



Boehringer Ingelheim  
Stiftung

2017  
HEINRICH WIELAND PRIZE



## AWARD SYMPOSIUM OF THE 2017 HEINRICH WIELAND PRIZE

Nymphenburg Palace, Munich, Germany  
Thursday, October 19, 2017

## HEINRICH WIELAND PRIZE

The international Heinrich Wieland Prize honours distinguished scientists for their outstanding research on biologically active molecules and systems in the fields of chemistry, biochemistry, and physiology as well as their clinical importance. The prize is endowed with 100,000 euros by the Boehringer Ingelheim Foundation and named after Heinrich Wieland (1877–1957), Nobel Laureate in Chemistry in 1927.

Every year, the foundation invites scientists to make nominations in an open call. It entrusts the selection of the awardees to a scientific Board of Trustees, all of whom work in an honorary capacity (see page 7 for current members). Presented annually since 1964, the Heinrich Wieland Prize has four subsequent Nobel Laureates among its awardees.

[www.heinrich-wieland-prize.de](http://www.heinrich-wieland-prize.de)



## AWARD SYMPOSIUM

- 3:30 P.M.      **Registration**
- 4:00 P.M.      **Welcome and opening remarks**  
Professor Dr Felix Wieland, Chair of the Board of Trustees of the  
Heinrich Wieland Prize, University of Heidelberg, Heidelberg, Germany
- 4:10 P.M.      **“Protein folding homeostasis in the endoplasmic reticulum”**  
Professor David Ron, MD,  
University of Cambridge, Cambridge, UK
- 4:50 P.M.      **“Twists and turns in ubiquitin conjugation”**  
Professor Brenda A. Schulman, PhD,  
Max Planck Institute of Biochemistry, Martinsried, Germany
- 5:30 P.M.      **Coffee break** including **“Meet the Speakers”** for selected students
- 6:10 P.M.      **“Editing of ubiquitin chains”**  
Professor Daniel Finley, PhD,  
Harvard Medical School, Boston, MA, USA
- 6:50 P.M.      **Award ceremony**  
Moderated by Dr Claudia Walther,  
Managing Director of the Boehringer Ingelheim Foundation, Mainz, Germany
- Musical Introduction**  
Wolfgang Amadeus Mozart (1756–1791):  
String Quartet in C major, KV 465, Mov. IV – Allegro molto
- Laudation**  
Professor Dr Franz-Ulrich Hartl,  
Max Planck Institute of Biochemistry, Martinsried, Germany
- Award presentation**  
to Professor Alexander Varshavsky, PhD,  
California Institute of Technology, Pasadena, CA, USA,  
by Christoph Boehringer, Chairman of the Executive Committee of the Boehringer  
Ingelheim Foundation, Mainz, Germany, and Professor Dr Felix Wieland
- Award lecture**  
**“The ubiquitin system, an immense realm”**  
Professor Alexander Varshavsky, PhD
- Musical conclusion**  
Antonín Dvořák (1841–1904),  
String Quartet in F major, “American”, Op 96, Finale – Vivace ma non troppo
- 8:00–10:00 P.M.      **Get-together**

Music performed by Schumann Quartet Munich (members of the Bavarian State Orchestra): Barbara Burgdorf (violin), Traudi Pauer (violin), Stephan Finkentey (viola), Oliver Göske (cello)

**Professor Alexander Varshavsky, PhD**

California Institute of Technology, Pasadena, CA, USA

Alexander Varshavsky receives the 2017 Heinrich Wieland Prize for discovering the biology of the ubiquitin system, a set of pathways regulating, among other things, protein degradation in living cells. Varshavsky and co-workers were the first to uncover the biological roles of ubiquitin conjugation, e.g. in the cell division cycle, DNA repair, cellular stress responses, protein synthesis, and transcriptional regulation. They were also the first to clone the genes encoding ubiquitin, deubiquitylating enzymes, and a ubiquitin ligase. Varshavsky discovered the first degradation signals (degrons) in short-lived proteins, including the N-end rule of protein degradation, and thus revealed how the ubiquitin system knows which proteins to target and when. He revolutionized our view of cellular physiology, placing the regulation of protein degradation on a par with regulation of transcription and translation. To achieve these and related results, his laboratory invented widely used genetic and biochemical methods. Over the last three decades, the fundamental discoveries by Varshavsky gave rise to major biomedical fields and have already led, directly or indirectly, to new medical therapies.



Alexander Varshavsky studied chemistry at the Moscow State University, Russia. In 1973, he received a PhD in biochemistry at the Moscow's Institute of Molecular Biology. He left Russia in 1977 and soon thereafter became a faculty member at the Massachusetts Institute of Technology in Cambridge, USA. Since 1992, he is Smits Professor of Cell Biology at the California Institute of Technology. Varshavsky is a member of the American Academy of Arts and Sciences and the US National Academy of Sciences. He received a number of major awards, including the Gairdner International Award, the Lasker Award in Medical Research, the Max Planck Award, the Albany Prize, and the Breakthrough Prize in Life Sciences.

## **Professor Daniel Finley, PhD**

Harvard Medical School, Boston, MA, USA

Daniel Finley is a renowned expert in the ubiquitin–proteasome pathway, which is responsible for cellular protein degradation, with the proteasome acting as selective shredder for ubiquitinated proteins. He – for example – developed the first purification of yeast proteasomes and described their composition and assembly pathway. He discovered that there are several types of multiubiquitin chains, some of which have regulatory functions. In addition, he identified a set of proteasome-associated ubiquitin chain-editing factors that regulate proteasome activity. One of these regulators is the deubiquitinase Usp14. Finley co-developed a small-molecule inhibitor for Usp14 that is currently being explored for its therapeutic use.

Daniel Finley studied biochemistry at Harvard University in Cambridge, MA, USA, where he graduated in 1980. He stayed in Cambridge for his PhD and joined the laboratory of Alexander Varshavsky at Massachusetts Institute of Technology (MIT). During his PhD, he showed that the ubiquitin pathway is essential for selective protein degradation and survival of mammalian cells. Finley continued at MIT for his post-doctoral work. In 1988, he joined the faculty of Harvard Medical School, where he became Professor of Cell Biology in 2000, a post he still holds. He is a member of the scientific advisory board of Proteostasis Therapeutics, Inc., which develops therapies for diseases caused by dysfunctional protein processing.

## **Professor Dr Franz-Ulrich Hartl**

Max Planck Institute of Biochemistry, Martinsried, Germany  
2011 Heinrich Wieland Laureate

Franz-Ulrich Hartl revolutionized our understanding of protein folding. He overturned the long-held dogma that proteins fold spontaneously into their correct 3D structure and showed that they need help from so-called molecular chaperones inside the crowded environment of cells. He unravelled, for instance, how the Hsp60 and Hsp70 chaperones bring about their protein clients' complex 3D structures and found that they act at different stages of protein synthesis to prevent protein misfolding and aggregation. Hartl also investigates how chaperones defend the cell against toxic protein aggregation in neurodegenerative disorders like Alzheimer's and Parkinson's disease.

Franz-Ulrich Hartl obtained his medical degree in Heidelberg in 1985. He did his postdoctoral work at the University of Munich, also Germany, and the University of California, Los Angeles, USA. In 1991, he accepted a professorship in cell biology and genetics at Memorial Sloan-Kettering Cancer Center and Cornell Medical College in New York, USA. Hartl returned to Germany in 1997 as a Director at the Max Planck Institute of Biochemistry in Martinsried. He is a member of the German Academy of Sciences, the American Academy of Arts and Sciences, and the National Academy of Sciences. Besides many other prizes, he received the Gairdner International Award, the Albert Lasker Basic Medical Research Award, and the Shaw Prize in Life Science and Medicine.

## **Professor David Ron, MD**

University of Cambridge, Cambridge, UK

David Ron has greatly advanced our understanding of how cells minimize and cope with the misfolding of proteins in the endoplasmic reticulum (ER). Working with nematodes and mammals, Ron deciphered how cells regulate their defence against ER stress unleashed by misfolded proteins. He showed how they can match the rates of protein synthesis to folding rates in the ER and, for example, identified PERK as a key regulator in the unfolded protein response. He also revealed how easily protein folding in the ER can be disturbed and that small homeostatic changes in protein folding are linked to diseases of ageing – concepts with fundamental implications to biology and therapeutic application.

David Ron received his medical degree from the Technion in Haifa, Israel, in 1980. He completed his clinical training in the USA at Mount Sinai Hospital in New York and Massachusetts General Hospital in Boston. In 1992, he established a research laboratory at the Skirball Institute of Biomolecular Medicine in New York. In 2009, he accepted a Wellcome Trust Fellowship and his current appointment as the Professor of Cellular Pathophysiology and Clinical Biochemistry at Cambridge University in the UK. David Ron is a Fellow of the Royal Society as well as of the Academy of Medical Sciences.

## **Professor Brenda A. Schulman, PhD**

Max Planck Institute of Biochemistry, Martinsried, Germany

Brenda Schulman is a leader in the field of structural biology studying post-translational protein modifications by ubiquitin-like proteins (UBLs). She unravelled how UBLs are specifically attached to targets by various E1, E2, and E3 enzymes in a complex series of steps. She, for instance, followed the UBL NEDD8 from being prepared by E1, escorted by E2 to being attached to its targets by E3 – in one such case ultimately boosting cell replication. She also studies how different UBLs regulate the function of their diverse targets, for example by changing their enzymatic activity, stability, or interactions with other proteins. Her results will help to tackle defects in UBL pathways seen in cancer, neurodegenerative disorders, and viral infections.

Until recently, Brenda Schulman pursued her academic career in the US. She studied biology at Johns Hopkins University, Baltimore, and received her PhD at Massachusetts Institute of Technology in Cambridge, in 1996. She then went on to postdoctoral fellowships at Harvard Medical School in Boston, MA, and Memorial Sloan-Kettering Cancer Center in New York. In 2001, she joined the faculty of St. Jude Children's Research Hospital. Schulman was granted a Pew Scholar Award, a Beckman Young Investigator Award, and the Presidential Early Career Award for Scientists and Engineers. She is an HHMI Investigator as well as a member of the National Academy of Sciences and the American Academy of Arts and Sciences. In July 2017, she became a Director at the Max Planck Institute of Biochemistry.

# THE PRIZE

**Heinrich Otto Wieland** was born on July 4, 1877, in Pforzheim, Germany. Wieland studied chemistry at the Ludwig-Maximilians-Universität München (LMU) in Munich, Germany, where he received his doctorate in 1901 and was appointed “außerordentlicher Professor” in 1909. At this time, he was already interested in oxidation processes in the living cell, one of the foundation stones of the field of biochemistry. He worked at the Technische Universität München (TUM), also in Munich, and LMU until 1921 as well as at the Kaiser Wilhelm Institute in Berlin-Dahlem, Germany. Wieland then accepted a call to the University of Freiburg, Germany, but returned to LMU in 1925 to succeed Richard Willstätter as Chair of Chemistry. He retired in 1952 and died in Munich on August 5, 1957.

Heinrich Wieland received numerous awards, among them the 1927 Nobel Prize in Chemistry for his pioneering investigations of bile acids and related substances.

Heinrich Wieland was a cousin of Albert Boehringer, the founder of the company Boehringer Ingelheim. As early as 1903, Wieland worked with the company and, in 1917, his advice led to the company establishing its first scientific department dedicated to innovative research. His scientific findings made it possible, for example, to produce drugs for cardiovascular and respiratory diseases.



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# 2017 HEINRICH WIELAND PRIZE

## BOEHRINGER INGELHEIM FOUNDATION

The Boehringer Ingelheim Foundation is an independent, non-profit organization committed to the promotion of the medical, biological, chemical, and pharmaceutical sciences. It was established in 1977 by Hubertus Liebrecht (1931–1991), a member of the shareholder family of the company Boehringer Ingelheim. With the Perspectives Programme “Plus 3” and the Exploration Grants, the foundation supports independent junior group leaders. It also endows awards for up-and coming scientists. In addition, the foundation has donated 100 million euros over ten years to the University of Mainz for the scientific running of the Institute of Molecular Biology (IMB) and a further 50 million euros for the development of the life sciences.



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