

An International Consortium Receives 12 Million Dollars from The National Institutes of Health in the United States of America to Study the Brain and Behavior in Individuals with 22q11.2 Deletion Syndrome

An international collaboration has received \$12 million from The National Institute of Mental Health of the National Institutes of Health to study the genetics of the brain and behavioral disorders, in particular psychiatric illnesses such as schizophrenia, associated with chromosome 22q11.2 deletion syndrome, a multisystem disorder which includes birth defects and developmental and behavioral differences across the life span.

The International Consortium on Brain and Behavior in 22q11.2 Deletion Syndrome is a large-scale effort among 22 clinical institutions and 5 genetics focused centers across North America, Europe, Australia and South America, led by The Children's Hospital of Philadelphia (CHOP) and the Perelman School of Medicine at the University of Pennsylvania (Penn).

Researchers will investigate the genetic reasons for the associated rates of schizophrenia (~25%) and other behavioral and intellectual disabilities in people who are affected with Chromosome 22q11.2 deletion syndrome.

Found in approximately 1 in 1,000 live births, 22q11.2 deletion syndrome has many possible signs and symptoms that can affect almost any part of the body, including heart abnormalities that often require surgery in the newborn period, an opening in the roof of the mouth, trouble fighting infection due to a poorly functioning immune system, seizures due to low calcium, and significant feeding and swallowing issues. Affected individuals may also have additional medical problems such as breathing difficulties, kidney abnormalities, scoliosis, and hearing loss. In contrast, some individuals with the 22q11.2 deletion have none of these medical issues. However, most children have developmental delays, including delayed acquisition of motor milestones as well as significant delays in emergence of language, and learning disabilities. Moreover, some children have autism or autistic spectrum disorder, ADHD, OCD, and anxiety. Later in life, persons with the 22q11.2 deletion are at an increased risk of developing mental illnesses such as schizophrenia, depression and anxiety.

"The funding from the NIH will provide us with the opportunity to advance the understanding of this under-recognized neurogenetic condition," said Raquel E. Gur, MD, PhD, Penn Medicine co-lead investigator, who is the director of the Neuropsychiatry Program and a professor of Psychiatry at Penn.

“The knowledge generated can provide a window to the brain that will benefit millions throughout the world.”

Beyond the potential for yielding a better understanding of a severe manifestation of 22q11.2 deletion syndrome, the results will help identify pathways leading to schizophrenia in the general population in a way that will inform novel treatments, she added.

There is a substantial risk for developing psychotic illness in approximately 25 to 30 percent of adolescents and young adults with 22q11.2 deletion syndrome. The illness presentation and course are similar to those of schizophrenia, which occurs in the general population at a much lower rate (about 1 percent).

The Consortium sites have extensive experience in applying sophisticated genetic and brain-behavior strategies to study individuals with 22q11.2 deletion syndrome and schizophrenia across the lifespan, and provide data on 1,000 well characterized individuals with the syndrome, the largest such available sample to date.

The genomic efforts will include whole-genome sequencing in order to uncover genetic variation that may contribute to the presence or absence of these features in individuals and may help predict who may or may not be affected with these problems in the future. Likewise, these studies may lead to better treatment strategies.

Donna McDonald-McGinn, MS CGC, Principle Investigator at the Children’s Hospital of Philadelphia and Co-Director of the Consortium, commented: “Not only does this successful application demonstrate the genuine commitment on the part of the National Institute of Mental Health to better understand the brain and psychiatric illness, but it highlights the need for such international collaborations, in this instance with 22 clinical and 5 basic science collaborating sites, all with extremely dedicated clinicians and researchers who have overcome the challenges of differing cultures, languages, time zones, and healthcare systems in working towards the common goal of improving patient care and long term outcome - truly an inspiring feat.”

In addition to Penn Medicine and the 22q and You Center at CHOP, participating academic sites in the United States include New York’s Albert Einstein College of Medicine, Duke University, Emory University, SUNY Syracuse, UCLA, , and UC Davis; with sites in Canada (Toronto), Europe (Leuven, Belgium; Marseille, France; Dublin, Ireland; Rome, Italy; Utrecht and Maastricht, the Netherlands;

Mallorca and Madrid, Spain; Geneva, Switzerland; Cardiff and London, United Kingdom); Tel Aviv, Israel; Australia (Newcastle); and Chile (Santiago).