

INSTITUT DU CERVEAU  
ET DE LA MOELLE ÉPINIÈRE, ICM  
BRAIN & SPINE INSTITUTE, PARIS

ANNUAL REPORT 2017

SEARCH, FIND, CURE, FOR YOU & WITH YOU.



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## ICM'S PLACE IN THE FUTURE OF MEDICINE

PROF GERARD SAILLANT, PRESIDENT OF ICM  
& PROF ALEXIS BRICE, C.E.O. OF ICM

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## ICM, A CORNERSTONE OF NEUROSCIENCE RESEARCH

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2017: PROGRESS, HOPES AND BREAKTHROUGHS

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## ICM'S PLACE IN THE FUTURE OF MEDICINE

PROF GERARD SAILLANT,  
PRESIDENT OF ICM

In 2017, we took a leap into a new era: the era of artificial intelligence, big data, innovative surgery, and tailored medicine. ICM found its place in the future of medicine. We have made the societal challenges raised by neuroscience a priority.

1 - Acquire understanding of 'normal' brain development and function could help us improve learning techniques (reading, language) and increase what we know about behaviour

2 - Improve our understanding of the underlying mechanisms of nervous system diseases and compensation mechanisms will help lower the number of affected individuals, a number currently on the rise.

ICM is ready to meet these 21st century challenges. Interactions

between researchers and clinicians are encouraged thanks to close collaboration with the Nervous System Diseases Hub with 100,000 patients on a yearly basis at Pitié-Salpêtrière Hospital. Thanks to the diversity of our activities and our many fields of expertise, we are set to meet the challenge of understanding the nervous system. A multidisciplinary approach, along with risk-taking and technological innovation developed at ICM, are assets for scientific and medical research.

Innovative approaches implemented by ICM researchers make it possible to design new ways of treating and curing diseases. Some of these include early diagnosis and prediction of disease progress to determine the

2017 CONFIRMED THAT OUR INSTITUTE IS HIGHLY CAPABLE OF PRODUCING KNOWLEDGE AND ACHIEVING MAJOR NEUROSCIENCE BREAKTHROUGHS.//

PROF ALEXIS BRICE,  
C.E.O. OF ICM

right treatment for the right patient at the right time, enabling treatments to cross into the brain to increase efficacy, building neurons from patient skin cells to understand disease mechanisms and test new treatments, and more.

2017 saw great scientific progress that gives our actions new meaning, confirms the expertise of our community and relevance of our organisation.

Our results come from cooperation, breaking down barriers between teams, and encouraging creativity.

Our financial model is balanced and our budget is on the rise; we boast 600 publications including 115 with an impact factor above 7, placing ICM second among 35 international

neurology institutes; 7 patents were filed in 2017, and prototypes were designed in our cLLAPS Living Lab; our researchers received numerous distinctions and awards; we welcomed two new teams and new startups; and 80 clinical trials took place in 2017. All of this represents tangible progress. 2017 confirmed that our Institute is highly capable of producing knowledge and achieving major neuroscience breakthroughs. We send warm thanks to those who, every single day, help us build our Institute to even greater heights: the 700 women and men who make up the Institute, our partners, our donors, and our volunteers for their immense and valued support.

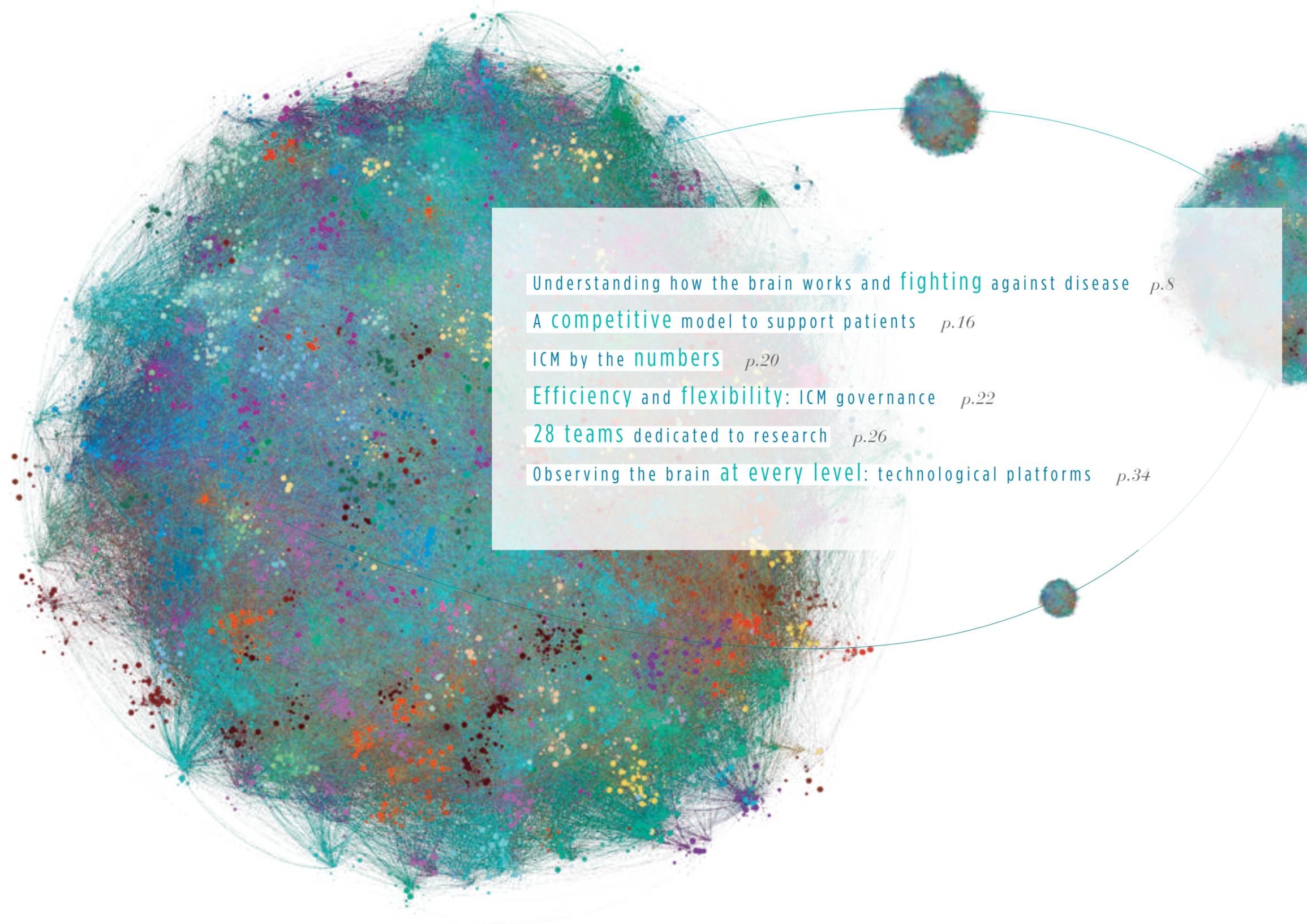
<sup>1</sup> Inserm/Thomson Reuters

# ICM, A CORNERSTONE OF NEUROSCIENCE RESEARCH

1 IN EVERY 8 INDIVIDUALS ARE AFFECTED BY NERVOUS SYSTEM DISEASE OR TRAUMA. WITH LIFE EXPECTANCY ON THE RISE, THE COMPLEXITY OF THE NERVOUS SYSTEM, AND COMPLICATED IDENTIFICATION OF NEW TREATMENTS, DEVELOPING INNOVATIVE STRATEGIES HAS BECOME ESSENTIAL.

IN THE 21<sup>ST</sup> CENTURY, WHERE TECHNOLOGICAL ADVANCES SURPASS HUMAN NATURE, HOW CAN WE ACCEPT THAT DISEASES ARE STILL ON THE RISE?

FACED WITH THIS MAJOR PUBLIC HEALTH CHALLENGE, CREATING AN INNOVATIVE, MULTIDISCIPLINARY, AND UNIQUE ENTREPRENEURIAL MODEL IS MUCH MORE THAN A NECESSITY: IT IS AN OBLIGATION.



Understanding how the brain works and fighting against disease *p.8*

A competitive model to support patients *p.16*

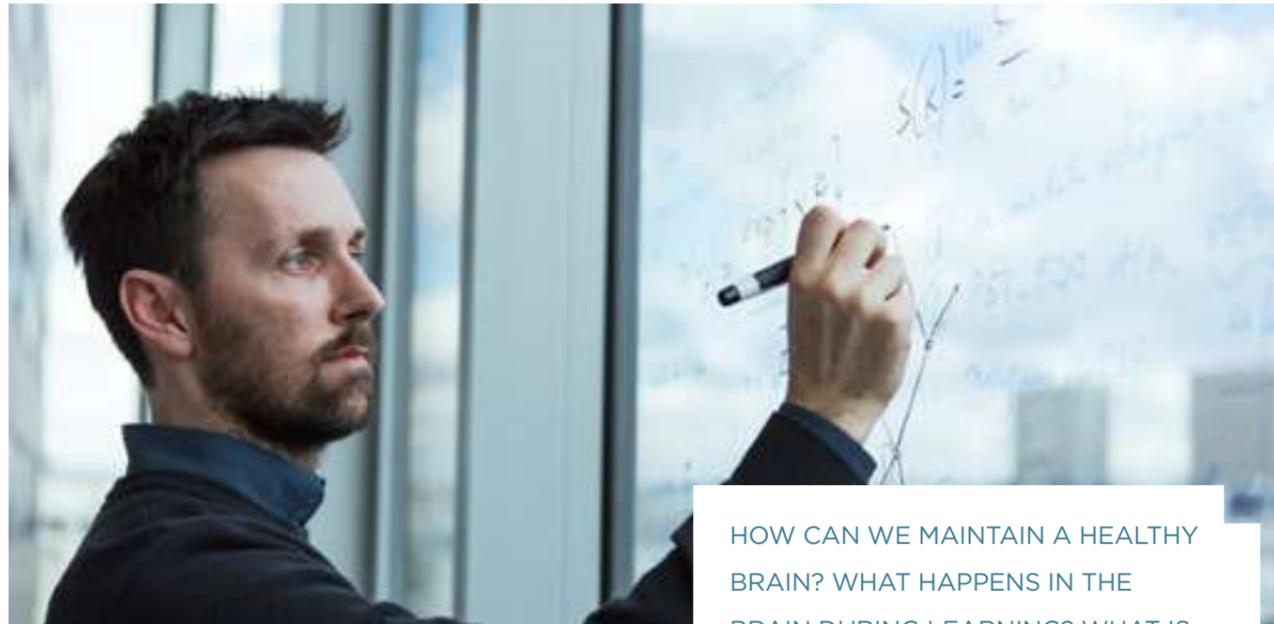
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Efficiency and flexibility: ICM governance *p.22*

28 teams dedicated to research *p.26*

Observing the brain at every level: technological platforms *p.34*

# UNDERSTANDING HOW THE BRAIN WORKS AND FIGHTING AGAINST DISEASE



HOW CAN WE MAINTAIN A HEALTHY BRAIN? WHAT HAPPENS IN THE BRAIN DURING LEARNING? WHAT IS CONSCIOUSNESS? HOW DOES THE BRAIN DEVELOP? HOW CAN WE HELP THOSE AROUND THE WORLD AFFECTED BY NEUROLOGICAL AND NEURODEGENERATIVE DISEASES FOR WHICH CURRENT TREATMENT ONLY HAS LIMITED EFFECTS? THESE ARE SOME OF THE QUESTIONS THAT MOTIVATE ICM TEAMS ON A DAILY BASIS.



## UNDERSTANDING

Although we are now familiar with the brain's anatomy and most of its components, how it functions as well as the interactions established between cells, essential to our behaviours and actions, remain in question.

Understanding how the central nervous system functions in individuals with no sign of neurological disease is necessary in identifying ineffective mechanisms that lead to altered motor, mental, or behavioural function specific to

neurological disease (gait disorders, tremors, memory loss, depression, autism...). Life expectancy is on the rise, making progress in neuroscience a major societal challenge for better ageing, now and in the future.

## CHALLENGES

### 1 UNDERSTANDING HOW BRAIN DEVELOPMENT INFLUENCES OUR BEHAVIOUR AS ADULTS

Several types of cells coexist in our brain, the most famous of which are neurons. During brain development, these cells interact based on a very specific code. Neurons, for example, establish very precise communication network amongst themselves to allow information to flow. Each network plays a very specific role.

#### ICM GOALS

- Identify genes, proteins, and molecular and cellular mechanisms involved in brain development
- Understand how neuron development and the connection building process are controlled
- Assess influence of brain development on behaviour

#### ICM STRENGTHS

- 12 researchers and clinicians with an expertise in brain development
- 5 cutting-edge technical platforms dedicated to molecular and cellular studies

#### ICM ACHIEVEMENTS

- Identification of a neuron network control anomaly in Fragile X Syndrome
- Identification of a gene responsible for agenesis of the corpus callosum, a brain malformation

## 2 UNDERSTANDING THE MECHANISMS BEHIND RESTRUCTURING AND NEUROPLASTICITY

Neural networks built during development can later be rendered inactive, or replaced by others according to our needs. Such is the case when learning to read or when learning a language, or when an area of the brain is affected by disease or trauma. These modifications in communications networks between neurons are known as neuroplasticity.

### ICM GOALS

- Identify and locate neural networks
- Understand how neural connexions evolve with time

### ICM STRENGTHS

- 26 researchers and clinicians, experts in neuroplasticity and network dynamics
- 2 cutting-edge technical platforms dedicated to brain imaging and recording of electrical and magnetic signals
- Multidisciplinary experts, researchers, doctors, mathematicians, statisticians, and MRI analysis specialists

### ICM ACHIEVEMENTS

- Identification of a brain area dedicated to recognising words in the visual cortex



## 3 IDENTIFYING CEREBRAL, INTELLECTUAL AND EMOTIONAL MECHANISMS THAT DETERMINE OUR ACTIONS AND BEHAVIOURS

Our “brain identity” can vary from normal to pathological states and influences our behaviours, including our motivation, our ability to make decisions, and our perception of social context.

### ICM GOALS

- Understand the mechanisms that control our behaviour and our actions
- Identify areas of the brain and neural networks as well as external stimuli that influence them

### ICM STRENGTHS

- 23 researchers and clinicians with expertise in social, cognitive and behavioural neuroscience
- 4 cutting-edge technical platforms dedicated to behavioural studies and brain imaging
- Multidisciplinary experts, researchers, neurologists, psychiatrists, mathematicians, and statisticians
- A world-class neurology and psychiatry hospital environment: Pitié-Salpêtrière Hospital in Paris

### ICM ACHIEVEMENTS

- Identification of an area of the brain involved in decision-making
- Implementation of an e-health instrument to assess variations in motivation and cognition capabilities in the general population

## 4 UNDERSTANDING MAJOR CEREBRAL MECHANISMS INCLUDING REASONING, CREATIVITY AND CONSCIOUSNESS

What are the various connections between neurons, the networks that link the different areas of the brain responsible for so-called “superior” cognitive function including reasoning and creativity?  
How are we able to assess consciousness in an individual that cannot communicate?

### ICM GOALS

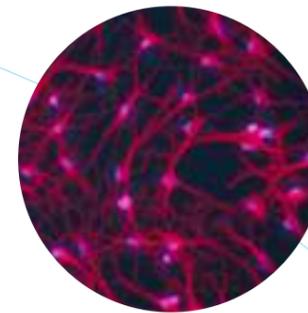
- Identify areas of the brain involved in reasoning and creativity
- Define how these areas developed with time
- Define and assess state of consciousness

### ICM STRENGTHS

- 15 researchers and clinicians with expertise in neurology, psychiatry, brain imaging, electrophysiology, and modelling
- 2 cutting-edge technical platforms dedicated to brain imaging analysis
- Multidisciplinary experts, researchers, neurologists, psychiatrists, mathematicians, and statisticians
- A world-class neurology and psychiatry hospital environment: Pitié-Salpêtrière Hospital in Paris

### ICM ACHIEVEMENTS

- Identification of two areas of the brain in the fronto-temporal cortex involved in verbal and artistic creativity
- Highlighted a correlation between strong neuroplasticity of certain areas of the brain and their late development in the evolution of species. These areas are at the heart of superior cognitive functions such as specific human reasoning
- Identification of new objective measurement instruments to assess state of consciousness in non-communicating patients after a stroke or trauma



## 5 IDENTIFYING MECHANISMS BEHIND LOCOMOTION IN THE BRAIN AND SPINAL CORD

Cerebrospinal fluid (CSF) runs along the brain and spinal cord. Beyond its protective virtues, the fluid seems to play an important part in certain complex mechanisms including locomotion and sleep as well as in the onset of certain anomalies, such as scoliosis. Specific neurons, CSF-cNs, create a link between the CSF and spinal cord.

### ICM GOALS

- Specify the role of CSG-cNs neurons in locomotion and postural anomalies
- Identify necessary and sufficient groups of neurons to generate movement

### ICM STRENGTHS

- 9 researchers and clinicians with expertise in genetics, optogenetics, spinal cord physiology and medullar trauma
- 2 cutting-edge technical platforms dedicated to optogenetics and microscopy

### ICM ACHIEVEMENTS

- Characterisation of specific neurons that control implementation of micro-networks in the spinal cord during locomotion



# FIGHTING

Nearly 1 billion individuals around the world are currently affected by a neurological disease, with a number on the rise. For 80% of these individuals, treatments implemented are unadapted

or insufficient. In France alone, 900,000 patients are affected by Alzheimer's Disease, over 150,000 have Parkinson's Disease, and nearly 85,000 individuals are affected by multiple sclerosis. Tailored and

personalised treatment for these pathologies is a challenge of the highest priority at ICM, to improve quality of life for patients, carers, and to lower the societal and economic impact of these diseases.

## CHALLENGES

### 1 PREDICT DISEASE ONSET BEFORE SYMPTOMS APPEAR

Neurological diseases are often diagnosed later due to late appearance of symptoms. In the case of Parkinson's and Alzheimer's Disease, as well as Multiple Sclerosis, certain brain lesions can be detected on an MRI scan although the patient does not display any clinical symptom. This paradox is explained by the fact that a lesion threshold or specific lesion location are necessary for symptom development.

### ICM GOALS

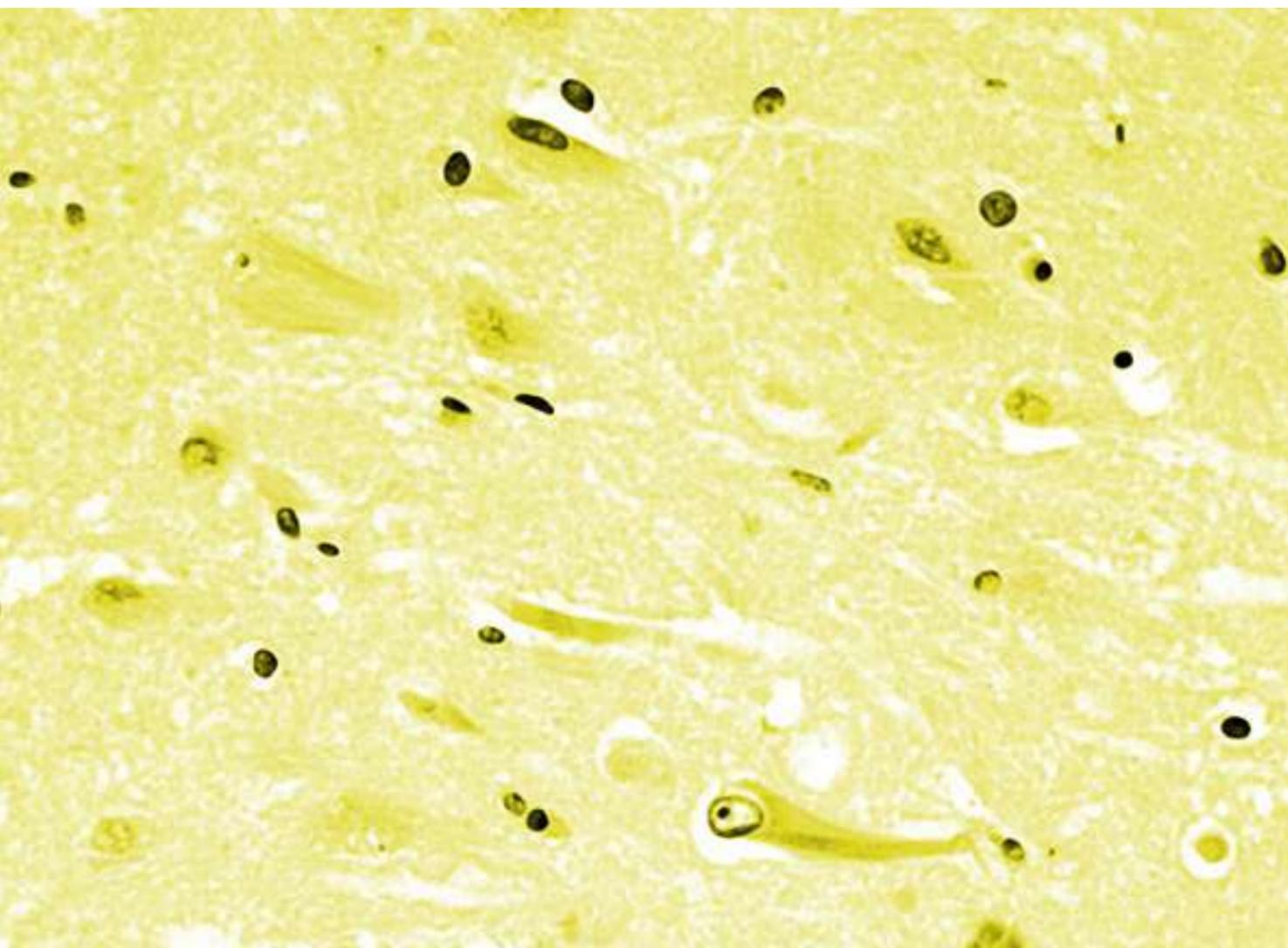
- Identify very early disease markers in at-risk individuals in a patient's close family, such as siblings and children
- Select markers measured using non-invasive techniques

### ICM STRENGTHS

- 300 researchers and clinicians with an expertise in neuroscience
- 5 cutting-edge technical platforms dedicated to molecular and cellular studies, MRI analysis, and neuropsychological assessment
- 1 Clinical Investigation Center - CIC at the heart of ICM
- A world-class neurology and psychiatry hospital environment: Pitié-Salpêtrière Hospital in Paris

### ICM ACHIEVEMENTS

- Identification of new genes related to Alzheimer's Disease risk
- Development of a diagnostic blood test for De Vivo Disease



## 2 TREAT DISEASES AS SOON AS EARLIEST SIGNS APPEAR

The later treatment is administered, the lower the chance of efficacy. Indeed, in the case of certain neurological diseases such as Multiple Sclerosis, chronic lesions develop with irreversible loss of neurons. Treating patients before this irreversible brain damage takes place is the main challenge of future therapies.

### ICM GOALS

- Confirm early diagnostic markers
- Identify risks and benefits of treating patients before symptom onset



### ICM STRENGTHS

- 300 researchers and clinicians with an expertise in neuroscience
- Close daily collaboration between clinicians and scientists
- Multidisciplinary experts, researchers, doctors, mathematicians, statisticians, and MRI image analysis specialists
- 1 Clinical Investigation Center - CIC at the heart of ICM to assess preclinical signs on patient cohorts
- 1 Research and Technology Office with a business incubator

### ICM ACHIEVEMENTS

- Highlighted early alteration of cognitive capabilities in Parkinson's patients with development of an instrument for early diagnosis



## 3 DEVELOP TREATMENT THAT CAN REACH THE BRAIN

The brain is the most isolated and protected organ of our body. It is surrounded by the blood-brain barrier, which filters potentially dangerous agents including viruses, bacteria, as well as certain molecules in the body. Unfortunately, this barrier remains an obstacle for drugs that target the brain.

### ICM GOALS

- Ensure that a specific therapy for a relevant cellular target reaches it thanks to chemical and proteinaceous engineering

### ICM STRENGTHS

- 300 researchers and clinicians with an expertise in neuroscience
- 1 Research and Technology Office with a business incubator
- A world-class neurology and psychiatry hospital environment: Pitié-Salpêtrière Hospital in Paris

### ICM ACHIEVEMENTS

- Ultrasound to increase diffusion of treatment in brain tumours

## 4 DEVELOP PERSONALISED MEDICINE

Some neurological diseases evolve differently depending on patients: in Multiple Sclerosis, for example, progress towards disability can take several years or decades. Additionally, response to treatment differs from one patient to another even when they share a same form of the disease. This implies that treatment must be adapted to each evolution and each type of disease as a form of tailored, personalised medicine. The challenge presented by "the future of medicine" resides in classifying patients using reliable criteria to adapt treatment.

### ICM GOALS

- Identify probable disease evolution markers from onset
- Identify patients that reply positively or negatively to given therapy (pharmacogenetics)

### ICM STRENGTHS

- 100 researchers and clinicians with expertise in genetics, neurology and clinical assessment
- 1 Clinical Investigation Center - CIC at the heart of ICM to assess preclinical signs on patient cohorts
- A world-class neurology and psychiatry hospital environment: Pitié-Salpêtrière Hospital in Paris

### ICM ACHIEVEMENTS

- Implementation of a study to assess probable evolution of multiple sclerosis by combining genetic, clinical, neuropsychological and cognitive markers

# A COMPETITIVE MODEL TO SUPPORT PATIENTS



THANKS TO CLOSE COLLABORATION BETWEEN 28 RESEARCH TEAMS, ENGINEERS, CUTTING-EDGE TECHNOLOGICAL PLATFORMS, THE CLINICAL INVESTIGATION CENTER - CIC, THE NERVOUS SYSTEM DISEASES HUB, AND THE ENTREPRENEURIAL ECOSYSTEM CREATED BY ITS BUSINESS INCUBATOR, ICM IS WORKING DAILY TO DEVELOP THE FUTURE OF MEDICINE.



## OUR VALUES

**SCIENTIFIC EXCELLENCE**  
■ Attract the best world-class scientists

**SUPPORTING PATIENTS**  
■ Gather patients, doctors, researchers and entrepreneurs in the same place

**FLEXIBILITY**  
■ Give science the means to be creative and to innovate

**AN OPEN ATMOSPHERE**  
■ Build a place to share, and encourage discussions with the general public and industry partners

**PASSING DOWN KNOWLEDGE**  
■ On a national and international scale  
■ Train students from around the world on the future of neuroscience

## OUR SCIENTIFIC PRIORITIES

### OUR SCIENTIFIC AGENDA, ON PAR WITH CURRENT CHALLENGES:

- Understand the development of a normal brain and how it works over the course of a lifetime
- Prevent, to stop diseases from appearing
- Slow down and, when possible, cure the ongoing pathological process
- Repair brain and spinal cord structures damaged by a disease
- Alleviate or eradicate symptoms including memory loss, speech disorders, pain, anxiety, depression...

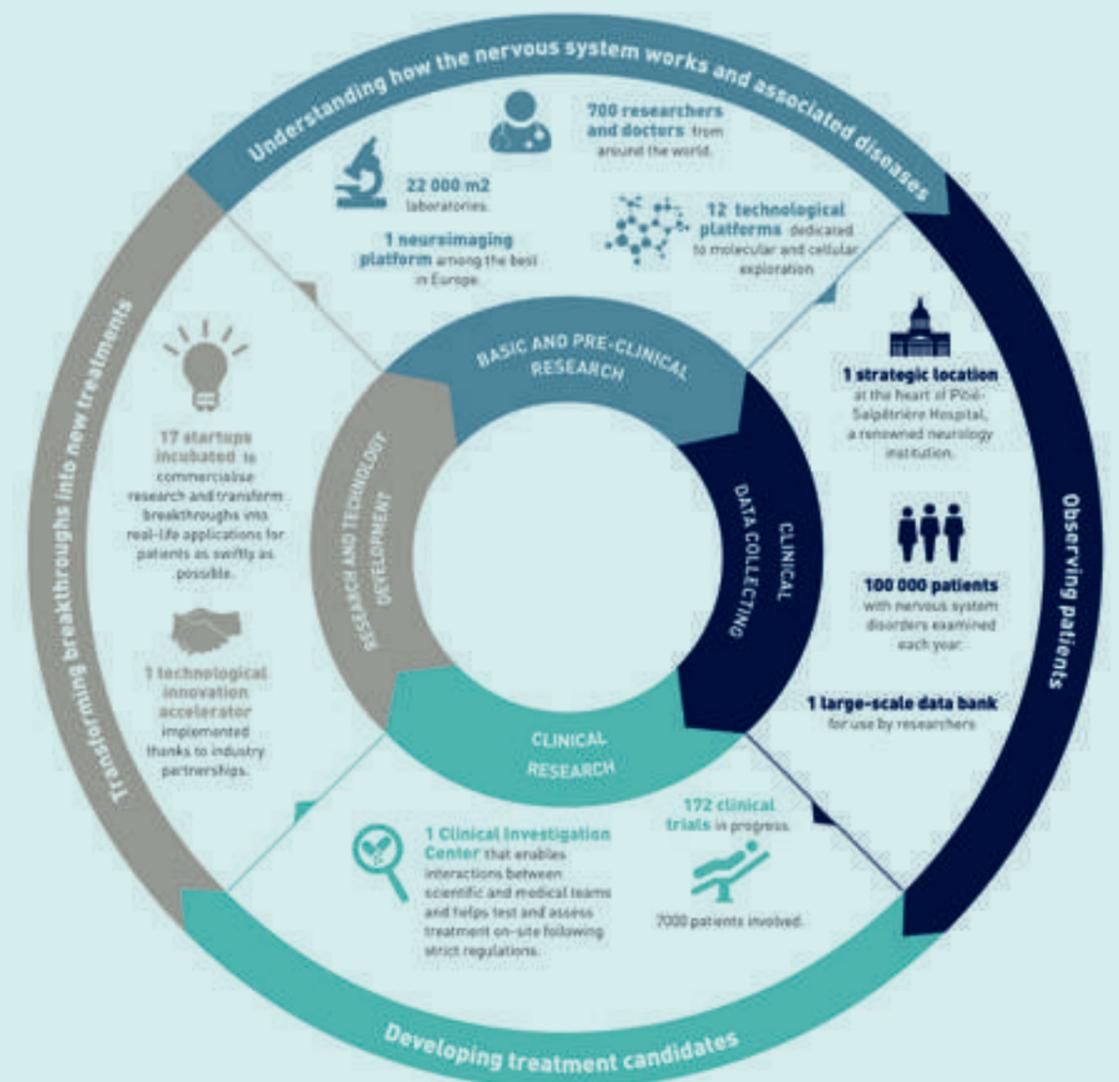
### AN AGENDA THAT NEEDS DRIVING TENETS:

- Create a strong research force, recruit the best French researchers and the best foreign investigators assessed by the International Scientific Council
- Make cutting-edge technological platforms available as well as a high-performance Center for Biological Resources
- Develop translational multidisciplinary research with industry partners and the best French and international research centers
- Define research priorities

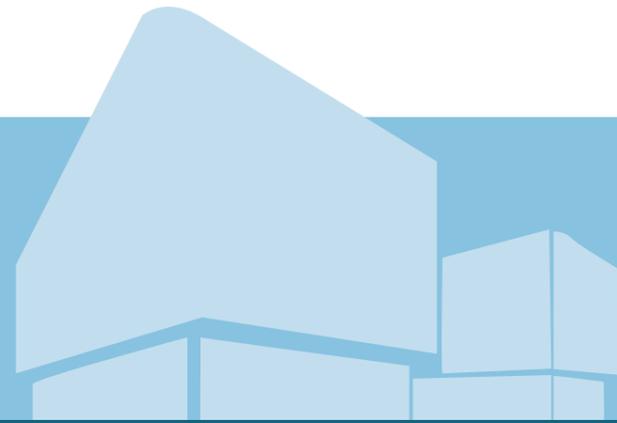
## A STRONG MODEL WITH ACADEMIC FOUNDATIONS

TWO NATIONAL RESEARCH AND ASSESSMENT INSTITUTES ENSURING THE HIGH LEVEL OF ICM RESEARCHERS AND ENGINEERS, ONE TOP UNIVERSITY AND THE LARGEST NERVOUS SYSTEM DISEASES HUB THROUGHOUT EUROPE

As a mixed research unit (UMR) with public partners, the Institute's governance is based on a strong partnership between the public and private sectors. At ICM, the mixed research unit brings together 4 public partners, AP-HP, INSERM, CNRS and Sorbonne Université



700 INDIVIDUALS AT ICM



42 NATIONALITIES

28 RESEARCH TEAMS

5 NEW TENURED RESEARCH FELLOWS

85 ENGINEERS AND TECHNICIANS

49 POST-DOCTORAL FELLOWS

92 DOCTORAL STUDENTS

101 ADMINISTRATIVE STAFF

51 MEDICAL AND PARAMEDICAL STAFF

150 RESEARCHERS AND PROFESSOR-RESEARCHERS

4

MAIN FIELDS OF RESEARCH

20

PATHOLOGIES STUDIED

12

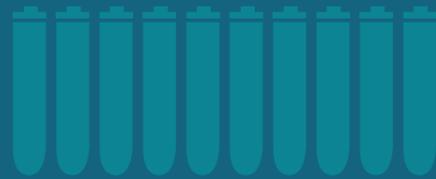
TECHNOLOGICAL PLATFORMS

1

CLINICAL INVESTIGATION CENTER

172

CLINICAL TRIALS



17

INCUBATED STARTUPS

1

CLLAPS LIVING LAB, THE ONLY ONE DEDICATED TO NEUROLOGY WORLDWIDE

11

ANR PROJECTS

55

PATENTS, 7 OF WHICH WERE FILED IN 2017

2

ERC PROJECTS

12

TRADEMARKS

88

TOTAL GRANTS OBTAINED IN 2017



*Our challenge is to create an Institute for Excellence in Research that is an international leader in Neuroscience.”*

Professor Alexis Brice, Chief Executive of ICM

## EFFICIENCY AND FLEXIBILITY: ICM GOVERNANCE

ICM'S GOVERNANCE IS BASED ON A STRONG PARTNERSHIP BETWEEN THE PUBLIC AND PRIVATE SECTORS, AS ILLUSTRATED BY ITS BOARD MEMBERS AND GOVERNING BODIES. THEY ENSURE THAT STRUCTURES AND RESOURCES PROPERLY MATCH SCIENTIFIC GOALS. THE EXECUTIVE COMMITTEE IMPLEMENTS MONITORING TO ENSURE EFFICIENT MANAGEMENT IS IN PLACE, AS WELL AS ONGOING EVALUATION OF WORK DONE BY THE TEAMS AND THEIR RESULTS, TO GUARANTEE CONTINUED EXCELLENCE. THROUGH ITS ANNUAL REPORT, ICM IS DEDICATED TO PROVIDING INFORMATION ON ITS MISSION AND RESULTS FOR TOTAL TRANSPARENCY TOWARDS PARTNERS AND DONORS.

In March 2011, ICM signed an agreement with academic partners AP-HP, CNRS, INSERM and UPMC to determine shared work arrangements for research teams under ICM management. The agreement details the creation of a Coordination Committee (stemming from the ICM Executive Committee) tasked with generating proposals on the Institute's research policy for the Board. In 2016, the Director of ICM was named C.E.O. of IHU-A-ICM to ensure streamlined governance between the two entities as they share a social mission and roadmap. The two entities officially merged on January 1st, 2018.

### THE BOARD OF DIRECTORS

The board of directors manages Institute affairs through its proceedings. It weighs in on strategic directions presented by the Chief Executive, adopts budgets and approves accounts.

The Foundation is governed by a board made up of fifteen members including:

- 5 founding college members;
- 3 members of the college of qualified persons;
- 4 ex officio members;
- 3 members of the college of friends of the foundation.

The college of founders includes not only the founders themselves, but also members selected by the founding college and renewed by it. The college of qualified persons includes individuals chosen for their competency in the foundation's field.

The college of ex officio members includes representatives from AP-HP, CNRS, INSERM and Sorbonne University. The college of friends of the foundation is comprised of individuals appointed by the Circle of Friends of ICM.

With the exception of founding members, all board members are appointed for a three-year term with one third renewed annually.

Their term can be renewed. The bureau meets at least four times per year at the initiative of the President of the Foundation in order to:

- Make arrangements, acting on authority of the Board of Directors when applicable, to ensure the foundation runs smoothly between board meetings;
- Manage preparation and monitoring of decisions made by the board of directors.

## MEMBERS

**Gérard SAILLANT**  
Professor of orthopaedic and trauma surgery, President of ICM

**Jean TODT**  
President of the FIA, Vice-President of ICM

### COLLEGE OF FOUNDERS

**Serge WEINBERG**  
**Jean GLAVANY**  
**Jean-Pierre MARTEL**  
**Gérard SAILLANT**  
**Jean TODT**

### COLLEGE OF QUALIFIED PERSONS

**Pierre CORVOL**  
Collège de France  
**Richard FRACKOWIAK**  
École Polytechnique  
Fédérale de Lausanne  
**Elisabeth TOURNIER-LASSERVE**  
Université Paris Diderot

### COLLEGE OF EX OFFICIO MEMBERS

**Bernard POULAIN**  
Representative of the National Center for Scientific Research (CNRS)  
**Thierry DAMERVAL**  
Representative of the National Health and Medical Research Institute (INSERM)  
**Bruno RIOU**  
Representative of Pierre et Marie Curie University (UPMC)  
**Ali FERHI**  
Representative of Assistance Publique – Hôpitaux de Paris (AP-HP)

### COLLEGE OF FRIENDS OF THE FOUNDATION

**Maurice LÉVY**  
**Jean-Philippe HOTTINGUER**  
**David de ROTHSCHILD**

### GOVERNMENT COMMISSIONER

**Philippe RITTER**

### AUDIT COMMITTEE

**Serge WEINBERG**  
Audit Committee President  
**Thierry DAMERVAL**  
Deputy Chief Executive of INSERM  
**Jean GLAVANY**  
Former Minister, Representative of the Hautes-Pyrénées  
**Jean-Pierre MARTEL**  
Attorney

### COORDINATION OF FOUNDATION AND PUBLIC PARTNER RELATIONSHIPS COMMITTEE

**Gérard SAILLANT**  
Professor of orthopaedic and trauma surgery, President of ICM  
**Ali FERHI**  
Representative of AP-HP  
**Bernard POULAIN**  
Representative of CNRS  
**Thierry DAMERVAL**  
Representative of INSERM  
**Bruno RIOU**  
Representative of UPMC

### AMBASSADORS

**Jean RENO**  
Actor  
**Michèle YEOH**  
Actress

### FRIENDS OF ICM

**Lily SAFRA**  
President of the philanthropic Edmond J. Safra Foundation  
Honorary President  
**Gérard SAILLANT**,  
Professor of orthopaedic and trauma surgery, President of ICM  
**Jean TODT**  
President of the FIA, Vice-President of ICM  
**Lindsay OWEN-JONES**  
Honorary President of L'Oréal, Honorary President of the Friends of ICM Committee  
**Maurice LÉVY**  
President of the Supervisory Board of Publicis Group, Co-President of the Friends of ICM Committee

**David de ROTHSCHILD**  
President of Rothschild & Cie bank, Co-President of the Friends of ICM Committee  
**Jean-Pierre MARTEL**  
Attorney  
**Serge WEINBERG**  
President of Weinberg Capital Partners, ICM Treasurer

## THE SCIENTIFIC ADVISORY BOARD

The International Scientific Advisory Board (SAB) assists the Board of Directors or Chief Executive on strategic directions, programs, or scientific strategies for the Institute. Its members are top international neuroscience experts. Every five years, ICM is assessed, as a Mixed Research Unit (UMR), on the quality of its research, its organisation, strategy, and five-year scientific plan. Research projects are assessed by the SAB, with the mission of advising the Institute and helping it define its overall approach. Following a period of discussions, the SAB provides input that is taken into account to build the file for assessment by the Committee for Assessment of Research and Higher Education (HCERES).

**Michael Shelanski** - President  
**Dimitri Kullman**  
**Gabor Tamas**  
**Peter Brown**  
**Brad Hyman**  
**Stephen Hauser**  
**Bill Richardson**  
**Helen Mayberg**  
**Christian Buchel**  
**Arnold Kriegstein**  
**Masud Husain**  
**Michael Heneka**

## PARIS TRANSLATIONAL NEUROSCIENCE INSTITUTE: A NEW PHASE IN 2017-2018



IN JULY 2010, THE MINISTRY OF HIGHER EDUCATION AND RESEARCH AND THE MINISTRY OF HEALTH LAUNCHED A CALL FOR PROJECTS FOR A TOTAL OF 850 MILLION EUROS DEDICATED TO BUILDING HOSPITAL-UNIVERSITY INSTITUTES (I.H.U.) WITHIN THE “FUTURE INVESTMENTS” PROGRAM. THIS CALL FOR PROJECTS AIMED AT DESIGNING WORLD-CLASS CENTERS TO STRENGTHEN FRANCE’S ATTRACTIVENESS IN MEDICAL AND SCIENTIFIC RESEARCH. ONLY 6 PROJECTS WERE SELECTED FOR THEIR EXCEPTIONAL QUALITIES.

### WHAT IS AN IHU?

An IHU is a world-class campus where the future of medicine is created, where the best public and private teams come together with exceptional flexibility to help patients, research and innovation.

### 6 FIELDS OF EXPERTISE, INCLUDING THE BRAIN

“ICM - Paris Translational Neuroscience Institute” IHU, recipient of a number of neuroscience awards, aims at developing best-in-class projects in healthcare, training, and technological transfer in nervous system diseases research. Using a multidisciplinary approach, its top priority is encouraging the design and development of innovative preventative, diagnostic and therapeutic products and solutions.

### WHAT DIFFERENTIATES ICM FROM IHU?

On January 1st 2018, both entities merged and IHU is now integrated within ICM. Operating budget, actions, teams, achievements and hopes were brought together for stronger coherence and a louder voice for the Institute’s scientific and medical project.

### RECENT ACHIEVEMENTS

#### RESEARCH-TO-MARKET

- IHU helped create iPEPS-ICM, the first startup incubator dedicated to nervous system disease with 28 incubated businesses, 115 M€ raised, 250 jobs and a special partnership with Station F, the world’s largest incubator
- 300 R&D partnerships were created, along with 43 patients and 30 licences
- Revenues of 42.1M€ thanks to the Carnot Institute Certification aimed at developing research partnerships between public laboratories and socio-economic players such as corporations and businesses to meet their needs.

#### TRAINING AND CARE

- IHU helped create a center that regroups early-stage clinical trials with 103 ongoing clinical trials
- Synergies between ICM and IHU helped build the cLLAPS Living Lab to place users involved in the healthcare process (doctors, patients, paramedical staff, hospital technicians, and more) at the heart of medical innovation to design new products and services for patient well-being, and to maximise efficiency of clinicians and all those involved (7 prototypes over the course of the year).
- IHU helped develop neuro-entrepreneur and future researcher training with a yearly entrepreneurship training program (Brain to Market Summer School) and with iMIND (International Master’s Degree on Neurodegenerative Diseases) in collaboration with Pierre and Marie Curie University.

# 28 TEAMS DEDICATED TO RESEARCH

RESEARCH TEAMS AT ICM WORK TO UNDERSTAND HOW THE CENTRAL NERVOUS SYSTEM WORKS IN HEALTHY INDIVIDUALS TO ACQUIRE FUNDAMENTAL RESEARCH, INCREASE OUR UNDERSTANDING OF NEUROLOGICAL AND PSYCHIATRIC DISEASES AND DISCOVER HOW AND WHY THEY APPEAR.

■ ICM has set 4 priorities for scientific research: molecular and cellular biology, neurophysiology, cognition, and clinical and translational research. Research projects in each of the 28 teams gravitate towards one primary field among these four, and may also include another field.

■ Direct funding acquired by research teams is known as competitive funding, acquired by calls for projects open to all teams working on a specific topic. Applications are prepared by applicant teams and include prior results obtained by researchers, their scientific project over the next few years, and detailed forecasted expenses to yield results in the specified amount of time (generally between 2 and 5 years). Calls for projects stem from national public institutions (ANR and ERC, for example) or from foundation and organisations dedicated to a specific disease or type of research (France Alzheimer or the Michael J. Fox Foundation, for example). Teams may also receive ICM funding for innovative projects such as BBT, cutting-edge equipment, or to hire staff.



## CELLULAR AND MOLECULAR BIOLOGY (15 TEAMS)

UNDERSTANDING THE SPECIFICITIES OF EACH CELL IN THE BRAIN, THEIR IDENTITY, AND IDENTIFYING MALFUNCTION

### ■ AMYOTROPHIC LATERAL SCLEROSIS (ALS): CAUSES AND MECHANISMS OF MOTOR NEURON DEGENERATION

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leader:** Séverine BOILLEE

**Principal investigators, researchers, clinicians:**

Séverine BOILLEE, PhD  
Delphine BOHL, PhD  
Stéphanie MILLECAMPS, PharmD, PhD  
Christian LOBSIGER, PhD  
François SALACHAS, MD  
Danielle SEILHEAN, MD, PhD

1 post-doctoral fellow  
3 engineers and technicians  
4 doctoral students

**Competitive funding granted in 2017**  
**National:** FRM, ARSLA

### ■ MOLECULAR BASIS, PHYSIOPATHOLOGY AND TREATMENT OF NEURODEGENERATIVE DISEASES

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leader:** Alexis BRICE

**Principal investigators, researchers, clinicians:**

Alexis BRICE, MD  
Alexandra DURR, MD, PhD  
Giovanni STEVANIN, PhD  
Frédéric DARIOS, PhD  
Morwena LATOUCHE, PhD  
Isabelle LE BER, MD, PhD  
Olga CORTI, PhD  
Jean-Christophe CORVOL, MD, PharmD, PhD  
Suzanne LESAGE, PhD  
Khalid Hamid EL HACHIMI  
Caroline NAVA, MD

Claire PUJOL, PhD  
Fanny MOCHEL, MD, PhD

9 post-doctoral fellows  
9 engineers and technicians  
11 doctoral students  
3 clinical research representatives

**Competitive funding granted in 2017**

**National:** ANR, H2020, Fondation de France, CHU Nîmes, FRM, ABM, France Parkinson, ARDOC, Fondation Vaincre Alzheimer  
**International:** NIH

### ■ ALZHEIMER'S DISEASE AND PRION DISEASES

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leaders:** Marie-Claude POTIER & Stéphane HAIK

**Principal investigators, researchers, clinicians:**

Marie-Claude POTIER, PhD  
Stéphane HAIK, PhD  
Nicolas BIZAT, PhD  
Benoit DELATOUR, PhD  
Stéphane EPELBAUM, MD  
Charles DUYCKAERTS, Md, PhD  
Serge MARTY, PhD  
Jean-Philippe BRANDEL, MD  
Véronique SAZDOVITCH, MD  
Jean-Maurice DELABAR, MD, PhD

6 post-doctoral fellows  
8 engineers and technicians  
2 doctoral students  
1 clinical research representative

**Competitive funding granted in 2017**

**National:** France Alzheimer, InVs  
**International:** CJD Foundation

### ■ EXPERIMENTAL THERAPIES IN PARKINSON'S DISEASE

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leader:** Etienne HIRSCH

**Principal investigators, researchers, clinicians:**

Etienne HIRSCH, PhD  
Stéphane HUNOT, PhD  
Marie-Laure WELTER, MD, PhD  
David GRABLI, MD  
Patrick Pierre MICHEL, PhD  
Rita RAISMAN-VOZARI, PhD

6 post-doctoral fellows  
6 engineers and technicians  
7 doctoral students

**Competitive funding granted in 2017**  
**National:** Fondation NRJ, FRM

### ■ NEUROGENETICS AND PHYSIOLOGY

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leader:** Bertrand FONTAINE

**Principal investigators, researchers, clinicians:**

Bertrand FONTAINE, MD, PhD  
Sophie NICOLE, PhD  
Cécile DELARASSE, PhD  
Isabelle REBEIX, PhD  
Laure STROCHLIC, PhD  
Mohamed EL-BEHI, PhD  
Gaëlle BRUNETEAU, MD, PhD  
Bruno EYMART, MD  
Emmanuel FOURNIER, MD  
Karine VIALA, MD  
Damien STERNBERG, MD  
Savine VICART, MD

2 post-doctoral fellows  
4 engineers and technicians  
2 doctoral students

Competitive funding granted in 2017  
**National:** AFM, ARSEP, Idex Sorbonne Université, DIM Biothérapies, INSERM

## GENETICS AND PHYSIOPATHOLOGY IN EPILEPSY

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leaders:** Stéphanie BAULAC & Eric LEGUERN

**Principal investigators, researchers, clinicians:**

Stéphanie BAULAC, PhD  
 Eric LEGUERN, MD, PhD  
 Christel DEPIENNE, MD, PhD  
 Michel BAULAC, MD  
 Cyril MIGNOT, MD  
 Rita RAISMAN-VOZARI, PhD

4 post-doctoral fellows  
 2 engineers and technicians  
 3 doctoral students

Competitive funding granted in 2017  
**National:** FRM, Ambassade de France au Japon, Institut National Polytechnique de Toulouse

## EXPERIMENTAL NEURO-ONCOLOGY

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leader:** Marc SANSON

**Principal investigators, researchers, clinicians:**

Marc SANSON, MD, PhD  
 Franck BIELLE, MD, PhD  
 Ahmed IDBAIH, MD, PhD  
 Michel KALAMARIDES, MD, PhD  
 Agusti ALENTORN, MD  
 Jean-Yves DELATTRE, MD, PhD  
 Khé HOANG-XUAN, MD, PhD  
 Karima MOKHTARI, MD  
 Mathieu PEYRE, MD, PhD

2 post-doctoral fellows  
 8 engineers and technicians  
 2 doctoral students

Competitive funding granted in 2017  
**National:** Cancéropôle Ile de France, Ligue National contre le cancer, Fondation NRJ, ARC  
**European:** MSCA-ITN/ETN

## MECHANISMS OF MYELINATION AND REMYELINATION IN THE CNS

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leaders:** Catherine LUBETZKI & Bruno STANKOFF

**Principal investigators, researchers, clinicians:**

Catherine LUBETZKI, MD, PhD  
 Bruno STANKOFF, MD, PhD  
 Nathalie SOL-FOULON, PharmD, PhD  
 Anne DESMAZIERE, PhD  
 Marc DAVENNE, PhD  
 Céline LOUAPRE, MD, PhD  
 Benedetta BODINI, MD, PhD  
 Caroline PAPEIX, MD  
 Elisabeth MAILLARD, MD  
 Géraldine BERA, MD

1 post-doctoral fellow  
 1 engineer  
 3 doctoral students

Competitive funding granted in 2017  
**National:** Fondation de France, ARSEP, FRM, ANR

## MOLECULAR AND CELLULAR APPROACHES FOR MYELIN REPAIR

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leaders:** Brahim NAIT-OUESMAR & Anne BARON VAN EVERCOOREN

**Principal investigators, researchers, clinicians:**

Brahim NAIT-OUESMAR, PhD  
 Anne BARON VAN EVERCOOREN, PhD  
 Violetta ZUJOVIC, PhD  
 Lamia BOUSLAMA, PhD

4 post-doctoral fellows  
 2 engineers  
 5 doctoral students

Competitive funding granted in 2017  
**National:** ENP, UPMC, ANR, AFM, Fondation Jérôme Lejeune, ARSEP  
**European:** ECTRIMS  
**International:** NMSS

## CELLULAR AND MOLECULAR MECHANISMS IN GLIOMA DEVELOPMENT

SECONDARY FIELD: NA

**Team leader:** Emmanuelle HUILLARD

**Principal investigators, researchers, clinicians:**

Emmanuelle HUILLARD, PhD  
 Isabelle LEROUX, PhD

1 post-doctoral fellow  
 2 engineers and technicians  
 2 doctoral students

Competitive funding granted in 2017  
**National:** Cancéropôle Ile de France, Ligue National contre le cancer, ARC

## OLIGODENDROCYTE DEVELOPMENT AND NEUROVASCULAR INTERACTIONS

SECONDARY FIELD: NA

**Team leaders:** Jean Léon THOMAS & Boris ZALC

**Principal investigators, researchers, clinicians:**

Jean Léon THOMAS, PhD  
 Boris ZALC, PhD  
 Michel MALLAT, PhD  
 Carlos PARRAS, PhD

2 post-doctoral fellows  
 4 engineers  
 1 doctoral student

Competitive funding granted in 2017  
**National:** ANR, ARC, FRC, ARSEP

## BIOTECHNOLOGY AND BIOTHERAPY

SECONDARY FIELD: NA

**Team leader:** Philippe RAVASSARD

**Principal investigators, researchers, clinicians:**

Philippe RAVASSARD, PhD  
 Hélène CHEVAL, PhD  
 Jacques MALLETT, Emérite

1 post-doctoral fellow  
 4 engineers  
 2 doctoral students

Competitive funding granted in 2017  
**National:** France PARKINSON

## TREATMENT OF AMYOTROPHIC LATERAL SCLEROSIS: FROM GENETICS TO ZEBRAFISH

SECONDARY FIELD: NA

**Team leader:** Edor KABASHI

**Principal investigators, researchers, clinicians:**

Edor KABASHI, PhD  
 Corinne BESNARD-GUERIN, PhD  
 Sorana CIURA, PhD

3 post-doctoral fellows  
 1 technician  
 3 doctoral students

Competitive funding granted in 2017  
**National:** ANR, ARSLA  
**Européens:** Frick fondation

## BRAIN DEVELOPMENT

SECONDARY FIELD: NA

**Team leader:** Bassem HASSAN

**Principal investigators, researchers, clinicians:**

Bassem HASSAN, PhD

8 post-doctoral fellows  
 4 engineers and technicians  
 4 doctoral students

Competitive funding granted in 2017  
**National:** Campus France

## STRUCTURAL NETWORK DYNAMICS

SECONDARY FIELD: NA

**Team leader:** Nicolas RENIER

**Principal investigators, researchers, clinicians:**

Nicolas RENIER, PhD

1 engineer  
 1 doctoral student

Competitive funding granted in 2017  
**National:** Ville de Paris  
**European:** ERC



## NEUROPHYSIOLOGY (7 TEAMS)

DISSECTING COMMUNICATION BETWEEN CELLS, IDENTIFYING THEIR INFORMATION NETWORKS WITHIN A SPECIFIC CELL TYPE AND WITHIN THE BODY

### ■ NORMAL AND ABNORMAL MOTOR CONTROL: MOTOR DISORDERS AND EXPERIMENTAL THERAPIES

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leaders:** Marie VIDAILHET & Stéphane LEHERICY

**Principal investigators, researchers, clinicians:**

Marie VIDAILHET, MD, PhD  
Stéphane LEHERICY, MD, PhD  
Charlotte ROSSO, MD, PhD  
Yulia WORBE, MD  
Pierre POUGET, PhD  
Isabelle ARNULF, MD, PhD  
Emmanuel ROZE, MD, PhD  
Andréas HARTMANN, MD  
Sabine MEUNIER, PhD  
Emmanuelle APARTIS-BOURDIEU, MD  
Smaranda LEU-SEMENESCU, MD  
Elodie HAINQUE, MD  
Nadya PYATIGORSKAYA, MD  
Alexandra PETIET, PhD

2 post-doctoral fellows  
2 engineers and technicians  
5 doctoral students

**Competitive funding granted in 2017**  
**National:** FRM, AMADYS, AP-HP, DMRF

### ■ SYNAPTIC INHIBITION AND SELF-REGULATION OF CEREBRAL CORTEX MICROCIRCUITS

SECONDARY FIELD: NA

**Team leader:** Alberto BACCI

**Principal investigators, researchers, clinicians:**

Alberto BACCI, PhD  
Joana LOURENCO, PhD  
Laurence CATHALA, PhD

2 post-doctoral fellows  
1 engineer  
4 doctoral students

**Competitive funding granted in 2017**  
**National:** ANR

### ■ CELL EXCITABILITY AND NEURAL NETWORK DYNAMICS

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leader:** Stéphane CHARPIER

**Principal investigators, researchers, clinicians:**

Stéphane CHARPIER, PhD  
Séverine MAHON, PhD  
Mario CHAVEZ, PhD  
Vincent NAVARRO, MD, PhD  
Michel LE VAN QUYEN, PhD

8 post-doctoral fellows  
1 technician  
2 doctoral students

**Competitive funding granted in 2017**  
**National:** ANR, FRM

### ■ CORTEX ET ÉPILEPSIE

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Chef d'équipe :** Richard MILES

**Principal investigators, researchers, clinicians:**

Richard MILES, PhD

5 post-doctoral fellows

### ■ OPTOGENETIC DISSECTION OF SPINAL CIRCUITS UNDERLYING LOCOMOTION

SECONDARY FIELD: MOLECULAR AND CELLULAR BIOLOGY

**Team leader:** Claire WYART

**Principal investigators, researchers, clinicians:**

Claire WYART, PhD  
Pierre-Luc BARDET, PhD  
Hugues PASCAL-MOUSSELARD, MD

6 post-doctoral fellows

1 engineer  
4 doctoral students

**Competitive funding granted in 2017**  
**National:** FRM, Campus France

**European:** EMBO, MSCA, Fondation Schlumberger  
**International:** NIH

### ■ EXPERIMENTAL NEUROSURGERY

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leader:** Brian LAU

**Principal investigators, researchers, clinicians:**

Brian LAU, PhD  
Carine KARACHI, MD, PhD  
Eric BARDINET, PhD

5 post-doctoral fellows  
1 engineer  
3 doctoral students

1 clinical research representatives

### ■ CELLULAR MECHANISMS IN SENSORY PROCESSING

SECONDARY FIELD: NA

**Team leader:** Nelson REBOLA

**Principal investigators, researchers, clinicians:**

Nelson REBOLA, PhD  
Annunziato MORABITO, PhD

1 doctoral student

**Competitive funding granted in 2017**  
**European:** ERC

## COGNITION (5 TEAMS)

UNDERSTANDING HOW COMMUNICATION AMONGST CELLS CAN MODIFY THEIR BEHAVIOUR AND HOW CELL MALFUNCTION CAN MODIFY INFORMATION RECEIVED BY OTHER CELLS

### ■ PHYSIOLOGICAL ASSESSMENT OF HEALTHY PATIENTS AND PATIENTS WITH COGNITIVE DISORDERS

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leaders:** Paolo BARTOLOMEO, Laurent COHEN & Lionel NACCACHE

**Principal investigators, researchers, clinicians:**

Paolo BARTOLOMEO, PhD  
Laurent COHEN, MD, PhD  
Lionel NACCACHE, MD, PhD  
Jacobo SITT, PhD

7 post-doctoral fellows  
1 technician  
7 doctoral students

**Competitive funding granted in 2017**  
**National:** Idex Sorbonne Université

### ■ FRONTAL SYSTEMS: FUNCTIONS AND MALFUNCTIONS

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leaders:** Bruno DUBOIS & Richard LEVY

**Principal investigators, researchers, clinicians:**

Richard LEVY, MD, PhD  
Bruno DUBOIS, MD, PhD  
Harald HAMPEL, PhD  
Michel THIEBAUT DE SCHOTTEN, PhD  
Antoni VALERO-CABRE, PhD  
Emmanuelle VOLLE, PhD  
Lara MIGLIACCIO, PhD  
Bénédicte BATRANCOURT, PhD  
Marc TEICHMANN, MD

5 post-doctoral fellows  
6 doctoral students

**Competitive funding granted in 2017**  
**National:** ANR

### ■ STUDY OF EMOTIONS AND SOCIAL INTERACTIONS

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leaders:** Nathalie GEORGE & Philippe FOSSATI

**Principal investigators, researchers, clinicians:**

Nathalie GEORGE, PhD  
Philippe FOSSATI, MD, PhD  
Stéphanie DUBAL, PhD  
Bruno MILLET, MD, PhD  
Jean-Yves ROTGE, MD

4 doctoral students

**Competitive funding granted in 2017**  
**National:** Fondation de France

### ■ BEHAVIOUR, EMOTION, AND BASAL GANGLIA

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leader:** Luc MALLET

**Principal investigators, researchers, clinicians:**

Luc MALLET, MD, PhD  
Eric BURGUIERE, PhD  
Philippe DOMENECH, MD, PhD  
Jérôme YELNIK, PhD  
Karim N'DIAYE, PhD  
Christiane SCHREIWEIS, MD, PhD

1 engineer  
4 doctoral students

### ■ MOTIVATION, BRAIN AND BEHAVIOUR

SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**Team leaders:** Mathias PESSIGLIONE, Sébastien BOURET, Jean DAUNIZEAU

**Principal investigators, researchers, clinicians:**

Mathias PESSIGLIONE, PhD  
Sébastien BOURET, PhD  
Jean DAUNIZEAU, PhD  
Fabien VINCKIER, MD, PhD  
Raphaël LE BOUC, MD

3 post-doctoral fellows  
7 doctoral students

**Competitive funding granted in 2017**  
**National:** ANR, FRM, Fondation de France, Idex Sorbonne Université, Ecole de l'INSERM Liliane Bettencourt

## CLINICAL AND TRANSLATIONAL RESEARCH

(1 TEAM)

COMBINE KNOWLEDGE FROM THE 3 FIELDS (MOLECULAR AND CELLULAR, NEUROPHYSIOLOGY AND COGNITION), COMPARE CONTROLLED CELLS TO PATIENT CELLS, COMPARE “NORMAL” AND PATHOLOGICAL PROCESSES, USE ARTIFICIAL INTELLIGENCE TO MODEL HOW THE BRAIN EVOLVES WITH AGEING AND DISEASES... THIS AMOUNTS TO RESEARCHING THE ORIGIN OF NEUROLOGICAL DISEASES AND IDENTIFYING MEANS TO PREVENT OR SLOW DISEASE PROGRESSION

### MATHEMATICAL MODELS AND ALGORITHMS TO PROCESS HUMAN BRAIN IMAGES AND SIGNALS

SECONDARY FIELD: NA

**Team leaders:** Olivier COLLIOT, Didier DORMONT

#### Principal investigators, researchers, clinicians:

Olivier COLLIOT, PhD  
Didier DORMONT, MD, PhD  
Stanley DURLEMAN, PhD  
Fabrizio De VICO FALLANI, PhD  
Stéphane EPELBAUM, MD  
Benjamin CHARLIER, PhD

4 post-doctoral fellows  
5 engineers  
16 doctoral students

#### Competitive funding granted in 2017

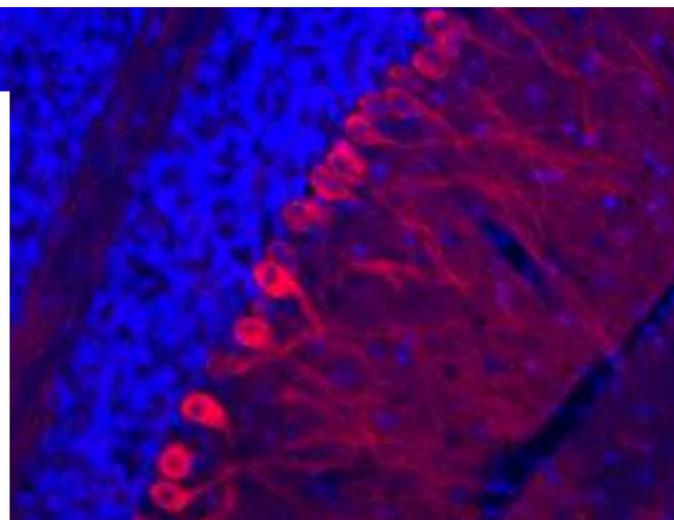
**National:** Idex Sorbonne Université, INRIA  
**European:** FET-HBP

ICM SUPPORT STAFF ARE FULLY DEDICATED TO SUPPORTING RESEARCH TEAMS IN THEIR WORK: PROCUREMENT, FINANCE, LEGAL, RESEARCH COMMERCIALISATION, COMMUNICATION AND DEVELOPMENT, SCIENTIFIC AND MEDICAL AFFAIRS, HUMAN RESOURCES, IT, AND LAUNDRY. THEY ARE ESSENTIAL TO THE INSTITUTE'S SUCCESS AND HELP RESEARCHERS DEDICATE THEIR TIME FULLY TO THEIR TALENT AND WORK: SEARCH FOR TOMORROW'S TREATMENTS!

**ABM** : Agence de Biomedecine  
**ADRMGNP** : Association Développement Recherche Maladies Génétiques Neurologiques Psychiatriques  
**AFAF** : Association Française de l'Ataxie de Friedreich  
**AFM** : Association Française contre les Myopathies  
**AHF** : Association Huntington France  
**AMADYS** : Association des Malades Atteints de Dystonie  
**ANR** : Agence Nationale pour la Recherche  
**ANSES** : Agence Nationale de Sécurité Sanitaire  
**AP-HP** : Assistance Publique - Hôpitaux de Paris  
**APTES** : Association des Personnes concernées par le Tremblement  
**ARC** : Association pour la Recherche sur le Cancer  
**ARDOC** : Association Régionale des Dépistages Organisés des Cancers  
**ARSEP** : Association pour la Recherche sur la Sclérose En Plaques  
**ARSLA** : Association pour la Recherche sur la SLA  
**ARTC** : Association pour la Recherche sur les Tumeurs Cérébrales Malignes  
**Association CSC** : Association Connaitre les Syndromes Cérébelleux  
**BBT** : Big Brain Theories (ICM)  
**BELSPO** : Politique scientifique fédérale belge  
**CJD Foundation** : Fondation maladie de Creutzfeldt-Jakob  
**DGCS** : Direction Générale de la Cohésion Sociale  
**DIM** : Domaine d'Intérêt Majeur- Région Ile de France  
**DMRF** : Dystonia Medical Research Foundation  
**ECTRIMS** : Comité européen pour le traitement et la recherche sur la sclérose en plaques  
**EJP** : European Joined Program  
**ELA** : Association européenne contre les leucodystrophies  
**EMBO** : Organisation européenne de biologie moléculaire  
**ENP** : Ecole des Neurosciences de Paris  
**ERC** : Conseil Européen de la Recherche  
**F-CRIN** : Réseau français d'infrastructure pour la recherche clinique  
**FMR** : Fondation Maladies Rares  
**FRC** : Fondation pour la Recherche sur le Cerveau  
**FRM** : Fondation pour la Recherche Médicale  
**FUI** : Fond Unique Interministériel  
**FWO** : Research Foundation - Flanders  
**H2020** : Programme européen horizon 2020  
**HFSP** : Human Frontier Science Program  
**Idex** : Initiative d'excellence  
**HBP** : Human Brain Project  
**MSCA-ITN/ETN** : Marie Skłodowska-curie Innovative Training Networks  
**PhD** : Postgraduate doctoral degree  
**MD** : Doctor of Medicine  
**PharmD** : Doctor of Pharmacy

# OBSERVING THE BRAIN AT EVERY LEVEL: TECHNOLOGICAL PLATFORMS

THE QUALITY OF SCIENTIFIC BREAKTHROUGHS DEPENDS ON THE PERFORMANCE OF TECHNOLOGICAL PLATFORMS. ICM IS REVOLUTIONARY IN ITS DESIGN, INNOVATIVE IN ITS ORGANISATION, AND UNIQUE IN ITS CUTTING-EDGE TECHNOLOGICAL EQUIPMENT. ICM RESEARCHERS WORK ON VARIOUS LEVELS: FROM MOLECULES (DNA, PROTEINS) TO CELLS AND INDIVIDUALS. AT EACH LEVEL, INNOVATIVE TECHNOLOGY IS MADE AVAILABLE TO RESEARCHERS AND CLINICIANS. THE PLATFORM NETWORK AT ICM ENABLES TRANSLATIONAL RESEARCH AND COLLABORATIONS BETWEEN RESEARCHERS AND CLINICIANS.



« Technological developments are essential to progress in medicine and science ».

Etienne Hirsch,  
Director of Platforms

## WHAT'S NEW IN 2017?

### Restructuring of cellular and molecular imaging

■ A major development of 2017 at ICM was the total restructuring of ICM. QUANT, the Institute's cellular and molecular imaging platform. Being at the forefront of cellular and molecular imaging is essential to observe and understand brain anatomy. This is one of the Institute's major challenges. Relationships with other platforms, such as the histology platform, helped develop strong technologies including the possibility of making brain tissue totally transparent and analysing very specific populations of neurons and neural connections using the latest microscopy technology.

### New equipment

■ New optic microscopes, a second spinning disk (straight) for rapid acquisition of 3D cell, tissue, or small organism imaging, a second inverted spectral confocal microscope for precise imaging of various fluorochromes and decrease of non-specific signal input with white light laser and time-gated detectors. Soon to come, a multiphoton microscope to observe thick tissue samples such as brain slices and holographic photo manipulation. "In vivo" microscopy to analyse cell dynamics within intact tissue, and a wide-field microscope equipped with a powerful deconvolution module.

### Several major projects currently in progress at the platform:

■ Development of correlative

microscopy (made possible by an ICM investment within the R&D call for projects), a approach to merge information acquired through various imaging techniques on the same sample, that can help bridge the gap between multiphoton microscopy and electron microscopy. Correlative microscopy spearheads interactions drawn between structures (electron microscopy) and their functions (multiphoton microscopy).

■ Development of large sample imaging strengthened by the arrival of Nicolas Renier at ICM.

■ Development of new sample building instruments for multiphoton microscopy and electron microscopy using computer-aided design and 3D printing, in collaboration with ICM's new micromechanics workshop.

### A PET-MRI technical facility at ICM

■ ICM and Pitié-Salpêtrière Hospital acquired a PET-MRI, a new generation of hybrid cameras that simultaneously perform Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI). Radioactive markers can be used to observe certain molecules in the brain combined with MRI imaging. ICM's equipment is one of the rare PET-MRIs in France made available for both clinical and research use. The new platform is a powerful tool in understanding neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, ALS as well as for oncology, research, diagnosis and treatment monitoring. The PET-MRI

was designed by GE Healthcare and acquired thanks to the generous support of the Alzheimer's disease Research Foundation and Dassault Group, the Bettencourt Schueller Foundation, the Gueules Cassées Foundation, The Conny-Maeva Charitable Foundation, and Etablissement Simonetta.

### "Technological development" calls for tender

■ To ensure that ICM platforms remain at the forefront of their field, technological developments are paramount. Competitive calls for tender were implemented in 2017 to support these efforts.

### What's next?

■ ICM is involved in an ongoing effort to improve and invest in its research. To support this effort, external assessment will take place in 2018 by a jury of scientific experts. This expertise also aims at determining new orientations for improvement in new fields for ICM platforms.

# ICM PLATFORMS

## MOLECULAR EXPLORATION

GENOME ANALYSIS AND DEVELOPMENT OF VIRAL VECTORS

### ■ iGenSeq - genotyping-sequencing platform

Genome analysis, detection of genetic mutations and variants and identification of the role of mutations in the onset of neurological diseases.

### ■ iVector - vectorology platform

Production of viral vectors used for gene therapy to counter the effects of genetic mutation.

## CELLULAR AND MOLECULAR IMAGING

OBSERVING CELLS, TISSUE, AND WHOLE ORGANISM MODELS USING MULTIPHOTON MICROSCOPY, ELECTRON MICROSCOPY AND IMAGE ANALYSIS.

### ■ ICM.Quant

The platform makes high-performance equipment available and advises, trains, and supports user in microscopy and cellular imaging.

## CELLULAR EXPLORATION

THE CELLULAR EXPLORATION SILO COMBINES TWO TECHNOLOGICAL PLATFORMS: CELIS FOR CELL CULTURE AND HISTOMICS FOR HISTOLOGY.

LA PLATEFORME CELIS DE CULTURE CELLULAIRE REGROUPE 3 ACTIVITÉS :

### ■ CELIS : cell culture

The platform implements cell models and cutting-edge technology used to study brain and spinal cord pathology, as well as screening of small drug molecules.

### ■ CELIS-E-PHYS: electrophysiology

The platform records electrical activity within cells and neural networks in various experimental models (cell lines with genes of interest, primary culture, iPS cells, brain slices, zebrafish) using patch-clamp (single cell) or multi-electrode arrays (cell networks).

### ■ CELIS-iPS : production of human induced pluripotent stem cells (iPS)

The platform develops human induced pluripotent stem cells (iPS), meaning cells capable of differentiating into different types of cells, and develops genetic modification techniques for these cells to design new therapies.

### HISTOMICS - HISTOLOGY PLATFORM

■ Equipment dedicated to histology techniques (slices, paraffin inclusion, dyeing, immunohistochemistry, tissue clearing, slide scanner and laser micro-dissector). The platform trains users and assists them in developing protocols and is also available for services.

## FUNCTIONAL EXPLORATION

STUDY OF LIVING ORGANISMS USING NON-INVASIVE AND RESPECTFUL METHODS, PARTICULARLY ADAPTED TO HUMANS, BOTH HEALTHY VOLUNTEERS AND AFFECTED PATIENTS.

### ■ CENIR - Human MRI - Research neuroimaging platform

High-quality imaging instruments for brain and spine research.

### ■ CENIR- MEG/EEG - Magnetoencephalography

(recording of magnetic fields in the brain) and electroencephalography (recording of the brain's electrical signals) platform

Non-invasive methods for visualisation of cerebral activity with millisecond precision.

### ■ CENIR - PET MRI - Platform combining Positron Emission Tomography and Magnetic Resonance Imaging

Instrument used to observe cerebral activity and integrity using anatomical, functional and molecular image acquisition. One same instrument for research and care for neurodegenerative diseases.

### ■ CENIR- STIM - Stereotaxic platform

Offers program development and analysis using stereotaxic imaging data (uses include deep brain stimulation, drug-resistant epilepsy and radiosurgery).

### ■ CENIR-PANAM - physiology and movement analysis platform

Clinical and therapeutic research using non-invasive brain stimulation, motor control studies and multidisciplinary association of various techniques.

### ■ CENIR - Small Animal MRI Platform

Experimental pathological model imaging for assessment of new biomarkers, the study of pathology mechanisms, and drug efficacy assessment.

## PRECLINICAL FUNCTIONAL EXPLORATION

STUDY OF LIVING ORGANISMS IN EXPERIMENTAL MODELS

### ■ PHENO-ICMice - Rodent Model Platform

### ■ PHENO-ZFish- Zebrafish Model Platform



## PRISME – HUMAN BEHAVIOUR EXPLORATION PLATFORM

Development of protocols to test cognitive functions and biological and cellular mechanisms in real-life situations (adapted environments, virtual reality, wireless measures) and in groups of participants representative of the general population (recruitment in an extended database with simultaneous testing).

## iCONICS BIOINFORMATICS

The role of the iCONICS Bioinformatics silo is to provide support for research teams from the start of a project requiring statistical analysis and data modelling. The silo is managed by experts in bioinformatics and biostatistics and is tasked with developing innovative data processing instruments for the data generated by research teams.

ICONICS operates in three fields. The “Database and Datawarehouse” division develops instruments used to organise and gather information using a shared model and makes them available through dynamic interfaces. The “Genomics” division builds and implements data treatment sequences and software to interpret genetic and -omic data (especially high-throughput sequencing data: transcriptomic, epigenomic). The “Biostatistics” division designs generic statistical analysis support and develops advanced methods for large-scale multimodal data integration.

## BIOLOGICAL RESOURCE CENTER

Samples collected during blood tests, biopsies, or other surgical actions are an extremely precious source of information in research. ICM helps manage 3 biobanks dedicated to managing these biological resources (biological samples and associated data): collecting, recording, processing, storing, and making them available to researchers in keeping with regulations and certified quality assurance (NF S96-900 certification).

- DNA and Cell Bank
- Biological Resource Center for the French Network for Multiple Sclerosis Genetic Studies (CRB-REFGENSEP)
- OncoNeuroTek Tumor Bank



# 2017 : PROGRESS, HOPES AND BREAKTHROUGHS

A YEAR FILLED WITH 600 PUBLICATIONS INCLUDING 115 WITH AN IMPACT FACTOR ABOVE 7, 7 PATENTS FILED, INNOVATIVE PROJECTS THAT GAVE RISE TO COLLABORATIONS, DEVELOPMENT OF NEUROINFORMATICS, TWO NEW WORLD-CLASS TEAMS AND STARTUPS, MANY DISTINCTIONS WITHIN THE SCIENTIFIC COMMUNITY, INNOVATIVE PROTOTYPES DEVELOPED FOR PATIENT WELL-BEING, 80 CLINICAL TRIALS, DEVELOPMENT OF RESEARCH-ORIENTED PHILANTHROPY, A BALANCED BUDGET AND A BUDGET ON THE RISE...2017 WAS FILLED WITH HOPE!

## 2017 HIGHLIGHTS

### GREAT STRIDES AND MAJOR BREAKTHROUGHS

- On the research side: search
- On the clinical side: predict and cure
- On the start-up side : innovate

### 2017 A CLOSER LOOK

- New collaborations: Big Brain Theory Program
- Towards medicine of the future: neuroinformatics
- New talents in research: recruitment of two new teams
- Excellence acknowledged: prizes and awards
- Research and care: patients as a primary concern
- Science and entrepreneurship: ICM, driving innovation
- Passing down knowledge: training and teaching
- Attractiveness: ICM at the crossroads of international research
- For innovative communication: sharing and spreading knowledge
- Patronage: philanthropy to benefit research
- Diligence and transparency at the heart of our actions:
- 2017 financial statement

WHAT WE DO IS ALSO THANKS TO YOU

# 2017 HIGHLIGHTS

## THE FRENCH PRESIDENT VISITS ICM

French President François Hollande visited ICM for the 2030 World Innovation Contest created to encourage development and growth of companies with breakthrough innovations. In the third phase of its program, the contest designated 12 award recipients among which BioSerenity, incubated at ICM since 2014.



## A GROWING NUMBER AND INCREASING QUALITY OF PUBLICATIONS IN MAJOR SCIENTIFIC JOURNALS

In 2017, ICM ranked 2nd among 35 international Neurology Institutes with 600 scientific publications stemming from its research (4th in 2013) (Inserm/Thomson Reuters). From an impact factor standpoint, 29% of these publications were published in the 10% most prestigious scientific journals, an illustration of the excellent results of ICM research teams.



## TWO NEW TEAM LEADERS AT ICM

Nicolas Renier joined ICM as head of the “Structural network dynamics” team. Nelson Rebola joined as head of the “Cellular mechanisms in sensory processes” team.



Nicolas Renier



Nelson Rebola

## iMIND, AN INTERNATIONAL MASTER’S PROGRAM AT PIERRE ET MARIE CURIE UNIVERSITY WITH ICM SUPPORT, DEDICATED TO NEURODEGENERATIVE DISEASES

The International Master’s Program in Neurodegenerative Diseases (iMIND) is an international and multidisciplinary 2-year training program geared towards the specific challenges raised by neurodegenerative diseases. iMIND helps students design a tailored course selection with classes and research projects. iMIND brings together numerous national and international partners including some of the most renowned universities: KU Leuven in Belgium, Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE) in Germany, CarloBesta Institute in Milan in Italy, and the MNI, Montreal Neurological Institute and Hospital in Canada.



## A HEALTHTECH PROGRAM ON THE STATION F CAMPUS WITH IPEPS-ICM

iPEPS-ICM was selected as Station F’s healthcare partner to develop medtech and e-health programs. The partnership is a great opportunity to bring Station F’s digital expertise together with ICM’s scientific and medical talent in the field of connected health. Thanks to this partnership, innovative digital solutions should be made available to patients and the market more quickly.



## SEGOLENE AYME JOINS ICM

Ségolène Aymé, a doctor, geneticist and epidemiologist and creator of the ORPHANET network, the major website dedicated to rare diseases and orphan drugs, joined ICM as an INSERM emeritus researcher. She brings her expertise to ICM to help direct “search, find and cure” to the 800 patients affected by a rare neurological disease.



INRIA PROJECT LAB: NEUROMARKERS

■ INRIA Project Labs help launch ambitious and multidisciplinary research projects that incorporate various skills. 5 teams from ICM were selected for their expertise, a good complement to skills developed at INRIA (National Research Institute in IT and Automation) to be at the heart of a project to identify imaging and genetic biomarkers of neurodegenerative diseases for use in clinical trials. The project touches on different fields including statistics, brain imaging, bio-informatics, data modelling and genomics. INRIA Project Lab: Neuromarkers aims at designing new IT and statistical approaches to predict disease onset and prognosis.



CERTIFICATION OF AN INTEGRATED CANCER RESEARCH CENTER

■ A new Integrated Cancer Research Center (SIRIC) received National Cancer Institute (INCa) certification. Its director is Professor Marc Sanson (Pitié-Salpêtrière-ICM) and, for the first time since these centers were created, brain tumours are a top priority.



ICM TAKES PART IN THE 3RD EDITION OF NEUROPLANET WITH LE POINT

■ The Neuroplanet forum, dedicated to neuroscience and the brain's extraordinary capabilities, welcomes renowned scientists and experts from various backgrounds to meet with the public for two days filled with conferences, debates and workshops.



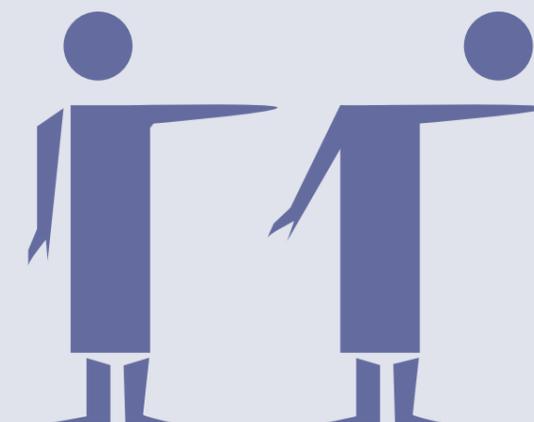
"THE BRAIN TO MARKET" 2017 SUMMER SCHOOL

■ "The Brain To Market" Summer School's 2017 edition was held from September 4th to 8th 2017 at the Brain and Spine Institute on the topic of depression. The week of training takes a novel approach and combines translational neuroscience and entrepreneurial training to give participants the opportunity to understand real-life economic and industrial challenges.



"THE MOVE EUROPE": LEARNING NEUROLOGY THROUGH MIME

■ The Move is an innovative teaching technique developed by Emmanuel Flamand-Roze, neurologist and ICM researcher, that helps medical school students better understand neurological disease symptoms. Using mime, this interactive teaching method helps understand and memorise clinical signs. The Move was a recipient of the second edition of the PEPS awards for innovation in teaching implemented by the Ministry of Higher Education, Research and Innovation in the "certificate of excellence" category.

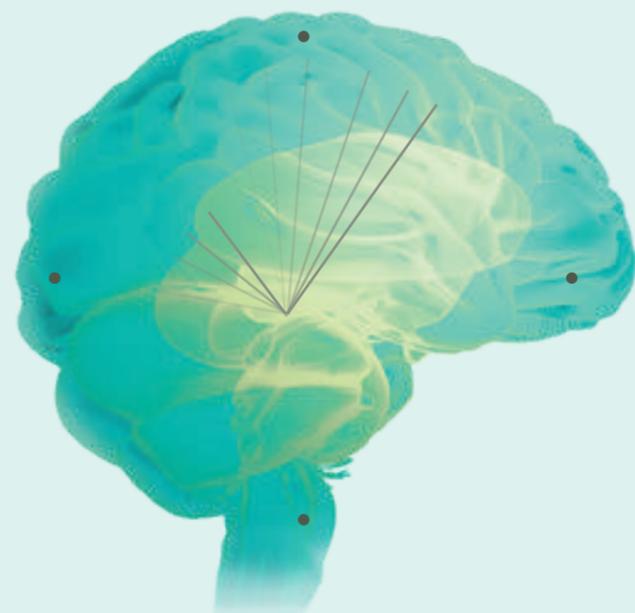


BIO SERENITY, ICM-INCUBATED STARTUP AND FRENCH E-HEALTH CHAMPION, RAISES 15 MILLION EUROS

■ BioSerenity, a startup hosted at iPEPS-ICM, develops smart clothing for patients with epilepsy. The company recently closed a series A funding round totalling 15M€, led by LBO France with the PSIM fund managed by BPI France in its Future Investments Program and with long-time shareholder Iinvest Partners.



# GREAT STRIDES AND MAJOR BREAKTHROUGHS



## SEARCHING TAKES TIME, AND TIME IS RARE FOR PATIENTS.

WHETHER IDENTIFYING A GENE OR DEVELOPING TREATMENT, THE RESEARCH PROCESS IS A LONG ROAD, WITH MANY COMPONENTS AND CONSTRAINTS.

ONE OF ICM'S TOP PRIORITIES IS TO DECREASE THE AMOUNT OF TIME BETWEEN A DISCOVERY, EVEN IF IT IS FUNDAMENTAL, AND ITS APPLICATION. EACH STEP, EACH BIT OF PROGRESS, EACH BREAKTHROUGH, BRINGS RENEWED HOPE.

WE ARE PROUD TO SHARE MAJOR DISCOVERIES  
FROM 2017 WITH YOU.

## ON THE RESEARCH SIDE: SEARCH

### 1. FRAGILE X SYNDROME A MECHANISM UNCOVERED

The team led by Bassem Hassan at ICM in collaboration with the VIB at KU Leuven and a Norwegian team found that lack of inhibitory characteristics in specific neurons may be a key mechanism in Fragile X syndrome. They shed new light on the neural process at work in Fragile X Syndrome. This neuronal damage leads to moderate to severe intellectual disabilities, attention deficit and social anxiety. Hyperexcitability of certain neural circuits due to lack of control of their activity could help explain patient symptoms.

Team Bassem Hassan

### 2. MULTIPLE SCLEROSIS MAJOR ROLE OF T LYMPHOCYTES IN MYELIN REGENERATION

A joint study conducted by ICM researchers, Violetta Zujovic, Isabelle Rebeix and Bertrand Fontaine highlighted the key role of T lymphocytes, responsible for inflammation, in the myelin regeneration process. Results pave the way for new treatments based on controlling these cells responsible for each patient's ability to repair their brain lesions. A patent was filed for 3 molecules that help encourage this repair process.

Team Brahim Nait-Oumesmar and Team Bertrand Fontaine

### 3. MULTIPLE SCLEROSIS KEY ROLE OF ENERGY REGULATION

Benedetta Bodini, from the team lead by Bruno Stankoff and Francesca Branzoli at CENIR, succeeded in visualising certain energy intake disruptions in neurons in multiple sclerosis patients. Restoring sufficient energy intake before neuron death could become a key goal in the development of future neuro-protective strategies.

Team Bruno Stankoff, Catherine Lubetzki and CENIR

### 4. HUNTINGTON'S DISEASE GENETIC INFLUENCE ON DISEASE PROGRESSION

ICM researcher Alexandra Durr participated in an international multicenter study with the same patient cohort that validated a new instrument to measure Huntington's disease progression and highlighted mutations in 3 new genes. These results pave the way for new treatment strategies in Huntington's disease and other diseases linked to genetic repeat expansion.

Team Alexis Brice

### 5. BRAIN ORGANISATION OUR BRAIN'S EVOLUTION, JUST LIKE GEOLOGICAL STRATA FROZEN IN TIME!

For the very first time, a study led by Michel Thiebaut de Schotten showed that areas with greater anatomical variability are the same as the areas that developed later in evolution, whereas more stable areas are also the most ancient from an evolutionary point of view. Researchers also found that variations can exist to a greater degree in humans compared to primates for specific areas of the brain. These results strengthen the idea of more important hemispheric specialisation in the human brain, which may be one of the underlying reasons explaining the divergence between humans and other primates.

Team Richard Levy and Bruno Dubois

### 6. ISOELECTRIC COMA NEURONS ARE STILL RESPONSIVE!

A study conducted by Stéphane Charpier was the first to show that in certain deep comas with flat-lined EEGs, where the brain displays no spontaneous electrical activity, and total disappearance of consciousness, neural networks still function and can process information from the surrounding environment. Neurons are thought to be in a silent or dormant state, with a structurally intact brain and interactions between neurons still in place. Neurons could therefore be reactivated by direct stimulation or environmental stimuli.

Team Stéphane Charpier

**7. DE VIVO DISEASE** A NEW BLOOD TEST TO DETECT THE DISEASE

Teams from AP-HP in collaboration with ICM researcher Fanny Mochel (Inserm/CNRS/UPMC) and CNRS-derived startup Metafora Biosystems have developed a diagnostic blood test for De Vivo disease, a rare yet treatable neurological illness. Early diagnosis of the disease will help prevent onset of symptoms including paediatric epilepsy, stunted growth of the cranial circumference, and developmental delay.

**Team Alexis Brice**

**8. ALZHEIMER'S DISEASE** TWO NEW GENES IDENTIFIED IN DISEASE RISK

Professor Alexis Brice and Professor Harald Hampel participated in an international study that identified new genes associated with a risk of developing Alzheimer's Disease. The identified genes find their expression in microglial cells, the brain's main immune cells, and suggest a causal role of the immune system in the disease.

**Team Bruno Dubois and Alexis Brice**

**9. ALZHEIMER'S DISEASE** BRAIN CONNECTIONS AND FREQUENCIES AS POTENTIAL BIOMARKERS

A study conducted by Jeremy Guillon and directed by Fabrizio De Vico Fallani developed a "complex multilayer model" to represent interactions between the different areas of the brain at varying frequencies. Researchers used data from healthy volunteers and patients with Alzheimer's disease to calculate an information diffusion capability score for each area of the brain. This score is significantly lower in patients with Alzheimer's disease, especially in deeper areas of the brain or those involved in memory. Results of the study, conducted in collaboration with the Memory and Alzheimer's Disease Institute (IM2A) suggest that this score could be used as a new non-invasive diagnostic instrument for Alzheimer's disease.

**Team Olivier Colliot and Stanley Durrleman**

**10. COGNITION** EVOLUTION AND HUMAN SOCIAL COGNITION

Jean Daunizeau, Shelly Masi from the National Museum of Natural History and colleagues compared levels of theory of mind sophistication, the ability to understand the mental states of others, in seven non-human primate species from lemurs to great apes. Results of the study contradict the general hypothesis that states that theory of mind was built to solve problems related to the social groups animals live in. Researchers found that the evolution of theory of mind may be determined first and foremost by limiting neurobiological factors such as brain size. They also identified an evolution gap between theory of mind capabilities in great apes and humans.

**Team Jean Daunizeau**

# ON THE CLINICAL SIDE: PREDICT AND CURE



## PREDICT

**1. ISOLATED CORPUS CALLOSUM AGENESIS** DISCOVERY OF A GENE INVOLVED IN A SPECIFIC BRAIN DEFECT, WHEN NOTHING LINKS THE TWO HEMISPHERES

Christel Depienne and colleagues were the first to identify DCC gene mutations, inherited in a dominant pattern and involved in pathological brain development. Results may have a major impact in prenatal diagnosis of the disease and diagnosis of associated intellectual disabilities.

**Team Alexis Brice**

**2. FRONTOTEMPORAL LOBAR DEGENERATION** IDENTIFICATION OF EARLY MARKERS FOR NEURODEGENERATIVE DISEASE IN AT-RISK INDIVIDUALS

Isabelle Le Ber, Anne Bertrand and Olivier Colliot conducted research at ICM at Pitié-Salpêtrière Hospital supported by AP-HP and found that those carrying mutation c9orf72, and therefore at risk of developing frontotemporal lobar degeneration (FTD) or amyotrophic lateral sclerosis (ALS) display very early cerebral, anatomical, and structural alterations without any other clinical sign of the disease. The



discovery of these early-stage biomarkers may help develop models to test treatment efficacy on onset or absence of symptoms.

**Team Alexis Brice and Olivier Colliot**

**3. PARKINSON'S DISEASE** AN INSTRUMENT TO PREDICT COGNITIVE DECLINE

Cognitive decline is one of the most disabling symptoms of Parkinson's disease for some patients. Jean-Christophe Corvol and other doctors and researchers from ICM participated in an international study that designed a clinical and genetic score with predictive value for cognitive decline in affected patients. The score is precise and can be reproduced, and predicts appearance of cognitive disorders within 10 years after disease onset. This instrument may help include patients in targeted clinical trials and give them the opportunity to receive early and personalised treatment.

**Team Alexis Brice**

**4. ALZHEIMER'S DISEASE** AN IMPORTANT INDICATOR IN PRECLINICAL FORMS OF THE DISEASE

A study carried out by ICM and the Memory and Alzheimer's Disease Institute (Institut de la Mémoire et de la Maladie d'Alzheimer (IM2A)) found that limited awareness of impairment by individuals may represent a specific early marker for Alzheimer's Disease. Indeed, individuals with the lowest levels of awareness of their cognitive impairment generally exhibited more objective signs of Alzheimer's disease and signs visible on an MRI, including increased amyloid aggregation and weaker cortical metabolism. These results may allow more targeted clinical trials in the future with better treatment for patients.

**Team Bruno Dubois**

**5. BRAIN TUMOURS** RAPID MOLECULAR DIAGNOSIS

Molecular classification of cancers has become a common yet very useful instrument for diagnosis, prognosis and selecting a type of treatment. Researchers and clinicians from ICM, Sorbonne University and AP-HP recently highlighted the efficacy of a cutting-edge DNA sequencing technique to analyse brain tumours. It is rapid and produces same-day results, making it a true breakthrough in precision medicine for each and every patient.

**Team Marc Sanson**



**6. CONSCIOUSNESS** IMPROVED ASSESSMENT OF STATE OF CONSCIOUSNESS THROUGH BRAIN-HEART INTERACTION

The team led by Lionel Naccache at ICM implemented a novel approach to assess state of consciousness in patients in comas: exploring interactions between the heart and the brain. « Unconscious » neurovegetative mechanisms, such as breathing and heartbeat, are actually modulated by conscious mechanisms. Perception of an external stimulation, auditory or other, may affect cardiac activity in proportion to the subject's level of consciousness. Researchers found that cardiac cycles are indeed modulated by auditory stimulation only in conscious or minimally conscious patients. They also highlighted that these results can be associated with EEG results with the same type of stimuli. Combining heart rate and EEG activity after external stimulation therefore helps assess state of consciousness and may offer a novel perspective on predicting coma recovery.

**Team Lionel Naccache**

**CURE**

**EPILEPSY** A NEW TREATMENT FOR FOCAL EPILEPSY SEIZURES

A stage 3 clinical trial conducted by neurologist Michel Baulac proved and confirmed efficacy of lacosamide alone to avoid focal epilepsy seizures; focal epilepsy seizures originate in very specific and limited areas of the brain and often affect recently diagnosed patients.

**Team Eric Leguern and Stéphanie Baulac**



## ON THE START-UP SIDE: INNOVATE

### 1 VIDEO GAMES FOR PATIENT REHABILITATION

Is it possible to develop physical rehabilitation and increase or stabilise cognitive capabilities for patients with a neurodegenerative disease or after head trauma using a video game? Apparently so, as demonstrated by the Brain e-Novation LabCom, co-directed by Pierre Foulon from Groupe Genius and Dr Marie-Laure Welter from the ICM, and incubated at ICM. The curapy.com platform was officially launched in 2017 and offers several "serious games", where video games become therapy, that are a type of physical and cognitive rehabilitation for patients with neurological diseases (Parkinson's, Alzheimer's, stroke) at home and on demand. Each game underwent or is currently undergoing clinical and therapeutic assessment on a large patient cohort with motor and cognitive function testing.

### 2 AD SCIENTIAM LAUNCHES MSCOPILOT\*, A MEDICAL DEVICE AND SOFTWARE TO MONITOR MULTIPLE SCLEROSIS

Ad Scientiam, startup incubated at the Brain and Spine Institute (ICM) at Pitié-Salpêtrière Hospital and at Station F, completed the development of its digital solution called MSCopilot\*. This multiple sclerosis monitoring application was developed to allow the patient to take his or her own medical tests right at home, on a smartphone. The clinical score that takes into account patient motor and cognitive capabilities and is usually assessed by a neurologist with a long time between appointments. Self-recording by patients helps determine the stage and severity of the disease with frequent measures. A clinical multicenter study coordinated by Doctor Elisabeth Maillart at ICM's Clinical Investigation Center - CIC is underway for clinical validation of the application.

### 3 BIOSERENITY, FRENCH E-HEALTH CHAMPION, RAISES 15 MILLION EUROS

BioSerenity, a startup incubated at iPEPS-ICM and managed by Pierre-Yves Frouin, develops smart and connected clothing to facilitate in-home diagnosis and care for patients with epilepsy, who are at risk for heart issues, with sleep disorders, or for pregnancy monitoring. The med-tech company currently collaborates with world-renowned hospitals, including Pitié-Salpêtrière Hospital thanks to its presence at ICM, and over 32 hospitals have signed on to use the company's digital solution, the "Neuronaute", for epilepsy monitoring. BioSerenity's e-health systems aim at speeding up diagnosis, providing easier monitoring solutions, and helping improve patient care.

BioSerenity recently completed a round of Series A fundraising for a total of 15 million euros, led by LBO France with Fonds PSIM managed by Bpifrance as part of the Future Investments Program and with long-time shareholder Idinvest Partners. This round of fundraising will help the company's growth and contribute to its international reach to attract investors who are digital innovation and medical innovation experts.

### 4 ARTIFICIAL INTELLIGENCE TO HELP PATIENTS WITH BRAIN LESIONS

The team led by Pascal Pradat-Diehl at Pitié-Salpêtrière Hospital developed a rehabilitation program to treat patients following a stroke or concussion in which patients follow a recipe. For patients with a brain lesion, this type of task is extremely complex as it requires many cognitive capabilities, some of which are altered. The cLLAPS Living Lab at ICM, in collaboration with startup A.I.Mergence incubated at iPEPS-ICM, designed a small companion robot named "BRO" to supervise patients during the recipe either at the hospital or at home. BRO can interact with patients and help them step by step with the recipe. BRO has numerous sensors allowing it to observe the patient's gestures and its artificial intelligence allows it to analyse recorded data. The prototype's first version is currently undergoing testing and initial results are promising.

### 5 THE FUTURE OF SURGERY: HELPING TREATMENTS CROSS THE BLOOD-BRAIN BARRIER

The blood-brain barrier (BBB) is an impermeable cell wall that protects the brain from the body's bacteria and viruses and therefore also prevents drugs from passing through. How can treatments cross the barrier, ensuring higher efficacy, without posing a risk to the brain? Teams from AP-HP, Sorbonne University, INSERM and CarThera, a company with offices at ICM, coordinated by Professor Alexandre Carpentier, neurosurgeon at Pitié-Salpêtrière Hospital, succeeded in using ultrasound technology to render the brain's blood vessels temporarily permeable in patients with a relapsing brain tumour. This innovative technique helps increase diffusion of treatments, especially chemotherapy, within the brain and may present an opportunity to treat other brain diseases. It is currently being tested with Alzheimer's disease patients.

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2. Adaptive human immunity drives remyelination in a mouse model of demyelination. El Behi M et al. *Brain.* 2017 Feb 22.
3. Dysregulation of energy metabolism in multiple sclerosis measured in vivo with diffusion-weighted spectroscopy. Bodini B et al. *Mult Scler.* 2017 Apr 1
4. Identification of genetic variants associated with Huntington's disease progression: a genome-wide association study. Moss DJH et al. *Lancet Neurol.* 2017 Jun 19
5. Structural variability across the primate brain and its relationship to evolution. Paula L et al. *Cereb Cortex.* 2017 Oct 13
6. Cortical neurons and networks are dormant but fully responsive during isoelectric brain state. Altwegg-Boussac T et al. *Brain.* 2017 Sep 1
7. A simple blood test expedites the diagnosis of glucose transporter type 1 deficiency syndrome. Gras D et al. *Ann Neurol.* 2017 Jul
8. Rare coding variants in *PLCG2*, *ABI3*, and *TREM2* implicate microglial-mediated innate immunity in Alzheimer's disease. Sims R et al. *Nat Genet.* 2017 Jul 17.



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10. Reading wild minds: A computational assay of Theory of Mind sophistication across seven primate species. Devaine M et al. *PLoS Comput Biol.* 2017 Nov 7
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12. Efficacy, safety, and tolerability of lacosamide monotherapy versus controlled-release carbamazepine in patients with newly diagnosed epilepsy: a phase 3, randomised, double-blind, non-inferiority trial. Baulac M et al. *Lancet Neurol.* 2017 Jan 16
13. Early Cognitive, Structural, and Microstructural Changes in Presymptomatic *C9orf72* Carriers Younger Than 40 Years. Bertrand A et al. *JAMA Neurol.* 2018 Feb 1
14. Prediction of cognition in Parkinson's disease with a clinical-genetic score: a longitudinal analysis of nine cohorts. Ganqiang Liu et al. *The Lancet Neurology*, June 16, 2017



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16. Same-day genomic and epigenomic diagnosis of brain tumors using real-time nanopore sequencing. Euskirchen P et al. *Acta Neuropathol.* 2017 Jun 21.
17. Brain-heart interactions reveal consciousness in non-communicating patients. Raimondo F et al. *Ann Neurol.* 2017 Sep 11

## 2017: A CLOSER LOOK



**THE RESEARCH ECOSYSTEM AT ICM IS EXPANDING AND DIVERSIFYING TO GIVE MEANING TO THE IDEA OF “ONGOING INNOVATION” ON A DAILY BASIS.**

BECAUSE RESEARCH ALSO MEANS CREATION, WE IMPLEMENTED INNOVATIVE PROGRAMS TO FOSTER COLLABORATION BETWEEN TEAMS WITH COMPLEMENTARY EXPERTISE. WE ALSO JOINED THE BIG DATA MOVEMENT BY DEVELOPING NEUROINFORMATICS, RECRUITED TWO NEW EXPERT TEAMS TO JOIN OUR RESEARCHERS, RECOGNISED YEARLY FOR THEIR TALENT. WE FOCUSED OUR EFFORTS ON RESEARCH APPLICATIONS, PLACING PATIENTS AT THE HEART OF OUR PRIORITIES, AND SUPPORTED ENTREPRENEURSHIP AS WELL AS PARTNERSHIPS WITH INTERNATIONAL RESEARCH CENTERS.

**DISCOVER HIGHLIGHTS FROM A YEAR OF SURPRISES!**



## NEW COLLABORATIONS: BIG BRAIN THEORY PROGRAM

“Big Brain Theory” was launched in June 2015 by ICM and IHU-A-ICM. Its goal? Fund ambitious, innovative, multidisciplinary and high-risk research projects. How does it work? By fostering collaborations between ICM researchers and clinicians from various teams with complementary expertise. 15 projects were financed in 2015, several of which have already proven very promising. In 2017, 8 new projects were selected. Let’s take a look at the future of science...

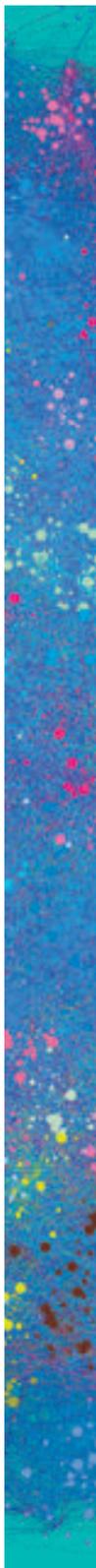
### PREDICTIVE MODELLING FOR PRECISION MEDICINE

#### 1 ATTACK : MODELLING RECUPERATION AFTER A STROKE

How do individuals recuperate after a stroke? How does the brain reorganise itself from a functional standpoint to regain lost motor function?

Two main goals: increase our understanding of brain reorganisation by modelling new connections among neurons and identify markers for these new connections to predict potential motor recuperation for each patient and adapt patient care accordingly.

By Fabrizio de Vico Fallani, expert in complex network modelling and Charlotte Rosso, neurologist with stroke expertise



**2 PD-PREDICT : PREDICTING LOSS OF IMPULSE CONTROL LINKED TO PARKINSON'S DISEASE TREATMENT**

Parkinson's disease treatment is based on dopamine replacements and leads to impulse control disorders in around 15 to 20% of patients. Why does treatment cause this disorder in some individuals and not others? Researchers are aiming to identify genetic variants and understand the process that leads to behavioural disorders based on research with several international cohorts. Results will help group patients based on their genetic profile depending on their level of risk to adapt therapy accordingly and prevent onset of these disorders.

**By Jean-Christophe Corvol, Professor of Neurology and Olivier Colliot, Expert in mathematical modelling**

**3 PPM-PD : TOWARDS PERSONALISED MEDICAL CARE FOR PARKINSON'S DISEASE**

The aim of this project is to collect and analyse clinical, behavioural, genetic, metabolic, and brain imaging data acquired with a large patient cohort using mathematical modelling. Modelling results should help identify biomarkers to recognise early signs of disease onset in at-risk individuals and monitor disease progression. With time, researchers hope to develop a personalised model for disease progression to adapt patient care to each profile using a targeted approach.

**By Stanley Durrleman, expert in mathematical modelling and Stéphane Lehericy, neuroradiologist and medical imaging expert**

**SEARCHING TO UNDERSTAND: FROM CLINICAL SIGNS TO BIOLOGY**

**4 COUNTING FLIES : THE ADVENT OF INDIVIDUALITY**

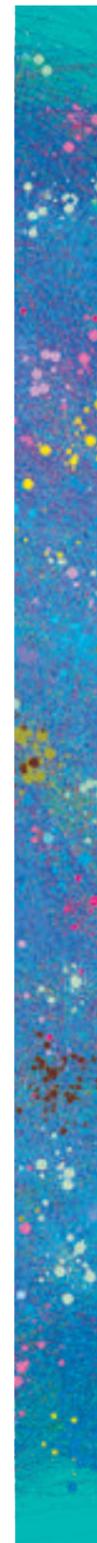
How does individual variability emerge in the brain? What are consequences of small variations in brain development on individual behaviour? The goal is to understand how brain development influences or causes certain character traits. Researchers will study the appearance of individuality in fruit flies in a laboratory setting, observing their visual pathways and behavioural differences depending on what they see. These discoveries may have an impact on research on psychiatric disorders.

**By Bassem Hassan, molecular geneticist and expert in development and Laurent Cohen, neurologist and expert in cognition**

**5 CURLY-FLOW : UNDERSTANDING WHAT CAUSES SCOLIOSIS**

Scoliosis affects 4% of the population with, very often, no known cause. Using a new model and cutting-edge imaging techniques, this projects aims at identifying mechanisms affected during development that may lead to spine malformation. Answers to this question could help understand how the body controls implementation and posture of the spine during embryonic and juvenile development.

**By Pierre-Luc Bardet, researcher and expert in development and Nicolas Renier, researcher and expert in cell imaging**



**6 BIO-FATIGUE : BIOLOGICAL FOUNDATIONS OF MENTAL FATIGUE**

What is mental fatigue? How can it be defined from a biological standpoint? This project aims at understanding the biological mechanisms within the brain that cause mental fatigue, using cutting-edge brain imaging techniques. Identifying these biological changes could help identify predictive and diagnostic markers as well as potential treatments for pathologies including depression and burnout, where mental fatigue is a major clinical symptom.

**By Mathias Pessiglione, neurobiologist and psychologist and Fanny Mochel, neurologist and expert in metabolic disorders**

**7 MOCONET : CORTICAL NETWORKS IN DOWN SYNDROME MODELS**

What are neural networks like in Down syndrome? Are cortical networks altered as a whole, or are specific and very local networks affected? Research has found that halting inhibition in certain synapses (where neurons communicate) helps improve cognitive deficit in experimental Down syndrome models. This project aims at studying synapses in the prefrontal cortex in mouse models of Down syndrome to assess behavioural changes after halting activity in specific synapses.

**By Alberto Bacci, neurophysiologist and Marie-Claude Potier, neuropharmacologist**

**8 DECIMOTIV : MOTIVATIONAL CONTROL IN DECISION-MAKING**

What makes us consider pros and cons when making a decision? This project aims at developing and validating a tool for quantitative and objective assessment of decision-making control. On the long term, research could help study certain neurological and psychiatric pathologies where impulsive and/or apathetic behaviour may be linked to lack of decision-making control. This is the case in Parkinson's disease, frontotemporal dementia, attention deficit disorder, obsessive compulsive disorder, and more.

**By Jean Daunizeau, expert in computational modelling and Eric Burguière, neurophysiologist and expert in behaviour and optogenetics**



# TOWARDS MEDICINE OF THE FUTURE: NEUROINFORMATICS

ICM's new neuroinformatics center aims at collecting and analysing scientific and medical data from research and clinical work with patients using an open and multidisciplinary approach. Using Big Data with powerful scientific and statistic calculation tool will lead to improved understanding of the human brain, new treatment strategies, and the development of support for diagnosis and treatment selection. Stanley Durrleman, coordinator, explains the center's goals and priorities.

## WHAT IS THE NEUROINFORMATICS CENTER?

It is a virtual, open center designed to put those managing and using data in touch. It aims at streamlining and sharing best practices in data management at ICM and is based on research as a partnership and coordinating researchers, engineers, doctors, IT specialists and technicians. At its heart is a team of 5 individuals who meet every week to monitor progress and present progress reports every three

months. The team is tasked with making shared tools available to all and with supporting research teams in the development of their data collecting and analysis.

A network of "neuroinformatics correspondents" ensures that each research team and platform is in contact with the center if needed. The team works hand in hand with the Institute's bio-statistics platform, iConics, and with the IT department.

## DO COMMUNICATION AND INTERACTION PLAY A KEY ROLE IN DEVELOPING A VIRTUAL CENTER?

We are implementing a number of specific activities to make our center thrive: trainings, seminars, and neuroinformatics coffee sessions will be launched in 2018 to create a community feel around the center and foster interactions between ICM teams. The center offers neuroinformatics training on topics including high-performance calculations and statistics. A series of workshops with CentraleSupélec was implemented in 2017. In 2018, we are planning on having neuroimaging training for CENIR as well as an open science symposium. The neuroinformatics center is also here to support all ICM initiatives.

In 2018, we will launch a dedicated website to deliver updated information on activities at the center.

## DOES THE CENTER PARTNER WITH OUTSIDE INITIATIVES?

The Center is open to ICM teams as well as those from outside ICM. We work with some obvious partners, such as AP-HP and its data warehouse, as well as INSERM and UPMC with whom we are working on a shared access to calculation and storage facilities. We believe in open and collaborative research. The center currently has access to outside databases for research and promotes data and software sharing throughout the international scientific community based on rules to be defined.

## WHAT IS THE CENTER'S MAIN AMBITION?

Our goal is to build the world's largest neuroscience research data warehouse. Availability and use of this data on an international level will help speed up research on nervous system diseases. Cross-exploitation of data may help identify new correlations and new hypotheses for research. It will also help us develop decision-making tools for doctors, to improve diagnosis and adapt patient care.



ONGOING PROJECTS THANKS TO THE GENEROUS SUPPORT OF ABEONA FOUNDATION:

### The MSBioProgress Project

uses high-throughput genomics and brain imaging to predict multiple sclerosis progression.

### The Brain@Scale Project

is developing a new algorithm to improve diagnosis of neurodegenerative diseases using medical imaging.

# NEW TALENTS IN RESEARCH: RECRUITMENT OF TWO NEW TEAMS

In 2017, ICM welcomed two new teams: one led by Nicolas Renier on “Structural network dynamics” and the other led by Nelson Rebola on “Cellular mechanisms in sensory processing”.



NICOLAS RENIER

STRUCTURAL NETWORK  
DYNAMICS

## CAN YOU TELL US ABOUT YOUR BACKGROUND PRIOR TO JOINING ICM?

■ **N. Renier** : I did my thesis at the Vision Institute with Alain Chédotal, who is focused on nervous system development and axon guidance. I wanted to understand how flaws in guidance during development were corrected by network plasticity in adults. I then joined Marc Tessier-Lavigne’s lab at the Rockefeller University in New York, renowned for its work on axon guidance molecules.

I wanted to improve our visualisation of axons during development, so I developed improvements on existing 3D imaging techniques, and more specifically on selective plane illumination microscope techniques, to study neural networks in intact-brain analysis.

■ **N. Rebola** : I wrote my thesis in Professor Rodrigo Cunha’s group in Coimbra (Portugal) on the impact of adenosine receptors on normal and pathological brain function. I then joined Dr Christophe Mulle’s laboratory in Bordeaux as a post-doc researcher on synaptic physiology, and more specifically synaptic plasticity in hippocampal circuits. In 2012, I was hired by CNRS and joined Dr David DiGregorio’s laboratory at Pasteur Institute, where I studied cellular mechanisms involved in synaptic transmission and neural integration of information using cutting-edge imaging.

## WHAT ARE YOU WORKING ON AT ICM?

■ **N. Rebola** : Integrating sensory information is a fundamental characteristic of our brain and is necessary to carry out daily actions. Analysing information coming from various

sources such as proprioception, sight, touch, and smell and turning them into a series of actions is essential to our interactions with our environment. However, cellular mechanisms involved in this cerebral processing are relatively unknown. At the lab, we are planning on using a combination of electrophysiology and imaging techniques both in vivo and in vitro to study the cellular aspects of how the brain analyses and integrates sensory information.

■ **N. Renier** : My team is working on large-scale overhauls in neural network structure in adults. We are hoping to understand how learning and adapting in the adult brain are illustrated by changes in neuron structure and connectivity over time.

We are looking at the question from two different perspectives. First of all, from a molecular and cellular perspective, which factors ensure survival and support of the many branches in adult neurons under normal conditions? Next, from a dynamic perspective, which factors encourage changes in neuron connectivity by creating new branches or with controlled destruction of other branches?

We are also studying these questions on a larger scale and attempting to understand if certain behavioural changes in adult mammals can be explained by massive overhauls in connections between specific groups of neurons.

## WHAT BROUGHT YOU TO ICM?

■ **N. Renier & N. Rebola** : ICM is the top neuroscience research facility in France. I’m motivated by the high quality of research conducted at the Institute, of course, but also by its ambition to become even better and compete with the greatest European research facilities. A close relationship with the hospital, and ICM’s strongly translational environment, are major assets that I would like to work with in the future. ICM is a unique institute where excellence in neuroscience research is integrated at the heart of a major European hospital, with a long tradition in treating brain diseases. Beyond clinical and translational research, ICM is



NELSON REBOLA

MÉCANISMES CELLULAIRES  
MECHANISMS IN  
SENSORY PROCESSING

home to outstanding fundamental research. Researchers work on neuroscientific issues at all levels: molecular, genetic, cellular, synaptic, on a circuit level, on systems, behaviour, as well as human cognition. The constant exchange of ideas between research teams, each with their own diverse experiences, is a wonderful way of looking at scientific questioning under different perspectives.

# EXCELLENCE ACKNOWLEDGED: PRIZES AND AWARDS

Each year, ICM researchers are acknowledged for their talent and efficacy among the scientific community and outside of it as well. Here are some of the main awards received in 2017.



■ **Carlos Paras**, researcher - Recipient of the 2017 **Prix Marie-Ange Bouvet-Labruyère 2017**.



■ **Nicolas Renier**, ICM team leader, received an **ERC Starting Grant** for his research project dedicated to understanding neuron connection stability in adult brains. He is also a recipient of the 2017 **"Emergence(s)"** award for his project on "Long-term remodelling mechanisms of neural networks in the adult brain".



■ **Nelson Rebola**, ICM team leader, received an **ERC Starting Grant** for his project on the "Impact of NMDA receptor diversity in sensory information processing".



■ **Emilie Poirion and Charline Benoît**, doctoral students in Team Bruno Stankoff and Catherine Lubetzki, were rewarded for the presentations on multiple sclerosis at the **international ECTRIMS-ACTRIMS congress**.



■ **Benedetta Bodini**, neurologist and researcher in Team Bruno Stankoff and Catherine Lubetzki at ICM, received the 2017 **Prix Rita Levi-Montalcini**. This award acknowledges Benedetta Bodini and Bruno Stankoff's work for the past 5 years on a new molecular imaging technique to understand development and progression of multiple sclerosis.



■ **The NRJ Foundation for neuroscience**, under the aegis of the **Institut de France**, acknowledged research on the contribution of genomics to classification, understanding and care of adult glial tumours by naming **Professor Jean-Yves Delattre**, Director of the Nervous System Diseases Unit at the Pitié-Salpêtrière Hospital and Medical Director at ICM, recipient of their Scientific Award.



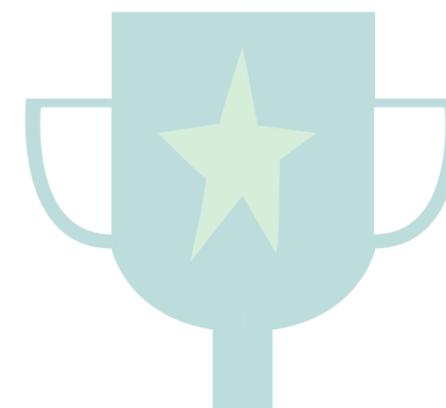
■ **Claire Wyart**, ICM team leader, received an award from **the Fondation Schlumberger for Research & Education**.



■ **Ségolène Aymé** received an award from the **European Society for Human Genetics**, acknowledging Professor Aymé's excellence in the field of rare diseases and the development of public and professional policy. She pioneered many projects pertaining to patient care, research, and education on rare diseases in Europe and beyond. ESHG also acknowledges her important contributions to the Society as President of the Professional and Public Policy Committee.



■ **Marie-Claude Potier**, ICM team leader, and **Luce Dauphinot**, research engineer, received **the SATT Lutec Trophy** for their involvement in the "SCM Made Easy" transfer project.



# RESEARCH AND CARE: PATIENTS AS A PRIMARY CONCERN

THE INSTITUTE'S 700 RESEARCHERS DEDICATED THEIR ENERGY TO ONE SINGLE PRIORITY, EVERY SINGLE DAY: DISCOVERING TREATMENTS FOR PATIENTS.

The Clinical Investigation Center - CIC (INSERM, AP-HP), housed on the first floor of ICM, is an incredible bridge between research and care. It help develop and approve innovative treatment for patients affected by neurological diseases. ICM and Pitié-Salpêtrière Hospital are allies in neuroscience, bringing together clinical and scientific strengths to cure brain diseases by developing new resources for improved patient care and faster access to treatment innovations developed at ICM and other international laboratories. At the core of these innovations is the collaboration between key players.



## 1 CLINICAL INVESTIGATION CENTER - CIC

“CLINICAL RESEARCH FOLLOWS BIOMEDICAL RESEARCH AND GOES FROM UNDERSTANDING DISEASE MECHANISMS AND IDENTIFYING TREATMENTS TO ASSESSING TREATMENT EFFICACY IN PATIENTS.”

Professor Jean-Christophe Corvol, CIC Director

CIC is a clinical research platform that brings together ICM researchers, neurologists, and psychiatrists from the Nervous System Diseases Hub at Pitié-Salpêtrière Hospital. CIC is also involved in national and international clinical research networks.

### PREDICT

In many neurodegenerative diseases, the physiopathological process begins years or even decades before the first symptoms appear. Acting as early as possible to prevent onset of symptoms is a major challenge. Several cohorts with individuals at risk for neurodegenerative diseases were implemented, including INSIGHT for Alzheimer's disease with preliminary results under analysis, PREVDEMALS for frontotemporal lobar degeneration and amyotrophic lateral sclerosis - ALS, and ICEBERG for Parkinson's disease. Another major challenge is predicting how severe the disease will be. CIC participated in studies to identify imaging markers for lesions in the brain stem to predict Parkinson's disease progression and develop a tool to predict cognitive decline.

### SUPPORT

In Huntington's disease, the WIN-HD trial is attempting to decrypt changes

in white matter that take place years before any visible clinical symptoms. These changes may place a key role in the appearance of symptoms. MSCopilot, the multiple sclerosis monitoring app developed by Ad Scientiam, an ICM-incubated startup, is currently involved in a multicenter clinical trial coordinated by Dr Elisabeth Maillart and conducted in part at CIC. A respiratory function trial assessment will begin soon as well; as respiratory failure is the leading cause of death in multiple sclerosis. As for epilepsy monitoring, a trial in collaboration with BioSerenity using a smart cap developed by the company began in 2017.

### PROTECT

A multicenter study coordinated by Professor Jean-Christophe Corvol in collaboration with IPSEN laboratories, the NS-Park/FCRIN network and ICM's DNA bank is currently underway to test a new neuroprotective treatment for a specific type of Parkinson's disease, ODS2005294a. ICM is also involved in a study to test deferiprone, an iron chelator, that supposedly lowers iron in dopaminergic neurons with neuroprotective effects. The study, coordinated by Professor Devos at

### CIC BY THE NUMBERS

80 ONGOING CLINICAL TRIALS  
1935 PARTICIPATING PATIENTS

- 1 CHIEF DOCTOR
- 1 DEPUTY DOCTOR
- 1 HEALTHCARE MANAGER
- 4 NEUROLOGISTS
- 2 NEUROPSYCHOLOGISTS
- 6 RESEARCH NURSES
- 2 ASSISTANT NURSES
- 3 LABORATORY TECHNICIANS
- 3 PROJECT MANAGERS
- 4 CLINICAL TRIAL TECHNICIANS
- 1 PHARMACY RESIDENT
- 1 STATISTICIAN
- 6 CLINICAL RESEARCH REPRESENTATIVES
- 6 HOSPITAL BEDS
- 11 DAYBEDS
- 6 APPOINTMENT ROOMS
- 1 BIOLOGICAL SAMPLE STORAGE AND ANALYSIS LABORATORY
- 1 METHODOLOGY EXPERTISE FOR DEVELOPMENT AND SUPPORT OF CLINICAL TRIALS (IDENTIFICATION OF PARTICIPATING PATIENTS, LENGTH OF TRIAL, DOSAGE, CONSENT, OBSERVATIONS...)

## ZOOM ON 102 CLINICAL TRIALS

### PARKINSON'S

20 CLINICAL TRIALS, 924 PATIENTS

### ALZHEIMER'S

13 CLINICAL TRIALS

### TUMOURS

26 CLINICAL TRIALS

### ALS

8 CLINICAL TRIALS, 101 PATIENTS

### STROKE

1 CLINICAL TRIAL, 47 PATIENTS

### DYSTONIA

1 CLINICAL TRIAL

### SUPRANUCLEAR PALSY

3 CLINICAL TRIALS, 54 PATIENTS

### ESSENTIAL/ORTHOSTATIC TREMOR

4 CLINICAL TRIALS, 52 PATIENTS

### DEMENTIA

5 CLINICAL TRIALS, 160 PATIENTS

### NEUROGENETICS

3 CLINICAL TRIALS, 155 PATIENTS

### MULTIPLE SCLEROSIS

14 CLINICAL TRIALS, 173 PATIENTS

### NEUROPSYCHIATRY

4 CLINICAL TRIALS, 31 PATIENTS

Lille CHU Hospital and funded by the European Union, has 24 participating sites in 8 European countries including 8 centers in the NS-PARK/FCRIN network. Three trials are underway for progressive supranuclear palsy, a rare disease.

### REPAIR

When brain lesions and clinical symptoms have appeared, solutions are needed to repair damage and lessen or eradicate symptoms.

Several clinical trials in the field of amyotrophic lateral sclerosis, or ALS, have already taken place to test a new drug and the effect of electrical stimulation of the diaphragm. However, results were negative. More clinical trials are planned for the near future, including gene therapy. In 2017, CIC participated in a Phase III clinical trial that confirmed lacosamide efficacy to treat focal epilepsy seizures on its own.

CIC was also involved in a key trial on Tourette syndrome that highlighted positive effects of deep brain stimulation. In the field of multiple sclerosis, promyelinating molecules will be tested in 2018 to assess myelin repair capabilities. In psychiatry, the Nervous System Diseases hub is coordinating the Paris MEM (Random-Access Memory) study with patients affected by post-traumatic stress disorder. The study was launched in September 2016 with AP-HP and is still recruiting patients beyond the 250 recruited up to date. This innovative therapy blends psychotherapy and a drug to lower the emotional burden related to the traumatic event, and may halt the encoding process in long-term memory. Additionally, two studies on stimulation techniques ended in 2017. The first aimed at finding the best target for Obsessive-Compulsive Disorder (OCD) treatment using deep brain stimulation. The second study used transcranial magnetic stimulation of the prefrontal cortex, with or without neuroimaging assistance, to treat depression. Results will be published in 2018.

### A PROACTIVE ROLE IN EDUCATION FOR CIC

CIC is fully involved in training doctors and medical school students from their very first years, with initiation to research. CIC also takes part in "The Move Europe", a neurology teaching program that uses mime, as well as resident exchanges with Yale University (United States). Doctors from across Europe also come to CIC to learn and work.

*"Our goal is to encourage new callings and raise awareness on research throughout medical school."*

**Dr. Céline Louapre, CIC Medical Officer**

Finally, Neurotrial and Neurocatalyst, two key programs for ICM and IHU-A-ICM, were launched in partnership with CIC. They aim at funding clinical proofs of concept for innovative medical technology or drug repositioning. Competitive funding is open to Institute researchers and clinicians hoping to assess a new treatment's efficacy or to assess the effect of one drug on a disease other than the one it was originally developed for.

## 2 INNOVATION IN PATIENT CARE

” Our healthcare system is considered as one of the best in the world. And it is, when it comes to equal access to care and our medical practice. In France, public medical care ensures that every citizen is taken care of regardless of their wealth, and we must make sure this never changes. However, we are not as strong when it comes to contributing to medical innovation: in this field, the main English-speaking countries lead the way. Our challenge is to reach their level and keep up with them while preserving our healthcare system’s qualities. ”

Professor Jean-Yves Delattre, ICM Medical Director

### CAP NEURO HUB: SUPPORTING AND CARING FOR NEUROLOGICAL DISABILITY

#### PROJECTS SUPPORTED WITHIN THE IHU PROGRAM



Each neurological disease has its own characteristics, yet they all share a foundation: neurological disability and its support.

■ With so many players and facilities in the area, how do we identify the best services for a patient’s specific needs? Cap Neuro Hub was created to support healthcare professionals to find the best care for individuals with neurological disabilities.

■ Cap Neuro Hub has cross-functional expertise on degenerative or traumatic neurological disability as well as solid knowledge of the available facilities to ensure continued healthcare as well as social support. The aim is to make the best services available to patients to assist them with their disability.

■ Cap Neuro Hub is funded on an experimental basis by the Ile de France Regional Healthcare Agency (ARS IdF) and ICM within the IHU program.

### BEHAVIOURAL NEURO-PSYCHIATRY UNIT - UNPC

#### CARING FOR BEHAVIOURAL DISORDERS

The Behavioural Neuro-Psychiatry Unit opened in 2013 at ICM with support from the IHU program in collaboration with AP-HP Pitié Salpêtrière Hospital.

Behavioural disorders (apathy, disinhibition, emotional or eating disorders...) are major symptoms in nervous system diseases. Behavioural disorders are still misunderstood, leading to complications in patient care and may lead to a disruption in long-

term care. To improve our understanding of where these disorders come and what their mechanisms are, and to find possible treatments, neurologists, psychiatrists, and researchers work hand in hand within the unit.

The unit is part of the Nervous System Diseases Hub and has 6 weekday hospital beds. The Behavioural Neuro-Psychiatry Unit has made it possible:

■ To open a recruitment pool

for patients with diseases requiring neuropsychiatric care;

■ To implement clinical research projects on apathy and motivation with patient cohorts. In 2017, a cohort of patients with behavioural disorders, mostly in frontotemporal dementia, was set up and is currently assessed by ICM research teams in collaboration with the Prisme platform;

■ To brainstorm future research

programs on neuro-behavioural disorders in nervous system diseases. Discussions between neurologists and psychiatrists improves patient care, with improved diagnosis and tailored treatment options.

### INNOVATION AT THE HEART OF THE NERVOUS SYSTEM DISEASES HUB

■ The Jump Program, coordinated by Professor Baulac and Professor Flamand Roze, is a day hospital to transition from paediatrics to adult care for young adults. The program was implemented a year and a half ago, with 150 patients included up to date.

■ The Neurosex Project gives patients with neurological diseases the opportunity to meet with nurses for sexual health appointments. The goal of the project is to tackle sexual concerns, difficulties, disorders or dysfunctions for patients with multiple sclerosis (Professor Lubetzki) and gliomas (Professor Khe Hoang-Xuan).

■ Docfeeling is a study launched by Professor Naccache aimed at comparing perceived assessment of patient state of consciousness by nursing staff for coma patients with assessment using a medical device.

### CLLAPS LIVING LAB: BUILDING MEDICAL INNOVATIONS OF THE FUTURE, TOGETHER

■ The collaborative platform prioritises co-creation of “futuristic” medical technology with patients, medical and paramedical staff, and experts in innovation and neuro-technology to improve quality of life for individuals living with a neurological disease.

## HOW IS INNOVATION BUILT AT THE CLLAPS LIVING LAB? THE STORY OF THE GAZU CANE



#### THE PROBLEM

A common issue in Parkinson’s Disease is known as “freezing”: individuals find it difficult to start walking and take the first step, and feet stay firmly anchored on the ground.

#### THE CREATIVE PATIENT

A patient with Parkinson’s disease noticed that faced with an obstacle, he has no trouble initiating his first steps. He made a few adjustments to his cane, adding a laser that draws a line on the ground to mimic an obstacle, helping him initiate a step.

#### THE ENGINEER

This device could help many patients in their daily life: we created an easy-to-use device, together, for patients.



#### THE ASSISTANT NURSE

Device usability testing was coordinated by an assistant nurse, and highlighted that an extra person is necessary to set up the device.

#### THE DOCTOR

A doctor with expertise in Parkinson’s Disease confirmed that this is a frequent symptom.

#### THE ICM NEUROSCIENCE EXPERT

Understanding the underlying mechanisms (when faced with an obstacle, another part of the brain that is not affected by the disease is enlisted) was essential in developing the right solution.

#### THE DEVICE

A tutorial for building the device was made available to all patients.

#### AN INNOVATION

The affected individual and a helper build the device together, for a price that is below market prices. This initiative also encourages social connections.





# SCIENCE AND ENTREPRENEURSHIP: ICM, DRIVING INNOVATION

THE RESEARCH AND TECHNOLOGY OFFICE AT ICM TRANSFORMS RESEARCH RESULTS INTO PRODUCTS AND NEW SOLUTIONS. THE OFFICE HAS 12 MEMBERS AND HAS SET 3 MAJOR POINTS OF FOCUS.

## ACCELERATING DEVELOPMENT OF NEW DRUGS

To develop new treatment efficiently and quickly, the team detects ICM innovations, searches for candidate drugs with potential, develops partnerships with industrial manufacturers and implements “maturation” programs. Neurocatalyst and Neurotrials, for example, confirm treatment potential for these new drugs. In 2017, 4 new molecules were identified and are currently undergoing development for Parkinson’s and Alzheimer’s disease, multiple sclerosis and spastic paraplegia.

## STARTUP CREATION AND DEVELOPMENT WITH THE IPEPS-ICM INCUBATOR

The iPEPS-ICM incubator, the first in France dedicated to nervous system diseases, expanded into Station F, the largest startup campus in the world. It is now Station F’s main healthcare partner. For the past 5 years, the incubator has supported the development of roughly 40 companies with over 130 million euros raised. Nearly 150 entrepreneurs currently work at the heart of the Institute.

## ACCELERATING DEVELOPMENT OF NEW TECHNOLOGY AND MEDICAL SERVICES

To make new services and medical devices available to patients as quickly as possible, the cLLAPS Living Lab brings patients, medical staff, engineers and entrepreneurs together to brainstorm new solutions for real-life needs. Since its inception in 2016, cLLAPS has helped develop 15 prototypes. In 2017, for example, a companion robot named BRO was designed to help patients with brain lesions in their own home; a series of instruments was developed to help young children with autism spectrum disorder and developmental disorders; and the gazu cane was created to help Parkinson’s disease patients walk.



## 2017 FACTS AND FIGURES

- NUMBER OF PATENTS: 7 filed in 2012
- NUMBER OF TRADEMARKS: 12
- NUMBER OF CONTRACTS: 34 contracts signed with industrial manufacturers in 2017 that brought in nearly 5 M€ for ICM research
- NUMBER OF STARTUPS: 19
- cLLAPS LIVING LAB PROJECTS: 6 new technology prototypes

### A PATENT FILED FOR SPASTIC PARAPLEGIA

The team led by Giovanni Stevanin and Frédéric Darios discovered a lipid metabolic disorder in the neurons of patients with Type 11 spastic paraplegia, a rare disease. After testing various approaches including drug candidates, they partially cured the disease in preclinical models. A patent was filed to protect these results.

### A PARTNERSHIP FOR MULTIPLE SCLEROSIS

Roche, ICM and AP-HP have started a collaboration to develop new imaging markers for multiple sclerosis using the PET-MRI platform at ICM. ICM will be in charge of coordinated a clinical trial to assess whether a monoclonal antibody found to be of interest in various types of multiple sclerosis is associated with a decrease in inflammation.

Roche has acknowledged the scientific expertise of ICM teams in multiple sclerosis issues, as well as the Institute’s ability to develop innovative imaging markers to monitor the effect of treatments on disease progression and make the underlying mechanism of treatments more easily understood.

” Entrepreneurship can truly get things done and is a great strength to have on our side. ICM as a whole, our researchers, doctors, engineers, and support staff encourage it and support many entrepreneurs in their fight against neurological disease. To reinforce our offer and give these initiatives a voice, ICM expanded its services for entrepreneurs in 2017 and launched ICMtech. ”

Alexis Génin - Research and Technology Office Director at ICM

## FOCUS ON

### NEUROCATALYST

In 2017, ICM launched “NeuroCatalyst”, an internal call for projects as part of the dynamic IHU Future Investments Program. With this program, ICM invests in clinical “proofs of concept” for new medical technology and treatment combinations.

### A FEW PROJECTS SELECTED IN 2017:

■ MEMOWAVE, a trial aimed at assessing tolerance and efficacy of a device used to improve memorisation in patients with mild cognitive disorders.

■ NEUROENVIROTECH, aimed at developing novel technology to assess state of consciousness and cognitive functions in patients in a state of modified consciousness (intensive care, for example).

### WHAT'S NEXT?

■ ICM-Tech, the branch of ICM dedicated to entrepreneurship, is the next step in the Institute’s development. Starting 2018, the first “Made by ICM” products will be launched to help patients with new treatments. Their development stems from ICM medical and scientific expertise and stringency. To meet this new challenge, ICM must strengthen its role as project accelerator, with new initiatives following the idea that “all ideas are good ideas until proven wrong”. In 2018, one to three international startups will join the Institute to carry out their development. Three national calls for projects will soon be launched: to test new candidate drugs, to develop preventive measures and to foster social entrepreneurship in the field of neuroscience.

### NEUROTRIALS

ICM developed a strategy in 2017 to create a new program aimed at improving “early” clinical research and assessing efficacy of innovative treatment on a first group of patients. Assessing drug efficacy at early stages of development is of great interest for patients, who are given the opportunity to test alternative treatments in the safe environment of the Clinical Investigation Center - CIC at ICM. NeuroTrials is unique in its organisation, with the goal of accelerating clinical research on new drugs and medical technology.



## STARTUPS INCUBATED AT ICM

ICM HAS ITS OWN INCUBATOR, IPEPS-ICM (PARIS SALPETRIERE INCUBATOR): IT SUPPORTS YOUNG AND INNOVATIVE COMPANIES THROUGHOUT THEIR DEVELOPMENT TO TURN IDEAS INTO TREATMENTS, IN AN IDEAL ATMOSPHERE AT THE HEART OF A CUTTING-EDGE RESEARCH INSTITUTE AND WITHIN A HOSPITAL SETTING..

## 2017 NEWCOMERS



**EVE DRUG** Outsourced solutions for health and safety surveillance



**A.I. MERGENCE** Artificial intelligence and autonomous robotics



**MOJOBOTS** Chatbot construction platform



**SCIPIO BIOSCIENCE** Innovative sample preparation for individual cell analysis



**MINDMAZE** Virtual reality platforms



**NEURALTIDE** Non-invasive medical device to treat ischemic strokes.



**TACTILAPTIC** New augmented reality concept using touch

WITH THE GENEROUS SUPPORT OF



## NEW PARTNERSHIP: IPEPS-ICM AND STATION F



### INTERVIEW WITH JULIEN ELRIC AND LOUIS REMIGEREAU, MANAGERS OF THE IPEPS-ICM/STATION F PARTNERSHIP



#### CAN YOU TELL US ABOUT THIS PARTNERSHIP?

When Station F opened in 2017 as the largest startup campus in the world, iPEPS-ICM was selected as its healthcare partner. This partnership offers numerous opportunities in the eHealth thanks to Station F's digital skills and ICM's scientific and medical expertise, to speed up market launches of innovative digital solutions for patients. Six startups incubated at iPEPS-ICM have moved to Station F so far. Station F's huge ecosystem is an amazing opportunity for iPEPS-ICM startups and strengthens the incubator's network of skills. Station F's international surveying activities will also help iPEPS-ICM gain more traction abroad.

#### WHAT ARE THE RESULTS AFTER 6 MONTHS WITH STATION F?

First of all, we filled every workstation allotted to us. We also received European ERDF funding (European Regional Development Fund) to give our startups the adequate digital environment for their development, with basic tools up to digital initiatives in clinical trials. Finally, we have witnessed the first illustrations of "cross-fertilisation" these past few months, and notably a partnership between Recast, a language processing startup incubated at Microsoft, and Mojobots, a chatbot production platform incubated at iPEPS-ICM.

#### WHAT IS IN THE WORKS FOR 2018?

We are working hard on dedicated part of our space at Station F to projects with unconventional market approaches. Projects developed by non-profits, for example, aimed at helping patients without profit. We are excited to help them accelerate their growth through our expertise and the startup ecosystem at Station F.



### LABCOM

Partnerships between startups and ICM can lead to the creation of a shared laboratory for research development. Each partner brings expertise, techniques, and human resources to the table to pursue a project together.

LabCom's success began with Brain e-novation, which led to the launch of therapeutic video game platform curapy.com. LabCom then went on to support Bioserenity, a startup focused on discovering and assessing digital biomarkers in the field of neurology. A new project is underway with another company incubated at iPEPS-ICM.

## ON THE START UP SIDE

### HIGHLIGHTS

#### BIOSERENITY

FUNDRAISING: 15 million euros in 2017

AWARD: Winner of the 2030 Innovation Awards in January 2017 for its smart clothing for epilepsy and long-term portable recording

#### ADSCIENTIAM

FUNDRAISING: 2 million euros in July 2017

PRODUCT: Launch of MSCopilot in December 2017

AWARD: Winner of the 2017 Digital Innovation Awards in the Healthcare category for MSCopilot

#### BRAIN E-NOVATION

PRODUCT: Launch of curapy.com





# PASSING DOWN KNOWLEDGE: LEARNING AND TRAINING

RESEARCH IS BY DEFINITION, AND IN ITS ESSENCE, LINKED TO SHARING KNOWLEDGE. SHARING INFORMATION MEANS DEVELOPING CUTTING-EDGE RESEARCH AND FOSTERING NEW INTERNATIONAL COLLABORATIONS. ICM HAS DEVELOPED A PANEL OF INNOVATIVE PROGRAMS FOR SUMMER SCHOOL TRAINING, WITH NEUROSCIENCE AND ENTREPRENEURIAL EDUCATION TO TRAIN FUTURE NEURO-ENTREPRENEURS AND TO FOSTER INTERACTIONS BETWEEN CLINICIANS AND RESEARCHERS.

## PASSING DOWN KNOWLEDGE

### TEACHING AND TRAINING AT THE HEART OF THE INSTITUTE'S MISSION

Developing cutting-edge research is deeply linked to sharing knowledge and fostering new collaborations. To pass on and share knowledge on a national and international level, in collaboration with Sorbonne University, ICM implemented ambitious seminar programs, summer schools, as well as student and clinician exchanges with prestigious international institutions. Thanks to the IHU Program awarded to ICM, learning and training activities have become a priority.

## PROMOTING SCIENTIFIC EXCELLENCE

### STUDENT FELLOWSHIPS PROGRAM

The "Student fellowship" program is a short-term exchange program for Master's or Doctoral students to help share the expertise of international institutions (Massachusetts Institute of Technology, Florey Institute of Neuroscience and Mental Health, Stanford) and create opportunities for potential collaboration.

### WORKSHOP CALL FOR PROJECTS

This call for projects is dedicated to ICM researchers and clinicians, to organise international seminars within the Institute and promote their skills and expertise among their peers to foster collaboration. 2017 topics were

electrophysiology, translational approaches in treating neuropsychiatric diseases, and single cell genomics.

### VISITING PROFESSOR CALL FOR PROJECTS

This call for projects aims at welcoming internationally-renowned senior researchers to ICM to pass along their knowledge. In 2017, ICM welcomed Professor Maurizio Corbetta, Professor of Neurology at the University of Padua in Italy.

### CARNOT TRAINING PROGRAM

This program is funded by the Carnot initiative and aimed at ICM teams and platforms. It aims at encouraging training in new techniques and fields by funding travel to other national and international research centers for researchers and technicians, or by inviting international researchers to ICM. Knowledge acquired is then passed down to ICM staff.

## PROMOTING CLINICAL RESEARCH

### THE MOVE

The Move is a unique program designed for medical students by Professor Emmanuel Roze, researcher and clinician. The Move is an innovative learning program using simulation and miming to teach medical students neurological semiology, meaning the clinical expression of neurological illnesses. The program, developed on a national and international level, is a remarkable example of innovation in education. In 2017, a battle was organised at ICM between France and Ireland, won by the Irish team.

### CLINICIAN EXCHANGE PROGRAM

A clinician exchange program with Yale (United States), within the Neurology department at Pitié Salpêtrière Hospital, allows clinicians to learn how our departments work and how we work.

### PROGRAM FOR PARAMEDICAL STAFF

A program designed for paramedical staff in partnership with the Public Health and Nursing School to develop innovative paramedical care and support research projects.

## A CROSS-DISCIPLINARY APPROACH

### SUMMER SCHOOL : BRAIN TO MARKET

"The Brain to Market" summer school is a yearly program that combines translational neuroscience and entrepreneurial training through intensive training to foster new projects, new initiatives and new ways of approaching neurological illnesses. In 2017, the program received 6 ECTS credits within

the Integrative Biology and Physiology Master's Program at Sorbonne University. The third edition focused on depression, with 39 national and international participants.

### POST-DOCTORAL PROGRAM

Attracting post-doctoral researchers with a degree in other fields than neuroscience such as mathematics, IT, healthcare economics... to apply their knowledge and expertise to neuroscience research.

### STARE

Professor Jean-Yves Delattre created STARE, an internship program for medical students to discover research from their third year of school to foster new callings and develop translational research.

## WHAT'S NEXT?

### CREATING AN INTERNATIONAL MASTER'S DEGREE

A high-level Master's program focused on neurodegenerative diseases is currently under development in collaboration with Sorbonne University and renowned international institutions including KU Leuven in Belgium. It will train neuro-centered professionals on the tools and information needed to meet the major challenges of neurodegenerative disorders. In 2017, funding from the Form'Innov initiative at Sorbonne University helped accelerate the program's development.

### MAINTAINING AND DEVELOPING CURRENT PROGRAMS

by offering a selection of training programs for initial and continuing education students.

### IMPLEMENTING THE LEADERSHIP AND SELF-CONFIDENCE PROGRAM

in collaboration with ICM's XX Initiative Group to promote women in science. This intensive workshop focuses on developing leadership skills and becoming an expert in communication.

” Education is an essential pathway for ICM, to generate new callings, develop new collaborations, and open ourselves to cross-disciplinary approaches on research projects with a long-term and international strategy. ”

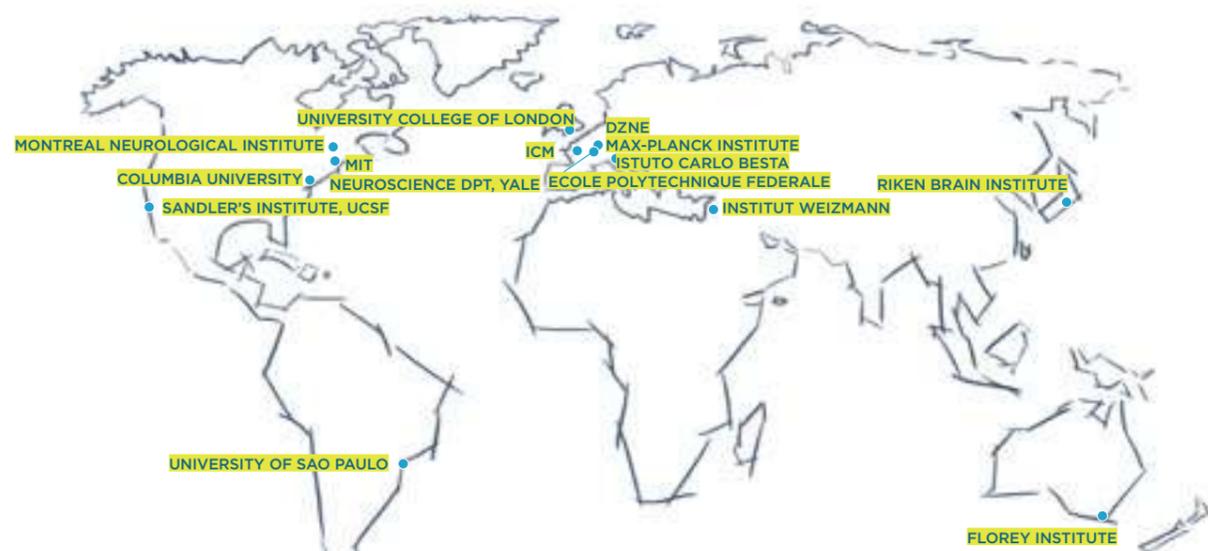
Alexandra Auffret - Director of the Medical and Scientific Affairs at ICM

# ICM AT THE CROSSROADS OF INTERNATIONAL RESEARCH

ICM IS PART OF AN INTERNATIONAL NETWORK THAT INCLUDES MAJOR NEUROSCIENCE CENTERS INVOLVED IN SHARED RESEARCH PROJECTS.

With nearly 300 partnerships developed worldwide, ICM's international reach is on the rise. These collaborations are an opportunity to share our breakthroughs and carry out shared research programs. Exchange programs are also in place to develop training and skill-pooling. ICM aims to develop partnerships with institutions specialised in complementary fields to meet transversal needs.

## INTERNATIONAL COLLABORATIONS



**UNIVERSITY COLLEGE OF LONDON** (United Kingdom) with research partnerships and the location of the first French-British workshop dedicated to doctoral students and post-doctoral researchers in 2017.

**Le DZNE** (Network of research centers focused on Neurodegenerative illness, Germany) with research partnerships and co-development of training and education.

**KU Leuven** (Katholieke Universiteit Leuven, Belgium) with close collaboration in the development of an international Master's program.

**YALE UNIVERSITY, NEW HAVEN** with a clinician exchange program.

**UNIVERSITY OF CALIFORNIA - SAN FRANCISCO** with the implementation of a Inserm-certified Associated International Laboratory with the team led by Bertrand Fontaine and Stephen Hauser.

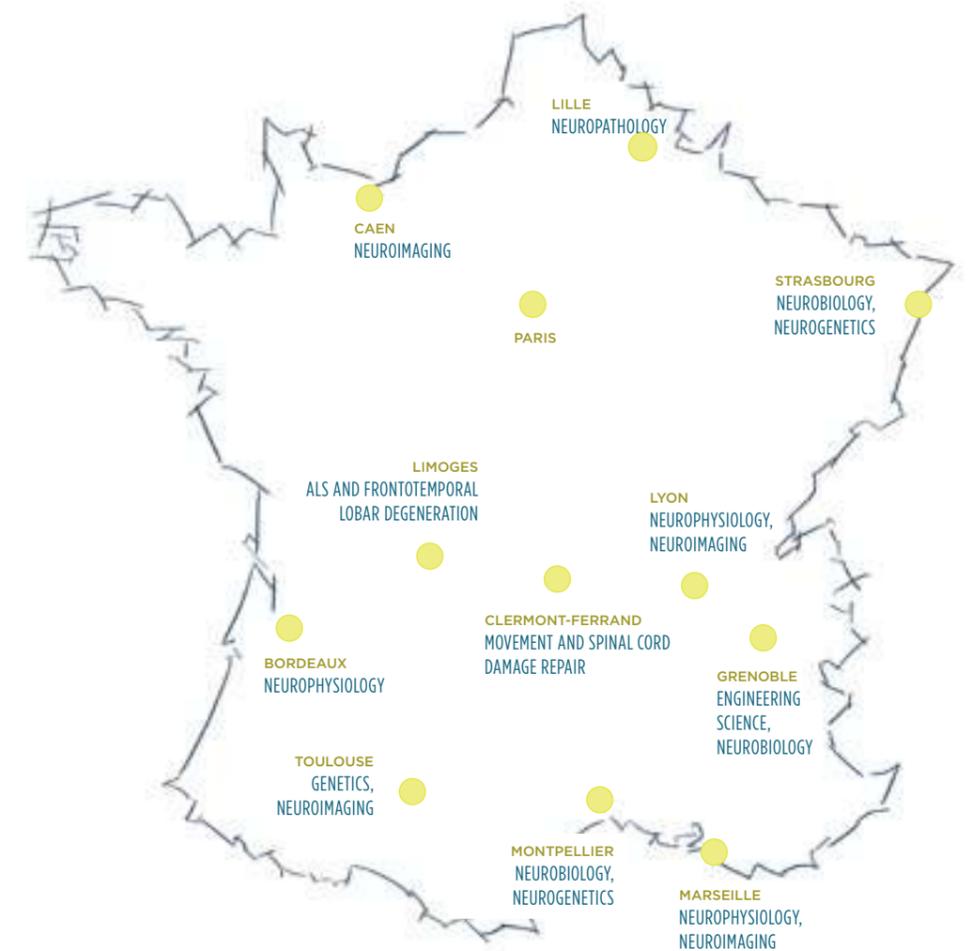
**MC GILL UNIVERSITY LE MNI (MONTREAL NEUROLOGICAL INSTITUTE)** in Canada, with which ICM has organised joint events in the past and welcomed many researchers on a variety of topics.

**MELBOURNE UNIVERSITY LE FLOREY INSTITUTE (AUSTRALIA)**, for a student exchange program with short-term internships. Shared seminars with our researchers aim at fostering relationships in research and education.

Research carried out at ICM is assessed by an International Scientific Committee composed of experts from around the world. ICM is therefore both an attractive medical and scientific research hub for high-level researchers as well as a generator of novel scientific information on an international level. Our research ambitions require close cooperation with the most prestigious French and international research institutions.

ICM is a cornerstone of the Greater Paris Research Neurohub (Neuropôle de Recherche Francilien - NERF) and the Paris School of Neuroscience (École des Neurosciences de Paris - ENP), and partners with other high-level research centers throughout Paris: Sorbonne University, Ecole Normale Supérieure, The Vision Institute, MIRCEN, NEUROSPIN, Pasteur Institute...

## RESEARCH AT ICM IS DEVELOPED IN COOPERATION WITH MAJOR FRENCH NEUROSCIENCE CENTERS, AMONG WHICH:



# FOR INNOVATIVE COMMUNICATION: SHARING AND SPREADING KNOWLEDGE

## COMMUNICATION AT ICM: OUR MISSION

DEVELOP ICM'S NOTORIETY, VISIBILITY, AND ATTRACTIVENESS IN FRANCE AND ABROAD

### HOW WE DO IT

- Put Institute experts in the spotlight
- Create a working relationship with editors and implement partnerships
- Develop events for the general public
- Highlight our social partnerships and communication with our partners (INSERM, CNRS, APHP, Sorbonne University, Patient organisations...)
- Develop communication to inform the general public and our donors



## OUR ACTIONS IN 2017

EVERY YEAR, ICM DEVELOPS EDUCATION INITIATIVES WITH EVENTS FOR CHILDREN AND THE GENERAL PUBLIC.

■ OPEN BRAIN BAR : These events step out of ICM walls to meet with citizens looking to understand how science interacts with their daily life. The aim of these twice-monthly events is to cover major societal challenges related to neurological diseases by discussing Institute breakthroughs and interviewing researchers, doctors and startups. Over 500 individuals participated in the first three editions of 2017.

### Topics:

- Will your watch replace your psychologist?
- A.I and human intelligence to defeat Alzheimer's
- Depression and burnout



- FÉE RARISSIME
- 20KM DE PARIS
- CLASSIC DAYS
- TROPHÉE LES ECHOS
- COURSE DES HÉROS
- MUSIC PASSION PARKINSON
- SOLIDAIR'S
- SOGNO DI CAVALLINO
- GROUPE IDEC
- RAID AMAZONES
- CHARITY DAY BGC
- BALADE POUR UN COPAIN
- LION'S CLUBS
- ROTARY CLUBS

**BRAIN WEEK:** Every March, Brain Week is coordinated by the Society for Neuroscience. In France, this national event is organised in over 25 cities at a time and intends to raise awareness on the importance of research on the brain. In Paris, ICM opens its doors to the general public to meet and interact with researchers and clinicians, share the latest breakthroughs and challenges when it comes to understanding the brain, and how this affects society as a whole with workshops, tours, exhibits and conferences.

**FUTURE RESEARCHERS:** For the 11th consecutive year, ICM in collaboration with INSERM and the Paris Board of Education organised the Future Researchers initiative. It gives middle and high school students the opportunity to take part in research projects one Wednesday per month throughout the school year.

**THE MOVE EUROPE :** The idea is simple: teach neurology to 3rd year medical school students using mime. Students perform sketches where they replicate neurological disease symptoms after a random draw. The event is inspired by TV show "The Voice", where mime replaces singing. Students learn real-life information with a fun, modern, and useful approach. Each season ends with a tournament with a jury of coaches (teachers) and students. After the battles, the jury selects a winning team based on medical authenticity and originality of their sketch.

**SCIENCE, ART & CULTURE CONFERENCES:** These conferences aim at making ICM a place for brainstorming and sharing ideas for researchers, to reflect on their ideas and push them further, and for the general public to learn more about research in the nervous system. It also consolidates ICM's position as a leader in neuroscience research and its international notoriety. Conferences are held every third Thursday of the month at 6 PM and are usually followed by an artistic performance. They are open to all, including scientists, doctors, entrepreneurs, members of the general public, donors... as long as they sign up in advance.

**S3ODEON :** For the third year, ICM has participated in this information initiative for the general public, to raise awareness on the future of healthcare research. At Odeon Theater in Paris, the most renowned specialists present the latest research breakthroughs in science and medicine for healthcare. Our research Institute's role is also to encourage sharing more information on Science, Healthcare and Society. To view videos of ICM researchers who participated in the 2015, 2016 and 2017 editions, visit: [www.s3odeon.fr](http://www.s3odeon.fr)



**MEDIA PARTNERSHIPS THROUGHOUT THE YEAR** (press conferences, press releases, meetings with reporters...): 70 press releases sent out, 300 press requests managed, 1,200 ICM mentions in the media, and 90 iPEPS-ICM mentions.

**CONFERENCE OF NOTARIES:** Each year, ICM takes part in the Conference of Notaries. The 2017 edition was held in Lille on the topic of "notaries at the heart of societal changes" and famille, support networks and digital issues. This ambitious topic is proof that notaries deal with real-life issues in their practice. Professor Gérard Saillant, President of ICM, spoke in the closing plenary.

**HANDICAPABLE :** ICM in collaboration with patient organisations launched a space for positive and innovative discussions on the individual and societal consequences of nervous system diseases: physical, cognitive, mental or psychological disability. The issue was raised through various exhibits and art performances as well as round table discussions, debates, and workshops with ICM experts.

**SCIENCE WEEK:** ICM opened its doors to visitors young and old for the 26th edition of Science Week on Saturday, October 14th 2017. The theme "When I grow up... I will help medical research advance" was selected by national organisers for the event. ICM introduced visitors to the brain, how it works, instruments used to explore it and the various research fields... and may have helped some future researchers discover their calling!

**NEUROPLANET:** The Neuroplanet forum organised with Le Point is dedicated to neuroscience and the powers of the brain, and invites renowned scientists and public figures from all horizons. The 3rd edition of the forum welcomed ICM experts as speakers.



# PATRONAGE: PHILANTHROPY TO BENEFIT RESEARCH

LE CERCLE DES AMIS DE L'ICM BRINGS TOGETHER THE INSTITUTE'S MAJOR BENEFACTORS (INDIVIDUALS, BUSINESSES, FOUNDATIONS AND ORGANIZATIONS). SUPPORT FROM PRIVATE PARTNERS AND THE GENERAL PUBLIC'S GENEROSITY ARE KEY IN ALLOWING ICM TO INCREASE ITS RESEARCH PROGRAMS, RECRUIT THE BEST SCIENTISTS, ATTRACT YOUNG TALENT AND PROVIDE THEM WITH CUTTING-EDGE TECHNOLOGICAL EQUIPMENT. THROUGHOUT THE YEAR, PRIVATE LABORATORY VISITS ARE ORGANISED FOR CIRCLE MEMBERS AS WELL AS SCIENTIFIC AND CULTURAL CONFERENCES AND MEETINGS WITH RESEARCHERS.

## PATRONS BOTH GENEROUS AND INVOLVED

In 2017, ICM was proud to count on the extremely generous support of its patrons. Dominique Desseigne and his two children provided exceptional financial support to the Institute to fund the Diane Barrière Chair for epilepsy research development. Klesia and EDF Foundation, two significant patrons for ICM, renewed their support for the 3 coming years to help fund research projects at the Institute: neuroinformatics development for Klesia and the Iceberg project on Parkinson's disease for EDF Foundation.



## EVENTS TO SUPPORT RESEARCH

In 2017, three events organised in support of ICM helped fund the Institute's research projects. Hermès Paris endorsed and provided support for ICM during the Saut Hermès (March 17th-19th 2017), a show jumping competition held yearly at Grand Palais in Paris, by inviting guests to make a donation to ICM. On October 18th 2017, ICM organised the 7th edition of its "Art and Science" breakfast in collaboration with FIAC Art Faire and its Director Jennifer Flay. In the spotlight was research by Stéphane Baulac and Professor Vincent Navarro on epilepsy: the morning was hosted by Claire Chazal, illustrator Benjamin Lacombe, Paris Opera Principal Léonore Baulac and dancer Amélie Joannidès, pianist Ephraïm Laor and countertenor Sébastien Fournier who presented their vision of the disease through their art. 120 guests attended the event with the Institute's Founding Members to help support ICM. On December 15th 2017, the **Automobile Club of France** also invited its guests to make a donation benefitting ICM during its annual ball.

## CERCLE DES AMIS DE L'ICM



### CERCLE DES AMIS DE L'ICM COMMITTEE

Its mission is to create relationships and enlist new patrons to help ICM achieve its goals.

#### MEMBERS

Lily SAFRA, Honorary President of the Friends of ICM Committee	Jean-Luc ALLAVENA
Lindsay OWEN-JONES, Honorary President of the Friends of ICM Committee	Cédric de BAILLIENCOURT,
Pr. Gérard SAILLANT, President of ICM	Jean BURELLE,
Jean TODT, Vice-President of ICM	Sylvain HEFES,
Maurice LÉVY, President of the Supervisory Board at Publicis Group, Co-president of the Friends of ICM Committee	François HENROT,
David de ROTHSCHILD, Co-president of the Friends of ICM Committee	Jean-Philippe HOTTINGUER,
	Jean-Claude LABRUNE
	Eddie MISRAHI
	Christian SCHMIDT de la BRELIE,
	François THOME,
	Isabelle WEILL,
	Serge WEINBERG,
	Alain WICKER

#### ICM'S FOUNDING MEMBERS

Gérard SAILLANT, Professor of orthopaedic and trauma surgery, President of ICM	Jean-Pierre MARTEL, Attorney
Jean TODT, President of the FIA, Vice-President of ICM	Max MOSLEY, former President of FIA
Yves AGID, Honorary Professor of neurology and neuroscience	Lindsay OWEN-JONES, Honorary President of the Friends of ICM Committee
Luc BESSON, filmmaker	David de ROTHSCHILD, President of Rothschild & Cie bank, Co-President of the Friends of ICM Committee
Louis CAMILLERI, President of Altria	Michael SCHUMACHER, former Formula 1 driver
Jean GLAVANY, Former Minister	Serge WEINBERG, President of Weinberg Capital Partners, ICM Treasurer
Maurice LÉVY, Co-President of the Friends of ICM Committee	
Olivier LYON-CAEN, Professor of neurology and former Director of the Nervous System Diseases Hub at Pitié-Salpêtrière Hospital	

# DILIGENCE AND TRANSPARENCY AT THE HEART OF OUR ACTIONS

ICM PROJECTS AND ADVANCES IN RESEARCH WERE CONDUCTED WITH THE UTMOST TRANSPARENCY, IN KEEPING WITH "CODE OF TRUSTED DONATIONS" GUIDELINES. THE ICM FOUNDATION RECEIVED ITS CERTIFICATION FROM THE CODE OF TRUSTED DONATIONS COMMITTEE IN NOVEMBER 2010 AND ITS RENEWAL TOOK PLACE IN 2016. CERTIFICATION GUARANTEES THAT ALL ACTIVITIES CARRIED OUT BY THE INSTITUTE ADHERE TO COMMITTEE GUIDELINES: STATUTORY DUTY AND SELFLESS MANAGEMENT, THOROUGH MANAGEMENT, STRONG COMMUNICATION AND FUNDRAISING AND FINANCIAL TRANSPARENCY. A DETAILED PRESENTATION OF ICM'S FINANCIAL STATEMENT FOLLOWS.

## FUNDRAISING

16.3 M€ WERE RAISED IN 2017, A 7% INCREASE COMPARED TO 2016.

Major patronage agreements signed with foundations or companies in 2017:

- UNIM to support research on consciousness
- Fonds St Michel to support a project on Parkinson's disease
- M.A. Mallart to support research on Parkinson's disease

Also of note is the exceptional donation made by Mr. Dominique Desseigne and his children to create the Diane Barrière Chair in support of research on epilepsy.

The Cercle des Amis de l'ICM brings together donors who have supported ICM from its inception with donations of 10,000€ or more. It was created as a means of giving special thanks to important donors, individuals, companies, or foundations, who very actively participated in the Fundraising Campaign launched by ICM in 2008. The Cercle des Amis de l'ICM currently has 718 donor members. Exclusive activities are organised to express our thanks for their support and to help donors meet and discuss with researchers, and are also a means of giving them more in-depth information regarding research outlooks and how donations are used.

Maurice Lévy and David de Rothschild, Founding Members of ICM, currently serve as Circle co-presidents.

In 2017, ICM continued its fundraising campaign to increase Institute resources.

Finally, ICM is especially grateful to families who collected donations in memoriam for the Institute.

## MIN-KIND DONATIONS AND SPONSORSHIPS

Many companies have offered their support by contributing skills from their field, or by donating products free of charge. In this section are also featured artists and collectors who have donated works of art to be sold, benefiting icm.

ICM has received in-kind support within the scope of communication and fundraising activities in the form of:

- Media placement from Air France, Reedexpo/FIAC
- Complimentary services and products: Air France, Publicis Group, ZenithOptimedia, Richard Mille, Orrick Ram- baud Martel, IDEC, ANACOFI, Hermès International

## BALANCE SHEET

### 2017 RESOURCES

2017 resources reached 45.5 M€, including fiscal year products of 36 M€ and a carryover of allocated and unused resources from previous fiscal years of 9.5 M€. Fiscal year profits are essentially made up of fundraising revenue (16.5 M€ or 45.8%), general public donations (13.9 M€ or 38.6%), companies and private foundations (2.6 M€ or 7.2%).

Additionally, they include:

- Revenue from technological platforms (3.9 M€), and research partnerships with industry partners (4 M€);
- Public subsidies (4.8 M€);
- Private subsidies (2.8 M€).

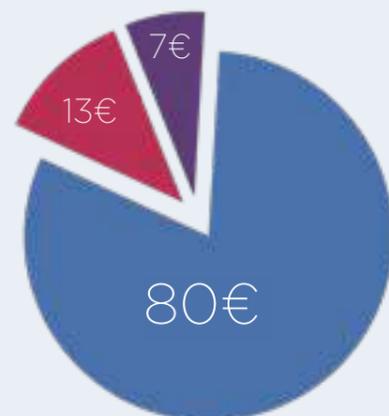


### 2017 APPLICATIONS

IN 2017, THE GRAND TOTAL OF APPLICATIONS REACHED 44.4 M€: 31.7 M€ USED OVER THE COURSE OF THE YEAR AND 12.7 M€ ALLOCATED FOR FUTURE USE. THE SHARE OF APPLICATIONS DEDICATED TO SOCIAL MISSIONS REACHED 25.3 M€, 80% OF TOTAL FISCAL YEAR APPLICATIONS. ICM SOCIAL MISSIONS INCLUDE:

- Research projects (63 %)
- Technological platforms (26 %)
- Scientific events and international partnership development (4 %)
- Innovative company incubation (7 %)

FOR 100€ SPENT  
 SOCIAL MISSIONS  
 FUNDRAISING AND COMMUNICATION FEES  
 OPERATING COSTS



Research project financing is primarily dedicated to nervous system diseases and spinal cord trauma. Technological platforms (neuroimaging, vectorology, genotyping sequencing, cell culture and histology) support these projects. Fundraising and communication costs (13%) represent expenses in canvassing of the general public (donations and bequests) as well as companies and private foundations (patronage and sponsorship) and communication. Operational costs (7%) represent support staff costs (finance, human resources, legal, IT and logistics). Applications on allocated resources (12.7 M€) primarily represent company and foundation donations received over the course of the year, to be utilised at a later date for specific multi-year research programs.

### ALLOCATION OF RESOURCES FROM THE GENERAL PUBLIC

RESOURCES RAISED FROM THE GENERAL PUBLIC AND USED IN 2017 TOTALLED 13.9 M€. IN SHORT, 69€ OF EVERY 100€ RAISED FROM THE GENERAL PUBLIC WERE USED TO FUND SOCIAL MISSIONS AND INVESTMENTS. 27€ WERE USED TO COVER FUNDRAISING AND COMMUNICATION COSTS, AND 4€ TO COVER ICM OPERATIONAL COSTS.

SOCIAL MISSIONS AND INVESTMENT  
 FUNDRAISING AND COMMUNICATION COSTS  
 OPERATIONAL COSTS



### SIMPLIFIED BALANCE SHEET

Assets (k€)	31 12 2016	31 12 2017
Net immobilised assets	54 276	52 257
Net available and realisable assets	50 399	56 072
<b>Total</b>	<b>104 675</b>	<b>108 329</b>

Liabilities (k€)	31 12 2016	31 12 2017
Organisation funds	44 498	45 099
Fiscal year result	1 191	1 114
Dedicated funds	7 919	11 131
Debts	51 067	50 985
<b>Total</b>	<b>104 675</b>	<b>108 329</b>

### COMMENTS

TOTAL ICM INVESTMENTS SINCE THE INSTITUTE'S LAUNCH REPRESENT NEARLY 26.8 M€, DEDICATED PRIMARILY TO TECHNOLOGICAL PLATFORMS SUPPORTING RESEARCH. FISCAL YEAR INVESTMENTS AMOUNTED TO 2.3 M€.

#### MAIN INVESTMENTS:

- Key equipment acquired in 2017 is a sequencer, for a total of 180 K€;
- Research team workspace reconfiguration and scientific equipment acquisition for 507 K€;
- Scientific IT storage capacity acquisition and calculation cluster for 630 K€.

Fixed assets amount to 52.3 M€. On December 31st 2017, cash ow amounted to 34.6 M€. ICM organisation funds represent 46.2 M€. This includes equity of 20.4 M€ as well as investment subsidies of 25.8 M€. Nonexpendable endowments total 1.2 M€. By fiscal year end, dedicated funds (to be allocated to various programs) amounted to 11 M€.

#### MONETARY RESERVE POLICY

ICM was supported by an 11.7 M€ grant when it was started in 2006. The board has a very cautious policy in terms of monetary reserve preservation. ICM reserves are invested in marketable securities (long-term investment contracts with major banks, capital guaranteed and 100% in euros).

#### VOLUNTARY CONTRIBUTIONS

■ Volunteering: ICM was supported by volunteering over the course of the fiscal year, especially for communication campaigns. Estimated volume is 1.4 yearly full-time equivalent, i.e. 37 K€ based on hourly minimum wage.

#### IN-KIND PATRONAGE:

■ ICM has received in-kind support within the scope of communication and fundraising activities in the form of:  
 -Media placement from Air France, Reedexpo/FIAC  
 -Complimentary services and products: Air France, Publicis Group, ZenithOptimedia, Richard Mille, Orrick Rambaud Martel, IDEC, ANACOFI, Hermès International

MAINTAINING A HIGH LEVEL OF EXCELLENCE IS KEY FOR ICM, WHICH IS WHY THE INSTITUTE IMPLEMENTED INTERNAL AND EXTERNAL AUDITING PROCEDURES TO ENSURE THOROUGH AND EFFICIENT MANAGEMENT: AS A MEMBER OF THE TRUSTED DONATIONS COMMITTEE AND INVOLVEMENT OF AN INDEPENDENT AUDITOR.



#### CODE OF TRUSTED DONATIONS COMMITTEE

On November 3, 2010, ICM received certification from the Comité de la Charte pour le Don en Confiance (Code of Trusted Donations Committee), renewed on October 6, 2016.

For over 20 years, the Committee has been a regulator of professional fundraising from the general public.

Its action is centered on 3 leading guidelines: certified organisations must respect ethics regulations, must abide by collective discipline with respect to donors, and must accept continuous monitoring of commitments.

ICM FOUNDATION 2017 EXPENDITURE STATEMENT

YEAR END DECEMBER 31 2017

APPLICATIONS	2017 APPLICATIONS	2017 ALLOCATION OF RESOURCES RAISED FROM THE GENERAL PUBLIC BY APPLICATION	RESOURCES	2017 RESOURCES COLLECTED	2017 RESOURCES COLLECTED AND USED
			Carryover of resources collected from general public not allocated/used at start of fiscal year		536 063
<b>1. Social Missions</b>	25 267 811	8 485 803	<b>1. Resources collected from general public</b>	13 898 583	13 898 583
Actions directly carried out			Unallocated monetary donations	10 891 601	10 891 601
Research Programs	15 826 359	4 461 149	Allocated monetary donations	2 357 599	2 357 599
Technological Research Platforms	6 671 505	2 213 254	Unallocated bequests and other gifts	649 383	649 383
Research Application and Incubator	1 643 453	921 693	Allocated bequests and other gifts	0	0
Other social missions	1 126 494	889 707	Other revenue from general public generosity	598 500	598 500
<b>2. Fundraising costs</b>	3 992 426	3 343 862	<b>2. Other private funds</b>	9 365 819	
Cost of appeals to the generosity of the general public	3 638 585	3 071 050	Patronage	2 622 303	
Costs related to private fund canvassing	338 368	259 753	Partnerships	3 981 544	
Communication costs	15 473	13 059	Private subsidies	2 761 972	
<b>3. Institute operational costs</b>	2 479 238	502 570	<b>3. Subsidies and other public financial support</b>	4 830 702	
<b>I. TOTAL APPLICATIONS</b>	31 739 475	12 332 235	<b>4. Other products</b>	7 970 173	
<b>II. PROVISIONS</b>	22 460		Financial products	303 607	
<b>III. PLEDGES ON ALLOCATED RESOURCES</b>	12 661 139		Services rendered	3 854 355	
<b>IV. FISCAL YEAR SURPLUS</b>	1 113 825		Other products	3 812 211	
<b>V. GRAND TOTAL</b>	45 536 899		<b>I. TOTAL RESOURCES</b>	36 065 277	
Share of fixed assets acquired during the fiscal year financed by collected funds			<b>II. CARRYOVER OF PROVISIONS</b>		
Neutralization of provisions for depreciation of fixed assets financed by collected funds			<b>III. CARRYOVER OF ALLOCATED RESOURCES UNUSED IN PREVIOUS FISCAL YEARS</b>	9 471 622	
<b>TOTAL APPLICATIONS FINANCED BY FUNDS COLLECTED FROM GENERAL PUBLIC</b>		12 332 235	<b>IV. VARIATION OF ALLOCATED FUNDS COLLECTED FROM GENERAL PUBLIC</b>		-2 102 411
			<b>V. INSUFFICIENT FISCAL YEAR RESOURCES</b>		
			<b>VI. GRAND TOTAL</b>	45 536 899	12 332 235
			<b>TOTAL APPLICATIONS FINANCED BY FUNDS COLLECTED FROM GENERAL PUBLIC</b>		12 332 235
			<b>BALANCE OF FUNDS COLLECTED FROM GENERAL PUBLIC NOT ALLOCATED/USED END OF FISCAL YEAR</b>		0
<b>EVALUATION OF VOLUNTARY IN-KIND DONATIONS</b>			<b>EVALUATION OF VOLUNTARY IN-KIND DONATIONS</b>		
Social missions	37 304		Volunteering	37 304	
Fundraising costs			In-kind services		
Operational costs			In-kind donations		
Total			Total		

# THANK YOU

## MAJOR PATRONS

Maria Rosa Bemberg  
 Dominique, Alexandre et Joy Desseigne  
 FIA FOUNDATION FOR THE AUTOMOBILE AND SOCIETY  
 FONDATION BETTENCOURT SCHUELLER  
 FONDATION EDF  
 FONDATION EDMOND J. SAFRA  
 FONDATION LILY SAFRA  
 FP JOURNE - INVENIT ET FECIT  
 HSBC FRANCE  
 KLESIA - CARCEPT PREV - IPRIAC  
 Docteur Léone-Noëlle Meyer  
 OCIRP  
 ORRICK RAMBAUD MARTEL  
 Lindsay Owen-Jones  
 PUBLICIS  
 RACE OF CHAMPIONS  
 Edouard et Martine de Royère  
 Michael Schumacher  
 Jean Todt et Michelle Yeoh  
 1 anonyme

## MAJOR BENEFACTORS

AIR FRANCE  
 Famille Jan Aron  
 Elisabeth Badinter  
 Luc Besson  
 BOLLORÉ  
 BOUYGUES  
 Lucienne Collin  
 FEDERATION FRANÇAISE DU SPORT AUTOMOBILE  
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