English pages

REPORT FROM THE 19TH ANNUAL MEETING OF THE JAPANESE SOCIETY OF IMMUNOTOXICOLOGY (TSIT2012)

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The 19th Annual Meeting of the Japanese Society of Immunotoxicology (JSIT2012) was held at "The Jikei University School of Medicine", Nishishimbashi, Tokyo during September 15-16, 2012. The main theme of this meeting was "Novel aspects of Immunotoxicological diseases". The meeting consisted of 2 special lectures, 2 master's lectures, symposium, workshop, 2 luncheon seminars, 2 JSIT Research Award lectures, 20 oral presentations and 6 student and young scientist presentations.

Special lecture

1. Overview and Application of the WHO/IPCS Harmonized Guidance for Immunotoxicity Risk Assessment for Chemicals (Henk van Loveren, National Institute of Public Health and the Environment, Maastrick University, The Netherlands)
2. New with old in immunotoxicological research – What has been and what shall be in our society of immunotoxicology (Motoyasu Ohsawa, Hatano Research Institute, Food and Drug Safety Center, Hatano, Japan)

Master's lecture

1. Molecular mechanism of fatigue and relationship between immunotoxicology and fatigue (Kazuhiro Kondo, Department of Virology, The Jikei University School of Medicine, Tokyo, Japan)
2. Pathological linkage of metabolic disease and autoimmunity by apoptosis inhibitor of macrophage (AIM) (Toru Miyazaki, Laboratory of Molecular Biomedicine for Pathogenesis, Center for Disease Biology and Integrative Medicine, Faculty of Medicine, The University of Tokyo, Tokyo, Japan)

The 20th Annual Meeting of JSIT 2013 (Japanese Society of Immunotoxicology)

September 12-13, 2013

Tokai University Takanawa Campus,
2-2-23 Takanawa, Minato-ku, Tokyo, Japan.

Theme:
"To explore the vision of Immunotoxicology."

The subject matter of the 20th Anniversary Annual Meeting of the Society is "To explore the vision of Immunotoxicology." Although the details of the 20th Memorial Lectures as well as Symposium are being prepared now, the contents should be apposite for the 20th anniversary, including invited speakers from overseas.
In addition, educational lectures on two separate subjects are also included in the plan.
Lecture 1 will be on "Epigenetics of the function and differentiation of immuno-competent cells – aspects of immunotoxicology", while Lecture 2 will deal with "Higher-order function analysis of the system of Notch / NotchL in the development and differentiation of the immune system".

Workshop :
Oral / Poster presentation:
Deadline for abstract submissions : June 24, 2013

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The website of this Anniversary Meeting is currently in preparation.

Symposium

"Progress in research for immunotoxicology"

1. Topics of research on sick house syndrome, with special reference to an immunotoxicologist aspect (Kou Sakabe, Department of human structure and function, Tokai University School of Medicine, Kanagawa, Japan)
2. Advances in gut immunity to gastrointestinal nematode infections (Kenji Ishiwata, Department of Tropical Medicine, The Jikei University School of Medicine, Tokyo, Japan)
3. Immunological analysis of asbestos-exposed people for identification of new diagnostic markers (Yasumitsu Nishimura et al., Department of Hygiene, Kawasaki Medical School, Kurashiki, Japan)

Workshop "In vitro immunotoxicology"

1. Current trend on in vitro immunotoxicology in EU (Emanuela Corsini, Laboratory of Toxicology, Dipartimento di Scienze Farmacologiche e Biomolecolari, Faculty of Pharmacy, Universita degli Studi di Milan, Italy)
2. Development and application of an in vitro skin sensitization test named h-CLAT based on alteration of dendritic cell surface markers expression (Hitoshi Sakaguchi, Safety Science Research Laboratories, Kao Corporation Tochigi, Japan)
3. Study on safety assessment for sensitization using alternative methods (Takao Ashikaga, Research Center, Shiseido Co., Ltd., Kanagawa, Japan)
4. Development of assay system for immunotoxicity using cytokine reporter cells (Multi-ImmunoTox assay) (Setsuya Aiba, Department of Dermatology, Tohoku University Graduate School of Medicine, Sendai, Japan)
5. Irradiation of light emitting diode at 850 nm inhibits T cell-induced cytokine expression (Ai-Young Lee et al. Department of Dermatology Dongguk University Ilsan Hospital, South Korea)

Luncheon seminar

1. Evaluation of ant-drug antibodies during non-clinical safety studies (Gray Bembridge, Huntingdon Life Sciences Ltd.)
2. Validation and use of several assays to monitor pharmacodynamic markers intended for human use, in the cynomolgus monkey (Lawrence D Jacob, Principal Immunologist and Molecular Biologist and Bioanalysis and Immunology Group, Charles River Laboratories Preclinacal services, Edinburg, UK)

In this year, "JSIT Prize for Encouragement" was received by Dr. Eiko Koike (Center for Environmental Health Sciences, National Institute for Environmental Studies, Tsukuba, Japan, Title: Study on the aggravation mechanism of allergy induced by environmental chemicals) and Dr. Yasumitsu Nishimura (Department of Hygiene, Kawasaki Medical School, Kurashiki, Japan, Title: Immunological analysis of asbestos-exposed people for identification of new diagnostic markers). "The Outstanding Researcher Award in Annual Convention" was received by Dr. Mitsuhiro Uchida (Meiji Seika Pharma Co., Ltd., Tokyo, Japan, Title: Application of Human Cell Line Activation Test (h-CLAT) as a new method for detecting allergic potential of systematically-treated drugs). "The Best Young Presenter Award" was received by Mr. Toshiro Hirai (Laboratory of Toxicology and Safety Science, Graduate School of Pharmaceutical Sciences, Osaka University, Osaka, Japan, Title: The novel immune-modulating effects of amorphous nanosilica particles following epicutaneous exposure) and Mr. Kazuyuki Okamura (National Institute for Environmental Studies, Graduate School of Life & Environmental Sciences University of Tsukuba, Tsukuba, Japan, Title: The involvement of p130 in arsenic-induced senescence of B cell).

I would like to appreciate all the participants who actively joined passive presentations and discussions. See you again in the coming JSIT2013 at Tokai University School of Medicine, Tokyo, Japan.

JSIT prize for encouragement

Study on the aggravation mechanism of allergy induced by environmental chemicals

Eiko Koike
(National Institute for Environmental Studies)

It is my great pleasure and honor to be awarded the JSIT prize for encouragement. I appreciate all members of JSIT and award selection committee.

Environmental pollutants are thought to be critical problems for the increase in allergy. Recently, we have been focusing especially on environmental chemicals, such as phthalates ubiquitously used as plasticizers in many polyvinylchloride consumer products. We have shown that diisononyl phthalate (DINP) aggravate atopic dermatitis-like skin lesions induced by mite antigen in NC/Nga mice. The aggravation was consistent with eosinophilic inflammation, mast cell degranulation, and TSLP expression in the inflammatory site. Then we have found that *in vitro* exposure to DINP enhance the expression of cell surface activation markers on BMDCs and their production of TARC and MDC, as well as their capacity to stimulate mite antigen-specific T-cell proliferation. DINP also enhanced interleukin-4 production from splenocytes. These results demonstrate that DINP can aggravate allergy and the mechanisms might be partly mediated through the activation of dendritic cells and through direct or indirect activation of T-cells.

Finally, I would like to say heartfelt thanks to Dr. Hirohisa Takano, Dr. Rie Yanagisawa, and all my collaborators for their help.

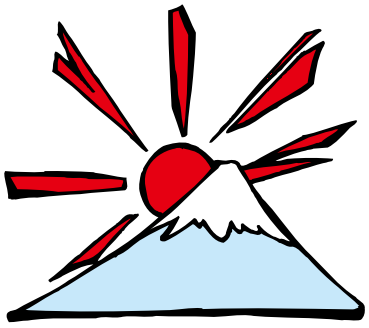
Asbestos and tumor immunity

Yasumitsu Nishimura
(Department of Hygiene, Kawasaki Medical School)

I am very honored to be awarded the JSIT second prize for encouragement. I would like to sincerely thank all of the members of the awarding committee.

This prize is awarded for the research about immunological analysis of asbestos-exposed people for identification of new diagnostic markers. I had learned immunology from Tomohide Hosokawa, a professor in Kyoto University of Education, and started the study about asbestos and alveolar macrophages at Hyogo College of Medicine in 2002, just after I had finished a doctorate at Kyoto University. At the beginning, I was not able to get interested in the study about asbestos, because asbestos looks like just a stone for me. However, as getting some results, I came to realize the significance and interest of study about effect of asbestos on cellular functions. And then, I started to work under the supervision of Prof. Takemi Otsuki at Department of Hygiene in Kawasaki Medical School. As you know, in our laboratory, Ayako Ueki, the former professor, had started the study about effect of exposure to silica and asbestos on immune cells, which Prof. Otsuki developed much more. Under such a great environment, we could accomplish the several outcomes about altered functions of tumor immunity related with asbestos exposure and malignant mesothelioma, in particular about suppressive effect on NK cell function. Recently, we have started the comprehensive immunological analysis for mesothelioma patients, showing several novel findings in immune cells. I will consistently exert an effort on studies about effects of asbestos and other materials on immune cells in the future, in order to contribute to clarification of mechanisms and development of strategies for health disorders caused by asbestos and other materials.

Finally, I thank all of people supporting me for their help and encouragement so much again.



The Outstanding Researcher Award in annual convention

Application of Human Cell Line Activation Test (h-CLAT) as a new method for detecting allergic potential of systematically-treated drugs

Mitsuhiro Uchida[1], Toshiyuki Tsuchiya[1], Maho Ukaji[2], Yoshiro Saito[2], Kouichi Kurose[2]
(1: Toxicology Laboratory, Pharmaceutical Center, Meiji Seika Pharma Co., Ltd., Kanagawa, Japan
2: Division of Medicinal Safety Science, National Institute of Health Sciences, Tokyo, Japan)

Allergic adverse reactions have been sometimes observed in a clinical development and/or on the market. Therefore, early detection of the sensitizing potential of chemicals is an emerging issue for pharmaceutical development. For skin sensitizing potential, human cell line activation test (h-CLAT) using monocytic cell line, THP-1, has been validated as a cell-based assay. We evaluated 18 systematically-treated drugs using h-CLAT to investigate the usefulness as a new method for sensitization potential of systematically-treated drugs.

As a result, 11 (ampicillin sodium, D-penicillamine, ticlopidine hydrochloride, cephalothin sodium, diclofenac sodium, levofloxacin hydrochloride, gefitinib, albendazole, amiodarone hydrochloride, carbamazepine and pravastatin sodium) out of 18 drugs which were reported allergic adverse reactions (e.g. rash, hepatitis) in human were determined positive in the h-CLAT. The other 7 drugs (phenytoin, hydrocortisone, penicillin G potassium, nevirapine, acetyl salicylic acid, allopurinol and amoxicillin) were not assayed due to poor water solubility or low cytotoxicity. This investigation demonstrated that h-CLAT might be the appropriate assay also for sensitizing potential of systematically-treated drugs.

The Best Young Presenter Award

The novel immune-modulating effects of amorphous nanosilica particles following epicutaneous exposure

Toshiro Hirai
(Laboratory of Toxicology and Safety Science, Graduate School of Pharmaceutical Sciences, Osaka University, Osaka, Japan)

I am very privileged to receive the students/young scientist best presentation award at the 19th annual meeting of the Japanese Society of Immunotoxicology and would like to appreciate the support from the selection committee.

I investigated the effects of epicutaneous exposure to silica nanoparticles (nSP), which is one of the most frequently used NMs in cosmetics, on allergic diseases using an AD model of NC/Nga mice. We showed that the combined applications of nSP and mite extract antigen (Dp) did not induce any effects on Dp-inducing AD skin lesion. In contrast, we revealed that epicutaneous exposure to nSP influences Dp-specific IgG/IgE balance and induce IgE-mediated hypersensitivity. It is known that epicutaneous allergen sensitizations play important role to make pathogenesis of not only AD, but also other IgE-mediated allergic diseases, such as food allergy and asthma. Therefore, when considering primary epicutaneous sensitization in asthma or food allergy, it may be better to consider environmental exposure to protein antigen with NM together.

I would also like to give special thanks to my research professor Dr. Yasuo TSUTSUMI, Dr. Yasuo YOSHIOKA, Dr. Kazuma HIGASHISAKA and other colleagues in Laboratory of Toxicology and Safety Science for supporting throughout the progress. I am thrilled to contribute much more for the immunotoxicology field by furthering my research topics.

The involvement of p130 in arsenic-induced senescence of B cell

Kazuyuki Okamura
(Graduate School of Life & Environmental Sciences, University of Tsukuba National Institute for Environmental Studies)

It's my great pleasure to get such a big award. In this paper, I described my project 'The involvement of p130 in arsenic-induced senescence of B cell'.

Chronic arsenic exposure induces immune suppression. We previously reported that long-term arsenic exposure of B cell lymphoma A20 cells induced senescence. In this study, I investigated the mechanism of arsenic-induced senescence. Reactive oxygen species (ROS)-mediated DNA damage response is implicated in senescence. Since arsenic is reported to induce ROS, I examined the contribution of ROS to arsenic-induced senescence. Treatment of cells with H_2O_2 for 5 days showed the features of senescence. However, while arsenic caused accumulation of cells at G0/G1 phase, H_2O_2 increased cells at G2/M phase, indicating that arsenic and H_2O_2 induce senescence by different mechanisms. Arsenic, but not H_2O_2, was found to greatly increase the amount of p130, the G0/G1-specific pRB family protein. Knockdown of p130 by siRNA abolished the arsenic-induced G0/G1 arrest. These results suggested that long-term arsenic exposure induces senescence at G0/G1 phase through accumulation of p130 protein.

Finally, I would like to sincerely thank you for giving me The Best Young Presenter Award. I want to study even harder to be a good scientist. I hope you will give me further guidance and encouragement in the future.

Contributed article

A memoirs on "Studies on experimental iodine allergy" for the purpose of developing diagnostic agent for predicting allergic adverse effect of iodinated contrast media

Hiroshi Shionoya
(Asama Chemical Co. Ltd)

The mechanism of "iodine allergy" has not yet been completely elucidated. However, from our studies and circumstantial evidence in humans, I speculate that the common allergens are autologous proteins having the antigenic determinant diiodotyrosine. A plan on diagnostic device development for preventing iodine allergy to iodinated contrast media was also addressed.

Words from new councilors

Etsushi Kuroda
(Particulate adjuvant and immunity
WPI Immunology Frontier Research Center, Osaka University
Laboratory of Vaccine Science)

My name is Etsushi Kuroda working in WPI Immunology Frontier Research Center, Osaka University. I took office as a councilor of the Japanese Society of Immunotoxicology. I am thankful to Dr. Otsuki in Kawasaki Medical School and Dr. Morimoto in University of Occupational and Environmental Health Japan for making a recommendation to the board on JSIT. I am going to contribute my best to the advances of JSIT.

My paramount interest is in the mechanisms of particulate-induced immune responses. Particulates and crystals stimulate the immune systems to induce inflammatory responses. A number of particulates, such as particle matter 2.5 (PM2.5), diesel particles and sand dusts induce pulmonary inflammation. In contrast, aluminum salts (referred to as alum) have been used to enhance antibody responses in animals and humans as vaccine adjuvant. Interestingly, a number of particulates, such as alum and silica, induce type 2 immune responses, which are characterized by the

accumulation of eosinophil at the site of inflammation and the elevation of serum IgE in vivo. However, the basis and mechanisms of adjuvanticity of these particulates remain poorly understood. Now I am strongly interested in the effect of particulates in immune responses. Of course, it is difficult to clarify the molecular mechanisms of adjuvanticity of particulates in detail. In addition, I'm still young fellow in the academic field of immunotoxicology. I ardently hope you will continue to guide me in the future, and I want to make a win-win relationship with all members in JSIT.

Thank you for your kind cooperation.

Tin Tin Win Shwe
(National Institute for Environmental Studies)

Currently, I am doing research studying the effects of environmental pollutants on nervous and immune systems at the Biological Impact Section, Center for Environmental Health Sciences, National Institute for Environmental Studies. I have been joining the Japan Society for Immunotoxicology every year from 11th meeting.

First I would like to introduce my research. Up to now, using brain *in vivo* microdialysis technique, molecular gene expression assay and learning performance test, I have been studying the effects of environmental toxic chemicals such as diesel exhaust nanoparticles, volatile organic compound toluene and organophosphate pesticide diazinon on neurotoxicity, neuroimmune crosstalk, chemical susceptibility and possible mechanism of action of these three substances in allergic model, athymic nude model, infectious model and inflammatory model of mice.

I deeply appreciate for giving opportunity for participating as a councillor of Japan Society for Immunotoxicology. I would like to contribute to development of a Japanese Immunotoxicology Society in the future. Finally I would like to invite all of you to visit my country golden land Myanmar and do collaborative research with Myanmar researcher from basic science, clinical and public health fields.

Ryota Kawai
(Daiichi Sankyo Co., Ltd.
Medicinal Safety Research Laboratories)

It is my honor to take office as a councilor of the Japanese Society of Immunotoxicology this year. I like the cozy atmosphere of this society which consists of many researchers from a broad range of fields.

It was in my masters-degree course that I began to study immunotoxicity. In those days, I tried to establish a system for evaluating allergenicity using Brown Norway rats and cell line for the identification of the allergen ingredients of food materials, evaluation of allergen removal effectiveness, and so on. I have been concerned with the non-clinical safety evaluation of the drug candidates since entering my current company. I engage in antigenicity studies, local irritation studies and immunotoxicity studies. Meanwhile I have studied to establish immunotoxicity evaluations, particularly T cell-dependent antibody response (TDAR), and participated in the validation of TDAR between institutions in this society.

These days, my attention is attracted to immunogenicity and infusion reaction of the biopharmaceuticals. This Society is a good area for exchange of information. Needless to say, the further development of immunotoxicology being important, I think that the role of this Society will become more important. I will make efforts to contribute to the development of this society and appreciate your further help and encouragement in advance.

Yasuo Yoshioka
(Graduate School of Pharmaceutical Sciences,
Osaka University, Osaka, Japan)

My name is Yasuo Yoshioka from the Graduate School of Pharmaceutical Sciences, Osaka University and it is my honor to announce that I was appointed as a member of the board. I would like to give an appreciation to Dr. Takemi Otsuki and Dr. Yasumitsu Nishimura at Kawasaki Medical School who recommended me for this position and also a great opportunity. With the

recent development of nanotechnology, nanomaterials are beginning to be used on a global scale. However, the increasing use of nanomaterials has raised public concerns about the potential risks to human health. Because nanomaterials have the potential to improve the quality of human life, it is essential to ensure their safety and obtain the information for designing safe nanomaterials. We are now trying to investigate the safety of nanomaterials for the development of nanomaterials with safety and efficacy. In the course of investigation, assistance from the members of the Japanese Society of Immunotoxicology will be much appreciated.

Sincerely,

Real Voices of International Immunotoxicologists

We had a chance to interview the three international researchers, Dr. Henk Van Loveren from National Institute of Public Health, the Netherlands, Dr. Emanuela Corsini from Università degli Studi di Milano, Italy and Dr. Ai-Young Lee from Dongguk University Ilsan Hospital, Korea, who gave us very exciting lecture and information at the 19th Annual Meeting of JSIT. Here, we introduce their answers for our questions. Those allow us to hear real voices of international immunotoxicologists.

Dr. Henk Van Loveren, Ph.D.
Head Section Immunotoxicology and Infection, Laboratory for Health Protection Research, National Institute of Public Health, The Netherlands

Q1. What was the most impressive event for you in your trip to Japan this time?

The most impressive of this meeting for me was to see how many scientists were gathered for this meeting. In Europe we do not have a Society for Immunotoxicology. We have, under EUROTOX, a Speciality Section for Immunotox, but even if EUROTOX covers the entire Europe, it does not attract so many scientists as there were in the JSIT meeting, which is basically a national meeting. Of course Japan is a big and innovative country, but still smaller than the entire Europe.

Q2. What is the most exciting thing in your career to date.

The most exciting thing in my career is undoubtedly to be in contact with many different people around the world, exchanging thoughts and ideas, and while doing so, improve risk assessment of chemicals. I hope to contribute to this, especially from the immunological angle.

Q3. What are the things you are doing energetically, right now?

A main activity that I am involved in now is being member of expert groups within the European Food safety Authority. They perform risk assessments, and I contribute from the immunotoxicological point of view. Here, the science that I am involved in is utilized and has an impact. That gives me quite a lot of energy.

Q4. What is required for breakthrough in immunotoxicology research in the future, do you think?

The further development of animal free, mechanism-based risk assessment approaches for identification of immunotoxic and sensitizing activity of chemicals, and the utilization of such approaches for quantitative risk assessment. Such approaches will most likely involve integral testing strategies made up of different tests, and include advanced technologies such as “omics”, in vitro testing etc. But we are not there yet. Acceptance by alternative testing by regulatory authorities is what is required, and these authorities should be aware that alternatives may not be full proof ever, while realizing that nor is the current practice using animals.

Q5. Any other comments

I was happy to be invited by the JSIT, and to see some good friends from Japan.

Emanuela Corsini, Ph.D.
Associated Professor of Toxicology
Department of Pharmacological Sciences
Università degli Studi di Milano
Italy

Q1. What was the most impressive event for you in your trip to Japan this time?

This year was my first visit of Japan, and the Congress of the Japanese Society of Immunotoxicology gave me the second opportunity to visit this wonderful country. It is very difficult for me to say which was the most impressive event, I have so many good memories that I don't know what to choose. Before coming to the Congress, I was in Kyoto and we visited the Royal Palace. I was impressed by the beauty, simplicity and elegance of the palace and gardens. I also have a wonderful memory of the dinner we had in Tokyo the day before the Congress started, where I tried all kind of sake although I do not usually drink alcohol.

Q2. What is the most exciting thing in your career to date.

One of the more exciting thing in my career was when I won the award for the best Young Investigator from the Immunotoxicology Specialty Section of SOT.

Q3. What are the things you are doing energetically, right now?

Even if next year I will be 50, I still like to work in the lab, but of course, I have to thank my collaborators for finishing all experiments I start, which I will never be able to finish due to a busy schedule that include a heavy teaching duty.

Q4. What is required for breakthrough in immunotoxicology research in the future, do you think?

I may have a bias of course, but I think that the development of better methods for in vitro immunotoxicology will be an important area of research in the near future due to economical, ethical and regulatory pressures.

Other important area of research in the field of immunotoxicology will be nanotoxicology, the immunotoxicity of biologicals or biosimilars and POPs.

Q5. Any other comments

I wish that all presentations during the Congress of the Japanese Society of Immunotoxicology would have been in English. The titles of all presentation were so interesting, but it was impossible for me to follow them as unfortunately I don't speak Japanese.

Ai-Young Lee
Professor / Chief
Department of Dermatology
Dongguk University Ilsan Hospital
Korea

Q1. What was the most impressive event for you in your trip to Japan this time?

I stayed at the Tokyu Hotel near by Jikei University School of Medicine. Although I've already known that the living expense in Tokyo is expensive, the size of hotel room was so small.

Q2. What is the most exciting thing in your career to date.

When I was in the late twenties, I saw a patient who had a generalized skin rash. From her medical history and skin tests, penicillin in milk was suspected. I collected related information and finally quantitated the rough amount of penicillin in commercialized milk products.

Q3. What are the things you are doing energetically, right now?

How dare I can tell that I do research energetically? Anyway, we have been interested in pathogenesis of the pigmentary skin diseases such as vitiligo and melasma.

Q4. What is required for breakthrough in immunotoxicology research in the future, do you think?

As an amateur, I think development of in vitro systems which can surrogate relevant in vivo systems may be required for breakthrough.