ImmunoTox Letter Digest

June, 2015

The 4th Japanese Society of Immunotoxicology Award (The 2014 JSIT Award)

"Immunotoxicity of environmental substances with special reference to heavy metals : Toxicological properties and evaluation" — Through with developing immunotoxicology of environmental heavy metals

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I feel honored that the 4th JSIT Award was given to me for my research career in environmental immunotoxicology, although first I was mystified by nomination of an early immunotoxicologist for the Award. My research for immunotoxicology has mainly focused on illustrating the concept for immunotoxicological evaluation of environmental substances through with experimental immunotoxicology of environmental heavy metals.

In the early stage of immunotoxicology, diverse immunotoxic findings were reported on environmental chemicals with a variety of testing systems[1]. For an overall assessment of their immunotoxicity, we have studied on immunotoxicites of heavy metals in the environment with special reference to cadmium (Cd).

For evaluating immunotoxicities of environmental heavy metals, the animal exposure to the metals is required at environmental levels, via actual route, and for the proper long duration. As described in the lecture, we reported on oral exposure of mice to Cd at environmental concentrations in the drinking water for 10 weeks[2] that: 1) immunotoxic alterations were very sensitive to the exposure, 2) acquired and natural immune indicators responded differently, as that the primed

The 22nd Annual Meeting of JSIT 2015 (Japanese Society of Immunotoxicology)

September 10–11, 2015

Kyoto University,
Clock Tower Centennial Hall International Conference Hall, Kyoto-city, Japan.
http://health.env.kyoto-u.ac.jp/jsit22-office/toiawase.html

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Deadline for abstract submission: June 26, 2014

The theme for this Meeting: "Revolutionary perspectives in the field of Immunotoxicology -Toxic effects and Disrupting effects"

Program (Tentative Schedule)

■September 10, 2015 (Thursday)

・Educational lecture 1:
Dr. Hidenori Ichijo
(The University of Tokyo,
Graduate School of Pharmaceutical Sciences)

・Symposium: Toxic effect to Disrupting effect
Dr. Takamichi Ichinose
Dr. Eiko Koike
Dr. Rie Yanagisawa
Dr. Shinji Fushiki
Dr. Taisen Iguchi

・Award lecture:
・Oral / Poster presentation
・Social gathering:
Kyoto University,
Clock Tower Centennial Hall International Conference Hall

■September 11, 2015 (Friday)
・Special lecture :
Dr. Stacey Anderson
(Team Leader,
Immunotoxicology and Hazard Identification laboratory
Allergen and Clinical Immunology Branch,
Health Effects Laboratory Division
National Institute for Occupational Safety and Health)

・Educational lecture 2:
Dr. Tomohiro Yoshimoto
(Hyogo College of Medicine,
Institute for advanced medical sciences)
・Workshop:
Immunotoxicological Methods
・Oral / Poster presentation
・Awards ceremony

antibody response was suppressed but the unprimed antibody response was non-specifically enhanced including production of autoantibodies like anti-nuclear and anti-dsDNA antibodies, even at less exposure level. These mean the immunotoxic effect of environmental substances should be assessed and evaluated differentially for immune regulation and immune defense, which work appropriately at host situation. Autoantibody formation and oral tolerance to food allergens are under suppressive immune regulation. Disturbance of the immune regulation by environmental substances may lead to autoimmune and/or allergic manifestations. Some examples were demonstrated with findings including our studies such as autoantibody production in autoimmune nephritis-prone mice enhanced by heavy metals[3], allergen-specific IgE production promoted with diesel particle[4], and sensitization of oral food protein aided with salitylate[5]. In these cases environmental substances including heavy metals act like an adjuvant to cause abnormal stimulation overcoming immune regulation. Such immunotoxicity of environmental substances should be considered further relating to pathogenesis of autoimmune and allergic diseases.

Our recent life becomes surrounded with more natural and/or artificial biopolymers that may act as immunostimulatory or immunogenic environmental substances. It may require a new paradigm in immunotoxicology that is left to the next generation of immunotoxicologists.

References

1) M. Ohsawa (1993) Prog. Clin. Biol. Res., 380: 283-398.
2) M. Ohsawa *et al.* (1988) Clin. Exp. Immunol., 73: 98-102.
3) M. Ohsawa (2009) Yakugaku Zasshi, 129: 305-319.
4) S. Yoshino *et al.* (1998) J. Pharmacol. Exp. Ther., 287: 679-683.
5) T. Shindo *et al.* (2012) J. Toxicol. Sci., 37: 307-315.

Real Voices of International Immunotoxicologists

What non-Japanese scientists think about immunotoxicology? What they have experienced and will do future. Their comments would allow us to realize the significance of study about immunotoxicology. This time, we interviewed Dr. Marc Pallardy from University Paris-Sud, France. Let's go to hear his voice. What do you feel and get from it?

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

There are numerous aspects that were impressive for me for my first trip to Japan. I have been very impress by how you welcome a guest scientist as me. The organization of my trip, the way you feel respected by your host it quite special of Japan. While travelling in the country, I was also very impressed by the organization, the willing of the people to help you if they feel that you are lost and also the respect between people.

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

Probably, to have been able to create, finance and manage a group of scientists since 1990 in the field of Immunotoxicology. Allowing the possibility to students to obtain their PhD with good publications and also to help them to find a job is also a great achievement for me.

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

The most energy consuming activity now is to manage the IMI (Innovativee Medicines Initiative) project ABIRISK (Anti-Biopharmaceutical Immunization: prediction and analysis of clinical relevance to minimize the RISK, http://www.abirisk.eu/). This project involves 38 partners from all Europe and aims at understanding how patients get immunized to therapeutic proteins (antibodies…) with the consequence of a loss of clinical response. This project aims also to optimize the monitoring of patients by closely monitoring anti-drug antibody.

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

Immunotoxicology is still an evolving field. All the aspects of immunotoxicology such as immunosuppression, hypersensitivity, autoimmunity and inappropriate stimulation of the immune system show intensive research activity. However, there are several aspects that need specific attention.

The link between immunosuppression/immunomodulation induced by chemicals and the risk of cancer is a matter of great importance. What are the components of the immune system most important to address, CD8+ cells, NK cells others? Are we able to establish a dose-relationship or to perform quantitative risk-assessment for this type of risk? What are the effects of mixtures of environmental chemicals with genotoxic and immunosuppressive properties?

Allergies due to drugs or environmental chemicals should also deserve more attention. The mechanisms of drug allergy have recently benefited from major breakthrough with the results published on Abacavir-induced toxic epidermolysis. However, we are still lacking some explanations on drug-induced liver injury due to immune mechanisms or on how people get immunized to drugs and how immunized/sensitized people become allergic.

The last point is the link between autoimmunity and exposure to chemicals or following drug treatment. These questions are very difficult to address and there are not a lot of support from public bodies. These latter points can explain the low activity in this field. Nevertheless, efforts should be made when we are facing the controversy with vaccines leading to a tendency for decrease in the rate of vaccinated people in Europe.