FONDATION
VOIR & ENTENDRE

Institut de la Vision

10 YEARS

OF FIGHTING BLINDNESS

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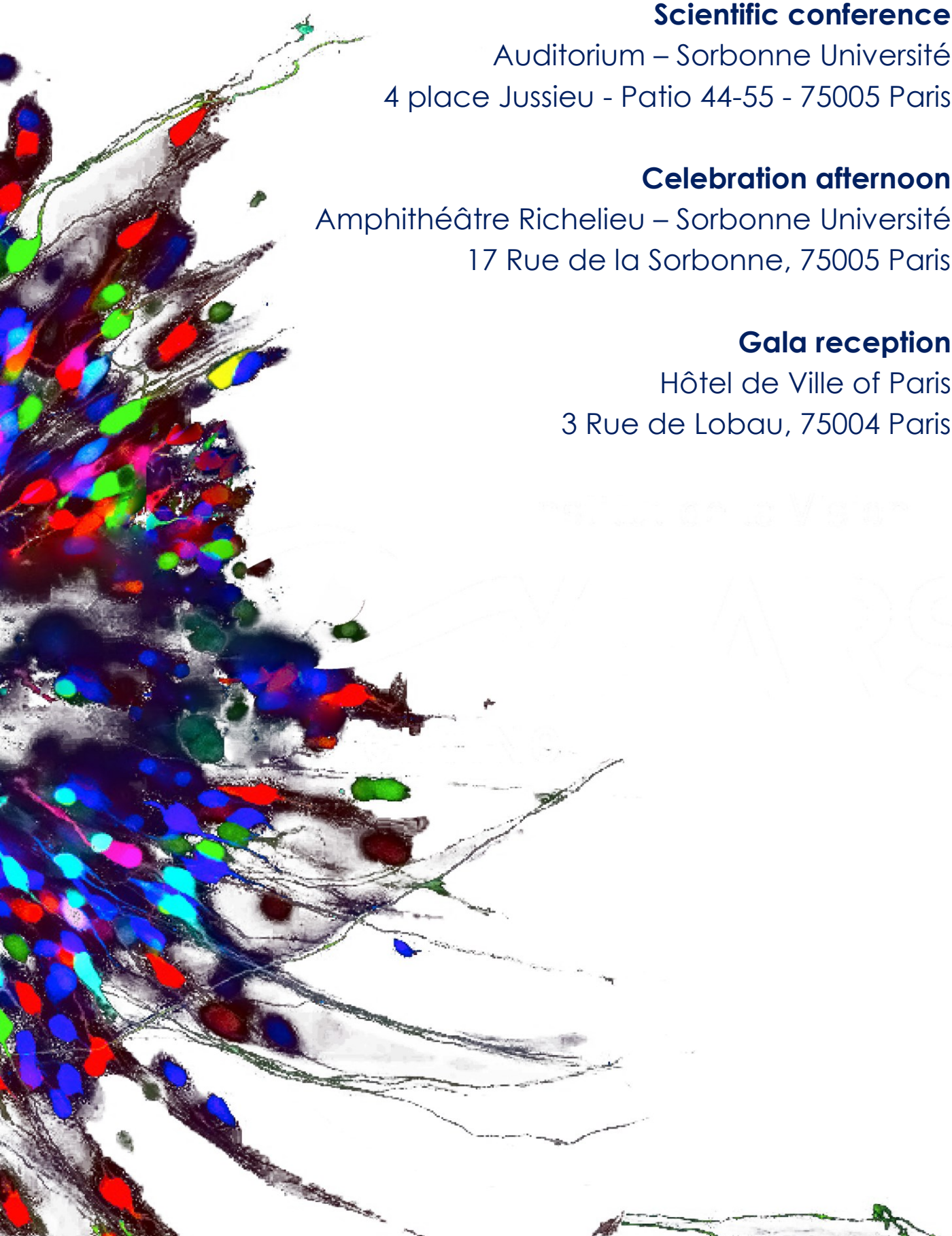
AGENDA

Celebration days 27-28-29 November 2019



Scientific conference
Auditorium – Sorbonne Université
4 place Jussieu - Patio 44-55 - 75005 Paris

Celebration afternoon
Amphithéâtre Richelieu – Sorbonne Université
17 Rue de la Sorbonne, 75005 Paris

Gala reception
Hôtel de Ville of Paris
3 Rue de Lobau, 75004 Paris

Special thanks for the help and support in the organization of this event
to Region Île de France, Sorbonne Université, Ville de Paris

Wednesday 27th November

Auditorium, 4 place Jussieu - Patio 44-55 - 75005 Paris

08:00h - 08:30h	Welcome coffee and conference registration
08:30 – 09:00	**Opening Lecture** "Where do we go from here: One new direction for vision research" by John Dowling *
09:00h – 09:40h	José-Alain Sahel (Director of the Institut de la Vision) Jean-François Segovia (General Director of National Ophthalmology Hospital Centre of 15-20) Martin Hirsch (CEO of AP-HP) Julien Gottsmann (CEO of Fondation Adolphe de Rothschild) Agnès Buzyn (Minister of Solidarity and Health)

"Understanding development and axon guidance I" Chaired by Jeff Gross

09:40h – 09:50h	"Development, evolution and function on commissural systems" by Alain Chedotal
09:50h - 10:00h	"Single cell analysis of neural circuit structure and development, from the retina to the brain" by Jean Livet
10:00h – 10:10h	"Visual system development and function: lessons from zebrafish" by Filippo Del Bene
10:10h - 10:30h	**Lecture** "Regeneration of the retinal pigmented epithelium" by Jeff Gross *
10:30h – 10:45h	Round table chaired by Jeff Gross
10:45h – 11:05h	**Special Lecture** "A new paradigm for biomedical imaging : the Matrix approach" by Mathias Fink
11:05h – 11:40h	Coffee break
11:40h – 12:10h	**Keynote Lecture** "An inclusive world for the visual impairment" by Masayo Takahashi *
12:10h – 12:25h	3 x "MT180" by 3 Young researchers (Dept. Development)
12:25h – 13:45h	Lunch with Posters

"Understanding development and axon guidance II" Chaired by Larry Benowitz

13:45h – 14:05h	**Lecture** "Optic nerve regeneration: Regulation by cell-autonomous and non-autonomous factors" by Larry Benowitz *

* Presentations with abstract

14:05h – 14:15h	"Retinal development and repair: a human pluripotent stem cell perspective" by Olivier Goureau
14:15h – 14:25h	"Retinal axon wiring by subcellular confinement of ubiquitous signals" by Xavier Nicol *
14:25h – 14:40h	Round table chaired by Larry Benowitz
14:40h – 15:00h	**Special Lecture** "3D Engineered photoreceptor/RPE/choroid to model and treat retinal degenerative diseases" by Kapil Bharti *
15:00h – 15:20h	**Special Lecture** "Non viral gene therapy for retinal diseases" by Francine Behar-Cohen

"Visual information processing" Chaired by Eberhart Zrenner

15:20h – 15:40h	**Lecture** "Electrical stimulation of retinal neurons and its clinical application" by Eberhart Zrenner
15:40h – 16:10h	Coffee break
16:10h – 16:20h	"From prostheses to optogenetic therapy : a journey towards visual restoration" by Serge Picaud
16:20h – 16:30h	"Computational neuroscience of sensory systems" by Romain Brette
16:30h – 16:40h	"Imaging of sensory processing and neurovascular coupling" by Serge Charpak
16:40h – 16:50h	"Visual aging and visuo-spatial cognition: clinical phenotyping, behavioral markers and neuroimaging" by Angelo Arleo *
16:50h – 17:00h	"Bidirectional prosthetics: from retina prosthetics and optogenetics to brain decoding and the future of computation" by Ryad Benosman
17:00h – 17:20h	5 x "MT180" by 5 Young researchers (Dept. Visual Information Processing)
17:20h – 17:35h	Round Table chaired by Eberhart Zrenner
17:35h – 17:55h	**Special Lecture** "Visual and visuomotor circuits in a genetically and optically accessible vertebrate" by Herwig Baier *

From 19h00 — A "get together" evening organized by the young researchers, location "LE TRAC" - Everybody is welcome!

"LE TRAC" 72 Avenue de France, 75013

* Presentations with abstract

Thursday 28th November

Auditorium, 4 place Jussieu - Patio 44-55 - 75005 Paris

08:30h – 09:00h **Keynote lecture** "The human retina" by Botond Roska *

"Genetics " Chaired by Botond Roska

09:00h – 09:10h "Identification of gene defects leading to non-progressive and progressive ocular diseases" by Isabelle Audo & Christina Zeitz

09:10h – 09:20h "Metabolic and redox signaling of the nucleoredoxin-like-1 gene for the treatment of rod-cone dystrophies" by Thierry Léveillard

09:20h – 09:40h **Lecture** "Best outcome measures for clinical trials in Stargardt disease: Lessons from the ProgStar study" by Hendrik Scholl *

09:40h – 10:00h **Lecture** "Syndromic Inherited Retinal Dystrophies: how rare is rare ? …" by Hélene Dollfus *

10:00h – 10:20h **Lecture** "Eye-Risk - identify, model and validate AMD risk factors and disease drivers" by Marius Ueffing *

10:20h – 10:35h 4 x "180 MT" by 4 Young researchers (Dept. Genetics & Photonics)

10:35h – 10:50h Round Table chaired by Botond Roska

10:50h - 11:50h Coffee break with Poster Session

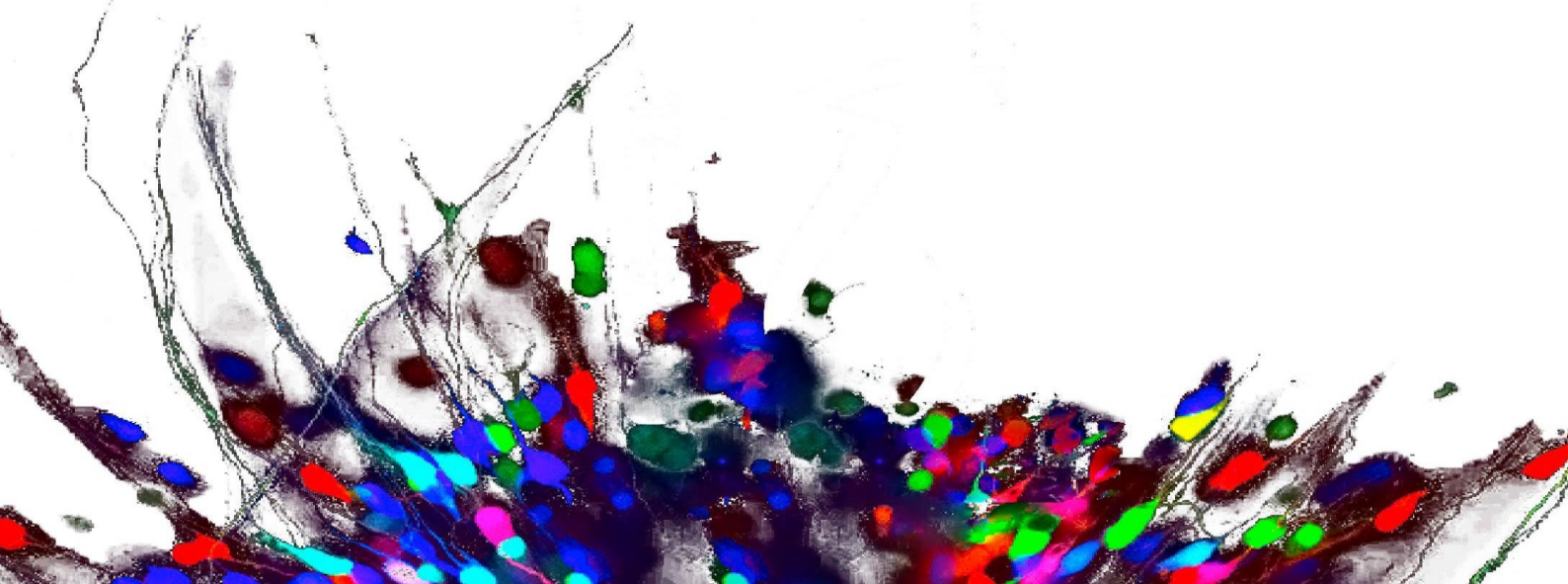
"Exploring by waves and frequencies" Chaired by Mickael Tanter

11:50h – 12:10h **Lecture** "Ultrasound in Neuroscience" by Mickael Tanter

12:10h – 12:20h "Holographic investigation of visual circuits" by Valentina Emiliani

12:20h – 12:30h "3D Microscopy" by Gilles Tessier

12:30h – 12:45h Round Table chaired by Mickael Tanter



Thursday 28th November

Amphithéâtre Richelieu, 17 rue de la Sorbonne 75005 Paris

Celebration Afternoon at the Amphithéâtre Richelieu, Sorbonne Université

Moderation par Jean-François Dhainaut

14:00h – 15:10h	Speeches by Antoine Petit (CEO of National Center of Scientific Research, CNRS) Jean Chambaz (President of Sorbonne University) Claire Giry (Deputy of the CEO of National Institute of Health and Medical Research, INSERM) Thierry Damerval (President & CEO of the French National Research Agency (ANR)) Jean-Louis Missika (Deputy of the Mayor of Paris) Valérie Pécresse (President of the Regional Council of Île-de-France) (all the speeches will be in French with simultaneous translation)
15:10h – 15:40h	"L'Institut de la Vision 10 years later" by José-Alain Sahel (in French and English)
15:40h – 16:30h	Success stories and roundtable moderated by Jean-François Dhainaut: "Ibionext : a model of partnership" by Bernard Gilly Roundtable : Audrey Derveloy (Novartis) / Emmanuel Gutman (StreetLab) / Florence Allouche (SparingVision) / Lloyd Diamond (Pixium Vision) / T.B.D. (Essilor) (in French with simultaneous translation)
16:30h – 16:50h	"The role of foundations" by Benjamin Yerxa (Foundation Fighting Blindness)(in English with simultaneous translation)
16:50h – 17:15h	From the patient's point of view by Gérard Muller, Christina Fasser, (in French with simultaneous translation)

Gala reception at the Hôtel de Ville of Paris

18:30h – 22:00h	Speeches by Marie-Christine Lemardeley (Deputy of the Mayor of Paris), José-Alain Sahel (Director of the Institut de la Vision), Jean-Charles Pomerol (President of the Fondation Voir et Entendre)

Friday 29th November

Auditorium, 4 place Jussieu - Patio 44-55 - 75005 Paris

"Answering needs" Chaired by Don Zack

08:30h – 08:50h	**Lecture** "Human Stem Cell-derived Retinal Cells for Disease Modeling and Drug Discovery" by Don Zack
08:50h – 09:00h	"Ten years of research from the front to the back of the eye, and beyond" by Christophe Baudouin *
09:00h – 09:10h	"Daily phagocytosis of the retinal pigment epithelium: timing is everything!" by Emeline Nandrot
09:10h – 09:20h	"On Phagocytes and Retinal Degeneration" by Florian Sennlaub *
09:20h – 09:40h	**Lecture** "Endophenotype and precision medicine for immune mediated ocular disorders" by Andrew Dick *
09:40h – 09:55h	Round Table chaired by Don Zack

"Gene Therapy" Chaired by John Flannery

09:55h – 10:15h	**Lecture** "Gene delivery to large animal retinas" by Leah Byrne
10:15h – 10:35h	**Lecture** "Retinal Gene Therapy" by Robert Mac Laren
10:35h – 11:05h	Coffee break
11:05h – 11:25h	**Lecture** "Designing mutation-Independent gene therapies" by John Flannery *
11:25h – 11:35h	"Gene therapies and animal models for neurodegenerative diseases" by Deniz Dalkara
11:35h – 11:50h	4 x "MT180" by 4 Young researchers (Dept. Therapeutics)
11:50h – 12:05h	Round Table chaired by John Flannery
12:05h – 12:25h	**Special Lecture** on "The expression of visual disorders in paintings, and their impact on the History of Art." by Avinoam Safran
12:25h – 13:30h	Lunch Break

"Clinical Research" Chaired by José Cunha-Vaz

13:30h – 13:40h	"Overview of Cochrane systematic reviews in ophthalmology: What is the quality of evidence?" by Agnès Dechartres
13:40h – 13:55h	**Lecture** "European Vision Clinical Research Network, EVICR.net" by José Cunha-Vaz *
13:55h – 14:05h	"Stalking infectious agents that cause uveitis : a long-term challenge" by Bahram Bodaghi
14:05h – 14:15h	"Role and Contributions of the Clinical Investigation Centre in the Fight against Blindness" by Saddek Mohand-Saïd
14:15h – 14:25h	"4D and 5D imaging of the living eye" by Michel Paques *
14:25h - 14:35h	"Static and dynamic full field OCT (FFOCT) in the field of eye research" by Claude Boccara *
14:35h – 14:50h	Round Table chaired by José Cunha-Vaz
14:50h – 15:20h	**Closing Lecture** "The acquisition of reading" by Stanislas Dehaëne *
15:20h	Conclusions and farewell by José-Alain Sahel

“MT180” presentations by the young researchers

Department of Development

1) Robin Vigouroux “Deciphering the origin of binocular vision in vertebrates”
2) Franck Maurinot “Color-filling the retina to decipher its development”
3) Sarah Baudet “Local network of second messengers modelling the connectivity of the visual system”

Department of Visual Information Processing

1) Gokul Rajan “Brain in Motion: Neuronal Correlates of Locomotion”
2) Anna Verschueren “Constructing a cellular mechanism hypothesis for the Stiles Crawford effect : Usher proteins, phototropism and planar cell polarity in photoreceptors.”
3) Sarah Goethals “The electrical impact of axon initial segment geometry”
4) Marion Durteste “The impact of visuo-cognitive ageing on spatial navigation”
5) Lenz Gregor “Teaching machines to see using bio-inspired cameras”

Department of Genetics

1) Juliette Varin “Developing therapy for CSNB : the challenges”
2) Geraldine Puel “One way from rod to cone”

Department of Photonics

1) Clement Molinier “Multiplexed temporally focused light shaping for high-resolution multi-cell targeting”
2) Clemence Gentner “Nanoprobes stroboscopy for 3D viscosity imaging”

Department of Therapeutics

1) Mathis Thibaud “Exploring the link between Parkinson disease and AMD”
2) Elora Vanoni “Prpf31-related RP: the need to set your RPE clock”
3) Catherine Botto “High flying scissors for precise retinal surgery
4) Leo Puyo “Clinical application of laser Doppler holography in ophthalmology for non-invasive blood flow imaging”

Poster presentations by the young researchers

Department of Development

1) Sergi Roig "Netrin-1 role in commissural axon guidance"

2) Takuma Kumamoto "A novel gene expression switch for direct readout of retinal stem cells transgenesis in vitro and in vivo"

3) Dragos Niculesu "Elucidating the Clonal Contribution to the Columnar Organization of the Mouse Cortex"

4) Fanny Eggeler "A novel gene expression switch for direct readout of retinal stem cells transgenesis in vitro and in vivo"

5) Shahad Al-Badri "Redox signaling controls the switch between cell proliferation and differentiation in the vertebrate retina"

6) Marion Rosello "Base editing technology in zebrafish, from signaling activation to human mutation mimicry"

7) Oriane Rabesandratana "Generation and characterization of transplantable retinal ganglion cells isolated from human iPS cell-derived retinal organoids"

8) Amelie Rodrigues "Characterization of an in vitro model of Retinitis Pigmentosa using human induced pluripotend stem cells"

9) Sacha Reichman "Drug discovery through HTS: The human iPS-derived RPE model for drug repurposing"

10) Coralie Fassier "Linking guidance signals to cytoskeleton remodelling: Fidgetin-like 1 as an integrator for axon repulsion"

11) Martijn C. Sierksma "Interactions between nearby retinal ganglion cells during eye-specific segregation"

12) Johann Becret "Modulation of focal adhesion dynamics by lipid raft-restricted cAMP signaling within RGCs"

13) Tadao Maeda and Yasuhiko Hirami "Clinical studies of iPS-RPE at Kobe Eye Center"

14)Suguru Yamazaki "Genetical modification to reduce graft bipolar cells in hESC derived retinas aming for enhanced graft integration "

15) Masaaki Ishida "Major histocompatibility complex class II defcient Retinal pigment epithelial cells reduce immune rejection"

16) Kiyoko Gocho "10 years of imaging with adaptive optics retinal cameras"

17) Akiko Maeda "High throughput drug screening found readthrough compounds for RP"

18) Takesi Matsuyama "Reconciling melanopsin tristability with action spectra"

19) Naohiro Motozawa "Proof of Concept about Human-free and versatile cell culture by LabDroid"

20) Hung-Ya Tu "Probing the partially reconstructed retinal circuitry after ES/iPS cell derived retinal transplantation"

21) Hirofumi Uyama "Survival and maturation of iPSC derived retina after transplantation in MHC matched and mismatched nonhuman primate"

Department of Visual Information Processing

22) Marcel Stimberg "Brian 2: Simulation of spiking neurons and networks"

23) Sarah Goethals "The electrical impact of axon initial segment geometry"

24) Huy Hoang Nguyen "A simple technique to immobilize motile cells for electrophysiology"

25) Francesco Trapani "Modeling the Spatial Integration of Rod Bipolar Cell output by Ganglion Cells"

26) Nissim Zerbib "Model free Anticipation in Sensorimotor Control"

27) Stephen Ramanoel "Geometric vs. Landmark based spatial navigation involved distinct cerebral networks"

28) Adrien Chopin "Stereoscopic vision, stereo-deficiency and its impact in the older adults"

29) Marcia Bécu "Modulation of spatial cue processing across the lifespan: a geometric polarization of space restores allocentric navigation strategies in children and older adults"

30) Tianyi Li "Modelling the impact of aging on the entorhinal-hippocampal network"

31) Omar Oubari "A spiking neural network with memristive synapses for neuromorphic event-based vision"

Department of Genetics

32) Juliette Wohlschlegel "First identification of ITM2B partners in human retina"

33) Marco Nassisi "Peripapillary Sparing With Near Infrared Autofluorescence Correlates With Electroretinographic Findings in Patients With Stargardt Disease"

34) Vassily Smirnov "Isolated retinal dystrophy linked with CLN3 mutations"

35) Lea Thiebault "The promoter of lactate transporter gene SLC16A8, a therapeutic target for age-related macular degeneration"

Department of Photonics

36) Nicolo Accanto & Florence Bui "Light shaping for precise in depth optogenetics"

37) Dimitrii Tanese & Imane Bendifallah "Characterization and modeling of temporally precise two-photon optogenetics experiments"

38) Emiliano Ronzitti "All-optical interrogation of retinal circuit by holographic wave front shaping"

39) I-wen Chen "In vivo submillisecond two-photon optogenetics with temporally focused patterned light"

40) Pascal Berto "Optical phase imaging and shaping"

Department of Therapeutics

41) Christophe Roubeix "Spleen-derived monocytes participate in pathogenic subretinal inflammation"

42) Darine Fakih "Upregulation of nociceptors in trigeminal ganglion and their role in the ocular pain physiopathology in a model of dry eye"

43) Romain Magny "Lipidomic analysis of an in vitro Dry Eye Disease model highlights the role of hyperosmolarity in Triglyceride, Oxysterol and Ceramide metabolisms"

44) Adrian Guerrero Moreno "Upregulation of the mu-opioid receptor in the cornea and trigeminal ganglion following corneal inflammatory pain"

45) Abdallah Hamieh "Mitochondrial failure and oxidative stress in Prpf31+/- mice: understanding PRPF31 implication in adRP"

46) Cardillia-Joe Simon "G-protein gated K+ channel-mediated vision restoration in Rod-Cone Dystrophy"

47) Marie Darche "Clearing the human eye"

Abstracts

"Where do we go from here: One New Direction for Vision Research" by John E. Dowling *

The progress made in vision research and at the Institut over the past decade, has been spectacular, but rather than focusing on the past, I will look forward and discuss briefly a new research approach that may help to understand the etiology of eye diseases about which we know too little. Light microscopy has advanced substantially over the past half century but today much focus is on electron microscopy and the higher resolution it provides.

Working in the laboratory of Jeffrey Lichtman who has developed connectome methods to study and reconstruct neural tissue, we can now cut thousands of serial sections, align them, and image areas of interest with a 61 beam electron microscope. With colleagues we are studying a control human fovea and a rare form of macular degeneration, Macular Telangiectasia (MacTel). Observations that will be discussed include the finding of cone pedicles in the foveal pit as well as a second type of Müller cell throughout the macula. In MacTel retinas, extending genetic and biochemical observations of serine deficiency there, we find specific changes in mitochondrial structure even outside the macula, but more dramatically in the macula itself. Müller cells, which synthesize retinal serine, are lacking in the macula, and a striking border exists between Müller cell presence and absence that may delimit the so-called MacTel zone.

"Regeneration of the retinal pigmented epithelium" by Jeff Gross *

Diseases resulting in degeneration of the retinal pigment epithelium (RPE) are among the leading causes of blindness worldwide and no therapy exists that can replace RPE or restore lost vision. Age-related macular degeneration (AMD) is one such disease and is the third leading cause of blindness in the world. While there are some effective treatments for exudative (wet) AMD, ~90% of AMD cases are atrophic (dry) and these are currently untreatable. Transplantation of stem-cell derived RPE has emerged as a possibility for treating geographic atrophy and clinical trials are underway. However, little is known about the fate of transplanted RPE and whether their survival and integration can be improved. An intriguing alternative approach to treating AMD and other RPE diseases is to develop therapies focused on stimulating endogenous RPE regeneration. For this to be possible, we must first gain a deeper understanding of the mechanisms underlying RPE regeneration. In mammals, RPE regeneration is extremely limited and, in some contexts, RPE cells overproliferate after injury, such as during proliferative vitreoretinopathy, where proliferative RPE cells invade the subretinal space and lead to blindness. Recently, a subpopulation of quiescent human RPE stem cells was identified that can be induced to proliferate in vitro and differentiate into RPE or mesenchymal cell types, suggesting that the human RPE contains a population of cells that could be induced to regenerate.

* Presentations with abstract

Despite these studies, little is known about the process by which RPE cells respond to injury to elicit a regenerative, rather than pathological, response. To address this issue and acquire a deeper understanding of the molecular mechanisms underlying RPE regeneration, we developed a transgenic zebrafish model to study RPE injury and regeneration. Our results demonstrate that the zebrafish RPE regenerates after severe injury and i) that RPE regeneration involves a robust proliferative response during which proliferative cells move to the injury site and differentiate into RPE, ii) that the source of regenerated cells is likely uninjured peripheral RPE and iii) the innate immune system plays a critical role in RPE regeneration.

"An inclusive world for the visual impairment" by Masayo Takahashi *

The induced pluripotent stem cell (iPSC) is a good source to evaluate human retinal diseases and to develop treatments. We utilize it by making retinal organoids. In view of clinical application of retinal transplantation therapy for retinitis pigmentosa, hESC/iPSC-derived retinal organoids were evaluated after subretinal transplantation in nude rats with retinal degeneration to confirm their potency as a graft source in terms of graft maturation and possible integration. Then in order to obtain preparatory information toward clinical application, we transplanted retinal organoids in monkey models and observed that the graft differentiated into various types of retinal cells including rod and cone photoreceptors with structured outer nuclear layers (ONLs). Host-graft synaptic connections were suggested by immunohistochemistry and electrophysiology in those animals. Our findings indicate the feasibility of retinal sheet transplantation in clinical practice and provide a tool to optimize transplantation strategies for future clinical application.

Besides promoting cell therapies, it is also important to inform the existence of another solution, low vision care, because excessive expectations are partly due to the idea that the cure is the only solution. It is necessary to make it known that regenerative medicine is completed in combination with rehabilitation (low vision care) at the beginning. In addition, it is necessary to change the image of visual impairment throughout society

"Optic nerve regeneration: regulation by cell-autonomous and non-autonomous factors" by Larry Benowitz *

The inability of retinal ganglion cells (RGCs) to survive and regenerate axons after optic nerve injury leads to an irreversible loss of vision in victims of traumatic or ischemic nerve damage or neurodegenerative diseases such as glaucoma. Studies from our lab and others have identified strategies to promote varying degrees of RGC survival and optic nerve regeneration, yet the extent of visual recovery remains modest, emphasizing the need for a deeper understanding of the factors that suppress or promote regeneration. Following the discovery that intraocular

inflammation leads to appreciable regeneration, we have identified three immune-derived proteins that stimulate appreciable RGC survival and axon regeneration. In addition, optic nerve injury activates a cascade of intercellular signaling events that involve glutamate release from bipolar cells, generation of nitric oxide from NOS1-positive amacrine cells, accumulation of mobile zinc in amacrine cell terminals, zinc exocytosis and RGC death. Chelating mobile zinc leads to long-term survival of many RGCs along with axon regeneration. Finally, identification of differentially expressed genes in RGCs stimulated to regenerate injured axons vs. RGCs subjected to nerve injury alone points to transcription factors that regulate the regenerative program, and the importance of these factors has been confirmed in gain- and loss-of-function studies. Leveraging these discoveries and ones made in other labs enables many RGCs to regenerate axons the full length of the optic nerve, and may one day enable us to promote substantial visual recovery in victims of acute or chronic insults to the optic nerve.

"3D Engineered photoreceptor/RPE/choroid to Model and Treat Retinal Degenerative Diseases" by Kapil Bharti *

Retinal degenerative diseases are the leading cause of untreatable blindness. Most forms of retinal degenerative disease are caused by degeneration of photoreceptors, RPE, and the choroid. We have combined bioprinting, tissue engineering, and induced pluripotent stem (iPS) cell technology to develop a 3D model of RPE/"choroid" as an in vitro model to study age-related macular degeneration, a disease that affects these two tissues. Using a collagen-based gel for encapsulation of patient-specific iPS cell-derived endothelial cells, choroidal fibroblasts, and pericytes, we successfully bioprinted a microvascular network on one side of a biodegradable scaffold. On the other side of the scaffold, we grow a RPE monolayer differentiated from the same patient's iPS cells. This 3D tissue mimics the anatomy and functional properties of native RPE/choroid unit. Similar to wet-AMD, the in vitro microvascular network also proliferates in response to VEGF. This 3D RPE/choroid construct is currently being combined with 3D retina derived from the same iPS cells to develop the entire back of the eye tissue relevant for AMD pathogenesis. This work provides a platform to discover disease initiating pathways and the possibility of identifying potential therapeutic drugs for AMD.

"Retinal axon wiring by subcellular confinement of ubiquitous signals" by Xavier Nicol *

The precise tuning of the visual system connectivity is crucial for the sound processing of visual information by the brain. When altered, abnormal connectivity can lead to a diversity of visual pathologies. The developmental mechanisms leading to precise connections from the retina to the brain are only partially understood. They involved a set of cellular second messengers including cAMP, cGMP and calcium, that are

also shared by many pathways. Although modulated by a plethoric number of intra and extracellular signals, second messengers drive selectively their myriad of downstream cellular events, including the pathfinding of retinal axons towards their targets of the brain and the shaping the terminal arbors of these projections. The spatial regulation of molecules within a cell emerged as a flexible strategy to provide specificity and coordinate distinct cellular processes. We developed a set of molecular tools enabling to investigate the subcellular localizations and regulations of second messengers and the diversity of their roles in developing retinal axons. Using this toolset, we clarified the cellular messenger-dependent mechanisms during the wiring of retinal projections into the brain. We identified lipid rafts (submicrometer compartments of the plasma membrane) as a critical region of the cell for the cAMP, cGMP and calcium signaling involved in wiring the visual system. We demonstrated that neighboring retinal ganglion cell axons co-stabilize their terminal arbors within the framework of competition with afferences from the other eye during the development eye-specific territories in the brain.

"Visual aging and visuo-spatial cognition: clinical phenotyping, behavioral markers and neuroimaging " by Angelo Arleo *

Visual aging leads to anatomical and functional changes, altering eye structures, sensory transduction, neural transmission, and sensory-cognitive functions. This talk will first present the SilverSight cohort study, launched in 2014 at the Vision Institute - CHNO des Quinze-Vingts. This population study aims at assessing, cross-sectionally and longitudinally, the anatomo-functional changes induced by healthy and pathological visual aging, to characterize the link between cellular changes (e.g., retinal structural alterations measured by adaptive optics high-resolution imaging), and associated visual symptoms (e.g., contrast and motion sensitivity measured psychophysically). Second, we will focus on a series of experiments conducted at the Vision Institute to investigate the impact of aging on visual-spatial cognition. These studies were carried out in ecological setups by using the Streetlab facility, thus reproducing everyday life situations under controlled conditions. Our body kinematics and eye movement analyses uncovered age-related effects on visual active exploration, encoding of spatial cues, and goal-oriented navigation strategies. Complementing these behavioral findings, anatomo-functional cerebral imaging (fMRI) shed light on the impact of aging on the network of brain areas subserving spatial cognition. Overall, these works identified dependency biomarkers and suggested solutions to counter spatial cognitive deficits leading to autonomy loss in older adults.

"Visual and visuomotor circuits in a genetically and optically accessible vertebrate" by Herwig Baier *

We are investigating how objects are encoded by the visual system and how their identification and localization results in goal-directed motor responses. Past work in the lab has established prey capture behavior of larval zebrafish as a paradigm to address this question. Machine vision analysis of hunting behavior in free-swimming larvae suggests that dedicated circuits exist that control orientation, pursuit and capture strike movements. Two-photon whole-brain imaging, laser ablations and optogenetic perturbations with single-cell resolution have identified the brain areas that detect prey stimuli and steer hunting maneuvers. Transcriptional profiling using single-cell RNA sequencing revealed retinal ganglion cell types that respond selectively to prey-like features of visual objects. These RGCs project into specific areas in the pretectum and tectal layers, whose activity, in turn, is necessary and sufficient for triggering hunting behavior. We similarly identified distinct pathways for the response to looming visual stimuli and to optic flow. This work is beginning to reveal the global circuit architecture of visuomotor transformations in a vertebrate brain.

"The human retina" by Botond Roska *

The cell types and circuits of the human retina are not well understood. Here I present a set of new technologies which enable us to study the structure, function and disease mechanism of human retinal circuits at single cell resolution. First, I will introduce our work on postmortem human retinas, either naturally light responsive or artificially made light sensitive by cell type targeted optogenetic tools. Then, I will discuss our work on human retinal organoids with multiple nuclear and synaptic layers that we developed in large quantities. Finally, I will show how we model diseases and develop therapies by using these organoids.

"Best outcome measures for clinical trials in Stargardt disease: Lessons from the ProgStar study" by Hendrik Scholl *

Stargardt disease (STGD1; OMIM: 248200) is the most common juvenile macular dystrophy. It is inherited as an autosomal-recessive trait associated with mutations in the ABCA4 gene, and more than 1000 disease-associated variants have been reported. Clinically, STGD1 is characterized by fundus flecks in the retinal pigment epithelium (RPE) and by macular atrophic lesions. Visual acuity (VA) and central visual fields deteriorate progressively commonly leading to legal blindness in adulthood. Currently there is no approved treatment for STGD1. The international multicenter Progression of Atrophy Secondary to Stargardt Disease (ProgStar) study aimed to understand the natural history of disease progression to help determine appropriate outcome measures for future treatment trials. The primary aim was to

assess the yearly rate of progression of STGD1 using the growth or the development of atrophic lesions as measured by fundus autofluorescence (FAF) imaging. Secondary aims include to assess the yearly rate of progression of STGD 1 using spectral-domain optical coherence tomography (SD-OCT) to measure the rates of retinal thinning and the loss of photoreceptors; to assess the yearly rate of loss of retinal sensitivity as measured by microperimetry (MP); to assess the yearly rate of VA changes; and to correlate the presence and progression of morphological abnormalities in FAF and SD-OCT images with visual function as measured by MP and VA.

"How rare is rare? What syndromic Inherited Retinal Dystrophies tell us … "
by Hélène Dollfus,*

Syndromic forms of Inherited Retinal Dystrophies (IRD) account for about 30 % of all IRDS with some well know entities such as Usher Syndrome or Bardet-Biedl syndromes and on the other hand some ultra rare syndromes occuring in a very small number of patients world wide.

For syndromic IRDs many biological pathways are implied illustrating the huge complexity and sensitivity of the photorector cells.

Today, our knowledge is expanding rapidely via high throughtput strategies such as Whole Genome Sequencing (WGS) and « omics » leading to an integrated biological vision concerning IRD pathogenesis. Thus IRDs can be considered as a continous spectrum of isolated and syndromic diseases.

This has a considerable impacts on: clinical and molecular diagnosis, genetic counseling, basic pathogenesis research and therapeutic avenues.

"Eye-Risk - identify, model and validate AMD risk factors and disease drivers"
by Marius Ueffing *

Current research aims to prevent, predict and treat Age-related macular degeneration (AMD). So far, genetic and epidemiologic studies have been able to pinpoint more than 35 genetic variants as well as environmental and lifestyle factors that define the individual risk for AMD. Turning this knowledge into prevention, prediction and treatment has been the goal of EYE-RISK (www.eye-risk.eu) The approach of EYE-RISK integrates clinical phenotyping and diagnosis, genotyping, next-generation targeted re-sequencing, bioinformatics and statistics, clinical data analysis, computational biology, systems-biology oriented pathway analysis and modelling. Five major goals have been pursued: 1) algorithms to identify personalized risks for development of advanced- and progression of dry AMD; 2) biomarkers for further stratification of disease risk; 3) molecular drivers/biological pathways relevant for onset and progression of advanced AMD; 4) clinical guidelines

for individuals at risk of developing AMD; 5) criteria of inclusion and stratification for patients entering clinical trials. Specifically, we have asked, how a combination of risks shifts the regulation of homeostasis in the choriocapillaris/Bruchs-membrane/RPE interphase towards a diseased state. Recent results on the interconnection of discrete genetic risks, the interaction with lifestyle factors, and the impact of local dysregulation of complement on the development and the progression of AMD will be discussed.

"Ten years of research from the front to the back of the eye, and beyond"
by Christophe Baudouin *

In line with previous research in inflammation and toxicological challenges to the surface and anterior segment of the eye, our achievements in preclinical and clinical research over the past decade have led to significant progresses in major ocular diseases and morbidities, such as glaucoma, dry eye disease, drug- or blue light-induced injuries or chronic ocular pain. New paradigms have thus raised, demonstrating dry eye as an inflammatory disease, showing the interest of immunomodulating agents, developing an extensive worldwide knowledge on inflammatory signatures, leading to new safer and well-tolerated preservative-free topical medications, or deciphering some of the mechanisms causing chronic intractable pain, along the trigeminal pathway and up to the brainstem and pain-associated cortical nuclei. Novel in vitro, ex vivo and in vivo models have been developed, based on high resolution imaging techniques, using complex cell cocultures or compartmentalized neuronal growth models, or by electrophysiological recording of ciliary nerve activity to discriminate corneal nerve functions and tackle pain-related mechanisms like those of the opioid system. Large-scale transcriptomic, proteomic or lipidomic strategies are now developed to identify disease signatures, both as biomarker developments and therapeutic approaches. Not only findings on iatrogenic inflammation allowed to develop new pharmacological formulations but deeper structures also showed inflammatory changes in glaucoma, a disease which takes its origin in the anterior segment and involves neuroinflammation in the retina and all along the visual pathway. All this extensive research will serve as the basis for future new therapies.

"On phagocytes, retinal degeneration, and vascular remodeling"
by Florian Sennlaub *

We focuses on the pathogenic role of the chronic accumulation of mononuclear phagocytes (MP) in age-related macular degeneration (AMD) and in ischemic proliferative retinopathies, such as retinal vein occlusion and diabetic retinopathy. Their work of the last 10 years has demonstrated how the chronic activation and accumulation of MPs drives retinal degeneration and they showed how the genetic AMD-risk variants affect MP function, impair subretinal immune suppression, and

inflammation resolution. Together these findings emphasise the role of the AMD-risk variants in inflammation and inflammation in AMD and open new therapeutic avenues to inhibit pathogenic non-resolving subretinal MP accumulation in AMD and other retinal affections.

"Endophenotype and precision medicine for immune mediated ocular disorders" by Andrew Dick *

The management of Ocular Inflammation until recently has lacked high level clinical trial evidence despite years of experience with Dmards and Biologics. On the backdrop of this data, I will be discussing future approaches no longer quixotic, through our understanding of the immunobiology of experimental models, advances in experimental medicine in man and our increasingly elegant imaging technologies to develop our future approaches that through endophenotypes of uveitis we will target patients appropriately.

"Designing mutation-Independent gene therapies" by John G. Flannery *

We have worked for the last few years to develop adeno-associated virus mediated gene therapies that are broadly applicable to many patients because they are 'agnostic' to the patient's gene defect. These approaches are not gene replacement strategies for recessive null conditions. To this end, we are developing improved AAV vectors to deliver from the vitreal space - secreted factors to rescue cone photoreceptors for patients in the early stages of retinal disease where there are substantial numbers of surviving photoreceptors to treat. For patients in later stages of retinal degeneration where there are few remaining photoreceptors, we are developing optogenetic methods to add a light receptive function to surviving inner retinal neurons.

"European Vision Clinical Research Network, EVICR.net" by José Cunha-Vaz *

EVICR.net is a network of European ophthalmological clinical research centers dedicated to performing multinational clinical research in ophthalmology, following the European and International regulations for clinical research and ICHGCP guidelines.

EVICR.net aim is to strengthen the capacity of Europe to perform multinational clinical research studies to develop and optimize the use of diagnostic, prevention, and treatment strategies in ophthalmology. EVICR.net offers a unique platform for ophthalmology multinational clinical research in Europe and a useful industry resource in order to contribute to the development of new drugs, gene and cell therapy products, medical devices, and biomarkers.

* Presentations with abstract

AIBILI, in Coimbra, Portugal, is the headquarters and coordinating center of the European Vision Institute Clinical Research Network – EVICR.net. At present, EVICR.net has 101 clinical ophthalmological centers as members from 15 European countries. The Network has coordinated already 20 studies and has at present 6 multinational clinical studies ongoing, of which 2 are funded by the European Commission.

Scientifically, it is organized by ophthalmology subspecialties expert committees, namely: age-related macular degeneration; retinal dystrophies (including pediatric ophthalmology); diabetic retinopathy and vascular diseases; glaucoma; anterior segment, and ocular surface, inflammation, dry eye and allergies. It also has transversal sections dedicated to reading centres, rare diseases, and medical devices.

"4d and 5D imaging of the living eye" by Michel Paques *

We see our environment by the light entering the eye, but only a very part (less than 1 /10,000 photons) is reflected and comes out of the eye. These few photons are extremely valuable because they carry a lot of information about the retina.The PARIS Group (Paris Adaptive Optics Retinal Imaging and Surgery) located in the Clinical Investigation Center 1423 of the Quinze-Vingts Hospital (http://parisgroup.org) was formed around doctors from the hospital of Quinze-Vingts and the Vision Institute, physicists from ESPCI and ONERA, and computer scientists from ISEP.Our team seeks to extract information from this light by deploying a set of technologies all aimed at understanding human diseases. We were able to set up a high-performance eye imaging unit that is unique in the world and dedicated to examining patients. The most popular of these techniques is adaptive optics, but we have also developed novel techniques such as full field optical coherence tomography, structured illumination and Doppler holography. These innovative technologies enable dynamic, multi-scale imaging (from cell to entire eye, from the surface of the eye to the optic nerve, and from decade to century). It is now possible to observe the subtle interactions between cells that are at work in diseases of the retina. The diseases concerned are as frequent diseases as age-related macular degeneration as rare diseases.

"Static and dynamic full field OCT (FFOCT) in the field of eye research" by Claude Boccara *

FFOCT takes en-face tomographic images, it uses a broadband, spatially incoherent illumination and microscope objectives to reach high resolutions in the 0.5 to 1.5 µm range (for the cornea). Using spatially incoherent full field illumination was found to be very useful to image through tissue: it strongly reduces low order aberration effects in retinal and corneal examination.

* Presentations with abstract

In order to take advantage of the weak influence of aberrations we have been able to image cornea without contact using air microscope objectives that could not be achieved with confocal imaging. In our experiments the field of view is about 16 times larger than with the confocal microscope. Moreover, our camera is fast enough to follow individual red blood cells and to quantify blood speed.

The low influence of the aberrations is even more spectacular on retinal images even with a 5 to 6 mm pupil and no adaptive optics for aberrations compensation, a diffraction limited resolution (< 3 □m) was achieved in retina allowing resolution of individual cone and rods photoreceptors near the fovea. Here also a much larger field of view than with adaptive optics setups is achieved.

For more biologically oriented research, using the same kind of setup and its ability to "section" in tissue we were able not only to add a clear view of cells but also of their metabolism. This Dynamic FFOCT approach brings indeed a new way of imaging by using a colour scale that represents increasing speed of subcellular dynamics, and a brightness the signal intensity.

"The acquisition of reading" by Stanislas Dehaëne *

Recent discoveries in cognitive psychology and neuroscience are starting to shed light on what is perhaps the most remarkable competence of the human brain: its capacity to change itself through education. In this talk, I will focus on reading. By scanning children every two months during the first year of school, as they acquire reading, and by comparing the results with those of illiterate adults, we obtained a detailed picture of how ventral visual cortex and language areas are enhanced by reading acquisition. Our growing understanding of the psychology and neuroscience of literacy has importance consequences for how our schools teach reading.

Invited scientific speakers

John Dowling (Harvard University, USA)
Jeff Gross (University of Pittsburgh School of Medicine, USA)
Mathias Fink (Institut Langevin, Paris)
Masayo Takahashi (Riken Institute, Japan)
Larry Benowitz (Boston Children's Hospital and Harvard Medical School, Boston, MA USA, USA)
Kapil Bharti (Ocular and Stem Cell Translational Research Unit NEI, Bethesda, USA)
Francine Behar-Cohen (Cordoliers Research Center, Paris Descartes University)
Eberhart Zrenner (Institute for Ophthalmic Research, Tübingen, Germany)
Herwig Baier (Max Planck Institute for Neurobiology, Germany)
Botond Roska (Institute of Molecular and Clinical Ophthalmology Basel, Switzerland)
Hendrik Scholl (Institute of Molecular and Clinical Ophthalmology Basel, Switzerland)
Hélène Dollfus (Hôpitaux Universitaires de Strasbourg, Université de Strasbourg, Strasbourg)
Marius Ueffing (Institute for Ophthalmic Research, Tübingen, Germany)
Mickael Tanter (European Academy of Science, ESPCI, Paris)
Don Zack (Johns Hopkins University School of Medicine, Baltimore, USA)
Leah Byrne (University of Pittsburgh School of Medicine, USA)
Robert Mac Laren (Nuffield Department of Clinical Neurosciences, University of Oxford, UK)
John Flannery (Helen Wills Neuroscience Institute, University of California, Berkeley, USA)
Andrew Dick (UCL Institute of Ophthalmology, London, UK)
Agnès Dechartres (Hôtel-Dieu AP-HP, Paris)
José Cunha-Vaz (European Vision Institute Clinical Research Network, University of Coimbra, Portugal)
Bahram Bodaghi (Sorbonne University, Paris 13 University and Medical School, Pitié-Salpêtrière Hospital, Paris)
Claude Boccara (ESPCI ParisTech, Institut Langevin, Paris)
Stanislas Dehaëne (CEA, College de France, Paris)
Jean-François Dhainaut (LabSanté-IDF Innovation)

Invited industrial speakers

Audrey Derveloy (Novartis)
Emmanuel Gutman (StreetLab)
Bernard Gilly (Gensight Biologics)
Florence Allouche (SparingVision)
Lloyd Diamond (Pixium Vision)
T.B.D. (Essilor)

Invited speakers

Benjamin Yerxa (Foundation Fighting Blindness, USA)
Gérard Muller (Association Yvoir)
Christina Fasser (Retina International)

1 - Scientific conference

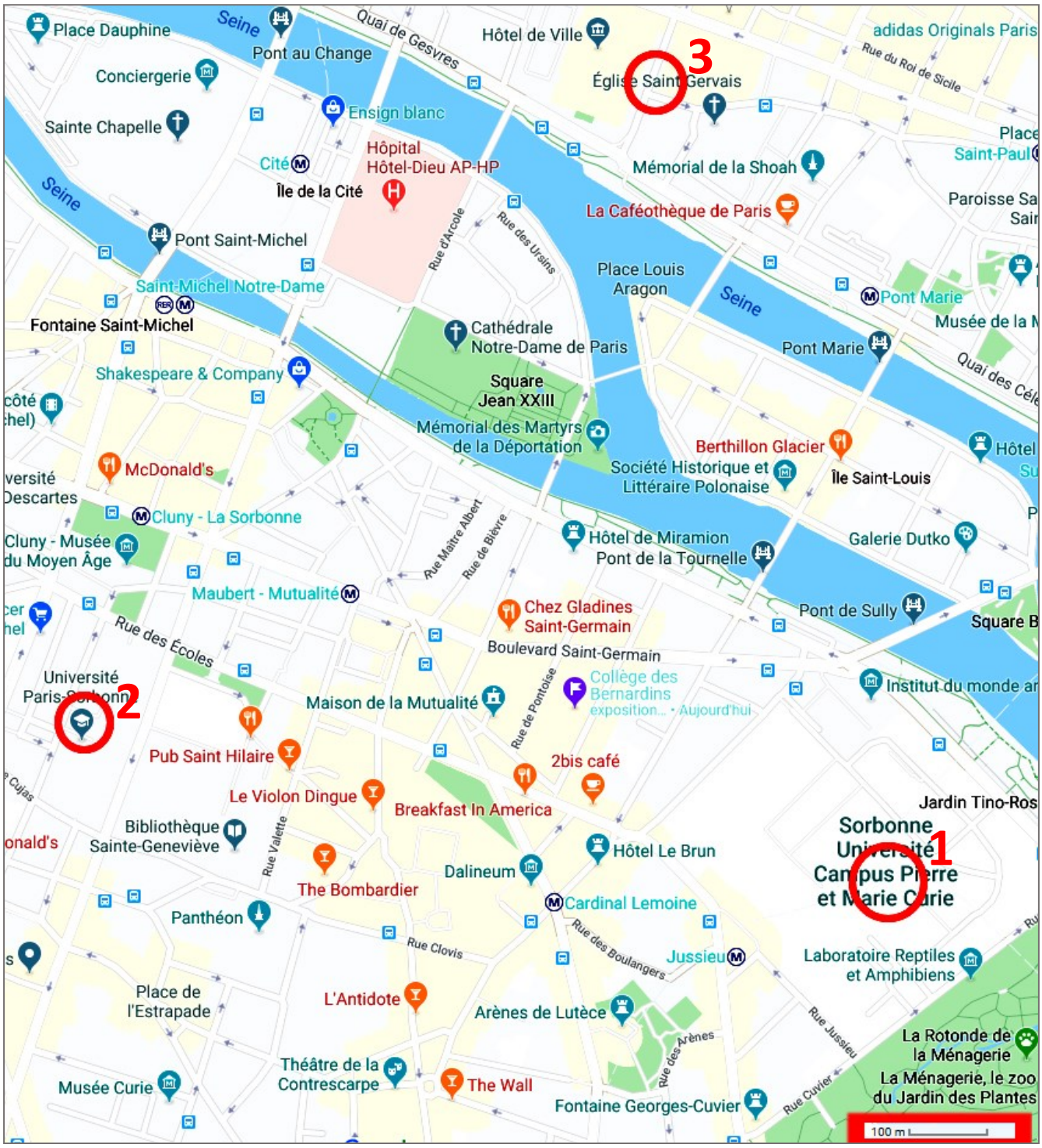
Auditorium - Sorbonne Université
4 place Jussieu - Patio 44-55 - 75005 Paris

2 - Celebration afternoon

Amphithéâtre Richelieu - Sorbonne Université
17 Rue de la Sorbonne, 75005 Paris

3 - Gala reception

Hôtel de Ville of Paris
3 Rue de Lobau, 75004 Paris

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