HEINRICH WIELAND PRIZE

PRESS RELEASE

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2025 HEINRICH WIELAND PRIZE FOR ADRIAN KRAINER: PIONEER IN RNA RESEARCH WHO GAVE CHILDREN WITH SMA A FUTURE

Boehringer Ingelheim Stiftung announces the winner of the 2025 Heinrich Wieland Prize: Adrian R. Krainer of Cold Spring Harbor Laboratory, USA. He will receive the 250,000 EUR award for his pioneering contributions to understanding how cells edit genetic messages before making proteins — a process known as pre-mRNA splicing — and for using this knowledge to develop the first therapy for spinal muscular atrophy (SMA), a genetic disease that used to be the leading cause of infant mortality. The award ceremony will take place in Munich, Germany, on Thursday, 11 December 2025.

SMA is a rare genetic disease, but it is the second most common severe inherited disorder of infancy and childhood after cystic fibrosis. It causes progressive muscle weakness and paralysis. About 1 in 11,000 babies are born with SMA; over half of them have the severe form, SMA type 1. These children are unable to sit or walk and have difficulty breathing, so they require ventilation. Until Adrian Krainer's groundbreaking work, a diagnosis with SMA type 1 was effectively a death sentence, with most affected children not surviving their first two years of life.

An idea takes shape

Some 25 years ago, Adrian Krainer was invited to a scientific symposium on SMA where he learned that the life-threatening form of this disease is related to a defect in pre-mRNA splicing. Already a leader in his field, he shifted the direction of his research to find a potential therapy. How so?

Pre-mRNA (messenger-RNA) splicing describes a crucial step that takes place in between the transcription of genetic messages from DNA and their translation into proteins, the building blocks of cells. This crucial step removes non-coding segments (introns) from a pre-mRNA and joins the coding regions of a gene (exons). The resulting mature mRNA then serves as a template for protein production. Through alternative splicing, cells can produce different proteins from the same gene by assembling various combinations of exons into distinct mature mRNAs, thereby greatly increasing the diversity of proteins in the body.

Adrian Krainer has made groundbreaking contributions to understanding how splicing works and how it is regulated. Early in his career, he developed a widely used method for studying RNA splicing in a test tube and identified the first human protein splicing factor. He showed how the relative levels of opposing splicing activators and repressors control alternative pre-mRNA splicing and that disruptions of this balance contribute to genetic disorders and cancer.

At the symposium on SMA, Adrian Krainer learned that patients with the disease carry a faulty gene, *SMN1*, which fails to produce enough of a protein essential for motor neurons. The human genome also contains a second, nearly identical gene, *SMN2*. However, *SMN2* cannot fully compensate for a faulty *SMN1*. A small difference in its genetic sequence, compared to *SMN1*, causes it to undergo alternative

splicing, so that it produces only limited amounts of the necessary protein. Adrian Krainer realised that by understanding the underlying mechanisms of splicing regulation in people with SMA, he might uncover a new way to combat this devastating disease.

Nusinersen [or Sprinraza] – a game-changing ASO drug

Through careful analysis, Adrian Krainer discovered that the alternative splicing of *SMN2* results from the failure of a splicing activator to bind to the *SMN2* pre-mRNA. In 2004, he began collaborating with Frank Bennett and his team at the company Ionis Pharmaceuticals. Together, they developed a short RNA-like molecule – a so-called antisense oligonucleotide (ASO) – that blocks the binding of a splicing repressor elsewhere on the *SMN2* pre-mRNA. This allows the pre-mRNA to be spliced in a way that enables production of enough functional protein to compensate for a faulty *SMN1*, at least in a transgenic mouse model of SMA harbouring the human *SMN2* gene. They first published their findings in 2008, and just three years later, the first clinical trials of their ASO (nusinersen) in children with SMA were launched. Several further clinical investigations followed over the next five years, culminating in approval of nusinersen – now marketed as Spinraza – by the U.S. Food and Drug Administration (FDA) in 2016 and by the European Medicines Agency (EMA) in 2017. Since then, more than 14,000 SMA patients have been treated with this groundbreaking therapy.

“Adrian Krainer is an exceptional scientist whose groundbreaking insights into fundamental biology have come full circle in their impact on human health,” says Franz-Ulrich Hartl, chair of the scientific board of trustees that selects the Heinrich Wieland Prize laureates from the many nominations submitted to Boehringer Ingelheim Stiftung (BIS) each year. “He uncovered the molecular mechanism behind a splicing defect in SMA patients and pioneered an entirely new approach to correcting it. The concept of ASO therapy holds great promise for treating other neurological diseases and beyond.” Christoph Boehringer, chair of the Executive Committee of BIS adds: “What began with a dedicated scientist’s curiosity has become a therapy that enables children to sit, stand, and walk for the first time. Adrian Krainer’s example shows how crucial freedom and excellent conditions are – not only for academic progress and the advancement of knowledge, but also for improving human health.”

Heinrich Wieland Prize

This international award honours outstanding research on biologically active molecules and systems in the fields of chemistry, biochemistry, and physiology as well as their clinical importance. The 250,000 EUR prize is named after the Nobel Laureate Heinrich Otto Wieland (1877–1957) and has been awarded annually since 1964. It is among the most prestigious awards for fundamental research in the life sciences in Europe.

Every year, BIS publishes an open call for nominations for the prize. Scientists worldwide can nominate a colleague for the award; self-nominations are not permitted. A scientific board of trustees consisting of nine internationally renowned scientists selects the laureate from submitted nominations. The trustees perform their duties on an honorary basis.

The long list of laureates includes five subsequent Nobel laureates: Michael Brown, Joseph Goldstein, Bengt Samuelsson, James Rothman, and Carolyn Bertozzi.

Boehringer Ingelheim Stiftung

Boehringer Ingelheim Stiftung is an independent, non-profit foundation that is committed to promoting 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 Boehringer Ingelheim company. Through its funding programmes Exploration Grants, Plus 3, and Rise up!, the foundation supports

excellent scientists during critical stages of their careers. It also endows awards for junior scientists in Germany. Additionally, it funds institutional projects in the life sciences, such as the AITHYRA Institute in Vienna and a new research department (BioAI) at the Center for Systems Biology in Dresden, which combine biomedicine with AI. Other supported institutions include the Institute of Molecular Biology (IMB) in Mainz and the European Molecular Biology Laboratory (EMBL) in Heidelberg, both in Germany.

Photos and additional information available at
https://boehringer-ingelheim-stiftung.de/en/scientific-awards/heinrich-wieland-prize/the-prize-winners.html

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