Genetics Can Provide Answers for Parents on the ‘Diagnostic Odyssey’

by Joel Schwarz

Parents who embark on the once frustrating journey that Fuki Hisama, M.D. characterizes as the “diagnostic odyssey” are looking for reasons why their child has been diagnosed with an autism spectrum disorder (ASD); reasons that were difficult to provide only a few years ago. Recent advances in medical genetics, such as the use of chromosomal microarray analysis (CMA), are making it possible for clinicians in some cases to give parents solid answers. Hisama, the medical director of the University of Washington’s Genetics Medicine Clinic based at the Center on Human Development and Disability, has established an Autism Genetics Clinic to address those issues.

“What we do in our clinic is true translational medicine by taking laboratory research findings and putting them into our practice,” said Hisama, who is also an associate professor of medicine and neurology. She was one of the authors of a 2010 paper in the journal Pediatrics that recommended using CMA as part of the initial diagnostic evaluation for patients with ASD. The American College of Medical Genetics and the American Society of Human Genetics have since adopted that recommendation. CMA is used at the UW where the technique is applied by the Department of Pathology’s Cytogenetics Laboratory. “CMA provides higher detection rates that are at least double those of other methods for all kinds of genetic conditions including ASD,” Hisama said.

Genetic testing for autism is important because it gives clinicians a way of explaining the genetic implications of an ASD diagnosis to a parent. “It is the most accurate way of giving parents an idea of the risk that any subsequent children might have ASD,” she said. Because genetic factors are responsible for a substantial portion of all ASD cases, there is a worldwide effort to identify all of the genes that contribute to the various forms of autism. So far, several dozen genes have been implicated, but this search has been complicated by the fact that autism often appears to be caused in part by de novo, or spontaneous genetic changes, according to Hisama. These changes can be copy number variations or alterations of DNA that have an abnormal numbers of copies of one or more sections of the DNA. These variations can be either deletions or duplications...
of parts of a chromosome. This means that a chromosome that normally has sections marked A-B-C-D, might have a deletion such as A-C-D or a duplication like A-B-B-C-D.

While the search for the genes contributing to ASD goes on, researchers also are trying to determine if there are individual genetic “recipes” for the various types of ASD. However, it is known that most of the candidate genes for ASD that have been identified thus far encode proteins that are involved in neural development and function. “This is important because it may help us to direct future treatments for ASD. It potentially suggests targets for pharmaceuticals and for the timing of treatment since this happens on the background of brain development,” Hisama said. If all of the genes involved in causing a specific type of ASD were identified “it would open up many possibilities on the clinical side including offering a ‘genetics first’ approach to treatment. We could institute therapy to counter the morbidity that comes from that condition. We also could look for other new avenues for treatment. Will genetic diagnosis change people’s treatment? We are not there yet, but we know we can improve patient outcomes with early diagnosis and intervention.”

While most of Hisama’s time is taken up by seeing patients, directing the Genetics Medicine Clinic and training residents who will make up the next generation of clinical geneticists, she still maintains a research agenda. In one project, with Dr. Gary Stobbe, a University of Washington clinical assistant professor of neurology, Hisama is in the early stages of looking at the spectrum of identifiable genetic causes of autism in young adults 18 to 40. They are trying to determine if the genetic causes and diagnostic yields are different in an adult population versus a pediatric population because many of these patients never had genetic testing when they were younger, and because the techniques for testing have improved.

To make an appointment in the Genetics Autism Clinic call 206-598-4030.