

The fourth category to be decided in the sixth edition of these awards

## Adrian Bird wins the Frontiers of Knowledge Award for mapping gene activation and opening new prospects for the cure of neurological disorders

- Bird identified DNA regions where genes are activated, a fundamental contribution in the field of epigenetics, which studies how environmental factors influence diseases such as cancer
- In 2007, he demonstrated in an animal model that the symptoms of a form of autism known as Rett syndrome could be made to disappear. This was the first time a neurological disease had been successfully reversed in an experimental context
- He currently combines his basic research activity with involvement in the scientific exploration to find a clinical treatment for Rett syndrome

**Madrid, January 28, 2014.**- The BBVA Foundation Frontiers of Knowledge Award in the Biomedicine category goes in this sixth edition to British biochemist Adrian Bird “for his discoveries in the field of epigenetics.” Bird’s signal achievement was to map the regions of DNA where genes are activated by the addition of a type of molecule known as a methyl group, in a process known as methylation. This contribution is of a fundamental nature, since DNA methylation, as the jury explains, “plays a crucial role in many diseases and in the progression of nearly all types of cancer.”

In the words of the award citation: “In a mammal, all cells have the same DNA sequence. However, cells involved in different functions express distinct subsets of genes. These different expression patterns are stabilized through epigenetic marks, of which DNA methylation was the first to be discovered and characterized. DNA methylation marks are inherited as cells divide, and in some cases inherited across generations.”

His work on methylation would later lead Bird to a discovery which could prove game-changing in the neurosciences domain. He found that by correcting defects in a protein associated with a severe form of autism known as Rett syndrome, the symptoms of the condition disappeared in mice. “This is the first time that a neurological disease has been reversed in an experimental context,

and offers hope that this approach can be translated into the clinic," the citation continues.

This result, obtained in 2007, has refocused research efforts on this congenital condition, which affects girls – one in every 10,000 – and causes severe mental retardation and the progressive and persistent loss of cognitive and motor skills. Bird has since combined his basic research with an active involvement in the quest "to do in humans what we have done in mice," he explained after hearing of the award. "I used to be quite content with myself just pursuing knowledge. But to see that your research can have such practical relevance in people's lives adds a new dimension, and makes the whole thing more exciting and engaging," he observed during the same conversation, after stating his gratitude for the jury's decision.

### **Importance in cancer and aging**

Epigenetic changes in the genome occur naturally during embryonic development and throughout life. They are also the mechanism through which the environment acts on our genes – smoking, for instance, affects DNA methylation. So understanding how these changes happen is a vital first step in order to understand diseases like Rett syndrome, and clarify the ways in which lifestyle and environmental factors influence cancer.

"DNA methylation is organized in a pattern, which is slightly different in each cell. And in the case of cancer cells, we know that these patterns are really messed up," Bird explains. "Although the relationship between DNA methylation and cancer is not fully understood, it seems pretty clear that certain genes in the tumor cell that depend on the absence of methylation become methylated and are shut down in consequence, which facilitates the development of cancer."

By the late seventies, scientists knew a relationship existed between methylation and gene activation, but not how it worked. Bird obtained the first ever DNA *methylation map*, demarcating the regions where the process unfolds.

### **New hope for Rett syndrome**

Bird not only revealed the precise form of organization of "the regions within the genome marked by DNA methylation," the jury remarks, but also "identified proteins that read the DNA methylation signals, mutation of which leads to human diseases."

His discovery of the MeCP2 protein that detects methylation signals in the genome occurred in the early nineties, before the human genome was sequenced. It was therefore a "huge surprise", Bird now recalls, for himself and everyone, when he was able to show, at the end of that decade, that it was a mutation in this protein that causes Rett syndrome.

Even more remarkable was his achievement in reversing the disorder in an animal model. In 2001, Bird switched research tack and created a mouse with the Rett syndrome genetic defect, presenting all the symptoms of the disease. In 2007, he found a way to activate the correct protein in these laboratory animals, and the symptoms disappeared.

“We didn’t expect it because it was assumed that once you have a neurological disorder, you have it forever. We thought we might, with luck, delay the animals’ death or perhaps alleviate some of the symptoms,” Bird reflects. “But what we got was a clear result, a spectacular improvement. It was one of those Eureka moments.”

The new laureate explained at the award announcement event that his experiment to treat mice with Rett syndrome started from the fact that the disease is not accompanied by the death of neurons, so it was theoretically possible to restore them to a fully functional state. This characteristic is shared by fragile X syndrome, another disabling hereditary disorder.

“We are still far from finding a cure for these diseases, but our work provides a proof of concept that has got a lot of other research groups involved in the search for therapies.”

Bird admits to feeling pressurized by the thought of people waiting for a cure and “frustrated” at the failure, so far, to replicate his results in human subjects. He also warns that “we cannot be sure” if the same cure will work in humans. Nevertheless, the hope felt by many families is not, in his view, unfounded: “The parents know it will take time, that their own daughters might not benefit from the advances. But they also know that there are lots of labs around the world working on Rett syndrome, and that wasn’t true before.”

Adrian Bird was nominated for the award by David Leach, Head of the School of Biological Sciences at the University of Edinburgh

### **Bio notes**

Sir Adrian Peter Bird earned his PhD in biochemistry from the University of Edinburgh in 1972. He then went on to occupy post-doctoral positions at the universities of Yale (United States) and Zurich (Switzerland). On returning to Edinburgh in 1975, he joined the Mammalian Genome Unit (Medical Research Council) where he would remain for eleven years. His next move was to Vienna, where he worked as a senior scientist in the Research Institute for Molecular Pathology.

In 1990, he was appointed to the Buchanan Chair of Genetics at the University of Edinburgh, a position he still holds today and which he combined for a time with the directorship of the same institution's Wellcome Trust Centre for Cell Biology.

He is a former governor of the Wellcome Trust (among the world's leading funders of medical research), serving for three years as its Deputy Chairman.

Author of more than 150 publications in international science journals, he is a Commander of the British Empire (2005) and has received numerous awards and honors, including a knighthood in 2014.

## The BBVA Foundation Frontiers of Knowledge Awards

The BBVA Foundation promotes, funds and disseminates world-class scientific research and artistic creation, in the conviction that science, culture and knowledge in its broadest sense hold the key to a better future for people. The Foundation designs and implements its programs in partnership with leading scientific and cultural organizations in Spain and abroad, seeking to identify and prioritize those projects with the power to move forward the frontiers of the known world.

The BBVA Foundation established its Frontiers of Knowledge Awards in 2008 to recognize the authors of outstanding contributions and radical advances in a broad range of scientific and technological areas congruent with the knowledge map of the late 20th and 21st centuries, and others that address central challenges, such as climate change and development cooperation, deserving of greater visibility and recognition. Their **eight categories** include classical areas like *Basic Sciences (Physics, Chemistry and Mathematics)* and *Biomedicine*, and other, more recent areas characteristic of our time, ranging from *Information and Communication Technologies*, *Ecology and Conservation Biology*, *Climate Change* and *Economics, Finance and Management* to *Development Cooperation* and the innovative realm of artistic creation that is *Contemporary Music*.

The **juries** in each category are made up of leading international experts in their respective fields, whose involvement endorses the rigor of the awards and has indeed been instrumental in consolidating their prestige. The BBVA Foundation is aided in the organization of the awards by the **Spanish National Research Council (CSIC)**, the country's premier multidisciplinary research organization. As well as proposing each jury chair, the CSIC is responsible for appointing the Technical Evaluation Committees that undertake an initial assessment of candidates and draw up a reasoned shortlist for the consideration of the juries.

In the Biomedicine category, Committee members were Dolores González-Pacanowska, research scientist at the Instituto de Parasitología y Biomedicina "López-Neyra" (IPBLN), and coordinator of the Council's Biology and Medicine Area; Rafael Giraldo, research scientist at the Biological Research Center (CIB); Víctor de Lorenzo, research scientist at the Spanish National Center for Biotechnology (CNB), working with an ERC Advanced Grant; Sergio Moreno, research scientist at the Instituto de Biología Funcional y Genómica (IBFG, a joint center of CSIC and the University of Salamanca); and Ángela Nieto, research

scientist at the Instituto de Neurociencias de Alicante (CSIC- Miguel Hernández University).

### Biomedicine jury

The jury in this category was chaired by **Angelika Schnieke**, Chair of Livestock Technology in the Department of Animal Science at Technische Universität München (TUM) (Germany). The secretary was **Óscar Marín**, Research Professor in the Department of Developmental Neurobiology at the Instituto de Neurociencias de Alicante, a joint center of CSIC and Miguel Hernández University (Spain). Remaining members were **Dario Alessi**, Director of the Protein Phosphorylation Unit, a Medical Research Council unit in the College of Life Sciences at the University of Dundee (United Kingdom); **Mariano Barbacid**, leader of the Experimental Oncology Group at the Spanish National Cancer Research Centre (CNIO); **Robin Lovell-Badge**, Head of the Division of Stem Cell Biology and Developmental Genetics at the MRC National Institute for Medical Research (United Kingdom); **Ursula Ravens**, Head of the Department of Pharmacology and Toxicology in the Carl Gustav Carus Medical School of Technische Universität Dresden (TU Dresden) (Germany); and **Bruce Whitelaw**, Head of the Developmental Biology Division at The Roslin Institute, a basic and translational research center belonging to the University of Edinburgh (United Kingdom).

### Previous laureates

The award in the last edition was shared by chemist **Douglas Coleman** and physician **Jeffrey Friedman** for "revealing the existence of the genes involved in the regulation of appetite and body weight, a discovery crucial to our understanding of human pathologies such as obesity." In the fourth edition, the award went to **Alexander Varshavsky** for "discovering the mechanisms involved in protein degradation." Preceding him were **Shinya Yamanaka** for his achievements "showing that it is possible to reprogram differentiated cells back into a state that is characteristic of pluripotent cells," and **Robert Lefkowitz** for "his discoveries of the seven transmembrane receptors." Finally, the winner in the inaugural edition was **Joan Massagué** for "developing novel approaches to identify genes involved in organ-specific metastasis."

### UPCOMING AWARD ANNOUNCEMENTS

CATEGORY	DATE
<b>Ecology and Conservation Biology</b>	February 4, 2014
<b>Contemporary Music</b>	February 11, 2014
<b>Economics, Finance and Management</b>	February 18, 2014
<b>Development Cooperation</b>	February 25, 2014

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