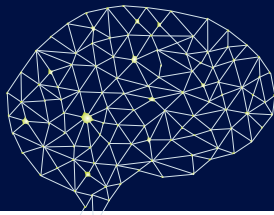




N°18 – AUGUST 2019



# FOR YOU & WITH YOU

The Brain and Spine Institute's donors Journal



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**SPECIAL REPORT**  
RARE NEUROLOGICAL  
DISEASES

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Today, the Brain and Spine Institute ranks 2<sup>nd</sup> in the world for neurological research. The ICM owes this positioning to its community of top researchers and to the recruitment of the best scientists worldwide - the arrival, next September, of Jaime de Juan-Sanz as new team leader in charge of the groundbreaking projects that he develops, stresses this point.

This year again, you are more than 100,000 donors to contribute to the life of our Institute and give it the means to achieve its ambitions. We are extremely grateful. Indeed, the support of donors and sponsors represents nearly half of the resources of our foundation.

In addition, after the merger between the ICM Foundation, recognised as being of public utility and the IHU-A-ICM Scientific Cooperation Foundation on December 31, 2017, the ICM Foundation's accounts (closed on December 31, 2018) include for the first time the "IHU programme", financed by the Future Investment Programme through the Agence Nationale de la Recherche (ANR).

The ICM is above all a human adventure, a community of experts who participate with passion, on a daily basis, in the fight against diseases of the nervous system. A strong interaction between basic research, applied research and the hospital environment. A successful convergence of the private and public cultures for optimal efficiency!

Your support is essential to continue and accelerate research work. We need resources, because there is still so much to discover about the brain to give hope for treatment and cure all those, patients and families, who suffer from diseases of the nervous system, which are today deprived of therapeutic solutions.

### Serge Weinberg

Treasurer and Founding Member of the ICM

## A RICH NEW YEAR WITH OPEN BRAIN BAR!



After a summer break, the Open Brain Bar (OBB) will be back in service. On the agenda: meetup as part of the International Scientific Film Festival, PARISCIENCE, which will be held from October 25 to 30, and an evening with HEC SANTE to discuss neuromanagement.

**More information to come on [icm-institute.org/fr/obb/](http://icm-institute.org/fr/obb/)**

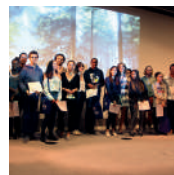
## NEW FOR THE IPEPS



Two new startups have joined the ICM incubator program. The iPEPS is therefore delighted to welcome StimulActiv, a young entity that develops professional solutions to support the dependency of people with Alzheimer's disease and autism; as well as Doctoconsult, which aims to improve access to care and continuous patient follow-up via a telemedicine platform and a therapeutic application.

**For more information: [ipeps.icm-institute.org/](http://ipeps.icm-institute.org/)**

## YOUNG PEOPLE IN THE SPOTLIGHT



Transmitting a taste for science and research is one of the Institute's vocations. To do this, several programs are organized throughout the year for teenagers. On April 6, the ICM hosted the France Brain Bee - an

international neuroscience competition testing students on their knowledge of the brain - and awarded Seung-Bin Joo of the International School of Paris. Another project: Researchers in the making, which aims to introduce secondary and high school students to research and its fundamental challenges by organizing ten sessions around scientific projects within the Institute. Finally, the Destination Lab Inserm operation, in which the ICM has been involved for many years by opening the doors of its laboratories. In 2019, 11<sup>th</sup> grade ST2S and 9<sup>th</sup> grade students were welcomed. Future vocations!

## CONGRATULATIONS TO THE HEROES



Nearly 13,700 euros; that's the amount collected by the 33 riders mobilized for this 10<sup>th</sup> edition of the Heroes' Race. Many thanks for their motivation and dedication, which enable the ICM to continue its fight against

neurodegenerative diseases.

## PARTNERS INFORMATION: THE ICM, WINNER OF THE 2019 GRAND PRIZE FOR PHILANTHROPY WITH ITS PARTNER EURYALE AM



On June 11, as part of the 3<sup>rd</sup> edition of the Grand Heritage Forum organized by the Ficade Group, the ICM and Euryale Asset Management received the Philanthropy Grand Prize for their joint initiative linking finance and philanthropy: the Pierval Santé SCPI sharing fund.

Launched in 2015 in partnership with the Crédit Mutuel Nord Europe and La Française AM, this scheme promotes medical research by creating this first sharing fund in France linked to an SCPI (Real Estate Investment Company) Prof. Gérard Saillant, President of the ICM, David Finck, General Manager of Euryale AM and Jean-Pierre Martel, founding member of the ICM, are delighted with this award.

**LE FIGARO**

### ARTICLES IN PARTNERSHIP WITH LE FIGARO

The mysteries of brain function

<http://sante.lefigaro.fr/dossier/institut-du-cerveau>

**For you & with you** is the ICM magazine sent to its donors. N°18 – August 2019 Editor-in-chief: **Axelle de Chaillé**. Editorial board: **Jean-Louis Da Costa, Astrid Crabouillet, Nicolas Brard and Claire Pennelle**. Completion: **Louis**. Printer: **BB création**. Print run: **1,500 copies**. © ICM – J.P. Pariente – Publicis – Gérard Saillant – INSERM – Michel Thiebaut de Schotten

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DE PARIS



**Inserm**  
La science pour la santé  
From science to health

**SORBONNE  
UNIVERSITÉ**

La recherche  
**CARNOT**  
pour les entreprises

## ICM on the web



- The beneficial effects of coffee in the treatment of dyskinesia
- When narcolepsy makes someone more creative

## VIDEOS

[icm-institute.org/videos](http://icm-institute.org/videos)

- Science, Art and Culture Conference on 16/05/19 with Professor Lionel Naccache: "Why should we be interested in the brain to understand human psychology?"
- Donor conference on 02/07/19 dedicated to brain function

[icm-institute.org/fr/actualites](http://icm-institute.org/fr/actualites)

- Open Brain Bar #12 on 06/06/19: "When emotions talk to us..."



Every month, discover ICM news and research breakthroughs by signing up to our website or newsletter.

Sign up at: [icm-institute.org](http://icm-institute.org)

## AGENDA

### ●●● September 19, 2019

– Donors Conference on Alzheimer's Disease

Online on our website  
[www.icm-institute.org](http://www.icm-institute.org)

### ●●● September 21, 2019

– European heritage days at the ICM

Information on [www.icm-institute.org](http://www.icm-institute.org)

### ●●● October 12, 2019

– A Circuit for the Brain

Information and registration on: [ucplc.fr](http://ucplc.fr)

# RARE NEUROLOG

A disease is considered rare when it affects less than one in 2,000 people. More than 7,000 rare diseases - including about 800 neurological diseases - are described, and new ones are identified every week. Rare diseases are usually severe, chronic and disabling. Half of the people affected have motor, sensory or intellectual deficits and in 9% of cases, a total loss of autonomy. It is in this context that research teams at the Brain and Spine Institute (ICM) are currently trying to identify the causes of 14 rare neurological diseases in order to accelerate their diagnosis and provide appropriate treatments, particularly by gene therapy.



**3.5 million** people affected  
by a rare disease in France

**7,000**

known rare diseases  
75% at early pediatrics



80% of genetic origin



Motor, sensory or intellectual impairment in **50%** of cases.  
For **9%** of patients, total loss of autonomy

## 13 TEAMS IN WORKING ORDER

In more than half of cases, rare diseases develop in childhood, but others occur later in adults. They are often referred to as "orphan" because there is currently no treatment for many of them. The 7,000 rare diseases identified today affect more than 3 million people, or 4.5% of the French population, and represent a major public health challenge.

These diseases are characterized by a wide variety of clinical signs that differ not only from one disease to another but also between two patients with the same disease. This variability makes diagnosis difficult, the latter occurring on average 5 years after the onset of symptoms in 25% of cases; in particular for non-hereditary diseases, i.e. 20% of them.

**"Better know the origin of diseases in order to better diagnose them and at the earliest stage"**

At the ICM, 13 research teams are working to discover the causes of 14 of these diseases, identify biomarkers to assist in the diagnosis and prediction of disease progression and develop treatments. The identification of genes, specific neural networks, brain imaging studies, and the identification of early markers of pathology are all promising results for the development of new therapeutic approaches. Investigation leads resulting from this research are already being studied, such as deep brain stimulation in Tourette's syndrome or gene therapy for Huntington's disease.

# GENETIC DISEASES

## RESEARCH ON RARE NEUROLOGICAL DISEASES AT THE ICM

### 14 MAIN PATHOLOGIES STUDIED BY OUR 13 RESEARCH TEAMS

Trisomy 21	•• Teams: M.C. Potier/S. Haik & A. Bacci
Tourette's syndrome	•• Teams: E. Burguiere, M. Vidhailet/S.Lehéricy & B. Lau/C. Karachi
X Fragile	• Team: B. Hassan
Cerebellar ataxias	•• Teams: A. Durr/G. Stevanin & N. Cartier
Leukodystrophies	•• Teams: B. Naït Oumesmar/Zujovic, M. Vidhailet/S.Lehéricy & N. Cartier
Brain tumors	• Team: M. Sanson/E. Huillard
Dystonia	• Team: M. Vidhailet/S.Lehéricy
Spastic paraplegias	• Team: A. Durr/G. Stevanin
Mirror Movement Syndrome	• Team: M. Vidhailet/S.Lehéricy
Huntington's disease	••• Teams: A. Durr/G. Stevanin, M. Vidhailet/S.Lehéricy & B. Lau/C. Karachi/N. Cartier
Fronto-temporal dementia	• Team: A. Durr/G. Stevanin & R. Levy
Prion diseases / Creutzfeldt-Jakob	• Team: M.C. Potier/ S. Haik
Amyotrophic lateral sclerosis	•• Teams: A. Durr/G. Stevanin & S. Boillée
Progressive supranuclear paralysis	••• Teams: A. Durr/G. Stevanin, M. Vidhailet/S.Lehéricy & E. Hirsch/S. Hunot, R. Levy

Many other rare neurological diseases are being studied by our researchers.



## RECENTLY AT THE ICM

— A European collaborative study, bringing together French, German, Belgian, Dutch and Italian centers, and conducted by Giulia Coarelli (Inserm) in the team of Giovanni Stevanin (Inserm/EPHE) and Alexandra Durr (Sorbonne University/APHP) revealed a mutated gene associated with the onset of later type 7 spastic paraplegia and a clinical picture combining paraplegia and cerebellar ataxia.

— A study by Marc Teichmann (APHP) in the team of Richard Lévy (Sorbonne University/APHP) and Carole Azuar, has allowed to identify an early marker of fronto-temporal degeneration. Indeed, patients with fronto-temporal dementia show a particularly profound impairment of moral emotions in a specific way compared to Alzheimer's patients, for example. They can be defined as "emotional experiences fostering cooperation or group cohesion" including, for example, admiration, shame or pity.

— A study conducted by the group of Isabelle Le Ber (AP-HP) and Olivier Colliot's team (CNRS) identified a new early biomarker in asymptomatic individuals at risk of developing fronto-temporal degeneration (DFT) or amyotrophic lateral sclerosis (ALS) because they carry a specific mutation of the C9orf72 gene. For the first time, researchers were able to measure a reduction in neuritis density, reflecting the amount of axons and dendrites in specific areas of the brain in these at-risk subjects. They also show that this marker is more sensitive than the standard imaging markers previously identified. This breakthrough is very important for this pathology but also for the study of other neurodegenerative diseases in which similar phenomena are found.

— The team of Nathalie Cartier (Inserm) recently demonstrated the efficacy of a gene therapy approach based on the contribution of an AAV vector, the key enzyme in the brain metabolism of cholesterol in a mouse model of a type 3 (SCA3) spinocerebellar ataxia or Machado Joseph's disease, the most frequent spinocerebellar ataxia. This strategy is particularly interesting because it could treat a whole family of diseases with a similar pathological mechanism - the accumulation of toxic proteins containing polyglutamine expansions, such as Huntington's disease. Nathalie Cartier is currently coordinating an E rare SCA-CYP European program aiming at confirming this strategy in several forms of SCAs, more specifically SCA3 and SCA7, to move towards therapeutic application (Phase I/II trial).

## A MAJOR ASSET: REFERENCE CENTERS

The lack of diagnostic tools for a majority of rare diseases requires a particular organisation of research and care. In this context, 109 reference centers have been labelled by the Health, Research and Innovation Ministries. These centers provide care and organize care circuits for people with rare diseases. They are in contact with patient associations and families and play an important role in the development of clinical trials. Indeed, in the case of rare diseases, the small number of patients affected severely limits the feasibility of clinical studies to test the efficacy of a drug. The ICM, located at the center of the Pitié-Salpêtrière Hospital, was designed on a unique ecosystem bringing together researchers, clinicians, technical and paramedical staff and patients in a single location to optimize the interactions between scientific research and medical applications. In the context of rare diseases, this continuity is based on the dual expertise of 7 physicians, both researchers at the ICM and coordinators of reference centers.

- Pr Bruno DUBOIS  
Rare or early dementia Reference Center
- Dr Isabelle LEBER  
Fronto-temporal degeneration (FTD) and progressive supranuclear paralysis (PSP) Reference Center
- Pr Alexandra DURR  
Neurogenetic Reference Center
- Pr Vincent NAVARRO  
Rare Epilepsy Reference Center
- Dr Cyril MIGNOT  
Malformation Reference Center and cerebellum diseases
- Dr Andreas HARTMANN  
Tourette's syndrome Reference Center
- Dr François SALACHAS  
Amyotrophic lateral sclerosis Reference Center (ALS)

## COLLABORATE TO PROVIDE BETTER CARE

Rare diseases affect 3 million people in France and 30 million in Europe. Patients with rare diseases generally pass through a long and arduous process, also known as diagnostic uncertainty, which sometimes lasts 10 or 15 years, before a pathology is linked with their symptoms. Scientific breakthroughs are also time-consuming because it is difficult to find a sufficient number of persons with the same rare disease to make significant progress in research. International networks play an extremely important role in the global identification of patients and help to accelerate research concerning these diseases.

The SPATAX network (spastic paraplegia and ataxia), for example, coordinated by the ICM, aims to study the genetic basis, natural history and treatment of hereditary diseases affecting the cerebellum and/or motor neuron, such as spastic paraplegia and ataxia whose lesions cause movement disorders. This consortium brings together 42 international research or clinical teams working together on common data. The ERN, European Reference Network, is a network for the management of rare diseases across borders. The ICM has actively participated in the establishment of the ERN-RND (Rare Neurological Disease) network, which brings together French sectors and European centers. The objective of this consortium is to share knowledge and thus allow patients to access the latest medical innovations.

This network will make it possible to create common databases in order to make an accurate diagnosis for as many patients as possible and to move towards the identification of new neurological pathologies, since 50% of rare pathologies of the nervous system are currently unidentified. This cooperation will also facilitate the conduct of clinical trials and the recruitment of patients when new therapeutic approaches arise. Clinicians at the ICM are very active in this network. They coordinate several working groups on clinical diagnosis, fronto-temporal dementia, dystonia, paroxysmal disorders and neurodegenerations with iron overload of the brain.

## INTERVIEW



**Nathalie Cartier**

Pediatrician and biologist, INSERM research director and head of the “Gene Therapy” team at the ICM.

### What is the focus of your research?

I have been working in the field of gene therapy for neurodegenerative diseases for many years, particularly in the field of rare diseases, such as leukodystrophies, which are very rare genetic demyelinating diseases, Huntington’s disease, spinocerebellar ataxias or amyotrophic lateral sclerosis. All are very severe diseases for which there are no treatments now.

### What is gene therapy?

Gene therapy consists in providing cells with a drug gene, particularly for diseases in which the gene is missing or deficient because it has mutated or is not sufficiently expressed. We can do this through gene therapy “vectors”, small viruses made totally harmless as a vehicle to bring the drug gene directly into the target cells and then produce the protein-drug permanently. A single administration of the virus carrying the drug gene allows long-term treatment of the disease.

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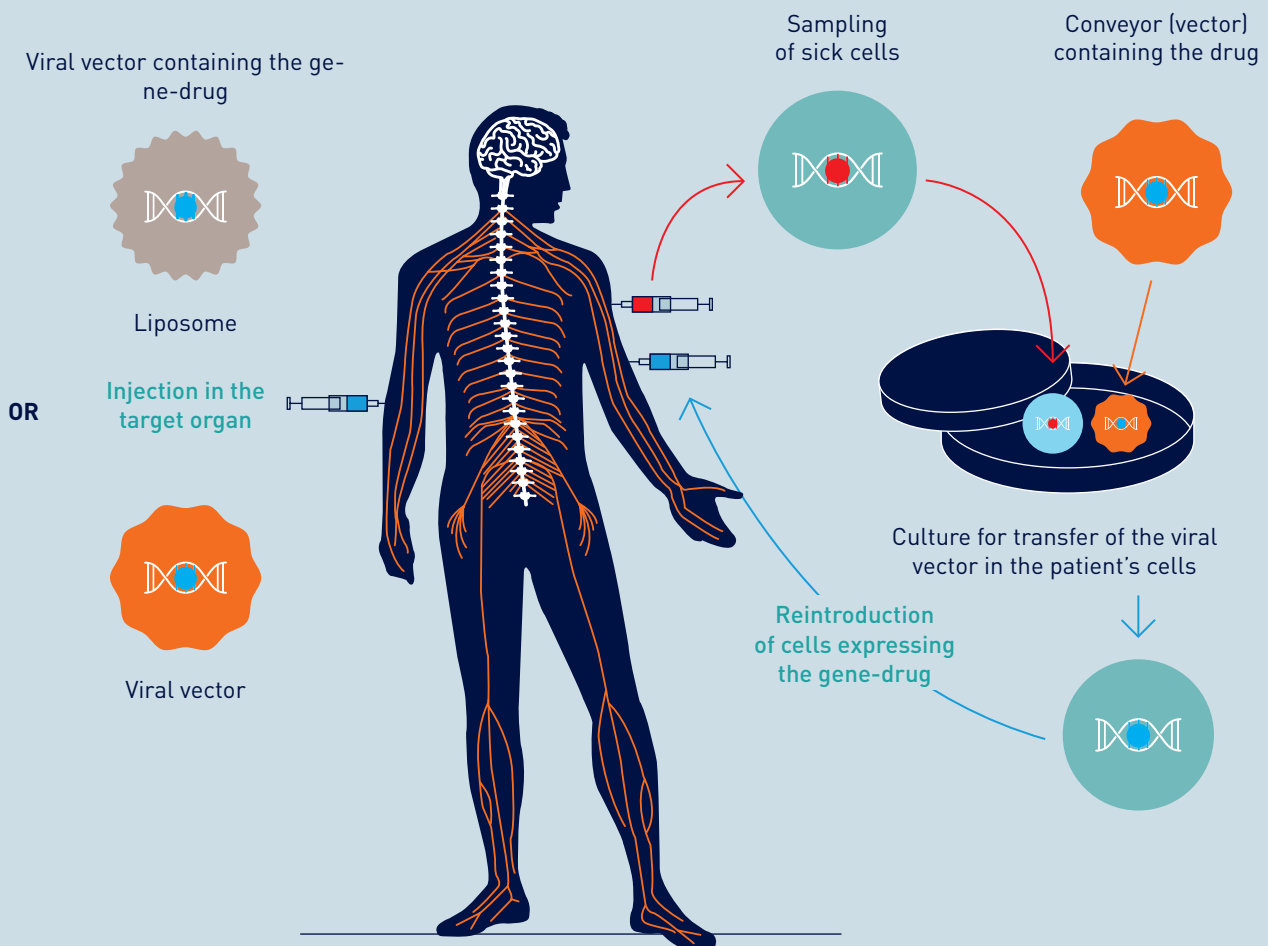


## How is research on gene therapies carried out?

Gene therapy research involves a whole series of stages. The first one is to know the gene to be replaced and the cells in which it is essential. In order to demonstrate the safety and efficacy of gene therapy, it is essential to perform "in vivo" tests. It is obviously inconceivable to carry out these tests on humans; that's why they are carried out on mouse models that reproduce, more or less entirely, human disease and make it possible to prove that the treatment is effective and, above all, safe. This is followed by a series of stages in patients to demonstrate the safety and efficacy of the treatment. All these stages are called translational.

## Why the ICM?

I joined the ICM on January 1, 2019 with a great joy shared with all the members of my team. Being at the ICM allows us to benefit from an absolutely exceptional environment, in terms of scientific and clinical equipment, structures and collaborations. The objective was to bring to the ICM the discipline of gene therapy for diseases of the nervous system, because it is a field where there are great opportunities for diseases that are currently not cured. Therapeutic trials are planned in the next few years for a number of these diseases, here at the ICM.







## A NEW TEAM AT THE ICM

In September, the ICM welcomed a new research team made possible by the creation of the Diane Barrière Chair for Epilepsy, a donation from the Desseigne family. Led by Jaime de Juan-Sanz, this team called “Molecular physiology of synaptic bioenergetics” studies the dysfunctions of mitochondria, the energy plants of our cells, which could be at the origin of epilepsy. As part of the reinforcement of the field of neurophysiology with an application to epilepsy\* and following the recommendations of the Scientific Advisory Board (SAB), the ICM launched an international call for applications in October 2017. The candidate hearings took place on June 13 and 14, 2018 under the aegis of Professor Michael Shelanski, President of the SAB, followed by meetings with researchers of the ICM and the Executive Management.

Jaime de Juan-Sanz, researcher at the Weill Cornell Medical College (USA), was thus selected as new team leader at the ICM. His team is studying mitochondrial dysfunctions that may be the cause of epilepsy. Mitochondria play a major role in the functioning of neurons by controlling fundamental and essential mechanisms for their biology and synaptic transmission, the passing of nerve information from one neuron to another. By using advanced optical technologies, the team will dissect the molecular mechanisms by which synaptic mitochondria control the normal and pathological neuronal function. The objectives of the team are:

- To better understand the neurophysiological role of mitochondria in the synaptic metabolic integrity;
- To consolidate knowledge on the link between mitochondrial dysfunctions and metabolic epilepsy;
- To be used as a basis for future studies to improve the bioenergetics of mitochondria in mitochondrial neurological diseases.



## A DIRECTORY OF UNEXPLORED AREAS OF DNA

Cellular functioning is based on protein synthesis. These are translated from RNA, the intermediate medium of genetic information transcribed from the DNA genome. In our genome, the proportion of sequences that encode proteins is low (2%), yet most of our DNA is transcribed into RNA in the form of “long non-coding RNAs - lncRNAs”, their importance has been stressed for the past ten years as powerful regulators of gene expression. A study\* conducted by Philippe Ravassard and H el ene Cheval at the ICM focused on dopaminergic neurons, the primary target of degeneration in Parkinson’s disease. They discovered 1294 lncRNAs, 80% of which are specific to dopaminergic neurons and are not found in other cell types. In addition, association studies have identified a number of genetic risk factors associated with Parkinson’s disease, the vast majority of which are DNA sequences that do not encode proteins. Characterizing non-coding

directories makes it possible to assess the existence of an increased association between these risk factors and the specific lncRNAs of dopaminergic neurons. If so, this could be a significant lead to explain their very specific vulnerability in Parkinson’s disease. The molecular mechanisms that lead to the dysfunction of dopaminergic neurons in Parkinson’s disease are still poorly understood. Identifying very specific regulators such as lncRNAs and studying their condition in the context of the disease, particularly in genetic forms, will help to better understand which regulatory pathways are altered in these cells and to detail their consequences.

\* Supported by the Edmond J. Safra Foundation



## L'ICM, A PILLAR OF NEUROSCIENCE RESEARCH

Created in 2010 and located in the heart of the Pitié-Salpêtrière Hospital, France's leading neurology hospital, the Brain and Spine Institute represents a strong link between research and care.

As a scientific and medical research institute, it includes, at the end of 2018, a network of 24 teams, more than 700 researchers and clinicians, 10 advanced technological platforms and 1,000 sq for startup incubation.

While one in eight people in Europe suffer from a disease of the nervous system, the ICM's objective is to produce ambitious research by combining scientific creativity and therapeutic purpose. By bringing patients, doctors and researchers together in a single place for a transversal approach of research, its model favors collaboration and accelerates the discovery of medical innovations. Partnerships between public and private sectors at the ICM made it possible to develop decompartmentalized and multidisciplinary research and to quickly translate discoveries into therapeutic solutions for the patient. Since 2017, the ICM has been STATION F's health partner and this location gives it a competitive advantage in the field of connected health.

In a few years, and in a very competitive environment, the ICM has ranked 2nd among 35 international neurology institutes. In addition to major scientific breakthroughs (see below), the ICM has supported or generated nearly thirty start-ups in our business incubator in the field of e-health or biotech, which now make it possible to create diagnostic tools on neurodegenerative diseases, but also digital tools to maintain autonomy (smartphone applications, connected objects, medical devices, serious games). These start-ups have raised more than €130 million and created 300 jobs.

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*"2018 was rich in scientific breakthroughs and renewal for our institute. First of all, our joint research unit, with the success of the teams presented during the evaluation by HCERES, the High Council for the Evaluation of Research and Higher Education; our Executive staff, with the arrival of Corinne Fortin as Secretary General and Bassem Hassan (Inserm) as Scientific Director and Deputy Director of the Unit (2019). It was also enriched by the success of our teams on a national and international scale, with an ever-increasing number of publications and prestigious awards. The ICM is a unique place, open to all. More than ever, we have to decompartmentalize, develop creativity, rely on cooperation, collaboration and share our expertise. A common mission at the service of the general interest brings us all together to go further and faster at the service of patients."*

Pr Alexis Brice, Executive Director of the ICM

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## MISSIONS AND SCIENTIFIC PRIORITIES UP TO THE CHALLENGES OF THE NEXT DECADE

Understanding brain function, preventing and curing neurological and psychiatric diseases. Facing the challenges of research on the brain and its pathologies, the ICM's objectives are clear and reaffirmed:

- Strongly contribute to the prevention and treatment of diseases of the nervous system;
- Participate in technological innovation and its medical applications;

For this purpose the institute has to:

- Attract the best international researchers, particularly in translational neurosciences;
- Develop advanced technological platforms;
- Foster entrepreneurial research;
- Create a unique, attractive, international training center which would be open to society.

To meet these challenges, the ICM supports innovative and creative approaches, led by teams bringing together high-level researchers and renowned clinicians. Thanks to the program of the University Hospital Institute (IHU) associated to a Clinical Investigation Center (CIC) within the ICM, prolific

translational research can be conducted. Cutting-edge technological platforms and the concentration of multidisciplinary expertise in a single location enable the ICM to gain optimal understanding of the nervous system. The international influence of the institute gives its researchers the opportunity to be actors in many international research consortia, sources of fruitful collaborations. Finally, the presence of a start-up incubator at the heart of the ICM ecosystem (iPEPS) makes it possible, on the one hand, to inspire an entrepreneurial spirit and, on the other hand, to accelerate the application of discoveries to the benefit of patients.

One of the ICM's major strengths in addressing the challenges associated with the understanding of diseases of the nervous system is to facilitate cross-sectional and multidisciplinary research. 28 teams, 4 major fields from fundamental to applied research, collaborative projects, clinical research networks, technological platforms always on the cutting edge of innovation.

### GOVERNANCE OF THE ICM

The ICM adopts a governance system based on a strong partnership between the public and private sectors, as evidenced by the representativeness of the members of its Board of Directors and its governing bodies.

As a joint research unit, the ICM brings together 4 public institutions: INSERM, CNRS and Sorbonne University, which are "guardians of the Joint Research Unit (UMR)" and AP-HP, the Institute's privileged partner. They finance part of the Institute's overall budget (34%) and are the employers of the Institute's public staff. These public partners also support us in the Institute's scientific projects, through the recruitment of staff or in financing specific projects.

The governance of the Institute, through its Board of Directors, ensures that scientific objectives and resources are in adequacy. The board of directors implements controls to ensure effective management, regularly evaluates the work and performance of teams, thus ensuring that excellence is maintained. In its annual report, the ICM communicates on its mission and results, with a view to ensuring full transparency towards its partners and donors.

The 2018 annual report can be downloaded from the website:  
[icm-institute.org/fr/publications-officielles/](http://icm-institute.org/fr/publications-officielles/)

# THE ICM'S KEY E

## OUR ORGANIZATION

- On January 1, 2018, the IHU-A-ICM Scientific Cooperation Foundation merged within the ICM Foundation. The intervention budget, achievements, teams, successes and hopes are now brought together to strengthen coherence and amplify the Institute's scientific and medical project;
- Creation of an ethics and moral code committee;
- French Excellence Award for the ICM; each year, this award honors different sectors of activity in which France stands out. These sectors are represented by companies or institutions themselves represented by their managers or by exceptional individuals, whose personal and professional success goes far beyond our borders;
- Evaluation of the platforms by a committee of international experts;
- The ICM has developed its practices to bring them into compliance with the General Data Protection Regulation (GDPR);
- Introduction of a selective sorting solution.

## RESEARCH

- Very positive report of the evaluation of the ICM Joint Research Unit (JRU) by HCERES. Recreation of the Joint Research Unit (UMR) associating INSERM, CNRS and Sorbonne University in partnership with APHP effective on January 1, 2019;
- Recruitment of a new team, Jaime de Juan-Sanz's, researcher at Weill Cornell Medical College (USA) in the context of strengthening the field of neurophysiology with an application dedicated to epilepsy;
- More than 600 scientific publications and 83 prestigious scholarships awarded in 2018;
- Further development of the neuroinformatics center to provide access to important and high quality data to monitor patient trajectories using advanced artificial intelligence and machine learning.

Find out about the ICM's major scientific advances on the website [www.icm-institute.org](http://www.icm-institute.org)

## PRESTIGIOUS AWARDS FOR OUR RESEARCHERS

- Fabrizio de Vico Fallani (Inria): Junior Scientific Award de la Complex Systems Society;
- Michel Thiebaut de Schotten (CNRS): Bronze medal of the CNRS;
- Alexandra Durr (Sorbonne University/APHP): Lamonica Prize in Neurology of the Academy of Sciences.

## CLINICAL RESEARCH & CARE

- Creation of the national clinical research network for multiple sclerosis, FCRIN-4-MS, coordinated by Céline Louapre (ICM, Paris) and Gilles Edan (Rennes);
- Support of 13 iCRIN (the ICM's clinical research infrastructure network) to develop interactions and sharing of expertise between the actors of the nervous system disease cluster and the ICM's research teams.

## THE ICM AND ITS INTERNATIONAL NETWORK

- 5 significant grants obtained by the ICM and DZNE (network of excellence research centers dedicated to neurodegenerative diseases, Germany);
- Hosting more than 40 doctoral and post-doctoral students from the University College London during a joint workshop with the ICM;
- International collaborations with more than 1,000 institutions.

## EVENTS IN 2018

TRAINING AND KNOWLEDGE  
TRANSFER

- 4<sup>th</sup> edition of “The Brain to Market” summer school on Parkinson’s disease, which takes a new dimension by being an integral part of the innovation chain in close collaboration with the Living Lab and the activities carried out by the iPEPS;
- Official opening in 2018 of M2 registrations for the iMIND Master’s degree in neurodegenerative diseases, conceived in collaboration with Sorbonne University and renowned foreign universities (University of Vienna, TUM, KU Leuven);
- Creation of the Open Brain School: the ICM’s training center aiming at developing all existing programs and creating new ones, particularly to train the general public in neuroscience.

INDUSTRIAL PARTNERSHIPS  
AND RESEARCH APPLICATIONS

- Launching the “Sleeping beauties” project to test and develop molecules of therapeutic interest in the field of nervous system diseases;
- Obtaining the “French Tech Visa” label, which facilitates the mobility of foreign start-ups within the iPEPS;
- Creation of NEUROTRIALS, an organization for so-called “early” clinical studies in partnership with healthcare manufacturers;
- Participatory innovation program for daily assistance of people with Parkinson’s disease: 150 participants and 5 ecosystem partners around the development of 5 technical aids;
- 4 digital health startups supported in an acceleration program in partnership with Pfizer and 3 startups from the social and solidarity economy on the theme of mental health and well-being in the Open Brain Initiative program.

## STRONG COMMUNICATION ACTIONS

- Publication of the Great Brain Atlas at Glénat, in collaboration with the ICM and Le Monde newspaper;
- Confirmed success of the Open Brain Bar, in partnership with Sciences & Avenir and Le Figaro;
- A new promotional film “Only our emotions should make us tremble”, created and offered by Publicis to the ICM, to raise public awareness on Parkinson’s disease;
- In 2018, the ICM opened its doors again during the Week of the Brain to offer to all privileged opportunities to interact with the institute’s researchers, clinicians, engineers and technicians.

## LOYAL AND NEW SUPPORT

- 2<sup>nd</sup> edition of the ICM gala at the Pavillon Cambon in Paris to support the Institute’s researchers;
- Gala of the Sclérose en Panne association, on the initiative of its president, Julien Taieb, to support the ICM’s research work on multiple sclerosis;
- The MSDAvenir Fund and the Abeona and Humanis foundations have joined the ranks of the Institute’s patrons by supporting each of the specific research programs;
- Development of legacies and life insurance policies to support research at the ICM, which become a major pillar of the institute’s resources.



## FINANCIAL SITUATION

### The ICM's budget is currently based on 5 levers:

1. Fundraising: patronage, donations and legacies;
2. Grants from public organizations and private foundations (national, European, and international funding), including the IHU funding (ANR);
3. Revenues from industrial collaborations, particularly with start-ups;
4. Technological platform services;
5. Miscellaneous revenues (rental income, financial products, etc.).

### These resources are essential to enable in particular:

- Support for innovative research projects;
- Recruitment of researchers;
- Investments in equipment;
- Incubator coordination;
- Functioning of the ICM;
- Development of collection and communication.

## RESOURCES OF 2018

The funding of research projects is characterized by a plurality of funding sources with a long-term perspective in order to produce major knowledge and advances in neuroscience. The 2018 resources amount to €54.6 million, including €43.6 million in revenue for the financial year and €10.7 million in carry-forward of resources allocated and not used in previous years. Revenues for the fiscal year mainly correspond to income from collections (€13.9 million or 32%), from the general public (€11.3 million or 26%) and from private companies and foundations (€2.6 million or 6%). They also include:

- Revenues from technology platform activities (€4.6 million) and research collaborations with industrial partners (€3.5 million);
- Public and private subsidies (€9.6 million);
- Financing of the "IHU program" (€8 million).



## EMPLOYMENT IN 2018

The overall total for employment in 2018 amounts to €54.6 million: €43.1 million used in 2018 and €11.5 million to be realised later on from allocated resources. For employment in 2018, the amount devoted to social missions is worth €36.7 million, representing 85% of total jobs for the fiscal year. The social missions of the ICM include:

- Research programs;
- Technology platforms;
- Scientific animation, implementation of international alliances and incubation of innovative companies.



Research project Fundings are mainly dedicated to diseases of the nervous system and spinal cord injuries. Technology platforms (neuroimaging, vectorology, sequencing, genotyping, cell culture, histology and bioinformatics) support these projects. Collection and communication research costs correspond to expenses incurred to collect funds from individuals (donations and legacies) and private companies and foundations (corresponding to patronage and sponsorship actions), as well as communication actions. They account for 10% of jobs

Operating expenses correspond to the expenses of support teams (general secretariat, finance, human resources, legal, IT and logistics), which represent 5% of total employment for the fiscal year. Commitments to be made from allocated resources (€11.5 million) correspond to multiannual project funding from private or public funds (ANR, donations from companies or foundations, etc.) received during the year, which will subsequently be used for specific multiannual research programmes.

## ALLOCATION OF RESOURCES COLLECTED FROM THE GENERAL PUBLIC

Resources raised from the general public used in 2018 amounted to €11.3 million. To summarize, on the €100 of resources raised from the general public, €66 were used to finance social missions and investments, €26 were used to cover fundraising and communication costs and €8 were used to cover the ICM's operating costs.

## SIMPLIFIED BALANCE SHEET

ASSETS (K€)	On 31-12-2017	On 31-12-2018
Net fixed assets	58,873	56,111
Realisable and available assets	72,027	65,131
<b>TOTAL</b>	<b>130,900</b>	<b>121,242</b>
LIABILITIES (K€)	On 31-12-2017	On 31-12-2018
Associative funds	63,392	56,549
Net operating result	1,113	- 238
Dedicated funds	12,255	12,952
Debts	54,140	51,979
<b>TOTAL</b>	<b>130,900</b>	<b>121,242</b>

## COMMENTS

The total amount of investments made by the ICM since its creation amounts to €30.3 million, mainly dedicated to technological platforms supporting research. Investments for the fiscal year amount to €3.5 million.

### Major investments

- Scientific investments: acquisition of a confocal microscope (€400k) and scientific equipment and material (€777k);
- Acquisition of scientific IT storage capacity and computing cluster (€1,500k).

Net fixed assets amount to €56.1 million. On December 31, 2018, the cash flow amounted to €42.5 million. The ICM's associative funds amount to €56.1 million. They include equity for €27.2 million, supplemented by investment grants worth €28.9 million. The ICM's non-expendable endowment is €1.2 million. At the end of the fiscal year, dedicated funds (funds still to be committed to multiannual programs) amounted to €13 million.

### Reserve policy

When it was created in 2006, the ICM Foundation received an endowment of €11.7 million, including €1.2 million in non-expendable funding. Thanks to rigorous budgetary management, the ICM Foundation has been balancing its expenses and revenues for the past 4 years, thus avoiding drawing on its reserves. In addition, the investment policy of the Board of Directors' members is extremely cautious. The ICM's cash flow is invested in marketable securities (capitalisation contract subscribed with leading banking institutions, guaranteed in capital and 100% in euro funds).

## VOLUNTARY CONTRIBUTIONS IN KIND

### Volunteering

The ICM benefited from volunteering hours during the fiscal year, in particular for communication activities. The volume is estimated at 1.2 FTE, i.e. on the basis of an hourly minimum, an amount of €32k.

### Sponsorship in kind

The ICM Foundation has benefited from sponsorship in kind as part of its communication activities and appeal to the public generosity, namely:

- Media spaces with Air France, Reedexpo/Fiac, ZenithOptimedia, Richard Mille, TF1, Klesia.
- Works of art, free of charge products or services: Fédération Internationale Automobile, David de Rothschild, François Pinault, Maurice Lévy, Laurent Dassault, Montres F.P. Journe, Air France, Publicis Groupe, Richard Mille, Orrick Rambaud Martel, Hermès international, Louis Cane, Noël Dolla, Claude Viallat, Didier Chamizo, André-Pierre Arnal, Vanessa Zitzewitz, Financière LOV, Domaines Barons de Rothschild (Lafite), Champagne Laurent-Perrier, Galerie Rive Gauche, Noirmontarproduction, IDEC, ANACOFI.

Particularly committed to maintaining its level of excellence, the ICM has set up internal and external control procedures to ensure the rigour and effectiveness of its management: member of the Trusted Gift Charter Committee and call for an independent auditor.

### Don en confiance



On November 3, 2010, the ICM received the approval of the Comité de la Charte, which was renewed on October 6, 2016. For more than 20 years, this committee

has been responsible for the professional regulation of the appeal to public generosity. Its action is based on 3 commitments: accredited bodies have to respect ethical rules, they have to comply with collective discipline towards donors, and accept the continuous monitoring of the commitments undertaken.

All ICM accounts are available on the website [icm-institute.org/fr/publications-officielles/](http://icm-institute.org/fr/publications-officielles/)

## YOUR MAGAZINE IS CHANGING: WE NEED YOU!

In 2020, the ICM will celebrate its 10th anniversary. 10 years of progress, hope and sharing, made possible thanks to your loyal support and that of thousands of donors. Because we work for you and with you, we are committed to meeting your expectations and sharing the great adventure of the conquest of the brain with you.

This is how the ICM teams strive to design the Donors' magazine every quarter: report to YOU on the progress made because YOU give us the means to move forward. Thank you so much! Every year, you are more and more to receive the Donors' magazine and we hope that the information you find live up to your expectations, both in terms of content and format.

At the ICM, we believe that science is intended to come out of laboratories and be spread to as many people as possible in order to benefit to society as a whole. To improve your magazine, we need your opinion!

**Help us design its new model** by answering a few questions. Your answers will allow us to measure your satisfaction and identify potential sources of improvement.

**Before October 15, visit**  
[www.icm-institute.org/journaldesdonateurs](http://www.icm-institute.org/journaldesdonateurs)  
**to participate. We are waiting for you, thanks!**



YOUR PERSONAL CONTACT:

Lucie Moutier  
01 57 27 40 32 – [cercle@icm-institute.org](mailto:cercle@icm-institute.org)



## WITH YOU



**Without children, I would like to leave my heritage to my nephew. My notary tells me that without changing anything for him, it is possible to bequeath to an association as well. I immediately thought of the ICM. What is this solution?**

This is a **universal legacy with charge**. To leave a legacy to a **person who is not a direct heir** (nephew, friend, etc.), all you have to do is make a universal bequest to the Brain and Spine Institute (ICM) by asking them to leave a specific bequest (net of costs and fees) to this person. The ICM will pay the part of the inheritance rights and notary fees in the person's place. The rest of your inheritance will go to the ICM\*.

### Example for a bequest of €100,000:

	TAXES	FOR THE PERSON	FOR THE ICM
If you leave directly to the person	€60,000	€40,000	€0
If you leave to the ICM with the responsibility of issuing a specific bequest to the person	€24,000	€40,000	<b>€36,000</b>

\* Example given according to French law.

Would you like to receive our brochure or discuss this subject, please contact:

Carole Clément, on +33 (0)1 57 27 41 41  
or [carole.clement@icm-institute.org](mailto:carole.clement@icm-institute.org)

As a Foundation Recognized for its public utility, the ICM is entitled to receive legacies, donations and life insurance while being totally exempt from the payment of inheritance rights.

## SUPPORT FORM

Thank you for sending us the completed form today with your donation to the address:  
ICM – Hôpital Pitié-Salpêtrière 47 boulevard de l'Hôpital 75013 Paris FRANCE



**Yes, I support the ICM in defeating diseases of the nervous system**

I am making a donation of: ..... €

Check payable to ICM

You can also make a donation online at:

[www.icm-institute.org](http://www.icm-institute.org)



I wish to receive complimentary information on bequests and donations. (Free of charge and obligations)



Your donation to the ICM is deductible up to 66% of income tax (limited to 20% of your taxable income), or up to 75% for the Real Estate Wealth Tax (up to a limit of € 50.000 deducted).

*Your contact details*

Mrs  Mr  Mr & Mrs

First name: .....

Surname: .....

Address: .....

.....

Zip Code: [ ][ ][ ][ ][ ]

City: .....

Email: .....

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Phone: .....

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The information on this form will be recorded in a digital file and placed under the responsibility of ICM, and used to send you a tax receipt, explain how your donation is used, invite you to conferences and events, contact you for further fundraising and to get to know you better, to ask for your opinion and improve our actions. Data is intended for use by ICM and can be transferred to third parties mandated by ICM to assist with fundraising campaigns and surveys. You have the right to access, rectify, remove, oppose, or limit the transfer of personal information that

concerns you by contacting the Bureau of Circle of Friends of ICM: ICM Hôpital Pitié-Salpêtrière - 47, boulevard de l'Hôpital - CS 21414 - 75646 Paris Cedex 13. You may also file a claim with a supervisory authority. Protection of your personal data and respecting your wishes is of the utmost importance for ICM and ICM will not transfer or exchange data pertaining to major benefactors.