ImmunoTox Letter Digest

June 2024

The 31th Annual Meeting of the Japanese Society of Immunotoxicology (JSIT2024)

1. Date

September 19-20th, 2024

2. Venues

Heisei Kinen Kaikan, Hyogo Medical University

(The following link is for Hyogo Medical University Nishinomiya Campus : https://www.hyo-med.ac.jp/about/access/campus_map/nishinomiya/)

3. President

Etsushi Kuroda.
(Department of Immunology, School of Medicine, Hyogo Medical University, Nishinomiya, Hyogo, Japan)

4. Main theme of the meeting

Scientific Exploration of Environment and Healthcare through Immunotoxicological Research.

5. Meeting secretariat

Department of Immunology, School of Medicine, Hyogo Medical University.
E-mail : jsit2024@hyo-med.ac.jp
URL :https://www.japanimmunotox.org/jsit2024/index.html

6. Program (tentative)

Special lecture

1) "Development of methods for assessing respiratory sensitizing potential."
Takayuki Yoshimoto (Tokyo Medical University)
2) "Development of AIDS prevention and treatment vaccines using live attenuated vaccines expressing adjuvant molecules."
Yasuhiro Yasutomi (National Institute of Biomedical Innovation, Health and Nutrition)
3) <TBA>
A Lecture by an invited speaker from SOT/ITSS.

Symposium 1

Environment and Allergy: Latest Findings

1) "Environmental factors that disrupt the epithelial barrier, leading to allergic inflammation."
Hideaki Morita (National Center for Child Health and Development)
2) "Molecular and cellular mechanisms through which tissue-resident memory T cells drive refractory disease formation."
Kiyoshi Hirahara. (Chiba University)
3) "Exploration of prevention/exacerbation factors for allergic rhinitis using mouse models."
Kazufumi Matsushita (Hyogo Medical University)

Symposium 2

The Efficacy and Safety of New Vaccines and Immunotherapies

1) "CpG ODN-mediated immunoprophylaxis against viral infection"
Kouji Kobiyama (The University of Tokyo)
2) "Disease modifying treatments: Allergy immunotherapy for type-1 allergy"
Katsuyo Doi (Torii Pharmaceutical Co Ltd)
3) "Preclinical immunogenicity and protective efficacy of new mRNA vaccines against Severe Fever with Thrombocytopenia Syndrome, SFTS"
Shiori Egasira (Daiichi Sankyo Co Ltd)

Special lecture of the recipient of the 14th JSIT award
"Immunotoxicology; the origins of medicine that protects lives in interaction with environment.
－From segmented research to research with an integrated perspective－"
Takahiko Yoshida (Professor emeritus, Asahikawa Medical University)

Special lectures of the recipients of the 13th JSIT prize for encouragement
"Molecular mechanisms of pathogen sensors-mediated cytokine production from innate immune cells."
Izumi Sasaki (Wakayama Medical University)

Workshop: Immunogenicity assessment
4) "Current status and issues in prediction and evaluation of immunogenicity of biopharmaceuticals."
Akiko Ishii (National Institute of Health Sciences)
1) "Strategy and case studies for assessing immunogenicity of biopharmaceuticals."
Eri Hamamura (Daiichi Sankyo Co Ltd)
2) "Immunogenicity assessment and deimmunization strategy of engineered therapeutic antibodies."
Eiichi Hashimoto (Chugai Pharmaceutical Co Ltd)
3) Comprehensive discussion

Oral sessions of young scientist
Oral presentations
Poster presentations
Luncheon seminars

7. Social gathering
Sakagura Dori Rengakan
September 19, 18:30~ (tentative)
https://www.rengakan.com/index.html

The 13th Japanese Society of Immunotoxicology Award
(The 2023 JSIT Award)

Establishment of a new concept "reproductive immunotoxicity" in immunotoxicology

Kazuichi Nakamura
Translational Research Unit, Veterinary Teaching Hospital,
Graduate School of Veterinary Medicine, Hokkaido University

I have been working on creating a new concept "reproductive immunotoxicity" in immunotoxicology. Here, I would like to briefly explain how pregnancy is immunologically maintained and to show some xenobiotics which immunotoxicologically impair the development of placenta and cause abortion.

Fetuses are semi-allogeneic to mothers because they inherit MHC class I genes from the father as well as the mother. Since the immune system recognizes and rejects non-self, pregnancy needs specialized immunological mechanism to accept the fetus. In the hemochorial placenta in human and rodents, placental villi directly contact maternal blood to receive oxygen and nutrient from the mother. The blood flows from remodeled uterus spiral arteries forming open circulation.

For remodeling of uterus spiral arteries, fetal extravillous trophoblasts (EVTs) enter maternal endometrium in collaboration with uterus NK (uNK) cells, subsequently decidual NK (dNK) cells. EVTs do not express classical MHC class I molecules HLA-A or HLA-B to avert killing by cytotoxic CD8 T cells. They bear classical MHC class I molecule HLA-C and nonclassical HLA-E, -F and -G to communicate with uNK cells. uNK cells (CD56brightCD16-) show lower cytotoxic activity in comparison with peripheral blood NK cells (CD56dim/-CD16bright). uNK/dNK cells also produce angiogenic factors such as vascular endothelial growth factor (VEGF). Receptors of uNK/dNK cells include killer cell immunoglobulin-like receptor (KIR), leukocyte immunoglobulin-like receptor (LILR) and natural killer group 2 (NKG2), each of which has inhibitory and activating subfamilies. Their cytotoxicity and the production of angiogenic factors depend on the combination of the EVTs' MHC class I molecules and the uNK/dNK cell receptors, which is critical for the placenta formation and fetal growth. To date, there have been some

researches in which Δ9-tetrahydrocannabinol, sphingosine-1-phosphate receptor modulator or titanium dioxide nanoparticles inhibit healthy placenta formation by affecting cytotoxicity and angiogenesis of the uNK/dNK cells in human or mice.

Normal pregnancy is associated with high levels of Th2 cytokines and low Th1/Th2 cell ratios. Progesterone produced by corpus stimulate the production of IL-4 from Th2 cells. IL-4 increases human chorionic gonadotropin (hCG) from syncytiotrophoblasts of fetal villi after implantation for the maintenance of pregnancy. As the consequence, Th2 cells are dominant over Th1 cells in the maternal immune system especially during early pregnancy. From the viewpoint of immunotoxicology, I and my colleagues in the Kitasato University demonstrated that Th1/Th2 imbalance caused by proteins affects pregnancy. For more details, please see https://www.jstage.jst.go.jp/article/jts/47/8/47_327/_article.

I think that some causes of recurrent pregnancy loss are attributed to reproductive immunotoxicity of environmental chemicals and pharmaceuticals. I hope these xenobiotics exhibiting “reproductive immunotoxicity” will be identified by our society of immunotoxicology.

Lastly, but most importantly, I really appreciate the JSIT and SOT ISS members for encouraging my ICH activities and basic researches for almost 30 years. Thank you very much.

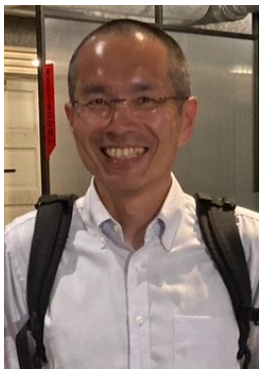
Thinking about “reproductive immunotoxicity” at;

Rurikoin Temple in Kyoto, December 2023

Ryoanji Temple, Rock Garden in Kyoto, March 2024

The 13th Japanese Society of Immunotoxicology Prize for Encouragement

Immunological mechanisms of metal allergy and its prevention and treatment



Toshinobu Kuroishi
Division of Oral Immunology,
Tohoku University Graduate School of Dentistry

I am deeply honored to have received the 13th JSIT Prize for Encouragement for the year 2023. I would like to sincerely express my appreciation to Dr. Masashi Tachibana who recommended me, and to the selection committee members as well as my supervisors, mentors, and all collaborators.

Metal allergies have been classified as type-IV allergies and induce allergic contact dermatitis. Nickel (Ni) is the most frequent metal allergen. We previously reported an effective Ni allergy mouse model with lipopolysaccharide as an adjuvant (Clin. Exp. Allergy, 2007). Using this mouse model, we have reported the pathological mechanisms of metal allergies. Biotin is a water-soluble B complex vitamin and function as a cofactor of 5 indispensable carboxylases. Biotin deficiency aggravated Ni allergy thorough the augmentation of IL-1ß production (J. Nutr., 2009). Moreover, biotin supplementation in drinking water attenuated Ni allergy, suggesting that biotin supplementation may have therapeutic effects on metal allergies. We also demonstrated that Ni induces nitric oxide production in dermal fibroblasts via the HIF-2α-dependent pathway (Tox. Sci., 2013). Although Ni ion is considered to bind to endogenous proteins, it remains unclear whether Ni-binding proteins are involved in Ni allergy in vivo. We demonstrated that CXC chemokine ligand 4 is a novel Ni-binding protein and augments Ni allergy at the elicitation and sensitization phases (Clin. Exp. Allergy, 2017). To understand the underlying mechanisms by which metal ions are recognized y the immune system, we investigated Ni-binding capabilities of antigen-presenting cells, and demonstrated that migratory dendritic cells in skin-draining lymph nodes have strong Ni-binding capabilities and elicit Ni allergy (Sci. Rep., 2020).

Encouraged by this award, I will continue my research to develop the effective methods to prevent and treat metal allergies.