

Yoshihiko Tomofuji. M.D., Ph.D. (Last update: 2023-10-19)

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Present Position:

Assistant Professor, Department of Genome Informatics, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan. 2023-

Visiting Scientist, Department of Statistical Genetics, Osaka University Graduate School of Medicine, Osaka, Japan. 2023-

Visiting Scientist, Laboratory for Systems Genetics, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan. 2023-

Education:

Osaka University, Osaka, Japan. 2020-2023

Ph.D. in Medicine

Dissertation: "Prokaryotic and viral genomes recovered from 787 Japanese gut metagenomes revealed microbial features linked to diets, populations, and diseases" ([URL](#))

Mentor: Dr. Yukinori Okada

The University of Tokyo, Tokyo, Japan. 2012-2018

Doctor of Medicine

Academic Appointments:

Assistant Professor, Department of Genome Informatics, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan. 2023-current

Clinical Residencies:

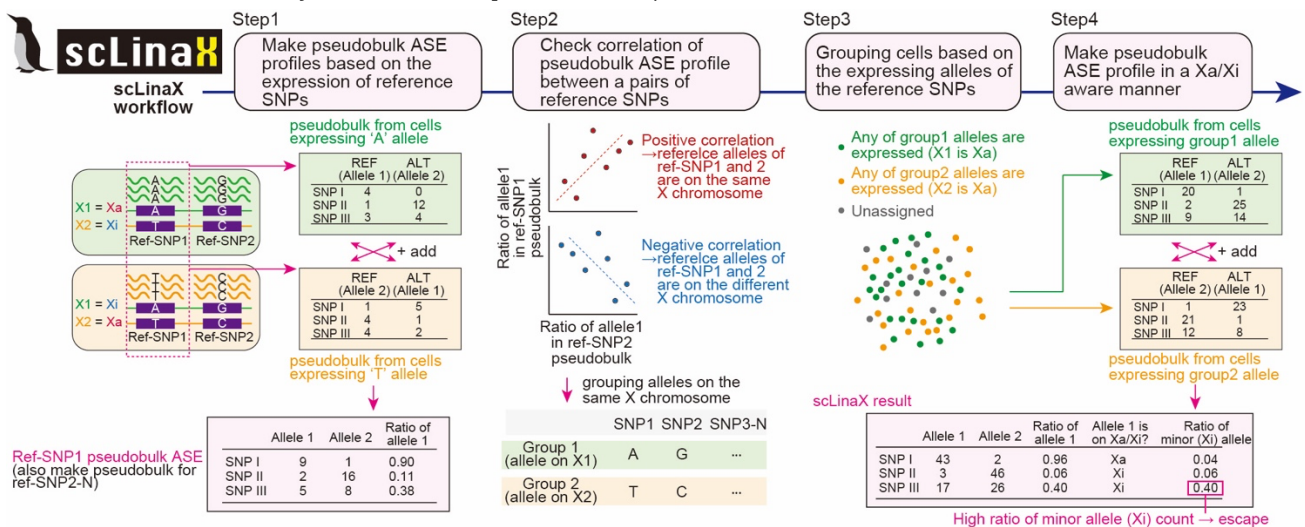
The University of Tokyo Hospital, Tokyo, Japan. 2019-2020

Personal Statements:

Yoshihiko is a researcher in the fields of medicine and bioinformatics. Currently, he is working on the analysis and method development of single-cell omics data at the University of Tokyo (PI: Dr. Yukinori Okada). He got a degree of M.D. from the University of Tokyo. During his time as a medical student, he conducted research on the thymic selection of T cells and autoimmunity (PI: Dr. Hiroshi Takayanagi), engaging in both wet and dry experiments (Tomofuji Y et al. *Nat. Immunol.* 2020). Following two years of clinical training, he started Ph.D. training under Dr. Yukinori Okada at Osaka University, focusing on bioinformatics research related to the gut microbiome and human genetics (Tomofuji Y et al. *Ann. Rheum. Dis.* 2021/2022, Tomofuji Y et al. *Cell Genom.* 2022, Tomofuji Y et al. *Nat. Microbiol.* 2023, Tomofuji Y et al. *Cell Rep.* in Press). After he got a Ph.D. from Osaka University, he moved to the University of Tokyo (Yukinori Okada's lab) as an assistant professor and started to work with single-cell omics technology. Specifically, he developed a new method to refine the understanding of the basic biological phenomena such as X chromosome inactivation (Tomofuji Y et al. *bioRxiv* 2023). He always loves to uncover the hidden treasures in omics data through the development of new methods.

Research Interests:

- Integrative analysis of the single-cell omics data and genome data for immune cells. In addition to the conventional functional genomics approaches such as pseudobulk eQTL mapping, I am specifically interested in the development of new methods to uncover hidden biology in the omics data.
 - Evaluation of the escape from X chromosome inactivation (Tomofuji Y et al. *bioRxiv* 2023; co-correspondence; This work is a part of Human Cell Atlas Consortium [Asian Immune Diversity Atlas Network] [Github URL](#))



- Analysis of the gut microbiome using metagenome shotgun sequencing. I am specifically interested in autoimmune diseases, Japanese-specific gut microbes, and integrative analysis with human genome data.
 - Integrative analysis of the gut microbiome, human genome, and plasma metabolites (Tomofuji Y et al. *Cell Rep.* in Press; co-correspondence)
 - Evaluation of the human genome in the metagenome shotgun sequencing data ([Tomofuji Y et al. *Nat. Microbiol.* 2023](#); co-correspondence)
 - Catalogue of the microbes in the Japanese gut ([Tomofuji Y et al. *Cell Genom.* 2022](#); co-correspondence)
 - Gut virome analysis of the RA/SLE/MS patients ([Tomofuji Y et al. *Ann. Rheum. Dis.* 2022](#))
 - Gut microbiome analysis of the SLE patients ([Tomofuji Y et al. *Ann. Rheum. Dis.* 2021](#))
- Transcription regulation of the thymic antigens which contribute to the thymic selection of T cells. I approached this question during medical school utilizing both wet and dry approaches.
 - Elucidating the role of chromatin remodeling protein Chd4 in the thymic antigen expression ([Tomofuji Y et al. *Nat. Immunol.* 2020](#))

Awards:

- JSPS Ikushi Prize, 2023/3 ([URL](#))
- Dean's Award of MD Researcher Training Program, Faculty of Medicine, The University of Tokyo, 2017/10

Presentation awards:

- The 14th International Workshop on Advanced Genomics, Poster Award, 2023/10
- Japan College of Rheumatology 2023 ICW Excellent Abstract Award, 2023/4
- The 7th Annual Meeting of the Japanese Society of Osteoimmunology, Best Presentation Award, 2022/6
- Japan College of Rheumatology 2022 ICW Excellent Abstract Award, 2022/4

Grants / Scholarships:

- Osaka University, Institute for Open and Transdisciplinary Research Initiatives, Junior Researcher Joint Projects, Project Leader, 2021/12 (Grant)
- Takeda Science Foundation Scholarship, 2020/4 - 2023/9

Teaching experiences:

- A practical course, Biochemistry, 2023-, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan

Publications:

The '*' and '†' symbols indicate equal contribution and correspondence, respectively, in the following list.

Tomofuji, Y.†, Sonehara, K., Kishikawa, T., Maeda, Y., Ogawa, K., Kawabata, S., Nii, T., Okuno, T., Oguro-Igashira, E., Kinoshita, M., Takagaki, M., Yamamoto, K., Kurakawa, T., Yagita-Sakamaki, M., Hosokawa, A., Motooka, D., Matsumoto, Y., Matsuoka, H., Yoshimura, M., Ohshima, S., Nakamura, S., Inohara, H., Kishima, H., Mochizuki, H., Takeda, K., Kumanogoh, A. & Okada, Y.† Reconstruction of the personal information from human genome reads in gut metagenome sequencing data. ***Nature Microbiology* 8**, 1079–1094 (2023).

Edahiro, R.*, Shirai, Y.*, Takeshima, Y., Sakakibara, S., Yamaguchi, Y., Murakami, T., Morita, T., Kato, Y., Liu, Y.-C., Motooka, D., Naito, Y., Takuwa, A., Sugihara, F., Tanaka, K., Wing, J. B., Sonehara, K., **Tomofuji, Y.**, Japan COVID-19 Task Force, Namkoong, H., Tanaka, H., Lee, H., Fukunaga, K., Hirata, H., Takeda, Y., Okazaki, D., Kumanogoh, A.† & Okada, Y.† Single-cell analyses and host genetics highlight the role of innate immune cells in COVID-19 severity. ***Nature Genetics* 55**, 753–767 (2023).

Tomofuji, Y.*, Suzuki, K.*, Kishikawa, T., Shojima, N., Hosoe, J., Inagaki, K., Matsubayashi, S., Ishihara, H., Watada, H., Ishigaki, Y., Yamanashi, Y., Furukawa, Y., Morisaki, T., Kamatani, Y., Muto, K., Nagai, A., Obara, W., Yamaji, K., Takahashi, K., Asai, S., Takahashi, Y., Suzuki, T., Sinozaki, N., Yamaguchi, H., Minami, S., Murayama, S., Yoshimori, K., Nagayama, S., Obata, D., Higashiyama, M., Masumoto, A., Koretsune, Y., Inohara, H., Murakami, Y., Matsuda, K., Okada, Y.†, Yamauchi, T.†, Kadowaki, T.†, & The BioBank Japan Project. Identification of serum metabolome signatures associated with retinal and renal complications of type 2 diabetes. ***Communications Medicine* 3**, 5 (2023).

Tomofuji, Y.†, Kishikawa, T., Maeda, Y., Ogawa, K., Otake-Kasamoto, Y., Kawabata, S., Nii, T., Okuno, T., Oguro-Igashira, E., Kinoshita, M., Takagaki, M., Oyama, N., Todo, K., Yamamoto, K., Sonehara, K., Yagita, M., Hosokawa, A., Motooka, D., Matsumoto, Y., Matsuoka, H., Yoshimura, M., Ohshima, S., Shinzaki, S., Nakamura, S., Iijima, H., Inohara, H., Kishima, H., Takehara, T., Mochizuki, H., Takeda, K., Kumanogoh, A. & Okada, Y.† Prokaryotic and viral genomes recovered from 787 Japanese gut metagenomes revealed microbial features linked to diets, populations, and diseases. ***Cell Genomics* 2**, 100219 (2022).

Itotagawa, E., **Tomofuji, Y.**, Kato, Y., Konaka, H., Tsujimoto, K., Park, J., Nagira, D., Hirayama, T., Jo, T., Hirano, T., Morita, T., Nishide, M., Nishida, S., Shima, Y., Narazaki, M., Okada, Y., Takamatsu, H. & Kumanogoh, A. SLE stratification based on BAFF and IFN-I bioactivity for biologics and implications of BAFF produced by glomeruli in lupus nephritis. *Rheumatology* **62**, 1988–1997 (2023).

Yan, M., Komatsu, N., Muro, R., Huynh, N. C.-N., **Tomofuji, Y.**, Okada, Y., Suzuki, H. I., Takaba, H., Kitazawa, R., Kitazawa, S., Pluemsakunthai, W., Mitsui, Y., Satoh, T., Okamura, T., Nitta, T., Im, S.-H., Kim, C. J., Kollias, G., Tanaka, S., Okamoto, K., Tsukasaki, M. & Takayanagi, H. ETS1 governs pathological tissue-remodeling programs in disease-associated fibroblasts. *Nature Immunology* **23**, 1330–1341 (2022).

Kishikawa, T., **Tomofuji, Y.**, Inohara, H. & Okada, Y. OMARU: a robust and multifaceted pipeline for metagenome-wide association study. *NAR Genomics and Bioinformatics* **4**, lqac019 (2022).

Tomofuji, Y., Kishikawa, T., Maeda, Y., Ogawa, K., Nii, T., Okuno, T., Oguro-Igashira, E., Kinoshita, M., Yamamoto, K., Sonehara, K., Yagita, M., Hosokawa, A., Motooka, D., Matsumoto, Y., Matsuoka, H., Yoshimura, M., Ohshima, S., Nakamura, S., Inohara, H., Mochizuki, H., Takeda, K., Kumanogoh, A. & Okada, Y. Whole gut virome analysis of 476 Japanese revealed a link between phage and autoimmune disease. *Annals of the Rheumatic Diseases* **81**, 278–288 (2022).

Tomofuji, Y.*, Maeda, Y.*, Oguro-Igashira, E.*, Kishikawa, T., Yamamoto, K., Sonehara, K., Motooka, D., Matsumoto, Y., Matsuoka, H., Yoshimura, M., Yagita, M., Nii, T., Ohshima, S., Nakamura, S., Inohara, H., Takeda, K., Kumanogoh, A. & Okada, Y. Metagenome-wide association study revealed disease-specific landscape of the gut microbiome of systemic lupus erythematosus in Japanese. *Annals of the Rheumatic Diseases* **80**, 1575–1583 (2021).

Harano, Y., Ishikawa, Y., Hattori, K., Ichinose, M., **Tomofuji, Y.**, Okano, H., Owada, G., Kimura, Y., Nanao, T., Fujimoto, J., Nishizawa, H., Ii, Y., Osada, J., Fujiwara, M. & Kita, Y. A case of complete atrioventricular block in secondary hemophagocytic syndrome/hemophagocytic lymphohistiocytosis recovered by plasma exchange and cytokine absorbing therapy with AN69ST continuous hemodiafiltration. *Immunological Medicine* **43**, 171–178 (2020).

Nitta, T., Tsutsumi, M., Nitta, S., Muro, R., Suzuki, E. C., Nakano, K., **Tomofuji, Y.**, Sawa, S., Okamura, T., Penninger, J. M. & Takayanagi, H. Fibroblasts as a source of self-antigens for central immune tolerance. *Nature Immunology* **21**, 1172–1180 (2020).

Tomofuji, Y.*, Takaba, H.*, Suzuki, H. I., Benlaribi, R., Martinez, C. D. P., Abe, Y., Morishita, Y., Okamura, T., Taguchi, A., Kodama, T. & Takayanagi, H. Chd4 choreographs self-antigen expression for central immune tolerance. *Nature Immunology* **21**, 892–901 (2020).

Tomofuji, Y., Ishikawa, Y., Hattori, K., Fujiwara, M. & Kita, Y. Successful treatment of refractory acute lupus haemophagocytic syndrome using rituximab: a case report. *Modern Rheumatology Case Reports* **4**, 222–228 (2020).

Nitta, T., Kochi, Y., Muro, R., **Tomofuji, Y.**, Okamura, T., Murata, S., Suzuki, H., Sumida, T., Yamamoto, K. & Takayanagi, H. Human thymoproteasome variations influence CD8 T cell selection. *Science Immunology* **2**, eaan5165 (2017).

Takaba, H., Morishita, Y., **Tomofuji, Y.**, Danks, L., Nitta, T., Komatsu, N., Kodama, T. & Takayanagi, H. Fezf2 orchestrates a thymic program of self-antigen expression for immune tolerance. *Cell* **163**, 975–987 (2015).

Preprints:

The ‘*’ and ‘†’ symbols indicate equal contribution and correspondence, respectively, in the following list.

Yoshihiko Tomofuji†, Ryuya Eda[†], Yuya Shirai, Kian Hong Kock, Kyuto Sonehara, Qingbo S. Wang, Shinichi Namba, Jonathan Moody, Yoshinari Ando, Akari Suzuki, Tomohiro Yata, Kotaro Ogawa, Ho Namkoong, Quy Xiao Xuan Lin, Eliora Violain Buyamin, Le Min Tan, Radhika Sonthalia, Kyung Yeon Han, Hiromu Tanaka, Ho Lee, Asian Immune Diversity Atlas Network, Japan COVID-19 Task Force, The BioBank Japan Project, Tatsusada Okuno, Boxiang Liu, Koichi Matsuda, Koichi Fukunaga, Hideki Mochizuki, Woong-Yang Park, Kazuhiko Yamamoto, Chung-Chau Hon, Jay W. Shin, Shyam Prabhakar, Atsushi Kumanogoh, & Yukinori Okada[†]. Quantification of the escape from X chromosome inactivation with the million cell-scale human single-cell omics datasets reveals heterogeneity of escape across cell types and tissues. *bioRxiv* 2023.10.14.561800 (2023) doi:10.1101/2023.10.14.561800.

Presentations:

Tomofuji Y., et al, "Quantification of the escape from X chromosome inactivation with the million cell-scale human single-cell omics datasets", The 14th International Workshop on Advanced Genomics, Short talk #2/Poster #1, Tokyo, Tokyo, Japan, October, 2023, Oral and Poster presentation

Tomofuji Y., et al, "Prokaryotic and viral genomes recovered from 787 Japanese gut metagenomes revealed microbial features associated with diets, populations, and diseases", The 8th Annual Meeting of

the Japanese Society of Osteoimmunology, D-8, Ishigaki, Okinawa, Japan, June, 2023, Poster presentation

Tomofuji Y, et al, "Leveraging the Japanese microbial genome database to identify rheumatic diseases-crAss-like phage associations", The 67th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology, Session ICW3-6, Hakata, Fukuoka, Japan, April, 2023, Oral presentation

Tomofuji Y, et al, "Prokaryotic and viral genomes recovered from 787 Japanese gut metagenomes revealed microbial features associated with diets, populations, and diseases", The 67th Annual Meeting of the Japan Society of Human Genetics, Session OE5-4, Yokohama, Kanagawa, Japan, December, 2022, Oral presentation

Tomofuji Y, et al, "Prokaryotic and viral genomes recovered from 787 Japanese gut metagenomes revealed microbial features associated with diets, populations, and diseases", American Society of Human Genetics 2022 Annual Meeting, PB3108, San Francisco, California, USA, October, 2022, Poster presentation

Tomofuji Y, et al, "Analysis for the gut bacteriome and virome in autoimmune diseases", The 7th Annual Meeting of the Japanese Society of Osteoimmunology, ST-2, Nago, Okinawa, Japan, June, 2022, Oral and Poster presentation

Tomofuji Y, et al, "Metagenome-wide association studies revealed the altered gut bacteriome and virome in autoimmune diseases", The 66th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology, Session ICW21-6, Yokohama, Kanagawa, Japan, April, 2022, Oral presentation

Tomofuji Y, et al, "A metagenome-wide association study revealed disease-specific landscape of the gut microbiome of systemic lupus erythematosus in Japanese", The 50th Annual Meeting of the Japanese Society for Immunology, 2-B-WS7-08-O/P, Nara, Nara, Japan, December, 2021, Oral and Poster presentation

Tomofuji Y, et al, "A metagenome-wide association study revealed disease-specific landscape of the gut microbiome of systemic lupus erythematosus in Japanese", The 8th JCR Basic Research Conference, P-35, Online, November, 2021, Poster presentation

Tomofuji Y, et al, "A Metagenome-wide Association Study Revealed Disease-specific Landscape of the Gut Microbiome of Systemic Lupus Erythematosus in Japanese", American College of Rheumatology Convergence 2021, 1496, Online, November, 2021, Poster presentation

Tomofuji Y, et al, "A metagenome-wide association study revealed disease-specific landscape of the gut microbiome of systemic lupus erythematosus in Japanese", American Society of Human Genetics 2021 Virtual Meeting, PrgmNr 2272, Online, October, 2021, Poster presentation

Tomofuji Y, et al, "A metagenome-wide association study revealed an alteration of the gut microbiome in systemic lupus erythematosus", The 66th Annual Meeting of the Japan Society of Human Genetics and the 28th Annual Meeting of the Japanese Society for Gene Diagnosis and Therapy 囊 Joint Conference 2021, Session OE12-5, Yokohama, Kanagawa, Japan, October, 2021, Oral presentation

Tomofuji Y, et al, "Distinct Features of Fezf2-induced Promiscuous Gene Expression", ThymOz 2018 an international conference on T lymphocytes, Session 11-8, Heron Island, Queensland, Australia, March, 2018, Oral presentation