Representatives from Illumina and ToMMo pose with a NovaSeq X System at ToMMo's sequencing facility in Sendai, Japan, April 2024

A landmark Japanese study reaches 100,000 genomes

The ToMMo Project is linking individual health and genomic data to understand dementia, disease, and more in the nation's population

THE TOHOKU MEDICAL MEGABANK Organization (ToMMo) was born from tragedy. In 2011, the Great East Japan Earthquake, the most powerful in Japanese history, and the associated tsunami destroyed large parts of the Tohoku region. Because it was close to the quake's epicenter, Tohoku University proposed the creation of a large biobank, both to advance medical research capabilities in the wake of the catastrophe and to help redevelop the devastated economy.

Relying heavily on Illumina instruments, ToMMo set the challenging goal of sequencing 150,000 people—and it recently achieved the milestone of 100,000. In addition to the genomic data, the bank has gathered health records and other information to better understand how a person's genotype influences their health.

This data will help researchers interpret the genomic variations that affect the Japanese population, refine reference genomes, and develop genomic arrays that are better at detecting single-nucleotide variations. The project is also embracing metabolomics, microbiome analysis, and other approaches to support personalized care. The results will diversify sequencing data and advance precision medicine.

"Japan is one of only a handful of countries that have sequenced so many genomes at this scale," says Arjuna Kumarasuriyar, PhD, Illumina's general manager in Japan. "We now have a tremendous opportunity to integrate this data with similar work being done all over the world to create a much better map of human diversity."

A two-pronged approach

To better assess the population's genomics, the project was divided into two studies: the Community-Based Cohort and the Birth and Three-Generation Cohort.

ToMMo researchers brought in Community-Based Cohort Study participants through their regular medical checkups, with around 70% participation. The team ultimately recruited more than 87,000 people in the Miyagi and Iwate prefectures, just north of Fukushima, which were both heavily affected by the earthquake and tsunami.

The researchers surveyed participants to learn more about their lifestyles, how the disaster affected them,

and other health-related data. They also collected blood and urine samples, conducted carotid echography to check vascular health, measured bone density, performed respiratory examinations, monitored oral health, and more. These approaches helped the group assess the disaster's impact and identify potential biomarkers that could advance personalized care.

The Birth and Three-Generation Cohort Study brought in more than 73,000 people, mainly from Miyagi. Pregnant women were recruited at obstetric facilities, and family members were also asked to join. This longitudinal study will follow participants for many years to understand how diseases develop and affect people at different stages of their lives.

In addition to meeting challenges inherent to any large genomic initiative (such as obtaining informed consent from 150,000 people), ToMMo has accomplished a lot with scarce resources. Starting in 2012, the team accumulated data in relatively small increments—a thousand participants at a time. However, as the group began to publish, fellow researchers, pharmaceutical companies, and the Japanese government increased their investment.

Improved technology helped as well. As sequencing and analysis sped up and costs came down, it became easier to conduct these massive studies. Without these advances, it's unlikely the project would have come so far, so fast.

Wide-ranging Illumina support

Illumina has been part of ToMMo from the beginning, initially by supplying HiSeq Systems, and most recently NovaSeq X Plus Systems. The company is also helping the ToMMo team improve their data analysis.

"Japanese institutions have been quite reliant on supercomputers, which have limitations," Kumarasuriyar says. "We are helping them transition to cloud-based solutions, such as DRAGEN on Illumina Connected Analytics, which also supports better variant detection."

Illumina is also helping ToMMo connect with pharma companies to possibly translate some of their discoveries into new therapies. This data could support more effective drug discovery, particularly for people of Japanese descent, and provide insights into how genomic variations influence drug efficacy.

"Studies like these pave the way to implement genomic medicine in Japan and other countries," Kumarasuriyar says. "The country has an excellent health care system, and now they will have the genomic data to make it even more effective."

An age of discovery

Because ToMMo has linked genomic and individual health data, it is gaining detailed information about how genotypic and phenotypic variations affect health, and its longitudinal approaches will yield long-term records showing how diseases evolve.

One high priority for the organization is dementia. Japan and many other nations face aging populations, and divining the genetic contributors of dementia could lead to improved treatments. In addition, the Birth and Three-Generation Cohort Study aims to produce more granular data about child development, while the project's Undiagnosed Diseases Initiative seeks to better understand rare genetic diseases.

These findings will help round out available global genomic data, since most research to date has been conducted on European populations. Focusing exclusively on large Japanese cohorts should shed more light on the full picture of human genetic diversity.

"There may be opportunities to rescue drugs that failed in early-stage clinical trials because of an unknown adverse effect," says Kumarasuriyar. "If we can pinpoint the genetic factors, and combine them with companion diagnostics, it may still be possible to take that drug to market in a way that improves both safety and efficacy."

The big picture

ToMMo will continue to sequence participants and provide long-term follow-ups. By better understanding the relationships between genetic factors and diseases, they hope to develop new clinical tools, such as polygenic risk scores, to help people understand their health risks and improve care.

There are also efforts to integrate information from ToMMo with other biobanks in the country, such as Biobank Japan, to create an even richer dataset. This virtual biobank could eventually exceed 500,000 samples.

"There are few efforts around the world that are looking at this kind of depth of phenotypic information," Kumarasuriyar says. "They have longitudinal, as well as proteomic, metabolomic, and other data. This is a massive foundation to adopt whole-genome sequencing to advance patient care." ◆