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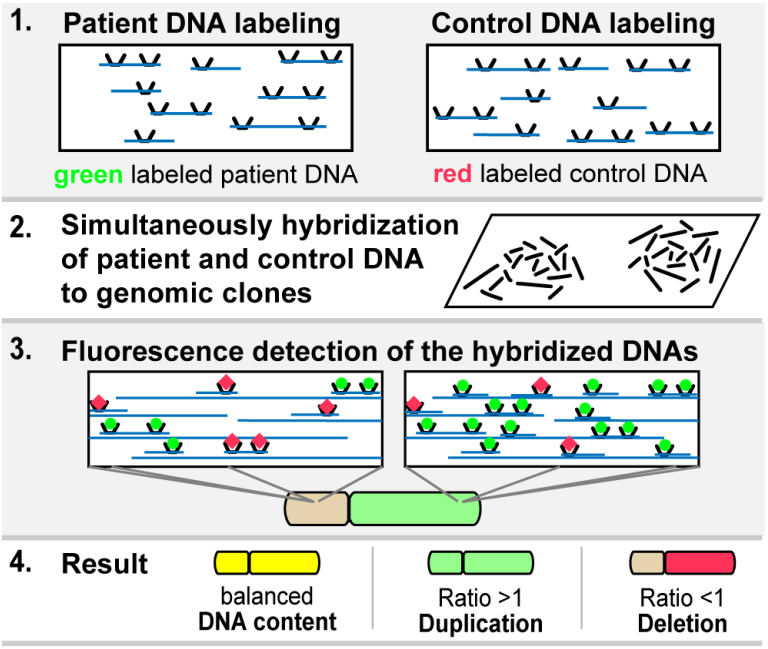
Testing Adults for Genetic Causes of Autism

by Sally James

Young adults and their families may discover crucial details about the possible genetic causes of autism thanks to a partnership between Fuki Hisama, M.D., Associate Professor of Medicine and Gary Stobbe, M.D., Clinical Assistant Professor of Neurology. The two recently completed research based on evaluating adults with autism, which has not been a widespread practice. Hisama is the Medical Director of the University of Washington's Genetic Medicine Clinic based at the Center on Human Development and Disability. Within this larger clinic, an Autism Genetics Clinic has been established by Hisama. Typically, autism clinics have answered questions of parents with newly diagnosed children, but Hisama and Stobbe decided to expand it to help families whose children were now adults. The rapid changes in what is known about the genomics of autism mean that those individuals diagnosed just a few years ago may have not been given as much information about possible genetic underpinnings as those diagnosed today. "The identification of a specific diagnosis is welcome information for families," Hisama said.



Chromosome microarray

Two particular reasons emerged among families seeking detailed genetic information for their adult children. Parents sought reassurance that they did not cause or contribute to their child's autism. "Parents often hold on to the idea that they did something wrong," Hisama said. In many cases, genetic evidence showed that their child's disability came from a genetic trait and not environmental factors. For many, that news is both powerful and emotional. One other reason for testing was to allow family or siblings of the child with autism to know if there was a heritable trait that they might carry. In that case, they might seek counseling or prenatal testing for their own children. "There is a reason to provide genetic risk counseling to the siblings of reproductive age," Hisama explained. Of course, the patients themselves might also wish for news of significance for potential offspring.

In some cases, news from the testing pointed the way to medical treatment or behavioral issues that were not obvious before testing. However, not every patient received conclusive information. If a genetic variation is of unknown significance, future research may become helpful for patients. Hisama said her team recommends genetic evaluation for adults with autism spectrum disorders but there are not many clinics nationwide that have genetic services for adults with these disorders. There is also a lack of awareness by general practice physicians about these services and their potential value to adult patients and their families.

Stobbe is director of a clinic focusing on the transition to adulthood for children with autism through Seattle Children's and refers patients to the CHDD Autism Genetics Clinic. He was a co-author on an article with Hisama about adult testing that was recently published in the journal *Genetics in Medicine*. Patients who were tested at the genetics clinic received results from a genetic counselor there, but also discussed their results with Stobbe.

In the recent study, 34 patients with a confirmed autism spectrum disorder diagnosis underwent evaluation, and 23 were tested by a method known as array comparative genomic hybridization or ACGH. Hisama said she was surprised that of the 23 patients tested, 39 percent had genetic variants, including 17 percent with abnormal or likely pathogenic abnormalities, and an additional 22 percent had variants of uncertain significance. In published studies in the pediatric population, array testing usually yields between 5-18 percent genetic abnormalities.

ACGH is also known as chromosomal microarray analysis. It is a technique that allows very careful comparison to show differences between a patient's DNA and that of a typical control. These include deletions (the absence of genetic material) or duplications (extra copies of genetic material) called copy-number variations. For example, a chromosome that normally has sections A-B-C-D might have A-B-C-C-D. Research is ongoing to understand which variations have a relationship to disease and which may not. In one CHDD Outlook story from last year, Hisama explained that there is a worldwide effort to find all the genes that contribute to various forms of autism. So far, several dozen have been implicated. Many of these genes lie within pathways known to control the development of neural signaling mechanisms in the brain.

The CHDD clinic sees over 2,000 patients every year. This makes it one of the largest genetics clinics in the United States, according to Hisama. One of her hopes is that more primary care providers will refer patients to genetics clinics. Another technology on the horizon is called exome sequencing and, as this becomes more widely available, it will shine a new light for patients and families. The exome is the protein-coding part of the genome, referred to as the "functional" part. It is less costly to sequence than the entire genome. Many genetic studies have required large families with multiple affected families members, or been conducted in large populations, but exome sequencing can allow a laboratory to find a rare variation that might explain a single patient's symptoms. Hisama predicted that exome sequencing may be more widely available to patients within the next few years.

CHDD is an interdisciplinary center dedicated to the prevention and amelioration of developmental disabilities through research, training, clinical service, and community outreach. CHDD includes the University Center of Excellence in Developmental Disabilities and the Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Center.

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