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EDITORIAL

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 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.
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 21st 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.

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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

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.

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

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.

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.
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
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

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, A CORNERSTONE OF NEUROSCIENCE RESEARCH | UNDERSTANDING & FIGHTING

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.

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

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

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- 9 researchers and clinicians with expertise in genetics, optogenetics, spinal cord physiology and medullar trauma
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ICM ACHIEVEMENTS
- Characterisation of specific neurons that control implementation of micro-networks in the spinal cord during locomotion
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

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
- 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

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

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

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.
ICM, A CORNERSTONE OF NEUROSCIENCE RESEARCH

ICM BY THE NUMBERS

700 INDIVIDUALS AT ICM

28 RESEARCH TEAMS

4 MAIN FIELDS OF RESEARCH

20 PATHOLOGIES STUDIED

12 TECHNOLOGICAL PLATFORMS

1 CLINICAL INVESTIGATION CENTER

172 CLINICAL TRIALS

1 CLLAPS LIVING LAB, THE ONLY ONE DEDICATED TO NEUROLOGY WORLDWIDE

55 PATENTS, 7 OF WHICH WERE FILED IN 2017

12 TRADemarks

42 NATIONALITIES

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

17 INCUBATED STARTUPS

11 ANR PROJECTS

2 ERC PROJECTS

12 TRADEMARKS

88 TOTAL GRANTS OBTAINED IN 2017

PATENTS, 7 OF WHICH WERE FILED IN 2017

4 MAIN FIELDS OF RESEARCH

20 PATHOLOGIES STUDIED

12 TECHNOLOGICAL PLATFORMS

1 CLINICAL INVESTIGATION CENTER

172 CLINICAL TRIALS

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12 TRADEMARKS

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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.

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

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;
- 3 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.
ICM, A CORNERSTONE OF NEUROSCIENCE RESEARCH

MEMBERS

Gérard SAILLANT
Professor of orthopaedic and trauma surgery, President of ICM
Jean TOOT
President of the FIA, Vice-President of ICM

COLLEGE OF FOUNDERS

Serge WEINBERG
Jean GLAVANY
Jean-Pierre MARTEL
Gérard SAILLANT
Jean TOOT

COLLEGE OF QUALIFIED PERSONS

Pierre CORVOL
Collège de France
Richard FRACKOWIAK
École Polytechnique
Fédérée de la Légion d’Honneur
Elisabeth TOURNIER-
ASSISTANCE AU SERVICE DE LA SOCIÉTÉ
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 TOOT
President of the FIA, Vice-President of ICM
Lindsay OWEN-JONES
Honorary President of L’Oreal
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
Heleen Mayberg
Christian Buchel
Arnold Kriegstein
Masud Huqain
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 I.H.U.?
An I.H.U 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” (I.H.U), 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 I.H.U.?
On January 1st 2018, both entities merged and I.H.U 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
ICM 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 42.4 M€ 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
ICM helped create a center that regroups early-stage clinical trials with 103 ongoing clinical trials
Synergies between ICM and I.H.U 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).
ICM 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.
ICM, A CORNERSTONE OF NEUROSCIENCE RESEARCH 28 TEAMS

28 TEAMS DEDICATED TO RESEARCH

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 applicants 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: Sérénine BOILLEE
Principal investigators, researchers, clinicians: Sérénine BOILLEE, PhD Delphine BOHÉ, PhD Stéphanie MILLECamps, PharmD, PhD Christian LOBSIGER, PhD François SALACHAS, MD Daniela SEILHEAN, MD, PhD 1 post-doctoral fellow 3 engineers and technicians 4 doctoral students
Competitive funding granted in 2017 National: ANR, FRM, ANRIS

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 DJURR, MD, PhD Giovanni STEVANIN, PhD Frédéric DARIOGS, PhD Monwena LATOUCHE, PhD Isabelle LE BER, MD, PhD Olga CORTI, PhD Jean-Christophe CORVOL, MD, PharmD, PhD Suzanne LESAGE, PhD Khalid Hamid EL HACHIMI Caroline NAVIA, MD
Clare PUJOL, PhD Fanny MOCHÉL, 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 HAİK
Principal investigators, researchers, clinicians: Marie-Claude POTIER, PhD Stéphane HAİK, PhD Nicolas BIZAT, PhD Benoît DELATOUR, PhD Stéphane EPELBAUM, MD Charles DUYCKHAERTS, MD, PhD Sarge MARTY, PhD Jean-Philippe BRANDEL, MD Véronique SAZDÖVITCH, MD Jean-Maurice DELABAR, MD, 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-BEH, 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

EXPERIMENTAL THERAPIES IN PARKINSON’S DISEASE
SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH
Team leader: Etienne HIRSC
Principal investigators, researchers, clinicians: Etienne HIRSC, 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
Competitive funding granted in 2017
National: AFM, ARSEP, Idex Sorbonne Université, DGH Biothérapies, INSERM

**GENETICS AND PHYSIOPATHOLOGY IN EPILEPSY**
SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH
Team leaders: Stéphanie BAULAC & Eric LEQUERN
Principal investigators, researchers, clinicians: Stéphanie BAULAC, PhD
Eric LEQUERN, MD, PhD
Christel DEPIENNE, MD, PhD
Michel BAULAC, MD
Cyril MIGNOT, MD
Rita RAŞMÂN-VOZAR, 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 IDDAH, MD, PhD
Michel KALAMARIDES, MD, PhD
Aguilbert ALENTORN, MD
Jean-Yves DELATTRE, MD
Kh Le HOANG-KHUAN, MD, PhD
Karima MOKHTARI, MD
Matthieu 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 MYELENATION AND REMYELENATION IN THE CNS**
SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH

**QUIGGODENDROCYTE 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
4 doctoral students
Competitive funding granted in 2017
National: France PARKINSON

**MOLECULAR AND CELLULAR APPROACHES FOR MYELEN REPAIR**
SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH
Team leaders: Brahmin NAJ-OUMESMAR & Anne BARON VAN EVERCOOREN
Principal investigators, researchers, clinicians:
Brahmin NAJ-OUMESMAR, PhD
Anne BARON VAN EVERCOOREN, PhD
Violetta ZUJOVIC, PhD
Lama BOULGLA, PhD
4 post-doctoral fellows
2 engineers
5 doctoral students
Competitive funding granted in 2017
National: ENP, UPMC, ANR, AFM
Foundation Jérôme Lejeune, ARSEP
European: ECTRIMS
International: NMSS

**CELLULAR AND MOLECULAR MECHANISMS IN GLIOMA DEVELOPMENT**
SECONDARY FIELD: NA
Team leader: Émilie HUILLARD
Principal investigators, researchers, clinicians:
Émilie 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

**GENETICS AND PHYSIOPATHOLOGY IN EPILEPSY**
SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH
Team leaders: Mathieu PEYRE, MD, PhD
Karima MOKHTARI, MD
Jean-Yves DELATTRE, MD, PhD
Agustí ALENTORN, MD
Michel KALAMARIDES, MD, PhD
Ahmed IDDAH, MD, PhD
Franck BIELLE, MD, PhD
Marc SANSON, MD, PhD
researchers, clinicians:
Principal investigators,
Team leader: Mathieu PEYRE

**BIOTECHNOLOGY AND BIOTHERAPY**
SECONDARY FIELD: NA
Team leader: Philippe RAVASSARD
Principal investigators, researchers, clinicians:
Philippe RAVASSARD, PhD
Hélène CHEVAL, PhD
Jacques MALLEL, Emérite
4 post-doctoral fellows
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 BESSNARD-GUERIN, PhD
Sorana CIURA, PhD
3 post-doctoral fellows
1 technician
3 doctoral students
Competitive funding granted in 2017
National: ANR, ARSEP, FRM
European: ERC

**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 POIJEU, PhD Isabelle ARNAUD, MD, PhD Emmanuel ROZE, MD, PhD Andrias HARTMANN, MD Sabrina MEUNIER, PhD Emmanuelle APARTIS-BOURDIEU, MD

SECONDARY FIELD: NA

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 Sáverine MAHON, PhD Mario CHAVEZ, PhD Vincent NAVARRO, MD, PhD Michel LE VAN QUYN, MD
8 post-doctoral fellows
1 technician
2 doctoral students

Competitive funding granted in 2017
National: ANR, FRM

CORTICAL ET ÉPILEPSIE
SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH
Chef d’équipe : Richard MILES
Principal investigators, researchers, clinicians: Richard MILES, PhD
5 post-doctoral fellows

COMPETITIVE FUNDING GRANTED IN 2017
National: FRM

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

Competitive funding granted in 2017
European: ERC

NEUROPHYSIOLOGY (7 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 BARROLOMOE, PhD Laurent COHEN & Lionel NACCACHE
Principal investigators, researchers, clinicians: Paolo BARROLOMOE, PhD Laurent COHEN, MD, PhD Lionel NACCACHE, MD, PhD Jacob SIT, 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: Bruno DUBOIS, MD, PhD Richard LEVY, MD, PhD
5 post-doctoral fellows

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 ALLARD, 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 leaders: Luc MALLEY & Richard LEVY
Principal investigators, researchers, clinicians: Luc MALLEY, MD, PhD Richard LEVY, MD, PhD Bruno DUBOIS, MD, PhD
2 post-doctoral fellows

Competitive funding granted in 2017
National: ANR

MOTION, BRAIN AND BEHAVIOUR
SECONDARY FIELD: CLINICAL AND TRANSLATIONAL RESEARCH
Team leaders: Mathias PESSAGLIONE, Sébastien BOURET, Jean DAUNIZEAU
Principal investigators, researchers, clinicians: Mathias PESSAGLIONE, 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 Lilianne 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
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 Pitie-Salpetriere 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.

« Technological developments are essential to progress in medicine and science »
Etienne Hirsch, Director of 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 path-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
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.

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: Progress, Hopes and Breakthroughs  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.

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 AYMÉ 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.

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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. INIRA 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.

BIOSERENITY, 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 Idinvest Partners.

2017: PROGRESS, HOPES AND BREAKTHROUGHS HIGHLIGHTS
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

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.
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 Guillot 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 neurological factors such as brain size. They also identified an evolution gap between theory of mind capabilities in great apes and humans.

Team Jean Daunizeau

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 Collior 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 Collot

### 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
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.

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.

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.


6. Cortical neurons and networks are dormant but fully responsive during isoelectric brain state. Altwegg-Boussac T et al. Brain. 2017 Sep 1


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
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

PPM-PD: TOWARDS PERSONALISED MEDICAL CARE FOR PARKINSON’S DISEASE

The aim of this project is to collect and analyse clinical, behavioural, genetic, metabolical, 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 Lehéricy, neuroradiologist and medical imaging expert

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

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, neuropathologist

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 project 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

NEW COLLABORATIONS

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

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 CentraleSupelec 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 TALES 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”.

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

Nicolas 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.

Nelson 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?

Nicolas 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.

Nelson 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.

WHAT BROUGHT YOU TO ICM?

Nicolas Renier & Nelson 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 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.


- **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”.

- **Nicolas Renier**, ICM team leader, received an ERC Starting Grant for his research project dedicated to understanding neuron connection stability in adult brains.

- **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.

- **Ségalène 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.

- **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 Pituité-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.

- **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.

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RESEARCH AND CARE: PATIENTS AS A PRIMARY CONCERN

The Clinical Investigation Center - CIC (INSERM, AP-HP), housed on the first floor of ICM, is an incredible bridge between research and care. It helps 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.

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 play 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...
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. These 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.
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

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

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

The Behavioural Neuro-Psychiatry Unit has made it possible: 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 projects 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

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

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.

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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

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 new 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.

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.

- **TOOLs**
  - You will find all the tools required for context of use analysis, developing your ideas and testing prototype use.
- **METHODS**
  - we provide support using our user-driven method of co-creation to ensure that your technology is accepted and used.
- **ENVIRONMENT**
  - cLLAPS provides access to a neutral and pleasant atmosphere, ideal for sharing experiences and coming up with new ideas.
- **PARTNERS**
  - We make it easier for you to access key skill sets, as well as the ICM and Nervous System Diseases Hub networks that could contribute to your project.
- **PARTICIPANTS**
  - You, us, ICM experts and researchers, Nervous System Diseases Hub medical and paramedical staff, carers and patients.

A PATENT FILED FOR SPASTIC PARAPLEGIA

The team led by Giovanni Stevanin and Frédéric Daris 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.
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**

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 combinations.

**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.

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**2017 NEWCOMERS**

- **EVE DRUG**  Outourced 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

**MAIRIE DE PARIS**
NEW PARTNERSHIP: IPEPS-ICM AND STATION F

INTERVIEW WITH JULIEN ERLIC 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.

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

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.
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: LEARNING AND TRAINING

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

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, École Normale Supérieure, The Vision Institute, MIRCEN,
NEUROSPIN, Pasteur Institute...
COMMUNICATION AND PATRONAGE

FOR INNOVATIVE COMMUNICATION:
SHARING AND SPREADING KNOWLEDGE

COMMUNICATION AT ICM: OUR MISSION

DEVELOP ICM’S NOTORIETY, VISIBILITY, AND ATTRACTION 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

OUR PARTNERS

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

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 families, 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

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-Pierre MARTEL, Attorney
Max MISLE, former President of FIA
Lindsay OWEN-JONES, Honorary President of the Friends of ICM Committee
Jean Todt, President of ICM
Yves AGID, Honorary Professor of neurology and neuroscience
Luc BESSON, filmmaker
Louis CAMILLERI, Former Minister
Jean d’AVIVY, former Minister
Maurice LÉVêque, Co-President of the Friends of ICM Committee
Serge WEINBERG, President of Weinberg Capital Partners, ICM Treasurer

ICM’S FOUNDING MEMBERS

Jean-Philippe HOTTINGUER, Jean-Claude LABRUNE
Dominique Desseigne and his two children
Klesia and EDF Foundation

COMMUNICATION AND PATRONAGE

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 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.

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 Fair 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 Joannides, pianist Efrain 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 benefiting ICM during its annual ball.

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

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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 Levy 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 Rambaud 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€).

General Public Fundraising

Private Foundation and Corporate Fundraising

Public and Private Subsidies

Activity Revenue

Other Revenue

39%
11%
21%
7%
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%)

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.

SIMPLIFIED BALANCE SHEET

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

<table>
<thead>
<tr>
<th>Liabilities (k€)</th>
<th>31 12 2016</th>
<th>31 12 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organisation funds</td>
<td>44 498</td>
<td>45 099</td>
</tr>
<tr>
<td>Fiscal year result</td>
<td>1 191</td>
<td>1 114</td>
</tr>
<tr>
<td>Dedicated funds</td>
<td>7 919</td>
<td>11 131</td>
</tr>
<tr>
<td>Debts</td>
<td>51 067</td>
<td>50 965</td>
</tr>
<tr>
<td>Total</td>
<td>104 675</td>
<td>108 329</td>
</tr>
</tbody>
</table>

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/PIAC

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.
## ICM FOUNDATION 2017 EXPENDITURE STATEMENT

### APPLICATIONS

<table>
<thead>
<tr>
<th>Social Missions</th>
<th>2017 Applications</th>
<th>2017 Allocation of Resources Raised from the General Public by Application</th>
<th>Resources</th>
<th>2017 Resources Collected</th>
<th>2017 Resources Collected and Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actions directly carried out</td>
<td>25 267 811</td>
<td>8 485 803</td>
<td>1. Resources collected from general public</td>
<td>13 898 583</td>
<td>13 898 583</td>
</tr>
<tr>
<td>Research Programs</td>
<td>15 826 359</td>
<td>4 461 149</td>
<td>Unallocated monetary donations</td>
<td>10 891 601</td>
<td>10 891 601</td>
</tr>
<tr>
<td>Technological Research Platforms</td>
<td>6 671 505</td>
<td>2 123 254</td>
<td>Allocated monetary donations</td>
<td>2 357 599</td>
<td>2 357 599</td>
</tr>
<tr>
<td>Research Application and Incubator</td>
<td>1 643 453</td>
<td>921 693</td>
<td>Unallocated bequests and other gifts</td>
<td>649 383</td>
<td>649 383</td>
</tr>
<tr>
<td>Other social missions</td>
<td>1 126 494</td>
<td>889 707</td>
<td>Allocated bequests and other gifts</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Other revenue from general public generosity</td>
<td>598 500</td>
<td>598 500</td>
</tr>
</tbody>
</table>

### 2. Fundraising costs

<table>
<thead>
<tr>
<th>2. Fundraising costs</th>
<th>3 992 426</th>
<th>3 343 862</th>
<th>2. Other private funds</th>
<th>9 365 819</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patronage</td>
<td>2 622 303</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partnerships</td>
<td>3 981 544</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private subsidies</td>
<td>2 761 972</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 3. Institute operational costs

| 3. Institute operational costs | 2 479 238 | 502 570 |

### 1. TOTAL APPLICATIONS

<table>
<thead>
<tr>
<th>I. TOTAL APPLICATIONS</th>
<th>31 739 475</th>
<th>12 332 235</th>
</tr>
</thead>
</table>

### II. PROVISIONS

<table>
<thead>
<tr>
<th>II. PROVISIONS</th>
<th>2 430</th>
</tr>
</thead>
</table>

### III. PLEDGES ON ALLOCATED RESOURCES

<table>
<thead>
<tr>
<th>III. PLEDGES ON ALLOCATED RESOURCES</th>
<th>12 661 139</th>
</tr>
</thead>
</table>

### IV. FISCAL YEAR SURPLUS

<table>
<thead>
<tr>
<th>IV. FISCAL YEAR SURPLUS</th>
<th>111 825</th>
</tr>
</thead>
</table>

### V. INSUFFICIENT FISCAL YEAR RESOURCES

<table>
<thead>
<tr>
<th>V. INSUFFICIENT FISCAL YEAR RESOURCES</th>
<th>45 536 899</th>
</tr>
</thead>
</table>

### 6. GRAND TOTAL

<table>
<thead>
<tr>
<th>6. GRAND TOTAL</th>
<th>45 536 899</th>
</tr>
</thead>
</table>

### TOTAL APPLICATIONS FINANCED BY FUNDS COLLECTED FROM GENERAL PUBLIC

<table>
<thead>
<tr>
<th>TOTAL APPLICATIONS FINANCED BY FUNDS COLLECTED FROM GENERAL PUBLIC</th>
<th>12 332 235</th>
</tr>
</thead>
</table>

### EVALUATION OF VOLUNTARY IN-KIND DONATIONS

<table>
<thead>
<tr>
<th>EVALUATION OF VOLUNTARY IN-KIND DONATIONS</th>
<th>Social missions</th>
<th>37 304</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fundraising costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operational costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>37 304</td>
</tr>
</tbody>
</table>

### SHARE OF FIXED ASSETS ACQUIRED DURING THE FISCAL YEAR FINANCED BY COLLECTED FUNDS

| Share of fixed assets acquired during the fiscal year financed by collected funds | 0 |

### NEUTRALIZATION OF PROVISIONS FOR DEPRECIATION OF FIXED ASSETS FINANCED BY COLLECTED FUNDS

| Neutralization of provisions for depreciation of fixed assets financed by collected funds | 0 |

## 2017: PROGRESS, HOPES AND BREAKTHROUGHS

2017 FINANCIAL STATEMENT

| Balance of funds collected from general public not allocated/used at end of fiscal year | 0 |

| Balance of funds collected from general public not allocated/used at end of fiscal year | 0 |

| ICM ANNUAL REPORT 2017 | ICM ANNUAL REPORT 2017 | 16 |
2017: PROGRESS, HOPES AND BREAKTHROUGHS

THANK YOU