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The 2020 Paul Ehrlich and Ludwig Darmstaedter Prize

Coveted award for Shimon Sakaguchi honors the discovery of regulatory T cells and their role in self-tolerance

Attack or peacekeeping? Immune cells answer this question countless times a day. If they regularly missed the mark, it would have serious consequences for human health. The regulatory T cells discovered by Shimon Sakaguchi help the immune system to distinguish between friend and foe and are instrumental for achieving self-tolerance. Strengthening or weakening this peacekeeping force gives the immune system a kick or a damper. Both strategies can be harnessed to develop new treatments for human diseases.

FRANKFURT am MAIN. Today, Shimon Sakaguchi, professor of Experimental Immunology at Osaka University (Japan) will receive the 2020 Paul Ehrlich and Ludwig Darmstaedter Prize for his pioneering discoveries of regulatory T cells and their role in self-tolerance. These cells have the potential to become the new heroes of medicine. They keep the immune system in balance and ensure that it doesn´t run amok or becomes inattentive. "Without regulatory T cells, the immune system would not be able to correct errors in distinguishing between friend and foe with the necessary precision," explained the Scientific Council of the Paul Ehrlich Foundation when presenting the award. "The immune system needs such regulatory control, because overreaction leads to autoimmune diseases such as rheumatoid arthritis and type 1 diabetes, whereas reduced activity gives cancer cells the opportunity to evade immune attack and eventually establish metastases. Therefore, Sakaguchi's discovery offers great potential for the development of new treatments."

Early on in his studies, Sakaguchi was convinced that an immunological peacekeeping force must exist in order to establish immune homeostasis. The difficulty he faced was that there was no molecular marker that would allow him to identify and isolate these cells. Therefore, Sakaguchi set out to search for such a telltale feature. After many years of painstaking work, he demonstrated that the surface protein CD25 is a reliable marker for these cells. "The discovery

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of CD25 was a watershed in immunological research. It proved the existence of regulatory T-cells and pointed a way forward to isolate and characterize them in greater detail," said Professor Thomas Boehm, Director at the Max Planck Institute of Immunobiology and Epigenetics in Freiburg, and Chairman of the Scientific Council. "This seminal discovery has given the field of immune regulation an enormous boost. Suddenly, many scientists became interested in the biology and use of regulatory T cells."

Subsequently, Sakaguchi was able to show that Foxp3 is the central on/off switch of regulatory T cells, a finding that was quickly confirmed by others. This discovery established an unexpected connection between regulatory T cells and a rare congenital syndrome known as IPEX, which had been shown to be due to the lack of Foxp3. IPEX patients develop severe autoimmune diseases shortly after birth, often leading to early death. Thus, the medical relevance of Sakaguchi´s earlier discovery of regulatory T cells became obvious: patients with IPEX syndrome suffered from lack of an immunological peacekeeping force.

Because of their fundamental importance for the immune system, the manipulation of regulatory T cells offers new forms of treatment for a wide range of conditions. In the case of autoimmune diseases such as rheumatoid arthritis, type 1 diabetes and multiple sclerosis, their activity must be strengthened so that they can take more decisive action against inappropriate attacks on the body's own tissue. In cancer, the activity of regulatory T cells needs to be attenuated. Although they no longer adhere to their normal cellular program, cancer cells are often not considered foreign by the immune system. Hence, the protection of tumor cells by regulatory T cells is unfortunate, as this prevents them from being eliminated. Therefore, to eliminate the tumor´s camouflage, regulatory T cells, which are disproportionately abundant in tumors, must be either reduced in number or their activity diminished to allow an efficient attack on the tumor.

Attenuation of regulatory T cell activity, however, needs to be very precisely controlled, both in space and in time, for they are needed elsewhere in the body to maintain immune homeostasis. "The challenge is to manipulate regulatory T cells only at the site of the tumor," Thomas Boehm explains. "In one approach, Sakaguchi is attempting to convert tumor resident regulatory T cells into conventional T-cells, which then switch sides and participate in attack. If this strategy is successful, an essential component of the body´s peacekeeping force will be converted into an aggressor directed at the malignant tissue ".

At present, various strategies for the treatment of autoimmune diseases and cancer based on the manipulation of regulatory T cells are being evaluated, although these approaches are still in an early phase of clinical development. As with many groundbreaking ideas, therapeutic application requires a long period of painstaking work before they can be offered to patients.

Short biography of Professor Shimon Sakaguchi

Professor Shimon Sakaguchi, M.D. (69) is a medical doctor. He studied medicine at Kyoto University in Japan, then moved to Johns Hopkins University in Baltimore as a post-doctoral fellow and then to Stanford University in California. In 1989 he became an "Assistant Professor" at the Scripps Research Institute in La Jolla. In 1991, Sakaguchi returned to Japan and worked at the Tokyo Metropolitan Institute of Gerontology and later at the Institute for Frontier Medical Sciences at Kyoto University, where he was temporarily director. Since 2011,

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he has been working at Osaka University. In 2012 he became a Foreign Member of the American National Academy of Sciences and in 2017 the Japanese government appointed him "Person of Cultural Merit". Sakaguchi has received many awards, including the William B. Coley Award from the Cancer Research Institute, the Keio Medical Science Prize, the Canada Gairdner International Award and the Crafoord Prize. Last year he was awarded the "German Immunology Prize 2019".

The Paul Ehrlich and Ludwig Darmstaedter Prize
The Paul Ehrlich and Ludwig Darmstaedter Prize is traditionally awarded on Paul Ehrlich's birthday, March 14, in the Paulskirche, Frankfurt. It honors scientists who have made significant contributions in Paul Ehrlich's field of research, in particular immunology, cancer research, microbiology, and chemotherapy. The Prize, which has been awarded since 1952, is financed by the German Federal Ministry of Health, the German association of research-based pharmaceutical company vfa e.V. and specially earmarked donations from the following companies, foundations and organizations: Christa Verhein Stiftung, Else Kröner-Fresenius-Stiftung, Sanofi-Aventis Deutschland GmbH, C.H. Boehringer Sohn AG & Co. KG, Biotest AG, Hans und Wolfgang Schleussner-Stiftung, Fresenius SE & Co. KGaA, F. Hoffmann-LaRoche Ltd., Grünenthal Group, Janssen-Cilag GmbH, Merck KGaA, Bayer AG, Holtzbrinck Publishing Group, AbbVie Deutschland GmbH & Co. KG, die Baden-Württembergische Bank, B. Metzler seel. Sohn & Co. and Goethe-Universität. The prizewinner is selected by the Scientific Council of the Paul Ehrlich Foundation.

The Paul Ehrlich Foundation
The Paul Ehrlich Foundation is a legally dependent foundation which is managed in a fiduciary capacity by the Association of Friends and Sponsors of the Goethe University, Frankfurt. The Honorary Chairman of the Foundation, which was established by Hedwig Ehrlich in 1929, is Professor Dr. Katja Becker, president of the German Research Foundation, who also appoints the elected members of the Scientific Council and the Board of Trustees. The Chairman of the Scientific Council is Professor Thomas Boehm, Managing Director at the Max Planck Institute of Immunobiology and Epigenetics in Freiburg, the Chair of the Board of Trustees is Professor Dr. Jochen Maas, Head of Research and Development and Member of the Management Board, Sanofi-Aventis Deutschland GmbH. Professor Wilhelm Bender, in his function as Chair of the Association of Friends and Sponsors of the Goethe University, is Member of the Scientific Council. The President of the Goethe University is at the same time a member of the Board of Trustees.

Further information
You can obtain selected publications, the list of publications and a photograph of the laureate from Dr. Hildegard Kaulen, phone: +49 (0)6122/52718, email: h.k@kaulen-wissenschaft.de and at www.paul-ehrlich-stiftung.de