

# FOR YOU & WITH YOU

The Brain and Spine Institute Donors Journal



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**SPECIAL FOCUS  
ON AMYOTROPHIC  
LATERAL SCLEROSIS**

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**FOR YOU & WITH YOU**

Knowledge of the brain has increased without stopping these last thirty years. This field of investigation, which offers immense possibilities and is a real

new frontier for science, fascinates but also raises questions. At a moment when the world is changing at an accelerating pace, it is essential to elucidate the functioning of the most extraordinary organ of the human body, both to advance our knowledge of its normal functioning and to understand its dysfunctions and imagine tomorrow's treatments.

For 5 years now, the Brain and Spine Institute has been an innovative and ambitious pilot project that offers more than 600 researchers, clinicians, engineers, technicians and support personnel, an environment, unique in the world, for discovering in the shortest time possible new treatments against the diseases of the brain and spinal cord. All is in place so that the Institute can make the great discoveries that will enable us to prevent, cure and repair.

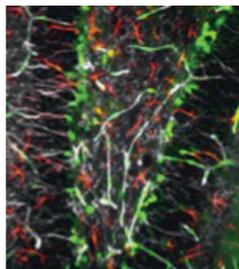
To celebrate this fifth anniversary with you, I have the pleasure of presenting the first edition of the Brain and Spine Institute Donors Journal, a bulletin dedicated to you, which will enable you to follow the activity of the Institute each trimester. The form and the contents have been elaborated for you, to enable you to discover with the researchers a timely subject, to express yourself and to receive answers to your questions.

I hope that this new format pleases you and will help reinforce our relations, so that we can continue, together, to write tomorrow's medicine.

**Pr Gérard Saillant**  
President of the ICM

**MAKE NEURONS TO FIGHT AGAINST ALZHEIMER DISEASE**

A decrease in the mechanism of neurogenesis during aging is implicated in the development of neurodegenerative pathologies such as



Alzheimer disease. Studies associating ICM researchers (Inserm / CNRS / Pierre and Marie Curie University), in collaboration with a team in the Cardiovascular research centre of Yale (USA), show the importance of the factor VEGF-C in the activation of

neural stem cells and consequently the production of neurons. These results, published in Cell Reports, bring new hope for the development of therapies to compensate for cognitive decline in persons with Alzheimer disease.

**ADVANCES IN THE NEUROSCIENCES QUESTION THE MORAL AND LEGAL RESPONSIBILITY OF RESEARCHERS**

The philosopher John Harris made a noteworthy presentation in the neuroethics colloquium that took place in the ICM, in June 2014. His lecture was published in the well-known journal "The Cambridge Quarterly on Healthcare Ethics." Find it on the site of the ICM / Communication / Conferences.

**ON JUNE 21, EVERYBODY CAN RUN, SICK OR IN PERFECT HEALTH, YOUNG OR LESS YOUNG, A RUNNER OR A SEDENTARY PERSON, BLOND OR BRUNETTE**

The race of heroes is accessible to just about everyone, athlete or not, because the participants have the choice of 3 formats, a 6 km walk, a 6 km race, a 6 km walk and a 10 km race. The Heroes



register then create a fundraising page to collect at least 250 € of donations for the association of their choice. D-day is the occasion to share a convivial and festive moment. This year, the ICM will once again be represented by Anne-Claire

Lenoir, our "super-hero" and her family. Find her testimony on the internet site of the Institute and, you too, come and participate in this unique and big-hearted sporting event.



A racetrack for the brain near the city of Bourg-en-Bresse.

**PARTNERS: LET'S DRIVE FOR RESEARCH ON THE BRAIN AND SPINAL CORD**

Four grand automobile events have been organized to support the ICM and help mobilize in the fight against the diseases of the nervous system.

Since its creation, the ICM has attracted many patrons and partners from the sporting and automobile world. September 12 and 13, 2015, the Lions Club Lyon-Doyen is organizing, for an entire weekend, a manifestation around luxury automobiles that is open to the public, with an exhibition and baptism in one of the dream cars. All of the profits will be donated to the ICM. Classic Days, Classic Festival and the Porsche Motor Club, gatherings of old and contemporary cars on famous automobile circuits, will also contribute their support this summer, adding pleasure to generosity for a day.

If you, too, wish to organise an event for the profit of the ICM, contact Agathe Gioli: [agathe.gioli@icm-institute.org](mailto:agathe.gioli@icm-institute.org).

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**Seen on the web**

Starting on May 19, the ICM will have the pleasure of presenting its **new web site**. The address remains the same.

- [icm-institute.org/news](http://icm-institute.org/news)  
A start-up in the ICM is developing a treatment for the **progressive form of multiple sclerosis**.
- [icm-institute.org/fr/the-conferences-of-the-icm](http://icm-institute.org/fr/the-conferences-of-the-icm)  
Find our researchers and a video of a lecture on **Parkinson disease**.

Find the lectures of **Brain Awareness Week 2015** and exclusive videos of the lectures of **Eric Orsenna** and **Philippe Labro**.

**AGENDA**

- **June 19, 2015, at 17:30\***  
Projection of the film "Une merveilleuse histoire du temps"—"The theory of Everything"—on ALS at the ICM
- **October 12, 2015\***  
Come and run the 20 km de Paris for the Institute

\*Reservation obligatory at [contact@icm-institute.org](mailto:contact@icm-institute.org)

# TO BETTER UNDERSTAND AND TREAT AMYOTROPHIC LATERAL SCLEROSIS

**A**myotrophic lateral sclerosis—ALS is characterized by a rapidly progressing paralysis (1 to 5 years after the appearance of the first symptoms) and a lack of effective treatments. Together with the core facilities and the clinicians of the Institute, the ICM team led by Séverine Boillée seeks to understand both how ALS is caused and how it evolves, in order to develop effective treatments for this fatal neurodegenerative disease

ALS is still not well known in France and little studied because it is considered to be one of the rare diseases. However,

## THE TEAMS AT WORK

■ Thanks to the privileged location of the ICM at the heart of the Pitié-Salpêtrière Hospital, the clinicians (Prs. Meininger and Seilhean and Drs. Pradat and Salachas) work in close collaboration with the researchers. Séverine Boillée has also brought together researchers with complementary skills (Dr. Delphine Bohl, Dr. Christian Lobsiger, Dr. Stéphanie Millecamps) to fight the disease more effectively.

the number of 8,000 persons affected by ALS in France hides another reality: the disease itself, for which effective treatments remain to be developed, causes a progressive, very disabling and fatal paralysis. It affects 5 persons in 100,000, generally when they are in their 50's, and its frequency increases with age; this means, for each of us, a risk of 1 in 1,000 of having ALS by the age of 65.

In France, ALS is known as "Charcot's disease", the name of the neurologist of the Salpêtrière, Jean-Martin Charcot (1825-1893) who described it for the first time. Thus, the ICM, situated right where ALS was discovered and affiliated with teams having found the only active treatment for ALS, has chosen as its mission to develop strong translational research to find new effective treatments for this disease.

Séverine Boillée's team at the ICM is searching for new causes of ALS and biochemical pathways implicated in the progression of the disease. ALS affects the neurons responsible for motricity, called motoneurons, which are situated in the brain and spinal cord. They are connected to muscles to which they send the signal to contract. In ALS, these signals are lost and the muscles



Séverine Boillée's team at the ICM

atrophy leading to paralysis.

Motoneurons are the cells that die in ALS, but cells of the immune system (macrophages) in the spinal cord also contribute to the disease. A recent study of the team showed the implication of these immune cells in the disease, in particular of a pathway called "system xc-", in ALS. They showed that system xc- was not expressed by the motoneurons themselves but by macrophages in the nervous system. They eliminated system xc- in models of ALS and slowed the progression of the disease. These results thus reveal the existence of communications between the immune cells and

the motoneurons and show that it is possible, by acting on the immune cells, to influence the survival of the motoneurons and the evolution of the disease. The development of pharmacological tools specific for system xc-, but also to target other factors expressed by the immune cells, might thus be able to slow the evolution of ALS.

This research relates to recent discoveries made by a European consortium to which one of the team members participated: mutations in a gene important for the immune system have just been implicated in ALS.

In order to find new therapeutic targets implicated in the interaction between the immune cells and the motoneurons, the team is developing experimental models of ALS, including human motoneurons obtained thanks to iPSc (pluripotent stem cell) technology, from skin biopsies taken from patients with ALS. This approach might lead to the development of new treatments that would slow the progression of the disease. ●●●

## Identify new causes of ALS thanks to the zebra fish

Edor Kabashi's team is specialized in the functional characterization of the genetics of ALS and has developed several models in the zebra fish to better understand the role of the major genes causing the disease. An essential advance in the work of this team was the development of the only vertebrate model reproducing the effects of the most important genetic cause of ALS in patients. These models have led to an understanding of the physiopathological mechanisms of the disease and helped the team identify several therapeutic targets for ALS and related diseases, including frontotemporal dementia.

Edor Kabashi  
Team leader





