The 42nd Annual Meeting of
the Japanese Society for Investigative Dermatology

Afternoon Seminar

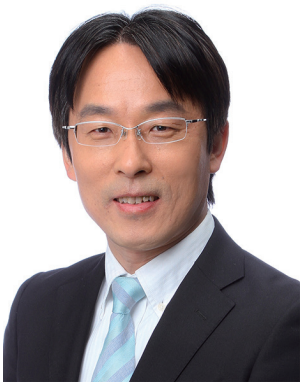
Accelerating Innovation of Clinical and Reseach with immune repertoire analysis

Date:
December 16 (Sat.) 16:00-17:00

Place:
KOCHI CITY CULTURE-PLAZA
Room D (7F Exhibition room No.4)
2-1, Kutanda, Kochi-shi, Kochi, 780-8529, Japan

Chairman:
Shin Morizane M.D.,Ph.D.
Department of Dermatology, Okayama University

Speakers:



Takaji Matsutani Ph.D.
Repertoire Genesis inc.

Presentation 1:
A new technology for high-throughput NGS-based antibody repertoire analysis

Munenari Itoh M.D.,Ph.D.
The Jikei University School of Medicine

Presentation 2:
Clinical and Research Application of T cell receptor repertoire analysis

Sponsors:
Repertoire Genesis Inc.
Wako Pure Chemical Industries, Ltd.
The 42nd Annual Meeting of the Japanese Society for Investigative Dermatology

HN-16

The 42nd Annual Meeting of
the Japanese Society for Investigative Dermatology
Afternoon Seminar

Accelerating Innovation of Clinical and Reseach with immune repertoire analysis

Speaker Profiles & Summaries

Takaji Matsutani Ph.D.

1992-2003	Research Scientist, Shionogi & Co., Ltd.
1999	Doctor of Medical Science (Ph.D.), Tohoku University School of Medicine
2003-2010	Assistant Professor, Department of Cell Biology, Tohoku University School of Medicine
2006-2008	Postdoctoral Fellow, Department of Microbiology and Immunology, University of Miami School of Medicine
2010-2013	Lecturer, Laboratory of Immune Regulation, Wakayama Medical University
2013-2014	Lecturer, Department of Immunobiology, Institute of Development, Aging and Cancer, Tohoku University
2014-Present	Director, R&D Dept., Repertoire Genesis Inc.

A new technology for high-throughput NGS-based antibody repertoire analysis

B cells play a significant role in an adaptive immune system by producing antibody capable of reacting with huge variety of foreign antigens. The antibody gene is primarily generated by gene rearrangement and subsequently acquires increased affinity to antigen by somatic hypermutation (SHM). Class switch recombination (CSR) generates several antibody isotypes or subclasses with different functional properties.

Next-generation sequencing (NGS) technologies have been remarkably advanced in recent years. By using the NGS, we have developed a new high-throughput sequencing method to identify all immunoglobulin (Ig) isotype and subclass genes in human and mouse. This method is based on an adaptor-ligation PCR and therefore allows us to amplify all Ig genes with high levels of SHMs without any bias by addition of adaptor primer to 5'-terminal of dsDNA. Following data acquisition, the CSR and the SHM levels are easily evaluated in respective isotypes and subclasses by bioinformatics analysis.

In this section, I' d like to show a representative result of comprehensive antibody repertoire in healthy individuals. The gene usage of V and J regions and diversity were similar among isotypes or subclasses (IgM, IgD, IgG3, IgG1, IgG2, IgG4, IgA1 IgE, and IgA2). Interestingly, clonal sequences were frequently shared among multiple Ig subclasses, especially, between IgG1 and IgG2 or IgA1 and IgA2. The frequency of SHM varied among the Ig subclasses. These results gave us an interesting insight into the development and the maturation of B cells.

This highly reliable NGS-based analysis will provide us significant information on in-depth antibody repertoire in healthy and disease conditions. The application of new technology will contribute to understanding mechanisms underlying protective immunity, pathogenesis of autoantibody and vaccine immunogenicity in studies on B cell immunology, dermatology, and oncoimmunology.

Munenari Itoh M.D.,Ph.D.

1999	M.D. The Jikei University School of Medicine
2005	Ph.D. The Jikei University School of Medicine
2005-2007	Assistant, Department of Dermatology, The Jikei University School of Medicine, Tokyo, Japan
2007-2008	Clinical staff, Department of Dermatology, NTT Kanto Medical Center, Tokyo, Japan
2008-2011	Postdoctoral Research Scientist, Department of Dermatology, Columbia University in the city of New York (Angela M. Christiano Lab), New York, U.S.A.
2012-2014	Assistant, Department of Dermatology, The Jikei University School of Medicine, Tokyo, Japan
2014-Present	Assistant Professor, Department of Dermatology, The Jikei University School of Medicine, Tokyo, Japan

Clinical and Research Application of T cell receptor repertoire analysis

T cell is a type of lymphocyte that plays an essential role in cellular adaptive immune system. There are several subsets of T cells, which each have a different function in immunological response: briefly, CD4+ helper T cells assist the other immune cells in being maturated and activated, CD8+ cytotoxic T cells bind to and kill virus-infected cells and cancer cells, and CD4+ regulatory T cells act to maintain and inactivate T cell-related immunity. All these processes are initiated by recognizing "non-self" targets through the presentation of peptide antigens on T cell receptor (TCR) expressing on the surface of T cell. TCR is composed of two different protein, mainly alpha and beta chains. To acquire huge diversity of TCR ($\sim 10^{18}$) for recognizing all sorts of antigens, TCR α- and β-chains have highly variable extracellular domain generated from genetic recombination of DNA encoding TCR fragments in individual somatic T cells.

Recently, the technology of next generation sequencing(NGS) has been remarkably emerged. A newly developed NGS-based TCR repertoire analysis has opened the way to comprehensively analyze not only the clonality and diversity of TCR but also expression quantification and antigen-specificity of TCR. This technology allows us to molecularly and genetically investigate abnormalities of T cells, including neoplastic proliferation, subset-imbalance and autoimmunity, which may occur various disorders. Such TCR-based profile analysis in the field of dermatology has been limited, although T cell infiltrations are frequently observed in skin inflammatory and allergic disorders.

We are now trying to utilize this novel technique to analyze the profile of T cells, which are infiltrated in several skin diseases and differentiated from patient-specific induced pluripotent stem cells (iPSCs). In this session, I would like to present our clinical and research applications of NSG-based TCR repertoire analysis.

Sponsors:

Repertoire Genesis Inc.
Wako Pure Chemical Industries, Ltd.
The 42nd Annual Meeting of the Japanese Society for Investigative Dermatology