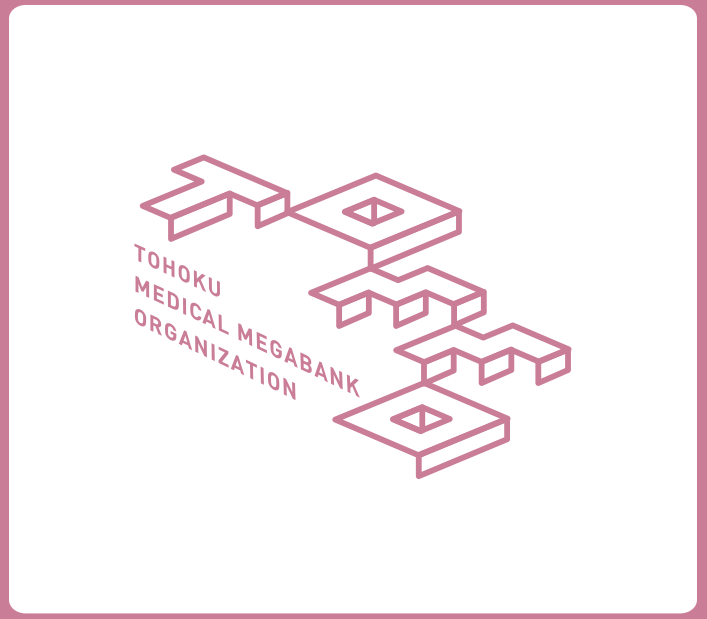
Overview & Organization

To the future, Together, Tohoku

www.megabank.tohoku.ac.jp/english



Tohoku University
Tohoku Medical Megabank Organization

Contents

Seeking to Establish an Advanced Community Medical System

Masayuki Yamamoto
Executive Director

The Great East Japan Earthquake gave rise to a catastrophic disaster, especially on the Pacific Coast of the Tohoku region. In an effort to recover from the disaster and to foster creative reconstruction of the Tohoku region, we have started "Tohoku Medical Megabank Project".
Our central goal is to set up an advanced medical system. As the number of medical practitioners in the Tohoku region has been decreasing, even prior to the 3.11 earthquake and tsunami, simple rebuilding of local institutions and medical service facilities are not adequate.
We needed to establish a core project that can revitalize the Tohoku region. Tohoku Medical Megabank Project provides supports to local medical services, constructs a community coalition for medical information, sets up an integrated biobank based on large-scale cohort studies, and provides educational training to produce highly specialized medical practitioners. We believe that this project will revitalize the Tohoku region, not only aiding in its recovery from the earthquake and tsunami but also making it an attractive and thriving center of innovation in Japan.
Tohoku Medical Megabank Project will be successful only when thousands of people in the Tohoku region and medical practitioners in other areas of Japan give their kind cooperation. Such cooperation is critical to our practice. We also would like to act as a medical center of the Tohoku region and sending out messages worldwide. Thank you for taking this leaflet in hand and please wish us luck.

Masayuki Yamamoto

Executive Director, Tohoku Medical Megabank Organization, 2012- Present
Dean, Tohoku University Graduate School of Medicine, 2008-2012

01 Rebuild community medicine on the Pacific

- Young doctors' rotation between the area suffered from tsunami and university laboratories

Photo by Kenichi Chiba

03 Construct biobank for the cutting-edge research

- Store the biospecimens and data from cohort studies
- Set-up the system for sample distribution and data-sharing

ToMMo's Work at a Glance

ToMMo = Friends

We wish to deliver the most advanced medicine to the people who suffered from the earthquake and tsunami

02 Survey of health status of the suffered area

- Two types of cohort study (long-term health studies)
- Set-up seven assessment centers (community support centers) in Miyagi Prefecture
- Support of victims by telephones and interviews
- Collecting biospecimens and data for biobank

04 Analyze genome and omics data for the personalized medicine and healthcare

- Sequence the DNA of cohort participants
- Analyze sequenced data and construct genome reference panel by using supercomputer

Cohort Studies

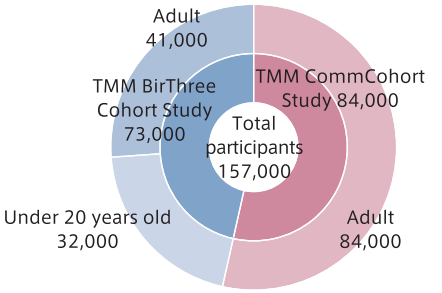
To study how genetic factors and environmental factors affect disease risk, two large-scale prospective studies, the Tohoku Medical Megabank Project Community-Based Cohort Study (TMM CommCohort Study) and the Tohoku Medical Megabank Project Birth and Three-Generation Cohort Study (TMM BirThree Cohort Study), are ongoing in Miyagi and Iwate Prefectures in Japan.

Since the cohort studies started in 2013, we successfully recruited more than 150,000 participants for baseline assessment by 2017. We collected biospecimens including serum, plasma, mononuclear cells, urine, and the answers to the questionnaires of their lifestyles and medical history. A part of participants took detailed assessment of the physiological health status in assessment centers we established.

After the baseline assessment was completed, we have started follow-up study "repeat assessment center-based survey during the second period" in which we ask participants to take a health survey similar to the baseline assessment they did at the centers. We made plan for this repeat assessment survey which they take once about 3 to 5 years. We also collect the data, disease or health information, using postal or web annually questionnaire and information survey from publicly constructed database.

Detail of cohort studies

Name of cohort study	Type	Recruitment target
TMM CommCohort Study	Population-based cohort	Local residents who are 20 years old or older
TMM BirThree Cohort Study	Family-based cohort, Birth and Three-generation cohort	Expectant mothers and their family



Results from Cohort Studies

From cohort studies, several aspects of devastated area were found. The severe damages of the Great East Japan Earthquake still remained here in Tohoku. Those results were informed to local governments and were utilized to the policy making.

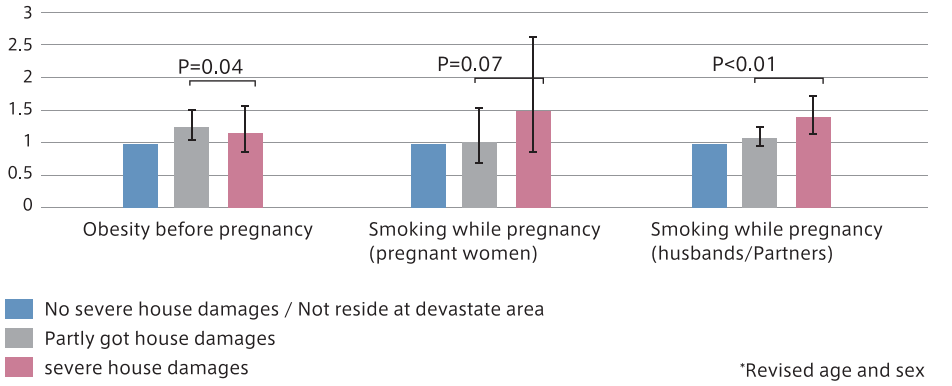
- The odds ratio of psychological distress, depressive symptoms, insomnia, and PTSR (post-traumatic stress reaction) are higher in the coastal area than in inland area.

- The damage extent of their own houses, physical activities, smoking, and drinking alcohol are significantly related to the metabolic syndrome.

- The damage by the Great East Japan Earthquake related to the therapeutics interruption of hypertension treatment.

- The ratio of salt intake, the infection by the H. Pylori, and potential latent cardiac insufficiency has not significantly changed.
- The damage extent of their own houses was related to BMI of pre-pregnancy and the smoking of pregnant women and her husbands/partners.

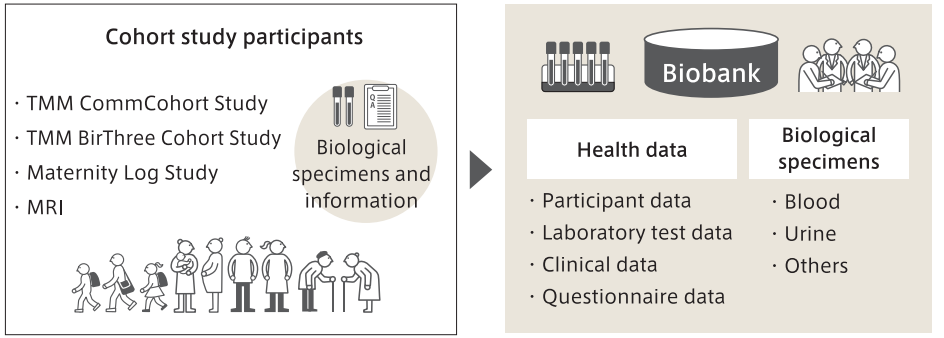
*Error bars are 95% confidence intervals.



*Revised age and sex

Biobank

We have been developing the biobank from the biological specimens of 150,000 cohort study participants. We store millions of tubes of biological specimens such as serum, plasma, mononuclear cells, DNA, health information, and genetic data from the cohort study participants. These biological specimens are preserved at appropriate temperatures and under suitable conditions. We also collect data from physiological examinations, physical measurements, medical and lifestyle information from the questionnaires, and MRI data of a part of the participants who offered their information at our assesment centers, which are located in several community areas. These series of information is stored in the data storage system. The results of analysis of the biological specimens are combined with information above to construct our integrated database.



Biological Specimens (Number of tubes on November 1, 2018)

Biological Specimens	Tubes
DNA	234,600
Plasma	860,200
Serum	858,400
Buffy Coat Cells	319,200
Peripheral Blood Mononuclear Cells	345,300
Cord Blood Mononuclear Cells	74,100
EBV-Transformed B Cells	9,700
Stimulated T Cells	12,500
Urine	601,900
Breast Milk	70,300
Saliva	4,600

Analytical Studies

We conduct genome analyses of biological specimens provided by cohort studies using next-generation sequencer. We also conduct omics analyses of protein and low-molecular metabolites using NMR, mass spectrometry, among other instruments. This data is processed using a supercomputer system and other technologies.

Genome Analysis

Whole genome sequencing and reference panel construction

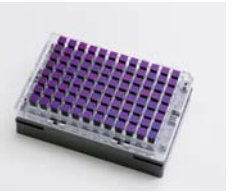
We preformed around 3,500 whole genome sequencing and construct genome reference panel for Japanese population (3.5KJPNv2 released in 2018). Information on frequencies and locations of all found single-nucleotide variants (SNV) including INDEL on the panel is available through the "jMorp"

Japanese genome reference assembly

We have been constructing the Japanese reference genome assembly with a long-read-type next generation sequencer, PacBio RSII (Pacific Biosciences), with 100 times depths.
Then, we have applied a method of information science called de novo assembly, assembling the sequences from scratch with high accuracy.

Microarray analysis

We developed a tool for analyzing the genomes of Japanese people, Japonica Array.
With the array, DNA from more than 100,000 paticipants have been analyzed. The data with microarray analysis will be imputated to whole genome sequence data with the reference panel and integrated to the biobank.



Metabolome Analysis

Constructing multi-omics reference panel

We are performing metabolome analysis on serum samples from cohort participants with proton NMR and LC-MS. The results of global metabolome analysis for metabolites from more than 10,000 people are opened on "jMorp" with other omics analysis data such as genome and proteome.

Public Database

jMorp

Japanese Multi Omics Reference Panel (jMorp) is an opened access database consisted of genome, metabolome and proteome data in plasma which is constructed by ToMMo. In this database, there are genome analysis data of 3,552 Japanese people and metabolome analysis data of 10,719 Japanese people from TMM cohort studies participants who are general local residents in Japan.

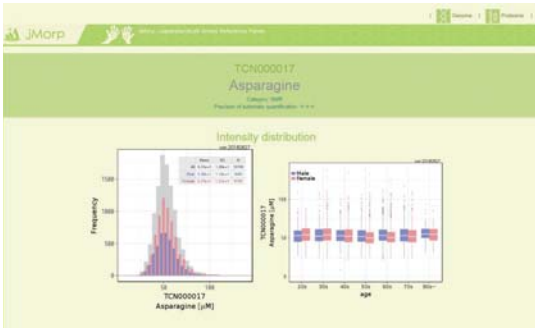
URL: https://jmorp.megabank.tohoku.ac.jp

Genome

You can search SNV (including INDEL) allele frequency dataset on the website. With login by ORCID ID, less than 1% of allele frequency information is searchable.

Metabolome

You can find intensity distribution (sex and age) for 37 metabolites from 10,719 cohort participants' serum. About 169 kinds of metabolites, the data of targeted GC-MS/MS measurements for more than 1,000 people is available.



Chronology

History of the Tohoku Medical Megabank Project

2011	Mar.	· The Great East Japan Earthquake
2012	Feb.	· Establishment of Tohoku University Tohoku Medical Megabank Organization (ToMMo)
	Jul.	· Establishment of Iwate Medical University Iwate Tohoku Medical Megabank Organization (IMM)
2013	May	· Commencement of the TMM CommCohort Study at Miyagi Prefecture
	Jul.	· Commencement of the TMM BirThree Cohort Study at Miyagi Prefecture
	Sep.	· Commencement of the TMM CommCohort Study at Iwate Prefecture
	Oct.	· Set-up of seven assessment centers (community support centers) in Miyagi Prefecture
	Nov.	· Completion of whole genome sequencing of 1,000 healthy Japanese people
2014	Mar.	· Completion of Tohoku Medical Megabank Organization facility; activation of the biobank and supercomputer system
	Aug.	· Online data sharing of the SNV allele frequency data from Japanese whole genome sequencing
	Dec.	· Commencement of the genotyping service of the Japonica Array provided by Toshiba Corporation
2015	Jul.	· Release of "jMorp" (metabolome and proteome analysis data of 500 Japanese people) database
	Aug.	· Commencement of registration of data and sharing of biological specimens
	Nov.	· Recruitment of 50,000 participants at the TMM CommCohort Study in Miyagi Prefecture
2016	Jan.	· Recruitment of 80,000 participants at the TMM CommCohort Study
	Mar.	· Closing recruitment of the TMM CommCohort Study
2017	Mar.	· Closing recruitment of the TMM BirThree Cohort Study with more than 70,000 participants
	Jun.	· Beginning of "Repeat assessment center-based survey during the second period"
	Oct.	· Commencement of the genotyping service of the Japonica Array v2
2018	Jun.	· Release of genome reference panel of 3,500 people (3.5KJPNv2)

Voice from Cohort Participants

I live in temporary housing along with many other people from the devastated area where we had our homes. I am worried about health of my oldest child who has predisposition of diseases, so I wanted to participate the research with all of my children. I appreciate the research for its role in the disaster recovery effort. Female, 30s

I lost my father to an incurable disease, and I am concerned about my children and grandchildren because I have heard that the disease is hereditary in males. Even if it is incurable at this moment, the research might elucidate something in the future. I hope our participation will contribute to the early detection and prevention of diseases in the future. Female, 50s

Even if it is research, I feel relieved that our family's health will be followed up longitudinally. Female, 30s

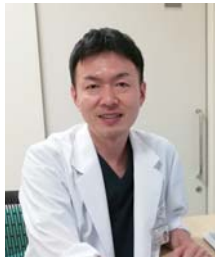
It is expected that precious data will be accumulated to the future. Concentrated efforts will be needed, and we cannot afford to not cooperate. Male, 60s

I hope the project lasts long enough for our children's and our grandchildren's generations. Female, 70s

My parent had breast cancer. Preventative treatment with genetic tests had already started in other countries and I wondered when those efforts would start in Japan. So I have been waiting for this kind of research. All of my family has or will participate in it. Please continue the research. Female

From the questionnaire sheet for the participant research results briefing

From Members



Yohei Hamanaka

Senior Assistant Professor, Center Director of Kesennuma Community Support Center, Oncologist

I make an effort to provide the best care for cancer patients as a surgeon. I realize deeply that the best way to reduce cancer mortality is evaluate the genetic and environmental risk factors of cancers and detect them at an early stage. Through the work at ToMMo, especially as a center director of Kesennuma Community Support Center, I try my best to implement these personalized medicine and healthcare.

Ichiko Nishijima

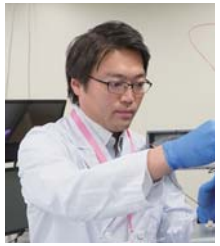
Senior Assistant Professor, Biobank Life Science

We have received millions of tubes of biospecimen from our cohort participants, and endeavor to keep them under best conditions for the purpose of supporting the progress of next-generation medicine.

Masayoshi Takashina

ToMMo GMRC (Genome Medical Research Coordinator)

I always try to explain about the research thoughtfully and have good communication with participants to make them feel relaxed. When I could see their smile after the health check-up, or they told me how satisfied they took the research, I feel sense of accomplishment and honored to take part in this job as a ToMMo GMRC.



Daisuke Saigusa

Senior Assistant Professor, Medical Biochemistry

A metabolic profiling for tens of thousands of people using mass spectrometry is promising avenue to realize the phenotypic changing by the genome and environmental effect, and contribute to establish the new health care program in the next-generation medicine.

Organization and Members

Tohoku Univ. President

Tohoku Univ. Board of Directors

Executive Director, Tohoku Medical Megabank Organization

- Masayuki Yamamoto
  Executive Director
- Shigeo Kure
  Deputy Executive Director
- Kengo Kinoshita
  Deputy Executive Director

Advisory Board

Ethics Committee

Governance Committee, Tohoku Medical Megabank Organization

General Affairs and Planning Sector

- Group of Planning
- Group of Public Relations
- Group of Education and Training
- Group of Strategy-Planning for Intellectual Property
- Group of Disease Risk Prediction
- Group of Return of Genomic Results
- Group of for Strategy-Planning for Medical Genomics
- Group of ToMMo-COI TOHOKU Collaboration

Cohort Studies Sector

- Group of the Birth and Three-Generation Cohort Study
- Group of Community Based Cohort Study
- Group of Community Support Center Operations
- Group of Information Management for Genome-Cohort Study
- Group of Community Medical Supports
- Group of Mental Health Promotion
- Group of MRI Project

Biobank and Databases Sector

- Group of Biobank
- Group of Metagenomics and Microbiome
- Group of Materials and Information Management
- Group of Integrated Database Systems
- Group of privacy controls

Genomic and Omics Analyses Sector

- Group of Integrative Data Analysis and Data Sharing Promotion
- Group of Genome Sequence Analysis
- Group of Microarray-based Genotyping Analysis
- Group of Genome Information Analysis
- Group of Omics Analysis
- Group of Early Prediction by Bioinformatics for Pregnancy Related Disorders

Center for Genome Platform Projects

Center for the Child Cohort

Access

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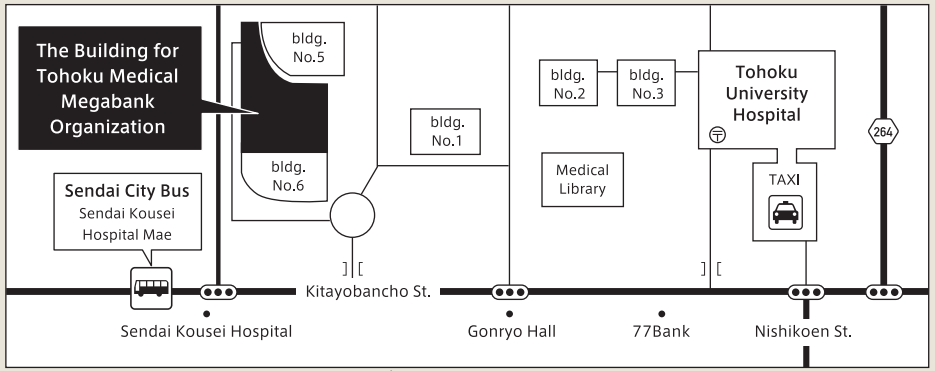
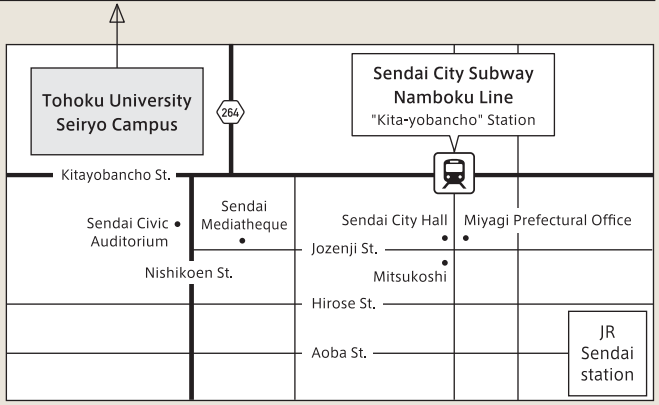
- **Sendai City Bus**
  From Sendai Station. West exit bus terminal No.10,15. Get on a bus for Routes passing through Tohoku University Hospital, get off at Sendai Kousei Hospital.
- **Sendai City Subway Namboku Line**
  From Sendai Station. Get off at "Kita-yobancho" Station (N07). It takes 15 min on foot from Exit north 2.





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