

Tohoku University

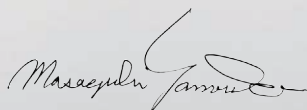
Tohoku Medical Megabank Organization



Tohoku University Tohoku Medical Megabank Organization (ToMMo) was founded to establish an advanced medical system to foster the reconstruction from the Great East Japan Earthquake. ToMMo has been developing a biobank that combines both medical and genome information during the process of rebuilding the community medical system and supporting health and welfare in the Tohoku region. The information from the brand-new biobank will allow a new medical system to be created. Based on the analytical findings, ToMMo aims to attract more medical professionals from all across the country to the area, promote industry-academic partnerships, create employment in related fields, and lastly reconstruct the medical system in the Tohoku region.



Towards the Development of Personalized Healthcare through the Promotion of Industry-Academia Collaboration



Masayuki Yamamoto
Executive Director



The year 2023 marks the 12th year since ToMMo was established in February 2012. Since then, we have enrolled over 157,000 participants into the cohort studies, which started in 2013. Our biobank has over 4.3 million specimens stored, with more healthcare surveys still ongoing. Additionally, we have analyzed the whole genome of 50,000 people, and combining this with other data, such as those from metabolome analyses; world-class information is stored in our supercomputer.

The following are the three priority issues to be addressed in 2023.

Firstly, the Center for Biobank Utilization and Academia-Industry Partnership will focus on further promoting the utilization of valuable specimens and

information stored in the integrated biobank by researchers from academic institutions and companies nationwide through distribution and collaborative research.

Secondly, we will promote collaboration with the Advanced Research Center for Innovations in Next-Generation Medicine (INGEM), which is one of the four Core Research Clusters established at Tohoku University as a founding member. Tohoku University Hospital and our organization will promote clinical research and strengthen efforts to tackle on the challenge of next-generation medicine.

Lastly, we will promote the completion of the whole genome sequencing of the 100,000 participants from the general population within our cohort

studies. We will update integrated analysis of the whole genome information together with various health information in our organization to build evidence that will serve as a foundation for personalized healthcare. The basis of being able to achieve these three major goals lies within the integrated biobank that we established in our cohort studies. We intend to continue the ongoing tertiary assessments, carry out additional recruitment as per our plans and expand our analytical information. We are determined to be the core of genome medical research in Japan and, in addition, share genomic information among many institutions in order to link medicine and healthcare together.

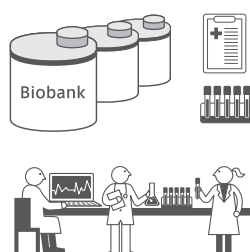
Concept

150,000 Cohort Study Participants

- Longitudinal Health Information
- Genome and Omics Analyses with Biospecimen from Cohort Studies



Integrated Biobank



Personalized Healthcare by Evidence-based Risk Prediction

Towards a Society Where Each Individual Chooses to Live in Accordance with His/her Own Health



Activities of ToMMo: Establishment of Integrated Biobank for Next Generation Medicine

The Tohoku Medical Megabank Project is pursuing the following studies:

- Long-term health survey for community residents
- Establishment and operation of large-scale biobank that integrates both biological specimens and health-related information
- Analyses of biological specimens and information amassed by the biobank using advanced technology

Through these activities, the project is enhancing the progression of future-oriented health care and cutting-edge research, while contributing to reconstruction efforts.

Long-term Health Survey

The Tohoku Medical Megabank Project has accumulated the longitudinal health survey information and genetic information of over 150,000 people. This was only achievable due to the generous cooperation and consent of community residents, while facing local health issues, after the Great East Japan Earthquake.

This project conducts two cohort study programs: The Community-Based Cohort Study (TMM CommCohort Study) and the Birth and Three-Generation Cohort Study (TMM BirThree Cohort Study). In a cohort study, information about the lifestyle habits of a large group of people are collected and studied to understand how their habits and their surrounding environment may correlate to disease. ToMMo's cohort studies also incorporate longitudinal MRI imaging and the collection of daily lifestyle information through smartphone applications to build a large data set.

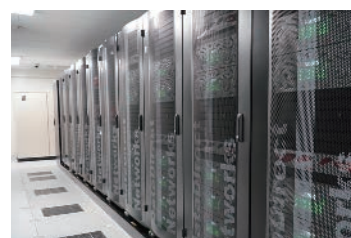
Building and Operating an Integrated Biobank

Our biobank is collecting and storing de-identified biological specimens including

DNA, plasma and serum from blood and corresponding health-related and clinical information obtained from the participants of cohort studies. Some biospecimens are analyzed and the information is incorporated into an integrated biobank. Researchers from various institutions are able to use these resources for health-related studies upon the approval of their research applications.

Detailed Analyses of Biological Specimens and Information

ToMMo is conducting whole genomic analyses of some of the participants from the cohort studies. In November 2013, ToMMo completed whole genomic analysis of 1,000 individuals in Japan and is continuing to expand the analysis to tens of thousands of individuals. By 2023, we aim to have completed whole genome analyses for approximately 70,000 individuals. The largest whole genome analysis of a general population in Japan has contributed widely to many related fields, including industry and academia. That is, a whole genome reference panel cataloging the variants detected by this analysis has led to significant support for patient genome analysis. The reference panel will greatly contribute to the development of innovative drug discovery and is indispensable for the realization of personalized healthcare. ToMMo also performs a variety of omics analyses, including large-scale metabolomic analysis of plasma, which continues to contribute to the enrichment of the integrated biobank. Taken together, we are attempting to elucidate the mechanisms of disease caused by complex interactions between genetic and environmental factors; and to realize evidence-based, personalized disease risk prediction.



jMorp

An accessible database from all over the world

ToMMo analyzed the genome and omics data of the cohort study participants in the Tohoku Medical Megabank Project and published the statistical data to the jMorp (Japanese Multi Omics Reference Panel) web database. The jMorp database was created in July 2015 to provide the analytical findings of proteome and metabolome data. Since then, it has been updated annually to include datasets for the genome, methylome, transcriptome, PGx, and metagenome.



The following data are present in jMorp. (As of May 2023)

Genome Sequence	• Japanese reference sequence constructed from the de-novo assembly of three Japanese males.
Genome Variation	• SNV/INDEL allele and genotype frequency data, and HLA allele frequency data derived from the short-read whole genome sequencing of over 38,000 Japanese individuals • Allele and genotype frequency data of structural variations(SVs) derived from the short-read whole genome sequencing of more than 8,300 Japanese individuals, and the long-read whole genome sequencing of 222 Japanese individuals
Other Genome-related Data	• Average depth information from short-read whole genome sequencing • Linkage disequilibrium map derived from 300 haploids • Lists of markers tiled on Japonica Arrays(SNP Arrays) developed by ToMMo
Methylome	• Data on DNA methylation, gene expression, and allele frequency for three different types of blood cells in approximately 100 Japanese individuals
Transcriptome	• Long-read transcriptome analysis of three Japanese male individuals • Data on DNA methylation, gene expression, and allele frequency for three different types of blood cells in approximately 100 Japanese individuals
Proteome	• Proteome analysis of about 500 Japanese plasma samples
Metabolome	• Metabolome analysis results obtained from around 53,000 Japanese plasma samples
Phenome	• Drug sensitivity-related enzymes' genome variants and enzyme activity • Microbiome analysis of plaque and saliva samples
Other	• A repository for the TMM project's GWAS analysis results



Key publication

- Fuse N *et al.* Establishment of Integrated Biobank for Precision Medicine and Personalized Healthcare: The Tohoku Medical Megabank Project. *JMA J.* 2, 113-122. 2019.
- Kuriyama S *et al.* Cohort Profile: Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study (TMM BirThree Cohort Study): Rationale, Progress and Perspective. *Int. J. Epidemiol.* 49, 1, 18–19m, 2019.
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- Minegishi N *et al.* Biobank Establishment and Sample Management in the Tohoku Medical Megabank Project. *Tohoku J Experiment Med.*, 248, 1, 45-55, 2019.
- Ogishima S *et al.* dbTMM: an integrated database of large-scale cohort, genome and clinical data for the Tohoku Medical Megabank Project. *Hum Genome Var.*, 8, 44, 202
- Yasuda J *et al.* Genome analyses for the Tohoku Medical Megabank Project towards establishment of personalized healthcare. *J. Biochem.* 165, 2, 139–158, 2018.
- Takayama J *et al.* Construction and integration of three de novo Japanese human genome assemblies toward a population-specific reference. *Nat Comm.*12, 226, 2021.
- Koshiba S *et al.* Omics research project on prospective cohort studies from the Tohoku Medical Megabank Project. *Genes Cells.* 23, 6, 406-417, 2018.
- Sakurai-Yageta M *et al.* Japonica Array NEO with increased genome-wide coverage and abundant disease risk SNPs. *J. Biochem.* 170, 3, 399–410, 2021.
- Saito S *et al.* Oral microbiome analysis in prospective genome cohort studies of the Tohoku Medical Megabank Project. *Front. Cell. Infect. Microbiol.* 10, 604596, 2020.



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