Researchers move 2 steps closer to understanding genetic underpinnings of autism

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Today's issue of the *American Journal of Human Genetics* (AJHG), describes what might be a corner piece of the autism puzzle—the identification and subsequent validation of a gene linked to the development of autism by three separate groups of scientists. An accompanying commentary by Dr. Dietrich Stephan, Director of the Neurogenomics Division at the Translational Genomics Research Institute's (TGen), further explains the findings.

Autism is a perplexing disease whose cause remains unexplained. It has long been suggested that environmental factors, linked with genetics, play a role in causing the disorder. As recently as last week, researchers in California published a study that found no proof linking autism with a mercury-based preservative found in childhood vaccines. While there are no clear-cut answers, researchers are one step closer to understanding autism's genetic cause.

In March 2006, Dr. Stephan, Director of TGen's Neurogenomics Division, led a team of researchers at TGen and collaborators at the Clinic for Special Children (CSC) in Strasburg, PA, that identified a gene called CNTNAP2. When mutated, this gene indicated a predisposition to autism in a specific population of Old Order Amish children from Pennsylvania.

One of the most important principles in science is the ability to replicate

results. Now, three groups of researchers from Yale University, the University of California, Los Angeles, and the Johns Hopkins University, have replicated the initial finding in the general population, unequivocally implicating this gene as causing the newly defined Type 1 autism. All three studies plus Dr. Stephan's commentary are published in the January edition of AJHG.

According to Dr. Erik Puffenberger, Laboratory Director of the Clinic for Special Children, "Our previous finding of association between loss of CNTNAP2 function and autistic behavior has been validated in the general population. This is a very exciting step for autism research. It also highlights the enormous potential of the 'small science' approach. Our initial work used only four affected Amish children. Careful study of these four patients uncovered the association between CNTNAP2 and autistic behaviors. From that small beginning, CNTNAP2 has now been implicated as a significant risk factor for autism."

Autism spectrum disorder (ASD) is a broadly used term for a set of developmental disorders that emerges in infants and young children. ASD impairs a child's intuitive thought, language and social development to varying degrees. Most individuals diagnosed with ASD require lifelong supervision and care; the most severely affected are unable to speak. ASD is the fastest growing developmental disability in the U.S. Two decades ago, roughly one child in 10,000 was diagnosed with ASD; it now affects one in 150 births.

"The field of genetics is replete with examples where researchers are unable to reproduce results. Here we have independent confirmation in multiple groups using large samples sizes," said Dr. Stephan. "Now that the results of the initial CNTNAP2 gene finding have been replicated, it strongly supports the notion that the 'broken version' of CNTNAP2 is recognized as a cause of autism in the general population."

In collaboration with the Phoenix-based Southwest Autism Research & Resource Center (SARRC), a nonprofit community-based organization dedicated to research, education and resources for individuals with ASDs and their families, TGen will apply these research findings to children in Arizona who have been diagnosed with ASD.

“The heterogeneity of the disorder has frustrated our past efforts in the search for causes of autism,” said Dr. Raun Melmed, medical director and co-founder of SARRC. “This exciting discovery will further our capacity to individualize approaches to the diagnosis and treatment of autism.”

The next step, noted Dr. Stephan in the commentary, is to develop a diagnostic to test for the CNTNAP2 mutation. If physicians could implement behavioral interventions early enough, children with autism may have a better chance of developing normally.

Source: The Translational Genomics Research Institute