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NYGC Psychiatric Disease Database Project Aims to Kickstart Precision Medicine for Mental Illness

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NEW YORK – Researchers from the New York Genome Center, working with the New York State Office of Mental Health (OMH) and a group of local medical centers, plan to build a vast clinico-genomic database focused on severe mental illnesses, including schizophrenia and bipolar disorder.

The aim is to collect and collate the information necessary to enable precision medicine for these illnesses, including tools for more accurate diagnosis and prognosis, and to build a resource for drug companies hoping to advance new therapies.

Called the Genomic Medicine for Mental Health Advancement (GeMMA) initiative, the effort was first proposed in 2020. Two years later, the team leading the project is on the cusp of obtaining the funding to begin its first recruitment and sequencing efforts, though they declined to provide details.

According to Tom Maniatis, NYGC's scientific director and CEO, while various genomic studies have now tackled psychiatric diseases like schizophrenia and bipolar disorder, along with neurological conditions like autism, what's been lacking is matched comprehensive clinical data.

Thus far, clinical implementation of genomics in psychiatry and mental health has been limited to pharmacogenomic testing, still greeted with some skepticism, along with more recent forays into polygenic risk scores that also face challenges.

Maniatis said that the time seems to be ripe for taking big next steps, citing a recent move by genomic big data company Tempus into neuropsychiatry as an example.

"Psychiatry is especially important, I think, [because of] the fact that in contrast to diseases of aging like Alzheimer's and cancers, psychiatric diseases emerge in adolescence, and they're with you the rest of your life," Maniatis said. "This has enormous consequences for families and society as a whole … so in many ways, it's one of the most important areas that we should be doing genetics [in]."

Progress made by previous studies has been significant, he added, but without being able to link genomic findings with information about patients' psychiatric history, their medications, and their overall care, molecular discoveries have failed to translate into better diagnoses and new treatments.

At the NYGC, a neuropsychiatric working group began discussing the possibility of creating a very large cohort that could be linked to robust longitudinal clinical data, Maniatis said.

While this might not be possible in other contexts, the New York state health system is organized in a way that enables such a project via an OMH database called PSYCKES (Psychiatric Services and

Clinical Knowledge Enhancement System), which Maniatis said includes 8.5 million patients, many of whom are or have been treated at the Genome Center's partner hospitals.

The database contains health records from patients who receive behavioral health services or psychotropic medication that are paid for by Medicaid, a population Maniatis highlighted as having an "extraordinarily diverse demographic makeup," which ensures a deeply population-representative research resource.

The plan for NYGC and its clinical partners at Mount Sinai, Columbia University, New York University, and Northwell Health is to consent patients whose data is available in PSYCKES to submit samples for whole-genome sequencing.

"Because the cost of sequencing has come down so much, and the time it'll take to recruit this cohort, we're absolutely committed to whole genomes," Maniatis said. "This is really important because … of where the variants that associate with these diseases lie — 99 percent of the genome is represented."

Maniatis highlighted Sander Markx at Columbia as a collaborator who has made significant strides in studying severe psychiatric illness, something crucial for the success of GeMMA moving forward.

"He has actually been accessing this population for many years and was recently part of an amazing [schizophrenia] study in which they specifically looked for really extreme cases," Maniatis said. "What was remarkable in that study was that they were able to detect variants in genes that could only be seen by much, much larger studies in the general [schizophrenia] population."

GeMMA's success will require effective patient engagement in a challenging population. "Doctors and nurses that are trained in accessing patients like this are really important," Maniatis said. "You can imagine that many of these patients can only be accessed through their families because their disease is so severe. But again, because we are working with the Office of Mental Health and these psychiatry departments, we believe that we'll have the expertise to be able to do this."

"When you look at the history of mental health in New York, like in most other places, they closed down all of the severe psychiatric hospitals in the '60s and '70s," he added. "The cases in Markx's study were taken from the remaining serious psychiatric hospitals in New York. But they constitute a tiny fraction of what they used to be. And so many of these people are on the streets, and that's a big problem, but I think that the fact that Sander could consent these really severe cases was a good sign that it's feasible to do this project."

Calling the effort a "massive undertaking," Maniatis said it will probably require 10 years to collect the hundreds of thousands of samples he and his colleagues are aiming for.

"But of course, as we go along, there will be constant access to the data. So it'll be impactful earlier than that," he said.

The hope is that the resulting linked clinical and genomic data will help improve diagnostic efficacy for these disorders, offering earlier and more sensitive measures of disease. It would also certainly accelerate therapeutic discovery, Maniatis said, with drug companies able to access this resource.

Although he declined to discuss funding details, he said the team believes it can get started "very soon" with collecting patients and running them through the program.

A few details still need to be worked out, including a sampling strategy. "We have to make a decision about whether to use blood or saliva to do the sequencing. Blood is more expensive and requires trained nurses and so on. Saliva doesn't, but it's contaminated with bacteria, so we are planning to do a very comprehensive study on that," Maniatis said.

A previous study under the SPARK Autism initiative found that a very high percentage of saliva samples were suitable for sequencing, but the group needs to test if the same holds true for this unique population.

"I think that because this [severely ill] population is somewhat hidden, it doesn't get a whole lot of publicity except when some horrible thing happens … and so a part of this program really has to be to publicize more effectively just how serious this is, and that we have the opportunity to really do something," Maniatis said.

However, because psychiatric conditions often overlap and diagnosis involves a great deal of subjectivity, the cohort will likely also yield information across other conditions like depression and anxiety, he added.

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