

## **Yoshihiko Tomofuji. M.D., Ph.D.** (Last update: 2023-10-11)

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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*

MD Researcher Training Program (Mentor: Dr. Hiroshi Takayanagi)

## **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

Yokohama Rosai Hospital, Yokohama, Japan. 2018-2019

## 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). 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; [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.

- Gut microbiome analysis of the SLE patients ([Tomofuji Y et al. \*Ann. Rheum. Dis.\* 2021](#))
  - Gut virome analysis of the RA/SLE/MS patients ([Tomofuji Y et al. \*Ann. Rheum. Dis.\* 2022](#))
  - Catalogue of the microbes in the Japanese gut ([Tomofuji Y et al. \*Cell Genom.\* 2022](#); co-correspondence)
  - Evaluation of the human genome in the metagenome shotgun sequencing data ([Tomofuji Y et al. \*Nat. Microbiol.\* 2023](#); co-correspondence)
  - Integrative analysis of the gut microbiome, human genome, and plasma metabolites (Tomofuji Y et al. *Cell Rep.* in Press; co-correspondence)

## Awards:

- The 14th International Workshop on Advanced Genomics, Poster Award, 2023/10

- Japan College of Rheumatology 2023 ICW Excellent Abstract Award, 2023/4
- JSPS Ikushi Prize, 2023/3 ([URL](#))
- 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
- 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
- Dean's Award of MD Researcher Training Program, Faculty of Medicine, The University of Tokyo, 2017/10

## 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., Iioka, 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).

## **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 ㊦ 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