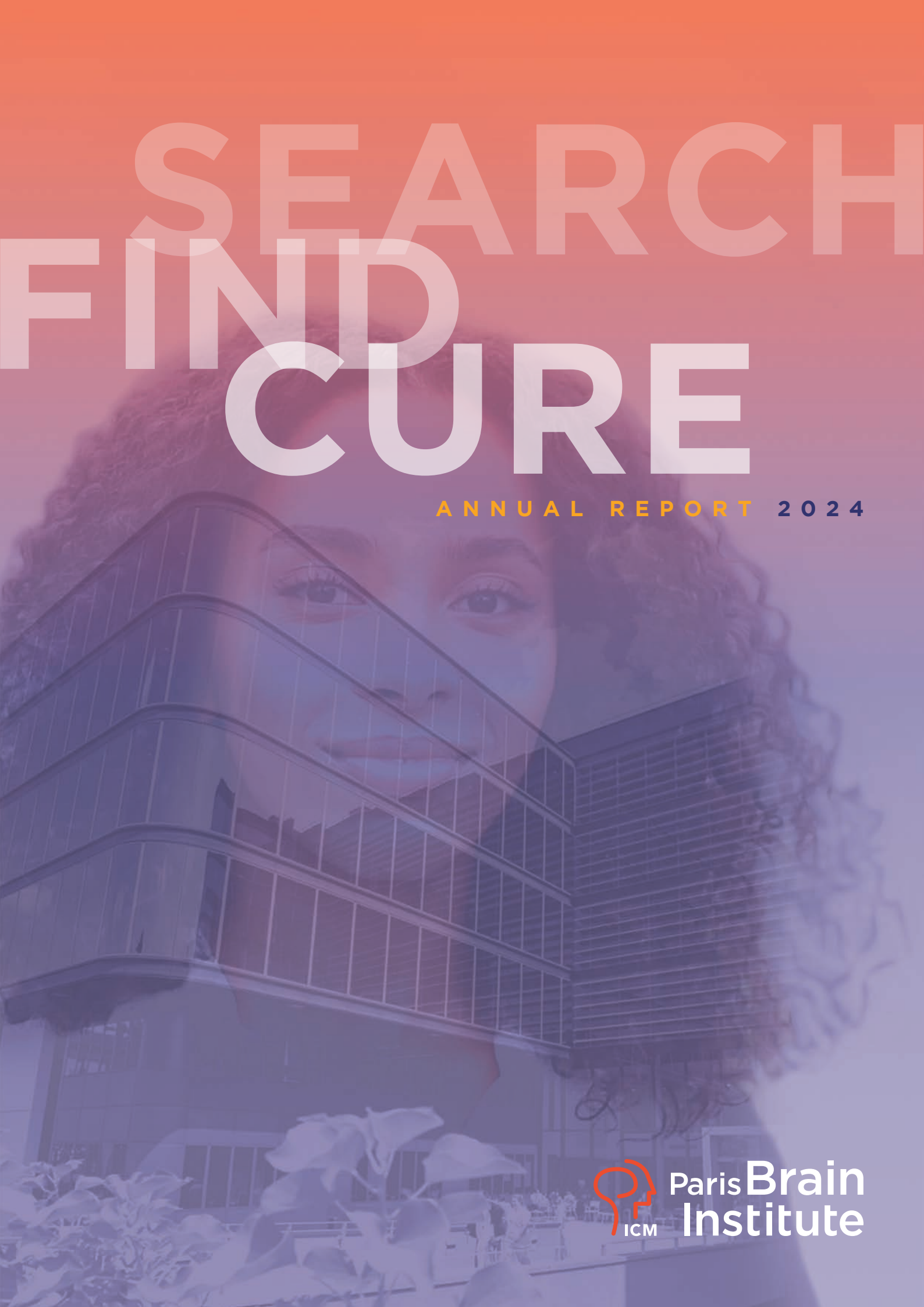
SEARCH FIND CURE

ANNUAL REPORT 2024



ICM Paris Brain Institute

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OUR MISSION

The most complex organ in the human body, the brain manages our social behavior, our emotions and our actions. It is the brain that makes us aware of the world around us, of ourselves and of others. But despite considerable progress achieved in science and technology, our understanding of how the brain works is still very patchy, and treating brain disorders remains a major challenge for the health of humanity.

Paris Brain Institute was established in 2010, and has created a collaborative, interdisciplinary research model that promotes innovation and groundbreaking discoveries. This environment, in which patients, researchers, clinicians, engineers, technicians, business leaders and students work side by side, has become one of Europe's leading centers for research into the central nervous system.

With drive and ambition, the Institute's teams work tirelessly to achieve a single objective: to transform fundamental discoveries into therapeutic solutions, so they can be accessed by patients and by society as quickly as possible.

Innovation and entrepreneurship supporting brain research

Prof. GÉRARD SAILLANT

PRESIDENT OF PARIS BRAIN INSTITUTE

EVERY YEAR since it was first established, Paris Brain Institute has made progress in its mission: to transform fundamental and basic research data into therapeutic innovations for patients with neurological or psychiatric diseases. This has been the ambition that has guided Paris Brain Institute since its inception. In 2024, our commitment and ambition in fulfilling this mission were strengthened with the arrival of a new Innovation Director, Géraldine Farjot, whose profile you can read in this annual report.

The Institute's entrepreneurial spirit was demonstrated this year with the launch of NeurAL. This neuroscience acceleration launchpad, supported by an entrepreneurial philanthropy fund, identifies the most promising scientific startups and helps them structure their business models from the earliest stages in order to develop solid business strategies. Two startups were selected – one on brain tumors and the other on Parkinson's disease – both aimed at developing new therapies.

To advance research, the Institute invests in cutting-edge technologies. The arrival of the 7-Tesla MRI scanner in June 2024 is a striking example of this approach and symbolizes our ability to bring ambitious projects to fruition. This high-precision equipment, acquired thanks to the very generous support of a patron, opens up unprecedented opportunities for exploring the human brain and promises major advances in research into neurodegenerative diseases. In addition, a twelfth core facility focused on proteomics was set up in 2024 to meet the growing needs of the teams in this field.

The past year has also been full of scientific advances, such as the clinical application of focused ultrasound, a non-invasive technique for the treatment of essential tremors, and other discoveries on multiple sclerosis and Parkinson's disease, for example, which you can read about throughout this document.

These successes would not have been possible without the wisdom and leadership of Professor Alexis Brice, who led the Institute for 12 years with unwavering commitment, and who ended his tenure at the end of 2024. I am deeply grateful to him for setting Paris Brain Institute on a path to excellence, establishing it as a world-class center for neuroscience that combines fundamental research, clinical practice, and technological innovation.

Building on these solid foundations, Professor Stéphanie Debette, our new Executive Director as from January 2025, will continue to pursue and develop our missions. Her recognized expertise and strategic vision will be valuable assets, and I wish her every success as head of our Institute. The first year of her leadership will see a series of major events, including the establishment of a new Joint Research Unit, presented in this report, and the celebration of the Institute's fifteenth anniversary: 15 years of commitment, innovation and discovery, serving and supporting patients and society. This anniversary will be an opportunity to celebrate our successes while renewing our ambition for the future.

All of these achievements are the result of the tireless efforts of the Institute's 900 employees: scientists, medical professionals, paramedics, and support staff. However, none of this could have been achieved without the invaluable support of our donors and patrons. Their commitment makes it possible for our teams to conduct cutting-edge, open, and multidisciplinary research. I would like to take this opportunity to thank them, and to thank you. Thanks to them, and thanks to you, we are able to respond to the boldest and most daring challenges, working to promote health for all.

Realization

CORINNE FORTIN

SECRETARY GENERAL OF PARIS BRAIN INSTITUTE

IN 2024, our scientific and support teams have demonstrated flawless synergy in joining forces to deliver a range of projects launched in the last few years, and to prepare for the redeployment of our Joint Research Unit (UMR), once again confirming our ability to respond to organizational and strategic challenges.

The installation and commissioning of two incredible new magnetic resonance imaging (MRI) devices – a 3-Tesla MAGNETOM Cima.X MRI and a 7-Tesla MAGNETOM Terra.X MRI – within our CENIR neuroimaging core facility are important examples of this ability. The Institute is the first such organization in France to access the latest advances in these technologies, with these acquisitions forming part of a broad program to develop strategic sectors in the the Île-de-France Region, funded by the regional authorities and the French Government as part of the France 2030 plan.

At the same time, the Institute has acquired new IT storage infrastructure and a new low-voltage switchboard, a key component in the building's electrical distribution system.

The Human Resources Department actively prepared for the redeployment of the UMR on January 1, 2025, in particular by developing a customized management training program for the 46 team leaders, 14 of whom are taking on this responsibility for the first time.

Innovation is the very core of our DNA, and this has been reinforced with the implementation of the MediTwin project, funded by the French public investment bank Bpifrance as part of the France 2030 plan, and the signing of a consortium agreement between 14 partners, including Dassault Systèmes, Inria, seven University Hospital Institutes (IHU), Nantes University Hospital (CHU) and four startups, including two – Qairnel and Neurometers – from Paris Brain Institute. MediTwin aims to create digital twins to transform patients' care pathways and accelerate the development of personalized therapies.

In clinical research, our Regulatory and Technical Support Unit (CART) secured authorization for the NeuroPrems study less than 10 months after the investigators began drafting the protocol. This is another demonstration of the effectiveness of Paris Brain Institute's unique model.

The Institute was also praised this year by the French High Council for Evaluation of Research and Higher Education (HCERES) in its assessments of the UMR and the Neuroscience Clinical Investigation Center (CIC). The conclusions of these reports acknowledge the remarkable results achieved thanks to this ecosystem of research, technology, logistics, and administration that drives scientific excellence and innovation.

Such successes are the result of strategic vision, ongoing commitment, and close cooperation among all parts of the Institute, which are united in their dedication to moving research forward and improving patient health.

INTERVIEW WITH

PROF. STÉPHANIE DEBETTE AND PROF. ALEXIS BRICE

On January 1, 2025, Professor Stéphanie Debette took over as Executive Director of Paris Brain Institute, succeeding Professor Alexis Brice, who led the Institute from 2012 to 2024.

How do you view the year 2024?

Alexis Brice: The year 2024 will be memorable in many ways. First and foremost, it marks recognition of the Institute's scientific and organizational excellence, with the very positive assessment by the High Council for Evaluation of Research and Higher Education (HCERES). This result, which also confirms the redeployment of our Joint Research Unit (UMR) as of January 1, 2025, is the outcome of a lengthy process of collective reflection. It has made it possible for us to strengthen major thematic areas within the Institute and create new ones. This includes the recruitment in 2024 of Nikolas Karalis' team, which is working on neural circuits and brain dynamics, the creation of a second team led by Inria researchers, focusing on brain-machine interfaces, and, of course, the arrival of Stéphanie Debette's team, introducing a field of research that is new to the Institute, focusing on the genetic epidemiology of cerebral vascular diseases.

Stéphanie Debette: First of all, I would like to express my gratitude to Professor Alexis Brice for setting the Institute on such a path to excellence. The success and reputation of Paris Brain Institute are the result of collective commitment, and I am excited to join this dynamic team. Recent successes, such as the excellent evaluations, the growing impact of international collaborations, and the development and implementation of major cross-disciplinary projects involving numerous teams working on topics of major interest, demonstrate the solid foundations of the Institute, which I intend to build upon in developing the strategy for the coming years.

A leadership transition is always a pivotal moment for an organization. How did you each prepare for and work through this transition?

A.B.: The preparations for the transition were completely transparent. Stéphanie and I had the opportunity to work closely together over the past few months with the Institute's governing bodies. This includes the evaluations we've already mentioned, but also a joint study trip to the United States, which helped strengthen ties with some of our international partners and ensure effective communication on strategic issues.

S.D.: This transition has been a valuable opportunity for dialogue. Alexis has been generous in making himself available and lending his support, as well as sharing his experience and in-depth knowledge of how the Institute operates. The US trip was a highlight, giving me the opportunity to bolster my understanding of international issues and build relationships of trust with our partners. This handover provided an opportunity for positive discussions about the future of the Institute, while recognizing its legacy and core values.

Alexis Brice, what is your assessment of your 12 years at the helm of Paris Brain Institute?

A.B.: The Institute was still only two years old when I took over as Executive Director. We had to develop a framework for how it would work, implement its vision and help it grow, building its identity together... I feel very proud of what our terrific community of researchers has achieved. Our center is now internationally recognized, attracting top experts and making important scientific discoveries that give hope to patients. I am aware of how far we still have to go, as the scientific and medical challenges are enormous, but I am confident because I know that the Institute, under the leadership of Professor Stéphanie Debette, is now ready to enter a new phase in its development.

Stéphanie Debette, as you take up the torch, what lessons can you take away from this assessment to help you begin building your own strategic vision?

S.D.: The Institute's solid track record points to exciting opportunities in the years ahead. I am thinking in particular of the very fruitful relationships we have built up over the past few years, and strengthened in 2024, with our partners in Europe and around the world. The Institute has continued to make its mark on the international stage with major collaborations, for example with Yale and Harvard Universities (United States), the extension of the Big Brain Theory (BBT) call for projects to several international partners, a source of promising synergies, and the appointment of Professor Philip de Jager from Columbia University (United States) as visiting professor. This will be a key area of focus for developing the Institute's influence, which we hope to extend to Asia and our global strategic partners such as the BrainLat Institute in Chile and the IIT and AIIMS institutes in India. Other major challenges lie ahead, in terms of both research and our ability to translate progress in the laboratory into concrete therapeutic solutions.

OCT 2023

SLEEP OPEN TO THE WORLD: WE CAN RESPOND TO EXTERNAL STIMULI WHILE SLEEPING

These observations, which appeared in *Nature Neuroscience* and are the result of a collaboration between teams at Paris Brain Institute and the Sleep Pathology Department at Pitié-Salpêtrière University Hospital in Paris (AP-HP), call into question the very definition of sleep and the associated clinical criteria.

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CAMILLE LAKHLIFI: SUCCESS AT THE POPULAR SCIENCE AWARDS

On Thursday October 5, Camille Lakhlifi, a Université Paris Cité PhD student at Paris Brain Institute (CNRS/Inserm/Sorbonne University), won 1st prize from the jury at the international final of "Ma thèse en 180 secondes" (My thesis in 180 seconds), the popular science competition organized by CNRS and France Universities.

NOV 2023

NICOLAS RENIER, RECIPIENT OF THE 22ND ERC FUNDING GRANT AWARDED TO THE INSTITUTE

The European Research Council (ERC) has awarded a Consolidator Grant to Nicolas Renier, an Inserm researcher and head of the Structural Dynamics of Networks team* at Paris Brain Institute. He was the recipient of a Starting Grant from the ERC in 2017.

European Research Council
Established by the European Commission

FIRST ROUND OF FINANCING FOR THE BRAIN FUND TO SUPPORT PARIS BRAIN INSTITUTE

Managed by Impact Partners, The Brain Fund, a private equity fund, has successfully raised €25 million in its first round of financing to provide Paris Brain Institute with long-term financial resources to support the research teams' projects and accelerate the development of new treatments for diseases of the nervous system.

DEC 2023

MULTIPLE SCLEROSIS: FIVE EARLY WARNING SIGNS

In a study published in *Neurology*, researchers from Paris Brain Institute have shown that, on a population scale, the frequency of symptoms such as depression, constipation, and urinary tract infections is associated with a diagnosis of multiple sclerosis five years later.

PROFESSOR ALEXIS BRICE ELECTED MEMBER OF THE ACADEMY OF SCIENCES

On December 12, 2023, Professor Alexis Brice was elected to the French Academy of Sciences for his work in improving our understanding of the mechanisms underlying neurodegenerative diseases and offering avenues for new therapies. His election will strengthen the neuroscience discipline within this prestigious institution.

JAN 2024

NIKOLAS KARALIS: EXPLORING THE BRAIN PROCESSES OF OUR INTERNAL STATES

Nikolas Karalis joined Paris Brain Institute in January 2024. He is a research associate (Inserm) and the leader of the Neuronal Circuits and Brain Dynamics team. His work will focus on the fundamental link between brain activity and neurotransmitter balance. In September 2024, he was selected as the recipient of an ERC Starting Grant for the innovative StateNeuromod project. This is the 23rd funding grant from the ERC obtained by Paris Brain Institute.

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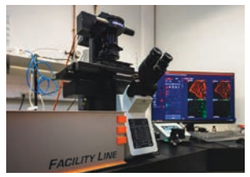
FEB 2024

A NEW STED MICROSCOPE TO ILLUMINATE THE BRAIN



Thanks to funding from the Fondation NRJ-Institut de France, Paris Brain Institute has acquired a STED microscope with an adaptive optics module, a state-of-the-art piece of equipment that will enable researchers to observe brain tissue under unique conditions.

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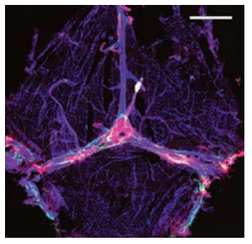
MUTATIONS THAT CAUSE MENINGIOMAS ARE WIDESPREAD IN HEALTHY TISSUES

In a new study published in *Acta Neuropathologica*, the Institute's Genetics and Development of Nervous System Tumors team* has shown, for the first time, that oncogenic mutations exist naturally in the meninges of healthy people.



MAR 2024

MINISTERIAL VISIT AND OPEN DAY FOR BRAIN AWARENESS WEEK

On Monday March 11, to open Brain Awareness Week, Paris Brain Institute was honored to welcome Ms Sylvie Retailleau, Minister of Higher Education and Research, Mr Roland Lescure, Minister Delegate for Industry, and Mr Frédéric Valletoux, Minister Delegate for Health and Prevention. Then, on Saturday, March 16, during an open day, more than 450 people were able to find out more about the Institute through workshops, tours, and lectures.

"We visited Paris Brain Institute to meet researchers and leaders of projects such as IGHOR, Neurometers and Brain & Mind, which have received €99 million in funding through France 2030. We will continue to support innovation in healthcare", stated Mr Frédéric Valletoux.

THE CONSTRUCTION OF VISUAL ATTENTION HIGHLIGHTED AT NEURONAL LEVEL

Findings published in the journal *Nature Communications* by researchers from Paris Brain Institute show that exogenous attention – the involuntary redirection of attention to a specific element in our environment – is built up in the cortex gradually, from the back to the front of the brain, within three fronto-parietal networks.

ARRIVAL OF THE 3-TESLA MRI PLATFORM AT PARIS BRAIN INSTITUTE

On Wednesday March 27, the CENIR neuroimaging core facility welcomed the new 3-Tesla MRI scanner (Siemens Healthineers). This acquisition forms part of a major investment plan for the Institute's core facilities, made possible by the valuable and loyal support of one of our patrons.

**2023–2024 team.*

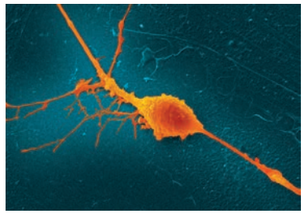
APR 2024

GÉRALDINE FARJOT APPOINTED INNOVATION DIRECTOR

In April 2024, Géraldine Farjot took over as head of innovation at Paris Brain Institute. She will be leading the ambitious activities of this department, which aims to transform scientific discoveries into concrete solutions for patients with neurological and psychiatric diseases.

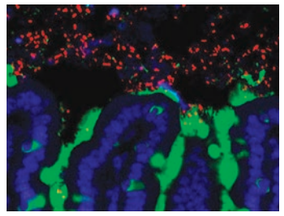
MULTIPLE SCLEROSIS: NEUROPROTECTIVE EFFECT AND EARLY CORTICAL REMYELINATION

In a study published in *Brain*, researchers at Paris Brain Institute have shown that spontaneous remyelination of nerve fibers in the cortex has a neuroprotective effect in patients with shorter disease duration and minor lesions. These results will be crucial for targeted patient recruitment in future clinical trials.



SEE P. 23

MAY 2024



THE COMPOSITION OF THE GUT MICROBIOTA COULD INFLUENCE DECISION-MAKING

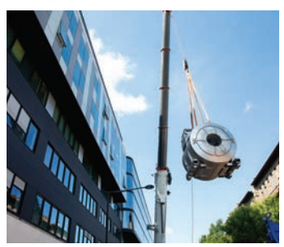
According to the findings of a joint study between Paris Brain Institute and the University of Bonn published in the journal *PNAS Nexus*, changes in gut microbiota can influence our sensitivity to injustice and how we treat others.

JUN 2024

A 7-TESLA MRI SCANNER AT PARIS BRAIN INSTITUTE

On Sunday June 9, 2024, thanks to the support of one of our generous patrons, Paris Brain Institute welcomed an extraordinary piece of equipment: the latest generation 7-Tesla MAGNETOM Terra.X MRI scanner from Siemens Healthineers. This 7-T MRI scanner will enable the Institute to take a technological leap forward for the benefit of the neuroscience community and, ultimately, for patients.

SEE P. 78



SPECIAL OPEN BRAIN BAR EVENT: ‘WHAT ATHLETES BRING TO NEUROSCIENCE’

Just a few weeks before the start of the 2024 Olympic Games in France, Paris Brain Institute hosted a special conference as part of its Open Brain Bar series, bringing together two worlds that have much more in common than one might think: neuroscience and sport.

SEE P. 56

THE DUAL EFFECT OF LERIGLITAZONE IN X-LINKED ADRENOLEUKODYSTROPHY (X-ALD)

The Institute’s Metabolism, Immunity and Neurodegeneration (MIND) team has shown that taking leriglitazone daily makes it possible to slow down the progression of myelopathy in patients with X-linked adrenoleukodystrophy, and above all, to reduce their risk of developing an acute cerebral form (CALD) of the disease. These findings have been published in the scientific journal *Brain*.

SEE P. 29

4TH EDITION OF THE BIG BRAIN THEORY PROGRAM FOR BOLD IDEAS (BBT4)

In 2024, Paris Brain Institute launched the 4th edition of the Big Brain Theory Program (BBT), created in 2016 and designed to foster new and bold projects addressing the next challenges in neuroscience. For the first time, this call for projects was open to researchers from the Institute’s international partners.

SEE P. 40

JUL 2024

“THE MOVE EUROPE 2024”: AN INTERNATIONAL NEUROLOGICAL SEMIOLOGY TOURNAMENT FOR MEDICAL STUDENTS

The 2024 edition of “The Move” took place on July 3 and 4 at Paris Brain Institute. An international, educational, and unifying event, this tournament is a special opportunity for young medical students from around the world to meet and exchange ideas about neurology.

SEE P. 54

RETT SYNDROME: A NEW GENE THERAPY ON THE WAY

The Technological Innovation Unit GENOV at Paris Brain Institute has looked closely at brain cholesterol metabolism, which is disrupted in young Rett Syndrome patients. By correcting this pathway through the injection of a gene drug, researchers have shown that the symptoms of the disease can be significantly reduced.

AUG 2024

GUESTS FROM THE INTERNATIONAL OLYMPIC COMMITTEE DISCOVER PARIS BRAIN INSTITUTE

On Wednesday July 31, the Institute had the pleasure of welcoming members of the International Olympic Committee (IOC) and their friends and families. Paris Brain Institute saw the IOC’s visit to Paris as the perfect opportunity to enrich international discussions about neuroscience. research.

ULTRASOUND ANALYSIS SHOWS UNEXPECTED EFFECTS ON MOTOR NEURON DISEASE

The ALS: Causes and Mechanisms of Motor Neuron Degeneration team, in collaboration with Alexandre Carpentier from the neurosurgery department at Pitié-Salpêtrière Hospital (AP-HP) and the startup CarThera, have demonstrated that an ultrasound-based technique can also be applied to the blood-spinal cord barrier and could be a promising avenue in motor neurone disease.

SEE P. 23

SEP 2024

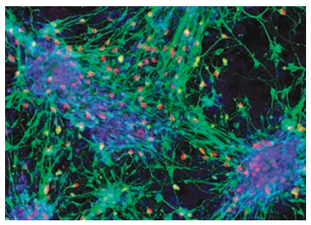
LAUNCH OF THE FOULÉES DU CORTEX CHALLENGE

A 100% connected sporting challenge, more than 1,000 participants, individuals and companies took part in the Foulées du Cortex for its first iteration (September 10–21, 2024) to give a major boost to research into brain diseases.

SEE P. 85

STIMULATING SPECIFIC NEURONS IN THE STRIATUM STOPS COMPULSIVE BEHAVIORS

Promising results, published in the journal *Nature Neuroscience*, obtained through the research of the Neurophysiology of Repetitive Behaviors team at Paris Brain Institute, have made it possible to better understand the biological mechanisms underlying compulsions, which are particularly common in obsessive-compulsive disorders (OCD).



*2023–2024 team.

Paris Brain Institute in 2024

878*
staff, including 84% scientific, medical and paramedical staff

** as at September 30, 2024*

45
industry contracts signed in 2024

29*
research teams selected by a Scientific Advisory Board

** as at January 1, 2025*

51
nationalities

12
core facilities and biobank

418
patients included in trials by the Neuroscience CIC

82
ongoing trials in the Neuroscience CIC

500
publications in scientific journals in 2024

13 clinical research facilities (iCRIN)

15
training programs at the Open Brain School, with over 515 participants

104,934
active donors between October 1, 2023 and September 30, 2024

63 active patents, including 7 new patent requests filed

24
startups hosted, including 1 spin-off created in 2024, and 3 maturing startup projects

Paris Brain Institute's research teams have won prestigious awards and funding, a recognition of the excellence of our scientists' work.

HONORS AND AWARDS

Election to the French Academy of Sciences

ALEXIS BRICE
Executive Director of Paris Brain Institute**

French Foundation for Medical Research Prize – Bernadette et Pierre Duban Prize

MARIE-CLAUDE POTIER
(CNRS)
Alzheimer's Disease and Prion Diseases team*

Schlumberger Foundation for Education and Research Prize

DELPHINE OUDIETTE
(Inserm) – Mov'It: Movement, Investigation, Therapeutics. Normal and Abnormal Motor Control: Movement Disorders and Experimental Therapeutics team*

Election as Chair of the ALBA Network

VIOLETTA ZUJOVIC
(Inserm)
Myelin Plasticity and Regeneration team*

International final, "Ma thèse en 180 secondes" (my thesis in 180 seconds) – 1st Prize from the Jury

CAMILLE LAKHLIFI
(CNRS/Inserm/ Sorbonne University)
PhD Student at Paris Brain Institute

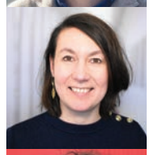
COMPETITIVE EXAMINATIONS

Research associate (normal grade), Inserm

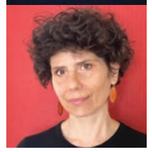
DAFNI HADJIECONOMOU
Gut-brain Axis Communication and Physiology

Research Director class 2 (DR2), Inserm

JEAN DAUNIZEAU
Motivation, Brain and Behavior team*



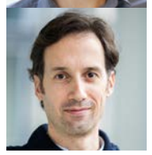
DELPHINE OUDIETTE
Mov'It team*



EMMANUELLE VOLLE
FrontLAB: Frontal Functions and Pathology team*

Research Director class 2 (DR2), CNRS

ÉRIC BURGUIÈRE
Neurophysiology of Repetitive Behaviors team*



NELSON REBOLA
Cellular Mechanisms of Sensory Processing team*

20.60 million euros: total competitive national and international funding obtained between October 1, 2023 and September 30, 2024.

17 ANR grants won in the same period, a success rate of 35%, including 3 ANR Early Career Scientist grants.

University Lecturer (CMF) (Sorbonne University)

MARIE VILLAIN
PICNIC – Physiological Investigation of Clinically Normal and Impaired Cognition team*

University Professors-Hospital Practitioners (PU-PH)

MATTHIEU PEYRE
Genetics and Development of Nervous System Tumors team*

BENJAMIN ROHAUT
PICNIC – Physiological Investigation of Clinically Normal and Impaired Cognition team*

Junior Professorship, Sorbonne University

YANN ZERLAUT
Cellular Mechanisms of Sensory Processing team*

GRANTS AND FUNDING

European Research Council (ERC) Consolidator Grant

NICOLAS RENIER
(Inserm)
Structural Dynamics of Networks team*

European Research Council (ERC) Starting Grant

NIKOLAS KARALIS
(Inserm)
Neuronal Circuits & Brain Dynamics team*

**2023–2024 team.*
***From 2012 to 2024.*

Paris Brain Institute's scientific and medical strategy is based on a transdisciplinary, synergistic approach combining basic and translational research, clinical expertise and support for cutting-edge technology platforms. This structure enables the Institute to meet the challenges involved in understanding the nervous system and the diseases that affect it, and to build a strong international reputation with growing visibility.

RESEARCH

MEHDI TOUAT
(AP-HP/SORBONNE UNIVERSITY)

Mehdi Touat is one of the young researchers who took charge of a team as part of the redeployment of Paris Brain Institute's Joint Research Unit (UMR) in January 2025. He is co-leader of the Brain Tumor Heterogeneity, Immunity and Therapy (BRIGHT) team.

Our research teams

In 2024, Paris Brain Institute brought together 26 research teams, working in five different fields, following a multidisciplinary approach.

26 RESEARCH TEAMS (2023–2024)

The list below summarizes all the teams and the funding they obtained between October 2023 and September 2024.

ARAMIS: Algorithms, Models and Methods for Images and Signals of the Human Brain


Olivier Colliot (CNRS),
Stanley Durrleman (Inria),
ANR – France 2030 – RHU,
Health Program, Horizon Europe

ALS: Causes and Mechanisms of Motor Neuron Degeneration

Séverine Boillée (Inserm),
ARMC, FilSLAN,
Fondation de France

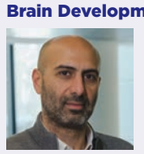
Neuronal Circuits & Brain Dynamics

Nikolas Karalis (Inserm),
ERC Starting Grant

Cognitive Control – Interoception – Attention


Philippe Fossati (AP-HP/Sorbonne University),
Liane Schmidt (Inserm),
FRM

Brain Development



Bassem Hassan (Inserm),
ANR-PRCI

Structural Dynamics of Networks

Nicolas Renier (Inserm),
ERC Consolidator Grant, FRM

Dynamics of Epileptic Networks and Neuronal Excitability


Stéphane Charpier (Sorbonne University),
Mario Chavez (CNRS),
Vincent Navarro (AP-HP/Sorbonne University),
MSCA-PF

FrontLAB: Frontal Functions and Pathology

Richard Lévy (AP-HP/Sorbonne University),
ANR-JCJC,
ANR-PRC (3), Arsla

Genetics and Development of Nervous System Tumors


Emmanuelle Huillard (CNRS),
Marc Sanson (AP-HP/Sorbonne University),
ARC (3), BRAINY, Cancéropôle Île-de-France (3), FRM, Gefluc Paris, Health Research Board, INCa (2), Institut Gustave Roussy, Ligue contre le cancer (2), Plan Cancer, Université Paris-Saclay (2)

Genetics and Pathophysiology of Epilepsy


Stéphanie Baulac (Inserm),
Éric Leguern (AP-HP/Sorbonne University),
Hope for HH, King Baudouin Foundation, MSCA-DN, MSCA-PF

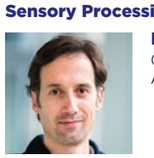
Repair in Multiple Sclerosis: from Biology to Clinical Translation


Catherine Lubetzki (AP-HP/Sorbonne University),
Bruno Stankoff (AP-HP/Sorbonne University),
ANR-PRC, Arsep (3), Fondation Hippocrène, FRC, FRM

Alzheimer's Disease and Prion Diseases


Marie-Claude Potier (CNRS),
Stéphane Haïk (Inserm, AP-HP),
ARMC, Campus France – Cofecub, CJD Foundation, Fondation pour la recherche sur Alzheimer (2), Fondation Alzheimer, FRM

Cellular Mechanisms of Sensory Processing



Nelson Rebola (CNRS),
ANR-PRC, FRM (2)

Motivation, Brain and Behavior



Mathias Pessiglione (Inserm),
Sébastien Bouret (CNRS),
Jean Daunizeau (Inserm),
ANR-JCJC, ANR-PRC, FRM,
DIM C-BRAINS, MSCA-PF

Mov'It: Movement, Investigation, Therapeutics. Normal and Abnormal Motor Control: Movement Disorders and Experimental Therapeutics


Marie Vidailhet (AP-HP/Sorbonne University),
Stéphane Lehéricy (AP-HP/Sorbonne University),
ANR-PRC, Cefipra, FRM (2), SFRMS (2)

Experimental Neurosurgery


Brian Lau (CNRS),
Carine Karachi (AP-HP/Sorbonne University),
France Parkinson, FRM

Basic to Translational Neurogenetics


Alexandra Durr (AP-HP/Sorbonne University),
Giovanni Stevanin (Inserm/EPHE),
ANR-PRC, Campus France, Friedreich's Ataxia Research Alliance, FRM, MJFOX, Target ALS

Neurophysiology of Repetitive Behaviors

Éric Burguière (CNRS),
ANR-JCJC

Cellular Physiology of Cortical Microcircuits

Alberto Bacci (Inserm)

Gut Sense Lab

Dafni Hadjieconomou (Inserm)

Molecular Physiology of Synaptic Bioenergetics (Diane Barrière Chair)

Jaime de Juan-Sanz (CNRS),
ANR-PRCI, FRM,
Fondation Fyssen,
Kavli Foundation

Molecular Pathophysiology of Parkinson's Disease


Olga Corti (Inserm),
Jean-Christophe Corvol (AP-HP/Sorbonne University),
ANR-PRC, CHU de Toulouse,
France Parkinson, FRM, Novartis

PICNIC – Physiological Investigation of Clinically Normal and Impaired Cognition



Laurent Cohen (AP-HP/Sorbonne University),
Lionel Naccache (AP-HP/Sorbonne University),
Paolo Bartolomeo (Inserm),
ANR-PRC, ANR-MRSEI, FRM (2)

Myelin Plasticity and Regeneration


Brahim Nait Oumesmar (Inserm),
Violetta Zujovic (Inserm),Arsep (2)

Sensory Spinal Signaling

Claire Wyart (Inserm),
ANR-PRC

Experimental Therapeutics of Parkinson's Disease


Étienne Hirsch (CNRS),
Stéphane Hunot (CNRS)

GLOSSARY

ANR – France 2030 – RHU: French National Research Agency (ANR) – Teaching Hospital Research
ANR-JCJC: ANR Early Career Scientist
ANR-MRSEI: ANR Setting up European or International Scientific Networks
ANR-PRC: ANR Collaborative Research Projects
ANR-PRCI: ANR Collaborative International Research Projects
AP-HP: Paris Public Hospital Network
ARC: Association for Cancer Research (ARC) Foundation
ARMC: Grant for Research on Brain Diseases
ARSEP: French Association for Multiple Sclerosis Research
ARSLA: French Association for Amyotrophic Lateral Sclerosis Research
CEFIPRA: Indo-French Center for the Promotion of Advanced Research
CJD Foundation: Creutzfeldt-Jakob Disease Foundation
COFECUB: French Committee for the Evaluation of Academic and Scientific Cooperation with Brazil
DIM C-BRAINS: Major Research and Innovation Field – Cognition and Brain Revolutions: Artificial Intelligence, Neurogenomics, Society
ERC: European Research Council
FILSLAN: French National Network for Rare Diseases: Amyotrophic Lateral Sclerosis and Motor Neurone Diseases
FRC: French Foundation for Brain Research
FRM: French Foundation for Medical Research
GEFLUC: Association of French Companies in the Fight against Cancer
INCA: French National Cancer Institute
MJFOX: The Michael J. Fox Foundation for Parkinson's Research
MSCA-PF: Marie Skłodowska-Curie Actions – Postdoctoral Fellowships
MSCA-DN: Marie Skłodowska-Curie Actions – Doctoral Networks
SFRMS: French Sleep Research and Medicine Society

29 RESEARCH TEAMS (2025)

The Joint Research Unit was redeployed following the evaluation by the Scientific Advisory Board (SAB) and then by the French High Council for Evaluation of Research and Higher Education (HCERES) in 2023–2024. Here is the list of the 29 teams in place since January 1, 2025.

Machine Learning and Data Science for Brain Disorders (ARAMIS)


Ninon Burgos (CNRS),
Olivier Colliot (CNRS)

ALS Causes and Mechanisms of Motor Neuron Degeneration (DecodALS)

Séverine Boillée
(Inserm)

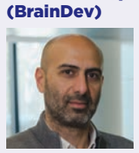
Neuronal Circuits & Brain Dynamics (NeuroCircuits)

Nikolas Karalis
(Inserm)

Belief Decision Neuroscience team


Philippe Fossati
(AP-HP/Sorbonne University),
Liane Schmidt (Inserm)

Brain Development (BrainDev)



Bassem Hassan
(Inserm)

Brain Development and Dysfunction in Neurogenetic Diseases (NeuroGen)


Alexandra Durr
(AP-HP/Sorbonne University),
Sandrine Humbert (Inserm)

From Movement to Cognition: Insights from Motor Disorders (MOV'IT)


Emmanuel Flamand-Roze
(AP-HP/Sorbonne University),
Pierre Pouget (CNRS)

Clinical and Experimental Epilepsy (EpiC)


Vincent Navarro
(AP-HP/Sorbonne University),
Jean-Christophe Poncer (Inserm)

Brain tumor Heterogeneity, immunity and Therapy (BRIGHT)


Franck Bielle
(AP-HP/Sorbonne University),
Mehdi Touat
(AP-HP/Sorbonne University)

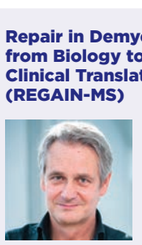
Neurovascular Interfaces in Brain Tumors and Vascular Malformations (NOVA)


Emmanuelle Huillard (CNRS),
Mathieu Peyre
(AP-HP/Sorbonne University)

Laboratory of Brain Plasticity (Plastic)

Nicolas Renier
(Inserm)

Repair in Demyelinating Diseases: from Biology to Clinical Translation (REGAIN-MS)



Bruno Stankoff
(AP-HP/Sorbonne University)

The Prefrontal Cortex as a Critical Hub for Higher Cognitive Functions: from Health to Disease (Frontlab)


Richard Lévy
(AP-HP/Sorbonne University),
Emmanuelle Volle (Inserm)

Alzheimer's Disease and Prion Diseases (ALZHEIMER-PRIONS)


Stéphane Haïk (Inserm),
Marie-Claude Potier (CNRS)

Cerebral Small Vessel Disease and Neurodegeneration (GENOVASC team)


Hugues Chabriat
(AP-HP/Université Paris Cité)
Stéphanie Debette
(Université de Bordeaux)

Cellular Mechanisms of Sensory Processing (CENSOR)

Nelson Rebola
(CNRS)

Metabolism, immunity and Neurodegeneration (MIND)


Fanny Mochel
(AP-HP/Sorbonne University),
Violetta Zujovic
(Inserm)

Genetic Mosaicism in Epilepsy and Neurodevelopmental Disorders (MOSAIC team)

Stéphanie Baulac
(Inserm)

Motivation, Brain and Behavior (MBB)


Jean Daunizeau (Inserm),
Mathias Pessiglione (Inserm)

Navigation, Sensorimotor Integration Brain & Body Integration Lab (SIBBIL)

Claire Wyart
(Inserm)

Experimental Neurosurgery (NEURXP)


Carine Karachi
(AP-HP/Sorbonne University),
Brian Lau
(CNRS)

Systems Neuroengineering to Model and interface Brain Networks (NERV)

Fabrizio De Vico Fallani
(Inria)

Neurophysiology of Social Cognition (SocialNeuro)

Julia Sliwa
(CNRS)

Physiological Investigations of Clinically Normal and Impaired Cognition (PICNIC Lab)



Paolo Bartolomeo (Inserm),
Lionel Naccache
(AP-HP/Sorbonne University),
Jacobo Sitt (Inserm)

Cellular Physiology of Cortical Microcircuits (CircuitLab)

Alberto Bacci
(Inserm)

Gut-brain Axis Communication and Physiology (GutSense)

Dafni Hadjieconomou
(Inserm)

Molecular Physiology of Presynaptic Function (PreSyn) (Diane Barrière Chair)

Jaime de Juan-Sanz
(CNRS)

Molecular Pathophysiology of Parkinson's Disease (MPP+)


Jean-Christophe Corvol
(AP-HP/Sorbonne University),
Philippe Ravassard (CNRS)

Sleep, Dreams, and Cognition (DreamTeam)


Isabelle Arnulf
(AP-HP/Sorbonne University),
Delphine Oudiette (Inserm)

Research boosted by new momentum

Brian Lau, Scientific Director, Director of Core Facilities, and Deputy Director of the UMR, looks back on the achievements of the past year and offers some perspectives for 2025.

A banner year

How would you sum up the past year?

Brian Lau: As we reflect on the Institute's accomplishments in 2024, it is clear that this year has been defined by outstanding evaluations, transformative initiatives, and the development of a robust foundation for future progress. The HCERES evaluation was a standout milestone, reaffirming our excellence in neuroscience research and the relevance of our strategic vision. This recognition underscores the dedication and innovation of our teams, whose pioneering work continues to push the boundaries of science.

Our strategic development efforts yielded remarkable results, including the arrival of two new team leaders, Nikolas Karalis and Dafni Hadjieconomou, who bring innovative and exciting new ways of studying fundamental aspects of brain function. In January 2025, we also welcomed our new Executive Director, Stéphanie Debette, whose commitment during this year of transition has been essential in the HCERES, Inserm, and CNRS evaluations, as well as in shaping new scientific perspectives for the years ahead. Her expertise in epidemiology and cerebrovascular disease opens new frontiers for research at the Institute.

What has been happening in clinical research?

B.L.: For clinical research, 2024 was a transformative year. The renewal of our clinical research facilities (iCRIN), which nowinclude two new hospital departments in the Neuroscience University Medical Department (DMU), demonstrates our steadfast commitment to patient-centered studies and addressing groundbreaking medical questions related to the nervous system.

This year also saw the launch of our four major cross-disciplinary projects, designed to elevate our science, tackle more ambitious questions, and transcend traditional research boundaries. These initiatives integrate contributions from across the Institute's teams, platforms, and international partners, fostering collaboration and innovation on a global scale.

State-of-the-art equipment arrived at the Institute in 2024. What can you tell us about it?

B.L.: Keeping pace with technological advancements is critical to advancing research. The Institute continually invests in its platforms, enhancing its human resources, with the recruitment of expert staff, and its cutting-edge equipment. The ICM.Quant platform is a good example of this, with the renewed employment of its scientific and operational managers, Nelson Rebola and Olivier Renaud, and the arrival of Astou Tangara, an expert in advanced imaging technologies. Notable additions include two advanced MRI scanners (3-Tesla and 7-Tesla) installed at our CENIR neuroimaging core facility, a super-resolution STED microscope, and the establishment of a dedicated proteomics core facility.

What projections do you have for 2025?

B.L.: As we look towards 2025, the horizon is filled with promise. We anticipate fresh perspectives and expanded collaborations that will further solidify our role in neuroscience research. When she was applying to the Institute, Stéphanie Debette presented an ambitious project to create a center dedicated to artificial intelligence and data science. That project will soon be established, reflecting our commitment to innovation, leveraging artificial intelligence to address complex brain disorders.

Together, we will continue to evolve, embracing challenges and forging paths that bring hope and breakthroughs to patients worldwide.

Outreach of scientific activities

The Institute has maintained a high publication volume, with a total of 500 publications in 2024, including 214 in journals with an impact factor greater than 7, representing 43% high-impact publications, a rate that has grown steadily in recent years (26.5% in 2018, the last year of the previous UMR's term of office). Researchers from the Institute have also been awarded prestigious competitive grants, including two from the European Research Council (Nicolas Renier and Nikolas Karalis) and 17 from the French National Research Agency (a success rate of 35%, twice the national average).

The Institute's international recognition also enables it to forge partnerships with other world-renowned research centers, particularly through joint calls for projects such as the Big Brain Theory program, which is becoming increasingly international. The purpose of this latter program is to foster collaborative and ongoing partnerships between researchers in order to broaden the impact of individual research programs and develop new pioneering projects that could lead to breakthroughs in any field of neuroscience. In 2024, three partners joined the program: the Pasteur Institute, The Neuro (Montreal), and Mission Lucidity (Belgium). Nine projects were selected: five bipartite projects between teams from Paris Brain Institute; two tripartite projects involving Paris Brain Institute, The Neuro, and the Pasteur Institute; and two bipartite projects with VIB-KU Leuven, part of Mission Lucidity.

ARRIVALS

NEW TEAM of Nikolas Karalis

Following Dafni Hadjieconomou in 2023, Paris Brain Institute welcomed researcher Nikolas Karalis and his team in early 2024. Specializing in the study of neural dynamics and their role in complex cognitive functions, this team will enrich the Institute's scientific landscape by bringing cutting-edge expertise in computational and experimental neuroscience. Their arrival demonstrates Paris Brain Institute's continued appeal to leading international talent.

Continued development of the clinical research strategy

Paris Brain Institute has placed particular emphasis on supporting young clinicians involved in research. Through specialized programs and targeted funding, the Institute supports their integration into the academic community while providing them with the resources they need to carry out ambitious and innovative projects. These initiatives aim to train a new generation of research-focused clinicians capable of tackling the complex challenges of neuroscience.

2024 saw the launch of three interface contracts enabling clinicians to devote more of their time to research activities, a positive step that was consolidated through the launch of a new call for applications in the same year. Support from Fondation André et Michel Bouriez also made it possible to recruit two clinical fellows, promising young international clinicians, to strengthen the links between research and clinical practice.

Finally, the Institute has launched a call for applications for the renewal of its clinical research facilities (iCRIN), with the aim of strengthening existing links between hospital departments and research conducted at Paris Brain Institute, and to further integrate clinicians into the Institute's systems and processes. The iCRIN newly selected at the end of 2024 began operating on January 1, 2025.

THREE QUESTIONS FOR

CLAIRE WYART,

leader of the Sensory Spinal Signaling team* and of the Deep Brain Stimulation (DBS) project

How did this project come about?

I wanted to draw on the unique expertise of Paris Brain Institute to explore the fundamental mechanisms of motor disorders. Since 2011, I have been researching the development of motor defects in various pathologies. Thanks to optogenetics and animal models such as zebrafish, I have been able to study the organization of motor circuits and their dysfunctions. The DBS project aims to combine all the expertise available at the Institute in one interdisciplinary approach to pave the way for new treatments for Parkinson's disease.

How does the environment at Paris Brain Institute foster the synergies needed to deliver this project?

Paris Brain Institute is a unique place where diverse areas of expertise come together to tackle complex issues. The genetic and anatomical pathology research on Parkinson's disease conducted at Pitié-Salpêtrière Hospital (AP-HP), and by Professors Alexis Brice and Yves Agid in particular, enriched by 15 years of international hires at Paris Brain Institute, provides a solid foundation for this project. The project will also draw on collaborations with external experts within France, notably with the Vision Institute, as well as internationally. Nine teams, four platforms, and more than 35 researchers are already involved, to maximize its impact.

What are the challenges ahead?

The current challenge is to establish robust methodologies and harmonize their application across specialties. We are also working on developing the Institute's platforms and the Neuro-CEB platform, in cooperation with the hospital, and on publishing innovative methodological advances.

Major cross-disciplinary projects

In 2023, the Institute launched four ambitious cross-disciplinary projects. These projects illustrate Paris Brain Institute's commitment to interdisciplinary and collaborative research, mobilizing expertise on a variety of approaches and pathologies to address the major challenges posed by diseases of the nervous system around a common issue. This first year of operation has enabled us to lay the foundations for the entire scientific organization of the projects: engaging experts and setting up working groups, seeking partnerships to make the best possible progress on the various aspects of each program, and recruiting technical and management staff.

NEUROPREMS

By accessing and making use of the resources of Pitié-Salpêtrière Hospital (AP-HP), which incorporates expert centers for neurodegenerative diseases and leading national centers for rare diseases, the main objective of the NeuroPrems project is to identify changes in biological markers and imaging data of neurodegeneration and neuroinflammation occurring during the presymptomatic stages of neurodegenerative and neuroinflammatory diseases.

The identification of distinct presymptomatic profiles during the silent phase preceding the onset of symptoms will make it possible to associate markers with disease onset or progression, and to identify critical periods of modification of different markers. This will make it possible to estimate the optimal time windows for early intervention for each disease.

NEIMO

The NEIMO program is being implemented in collaboration with Yale University (United States), with the primary goal of generating and integrating the most advanced procedures to simultaneously image and profile the cellular and molecular states of neuroinflammation in multiple sclerosis and early Parkinson's disease, to understand how monitoring neuroinflammation can inform the prediction of disease onset and assess its progression and response to treatments. The project draws on the expertise of those involved in this transatlantic collaboration.

BRAIN FUNCTIONAL GENOME PROGRAM

The Brain Functional Genome Program (BFGP) aims to deepen our understanding of the human brain during development by linking gene expression locations to their functions, providing the broad community working on neurological and neurodegenerative diseases with established and robust techniques and targeted tools. It is based on cutting-edge technologies in which Paris Brain Institute is an expert: 3D visualization (iDISCO) of transcripts, spatial transcriptomics, and the generation of induced pluripotent stem cell (iPSC) lines.

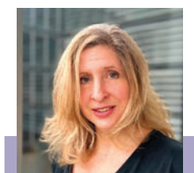
DEEP BRAIN STIMULATION

By combining approaches from human genetics, cellular neurobiology, computational methods, and motor circuit physiology, ranging from genetic model organisms to humans, the Deep Brain Stimulation (DBS) project is intended to develop new strategies for stimulating resilient motor circuits in Parkinson's disease.

**2023–2024 team.*

Cellular and molecular neurobiology

The primary objective of the researchers working in this field is to identify the genetic, molecular and cellular mechanisms underlying brain function during development and aging.
This fundamental knowledge is essential for understanding major brain functions and neurological and psychiatric diseases, and for developing new therapeutic targets.

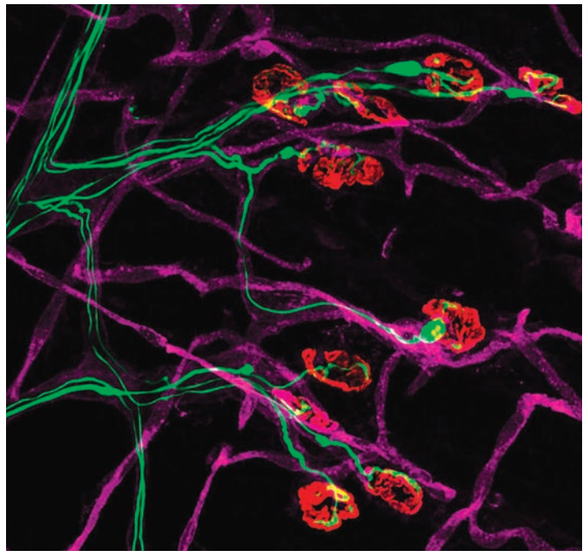


Manager for the research field: Stéphanie Baulac, Inserm Research Director and Team Leader.

FOCAL CORTICAL DYSPLASIA AND EPILEPSY: A NEW THERAPEUTIC APPROACH

Cortical malformations such as focal cortical dysplasia type II (FCD II) are associated with drug-resistant pediatric epilepsy, often requiring neurosurgery. FCD II results from somatic mosaicism, which leads to the presence of dysmorphic cells in the brain tissue among non-mutated neurons. A correlation between pathological neuron density and epileptiform activity has been demonstrated in FCD II tissue sections. At the same time, this work has shown that dysmorphic neurons exhibit characteristics of senescence and that treatment offering the possibility of eliminating senescent cells (dasatinib/quercetin) reduces the number of senescent neurons and the frequency of seizures in an experimental model. These results pave the way for therapeutic strategies that selectively target mutated senescent cells in the brain tissue of FCD II patients, regardless of the mutated gene.

Ribierre T. *et al. Nat. Neurosci*. 2024
Genetics and Pathophysiology of Epilepsy team*



The motor nerves in the spinal cord extend to the periphery, where they come into contact with muscles, forming connections called neuromuscular junctions.

A NEW DIAGNOSTIC CRITERION FOR SPINOCEREBELLAR ATAXIA TYPE 27B (SCA27B)

GAA trinucleotide repeat expansions in the FGF14 gene are a common cause of spinocerebellar ataxia type 27B (SCA27B), characterized by a slowly progressive cerebellar syndrome (balance and walking disorders, clumsiness, etc.) that begins after the age of 45. There is a familial bias in the transmission of the disease and significant genetic and clinical variability. A study on 1,169 people with cerebellar ataxia showed a 10% frequency of allele carriers with GAA repeat expansions exceeding 300 repeats and highlighted specific clinical characteristics in these patients. Diagnosis of SCA27B ataxia must take into account both the patient's clinical picture (onset after age 45, rhythmic involuntary downward eye movements, double vision, normal speech) and the scale of GAA expansion.

Méreaux J.-L. *et al. eBioMedicine*. 2024
Basic to Translational Neurogenetics team*

ULTRASOUND ANALYSIS SHOWS UNEXPECTED EFFECTS ON MOTOR NEURONE DISEASE

The blood-brain barrier (BBB), made up of small blood vessels, protects the central nervous system (CNS) from potentially toxic substances circulating in the blood, including drugs. In amyotrophic lateral sclerosis (ALS), or motor neurone disease, the challenge is to enable therapeutic molecules to reach the motor neurons located in the CNS that specialize in controlling movement. To assist the action of a therapeutic molecule known to be effective in the disease, researchers used pulsed ultrasound in the lumbar region of mice once a week for five weeks. Their findings are very encouraging: a single session enabled the drug to be highly concentrated in the spinal cord. A therapeutic trial will soon begin in patients with ALS to assess the absence of ultrasound toxicity and the tolerance of the device, followed by its effectiveness on symptoms.

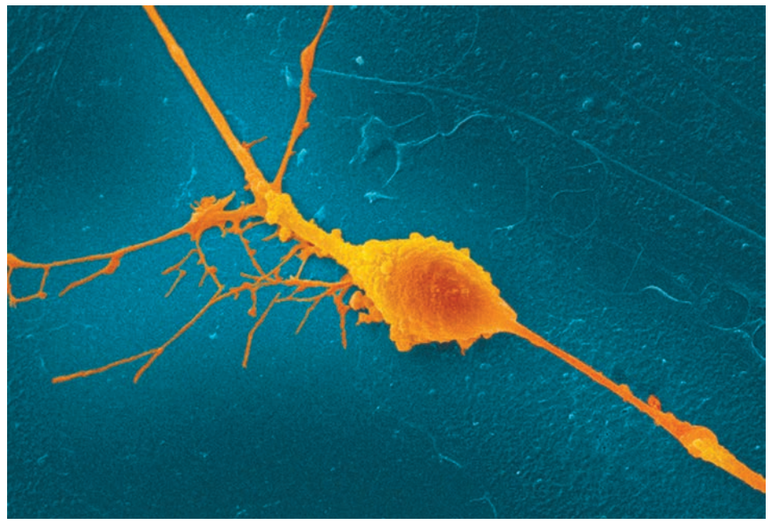
Montero A.-S. *et al. eBioMedicine*. 2024
ALS: Causes and Mechanisms of Motor Neuron Degeneration team*

EARLY CORTICAL REMYELINATION HAS A NEUROPROTECTIVE EFFECT IN MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is an inflammatory disease in which the immune system attacks myelin, the protective sheath surrounding nerve fibers. This anomaly causes lesions of varying extents in the brain and spinal cord, which are associated with motor, sensory, and cognitive disorders. Studying 140 patients with multiple sclerosis (37 with clinically isolated syndrome, 71 with a relapsing-remitting form, and 32 with a progressive form) using a specific type of imaging (quantitative magnetization transfer (qMT) imaging) showed that, in patients with early-stage disease and limited lesions, spontaneous remyelination of nerve fibers in the cortex has a neuroprotective effect: it halves the risk that symptoms will worsen five years later. These results indicate that treatments promoting myelin repair, which are currently being researched, should be administered as soon as first symptoms appear for maximum effectiveness.

Lazzarotto A. *et al. Brain*. 2024
Repair in Multiple Sclerosis: from Biology to Clinical Translation team*

Retinal neuron extended by a long axon surrounded by its myelin sheath.



**2023–2024 team.*

INTERFACE CONTRACT

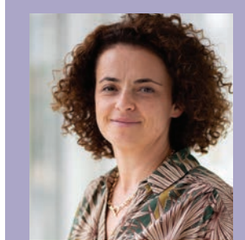
FRANCK BIELLE

(AP-HP/Sorbonne University) has been awarded an interface contract under an initiative launched by the Institute in 2023 to enable doctors in the Neuroscience DMU to dedicate 50% of their time to research as part of an Institute team for a period of three to five years. Franck Bielle is conducting research into understanding the molecular and cellular mechanisms of brain tumors. Since January 1, 2025, he has been co-leader of the Brain Tumor Heterogeneity, Immunity and Therapy (BRIGHT) team.

AWARD

VIOLETTA ZUJOVIC

(Inserm), co-leader of the Myelin Plasticity and Regeneration team*, was elected in September 2024 as Chair of the Alba Network, which promotes equity and diversity in brain science.



Integrative neurophysiology

Scientists specializing in neurophysiology study the mechanisms and neuronal interactions underlying sensory processing, cognition and motor control. Their main goal is to characterize the activity of synapses – areas between several neurons where information is exchanged – and of microcircuits and whole-brain networks. This research also seeks to understand the how and why of neuronal activity linked to behaviors or movement malfunctions in pathological conditions such as an epileptic seizure, or a motor block during gait in Parkinson's disease.

Manager for the research field: Claire Wyart, Inserm Research Director and Team Leader

EPILEPSY: BETTER UNDERSTANDING THE CONTROL OF SYNAPTIC EXCITABILITY

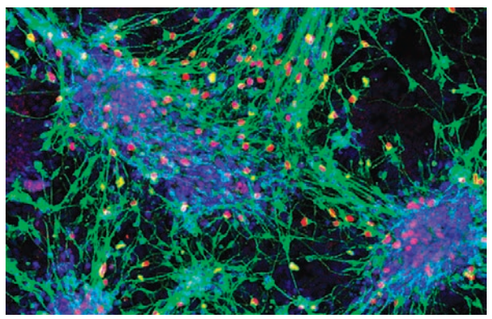
Autoimmune limbic encephalitis associated with LGI1 autoantibodies is a form of epilepsy characterized by seizures caused by disruptions in synaptic function. The underlying molecular defects are still not clearly understood. Using LGI1 autoantibodies obtained from patients with this disease, researchers were able to accurately track LGI1 regulation by neuronal activity at the synapse and assess the impact of pathological autoantibodies on this process using innovative optical tools. They discovered that LGI1 is not simply secreted, but is instead dynamically recycled through exocytosis and endocytosis, and that its concentration finely adjusts glutamate release. This work has enabled a better understanding of how LGI1 dysfunction leads to hyperexcitability and confirms its role in epilepsy, paving the way for future targeted therapeutic strategies.

Cuhadar U., Calzado-Reyes L. *et al. Cell Rep.* 2024
Molecular Physiology of Synaptic Bioenergetics team*

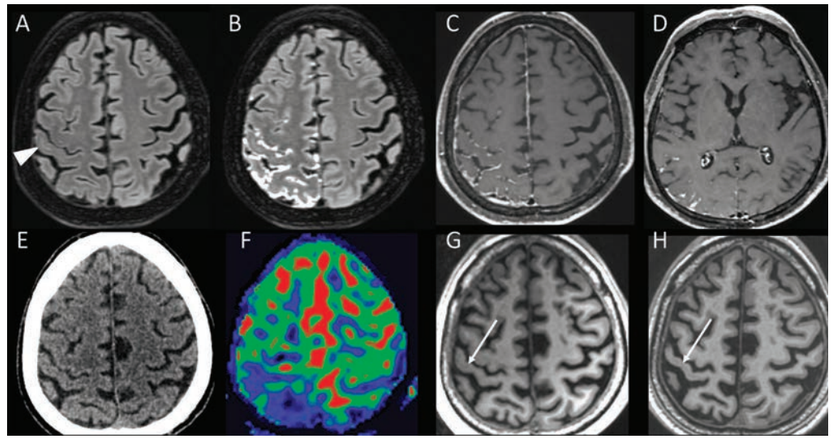
ROLE OF DISINHIBITORY INTERNEURONS IN THE MODULATION OF CORTICAL FUNCTIONS

The cerebral cortex, an essential structure of the brain, governs our higher cognitive functions. It allows us to understand and interact dynamically with our environment, adapting our perception according to our behavioral state. In fact, our sensory perception varies considerably depending on our activity and our physiological state at a given moment. The mechanism behind this sensory flexibility remains unknown, but it may involve neocortical interneurons releasing γ-aminobutyric acid (GABA), which is essential for neuronal inhibition. This research shows that the activation of these interneuron populations is not uniform across cortical areas, but varies depending on the activity of sensory systems. The results emphasize the critical role of a specific subtype of interneurons – somatostatin-positive (SST+) interneurons – as key regulators in these processes. Furthermore, the results reveal that these interneurons are dynamically regulated by a combination of neuromodulation and sensory inputs transmitted to the neocortex via the thalamus. These findings shed light on fundamental mechanisms explaining how behavioral states influence the functioning of the neocortex.

De Brito Van Velze M. *et al. Cell Rep.* 2024
Cellular Mechanisms of Sensory Processing team*



Interneurons.



Brain MRI of a patient with Sturge-Weber syndrome: observation of leptomeningeal angioma after injection of a contrast agent (B, C, and D), with a decrease in cerebral blood flow opposite (F) and the gradual onset of cerebral cortex atrophy over six months (G and H).

Illustration taken from: Late-Onset Status Epilepticus Associated With Isolated Leptomeningeal Angioma and Sturge-Weber Syndrome-Related GNA11 Pathogenic Variation. Cousyn L. *et al., Neurology*. 2023 Nov 27; 101(22): 1021-1022. doi: 10.1212/

AN ATYPICAL CASE OF LATE-ONSET STURGE-WEBER SYNDROME

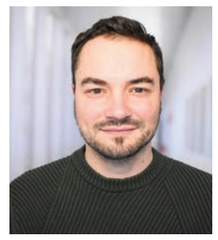
A 61-year-old man with no history of neurological disorders presented with two episodes of refractory status epilepticus requiring intensive care, five months apart. After each episode, he developed prolonged weakness on the left side (hemiparesis), which gradually improved over several weeks. He also developed recurrent, transient episodes of paralysis on the left side (hemiplegia), this time unrelated to epileptic seizures, which occurred after hypovolemic (decrease in the amount of circulating blood) and septic (caused by infection) shocks.
A brain MRI showed a vascular malformation located in the meninges (leptomeningeal angioma) in the right temporal, parietal, and occipital regions ***(see illustration),*** consistent with Sturge-Weber syndrome. However, the age of onset of the disease was too late, since the vast majority of patients (approximately 80%) develop symptoms before the age of 1. A meningeal biopsy revealed a somatic R183C mutation in the GNA11 gene, as described in Sturge-Weber syndrome, confirming the diagnosis. The authors point out that this is the first reported case of genetically proven late-onset Sturge-Weber syndrome. The presence of a leptomeningeal angioma with epilepsy that appears late in adulthood should not rule out a diagnosis of Sturge-Weber syndrome.

Cousyn L. *et al. Neurology.* 2023
Dynamics of Epileptic Networks and Neuronal Excitability team*

COMPETITIVE EXAMINATION

YANN ZERLAUT

(CNRS), who is studying the principles of information processing in cortical networks by combining approaches and tools from theoretical neuroscience, data science, data engineering, and software engineering in the Cellular Mechanisms of Sensory Processing team*, has been appointed junior professor of computational neuroscience at Sorbonne University.



**2023–2024 team.*

Cognitive neuroscience

The aim of research in this field, at the intersection of psychology and biology, is to identify the circuits in the brain behind mental processes and how they are impaired by disease, treatment and rehabilitation. Researchers in this field study how the brain consciously forms language, guides attention, and accesses information. They explore where motivation and decision-making are localized in the brain and how they are represented. They also seek to understand how behavior is influenced by cognitive biases, creativity, mood, or social factors such as suggestion and interaction with others. To shed light on the neurocognitive foundations of these mental processes and effects, scientists combine behavioral testing, mathematical modeling, and brain imaging. They apply these tools to investigate cognition in healthy people, and in patients with disorders such as depression, apathy, dementia, aphasia, and impaired planning, reasoning and behavioral control. Findings from this field of research offer an understanding of neurological and psychiatric diseases through the lens of behavior and brain imaging, which has implications for the development of novel treatment strategies.

THE INTERMEDIATE STATES BETWEEN WAKEFULNESS AND SLEEP

Sleep is not a state in which we are completely isolated from our environment: while we sleep, we are capable of hearing and understanding words. For this study, 22 people without sleep disorders and 27 narcoleptic patients were given a "lexical decision" test in which a human voice read out a series of real words and made-up words. Participants were asked to respond by smiling or frowning, in order to classify them into one of these categories. On waking up, participants were asked to report whether they remembered interacting with anyone. By cross-referencing physiological and behavioral data with participants' subjective reports, researchers showed that it is possible to predict when sleepers were able to respond to stimuli, as this correlated with increased brain activity and physiological indicators typically associated with conscious cognitive activity.

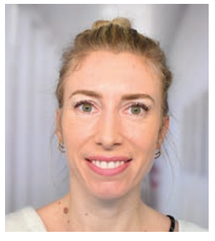
Türker B. *et al. Nat. Neurosci.* 2023
Mov'It: Movement, Investigation, Therapeutics. Normal and Abnormal Motor Control: Movement Disorders and Experimental Therapeutics team*

Manager for the research field: Liane Schmidt, Inserm Research Associate and Team Leader

COMPETITIVE EXAMINATION

MARIE VILLAIN,

a speech therapist in the Department of Physical and Rehabilitation Medicine (PRM) at Pitié-Salpêtrière Hospital (AP-HP/Sorbonne University) and a researcher with the PICNIC – Physiological Investigation of Clinically Normal and Impaired Cognition team*, has been appointed lecturer at Sorbonne University.



MAPPING THE PLACEBO EFFECTS ON APPETITE IN THE BRAIN

This study highlighted the cerebral and cognitive mechanisms behind the placebo effect on the ability to feel hunger and how food preferences are formed. The placebo intervention involved giving participants a glass of water with the explicit suggestion that it would either increase or decrease their hunger. The group to which reduced hunger was suggested reported feeling less hungry during the experiment and preferred healthier foods compared to the control group. Conversely, the group to which increased hunger was suggested reported feeling hungrier and craving more flavorful foods than the control group. The results show that the activation and interaction of different areas of the prefrontal cortex guided participants to pay attention either to taste or to healthier eating, depending on their expectations about the effectiveness of drinking a glass of water. These data contribute to our understanding of the effects of subjective beliefs on sensations and decision-making. They open up the field of research into interventions that would reinforce beliefs and personal reasons for changing eating behavior, often used as a complement to treatments for adverse changes in hunger sensation and eating disorders.

Khalid I. *et al. Nat. Commun.* 2024
Cognitive Control – Interoception – Attention team*

THE NEURAL MECHANISMS OF VISUAL ATTENTION

The involuntary redirection of attention to a specific element in our environment – referred to as "exogenous attention" – is built up in the cortex gradually, from the back to the front of the brain, within three fronto-parietal networks. These neural networks allow us to explore space efficiently by disregarding familiar objects in favor of new or unexpected visual stimuli. Twenty-eight patients who had deep electrodes implanted as part of a pre-surgical assessment for treatment-resistant epilepsy underwent tests to measure the conditions under which attention is captured by one event or redirected to another, and the subjects' reaction times. For the first time, this study shows the dynamics of exogenous attention networks and their place in the organization of the cortex. Researchers have also identified the brain mechanism behind inhibition of return, an attentional phenomenon that allows us to ignore familiar visual information in order to focus on unfamiliar visual stimuli.

Seidel Malkinson T. *et al. Nat. Commun.* 2024
PICNIC – Physiological Investigation of Clinically Normal and Impaired Cognition team*

INTERFACE CONTRACT

PAULINE DODET,

a neurologist in the Sleep Disorders Department at Pitié-Salpêtrière Hospital (AP-HP) and member of the Mov'It: Movement, Investigation, Therapeutics. Normal and Abnormal Motor Control: Movement Disorders and Experimental Therapeutics team*, has been awarded an interface contract that allows her to devote 50% of her time to research.

**2023–2024 team.*

Clinical and translational neuroscience

From the laboratory to the patient's bedside and vice versa, the main objective of the researchers in this field is to promote the development of translational research into neurological and psychiatric diseases. Their scientific approach aims to understand the physiology and pathophysiology of the brain, using human diseases as models. The objective is to provide innovative tools for clinical assessment of symptoms, diagnosis, identification of biomarkers of progression, and the design of new therapies. This research requires the creation of patient cohorts that are clearly characterized in terms of their phenotypic and biological features, using molecular biomarkers, brain imaging or electrophysiological criteria. These approaches make it possible to study molecular and cellular pathological mechanisms and promote targeted, personalized medicine.

Manager for the research field: Céline Louapre, neurologist (AP-HP/Sorbonne University), co-leader of the Neuroscience CIC and researcher at Paris Brain Institute.

ULTRASOUND AND GLIOBLASTOMAS

An ultrasound implant was fitted on completion of tumor removal surgery in 33 patients with recurrent glioblastoma treated with chemotherapy (carboplatin). After surgery, the implant was activated to disrupt the blood-brain barrier (BBB) every four weeks, either before or after carboplatin infusion, to assess whether the amount of drug entering the brain was improved. The results show transient opening of the BBB in 90% of cases. In the 12 patients who were given carboplatin just before ultrasound activation, the time to tumor progression was three months, the overall one-year survival rate was 58%, and the median overall survival was 14 months from surgery.

Carpentier A. *et al. Nat. Commun.* 2024
Genetics and Development of Nervous System Tumors team*

PREDICTING POST-STROKE RECOVERY

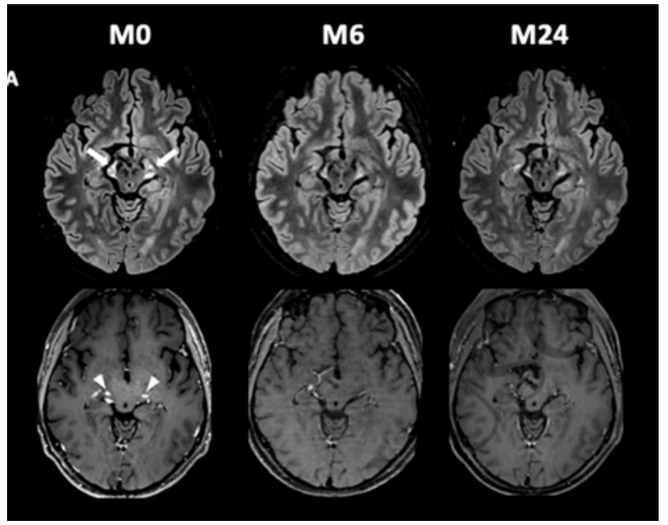
Assessment of the structural integrity and functional excitability of the corticospinal tract (CST), a bundle of nerve fibers connecting one hemisphere of the brain to the motor neurons, could be important for predicting motor recovery after stroke. Seventy patients who had suffered an acute ischemic stroke and presented with unilateral upper limb weakness underwent an assessment that included clinical severity, MRI, and transcranial magnetic stimulation. This extensive multimodal study of CST structure/function and recovery after stroke sheds more light on the nature of the link between structural integrity and neurophysiological function, which has implications for recovery prognosis.

Daghsen L. *et al. J. Neurol. Neurosurg. Psychiatry*. 2024
Mov'It: Movement, Investigation, Therapeutics. Normal and Abnormal Motor Control: Movement Disorders and Experimental Therapeutics team*

INTERFACE CONTRACT

GIULIA COARELLI,

a neurologist in the Department of Medical Genetics at Pitié-Salpêtrière Hospital (AP-HP) and a member of the Basic to Translational Neurogenetics team* at Paris Brain Institute, has been awarded an interface contract allowing her to devote 50% of her time to research.



Lesions in a patient at inclusion in the protocol (M0) disappeared after two years of treatment with leriglitazone (M24).

X-LINKED ADRENOLEUKODYSTROPHY

The acute cerebral form of X-linked adrenoleukodystrophy (CALD) is an aggressive inflammation of the brain that can occur in patients with X-linked adrenoleukodystrophy, leading to rapid cognitive and motor decline, with a median survival of three years. In a therapeutic trial, 13 patients aged 19 to 67 with CALD were treated orally with leriglitazone. This molecule has the ability to protect oligodendrocytes (cells that produce myelin), reduce pro-inflammatory cytokine levels and therefore inflammation, and preserve neurons. Each participant underwent motor and cognitive neurological examinations and magnetic resonance imaging (MRI) scans every three months, as well as blood tests, over a period of 24 months. The clinical, radiological, and biological stability observed in the majority of patients during the two-year follow-up suggests that daily administration of leriglitazone may halt brain inflammation and disease progression.

Golse M. *et al. Brain*. 2024
Mov'It: Movement, Investigation, Therapeutics. Normal and Abnormal Motor Control: Movement Disorders and Experimental Therapeutics team*

AUTOSOMAL DOMINANT SPINOCEREBELLAR ATAXIAS

This study aimed to identify longitudinal changes over a one-year period in biological, clinical, and/or imaging biomarkers in 30 patients with spinocerebellar ataxia (SCA) types 2 and 7, or asymptomatic mutation carriers (pre-ataxic individuals). The initial assessments, and those at 6 and 12 months, included neurological examinations, orofacial motor function assessments, neuropsychological evaluations, ophthalmological tests, and gait and oculomotor recordings. Additionally, a brain MRI, cerebrospinal fluid (CSF) sampling, and blood sampling were carried out. The results show annual changes in pre-ataxic and early ataxic carriers in brain MRI, clinical scores, gait parameters, and retinal thickness. These radiological and clinical markers could be used to measure the effectiveness of treatments in future therapeutic trials in the pre-ataxic phase.

Coarelli G. *et al. Neurology*. 2024
Basic to Translational Neurogenetics team*

FUNDING

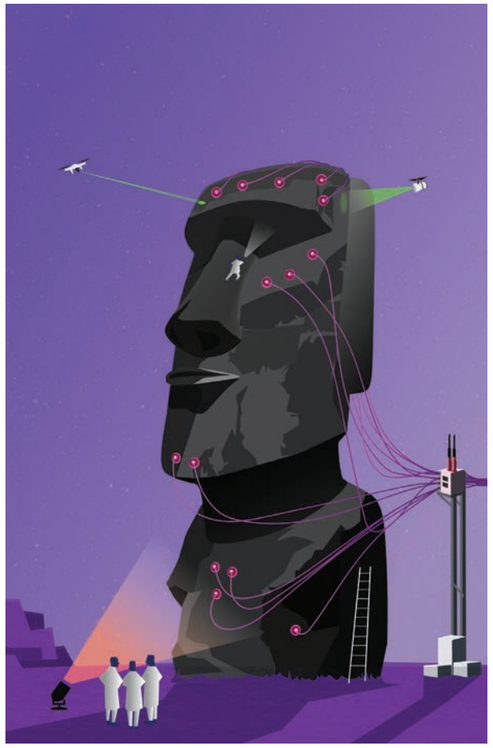
FRANCESCA BRANZOLI,

an Inserm research associate and a member of the Genetics and Development of Nervous System Tumors team* and the CENIR core facility, was given "equipment" funding from the Cancer Plan in 2024. This will strengthen translational research in oncology, with the development of new MRI biomarkers for non-invasive characterization of tumors and response to targeted therapies. These new biomarkers are essential for precision medicine and will be translated into clinical practice to provide optimal patient care.

**2023–2024 team.*

Computational modeling in neuroscience

Mathematical and computational modeling of brain mechanisms on a varying scale is essential to our understanding of healthy and pathological brain function. Scientists in this field are developing exploratory methods, including network science, signal and image processing, machine learning and artificial intelligence, to interpret and analyze data from neuroscience research and improve diagnosis and prognosis of neurological and psychiatric diseases.



ACUTE BRAIN INJURY AND NEUROLOGICAL PROGNOSIS

Accurately predicting the recovery of unconscious and uncommunicative patients with acute brain injuries is a medical, scientific, and ethical challenge. This 12-year prospective study evaluates how a multimodal approach (combining different behavioral markers, brain imaging, and electroencephalography) could aid prognosis. The results validate the concept that increasing the number of markers measured by a team of experts and included in the assessment improves prognostic performance. They emphasize the value of multimodal assessment as a basis for clinical decision-making for patients with acute brain injury. This research must be continued in order to extend the relevance of the multimodal approach to teams with varying levels of expertise.

Rohaut B. *et al. Nat. Med.* 2024
PICNIC – Physiological Investigation of Clinically Normal and Impaired Cognition team*

THE BRAIN: A COMPLEX MULTILAYERED SYSTEM

Biological systems are often characterized by numerous local interactions (nodes) that generate emergent properties affecting the structure and dynamics of the overall network. In this network, nodes are connected through different types of interactions or relationships, which are represented as distinct layers. The brain represents a multilayered network, encompassing various scales and levels of interaction. This study reveals, for the first time, the fundamental property of node/layer duality. This opens up new avenues in modern neuroscience to better understand how neurons communicate by integrating different modes of connectivity. These results could significantly improve our models of brain function during cognitive and motor tasks, and help to identify predictive biomarkers for brain diseases such as neurodegeneration and recovery after stroke.

Presigny C. *et al. Nat. commun.* 2024
ARAMIS: Algorithms, Models and Methods for Images and Signals of the Human Brain team*

Manager for the research field: Jacobo Sitt, Inserm Research Director and researcher at Paris Brain Institute.

DETECTING ARTIFACTS IN BRAIN IMAGES

Magnetic resonance imaging (MRI) is particularly sensitive to patient movement during acquisition, resulting in MRI artifacts (blurring, etc.) in the reconstructed image. To detect these artifacts, we need to develop tools that can automatically exclude, or at least identify, images containing movement. This study proposes a novel method of learning by transferring research data to clinical data to enable automatic movement detection in brain MRIs obtained during routine care. The method involves two steps: pre-training on research data using synthetic movement, followed by a fine-tuning step to extend the pre-trained model to clinical data. The objectives are to be able to exclude images with significant movement and to detect MRI artifacts caused by slight movement.

Loizillon S. *et al. Med. Image Anal.* 2024
ARAMIS: Algorithms, Models and Methods for Images and Signals of the Human Brain team*

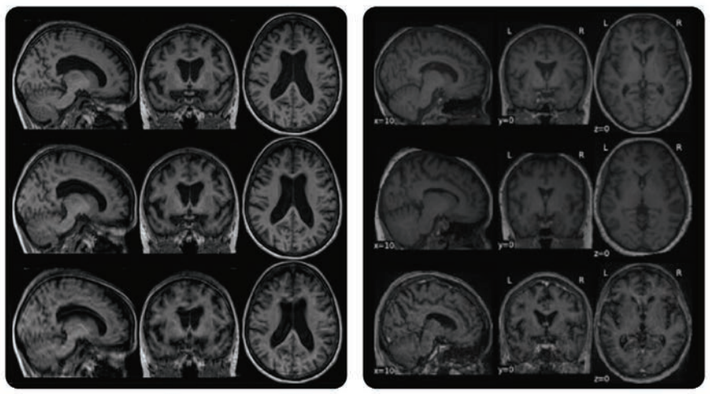
COMPETITIVE EXAMINATION

JEAN DAUNIZEAU,
co-leader of the Motivation, Brain and Behavior team*, has been promoted to class 2 Inserm Research Director (DR2).

DECISION-MAKING AND MENTAL EFFORT

Reward usually requires effort. This is also true in the mental realm: achieving a difficult goal (for example, memorizing or understanding something) can require significant mental effort. When we invest little mental effort, we make hasty decisions that are prone to cognitive biases. How does the brain regulate mental effort? This work is based on the assumption that the allocation of mental resources balances the cost of investing resources (mental effort) and the expected benefit (confidence in the decision). Using optimal control theory, we can break down the computational mechanisms involved in regulating mental effort and quantitatively predict the complex links between mental effort, cognitive performance, and subjective impressions of confidence.

Bénon J. *et al. Commun. Psychology.* 2024
Motivation, Brain and Behavior team*



Left: research images showing simulated artifacts of varying degrees of movement. Right: examples of images from routine care showing actual artifacts from movement.

**2023–2024 team.*

Research and treatment: the Institute's actions focused squarely on the patient

Paris Brain Institute's outstanding clinical and translational research activities, which have always been a core part of its mission, are built around partnership and teamwork between the Neuroscience Clinical Investigation Center (Neuroscience CIC), the clinical research facilities (iCRIN), and national and international networks of experts. Once again this year, the Institute's excellence in medical innovation to support patients with neurological and psychiatric diseases has been demonstrated through very promising clinical trial results, and recognition of the Neuroscience CIC's approach.

Two important recognitions for the Neuroscience CIC

In December 2023, the Neuroscience CIC (AP-HP/Inserm/Paris Brain Institute) obtained ISO 9001 certification, an internationally recognized standard for quality management. This certification confirms the Neuroscience CIC's commitment to rigorous quality standards, both in the conduct of clinical studies and in the management of the data generated. This standard guarantees not only safety and transparency for study participants, but also the reliability of results for academic and industrial partners.

Meanwhile, in June 2024, the Neuroscience CIC passed its evaluation by the HCERES with flying colors. This process praised the quality of the Neuroscience CIC's research projects, its structured organization, and the resources allocated to support its activities. This recognition cements its position as a key player in the field of clinical neuroscience research, ready to take on future challenges with a clear and structured vision.

Clinical studies: significant progress

A STATE-OF-THE-ART CENTER FOR ANTISENSE THERAPY TRIALS

The Neuroscience CIC is now a leading center for conducting trials based on antisense oligonucleotide (ASO) technology. One such treatment is tofersen, which is intended for patients with amyotrophic lateral sclerosis (ALS) associated with the SOD1 gene mutation and which, since this year, has been transferred to clinical practice. Several trials using this same technology are in progress on spinocerebellar ataxia, Alzheimer's disease, Creutzfeld-Jacob disease, and multisystem atrophy.

ESSENTIAL TREMOR: A MAJOR TECHNOLOGICAL BREAKTHROUGH

Paris Brain Institute is pioneering the treatment of essential tremor through the innovative use of focused ultrasound. This technology integrates directly into the MRI scanner and allows precise targeting of a specific region of the thalamus in order to perform a controlled therapeutic lesion. Studies conducted at the Institute have demonstrated the effectiveness of this method, which has now been transferred to routine neuroradiology care.

This success is achieved through close collaboration between neurologists, neurosurgeons, and neuroradiologists, illustrating the scientific and clinical excellence of Paris Brain Institute in the development and application of innovative solutions for complex pathologies.
Bancel T. ***et al., Brain stimul.,*** **2024**

ADVANCES IN MULTIPLE SCLEROSIS

InflaSEP

The past year has seen major advances in the understanding and treatment of multiple sclerosis (MS). Advanced imaging tools, including PET-MRI, have revealed that nearly half of MS lesions considered old, chronic, and inactive on standard MRI scans actually show persistent microglial inflammation. This discovery sheds light on a previously unseen dimension of the disease and paves the way for better assessment of inflammatory activity.
Hamzaoui M. ***et al., Ann. Neurol.,*** **2023**

Respiratory involvement in multiple sclerosis

Another significant advance concerns respiratory impairment in MS patients presenting with severe disability. Although this symptom is not typical of the disease, it is crucial because it is one of the leading causes of death in severe cases. Thanks to collaboration with the Respiratory Diseases and Sleep Disorders Departments at Pitié Salpêtrière Hospital (AP-HP), specific markers have been identified, enabling better assessment of respiratory function. This discovery is essential for providing early treatment and improving patients' quality of life.
Maillart E. ***et al., Mult. Scler.*****, 2024**

Progress in optic neuritis

Research into optic neuritis, a common condition in patients with MS, has led to the development of accurate biomarkers using magnetoencephalography (MEG), improving the assessment of optic nerve damage and creating a foundation for more effective therapeutic developments.

The impact of physical activity on remyelination

An innovative project is exploring the effect of physical activity on remyelination of the nervous system in healthy subjects. Based on the assumption that physical activity can stimulate myelination processes, this project includes different types of supervised and unsupervised exercise. Supported by the French National Research Agency (ANR) since 2023, this program aims to better understand the mechanisms of remyelination and open up prospects for future applications in patient care.

RESULTS FOR PARKINSON'S DISEASE

The promising results of the LixiPark study

The LixiPark study found that a drug used to treat diabetes, lixisenatide, could slow the progression of Parkinson's disease in its early stages. These results, from a clinical trial conducted within the NS-Park network ***(see page 35)***, show a stabilization of motor symptoms in treated patients. This discovery suggests promising avenues for therapeutic repositioning in neurodegenerative diseases.

Ten years of the ICEBERG study

The ICEBERG study, which has been running for 10 years now, thanks to initial support from the EDF Group Foundation and then the Saint-Michel Fund, focuses on the early stages of Parkinson's disease, including healthy subjects, patients in the prodromal or silent stages, and those in the early stages of the disease. Its aim is to identify biomarkers that predict the onset and progression of the disease through annual clinical testing, incorporating imaging, biomarkers, and neurophysiology analysis. The results have shown promising imaging markers, but also some more atypical ones such as voice disorders, which could enable early prediction of the risk of Parkinson's disease. This cohort paves the way for new approaches to disease detection and monitoring.

Major funding for addiction research

At the end of 2023, Louise-Laure Mariani, a clinician involved in research at Paris Brain Institute, secured essential funding from the hospital clinical research program (PHRC) to test the effectiveness of an algorithm for preventing addictive disorders secondary to the treatment of Parkinson's disease. This project will be carried out within the NS-Park network's expert centers.

Renewal of clinical research facilities (iCRIN)

The aim of Paris Brain Institute's clinical research facilities (iCRIN) is to deepen interactions and the sharing of expertise between the Neuroscience Department (DMU) of Pitié-Salpêtrière Hospital (AP-HP) and the Institute's research teams.

Certified for a period of five years, the first 13 iCRIN reached the end of their term in December 2024. To prepare for their renewal, a call for applications was launched in the first half of 2024. Twenty applications were submitted, and the panel met at the end of September 2024 to select the new projects, which were launched on January 1, 2025.

THE 13 ICRIN AT PARIS BRAIN INSTITUTE (2019–2024)

Stroke

Charlotte Rosso
(AP-HP/Sorbonne University)

Orthopedic Surgery

Hugues Pascal-Mousselard
(AP-HP/Sorbonne University)

Alzheimer's Disease

Richard Lévy
(AP-HP/Sorbonne University)

Parkinson's Disease and Movement Disorders

David Grabli
(AP-HP/Sorbonne University)

Neurosurgery

Carine Karachi and **Alexandre Carpentier**
(AP-HP/Sorbonne University)

Neurogenetics

Alexandra Durr
(AP-HP/Sorbonne University)

Neuro-oncology

Ahmed Idbaih
(AP-HP/Sorbonne University)

Adult Psychiatry

Bruno Millet
(AP-HP/Sorbonne University)

Multiple Sclerosis

Bruno Stankoff and **Catherine Lubetzki**
(AP-HP/Sorbonne University)

Amyotrophic Lateral Sclerosis (ALS)

François Salachas
(AP-HP/Sorbonne University)

Neurological Intensive Care

Sophie Demeret
(AP-HP/Sorbonne University)

Sleep

Isabelle Arnulf
(AP-HP/Sorbonne University)

Cranial Trauma

Éléonore Bayen
(AP-HP/Sorbonne University)

THREE QUESTIONS FOR

JEAN-CHRISTOPHE CORVOL,

Medical Director at Paris Brain Institute and Co-Coordinator of the NS-Park network

One of the NS-Park network's major activities is supervision of a unique cohort study. Could you tell us a bit about it?

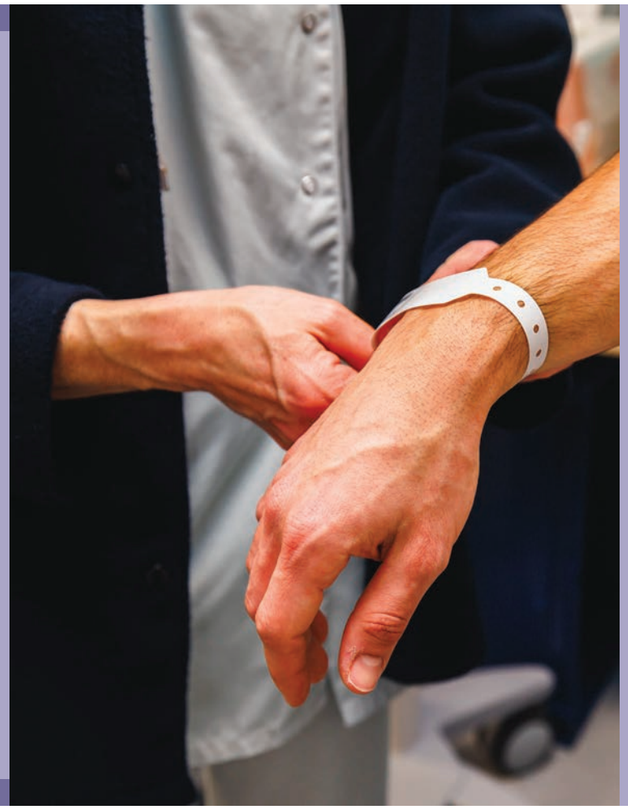
The NS-Park cohort study collates clinical data collected during routine care from more than 20,000 patients with Parkinson's disease who are being monitored at specialist centers. For the past two years, we have also been collecting biological samples (more than 1,500 patients included to date, including 400 at the Neuroscience CIC) and will soon begin collecting brain imaging data (MRI). This provides a unique platform for research, enabling the pre-selection of patients for innovative clinical trials and in-depth study of disease mechanisms.

What are the latest advances enabled by this cohort?

The NS-Park cohort enables the analysis of real-life progression data to model different disease trajectories and ultimately offer personalized treatment using artificial intelligence tools. It also offers patients the option to enroll in neuroprotection trials that match their profiles, as was done for the LixiPark study *(see page 33)*. The cohort has recently enabled us to include patients carrying a specific genetic mutation that is being researched in biological samples taken in an industrial trial known as a "precision trial".

What's in store for the network?

The NS-Park network will continue to bring together scientific expertise, therapeutic innovation, and interdisciplinary collaboration to benefit patients with Parkinson's disease.
Some great recent news is that the network is one of two winners of an F-CRIN (the French Clinical Research Infrastructure Network) call for proposals to set up a platform trial in France. This innovative type of trial makes it possible to test several drugs simultaneously, accelerating the development of new treatments, particularly those related to drug repositioning. Patients with Parkinson's disease will be involved in the design of the project, thanks to a partnership with France Parkinson. The launch of this ambitious project is scheduled for 2026.



FOCUS ON

THE NS-PARK NETWORK

A key player in clinical research into Parkinson's disease

The NS-Park network, coordinated by Olivier Rascol (Toulouse), David Devos (Lille), Stéphane Thobois (Lyons) and Jean-Christophe Corvol (Paris Brain Institute – ***see opposite***), plays a central role in clinical research into Parkinson's disease in France. Certified by F-CRIN, it brings together 26 specialized centers on the disease across the country, with the aim of facilitating both academic and industrial clinical research.

nspark

CLINICAL RESEARCH – KEY FIGURES

418
patients included in clinical trials at the Neuroscience CIC and 850 enrollments in iCRIN trials

82
trials under way in the CIC, including 14 new studies launched in 2024. 46% are sponsored by institutional partners and 54% by industrial partners

118
studies in progress in the iCRIN

1,764
visits to the Neuroscience CIC and 2,017 visits to the iCRIN

Core facilities: constant innovation and development

Paris Brain Institute's technology platforms play a central role in advancing knowledge in neuroscience by providing researchers with more powerful tools that are better suited to the scientific challenges of tomorrow.

IGENSEQ

Sara Baldassari

The ISO 9001* and GIS IBiSA-certified genotyping and sequencing core facility specializes in genome analysis techniques (DNA and RNA) to detect mutations or variations in the expression of disease-associated genes.
iGenSeq is part of the France Génomique network.

**ISO 9001:2015 (excluding provision of equipment and animal DNA and RNA genotyping).*

Yannick Marie

ICV

Philippe Ravassard

The Cellular Engineering and Vectorology (ICV) core facility is organized around three technical platforms:

ICV-3C (cell culture and flow cytometry) – cellular models and tools designed for cell culture, multiparameter flow cytometry, cell sorting, and characterization of cytokines and chemokines.

Laetitia Strehl

ICV-Vectorology* – construction and production of viral vectors for gene transfer.

**ISO 9001:2015 (excluding provision of equipment).*

Blandine Bonnamy

ICV-iPS – human induced pluripotent stem cells (iPSc).

Stéphanie Bigou

EPHYS

Jean-Christophe Poncer

The ePhys platform specializes in electrophysiology and offers a wide range of technology approaches such as functional screening of cell excitability, functional characterization of iPS-derived human neurons, and exploration of drug effects.



Carine Dalle, Charlotte Deleuze and Delphine Roussel

HISTOMICS

Brahim Nait Oumesmar

The Histomics facility provides scientific teams with all the infrastructure they need for histological tissue analysis: from standard analysis (sectioning, staining, immunohistochemistry) to advanced analysis such as artificial intelligence image analysis and spatial transcriptomics.

Annick Prigent

ICM.QUANT

Nelson Rebola

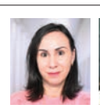
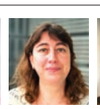
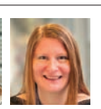
ICM.Quant offers access to multiple cutting-edge imaging technologies and essential scientific know-how in electron microscopy, light microscopy and image analysis.

Olivier Renaud

PHENOPARC

Philippe Ravassard

The PhenoParc facility specializes in preclinical exploration. It provides a wide range of animal models and state-of-the-art equipment, while the expertise of its staff contributes to ambitious and innovative research projects that comply with animal welfare and ethical guidelines.

Sophie Nunes-Figueiredo, Nadège Sarrazin and Morgane Weissenburger

CENIR

Stéphane Lehéricy
Nathalie George
Aurélie Kas
Marie-Odile Habert
Pierre Pouget

The CENIR neuroimaging core facility comprises five technical platforms:

MRI neuroimaging

Éric Bardinet

MEG-EEG

Laurent Hugueville

PANAM – physiology and movement analysis center.

Jean-Charles Lamy

PET-MRI

Éric Bardinet

Preclinical MRI for imaging experimental disease models for translational research projects.

Mathieu Santin

PRISME

Alizée Lopez-Persem

PRISME specializes in the study of brain function and normal and pathological human behavior.

Karim N'Diaye

DATA ANALYSIS CORE

Violetta Zujovic

The Data Analysis Core (DAC) facility provides support and expertise in data processing, integration, analysis, and management, from study design to data interpretation.

Stephen Whitmarsh

DNA & CELL BANK

Alexis Brice and Alexandra Durr

The DNA & Cell Bank is a Biological Resource Center (BRC) specializing in the collection, processing, conservation and provision of samples from patients and controls.

Sylvie Forlani

F.P. JOURNE CHARITY FUND R&D UNIT

Charly Rousseau

The purpose of the F.P.Journe Charity Fund R&D Unit is to provide equipment and advice to develop innovative and unique tools not available on the market.

Pierre Tissier

PROTEOMIC

Stéphane Haïk

The ProteomIC facility has state-of-the-art equipment for in-depth protein analysis. The team assists in sample preparation (fractionation, ultracentrifugation), biomarker analysis using ultrasensitive immunodetection, recombinant protein production, protein misfolding amplification, study of protein-protein interactions (PPIs), screening of compounds for therapeutic purposes, and performance of mass spectrometry analysis in collaboration with partners.

Katarina Grznarova

Scientific Manager
Operational Manager

A new proteomics facility to address a growing need

Paris Brain Institute is constantly developing its technology in terms of equipment and expertise to meet the needs expressed by scientists. In 2024, thanks to support from our generous donors, work began on developing a proteomics facility called ProteomIC, set for launch in 2025. This new facility will meet the Institute's needs for in-depth protein research: recombinant protein production, mass spectrometry and complex sample management. A three-year strategic plan has been developed to address these needs, with input from the operational manager Katarina Grznarova. Partnerships are planned with the École supérieure de physique et de chimie industrielles de la Ville de Paris (ESPCI Paris, a prestigious industrial physics and chemistry graduate school) for mass spectroscopy, and with other entities specializing in metabolism, such as the ICAN university hospital institute (IHU). An extension to high-throughput proteomic facilities to facilitate large-scale biomarker identification is envisaged.

Developing organoid-focused services

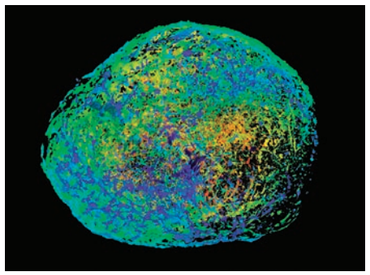
In response to the boom in research using organoids – 3D cell models – Paris Brain Institute has chosen to focus on a cross-disciplinary approach in this field. Several of the Institute's core facilities offer complementary expertise for the study these models: ICV for the generation and maintenance of these cell models, ePHYS for electrophysiology, iGenSeq for sequencing, and ICM.Quant for microscopic imaging. The aim is to harmonize protocols and strengthen collaboration between these facilities and research teams to guarantee standardized, high-quality production of organoids, maximizing the scientific impact of these *in vitro* models.

2024 call for R&D projects: encouraging innovation

Each year, Paris Brain Institute issues a call for R&D projects to stimulate innovation within its core facilities. These calls for projects strengthen collaboration between research teams and core facilities, while encouraging the development of innovative solutions for neuroscience.

In 2024, three winning projects were selected:

- NeuroFibre Insight, which aims to combine *in vivo* electrophysiological recordings with fiber photometry imaging in rodents;
- GlioExplant, which has the objective of establishing, characterizing and cryopreserving brain tumors;
- A Brain Mapping Hub at ICM, which will provide cutting-edge services in brain microscopy imaging, including marking, clarification, acquisition, and analysis.



Three-dimensional multicellular culture.

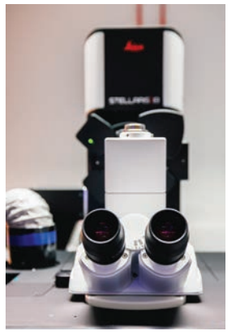
3-Tesla and 7-Tesla MRI: a new era for brain imaging

2024 marks the arrival of new MRI scanners: a 3-Tesla MRI and a 7-Tesla MRI (Siemens Healthineers) for the neuroimaging facility (CENIR), acquired through generous support from Richard Mille. Incorporating the most recent technologies, including super-powerful gradients, the MAGNETOM Cima.X 3-Tesla MRI scanner opens up new research possibilities for the Institute, a huge improvement on the old machine it replaces. For its part, the latest generation MAGNETOM Terra.X 7-Tesla MRI scanner offers the ability to produce data at sub-millimeter resolution, making it possible for the Institute's researchers to gain a better understanding of neurological disorders and brain function. The arrival of the 7-Tesla MRI scanner has enabled Paris Brain Institute to obtain SÉSAME Filières funding from the Île-de-France Region and the French Government as part of the France 2030 program. These equipment acquisitions are part of Paris Brain Institute's comprehensive strategy for accelerated technological development. They also make the Institute the first user in France of the latest advances in MAGNETOM Terra.X technology.

A video of the scanner arriving can be viewed on the Institute's YouTube channel.

A more powerful microscopy core facility

In addition to the new MRI scanners, Paris Brain Institute has invested in several cutting-edge pieces of equipment to strengthen its capabilities in cellular and molecular exploration: xCELLiGence, which enables real-time monitoring of the health, behavior and biological processes of cells using multiple systems, Celldiscoverer 7 microscopes (high-content screening), with superior performance in terms of resolution, sensitivity and acquisition speed, a Stellaris 8 Dive multiphoton microscope, a STED microscope ***(see below),*** an InSight X3 (MKS) laser, and a bioluminescence system, enabling non-invasive, real-time monitoring of disease progression in model organisms. These acquisitions illustrate the Institute's commitment to remaining at the forefront of technological innovation by providing researchers with the resources they need to tackle the most ambitious scientific challenges.



PORTRAIT

Expertise to boost dynamic imaging

Astou Tangara joined the ICM.Quant core facility in June 2024 as part of an Inserm mobility program. With experience gained at the University of California (Berkeley, United States) and École Normale Supérieure in Paris, she brings valuable expertise in bioimaging for research, particularly in *in vivo* multiphoton microscopy and optical development.
Through her knowledge of advanced imaging technologies, Astou is able to support users in adapting optical devices to their experimental protocols, in collaboration with the F.P. Journe Charity Fund R&D Unit at Paris Brain Institute.

THREE QUESTIONS FOR

OLIVIER RENAUD,

Operational Manager of the ICM.Quant core facility since October 2023.

What were your goals when you arrived?

My first objective was to strengthen collaboration between the research teams and the facility's experts. The ICM.Quant core facility has a wide range of cutting-edge equipment, but like all advanced technology, this requires dedicated experts. With support from the Institute's management, I consolidated the team by recruiting several engineers with complementary skills. These hires are intended to improve support for teams in using the facility's microscopes, including those we have recently acquired.

What are the latest developments for the facility?

Several major initiatives have been implemented in a range of fields: super-resolution, correlative microscopy, dynamic imaging and image analysis. The acquisition of a state-of-the-art STED (Stimulated Emission Depletion) super-resolution microscope, funded by Fondation NRJ – Institut de France, is an incredible opportunity, as there are only a few microscopes of this kind in the world. We also had the honor of welcoming Nobel Prize winner Stefan Hell for a lecture on this revolutionary technology. At the same time, our electron microscopy experts are developing correlative light and electron microscopy (CLEM) approaches combining photonics and electronics to explore cellular ultrastructure. Several research teams are interested in dynamic *in vivo* imaging, which makes it possible to observe processes in real time. To meet their needs, we have recruited an expert on this very subject – Astou Tangara *(see above)*. Finally, we have bolstered our image analysis capabilities with the recruitment of Gabriel Jiménez and Louise Mathé, who support researchers in collaboration with the Data Analysis Core (DAC) facility.

What is your vision for the future of the facility?

**The objective is to maintain and strengthen the expertise available at the facility. We expanded significantly in 2024, in terms of equipment and human resources. We need to make sure this continues.
We are also constantly developing new technologies so we can provide our teams with what they need, for example in the areas of organoids and calcium imaging. Finally, we plan to obtain ISO 9001 certification in 2025, with the support of the Institute's Organization, Quality and Risk Management Department (ROQ) *(see page 67)*.**

International partnerships

In 2024, Paris Brain Institute consolidated its international presence through strengthened partnerships with prestigious institutions such as Yale and Stanford Universities (United States) and The Neuro (Canada). From Latin America to India, not forgetting North America and Europe, the Institute's researchers and teams have stepped up exchanges, visits and joint projects. By building our network, we demonstrating our ongoing commitment to playing a leading role in international research on brain diseases.

A Europe-wide investment

Paris Brain Institute was represented at the European Parliament in 2024 as part of a program to support research into the brain and neurodegenerative diseases. This provided an opportunity for discussion with representatives of the Parliament, public decision-makers, patient associations and other scientific stakeholders on research and healthcare policy in the field of neuroscience.

CURE-ND CONSORTIUM (FRANCE, GERMANY, BELGIUM, UNITED KINGDOM)

The aim of CURE-ND (Catalyzing a United Response in Europe to Neurodegenerative Diseases) is to strengthen collaboration between European institutes to accelerate research into neurodegenerative diseases. The network is made up of the UK Dementia Research Institute (UK-DRI), Germany's DZNE, Mission Lucidity (VIB, UK-Leuven, UZ Leuven, imec) in Belgium, and Paris Brain Institute. In 2024, 120 PhD students and postdoctoral researchers came together on a three-day retreat in Bonn, Germany, promoting exchanges of scientific knowledge and discussions about their future career opportunities. Meanwhile, researchers from the Institute participated in several lectures organized by the network within Europe, while Professor Alexis Brice, Executive Director of Paris Brain Institute*, was a keynote speaker at an event held in Leuven.

CURE-ND retreat in Bonn (Germany).

* From 2012 to 2024.

SAME-NEUROID (POLAND, FRANCE, GERMANY, NETHERLANDS)

The SAME-NeuroID project brings together Paris Brain Institute, the Łukasiewicz Research Network PORT – Polish Center for Technology (Poland), the Erasmus Medical Center (EMC, Netherlands) and the Max Planck Institute of Psychiatry (MPI, Germany). The aim is to establish standardized protocols for researching and modeling neuropsychiatric disorders (SAME-NeuroID) at Łukasiewicz PORT.

As part of this collaboration, a delegation of Polish PhD students and postdoctoral students was welcomed for a three-day joint retreat with young researchers from Paris Brain Institute.

Delegation from Łukasiewicz PORT (Poland) welcomed at Paris Brain Institute.

FOCUS ON

The Big Brain Theory program goes international for the first time

The international expansion of the Big Brain Theory (BBT) program embodies the Institute's collaborative vision on a large scale. This scheme provides funding for innovative, cross-disciplinary projects carried out jointly by two teams. Thanks to the support of Fondation Marie-Françoise Parayre-Chaufour, this program went international in 2024: eight projects were funded, including two as part of a tripartite collaboration with Pasteur Institute and The Neuro in Montreal (Canada) ***(see page 42)***, and two with VIB and KU Leuven (Belgium). This is how the program contributes to scientific excellence shared between partner institutions and to the Institute's international reputation.

A stronger presence in North and South America

Paris Brain Institute consolidated its partnerships with several leading US institutions in 2024, while raising its profile at major scientific events.

AN AMERICAN TOUR

A delegation from the Institute conducted a 10-day strategic tour of the United States. This journey involved five major stops: New York, New Haven, Boston, Washington, D.C., and Houston. Each visit was an opportunity to meet with prestigious scientific institutions to strengthen existing partnerships and explore new collaborative opportunities. An exclusive evening event at the French Embassy in Washington, D.C., also showcased the Institute to key players in US research and representatives of scientific diplomacy between France and the United States. This tour also tied in with the recent establishment of Paris Brain Institute America, which aims to develop new partnerships and philanthropy between France and the United States.

STRONG PARTNERSHIPS WITH YALE AND STANFORD

Collaboration with Yale University (United States) on clinical and scientific knowledge exchange and researcher mobility continued and was strengthened this year with the introduction of clinical rounds, where complex medical cases are discussed by clinicians from both institutions. For Stanford, academic exchanges continue with the arrival of several students at the Institute's laboratories and reciprocal mobility programs for researchers.

France Neurosciences stand at the SFN Annual Meeting in Chicago.

Paris Brain Institute delegation to the United States.

THE NEURO (MONTREAL, CANADA): A LONG-STANDING COLLABORATION

The Neuro, formerly known as the Montreal Neurological Institute (MNI), is a long-standing partner of Paris Brain Institute. This visit was an opportunity to strengthen existing coordination, discuss ongoing programs and explore new initiatives. The Big Brain Theory (BBT) program, which funds joint projects, is at the heart of this partnership.

STRENGTHENING COLLABORATION WITH CHILE

Paris Brain Institute has continued to develop its partnership with the Latin American Brain Health Institute (BrainLat) in Chile, notably by co-organizing a summer school with VBHI university hospital institute (IHU) in Santiago in October 2024. This strategic cooperation promotes the sharing of advanced methodologies and knowledge exchange between Chilean and French teams. This partnership could potentially offer promising opportunities for collaborative research and the development of innovative solutions in neuroscience.

PARTICIPATION IN THE SOCIETY FOR NEUROSCIENCE CONFERENCE

In October, a delegation from the Institute participated in the world's largest conference dedicated to neuroscience, organized by the American Society for Neuroscience (SFN) in Chicago (United States). The Institute was represented at the France Neurosciences stand, where very promising discussions helped to raise its profile, attract new talent and promote its research programs.

THREE QUESTIONS FOR

JULIA SLIWA,

is a researcher at the CNRS and, since January 1, 2025, leader of the Neurophysiology of Social Cognition (SocialNeuro) team at Paris Brain Institute. For several months, she has been developing a collaborative project with Justine Cléry, team leader at The Neuro and the Azrieli Centre for Autism Research (McGill University, Montreal), and Roberto Toro, team leader at Pasteur Institute. Their project was selected as one of the winners in the 2024 Big Brain Theory call for projects, which was open to international applicants for the first time.

How did this collaboration come about?

Justine Cléry and I completed our postdoctoral research on similar topics, namely social interactions. We discovered the specific brain bases for analyzing these interactions in two species (macaques and marmosets), in parts of the brain that support the highest forms of social cognition in humans: the ability to assess the mental state of others. We independently identified the first animal models, enabling the study of higher-level social cognition at the whole-brain level. This opened up new avenues for understanding the underlying causes of social impairments in neurological and psychiatric disorders. A few years later, we got back in touch and came up with the idea for this project, guided by one big question: how do we move from perceiving social interactions to conceptualizing them in our adult brains, but also as our brain develops?

What exactly does the project involve?

Three main types of relationships between individuals are conventionally defined: friendship, familial relationship, and hierarchy. As we develop, the establishment of these relationships and their integration into our brain play a crucial role. For example, marmosets, like humans but unlike macaques, will have a second baby even though the first is not necessarily able to feed itself. This requires that first baby to interact with the various adults in the group and form social relationships in order to survive. Our objective is to better understand how the brain regions associated with situations requiring social cognition develop, with the aim of building better models of pathological trajectories in autism. This is where Roberto Toro comes in. He specializes in modeling brain morphology over time and throughout the evolution of species.

What will the funding for the Big Brain Theory program allow you to do?

We have designed a cognitive task to measure understanding of social relationships; not just their visual perception, such as two individuals doing something together, but also their conceptualization. The goal now is to expand this to three groups – marmosets, macaques, and humans – combining it with brain imaging measurements. We hope that this will enable us to model trajectories of development and evolution of the brain regions involved in social relationships.

Stronger ties with Asia and the Pacific

THE FLOREY (MELBOURNE, AUSTRALIA)

In June 2024, Paris Brain Institute welcomed a delegation from the Florey, a major research center in Australia with which the Institute has close ties. Discussions were held to establish joint funding initiatives, scientific meetings, and exchanges between PhD and postdoctoral students.

GROWING MOMENTUM IN EXCHANGES WITH INDIA

The year 2024 also saw a lot more exchanges with the Indian Institute of Technology (IIT) in New Delhi. Professor Alexis Brice welcomed a delegation from IIT and several researchers from the Institute, including Rahul Gaurav, Hélène Cheval and Violetta Zujovic, made several trips to organize joint projects and strengthen academic and clinical exchange programs. These collaborations are part of the Franco-Indian Campus for Health coordinated by Sorbonne University, with a particular focus on neuroscience.

Delegation from the Indian Institute of Technology, New Delhi.

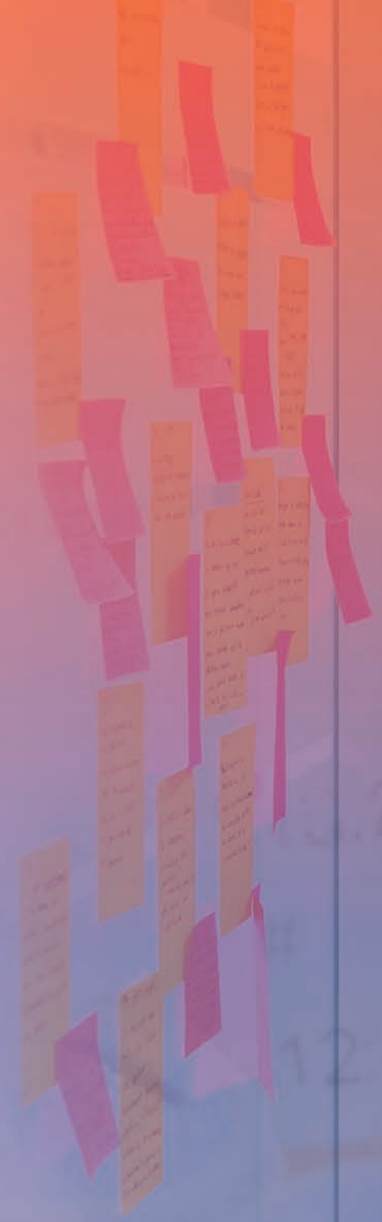
FOCUS ON

Delegation from the Weizmann Institute of Science.

Numerous strategic visits by delegations

Paris Brain Institute welcomed numerous international delegations this year, highlighting its visibility and central role within the scientific community. These included representatives from Canada, University College London (UCL), Lithuania, the Weizmann Institute of Science, and Norway. These visits are often the first step towards future collaborative work and some of these recent visits have helped to identify concrete avenues for educational and research partnerships.

Paris Brain Institute's Innovation Department is focused on accelerating the delivery of therapeutic solutions in neurology and psychiatry that can benefit patients and society as a whole.



2 INNOVATION

CASSANDRA ZORAYAN

Cassandra Zorayan is a designer in the Care Lab. This innovation unit is dedicated to the collaborative design of concrete solutions with immediate impact, to improve patients' quality of life.

Transforming discoveries into solutions for patients

Paris Brain Institute focuses on innovation as the key component of its mission to transform scientific discoveries into concrete solutions for patients with neurological and psychiatric diseases.

Promoting research discoveries

Paris Brain Institute builds its innovation strategy around the promotion of scientific discoveries. This ambition is reflected in a rigorous intellectual property policy. The Institute focuses on the quality and effective exploitation of patents, with particular attention paid to the maturing of protected innovations and their transfer to spin-off startups from the Institute, supported by researchers or industrial partnerships for further development and market launch. This year, for example, saw this process applied to a portfolio of five patents for the Neurometers spin-off ***(see page 50).***

At the same time, the Institute continues to strengthen its industrial partnerships to accelerate the development of new technologies and treatments. Strategic partnerships such as the MediTwin project epitomize this ambition. This major French initiative, bringing together seven University Hospital Institutes (IHU), Nantes University Hospital (CHU), Inria, associated startups, and Dassault Systèmes, aims to develop personalized virtual twins of organs, the metabolism, and cancerous tumors to enable better diagnosis and treatment.

Innovation units, unique structures

Paris Brain Institute's innovation units offer an agile, structured framework for exploring promising avenues of innovation that might not be immediately attractive to industry but offer real added value for society and medicine.

GENOV: A MATURE GENE THERAPY PORTFOLIO

The GENOV unit perfectly embodies this success. Now mature, it has a robust portfolio of gene therapy projects based on the non-invasive intravenous injection of vectors (adeno-associated viruses, or AAV), including three candidates ready to enter clinical trials for rare lysosomal storage diseases (mucopolysaccharidoses and metachromatic leukodystrophy). Other candidates are still being developed in preclinical stages, particularly for Alzheimer's and Parkinson's diseases.

GENOV also enjoys the unwavering support of patient associations, with funding obtained from Vaincre les Maladies Lysosomales, the ELA Association, and the Cure Sanfilippo Foundation.

In addition, collaborations with startups such as Release Therapeutics and WhiteLab Genomics enable these entities to explore new avenues for developing viral vectors or cell therapies by leveraging GENOV's expertise and technological tools.

This success demonstrates the relevance of the innovation unit model, which is capable of transforming innovative ideas into concrete projects at a level of maturity necessary for industrial collaborations or the development of specialized startups.

SPOTLIGHT

The Brain & Mind biocluster

Thanks to public investment of nearly €100 million from the France 2030 plan, the Brain & Mind biocluster was officially created in 2024. It has been built through sound governance and a number of recruitments. The result of a partnership between the FondaMental Foundation, the Vision Institute, and Paris Brain Institute, this biocluster will roll out large-scale innovation projects supported by multidisciplinary technology platforms dedicated to neurological and psychiatric diseases and sensory impairments.

THREE QUESTIONS FOR

GÉRALDINE FARJOT,

Innovation Director, who joined Paris Brain Institute in April 2024.

Why did you choose Paris Brain Institute?

The common thread throughout my career has always been innovation in healthcare, particularly the development of therapeutic products. I worked in various research and development roles in the pharmaceutical industry and biotechnology startups before joining the Institute in April 2024. What motivated me was the opportunity to bring what I have learned to this extremely stimulating, outstanding academic environment. I believe in cross-disciplinary methodologies and approaches. Like the Institute's founders and management team, I believe very strongly that bringing together researchers, doctors, and innovative companies is a key factor for success. I was really drawn to the Institute's ambition and clear vision: focusing on innovation as the key component of its strategy to transform scientific discoveries into concrete solutions for patients with neurological and psychiatric diseases. It was an ambitious project that I wanted to be actively involved in.

What was your impression when you joined?

Beyond the excellence and energy of the research teams, I quickly realized that the Institute's ambition was not just a statement of intent, but a tangible reality. An innovation roadmap had already been established, combining traditional approaches such as industrial partnerships with more daring models such as the creation of startups arising from our research. I was also impressed by the innovation units, which are real ideas factories where researchers can explore promising avenues without the immediate constraints of profitability. All of this demonstrates strong scientific and entrepreneurial momentum. My industrial experience has also enabled me to quickly identify areas for improvement in the functioning of these existing structures, particularly in the development of therapeutic solutions, a field in which I would like to bring a new dimension by leveraging partnerships to maximize their potential.

What are the next steps for the Innovation Department?

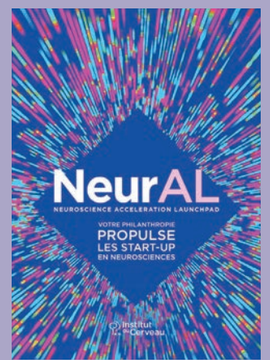
With our roadmap in place, we are strengthening the team with a few missing areas of expertise. 2025 will be a particularly important year for the implementation of the new startup incubation model, which will provide enhanced support for startups from the earliest stages of project development. At the same time, innovation units will continue to play a key role, particularly by developing projects that, although not very attractive to industry in their current form, have significant societal value, such as molecule repositioning or the development of solutions identified by the Care Lab. Finally, we remain committed to partnership-based research, a core value of innovation at the Institute, with a particular focus on intellectual property and industrial collaborations.

FOCUS ON

NeurAL: philanthropy supporting innovation

One of the cornerstones of the strategic change in the department is the Neuroscience Acceleration Launchpad (NeurAL) philanthropy fund, a funding vehicle for Paris Brain Institute's startup studio, which was successfully launched at the end of 2022. NeurAL was created because of the difficulties encountered in neuroscience in bringing together leading technical, medical, regulatory, and industrial expertise to transform research and development projects from research laboratories into viable startups. By creating this unique seed funding program open to all of Europe, Paris Brain Institute and its incubator iPEPS – which already boast several successes in innovation – have decided to put their expertise to work for the entire neuroscience community.

Thanks to bespoke, multi-faceted support supplemented by funding, this program promotes the creation of structured startups capable of attracting investors. This lever is essential to the emergence of innovative solutions that address the major challenges of neurological and psychiatric diseases. In 2024, the second iteration of the program was launched and was once again a great success, with numerous applications, attracting project leaders from outside the Institute. The NeurAL program has received support from the Fondation Anne et Claude Berda since 2023 and from Indosuez Wealth Management.



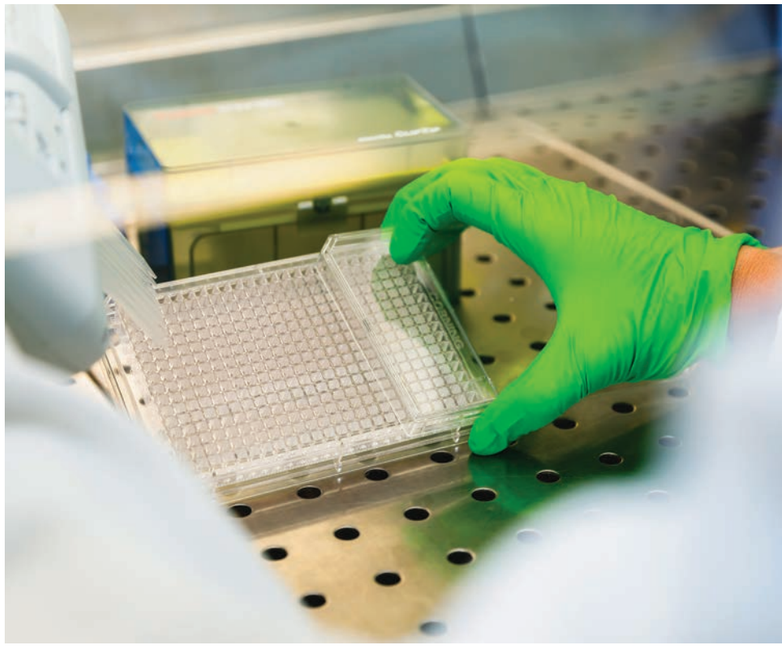
THE CARE LAB: EXPERTISE SUPPORTING THE PATIENT JOURNEY

Positioned in a unique open-innovation ecosystem within the Neurosciences DMU at Pitié-Salpêtrière Hospital (AP-HP), the Care Lab is made up of a team of three designers whose mission is to develop concrete solutions with an immediate impact, to improve patients' quality of life. The model is based on close involvement between patients, healthcare professionals and innovation players, from needs assessment and idea generation through to market entry.

In 2024, the Care Lab rolled out patient information tools for the memory clinic and child psychiatry services, and developed a digital app to help patients with brain injuries live more independently. To ensure maximum impact, the Care Lab works with partners to develop and deploy prototypes created in previous years. For example, a clinical study has been launched to evaluate "Bro", a digital solution for therapeutic cooking (kitchen therapy).

Finally, the Care Lab is pursuing an ambitious path through the strategic development of a new offering designed to support the patient journey. Key partnerships were established during the year, with the Biogen laboratory for Friedreich's ataxia and with the French Association for Amyotrophic Lateral Sclerosis Research (ARSLA), to improve patient management in the Auvergne-Rhône-Alpes region, in private practice and hospital scenarios.

Co-construction workshop with care staff conducted by the Care Lab.



SLEEPING BEAUTIES: EXPLORING THE POTENTIAL OF SMALL MOLECULES

Paris Brain Institute's Sleeping Beauties program develops new drugs by exploring existing molecules that have not yet revealed their full therapeutic potential. This project is based on an innovative approach to pharmacological repositioning, applying an agile and promising strategy.

The Sleeping Beauties innovation unit continued its small molecule screening efforts, in partnership with medicinal chemists and internal teams, using disease models developed by the Institute's researchers, particularly for neuroinflammation, multiple sclerosis, and glioblastoma.

A review of this unit's portfolio and strategy was conducted in 2024, and it will now focus its development efforts on ambitious translational programs based on discoveries made by the Institute's researchers, with the aim of identifying new molecules or molecules for repositioning. These programs will be coordinated between research teams and external private or academic partners.

EXPERTISE

Neurotrials: a certified team of experts with experience in clinical trial management

Since 2018, Paris Brain Institute has been committed to developing a team dedicated to managing early-stage clinical studies for industrial promotion. Its services have been extended to researchers for the management of their studies promoted by the Institute. As of September 30, 2024, this team had 13 members, bringing together a set of expertise essential to the management of clinical trials: technical and regulatory support, medical and scientific consulting, medical writing, quality management, project coordination, and clinical operations management.

The unit has been ISO 9001-certified since December 2023, attesting to the rigor and efficiency of its structure in project management, consulting, and expertise in clinical research, particularly in neuroscience, and to its quality management system. This recognition is a major asset that strengthens the standing of the Neurotrials unit among industrial and academic players who use its services.

Currently, 14 clinical studies are being supported. Between October 2023 and September 2024, three new trials began and ten others were approved (new protocols and amendments). Against a backdrop of strong growth, the team continues to offer its expertise to the unique environment provided by the Neurosciences DMU and Paris Brain Institute. This unique framework means that Neurotrials can be a driving force for the optimal development of clinical studies in neuroscience.

NEUROTRIALS
Paris Brain Institute

A change of strategy for iPEPS

iPEPS is undergoing a major strategic shift. Formerly focused on providing hosting and support to companies at all stages of maturity, the incubator now aims to become a true catalyst for business creation by intervening earlier in the innovation process and developing new maturation and acceleration programs.

THE EMERGENCE OF PROMISING NEW STARTUPS

This renewed strategy has already borne fruit, with the creation of new innovative startups. These successes include the Neurometers startup ***(see below)***, which emerged from an internal scientific project led by Lionel Naccache and Jacobo Sitt, two co-leaders of the PICNIC: neuropsychology and functional neuroimaging team since January 1, 2025. This startup perfectly embodies this promotional development model. Specializing in the development of electroencephalogram analysis algorithms, the startup offers solutions for predicting the state of consciousness of patients in comas.

NEW STARTUPS

Neurometers

Neurometers is a spin-off startup from Paris Brain Institute, developed from the work of the PICNIC: neuropsychology and functional neuroimaging team. The ambition of this startup is to aid the monitoring of brain function using electroencephalograms (EEGs), similar to how heart function is assessed using electrocardiograms (ECGs). To do this, several artificial intelligence algorithms have already been developed to assess the state of consciousness of patients in chronic and acute comas and produce a “consciousness score”. In addition, a box has been designed to provide patients with auditory stimuli and collect data from electroencephalograms. The next steps will focus on developing solutions for monitoring patients under general anesthesia, as well as early diagnosis of neurodegenerative disorders such as Alzheimer’s disease.

SPOTLIGHT

The Carnot label: essential support for innovation research

The Carnot label was renewed in 2020 and represents an essential strategic lever for Paris Brain Institute. Awarded to research organizations capable of developing effective partnerships with industrial and economic players, this label is both a recognition of scientific excellence and a concrete tool for strengthening innovation.

Through this support, the Institute benefits from a virtuous process in which research partnerships with industry are supplemented by funding that enables it to build and sustain its innovation activities.

Specifically, the Carnot label plays a key role in:

- **the maturing of research projects, facilitating their transition from idea to proof of concept and patent;**
- **the development of industrial partnerships that ensure scientific advances are put into practice;**
- **support for innovation units exploring promising avenues.**

La recherche CARNOT pour l’innovation des entreprises

The Carnot scheme also raises awareness among researchers about protecting their discoveries by filing patents and contributes to scientific resource development initiatives, such as conferences organized by the Institute and training for young researchers in cutting-edge techniques.

The Carnot label demonstrates not only the quality of the work carried out by Paris Brain Institute, but also its role as a key player in the landscape of collaborative neuroscience research. Thanks to this support, which the Institute hopes will be renewed once again, we continue to push the frontiers of innovation to address the major challenges posed by neurological diseases.

INNOVATION AT THE INSTITUTE

45
industrial agreements signed in 2024 (including two Cifre* theses)

1
new subsidized public-private consortium (MediTwin)

63
active patents (including 7 new patent requests filed in 2024)

32
active therapeutic development projects

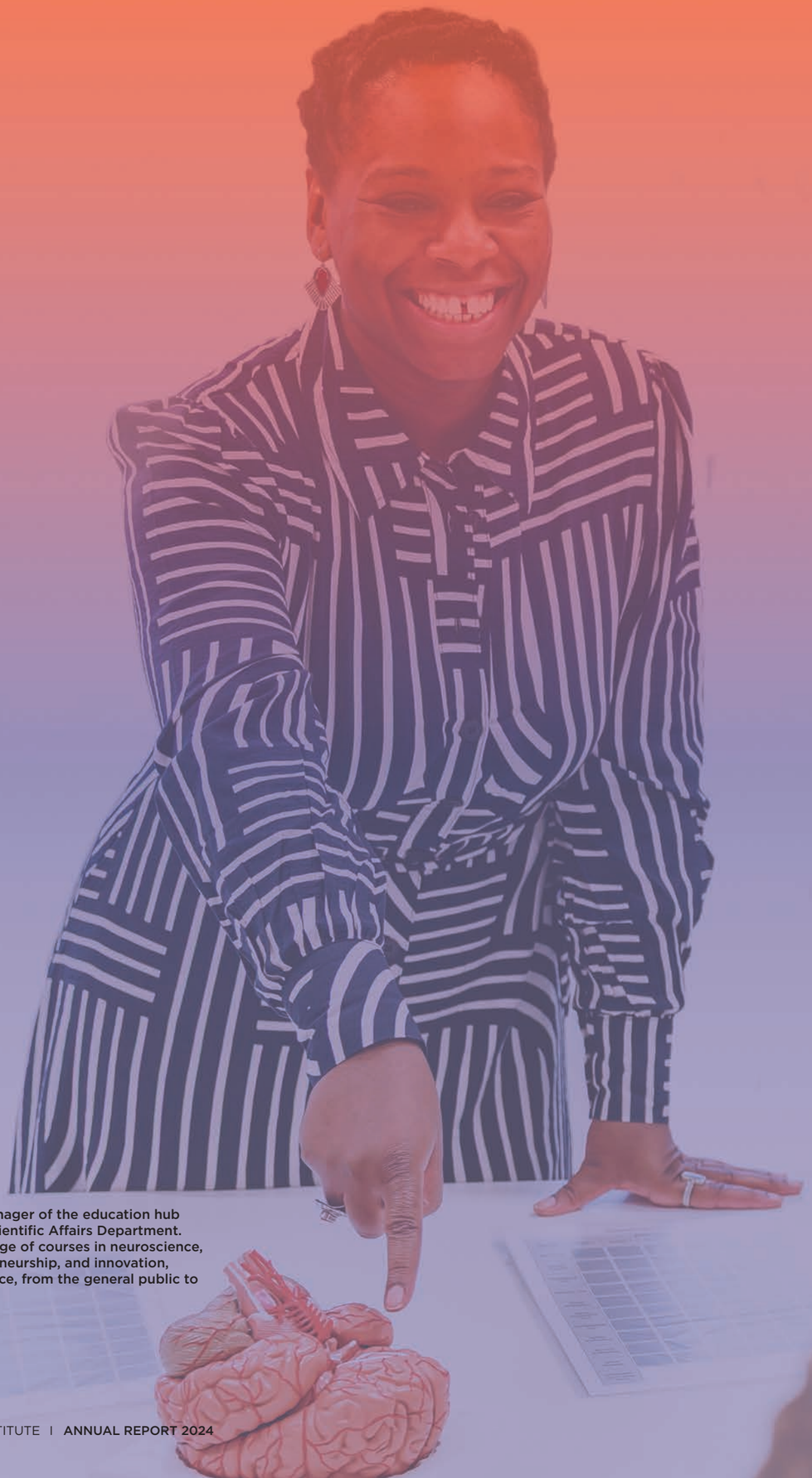
12
prototypes being developed

24
startups being incubated (including 1 spin-off created in 2024)

3
startup projects maturing (including 2 through the NeurAL philanthropy fund)

** Industrial agreements for training through research.*

Transmitting knowledge and sharing it with as many people as possible are two of Paris Brain Institute's core missions. Through its teaching activities, the Open Brain School trains research and healthcare professionals who wish to optimize their practices, but also offers training to external audiences. The Institute is also committed to making neuroscience accessible to everyone through extensive communication initiatives targeting patients, their caregivers, and the general public.



CLARISSE
MARIE-LUCE

Clarisse Marie-Luce is manager of the education hub within the Medical and Scientific Affairs Department. This unit offers a wide range of courses in neuroscience, clinical research, entrepreneurship, and innovation, aimed at a diverse audience, from the general public to neuroscience specialists.

3 TRAINING AND OUTREACH

A key player in neuroscience education

Boosted by a rich and innovative scientific ecosystem supported by prestigious public partners, in January 2022 the Institute created an education hub, the Open Brain School, with the aim of offering a wide range of multidisciplinary programs for a variety of audiences (students, researchers, clinicians, paramedical staff, and healthcare professionals).

Inspiring a vocation

France Brain Bee award ceremony.

Sparking interest in scientific careers from an early age is a priority for encouraging and supporting neuroscience research. With this in mind, Paris Brain Institute is stepping up its initiatives and regularly organizes dedicated neuroscience events open to all audiences, and especially to young people.

These initiatives include the France Brain Bee neuroscience competition, part of the International Brain Bee (IBB), which encourages students in grades 9 through 12 to consider careers in research and neuroscience. Since 2019, Paris Brain Institute has been coordinating the French version of this prestigious competition. The 2024 competition brought together 25 students from all over France at the Institute. The winner, Ayda Durubal, represented France at the world championships in October 2024.

The Move Europe, an international event organized in July 2024 at Paris Brain Institute.

Developing skills

Paris Brain Institute is committed to scientific excellence and offers a wide range of neuroscience training programs for students as part of the Open Brain School.

DIM C-BRAINS

Since 2022, thanks to the support of DIM C-BRAINS, ten doctoral researchers have had the opportunity to receive study grants. This program is different from others in that it is international, being open to candidates from Germany, Brazil, Spain, Greece, and India. In 2025, a tailor-made training program will be offered to these doctoral researchers.

STARE

The STARE program (introductory course in translational research), recognized as a teaching unit at Sorbonne University, is an educational project introducing third-year medical students to research in the field of neuroscience. In 2024, 20 new students were welcomed into ten research teams and facilities at the Institute from April 22 to 26.

THE MOVE

The 2024 iteration of The Move Europe, an educational program that uses mime to teach medical students neurological semiology, was held on July 3 and 4, 2024, at Paris Brain Institute. This unifying event provides an opportunity to develop future international collaborations in the fields of education, healthcare, and research.

Strengthening knowledge

To support professionals in the field of neuroscience throughout their careers, Paris Brain Institute offers high-quality continuing education programs in cooperation with its partners. These programs, designed using a multidisciplinary approach, are available in a variety of flexible formats tailored to the needs and pace of participants.

BRAIN TO MARKET

The Brain to Market Summer School is an intensive five-day training program that provides hands-on learning of key entrepreneurial skills in healthcare, focusing on a specific disease (Alzheimer's, epilepsy, depression, etc.). The 2024 version (September 9-13) of this unique training program in neuroscience and entrepreneurship focused on amyotrophic lateral sclerosis and involved 48 international participants. It was also an opportunity to celebrate the 10th anniversary of this summer school, which has trained 401 participants since its inception.

TRAINING IN ENTREPRENEURSHIP AND INNOVATION

The health entrepreneurship program offers interactive online modules combining theory, case studies, and expert guidance. In addition, the EPICA program guides learners in the development of collaborative innovation projects in healthcare.

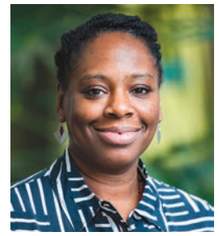
Contributing to the Institute's international visibility

Various calls for projects are launched by Paris Brain Institute, with the aim of developing its appeal to researchers from around the world, but also to enable internal staff to train abroad. Some recent cases include the DIM C-BRAINS international PhD call for applications aimed at master's students outside France (enabling the Institute to offer five doctoral contracts), the Carnot training call for projects (to train in specific technical skills), the Workshop call for projects (to exchange knowledge with international experts in specific fields and develop international collaborations), and the Resident exchange fellowship (exchange of clinicians with foreign clinical services).

THREE QUESTIONS FOR

CLARISSE MARIE-LUCE,

manager of the education hub within the Medical and Scientific Affairs Department, who joined the Institute in 2014.



The Institute has now been offering training courses for over ten years. What's your assessment of what it has achieved?

Since 2012, with the award of the IHU label, the Institute's educational mission has grown to become an integral part of its development strategy. This led to the creation of a training organization in 2019 and the Open Brain School education hub in 2022. We have grown from two programs in 2014 to 15 programs in 2024, attracting more than 2,500 participants from diverse international backgrounds.

What achievements are you most proud of?

Over the years, we have successfully developed and expanded our training offerings to the point where a dedicated education hub was created within the Medical and Scientific Affairs Department. We have diversified our programs and target audiences by offering both initial training (in partnership with Sorbonne University) and continuing education with a multidisciplinary approach. We have tested various educational approaches, and some programs are now recognized as teaching units in renowned schools and universities (Sorbonne University, Collège des Ingénieurs, CY School of Design, etc.). For example, the iMIND international master's program (second stage) is one of our flagship programs, with exciting potential for future development in several areas, including teaching methods, collaborative research, partnerships, and European accreditation.

What developments can we expect in the coming years?

We will continue to enrich our training catalog and broaden the profiles of our learners, while maintaining a multidisciplinary approach and strengthening our ties with our main partner, Sorbonne University. Some examples of areas for development are currently under consideration, such as the integration of neuroscience into school curricula, the creation of a series of high-level advanced scientific training courses showcasing our expertise (in the form of workshops or summer schools and linked to our university partner, which we hope will gain international recognition), and a focus on society, with programs dedicated to patients who wish to train in research.

Open communication to share knowledge and make it accessible

With its wealth of expertise, Paris Brain Institute works to share reliable, understandable, and useful information with all of its audiences, in a spirit of openness and dialogue. To do so, the Institute is committed to ensuring everyone can access information about advances in research on brain function and diseases, and the work carried out by its scientific teams. With this objective in mind, in 2024 the Institute focused particularly on redesigning its website and developing its range of events.

Visit to the CENIR facility during Brain Awareness Week in March 2024.

Lectures and events: meetings to promote understanding

This year once again, Paris Brain Institute has expanded its range of events to encourage direct interactions between the general public and its researchers. The communications team was particularly active during three major national events. In October 2023, during the Fête de la Science (Festival of Science), two lectures were organized in the Edmond and Lily Safra Auditorium, entitled "Brain and creativity" and "Brain death: at the frontiers of consciousness".

Brain Awareness Week in March 2024 also saw the Institute open its doors, offering more than 450 visitors – including members of the general public and donors – an immersive experience within the beating heart of research. The program included six interactive workshops, guided tours of four laboratories and core facilities, and two lectures ("From books to synapses: the neuroscience of reading" and "Different perspectives on bipolar disorder today").

Keen to inspire future scientists, the Institute also welcomed three high school classes during this week dedicated to neuroscience. They had the opportunity to visit the laboratories, talk to researchers, and discover what research jobs actually involve.

Finally, in June 2024, shortly before the opening of the Paris 2024 Olympic Games, the Institute organized an exclusive lecture at the offices of the French National Olympic and Sports Committee (CNOSF), entitled "What athletes bring to neuroscience" ***(see opposite)***, with the participation of big names from the world of sport and scientists from the Institute.

These educational events illustrate Paris Brain Institute's ongoing commitment to broadening access to research, strengthening dialogue between science and society, and inspiring future careers.

Shaping the digital content offering

Paris Brain Institute's digital activity in 2024 focused on the launch of its new website: institutducerveau.org. In addition to its new design and technical and user experience improvements, it now also offers new content and intuitive access to numerous video resources, event replays, podcasts, fact sheets on diseases and brain functions, and more. The site also features innovative functionalities such as a smarter search engine, a dynamic calendar displaying all of the Institute's events, and customized, contextualized content suggestions on each page. The website's transformation is set to continue in 2025, particularly on pages showcasing the scientific teams and their members.

Paris Brain Institute's presence on social media (Facebook, LinkedIn, X, YouTube, Instagram, and Threads, as well as Bluesky since late 2024) confirms its momentum, surpassing the symbolic milestone of 100,000 followers across all channels (up 10% in 2024 compared to 2023).

Lastly, the Institute's audiovisual content ("Comprendre en 2 minutes", "Just Published", "Les Matinales de Paris Brain Institute" playlists, etc.), available on its YouTube channel, bring together a united and engaged community every month, demonstrating the support for and interest in the work of the Institute's scientists among a range of different audiences.

SPOTLIGHT

"Dans le coin du ciboulot" podcast: a second season full of discoveries

Season 2 of the podcast "Dans le coin du ciboulot" (In the corner of your mind), which provides simple, accessible answers to young people's questions about the brain and how it works, was released between April and November 2024. After a first season devoted to the brain's major functions, this second season explores brain anatomy, nightmares, learning in sports, and certain pathologies explained in a way that children can understand. Each episode averages 2,000 listens. Effective content available to everyone.

EVENT

Open Brain Bar: "What athletes bring to neuroscience"

On June 13, 2024, in the build-up to the 2024 Olympic Games, Paris Brain Institute hosted an exclusive Open Brain Bar lecture at the Maison du Sport Français, headquarters of the French National Olympic and Sports Committee (CNOSF), bringing together two worlds that have much more in common than one might think: neuroscience and sports. This Open Brain Bar, organized with the support of Groupe Pasteur Mutualité, brought together Professor Gérard Saillant, President of Paris Brain Institute, Cécile Gallea and Mathias Pessiglione, researchers at the Institute, and three top athletes, Cyril Benzaquen (world kickboxing champion), Anaïs Ebayilin (footballer for Paris Saint-Germain and the French U17s team) and Thomas Lombard (former international and professional rugby player, CEO of Stade Français Paris). The discussions highlighted the brain mechanisms underlying motivation, attention, coordination, and many other cognitive and motor skills involved in intensive sports training. This knowledge is valuable for developing therapeutic solutions for patients whose functions are impaired. The replay of the event is available on the Institute's YouTube channel **(QR code below).**

4

GOVERNANCE

Paris Brain Institute is built around a private foundation with recognized charitable status – ICM Foundation and a strong partnership between a public joint research unit (CNRS, Inserm and Sorbonne University) – working with the AP-HP Paris Public Hospital Network.

The board representation in the Institute's governing bodies – on the Board of Directors and management and other committees – reflects the strength of this partnership.

Meeting of the Institute's Scientific and Medical Steering Committee. This consultative body addresses all matters related to the Institute's scientific and medical strategy and provides opinions to the Management Committee.

Governing bodies

Board of Directors

The Board of Directors is made up of 15 members divided into four colleges. It governs the affairs of the Institute through its deliberations and decides on the strategic direction proposed by executive board.
It also votes on budgets and approves the Foundation's accounts.

COLLEGE OF FOUNDERS

- **President: Gérard Saillant,** Honorary Professor of Orthopedic and Trauma Surgery
- **Vice-President: Jean Todt,** UN Secretary-General's Special Envoy for Road Safety
- **Treasurer: Serge Weinberg,** President of Weinberg Capital Partners
- **Jean Glavany,** Former Minister
- **Jean-Pierre Martel,** Attorney

COLLEGE OF QUALIFIED PERSONS

- **Richard Frackowiak,** Emeritus Professor at University College London
- **Philippe Menasché,** Professor of Thoracic and Cardiovascular Surgery at Université Paris-Cité
- **Élisabeth Tournier-Lasserve,** Professor of Medical Genetics at Université Paris-Cité

COLLEGE OF FULL MEMBERS

- **André Le Bivic,** Director of the CNRS National Institute of Biological Sciences (INSB)
- **Didier Samuel,** President and CEO of the French National Institute for Health and Medical Research (Inserm)
- **Bruno Riou,** Dean of the Faculty of Medicine at Sorbonne University
- **Nicolas Revel,** CEO of the Paris Public Hospital Network (AP-HP)

COLLEGE OF FRIENDS OF THE FOUNDATION

- **Martine Assouline,** Founder and Director of the Assouline publishing house
- **Maurice Lévy,** Honorary Chairman of Publicis Groupe
- **Christian Schmidt de La Brélie,** CEO of Klesia

GOVERNMENT COMMISSIONER

- **Jean-Marie Paulot**

FOUNDERS OF PARIS BRAIN INSTITUTE

- **GÉRARD SAILLANT,** Honorary Professor of Orthopedic and Trauma Surgery, President of Paris Brain Institute
- **JEAN TODT,** UN Secretary-General's Special Envoy for Road Safety, 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,** Honorary President of Publicis Groupe, Co-Chair of Paris Brain Institute Circle of Friends
- **OLIVIER LYON-CAEN,** Professor of Neurology, former Director of the Nervous System Diseases Department at Pitié-Salpêtrière University Hospital
- **JEAN-PIERRE MARTEL,** Attorney
- **LINDSAY OWEN-JONES,** Honorary Chairman of L'Oréal and of Paris Brain Institute Friends Committee
- **DAVID DE ROTHSCHILD,** Honorary Chairman of the Supervisory Board of Rothschild & Co
- **MICHAEL SCHUMACHER,** Former Formula 1 Driver
- **SERGE WEINBERG,** President of Weinberg Capital Partners and Paris Brain Institute Treasurer

Board committees

SCIENTIFIC ADVISORY BOARD

Consisting of leading international neuroscience experts, the Scientific Advisory Board (SAB) has the task of advising Paris Brain Institute and providing the necessary support in defining its overall strategy.

- **President: Prof. Dimitri Kullmann,** Department of Clinical & Experimental Epilepsy, UCL Queen Square Institute of Neurology, UK
- **Prof. Adrienne Fairhall,** Department of Physiology and Biophysics, Department of Physics and Department of Applied Mathematics, Washington University, USA
- **Prof. Tamas Gabor,** Department of Physiology, Anatomy and Neuroscience, University of Szeged, Hungary
- **Prof. Magdalena Goetz,** LMU Munich, Department of Physiological Genomics, Helmholtz Center Munich, Institute Stem Cell Research, Germany
- **Prof. Masud Husain,** Professorial Fellow of Neurology and Cognitive Neuroscience, Department of Experimental Psychology, University of Oxford, UK
- **Prof. Sabine Kastner,** Princeton Neuroscience Institute, USA
- **Prof. Giovanna Mallucci,** Principal Investigator at the Altos Labs Cambridge Institute of Science, UK
- **Prof. Eve Marder,** University Professor and the Victor and Gwendolyn Beinfield Professor of Neuroscience, Brandeis University, USA
- **Prof. Elizabeth Phelps,** Department of Psychology, Harvard University, USA
- **Prof. Carmen Sandi,** Laboratory of Behavioral Genetics, Brain Mind Institute, École Polytechnique Fédérale de Lausanne (EPFL), Switzerland
- **Prof. Erin Schuman,** Department of Synaptic Plasticity, Max Planck Institute for Brain Research, Germany
- **Prof. Mikael Simons,** Institute of Neuronal Cell Biology (TUM-NCB), Technical University of Munich, German Center for Neurodegenerative Diseases (DZNE), Germany

BUREAU OF THE BOARD

- **President: Gérard Saillant,** Honorary Professor of Orthopedic and Trauma Surgery
- **Vice-President: Jean Todt,** UN Secretary-General's Special Envoy for Road Safety
- **Treasurer: Serge Weinberg,** President of Weinberg Capital Partners
- **Jean Glavany,** Former Minister

AUDIT COMMITTEE

- **President: Serge Weinberg,** Treasurer of Paris Brain Institute Foundation
- **Elli Chatzopoulou,** Inserm Representative
- **Jean Glavany,** Former Minister
- **Jean-Pierre Martel,** Attorney

GENERAL AGREEMENT COORDINATION COMMITTEE

- **President: Gérard Saillant,** President of Paris Brain Institute
- **André Le Bivic,** CNRS Representative
- **Didier Samuel,** Inserm Representative
- **Bruno Riou,** Sorbonne University Representative
- **Erik Domain,** AP-HP Representative

ETHICS AND PROFESSIONAL CONDUCT COMMITTEE

The mission of Paris Brain Institute's Ethics and Professional Conduct Committee (Cometh) is to guide reflection on ethical and professional conduct issues raised by our scientific and medical research programs.
It helps all those involved in research at Paris Brain Institute to comply with the principles governing ethics and professional conduct by encouraging reflection on own practices and contributing to general thinking based on pioneering experiences.
Cometh hosts monthly ethics and professional conduct training sessions for new recruits.

Management Committee (CODIR)*

The senior management team implements the policy developed by Paris Brain Institute's Board of Directors. The Executive Director, appointed by the Board of Directors, leads the six-member Management Committee.

Prof. Stéphanie Debette, Executive Director of Paris Brain Institute (ICM Foundation and Joint Research Unit)

Corinne Fortin, Secretary General of Paris Brain Institute and of the Joint Research Unit

Prof. Jean-Christophe Corvol, Medical Director

Jean-Louis Da Costa, Communication and Development Director

Brian Lau, Scientific Director, Director of Core Facilities, and Deputy Director of the Joint Research Unit

Géraldine Farjot, Innovation Director

The **Support Function Management Committee** (CODIS) also leads institutional and interdisciplinary projects and has the following members:

- **Stéphanie Debette,** Executive Director
- **Corinne Fortin,** Secretary General
- **Pierre Couraud,** Deputy Secretary General
- **Jean-Louis Da Costa,** Communication and Development Director
- **Géraldine Farjot,** Innovation Director
- **Pierre Georges-François,** RIPH Unit Manager
- **Mathilde Gibert,** Legal Affairs Director
- **Géraldine Gouzer,** Scientific and Medical Affairs Director
- **Sylvain Gugliermina,** Procurement, Equipment and Logistics Director
- **Laurine Lenoir,** Organization, Quality & Risk Management Department Director
- **Frédérique Lesaulnier,** Data Protection Officer
- **Cécile Proust,** Human Resources Director
- **Antoine Souquière,** Information Systems Director
- **Marc Thévenot,** CFO

** As at March 1, 2025.*

CODIR Committees

SCIENTIFIC AND MEDICAL STEERING COMMITTEE (COPIL)

The Scientific and Medical Steering Committee (Copil) is a consultative body on all matters related to the Institute's scientific and medical strategy. It provides opinions to the Management Committee (CODIR). Additionally, it has decision-making authority on funding allocations for internal calls for proposals. Alongside senior management, scientific management, and medical management, it includes five researchers representing the Institute's scientific fields:

- **Stéphanie Baulac,** representative for cellular and molecular neurobiology
- **Céline Louapre,** representative for clinical and translational neuroscience
- **Liane Schmidt,** representative for cognitive neuroscience
- **Jacobo Sitt,** representative for computational modeling in neuroscience
- **Claire Wyart,** representative for integrative neurophysiology

TEAMS COUNCIL

The Teams Council, comprising the senior management team and all team leaders, meets once a month. It is consulted on scientific policy, budgetary matters, and resources to be allocated for the UMR.

GENDER EQUITY COMMITTEE

The Gender Equity Committee (GEC) performs an advisory and monitoring role for Paris Brain Institute's governing bodies, and takes action to promote gender equity. The work of the GEC is supported by the GEM *(Gender Equity Movement)* initiative, a collective of Paris Brain Institute staff who have come together to raise awareness of gender bias and inequities and propose measures to address them.

Following the adoption of the Institute's gender equality charter in 2021, the GEC developed an action plan and continued its work on awareness raising, monitoring statistics and indicators measuring gender distribution at all professional levels, along with communication campaigns and initiatives. Paris Brain Institute's workplace gender equality index has progressed in recent years, rising from 75 in 2020 to 89 in 2024, out of a maximum score of 100.

The GEM has been organized into working groups for planning a biennial international workshop and developing a website, journal club, scientist mentoring program and broader educational activities.

Staff representative bodies

SOCIAL AND ECONOMIC COMMITTEE

The task of the Social and Economic Committee (CSE) is to represent staff at ICM Foundation. It liaises with management on issues relating to quality of life at work and relays any individual or collective complaints concerning the application of labor regulations (labor code, pay, working hours, health and safety, etc.).

The role of its Health, Safety and Working Conditions Committee (CSSCT) is to oversee compliance with legal and regulatory requirements. It helps protect the health and safety of staff and implements measures to improve their well-being, analyzes occupational risks, is available for consultation by the employer and assists in reviewing working conditions.

LABORATORY COMMITTEE

The Laboratory Committee is the representative body for staff of the Joint Research Unit (UMR). It advises the UMR's management on scientific, budgetary and human resources policy, and on all other matters related to UMR operations. Members are elected by the Institute's public sector staff. They represent the various categories of staff: researchers and teacher-researchers, engineering, technical and administrative staff, doctoral students, and permanent and contracted civil servants.

5

SUPPORTING RESEARCH

The research conducted at Paris Brain Institute is underpinned by sound, diversified financial resources, and by support teams that collectively provide all the expertise needed to help researchers in the design and implementation of their scientific projects.

SYLVAIN GUGLIERMINA

Sylvain Gugliermina is the Procurement, Equipment and Logistics Director. His team played a key role in the integration and commissioning of the 3-Tesla and 7-Tesla MRI scanners, two state-of-the-art pieces of equipment that arrived at the Institute in 2024.

Fostering, supporting, and securing research

Paris Brain Institute's research activities are supported by a network of services and expertise that provides an essential framework on law, safety, compliance, quality, and scientific ethics and integrity. These services work together to provide an enabling environment for innovation and scientific excellence.

The Ethics Committee: promoting responsible research

The mission of Paris Brain Institute's Ethics and Professional Conduct Committee (Cometh) is to guide reflection on ethical and professional conduct issues raised by our scientific and medical research programs. It helps all those involved in research to comply with the principles governing ethics and professional conduct by encouraging reflection on own practices and contributing to general thinking on these issues.

Since its creation in 2018, Cometh has issued opinions in response to referrals or on the basis of internal discussions (for example, on communication about animal research or the use of artificial intelligence) and drafted the Institute's ethical charter in 2020. In addition, debates have regularly been organized to stimulate collective reflection, along with training sessions for newcomers and students.

Cometh members meet every month to accomplish the committee's various tasks. The positions of several officers of the committee were renewed in 2024. These officers strive to ensure that its members are representative of the Institute's various professional disciplines and staff categories, and the committee therefore also includes a donor and a representative of a patient association. Pierre Pouget, a researcher within the Mov'It: Movement, Investigation, Therapeutics team. Normal and Abnormal Motor Control: Movement Disorders and Experimental Therapeutics team*, became the President of the committee on January 1, 2025 ***(see box opposite).***

COMPOSITION OF THE COMMITTEE

- **Maria del Mar Amador,** Researcher on the ALS: Causes and Mechanisms of Motor Neuron Degeneration team*, Hospital Doctor.
- **Étienne Blanc,** Manager of the Intellectual Property and Strategic Partnerships Unit.
- **Anne Desmazières,** Researcher on the Repair in Multiple Sclerosis: from Biology to Clinical Translation team*.
- **Caroline Dumas,** Donor.
- **Claire Ewenczyk,** Researcher on the Mov'It: Movement, Investigation, Therapeutics team. Normal and Abnormal Motor Control: Movement Disorders and Experimental Therapeutics team*, Hospital Doctor.
- **Frédérique Lesaulnier,** Data Protection Officer.
- **Graziella Mangone,** Doctor in the Neuroscience CIC, Researcher on the Molecular Pathophysiology of Parkinson's Disease team*.
- **Eliott Owczarek,** PhD student on the Experimental Neurosurgery team*.
- **Maï Panchal,** CEO and Chief Scientific Officer of Fondation Vaincre Alzheimer.
- **Pierre Pouget,** Researcher on the Mov'It team*.
- **Magali Regnier,** Neurotrials Quality Assurance Manager.
- **Benjamin Rohaut,** Researcher on the PICNIC – Physiological Investigation of Clinically Normal and Impaired Cognition team*.
- **Danielle Seilhean,** Neuropathologist, Chief Scientific Officer of the Neuro-CEB National Brain Donation Network for Research, Manager of the Neurosciences DMU.

**2023–2024 team.*

THREE QUESTIONS FOR

PIERRE POUGET,

President of the Ethics and Professional Conduct Committee

What motivated you to take on the role of committee president?

I have a keen general interest in this area, rather than there being one single reason. After a year serving on the committee, I wanted to get more involved. I'm particularly interested in ethical issues, which reflect my educational background, including courses in the philosophy of science, psychology, and sociology. This role represents a rare opportunity: it offers the chance to participate in a fundamentally important project that is different from my work within my research team. It allows us to take a step back, reflect on our practices, and consider research from a different angle.

What would you like to achieve on Cometh?

Cometh must, of course, continue the efforts and work it has already begun. To my knowledge, there are few research centers with a committee as active and productive as ours. I would also like to strengthen the ways we interact with senior management, human resources, the scientific integrity unit, and the Social and Economic Committee. Alongside those goals, inviting external speakers to address the committee on an ad hoc basis could enrich our discussions and provide informed perspectives on specific issues.

In your opinion, what major issues will the committee focus on?

Certain key themes specific to the Institute's activities will continue to play an important role: clinical research and the promotion of these activities, the use of animals for scientific purposes, and the use of artificial intelligence in research. These topics have already been addressed by the committee and will most likely return to the forefront of our discussions in the near future.

The ROQ unit: a driver for continuous improvement

The Organization, Quality and Risk Management (ROQ) Department was created in 2018 and plays a key role in supporting the Institute's core facilities, scientific teams and support functions. The department's primary mission is to promote and maintain a rigorous quality approach while optimizing internal practices. This work focuses on identifying and managing risks, helping to strengthen the Institute's operational and scientific excellence.

QUALITY: IMPLEMENTING GOOD PRACTICES

The development of the quality management system and the promotion of staff awareness are among the main tasks of the ROQ Department. In 2024, the team helped the iGenSeq and ICV-Vectorology facilities renew their ISO 9001 certification. New certifications are also being prepared for ICM.Quant ***(see page 39)*** and the NDA & Cell Bank. The ROQ Department also supports volunteer teams (core

The ROQ team.

New Pure Storage® scientific data storage solution, powered on in April 2024.

facilities, scientific teams, and support functions) in harmonizing practices and continuously improving their quality approaches.

ORGANIZATION: OPTIMIZING PROCESSES AND UNITING AROUND COMMON PROJECTS

In translating the specific needs of each department, the ROQ unit acts as a facilitator to optimize internal processes and manages a range of cross-functional projects at the Institute. These include two initiatives focused on environmental issues that involved huge numbers of the Institute's teams:

- **Cleanup Day,** held in late 2023, which encouraged the sorting of freezers, furniture, IT equipment, and digital and paper archives, as well as the reuse of building equipment;
- **The international Freezer Challenge** in spring 2024, which focused on improving the energy efficiency of refrigeration units in laboratories. This competition saw the ICV-3C facility gain an award for the Institute's first participation.

RISK MANAGEMENT: IMPROVED ANTICIPATION THROUGH PREPAREDNESS

The Institute manages its risks using a risk map developed in 2020 and updated annually by the ROQ team. This tool identifies operational and strategic improvement actions that need to be implemented during the year by scientific teams, core facilities, support functions, and the Management Committee, to ensure proactive, effective risk management.

Supporting the Institute's teams: a daily mission for the Information Systems Department

SCIENTIFIC DATA HOSTING: REPLACEMENT OF THE STORAGE SOLUTION

In 2024, Paris Brain Institute chose a Pure Storage® scientific data storage solution, replacing Lustre®. This solution was switched on in April 2024 and enabled the migration of 5 petabytes (5 million billion bytes) of data in just three and a half months. Hosted at two sites in France, with replication every 15 minutes, Pure Storage® has been selected to strengthen high-performance computing environments because of its superior performance and stability. This meets the demanding needs of scientists, particularly in scientific modeling, artificial intelligence, and complex simulations. The Information Systems Department will embark on a new key phase in 2025: data classification and archiving, to support the Institute's continually growing research needs.

TWO COMMITTEES CREATED TO BETTER UNDERSTAND THE NEEDS AND SPECIFIC REALITIES OF RESEARCH

Two specific committees were created in 2024 to strengthen collaboration between the Information Systems Department and the Institute's teams, while promoting the sharing of best practices:

- **The Information Systems Representatives Committee**, which will meet on a bimonthly basis from 2025, focuses on identifying and resolving specific needs, particularly those related to recurring issues.
- **The Scientific Experts Committee**, for its part, addresses longer-term scientific issues related to the information system, such as data compression and the dissemination of best practices among teams.

BUILDING PROFESSIONAL EXPERTISE IN TEAMS

One of the key events of 2024 was a restructuring of the Information Systems Department, with the recruitment of four new employees. These changes have strengthened the professional credentials of the teams and enabled the integration of proven methodologies, such as ITIL and Lean IT, along with other approaches, with a view to preparing the information system for ISO 27001 certification.

Over the past year, more than 120 projects have been carried out, including initiatives to share data with the scientific community in the form of online atlases. The first of these, LAMBADA, is a benchmark initiative on postnatal brain development in mice. A new atlas dedicated to the human brain stem will be added to this collection in 2025.

ENHANCED CYBERSECURITY

Paris Brain Institute is particularly focused on the security of data produced by scientific teams. The recruitment of a computer systems security engineer in 2024 marked a key step in strengthening cyber vigilance and raising awareness of digital risks among all Institute staff.

This expert plays a central role in structuring and securing the Institute's information system, and works closely with the ROQ Department ***(see page 67)***, the personal data protection team, and the Legal Department to standardize and optimize computer systems security processes.

Supporting and shaping the growth of the Institute and its staff

In 2024, the Human Resources Department played a central role in supporting structural transformations within Paris Brain Institute, strengthening its attractiveness as an employer, and implementing a customized management development program. Here we look back at a key year for the Institute's human and organizational development.

Supporting the renewal of the UMR

Preparing for the renewal of the Joint Research Unit (UMR) on January 1, 2025 required significant work by the Human Resources Department to support each stage of this transition. Some teams are reconfigured, while others are split to form new entities, often led by young team leaders. This reorganization also demonstrated the Institute's ongoing commitment to achieving gender parity in the management of research teams. Although Paris Brain Institute has not yet achieved complete equality, significant progress has been made, with increased promotion of young female researchers to team leader positions.

A management program tailored to the challenges of research

The Institute launched an innovative management program in 2024 specifically designed to meet the unique needs of the scientific research sector. The aim of this bespoke program is to equip all of the Institute's research team leaders with the skills they need to meet management challenges and keep pace with changes in the field.

The program is structured around three complementary activities: individual coaching, practical workshops in small groups, and peer-to-peer discussion sessions. Extremely valuable discussions on practical managerial issues took place within groups made up of participants with diverse backgrounds (new and experienced team leaders, men and women from different scientific fields).

Feedback from participants was overwhelmingly positive. Many emphasized the importance of such an initiative in an environment where researchers, often experts in their fields, are not necessarily trained in management. This training not only boosted their organizational skills, but also helped managers better understand the expectations of each member of their teams.

Employer brand and attractiveness

Paris Brain Institute continued its efforts to enhance its appeal to job applicants, in particular through the online recruitment platform Welcome to the Jungle. This system provides a modern, engaging showcase that presents the Institute, its values, its professional disciplines, and the benefits offered to employees. The rollout of the Tool4Staffing (T4S) software has also made it possible to modernize and formalize the application tracking process. This tool creates a central collection point for resumes received, streamlines communication with applicants, and automates a number of steps in the recruitment process.

Meeting the needs of international personnel

In response to the steady growth in the number of international researchers, Paris Brain Institute has been offering French as a foreign language (FLE) courses for several years. These sessions are organized in small groups and tailored to different levels, and aim to support the linguistic and cultural integration of foreign researchers.

The courses, which run over several months, are designed to fit into participants' schedules. They alternate between theory and practical exercises, emphasizing language skills that are directly applicable in professional contexts and in everyday life.

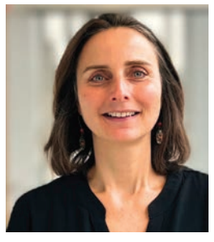
This program plays a key role in building a greater sense of belonging among international researchers, helping them to integrate, and promoting smooth communication within teams.

THREE QUESTIONS FOR

EMMANUELLE HUILLARD,

co-leader of the Genetics and Development of Nervous System Tumors team*

Like all research team leaders at the Institute, Emmanuelle Huillard has been able to access the management training program set up by the Human Resources Department.



How did the training go?

It has been a really positive experience. I had already taken a management training course a few years ago, but revisiting the subject with the experience I had gained since then was extremely helpful. The sessions were engaging, alternating between feedback, role-playing, and theoretical input. The opportunity to share notes with other team leaders was particularly helpful. You realize that, despite our differences, we are all facing the same challenges and that sharing our approaches is so valuable. I also appreciated the friendliness of the group and the skills of the trainer, who was able to create a climate of trust.

What are the benefits for you?

This training enabled me to take a step back and look at my management style, and identify concrete areas for improvement. For example, being better at adapting my communication style to each member of my team, taking into account each person's own style. I also learned the importance of celebrating successes, analyzing why they happened, and learning from them, just as much as from failures. Finally, the training encouraged me to form a clearer idea of my own expectations and those of my colleagues, and to plan more regular follow-ups.

How are you going to apply this training now?

I have already scheduled meetings with my team members. We will sit down together to formalize our mutual expectations and clarify objectives. I also plan to improve the structure of team meetings and project follow-up. Finally, we have decided to organize regular meetings with some of the colleagues we met during the training to continue sharing our practices.

**2023–2024 team.*

IN-HOUSE NEWS

Redesign of internal tools to enable enhanced communication

To better meet the expectations of its teams, the Institute has redesigned its internal communication tools following a survey of all staff. The new version features a modernized editorial policy and a revamped design. Two formats have been developed: a weekly bilingual newsletter covering key news about teams, core facilities, projects, and events; and occasional push emails reserved for priority and urgent information. These changes are designed to strengthen ties between teams while providing a more fluid, tailored, and effective communication experience.

Lunch & Learn: the event that promotes inter-team dialogue

As part of the internal events program, Lunch & Learn sessions have become a highlight for Institute staff. More than 80 participants attend these sessions every month: they are open to all employees, and provide an opportunity to learn more about the activities and talents that drive the Institute. The aim of this friendly and informal format is to encourage inter-team dialogue. Different teams have a chance to talk about their projects and services, or share their thoughts on specific topics. In 2024, participants were able to engage with teams from the PhenoParc, ICV-3C, and DAC core facilities, discover initiatives from the education hub, the Open Brain School, and learn about the startup studio program run by the Innovation Department.

Lunch & Learn offered to Institute staff.

KEY FIGURES

THE MEN AND WOMEN who are the Institute*

878 employees, including 449 Foundation staff and 429 employees of our public partners

51 nationalities, representing 23% of the Institute's workforce

12% medical and paramedical personnel

16% administrative and support staff

72% scientific personnel

€179,930

Amount invested in training in 2024 (excluding contributions)

2024 Gender Equality Index

89/100

61% women

39% men

402

staff trained in 2024, representing 4,446 hours of training

** As at September 30, 2024.*

Financial Report: rigor and transparency central to our action

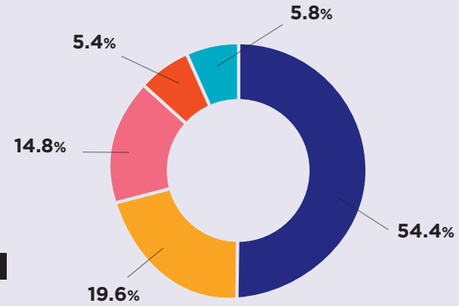
Funding for research projects came from multiple sources, with a resolute focus on the long-term prospect of gaining knowledge and achieving major breakthroughs within the field of neuroscience.
The balance sheet presented here covers the period from October 1, 2023, to September 30, 2024.

INCOME STATEMENT BY NATURE AND FUNCTION (ISNF) AND EXPENDITURE STATEMENT (ES)

2024 INCOME BY NATURE

2024 income amounted to €108.10 M: this includes €87.70 M in income and €20.40 M carried forward from resources allocated and not used in previous years. Income for the fiscal year consisted of fundraising income (€47.70 M or 54.4%), which includes donations (€17.60 M or 36.9%), bequests and gifts (€4.10 M or 8.6%), and sponsorship (€26 M or 54.5%).

It also includes:
- income from core facility activities (€11.40 M) and research collaborations with industry partners (€1.60 M);
- public and private grants (€17.20 M);
- funding of the "IHU Program" (€4.70 M);
- miscellaneous income (rental income, re-invoicing of charges, financial income) (€5.10 M).



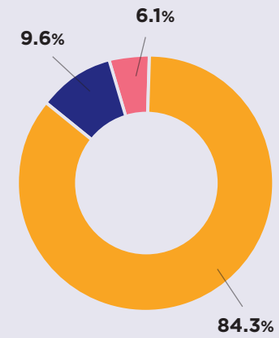
INCOME BREAKDOWN

- Revenue from fundraising
- Public and private competitive funding
- Revenue from core facilities activity and industry partnerships
- Financing of the "IHU program"
- Other revenue (rental income, re-invoicing of charges, financial income)

2024 ALLOCATION BY FUNCTION

Overall expenses in 2024 amounted to €105.60 M: €64.60 M used in 2024 and **€41 M** to be used subsequently from the allocated resources. A total of €54.30 M was allocated to **social missions**, representing **84.3%** of total ISNF allocations.

Paris Brain Institute's social missions include:
- research programs;
- core facilities;
- scientific leadership, international partnerships and training programs;
- promotion of research and incubation of startups.



BREAKDOWN OF ALLOCATION

- Social missions
- Fundraising and communication costs
- Operating costs

Funding for research projects is primarily dedicated to nervous system diseases and spinal cord injuries. The core facilities (neuroimaging, vectorology, genotyping and 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 initiatives), as well as communication initiatives. They represent a total of €6.20 M, or **9.6%** of total ISNF allocations.

Operating costs are expenses incurred in support of research (finance, human resources, legal, and communication) and represent **6.1%** of total ISNF allocations, or €3.90 M.

ALLOCATION OF RESOURCES FROM PUBLIC GIVING

Resources from public fundraising and used in 2024 amounted to €47.70 M. To summarize, for every €100 raised, €74.40 was used to finance social missions and investments, €23.30 was used to cover fundraising and communication costs, and €2.30 was used to cover Paris Brain Institute operating costs.

€2.3
Operating costs

+

€23.3
Fundraising and communication costs

+

€74.4
Financing of social missions and investments

€100
from funds raised

It should be noted that these ratios are established, by accounting convention, solely on the basis of funds used during the fiscal year. This effectively excludes funds assigned to social missions that will be used in future fiscal years and are carried forward as allocated resources, while all costs, particularly fundraising costs, including these multi-year funds, are included in full over the fiscal year. In 2024, Paris Brain Institute Foundation received support from major donors to fund large-scale multi-year projects *(see pages 20-21)*. This resulted in an apparent increase in its fundraising costs, solely because of the significant increase in carryovers of allocated resources from public giving (€23.60 million, compared with €5.40 million in 2023).

BALANCE SHEET FOR THE FISCAL YEAR*

Assets (M €)	2023	2024
Net fixed assets	65	77
Realizable and available assets	86	109
Total	151	186

Liabilities (M €)	2023	2024
Equity	49	51
Fiscal year profit/loss	2.5	2.5
Dedicated funds	31	52
Debt	42	50
Deferred income	26	30
Total	151	186

** As at 30 September 2024.*

Total investments (excluding buildings) made by ICM Foundation since its inception amount to €81.30 M, allocated primarily to the core facilities supporting research.

Investments for the October 2023 to September 2024 fiscal year amounted to €19.30 M (including variation in assets in progress) and include significant investments in scientific materials and equipment of €17.50 M, including €15.20 M for two state-of-the-art 3T and 7T MRI machines.

Net fixed assets amounted to €77 M. As at September 30, 2024, cash holdings amount to €64.30 M, including €41.40 M allocated to earmarked funding. ICM Foundation's equity stands at €53.50 M (including the profit for the fiscal year of €2.50 M). This includes €33.40 M in net position, supplemented by investment grants of €19.60 M. The non-expendable endowment amounts to €1.20 M. At fiscal year-end, allocated funds (funds still to be invested in multi-year programs) amount to €48.40 M.

RESERVE POLICY

When it was established in 2006, ICM Foundation had an endowment of €11.70 M, including €1.20 M in non-expendable endowments. Thanks to careful budget management, the Foundation has balanced its expenses and income for the past eight years, thus avoiding any need to draw on its reserves. These reserves contribute to building assets that can be used for the development of scientific research, as is the case for any non-profit foundation with recognized charitable status. However, since the Foundation is still young, there is not yet any reserve policy aimed at setting a target reserve amount. Instead, the Board of Directors ensures each year that reserves allow for short-term coverage of capital commitments (primarily payroll and building costs, including the repayment of property loans). In addition, the investment policy applied by the members of the Board of Directors is extremely prudent. Cash holdings are invested in marketable securities (capitalization contracts taken out with leading banking institutions, which are 100% capital-guaranteed euro funds) and capital-guaranteed term deposits.

VOLUNTARY IN-KIND CONTRIBUTIONS

VOLUNTEERING

Paris Brain Institute was supported by volunteer hours during the 2024 fiscal year, primarily for communication initiatives. The volume is estimated at 0.6 FTE, or, on the basis of an hourly minimum wage, a sum of €19,000.

IN-KIND PATRONAGE

Paris Brain Institute was also supported by in-kind patronage and patronage in skills in connection with its communication and public fundraising activities, namely:

- media space with: Richard Mille, Klesia, Amaury Média, Bayard Média Développement, Canal+, France TV, *Le Figaro*, NRJ Groupe, Radio Classique, Radio France, RTL.
- donated products and services: Publicis Groupe, Orrick Rambaud Martel, Anacofi, Française de financement et d'édition (FFE), Butard Enescot, Lakiko, M6 Groupe, Orange, Pinault Collection, *Télérama*, Fondation Air France, Willkie Farr & Gallagher LLP, Mediavision, DataOnDemand, Sport Market, MaGwen, Publicis Cinéma, Assouline, Olympic Museum.

To maintain its standards of excellence, Paris Brain Institute has internal and external control procedures in place to guarantee effective and efficient management. It holds Trusted Donations Charter Committee certification and uses independent auditors.

label DON en CONFIANCE
Vous donnez. Il vous rassure.

TRUSTED DONATIONS

On November 3, 2010, Paris Brain Institute was granted certification by the Trusted Donations Charter Committee. This was renewed in October 2022. For over 20 years, this Committee has acted as a professional regulator for public fundraising initiatives. Its action is based on three commitments: accredited organizations must respect ethical rules, they must comply with a collective discipline towards donors and they much accept the continuous monitoring of commitments made.

INCOME STATEMENT BY NATURE AND FUNCTION IN EUROS

Income and expenses by nature and function	Fiscal year Oct 2023–Sept 2024	
	Total	Including public support
INCOME BY NATURE		
1. Resources collected from public giving	**47,665,224**	**47,665,224**
1.1 Donations free of equivalent compensation		
1.2 Patronage, donations and bequests	47,665,224	47,665,224
Personal donations	*17,513,474*	*17,513,474*
Bequests, donations and life insurance policies	*4,131,373*	*4,131,373*
Patronage	*26,020,377*	*26,020,377*
1.3 Other revenue from public support	0	0
2. Resources unrelated to public support	**22,810,994**	
2.1 Donations free of equivalent compensation		
2.2 Corporate patronage		
2.3 Financial contributions free of equivalent compensation	4,702,008	
2.4 Other revenue unrelated to public support	18,108,986	
Services rendered	*11,381,933*	
Partnerships	*1,585,594*	
Other revenue	*5,141,459*	
3. Grants and other public funding	**17,152,722**	
4. Reversals of provisions and impairments	**149,190**	**0**
5. Use of allocated resources from previous fiscal years	**20,361,911**	**2,461,266**
Total	**108,140,041**	**50,126,489**
EXPENSES BY FUNCTION		
1. Social missions	**54,266,020**	**19,754,154**
1.1 Carried out in France	54,266,020	19,754,154
Actions directly carried out	*54,266,020*	*19,754,154*
Payments to a central body or other bodies acting in France		
1.2 Carried out abroad	0	0
Actions directly carried out		
Payments to a central body or other bodies acting in France		
2. Fundraising costs	**6,171,818**	**6,171,818**
2.1 Costs of public appeals	5,124,634	5,124,634
2.2 Costs related to canvassing	1,047,184	1,047,184
3. Operating costs	**3,958,370**	**611,777**
4. Allocations for provisions and impairments	**183,192**	0
5. Income tax		
6. Carryover of fiscal year allocated resources	**41,027,653**	**23,588,740**
Total	**105,607,055**	**50,126,489**
Surplus or deficit	**2,532,986**	**0**

EXPENDITURE STATEMENT IN EUROS

Allocations by function	Fiscal year Oct 2023–Sept 2024	Resources by nature	Fiscal year Oct 2023–Sept 2024
Allocations for the fiscal year		**Resources for the fiscal year**	
1. Social missions	**19,754,154**	**1. Resources collected from public giving**	**47,665,224**
1.1 Carried out in France	19,754,154	1.1 Donations free of equivalent compensation	
Actions directly carried out	*19,754,154*	*1.2 Patronage, donations and bequests*	*47,665,224*
Payments to a central body or other bodies acting in France	*0*	*Personal donations*	*17,513,474*
1.2 Carried out abroad	*0*	*Bequests, donations and life insurance policies*	*4,131,373*
Actions directly carried out	*0*	*Patronage*	*26,020,377*
Payments to a central body or other bodies acting in France	*0*	1.3 Other revenue from public support	*0*
2. Fundraising costs	**6,171,818**		
2.1 Costs of public appeals	5,124,634		
2.2 Costs related to canvassing	1,047,184		
3. Operating costs	**611,777**		
Total allocations in the income statement	**26,537,750**	**Total resources**	**47,665,224**
4. Allocations for provisions and impairments	**0**	**2. Reversals of provisions and impairments**	**0**
5. Carryover of fiscal year allocated resources	**23,588,740**	**3. Use of allocated resources from previous fiscal years**	**2,461,266**
Resource surplus for fiscal year		Public giving deficit for fiscal year	
Total	**50,126,489**	**Total**	**50,126,489**

Philanthropy: supporting the Institute and being a partner in its progress

The Circle of Friends offers its donors and patron members a unique opportunity to connect with the research teams they support. The members of Paris Brain Institute's scientific and medical community would like to express their sincere gratitude to the philanthropists and patrons who continue to support the Institute for their unwavering trust and generosity.

Securing technological investments

A 7-TESLA MRI MACHINE AT PARIS BRAIN INSTITUTE: ACHIEVING SCIENTIFIC AMBITION WITH CUTTING-EDGE TECHNOLOGY

In June 2024, Paris Brain Institute welcomed an extraordinary piece of technology: the latest generation 7-Tesla MRI scanner, the MAGNETOM Terra.X from Siemens Healthineers. This acquisition was possible thanks to the ongoing and unwavering support of Richard Mille and in partnership with the Île-de-France Region, and forms part of an ambitious investment plan for the Institute's core facilities. Thanks to this 7-Tesla MRI machine, Paris Brain Institute is taking a technological leap forward for the neuroscience community and, ultimately, for patients.

First commissioned in November, the machine generates images with unparalleled precision and opens up new fields of application such as very high-resolution imaging, sodium MRI in brain tumors, and precise tracking of bundles of neuronal fibers. The use of a non-invasive technique like the 7-Tesla MRI makes it possible to produce incredibly accurate micro-anatomical brain mapping. Ultimately, it could identify new therapeutic targets and expand the use of brain stimulation.

Richard Mille's team welcomes the state-of-the-art 7-Tesla MRI, the MAGNETOM Terra.X, at Paris Brain Institute in June 2024.

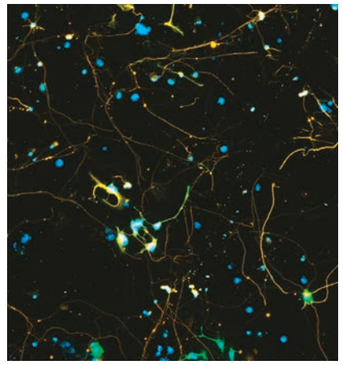
STED MICROSCOPE ACQUIRED THROUGH GENEROUS FUNDING FROM FONDATION NRJ – INSTITUT DE FRANCE

Thanks to Fondation NRJ – Institut de France, founded by Mr Jean-Paul Baudecroux, Paris Brain Institute was able to purchase a STED (Stimulated Emission Depletion) microscope with adaptive optics module, and this was commissioned in 2024. The configuration chosen by the Institute's microscopy platform, ICM.Quant, features two depletion lasers, an adaptive optics module, and a Matrix detector. This is a first in France. This microscope, which can study tiny structures such as organelles up to 20 nanometers, will help neuroscientists unravel the mysteries of neural cells and their components, to determine the biological mechanisms behind normal or pathological brain function. This acquisition has made the Institute a leading center for this technology and opens up new research avenues for its teams and its academic and industry partners, as well as for the neuroscience community in general.

Jean-Paul Baudecroux, founder of Fondation NRJ – Institut de France, and the STED microscope at the Institute's ICM.Quant microscopy facility.

FAMILY PLEDGE TO SUPPORT THE ACQUISITION OF AN APOTOME 3 MICROSCOPE

As members of the Circle of Friends for several years, Mr and Mrs Dumas got involved as a family in 2024. In memory of Mrs Dumas' parents, the family wanted to support the purchase of a state-of-the-art microscope for the ICM.Quant facility. This equipment provides optical sectioning on fixed fluorescent samples, creating the possibility of extracting three-dimensional information with an incredible level of automation and image quality.



This choice of family philanthropy is a mark of trust in the Institute and part of a long-standing wish to pass on the family values of generosity and action to benefit medical research. For the family, it was important to enable the Institute to acquire sustainable equipment that makes the day-to-day work of researchers easier and encourages knowledge-sharing between teams.

20 YEARS OF PARTNERSHIP WITH F.P.JOURNE

Paris Brain Institute is proud to celebrate 20 years of support from its longest-standing patron: Geneva-based fine watchmaker F.P.Journe. Through this philanthropic partnership, founded on common values of trust, loyalty and excellence, F.P.Journe has given more than two million euros to support the Institute's work.

In 2024, to mark this anniversary, F.P.Journe renewed its commitment by providing multi-year funding to the R&D Unit, Paris Brain Institute's innovative prototyping facility. With its new name, "F.P.Journe Charity Fund R&D Unit", the unit is a key asset in the Institute's innovation strategy. In addition to this incredible support, since 2008, 30% of profits from sales of the iconic "Centigraphe" watch have been donated to the Institute. In 2021, F.P.Journe also funded a Big Brain Theory program project on myelin repair in multiple sclerosis. Together, F.P. Journe and Paris Brain Institute are demonstrating how philanthropy accelerates innovation in health.

Event celebrating 20 years of partnership with F.P.Journe with Lionel Naccache, Gérard Saillant, François-Paul Journe and Jean Todt *(left to right)*.

FOCUS ON...

2024 Art-Science Breakfast

With support from Art Basel Paris, and alongside the Institute's founders and Circle of Friends, the 13th edition of the Art-Science Breakfast was held on October 16. The event showcased brain-machine interfaces as an innovative solution for post-stroke rehabilitation. These devices use brain signals to stimulate motor imagination and promote the reorganization of neuronal circuits, essential in the therapeutic window that is the first six months after a stroke. At the event featuring poet Laura Vazquez, artist Florian Zumbrunn and the Obvious collective, Fabrizio De Vico Fallani, NERV Lab team leader, and Camile Bousfiha, a neurologist specializing in strokes, presented their collaborative work done at Paris Brain Institute to the assembled philanthropists, highlighting the potential of brain-machine interfaces for the non-invasive rehabilitation of patients with motor disabilities. The event was a prominent celebration of the generosity that supports Paris Brain Institute.

Continuing support for research teams

OLIVIER GOY: AN INVINCIBLE AMBASSADOR FOR PARIS BRAIN INSTITUTE

In 2024, Olivier Goy continued his generous commitment to supporting the research conducted at Paris Brain Institute into amyotrophic lateral sclerosis (ALS). His efforts have not only generated crucial funding to accelerate research, but have also raised the profile of this disease as a major public health challenge. Landmark initiatives in 2024 include several screenings of *Invincible été* (Invincible Summer) around the world and throughout France, thanks to the involvement of France Tutelle, the release of his book written with Anne Fulda, *Invincible*, and published by Éditions l'Observatoire, and the formidable momentum built by Les Invincibles – All United association. Founded by Ludovic Besombes, John Scala and Olivier Goy, the association has been a huge success, with a concert at the Olympia concert venue with France's biggest singers, a gala at the Grand Palais, 35 ambassadors on board, including Thomas Pesquet, and wide media coverage highlighting the urgency of combating ALS.

THE ENCODE-ID PROJECT ON INTELLECTUAL DISABILITIES RECEIVES PATRONAGE SUPPORT FROM MUTUELLES AXA

Aimed at accelerating innovation in research, prevention, health education, patient management and high-quality training for young researchers and doctors, the healthcare patronage program launched by Mutuelles AXA in early 2022 is a new commitment that complements its traditional patronage focus areas supporting social, environmental and community causes.

The ENCode-ID project, led by Laïla el-Khattabi within the Brain Development team (BrainDev), and in partnership with the Armand Trousseau and Pitié-Salpêtrière (AP-HP) Hospitals' clinical and biological genetics teams, as well as Lille and Rennes teaching hospitals, has received support from Mutuelles AXA, as part of the second call for projects launched in February 2023.

The initiative focuses on intellectual development disorders (IDDs), which are cognitive skills development disorders occurring in early childhood and affecting 1%-2% of the population. Despite advances in genetics, in around 50% of cases the cause is not identified. Thanks to this incredible support over two years (2024 and 2025), EnCode-ID seeks not only to identify new genetic causes of IDDs, but also to identify severity biomarkers and new therapeutic approaches. The project aims to have an immediate impact on patients and on their families, particularly for their treatment, care and genetic counseling.

THE BOUVET-LABRUYÈRE PRIZE: 15 YEARS OF SUPPORTING MULTIPLE SCLEROSIS RESEARCH

Established in 2005 by Mrs Bouvet-Labruyère's four children, the Fondation Marie-Ange Bouvet-Labruyère, housed at Fondation de France, has been supporting research into multiple sclerosis (MS) conducted at Paris Brain Institute since 2011, in the form of a €25,000 prize. It is the first at the Institute created by patrons, and is intended to fund innovative research led by young researchers. Mary-Amélie Masson, winner of the prize and doctoral student on the Myelin Plasticity and Regeneration team*, presented her work to the family under the leadership of her research director, Brahim Nait-Oumesmar. Her thesis focuses on the role of postsynaptic density protein 95 in the manufacture of the neuron protective sheath, myelin.Her work aims to shed light on the demyelination and remyelination processes in MS. *"As truly a family project ..., each year we contribute to understanding and fighting this disease, as part of a process of passing on this commitment within our family,"* say the founders of the Fondation Marie-Ange Bouvet-Labruyère.

** 2023-2024 team.*

ALEXANDRA CURIEL-JOFFO, AMBASSADOR FOR RESEARCH INTO GLIOBLASTOMA

In memory of her husband, Franck Joffo, who died at the age of 51, Alexandra Curiel-Joffo campaigns in France and internationally to raise funds to support research into glioblastoma, the most aggressive and common form of brain tumor. Alexandra's efforts are focused on funding a joint research project between Paris Brain Institute and Harvard Medical School, led by Mehdi Touat and Keith Ligon. This ambitious transatlantic project, which has a budget of €2 million over four years, aims to identify new treatment strategies for people with glioblastoma. More than €150,000, and around $350,000 (via Paris Brain Institute America), has already been raised thanks to campaigning by Alexandra Curiel-Joffo and her network.

Alexandra Curiel-Joffo, ambassador for research into glioblastoma.

FREE TO MOVE: FRANCE PARKINSON CREATES A DEDICATED FUND WITH PARIS BRAIN INSTITUTE

France Parkinson and Paris Brain Institute share the same founder: Professor Yves Agid, a leading specialist in the disease. It was therefore logical that these two institutions came together in 2024 to step up the funding of basic and clinical research into Parkinson's Disease, which now affects 270,000 people in France and several million people worldwide. By creating a dedicated fund, France Parkinson is enabling researchers at the Institute whose scientific projects have been selected by the association's Scientific Advisory Board to immediately access the funding needed for innovation. The first two winners, Claire Dussard and Hélène Cheval, will be able to explore two new innovative and promising avenues in 2025: neuro-feedback, as a non-invasive therapy, and organoids, as a model for detecting mitochondrial stress in dopaminergic neurons. A winning formula for new progress in research into Parkinson's Disease, for the benefit of patients.

PARIS BRAIN INSTITUTE IS EXPANDING ITS HORIZONS THANKS TO SUPPORT FROM THE FONDATION MARIE-FRANÇOISE PARAYRE-CHAUFOUR

Thanks to support from the Fondation Marie-Françoise Parayre Chaufour, a Belgian non-profit, Paris Brain Institute launched its first Big Brain Theory (BBT) international appeal in partnership with Mission Lucidity in Belgium. The BBT program was created by Paris Brain Institute to fund innovative, interdisciplinary and high-risk research projects by the Institute's teams. The first project to win the international BBT is led by Bassem Hassan (Paris Brain Institute) and Pierre Vanderhaeghen (VIB-KU Leuven) and its purpose is to explore the mechanisms of synapse formation synchronization and their impact on the organization and plasticity of brain circuits.

Paris Brain Institute America: philanthropy supporting transatlantic research into brain diseases

2024 was the first full fiscal year of Paris Brain Institute America (PBIA), Paris Brain Institute's US foundation launched in 2023 in New York under the leadership of Martine Assouline. The purpose of the Foundation is to provide crucial support for Paris Brain Institute's research projects carried out in partnership with top US universities. In 2024, thanks in particular to a charity dinner held at the French Consulate in New York, attended by Mr Laurent Bili, France's ambassador to the United States, and Mr Cédrik Fouriscot, Consul General of France in New York, PBIA enabled Paris Brain Institute to launch two research projects: the first in partnership with Harvard Medical School on glioblastomas, led by Mehdi Touat, and the second on head traumas, in partnership with Columbia University, led by Jacobo Sitt.

Dinner organized in 2024 by Paris Brain Institute America (PBIA) at the French Consulate in New York, attended by Jean Reno, ambassador of the Institute.

Accelerating innovation

NEURAL PHILANTHROPY FUND: SUCCESSFUL LAUNCH THANKS TO THE FONDATION ANNE ET CLAUDE BERDA AND INDOSUEZ WEALTH MANAGEMENT

Paris Brain Institute strives to transform basic research results into useful health products for patients in the field of neuroscience. One of the key pillars of this approach is to draw on the strength of entrepreneurship, for example through NeurAL *(Neuroscience Acceleration Launchpad,* ***see page 48***), its innovative neuroscience seed program, which relies on an entrepreneurial philanthropy fund. Launched in 2023 with support from the Fondation Anne et Claude Berda, NeurAL also received support from Indosuez Wealth Management in 2024.

The Institute's startup studio selects promising research and development projects in European neuroscience laboratories through a call for proposals and supports them for 12 to 18 months, providing them with technological, scientific, clinical, and regulatory expertise with the aim of increasing their chances of success, convincing investors, and securing the necessary funding. Winning projects also receive funding of up to €400,000 for the purpose of obtaining robust data.

THE 2023 WINNERS

- The aim of the IGHOR project (led by Maïté Verreault and Ahmed Idbaihis) is to develop and test a new chemical entity for the treatment of glioblastoma, designed to specifically target a hormone receptor affected in almost a third of patients.

- The CicaNeuro project (led by Bruno Figadère, Rita Raisman-Vozari, Patrick Michel and Laurent Ferrié) is developing a process for modifying compounds that were originally antibiotics, transforming them into neuroprotective molecules that can be applied to Parkinson's disease. By supporting the NeurAL program, the Fondation Anne et Claude Berda and Indosuez Wealth Management are demonstrating their commitment to innovation and helping to accelerate the market entry of innovative therapeutic solutions for brain diseases.

Focus on two private initiatives

GENEROUS PATRONAGE FROM THE B SIGNATURE HOTELS & RESORTS GROUP

In addition to her individual support as a philanthropist and member of the Paris Brain Institute Circle of Friends, Anne Jousse also supports the Institute through her hotel group, B Signature Hotels & Resorts, which has five hotels in Paris, as well as one in Brittany and in Saint Barthélemy. Alongside generous funding, the group offers its customers the opportunity to support Paris Brain Institute via a micro-donation at checkout. Beyond the support this generates, it also offers great visibility for the Institute among the group's international clientele.

A SOLO CROSSING IN SUPPORT OF PARIS BRAIN INSTITUTE

Thierry Scheur, Chief Operating Officer of Euryale Services, partner and major patron of the Institute, set himself the challenge of sailing 1,000 miles aboard a yacht. For this seven-day solo challenge, departing from La Rochelle, Thierry Scheur raised funds for the Institute through his network. The generosity of Thierry and of his donors has raised nearly €50,000.

Signing the funding agreement by Jacques Prost, CEO of Indosuez Wealth Management, and Professor Alexis Brice on June 28, 2024.

PARIS BRAIN INSTITUTE CIRCLE OF FRIENDS

The Circle of Friends is a group of philanthropists who are not only generous donors but are also committed to the development of Paris Brain Institute*.

- **Lindsay Owen-Jones, Honorary President of Paris Brain Institute Circle of Friends**
- **Gérard Saillant, Founding Member and President of Paris Brain Institute**
- **Jean Todt, Founding Member and Vice President of Paris Brain Institute**
- **Martine Assouline and Maurice Lévy, Co-Presidents of the Circle of Friends**
- **Jean-Luc Allavena**
- **Cédric de Bailliencourt**
- **Frédéric Banzet**
- **Alexandre Barrière**
- **Florence Courbit****
- **Stéphane Courbit****
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- **Jean-Philippe Hottinguer**
- **Anne Jousse****
- **Richard Mille**
- **Eddie Misrahi**
- **Margaux Primat**
- **Arnaud de Puyfontaine****
- **Christian Schmidt de La Brélie**
- **Serge Weinberg**

**** As at September 30, 2024.***
***** Joined the Circle of Friends in 2024.***

DONORS AND PATRONS
who joined the Circle of Friends in 2024

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Philippe Klocanas
Family and Friends of Franck Joffo
LAKIKO – Charlotte Psaume, Michel Kikoïne and Paul Marques-Duarte
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Beatrice Stern
Jean Raby and Christine Tarbouriech
Marie-Laure Traux-Binsse
16 anonymous donors and patrons

Circle of Friends
Paris Brain Institute

THE AMBASSADORS
of Paris Brain Institute

- **Michelle Yeoh, actress**
- **Jean Reno, actor**
- **Guillaume de Tonquédec, actor**

OFFICE OF THE CIRCLE OF FRIENDS:
+33 (0)1 57 27 40 32
cercle@icm-institute.org

Public fundraising: a collective push for scientific progress

Each year, tens of thousands of donors join forces to support brain research.
This collective push makes it possible to fund brand new projects in basic and clinical research, to equip teams with the resources they need and to acquire state-of-the-art equipment that enables researchers at Paris Brain Institute to rise to new scientific challenges and accelerate our understanding of neurological and psychiatric diseases.

Charitable giving on the rise

Over the 2023-2024 fiscal year, public fundraising appeals continued through multiple campaigns for donations. All of the initiatives together raised €11.7 million in donations, an increase of 11% on the previous year. This fundraising was supported by more than 103,000 dedicated regular and new donors. Paris Brain Institute would like to thank all donors who each year continue to support neuroscience research.

Through the various campaigns developed and addressed to donors throughout the year, the Institute reports on progress made by its research teams. Each campaign focuses on a particular topic, presenting the latest knowledge, as well as presenting one or more ongoing research projects and research avenues.

Donor-focused events

At the "Matinales" quarterly conferences led by researchers, four topics were covered this year: ataxias, mental health, dementia, and patient-focused artificial intelligence. These events are held in the Edmond and Lily Safra Auditorium at the Institute and were also streamed live and available for replay on the Institute's YouTube channel.

Specific events are organized to thank donors and show them the progress made possible thanks to their generous support. For example, in November 2023, the "En tête à tête" event was an opportunity for an exclusive discussion between Lionel Naccache, co-leader of the PICNIC Lab team, which focuses on neuropsychology and functional neuroimaging at Paris Brain Institute, and the actor Guillaume de Tonquédec, Institute ambassador. This event also featured a live reading from Guillaume de Tonquédec's book about his difficulties learning to read, combined with neuroscientific analysis of the mechanisms at play.

In addition, each quarter, the magazine for donors, *Synapse,* offers insights into key aspects of research, developed as part of a topic-focused issue. Each issue also features news on the work of the Institute's researchers and its day-to-day activities, allowing donors to see the true impact of their support.

SPOTLIGHT

Generous support for the Discoverers of Hope (Découvreurs d'Espoir) campaign

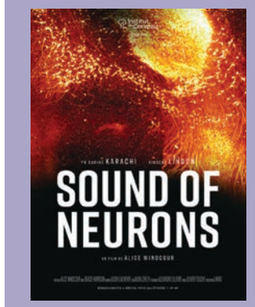
In November 2023, for the sixth consecutive year, actor Guillaume de Tonquédec once again lent his support to Paris Brain Institute by championing the message of hope for the "Découvreurs d'Espoir" annual fundraising campaign. For this latest campaign, he was accompanied by five other big names from film and television to give an even louder voice to this cause: Lionel Abelanski, Valérie Bonneton, Thomas Da Costa, Sabrina Ouazani and Charlotte de Turckheim. Together, they volunteered to film a powerful and moving advert with a main message inviting everyone to become "Découvreurs d'Espoir" (discoverers of hope) by donating. The Mediavision, M6 and Barrière groups helped to gain media coverage for the film by broadcasting it free of charge over several weeks on TV and in cinemas.

Guillaume de Tonquédec (left) alongside Sabrina Ouazani and Lionel Abelanski.

FOCUS ON...

A film to promote research

This year was an opportunity for incredible partnerships, including the making of a short documentary film called *Sound of Neurons*, kindly directed by multi-award-winning director Alice Winocour, highlighting progress in clinical research into Parkinson's disease. In this film, viewers see behind the scenes of the work of Prof. Carine Karachi, a neurosurgeon at Pitié-Salpêtrière Hospital (AP-HP) and co-leader of the experimental neurosurgery team. Actor Vincent Lindon is also filmed meeting three Parkinson's patients who have received neurosurgical care. Throughout the documentary, viewers are immersed in the fascinating world of neurosurgery research. Paris Brain Institute would like to extend its sincere thanks to Alice Winocour and Vincent Lindon for their time, generosity, and commitment to this remarkable project.



Sound of Neurons is regularly screened at events organized by Paris Brain Institute. If you have any questions about future screenings, please contact Claire Pennelle: **claire.pennelle@icm-institute.org**

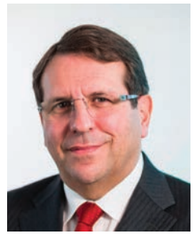
SPORTS CHALLENGE

Les Foulées du Cortex challenge New impetus for brain research

September 2024 saw the launch of the "Foulées du Cortex", the very first edition of Paris Brain Institute's 100% connected fundraising and fitness challenge. This innovative challenge, organized from September 10-21, brought individuals and companies together around a simple principle: 1 km completed = €1 donated to Paris Brain Institute. Over 1,100 people enthusiastically took part in the challenge. Amandine Petit, Miss France 2021, was the challenge's ambassador, while Crédit Mutuel Nord Europe, long-standing sponsor of the Institute and main partner of Foulées du Cortex, pledged to fund 35,000 km. Thank you to our generous partners for their valuable support. In total, more than €80,000 was raised in connection with this event, named the "2024 Great National Cause". This unifying fitness challenge embodies a new way of combining sport and charitable giving, and lays the foundations for an annual event that benefits neuroscience research.

"When you arrive at Paris Brain Institute, you discover a world of progress where researchers come from all over the world to revolutionize the treatment of brain diseases. I have believed in it from the beginning, and that belief is constantly reaffirmed by the Institute's development and the breakthroughs published by its researchers. At CMNE, we are proud to support the Institute's excellent teams who share their discoveries with us beyond the lab."

Éric Charpentier, Chief Executive of Crédit Mutuel Nord Europe (CMNE).



Meaningful support from bequests and life insurance policies

In the knowledge that brain diseases pose a major public health challenge, generous donors are increasingly opting to donate all or part of their estates to Paris Brain Institute by leaving gifts in their wills or naming the Institute as a beneficiary in their life insurance policies. This is a way of extending their support, to enable the Institute to remain at the forefront of neuroscience research, and to protect the future of current generations and those to come.
In 2024, bequests and life insurance donations received by the Institute amounted to €5.5 million, an increase of over 12% compared to 2023.

Art articulating disease: a new bequest awareness campaign

In 2024, the Institute launched a new bequest awareness campaign in response to the scale of the scientific, medical and human challenges posed by brain conditions.

The campaign chose art as the medium to represent a feeling widely held among Alzheimer's disease patients: a loss of identity.

William Utermohlen (1933-2017), an American artist and painter affected by this progressive disease, produced a series of self-portraits during his lifetime. As the years passed and his disease progressed, the features he drew became less precise and his face eventually disappeared from the sketches. This poignant, rich insight helps us understand how this condition affects patients.

William Utermohlen's artistic legacy illustrates, better than words ever could, the need for campaigns to increase knowledge about the brain and the mechanisms at work in the diseases that affect it.

Watch the campaign video here:

CLAUDE S.

has named Paris Brain Institute as co-beneficiary of her life insurance policy

I worked in research for 40 years, so I knew the funds were needed. It was a natural choice for me to choose to name research bodies such as Paris Brain Institute as beneficiaries of my life insurance upon my death. This cause is particularly close to my heart because my husband died from a brain tumor five years ago. I believe that research must be able to progress, but that it does not have enough resources to do so. I hope that my money will give researchers a lot more freedom. It is so important for them to spend less time fulfilling administrative duties and applying for funding. My life insurance policy must be the oxygen researchers need!

Évolution des autoportraits de William Utermohlen, artiste et malade d'Alzheimer.

2024 bequests campaign: William Utermohlen (1933-2007), *Self-portrait*, *Self-portrait (with saw)*, *Self-portrait (with easel)*, and *Head* (August 30, 2000). With permission from Chris Boïcos Fine Arts (Paris) and with the support of Bridgeman Images.

FIND OUT MORE

For more information about leaving bequests and life insurance to Paris Brain Institute, visit legs.institutducerveau.org

A legacy for the future

The Institute wishes to pay tribute to all its benefactors for their immense contribution to brain disease research. By printing their names onto its wall of donors and testators, it can ensure that their legacy will be forever remembered at the Institute.

Specific support and organized visits

Carole Clément, Testator Relations Manager, is available to speak with anyone considering passing on assets to the Institute and seeking advice on how to proceed or simply wishing to find out more. A meeting can also be arranged with Marion Bouletin, the Institute's legal expert and notary ***(see below).***

Any discussions are completely confidential and non-binding, and follow a rigorous code of ethics and conduct.

Testators can also arrange a visit to the Institute to meet with researchers and find out about its laboratories. These meetings are very much appreciated, as they provide an essential opportunity for people considering gifting their assets to discuss possible options.

To contact Carole Clément:
+33 (0)1 57 27 41 41 or carole.clement@icm-institute.org

THREE QUESTIONS FOR

MARION BOULETIN,

Legal Expert and Notary

Why did you decide to join Paris Brain Institute in 2024?

➡ As a specialist notary, I had worked for 13 years at several notarial offices. This enabled me to gain extensive experience in real estate law and family law. With this experience, I decided to use my legal knowledge for a cause that is close to my heart: scientific research and progress to fight against diseases that affect us all.

What does your daily work involve?

➡ Because the number of bequests has increased (36 new bequests registered in 2024), Paris Brain Institute decided to bring the management of bequests in-house. My role is to ensure the legal paperwork is carefully handled with notaries, to ensure that bequests to the Institute are promptly and efficiently administered. I ensure the testators' wishes are respected and fully implemented at every step. My mission is also to release capital from life insurance policies for which the Institute is beneficiary.

How do you liaise with people who want to leave a bequest to the Institute?

➡ I work closely with Carole Clément to provide legal support to our benefactors, reviewing which gifting solutions are best suited to their circumstances and wishes, and guiding them on the more technical aspects, such as drafting a will.

Thank you

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Monique Guérinat – FISA

THANK YOU

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39 anonymes

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Hôpital Pitié-Salpêtrière
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