THE Crafoord PRIZE

Crafoord *Days* 2017

16–18 MAY IN LUND AND STOCKHOLM, SWEDEN

The Crafoord Prize in Polyarthritis 2017

Abstracts and Programmes

PHOTO: NAKAO PHOTO

SHIMON SAKAGUCHI

PHOTO: TODD LEYECK, EPIC PHOTOJOURNALISM

FRED RAMSDELL

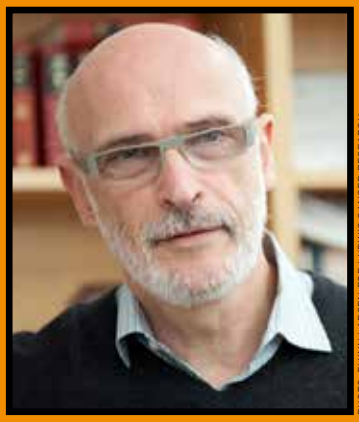

PHOTO: FLYNN LARSEN FOR LUDWIG CANCER RESEARCH

ALEXANDER RUDENSKY

Anna-Greta and Holger Crafoord Fund

THE FUND WAS ESTABLISHED in 1980 by a donation to the Royal Swedish Academy of Sciences from Anna-Greta and Holger Crafoord. The Crafoord Prize was awarded for the first time in 1982. The purpose of the fund is to promote basic scientific research worldwide in the following disciplines:

- Mathematics
- Astronomy
- Geosciences
- Biosciences (with particular emphasis on Ecology)
- Polyarthritis (e.g. rheumatoid arthritis)

Support to research takes the form of an international prize awarded annually to outstanding scientists and of research grants to individuals or institutions in Sweden. Both awards and grants are made according to the following order:

year 1: Mathematics and Astronomy
year 2: Geosciences
year 3: Biosciences (with particular emphasis on Ecology)
year 4: Mathematics and Astronomy
etc.

The Prize in Polyarthritis is awarded only when the Academy's Class for medical sciences has shown that scientific progress in this field has been such that an award is justified.

Part of the fund is reserved for appropriate research projects at the Academy's institutes. The Crafoord Prize presently amounts to SEK 6 million.

The Crafoord Prize is awarded by the Royal Swedish Academy of Sciences.

Content

PROGRAMMES

LAUREATES

Crafoord *Prize* 2017

The Crafoord Laureates in Polyarthritis 2017

PHOTO: NAKAO PHOTO

SHIMON SAKAGUCHI
OSAKA UNIVERSITY, OSAKA, JAPAN

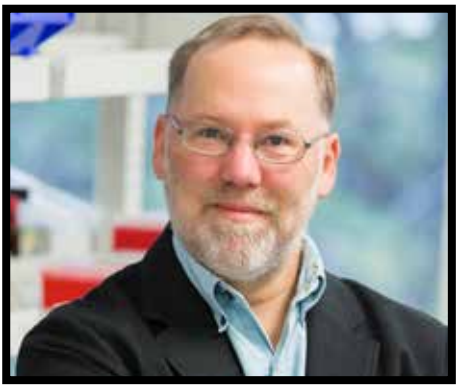

PHOTO: TODD LEVECK, EPIC PHOTOJOURNALISM

FRED RAMSDELL
PARKER INSTITUTE FOR CANCER IMMUNOTHERAPY, SAN FRANCISCO, CA, USA

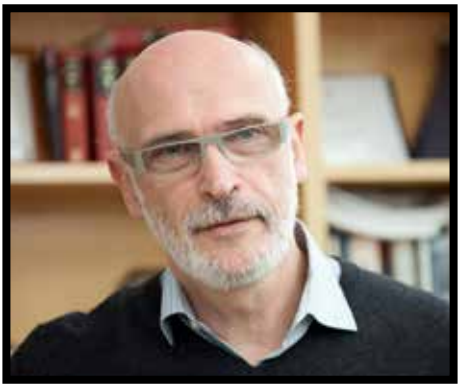

PHOTO: FLYNN LARSEN FOR LUDWIG CANCER RESEARCH

ALEXANDER RUDENSKY
MEMORIAL SLOAN KETTERING CANCER CENTER, NEW YORK, NY, USA

Shimon Sakaguchi, Osaka University, Osaka, Japan, **Fred Ramsdell**, Parker Institute for Cancer Immunotherapy, San Francisco, CA, USA, and **Alexander Rudensky**, Memorial Sloan Kettering Cancer Center, New York, NY, USA "*for their discoveries relating to regulatory T cells, which counteract harmful immune reactions in arthritis and other autoimmune diseases*".

The Crafoord *Prize* in Polyarthritis

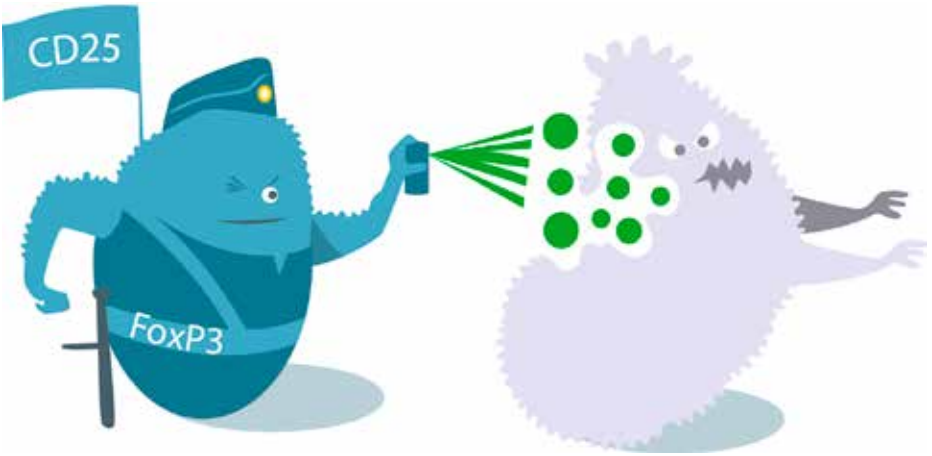

Illustration: © Johan Jarnestad/The Royal Swedish Academy of Sciences

Three immunology researchers share 2017's Crafoord Prize in Polyarthritis, for which the prize money is 6 million Swedish krona. The research being rewarded deals with the discovery of regulatory T cells, cells that can be regarded as our immune system's security guards. They put a brake on cells that are overzealous and attack the body's own tissue. There are hopes that their discoveries will lead the way to new, highly effective treatment methods for autoimmune diseases, such as rheumatoid arthritis, MS and type 1 diabetes.

Autoimmune diseases arise when the body's immune system malfunctions, attacking normal tissue. Globally, these diseases cause great suffering and premature death for millions of people. Autoimmune diseases include multiple sclerosis (MS), type 1 diabetes and polyarthritis. The latter is a term used for rheumatic diseases in which multiple joints are affected.

There are great hopes that highly effective treatments for autoimmune diseases will be possible, based on new knowledge about the immune system that was gained over the last few decades. Three researchers are now being rewarded for their fundamental discoveries in the field: Shimon Sakaguchi, Fred Ramsdell, and Alexander Rudensky.

The Laureates' discoveries relate to regulatory T cells, which are the immune

system's security guards. Their task is to keep an eye on other white blood cells that are overzealous in their task of defending the body from intruders and could harm things they should leave alone, such as healthy cells in joints, the pancreas or brain.

Even back in the 1960s, researchers were searching for suppressor cells in the immune system, but the research results were contradictory. Accordingly, over time, the consensus became that no such cells existed.

Despite this, Shimon Sakaguchi persevered with the search and, after many years, he succeeded in identifying the cells that are now called regulatory T cells. Some years later, Fred Ramsdell approached the same area from a different direction; he isolated and identified the gene that is linked to severe autoimmune disease in a particular strain of mice. He also demonstrated that mutation in the same gene in humans, now known as FOXP3, causes a severe congenital disease called IPEX. Shortly afterwards, decisive findings were made, linking these two pieces of knowledge together. Alexander Rudensky, Shimon Sakaguchi and Fred Ramsdell each described how the FOXP3 gene is vital to a process that results in some T cells becoming security guards in the immune system. These are the regulatory T cells, which can prevent autoimmune reactions because they detect and suppress overzealous colleagues in the immune system.

A great number of clinical trials are now being conducted globally, with research teams testing various ways of using regulatory T cells to subdue the immune system's attacks that cause autoimmune diseases. The long-term vision is that of a breakthrough in the treatment of polyarthritis and other autoimmune syndromes, which could be treated more effectively than they are today.

ABSTRACTS

Crafoord *Days* 2017

Targeting transcriptional and epigenetic control of Treg cell development

SHIMON SAKAGUCHI, OSAKA UNIVERSITY, OSAKA, JAPAN

Regulatory T (Treg) cells, which specifically express the transcription factor Foxp3, are actively engaged in the maintenance of immunological self-tolerance and homeostasis. The majority of them develop in the thymus as a functionally distinct and mature T-cell subpopulation with stable Foxp3 expression, which is dependent on Treg-specific DNA demethylation. Addressing how Treg-specific transcriptional and epigenetic events determine the Treg cell lineage in the thymus, we have recently identified Treg-specific super-enhancers (Treg-SEs), many of which were associated with the Treg signature genes, such as *Foxp3*, *Ctla4* and *Il2ra*. The activation of the Treg-SEs, assessed by specific histone modification, developmentally began in Treg progenitor cells before transcription of Treg signature genes and Treg-specific DNA demethylation. Impaired Treg-SE formation in Treg precursor cells, for example, by deleting the genome organizer Satb1 arrested Treg cell differentiation and caused severe autoimmunity due to Treg cell deficiency. Thus, early genomic changes determine Treg cell lineage specification in the thymus. Molecular anomaly in the process causes autoimmune and other immunological diseases via affecting Treg cell development. In addition, functionally stable Treg cells can be induced from conventional T cells (Tconvs) if Treg-specific transcriptional and epigenetic events, in particular activation of Treg-SEs, which are dormant in Tconv cells, can be evoked.

References

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Kitagawa Y, et al. Guidance of regulatory T cell development by Satb1-dependent super-enhancer establishment. *Nat. Immunol*. 18:173–183, 2017.

History of FoxP3 and implications for therapeutic intervention in disease

FRED RAMSDELL, PARKER INSTITUTE FOR CANCER IMMUNOTHERAPY, SAN FRANCISCO, CA, USA

The primary function of the immune system is to protect the host from pathogens. This elegant system has developed over 1 billion years – and versions of it are found in virtually every multicellular organism known, including plants. The mammalian immune system utilizes roughly 10 % of all our genes and is comprised of 100s of different cell types that act in concert to maintain health. While the system is both remarkably efficient and simultaneously comprehensive – it can also mount a response against our own tissues. Essentially, it gets its target wrong. This can result in diseases that range from Type 1 Diabetes to Rheumatoid Arthritis to Multiple Sclerosis to many others.

In order to develop effective approaches to treat these diseases, it is extremely helpful, if not necessary, to understand how the system works at some level. In general, such understanding is often gained through the integration of knowledge obtained in incremental steps. At times however, singular observations can lead to a more substantial leap forward – and the discovery of the role of the FoxP3 gene in immunity provided such a leap. By linking a compelling phenotype (the scurfy mouse) to the responsible genotype (FoxP3), a new window was opened for immunologists. The subsequent characterization FoxP3 function – many pioneered by my colleagues here today – has led to remarkable insights into how the immune system is regulated. Perhaps more significantly, the insights are leading to novel attempts at treating autoimmune diseases.

Although genomic sequencing is now routine and rapid, there is no equivalent method to determine the function, or functions, of a given gene. Thus, phenotype-first analyses (including 'experiments of nature' such as the Scurfy mouse) remain a powerful way to provide not only biological understanding but also the foundation for therapeutic intervention and represent one of the great opportunities of the current century.

References

Brunkow, M.E., Jeffery, E.W., Hjerrild, K.A., Paeper, B., Clark, L.B., Yasayko, S.A., Wilkinson, J.E., Galas, D., Ziegler, S.F. and F. Ramsdell. 2001. Disruption of a new forkhead/winged-helix protein, scurfin, results in the fatal lymphoproliferative disorder of the scurfy mouse. *Nat Genet* 27: 68–73.

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Regulatory T Cell Differentiation

ALEXANDER RUDENSKY, MEMORIAL SLOAN KETTERING CANCER CENTER, NEW YORK, NY, USA

The emergence of self-MHC restricted recognition by antigen-specific receptors of T cells (TCR) afforded an exquisite sensing of, and powerful resistance to diverse, rapidly evolving intracellular pathogens. The "self-referential" basis of T cell recognition and differentiation and T cell-mediated amplification of inflammation likely required a novel, dominant means of negative regulation – suppression of immune mediated inflammation by regulatory T cells. The latter represent a dedicated suppressive cell lineage and feature prominently in autoimmune and inflammatory disorders, allergy, acute and chronic infections, cancer, and metabolic inflammation. The cellular and molecular mechanisms of differentiation of regulatory T cells will be discussed with an emphasis on the control of expression of the transcription factor Foxp3 and its role in the biology of these cells.

Unraveling central tolerance through multi-organ autoimmunity

MARK ANDERSON, DIABETES CENTER, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, CA, USA

Autoimmunity is a complex condition that results from a breakdown of immune tolerance to self. The human immune system has an adaptive arm that allows for the generation of a diverse set of immune receptors that can detect a wide array of pathogenic specificities. The generation of this diverse array of receptors occurs in both T cells and B cells. Because of the stochastic properties of this receptor generation process, a subset of immune receptors gets generated with reactivity against self specificities. Thus, key mechanisms must be in place to prevent or silence such cells from the immune system or autoimmunity will ensue. One clue into a key switch of how this is controlled in T cells has come from the study of patients with a rare clinical syndrome termed Autoimmune Polyglandular Syndrome Type 1 (APS1). These patients develop a series of organ-specific autoimmune diseases that can be attributed to a defect in a single gene termed *AIRE* (for Autoimmune Regulator). Our lab group and others have determined that AIRE plays a key role in enforcing T cell tolerance in the thymus by promoting the display of "self" to developing T cells. This key process now appears to have a role in common autoimmune diseases and also an important intersection with the selection of T regulatory cells. These findings underscore the rapid advances that are now occurring in complex biology through the study of extreme forms of autoimmunity.

CTLA-4 and T regulatory cells in autoimmunity

KAJSA WING, KAROLINSKA INSTITUTET, STOCKHOLM, SWEDEN

Foxp3$^+$ regulatory T cells (Treg) are professionals in tolerance and seem to have incorporated multiple immune suppressive mechanisms in their repertoire in order to control immune responses. A key suppressive mechanism for Treg cells that also operates in conventional T cells (Tconv) is cytotoxic T-lymphocyte antigen 4 (CTLA-4). Genetic variants and also functional defects of this immunosuppressive protein have been shown to be related to various autoimmune disorders including rheumatoid arthritis (RA). Moreover CTLA-4 is used for clinical therapy in both RA patients but also to release cancer immunity. Thus, CTLA-4-mediated regulation of already tolerized autoreactive T cells is critical for understanding autoimmune responses. However due to the early fatality of CTLA-4 KO mice the specific role of CTLA-4 in Treg and Tconv cells in systemic autoimmunity have been difficult to sort out. By deleting CTLA-4 in adult mice we circumvented this and found that although these mice developed autoimmunity to certain organs the exocrine pancreatitis and the myocarditis seen in congenitally CTLA-4 deficient mice was avoided. This allowed model studies of immunity towards the dominant collagen type-II (CII) T cell epitope in collagen-induced arthritis (CIA). CTLA-4 was found to regulate all stages of arthritis, including the chronic phase and affected the priming of autologous but not heterologous CII-reactive T cells. CTLA-4 expression by both conventional T cells (Tconv) and Treg cells was required but while Tconv cell expression was needed to control priming of naïve autoreactive T cells, CTLA-4 on Treg cells prevented the inflammatory tissue attack. This identifies a time window when cell type-specific CTLA-4-mediated tolerance is most powerful, which has important implications for clinical therapy with immune modulatory drugs.

Targeting Fibroblasts to regulate inflammation

CHRISTOPHER BUCKLEY, INSTITUTE OF INFLAMMATION AND AGEING, UNIVERSITY OF BIRMINGHAM, UK

Despite the introduction of biologic treatments, a significant proportion of patients continue to have stubbornly resistant disease. Moreover many patients, in whom clinical remission has been achieved, subsequently relapse once treatment is withdrawn, suggesting that additional therapeutic targets, responsible for complete resolution of chronic inflammation, remain to be discovered.

Inflammation results from the complex interaction between haematopoietic and stromal cells. Yet almost all current therapies target haematopoietic cells and ignore stromal cells, such as fibroblasts. Our work over the last decade has demonstrated that in addition to their well-known structural role in "landscaping" the microenvironment, fibroblasts modify the quality, quantity and duration of leucocyte accumulation within tissues. They also contribute to the resolution of inflammation by normalizing chemokine gradients, allowing infiltrating leukocytes to leave the tissue through the draining lymphatics and enhancing regulatory T cell function.

We have proposed that inflammation is contextual and since fibroblasts help define tissue topography we have suggested that fibroblasts represent an attractive, site specific, therapeutic target. We now propose that fibroblasts exist in discrete subsets, some of which are pro-inflammatory while others, more functionally similar to MSC, are anti-inflammatory and regulate tissue homeostasis and organ repair. This has led to a therapeutic dilemma: which fibroblast subsets to delete and which to replace? Therefore a clear understanding of the biology and significance of fibroblast heterogeneity is essential to provide a coherent rationale for their targeting in the treatment of rheumatic diseases. In this lecture I will describe recent evidence that suggests that like effector and regulatory T cells, fibroblasts can exist in distinct effector and regulatory sates.

IPEX Syndrome: Clinical History, Immunological Characterization and Therapeutic Perspectives

ROSA BACCHETTA, STANFORD UNIVERSITY, CA, USA

Defective *FOXP3* leading to regulatory T (Treg) cell dysfunction is the primary cause of Immune-dysregulation Polyendocrinopathy-Enteropathy-X-linked (IPEX) syndrome a severe genetic autoimmune disease that can be fatal within the first year of life. IPEX is an X-linked recessive disorder with exclusive expression in males that most commonly manifests with early onset Type 1 Diabetes, severe diarrhea with associated failure to thrive and extensive dermatitis. Mutations of *FOXP3* cause dysfunction of Treg cells, but FOXP3 is also transiently expressed in activated T effector (Teff) cells, broadly impacting T cell lymphocytes and indirectly B cells. IPEX is considered a rare disease but the disease awareness and diagnosis has increased during the past decade. Thus, the increasing challenge is to develop a long-term treatment and cure. Current treatment options include immunosuppression, only partially effective, and allogeneic hematopoietic stem cell (HSC) transplantation, limited by lack of suitable donors and toxicity from pre-transplant conditioning.

To improve therapies for IPEX patients, we have developed a lentivirus (LV)-mediated *FOXP3* gene transfer method that converts pathogenic IPEX patient CD4+ T cells to functional Treg cells ($CD4^{FOXP3}$). Autologous $CD4^{FOXP3}$ T cells are cell-based therapeutics that should dramatically improve IPEX patient pathology, reducing the need for pharmacological immunosuppression. However, to establish long-lasting treatment, we are currently pursuing a gene editing approach in HSC. The site-specific gene correction of FOXP3 would permit endogenously regulated expression of the functional FOXP3 protein not only in Treg but also in Teff cells. To edit FOXP3, we used CRISPR-Cas9 protein combined with an AAV6 packaged donor DNA template. Preliminary results demonstrate the feasibility of *FOXP3* gene editing in HSC. Our data indicates that both LV-FOXP3 gene transfer and FOXP3 gene editing can be proposed for the cure of IPEX syndrome.

Switching off rheumatoid arthritis – vain hope or future reality?

JOHN D. ISAACS, INSTITUTE OF CELLULAR MEDICINE, NEWCASTLE UNIVERSITY, UK

The human immune system is a highly complex organ, comprising a multitude of cell types in various locations around the body. It is designed to recognise and fight foreign invaders, such as microbes and tumours. However, in order to do this, it requires highly sophisticated control mechanisms to avoid damaging 'self' tissues. This is the concept of immune tolerance and our immune system actually spends much of its time maintaining a tolerant state. Autoimmune disease is the consequence when this equilibrium breaks down, encompassing diseases such as type 1 diabetes, multiple sclerosis and rheumatoid arthritis (RA).

In the last quarter of the 20th century our understanding of immunology increased exponentially, allowing us to dissect and understand the various cells and interactions that formed a classical immune response. However, this also suggested ways to interrupt unwanted immune responses, such as occur in autoimmune diseases. In fact, using animal models, it became clear that it was possible to 're-educate' a diseased immune system and potentially switch off unwanted immune responses permanently, so-called therapeutic tolerance. If these findings could be translated to humans, this raised the possibility of cures for diseases such as type 1 diabetes and RA.

For the past 30 years, translational researchers have attempted to achieve immune 're-education' in humans. Mostly these attempts have focussed on the interaction between T-cells and antigen presenting cells, the cells at the core of all immune responses. Techniques have ranged from monoclonal antibodies that non-specifically kill a variety of immune cells, to small peptides designed to specifically interrupt the interactions central to a particular disease. More recently there have been attempts to utilise cells generated outside of the body to achieve therapeutic tolerance. In this lecture I will highlight my own journey along the path of therapeutic tolerance in RA, one of the commonest autoimmune diseases.

CD4+ T cells in Rheumatoid Arthritis – the questions of subsets, time and location

VIVIANNE MALMSTRÖM, KAROLINSKA INSTITUTET, STOCKHOLM, SWEDEN

Rheumatoid Arthritis (RA) is a heterogenous chronic inflammatory disease manifesting in peripheral joints. A distinct subset of RA patients have an autoimmune disease as characterized by HLA class II associations and autoantibody production. Still, our current view is that RA does not start as a joint inflammation, but loss of tolerance is likely to happen many years prior to disease onset at mucosal sites.

The contribution of CD4+ T cells is still only partly understood, and I will exemplify this both by our studies of joint-derived plasma cells and the antibodies they produced (which are likely to be T-cell driven) and by direct assessment of effector T cell phenotypes and of autoreactive T cells in different sites and during different stages of disease.

Manipulating Tregs to control tolerance in autoimmunity and cancer

JEFFREY A. BLUESTONE, HORMONE RESEARCH INSTITUTE, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, CA, USA

The breakdown of tolerance has been attributed to an imbalance of effector function and immune regulation, specifically defective regulation due to defects in the T regulatory cells (Treg) subset. Thus, multiple efforts have been forged to re-instate that balance in setting such as autoimmune disease and organ transplantation or disrupt it as a means to promote anti-tumor immunity. In this presentation, I will discuss recent studies demonstrating Treg instability in the autoimmune and cancer settings. One focus will be on the epigenetic enzyme, EZH2, which are critical for maintaining the stability and function of Tregs upon activation. Disruption of the EZH2 activity specifically disrupts intratumoral Treg function without compromising systemic control of immune homeostasis and with clear therapeutic implications, EZH2-deficient Tregs acquires activities that promote tumor clearance and may be responsible for autoimmunity in certain settings. In addition, FOXP3 mutants, causing IPEX disease in humans, has been informative in elucidating mechanism of action for this key transcription factor discovered by this year's Crafoord awardees. The effects of one such mutation, in the FOXP3 dimerization domain, will be discussed as it has led to important insights into germinal center formation, T cell differentiation and functional status of immunity. Finally, early pre-clinical and clinical studies will be presented translating the insights gained from the mouse studies to deliver Tregs therapeutically, including for rheumatoid arthritis, to promote rebalancing of effector and Treg function in autoimmunity and transplantation. This work has been supported by NIH, JDRF, and the Sean N. Parker Autoimmunity Research Laboratory.

Overview programme Crafoord *Days* 2017

Tuesday 16 May

09:30

Prize Lectures

Held by the Crafoord Laureates **Shimon Sakaguchi, Fred Ramsdell** and **Alexander Rudensky.**

LUND, GRAND AUDITORIUM, LUX, LUND UNIVERSITY,
HELGONAVÄGEN 3, LUND

Registration at www.crafoordprize.se or http://kva.se

Wednesday 17 May

09:00

Prize Symposium

The control of inflammation; regulatory T cells in health and disease

Lectures by the Crafoord Laureates **Shimon Sakaguchi, Fred Ramsdell** and **Alexander Rudensky** and invited speakers.

STOCKHOLM, THE BEIJER HALL, ROYAL SWEDISH ACADEMY OF SCIENCES,
LILLA FRESCATIVÄGEN 4A, STOCKHOLM

Registration at www.crafoordprize.se or http://kva.se

Thursday 18 May

16:30

Prize Award Ceremony

In the presence of H.R.H. Crown Princess Victoria and H.R.H. Prince Daniel.

STOCKHOLM, THE BEIJER HALL, THE ROYAL SWEDISH ACADEMY OF SCIENCES,
LILLA FRESCATIVÄGEN 4A, STOCKHOLM

Registration at www.crafoordprize.se or http://kva.se

Detailed programme

THE CRAFOORD PRIZE IN POLYATRITIS 2017

The Crafoord *Prize* Lectures in Polyatritis

09:30

LUND
GRAND AUDITORIUM, LUX,
LUND UNIVERSITY, HELGONAVÄGEN 3, LUND

Tuesday 16 May

*Registration at **www.crafoordprize.se** or **http://kva.se***

09:30	Welcome remarks	*Klas Kärre*, Chair, the Crafoord Prize Committee
09:35	Introduction of the Crafoord Prize Laureates	*Åke Lernmark*, Lund University, Sweden
09:45	*Control of Immune Responses by Regulatory T Cells*	CRAFOORD LAUREATE 2017 ***Shimon Sakaguchi***, Osaka University, Osaka, Japan
10:15	Questions from the auditorium	Moderated by *Åke Lernmark*, Lund University, Sweden
10:25	*On the virtue of restraint*	CRAFOORD LAUREATE 2017 ***Alexander Rudensky***, Memorial Sloan Kettering Cancer Center, New York, NY, USA
10:55	Questions from the auditorium	Moderated by *Åke Lernmark*, Lund University, Sweden
11:05	COFFEE	
11:35	*History of FoxP3 and implications for therapeutic intervention in disease*	CRAFOORD LAUREATE 2017 ***Fred Ramsdell***, Parker Institute for Cancer Immunotherapy, San Francisco, CA, USA
12:05	Questions from the auditorium	Moderated by *Åke Lernmark*, Lund University, Sweden
12:15	Concluding remarks	*Klas Kärre*, Chair, the Crafoord Prize Committee
12:20	LUNCH	Lunch is served outside the lecture hall and is included form registered participants.

Detailed programme

THE CRAFOORD SYMPOSIUM IN POLYATRITIS 2017

The control of inflammation; regulatory T cells in health and disease

09:00

STOCKHOLM
THE BEIJER HALL, THE ROYAL SWEDISH ACADEMY OF SCIENCES,
LILLA FRESCATIVÄGEN 4A, STOCKHOLM

Open to the public and free of charge. Seating is limited.
For registration and further information visit
http://kva.se/crafoordsymposium2017

Wednesday 17 May

09:00	Opening address	*Göran K. Hansson*, Secretary General, the Royal Swedish Academy of Sciences
09:05	Introduction of the Crafoord Laureates	*Klas Kärre*, Chair of the Crafoord Prize Committee
09:15	*Targeting transcriptional and epigenetic control of Treg cell development*	CRAFOORD LAUREATE 2017 ***Shimon Sakaguchi***, Osaka University, Osaka, Japan
10:00	*History of FoxP3 and implications for therapeutic intervention in disease*	CRAFOORD LAUREATE 2017 ***Fred Ramsdell***, Parker Institute for Cancer Immunotherapy, San Francisco, CA, USA
10:45	BREAK WITH REFRESHMENTS	
11:15	*Regulatory T Cell Differentiation*	CRAFOORD LAUREATE 2017 ***Alexander Rudensky***, Memorial Sloan Kettering Cancer Center, New York, NY, USA
12:00	LUNCH	(Included for registered participants)
13:00	*Unraveling central tolerance through multi-organ autoimmunity*	*Mark Anderson*, Diabetes Center, University of California, San Francisco, CA, USA
13:35	*CTLA-4 and T regulatory cells in autoimmunity*	*Kajsa Wing*, Karolinska Institutet, Stockholm, Sweden
14:10	*Targeting Fibroblasts to regulate inflammation*	*Christopher Buckley*, Institute of Inflammation and Ageing, University of Birmingham, UK
14:45	BREAK WITH REFRESHMENTS	
15:15	*IPEX Syndrome: Clinical History, Immunological Characterization and Therapeutic Perspectives*	*Rosa Bacchetta*, Stanford University, CA, USA
15:50	*Switching off rheumatoid arthritis – vain hope or future reality?*	*John D. Isaacs*, Institute of Cellular Medicine, Newcastle University, UK
16:25	*CD4+ T cells in Rheumatoid Arthritis – the questions of subsets, time and location*	*Vivianne Malmström*, Karolinska Institutet, Stockholm, Sweden
17:00	*Manipulating Tregs to control tolerance in autoimmunity and cancer*	*Jeffrey A. Bluestone*, Hormone Research Institute, University of California, San Francisco, CA, USA
17:40	End of symposium	

Anna-Greta and Holger Crafoord

Holger Crafoord (1908–1982) was prominent in Swedish industry and commerce. He began his career with AB Åkerlund & Rausing and devoted a larger part of his working life to this company. In 1964, Holger Crafoord founded Gambro AB in Lund, Sweden, where the technique of manufacturing the artificial kidney was developed. This remarkable dialyser soon became world famous. Since then, a series of medical instruments has been introduced on the world market by Gambro.

HOLGER AND ANNA-GRETA CRAFOORD

In 1980, Holger Crafoord founded the Crafoord Foundation, which annually contributes greatly to the Anna-Greta and Holger Crafoord Fund.

Holger Crafoord became an honorary doctor of economics in 1972 and in 1976 an honorary doctor of medicine at the University of Lund.

Anna-Greta Crafoord (1914–1994) took, as Holger Crafoord's wife, part in the development of Gambro AB. Through generous donations and a strong commitment in the society around her, she contributed to the scientific and cultural life. In 1986 she founded the Anna-Greta Crafoord foundation for rheumatological research and in 1987 Anna-Greta Crafoord became an honorary doctor of medicine at the University of Lund.

Over the years, the Crafoords have furthered both science and culture in many ways and it is noteworthy that research in the natural sciences has received an important measure of support from the Anna-Greta and Holger Crafoord Fund.

THE ROYAL SWEDISH ACADEMY OF SCIENCES is an independent, nongovernmental organization whose aim is to promote the sciences and strengthen their influence in society. Traditionally, the Academy takes a special responsibility for the natural sciences and mathematics, and strives to increase exchanges between various disciplines.

The activities of the Academy are aimed mainly at

- spreading knowledge of discoveries and problems in current research
- providing support for young researchers
- rewarding outstanding contributions in research
- stimulating interest in mathematics and the natural sciences in schools
- spreading scientific and popular-scientific information in various forms
- offering unique research environments
- maintaining contact with foreign academies, learned societies and other international scientific organisations
- representing the sciences in society
- carrying out independent analyses and evaluations based on scientific grounds on issues of importance for society

THE ACADEMY HAS has about 450 Swedish members and 175 foreign members. The Swedish members are active within Classes and committees. They initiate investigations, responses to government proposals, conferences and seminars. Once a month, the Academy holds a General Meeting, with a connected public lecture.

THE ACADEMY´S OWN INSTITUTES offer unique research environments for botany, ecological economics, the history of science and mathematics.

IN ADDITION TO THE CRAFOORD PRIZE, the Academy annually awards a number of prizes, the best known of which are the Nobel Prizes in Physics and Chemistry and the Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel. Others are the Söderberg Prize and the Göran Gustafsson Prize. The latter are awarded to outstanding young researchers and are a combination of a personal prize and a research grant. The Academy also supports researchers through scholarships and mentoring programmes, and is engaged in appointing many promising young researchers to long-term positions that are financed by foundations.

THROUGH ITS VARIOUS COMMITTEES, the Academy also works for the development of a society based on scientific grounds. Great interest in environmental and educational issues has resulted in a wide variety of Academy activities in these areas.

THE CRAFOORD PRIZE IS AWARDED IN PARTNERSHIP BETWEEN THE ROYAL SWEDISH ACADEMY OF SCIENCES AND THE CRAFOORD FOUNDATION IN LUND. THE ACADEMY IS RESPONSIBLE FOR SELECTING THE CRAFOORD LAUREATES.

WWW.CRAFOORDPRIZE.SE

KUNGL. VETENSKAPS-AKADEMIEN
THE ROYAL SWEDISH ACADEMY OF SCIENCES

BOX 50005, SE-104 05 STOCKHOLM, SWEDEN
TEL: +46 8 673 95 00 | INFO@KVA.SE | HTTP://KVA.SE