ImmunoTox Letter Digest

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Report on the 32nd Annual Meeting of the Japanese Society of Immunotoxicology (JSIT2025)

Tsuyoshi Nakanishi
President of the 32nd Annual Meeting of the JSIT
Gifu Pharmaceutical University

The 32nd Annual Meeting of the Japanese Society of Immunotoxicology was held over two days, September 4 (Thu)–5 (Fri), 2025, at the Gifu City Culture Center (Gifu, Japan). The meeting was conducted entirely in person, with all presentations delivered on site and no online component. The meeting was co-hosted by Gifu Pharmaceutical University, which provided substantial support, including assistance in securing the venue. I first attended this society's meeting as a young faculty member at Osaka University at the 5th Annual Meeting (1998) held at the Senri Life Science Center. More than a quarter of a century has passed since then, and it is deeply meaningful to me to serve as President for this annual meeting. With the generous support of the organizing committee and all participants and stakeholders, the meeting concluded successfully. In total, 154 people (including staff) attended the meeting. The industry exhibition also received applications from six companies, and the meeting was much more vibrant than initially anticipated.

The theme of this annual meeting was "Aiming to Contribute to Innovation in Immunotoxicology Research." Gifu is historically associated with Oda Nobunaga, and I wished to connect the spirit of "innovation and challenge" embodied by Nobunaga with the current landscape of immunotoxicology. Immunotoxicology is a foundational science that supports public health and societal safety across diverse fields such as pharmaceuticals, chemicals, food, and the environment. In this context, it is increasingly important to continuously advance methodologies, analyses, and concepts for evaluation, and to translate scientific knowledge into practical implementation. With these aims in mind, we designed the program so that the meeting would not merely share the latest findings, but also foster cross-disciplinary integration and new perspectives, thereby nurturing "seeds" for the next generation of research, testing methods, and risk assessment.

The program included general oral sessions and poster discussions, as well as sessions for students and young scientists. In addition, the meeting featured Special Lectures (SL-01, SL-02), a Tutorial Lecture (TL-01), a Symposium (S-01–S-04), Award Lectures (AL-01, AL-02), and a Workshop (WS-01–WS-04). In particular, we sought to invigorate

the society by strengthening the general oral sessions and creating more opportunities for in-depth discussion among participants, regardless of membership status. To this end, we reviewed the overall balance of invited program slots (e.g., symposia and special lectures) and secured more time for general oral presentations than in previous years. As a result, the number of general abstracts reached a record high: 33 general presentations (oral/poster) and 16 student and young-scientist presentations (oral/poster), for a total of 49 presentations, the largest number in the society's history. As President of this annual meeting, I was delighted to see this strong response, which I believe reflects the vitality of our society. As another initiative to increase participation from the younger generation, we made undergraduate registration free of charge and established a new Undergraduate Student Presentation Award. We believe that expanding opportunities for undergraduate students to experience scientific presentations and discussions will contribute to strengthening the foundation of the immunotoxicology research community in the future.

On Day 1, Special Lecture 1 (SL-01) was delivered by Dr. Jun Kunisawa (National Institutes of Biomedical Innovation, Health and Nutrition), entitled "Immunotoxicity Regulation Through Gut Microbiota-Based Strategies". Centered on the linkage between the gut environment and immune responses, the lecture presented emerging directions and future perspectives from the standpoint of immunotoxicology. Special Lecture 2 (SL-02) was delivered by Dr. Marie-Soleil Piche (Immunology Department, Charles River Laboratories, Senneville, Canada), entitled "Immunotoxicology testing for biotherapeutics: strategies and applications." Despite her busy schedule, Dr. Piche traveled to Japan for a whirlwind trip to give this lecture. She provided a well-organized overview of immunotoxicology evaluation for biotherapeutics from both strategic and practical perspectives, offering many insights directly relevant to real-world practice. I would like to express my sincere gratitude to Dr. Piche for her generous contribution. The Tutorial Lecture (TL-01) was delivered by Dr. Shuichi Shimma (The University of Osaka) and was titled "Mass Spectrometry Imaging -Basics and its applications-". The lecture systematically covered key principles and practical considerations in measurement, the value of molecular analyses with spatial information, and the expanding range of applications. It provided an excellent opportunity to consider the potential of mass spectrometry imaging as a novel analytical platform in immunotoxicology research.

On Day 2, the symposium was held under the theme "Immune toxicity involvement in brain dysfunction". Dr. Gi-Wook Hwang (Tohoku Medical and Pharmaceutical University) presented "Methylmercury-induced neurological damage mediated by

microglial activation and future prospects", deepening discussion from the viewpoint of immune–nervous system crosstalk. Dr. Yasuhiro Ishihara (Hiroshima University) delivered "Oligodendrocyte Toxicology -Beyond Microglia-", sharing a framework for understanding based on glial–glial interactions in the brain. Dr. Yuhei Nishimura (Mie University) introduced "Assessment of microglial morphology and function using in *vivo* whole-brain imaging of larval zebrafish". Dr. Michio Miyajima (The University of Tokyo/RIKEN) presented "Mechanistic insights into brain functional alterations associated with peripheral immune dysregulation", leading to active discussion on the interface between peripheral immune perturbations and changes in brain function.

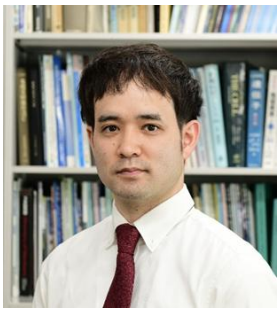
The Workshop (WS-01–WS-04) was organized under the theme "Trends in the development of respiratory sensitization tests and domestic initiatives". Dr. Tomoki Fukuyama (Azabu University) presented "The feature and detection methods of respiratory sensitization induced by chemicals including pesticides". Dr. Eiko Koike (National Institute for Environmental Studies) and Dr. Takao Ashikaga (National Institute of Health Sciences) addressed "Global trends of in *vitro* respiratory sensitization tests to the regulatory use and JaCVAM's efforts". In addition, Dr. Shinkichi Ishikawa (Japan Tobacco Inc.) and colleagues presented "Utilization of Reconstructed Human Bronchial Epithelium in *In Vitro* Evaluation of Respiratory Sensitization Potential of Chemicals". Finally, Dr. Izuru Mizoguchi (Tokyo Medical University) and colleagues presented "Development of the 3D coculture systems (DCsens and DC/Tsens) capable of accurately predicting chemical respiratory sensitizing potential", stimulating concrete discussions on the future of alternative methods and integrated testing strategies.

For the Award Lectures, commemorative talks were delivered by Dr. Hiroyuki Yanagisawa (The Jikei University School of Medicine) in the JSIT Award Lecture (AL-01) and by Dr. Takeshi Susukida (University of Toyama) in the JSIT Young Investigator Award Lecture (AL-02). For the Annual Meeting Awards, one awardee was selected from oral presentations and one from poster presentations: Dr. Ryoji Kawakami (Kyoto University) received the award for oral presentation, and Dr. Yoshika Iwata (Translational Research Division, Chugai Pharmaceutical Co., Ltd.) received the award for poster presentation. The Young Scientist Excellent Presentation Award was presented to Ms. Aoi Ezawa (Osaka University). In addition, the newly established Undergraduate Student Presentation Award was presented to Ms. Saya Tanaka (Gifu Pharmaceutical University) and Mr. Ryunosuke Gohara (Ritsumeikan University). I extend my heartfelt congratulations to all awardees and look forward to their continued success.

In conclusion, this annual meeting provided ample opportunities to share a wide range of research outcomes and to engage in lively discussions among members and non-members alike. As President of this annual meeting, I would like to express my sincere appreciation to all speakers and session chairs, all participants, the companies involved in the exhibition, Gifu Pharmaceutical University for its support as co-host, and the staff members who contributed to the operation of the meeting. I sincerely hope that this momentum will continue, leading to further revitalization of our society, advances in immunotoxicology research, and meaningful contributions to society.

The Best Presentation Award

De novo generation of lineage-stable regulatory T cells promotes immune tolerance to food antigens



Ryoji Kawakami
Institute for Life and Medical Sciences (LiME)
Kyoto University

I am deeply honored to receive the Annual Award of the 32nd Meeting of the Japanese Society of Immunotoxicology, and I sincerely thank the meeting chair, Prof. Tsuyoshi Nakanishi, the selection committee, and all members involved in the organization.

My research focuses on T-cell immunity and mechanisms of peripheral immune tolerance, particularly how the immune system determines whether ingested food antigens are accepted as self or eliminated as foreign invaders. In this meeting, I presented our recent findings on the induction and stability of food antigen–specific regulatory T cells (Treg). Using a defined oral egg white-derived antigen exposure mouse model, we observed that naïve egg white-specific specific $CD4^+$ T cells preferentially differentiate into $Foxp3^+$ Treg rather than effector T cells under steady-state conditions. Genome-wide epigenetic profiling further demonstrated that these peripherally induced Treg acquire a stable Treg-type epigenome comparable to thymus-derived Treg, although their long-term maintenance requires continued antigen exposure.

We also showed that prior skin-sensitization disrupts oral tolerance and promotes allergic pathology. However, blockade of co-stimulation using abatacept during oral antigen exposure induced $CD101^+$ Treg and restored tolerance, suppressing effector T-cell responses. Depletion studies confirmed that these induced Treg are essential for therapeutic effects.

These results highlight the importance of peripherally induced antigen-specific Treg in food allergy and suggest that modulation of antigen presentation and co-stimulation may provide a novel therapeutic strategy. I hope to further advance this work toward broader applications in immune-mediated diseases.

The Student and Young Scientists Award

Analysis of adjuvant factors involved in the development of cochineal allergy

Aoi Ezawa
Graduate School of Pharmaceutical Sciences
The University of Osaka

It is a great honor to receive the Young Scientists Award at the 32nd Annual Meeting of the Japanese Society of Immunotoxicology. I would like to express my sincere gratitude to the organizing committee and to all those who have supported my research.

My interest in immunotoxicology was inspired by seeing my younger brother struggling with allergies for many years. This experience motivated me to pursue immunological research and led me to enroll at The University of Osaka, where I joined the Laboratory of Bioresponse Regulation. I am currently engaged in the study aimed at elucidating the pathological mechanisms underlying cochineal allergy.

Cochineal allergy is an immediate hypersensitivity reaction caused by cochineal dye derived from Dactylopius coccus extract, which is widely used in foods and cosmetics. Severe symptoms such as swelling and anaphylaxis have been reported. Since most patients are adult women, sensitization to insect-derived antigens in cochineal dye is considered to occur more readily through cosmetics use, although the mechanism remains unclear. Importantly, cochineal dye is typically used in cosmetics as carmine, an insoluble metal salt produced by reacting carminic acid, the main component of cochineal dye, with metal ions, including aluminum. In this study, we demonstrated that carmine induces pyroptosis in macrophages and enhances antigen-specific IgE production, suggesting that it may function as a particulate adjuvant in a manner similar to aluminum hydroxide gel. These findings provide new insights into the environmental factors that promote allergic sensitization. In future studies, I aim to identify the inflammatory mediators involved in the production of antigen-specific IgE induced by carmine. Moreover, it will be important to establish reliable safety assessment methods to evaluate whether insoluble pigments, including carmine, possess particulate-like immunostimulatory activity that can promote antigen sensitization.