RENÉE ALTROV FOR *NATURE*

A BANKER OF GENOMIC POTENTIAL

At the Estonian Genome Centre, Lili Milani and her team are investigating the impact of genetic variations on drug metabolism and adherence to prescriptions. She spoke with Bec Crew.

The Estonian Genome Centre at the University of Tartu is one of the largest biobanks in Europe, containing biological samples and personal health information volunteered by more than 150,000 people, over 20% of the country's adult population. This trove of data and materials is emblematic of Estonia's ambitious personalized medicine programme and drive to be one of the world's most advanced digital societies. It is a resource for genome-wide association studies to identify genetic variations linked with disease detection, treatment and prevention.

At the heart of the Estonian initiative is geneticist Lili Milani, group leader in pharmacogenomics at the biobank and one of the leading biomedical researchers by article count in the Nature Index.

Which conditions are you investigating?

My group focuses on adverse reactions to drugs, as well as on problems with adherence — patients not taking their medications as prescribed. These issues are seriously underreported, so we need to be creative in trying to discover genetic variants that are associated with poor treatment response or side-effects.

We are using biobank samples to look at the genetic effects and associations that may cause discontinuation of medications such as antidepressants or statins. We can do this in Estonia because we have such rich electronic health records. We're working on this with colleagues from Finland and Norway, and feeding a lot of information into the Estonian National Personalised Medicine Initiative.

What have your studies revealed?

A person's specific genetic variants affect how quickly he or she metabolizes certain drugs. These results are being published by the Clinical Pharmacogenetics Implementation Consortium, an international group of volunteers that provides recommendations for healthcare professionals on dosing or drug selection based on genetic variants. Our latest study took these guidelines and genotype data in the biobank, and translated them into specific plans of action for the participants. In one case, a biobank volunteer had been prescribed two different antidepressants and had experienced serious side-effects. She got her genetic report and discovered that she's actually a very slow metabolizer of both medications, and needed much smaller dosing. Prior knowledge of this information could have really helped.

How does the biobank inform research?

Our data reflect the general population, which is why we deal mostly with common disorders such as cardiovascular disease and type 2 diabetes. We work with many international consortia, including the UK Biobank, which has about 500,000 samples, and deCODE in Iceland, with roughly 130,000. Sweden and Finland and the other Nordic countries also have a lot of clinical biobanks, and those collections are also valuable.

Why is the Estonian biobank so large, relative to its population?

Since the launch of the Estonian biobank in 2000, we have been using the genotype and health data of the first 50,000 participants for large genomic studies. We've been very active in communicating the results to the general population through the media, which has created great awareness and interest in genomics.

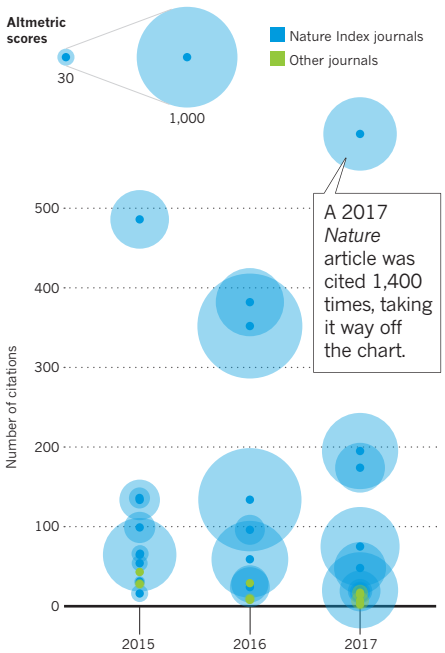
With a lot of excellent IT systems in place, and with genetic findings that could be used to improve health care, Andres Metspalu, director of the Estonian Genome Centre, came up with a vision about five years ago for implementing personalized medicine to prevent common complex diseases. After a few years of studies showing the increased incidence of disease among individuals with a high genetic risk, the Ministry of Social Affairs decided to fund the biobank with €5 million in 2018 to increase the sample size with 100,000 new participants, and to launch the national programme for the implementation of personalized medicine.

Can you elaborate on how the biobanks around Europe work together?

Our team mostly collaborates through the BBMRI-ERIC, which brings together researchers, biobankers, industry and patients from 20 countries, making it one of the largest research infrastructures in Europe. Meanwhile, scientists mostly collaborate directly. If I'm working on a specific phenotype, I will look for scientists with similar data sets. Usually we build capacity by running analyses locally, and then running meta-analyses together.

RESEARCH RECORD

Lili Milani's publication history. Each small dot represents one paper published in one of the journals tracked by the Nature Index. Some dots overlap. Citation figures correct as at 12 April 2019.



SOURCE: NATURE INDEX/DIMENSIONS FROM DIGITAL SCIENCE

Different consortia have different routines. There are regular teleconferences and webinars, but usually we interact with the writing groups — the papers' lead authors. They have the task of specifically sharing the analysis plans and interacting with all the analysts to get the results, that is, the input on cohort and data that should be reported back. Then a draft of the manuscript is circulated. My record is running such studies with two or three cohorts and 15 to 20 co-authors. I found that challenging, so I really admire the principal investigators who are managing more than 100 co-authors. Although most of the communication and collaboration is done via e-mail, chats and video/teleconferences, the highlight is always meeting up at conferences, such as the American Society of Human Genetics annual conference.

How did you get into the field?

I've always found genetics fascinating. I started as a student in gene technology at the University of Tartu, and ended up doing my PhD in molecular medicine at Uppsala University in Sweden. The advances in technology over the past 20 years have been amazing. In 2005 we were printing our own microarrays and trying to simultaneously sequence hundreds of SNPs — single nucleotide polymorphisms, the most common type of genetic variation. Then in 2006, Illumina came to the market with machines that allowed us to analyse hundreds of thousands of SNPs in parallel on a single microarray. I'm just as excited now as I was when I started.

What has your experience been like as a woman in the field?

I've been lucky. My mentor and supervisor during my PhD studies, Ann-Christine Syvänen, was one of the few women in the field back then. My postdoc supervisor at the Estonian biobank was also very supportive when I was raising small children. He once asked me to go to a conference and I said, "I can't go; my son is nine months." He said, "Don't say you can't go. Just tell me what you need to make it possible."

He said the institute would send a babysitter with me and cover the costs, and it showed me that there is always a way. I felt empowered. And although I did not want the institute to pay, I realized that I could take my dad along with me and pay for his ticket myself. It was such an easy solution and it was an excellent conference that gave me lots of new ideas and enthusiasm.

What is your ultimate research goal?

I used to be more interested in molecular mechanisms and functional studies around genomics. Since we launched the personalized medicine initiative, I'm very motivated to run research projects with results that can be implemented in the near future. With all the outreach that we've done, in the hopes of getting general support for increased scientific funding and our work in general, I feel a responsibility to deliver some kind of scientific output that people will benefit from sooner. ■

Leading authors

Based on article counts higher than 50 between 2015 and 2017 in biomedical sciences in the Nature Index

KARL DEISSEROTH
Bioengineer, neuroscientist
Stanford University

Credited with developing neuroscience techniques, including optogenetics, which uses light to control cells such as neurons in living tissue, lauded as the most precise known method for studying the brain.

STEVEN P GYGI
Cell biologist
Harvard Medical School

Develops and applies new technologies in mass spectrometry and proteomics (the large-scale study of proteins). Jointly credited for the BioPlex network, with 9,000 proteins the largest open access resource for studying protein interactions.

ALBERT HOFMAN
Epidemiologist
Harvard T.H. Chan School of Public Health

A world leader in the epidemiology of common neurologic and vascular diseases, such as dementia and stroke; author of influential studies on the role of vascular factors in Alzheimer's disease.

KÁRI STEFÁNSSON
Geneticist
University of Iceland

Has published widely on the genetics of common and complex diseases and is a leading figure in the identification of genetic risk variants in the genome.

BO TANG
Chemist
Shandong Normal University, China

Research on application of nanomaterials and molecular probes in biochemical analysis, clean synthesis of chemicals, and technologies for solar power generation and storage. ■

SOURCE: NATURE INDEX/DIMENSIONS FROM DIGITAL SCIENCE

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DECODE GENETICS