INSTITUT DE FRANCE

Awards ceremony for the attribution of Grand prizes

Wednesday June 15 2005 at 15 h

Presided over by Mr. Jean PRODROMIDÈS

President of the Institute
President of the Academy of Fine Arts

Opening

By Mr. Pierre MESSMER, chancellor of the Institute

« The 3rd brumaire year IV, during one of the final sessions, the Convention adopted the Daunou report which created the Institut de France, designated as a "summary of the scholarly world, the representative body of the Republic of letters". This Institute, the author writes, "will publicize scientific discoveries so that the most outstanding will benefit from the free influence of the public's esteem and therefore become universal in being seen as the most significant."

The founders of the Institut de France hold it as their duty to endow the Institute with the benefit of public funds in order to achieve such a noble ambition. More than 200 years of this institution have shown that our missions – which serve the public interest and have been confided to us by the State – have been accomplished with the gracious assistance and generosity of private donors.

It is due to the contributions of such private donors that the Institute exercises the influence and service entrusted to it; and thanks to their generosity it can, in full autonomy, work effectively in the areas of the arts and sciences"… (extract from the speech)

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The Institut de France and its major Foundations: Patronage with a resolute eye on the future

The prizes and financial assistance provided by the Foundations go to support work in **four areas**:

- **Scientific research**, particularly research in health, including substantial grand prizes to reward confirmed researchers and many subsidies to support laboratories (Fondation Yves Cotrel, Fondation Simone et Cino del Duca, Fondation Lefoulon-Delalande, Fondation Rodolphe Mérieux and Fondation NRJ).

- **Humanitarian Aid**, particularly the fight against extreme poverty, aid to civilian victims of war and aid to disadvantaged children (Fondation Blancmesnil, Fondation Janelly and Jean-René Fourtou, Fondation Louis D., Fondation Rodolphe Mérieux).

- **Cultural Heritage**, financial assistance for the conservation of works of art or the creation of a collection (Fondation Blancmesnil, Fondation Janelly et Jean-René Fourtou, Fondation Louis D., and Fondation Lefoulon-Delalande).

- **Education, sustainable development, cultural and scientific development** (Fondation Blancmesnil, Fondation Rodolphe Mérieux and Fondation Louis D.).

Prizes to be awarded by the Institut de France in 2005

Fondation Louis D. (founded in 2000)
Scientific Prize *(750,000 euros)*
Humanitarian Prize *(750,000 euros)*

Fondation Lefoulon-Delalande (founded in 2000)
Scientific Prize *(5,000,000 euros)*

Fondation Simone et Cino del Duca (under the gouvernance of the Institut de France since 2005)
Scientific Prize (250,000 euros)
World Prize (250,000 euros)
Archeology Prize (200,000 euros)

Fondation NRJ (founded in 1999)
Scientific Prize (100,000 euros)

Fondation Blancmesnil (founded in 1998)
Subsidies (approximately 220,000 euros)

Fondation Yves Cotrel (founded in 1999)
Subsidies (approximately 324,000 euros)

Fondation Janelly et Jean-René Fourtou (founded in 2002)
Subsidies for the arts and humanitarian aid (approximately 308,000 euros)

Fondation Rodolphe Mérieux (founded in 2001)
Subsidies (approximately 1,320,000 euros)

Ceremony Programme

Scientific Patronage of the Foundations of the Institut

By Mrs Nicole LE DOUARIN, secrétaire perpétuel de l'Académie des sciences

Scientific prize-winners for 2005

La Fondation Lefoulon-Delalande awards the scientific prize of 600,000 euros to Professor **Harold F. Dvorak** (Harvard Medical School – Boston MA – USA) and to **Doctors Napoleone Ferrara** (Genentech – San Francisco CA – USA) and **Moses Judah Folkman** (Children's Hospital – Boston MA – USA).
by M. Alain CARPENTIER, de l'Académie des sciences

La Fondation Louis D. awards the Grand Prix Scientifique of 750,000 euros to **Professors David P. Bartel**, member of the Whitehead Institute for Biomedical Research/MIT and **Ronald H.A. Plasterk**, Hubrecht Laboratory/University of Utrecht (Netherlands), for their work on the "The new world of small, non-coding RNAs and their roles in the control of cellular functions".
by M. François GROS, secrétaire perpétuel honoraire de l'Académie des sciences

La Fondation Simone et Cino del Duca awards the scientific prize of 250,000 euros to Pr. **Massimo Inguscio**, of the University of Florence for his research in the area of degenerate fermion gases.
by M. Édouard BRÉZIN, président de l'Académie des sciences

La Fondation NRJ awards a scientific prize of 100,000 euros to Professors **Patrice Tran Ba Huy,** Chief of Service (ORL) at the Lariboisière hospital in Paris and **Guy Richardson,** of the University of Sussex, GB, for their work on the "physiology and pathology of the inner ear."
by M. Jean ROSA, de l'Académie des sciences

The humanitarian and cultural sponsorship of the Foundations of the Institut

By Mr. Gabriel de BROGLIE, of the French Academy
and of the Academy of Moral and Political Sciences

Proclamation of the laureates of the Grand Prizes of cultural and humanitarian achievement

Attribution of the Louis D. Foundation Prize for humanitarian work valued at 750,000 euros to Catholic Relief, for the medicalized halfway house for autistic adults at Bagneux (Hauts-de-Seine) on behalf of its associate the Association of Catholic Relief Services by Mr. Michel ALABERT, permanent secretary of the Academy of moral and Political Sciences,

Attribution of the Simone and Cino del Duca World Prize worth 250,000 euros
to Mr. Simon LEYS, Belgian author and Sinologist for his collected works, by Mme. Hélène CARRÈRE d'ENCAUSSE, permanent secretary of the French Academy.

The Louis D. Foundation (established in 2000)

The purpose of the Foundation is to **support associations**, non-profit organizations or N.G.O's (Non-Governmental Organizations), not including individuals, which are either charities or engaged in a cultural activities, or **whose purpose it is to encourage research**.

Since its inception, the Louis D. Foundation has awarded each year **two Grand Prizes each worth 750,000 euros**: a science prize and a humanitarian or cultural prize, alternately awarded.

In 2005, the Grand Prizes were awarded to:

- The **Grand Prize for science** on the topic of "*The 'new world' of small non-messenger RNAs and their roles in the control of cellular functions*", shared between **the American team of Dr. David P. Bartel and the Dutch team of Dr. Ronald H.A. Plasterk**.

- The **Grand Prize for humanitarian work**, awarded **to Catholic Relief** for its *project for a medicalized halfway house for autistic adults at Bagneux* (Hauts-de-Seine) under the aegis of the **Association of Catholic Relief Services**.

The naming of laureates for the science prize was accomplished in two steps:

- First, an international jury made up of experts nominated by eight of the most prestigious foreign Academies of Science drew up a short list of nine candidates of which five were accepted.
- Second, the list of five candidates was submitted to a jury composed of members of the Institut de France – Academy of Science – who ranked the heads of the research groups or laboratories into finalists and semifinalists according to the importance of their work. The final selection was made by the Administrative board.

Members of the scientific committee

- M. Édouard Brézin, of the Académie des sciences, President of the committee
- M. Michel Caboche, of the Académie des sciences
- M. Antoine Danchin, of the Institut Pasteur
- M. Roland Douce, of the Académie des sciences
- M. Bernard Dujon, of the Académie des sciences
- M. Christian Dumas, of the Académie des sciences
- M. Jules Hoffman, of the Académie des sciences
- M. Axel Kahn, of the Académie des sciences
- M. Michel Labouesse, director of research at the université Louis Pasteur de Strasbourg
- M. Jean-Yves Lallemand, of the Académie des sciences
- Mme Nicole Le Douarin, permanent secretary of the Académie des sciences
- M. Jean-Antoine Lepesant, of the Académie des sciences
- M. Jean-Louis Mandel, of the Académie des sciences
- M. Roger Monier, of the Académie des sciences
- M. Gérard Orth, of the Académie des sciences
- Mme Christine Petit, of the Académie des sciences
- M. Jean Rosa, of the Académie des sciences
- M. Jean Weissenbach, of the Académie des sciences
- M. Éric Westhof, of the Académie des sciences
- M. Moshe Yaniv, of the Académie des sciences

Members of the jury for the Grand Prize for humanitarian work

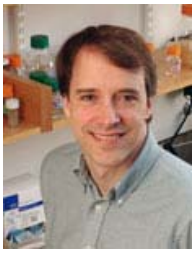
- M. Michel Albert, permanent secretary of the Académie des sciences morales et politiques, president of the jury
- Mme Marianne Bastid-Bruguiere, of the Académie des sciences morales et politiques
- M. Jean-Pierre Caillard, president and director general of the media group Centre France – La Montagne
- M. Michel Didier, professor at the Conservatoire national des arts et métiers (CNAM)
- M. Claude Malhuret, former Minister for Human Rights, Maire de Vichy
- M. Henri Pigeat, president of the Institut International de Communication
- M. Yves Pouliquen, of the Académie française, of the Académie nationale de Médecine
- Mme Michèle Puybasset, president of the Commission d'Accès aux Documents Administratifs (CADA)

The 2005 Science Prize

Worth 600,000 euros

Awarded to Professors David Bartel and Ronald Plasterk

Professor Bartel



Whitehead Member David Bartel has made major contributions to recent advances in understanding the roles that ribonucleic acid (RNA) plays in contemporary biology and may have played in early evolution.

Bartel and co-workers have discovered hundreds of tiny RNAs, known as microRNAs, which are thought to regulate gene expression in animal and plant cells. The lab employs biochemical, molecular, genetic, and computational approaches to identify additional microRNAs and determine their biological roles and the molecular mechanisms of their action. Among other findings, their analyses indicate that microRNA genes comprise nearly one percent of human genes, and that microRNAs play important regulatory roles during the development of mammals and plants.

Additionally, Bartel and his colleagues have investigated RNA's ability to catalyze reactions and studied how new RNA enzymes (ribozymes) emerge. The group has created new ribozymes with enzymatic activities thought to have been required early in evolution, before the emergence of enzymes made of protein. For example, the researchers have generated a ribozyme that synthesizes small pieces of RNA, supporting the idea of an "RNA world" during the early evolution of life that featured RNA self-replication. Further work in this area may point toward the eventual synthesis of minimal forms of life based on RNA.

Among its work, the group also has designed a single RNA sequence that can fold into either of two ribozymes, raising the possibility that biological RNAs without structural or functional similarity might still share a common ancestry.

The Bartel group also made significant contributions in developing RNA interference, a powerful biochemical tool that works by blocking the delivery of genetic messages from DNA. Important advances for the new small interfering RNA technique, which extends RNAi to mammalian cells, began in Bartel's laboratory.

Bartel joined Whitehead Institute in 1994 as a Whitehead Fellow, following the completion of his PhD at Harvard University. In 1996 he was appointed an Associate Member of Whitehead and assistant professor of biology at MIT. Bartel is now a Member at Whitehead and professor at MIT.

Ten Publications Relevant to siRNAs and miRNAs

- Zamore, P.D., T. Tuschl, P.A. Sharp, and D.P. Bartel. 2000. RNAi: dsRNA directs the ATP-dependent cleavage of mRNA at 21 to 23 nucleotide intervals. **Cell** 101:25-33.

- Lau, N.C., L.P. Lim, E.G. Weinstein, and D.P. Bartel. 2001. An abundant class of tiny RNAs with probable regulatory roles in *Caenorhabditis elegans*. **Science** 294:858-862.

- Reinhart, B.J., E.G. Weinstein, M.W. Rhoades, B. Bartel, and D.P. Bartel. 2002. MicroRNAs in plants. **Genes Dev.** 16:1616-1626.

- Rhoades, M.W., B.J. Reinhart, L.P. Lim, C.B. Burge, B. Bartel, and D.P. Bartel. 2002. Prediction of plant microRNA targets. **Cell** 110:513-520.

- Reinhart, B.J. and D.P. Bartel. 2002. Small RNAs correspond to centromere heterochromatic repeats. **Science** 297:1831.

- Lim, L.P., M.G. Glasner, S. Yekta, C.B. Burge, and D.P. Bartel. 2003. Vertebrate microRNA genes. **Science** 299:1540.

- Lewis, B.P., I-H. Shih, M.W. Jones-Rhoades, D.P. Bartel, and C.B. Burge. 2003. Prediction of mammalian microRNA targets. **Cell** 115:787-798.

- Chen, C.Z., L. Li, H.F. Lodish, and D.P. Bartel. 2004. MicroRNAs modulate hematopoietic lineage differentiation. **Science** 303:83-86.

- Yekta, S., I-H. Shih, and D.P. Bartel. 2004. MicroRNA-directed cleavage of *HOXB8* mRNA. **Science** 304:594-596.

- Lewis, B.P., C.B. Burge, D.P. Bartel. 2005. Conserved seed pairing, often flanked by adenosines, indicates that thousands of human genes are microRNA targets. **Cell** 120:15-20.

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Professor Plasterk

Curriculum vitae

Married to Els Beumer, father of Wouter (13) and Willem (11)

1957	born in The Hague on 12 April
1984	Ph.D. thesis "Inversion of the G segment of bacteriophage Mu; analysis of a genetic switch", thesis supervisor: prof.dr. P. van de Putte, University of Leiden (cum laude)
1984-1985	post-doc in California Institute of Technology (Pasadena) in the lab of dr. M.I. Simon (study of DNA transposition in *Borrelia hermsii*)
1986	post-doc at the LMB-MRC Cambridge, in the lab of Dr. J. Sulston (study of the nematode *Caenorhabditis elegans*)
1987-2000	group leader at the Netherlands Cancer Institute, Amsterdam
1993-1997	professor of Molecular Microbiology, Medical School Free University of Amsterdam
1995	member of EMBO (European Molecular Biology Organization)
1997-2003	professor of Molecular Genetics, University of Amsterdam
1999	Spinoza Prize, awarded by the Netherlands Organization for Scientific Research
2000-	director of Hubrecht Laboratory/Netherlands Institute of Developmental Biology, Utrecht professor of Developmental Genetics (Academic Biomedical Cluster), University of Utrecht
2000-	member of the Royal Netherlands Academy of Arts and Science
2002	EMBO award for Communication in the Life Sciences
2004-	member of the Board of Governors of The Wellcome Trust
1999-	columnist for De Volkskrant (Dutch newspaper) columnist for Buitenhof (Dutch television program)

Summary of Professor Plasterk reserach

Plasterk's research interests are in the areas of genetics and functional genomics, mainly studying the nematode *C. elegans* (and more recently also the zebrafish). He focuses on the mechanism and regulation of DNA transposition, the question how genomes are protected against mutation, and the function of small RNAs in animal development.

Small RNA molecules and their roles in animal development

The central dogma of molecular biology is: "DNA makes RNA makes protein". Humans, and most other animals, have a repertoire of roughly 30,000 protein encoding genes. Differentiation of cells into specific fates, neurons, muscle cells, bone cells, is a consequence of the fact that not all of these genes are expressed to the same level. It is assumed, and partially proven, that the fundamental difference between differentiated cells is the result of expression of different subsets of the gene repertoire. Given the central dogma, one might assume that a high expression of a protein correlates with high expression of the messenger RNA. Indeed such a correlation does exist. However, it has recently become clear that important networks of regulation exist in the second step of the central dogma, translation from mRNA into protein. Part of this regulation is carried out by small regulatory RNAs.

RNA as the immune system of the genome

Ronald Plasterk and his collaborators, initially at the Netherlands Cancer Institute in Amsterdam, The Netherlands, and since five year at the Hubrecht Laboratory in Utrecht, The Netherlands, discovered the role of small regulatory RNAs in one specific function, the protection of the genome of the nematode *Caenorhabditis elegans* against jumping of transposable elements.

The history of this is the following. The nematode is known to contain in its genome multiple transposons of quite different sequences. These transposons can jump, as witnessed by excision and insertion in somatic cells. Strikingly, the germ line of the animal seems protected against transposition: one can culture such an animal for many generations, and all progeny will have precisely the same transposon insertions as their parents. Therefore Plasterk concluded that most likely there was an active protection system in the germ line, and together with his graduate student René Ketting he undertook a genetic screen to isolate mutants defective in transposon silencing. They found multiple mutants. Surprisingly, these mutants had lost the silencing of all transposable elements at once, showing that there was one common mechanism that silenced all transposons of different sequence. The second surprise was that most of these mutants, isolated for their loss of transposon silencing, were found to be also deficient in the phenomenon of RNA interference or RNAi. This phenomenon had at that time just been discovered by Mello and Fire, as a means to silence genes by injection of double-stranded RNA. In follow-up studies Plasterk showed that most likely these transposons, which contained long terminal inverted repeats, produce RNA that can fold into double-stranded RNA, which triggers activity of the RNAi-system, resulting in silencing of the expression of the transposon-encoded protein transposase. Given the strong interrelation between RNAi and transposon silencing the group then initiated mechanistic studies on the mechanism of RNAi, resulting in the discovery of an active amplification system, in which an RNA dependent RNA polymerase can generate secondary silencing signals.

miRNAs in animal development

The group of Greg Hannon (Cold Spring Harbor) demonstrated the central role of the Dicer enzyme as the nuclease that turns double-stranded RNA into small interfering RNAs (siRNAs). These approximately 21 nucleotide long RNA molecules are at the heart of all RNA-silencing systems. Almost immediately after the discovery of the Dicer enzyme, many researchers (including the laboratory of Ronald Plasterk) realized that the products of Dicer, RNA molecules of 21 bases, were strikingly similar to the small regulatory RNAs previously discovered by Ambros and Ruvkun (let-7 and lin-14). Therefore several researchers independently knocked-out the *dicer* gene in different systems, and indeed found that this resulted in the failure to make microRNAs. Plasterk and his coworkers, in collaboration with Greg Hannon, first demonstrated this in C. elegans and then Plasterk chose to further study the role of microRNAs in development of the vertebrate embryo of the zebrafish *Danio rerio*. Knock-out of the Dicer enzyme resulted indeed in failure to make microRNAs, which resulted in developmental arrest after two days. By bioinformatic studies the group discovered that the list of microRNAs was probably significantly longer than the approximately 250 that had previously been recognized. What then is the specific role of microRNAs in animal development? This question is currently not answered yet. However, in a recent study the Plasterk laboratory has initiated studies into roles of specific microRNAs in the vertebrate embryo by determining their expression patters *in situ*. A comprehensive set of all microRNAs known to be conserved between zebrafish and human was studied *in situ,* and the expression patterns were found to be strikingly tissue and organ specific. Based on the timing of expression, and other arguments, it seems likely that microRNAs do not primarily act in switching on specific cell fates, but rather in maintaining these fates. One could say that microRNAs remind the cells of what they are. The beauty of the microRNA regulation system is that many different mRNAs can be regulated by the same microRNAs, while at the same time one messenger RNA can be regulated by different microRNAs. This provides a high degree of possible coordination, which is precisely what one requires of a system that maintains cell fates.

One of the new challenges in biology is now to determine the mechanism of microRNA action, dissect the roles of different microRNAs individually, and investigate the possible contribution of microRNA disfunction to human disease, and potentially even their therapeutic relevance.

Selected list of 10 recent major publications

- Ketting, R., Haverkamp, Th.H.A., van Luenen, H.G.A.M., Plasterk, R.H.A. (1999). *mut-7* of *C. elegans*, required for transposon silencing and RNA interference, is a homolog of Werner Syndrome Helicase and RNaseD. Cell 99: 133-141.

- Ketting, R.F., Fischer, S.E.J., Bernstein, E., Sijen, T., Hannon, G.J., Plasterk, R.H.A. (2001). Dicer functions in RNA interference and in synthesis of small RNA involved in developmental timing in C. elegans. Genes Developm. 15: 2654-2659.

- Sijen, T., Fleenor, J., Simmer, F., Thijssen, K.L., Parrish, S., Timmons, L., Plasterk, R.H.A., Fire, A. (2001). On the role of RNA amplification in dsRNA-triggered gene silencing. Cell 107: 465-476.

- Tijsterman, M., Ketting, R.F., Okihara, K. L., Sijen, T. and Plasterk, R. H. A. (2002) Short antisense RNAs can trigger gene silencing in *C. elegans*, depending on the RNA helicase MUT-14. Science 295 (5555): 694-697.

- Plasterk, R.H.A. (2002) RNA silencing: the genome's immune system. Science 296:1263-1265.

- Wienholds, E., Schulte-Merker, S., Walderich, B., Plasterk, R.H.A. (2002) Target-selected inactivation of the zebrafish *rag1* gene. Science 297 (5578): 99-102.

- Sijen, T., Plasterk, R.H.A. (2003) Transposon silencing in the Caenorhabditis elegans germ line by natural RNAi. Nature 426: 310-314.

- Caudy, A.A., Ketting, R.F., Hammond, S.M., Denli, A.M., Bathoorn, A.M.P., Tops, B.B.J., Silva, J.M., Myers, M.M., Hannon, G.J., Plasterk, R.H.A. (2003) A micrococcal nuclease homologue in RNAi effector complexes. Nature 425: 411-414.

- Denli, A.M., Tops, B.B.J., Plasterk, R.H.A., Ketting, R.F., Hannon, G.J. (2004) Processing of primary microRNAs by the microprocessor complex. Nature 432: 231-235.

- Berezikov, E., Guryev, V., van de Belt, J., Wienholds, E., Plasterk, R.H.A., Cuppen, E. (2005) Phylogenetic shadowing and computational identification of human microRNA genes. Cell 120: 21-24.

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