

# FOR YOU & WITH YOU

The brain and spine institute donors journal



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## **SPECIAL FOCUS MULTIPLE SCLEROSIS**

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## EXEMPLARITY AND EFFICACY

During this summer's heat wave, the ICM persists in its development. You will find in this edition the essentials of the annual accounts of the ICM, taken from the annual

report and the report on the moral and financial situation of the year 2014. You will see that our situation is healthy and that the management of the Institute is rigorous.

In addition, you will surely be glad to learn that MedDay, a start-up in the ICM's business incubator, has developed a new treatment for progressive multiple sclerosis. You will find, in this edition, all the informations you wish about this good news, which is further proof that our model "from the patient to the treatment" via physicians and researchers is exemplary and efficacious.

Finally, Smuggler, a brand of men's suits "Made in France" has become a partner of the ICM. There also, we have more proof that our "mixed economy" in which partnerships with you, our donor friends, and private enterprises is an exemplary and efficacious model that offers our researchers, many of whom belong to public organisms, supplementary means, even the recruitment of "private" teams.

You see that our Institute, in a tormented universe and a difficult environment in terms of public financing, demonstrates its dynamism daily.

**Jean Glavany**  
Founding Member

## A PARTNERSHIP WITH THE CHU OF CLERMONT-FERRAND HAS BEEN ESTABLISHED

A first research project has been initiated with the team of Dr. Laurent Sakka at the Clermont-Ferrand Medical School and the team of Claire Wyart at the ICM. This first collaborative research project will address the question of motricity and the development of new regulatory pathways on which to act to improve post-traumatic repair of the spinal cord.



## SMUGGLER

This French brand of men's suits "Made in France" has established a partnership with the ICM in order to support research on the diseases of the brain and lesions of the spinal cord. For each suit or jacket sold, ten euros will be donated to the Institute.



## AN ANTI-STRESS HEADSET

MyBrain Technologies is a young company, started by two young ICM researchers, that is incubated in the business incubator of the Institute the iPEPS-ICM. On the basis of their work on EEG (electroencephalographic) technology, the founders developed, in conjunction with the EEG platform of the ICM and the team of Nathalie George, a "neurofeedback" headset to fight against stress. Long term, this technology should also help fight against attentional disorders, hyperactivity or sleep problems.



## PARTNERS: 20 KM DE PARIS

On October 11, 2015, the Brain and Spine Institute will be present at the "20 KM DE PARIS". An 11-year partnership that contributes support equal to the challenge posed by the diseases of the brain and spinal cord.

The "20 KM de Paris" race is a personal and collective challenge. October 11, 2015, at 10 o'clock at the Léna Bridge, will be another wonderful morning under the sign of the passion for sports and generosity. If you wish to support the Institute during this event, there are two possibilities:

- The first is to run wearing the colours of the ICM. The Institute will be present in the village during the distribution of numbers to alert the public to the challenges and propose tee-shirts with its colours.
- The second is to collect funds to help research. The runners can create a free personalized web page on the Alvarum platform calling for donations and invite their friends to support them during the race to finance research.

If you also wish to organize an event for the benefit of the ICM, please contact Agathe Gioli: [agathe.gioli@icm-insitute.org](mailto:agathe.gioli@icm-insitute.org)

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## Seen on the Web

• [icm-institute.org/fr/legs-donations-et-assurances-vie/](http://icm-institute.org/fr/legs-donations-et-assurances-vie/)  
You will find a special focus on bequests, donations, life-insurance

• [icm-institute.org/fr/les-conferences-de-licm/](http://icm-institute.org/fr/les-conferences-de-licm/)

- You will find an exceptional lecture on multiple sclerosis
- View the lecture "Science, Art et Culture" with Jean-Didier Vincent
- Discover the video of the sessions of "connected health" on the impact of connected objects on clinical and epidemiological research

## AGENDA

●●● September 12 and 13

- At the Parc des Expositions of Toulouse, Fée-Rarissime will propose, as usual, baptisms behind the wheel of a Ferrari for the benefit of the Hôpital Sourire and the ICM.

- All information on "A circuit for the brain", at <http://ucplc.fr/>

●●● September 24

The ICM will celebrate the 5<sup>th</sup> anniversary of its inauguration

# MULTIPLE SCLEROSIS: DECIPHER, MEASURE AND TREAT

**M**ultiple sclerosis (MS) is the first cause of severe handicap in persons in their thirties not due to trauma. It affects about 1 person in 1,000 in France and about 2.8 millions worldwide. It is an inflammatory disease of the central nervous system in which the immune system, normally implicated in the fight against viruses and bacteria, becomes activated and attacks elements normally present in the body.

In the case of MS, the inflammatory reaction destroys the myelin sheath that surrounds neuronal projections, the axons, which transmit the nervous influx (like the insulation that surrounds electrical wires to assure good conductance of current). The principal aim of this protection is to assure rapid transmission of the nervous influx in order that information originating in the brain can rapidly reach the muscles. Repeated attacks of inflammation alter the transfer of information and lead to motor, sensory, balance and visual disorders. ICM researchers try to understand the mechanisms of de- and remyelination, not only to stop destruction of the myelin but also to stimulate its repair.

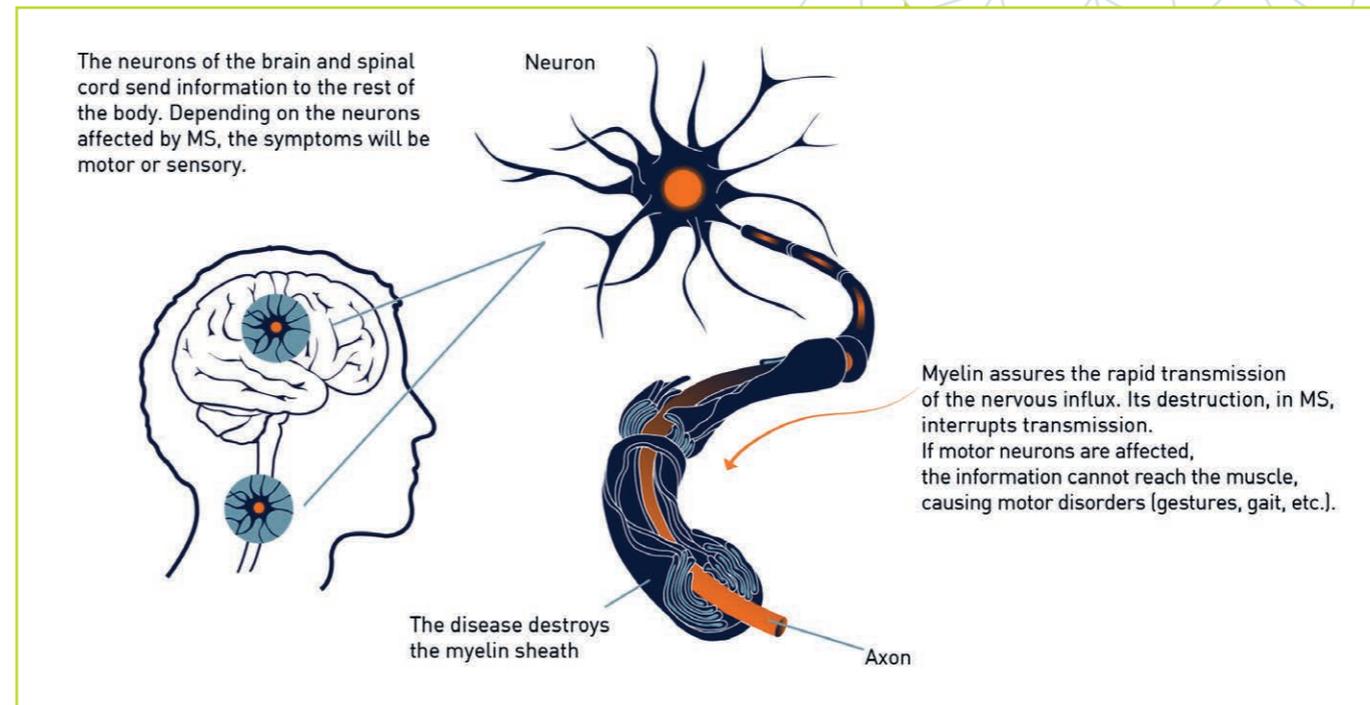
## 1/ DECIPHER

### The mechanisms of destruction

The team of Bertrand Fontaine and Sophie Nicole has discovered five new groups of genes associated with a predisposition to MS. These gene networks are implicated in the adhesion and migration of certain cells of the immune system, the T lymphocytes, into the brain. The entry of T lymphocytes into the brain is a crucial step in the development of MS, because they are responsible for the destruction of the myelin sheath. By blocking their migration towards the nervous system, degradation of the myelin sheath is reduced, favouring its repair and the restoration of nerve functions. One of the gene networks identified by this analysis is of major importance for the identification of new therapeutic targets in MS.

### The recruitment of reparative cells

The team of Catherine Lubetzki and Bruno Stankoff studies the



The mechanism of multiple sclerosis

cellular and molecular mechanisms of de/remyelination, notably those that control the migration and recruitment of the cells that produce myelin. These researchers have just shown that these cells are activated during demyelination, become more motile and express factors that increase their mobilization. In collaboration with other researchers of the ICM, this team demonstrated the role of a molecule (netrine) that prevents the recruitment of these reparative cells. Blocking this molecule accelerates myelination. This discovery is extremely important because accelerated recruitment of myelin-producing cells permits repair of the axon during a period in which the lesions are still reversible. The team of Brahim Nait Omesmar

and Anne Baron-Van Evercooren showed that cells in the peripheral nervous system also contribute to remyelination in the central nervous system (CNS). When the CNS is lesioned, cells in the periphery can migrate and contribute to the production of myelin. These cells are of interest because they are not destroyed by the immune system in MS, and can thus play a major role in remyelination.

### Factors implicated in repair

Brahim Nait Omesmar and Anne Baron-Van Evercooren have discovered the beneficial role of several molecules in myelin repair. Their latest advance was the identification of a "pro-myelinating" molecule, called Olig2. This discovery could play a major role

in the development of treatments aimed at stimulating the repair of damage caused by MS. The team of Catherine Lubetzki and Bruno Stankoff are also interested in the early mechanisms underlying the formation of Nodes of Ranvier, regions of the axon which are not myelinated and transmit the nerve influx. They have demonstrated that structures resembling Nodes of Ranvier, called pre-nodes, appear before myelination starts. These pre-nodes are important because they accelerate conductance of the nervous influx along the axon. The fact that another element, in addition to myelin, can accelerate the nervous influx is an innovative concept. A study is underway on the role of these pre-nodes during remyelination.

## 2/ MEASURE

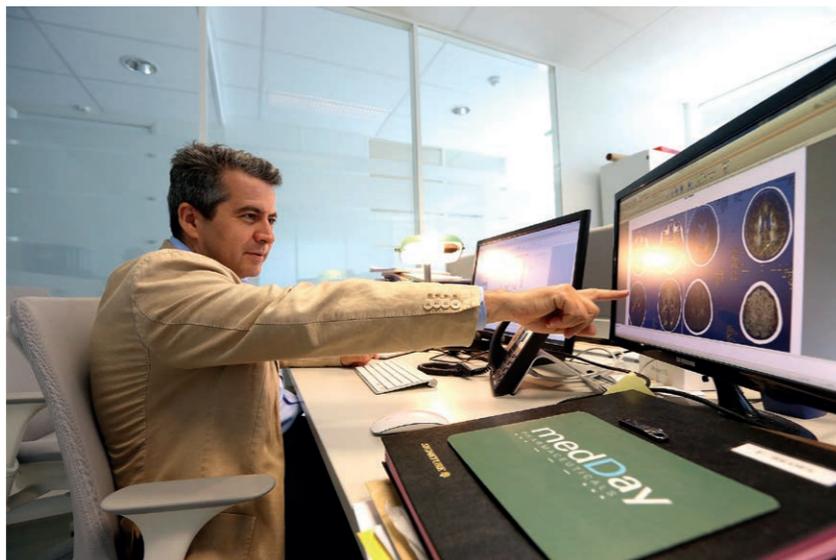
The team of Catherine Lubetzki and Bruno Stankoff is looking for ways to measure the evolution of the disease (undetectable by MRI). To this end, the researchers developed an innovative imaging program associating several techniques. One of their research axes is to visualize myelin by PET-SCAN. With this method, the rate of de/remyelination can be measured and patients characterized according to their capacity to remyelinate. This new method could serve as a predictive marker of the evolution of the disease.

By combining several MRI techniques and analyzing functional connectivity in the brain, the researchers have shown that certain networks are particularly disconnected in patients with cognitive disorders. This disconnection is related to the death of the neurons in specific regions, which underlies the loss of cognitive functions. The team also works on an imagery project specific to neurodegeneration (MS is a myelin disease, but neuronal degeneration causes the handicaps). With these methodologies, one can predict the evolution of the patients, understand why the disease progresses and evaluate therapeutic targets for remyelination, neurodegeneration or neuroinflammation.

focus continues on next page ●●●

## ALEXIS GENIN, Director of Research Applications

"The ambition of the ICM is not only to perform excellent research, but especially to use it as a basis for the development of new treatments, applying the knowledge obtained by research and the competencies of the researchers. The iPEPS-ICM incubator establishes a bridge that aims at valorising all work done in the ICM, help Institute researchers to create their "start-up" and rapidly develop medical applications. The adventure of Frédéric Sedel and MedDay is a fine example, and we are proud to have accompanied this start-up in the development of the new treatment. Examples of such a rapid success are extremely rare!"



### 3/ TREAT

**After a surprising clinical observation, the founder of MedDay, Frédéric Sedel, followed-up on his idea and registered a patent. Once patented, his idea gave rise to the creation of a company to realize his project. The company, MedDay is incubated at the ICM.**

**In less than two years, this scientific adventure resulted in the development of a treatment for progressive multiple sclerosis, an achievement that many important pharmaceutical companies take more than 15 years to realize.**

MedDay is today a private biotechnology company, incubated in the Brain and Spine Institute, which develops new treatments for nervous system disorders. Last April, it announced that the main criterion in its clinical trial of a treatment for progressive MS had been reached. The effectiveness of biotine, a new treatment for the progressive form of MS, has just been confirmed by a phase III study on 154 patients. This treatment not only slows the progression of the disease, it also significantly improves the state of health of the patients. The MedDay team hopes that the treatment will be available on the market within a year, a period that is particularly short and encouraging for the team as well as the patients. ●●●



See the complete interview with Frédéric Seidel at <http://icm-institute.org/fr/actualite/sclerose-en-plaques-progressive-un-succes-pour-medday/>



## ALZHEIMER DISEASE A GENETIC FACTOR IDENTIFIED

About 860,000 persons have Alzheimer type dementia in France and 35 million worldwide. Alzheimer disease is thus, today, at the centre of our preoccupations. Alzheimer disease is characterized by the slow degeneration of neurons that begins in a specific region of the brain (the hippocampus) then extends to the rest of the brain.

Understanding the genetic bases of the disease is fundamental, on the one hand to make the diagnosis and on the other to understand the mechanisms responsible for neuronal death. In a study involving 2,600 Islanders, Harald Hampel (Pierre and Marie Curie University/IM2A/ICM) and his colleagues discovered a correlation between the presence of a mutation (modification of information) in the gene ABCA7 and the development of Alzheimer disease.

If the role played by the ABCA7 protein in Alzheimer disease is still unknown, these studies open the way for new methods of diagnosing Alzheimer disease as well as other neurodegenerative disorders.



## AUTISM WHAT IF IMITATION HAS A THERAPEUTIC EFFECT?

If they are imitated, the social behaviour of autistic patients improves via effects on strategic regions of the brain. This is suggested by a recent study conducted by ICM researchers using functional magnetic resonance imagery (fMRI). Autism affects 430,000 persons in France, 25% of which are children. This pathology is characterized by difficulties of communication with others and developing social relations. Several studies have shown that the administration of oxytocin to autistic patients in the form of a nasal spray improves their social interactions and cooperation with others. Recent studies by the teams of Jacqueline Nadel and Philippe Fossati, published in Brain show that the imitation of autistic patients has an action similar to that of oxytocin.

The study involved six autistic men and consisted, for the researchers, of imitating, or not, a movement of the hand made by the patients whose brain activity was measured by fMRI. The researchers observed an activation of the right side of the insula in autistic patients when they were imitated and a reduction in the activity of regions of the brain that are exaggeratedly active in the autistic subjects.

The region of the insula, also activated by oxytocin, plays a central role in social behaviour and the development of emotions.

By suggesting that the imitation of autistic patients has a therapeutic effect via the modulation of specific brain regions, these results open new perspectives for the treatment of autism.

## THE ESSENTIALS OF THE ANNUAL ACCOUNTS OF THE ICM FOR 2014

Understand and treat the diseases and traumatisms of the nervous system are a major challenge worldwide for the 21<sup>st</sup> century. Today, medicine relieves... Tomorrow, it must prevent, cure and repair. These disorders affect about a billion persons throughout the world,\* a number that will continue to increase as the population ages. In France, life expectancy has increased by 15 years during the last 50 years: 1 girl out of 2 who are born today will become a centenarian. In 2050, 1 French person out of 3 will be 60 or more (1 in 5 in 2005). Each year in the world, 50 million persons\* are injured or become invalids following a cranial or spinal traumatism. These numbers will increase considerably between now and 2020, particularly in developing countries.

### FACED WITH THIS CHALLENGE, THE MISSIONS OF THE ICM ARE TO:

- **Prevent**, i.e. to prevent the disease from developing;
- **Cure**, i.e. to slow, even stop, the evolution of the pathological process;
- **Repair**, i.e. to reconstruct the neuronal circuits affected in the nervous system;
- **Relieve**, to attenuate or suppress symptoms such as memory loss, language disorders, pain, anxiety, depression...

### THE AIM IS TO PRODUCE INTERNATIONAL LEVEL RESEARCH BY COMBINING SCIENTIFIC CREATIVITY WITH A THERAPEUTIC GOAL.

### THE SCIENTIFIC PROGRAM IS FOUNDED ON THE FOLLOWING PRINCIPLES:

- Create a research "strike force", which means recruiting the best French researchers classed by AERES (agency for the evaluation of research and higher education) and the best foreign researchers evaluated by the Institute's International Scientific Advisory Board;
- Offer researchers the most advanced technological platforms and a very efficient Biological Resource Centre;
- Develop multidisciplinary "translational" research in association with industrial partners and the best French and international research centres;
- Define privileged research axes.

### THE ICM: A NEW MODEL

For its investments and functioning, the ICM, a "Foundation of recognized public utility" since 2006, is accompanied by its institutional partners: Ile-de-France, Mairie de Paris, Caisse des Dépôts, Assistance Public-Hôpitaux de Paris, CNRS, Université Pierre et Marie Curie.

### The generosity of its donors and partnerships with sponsoring enterprises provide support, notably to permit:

- Financing, on its own resources, of the teams or researchers recruited worldwide on criteria of excellence;
- The realization of innovative research programs;
- Investments in advanced equipment.

\* Sources: OMS, continentalnews, sante-medecine.creapharm.psymad

## FINANCIAL REPORT

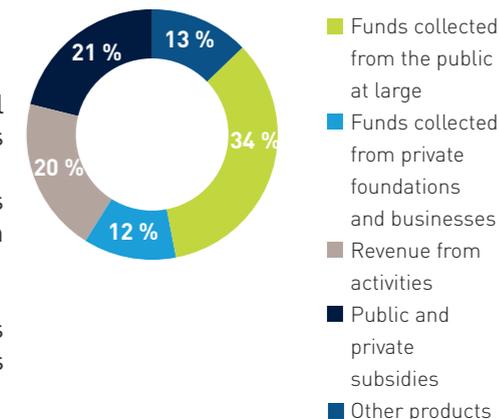
### 1-RESOURCES

Resources for 2014 reached 26.2 M€. They include 24 M€ for the fiscal year and 2.2 M€ of affected resources carried over from previous fiscal years.

The products of the fiscal year correspond essentially to funds collected (46%) either from the public at large (34%) or from businesses or private foundations (12%).

They also include:

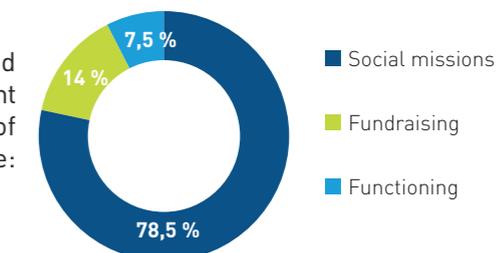
- Revenues from the activities of the technological platforms (2.2 M€) and research collaborations with industrial partners (2.6 M€);
- Subsidies from public (3.3 M€) and private (1.8 M€) sources.



### 2-USES

Total of uses in 2014 reached 27.2 M€: 24.1 M€ used in 2014 and 3.1 M€ of already affected resources. Among uses in 2014, the amount dedicated to social missions was 19 M€, which represents 78.5% of total uses for the fiscal year. The social missions of the ICM include:

- The research projects (58%);
- The technological platforms (30%);
- Other scientific activities and the development of international alliances (9%);
- Incubation of innovative enterprises (3%).



The research projects financed mainly concern neurodegenerative diseases and traumatisms of the spinal cord. The technological platforms (neuroimaging, vectorology, sequencing/genotyping, cell culture and histology) added support for these projects. The costs of fundraising correspond to the expenses engaged to collect funds from private individuals (donations and bequests) and business and private foundations (sponsoring or patronage). They represent 14% of uses.

The costs of functioning correspond to the expenses of support teams (finance, human resources, informatics and logistics), which represent 7.5% of total uses for the fiscal year. Engaged affected resources (3.1 M€) correspond mainly to donations by enterprises and foundations received during the year that will be used for specific pluriannual research programs.

### 3-USES OF RESOURCES COLLECTED FROM THE PUBLIC

Resources collected from the public at large, used in 2014, reached 9.6 M€.

**In brief, out of 100€ of resources collected from the general public, 71€ were used to finance the social missions and investments of the Institute, 27€ were used for fundraising and 2€ covered the costs of functioning of the ICM.**

