

In the fourth edition of these awards upholding science as a motor of progress

## Varshavsky wins the BBVA Foundation Frontiers of Knowledge Award in Biomedicine for discovering the mechanism of protein destruction whose failure is a cause of disease

- Alexander Varshavsky, born in Moscow and now a U.S. citizen, revealed that ubiquitins act as labels marking out other proteins for destruction; a mechanism whose failure underlies a range of immune-system and neurodegenerative diseases, as well as cancer.
- Universities and pharmaceutical companies are now working to find therapeutic applications for his discoveries.
- The BBVA Foundation Frontiers of Knowledge Awards recognize the role of science and cultural creation as levers of society's progress and wellbeing. Their eight categories address the main scientific, technological, social and economic areas and challenges of our times

**Madrid, January 31, 2012.-** The BBVA Foundation Frontiers of Knowledge Award in the Biomedicine category goes in this fourth edition to Alexander Varshavsky of California Institute of Technology (United States) for discovering "the mechanisms involved in protein degradation and their critical importance in biological systems," in the words of the jury's citation.

Varshavsky (Moscow, 1946) discovered that the proteins known as ubiquitins act as labels signaling proteins for destruction, as well as revealing their source of specificity. "Varshavsky showed how ubiquitin (...) is attached to other proteins, marking them for destruction," the citation continues. "This system is essential for normal cellular functions, ranging from the control of gene transcription, protein synthesis and DNA repair to cell division and the response to stress."

According to the jury, Varshavsky's research has spawned a whole new field in biomedicine, since we now know that defects in his protein degradation mechanism underlie a wide variety of pathologies. His work, as such, has a

bearing on our understanding of cancers, immune system disorders and neurodegenerative diseases, "including Parkinson's", as the citation points out. "It is likely that drugs that target components of the system will be of wide significance in medicine".

While some proteins remain stable for days, others turn over in a matter of hours. The process of protein degradation is accordingly vital to the life of the cell, and it was Alexander Varshavsky's research that uncovered its inner workings.

In the 1980s, the new laureate discovered that ubiquitins attach themselves to proteins that are due to be destroyed through ubiquitin-ligases – a kind of enzyme of which we now know that there are many hundreds, whose role is to recognize specific proteins and target them selectively for degradation.

Varshavsky offered some glimpses of the scope and importance of his work during a phone conversation yesterday, after hearing of the award: "I feel privileged to have contributed to the birth of this field, and to partake in its later development. This arena grew rapidly in the 1990s and has become, by now, a vast and diverse field."

"One amazing thing about the ubiquitin field is that it refuses to age. After three decades of ever-expanding research, new directions of inquiry, new problems and new applications continue unabated." In fact one of his recent contributions was a 2010 paper unveiling a new mechanism involved in protein degradation: N-terminal acetylation of cellular protein.

The search for ubiquitin-based therapies and drugs is a particularly thriving area. "There is a great deal of ongoing medical research, at both pharmaceutical companies and universities, to design small molecules that either inhibit or augment functional aspects of the ubiquitin system", Varshavsky relates. In other words, translation research spurred by his insights is attempting to activate or deactivate the degradation mechanism depending on the target condition.

Alexander Varshavsky was nominated for the award by 2006 Nobel Chemistry laureate Roger Kornberg of Stanford Medical School, California; Ulrich Hartl, of the Max Planck Institute of Biochemistry (Marstried, Germany); and Elliot Meyerowitz, of California Institute of Technology (United States).

The name of the new laureate was announced this morning in the Marqués de Salamanca Palace, Madrid headquarters of the BBVA Foundation, at an event attended by the chair of the jury, Nobel medicine laureate Werner Arber, and Rafael Pardo, Director of the BBVA Foundation.

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

The BBVA Foundation established the Frontiers of Knowledge Awards in 2008 to recognize the authors of outstanding contributions and significant advances in a broad range of scientific and technological areas characteristic of our times. The

quality of the nominations received, the stature of the international judges, appointed in consultation with the Spanish National Research Council (CSIC), and the excellence of the laureates in their first three editions have earned them a place among the world's foremost award families.

In the midst of a severe economic crisis which has pushed science, culture and the environment lower down the list of public priorities, the BBVA Foundation Frontiers of Knowledge Awards enter this fourth edition firm in their commitment to the individuals and teams working for a better future for people through the advancement of knowledge and its dissemination to society.

The eight categories of the BBVA Foundation Frontiers of Knowledge Awards, each carrying prize money of 400,000 euros, reflect both the knowledge map of the early 21st century and the great global challenges of the day. Hence their inclusion of two dedicated environmental categories in the form of "Climate Change" and "Ecology and Conservation Biology".

The BBVA Foundation primarily engages in the generation and diffusion of scientific knowledge and culture. This effort materializes in research projects, advanced training, lectures and publications, and a series of award families aimed at recognizing and drawing public attention to the work of scientists and creative practitioners.

Among the BBVA Foundation's areas of activity are basic sciences, biomedicine, ecology and conservation biology, the social sciences and literary and musical creation. Its initiatives mesh with the BBVA Group's strategy of fostering innovation and knowledge as development drivers and an effective means to expand our individual and collective choices.

### **International jury**

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

Remaining members were **Adriano Aguzzi**, Chairman of the Department of Pathology and Director of the Institute of Neuropathology at the University Hospital of Zurich (Switzerland); **Dario Alessi**, Deputy Director of the Protein Phosphorylation Unit, a Medical Research Council unit in the College of Life Sciences of Dundee University (United Kingdom); **Francisco Sánchez Madrid**, Scientific Director of the Instituto de Investigación Princesa, Professor of Immunology at the Universidad Autónoma de Madrid (UAM) and Head of the Department of Immunology in La Princesa University Hospital (Spain); **Ursula Ravens**, Head of the Department of Pharmacology and Toxicology at TU Dresden (Germany); **Angelika Schnieke**, holder since 2003 of the Chair of Livestock Technology in the Department of Animal Science of the Technical University of Munich (Germany); and **Bruce Whitelaw**, Head of the Developmental Biology Division at The Roslin Institute in Edinburgh (United Kingdom).

Last year's award in this category went to **Shinya Yamanaka** Yamanaka for "showing that it is possible to reprogram differentiated cells back into a state that is characteristic of pluripotent cells", said the jury in its citation. His work, it continued "has accelerated the possibility of translating regenerative medicine from the bench to the clinic."

In the second edition, the winner was **Robert Lefkowitz**, investigator in the Department of Medicine at Duke University (United States). The award was granted, in the words of the jury, "for his discoveries of the seven transmembrane receptors (G protein-coupled receptors), the largest, most versatile and most therapeutically accessible receptor signaling system, and of the general mechanism of their regulation."

Finally, the winner in the inaugural edition of the awards was **Joan Massagué**, Chairman of the Cancer Biology and Genetics Program at the Sloan-Kettering Institute in New York.

## Biography

Alexander Varshavsky was born in Moscow in 1946. With his father a physicist-chemist, wounded in the Second World War, and his mother a doctor, Varshavsky was raised in a scientific environment. "So my interest, and later love for science were a case of 'nature' and 'nurture' together," he has remarked in an interview.

In his teenage years he was already familiar with the Moscow science world thanks to gatherings in his parents' home. His excellent grades subsequently earned him a place at the prestigious Moscow State University, in the year 1964. He wanted to study biology, but also physics, mathematics and chemistry. And one year later, he was already a regular visitor to the biochemistry labs. However his habit of skipping practical courses came close to costing him expulsion and three years in the Soviet army. What saved him, again, from "a disaster of my own making" was his status as a straight-A student.

In January 1968 he published a paper in Russian in "Molecular Biology", then a new journal; a theoretical piece full of differential equations that described the behavior of circuits in which repressors regulated themselves; three years before such models were even considered in the English-language literature.

Between 1970 and 1977, Varshavsky worked at the Institute of Molecular Biology. He obtained his PhD in 1973 and began to devote himself with passion to the still mysterious structure and organization of chromosomes. One of his findings was written up in USSR journals but also in the west. The result was a series of invitations to give talks abroad, all of which were summarily declined except those from two Communist-bloc countries: Bulgaria and the German Democratic Republic. Shortly, however, an invitation to London from the structural biologist Aaron Klug would change Varshavsky's fate. With the OK of the IMB's director, Vladimir Engelhardt, he flew from Moscow to London in 1977, returning on schedule so as not to let his mentor down. Thanks to this, he was allowed out again without too

many restrictions. And it was on one of these occasions, at a conference in Helsinki, that he managed to escape by ferry to Stockholm and make his way to Frankfurt, where he got in touch with David Baltimore of Massachusetts Institute of Technology (MIT). Thanks to the mediation of the 1975 Nobel medicine laureate, he obtained a visa for the United States.

That same year he managed to get an article written in the USSR into the journal *Cell*, an usual occurrence back then. (Bakayev, V. V., Bakayeva, T. G. and Varshavsky, A. (1977) Nucleosomes and subnucleosomes: heterogeneity and composition. *Cell* 11, 619-630).

After delivering a seminar in the MIT Department of Biology, the university offered him a post. From assistant professor (1977-1980), he progressed to associate professor (1980-1986) and finally full professor of biology. In 1992, he was appointed Howard & Gwen Laurie Smits Professor of Cell Biology in the Division of Biology at California Institute of Technology.

### UPCOMING AWARD ANNOUNCEMENTS

<b>CATEGORY</b>	<b>DATE</b>
<b>Ecology and Conservation Biology</b>	Tuesday, February 7
<b>Contemporary Music</b>	Tuesday, February 14
<b>Economics, Finance and Management</b>	Tuesday, February 21
<b>Development Cooperation</b>	Tuesday, February 28

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

A video recording of the new laureate's first impressions on receiving news of the award is available from the Atlas FTP with the following name and coordinates, along with photographic images and an audio MP3 recording of the announcement event, featuring more declarations:

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

The name of the video is:  
 "FBBVA PREMIO BIOMEDICINA"

## Fundación **BBVA**

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