Largest-ever autism genome study finds most siblings have different autism-risk genes

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Quinn, an autistic boy, and the line of toys he made before falling asleep. Repeatedly stacking or lining up objects is a behavior commonly associated with autism. Credit: Wikipedia.

The largest-ever autism genome study, funded by Autism Speaks, reveals that the disorder's genetic underpinnings are even more complex than previously thought: Most siblings who have autism spectrum disorder (ASD) have different autism-linked genes.

Led by the director of the Autism Speaks MSSNG project, the report made the cover of today's *Nature Medicine*.

Simultaneous with publication, the study's data became part of the historic first upload of approximately 1,000 autism genomes to the Autism Speaks MSSNG portal in Google Cloud Platform. Autism Speaks is making the de-identified data openly available for global research in order to speed understanding of autism and the development of individualized treatments.

"This is a historic day," says study leader Stephen Scherer, "as it marks the first time whole genome sequences for autism will be available for research on the MSSNG open-science database. This is an exemplar for a future when open-access genomics will lead to personalized treatments for many developmental and medical disorders." In addition to leading Autism Speaks' MSSNG program, Dr. Scherer directs the Centre for Applied Genomics at Toronto's Hospital for Sick Children and the McLaughlin Centre at the University of Toronto.

"By using the cloud to make data like this openly accessible to researchers around the world, we're breaking down barriers in a way never done before," says Robert Ring, chief science officer of Autism Speaks and co-author on the *Nature Medicine* paper. "As always, our goal at Autism Speaks is to accelerate scientific discovery that will ultimately improve the lives of individuals with autism at home and around the world."

In total, the MSSNG project aims to make at least 10,000 autism genomes available for research, along with a "tool box" of state-of-the-art tools to aide analysis.

Autism's Surprising Diversity

In the new study, Dr. Scherer's team sequenced 340 whole genomes from 85 families, each with two children affected by autism. The majority of siblings (69 percent) had little to no overlap in the gene variations known to contribute to autism. They found that the sibling pairs shared the same autism-associated gene changes less than one third of the time (31 percent).

The findings challenge long-held presumptions. Because autism often runs in families, experts had assumed that siblings with the disorder were inheriting the same autism-predisposing genes from their parents. It now appears this may not be true.

"We knew that there were many differences in autism, but our recent findings firmly nail that down," Dr. Scherer says. "We believe that each child with autism is like a snowflake - unique from the other."

"This means we should not be looking just for suspected autism-risk genes, as is typically done in diagnostic genetic testing," Dr. Scherer adds. "A full assessment of each individual's genome is needed to determine how to best use knowledge of genetic factors in personalized autism treatment." Whole genome sequencing goes far beyond traditional genetic testing to analyze an individual's complete DNA sequence.

Known autism-risk genes showed up in 42 percent of the families participating in the study. "This may help explain why autism came about in their child or provide insight into related medical conditions," Dr. Scherer says. In a 2013 pilot genome sequencing study, Dr. Scherer's team identified autism-linked genes in more than half of 32 participating families. That study provided several families with medically important information.

More information: *Nature Medicine*, DOI: 10.1038/nm.3792"

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Provided by Autism Speaks