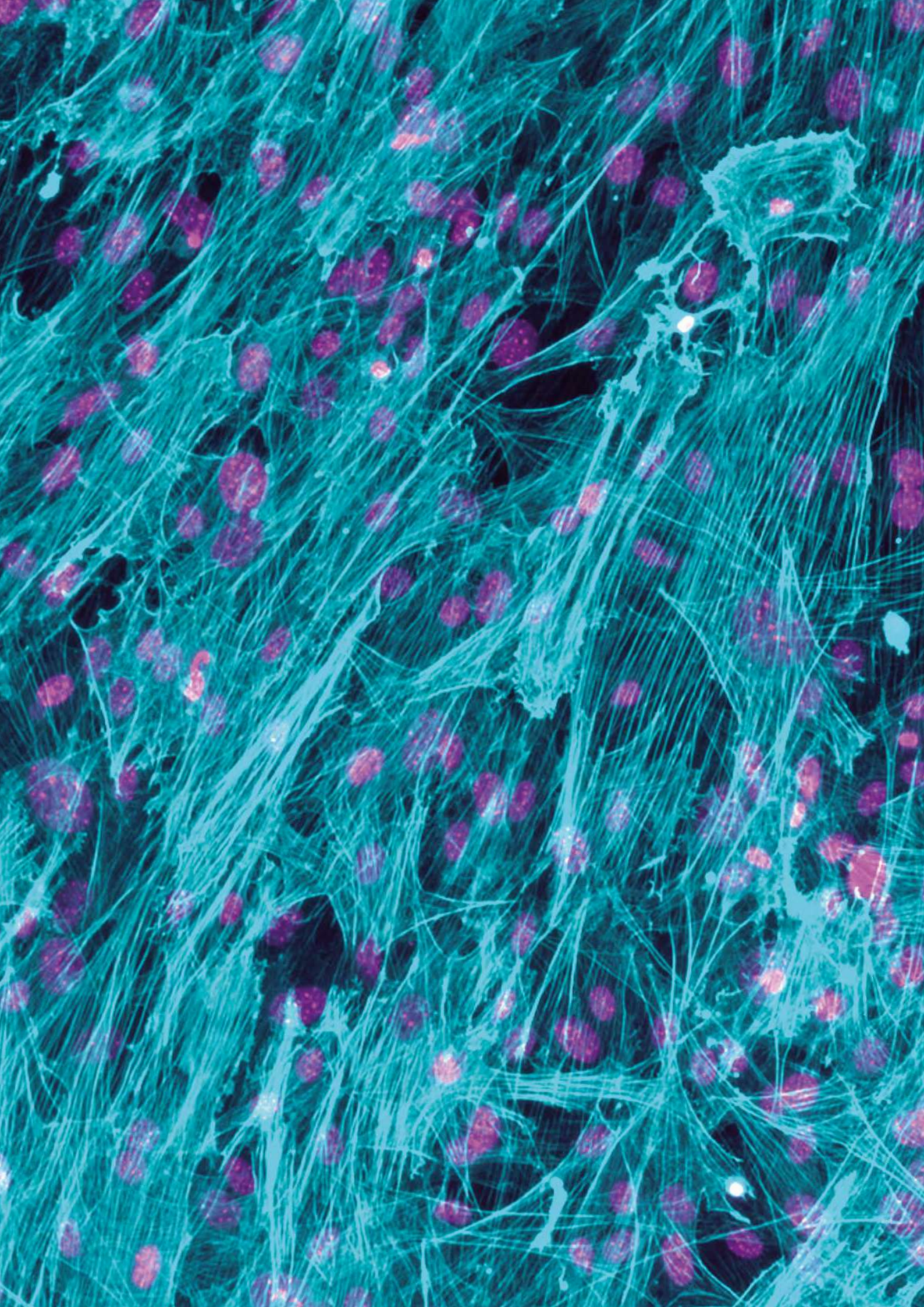
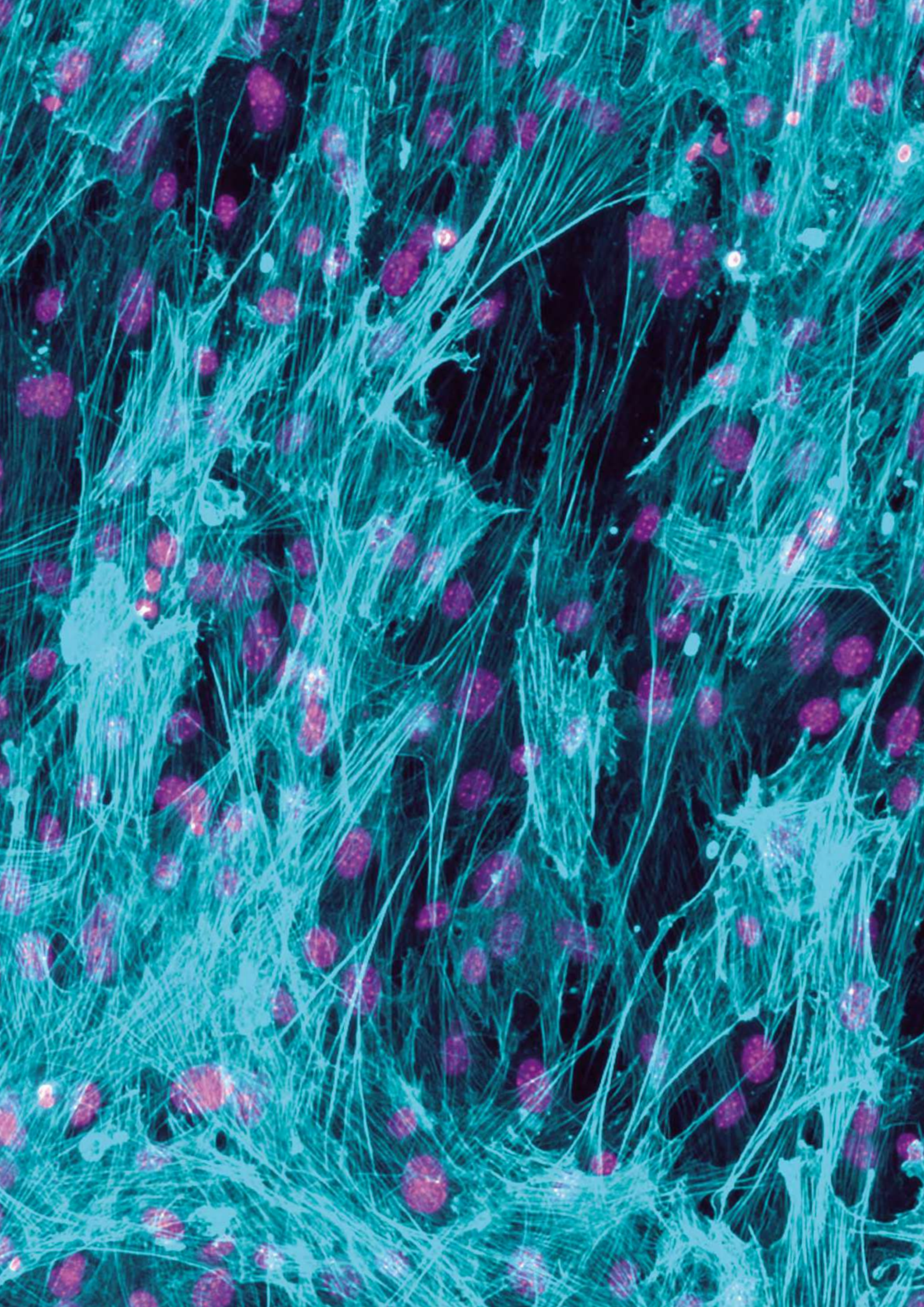


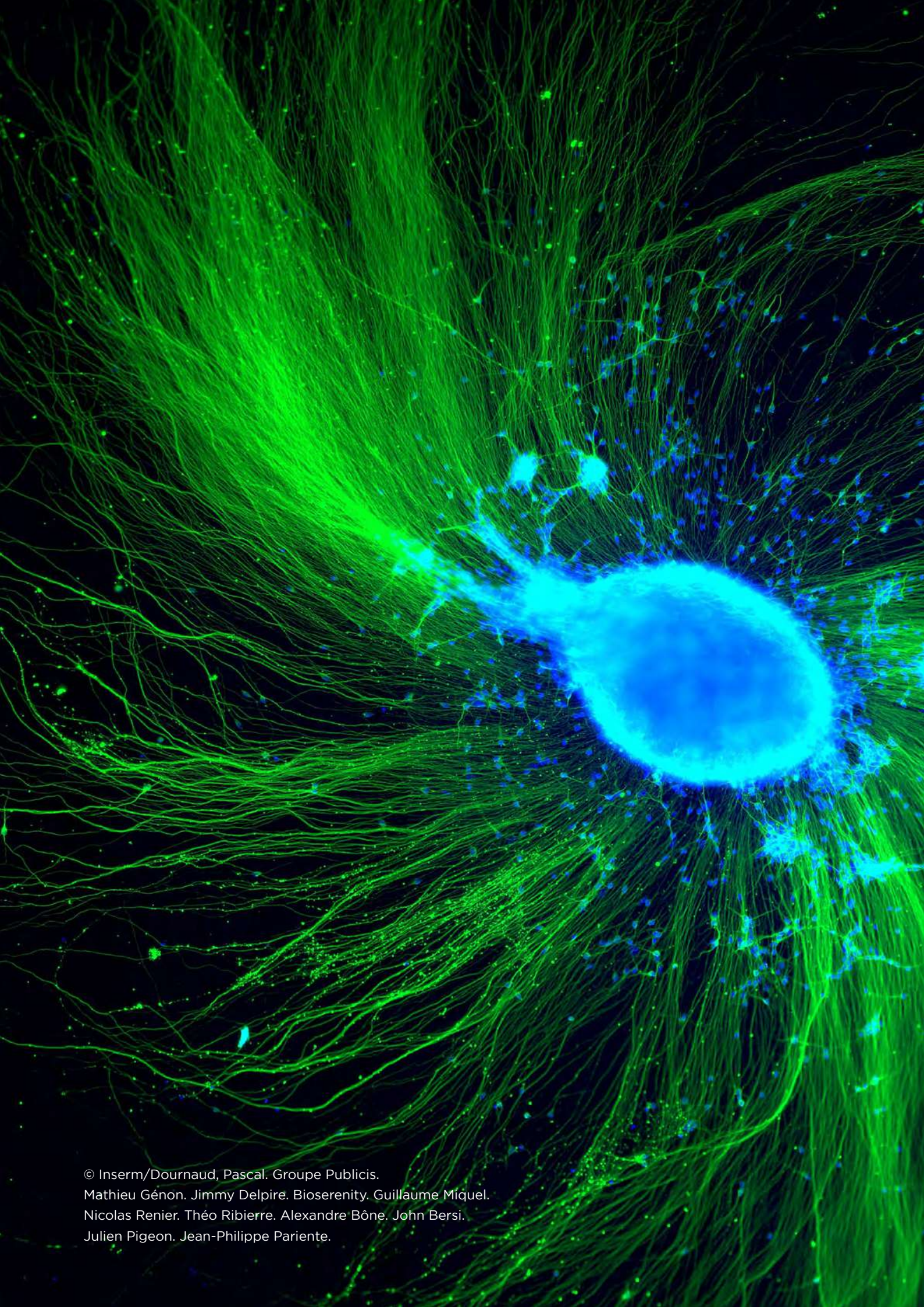
2020 ANNUAL REPORT

10 YEARS

**of progress  
& innovation**







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Mathieu Génon. Jimmy Delpire. Bioserenity. Guillaume Miquel.  
Nicolas Renier. Théo Ribierre. Alexandre Bône. John Bersi.  
Julien Pigeon. Jean-Philippe Pariente.

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# EDITORIAL



**Prof. Gérard Saillant,**  
President of  
Paris Brain Institute

” AS WE LOOK BACK ON THE YEAR 2020, WE MUST FIRST THINK OF ALL THOSE WHO HAVE BEEN AFFECTED, ARE STILL AFFECTED OR HAVE DISAPPEARED BECAUSE OF COVID-19. WE HAVE ALL BEEN AFFECTED PHYSICALLY, SOCIALLY AND ECONOMICALLY. IN THIS DIFFICULT PERIOD, THE PARIS BRAIN INSTITUTE HAS SHOWN A FANTASTIC CAPACITY FOR ADAPTABILITY, FLEXIBILITY AND REACTIVITY. TOWARDS THE HOSPITAL, WITH THE MOBILISATION OF HUMAN AND MATERIAL RESOURCES; TOWARDS ITS STAFF, TO GUARANTEE THEIR SAFETY AND TO DEVELOP SALIVARY TESTS TO DETECT COVID-19; TOWARDS SCIENCE, BY DEVELOPING NEW RESEARCH SUCH AS THE COVID NEUROSCIENCE COHORT TO MONITOR THE NEUROLOGICAL AND PSYCHIATRIC CONSEQUENCES OF COVID-19, AND BY CONTINUING ITS WORK ON THE NERVOUS SYSTEM, MAINTAINING A HIGH LEVEL OF SCIENTIFIC PUBLICATIONS.

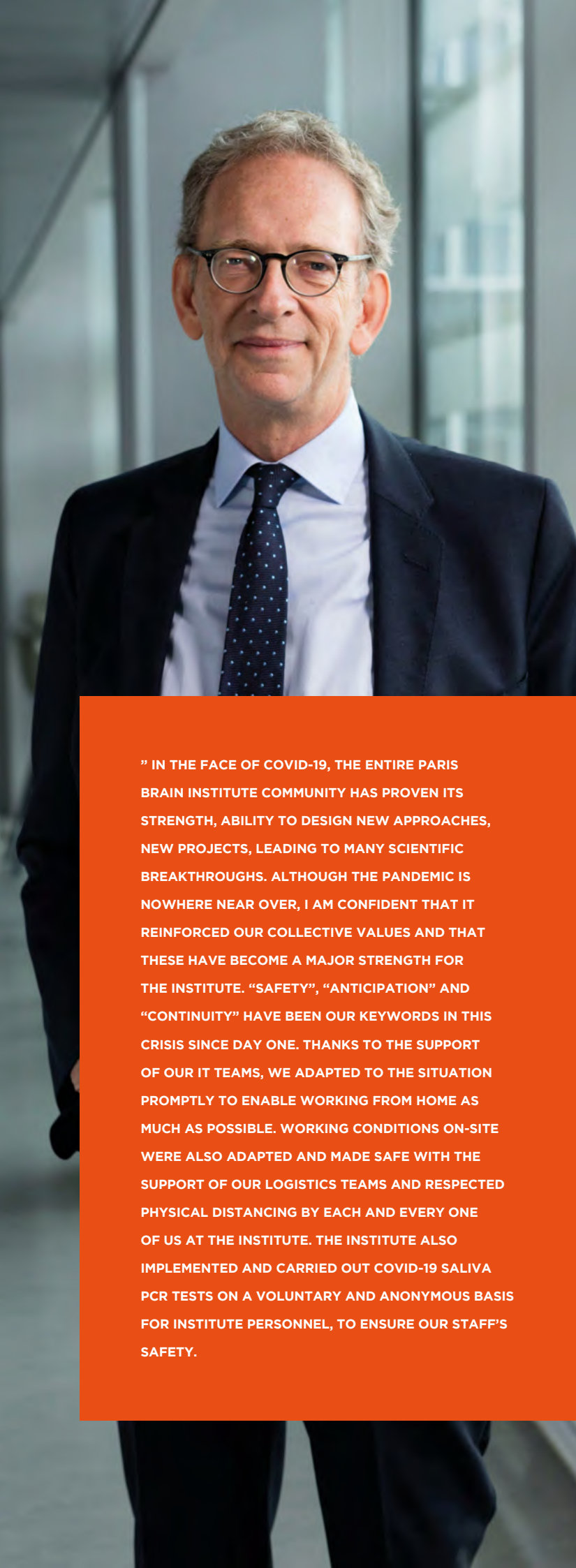
DESPITE CONTINUING UNCERTAINTIES, WE HAVE CONTINUED TO EVOLVE AND GROW. THE CHEVALERET CAMPUS, AN INCUBATOR DEDICATED TO MEDICAL TECHNOLOGIES AND ARTIFICIAL INTELLIGENCE, WHICH WILL OPEN IN 2021, PROMISES GREAT SUCCESS; THE GREATER INTEGRATION OF THE PARIS BRAIN INSTITUTE IN THE VARIOUS ASPECTS OF CLINICAL RESEARCH, IN CLOSE COLLABORATION WITH THE MEDICAL-UNIVERSITY DEPARTMENT OF NEUROSCIENCES AT THE PITIÉ-SALPÊTRIÈRE HOSPITAL; THE PURSUIT OF HIGH-LEVEL RESEARCH ON NEUROLOGICAL AND PSYCHIATRIC DISEASES, BUT ALSO ON THE FUNDAMENTAL UNDERSTANDING OF THE BRAIN IN NORMAL CONDITIONS, THE PROGRESSION OF ARTIFICIAL INTELLIGENCE AND THE IMPROVEMENT OF COGNITIVE CAPACITIES.

I WOULD LIKE TO THANK YOU, PARTNERS, DONORS AND VOLUNTEERS, FOR YOUR INVOLVEMENT AND YOUR UNFAILING SUPPORT FOR THE PARIS BRAIN INSTITUTE IN THIS VERY SPECIAL CONTEXT. THE RESEARCH CARRIED OUT HERE IS ONLY POSSIBLE THANKS TO THE MOBILISATION OF EVERYONE. ”



” THE COVID-19 PANDEMIC RADICALLY CHANGED OUR PROFESSIONAL LIVES AND FORCED US TO REINVENT THE WAY WE WORK. OUR MODEL AND THE STRENUOUS FLEXIBILITY WE APPLY ON A DAY-TO-DAY BASIS HAVE PROVEN THEIR STRENGTHS IN THIS TIME AND ALLOWED US TO MAINTAIN A HIGH LEVEL OF EFFICACY. THROUGH COLLABORATION, PERMANENT AND FLEXIBLE COMMUNICATION AND HIGH STANDARDS, WE WERE ABLE TO ENSURE THAT EVERYONE CONTINUED TO WORK IN THE BEST CONDITIONS. FOR TEAMS TO DEDICATE THEMSELVES FULLY TO RESEARCH, WITH LIMITED ADMINISTRATIVE CONSTRAINTS. FOR PLATFORMS TO ENSURE OPTIMAL SERVICE AND SUPPORT TEAMS WHILE DEVELOPING THEIR ORGANIZATION. FOR SUPPORT TEAMS TO REMAIN AS OPEN AS POSSIBLE TO RESEARCH TEAMS WHILE MAKING SURE THAT WE FOLLOW THE NECESSARY RULES FOR THE SITUATION. THE INVOLVEMENT OF THE ENTIRE INSTITUTE COMMUNITY IS WHAT HAS MADE SUCCESS POSSIBLE TODAY AND WILL GUARANTEE THE SUCCESS OF FUTURE ORGANIZATIONAL AND SCIENTIFIC PROJECTS AS WELL. ”

**Corinne Fortin,**  
Secretary General of Paris Brain Institute

A portrait of Prof. Alexis Brice, a middle-aged man with short, light-colored hair and glasses, wearing a dark suit, a light blue shirt, and a dark tie with small white polka dots. He is standing in front of a large window with a view of a city building.

” IN THE FACE OF COVID-19, THE ENTIRE PARIS BRAIN INSTITUTE COMMUNITY HAS PROVEN ITS STRENGTH, ABILITY TO DESIGN NEW APPROACHES, NEW PROJECTS, LEADING TO MANY SCIENTIFIC BREAKTHROUGHS. ALTHOUGH THE PANDEMIC IS NOWHERE NEAR OVER, I AM CONFIDENT THAT IT REINFORCED OUR COLLECTIVE VALUES AND THAT THESE HAVE BECOME A MAJOR STRENGTH FOR THE INSTITUTE. “SAFETY”, “ANTICIPATION” AND “CONTINUITY” HAVE BEEN OUR KEYWORDS IN THIS CRISIS SINCE DAY ONE. THANKS TO THE SUPPORT OF OUR IT TEAMS, WE ADAPTED TO THE SITUATION PROMPTLY TO ENABLE WORKING FROM HOME AS MUCH AS POSSIBLE. WORKING CONDITIONS ON-SITE WERE ALSO ADAPTED AND MADE SAFE WITH THE SUPPORT OF OUR LOGISTICS TEAMS AND RESPECTED PHYSICAL DISTANCING BY EACH AND EVERY ONE OF US AT THE INSTITUTE. THE INSTITUTE ALSO IMPLEMENTED AND CARRIED OUT COVID-19 SALIVA PCR TESTS ON A VOLUNTARY AND ANONYMOUS BASIS FOR INSTITUTE PERSONNEL, TO ENSURE OUR STAFF’S SAFETY.

DESPITE THE PANDEMIC, THE INSTITUTE UPHELD A REMARKABLE RESEARCH DYNAMIC IN 2020 WITH CONTINUED SUCCESS, INCLUDING THE RECRUITMENT OF SEVERAL RESEARCHERS, AWARDS, AND HIGHLY COMPETITIVE FUNDING INCLUDING OUR 15<sup>TH</sup> ERC (EUROPEAN RESEARCH COUNCIL) GRANT. THIS YEAR ALSO SAW AN UNPARALLELED NUMBER OF PUBLICATIONS FROM OUR RESEARCHERS IN TOP SCIENTIFIC AND MEDICAL JOURNALS. THIS IS A DIRECT RESULT OF AMBITIOUS AND HIGH-RISK PROJECTS LAUNCHED 3 TO 5 YEARS AGO THAT ARE COMING TO FRUITION.

THE INSTITUTE WAS ALSO INVOLVED IN RESEARCH ON COVID-19 WITH THE LAUNCH OF THE COVID NEUROSCIENCE COHORT TO STUDY NEUROLOGICAL AND PSYCHIATRIC CONSEQUENCES OF SARS-COV-2 INFECTION.

I WOULD LIKE TO TAKE A MOMENT TO ACKNOWLEDGE PROF JEAN-YVES DELATTRE, OUR INSTITUTE’S MEDICAL DIRECTOR AND DIRECTOR OF THE MEDICAL-UNIVERSITY NEUROSCIENCE DEPARTMENT AT PITIÉ-SALPÊTRIÈRE AP-HP HOSPITAL, WHO RETIRED LAST NOVEMBER. HIS RETIREMENT WAS A VERY TOUCHING MOMENT FOR THE INSTITUTE COMMUNITY, AND A TRIBUTE TO HIS CONCERN FOR HUMANKIND AND HIS EXCEPTIONAL INVOLVEMENT. PROF CATHERINE LUBETZKI IS TAKING OVER TO CONTINUE OUR ACTIONS TO REINFORCE THE RELATIONSHIP BETWEEN OUR INSTITUTE AND CLINICAL UNITS AT THE HOSPITAL. PATIENTS ARE TRULY AT THE HEART OF OUR RESEARCH.

WE KNOW THAT THE NEXT FEW MONTHS WILL REMAIN UNCERTAIN AS WE WAIT FOR VACCINATION LEVELS TO RISE. IN ADDITION TO PROTECTING HEALTH AND WELL-BEING, WE MUST ALSO PROTECT OUR RESEARCH DYNAMIC. DEVELOPING NEW COLLABORATIONS AND INTERDISCIPLINARY APPROACHES, GROUNDBREAKING PROJECTS ON THE NERVOUS SYSTEM AND ITS PATHOLOGIES, AND INVESTING IN NOVEL TECHNOLOGY DEVELOPMENT REMAIN ABSOLUTELY ESSENTIAL. MEDICAL RESEARCH MUST REMAIN A PRIORITY FOR SOCIETY, AND WE HAVE AN A MAJOR ROLE TO PLAY. ”

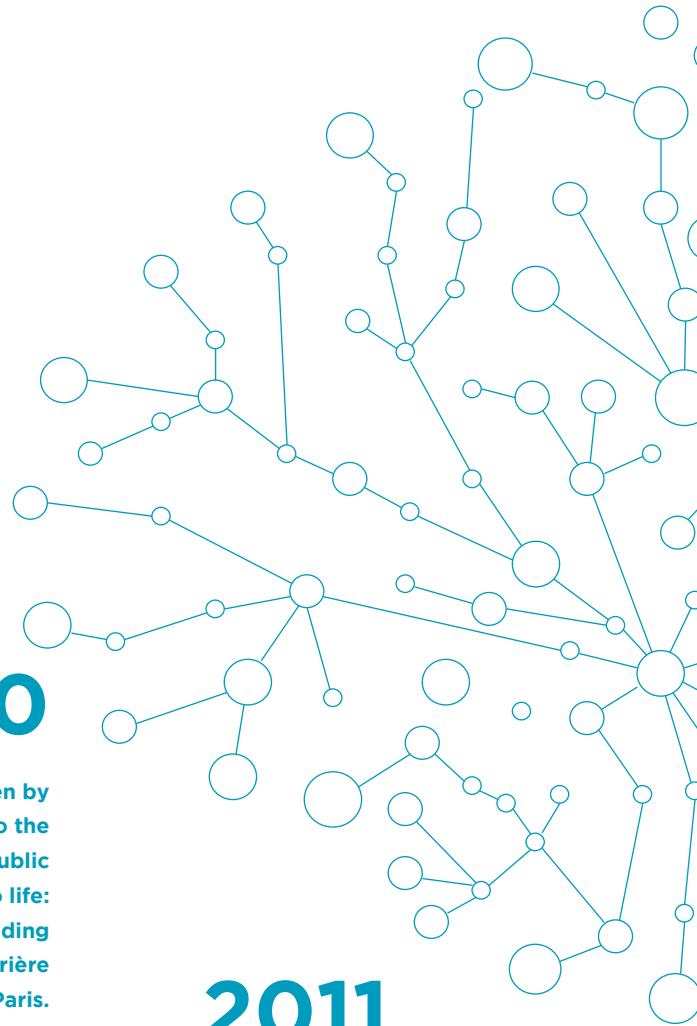
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**Prof. Alexis Brice,**  
Executive Director of Paris Brain Institute



# PARIS BRAIN INSTITUTE, A REVOLUTIONARY MODEL TO ACCELERATE THE FIGHT AGAINST BRAIN DISEASES

PARIS BRAIN INSTITUTE WAS BUILT ON THE INVOLVEMENT OF CELEBRITIES AND PUBLIC INSTITUTIONS WITH A SHARED GOAL : UNDERSTANDING THE BRAIN AND TREATING NEUROLOGICAL AND PSYCHIATRIC ILLNESS.



## 2003 - 2010

An idea turns into a project, driven by hope and motivation ! Thanks to the founding members, donors and public stakeholders, the Institute comes to life: in 2020, the Paris Brain Institute building was inaugurated within Pitié-Salpêtrière Hospital in Paris.



## 2011

The Clinical Investigation Center (AP-HP, Inserm) opens its doors to patients taking part in clinical trials within the Institute.

Obtaining the Carnot label, to accelerate the development of new technologies in the fields of neurology and psychiatry



## 2012

ICM becomes one of 6 centers for scientific and medical excellence supported by the Investments in the Future project implemented by the Ministry of Higher Education and Research and the Ministry of Health (IHU).

Inauguration of iPEPS-ICM, the first startup incubator dedicated to nervous system diseases.







ICM's funding is renewed and supplemented for the IHU program.

ICM receives state certification as part of the "French Tech Seed" fund managed by Bpifrance.

This certification confirms the dynamic strategy implemented by the iPEPS bio-incubator to promote entrepreneurship with strong expertise in the fields of neurology and psychiatry.



# 2019

# 2018

**Identification of compensation mechanisms in Alzheimer's disease**

with the INSIGHT cohort of elderly subjects by Professor Bruno Dubois's (AP-HP, Sorbonne Université) team with Pitié-Salpêtrière Hospital.



**Paris Brain Institute launches its training center, Open Brain School,**

to share neuroscience knowledge and strengthen training for future researchers and doctors on a national and international level.

# 2017

**Creation of the Neuroinformatics Center** for cutting-edge research and medicine.



# 2014

**Acquisition and operation of a PET-MRI** with AP-HP, the first in France with both clinical and research use.

# 2016

**Development of a new imaging technique** to visualize remyelination in patients with multiple sclerosis, impossible to see with classic imaging techniques.

# 2015

Along with its institutional partners, **the Institute receives certification as a "Center for excellence in neurodegenerative diseases"** as part of a national program on neurodegenerative diseases.

**Bioserenity, a startup incubated at Paris Brain Institute, designs the Neuronaut :** smart clothing for at-home care and monitoring of patients with epilepsy. Today, Bioserenity has over 500 employees worldwide. The company is part of the Next 40, an index created by the French government in 2019 to track the 40 French start-ups with very high potential.



**A decade of progress and innovations**

# IN 2020

## **COVID-19 PANDEMIC : PARIS BRAIN INSTITUTE CONTINUES TO MOVE FORWARD**

As you will discover throughout this report, in the context of the COVID-19 pandemic, Paris Brain Institute has made every effort to continue its research activity as best as possible and has actively participated in the fight against the virus and in helping those affected by it.

From the start of the pandemic, Paris Brain Institute was in close contact with the medical teams at Pitié-Salpêtrière Hospital (AP-HP) and made equipment, goods, and expertise available. All clinicians working at Paris Brain Institute and in the hospital's university medical neuroscience department are on board to support the medical teams caring for patients with COVID-19.

## **PARIS BRAIN INSTITUTE'S CARNOT CERTIFICATION RENEWED FOR 4 YEARS**

Carnot certification is a French certification created in 2006 with the aim of developing research partnerships between public laboratories and economic players (mainly companies). The Ministry of research awards this certification to Carnot institutes following a very selective call for applications.

The renewal of our Carnot certification for 4 years will allow us to fund Carnot Maturation projects, the Skills Build-up program, Carnot Training and scientific resourcing actions including the organization of conferences at Paris Brain Institute, editor days, and more.



## NATIONAL AWARENESS CAMPAIGN

#VOTRECERVEAUVOUSRENDREMARQUABLE

To support its recent name change, Paris Brain Institute launched a national awareness poster campaign entitled #votrecerveauvousrendremarquable (“your brain makes you remarkable”), produced pro bono by historical partners Publicis and JCDecaux.

Through portraits of great personalities from the politics, sports, culture and the arts including Simone Veil, Rafael Nadal, and Jean Reno, and a slogan filled with meaning, this campaign aims to make each of us aware of the vital importance of this fascinating organ, the most complex in the human body.



## PARIS BRAIN INSTITUTE CELEBRATES THE EXCEPTIONAL INVOLVEMENT OF PROFESSOR JEAN-YVES DELATTRE AND THE ARRIVAL OF PROFESSOR CATHERINE LUBETZKI

Professor Jean-Yves Delattre, Director of the Medical University Neuroscience Department and former Medical Director of Paris Brain Institute, retired in November 2020. The entire Paris Brain Institute teams thank Professor Jean-Yves Delattre for his exceptional commitment and recognize his remarkable career at patients' bedsides.

Professor Jean-Yves Delattre is replaced in these positions by Professor Catherine Lubetzki (AP-HP/Sorbonne Université).



” I AM HAPPY TO HAVE WORKED WITH THE TEAMS AT PARIS BRAIN INSTITUTE. I THINK IT'S A WONDERFUL INSTITUTION, A TREMENDOUS OPPORTUNITY FOR THE UNIVERSITY MEDICAL NEUROSCIENCE DEPARTMENT. OUR RELATIONSHIPS ARE STRONG, OUR DIFFERENCES MAKE US RICHER. I WISH GOOD LUCK AND MUCH SUCCESS TO PROF. CATHERINE LUBETZKI, MY TRAVELING COMPANION AT PITIÉ-SALPÊTRIÈRE HOSPITAL FOR DECADES, WHO HAS ALL THE QUALITIES NEEDED TO HELP THE INSTITUTE ACCOMPLISH ITS MISSION TO "SEARCH, FIND, CURE" ! ”

Prof. Jean-Yves Delattre



” IT IS AN HONOR FOR ME TO REPLACE JEAN-YVES DELATTRE, A LONGTIME FRIEND, FOR WHOM I HAVE SUCH ESTEEM AND AFFECTION. AS A CONTINUATION OF HIS ACTIONS, I HOPE TO PROMOTE INTERACTIONS BETWEEN CAREGIVERS AND RESEARCHERS, AND DEVELOP CLINICAL RESEARCH IN CONNECTION WITH FUNDAMENTAL RESEARCH. ”

Prof. Catherine Lubetzki

## ADIÓS CORONA, THE WEBSITE THAT DECODES INFORMATION ON COVID-19

It can be difficult to find the right information in real time regarding the pandemic we are currently experiencing. That's why a team of scientists, and notably several researchers from Paris Brain Institute including **Claire Wyart ( Inserm), designed a website that analyzes publications on COVID-19 and gives advice on proper collective behavior to stop the spread of the virus.**

## CURE-ND - A UNIFIED RESPONDE TO NEURODEGENERATIVE DISEASES

A new alliance, CURE-ND, was launched at the end of 2020. It brings together four highly recognized European partners in neurodegenerative diseases: DRI in Great Britain, VIB in Belgium, DZNE in Germany and our Institute. A first launch event was organized in December with more to follow at the start of 2021.



" TOGETHER, WE REPRESENT A CRITICAL MASS OF OVER 2,000 RESEARCHERS. WE HAVE OBVIOUS SYNERGIES AND COMPLEMENTARITIES BETWEEN OUR CENTERS, WHICH SHOULD ALLOW FOR A VERY EFFECTIVE AND POWERFUL RESPONSE. OUR ALLIANCE IS PART OF A SHARED EFFORT TO ACCELERATE THE PACE OF SCIENTIFIC DISCOVERY AND PROMOTE BREAKTHROUGHS IN THE FIELD OF NEURODEGENERATIVE DISEASES. "

**Prof. Alexis Brice,**  
Executive Director of Paris Brain Institute

## THE MEDTECH GENERATOR & ACCELERATOR PROJECT REPRESENTED BY IPEPS, RECIPIENT OF THE SIA/ FUTURE INVESTMENT CALL FOR PROJECTS

**This consortium, led by Paris Brain Institute, Institut Imagine, Institut de la Vision and Institut Pasteur, aims at developing innovative support programs to accelerate growth and development of startups specializing in health and artificial intelligence in the field of neurosciences, genetics, and rare diseases.**

Public funding will be provided by the Future Investment Program (PIA) over the first two years. This announcement marks the Institute's desire to combine research with innovative projects to increase discoveries to benefit patients, in particular through its iPEPS - The Healthtech Hub incubator.



## A NEW CAMPAIGN ON BEQUESTS

Through the message of this campaign based on the message "**At Paris Brain Institute, it is not only researchers who advance research**", the Institute wished to honor those who decide to transfer their estate to the Paris Brain Institute or to designate it as the beneficiary of a life insurance contract. Thanks to them and their financial support, Paris Brain Institute can go further in its research and accelerate its discoveries, by carrying out innovative research programs, by acquiring cutting-edge equipment or by recruiting teams of researchers based on criteria of excellence.

# OUR RESEARCH TEAM'S ACHIEVEMENTS



## PRESTIGIOUS AWARDS



**Mathias Pessiglione (Inserm)**  
Halphen Award



**Alberto Bacci (Inserm)**  
Camille Woringer Award from the Medical Research Foundation



**Stanley Durrleman (Inria)**  
Young Researcher Award – INRIA/Académie des Sciences



**Maha Dahawi**  
L'Oréal - UNESCO for women in science 2020 Young talent award



**Mathilde Lapoix**  
Pariscience Festival Symbiose Award



**Claire Wyart (Inserm)**  
ERC Consolidator Grant

## EXCELLENT RESULTS FROM THE ANR GENERIC CALL FOR PROPOSALS

Every year, the generic call for proposals from the ANR (National Research Agency) funds research by various players in the scientific community. This very competitive call for projects rewards innovative projects according to four categories :

- **JCJC** : Young researcher ;
- **PRC** : Collaborative research project ;
- **PRCE** : Collaborative research project - Company ;
- **PRCI** : Collaborative research project - International

**This year, 16 projects by researchers from Paris Brain Institute were among the final recipients. The Institute's success rate is 34%, which is twice the national average (16.8%), a sign of the quality and soundness of the projects put forward.**



## 15<sup>th</sup> ERC FUNDING FOR THE INSTITUTE

**In 2020, Claire Wyart, team leader (Inserm) at Paris Brain Institute, was awarded an ERC Consolidator Grant, competitive European funding, for the scientific excellence of her "Exploratome" project. This project aims to decipher the spatial-temporal structure of motor patterns by studying how sensory information can induce change in locomotor states.**

Each year, the European Research Council (ERC) encourages the best scientific projects through competitive calls for projects open to all researchers in the European community. The ERC Consolidator Grants are awarded to researchers with at least seven and up to twelve years of experience after their doctoral degree and an excellent scientific background.

# KEY FIGURES

## PARIS BRAIN INSTITUTE IN THE PAST **10 years**



**11**

new  
teams

recruited by international  
calls for applications



**6281**

**PUBLICATIONS**

since 2012, including 1500  
with an Impact Factor > 7  
and **1,318 in the top 10%**  
of citations  
(**265 in the top 1%**)

Over

**70**

incubated  
companies



**88 M€**

**IN GRANTS**

received since 2012

**7**

**MEDICAL  
DEVICES**

designed  
at the  
Living Lab

**15**

**ERC GRANTS**

(European Brain Council)

**400 M€**

**IN  
FUNDRAISING**

Over  
**900**

**JOBS CREATED**

**8**

innovative  
products  
launched

**10** YEARS

of progress  
& innovation



PARIS BRAIN INSTITUTE  
IN **2020**

**25**

**RESEARCH  
TEAM**

selected by an International  
Scientific Committee



**734**  
people



**37** start-ups incubated

in 3 locations



**5 fields of research :**

- Molecular & cellular neurobiology
- Integrative neurophysiology
- Cognitive neuroscience
- Clinical & translational neuroscience
- Computational neuroscience

**13**

clinical research  
infrastructures

**173**

clinical trials

**10**

**CUTTING-EDGE  
TECHNICAL  
PLATFORMS**

including BioBanks  
(>55,000 patients,  
10,000 tumors, 330 brains)

**1 CARE LAB**

and

**1 FABLAB**



**600 publications** in international  
scientific journals

**12 training programs**  
at the Open Brain School  
with **over 1,500 participants**

**244,283**  
donors







2020

A YEAR

FILLED WITH

SCIENTIFIC

BREAKTHROUGHS

---

**2020 SAW THE CULMINATION OF MAJOR BREAKTHROUGH PROJECTS LED BY RESEARCHERS AT PARIS BRAIN INSTITUTE WITH MAJOR SCIENTIFIC PROGRESS. MAJOR PUBLICATIONS SPANNED ALL FIELDS OF RESEARCH COVERED BY OUR TEAMS, FROM MOLECULAR AND CELLULAR NEUROBIOLOGY TO COMPUTATIONAL NEUROSCIENCE, NEUROPHYSIOLOGY, CLINICAL WORK AND COGNITION. PROOF THAT DESPITE THE DIFFICULT CONTEXT, PARIS BRAIN INSTITUTE TEAMS REMAIN INVOLVED TO BRING THEIR PROJECTS TO FRUITION.**

---

### **THE MENINGEAL LYMPHATIC NETWORK, A NEW POSSIBILITY FOR TREATMENT OF BRAIN TUMORS**

Does the recently characterized meningeal lymphatic network play a role in the brain's immune protection? Does this network facilitate the entry of antigen-specific immune cells into brain tissue? The research carried out by Éric Song from Akiko Iwasaki's team (Yale, United States) and Jean-Léon Thomas (Inserm/Yale) at Paris Brain Institute highlighted a beneficial role for the meningeal lymphatic vascular network in the short and longer-term treatment of glioblastoma multiforme (GBM). Strengthening the meningeal lymphatic vessel network increases the traffic of tumor antigen-presenting cells from the meninges to the lymph nodes. The authors conclude that the major role of the meningeal lymphatic network would be to transport the immune alert message, triggering the activation of lymphocytes directed against the tumor, from the meninges.

- Song E, et al. *Nature*, January 2020.

### **TOURETTE'S SYNDROME : MOTOR IMPULSES DO NOT PREDICT PATIENT TICS**

Tourette's syndrome is a highly heterogeneous neuropsychiatric and neurodevelopmental pathology characterized by tics, which are sudden and repeated involuntary movements. Cyril Atkinson-Clément and Yulia Worbe (Sorbonne University/AP-HP) found that control of motor impulsivity, which characterizes the ability to inhibit a movement or an action that has already been initiated, is not correlated with tics in patients with Tourette's syndrome. This discovery sheds light on this pathology, where the search for predictive markers for the progression of the disease is a major issue in order to better manage patient care.

- Atkinson-Clément C, et al. *Cortex*, 2020.

## Research

### **THE FIRST COMPLETE MAPPING OF CEREBRAL VASCULARIZATION**

Nicolas Renier's team (Inserm) succeeded in reconstructing the entire cerebral vascular system of mice with unprecedented precision. While many neurological and psychiatric pathologies have a vascular component, the complexity of the network of blood vessels, intimately intertwined with neural cells, complicates research. The instrument developed by the research team paves the way for important findings on the role of cerebral vascularization in the development of many brain diseases.

- Kirst C, et al. *Cell*, February 2020.



### **ONSET OF BEHAVIORAL INDIVIDUALITY IN THE BRAINS OF FLIES : A GENERAL PRINCIPLE FOR NEURODEVELOPMENTAL ORIGIN OF PERSONALITY ?**

Where does our individuality come from? What makes us unique in our behavior? Could the answer lie in our brain? Bassem Hassan and his team discovered a random neural circuit formation mechanism in the brain of the *Drosophila melanogaster* fly that causes individual behavior. These findings may represent a general principle of how certain aspects of individuality emerge in the brain.

- Linneweber GA, et al. *Science*, March 2020.

### **FUNDAMENTAL PROPERTIES OF VALUE SYSTEMS WITHIN THE BRAIN**

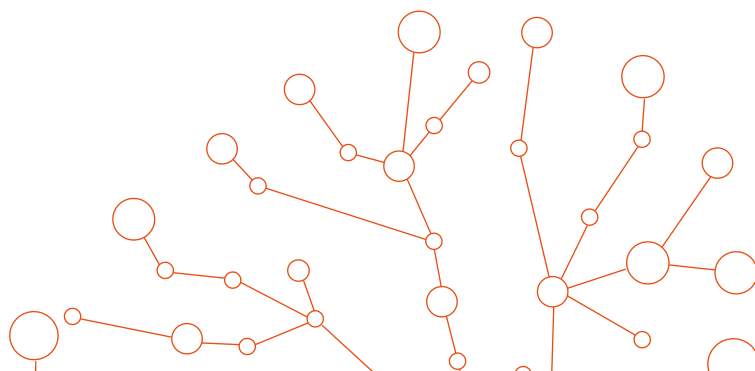
Which cognitive mechanisms help us make decisions? Why do we prefer some options over others? How is the value of an option estimated by the brain? A study conducted by Alizée Lopez-Persem in Mathias Pessiglione's team (Inserm) highlighted the main characteristics of the neural signal involved in value judgments. This study identified four essential properties of the neural signal observed in the orbitofrontal cortex (area of the brain located in the prefrontal cortex, just behind the eye sockets). These four properties explain attribution errors in value judgments. We sometimes believe we are estimating the value of one option, while we are in fact influenced by the value of another.

- Lopez-Persem A, et al. *Nature Neuroscience*, April 2020.

### **GENETICS AND MECHANISMS INVOLVED IN DRUG RESISTANCE IN BRAIN TUMORS**

Mehdi Touat and Franck Bielle (AP-HP/Sorbonne University), from the team led by Marc Sanson and Emmanuelle Huillard and from the neuro-oncology and neuropathology departments of the Pitié-Salpêtrière AP-HP Hospital, in collaboration with Yvonne Li, Rameen Beroukhim, Pratiti Bandopadhyay and Keith Ligon of the Dana Farber Cancer Institute (Harvard Medical School, Boston), highlighted genetic changes in certain recurrent gliomas that lead to resistance to chemotherapy. The study, beyond its very comprehensive approach in molecular and mechanistic analysis, deals with the largest sample ever to be explored in brain tumors. The results obtained will make it possible to provide information on the response to chemotherapy during the diagnosis of tumors and during treatment, in particular in the event of recurrence after chemotherapy, where the use of high-throughput DNA sequencing techniques would make it possible to tailor treatments to patient's needs.

- Touat M, et al. *Nature*, April 2020.



## **ACTIVATION OF THE INNATE IMMUNE SYSTEM WITHIN THE CENTRAL NERVOUS SYSTEM : A BIOMARKER FOR DISEASE PROGRESSION IN MULTIPLE SCLEROSIS ?**

A study conducted by Benedetta Bodini (AP-HP / Sorbonne University) and Émilie Poirion, in the team led by Bruno Stankoff and Catherine Lubetzki (AP-HP/Sorbonne University), has enabled the development of a new method to map activation of microglia in the white matter of the central nervous system that contains the majority of neuron axons. The researchers succeeded in reconstructing individualized activation profiles of innate immune cells, and pinpointed white matter lesions presenting a persistent activation of the microglia in patients when they were considered as perfectly stable and inactive in standard MRIs. Activation of microglia in lesions is a promising biomarker for the evolution of patient disability, which will need to be confirmed by future prospective studies. This will hopefully lead to more efficiently adapting the treatment of patients with multiple sclerosis, assessing new therapies, and preventing the progression of disability as much as possible.

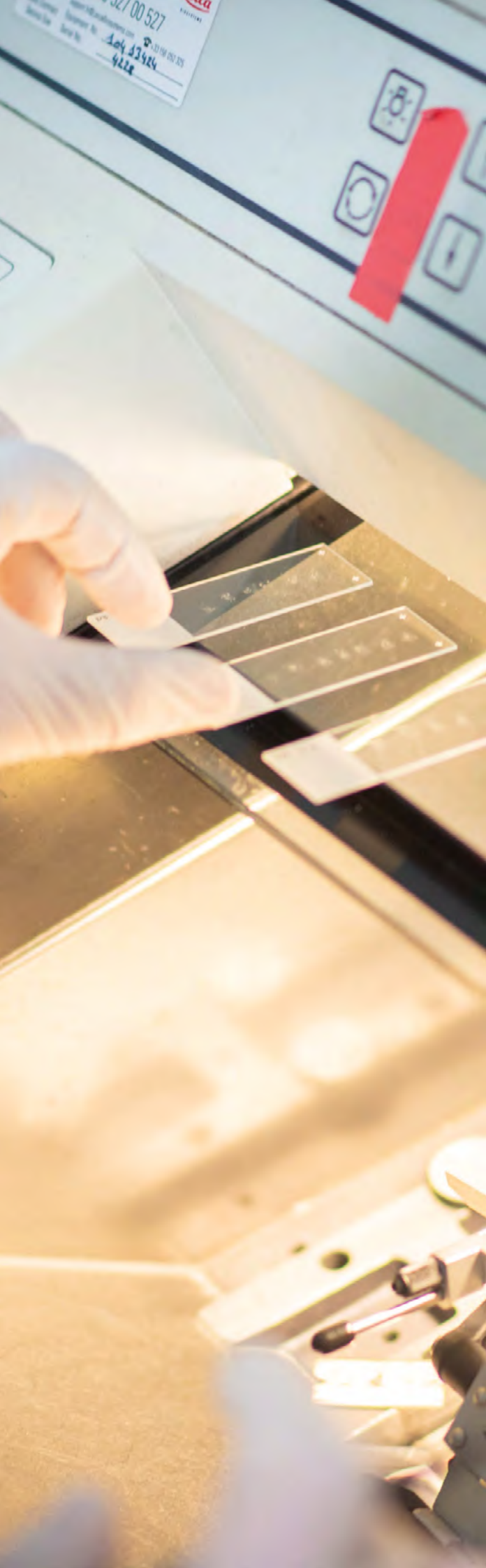
**- Bodini B, et al. *J Nucl Med*, 2020.**

## **MYELIN DEFICIT LEADS TO COGNITIVE DISORDERS IN A SCHIZOPHRENIA MODEL**

Using an experimental model of schizophrenia, Dorien Maas and Brahim Nait-Oumesmar (Inserm) in collaboration with Gerald Martens (Donders Institute, Nijmegen, Netherlands) demonstrated that spatial memory and social behavior disorders depend on the prefrontal cortex. These cognitive disorders have been associated with hypomyelination of parvalbumin interneurons in the prefrontal cortex, following a halt in oligodendrocyte maturation. In addition, researchers have shown that environmental enrichment (physical activity, social interactions, etc.) corrects developmental alterations in myelination of the prefrontal cortex. These results pave the way for new behavioral and/or pharmacological treatment perspectives to promote myelination in schizophrenia.

**- Maas DA, et al. *Nature Communications*, 2020.**





## **A NEW CLINICAL SIGN**

### **POUR SONDER L'ÉTAT DE CONSCIENCE**

Lionel Naccache (AP-HP/Sorbonne University) and his team have identified and validated a new clinical examination sign that highlights enhanced brain function in non-communicating patients. They observed that the startle reflex response to noise (eyelid blinking after a sudden sound) exhibited habituation in patients who were able to predict and anticipate this repetition. Beyond this precious diagnostic information, the presence of this clinical sign that is easy to spot at the patient's bedside also made it possible to predict an improvement in their state of consciousness six months later. The invention of new clinical signs based on the latest structural and functional brain imaging techniques also demonstrates the contemporary vitality and constant renewal of neurological semiology.

- Hermann B, et al. *Brain*, June 2020.

## **IMPROVING CONSCIOUSNESS WITH ELECTRICAL STIMULATION OF THE BRAIN CORTEX**

A study by Lionel Naccache's team (AP-HP/Sorbonne University) reveals how transcranial direct current electrical stimulation (tDCS) of the frontal lobe of patients with disorder of consciousness improves their state of consciousness. These results are important both from a clinical standpoint - by paving the way for the development of new treatment strategies for tailored stimulation - and from a fundamental research standpoint by confirming the importance of the prefrontal cortex and the fronto-parietal network in the physiology of consciousness. These findings are in line with the global neuronal space theory developed over the past twenty years by Stanislas Dehaene, Jean-Pierre Changeux and Lionel Naccache.

- Hermann B, et al. *Scientific reports*, June 2020.

## **LARGE-SCALE EXPLORATION OF GENETIC FORMS OF PARKINSON'S DISEASE**

In 1990, a large cohort on Parkinson's disease was set up by Professor Alexis Brice as part of a national and international network coordinated by Paris Brain Institute at Pitié-Salpêtrière Hospital. The patients included participate in genetic analysis as well as a clinical evaluation. Within this cohort and in over 1,600 individuals, Suzanne Lesage (Inserm) and her collaborators searched for abnormalities in three genes, PRKN (Parkin), PINK1 and DJ-1, the mutations of which are the

most frequent cause of recessive genetic forms of early-onset Parkinson's disease before the age of 40. Their recent findings also provide valuable information to guide genetic testing and counseling in newly diagnosed patients and their families. They will also make it possible to stratify patients into cohorts for future clinical trials targeting deficits associated with PRKN and PINK1 mutations, and more generally to monitor symptom progression.

- Lesage S, et al. *Annals of Neurology*, May 2020.

### **HUNTINGTON'S DISEASE :** **CEREBRAL ANOMALIES** **COULD BE DETECTED IN EMBRYOS**

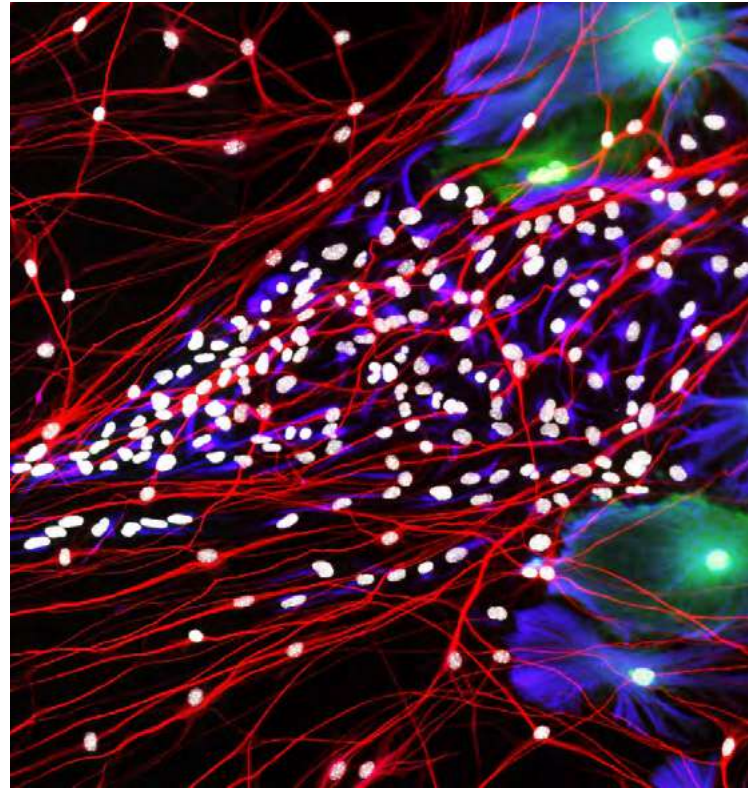
Huntington's disease is a genetic neurological disease with typical onset in adulthood. Sandrine Humbert (Inserm) at the Grenoble Institute of Neuroscience and Alexandra Durr (AP-HP/Sorbonne University) at Paris Brain Institute discovered abnormalities in the brains of human embryos carrying the mutation responsible for Huntington's disease. This research sheds light on mechanisms of silent disease progression, and when and how to treat patients in the future.

- Barnat M, et al. *Science*, July 2020.

### **CHARACTERIZING** **NEURODEGENERATION OF** **SUBSTANTIA NIGRA THROUGH SPACE** **AND TIME IN PARKINSON'S DISEASE**

Emma Biondetti, a member of the team led by Marie Vidailhet and Stéphane Lehéricy (AP-HP/Sorbonne University), found that there is a progressive decrease in neuromelanin in Parkinson's Disease, visible on MRI, as well as an overall reduction in substantia nigra volume. Changes in neuromelanin begin in the posterior regions of the substantia nigra, more specifically involved in motor function. The results also highlight that the various symptoms (motor, cognitive and behavioral) associated with black matter involvement are observed in distinct regions of this structure. The substantia nigra region therefore associated with the development of motor symptoms is different from that associated with cognitive or behavioral symptoms. This data confirms the value of neuromelanin as a biomarker for the progression of Parkinson's disease and its symptoms. It provides new research directions in the evaluation of the effectiveness of treatments on the progression of the disease in future clinical trials.

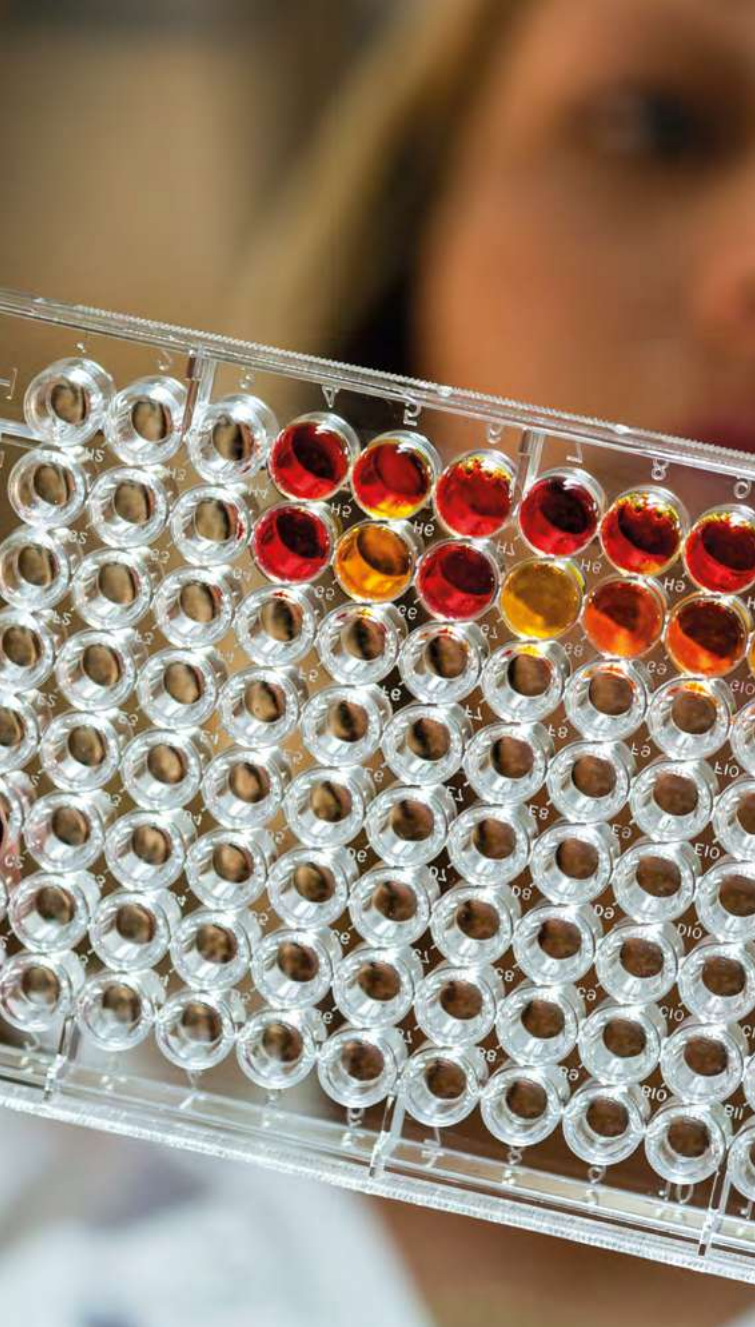
- Biondetti E, et al. *Brain*, 2020.



### **TO PERSEVERE OR TO EXPLORE :** **NEURAL BASES OF THE** **EXPLOITATION - EXPLORATION** **DILEMMA**

Psychiatrist and researcher Philippe Domenech (Henri Mondor AP-HP Hospital), in the "Neurophysiology of repetitive behaviors" team at Paris Brain Institute, along with Sylvain Rheims from the neurology and epileptology department of the Hospices Civils de Lyon Hospital and Étienne Koechlin of École Normale Supérieure - PSL revealed the brain mechanisms behind the decision to explore one's environment in order to establish new strategies. This is the first electrophysiology study to identify brain mechanisms underlying the resolution of the exploitation-exploration dilemma in humans. The identification of a predictive encoding process, the importance of which was already known for perception, demonstrates that it is also essential to executive functions such as decision making, suggesting that it may be a general mechanism implemented throughout the cerebral cortex.

- Domenech P, et al. *Science*, August 2020.



## **NEW DATA CONFIRMS BENEFITS OF DEEP BRAIN STIMULATION TO TREAT OBSESSIVE-COMPULSIVE DISORDER**

A study by researchers and clinicians from Paris Brain Institute and AP-HP (Henri Mondor and Pitié-Salpêtrière Hospitals) confirmed the beneficial effect of deep brain stimulation on several brain structures in severe drug-resistant obsessive-compulsive disorders, highlighting the importance of precise identification of underlying neural networks. Research is still needed to identify precise characteristics predicting patient response to deep brain stimulation.

- **Welter ML, et al. *Biological Psychiatry*, October 2020.**

## **PROMISING RESEARCH ON THERAPY IN AMYOTROPHIC LATERAL SCLEROSIS (ALS)**

ALS is characterized by degeneration of motor neurons, that are directly connected to a muscle and control its contractions. The spinal motor neurons affected in ALS have the specificity of being surrounded both by microglial cells in the spinal cord and by peripheral macrophages in the nerve, the part of the motor neuron that exits the spine to connect the muscle to the periphery. Séverine Boillée's team (Inserm) has found for the very first time that peripheral macrophages play an important role in the development of amyotrophic lateral sclerosis (ALS), paving the way for new therapeutic approaches for patients. In the longer term, development of research aimed at treating neurotoxic macrophages outside the central nervous system, in a less invasive way, could lead to a significant decrease in the death of motor neurons in patients with ALS. These results pave the way for promising research opportunities on treatment.

- **Chiot A, et al. *Nature Neuroscience*, September 2020.**

## **MAKING SENSE OF THE WORLD : THE NEURAL BASIS OF ABSTRACTION**

We are constantly confronted with immense amounts of information from our environment: what we see, hear, smell, the objects we interact with and the situations we experience. In order to navigate this, our brain integrates all of these explicit factors, simplifies and aggregates them to create implicit rules. A study conducted at the Zuckerman Institute at Columbia University (United States) by Jérôme Munuera, co-first author and researcher at Paris Brain Institute, and his collaborators, highlights a «geometry of abstraction». During the neural response, the number of dimensions is reduced to the most essential, leaving only major contextual elements to generate optimal behavior without saturating the brain with unnecessary information. This discovery opens new perspectives in certain neuropsychiatric deficits and in the field of artificial intelligence. By better understanding the integration of different dimensions in the brain and neural networks, it may be possible to apply this integration to algorithms and to develop new and more efficient machine learning techniques.

- **Bernardi S, et al. *Cell*, October 2020.**

## **CLINICAL VALIDATION OF AN AUTOMATIC LEARNING ALGORITHM FOR DIAGNOSIS OF PARKINSONIAN SYNDROMES**

Researchers and clinicians from Paris Brain Institute at Pitié-Salpêtrière AP-HP Hospital have validated the clinical use of a machine learning algorithm using magnetic resonance imaging (MRI) data. This algorithm differentiates subjects suffering from parkinsonian syndromes such as Parkinson's disease, progressive supranuclear palsy or multisystem atrophy. In the future, the addition of new biomarkers, such as the measurement of iron deposits in tissues, could increase diagnostic precision. The integration of this type of algorithm into the clinical management of Parkinson's disease may improve future diagnosis of parkinsonian syndromes at an early stage.

- Chougar L, et al. *Movement Disorders*, November 2020.

## **A NEW CEREBRAL CHANNELOPATHY THAT ASSOCIATES INTELLECTUAL DISABILITY AND ABNORMAL MOVEMENTS**

Dysfunctions of ion channels – or channelopathies – in the brain are currently associated with over 30 neurological diseases such as epilepsy or cerebellar ataxia. A study conducted by Fanny Mochel (AP-HP/Sorbonne Université) and Christel Depienne identified a new cerebral channelopathy originating from dominant mutations in the KCNN2 gene, encoding the SK2 ion channel. This new pathology includes strongly heterogeneous symptomatology and requires multidisciplinary care with genetics, to look for KCNN2 mutations, neuropediatrics, and neurology to manage cognitive and motor symptoms in patients.

- Mochel F, et al. *Brain*, 2020.



## **MULTIPLE SCLEROSIS : CELLS IN CHARGE OF MYELIN REPAIR DISPLAY NO INTRINSIC ANOMALIES**

As part of an international consortium, Anne Baron-Van Evercooren (Inserm) and Tanja Kuhlmann (Münster, Germany) found that the lack of remyelination in some patients with relapsing-remitting multiple sclerosis is not linked to an intrinsic defect in oligodendrocytes, myelinating cells of the brain, but in the toxic and inflammatory environment of the lesions.

- Starost L, et al. *Acta Neuropathologica*, September 2020.

- Mozafari S, et al. *Science Advances*, September 2020.



## **NEW FINDINGS ON A MAJOR PROTEIN INVOLVED IN ALZHEIMER'S DISEASE**

A study conducted by Irimi Kessissoglou, in Bassem Hassan's team (Inserm), reveals new functions for the equivalent of the amyloid precursor protein (APP) in *Drosophila* flies in a physiological context and underlines its importance for homeostasis of the adult brain. Findings regarding the consequences of loss of APP suggest a strong link between its physiological functions and the deficiencies observed in familial Alzheimer's disease. The initial effects observed in flies lacking APP support the idea of long-term changes in the brain occurring before the onset of clinical symptoms, suggesting new research into early endosomes and neuron and glial cell interactions in this disease.

- Kessissoglou IA, et al. *PLoS Biology*, December 2020.

### **DISCOVERY OF A PLASMA SIGNATURE OF FRONTO-TEMPORAL DEGENERATION AND AMYOTROPHIC LATERAL SCLEROSIS LINKED TO C9ORF72 GENE MUTATION**

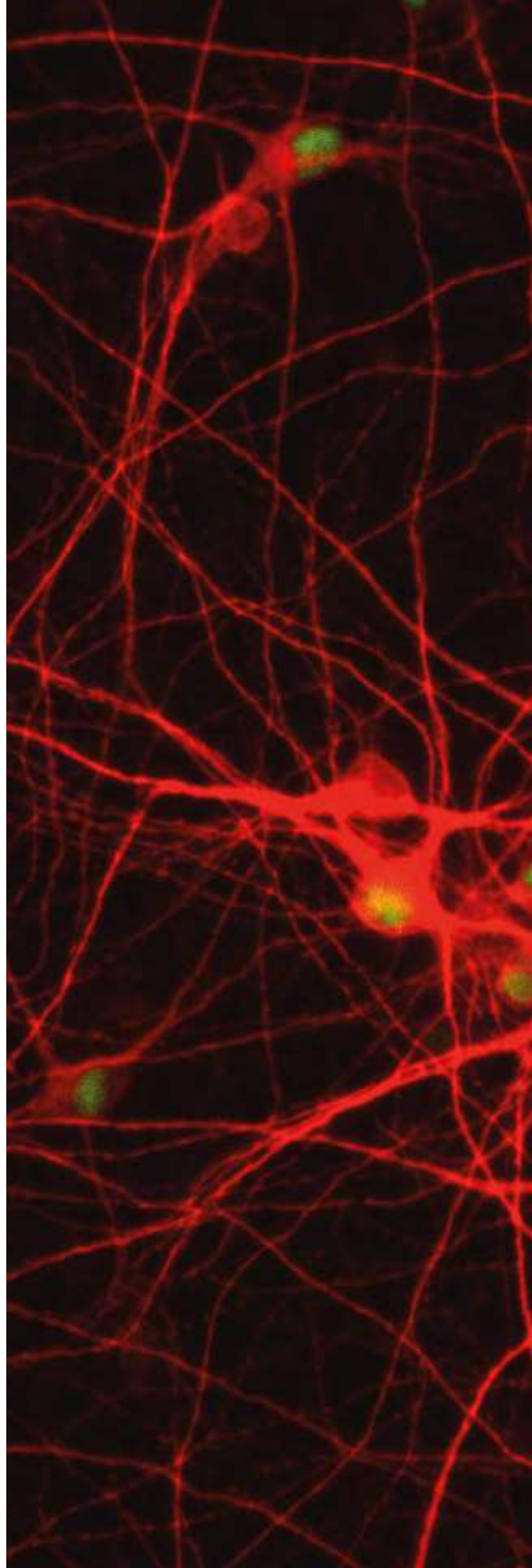
A joint study by the teams led by Olivier Colliot (CNRS) and Isabelle Leber (AP-HP) at Paris Brain Institute and Inria (Rennes and Paris centers) revealed, for the very first time, microRNA plasma signatures in individuals with symptomatic or pre-symptomatic frontotemporal degeneration and amyotrophic lateral sclerosis. The discovery of this potential new biomarker represents an important advance in assessing clinical progression of patients and efficacy of future treatment candidates in therapeutic trials.

- Kmetzsch V. et al. *Journal of Neurology, Neurosurgery and Psychiatry*, 2020.

### **EARLY COGNITIVE DISORDERS IN SUBJECTS AT RISK OF DEVELOPING FTD/ALS**

Patients with frontotemporal degeneration show impairment in cognitive and behavioral inhibition, which allows us not to respond to all the stimuli we are confronted with on a daily basis and to suppress behaviors unsuited to the different situations we face. A study that stemmed from a collaboration between the teams of Isabelle Leber (AP-HP) and Lara Migliaccio (Inserm) at Paris Brain Institute found that assessing cognitive inhibition is a highly important marker in the early detection of abnormalities in individuals at risk of developing a neurodegenerative pathology. This assessment of cognitive inhibition may prove to be essential to stratify patients and identify asymptomatic carriers of the mutation in order to set up treatment trials.

- Montembeault M, et al. *Journal of Neurology, Neurosurgery and Psychiatry*, 2020.







## NEUROCOVID -19 CALL FOR PROJECTS

Very shortly after the onset of the pandemic, neurologists suspected that the nervous system may be affected, directly or indirectly, during a COVID-19 infection. In June, Paris Brain Institute launched an internal call for projects in collaboration with Institut Pasteur (IP) to finance new proofs of concept (new models, development of instruments and technology for analysis, etc.) on how infection impacts a healthy or pathological nervous system. This call for projects was launched thanks to the support of its patrons and donors, including the OCIRP Foundation and Accuracy.

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4

### PROJECTS

#### WERE SELECTED :

- > **COV-2 BRAIN** : Pathophysiology of central nervous system infection by the SARS-CoV-2 coronavirus, by Nicolas Renier (Inserm) and Stéphane Haik (Inserm)
- > **COV-2-NEURO-SENSING** : Study of the interaction between SARS-CoV-2 and sensory neurons of the central nervous system, by Claire Wyart (Inserm) and Jean-Pierre Levrard (IP)
- > **BRAIN-COV** : Characterization of brain lesions due to infection by SARS-CoV-2, by Mathieu Santin (Paris Brain Institute), Danièle Seilhean (AP-HP/Sorbonne University), and Roberto Toro (IP)
- > **COVESSEL** : Identification of the infection pathways of the SARS-CoV-2 coronavirus in the central nervous system, by Nicolas Renier (Inserm) and Pierre-Marie Lledo (IP)

# CUTTING-EDGE TECHNOLOGICAL PLATFORMS

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**IN 2020, THE INSTITUTE COMMITTED TO INCREASING PLATFORM INTERDISCIPLINARITY, AND OFFER RESEARCH TEAMS A WIDER ARRAY OF SERVICES. DESPITE THE HEALTH CRISIS, INSTITUTE PLATFORMS MAINTAINED HIGH-LEVEL SERVICE THAT ALLOWED SCIENTIFIC PROJECTS TO PROGRESS AND ATTAIN COMPLETION.**

**STRATEGIC CHANGES ARE IN PROGRESS TO OPTIMIZE PLATFORM ACTIVITY AT THE INSTITUTE. THEY WILL ALLOW FOR BETTER INTEGRATION WITHIN THE SCIENTIFIC ECOSYSTEM AND THE INSTITUTE'S STRATEGY, WILL HELP PRIORITIZE SCIENTIFIC AND TECHNICAL GOALS, AND MAINTAIN A LEVEL OF EXCELLENCE FOR THE INSTITUTE'S PLATFORMS.**

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## **EVOLUTION OF THE BIOINFORMATICS PLATFORM**

Lars Jorgensen joined the bioinformatics platform in 2020 in the role of operational manager. He brings extensive international experience to his new position and is currently working with his team on a full redesign of platform activities and greater integration with other departments and platforms.

## **ACQUISITION OF A NEW CUSTOM-MADE MULTIPHOTON MICROSCOPE**

Paris Brain Institute acquired a new multiphoton microscope with the generous support of the Edmond J. Safra foundation. It is custom-made and will allow various Institute teams to develop in-depth and multiscale research. Multiphoton microscopy allows scientists to acquire imaging of the depths of animals' brains during development or while undertaking a behavioral task. This type of instrument is essential to establish relationships between brain activity and behavior.

**” DEVELOPMENTAL AND BEHAVIORAL IMAGING INVOLVES LENGTHY EXPERIMENTS WHERE AN INSTRUMENT CAN REMAIN IN USE FOR HOURS AT A TIME, AND SOMETIMES UP TO 24 HOURS IN A ROW. THIS ACQUISITION, MADE POSSIBLE WITH SUPPORT FROM THE EDMOND J. SAFRA FOUNDATION, WILL HELP BOOST OUR RESEARCH, AND ESPECIALLY OUR PROJECT DEDICATED TO UNDERSTANDING THE NEURAL BASIS OF INDIVIDUALITY. ”**

**Prof. Bassem Hassan**, team leader and scientific director at Paris Brain Institute

## **EVOLUTIONS IN RESEARCH AND DEVELOPMENT PROGRAMS**

FabLab, also known as a “workshop”, is set to evolve towards becoming an R&D platform with a wider array of services offered. This new R&D unit will combine design, production and personalization for the entire Paris Brain Institute ecosystem.



## **NOVASEQ SEQUENCER ON IGENSEQ PLATFORM GETS AN UPGRADE**

In 2019, the Paris Brain Institute acquired the Novaseq 6000 ILLUMINA, the world's most powerful short fragment DNA sequencer, for the iGenSeq core facility.

Sequencing capacity was increased as well as single-cell sequencing capabilities

## **TOWARDS NEW CUTTING-EDGE EQUIPMENT**

Paris Brain Institute values access to cutting-edge equipment for its researchers. A current institute priority is the acquisition of a 7T MRI. Various calls for tender and fundraising options are under consideration.



# 10

## TECHNOLOGICAL PLATFORMS AND BIOBANKS

The progress and quality of science depend as much on technological progress as on good ideas. At Paris Brain Institute, researchers and core facilities managers work together to keep abreast of technological advances in order to provide the most advanced equipment and techniques, operated by highly competent staff, to advance brain research.

The Institute's researchers work at different scales: from the molecule (DNA, proteins, etc.) to the individual, as well as the cell. For each of these scales, innovative technologies are made available to researchers, clinicians and start-ups. This network of core facilities at the Paris Brain Institute facilitates translational and trans-disciplinary research.





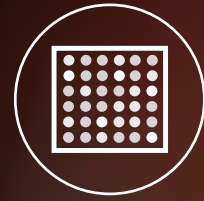
## IGENSEQ

Next generation RNA and DNA sequencing



## IVECTOR

Development of molecular instruments for genetrasfer (lentivirus, adenovirus, CRISPR)



## CELIS

Screening, cell culture, iPSC, electrophysiology



## HISTOMICS

Histomics research using specific equipment to cut tissue and process samples



## PHENOPARK

Preclinical functional exploration, behavioral analysis, surgery, electrophysiology



## DAC

Genomics, bioinformatics and biostatistics



## ICMQUANT

conventional fluorescence microscopy, confocal laser scanning microscopy, bi-photonic microscopy, confocal rotating disk microscopy and transmission electron microscopy



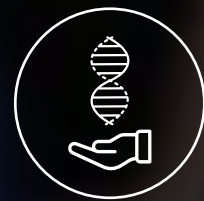
## CENIR

Center for Neuroimaging Research : 3T MRI, PET-MRI, TMS, MEG-EEG, Gait analysis, Stereotactic imaging



## PRISME

Cognitive and social assessment in real-life conditions and virtual reality



## BIOBANKS

Biological resource collection, DNA, plasma, cells, brain tissue

# IHU

## PARIS

### INSTITUTE OF

### TRANSLATIONAL

### NEUROSCIENCE

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**SINCE 2012, INITIATIVES FUNDED BY THE HOSPITAL-UNIVERSITY INSTITUTE (IHU) DEVELOPED AS PART OF THE "INVESTMENTS IN THE FUTURE" PROGRAM, HAVE HAD MAJOR SCIENTIFIC, CLINICAL AND ECONOMIC IMPACT.**

**IN 2019, PARIS BRAIN INSTITUTE SAW ITS IHU PROGRAM RENEWED WITH AN ADDITIONAL 17 MILLION EUROS, DEMONSTRATING THE EFFICIENCY OF THE "IHU MODEL".**

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2020 was a very important year for the Institute with **a high number of publications in the best journals** : 3 *Science*, 1 *Nature*, 2 *Nature. Neuroscience*, 1 *Cell*. In 2020, Paris Brain Institute now hosts its **15<sup>th</sup> ERC** (funding from the European Research Council). The year 2020 was also the year of the COVID-19 pandemic. Measures implemented by Paris Brain Institute management have been effective in guaranteeing staff safety, participating in national collective efforts and maintaining research momentum.

A total of **173 clinical trials** are underway, a testament to our high level of clinical research. The Neurotrials framework created to assess drugs in early development achieved major results in 2020 with 3 ongoing studies in collaboration with the pharmaceutical industry.

The Institute signed **42 new industrial contracts** with biotechnology, pharmacy and medical technology companies for both preclinical research programs and clinical programs. In 2020, the incubator operated **the second acceleration program for the "Pfizer Innovation France"** endowment fund and launched its **first acceleration program with Janssen**. Around ten digital health startups have benefited from the support of the incubator and the Care Lab, as well as the expertise of a leader in the pharmaceutical industry.

This past year also saw **investments in digital technology and the integration of Education Technology approaches in the Open Brain School curriculum**. Our concern was to maintain access to our events and training programs while taking into account the effects of distance learning on participants.



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**BASED ON THE PLAN  
PRESENTED TO THE IHU  
JURY AND IN LINE WITH OUR  
ROADMAP, WE PURSUED  
OUR AMBITIOUS GOALS IN  
SCIENCE, MEDICAL RESEARCH,  
EDUCATION AND INNOVATION  
BY CONTINUOUSLY WORKING  
TO INCREASE OUR ECONOMIC  
IMPACT DESPITE THE PANDEMIC.**

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**15**  
ERCs

**173**  
clinical trials

**42**  
new industrial contracts

# PARIS BRAIN INSTITUTE

## TEAMS

### ALS : CAUSES AND MECHANISMS OF MOTOR NEURON DEGENERATION

**Séverine Boillée (Inserm)** Competitive grants received in 2020 : ANR-PRCE, ARSLA, FRM

### BASIC TO TRANSLATIONAL NEUROGENETICS

**Giovanni Stevanin (Inserm/EPHE) and Alexandra Durr (Sorbonne Université/AP-HP)** Competitive grants received in 2020 : FRM, NIH, Association CSC

### MOLECULAR PATHOPHYSIOLOGY OF PARKINSON'S DISEASE

**Olga Corti (Inserm) and Jean-Christophe Corvol (Sorbonne Université/AP-HP)** Competitive grants received in 2020 : ANR-PRC, FRM, MJFOX, ANR-ERAPerMed, Fondation de France

### ALZHEIMER'S DISEASE AND PRION DISEASES

**Marie-Claude Potier (CNRS) and Stéphane Haik (Inserm)** Competitive grants received in 2020 : ANR-PRC, ANR-ERAPerMed, LRTCA, Fondation pour la Recherche sur Alzheimer

### EXPERIMENTAL THERAPEUTICS OF PARKINSON'S DISEASE

**Étienne Hirsch (CNRS) and Stéphane Hunot (CNRS)** Competitive grants received in 2020 : ANR-CoEN, Fondation de France

### MOV'IT : MOVEMENT, INVESTIGATION, THERAPEUTICS, NORMAL AND ABNORMAL MOTOR CONTROL : MOVEMENT DISORDERS AND EXPERIMENTAL THERAPEUTICS

**Marie Vidailhet (Sorbonne Université/AP-HP) and Stéphane Lehericy (Sorbonne Université/AP-HP)** Competitive grants received in 2020 : ANR-JCJC, ANR-JNPD, ANR-PRC, AMADYS, Fondation Generali, ANR-TREMPIN, SFRMS, Fondation pour la Recherche sur Alzheimer, PSP France

### CELLULAR PHYSIOLOGY OF CORTICAL MICROCIRCUITS

**Alberto Bacci (Inserm)** Competitive grants received in 2020 : ANR-PRC, FRM, Fondation Jérôme Lejeune

### CELLULAR EXCITABILITY AND NEURAL NETWORK DYNAMICS

**Stéphane Charpier (Sorbonne Université), Mario Chavez (CNRS) and Vincent Navarro (Sorbonne Université/AP-HP)** Competitive grants received in 2020 : FRM, Fondation Generali, FFRE

### GENETICS AND PHYSIOPATHOLOGY OF EPILEPSY

**Éric Leguern (Sorbonne Université/AP-HP) and Stéphanie Baulac (Inserm)** Competitive grants received in 2020 : FRM, Prix L'Oréal UNESCO, LFCE

### SENSORY SPINAL SIGNALING

**Claire Wyart (Inserm)** Competitive grants received in 2020 : FRM, Fondation des Treilles, ERC-Consolidator

### GENETICS AND DEVELOPMENT OF NERVOUS SYSTEM TUMORS

**Emmanuelle Huillard (CNRS) and Marc Sanson (Sorbonne Université/AP-HP)** Competitive grants received in 2020 : INCA, DoD - Department of Defense, FRM, Ligue contre le cancer, APHP, ARTC, ANSES, Cancéropôle Île-de-France, FRM, GEFLUC Paris

### REMYELINATION IN MULTIPLE SCLEROSIS : FROM BIOLOGY TO CLINICAL TRANSLATION

**Catherine Lubetzki (Sorbonne Université/AP-HP) and Bruno Stankoff (Sorbonne Université/AP-HP)** Competitive grants received in 2020 : NeurATRIS, FRM, ARSEP, Fondation Sorbonne Université

### MYELINE PLASTICITY AND REGENERATION

**Brahim Nait-Oumesmar (Inserm) and Violetta Zujovic (Inserm)** Competitive grants received in 2020 : ARSEP

### PICNIC- PHYSIOLOGICAL INVESTIGATION OF CLINICALLY NORMAL AND IMPAIRED COGNITION - NEUROPSYCHOLOGY AND FUNCTIONAL NEUROIMAGING

**Laurent Cohen (Sorbonne Université/AP-HP), Lionel Naccache (Sorbonne Université/AP-HP) and Paolo Bartolomeo (Inserm)** Competitive grants received in 2020 : MSCA-IF/GF, ANR-PRC, Fondation pour la recherche sur les AVC, Foundation for Polish Science, FRM, HAS-Haute Autorité de Santé

### FRONTLAB : FRONTAL FUNCTIONS AND PATHOLOGY

**Richard Lévy (Sorbonne Université/AP-HP)** Competitive grants received in 2020 : MSCA/IF-GF, ANR-PRC, FRC, ANR-LABCOM, FRM

### CIA : COGNITIVE CONTROL - INTEROCEPTION - ATTENTION

**Philippe Fossati (Sorbonne Université/AP-HP) and Liane Schmidt (Inserm)** Competitive grants received in 2020 : ANR-PRC

### NEUROPHYSIOLOGY OF REPETITIVE BEHAVIORS

**Éric Burguière (CNRS)** Competitive grants received in 2020 : Fondation FondaMental, ANR-PRC

**MOTIVATION, BRAIN AND BEHAVIOR**  
**Mathias Pessiglione (Inserm), Sébastien Bouret (CNRS) and Jean Dauterive (Inserm)** Competitive grants received in 2020 : ANR-PRC, H2020, Académie des Sciences





**ARAMIS :**  
**ALGORITHMS, MODELS AND METHODS FOR IMAGES AND SIGNALS OF THE HUMAN BRAIN**

**Olivier Colliot (CNRS) and Stanley Durrleman (Inria)**

Competitive grants received in 2020 : ANR-PRC, Plan cancer, Inserm, Académie des Sciences

**EXPERIMENTAL NEUROSURGERY**

**Brian Lau (CNRS) and Carine Karachi (Sorbonne Université/AP-HP)**

Competitive grants received in 2020 : MSCA/IF-GF, ANR-CoEN, ANR-PRC, ANR-CRCNS, Fondation pour la Recherche sur Alzheimer, France Parkinson

**BRAIN DEVELOPMENT**

**Bassem Hassan (Inserm)**

Competitive grants received in 2020 : FRM, Fonds de dotation Neuroglia, ANSES

**STRUCTURAL DYNAMICS OF NEURAL NETWORKS**

**Nicolas Renier (Inserm)**

Competitive grants received in 2020 : MSCA-ITN/ETN, FRM

**CELLULAR MECHANISMS OF SENSORY PROCESSING**

**Nelson Rebola (CNRS)**

Competitive grants received in 2020 : MSCA/IF-GF, ANR-PRC

**GENE THERAPY**

**Nathalie Cartier (Inserm)**

Competitive grants received in 2020 : IMI, ANR-JCJ, ARSLA, Inserm, Association française du Syndrome de Rett

**DIANE BARRIÈRE CHAIR : “MOLECULAR PHYSIOLOGY OF SYNAPTIC BIOENERGETICS”**

**Jaime De Juan-Sanz (CNRS)**

**SUPPORTING RESEARCH AND ITS NEED FOR FUNDING**

Research institutes have developed a dynamic financial strategy to cope with the ever-changing regulations of public financial support and to adapt to the industrial environment, where new trends and new needs arise almost daily. The Department of Medical and Scientific Affairs (DAMS) is home to a grants office that offers numerous services to the Paris Brain Institute community and is available to assist in developing new external collaborations. With a wide range of skills, DAMS offers sourcing and engineering assistance to obtain competitive research grants on a national, European and international level.

**1**

**ERC consolidator grant in 2020**

i.e. 15 since the creation of the Institute

**16,7** M€

of external competitive grant income 2020

**3**

**MSCA fellowships in 2020**

i.e. 22 since the creation of the Institute

**ACRONYMS**

- **ANR-CoEN** : National Research Agency – Expert Centers for Neurodegenerative Diseases
- **ANR-CRCNS** : National Research Agency – Collaborative Research in Computational Neuroscience
- **ANR-ERAPerMed** : National Research Agency – Translational Medicine Project
- **ANR-JCJC** : National Research Agency – Young Researcher
- **ANR – JPND** : National Research Agency – Joint program on neurodegenerative diseases
- **ANR – PRC** : National Research Agency – Collaborative research projects
- **ANSES** : National Food and Hygiene Safety Agency
- **APHP** : Assistance Publique – Hôpitaux de Paris (Paris Hospital System)
- **ARDRM** : Robert Debré Association for Medical Research
- **Association CSC** : Understanding Cerebellar Syndromes
- **ARSEP** : Association for Research on Multiple Sclerosis
- **ARSLA** : Association for Research on Amyotrophic Lateral Sclerosis
- **ERC** : European Research Council
- **FFRE** : French Epilepsy Research Foundation
- **FRM** : Foundation for Medical Research
- **H2020** : Horizon 2020 European Program
- **IMI** : Innovative Medicine Initiative
- **LFCE** : French Epilepsy League
- **LRTCA** : Advanced Surgical Technology Research Laboratory
- **MSCA-IF/GF** : Marie Skłodowska-Curie actions – Individual and Global Fellowships (Europe)
- **MSCA-ITN/ETN** : Marie Skłodowska-Curie actions – Innovative Training Network/ European Training Network
- **NIH** : National Institutes of Health (United States)

# INTERNATIONAL PARTNERSHIPS

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**DESPITE THE PANDEMIC, THE INSTITUTE WAS ABLE TO MAINTAIN AND INCREASE ITS INTERNATIONAL COOPERATION EFFORTS THROUGHOUT THE YEAR. ALTHOUGH INTERNATIONAL TRAVEL WAS IMPOSSIBLE AND EXCHANGES WERE SUSPENDED (MIT, STANFORD, YALE, ST JOHN'S UNIVERSITY IN THE UNITED STATES), WE ADAPTED MANY OF OUR ACTIONS TOWARDS DIGITAL PLATFORMS. THIS YEAR, ONCE AGAIN, THE INSTITUTE COOPERATED WITH RESEARCHERS FROM DIFFERENT INSTITUTES THROUGH PUBLICATIONS AND BY OBTAINING NATIONAL, EUROPEAN AND INTERNATIONAL FUNDING.**

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## **YALE UNIVERSITY** **(USA)**

While no clinician exchange took place this year due to the situation, clinical collaboration was nevertheless strengthened by pooling our clinical rounds on the initial topics of epilepsy and abnormal movements. A multidisciplinary workshop in September saw the start of a new research collaboration on epilepsy and was a chance to take stock of the recent collaboration between our teams on COVID-19, with initial results published in the Fall.

## **MONTREAL NEUROLOGICAL INSTITUTE** **(Canada)**

Although the multidisciplinary workshop scheduled for June 2020 was postponed for a year due to the health crisis, collaboration with the MNI grew. An online workshop dedicated to organoids and iPSCs applied to nervous system diseases prompted our researchers to come together and fostered discussions on new joint projects. The renewal of our cooperation agreement was agreed upon, and discussions are underway regarding further collaboration in other specialties : iPSC-based screens, multimodal data analysis and neurodevelopmental disorders.



## **CURE-ND**

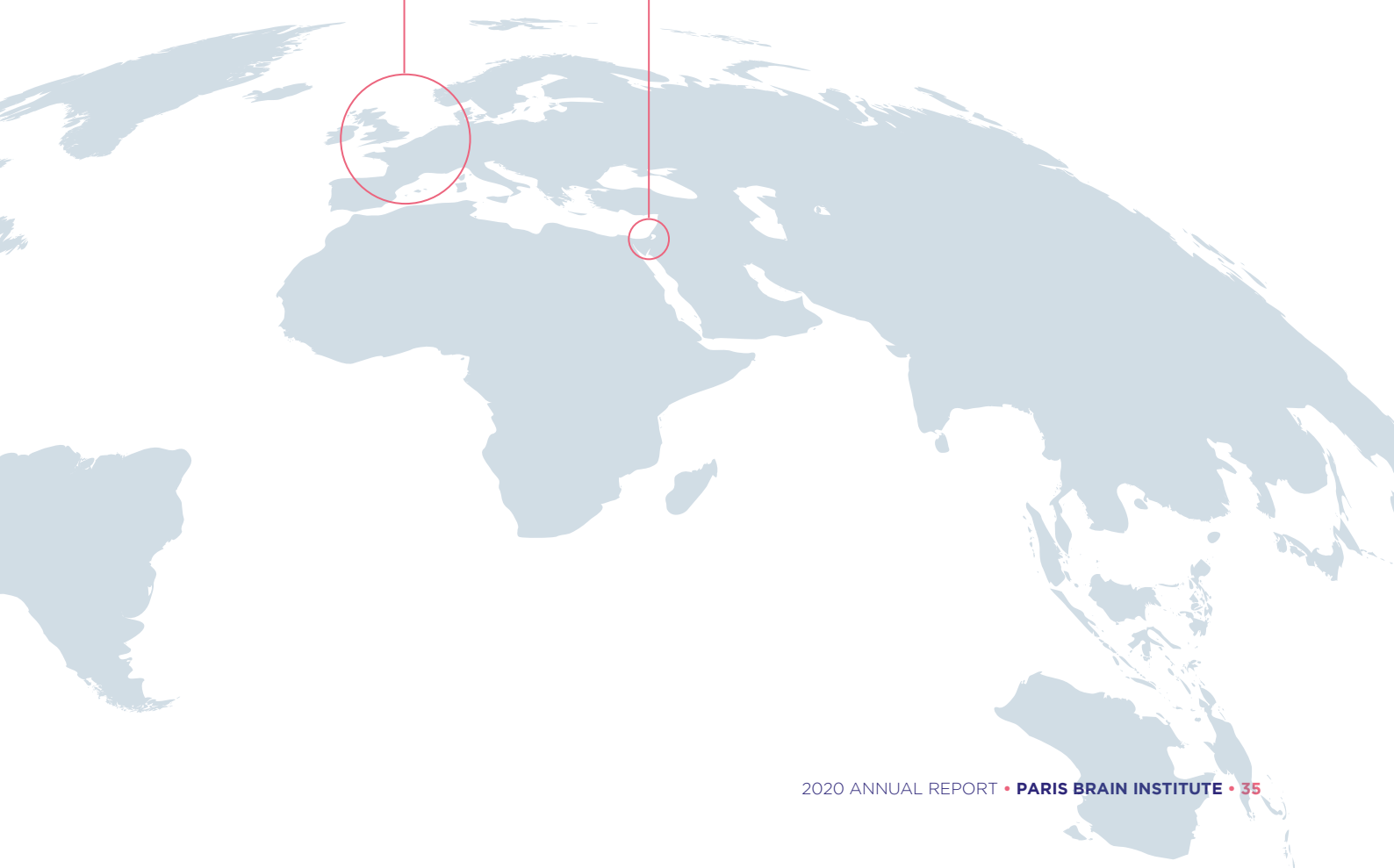
### **(France, Germany, United-Kingdom, Belgium)**

A highlight the year 2020 was the creation of the CURE-ND “Catalyzing a United Response in Europe to Neurodegenerative Diseases” consortium, which brings together Paris Brain Institute and our long-standing partners the UK Dementia Research Institute, the German DZNE and the Belgian Mission Lucidity (VIB). With a critical mass of over 2,000 researchers, this working group aims to develop a new European network of excellence in neurodegenerative diseases. The launch event was held online in December 2020 with the development of a shared framework.

## **WEIZMANN INSTITUTE**

### **(Israel)**

In 2020, we decided to strengthen our cooperation with the Weizmann Institute, initiated by a scientific collaboration centered on the fundamental bases of states of consciousness and non-consciousness. In order to promote meetings and the development of innovative projects, we have planned scientific workshops as well as organization and support for research and student exchanges between the two Institutes on a regular basis.



# COVID-19 PANDEMIC : THE INSTITUTE'S CLINICAL FORCES UNITE

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FROM THE FIRST WEEKS OF THE COVID-19 PANDEMIC, THE ENTIRETY OF PARIS BRAIN INSTITUTE'S CLINICAL FORCES WAS TRANSFERRED TO THE HOSPITAL'S INTENSIVE CARE, INFECTIOUS DISEASES AND PNEUMOLOGY UNITS TO SUPPORT TEAM ONSITE.

STAFF FROM THE CLINICAL INVESTIGATION CENTER ALSO PROVIDED THEIR EXPERTISE FOR PATIENT RECRUITMENT IN SEVERAL COVID-19 TRIALS :

- > DISCOVERY
- > COVID-ICU
- > CORIMMUNO

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These trials evaluated several therapeutic strategies against SARS-CoV-2, allowing us to gain a better understanding of risk factors for severity.

## **COVID-NEUROSCIENCE COHORT : STUDYING THE NEUROLOGICAL AND PSYCHIATRIC CONSEQUENCES OF SARS-COV-2 INFECTION**

From the very first weeks of the pandemic, doctors reported neurological symptoms in patients affected by COVID-19 such as loss of smell or taste, but also more serious effects such as seizures or strokes. Faced with this challenge, within a few weeks in April 2020, the Cohort Covid Neuroscience project coordinated by Prof. Jean-Christophe Corvol (AP-HP/Sorbonne University) and Dr. Cécile Delorme (AP-HP) was launched and brought together the entire medical-university Neuroscience department of Pitié-Salpêtrière AP-HP Hospital and Paris Brain Institute. This was made possible with support by the International Automobile Federation (FIA), the FIA Foundation and Institute donors. Over 600 subjects have been recruited and the first results of the project have already identified a number of effects of this disease as well factors impacting the COVID-19 severity.

Several types of brain abnormalities were identified in patients with COVID-19 using brain imaging. These findings were published in Radiology and provide important data in patients with this disease, and also identify several potential brain targets for SARS-CoV-2 infection. Other publications in the European Journal of Neurology describe common features of encephalopathies, visible by positron emission tomography, following infection with SARS-CoV-2, which may reflect an immune system mechanism. Given that these features may appear several weeks after infection or upon discharge from intensive care units, several hypotheses will be examined in the future regarding mechanisms involved, including direct damage to the central nervous system by SARS-CoV-2, thrombosis, immune mechanisms, and metabolic disorders.

This study now goes beyond a national framework, with collaborations with prestigious research centers including Yale and Liverpool Universities as well as with international groups. Funding from Fondation de France will allow patient monitoring throughout 2021 with the study of long-term consequences on the nervous system. They will be key to increasing our knowledge of the infection and its consequences on the central nervous system, to benefit patients first and foremost.

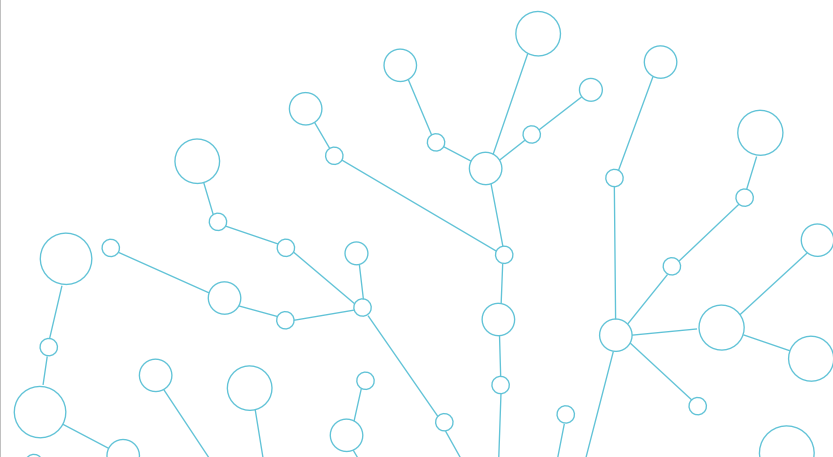
## **COVID NEUROSCIENCE BIO-COHORT**

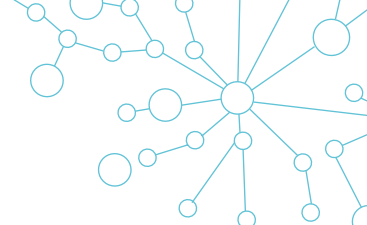
In line with the Covid Neuroscience Cohort study, a collection of biological data is being set up to follow patients affected by COVID-19 who presented post-infection and post-vaccination neurological or psychiatric symptoms over time.

## **COVISEP : COVID-19 IN PATIENTS WITH MULTIPLE SCLEROSIS**

The COVISEP registry is based on a cohort of patients from all expert centers and neurologists who follow patients with multiple sclerosis (MS) in France. It includes nearly 1,000 patients.

A retrospective and observational study, coordinated by Dr. Céline Louapre (AP-HP/Sorbonne University), was published in the scientific journal JAMA Neurology. It focused on 347 patients with multiple sclerosis and infected with COVID-19 between March 1 and May 21, 2020. The results of this study show that risk factors for severe forms of COVID-19 (requiring at least one hospitalization) are the EDSS score (scale reflecting neurological disability severity), age and obesity. In contrast, immunomodulatory or immunosuppressive treatments are not associated with severe COVID-19. This study is ongoing, with over 1,000 patients included and a Franco-Italian collaboration is underway to compare results obtained in each country's patient registry.





# THE CLINICAL INVESTIGATION CENTER

WORKS TOWARDS  
TAILORED TREATMENT  
FOR EACH PATIENT

## **IMPORTANT RESULTS FOR TRIALS CARRIED OUT AT THE NEUROSCIENCE CLINICAL INVESTIGATION CENTER**

### **Antisense oligonucleotides in Amyotrophic Lateral Sclerosis (ALS)**

Currently, many promising therapeutic innovations are based on antisense oligonucleotide technology, using fragments of genetic material that will interfere with message RNA and thereby mediate the expression of certain proteins in the central nervous system. Encouraging results were obtained in ALS in a study testing the effect of anti-SOD antisense oligonucleotides, conducted by Dr. François Salachas (AP-HP) at the Clinical Investigation Center.

### **Two immunotherapy trials in progressive supranuclear palsy (PSP)**

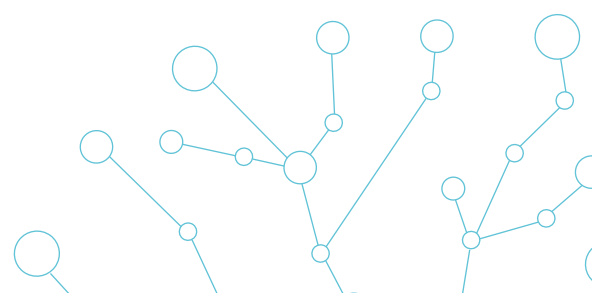
PSP is a neurodegenerative disease caused by the progressive destruction of neurons in different areas of the brain. A trial coordinated by Prof. Corvol (AP-HP/Sorbonne University) at the Paris Brain Institute CIC was conducted to assess the therapeutic effect of an anti-TAU antibody. TAU protein aggregates abnormally in neurodegenerative diseases such as PSP or Alzheimer's disease. The results are unfortunately negative and do not conclude on the effectiveness of these therapies.

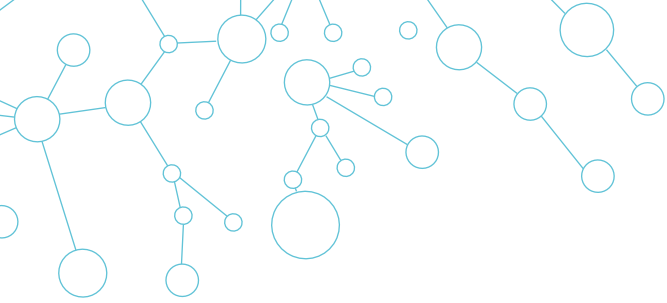
### **Remyelination and inflammation in multiple sclerosis**

The ON-STIM trial, aimed at promoting remyelination by electrical stimulation after an episode of optic neuritis in patients with multiple sclerosis, has launched. Another trial on neuroprotection has also started. Encouraging results have been obtained on the use of IL-2 immunotherapy in the disease.

### **Active clinical research in Parkinson's disease**

Precision therapeutic trials have launched in patients with genetic forms of Parkinson's disease affecting GBA and LRRK2 genes. The Precise-PD project, coordinated by the NS-Park/FCRIN network and supported by France Parkinson, aims to collect clinical data from patients monitored in expert centers throughout France, associated with a collection of biological samples. The goal is to understand the wide variability in disease progression trajectories using computational approaches and artificial intelligence for precision and personalized medicine in this illness. A study conducted with Roche laboratory has also obtained encouraging results on slowing the progression of motor symptoms in the disease. A phase 3 trial is due to start soon.





## **AP-HP/PARIS BRAIN INSTITUTE FAST-TRACKS : ACCELERATING CLINICAL RESEARCH**

Before starting, a clinical trial must receive a green light from a CPP (Committee for the Protection of Persons) and authorization from the National Drug Safety Agency (ANSM). Research must be carried out under the direction of a qualified investigator in the research field and be supervised and insured by an institutional (INSERM, AP-HP, etc.) or industrial promoter.

In order to best facilitate this process and allow clinical trials to start as quickly as possible under the best conditions, a «fast-track» has been set up between Paris Brain Institute and AP-HP. A project manager, a data manager and a scientific committee are available for investigators of the medical-university neuroscience department to accelerate the regulatory submission process and completion of studies.

## **A NEW STEP FOR PARIS BRAIN INSTITUTE'S CLINICAL RESEARCH INFRASTRUCTURE (iCRIN)**

The clinical research infrastructures of Paris Brain Institute (iCRIN) develop interactions and expertise-sharing among the Neuroscience Medical-University Unit (DMU) at Pitié-Salpêtrière Hospital and Paris Brain Institute research teams. They underwent assessment for the second time this year : the 3 emerging projects were renewed for 3 more years, and 2 of them received a certification of excellence. Currently, 12 iCRINs hold a certification of excellence, and one is considered an emerging iCRIN. This initiative makes it possible to support clinical research projects directly with patients of the Neuroscience Medical-University Unit.



## **LAUNCH OF THE FIRST CLINICAL TRIAL FOR NEUROTRIALS, EARLY CLINICAL DEVELOPMENT UNIT**

In 2020, the Neurotrials team was structured to become fully operational in its consulting and clinical trial management activities with industrial sponsors. This year was marked by the submission to the health authorities and the implementation of a phase IIa clinical protocol in acute optic neuritis, with several patients already included by the investigating teams. Neurotrials is supporting other gene therapy biotechnology companies in Huntington's disease and cerebellar ataxias, as well as a biomarker study in Parkinson's disease. The unit has also provided consulting services to medtechs (in pain management and gait disorders) and biotechs in neurodegenerative diseases such as Alzheimer's and Parkinson's. The perfect integration of Neurotrials within the Paris Brain Institute, in particular in its technological and entrepreneurial ecosystem, and its proximity with clinicians and expert and reference biologists constitute a major asset in supporting healthcare industrialists for the early clinical development of their product in neurology and psychiatry.

**More information will be available soon on [www.neurotrials.fr](http://www.neurotrials.fr)**





Innovation and knowledge transfer

# RESEARCH APPLICATIONS

## **A NEW SITE FOR ACCELERATED PRODUCT DEVELOPMENT**

Despite a year that was strongly disrupted by the COVID-19 crisis, the Institute was able to initiate the development work of its third business incubation site in 2020. Over 1,500 square meters and halfway between Paris Brain Institute and Station F campus, the new “Chevaleret” site will be an accelerator dedicated to medical technologies and artificial intelligence in healthcare. It will allow the development of healthcare technology that is socially responsible, financially affordable and can be used in prevention and in maintenance of autonomy. Through supported projects, the Institute will ultimately help offer new diagnostic and imaging tools, therapeutic solutions to patients suffering from neurodegenerative and psychiatric illnesses, as well as help develop new tools intended to improve quality of life and autonomy of these patients.

**The development of the activities at the new Chevaleret site is made possible by the triple financial support of the City of Paris, the Île-de-France Region and the BPI through the funding of the MGA project (Medtech Generator & Accelerator).**

MAIRIE DE PARIS



 **île de France**

**bpi**france



## **THE MEDTECH GENERATOR & ACCELERATOR PROJECT (MGA)**

The MGA Project, coordinated by Paris Brain Institute, brings together the Institut Imagine, the Institut de la Vision and the Institut Pasteur. Supported by BPI with a budget of 1.2 million Euros over 2 years, it aims at developing innovative programs to accelerate the growth and development of startups specializing in healthcare and artificial intelligence in the field of neuroscience, genetic and rare diseases.

The MGA project will structure and enliven the regional community of deep tech researchers and entrepreneurs to boost the creation of startups hailing from academic research and support the acceleration of their commercial development. To do so, the project creates a clear path for entrepreneurs from the first phases of their project, closely steers its progress and adjusts it to ensure effectiveness. The members of the consortium will carry out simultaneous high-leverage targeted actions for the development of the most advanced startups, including support for clinical validation of their products.

The ultimate goal is to offer an integrated approach to entrepreneurial support through balance between collective and individual actions, putting researchers and entrepreneurs in contact with experts within our ecosystems. It should thereby help double the number of startups created within the four member Institutes.


## **CARNOT**

Paris Brain Institute coordinates the national FINDMED initiative dedicated to supporting French SMEs in pharmaceuticals. It brings together the following Institutes: Carnot Calym, Chimie Balard Cirimat, Curie Cancer, I2C, Institut du Cerveau, Imagine, Pasteur MS, Qualiment, FFE, MINES, TN @ UPSaclay, Voir et Entendre, and was recently joined by Carnot Opale and APHP. Since 2016, this consortium has quadrupled its results with French small and medium-sized companies, a proactive approach hailed by government assessors as "structured and efficient".

In early 2020, when the Board of Directors of the Carnot Institutes Association was renewed, the Paris Brain Institute representative was elected vice-president of the network, in charge of startups and SMEs.



# KEY FIGURES

 **15**  
promising  
molecules  
undergoing  
characterization

 **8** novel technology  
development programs  
currently underway

 **5,6** M€  
in new industrial  
partnerships

Active portfolio of  
**55** patents

 **37**  
startups  
currently incubated

### **NEW** **CANDIDATE DRUGS**

2020 saw the development of a transatlantic collaboration on Huntington's disease and spinocerebellar ataxias between an American SME and Prof. Alexandra Durr (AP-HP/Sorbonne University), a physician specialized in hereditary neurodegenerative diseases. These rare diseases are hereditary and incurable neurological pathologies associated with neural degeneration in an area of the brain involved in motor, cognitive and behavioral functions. Understanding the biological mechanisms underlying these pathologies is a fundamental issue in the search for treatment.

The Institute's proximity to patients has given rise to a promising scientific project between a research team specializing in models of neuroinflammation and neurodegeneration and a startup founded by a patient with Parkinson's disease. These interactions between researchers and patients allowed better scientific understanding of clinical observations and helped consolidate a patent filing for possible therapeutic applications.

2020 was also a year with three patent filings, thanks to the work of different teams at the Institute. The first is based on findings suggesting that a new medical technology can slow the build-up of amyloid plaques in Alzheimer's disease. The second, resulting from a collaboration with academic chemists, demonstrates the potential for new molecules to act on the neuroinflammatory component of neurodegenerative diseases including Parkinson's disease, using unique biological models. The third is about the anticipation of epileptic seizures by electroencephalography.

The second year of the «Sleeping Beauties» project allowed continued assessment of drugs for therapeutic purposes in glioblastoma, the most common brain cancer in adults, through new partnerships. The growing number of academic partnerships around this project led to the hiring of an undergraduate professional apprentice. The development of high-throughput phenotypic screening protocols on an automated system will also allow optimization of the volume of molecules tested in the near future.

### **TECHNOLOGY** **DEVELOPEMENT**

The team responsible for technology development (medical and/or research) structured 2020 by launching two calls for projects. The first, CARNOT TOOLS, is intended for researchers at Paris Brain Institute. It aims at developing new research technologies by relying on developers, the Institute's prototyping laboratory and the skillsets at CARE LAB, the Paris Brain Institute LivingLab, for user interface development. Among the first projects, a digital tool for processing and archiving electrophysiological data, a new system for 3D cell cultures, and a tool to measure motor behavior of *Drosophila* flies. The second call for projects, CARER INITIATIVE, is a sister initiative to support the development of tools and solutions to facilitate patient care. Among the first projects selected are an application to facilitate decision-making for clinical teams, another to help private practices in the follow-up of patients after a hospital stay, and an instrument to detect sense of smell disorders.

In the spirit of «Made@ICM», these projects must be mature enough after prototyping to allow industrial transfer and subsequent wide dissemination of innovation. At the end of 2020, a partnership was signed with SBT-HappyNeuron, a French SME specializing in digital therapy, to develop projects resulting from a recent participatory innovation program dedicated to traumatic brain injuries and carried out with the Department of Physical Medicine and Rehabilitation of the hospital. Thanks to these new instruments, CARE LAB is now equipped to support strong development for made@ICM.



## INCUBATING INNOVATIVE COMPANIES

iPEPS, Paris Brain Institute's innovative business incubator, is located at the heart of the Institute as well as within STATION F, the largest startup campus in the world since 2017. 2020 also saw the construction of the new Chevaleret campus which will open its doors in 2021. The combination of these three sites supports the incubator's growth and will allow Paris Brain Institute to support startups in medicine, medical devices and digital health.

In 2020, the incubator operated the second edition of the "Pfizer Innovation France" endowment acceleration program. Five digital healthcare startups benefitted from the support and resources of the incubator, as well as the expertise of a leader in the pharmaceutical industry. This year also marks the start of two new industrial partnerships for the

incubator : with Jansen EMEA, a pan-European support program, and with Janssen France, AstraZeneca, AG2R La Mondiale and Geopost, a multi-partner initiative in response to the COVID-19 crisis.

Several incubated companies have taken important steps in their development. Scipio Bioscience raised 6 million euros in funds to revolutionize single-cell sequencing analysis. Carthera received 2 million euros in grants and 10.5 million euros in equity from the European Council to deploy its SonoCloud device on a clinical level White Lab Genomics, a young startup, obtained an additional 300,000€ thanks to the French Tech Seed program, recommended by Paris Brain Institute.



# OPEN BRAIN SCHOOL

THE PAST YEAR HAS BEEN OVERSHADOWED BY THE PANDEMIC. THROUGHOUT THE YEAR, WE WORKED TO MAINTAIN THE TEACHING ACTIVITIES OF THE OPEN BRAIN SCHOOL TRAINING ORGANIZATION. THIS PERIOD WAS AN OPPORTUNITY TO REALIZE HOW MUCH OUR DAILY LIFE IS CLOSELY LINKED TO NEUROSCIENCE. AN INCREASING NUMBER OF TRAINING COURSES SEEK TO DRAW ON NEUROSCIENCE-BASED KNOWLEDGE IN ORDER TO IMPROVE TEACHING APPROACHES.

To seize this opportunity, Paris Brain Institute has placed an emphasis on digital technology to make Institute discoveries available to as many people as possible.

For the Open Brain School, 2020 was the year of the launch of its website, where all training activities are currently listed. Registration for the various programs is now open !



## INVESTING IN DIGITAL LEARNING AND EDTECH INTEGRATION

2020 saw an investment in digital technology and the integration of EdTech approaches. Our priority has been to maintain access to our events and training while taking into account the effects of distance learning on participants (access to content, concentration, memorization, need for interactions, understanding, etc.). Consequently, Paris Brain Institute has implemented videoconferencing whenever possible, and the Open Brain School set up a Learning Management System for program and enrollment monitoring.

**IN 2020, THE OPEN BRAIN SCHOOL BEGAN THE DIGITAL TRANSITION OF ITS CONTENT.**

CORNERSTONE #1 :

**PROMOTING  
SCIENTIFIC  
EXCELLENCE**

**International**

**BRAIN BEE PROGRAM**

This program is an international neuroscience competition for high school students. The Brain Bee's mission is to help students learn more about the brain and its basic functions, neuroscience research, and misconceptions about brain disorders. Since 2019, Paris Brain Institute has been the official organizer of the French national competition. It was initially scheduled for a face-to-face event in March 2020, and the team made a point of maintaining the event by transitioning to an entirely remote solution. Of the 50 participants initially registered, on June 5, 35 students from Cusset, Lyon, Paris and Toulouse were able to connect simultaneously to perform the tests via their screens. Matsuko Sano, who is home-schooled, is the winner of this edition, Carole Hosono from Lycée Louis le Grand got second place and Théo Damiaty from Lycée Louis le Grand ranked third.

At the same time, an e-learning module on Multiple Sclerosis was produced and made available to participants to prepare for the competition. We are working to adapt this module to different themes. This marks the start of the deployment of user-centric digital content.

**INTERNATIONAL iMIND  
MASTER'S PROGRAM**

The iMIND master's program is an international and interdisciplinary two-year program. This master's program is the first of its kind specifically dedicated to neurodegenerative diseases, a

current major societal challenge. In 2020, the number of master's program enrollments doubled and registration has opened to international students. All courses in the program, including platform visits, were taught through distance learning with videoconferencing..

CORNERSTONE #2 :

**PROMOTING  
CLINICAL  
RESEARCH**

**STARE**

An introductory educational program for neuroscience for 3rd year medical students.

The program was initially created on a voluntary basis for 5 half-days, and we have now welcomed 60 students since 2017. Building on this success, STARE has become a Teaching Unit within the Sorbonne University Faculty of Medicine since 2020 and its organization is developing. The program will last 2 weeks with one session per year. Although the 2020 session was canceled due to the pandemic, we actively prepared the arrival of 20 students within our teams, platforms and incubated companies for 2021.

**DECLIC**

Like STARE, DECLIC is a program that aims to meet the needs of research staff to become familiar with clinical neurology departments. In collaboration with Medical-University teams, we developed an immersion program for researchers, post-docs and doctoral students that will be tested at the start of the 2021 school year.

CORNERSTONE #3 :

**FOSTERING  
INTERDISCIPLINARY  
COLLABORATION**

**Summer School : BRAIN  
TO MARKET**

The "Brain to Market" Summer School is an annual program combining translational neuroscience and entrepreneurial training thanks to intensive training to foster new projects, new initiatives and new approaches to neurologic and psychiatric pathologies. In 2020, the sixth edition was held remotely on the topic of Multiple Sclerosis, with 31 participants from the following schools : SU, Strate, Epitech, and Collège des Ingénieurs.

**Masterclass for young  
researchers**

**> "Writing a scientific/medical  
paper" Masterclass.**

This training course was organized with Duc Le (*eBioMedicine* Editor-in-Chief).

**> "Becoming a PI" Masterclass.**

This training course was developed to prepare young researchers for the "Research Manager" selection at INSERM and CNRS and benefitted from the experience and advice Paris Brain Institute researchers who have been part of selection committees.

**> "Writing a grant" Masterclass.**

This training was organized for young researchers preparing grant applications, with a special focus on EU Marie-Curie Grants.

# THE PARIS BRAIN INSTITUTE'S HUMAN RESOURCES

## GUARANTEEING THE INTEGRATION AND QUALITY OF LIFE AT WORK FOR EMPLOYEES

The Human Resources team is available to assist the Institute's employees in all aspects of their integration and daily life: recruitment, leave, employment law, employment contracts, remuneration, training, career management, international welcome.

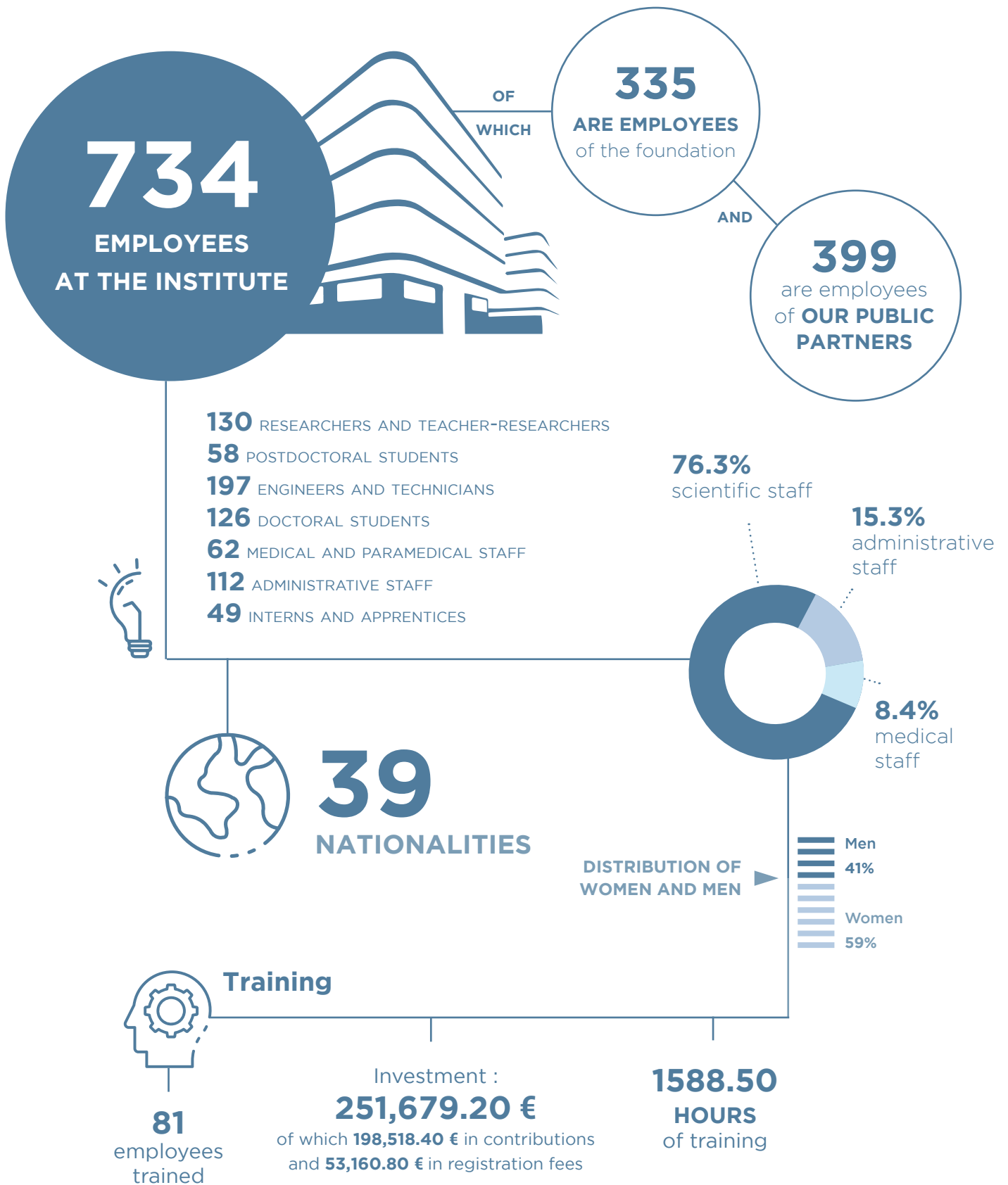
As a research environment of excellence, the Institute works to provide a professional environment that offers the best possible working conditions. The quality of life at work, the fight against harassment, the prevention of psycho-social risks, the collaborative spirit and diversity are all values that the Institute shares within its teams.

## MOBILISATION DURING THE COVID-19 PANDEMIC

Mobilised from the start of the Covid-19 pandemic, the HR team supported the Institute and its staff at the height of the lockdown on various aspects related to teleworking, remote management, management of partial unemployment benefits, sick leave/childcare, communication ("Com'In HR tips") and assistance for international staff.

In support of the teams, the HR department participated in the resumption of on-site activity while maintaining the telework dynamic in a bid to guarantee the health and safety of staff: identification of telework, management of staff in the Covid-19 management system (contact cases and positive cases) in conjunction with the Institute's Covid-19 referent, prevention of RPS and deployment of psychological support systems (telephone cells, partnerships with smartphone applications Mind, Monsherpa).

# 2020 SOCIAL REPORT



# GOVERNANCE OF THE PARIS BRAIN INSTITUTE

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THE BOARD OF DIRECTORS REGULATES THE AFFAIRS OF THE INSTITUTE THROUGH ITS DELIBERATIONS. IT DECIDES ON THE STRATEGIC ORIENTATIONS PUT FORWARD BY THE GENERAL MANAGER, VOTES ON BUDGETS AND CERTIFIES THE ACCOUNTS. IT IS CHAIRED BY PROFESSOR GÉRARD SAILLANT AND HAS 15 MEMBERS DIVIDED IN 4 COLLEGES : FOUNDERS, QUALIFIED PERSONS, FULL MEMBERS (INSERM, CNRS, SORBONNE UNIVERSITY, AP-HP) AND FRIENDS OF THE FOUNDATION.

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## BOARD OF DIRECTORS

### College of founders and members of the board

- **Gérard Saillant**, Professor of Orthopaedic and Traumatological Surgery, President of Paris Brain Institute
  - **Jean Todt**, President of FIA, Vice-President of Paris Brain Institute
  - **Serge Weinberg**, President of Weinberg Capital Partners, Treasurer of Paris Brain Institute
  - **Jean Glavany**, Former Minister
  - **Jean-Pierre Martel**, Attorney
- 

### College of qualified persons

- **Philippe Ménasché**, Professor of Thoracic and Cardiovascular Surgery at Université de Paris
  - **Richard Frackowiak**, Emeritus Professor at University College London
  - **Élisabeth Tournier-Lasserre**, Professor of medical genetics at Université de Paris
- 

### College of full members

- **Gilles Bloch**, CEO and representative of the National Institute for Health and Medical Research (INSERM)
  - **Bernard Poulain**, Scientific deputy director of INSB and representative of the National Center for Scientific Research (CNRS)
  - **Bruno Riou**, Dean and representative of Sorbonne University
  - **Erik Domain**, Director of Relations with Universities and Research Organisations and representative of Paris Hospital Administration (AP-HP)
- 

### College of friends of the foundation

- **Maurice Lévy**
  - **Christian Schmidt de la Brélie**
  - **Martine Assouline**
- 

### Public commissioner

- **Philippe Ritter**



## **BOARD COMMITTEES**

### **Scientific advisory board**

Every 5 years, Paris Brain Institute as a joint research unit (UMR) is assessed on the quality of its research, its organization, its strategy and its five-year scientific strategy. **Team research projects are assessed by the International Scientific Advisory Board (SAB), whose mission is to advise the Institute and assist it in defining its general orientations.** After discussion, the SAB submits an opinion that is taken into account to build the file submitted for evaluation by the High Council for the Evaluation of Research and Higher Education (HCERES).

- **Michael Shelanski** – President of the SAB, Columbia University, New York, USA
- **Dimitri Kullman** – ION, University College of London, UK
- **Gabor Tamas** – University of Szeged, Hungary
- **Peter Brown** – University of Oxford, UK
- **Brad Hyman** – Massachusetts Alzheimer Disease Research Center, USA
- **Stephen Hauser** – UCSF Sandler Institute, San Francisco, USA
- **Bill Richardson** – University College of London, UK
- **Helen Mayberg** – Center for Advanced Circuit Therapeutics, USA
- **Christian Buchel** – University Medical Centre Hamburg-Eppendorf - Department of Systems Neuroscience, Germany
- **Arnold Kriegstein** – UCSF, San Francisco, USA
- **Masud Husain** – University of Oxford, UK
- **Michael Heneka** – DZNE, University of Bonn, Germany

### **Audit committee & nominations and wages committee**

- **Serge Weinberg**, President of the Audit Committee
- **Claire Giry**, President of the Nominations and Wages
- **Jean Glavany**, Former Minister
- **Jean-Pierre Martel**, Attorney

### **Committee for coordination of foundation and public stakeholder activities**

- **G rard Saillant**, President of Paris Brain Institute
- **Gilles Bloch**, Representative for INSERM
- **Bernard Poulain**, Representative for CNRS
- **Bruno Riou**, Representative for Sorbonne University
- **Erik Domain**, Representative for AP-HP

### **Management committee**

Decisions are made by Executive director on the basis of CODIR recommendations.

#### **Executive Director of Paris Brain Institute and the Joint Research Unit (UMR)**

- **Prof. Alexis Brice**

#### **Scientific director and Deputy Director of the UMR**

- **Prof. Bassem Hassan**

#### **Medical Director**

- **Prof. Jean-Yves Delattre**
- **Prof. Catherine Lubetzki**

(since November 2020)

#### **Secretary General of Paris Brain Institute and the Joint Research Unit (UMR)**

- **Corinne Fortin**

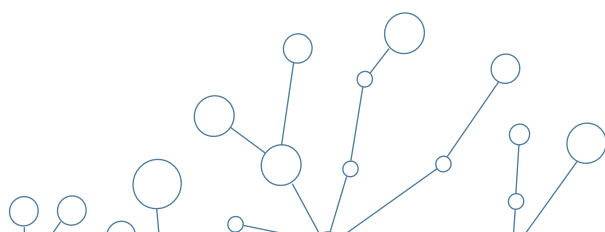
#### **Director of Communications and Development**

- **Jean-Louis Da Costa**

In addition, the Support functions management Committee (CODIS) steers several institutional and transversal projects. The platforms' expert committee is consulted twice a year on the strategic orientations of each platform, in line with the Institute's overall strategy.

### **Ethics & deontology committee**

The Paris Brain Institute Ethics and Deontology Committee was established with the dual responsibility of **contributing to the ethical conduct of research and compliance to the ethical rules of the activities that contribute to its production.** Its members are in part Institute and Piti -Salp tri re Neuroscience Medical University Department employees, appointed by the Board of Directors for 3 years, and two external members, one representing patients and the other representing donors.



## 5 ADVISORY COMMITTEES

### THEY ISSUE OPINIONS AND RECOMMENDATIONS BASED ON THEIR AREA OF EXPERTISE.

#### The scientific and medical steering committee

The Scientific and Medical Steering Committee brings together representatives from the 4 research fields (5 in 2021). Its mission is to integrate the concerns and interests of researchers into the Institute's overall mission by participating in the development and evolution of the scientific strategy, advising the Management Committee, regularly dealing with substantive issues raised by the principal investigators and providing feedback to researchers in each field.

#### Teams council

The teams council, made up of the General Manager and all the team leaders (25 in 2020), meets once a month. It is consulted on the scientific policy, budgetary measures and priorities for the UMR.

#### The Social and Economic Committee

The Social and Economic Committee (CSE) represents the Foundation's staff in dealings with the employer and informs him of any individual or collective complaint concerning the application of labour regulations (Labour Code, salaries, working hours, health and safety, etc.).

#### Laboratory committee

The mission of the Laboratory Committee is to advise UMR management on UMR activities, scientific policy, budgetary and human resources policy, and all other questions related to UMR administration. The members of the laboratory council are elected by their college (5 colleges in 2020). The number of representatives is proportional to the number of members in the college (15 members in 2020).

#### Committee on gender equity


The mission of the Gender Equity Committee, which grew out of the XX initiative at Paris Brain Institute, is to raise awareness of inequalities of opportunity and to point out biases, promote the recruitment and promotion of women, act for the visibility of women in science and propose training to change practices and culture at the Institute.

## FOUNDING MEMBERS

- **Gérard Saillant**, Professor of Orthopaedic and Traumatological Surgery, President of Paris Brain Institute
- **Jean Todt**, President of FIA, Vice-President of Paris Brain Institute
- **Yves Agid**, Honorary Professor of Neurology and Neuroscience
- **Luc Besson**, Film Director
- **Louis Camilleri**, Former CEO of Ferrari
- **Jean Glavany**, Former Minister
- **Maurice Lévy**, Chairman of the Executive Board of Publicis Group, Co-Chair of the Paris Brain Institute Friends Committee
- **Olivier Lyon-Caen**, Professor of Neurology, former Director of the Nervous System Diseases Centre of Pitié-Salpêtrière University Hospital
- **Jean-Pierre Martel**, Attorney
- **Max Mosley**, Former President of FIA
- **Lindsay Owen-Jones**, Honorary President of L'Oréal, Honorary President of the Paris Brain Institute Friends Committee
- **David de Rothschild**, Chairman of the Rothschild Bank & Co Supervisory Board
- **Michael Schumacher**, Formula 1 Driver
- **Serge Weinberg**, President of Weinberg Capital Partners, Treasurer of Paris Brain Institute

## FRIENDS OF PARIS BRAIN INSTITUTE ASSOCIATION

- **Lily Safra**, Honorary President, President of the Edmond J. Safra Foundation
- **Gérard Saillant**
- **Jean Todt**
- **Lindsay Owen-Jones**
- **Maurice Lévy**
- **David de Rothschild**
- **Jean-Pierre Martel**
- **Serge Weinberg**



Paris Brain Institute

# FINANCIAL REPORT

THOROUGH TRANSPARENCY

AT THE CORE OF OUR ACTIONS

**THE ADVANCES AND ACTIONS OF PARIS BRAIN INSTITUTE WERE CARRIED OUT WITH THE UTMOST TRANSPARENCY, WITH “TRUSTED DONATION” ACCREDITATION SINCE NOVEMBER 2010 AND RENEWED IN OCTOBER 2019. THIS ACCREDITATION ATTESTS THAT THE ACTIVITIES OF THE INSTITUTE ARE IN LINE WITH THE COMMITTEE’S PRINCIPLES : STATUTORY FUNCTIONING AND IMPARTIAL MANAGEMENT, THOROUGH MANAGEMENT, QUALITY OF COMMUNICATION AND FUNDRAISING ACTIONS, AND FINANCIAL TRANSPARENCY.**

## FUNDRAISING

**2020 fundraising revenue reached €18.3M.**

In 2020, the main new patronage agreements signed were the following :

- Fondazione Generali - The Human Safety Net
- Fondation d'entreprise IRCEM
- FIA Foundation

The Circle of Friends of Paris Brain Institute brings together donors who have been involved since the very beginning of the Paris Brain Institute adventure by accumulating large donations (€15,000 per year and more). This Circle was created to specifically thank the major donors, individuals, companies and foundations, who have been working with the Institute since 2008. It brings together donors who have donated at least €10,000 in a given year. At the end of 2020, the Circle of Friends had 578 donors. Since October 2020, the Circle has been co-chaired by Ms. Martine Assouline and Mr. Maurice Lévy, Founding Member of Paris Brain Institute.

In order to increase its resources, Paris Brain Institute continued its fundraising campaigns in 2020. Paris Brain Institute is particularly grateful and extends its thanks to loved ones who organized fundraising in memoriam benefitting the Institute.



## 2020 FINANCIAL SITUATION

### Income Statement by Nature and Function (ISNF) and Expenditure Statement (ES)

New accounting regulations relating to the annual accounts of private non-profit legal persons require the presentation of an income statement by nature and function (ISNF) to reflect the economic model of the entity and an annual fundraising expenditure statement (ES) using the data from the previous income statement.

The purpose of these documents is to give a quick overview of the use that any foundation or association makes of resources collected from the public to finance its social missions. The tables presented here thus reflect the economic model and social missions of the Institute.

In accordance with accounting regulations, allocation mechanisms underlying the development of these statements reflect management and allocation rules defined by Paris Brain Institute and are therefore based on distribution keys established internally (analytical breakdowns). Allocations are valued at full cost per destination.

### 2020 Income by Nature

**Funding of research projects is characterized by a plurality of funding sources with anchoring in a long-term perspective in order to produce knowledge and major breakthroughs in neuroscience.**

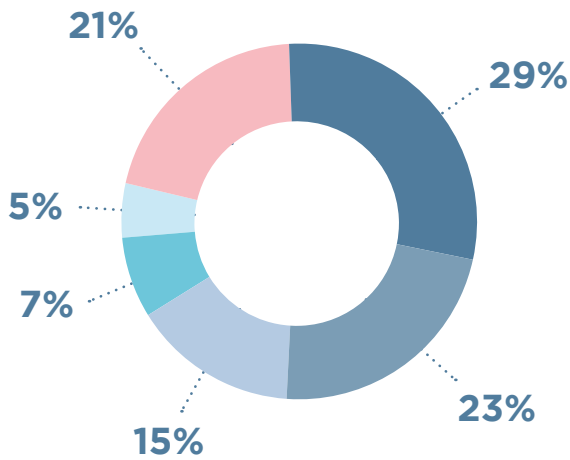
2020 income amounted to € 63.2 million, including € 50.1 million in income for the year and € 13.1 million in carry-over of resources allocated and not used in previous years. Income for the financial year mainly represents fundraising income (€ 18.3 M or 37%), which includes donations (€ 11.6 M or 63%), sponsorship (€ 5.3 M or 29%), bequests and donations (1.4 M €, or 8%).

Total income also includes :

- Income from technological platforms activities (€ 6.2 M), and from research collaborations with industrial partners (€ 3.4 M),
- Public and private subsidies (€ 14.3 M),
- Funding of the "IHU program" (€ 4.7 M),
- Miscellaneous income (rental, re-invoicing of charges, financial income) (€ 3.1 M).

Note : The overall amount of bequests, donations and life insurances accepted in 2020 amounts to € 1.9 M (compared to € 1.7 M in 2019, i.e. +11%). The legal application of the new accounting regulations from 1 January 2020 implies that bequests accepted in the course of processing and not collected are now recognised in the balance sheet. The impact of these deferred funds on the 2020 financial year amounts to € 0.5 M.

## 2020 distribution of income



### Income

- Fundraising income
- Public and private subsidies
- Income from technological platforms activities and from research collaborations with industrial partners
- Funding "IHU program"
- Miscellaneous income (rental, re-invoicing of charges, financial income)
- Report de ressources antérieures

## 2020 Expenses by Function

Overall 2020 expenses amounted to € 62.2 million : € 45.7 million used in 2020 and € 16.5 million to be used subsequently from the allocated resources. Of the 2020 allocations, € 38.2 million were allocated to **social missions**, representing **84%** of total ISNF allocations.

Paris Brain Institute social missions include :

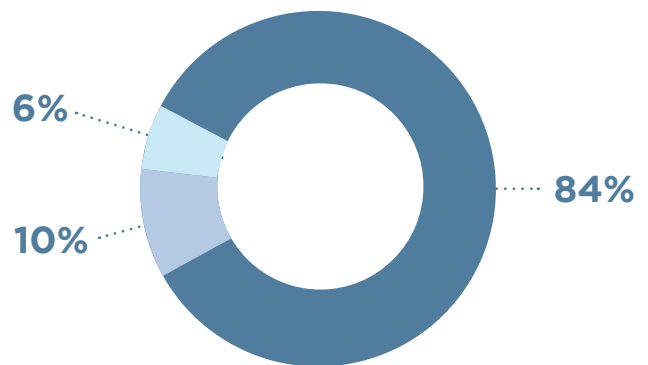
- Research programs,
- Technological platforms,
- Scientific leadership and implementation of international alliances,
- Incubation of innovative businesses.

Funding for research projects is primarily dedicated to nervous system diseases and spinal cord injuries. Technological platforms (neuroimaging, vectrology, genotyping sequencing, cell culture, histology and bioinformatics) support these projects.

**Fundraising and communication costs** are expenses incurred to collect funds from individuals (donations and bequests), companies and private foundations (patronage and sponsorship actions), as well as communication actions. They represent a total of 4.3 M €, or **10%** of total ISNF allocations

**Operating costs** are expenses in support of research (general administration, finance, human resources, legal, IT and logistics) and represent **6%** of total ISNF allocations, i.e. € 2.7 M.

## 2020 distribution of expenses



### Expenses

- Social missions
- Fundraising and communication costs
- Operating costs

## Allocation of General Public Fundraising Resources

Resources collected from the general public used in 2020 amounted to € 18.3 M. For every € 100 collected from the general public, € 73.8 were used to finance social missions and investments, € 23.6 were used to cover the costs of fundraising and communication and € 2.6 to cover Paris Brain Institute operating costs.

## 2020 Balance Sheet

Assets (M€)	2019	2020
Fixed net assets	65	63
Realizable and available assets	67	86
<b>Total</b>	<b>132</b>	<b>149</b>

Liabilities (M€)	2019	2020
Association funds	51	55
Fiscal year profit	1,7	0,95
Dedicated funds	15	20
Debt	41	41
Deferred income	23	32
<b>Total</b>	<b>132</b>	<b>149</b>

## Comments

**Total investments made by Paris Brain Institute since its creation amount to € 49 million, dedicated primarily to technological platforms that support research.**

Investments for fiscal year 2020 amount to € 3 million and include :

- [Investments in scientific materials and equipment](#) (€ 1.5 M including 4 microscopes for a total of € 0.75 M),
- [Investments to update the IT network](#) (€ 1 M),
- [Continued construction at the Rue du Chevaleret site](#) (change in assets in progress).

Net fixed assets amount to € 63 million. As of December 31, 2020, cash holdings amount to € 40.1 million, including € 14 million dedicated to earmarked funding. Association funds of Paris Brain Institute amount to € 55 million. They include equity for € 33 million supplemented by investment grants of € 22 million. Non-expendable endowment totals € 1.2 million. At the end of the fiscal year, dedicated funds (funds still to be committed to multi-year programs) amount to € 20 million.

### > Reserve policy

When it was created in 2006, the Paris Brain Institute Foundation received an endowment of € 11.70 million, of which € 1.2 million was non-expendable. Thanks to thorough budget management, the Foundation has balanced its expenses and income for the past 5 years, thus avoiding drawing on its reserves. Furthermore, the Board of Directors' investment policy is extremely cautious.

Paris Brain Institute's cashflow is invested in marketable securities (capitalization contract taken out with leading banking institutions, capital-guaranteed and 100% in euro funds).

## Voluntary in-kind contributions

### > Volunteering :

Paris Brain Institute benefited from volunteer hours during the fiscal year, primarily for communication actions. Total volume is evaluated at 0.6 FTE, or on the basis of an hourly minimum wage, a total amount of € 17 K.

### > In-kind patronage :

In 2020, the Paris Brain Institute Foundation benefited from in-kind patronage in the scope of its communication actions and appeal for public generosity, namely :

- **Media space :** FIA-Fédération Internationale Automobile, Groupe Barrière, JC Decaux, Klesia, Richard Mille, Next Radio TV, Media VB, NRJ Global, M6, Lagardère Publicité, Radio France, France TV, Amaury Media, Canal+, BeinSports, Les Echos/Le Parisien, Figaro Magazine, Réseau S4M, Le Bon Coin, Réseau Adikteev, Réseau Emoteev, Réseau Equipe.fr, Réseau Teads, Réseau Cerise, Réseau Madvertise, Réseau Tabmo, Réseau DailyMotion, Réseau Webedia, Réseau Tfi, Réseau SublimeSkinz, Réseau Capityfy, Réseau Criteo, Réseau Ogury,

- **Donated products and services :** ANACOFI, IDEC, Orrick Rambaud Martel, Publicis Groupe, ZenithOptimedia.

**To maintain its level of excellence, Paris Brain Institute has set up internal and external control procedures to guarantee thorough and efficient management: contributions to the Trusted Donations Charter Committee and services of an independent auditor.**



## TRUSTED DONATIONS

On November 3rd 2010, Paris Brain Institute received certification from the Trusted Donations Charter Committee. This certification was renewed in October 2019. For over 20 years, this Committee has acted as a regulator: certified organizations must respect ethics rules, implement a stringent policy towards donors, and accept ongoing monitoring of their commitments.

## 2020 Income Statement by Nature and Function (in €)

EXPENSES BY FUNCTION	Total	Including general public support
<b>1. Social Missions</b>	<b>38 181 383</b>	<b>13 002 106</b>
<b>Carried out in France</b>	<b>38 181 383</b>	<b>13 002 106</b>
- Actions directly carried out	38 181 383	13 002 106
- Payments to an acting organization in France	-	-
<b>Carried out abroad</b>	<b>0</b>	<b>0</b>
- Actions directly carried out	-	-
- Payments to an acting organization in France	-	-
<b>2. Fundraising Costs</b>	<b>4 326 986</b>	<b>4 326 986</b>
<b>Cost of appeals to the generosity of the general public</b>	<b>4 010 869</b>	<b>4 010 869</b>
<b>Costs related to canvassing</b>	<b>316 117</b>	<b>316 117</b>
<b>3. Institutional Operational Costs</b>	<b>2 738 510</b>	<b>2 738 510</b>
<b>4. Provisions &amp; Impairments</b>	<b>454 448</b>	<b>0</b>
<b>5. Income tax</b>	<b>-</b>	<b>-</b>
<b>6. Carryover of fiscal year allocated resources</b>	<b>16 523 021</b>	<b>2 053 723</b>
<b>GRAND TOTAL</b>	<b>62 224 348</b>	<b>19 857 961</b>
<b>SURPLUS OR DEFICIT</b>	<b>950 195</b>	

INCOME BY NATURE	Total	Including general public support
<b>1. Resources collected from the general public</b>	<b>18 355 192</b>	<b>18 355 192</b>
<b>Donations free of equivalent compensation</b>		
<b>Patronage, donations and bequests</b>	<b>18 345 385</b>	<b>18 345 385</b>
- Personal donations	11 620 122	11 620 122
- Bequests and life insurance policies	1 440 408	1 440 408
- Patronage	5 284 854	5 284 854
<b>Other revenue from general public support</b>	<b>9 807</b>	<b>9 807</b>
<b>2. Products unrelated to general public support</b>	<b>17 381 014</b>	<b>-</b>
<b>Donations free of equivalent compensation</b>	<b>-</b>	<b>-</b>
<b>Corporate patronage</b>	<b>-</b>	<b>-</b>
<b>Financial contributions free of equivalent compensation</b>	<b>4 728 491</b>	
<b>Other products</b>	<b>12 652 523</b>	
- Financial products	6 627 162	
- Services rendered	3 388 093	
- Other products	2 637 268	
<b>3. Grants and other public funding</b>	<b>14 286 154</b>	
<b>4. Reversals of provisions and impairments</b>	<b>73 402</b>	<b>0</b>
<b>5. Use of allocated resources from previous fiscal years</b>	<b>13 078 781</b>	<b>1 502 769</b>
<b>GRAND TOTAL</b>	<b>63 174 543</b>	<b>19 857 961</b>

## 2020 Expenditure Statement (in €)

APPLICATIONS BY FUNCTION	2020
<b>1. Social Missions</b>	<b>13 002 106</b>
<b>Carried out in France</b>	<b>13 002 106</b>
- Actions directly carried out	13 002 106
- Payments to an acting organization in France	0
<b>Carried out abroad</b>	<b>0</b>
- Actions directly carried out	0
- Payments to an acting organization in France	0
<b>2. Fundraising Costs</b>	<b>4 326 986</b>
<b>Cost of appeals to the generosity of the general public</b>	<b>4 010 869</b>
<b>Costs related to canvassing</b>	<b>316 117</b>
<b>3. Institutional Operational Costs</b>	<b>475 146</b>
<b>TOTAL APPLICATIONS</b>	<b>17 804 237</b>
<b>4. Provisions &amp; Impairments</b>	<b>0</b>
<b>5. Carryover of fiscal year allocated resources</b>	<b>2 053 723</b>
<b>Resource surplus for the year</b>	<b>-</b>
<b>TOTAL</b>	<b>19 857 961</b>

RESOURCES BY NATURE	2020
<b>1. Resources collected from the general public</b>	<b>18 355 192</b>
<b>Donations free of equivalent compensation</b>	
<b>Patronage, donations and bequests</b>	<b>18 345 385</b>
- Personal donations	11 620 122
- Bequests and life insurance policies	1 440 408
- Patronage	5 284 854
<b>Other revenue from general public support</b>	<b>9 807</b>
<b>TOTAL RESOURCES</b>	<b>18 355 192</b>
<b>2. Reversals of provisions and impairments</b>	<b>0</b>
<b>3. Use of allocated resources from previous fiscal years</b>	<b>1 502 769</b>
<b>Deficit of the general public fundraising of the year</b>	<b>-</b>
<b>TOTAL</b>	<b>19 857 961</b>

# SHARING AND DISSEMINATION OF KNOWLEDGE

## ABOUT THE BRAIN AND ITS PATHOLOGIES

THE MAIN GOALS OF PARIS BRAIN INSTITUTE'S COMMUNICATION ARE TO SHARE ADVANCES IN OUR RESEARCH WITH THE PUBLIC AT LARGE AND TO DEVELOP THE IMAGE AND ATTRACTIVENESS OF THE INSTITUTE IN FRANCE AND ABROAD. TO DO SO, WE HAVE FORGED A RELATIONSHIP WITH THE MEDIA, SET UP PARTNERSHIPS, DEVELOPED COMMUNICATION CAMPAIGNS, EVENTS AND JOINT ACTIONS WITH OUR ACADEMIC PARTNERS (INSERM, CNRS, AP-HP, SORBONNE UNIVERSITY, INRIA ...).

Despite the pandemic, the Institute carried out noteworthy communications actions for its 10th anniversary as well as to promote research, COVID-19 efforts, and recent developments in its organization.



### THE BRAIN & SPINE INSTITUTE - ICM BECOMES THE PARIS BRAIN INSTITUTE !

In 10 short years, ICM has become a leading neuroscience research center in Europe. Thanks to the involvement of its 734 researchers, physicians and experts, many scientific, medical and technological advances have been made possible. To go even further in its development, Paris Brain Institute decided to strengthen its visibility and attractiveness. The Brain & Spine Institute - ICM becomes Paris Brain Institute. A progression, not a radical change: we are not letting go of the spinal cord, an essential relay that helps an enormous quantity of information move throughout the body. We are moving forward towards greater clarity and simplicity as we increase societal awareness of challenges in neuroscience research. Our acronym remains: we have been the Brain & Spine Institute for the past 10 years and do not wish to erase our history and the great breakthroughs we achieved in nervous system diseases. It is also our way of recognising the support of those in our community who have been by ICM's side from the start.



## AN EXHIBIT TO CELEBRATE THE INSTITUTE'S 10 YEAR ANNIVERSARY

To make these 10 past years even more visible, an exhibit was designed to take the public at large on a discovery of "10 years at the Institute". With 5 different themes, this retrospective is an opportunity to discover Paris Brain Institute's vision, its ecosystem, major scientific and medical findings in the past decade, and major challenges to come in the field of neuroscience. The exhibit is ongoing.

## NATIONAL AWARENESS CAMPAIGN

#YOURBRAINMAKESYOUREMARKABLE

#VOTRECERVEAUVOUSRENDREMARQUABLE

To support its recent name change, Paris Brain Institute launched a national awareness outdoor media campaign with the hashtag #votrecerveauvousrendremarquable, #yourbrainmakesyouremarkable, produced *pro bono* by historical partners Publicis and JCDecaux. Through portraits of great personalities from the political, sporting, cultural and artistic worlds, including Simone Veil, Rafael Nadal, and even Jean Reno as well as a strong slogan, this campaign aims to make each of us aware of the vital importance of this fascinating organ, the most complex in the human body.

The campaign took place in two stages. A first national 100% outdoor media plan was implemented throughout France between June and August on 6,500 facings and 5,000 bus stops. In November, a second phase of the campaign was carried out on the radio (with the voice of Jean Reno and broadcast on Chérie FM, Europe 1, France Bleu, France Inter, RMC, RTL, and more) and online (digital banners on 20 Minutes, Atlantico.fr, Aufeminin.com, Télé 7 jours, Telerama.fr, and more). A "relay" website was also launched with the various campaign visuals.

The objective was to remind the general public that :

- The brain is the conductor of our orchestra, our organism, and it is thanks to it that we can dream, think, move, write, imagine, speak, create, and more ;
- Paris Brain Institute needs support to face the many challenges towards «healthy aging», especially knowing that 1 in 8 people in France are affected by a brain disease.

## LIVE S3COVID-19 CONFERENCE

S3ODEON, in association with the Academy of Sciences, Institut de France and Paris Brain Institute, organized a special edition of "S3COVID-19, what does science say ?". The conference brought together an exceptional panel of 12 key experts. They shared what we know and what we do not know about the virus, insights on management of the health crisis, and control of the pandemic.

## PARTNER EVENTS

Due to the health situation, Paris Brain Institute saw many of its partner events canceled or modified in the way they were held. This was particularly the case for the Course des Héros, or Heroes Race, a charity sporting challenge. It took place online for the benefit of Paris Brain Institute. A team of runners from Paris Brain Institute was also been set up for the online Paris 20K to support this long-term partner.

The Institute also organized 100% online partner seminars such as the Demoday of the Pfizer Healthcare Hub France's second edition. The live conference was hosted by Franck Le Meur, President of TechtoMed, and brought together all those involved in the program to look back on this second edition and highlight the agile and innovative framework set up by Paris Brain Institute and its incubator iPEPS - The Healthtech Hub.

## BRAINCAST PODCAST : GIVING NEURONS A VOICE, IN COLLABORATION CERVEAU & PSYCHO MAGAZINE

To highlight the Foundation's influence as an internationally renowned research institute specializing in neurodegenerative diseases, we initiated a partnership with Cerveau & Psycho Magazine. A total of five Braincast podcasts with exciting content were recorded with Profs. Yves Agid, Laurent Cohen, Alexis Genin, Lionel Naccache and Alexandra Durr and were listened to nearly 30,000 times in 2020.



# PATRONAGE, DONATIONS AND BEQUESTS

THE SUPPORT OF OUR DONORS (INDIVIDUALS, COMPANIES, FOUNDATIONS AND ASSOCIATIONS) AS WELL AS FROM THE GENERAL PUBLIC IS ESSENTIAL FOR PARIS BRAIN INSTITUTE TO STRENGTHEN ITS RESEARCH PROGRAMS, RECRUIT THE BEST SCIENTISTS, ATTRACT YOUNG TALENTS AND MAKE STATE-OF-THE-ART EQUIPMENT AVAILABLE TO THEM.

## **BEQUESTS, DONATIONS AND LIFE INSURANCE**

Thanks to the great generosity of women and men who have decided to pass on all or part of their assets to the Institute, bequests and life insurance in 2020 amounted to € 1.9 million, a 12% increase compared to 2019. This was especially made possible thanks to a life insurance contract of over € 489,000 for which Paris Brain Institute was designated as sole beneficiary by Ms. André G. This highlights that an increasing number of people perceive the exceptionality of the Institute's research model and put their trust in it.

These are strategic resources for the Institute: as a public-interest foundation, it is exempt from inheritance tax and 100% of what is transmitted therefore benefits our 700 researchers' work directly.

To help understand the development of brain diseases that affect 1 billion people around the world, making room for the Institute in your will or designating it as the beneficiary of a life insurance contract are powerful accelerators for discoveries that will benefit future generations.

Carole Clément, testator relationship manager, has been answering an increasing number of queries from single individuals and couples without children, as well as from donors who wish to extend their commitment.

Carole Clément can offer visits to the Institute for those wishing to learn more about how researched is organized. She can also coordinate discussions with our notary for personalized solutions

**Please feel free to contact her in full confidentiality and without any commitment on your part, to share your project, receive answers to your questions or receive our new bequest, donation and life insurance brochure : [Carole Clément at +33\(0\)1 57 27 41 41](mailto:Carole.Clément@icm-institute.org) or by email: [carole.clement@icm-institute.org](mailto:carole.clement@icm-institute.org).**

## **GENERAL PUBLIC FUNDRAISING**

Although 2020 was affected by an unprecedented health crisis, donor support towards Paris Brain Institute allowed for solid and continued growth in the number of donations and in general public fundraising, with over € 8.53M raised. This represents an increase of 9% compared to 2019. Over the year, we welcomed no less than 25,000 new donors.

There were incredible appeals for donations throughout the year, especially in April with an emergency campaign in connection with the COVID Neuroscience Cohort project. The other highlight of the year was between November and December with the annual Discoverers of Hope campaign. Actor Guillaume de Tonquédec, sponsor since 2018, was once again the spokesperson for this fundraising campaign in which all of the Institute's supporters are called upon to join forces in the hope of fighting brain disease.



With the aim of optimizing spending and reducing paper mailings, online media strategy helped increase online fundraising by +31% in 2020, bringing the share of online collection to 23% of total general public fundraising. The other strategic axis for increasing the share of resources directly allocated to research lies in the growth of recurring donations made by direct debit thanks to a reduction in management fees and expenses related to solicitation. This recurring donation method increased by +15% in 2020.

**Donations to Paris Brain Institute are income tax-deductible up to 66%, real estate tax-deductible up to 75%, and corporate tax-deductible up to 60%.**

**[The Donor Service can be reached on +33\(0\)1 57 27 47 56 or at \[contact@icm-institute.org\]\(mailto:contact@icm-institute.org\)](#)**

## **PATRONAGE : PHILANTHROPY FOR RESEARCH**

The Paris Brain Institute Circle of Friends brings together Institute patrons and major donors. Throughout the year, members of the Circle are offered private visits to laboratories, scientific and cultural conferences, and meetings with researchers.

**[The Circle of Friends Office can be reached on +33 \(0\)1 57 27 40 32 or at \[cercle@icm-institute.org\]\(mailto:cercle@icm-institute.org\)](#)**

## **Exceptional generosity towards the Institute's research programs despite the health situation**

**As of December 31<sup>st</sup>, 2020, the Circle of Friends of the Institute included 578 donors (individuals, foundations and companies).** The year was marked by the arrival of Fondazione Generali-The Human Safety Net and IRCEM Corporate Foundation as patrons. Klesia group (through its institutions Carcept Prévoyance, Ipriac and Klesia Prévoyance), the Bettencourt Schueller Foundation, the Edmond J. Safra Foundation, the Saint-Michel Fund, Boston Scientific, UNIM, the Philippe Foundation, Ever Neuro Pharma, IPSEN, the Abeona Foundation, Rousselet Group, Barrière Group and PHARMADOM ORKYN renewed their support for research on nervous system diseases by signed agreement.

Watchmakers Richard Mille and F.P.Journe once again decided to sell one of their creations to benefit Paris Brain Institute, contributing to the support of research projects. Crédit Mutuel Nord Europe, La Française and Euryale AM renewed their commitment through the SCPI Pierval Santé sharing fund.

Finally, in a time when certain scientific experiments were suspended during the first lockdown, Paris Brain Institute was able to count on the spirit of understanding of the patrons committed to multi-year agreements who agreed to maintain payments despite the research delays.

## **Donors and patrons committed alongside researchers against SARS- CoV-2**

Faced with an unprecedented upheaval caused by the COVID-19 pandemic along with the rest of humanity, Paris Brain Institute immediately appealed to the commitment of its donors and patrons to support unprecedented research projects intended to understand the effects and neurological complications of the virus. Along with the support of our donors, researchers also received the loyal support of the FIA and the FIA Foundation, OCIRP "at the heart of the family" Foundation and Accuracy.

In addition, given the health context, Paris Brain Institute was forced to cancel its fundraising breakfast at the opening of the International Contemporary Art Fair (FIAC) at Grand Palais as well as its biannual fundraising dinner. However, a fundraising dinner was organized in October 2020 at the Monaco Yacht Club in the presence of HSH Prince Albert II.

**CERCLE  
DES AMIS  
de l'Institut  
du Cerveau**



## **CIRCLE OF FRIENDS OF PARIS BRAIN INSTITUTE**

- **Lily Safra**, Honorary President of the Circle of Friends of Paris Brain Institute
- **Lindsay Owen-Jones**, Honorary President of the Circle of Friends of Paris Brain Institute
- **Pr. Gérard Saillant**, Founding Member and President of Paris Brain Institute
- **Jean Todt**, Founding Member and Vice-President of Paris Brain Institute
- **Martine Assouline et Maurice Lévy**, Co-Presidents of the Paris Brain Institute's Campaign Committee
- **Jean-Luc Allavena** • **Cédric de Bailliencourt** • **Natacha et Jean-Charles Decaux** • **Alexandre Desseigne-Barrière** • **Sylvain Héfès** • **François Henrot** • **Jean-Philippe Hottinguer** • **Véronique de Kepper** • **Richard Mille** • **Eddie Misrahi** • **Margaux Primat** • **Christian Schmidt de La Brélie** • **Sophie Seydoux** • **François Thomé** • **Serge Weinberg**  
Members of the Campaign Committee on December 31<sup>st</sup>, 2020

## **AMBASSADORS**

**Michelle Yeoh**, actress, and **Jean Reno**, actor



# THANK YOU

## MAJOR PATRONS

- Elisabeth Badinter
- Maria Rosa Bemberg
- Dominique, Alexandre et Joy Desseigne
- FIA FOUNDATION
- FONDATION BETTENCOURT SCHUELLER
- FONDATION GROUPE EDF
- FONDATION EDMOND J. SAFRA
- FONDATION LILY SAFRA
- FP JOURNE - INVENIT ET FECIT
- HSBC FRANCE
- KLESIA - CARCEPT PREV - IPRIAC
- Maurice Lévy
- Docteur Léone-Noëlle Meyer
- Richard Mille
- MSDAVENIR
- OCIRP
- ORRICK RAMBAUD MARTEL
- Lindsay Owen-Jones
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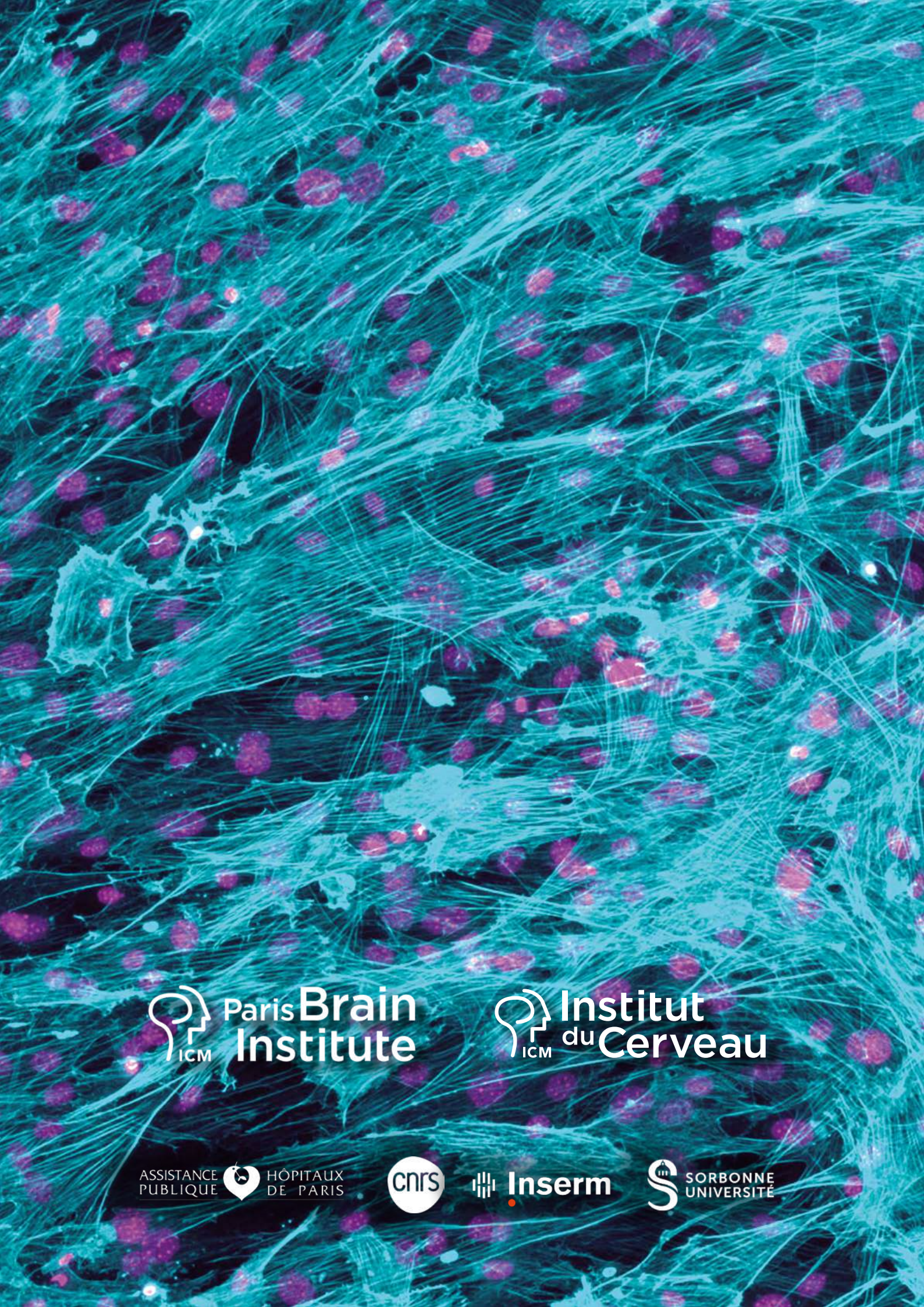
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