EUROPEAN SCIENCE FOUNDATION
SETTING SCIENCE AGENDAS FOR EUROPE

JSPS
Japan Society for the Promotion of Science

RESEARCH CONFERENCES

ESF-JSPS Frontier Science Conference for Young Researchers

Cutting Edge Immunology and its Clinical Application

Apollo Hotel de Beyaerd, Hulshort, The Netherlands

1-6 March 2011

Chairs:

- **Prof. Åke Lernmark** - Department of Clinical Sciences, Lund University and CRC, Lund, SE
- **Prof. Kazuo Sugamura** - President of Miyagi Cancer Center Research Institute, JP

Co-Chair:

- **Prof. Hajime Karasuyama** - Department of Immune Regulation, Tokyo Medical and Dental University Graduate School, JP

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Conference Highlights

Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)

The conference centered on the immune system, which has evolved to protect our body against a large number of infectious agents. The infection itself may cause serious and often fatal diseases. An infection may also cause severe sequelas i.e. pathological conditions resulting from an infection. It was possible in the conference through leaders in diverse areas of the immune system as well as by the participants to cover key functions of the immune system to better understand its' role in human health and disease. The conference was able to provide an academic environment in which young researchers readily met distinguished front-runners in the field of basic and clinical immunology to discuss the frontline of immunological research and its clinical application.

The highlights of the conference included Japanese and European leaders. The participants were also equally represented from Japan and Europe in a extremely successful mix allowing an outstanding opportunity to meet young investigators to establish contacts and novel network.

The program involved presentations of the development of the hematopoeitic and immune system. Novel findings in the ontogeny of the hematopoetic revealed early and novel roles of cytokines in the development process. Similarly the role of the thymus in T cell selection was detailed also to detail the importance of dendritic cells to remove T cells that may harm the body. As one third of the human population is infected with parasites it was an important task to detail the state of the art of understanding the mechanisms by which the immune system cope with parasites and other infectious agents. The understanding of these mechanisms is close to the survival of the human race and novel approaches to combat the infections and epidemics were reviewed and discussed. It has been estimated that 15-20% of all hospital visit may be related to different types of autoimmune or allergic disease. The worldwide epidemic of autoimmune diseases, their etiology, pathogenesis and possible treatment and cure was discussed in detail both in plenary lectures and in participant presentations. The role of the innate immune system and its' ability to influence specific immune reactions to both exogenous and endogenous antigens were detailed. It was evident from the discussions that while basic knowledge in laboratory animals dominate the more complicated investigations in man are catching up in our ability to dissect the human immune response to pathogens.

Treatment and prevention of diseases included the development and use of novel human monoclonal antibody reagents to target key immune response mechanisms in man. Plenary lectures on the emerging use of IL-6 and other cytokines reagents and novel monoclonal antibody reagents that modulate the function of both T and B lymphocytes showed promising results in early clinical trials. Novel findings to use T cell reagents in the combat of allergic disorders were also discussed.

The conference was a success since the participants were exposed to interdisciplinary approaches that have advanced our understanding of basic mechanisms underlying immune responses in a variety of physiological and pathological settings. It was also revealed how critical findings in laboratory animals are being applied in the clinic. Monoclonal antibodies specific to proinflammatory cytokines and cell surface signaling molecules or their receptors are successfully used to treat human disorders such as rheumatoid arthritis and inflammatory bowel disease. The conference also succeeded in exposing young and senior researchers with different backgrounds and interests, and in promoting closer interaction between the bench and the clinic.

☐ I hereby authorize ESF – and the conference partners to use the information contained in the above section on 'Conference Highlights' in their communication on the scheme.

Scientific Report

Executive Summary

(2 pages max)

ESF-JSPS Frontier Science Conference for Young Researchers: “Cutting Edge Immunology and its Clinical Application” was held on 1-6 March 2011. The organization from the ESF and JSPS was outstanding. The conference was held at Apollo Hotel de Beyaerd, in Hulshorst, the Netherlands. The 45 min transport from Amsterdam was taken care of by the organizers. The conference facilities were excellent in terms of accommodation and meals. It allowed the participants to mingle and have meals together. There were no opportunities to sneak away from the meeting as the location was way out in the countryside. Hence, the interaction between speakers and participants was very successful and the young investigators all took the opportunity to discuss with the more senior investigators.

The invited speakers mostly stayed for a large proportion of the meeting. A couple of speakers stayed for the entire meeting which enhanced the quality of the discussions. Indeed, very few speakers showed up at the meeting only to give their presentations. The relatively small meeting room allowed the participants to ask questions and the presentations were characterized by question and answer sessions both during and after the formal presentations.

Overall the presentations were of very high quality. The best of Japanese and European immunology researchers attended the meeting. It gave an atmosphere of pioneering as the program was highly interdisciplinary. The group of seasoned speakers and researchers had to address and audience that was new to them and not the usual crowd that shows up at conferences of specialized fields.

The young investigators had submitted abstracts of their on-going research. It made it possible for the organizers to select abstracts for oral as well as poster presentations. Several of the participants took the opportunity to present both. As time had been allocated to poster presentations in conjunction with wine and cheese this conference provided an outstanding opportunity also for younger scientists to present their research and have it thoroughly discussed by their fellow participants. The program shows that the presentations represented a broad spectrum of immunology research being done in both Japan and Europe. The opportunity to cross-fertilize ideas and exchange reagents as well as to establish collaborations and contacts was outstanding.

The Japanese delegation included the following ten speakers and the title of their presentations illustrating the broad coverage of immunology:

Kazuo Sugamura, Miyagi Cancer Center Research Institute, Miyagi: Regulation of memory T cell development by OX40 costimulatory signals.

Hajime Karasuyama, Department of Immune Regulation, Tokyo Medical and Dental University Graduate School, Tokyo: Novel roles for basophils in allergy and protective immunity.

Toshiaki Ohteki, Tokyo Medical and Dental University, Tokyo: Regulatory role of interferon in HSC homeostasis – an old cytokine with a new function.

Yousuke Takahama, University of Tokushima, Tokushima: Thymic microenvironments that shape T lymphocyte repertoire.

Yoshinori Fukui, Kyushu University,Fukuoka: Regulation of leukocyte trafficking and other

immunological functions by the CDM family of proteins.

Tadamitsu Kishimoto, Osaka University, Osaka: IL-6: from its discovery to medicine and back again.

Kiyoshi Takeda, Osaka University, Osaka: Regulation of intestinal homeostasis by innate immunity.

Sidonia Fagarasan, RIKEN, Yokohama: New aspects of IgA synthesis in gut.

Toshio Hirano, Osaka University and RIKEN, Osaka: Interleukin 6 amplifier and autoimmune disease: a four step model.

Hiroshi Kiyono, The University of Tokyo, Tokyo, JP: Mucosal immunity and symbiosis for the development of needle-free vaccine.

The European delegation included the following twelve speakers:

Ana Cumano, Institut Pasteur, Paris, FR : Ontogeny of the hematopoietic system.

Maria Yazdanbakhsh, Leiden University Medical Center,Leiden, NL**:** Immune polarization by parasites.

Jean-François Bach, Hôpital Necker, Paris, FR **:** Infections, immunoregulation and autoimmune diseases.

Philippe Pierre, Centre Immunologie de Marseille Luminy, Marseille, FR **:** Activation of the integrated stress response pathway is essential for innate immunity.

Andreas Radbruch, Universitätsklinikum Berlin, DE: The organisation of immunological memory.

Ed Palmer, University of Basel, Basel, CH**:** Affinity thresholds determine central and peripheral tolerance.

Bart Lambrecht, Ghent University, Ghent, BE: Dendritic cell-epithelial cell crosstalk in asthma.

Antonio Lanzavecchia, Institute for Research in Biomedicine, Bellinzona, CH**:** Dissecting the human immune response to pathogens.

Peter Taylor, Imperial College London, London, UK**:** TNF blockade in rheumatoid arthritis and other chronic inflammatory diseases.

Herman Waldmann, University of Oxford, Oxford, UK**:** Infectious tolerance and immune therapy.

Rudolf Valenta, University of Vienna, Vienna, AT**:** Regulation of allergen responses.

Åke Lernmark, Lund University/CRC, Malmö, SE: Immunotherapy of type 1 diabetes.

All participants submitted abstracts. The program committee selected a total of 24 for short oral presentations (10 min and 5 min discussion). In addition, there were 40 abstracts accepted for poster presentation. These presentations were divided into two poster sessions prior to dinner to allow poster presentations and discussions to take place over beverages and some snacks.

The organizers provided an excellent and much appreciated afternoon excursion to and guided tour of the Kröller Müller Museum. The tour took place the day before the last day of the conference.

Scientific Content of the Conference

(1 page min.)

- *Summary of the conference sessions focusing on the scientific highlights*
- *Assessment of the results and their potential impact on future research or applications*

The conference had two plenary lectures and seven sessions. The entire meeting lasted for four days. The fist session on **Development of hemato-poietic and immune system** highlighted novel data on stem cells and mechanisms of development and differentiation. The importance of cytokine regulation of the cell cycle was discussed. The role of the thymus in T selection focused on the mechanisms of positive selection to avoid useless T cells to leave the thymus as well as negative selection as a way to avoid harmful T cells. The second session focused on **Immune regulation.** The role of parasites to polarize the immune system was discussed in detail. The mechanisms of parasites affecting T regulatory cells and subsequent regulation of antibody production may offer novel approaches to treatment. The interaction between the adaptive and innate immune responses were further analyzed and discussed in session three: **Innate and mucosal immunity.** This is a rapidly expanding area of research and novel data on the integrated stress response pathway revealed its importance for innate immunity. There is an extended role of Vitamin A and the gut immunity responses to vaccines and infections may provide differences in innate immune responses dependent on the function of follicular dendritic cells in the gut. **Immunogical memory and tolerance** was discussed in session 4. OX40 and OX40 ligands are demonstrated to play important roles in the generation and control of memory precursor T cells. It is possible to identify and analyze distinct effector memory T cells through their cell surface receptors. The role of plasma cells in immune response has been a problem to dissect in human immunology. Recent advances were highlighted and the possibility to identify and isolate human plasma cells should make it possible in the future to clarify to what extent these cells are antigen presenting cells for T cells. The T cell receptor interaction with the major histocompatibility complex class I and II heterodimeric proteins was dissected in binding experiments. The role of the time that T cell receptor dwell on the surface of the antigen presenting cell may be related to a signal for positive or negative selection. Such mechanisms are likely to be important to the risk that autoreactive T cells may appear and contribute to autoimmune disease. In session five on **immune disorders,** new information on the role of basophils as controllers of immune responses to allergens such as dust mites and ticks were presented. Advances have been made in the understanding of the interaction between dendritic cells and basophils in advancing the immune responses allergens or other infectious agents. Translational research is at the verge of implementation to include the role of adjuvants as well as intestinal parasites. The role of Il-6 in transient and chronic immunopathogenesis showed unexpected involvement of IL-17 leading to an increase in tissue sensitivity to different cytokines. Novel technologies have allowed the screening for single plasma cell cultures from humans. Focus has been on the generation of human monoclonal antibodies that would show immunomodulatory effects. Similar technologies have also made it possible on a large scale to identify memory T cells and establish memory T cell libraries. On-going research focus on specific T cell responses to C. Albicans, and S. aureus and their differences in cytokine release patterns. In a first session on **Treatment and prevention of diseases (session 6)** the use of soluble receptors of monoclonal antibodies specifically developed against cytokine such as TNFalpha receptors were discussed. Despite success patients continue to fail treatment and novel approaches in drug combination trials will be needed. The question and approaches to tolerance induction showed the need for better understanding of alternative regulatory molecules such as CTLA-4, CD39, IDO and mTOR. The second session of **Treatment and prevention of diseases,** focused on type I allergic reactions and the mechanisms of possible allergen presentation by B lymphocytes. The development of allergen identification

and molecular cloning has been rapid and the translation into clinical trials has been swift. Allergen T cell epitopes are recognized and novel approaches to specific immune tolerance are being developed. Oral vaccines are modified to tale into account adjuvant effects by different proteins or protein adducts. Antisense therapies may offer a novel approach to vaccination and immune tolerance induction. Although mechanisms are not clear it is possible that immune tolerance induction with autoantigens may reduce autoreactivity in organ-specific autoimmune diseases such as type 1 diabetes. One plenary session summarized the state of the art of **Infections, immunoregulation and autoimmune diseases** indicating the possible role of hygiene as a contributing phenomenon to the present escalation in autoimmune diseases. While infections overall are decreasing in the society, the incidence of autoimmunity is steadily increasing. Another plenary lecture discussed **IL-6: from its discovery to medicine and back again,**an important lesson to be learned about Il-6 and the effects of this cytokine in disease development but also on the use of monoclonal IL-& antibodies to modulate a large variety of immune mediated disorders**.**

Forward Look

(1 page min.)

- *Assessment of the results*
- *Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe*
- *Identification of emerging topics*

This conference on **Cutting Edge Immunology and its Clinical Application** brought an unprecedented opportunity to discuss key events in immune regulation and immune mediated and associated diseases together. It was an opportunity for Japanese and European scientists to get together and discuss the new data in the very frontline of immunological research. The focus was mechanisms that would be possible to translate into clinical application. Investigator-initiated clinical research is a rare commodity and the initiative to apply recent bench-related research to clinical practice needs major support. The advancement in immunology research with clinical application was clearly a focus at this meeting. The technologies are overlapping an the experience at the conference was that both senior and young investigators had more in common than they were separated in thoughts and approaches to answer fundamental questions. Novel ideas raised at the conference will beyond doubt to be disseminated. Some 5-10 years from now there will be a need to meet again and benefit from the platform established at the present conference to take the next humble steps towards effective measures to prevent or cure the many serve autoimmunity diseases that affect mankind today.

- Is there a need for a foresight-type initiative?

Diseases associated with immunological dysfunction are poorly understood. The treatment success is directly proportional to the poor understanding. Major research efforts are required to improve the situation for patients. The growing increase in autoimmune diseases including a world-wide increase in type 1 diabetes and other organ-specific immune disorders will require extraordinary efforts. The cutting edge immunology and its clinical application should be the focus of fore-sight initiatives to speed up the development of novel approaches to prevention, intervention and cure.

Atmosphere and Infrastructure

▪ *The reaction of the participants to the location and the organization, including networking, and any other relevant comments*

This conference provided an outstanding opportunity for invited speakers to meet with younger scientists to present their research and have it thoroughly discussed. The presentations represented a broad spectrum of immunology research being done in both Japan and Europe. The opportunity to cross-fertilize ideas and exchange reagents as well as to establish collaborations and contacts was outstanding. The cooperation between ESF and the JSPS to bring together the best scientists in the field was the heart of success of the ESF-JSPS Frontier Science Conference for Young Researchers.

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None

Date & Author:

2011-12-03 Åke Lernmark