

Biomedicine is the fourth category decided in the fifth edition of the awards

## The BBVA Foundation Frontiers of Knowledge Award goes to Coleman and Friedman, discoverers of the appetite hormone

- In 1969, biochemist Douglas Coleman published a paper on a physiological factor that regulated appetite. In 1994, physician Jeffrey Friedman identified this factor as the hormone leptin
- The work of the new laureates has brought about a paradigm change in the study and perception of obesity, now viewed as a medical condition rather than a personal failing of the individual

**Madrid, January 29, 2013.-** The BBVA Foundation Frontiers of Knowledge Award in the Biomedicine category has been granted in this fifth edition to 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 words of the prize jury.

Their work showed conclusively that leptin is a hormone made by fat which acts on the hypothalamus in the brain, in order to “maintain control of food intake, energy expenditure and the amount of fat that accumulates,” the citation continues. “The absence of leptin or its receptor leads to obesity,” a mechanism initially identified in mice but that also “holds true for humans, and is therefore of obvious critical importance.”

Coleman and Friedman's findings, in the view of the jury, have not only opened up a new era of research into the biological roots of obesity, but have also brought about a paradigm shift in social attitudes by showing that obesity is not due to “inappropriate behavior, but is the consequence of imbalance in a hormone-driven process,” the citation concludes.

Douglas Coleman (1931, Ontario, Canada) holds dual Canadian-American nationality and is Senior Staff Scientist Emeritus at The Jackson Laboratory in Maine (United States). Jeffrey Friedman (1954, Orlando, United States) is a professor at The Rockefeller University in New York. Their names were put forward for the award by Paul Greengard, winner of the 2000 Nobel Prize in Medicine and a professor at The Rockefeller University, Alexander Varshavsky, professor at the California Institute of Technology and 2011 BBVA Foundation Frontiers of Knowledge laureate in Biomedicine, and Robert E. Braun, Chair of Research at The Jackson Laboratory.

Although the two men have not worked together, their relationship is about as close as one can get in science, for it was Friedman who proved that Coleman's scientific hypotheses were in fact correct.

Hence Coleman's insistence, on hearing of the award, that he was "especially delighted" to be sharing it with Jeffrey Friedman: "We are good friends, and have known each other for many years. One day he called me to say he wanted to work with the mice I was studying, and, several decades later, it was he who found the hormone that I had predicted."

In the late 1960s, Coleman had demonstrated the existence of a still unknown hormone that regulated food intake and body weight. He had done so through his studies of mice carrying a mutation that made them morbidly obese. And his team could tell from the genetic crosses that the defect lay in a single gene. Then Friedman took up the baton in the mid 1980s, determined to find and name the guilty gene.

"Back then we didn't have the technology we have now to isolate genes," remarked Friedman on the phone, "so I knew it was going to be a hard task and decided to call Coleman to get more background." Eight years later, in 1994, Friedman discovered the gene of the leptin hormone, which functions just as Coleman had anticipated.

Informed of the jury's decision, Friedman said yesterday: "It is a great honor to receive this particular award, which emphasizes such diverse aspects of science. And I couldn't be happier than to share it with Douglas Coleman, who laid the foundations for this work."

### **The action of leptin**

"Leptin is designed to maintain a certain body weight," explains Friedman. The way the system works is that the more fat you have, the more leptin your body makes and the less hungry you feel. The ultimate goal is to shut down the appetite of individuals with a lot of fat, so they eat less and stop gaining weight. And vice versa. If you lose weight, your body produces less leptin and your appetite increases. The fact that the body possesses this mechanism has an evolutionary origin: "It would be very dangerous to have no fat, because you would risk dying

of starvation, but it would also be dangerous to be too fat, because you would be at the mercy of predators. So the system tries to maintain an optimal level."

The lab also discovered that leptin "circulates in the blood and acts on centers in the brain to regulate appetite, just as Coleman predicted," adds Friedman, an admirer of his colleague's work: "His observations were very non-obvious. There were probably thousands of scientists looking at the same problem, but he was the one who got it right."

The discovery of leptin opened up a whole new field of research into the causes of obesity, propelled by a radical change of mentality in society and science: "Before people thought that how much we ate was completely a matter of willpower," Friedman reflects, "but we now know that body weight, in humans and other animals, is regulated by cells in the brain that receive important signals such as leptin and then unconsciously regulate appetite. And this system is absolutely crucial for the survival of any species."

This means, ultimately, that obesity is "in the mind": "As well as leptin and the leptin receptor, we know that 10% of morbidly obese individuals carry defects in genes that regulate food intake, metabolism and body weight. And all these genes act on the brain, which tells us that the main reason people get fat is an alteration of their brain chemistry."

Leptin, in other words, is not the only gene linked to obesity – Friedman predicts that more will come to light – but it does play a leading role, and will certainly be important in future drug therapies against obesity: "There is a lot left to be learned about the regulation of obesity, but the identification of leptin will undoubtedly lead us to a better understanding of the factors controlling appetite, which will lead, in turn, to new avenues for treatment."

For Friedman, however, the objective is not to get everyone who is obese to lose weight, but "to make unhealthy people more healthy." And this, he points out, can be achieved with even moderate weight loss.

## Bio notes

**Douglas L Coleman** was born in Ontario, Canada, in 1931. After attending elementary and secondary schools in the town of Stratford, he went on to McMaster University, Hamilton, Ontario, where he received a BSc in chemistry. Coleman then continued his studies in the United States, at the University of Wisconsin, obtaining his doctorate there in 1958.

That same year he joined the staff of The Jackson Laboratory and, although his original intention was to stay for just a couple of years, he would end up spending his entire research career with this institution. He retired in 1991 and, since then, has devoted much of his time to ecological issues like forest management and land conservation, with the same enthusiasm he brought to research.

**Jeffrey M. Friedman** was born in Orlando, Florida, United States, in 1954, but was brought up in the suburbs of New York City. His father was a radiologist and his mother a teacher. He finished polytechnic studies in 1971 and went on to complete an MD at Union University in 1977. During his medical studies he got his first taste of research, and soon took up a recommendation from one of his teachers to enter the basic research lab at The Rockefeller University, where he started out studying the effects of endorphins on the development of narcotic addiction under Dr. Mary-Jane Kreek. After receiving his PhD in 1986, he stayed on at Rockefeller in a professorial post, while continuing his investigation into the nature of the ob/ob gene present in obese mice. This research project culminated in 1994 with his discovery and characterization of the leptin hormone.

### **BBVA Foundation Frontiers of Knowledge Awards**

The BBVA Foundation primarily engages in the generation and diffusion of scientific knowledge and culture, through ongoing programs in the areas of basic sciences, biomedicine, ecology and conservation biology, social sciences, literary and musical creation, and the visual arts.

Its focus on the core concerns of today's society, like health or the environment, has materialized in major research projects, including those involving the study of cancer. The Foundation's support for research, advanced training and knowledge dissemination is also manifest in a series of award families which not only honor the winners' contributions but also shed a wider light on their fields of work, the values they represent and the combined endeavors of the research and creative communities.

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 characteristic of our times. They are in this sense a prize family congruent with the knowledge map and central challenges of the 21st century.

The nominations received from leading universities and research and cultural centers all round the world, the independence and objectivity of the prize juries formed by reputed specialists in their respective fields, and the excellence of the laureates in their earlier editions have earned these awards, devised and organized from Spain, a firm place among the world's foremost award schemes. The BBVA Foundation is assisted in this initiative by the country's premier multidisciplinary research organization, the Spanish National Research Council (CSIC), and by the presence of Spanish scientists and creative practitioners on the international juries.

The CSIC collaborates in the appointment of Technical Evaluation Committees for each prize category made up of acknowledged experts in the relevant domain. This Committee undertakes an initial assessment of candidates and draws up a reasoned shortlist for the consideration of the juries.

In the Biomedicine category, Committee members were Dolores González-Pacanowska, scientific researcher in the López-Neyra Institute of Parasitology and Biomedicine (CSIC) and coordinator of the Council's Biology and Medicine Area; Lisardo Boscá, Research Professor at the Alberto Sols Institute of Biomedical Research (UAM-CSIC); José Ramón Naranjo, scientific researcher with the National Centre for Biotechnology (CNB, CSIC); Sergio Moreno, Research Professor at the Salamanca Institute of Biomedical Research (IBSAL, University of Salamanca-CSIC); and Germán Rivas, Research Professor at the Centre for Biological Research (CIB, CSIC).

The Frontiers awards provide an international showcase for the best qualities of Spain and Spanish science, and have achieved the endorsement of the world scientific community, whose members have served on the juries and put forward nominations from their posts in eminent Spanish and international academic and research institutions.

In their fifth edition, the BBVA Foundation Frontiers of Knowledge Awards wish to offer support and recognition to the individuals and teams working for a better future for people through the advancement of knowledge, innovation and culture and their dissemination to society; goals and practices that are also at the center of the BBVA Group culture.

In an economic context marked by a prolonged economic crisis and the adoption of short-term measures to tackle its multiple causes and manifestations, science, the environment and culture have dropped further down the list of public priorities. The BBVA Foundation Frontiers of Knowledge Awards, and the Foundation's broader program to foster scientific knowledge and culture, wish to drive home the message that these three areas are of transcendental importance for our collective wellbeing and individual opportunities.

The eight categories of the BBVA Foundation Frontiers of Knowledge Awards, each carrying prize money of 400,000 euros, respond to the knowledge map of the early 21st century, but also to key global challenges that have never before merited a specific honor on this scale, as with the two environmental categories – Ecology and Conservation Biology and Climate Change – and the category of Development Cooperation. These stand alongside the classic categories of Basic Sciences, Biomedicine and Economics, Finance and Management. Finally, the award family is completed by Contemporary Music, an art at the leading edge of cultural innovation to which the BBVA Foundation devotes a broad-ranging support program, and where Spain is home to a wide and talented community of authors, conductors and performers.

## International jury

The jury in this category was chaired by **Werner Arber**, winner of the Nobel Prize in Medicine and Emeritus Professor of Molecular Microbiology at Biozentrum, an interdisciplinary research institute belonging to the University of Basel (Switzerland). The secretary was **Robin Lovell-Badge**, Head of the Division of Stem Cell Biology and Developmental Genetics at the National Institute for Medical Research (Medical Research Council, United Kingdom). Remaining members were **Dario**

**Alessi**, Director of the Protein Phosphorylation Unit, a Medical Research Council center in the College of Life Sciences at Dundee University (United Kingdom); **Mariano Barbacid**, AXA-CNIO Professor of Molecular Oncology in the Spanish National Cancer Research Centre (CNIO)(Spain); **Óscar Marín**, Principal Investigator in the Department of Developmental Neurobiology of the Instituto de Neurociencias de Alicante (Spain); **Ursula Ravens**, Chair of the Department of Pharmacology and Toxicology at Dresden University of Technology (Germany); **Angelika Schnieke**, since 2003, Chair of Livestock Biotechnology in the Department of Animal Science at the Technical University of Munich (Germany); and **Bruce Whitelaw**, Head of the Developmental Biology Division at The Roslin Institute in Edinburgh (United Kingdom).

The winner in this category in the last edition of the awards was **Alexander Varshavsky** for “discovering the mechanisms involved in protein degradation.” In the third edition, the award went to **Shinya Yamanaka** for “showing that it is possible to reprogram differentiated cells back into a state that is characteristic of pluripotent cells.” The award in the second edition was granted to **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 5, 2013
<b>Contemporary Music</b>	February 12, 2013
<b>Economics, Finance and Management</b>	February 19, 2013
<b>Development Cooperation</b>	February 26, 2013

#### **LAUREATE'S FIRST DECLARATIONS AND IMAGES**

A video recording of the new laureate's first interview on receiving news of the award is available from the Atlas FTP with the following name and coordinates.

Server: **213.0.38.61**  
 Username: **agenciaatlas1**  
 Password: **amapola**

The name of the video is:  
 “FBBVA PREMIO BIOMEDICINA”

In the event of connection difficulties, please contact Alejandro Martín at ATLAS:

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## Fundación **BBVA**

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