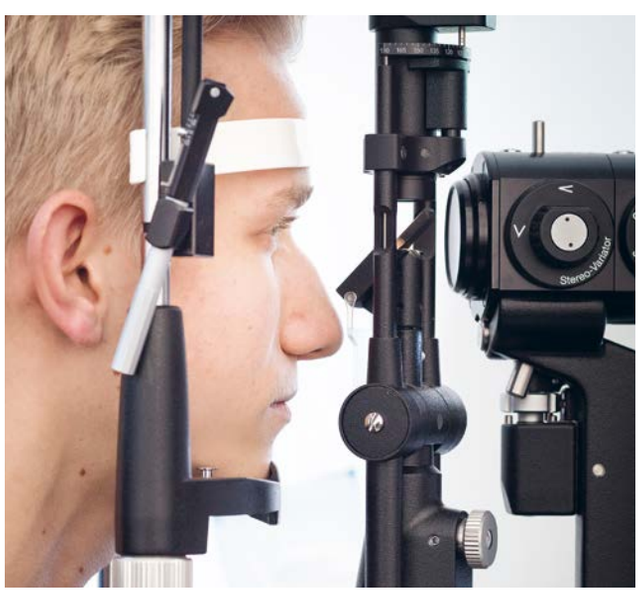
CLINICAL TRIAL CENTER PLATFORM

The Clinical Trial Center Platform is organized as a service center to support all clinical research studies performed at IOB and the University Eye Clinic Basel.

Important activities in 2020 included the standardization and certification of trial processes as well as setting up a quality control system. We continue to be a member of the European Vision Institute Clinical Research Network (EVICR.net), a network of European Ophthalmological Clinical Research Sites, dedicated to performing multinational clinical research in ophthalmology with the highest standards of quality. In 2020, we joined the Foundation Fighting Blindness (FFB) Consortium, in which investigators from currently 40 clinical centers worldwide collaborate on ideas for hypotheses, study designs, and publications. Emphasis is on long-term data about disease onset and progression and the identification of sensitive structural and functional outcome measures for future clinical trials.

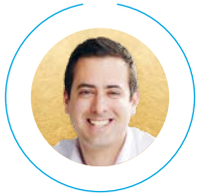


Currently, the team consists of three trial coordinators and two medical physicians, who are supervising and conducting ten clinical trials including randomized international multicenter studies and three investigator-initiated trials (IITs) that were planned and initiated at IOB in collaboration with the Eye Clinic. Another ten studies, including two IITs, are in preparation and will be launched in 2021. In most of these trials, members of IOB and the Eye Clinic function as principal investigator.



A highlight of 2020 was the certification of the Eye Clinic and the Trial Center as the first and only gene therapy center in Switzerland to perform Luxturna© gene therapy for patients with severe retinal dystrophies due to mutations in the RPE65 gene. ●

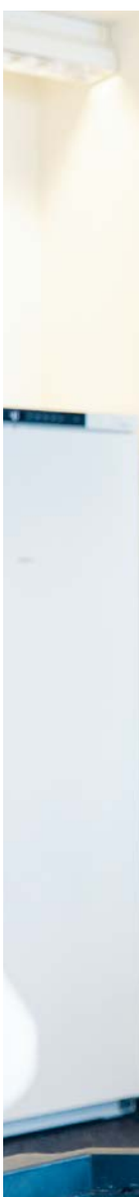
AWARDS 2020

Felix Franke		**SNSF Eccellenza Professorial Fellowship**	*Swiss National Science Foundation (SNSF)*
Bence György		**Swiss RetinAward** 2020	*Swiss VitreoRetinal Group*
Josephine Jüttner		2020 **PRO RETINA Germany & Retina Suisse Research Award** Category “Basic Research”	*PRO RETINA Deutschland and Retina Suisse*
Andreas Keller		**SNSF Eccellenza Professorial Fellowship**	*Swiss National Science Foundation (SNSF)*
Dasha Nelidova		**Research Prize in Molecular Medicine** 2020	*Science and SciLifeLab*
		Ophthalmology Star Award 2020	*VSY Biotechnology*
		2020 **PRO RETINA Germany & Retina Suisse Research Award** Category “Basic Research”	*PRO RETINA Deutschland and Retina Suisse*
		Swiss Ophtha Research Award 2020	*Swiss Ophthalmology Society*
Botond Roska		**Körber European Science Prize** 2020	*Körber-Stiftung*
		Member of Academia Europaea	*Academia Europaea*
		Sanford and Susan Greenberg End Blindness Visionary Prize 2020	*End Blindness by 20/20*
Hendrik Scholl		**Paul Henkind Memorial Award and Lecture for outstanding retinal research**	*American Macula Society*

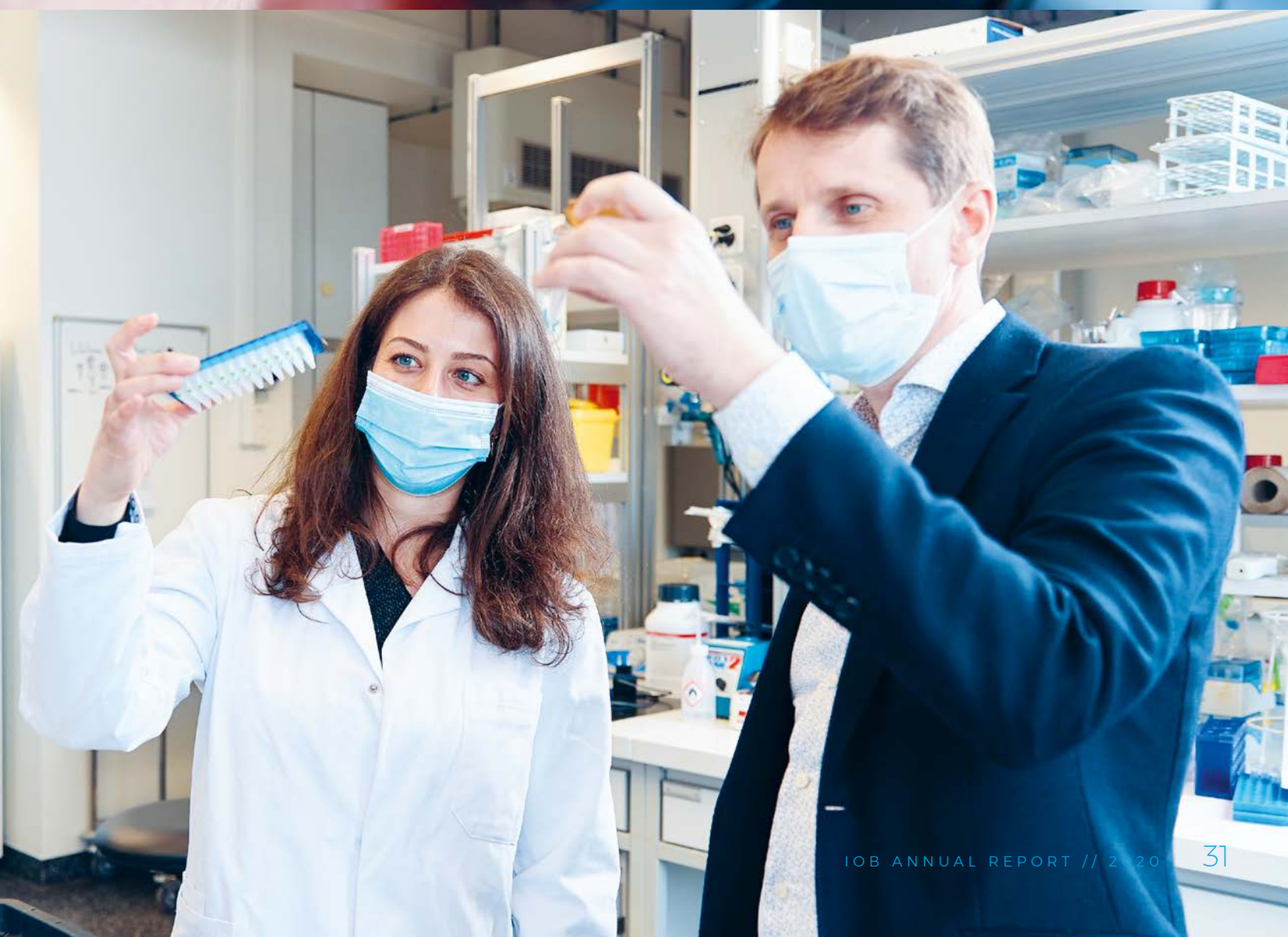
KEY PUBLICATIONS IN 2020

Title	*Authors*	*Journal/Book*
Cell types of the human retina and its organoids at single-cell resolution	*Cowan CS, Renner M, De Gennaro M, Gross-Scherf B, Goldblum D, Hou Y, Munz M, Rodrigues TM, Krol J, Szikra T, Cuttat R, Waldt A, Papasaikas P, Diggelmann R, Patino-Alvarez CP, Galliker P, Spirig SE, Pavlinic D, Gerber-Hollbach N, Schuierer S, Srdanovic A, Balogh M, Panero R, Kusnyerik A, Szabo A, Stadler MB, Orgül S, Picelli S, Hasler PW, Hierlemann A, Scholl HPN, Roma G, Nigsch F, Roska B.*	*Cell*
Restoring light sensitivity using tunable near-infrared sensors	*Nelidova D, Morikawa RK, Cowan CS, Raics Z, Goldblum D, Scholl HPN, Szikra T, Szabo A, Hillier D, Roska B.*	*Science*
Worldwide carrier frequency and genetic prevalence of autosomal recessive inherited retinal diseases	*Hanany M, Rivolta C, Sharon D.*	*Proc Natl Acad Sci U S A*
Validation of virtual reality orbitometry bridges digital and physical worlds	*Maloca PM, Faludi B, Zelechowski M, Jud C, Vollmar T, Hug S, Müller PL, de Carvalho ER, Zarranz-Ventura J, Reich M, Lange C, Egan C, Tufail A, Hasler PW, Scholl HPN, Cattin PC.*	*Sci Rep*
Longitudinal microperimetric changes of macular sensitivity in stargardt disease after 12 months: ProgStar Report no. 13	*Schönbach EM, Strauss RW, Muñoz B, Wolfson Y, Ibrahim MA, Birch DG, Zrenner E, Sunness JS, Ip MS, Sadda SR, West SK, Scholl HPN; ProgStar Study Group.*	*JAMA Ophthalmol*
Resolving neurodevelopmental and vision disorders using organoid single-cell multi-omics	*Brancati G, Treutlein B, Camp JG.*	*Neuron*
Genomic and transcriptomic landscape of conjunctival melanoma	*Cisarova K, Folcher M, El Zaoui I, Pescini-Gobert R, Peter VG, Royer-Bertrand B, Zografos L, Schalenbourg A, Nicolas M, Rimoldi D, Leyvraz S, Riggi N, Moulin AP, Rivolta C.*	*PLoS Genet*
Whole exome sequencing and homozygosity mapping reveals genetic defects in consanguineous Iranian families with inherited retinal dystrophies	*Salmaninejad A, Bedoni N, Ravesh Z, Quinodoz M, Shoeibi N, Mojarrad M, Pasdar A, Rivolta C.*	*Sci Rep*
A 3D model to evaluate retinal nerve fiber layer thickness deviations caused by the displacement of optical coherence tomography circular scans in cynomolgus monkeys (macaca fascicularis)	*Niklaus S, Hasler PW, Bryant T, Desgent S, Vezina M, Schnitzer TK, Maloca PM, Denk N.*	*PLoS One*
New technologies for outcome measures in retinal disease: review from the European Vision Institute Special Interest Focus Group	*Della Volpe-Waizel M, Traber GL, Maloca P, Zinkernagel M, Schmidt-Erfurth U, Rubin G, Roska B, Otto T, Weleber RG, Scholl HPN.*	*Ophthalmic Res*

View all our papers listed in PubMed:




OLYMPUS



SCIENTIFIC ADVISORY BOARD

José-Alain Sahel, *M.D.*
Chairman of the IOB Scientific Advisory Board –
Distinguished Professor and Chairman,
Department of Ophthalmology,
University of Pittsburgh School of Medicine –
Professor of Ophthalmology, Sorbonne Université

» Within a few years IOB has arisen as a leading international center. The joint investment from industry and academia in the best scientific and clinical leaders worldwide is paying off at an unprecedented speed as demonstrated by the recruitment of outstanding team leaders, the quantity and quality of the publications and awards, the launch of innovative translational programs. A lot to be proud of and to expect in the coming years. «

Alexander Borst, *Ph.D.*
Director Max Planck Institute of Neurobiology,
Martinsried

» The newly founded Institute of Molecular and Clinical Ophthalmology Basel (IOB) represents one of the rare places in the world where basic research meets clinical treatment to understand the human eye and treat its diseases. Given the unique expertise of the two directors, Dr. Botond Roska and Dr. Hendrik Scholl, and their unlimited dedication to research, IOB is bound to succeed and to provide breakthroughs in the years to come. «

Constance Cepko, *Ph.D.*
Professor of Genetics and Ophthalmology, Harvard Medical School, Howard Hughes Medical Institute

» IOB brings together top scientists and clinicians focussed on both understanding and curing diseases that can lead to blindness. The talent that they have assembled, the approaches that they are developing, and their intense focus will make this one of, if not the, premier Institute in the world working on these problems. I am thrilled to be able to watch first hand how they are launching this Institute and realizing their plans. «

Cynthia Grosskreutz, *M.D., Ph.D.*
Global Head of Ophthalmology,
Novartis Institutes for BioMedical Research

» I continue to be impressed with the scientific progress being made at IOB linking laboratory observations and clinical assessments to human disease. This, in spite of the challenges introduced by the COVID-19 pandemic. «

Paul Sieving, *M.D., Ph.D.*
Professor, Department of Ophthalmology, School of Medicine – Director, Center for Ocular Regenerative Therapy, CORT, University of California Davis

» As the Institute of Molecular and Clinical Ophthalmology Basel nears the three-year anniversary of its founding, I am pleased to see the remarkable scientific progress they are making toward understanding Inherited Retinal Dystrophy (IRD) conditions in the clinic and in the lab. These genetic conditions cause progressive loss of vision that affects millions of individuals worldwide. The Institute's focus on developing therapies for IRD conditions is advancing at a significant pace toward addressing this medical need. «

Eberhart Zrenner, *Prof. Dr. med. Dr. h.c.mult.*
Distinguished Professor of Ophthalmology,
Eberhard Karls University of Tübingen,
Institute for Ophthalmic Research

» The group of eminent scientists and clinicians focussing on new therapeutic approaches to urgent ophthalmological problems within the IOB teams is a key to unprecedented success. «

FINANCIAL STATEMENT FOR 2020

General information

The Institute of Molecular and Clinical Ophthalmology Basel exists as a foundation in accordance with articles 80 et seq. of the Swiss Civil Code. The purpose of the foundation is to conduct basic and translational research in human health, for example, to improve society's understanding of the function and diseases of the human eye, to counter degeneration, and to treat impaired vision and blindness and hereby to foster Basel as a center of life science research. The Board of Trustees can expand the research activities to other fields of research.

Organization and governance

Board of Trustees

- Hans Jörg Reinhardt – *President of the Board of Trustees*
- Werner Friedrich Kübler – *Member of the Board of Trustees*
- Andrea Schenker-Wicki – *Member of the Board of Trustees*

The Board of Trustees works on a voluntary basis.

Supervisory Authority

BVG- and Stiftungsaufsicht beider Basel (BSABB)

Auditors

PricewaterhouseCoopers AG, Basel

Basis of preparation and accounting policies

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).

Currency

The IOB presentation currency is CHF (Swiss francs).

Foreign currency positions

The items in foreign currencies were converted into CHF at the following exchange rates:

31.12.2020	*Foreign currency*	*Balance*
	EUR	1.0840

Trade account receivables

Trade account receivables and other short-term receivables are initially recognized at their invoiced amounts including any related VAT. Provisions for doubtful trade receivables are established once there is an indication that a loss will be incurred.

Non-current assets and leasing

Property, plant and equipment are carried at cost less accumulated depreciation. Assets financed by long-term leasing contracts are not recognized in the balance sheet.

The following useful life spans and depreciation methods are used to calculate the depreciation amounts:

Non-current assets	*Durability*	*Method*
Research equipment	8 Years	25% degressively
Software	8 Years	25% degressively
Buildings	6 Years	33.3% degressively

Notes to the financial statements

1 Unrestricted and restricted funds

In 2020, the income from fund raising amounted to CHF 5 563 062, thereof CHF 2 411 534 have already been used for projects. This results in net funds available as per 31 December 2020 in the amount of CHF 3 151 528, whereof CHF 1 302 563 are restricted (unrestricted: CHF 1 848 965).

	31.12.2020	***31.12.2019***
Net amount of funds received from	CHF	CHF
Private entity	1 398 066	234 213
Legal entities	450 899	1 148 015
Total unrestricted funds	**1 848 965**	**1 382 228**
Private entity	212 651	
Legal entities	1 089 911	
Total restricted funds	**1 302 563**	
Total funds	**3 151 528**	**1 382 228**

2 Income from contributions

Income from contributions	**14 110 000**	**11 570 000**
Novartis	7 050 000	5 805 000
Canton of Basel-Stadt	3 530 000	2 865 000
USB	2 120 000	1 740 000
University of Basel	1 410 000	1 160 000

3 Research expenses

Research expenses	**4 630 797**	**3 734 787**
Consumables	2 392 681	1 685 800
Non-capital equipment	944 773	798 022
External services	1 293 343	1 250 964

4 Administrative expenses

Administrative expenses	**2 341 222**	**2 293 403**
Planning expenses for modular building IOB		249 925
Legal and consulting expenses	1 016 151	1 043 968
Transport and travel expenses	54 478	148 685
Board and lodging expenses	36 854	142 646
IT expenses	1 024 576	488 624
Other expenses	209 163	219 555

Balance sheet

Assets	*Notes*	***31.12.2020*** CHF	*31.12.2019* CHF
Cash and cash equivalents		1 671 307	997 595
Accounts receivable		726 051	588 018
from third parties		518 527	371 822
from affiliated parties		207 524	216 196
Other short-term receivables		39 403	57 567
from third parties		39 403	57 567
Prepaid expenses		634 239	171 955
Current assets		**3 071 000**	**1 815 135**
Property, plant and equipment		7 922 597	4 885 669
Non-current assets		**7 922 597**	**4 885 669**
Total assets		**10 993 597**	**6 700 803**
Liabilities and equity			
Accounts payable		1 411 985	1 710 847
from third parties		883 218	1 233 621
from affiliated parties		528 767	477 226
Accrued expense and deferred income		860 565	244 017
Restricted funds		1 302 563	
Short-term liabilities		**3 575 112**	**1 954 864**
Long-term interest-bearing liabilities		6 500 000	3 000 000
from third parties		3 500 000	1 000 000
from affiliated parties		3 000 000	2 000 000
Long-term liabilities		**6 500 000**	**3 000 000**
Total liabilities		**10 075 112**	**4 954 864**
Foundation capital		500 000	500 000
Profit brought forward		-136 288	854 945
Unrestricted funds	1	1 848 965	1 382 228
Net result of the year		-1 294 192	-991 233
Total equity		**918 485**	**1 745 940**
Total liabilities and equity		**10 993 597**	**6 700 803**

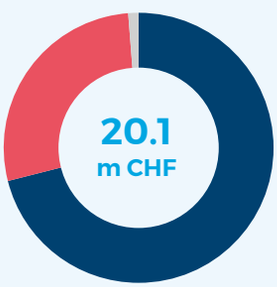
Income statement

	Notes	01.01.2020 – 31.12.2020	01.01.2019 – 31.12.2019
		CHF	CHF
Income from contributions	2	-14 258 934	-11 590 472
Income from fundraising		-5 563 062	-2 564 121
Other income		-248 844	-183 276
Total operating income		**-20 070 841**	**-14 337 868**
Personnel expenses		9 227 121	5 807 795
Research expenses	3	4 630 797	3 734 787
Maintenance, repair, replacement		241 781	50 241
Rent and utility expenses		1 926 822	1 497 276
Energy, gas, water, disposal		153 938	18 614
Administrative expenses	4	2 341 222	2 293 403
Other expenses		62 133	357 981
Depreciation on property, plant and equipment		881 403	271 004
Total operating expenses		**19 465 217**	**14 031 099**
Operating result		**-605 624**	**-306 768**
Financial income		-60 537	-40 512
Financial expenses		134 589	67 588
Ordinary result for the period		**-531 571**	**-279 692**
Extraordinary, non-recurring or prior period income			
Extraordinary, non-recurring or prior period expenses		56 464	214 441
Net result for the period		**-475 108**	**-65 251**
Net allocation to restricted funds	1	1 302 563	
Net result for the period before net allocation to restricted funds		**827 455**	**-65 251**
Net allocation to unrestricted funds	1	466 737	1 056 484
Net result for the period after net allocation to unrestricted funds		**1 294 192**	**991 233**

Cash flow statement

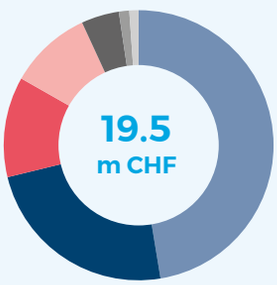
	01.01.2020 – 31.12.2020	01.01.2019 – 31.12.2019
	CHF	CHF
Net result for the period before allocation to unrestricted funds	-827 455	65 251
Depreciation on property, plant and equipment	881 403	271 004
Changes in accounts receivable and other short-term receivables	-119 870	4 614 937
Changes in prepaid expenses	-462 284	-48 679
Changes in accounts payable	-298 862	-4 419 972
Changes in accrued expenses and deferred income	616 548	179 058
Changes in restricted funds	1 302 563	0
Cash flow from operating activities	**1 092 043**	**661 600**
Capital expenditure on property, plant and equipment	-3 918 331	-4 589 342
Cash flow from investing activities	**-3 918 331**	**-4 589 342**
Changes in long-term liabilities	3 500 000	3 000 000
Cash flow from financing activities	**3 500 000**	**3 000 000**
Changes in cash and cash equivalents	**673 712**	**-927 741**
Verification of changes in cash and cash equivalents		
Beginning of period	997 595	1 925 336
End of period	1 671 307	997 595
Changes in cash and cash equivalents	**673 712**	**-927 741**

Funding 2020



- Income from contributions: **71%**
- Income from third parties: **28%**
- Other income: **1%**

Expenses 2020



- Personnel expenses: **47%**
- Research expenses: **24%**
- Administrative expenses: **12%**
- Rent and utility expenses: **10%**
- Depreciation on non-current assets: **5%**
- Maintenance, repair: **1%**
- Other expenses: **1%**

PARTNER INSTITUTIONS

A network around the world

Switzerland	**1**	Alfred Vogt-Foundation for Research in Ophthalmology	*Zurich*	Switzerland
	2	Apellis Switzerland GmbH	*Zug*	Switzerland
	3	Arctos Medical AG	*Bern*	Switzerland
	4	Biozentrum, University of Basel	*Basel*	Switzerland
	5	Brain Mind Institute, Swiss Federal Institute of Technology Lausanne	*Lausanne*	Switzerland
	6	Department of Biomedical Engineering, University of Basel	*Basel*	Switzerland
	7	Department of Biomedicine, University of Basel	*Basel*	Switzerland
	8	Department of Clinical Research, University of Basel	*Basel*	Switzerland
	9	Ecole Polytechnique fédérale de Lausanne	*Lausanne*	Switzerland
	10	F. Hoffmann-La Roche Ltd, Pharmaceutical Research and Early Development (pRED)	*Basel*	Switzerland
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	17	National Centre of Competence in Research (NCCR) of Molecular Systems Engineering	*Basel*	Switzerland
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	20	ProgStar study group	*Basel*	Switzerland
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	22	Retina Suisse	*Zurich*	Switzerland
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	26	University of Applied Sciences and Arts Northwestern Switzerland	*Windisch*	Switzerland
	27	University of Basel	*Basel*	Switzerland
Middle East	**28**	Hebrew University of Jerusalem	*Jerusalem*	Israel
Asia	**29**	Nanyang Technological University, Ophthalmology and Biomedical Engineering	*Singapore*	Singapore
	30	Singapore Eye Research Institute	*Singapore*	Singapore
	31	Japan Eye Genetics Consortium	*Tokyo*	Japan

Europe	**32**	Department of Ophthalmology, Kepler University Clinic	*Linz*	Austria
	33	Department of Ophthalmology, Medical University of Graz	*Graz*	Austria
	34	Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA)	*Vienna*	Austria
	35	Medical University of Vienna	*Vienna*	Austria
	36	European Vision Institute	*Brussels*	Belgium
	37	Ecole Normale Supérieure	*Paris*	France
	38	GenSight Biologics	*Paris*	France
	39	Institut de l'Audition, Institut Pasteur	*Paris*	France
	40	Institut de la Vision Paris	*Paris*	France
	41	SILABE	*Strasbourg*	France
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	43	Boehringer Ingelheim	*Ingelheim*	Germany
	44	Forschungsplattform Degenerative Erkrankungen, Deutsches Primatenzentrum	*Göttingen*	Germany
	45	Heidelberg University	*Heidelberg*	Germany
	46	Institute for Ophthalmic Research, University of Tübingen	*Tübingen*	Germany
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	53	PRO RETINA Deutschland e. V.	*Bonn*	Germany
	54	STZ eyetrial, Department für Augenheilkunde, University of Tübingen	*Tübingen*	Germany
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	57	Semmelweis University	*Budapest*	Hungary
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	59	Radboud University Medical Center, Radboud University Nijmegen	*Nijmegen*	Netherlands
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	61	Gyroscope Therapeutics Ltd.	*London*	UK
	62	Imperial College London	*London*	UK
	63	Institute of Ophthalmology, University College London	*London*	UK
	64	King's College London	*London*	UK
	65	Moorfields Eye Hospital	*London*	UK
	66	Novartis Pharma AG (CORE)	*London*	UK
	67	PINNACLE study group	*Southampton*	UK
	68	ReNeuron Group Plc/Ora Inc. and member of the Steering Committee of Novo Nordisk	*Bridgend, Bagsværd*	UK, Denmark
	69	Sainsbury Wellcome Center	*London*	UK
	70	University of Southampton	*Southampton*	UK
	71	Wellcome Trust	*London*	UK
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	73	Allen Institute for Brain Science	*Seattle*	USA
	74	Astellas Pharma Global Development, Inc./ Astellas Institute for Regenerative Medicine	*Deerfield/ Marlborough*	USA
	75	Beam Therapeutics	*Cambridge*	USA
	76	Belite Bio	*San Diego*	USA
	77	Biogen MA Inc	*Cambridge*	USA
	78	Byers Eye Institute, Stanford University	*Palo Alto*	USA
	79	Cole Eye Institute, Cleveland Clinic	*Cleveland*	USA
	80	David Geffen School of Medicine, University of California	*Los Angeles*	USA
	81	Department of Ophthalmology, Case Western Reserve University	*Cleveland*	USA
	82	Doheny Eye Institute, University of California	*Los Angeles*	USA
	83	End Blindness by 20/20	*Washington DC*	USA
	84	Foundation Fighting Blindness	*Columbia*	USA
	85	Foundation Fighting Blindness (FFB) Consortium, coordinated by the Center at Jaeb Center for Health Research (JCHR)	*Tampa*	USA
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	87	Harvard Medical School	*Cambridge*	USA
	88	Inscopix, Inc.	*Palo Alto*	USA
	89	Janssen Research & Development, LLC (Johnson & Johnson)	*Raritan*	USA
	90	Moran Eye Center, University of Utah	*Salt Lake City*	USA
	91	Novartis Institutes for Biomedical Research	*Cambridge, Basel*	USA, Switzerland
	92	Retina Foundation of the Southwest	*Dallas*	USA
	93	ReVision Therapeutics, Inc.	*Ridgewood*	USA
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	95	Stargazer Pharmaceuticals, Inc.	*Boston*	USA
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	97	University Hospitals Clinical Research Center, Cleveland Medical Center	*Cleveland*	USA
	98	University of Houston College of Optometry	*Houston*	USA
	99	University of Michigan	*Michigan*	USA
	100	University of Pittsburgh	*Pittsburgh*	USA
	101	Wilmer Eye Institute, Johns Hopkins University	*Baltimore*	USA

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Researchers and Clinicians united to restore vision.

CONTACT

IOB – Institute of Molecular and
Clinical Ophthalmology Basel
Mittlere Strasse 91
CH-4031 Basel
Switzerland

T +41 61 265 92 14
info@iob.ch
www.iob.ch