INSTITUT DE FRANCE

Press release
Paris, May 2010

SIMONE AND CINO DEL DUCA FOUNDATION

The Grand Prix scientifique 2010
of the Simone and Cino del Duca Foundation was awarded to

Prof. PATRICK AUBOURG

Director of Inserm 745 Unit "Genetics and biotherapies of degenerative and proliferative diseases of the nervous system" - Saint-Vincent de Paul Hospital, Paris

The Grand Prix scientifique of the Simone and Cino del Duca Foundation, worth **300,000 euros**, aims to reward either a French or foreign research team. The 2010 Prix theme was "Vectorization of bioactive molecules for the treatment of severe pathologies".

The Jury, composed of eminent scientists, most of whom members of the Académie des sciences, awarded the 2010 Prix to **Prof. Patrick Aubourg** and his team, to reward their critical findings in the field of **genetic diseases of the central nervous system**.

Prof. PATRICK AUBOURG

Born in Paris in 1953, Patrick Aubourg is a Doctor of medicine and Professor at the Université Paris-Descartes. He directs the Inserm 745 Unit "Genetics and biotherapies of degenerative and proliferative diseases of the nervous system" at the Saint-Vincent de Paul Hospital. His work has mainly focused on a group of particularly severe neuro-degenerative diseases, leukodystrophies, caused by the progressive disappearance of neurone myelin (myelin insulates the axon of each neurone). Prof. Aubourg has brought the most sophisticated concepts and techniques of molecular biology to his patients over a period of more than twenty years.

The Prix will be awarded under the Cupola of the Institut de France

Wednesday June 9th 2010 at 3pm

as will all other scientific and cultural Grands Prix of the Foundations of the Institut de France:
the Mérieux, Louis D., NRJ, Lefoulon-Delalande and Simone and Cino del Duca Foundations

Treatment of Adrenoleukodystrophy (ALD) using gene therapy

Adrenoleukodystrophy is the most common of the leukodystrophies (***see box***). In 1993, Patrick Aubourg and Jean-Louis Mandel identified the gene which causes the condition. This discovery clarified the mechanisms of the disease and opened the door to prenatal diagnosis. Above all, it encouraged Patrick Aubourg, his colleague Nathalie Cartier (Inserm) and his team to launch an ambitious **gene therapy** project, replacing the mutated gene by a gene with normal function, with the help of Pierre Bougnères (Saint-Vincent de Paul Hospital). Gene therapy was just beginning to prove its efficacy in humans, especially thanks to the work of Alain Fischer, Marina Cavazzana and Salima Haceyn-Bey-Abina (Necker Children's Hospital) with whom Patrick Aubourg has worked closely. The results, published in *Science* in 2009, led to an amazing improvement in the clinical manifestation in a number of patients and made history in human gene therapy. Previously, Patrick Aubourg, in collaboration with Claude Griscelli and Alain Fischer, had obtained promising yet more limited results by "allogeneic" bone marrow transplants from healthy humans.
The treatment awarded the Prix scientifique 2010 of the Simone and Cino del Duca Foundation consists of taking stem cells from the patient's bone marrow and correcting the malfunction by the transfer of a normal gene using a **gene therapy vector derived from the HIV virus which has been modified and deactivated**. The corrected cells are then reinjected into the patient. By a natural mechanism, some will go directly to the brain of the patient and correct the malfunction.

This is the first time that a serious brain disease has been successfully treated using gene therapy, and the results have contributed to renewed interest in the treatment of human diseases using this kind of approach.

Adrenoleukodystrophy *is a rare disease (affecting 1 / 17,000 births) which has three clinical presentations. The first is a cerebral form which presents in children between age 4 and 8, with progressive vision loss and loss of cognitive and motor functions, leading to total disability in less than two years. The second, adrenomyeloneuropathy, presents at a later age. At around the age of 20, progressive paralysis sets in, together with sphincterian problems and variable vision loss. The third is an adrenocortical insufficiency which appears between the ages of 2 and 20, most commonly around the age of 7, with no neurological indicators.*

Projects for treatment of Alzheimer's and Friedreich's disease

The grant awarded by the Simone and Cino Del Duca Foundation is also intended to support the research project proposed by the laureate and his team. This project aims to improve the remarkable gene transfer method used, and apply it to two further cerebral pathologies: Alzheimer's disease and Friedreich's cerebellar ataxia.

- In **Alzheimer's** patients, the research focuses on the correction of cholesterol anomalies, as conventional cholesterol-lowering agents do not work on the brain. The aim is to use a suitable vector to introduce into the brain the coding gene for "cholesterol-24-hydroxylase", an enzyme which participates in the elimination of cholesterol from this organ.

- In patients suffering from **Friedreich's ataxia**, the study aims to introduce the functional gene of frataxine, a protein essential to the function of the cerebellum, found in precise cellular organelles: mitochondria. A lack of frataxine in these organelles leads to disturbance of a structure which is essential to their healthy functioning, and later an accumulation of iron. Patrick Aubourg's team are testing two new viral vectors for gene therapy to determine which, after, intra-venous injection, is most conducive to frataxine expression not only in cerebellum cells but also in the heart and in spinal marrow.

About the Simone and Cino del Duca Foundation – Institut de France

The **Simone and Cino del Duca Foundation**, situated in the Institut de France since 2005, aims to promote scientific research and conserve, enhance and draw attention to scientific and cultural heritage. It offers bursaries and prizes in France and overseas. The Foundation awards three Grands Prix each year: a Prix mondial, a Prix scientifique, and a Prix d'archéologie.

The Prix scientifique, worth **300,000 euros**, aims to reward either a French or foreign research team. Following very diverse themes such as "mathematics and its applications" or "Biodiversity and/or evolution", the theme of the 2010 Prix was "Vectorization of bioactive molecules for the treatment of severe pathologies". In the scientific field, the Foundation also awards three grants a year to encourage young French teams.

Composition of the Jury for the Prix scientifique 2010

- Mr. Alain Carpentier, Vice-President of the Académie des sciences, President of the Jury
- Mr. Jean-François Bach, Permanent secretary of the Académie des sciences
- Mr. Jean-Paul Behr, Académie des sciences
- Mr. Marc Fontecave, Académie des sciences
- Mr. Daniel Mansuy, Académie des sciences
- Mr. Jean-Marc Egly, Académie des sciences
- Mr. Daniel Louvard, Académie des sciences
- Mr. André Sentenac, Académie des sciences
- Mr. Henri Korn, Académie des sciences
- Mr. Bernard Malissen, Académie des sciences
- Mr. Daniel Ricquier, Académie des sciences
- Mr. Yves Agid, Académie des sciences
- Mr. Sébastien Amigorena, Académie des sciences
- Mr. Jean-Charles Schwartz, Académie des sciences
- Mr. Christian Amatore, Académie des sciences
- Mr. Jacques Livage, Académie des sciences
- Mr. Bernard Meunier, Académie des sciences
- M. Lucien Israël, Académie des sciences morales et politiques

About the Institut de France

The Institut de France, also known as "the parliament of the learned", brings together **five Academies**: the Académie française, the Académie des inscriptions et belles-lettres, the Académie des sciences, the Académie des beaux-arts and the Académie des sciences morales et politiques. Its non-profit mission is to contribute to the improvement and influence of humanities, sciences and the arts.

As an association, it houses **foundations** whose support from their administrative and financial structures allows them to play an essential role in modern patronage, through the award of grants and prizes.

The actions the foundations support cover a variety of fields, such as:

- **Scientific research**: rewarding established researchers, supporting young talents and laboratories.
- **Humanitarian action**: fighting against endemic illnesses and poverty
- **Cultural heritage**: conserving works of art, creating collections or supporting young artists
- **Education and training**: study or research bursaries
- **Sustainable or environmental development projects**: protecting rural and natural heritage

Faculté des Sciences Pharmaceutiques et Biologiques – UMR Inserm 745 Prof. Patrick Aubourg 4, avenue de l'Observatoire - 75279 Paris cedex 06 Telephone: +33 (0)1 40 48 80 74 Email: patrick.aubourg@inserm.fr	**Institut de France** Camille Bouvier Service communication CS90618 - 23, quai de Conti – 75270 Paris cedex 06 Telephone: +33 (0)1 44 41 43 40 Email: com@institut-de-france.fr www.actualites.institut-de-france.fr