Introduction of Tohoku Medical Megabank Cohort Study.
How to achieve personalized health care using big data.

Feb 12, 2020
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Tohoku University Tohoku Medical Megabank Organization
The Great Eastern Japan Earthquake
March 11, 2011

- The total number of dead and missing persons is 18,550
- Many key hospitals suffered from the Tsunami
- As an emergency support, Tohoku University Hospital and Medical School sent more than 1,500 doctors (total) to the damaged coastal area

What shall we do as medical scientists?

Creative Reconstruction

- A core project is required to revitalize the Tohoku region
- Create an attractive and thriving center of innovation leading to fast-track recovery of the Tohoku region
ToMMo’s Residents Cohort and Birth & Three Generation Cohort

- **Community / Residents Cohort**
  Recruit 80,000 residents from coastal areas in Miyagi and Iwate provinces
  Recruit through joint session with health check by local government and use of seven regional support centers in the area

- **Birth & Three Generation Cohort**
  Recruit 70,000 people including offspring, parental and grandparental generations
  Request expectant mothers for cooperation in maternity hospitals

At March 31, 2016, we have finished recruit of 84,000 participants for Resident Cohort and at March 31, 2017, we have finished recruit of more than 73,000 for the Birth and Three Generation Cohort.

We recruited more than 150,000 participants in total.
TMM Community Based Cohort Study
Follow-up

- Increment of Life style related disease
- Early detection of problem and counteraction

Prospective cohort study design
Clarify the causal relationship and elucidate risk factors of diseases.

Gene–environmental interaction is not fully clarified

Gene X Environment

Monitor

- Monitoring of disease incidence
- Early intervention if risk factors are clarified

Prevention of secondary health damage

Establishment of personalized healthcare and medicine
Baseline survey enabled us to assess the current condition.

**Data collection**
- Blood • Urine
- Questionnaire
- Gene
- Other test

**Data Banking**
Storage of information and specimen
- Blood, urine
- Gene
- Disease incidence
- Death • Moving
- Questionnaire
- Other test

**Short term follow-up**
- Annual Follow-up
  - Lifestyle related disease incidence
  - Change in mental health

**Long-term follow-up**
- Follow-up
  - Disease incidence
  - Death • moving

**Contribution for next generation**
- Tohoku Univ
- Other Univ
- Other Company
How participants were recruited?

Inclusion criteria: Aged > 20 years and live in Miyagi and Iwate prefecture

Type 1 survey based on municipal health check-up

At the sites of annual health check-up in the local communities

- Trained staff approached and obtained additional blood sample and urine sample with informed consents

- Questionnaire was distributed

Type 2 survey based on assessment center-based survey

Volunteer based recruitment at 7 community support centers

Participants voluntarily made appointments and visited community support centers nearby
## Data Collected from All Participants in TMM Cohort Studies

### Baseline Measurements
- Height
- Weight
- Blood pressure
- Blood glucose
- Serum cholesterol
- Liver function
- Uric acid
- Renal function
- Specific Ig E (Allergy)
- Helicobacter pylori
- Pepsinogen I and II
- Microalbuminuria
- Urinary Na
- Urinary K

### Questionnaire-Based Data
- Smoking
- Alcohol consumption
- Physical activity
- Depression (CES-D)
- Psychological disorder (K6)
- Insomnia (Athene insomnia scale)
- Food Frequency Questionnaire
- Disaster related scale
- History of diseases
- Occupation
- Social connection
Type 1 recruitment, Miyagi prefecture

Recruitment period: 2013.5 – 2016.3

About 63,000 participants participated in Miyagi and Iwate

http://edit.freemap.jp/
About 20,000 participants participated in Miyagi and Iwate

- Carotid echography
- Body composition
- Blood pressure Measurement (Office, Home)
- Calcaneal Bone density
- Fundus test

Lung test, hearing test, oral test by dentist, and Leg extension test, or grip strength were also measured
Compared with inland area, coastal area showed

Higher prevalence of depression or psychological distress.

Higher risk of withdrawing treatment for hypertension.

Higher prevalence of metabolic disorder.

⇒

They might have higher risk of atherosclerotic disease, stroke or ischemic heart disease in future.
Compared with inland area, coastal area showed
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They might have higher risk of atherosclerotic disease, stroke or ischemic heart disease in future.

Secondary damage from disaster might be occurred.

Government allowed us to measure change in subclinical atherosclerosis or other factors.
Repeat assessment center-based survey during second period have just started 1 June 2017 -

- Ask all participants to visit the community support centers nearby.

In Miyagi, more than 26,000 participants has already measured this repeated measurement within 3 year

- Questionnaire

- New devices measured at home (urine Na/K test, activity monitor, sleep monitor)
Follow-up rate

- Follow-up survey

We confirmed 509 deaths until October 2018.
ToMMo is an integrated biobank

Integrated biobank
- ToMMo sets up an analytical center that executes standard analyses of samples
- To avoid rapid depletion of samples, ToMMo distributes analysis information first, and then bio-samples

Blood & Urine
- Whole Blood, Serum, WBCs are stored → metabolome & proteome
- DNA extracted from blood is also stored → genomics & transcriptome
- Main part is for life style (including food), psychological condition, experiences of the disaster

Questionnaire
- + MRI & more than 10 physiological examinations, and cognitive and psychological assessment
Tohoku Medical Megabank (TMM) is an integrated biobank retaining both Biobank and Genome / Omics Analytical Facilities.
Follow-up measurements

• As well as detailed survey, we sent brief questionnaire every 1–2 years.

• We also have obtained mortality data from residence card.

• We have already linked our data to cancer registry.

• Furthermore, we have obtained insurance data regarding medical cost and long term health care.

• From these resources, we are collecting the information on stroke or MI incidence of our participants.
Outlines of our dataset

Lifestyle
  Smoking
  Physical activity
  Diet, nutrition

Gene
  Whole genome
  SNP array

Damage from Disaster
  House destruction
  Loss of family or kin

Physiological data
  Blood pressure
  Atherosclerosis
  Lung function

Follow-up
  Physiological data
  Disease incidence
  Mortality

Metabolome data
Examples of biobank data

• We have started data distribution of type 1 recruitment data (about 67,000 participants).
• The data set consists of the following data.
• We confirmed the relation of blood pressure with traditional risk factors, such as BMI, alcohol, and NaCl.

- Height
- Weight
- Blood pressure
- Blood glucose
- Serum cholesterol
- Liver function
- Uric acid
- Renal function
- Specific Ig E (Allergy)
- Helicobacter pylori
- Pepsinogen I and II
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- Smoking
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- Food Frequency Questionnaire
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- Social connection
Examples of add-on cohort in ToMMo

As a cooperative study with industrial companies, we have added several component to our detailed survey.
乳酸菌摂取の保健効果を明らかにする共同研究を開始 ～数万人以上の規模

東北メディカル・メガバンク機構、疾病罹患・生理機能低下と腸内細菌叢との関連性を明らかにする共同研究を開始【プレスリリース】

本研究では、東北メディカル・メガバンク機構（機構長 山本 雅之、以下、ToMMo）と株式会社ヤクルト本社（社長 根岸 孝成、以下、ヤクルト）は、腸内細菌叢*1を標的とした新規の疾患予防法や治療法の創出、予防医学に基づく乳酸菌飲料および発酵乳の生理的意義を明らかにすることを目的とした共同研究を開始しましたのでお知らせします。
Questionnaire survey (Started on August 2017)
Investigate detailed information on dairy products containing probiotics. About 40,000 participants answered the questionnaire.

Most of dairy products are covered and they are ordered according to sales volume.

Study regarding intestinal flora (Started on April 2018).
The first wave collection has completed (about 2700 samples).
Potassium (vegetables and fruits etc.) intake is inverse blood pressure (INTERSALT Co-operative Research Group. BMJ 1988)

The balance between sodium intake and potassium intake (sodium to potassium ratio: Na/K ratio) has been drawing attention recently.
Add physical activity monitor, Na/K ratio monitor, and Sleep monitor on our second wave study.
OMRON Healthcare Co., Ltd. developed a handy-sized urinary Na/K ratio monitor. It can quickly and easily measure Na/K ratios from urine sample for long-term.

ToMMo began a collaborative study in June 2017 with OMRON Healthcare Co., Ltd.
Relationship between Hypertension and day1 to day1-4 Na/K ratio

**Day 1**

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**Day 1+Day2**

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**Day 1+2+3**

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**Day 1+2+3+4**

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Prevalence of home hypertension per one unit increase in urinary Na/K ratio from 1 day to 10 days about 3000 data

The aOR of home hypertension per one unit increase in urinary Na/K ratio increased from 1 days to around 5 days.
The aOR of home hypertension per one unit increase in urinary Na/K ratio was stable after around 6 days

We also published sleep efficiency and hypertension. Poor sleep efficiency associated with higher prevalence of hypertension.

Conclusion

• We have established community-based and three generation cohorts after Great Eastern Japan Earthquake.

• We have reported several effect of damage from GEJE on community health.

• We have also collected information on genome metabolome, and several add-on measurements.

• We have started several set of data distribution.

• We have collaborated with industrial companies.

• We consider that using our data accelerate health information.

• We would like to ask your good practice.