

Press Release of the Boehringer Ingelheim Foundation

Editing the book of life – 2016 Heinrich Wieland Prize goes to Professor Peter Schultz

Mainz, 11. Oct. 16: The chemist Peter Schultz will be honoured with the 2016 Heinrich Wieland Prize for his fundamental contributions to the biologically inspired synthesis of new molecules and, in particular, for the expansion of the genetic code. Schultz, professor at The Scripps Research Institute in California, combines nature's own methods with principles from the chemistry laboratory to create molecules with new functions to use as drugs, study life, or synthesize new materials. His findings have already led to the development of new drugs – some approved, others in the clinical trial stage – against degenerative diseases, cancer, autoimmune, and neglected diseases. The Boehringer Ingelheim Foundation will present him with the international 100,000-euro award during a scientific symposium on synthetic biology on 13 October 2016 in Munich.

Nature is extremely good at building and creating molecules with amazing properties – from antibodies that recognize dangerous pathogens to complexes that harvest energy from sunlight. Chemistry, on the other hand, struggles hard when it comes to reliably and precisely synthesizing large biological molecules with a desired function. The Heinrich Wieland Prize honours Schultz for his pioneering methods that combine chemical and biological tools to reprogramme the cell's own construction machinery to incorporate amino acids beyond the common 20 into the proteins it builds. These non-coded amino acids expand nature's own set of protein building blocks, thus enabling the creation of proteins with new chemical, physical, or biological properties. After all, almost all organisms use a very limited set of building blocks, consisting of the same 20 amino acids. In addition – and in contrast to purely chemical methods – his tools allow him to insert these new building blocks at the exact spot he desires in living cells. With the methods he and his team have devised, we are now able to build probes that help us to understand how proteins act within living cells and to improve diagnostics, vaccines, and drugs more quickly, precisely, and reliably.

Professor Baumeister, chair of the Selection Committee of the Heinrich Wieland Prize says: "Peter Schultz has given us a wide array of invaluable tools that enable us to rationally design molecules and cells to understand the processes of life and to treat medical conditions."

So far, the new tools have enabled researchers to teach cells to insert more than 100 artificial amino acids with different functions with surgical precision into the proteins of individual cells of bacteria, plants, and mammals or even into entire organisms such as fruit flies and roundworms. Using Schultz's approaches, researchers can attach one or several probes to almost any protein and study its function in a living cell in unprecedented detail. Tools based on his work have also

been used to design and refine a variety of drugs, including those that deliver a deadly cargo to the doorsteps of cancer cells.

For many years, researchers have tried to hitch cell-killing drugs to antibodies that recognize and bind to cancer cells and thus deliver the drug only to them. However, it has been difficult with conventional chemistry to control the precise location and amount of a drug attached to the antibody. Both parameters are critical for antibody-binding and the drug's effects – intended or otherwise.

By using the new toolbox, researchers can in principle attach cancer-killing agents at the site that is most effective and safest. Engineered antibody-drug conjugates based on Schultz's method are now showing remarkable results in clinical trials for breast cancer. Because payload and antibody-shuttle can be combined according to need, Schultz thinks that his tools will also improve the safety and efficiency of drugs for inflammatory, autoimmune, and metabolic disease.

Schultz has also developed new ways to screen large numbers of chemicals to find promising candidates for drug development. This promises to greatly improve the search for the proverbial needle in the haystack.

Expanding the genetic code – the how

The genetic code contains the blueprint for life, or, more specifically, for the organisms' proteins. Proteins do all the work in the cell: they transport nutrients, deliver messages, sense the environment, and take many other required actions. Despite their versatility, they start out as linear strands of amino acids strung together like pearls. The order of the amino acids in these strands is written in the DNA using just four letters: A, C, G, and T – short for the bases adenine, cytosine, guanine, and thymine. They spell out 64 different three-letter words, the codons. With three of them not coding for an amino acid and thus functioning as stop signals, DNA can code for 61 different amino acids. However, almost every organism uses the same set of just 20 amino acids – the so-called natural amino acids. Some of these are encoded by just one, others by up to six different codons. But when it comes to translating the codons, each codon uses its own "translator", the so-called tRNA. It works in tandem with another protein, the synthetase. Together they ensure that their specific amino acid is delivered and attached to the growing protein strand.

Schultz has expanded the genetic code by reprogramming both a tRNA and a synthetase so that they can use the stop codon or even four-base unnatural codons to attach an amino acid of his design to the protein. He then inserts this unique codon into the DNA strand at the desired site for his artificial amino acid.

Peter Schultz – the laureate

Peter Schultz received his PhD from the California Institute of Technology, Pasadena, CA, USA, in 1984. After a postdoctoral year at the Massachusetts Institute of Technology, Boston, MA, USA, he became a professor at the University of California, Berkeley, and a principal investigator at the Lawrence Berkeley National Laboratory. Later he was also appointed an investigator at Howard Hughes Medical Institute. In 1999, he moved to The Scripps Research Institute, La Jolla, CA, USA, where he is currently professor of chemistry and CEO. Schultz founded his first biotech company, Affymax Research Institute, in

1988. Eight institutions at the interface between chemistry, material science, and medicine followed; among them are the Genomics Institute of the Novartis Research Foundation and the non-profit California Institute for Biomedical Research, which aims to discover paradigm-changing medicines for unmet needs. Schultz holds almost 100 patents and was named the top translational researcher in 2013 by *Nature Biotechnology*.

Heinrich Wieland Prize – the award

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 100,000-euro prize is named after the Nobel Laureate Heinrich Otto Wieland (1877–1957) and has been awarded annually since 1964. Among the awardees – selected by a scientific Board of Trustees – are four later Nobel Laureates. Since 2011, the prize has been endowed by the Boehringer Ingelheim Foundation.

www.heinrich-wieland-prize.de

Boehringer Ingelheim Foundation – the donor

The Boehringer Ingelheim Foundation is a charitable foundation. It was established in 1977 by Hubertus Liebrecht (1931–1991), a member of the shareholder family of the company Boehringer Ingelheim. The foundation aims to support excellent scientific work in medicine, biology, chemistry, and pharmacy. With its PLUS 3 Perspectives Programme and the Exploration Grants, the foundation supports junior group leaders. It also provides funds of 100 million euros over ten years to support the scientific running of the Institute of Molecular Biology (IMB) and 50 million euros for the development of the life sciences at the University of Mainz. The foundation also endows the internationally renowned Heinrich Wieland Prize and the Boehringer Ingelheim Prize for outstanding research in clinical and theoretical medicine at the University of Mainz.

www.bistiftung.de

An image of Professor Peter Schultz is provided on the webpage www.heinrich-wieland-prize.de (© The Scripps Research Institute).

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