

VII edición

Premios Fundación BBVA Fronteras del Conocimiento

BBVA Foundation Frontiers of Knowledge Awards

7th edition

## The BBVA Foundation Frontiers of Knowledge Award in Biomedicine goes to Tony Hunter, Joseph Schlessinger and Charles Sawyers for opening the door to the personalized treatment of cancer

- The winners represent the three steps in research leading to this advance: Tony Hunter discovered tyrosine kinases, Joseph Schlessinger identified the principle through which they function, and Charles Sawyers brought this knowledge to the clinic and the development of novel cancer therapies
- Their contributions served initially to treat a variety of leukemia, transforming it from a fatal into a chronic disorder, but have since given rise to effective therapies for lung and breast cancer, melanoma and lymphomas, among other conditions
- José Baselga, Physician-in-Chief at the Memorial Sloan Kettering Cancer Center in New York and nominator of Charles Sawyers, described the contributions of the three laureates as marking “the birth of personalized anti-cancer medicine”

**Madrid, January 27, 2015.-** The BBVA Foundation Frontiers of Knowledge Award in the Biomedicine category is shared in this seventh edition by Tony Hunter, professor and Director of the Salk Institute Cancer Center in La Jolla, California; Joseph Schlessinger, Chairman of the Department of Pharmacology at Yale University School of Medicine, New Haven, and Charles Sawyers, Human Oncology and Pathogenesis Program Chair at the Memorial Sloan Kettering Cancer Center in New York, for “carving out the path that led to the development of a new class of successful cancer drugs.”

For José Baselga, Physician-in-Chief at the Memorial Sloan-Kettering Cancer Center in New York and nominator of Charles Sawyers, the three men's contribution signifies “the birth of personalized anti-cancer medicine.” In the words of the jury, meantime, the award recognizes “the contributions of three eminent scientists who have taken the field all the way from initial basic discoveries to clinical applications that save lives.”

The new treatments, all of them approved in the last ten years, differ from traditional chemotherapy in that they specifically target the mechanisms causing

each type of cancer, making them less toxic for the patient. They are, as such, the first dividend of a profound understanding of the biology of cancer rather than scatter-gun molecular test activity. Imatinib, approved in 2001 and the first of this new class of pharmaceuticals, transformed chronic myeloid leukemia from a fatal cancer into one that is nearly always treatable. Now dozens of such "targeted" drugs are in use for lung and breast tumors, melanoma and lymphomas.

The jury remarked that the three laureates have participated independently in a chain of advances running from "the basic discoveries of tyrosine kinase proteins to clinical applications that save lives."

Tony Hunter, of the Salk Institute, launched the field in 1979 with his discovery of tyrosine kinases, a family of proteins instrumental in regulating vital cell processes like metabolism and proliferation. Some time later, Joseph Schlessinger identified how these tyrosine kinases were activated. And, finally, Charles Sawyers found a way to interfere with their activity in the presence of mutation, "leading to the clinical translation of these basic concepts into the treatment of cancer," the citation continues.

Since many human cancers are driven by mutations in tyrosine kinase activity, these proteins and the molecules they interact with have come center stage as therapeutic targets. As the citation explains it: "Today, it is estimated that about a third of pharmaceutical research and development effort goes into targeting tyrosine kinase receptors and their signaling pathways for cancer therapies."

### **A product of basic research**

The breakthrough that set the story in motion was a product of basic research: the 1979 discovery of the tyrosine kinase that enables the cell to perceive its environment. Like a key it opens a specific door in the cell membrane, inducing a cascade of signals with a vital role in regulating cell proliferation and multiple other processes.

The next step was the establishment of a link with tumoral processes. This part fell to Schlessinger (Topusko, now Croatia, 1945), who explained by phone after hearing of the award: "Very quickly we found that tyrosine kinase receptors became mutated in cancer. So suddenly it was a big story. There was a mechanism for the information to flow from outside the cell to the interior of the cell and that mechanism was hijacked by cancer."

From then to midway through the 1990s, "we explored the way these signaling pathways operated, and it became clear that if we developed inhibitors we could have drugs to treat cancer," Schlessinger continues. "What I mean is that when we started this we did not know it was going to be so important for cancer, and now there are maybe thirty cancer drugs based on this work." Indeed Schlessinger himself has been behind the development of several.

They are, he adds "much more selective and not so toxic. Most of them cannot be considered a cure, but they do extend life expectancy, which is a real

revolution. These new drugs, moreover, are based on an understanding of what causes cancer. And that is why we can talk about personalized medicine. Even so, we are only scratching at the surface. Cancer is a very complicated disease, and the challenge now is how to overcome resistances."

It is precisely this problem of resistance that is at the heart of Sawyer's contribution. He recalled yesterday how his group took part in the first human trial of imatinib, a drug that is "very selective in its action because it only attacks the mutating protein in chronic myeloid leukemia, so has no side effects. When patients began to develop resistance our lab figured out why: there were additional mutations in the gene encoding the protein that imatinib targets. So, based on that, we developed another agent, dasatinib, that inhibits the same protein but in a different way."

For Sawyers, imatinib was the drug that proved it was possible to fight cancer by acting on a mechanism found through basic research. "In ten years," he insists, "it has completely changed the approach of the entire pharma industry, at least in cancer."

And it has also transformed treatment. The concept now is to match the right drug to the right patient after running the relevant genetic tests: "The kind of mutation determines the choice of drug. Now we know hundreds of mutations, and have progressed in no time at all from having imatinib alone to having dozens of drugs that act upon them," Sawyers points out. "It's a success story that could never have happened without basic research revealing the deep-seated mechanisms of cancer."

The next step, he believes, is giving drugs in combination to prevent resistances. "It's happening already, we are still at the start but now have an approved therapy for melanoma."

## Bio notes

**Tony Hunter** was born in Ashford, Kent (United Kingdom) in August 1943. He graduated in 1966 from the University of Cambridge, where he also obtained his PhD. In 1975 he joined the Salk Institute, rising to a professorship in 1982. Since 1983, he has also held a professorship at the University of California, San Diego. He has headed the Salk Institute Cancer Center since 2008.

Author of almost 550 publications, he has held editorial posts with 26 journals, including *Cell*, *Proceedings of the National Academy of Sciences* and *eLife*.

Among his multiple distinctions, he is a fellow of the Royal Society, a member of the United States National Academy of Sciences and the Institute of Medicine of the National Academies, and Einstein Professor of the Chinese Academy of Sciences.

**Charles Sawyers** was born in Nashville, Tennessee (United States) in 1959. He studied medicine at Johns Hopkins University (1985) before going on to complete

his training at the University of California, San Francisco, and the Howard Hughes Medical Institute at the University of California, Los Angeles (UCLA), where he is currently an investigator.

Between 1991 and 2006, he pursued his clinical, academic and research career at UCLA, taking up a professorship there in 2000. In 2006, he joined the Memorial Sloan-Kettering Cancer Center, where he heads the Human Oncology and Pathogenesis Program. Since 2011, he has combined this position with a professorship at the Joan & Sanford Weill Graduate School of Medical Sciences (Cornell University).

Sawyers is author of around 200 published papers and twelve issued patents. He serves on the editorial boards of several publications including *Cell*, *Cancer Cell* and *Science Translational Medicine*. Among his various honors, he is a past president of the American Society of Clinical Investigation Science, and a member of the Institute of Medicine, the U.S. National Academy of Science and the American Academy of Arts and Sciences.

**Joseph Schlessinger** was born in March 1945 in Topusko (now Croatia). In 1948, his family moved to Israel. He studied physics and chemistry at the Hebrew University of Jerusalem, going on to earn a PhD in biophysics in 1974 from The Weizmann Institute of Science (Israel). Since 2001, he has been Chairman of the Department of Pharmacology and William H. Prusoff Professor at Yale University School of Medicine in Connecticut (United States), and, since 2010, has headed the Cancer Biology Institute on the Yale West Campus.

Author or co-author of over 480 scientific papers and publications, in 2001 ISI Highly Cited listed him among the 30 most cited scientists of the 1990s, with over 76,699 citations. He also sits on the editorial boards of leading scientific journals such as *EMBO Journal*, *Cell*, *Molecular Cell* and *Molecular Biology of the Cell*.

He is a member, among others, of the U.S. National Academy of Sciences, the American Academy of Arts and Sciences, the Institute of Medicine of the National Academies, and the European Molecular Biology Organization (EMBO).

### **About 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 hold the key to building a better future for people. The Foundation implements its programs in partnership with leading scientific and cultural organizations in Spain and abroad, striving 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, representing cultural creativity at its expressive height, the area of music. The Awards also reserve space for two

central challenges of the present, those of climate change and development cooperation. 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 artistic realm of *music, both classical and of our time*.

The **juries** in each category are made up of leading international experts in their respective fields, who arrive at their decisions in a wholly independent manner, applying internationally recognized metrics of excellence. The BBVA Foundation is aided in the organization of the awards by the **Spanish National Research Council (CSIC)**, the country's premier multidisciplinary research body. As well as designating 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.

Committee members in the Biomedicine category were Balbino Alarcón Sánchez, Research Professor at the Instituto de Biología Molecular "Eladio Viñuela" (IIBMEV-CBM); Lisardo Bosca Gomar, Research Professor at the Instituto de Investigaciones Biomédicas "Alberto Sols" (IIBM); Mariano Esteban Rodríguez, Research Professor in the Centro Nacional de Biotecnología (CNB); Dolores González-Pacanowska, CSIC Coordinator in the Biology and Biomedicine Area and Research Professor at the Instituto de Parasitología y Biomedicina "López Neyra" (IPBLN); and Ángela Nieto Toledano, Research Professor in the Instituto de Neurociencias (IN).

### Biomedicine jury

The jury in this category was chaired by **Angelika Schnieke**, Chair of Livestock Biotechnology in the Department of Animal Sciences of Technische Universität München (TUM) (Germany), with **Óscar Marín**, Professor of Neurosciences and Director of the MRC Centre for Developmental Neurobiology at King's College London (United Kingdom), acting as secretary. Remaining members were **Dario Alessi**, Director of the Protein Phosphorylation Unit, a Medical Research Council unit in the College of Life Sciences of Dundee University (United Kingdom), **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**, Senior Professor in the Department of Pharmacology and Toxicology in the Carl Gustav Carus Medical School of Technische Universität Dresden (TU Dresden) (Germany), and **Bruce Whitelaw**, Deputy Director and 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 winner in the last edition was British biochemist **Adrian Bird** for "his discoveries in the field of epigenetics." The award in the fifth 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 "showing that it is possible to reprogram differentiated cells back into a state that is characteristic of pluripotent cells," and, in the second edition, **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 3, 2015
<b>Contemporary Music</b>	February 10, 2015
<b>Economics, Finance and Management</b>	February 17, 2015
<b>Development Cooperation</b>	February 24, 2015

#### 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: **AgenciaAtlas4**

Password: **premios**

The name of the video is:

"PREMIO FRONTERAS DEL CONOCIMIENTO CATEGORÍA BIOMEDICINA"

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

**Mobile:** +34 639 16 58 61

**E-Mail:** [amartin@atlas-news.com](mailto:amartin@atlas-news.com)

Fundación **BBVA**

For more information, contact the BBVA Foundation Department of Communication and Institutional Relations (+34 91 374 5210,+34 91 537 3769 / [comunicacion@fbbva.es](mailto:comunicacion@fbbva.es)) or visit [www.fbbva.es](http://www.fbbva.es)