

HONDA FOUNDATION

2-6-20, Yaesu, Chuo-ku, Tokyo 104-0028 Japan

Tel +81-(0)3-3274-5125 Fax +81-(0)3-3274-5103 https://www.hondafoundation.jp/en

September 30, 2021

The Honda Prize 2021 Awarded to Dr. Alim Louis Benabid, Professor Emeritus of Joseph Fourier University and Chairman of the Board of Clinatec*

—Pioneering research into deep brain stimulation (DBS)^{*1} and its contribution to practical application for the treatment of involuntary movement caused by Parkinson's disease^{*2} and other neurological disorders
*Clinatec : Clinatec, Edmond J. Safra Biomedical Research Center

The Honda Foundation, the public interest incorporated foundation established by Soichiro Honda and his younger brother Benjiro and currently led by President Hiroto Ishida, is pleased to announce that the Honda Prize 2021 will be awarded to Dr. Alim Louis Benabid, Professor Emeritus of Joseph Fourier University and Chairman of the Board of Clinatec, Edmond J. Safra Biomedical Research Center, both of France, for his contribution to pioneering research and practical application of deep brain stimulation (DBS) to the treatment of involuntary movement caused by progressive Parkinson's disease and other neurological disorders.

The Honda Prize, established in 1980 and awarded once each year, is an international award that recognizes the work of individuals or groups generating new knowledge to drive the next generation, from the standpoint of ecotechnology^{*3}. Dr. Benabid was the first to make use of DBS for the treatment of involuntary movement, caused mainly by progressive Parkinson's disease, and other neurological disorders and to succeed in its practical application. DBS is a surgical procedure in which electrodes are implanted in the subthalamic nucleus in the brain. Stimulation by high-frequency electric current from electrodes reduces tremors and restores the motor function of Parkinson's disease patients. Recognition of its effectiveness in clinical studies led to the dissemination of DBS worldwide, with more than 150,000 patients undergoing this procedure to date.

If involuntary tremors cannot be controlled with drug therapy considered best suited to treat Parkinson's disease, a surgical procedure known as thalamotomy was commonly performed to destroy a tiny portion of the brain. On the other hand, DBS is a reversible procedure in which the implanted electrodes can not only be removed but also adjusted to fine-tune the strength of the current. DBS can be used to treat not only Parkinson's but also dystonia and other motor disorders, and contributes to improving the quality of life of many, including restoring the ability to stand alone, for example. The Prize will be awarded to Dr. Benabid for this innovative treatment method, which is worthy of the highest recognition.

This year, the presentation ceremony for the 42nd Honda Prize will be held on November 17, 2021, in an online format. The medal and certification, along with an honorarium of 10 million yen, will be presented to Dr. Benabid.

<Research by Dr. Alim Louis Benabid >

Thalamotomy was developed in 1947 as a surgical procedure for treating Parkinson's disease. This procedure, aimed at thermally destroying nerve cells in a tiny portion of the brain (either the thalamus or palladium) that had been activated by the disease, was commonly practiced in the 1950s through 1960s. Although the number of surgeries declined with the development of drugs (L-dopa) that compensate for the drop in dopamine levels, there were side effects and problems of medication over a long period of time (once started, continuing for a lifetime for a majority of cases), drawing renewed interest in surgical procedures.

Because the existing procedure, which aimed at thermal destruction of the target, was irreversible, Dr. Benabid explored safer and more effective treatment methods since 1980s. In the procedure to burn a target in the brain with heat, electrical stimulation was used to predict the effect of the surgery. Dr. Benabid placed electrodes around the target site and stimulated them at the physiological frequency range of 20–50 Hz. While observing the movements of the patient during simulation, he noticed that electrical stimulation stopped tremors at high frequency around 130 Hz. He proceeded to conduct tests from very low frequencies of 1, 5 and 10 Hz to up to 100 Hz and found that effects similar to the existing surgical procedure could be achieved at 130 Hz without destroying the brain tissue.

After Dr. Benabid's discovery that electrodes placed in the subthalamic nucleus and sending adjustable high-frequency simulation produces the same improvement as stereoencephalotomy, he conducted the first thalamic stimulation treatment on an advanced Parkinson's patient for the first time in the world in 1987, and subthalamic stimulation treatment for the first time in the world in 1997. Reports of the mitigation of tremors and muscle rigidity and of favorable results after five years led to DBS becoming the mainstream treatment method for Parkinson's around the world.

When DBS is applied to surgery for globus pallidus internus (GPi), it is reported to produce dramatic improvements in persons suffering from deformity of the legs with dystonia (abnormal contraction of the muscles that cause unnatural posture and movement), enabling

them to walk. DBS is also being used in Germany to treat depression by targeting the habenular nucleus. In the United States, it is being used to target stimulation of the hippocampus for treatment of Alzheimer's disease. It is also applied to restore normal function to neural circuits in the brain, when drug therapy does not show any improvement, and has contributed to improving the quality of life for many people.

"Make people happy with technology." This is the fundamental vision for ecotechnology set out by Soichiro Honda. The achievements of Dr. Benabid have been recognized as worthy of the Honda Prize. For these reasons, the Prize will be awarded to Dr. Alim Louis Benabid.

- *1 Deep brain stimulation (DBS): Electrodes are implanted around the subthalamic nucleus of the brain, along with a stimulation generator placed in the chest. The two are connected with a lead for high-frequency electrical stimulation. This aids in restoring movement functions, and curbing tremors and other symptoms for improved mobility in everyday living.
- *2 Parkinson's disease: Disorder in the function that makes movement adjustments, caused by insufficient production of the neurotransmitter dopamine that carries commands from the cerebral cortex to muscles throughout the body. It progresses slowly over many years, causing movement problems such as tremors at rest (small tremors of the limbs while at rest), akinesia (reduced speed, frequency and range of movement), muscular rigidity (difficulty in moving the joints when trying to move the arm or leg) and impairment of postural reflexes (inability to restore postural balance when losing the center of gravity).
- *3 Ecotechnology: a neologism combining imaging of the natural world (ecology), including civilization as a whole, and technology. Advocated by the Honda Foundation in 1979, it seeks new technological concepts required by human society in the sense of coexistence of people and technology.

For more information, contact the Honda Foundation via:

phone at +81-3-3274-5125 or fax at +81-3-3274-5103

Honda Yaesu Building, 2-6-20 Yaesu, Chuo-ku, Tokyo 104-0028, Japan

https://www.hondafoundation.jp/en/

You may also contact Honda Motor's Corporate PR Department via phone at +81-3-5412-1512.

Alim Louis Benabid, MD, PhD

Professor Emeritus of Biophysics: Joseph Fourier University Medical School

Honorary Professor at Institut Universitaire de France (Senior Member)

Scientific Advisor to the Director of Technological Research at CEA (Atomic Energy Agency)

Chairman of the Board of the Clinatec Institute at CEA Grenoble

<u>Born</u>

May 2, 1942, Grenoble, France (French citizenship)

Education and Training

Medical Degrees (University of Grenoble)

- 1970 MD Thesis
- 1972 Staff Neurosurgeon
- 1978 Professor, Experimental Medicine
- 1984 Professor, Biophysics
- 1989-2004 Head of Neurosurgery

Scientific Degrees (University of Grenoble)

- 1973 Masters of Science
- 1978 Thesis (PhD) Physics

Military Service: Lyon (CRSSA Research Center of the Military Health Services) Oct 1967-Apr 1969

Member of Scientific Societies

| 1977 | European Society for Stereotaxy and Functional Neurosurgery |
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| 1980 | American Society for Neurosciences |
| 1981 | European Society for Neurosciences |
| 1998 | Society for Movement Disorders |
| 1999 | American Association of Neurological Surgeons |
| 2000 | Congress of Neurological Surgeons (USA) |

Scientific Responsibilities

- 1978-2007 Director of LMCEC (Laboratoire de Médecine et Chirurgie Expérimentales et Comparées) and then Laboratoire de Neurobiophysique
- 1984-1990 Director of IRMBM (Institut de Résonance Magnétique Biologique et Médicale) from
- 1988-2007 Director of Research Unit INSERM 318 (Neurobiologie Préclinique)
- 1995-1997 Director of Center for Gene Therapy "Brain Tumors"
- 2007- Director of the Clinatec Institute Project at CEA Grenoble
- 2008-2021 Chairman of the Board, Clinatec, Biomedical Research Center Edmond, Safra, CEA, Grenoble

Medical Responsibilities

1989-2004 Head of Neurosurgery Department -Coordinator of the Epilepsy and Movement Disorders Center "Claudio Munari", Niguarda ca Grande Hospital, Milano, Italy



Administrative Responsibilities

| Scientific Council of: | |
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| 1976-1986 | Medical School Grenoble |
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| 1976-1986 | University of Grenoble |

Administrative Council of:

| 1989-1993 | INSERM (appointed by the Ministry) |
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| 2006-2012 | Science Advisory Committee of ESRF (European Synchrotron Radiation Facility) Special Advisor |
| 2007- | Scientific Advisor of the Director of Research and Technology at CEA |
| 2016- | Scientific Advisory Board of the WYSS Foundation, Geneva |

Prizes and Honors

| 1971 | Prix Beytout |
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| 1972 | Prix de Thèse de l'Université de Grenoble |
| 1993 | Prix Electricité-Santé de l'EDF |
| 1994 | Prix du Club de la Presse de l'Isère |
| 1996 | Prix Médecine et Biologie du Comité du Rayonnement Français |
| 1997 | Grand Prix de la Recherche Biomédicale PCL de l'Académie des Sciences |
| 1999 | Prix de l'œuvre Scientifique (Fondation Nationale pour la Promotion de la Santé, |
| | et le Développement de la Recherche, Algérie) |
| | Prix Jean Valade. Fondation de France |
| 2000 | Prix Klaus Joachim Zülch. Gertrud Reemtsma Foundation (Cologne) |
| | Scientific Award 2000. International Neurobionics Foundation (Hannover) |
| | Cotzias Award, Spanish Society of Neurology, Barcelona |
| 2002 | Sherrington Medal of the Royal Society of Medecine, London |
| | Prix Recherche et Santé de l'Institut des Sciences et de la Santé |
| | Prix Betty and David Koetser Foundation (Zurich) |
| | Prix Dingebauer of the German Society of Neurology (Manheim) |
| 2005 | Spiegel and Wycis Medal of the WFSSN, Roma |
| 2006 | Prix Matmut de l'Innovation médicale et de la Fondation de l'avenir |
| 2007 | James Parkinson Award, Parkinson's Disease Foundation, New York, |
| | Victor Horsley Medal, London, UK |
| 2008 | Movement Disorders Award of the American Academy of Neurology |
| | First International Highest Recognition Award of the Secretary of Health and Human Services, |
| | Washington.DC |
| | Prix d'Honneur de l'INSERM |
| | Victoires de la Médecine, Association of University Hospitals for the last 50 Years |
| 2009 | IPSEN Prize, IPSEN Foundation |
| 2012 | Légion d'Honneur (Officer) |
| 2013 | Pritzker Prize, Michael J Fox Foundation |
| | Jay van Andel Prize, Jay van Andel Foundation |
| 2014 | Lasker Prize |
| | Breakthrough Prize for Life Sciences |
| | Lifetime Achievement Prize |
| 2015 | Giant in Neuromodulation Award |
| 2016 | European Inventor Award Research |
| | Ambroise Paré Medal (French Academy of Surgery) |
| 2021 | Vilhelm Magnus Medal, Norwegian Neurosurgical Society |
| 2021 | 2021 International Brain Stimulation Award |
| | Jean Talairach Award, SSFN |

Honoris Causa Doctorates

| 2005 | Doctor Honoris Causa University of Galway, Ireland |
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| 2006 | Doctor Honoris Causa University of London, Ontario |
| 2008 | Doctor Honoris Causa McGill University, Montreal, Quebec |
| 2012 | Doctor Honoris Causa Porto University, Porto, Portugal |
| 2018 | Doctor Honoris Causa KUL, Leuwen, Belgique |
| | Doctor Honoris Causa Chan Tun University, Taipei, Taiwan |

Medals and Academies

| 1997 | Chevalier des Palmes Académiques |
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| 1999 | Member (corresponding) of Academy of Medicine |
| 2002 | Chevalier de l'Ordre National de la Légion d'Honneur |
| | Member of the Royal Academy of Medicine of Belgium |
| | Member of the Academy of Sciences, Institut de France |
| 2012 | Officier de l'Ordre National de la Légion d'Honneur |
| 2016 | Officier des Palmes Académiques |
| 2021 | Commandeur des Palmes Académiques |

Honorary Membership of Scientific Societies:

| | 1998 | Belgian Society of Neurology |
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| ź | 2007 | Spanish Society of Neurosurgery |
| | | Japanese Society of Neurosurgery |
| | | Italian League against Epilepsy |
| ź | 2008 | Movement Disorders Society |
| ź | 2012 | German Clinical Neurophysiology Society |
| ź | 2016 | Brazilian Functional and Stereotactic Neurosurgery Society |
| ź | 2017 | Spanish Society of Functional and Stereotactic Neurosurgery |
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Published Articles From Web of Science

January 2021: *h*-index *96/95* Results found Sum of the Times Cited 42272 Citing Articles 1357

Published Articles From Google scholar

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May 2021: h-index 107
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Results found 336 articles Sum of the Times Cited 50842 Citing Articles

Publications

Benabid AL, Pollak P, Louveau A, Henry S, de Rougemont J: Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson disease. Appl Neurophysiol,1987, 50:344-346.

Krack P, Pollak P, Limousin P, Benazzouz A, Benabid AL. Stimulation of subthalamic nucleusalleviatestremor in Parkinson's disease. Lancet. 1997 Dec 6;350(9092):1675.

Krack P, Limousin P, Benabid AL, Pollak P. Chronic stimulation of subthalamic nucleus improves levodopainduced dyskinesias in Parkinson's disease. Lancet. 1997 Dec 6;350(9092):1676.

Limousin P, Krack P, Pollak P, Benazzouz A, Ardouin C, Hoffmann D, Benabid AL: Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease. N Engl J Med. 1998 Oct 15;339(16):1105-1111.