

English pages

Report from the holding of the 16th Annual Meeting of the Japanese Society of Immunotoxicology

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The 16th Annual Meeting of the Japanese Society of Immunotoxicology (JSIT) was held at Asahikawa Cultural Hall in Asahikawa City with the theme of "Children and Immunity" during August 27-28, 2009. This meeting was hold by joint hosting with the 55th Meeting of Allergy and Immunotoxicology Scientific Committee / Japan Society for Occupational Health.

Dr. Dori R. Germolec (NIEHS, NIH, USA) presented the first special lecture entitled "Does immunomodulation early in life increase disease risk in children and beyond?". The content of presentation was started with basic animal studies and referred to the points of public health problems, and was also significant as introduction to the symposium "Children and Immunity". Symposia entitled, "Children and Immunity" chaired by Drs. Fujio Kayama (Jichi Medical Collage) and Dr. Kazuichi Nakamura (Shionogi Pharmaceutical Co.). The symposium featured presentations by Dr. Sho Ishikawa (Tokyo University) on the breakdown of mucosal immunity in the gut and allergic sensitization by dioxins, Dr. Chisato Mori (Chiba University) on a health examination system to prevent fetal exposure to persistent organic pollutants and atopic dermatitis in infants and Dr. Judith T. Zelikoff (New York Univ. USA) on the prenatal exposure to cigarette smoke increases tumor susceptibility of juvenile mice via changes in anti-tumor mechanisms. The beginning of afternoon, the JSIT had the general assembly of this fiscal year. That evening, the reception had hosted at the Asahikawa Grand Hotel. Dr. Nakamura reported on the progress of cooperation and scientific interchange between the JSIT and the Immunotoxicology Specialty Section of Society of Toxicology (ISS SOT). Then Dr. Judy Zelikoff gave a greeting as the representative of ISS SOT. Both scientific meetings of the 49th annual meeting of the SOT in Salt Lake City and the 17th annual meeting of the JSIT in Tsukuba City in 2010 were announced. Dr. Otsuki

performed his original tunes on the piano and voice.

The second day, the second special lecture was presented by Dr. Masao Kosuge, the Director Emeritus of the Asahikawa Asahiyama Zoo entitled "The role of the Asahiyama Zoo in education and species preservation". The workshop focused on the immunotoxicological testing methodology was chaired by Dr. Naohisa Tsutsui focused on "Standardization of an immunotoxicity test: T cell-dependent antibody response to keyhole limpet Hemocyanin". Dr. Tsutsui started by mentioning "Background for a discussion on standardized protocols of KLH-TDAR". Four cases were presented; "Rat strain

The 17th Annual Meeting of the Japanese Society of Immunotoxicology

September 9-10, 2010

Ohyama Memorial Hall,

National Institute for Environmental Studies

Theme: Immunotoxicology and Susceptibility

Invited Plenary Lecture:

Professor A Dean Befus (University of Alberta, CANADA)

Invited Special Lecture: Professor Kensuke Miyake (The Institute of Medical Science, The University of Tokyo)

Master's Lecture: Jun-ichi Sawada, Ph.D. (President of JSIT)

Symposium: "Immunotoxicity and chemical susceptibility".

Invited Speaker: Mary Jane Selgrade, Ph.D. (USEPA)

Workshop

Oral/Poster presentation

Students session

President: Dr. Hidekazu Fujimaki

Research Center for Environmental Risk

Secretary office: Dr. Keiko Nohara

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comparison of TDAR using KLH as an antigen” by Dr. Ryota Kawai, “Protocol for rat KLH-TDAR in Takeda Pharmaceutical Company Limited” by Dr. Kanako Mori, “TDAR method using the commercial anti KLH-ELISA kit -Comparison with SRBC method-” by Hiroyuki Komatsu and “Case study of both anti-KLH IgM and IgG antibody measurement in TDAR testing” by Hideki Harada.

Totally 22 oral and 13 poster presentations were submitted to the meeting and around 160 participants spent fruitful opportunity and had enthusiastic discussion during the sessions. The meeting was closed successfully with hoping reunion in the next meeting.



At the welcoming reception. (From left to right) Dr. Yoshida, Dr. Kayama, Dr. Germolec, Dr. Zelikoff, and Dr. Kouchi.

Report from the 16th Annual Meeting of the Japanese Society of Immunotoxicology

Submitted by Dori Germolec¹
and Judith Zelikoff²

¹National Institute of Environmental Health Sciences,

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As part of the ongoing cooperation and scientific interchange that the Immunotoxicology Specialty Section (ISS) has with the Japanese Society of Immunotoxicology, Judy and I were chosen to represent the ISS at the 16th Annual Meeting of the Japanese Society of Immunotoxicology (JSIT). The theme for this year’s meeting, held in the beautiful city of Asahikawa on the Island of Hokkaido, was “Children and Immunity”.

We arrived in Tokyo on the 25th of August and were whisked to our hotel near the Haneda airport. There

we were met by one of our hosts for this journey, Dr. Kazuichi Nakamura, who introduced us to Tokyo and the wonders of Japanese noodle soup. On the 26th we joined Dr. Nakamura and a large group of JSIT members for the flight from Tokyo to Asahikawa. Hokkaido is a volcanic island, and on our journey to Asahikawa we were treated to spectacular mountain views and given a taste of the beautiful gardens that front local homes and farms. That evening we joined our hosts for the JSIT conference opening dinner. Dr. Takahiko Yoshida, from the Asahikawa Medical College and the President and Organizer of the 16th Annual Meeting, and the Executive Committee welcomed us. The dinner was an excellent opportunity for us to have superb Japanese cuisine and discuss current and future collaborations between the JSIT and the ISS.

Dr. Yoshida opened the meeting on Thursday morning, and the sessions began with oral presentations on the effects of environmental chemicals on allergic and infectious disease. In a session chaired by Dr. Yoshida, Dr. Germolec presented the first special lecture of the meeting entitled “Does immunomodulation early in life increase disease risk in children and beyond?” Oral presentations continued in the early afternoon in a session chaired by Dr. Yasuhide Kouchi and focused on novel methods in immunotoxicity. The meeting theme was highlighted in a symposium entitled, “Children and Immunity” chaired by Drs. Fujio Kayama and Dr. Kazuichi Nakamura. The symposium featured presentations by Dr. Sho Ishikawa on the breakdown of mucosal immunity in the gut and allergic sensitization by dioxins, Dr. Chisato Mori on a health examination system to prevent fetal exposure to persistent organic pollutants and atopic dermatitis in infants and Dr. Judy Zelikoff, on how prenatal exposure to cigarette smoke increases tumor susceptibility of juvenile mice via changes in anti-tumor mechanisms. That evening, the JSIT hosted a wonderful dinner reception at the Asahikawa Grand Hotel. We were fortunate that Dr. Takemi Otsuki was willing to perform his “Song for the JSIT” which he debuted at an earlier JSIT meeting. It was a treat to see old friends, begin new collaborations and hear about the exciting plans for the sessions being planned for both the 49th annual meeting of the SOT in Salt Lake City and the 17th Annual Meeting of the JSIT in Tsukuba next

September.

The second day featured a special lecture chaired by Dr. Jun-ichi Sawada and presented by Dr. Masao Kosuge, the Director Emeritus of the Asahikawa Asahi-yama Zoo regarding the role of the Asahi-yama Zoo in education and species preservation. We were fortunate to get an “up close and personal” view of the zoo and all of its inhabitants that afternoon. The afternoon Workshop focused on “Standardization of an immunotoxicity test: T cell-dependent antibody response to keyhole limpet hemocyanin.” Oral and poster presentations highlighted the outstanding contributions of our Japanese colleagues in all aspects of immunotoxicology.

After the meeting, we were entertained by Dr. Yoshida who brought us up to the mountains for a visit to Daisetsuzan National Park and its volcanic hot springs, followed by a magnificent Japanese meal with many of our meeting colleagues. Our flight back to Tokyo from Asahikawa was just the beginning of another adventure, in which we traveled through the Ginza and up to the top of the Tokyo Tower. Dr. Nakamura acted as our tour guide for a final day in Tokyo, where we saw the Great Buddha of Kamakura, the port of Yokohama and its magnificent Chinatown, as well as beautiful shrines and temples. Our discussions on immunotoxicology and future collaborations did not end until we stepped on the plane headed back to New York.

We would like to sincerely thank all of our hosts in Japan for their warmth, welcome and kindness. We had many fruitful discussions about the future of our Specialty Section and toxicology in general. The hospitality that was extended to us was remarkable and made our trip a never to be forgotten experience. We look forward to continued collaborations with our JSIT colleagues.

A prize for annual convention

Development of a novel allergy test using a cultured mast cell line

Ryosuke Nakamura, Yoshimi Uchida,
Masakazu Higuchi and Reiko Teshima

(Div. Novel Foods Immunochem., Natl. Inst. Health Sci., Tokyo, Japan)

Rationale

Food allergy is a very popular disease among children, and the avoidance of causative foods is essential for children with allergies. However, inappropriate food avoidance can lead to nutritional deficits, especially in infants and children. The most reliable allergy test is an oral food challenge (OFC) test; however, *in vivo* tests are associated with a risk of possible anaphylaxis. *Ex vivo* tests, such as the basophil-activation test, are also known to be effective; however, the basophil test requires whole blood, which cannot be preserved for lengthy time periods. To detect allergen-specific IgE in sera, solid-phase IgE-binding assays like the CAP test are commonly used. Although such immunochemical methods are very sensitive, they frequently produce false-positive results. The degranulation of human IgE receptor (FcεRI)-transfected rat mast cell (RBL) lines seems to be a possible indicator for human IgE, but the spontaneous release of mediators from these cells in the presence of human sera is not negligible.

Methods

We have established a new mast cell line, RS-ATL8, that has been stably transfected with human FcεRI genes and NF-AT-responsive luciferase gene. The cells were sensitized with a 1:100-dilution of sera from egg white allergy patients and then stimulated with a purified or crude extract of egg white allergen. A two-fold increase in the luciferase level was adopted as a cut-off point. The OFC tests were performed at the Fujita Health University after obtaining informed consent.

Results

Sensitization with 15 pg/ml of IgE was sufficient to detect IgE Crosslinking-induced Luciferase Expression (EXiLE) using anti-IgE stimulation (data not shown). Sera from a patient with egg white allergy diluted

to at least 1:100 was sufficient to elicit an EXiLE reaction in RS-ATL8 cells without marked cytotoxicity, whereas a higher spontaneous release was observed in the degranulation-based assay. The EXiLE results were strongly correlated with the results of OFC tests in patients with egg white allergy ($P=0.001687$, Fisher's exact test). The measured Max EXiLE and CAP test values were also strongly correlated ($R=0.9127$, Spearman's rank test).

Discussion

Unlikely the degranulation-based mast cell activation test, the EXiLE test was able to produce consistent results without inducing cytotoxicity. We observed that 1 fg/ml of egg antigen was sufficient to detect cell activation using the EXiLE test (data not shown). Of note, the medium used here was supplemented with 10% FCS, which includes incredible amounts of non-specific proteins, ensuring the robustness of the system. Additionally, the EXiLE test and OFC test results were strongly correlated, whereas the correlation between the OFC and CAP tests was not very good ($P = 0.3684$). The values of the Max EXiLE and CAP tests were also strongly correlated; therefore, the inconsistencies between the OFC and CAP test results reported here might be partly due to the excessive sensitivity of the CAP test. However, at least one serum, which contained a high level (4.46 U_A/ml) of egg white-specific IgE, did not elicit an EXiLE reaction in RS-ATL8 cells. This patient was also OFC negative. Therefore, the EXiLE test seems to be a promising *in vitro* IgE test for evaluating whether IgE binding to an allergen is biologically meaningful.

Acknowledgements

We are greatly honored to receive this prize for annual convention. This study was supported by Grants-in-Aid from the Food Safety Commission, Japan (No.0708). We are also grateful to Dr. Atsuo Urisu of Fujita Health University for his kind gift of the allergic patients' sera.

A prize for encouragement

Analysis for suppressed expression of NKp46 on NK cells exposed to asbestos, possible predictive molecular marker for anti-tumor immune function

Yasumitsu Nishimura¹, Naoko Kumagai¹,
Megumi Maeda¹, Hiroaki Hayashi¹,
Takumi Kishimoto² and Takemi Otsuki¹

(¹Department of Hygiene, Kawasaki Medical School,

²Okayama Rosai Hospital)

The present study tried to explore how expression of NKp46 on NK cells is suppressed by exposure to chrysotile B (CB) asbestos, as shown in our previous report, and compared cytotoxicity of NK cells among pleural plaque-positive people with high or low expression of NKp46 and patient with mesothelioma, which were assigned a score of 1, 2 and 3, respectively. NK cells in PBMCs cultured with CB showed a decrease in NKp46 mRNA, whereas they show no accumulation of intracellular NKp46. The suppressed expression of NKp46 was also observed in NK cells in the culture insert over the culture of PBMCs with CB. The cytotoxicity of NK cells was inversely correlated with the score determined for each patient-group. These results indicate that exposure to asbestos causes suppressed expression of NKp46 at the mRNA level by alteration in production of cytokines related with NK cell function, and suggest that NKp46 might be a possible marker for anti-tumor immune function in people exposed to asbestos.

An interim report about the guidance on immunotoxicity for chemical risk assessment discussed by WHO/IPCS harmonization project

Reiko Teshima
(National Institute of Health Sciences)

WHO/IPCS harmonization project are now preparing harmonized guidance for immunotoxicity risk assessment for chemicals. The Immunotoxicity drafting group meeting was held at the Netherland in April 2009. At the meeting, text of draft guideline (Chapter 1-7) and case

study report of platinum was discussed. In Next year finalized draft document and several case study reports will be public and peer reviewed.

