Population Diagnostics, Inc. and The Hospital for Sick Children Discover Novel Genetic Variants Associated with Autism Spectrum Disorder

The Associated Press

MELVILLE, N.Y.--(BUSINESS WIRE)--Dec 10, 2012--Population Diagnostics, Inc. (“PDx”), a private company with a novel approach for systematically uncovering the genetic causes of disease as well as the genetic basis of drug efficacy and safety, together with collaborators from The Hospital for Sick Children (SickKids) in Toronto, reported today in the journal G3 (Genes│Genomes│Genetics) the discovery of a collection of gene variants for autism spectrum disorder. These variants confer clinical utility and will enable a new generation of early detection diagnostic tests that will be highly sought after by the patient community. The newly discovered variants will also provide insights into the emerging field of drug discovery for autism.

“Our collaboration with Population Diagnostics has been very fruitful,” said the primary investigator, Dr. Stephen Scherer at The Hospital for Sick Children. “We set out to understand microarray platform differences in c opy n umber v ariant (CNV) detection but because of PDx’s technical contribution, which delineates benign variants from those that are pathogenic, we were able to effectively interpret the genome at a higher resolution than obtained with previously utilized microarrays. This focused our attention on smaller variants associated with autism. Not only were we able to confirm variants in genes that we and others have previously discovered using alternate methods, but more importantly, we are pleased that an abundance of novel variants have been uncovered. We intend to report on additional discoveries in future publications that are based on an even finer-scale interpretation of the data in this joint project.” In addition to discovering sixteen novel genes associated with autism (many implicated in neurodevelopment), this study highlights the general importance of analyzing genomes specifically for CNVs, which is a type of genetic variant that can disrupt, delete, or generate multiple copies of a gene. However, the analytical tools that detect CNVs differ significantly in their output. For example, 64% of the CNVs observed in this study – using a high resolution platform specifically designed to detect CNVs – were missed in a prior CNV study that used SNP microarrays, which are not optimized for CNV detection because they were originally designed to detect another class of variants called s ingle n ucleotide p olymorphisms (SNPs). Many SNP-based studies did not yield sufficient medically useful information and the SNP microarray data were subsequently mined for the presence of CNVs, which is a suboptimal strategy. The size of CNVs that can be detected is a key difference, and in this study the researchers found that 75% of the CNVs missed by SNP microarrays were small and these afford a greater opportunity to pinpoint single genes involved in autism. A more refined analysis of the autism patients used in the present study is underway and is revealing additional small CNVs in novel autism genes as well as novel variants in previously known autism genes.

Population Diagnostics holds two US patents (7,702,468 and 7,957,913) that describe a method of comparison of CNVs in subjects with a given condition to those present in a cohort comprised of healthy individuals. By eliminating benign and irrelevant CNVs in such a comparison, one is quickly led to genes that are pathogenic, which can then be interrogated using higher resolution genetic analysis techniques such as sequencing. In addition to disease gene discovery, PDx's methods can also reveal genetic biomarkers applicable for patient stratification (optimization of clinical trials), such as genetically differentiating a drug responder from a non-responder (efficacy) or identifying individuals most likely to experience a serious adverse event to a given drug.

"The discoveries reported in this study underscore that the genetic landscape for autism involves numerous genes containing many low frequency genetic variants with large effect," said Dr. Peggy Eis, Chief Technology Officer at Population Diagnostics. "Collectively, these newly discovered genes from our collaboration with SickKids, along with novel genes from our finer-scale analysis that will be reported in a future paper, represent a significant portion of the unexplained genetic contribution to autism and greatly expand our understanding of the underlying genetic causes of autism. We are excited about the opportunity to accelerate their clinical use in diagnostic tests, as potential drug targets and as genetic biomarkers in therapeutics development." The US CDC estimates 1 in 88 children have autism. Genetics is believed to be the major causal factor, with up to 90% of cases having a genetic contribution. Rare gene variants are usually sufficient to cause autism by themselves. There is no single cause or type of autism. The average age of diagnosis is 4.5 years via observational methods and it is clear that the earlier the diagnosis the better the treatment outcome through early intervention modalities. With knowledge of the various genetic causes, a genetic test can be performed immediately after the birth of a child and provide the maximum opportunity for treatment. There are ~4 million live births in the US per year and 45,000 of these newborns will develop autism.

About Population Diagnostics, Inc. Population Diagnostics, Inc. (PDx, www.populationdiagnostics.com) is applying its discoveries in human genetics to the development of DNA-based diagnostics and personalized medicine tests. PDx's technology, which reveals the genetic causes of complex diseases such as autism, Parkinson's, Alzheimer's, and food allergies, enables development of early detection diagnostic tests that predict pre-symptomatically why some individuals will suffer from debilitating diseases while others will not. When applied to drug discovery, the technology enables pharmaceutical companies to develop targeted therapies and companion diagnostics. Its novel technology and exclusive products places PDx in a prime position to (i) transform how physicians diagnose and manage disease in their patients and (ii) enable pharmaceutical companies to expand the number of available therapies and market drugs with higher efficacy and safety.

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