Quest Diagnostics Discovers New Genetic Mutations Affecting Cystic Fibrosis Screening

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Company's Scientists also Enhance Industry Standards for Quality Screening in Three Articles Published in The Journal of Molecular Diagnostics

MADISON, N.J., April 27 /PRNewswire-FirstCall/ -- Quest Diagnostics scientists provide new insights into genetic factors affecting the accuracy and quality of Cystic Fibrosis (CF) carrier and newborn screening in three separate articles published in the May 2009 issue of The Journal of Molecular Diagnostics. Quest Diagnostics Incorporated (NYSE: DGX) is the world's leading provider of diagnostic testing, information and services.

The research may enhance the accuracy of carrier and newborn screening for CF, a genetically inherited disease that damages the respiratory and gastrointestinal systems. One in 29 Americans of Northern European Caucasian or Ashkenazi Jewish descent are symptomless carriers of the defective, or mutated, cystic fibrosis transmembrane regulator (CFTR) gene. A child whose parents are both carriers has a one in four chance of developing the disease.

"Taken together, these three papers demonstrate how the widespread and thoughtful experience with [cystic fibrosis] mutation testing and screening continues to reveal new insights about the mutational alleles of the CFTR gene and further refinements in how best to detect them and assure appropriate quality control while doing so," said Wayne W. Grody, M.D., Ph.D., professor in the Departments of Pathology and Laboratory Medicine, Pediatrics, and Human Genetics at the UCLA School of Medicine. Dr. Grody, who wrote the commentary "Cystic Fibrosis Testing Comes of Age(1)" in the journal's May issue, is not affiliated with the studies.

"Since the CFTR gene was discovered two decades ago this year, scientists have acquired significant insights into the genetics of CF, one of the most common autosomal recessive genetic disorders," said Charles (Buck) Strom, M.D., Ph.D., medical director of the genetic testing center of Quest Diagnostics Nichols Institute, the esoteric research, development and testing services operation of Quest Diagnostics. "As the world's leading provider of genetic testing for cystic fibrosis, Quest Diagnostics has been at the forefront of efforts to advance scientific understanding of the disease and promote testing quality across the laboratory industry. These efforts are noteworthy because insights into the more than 1,500 mutations affecting the CFTR gene are enhancing the medical understanding of cystic fibrosis as well as the mechanisms of other genetic diseases."

In "Apparent homozygosity of a novel frame shift mutation in the CFTR gene because of a large deletion,(2)" Strom and his colleagues at Quest Diagnostics present a patient with classic cystic fibrosis who exhibits previously undescribed (novel) mutations that include deletions, or the absence, of large parts of the CFTR gene. The investigators demonstrate that conventional screening techniques may not accurately identify both defective CFTR genes in patients who have inherited CFTR genes with large deletions. "The failure to identify these CFTR mutations in carriers could increase the potential that their family members are falsely identified as non-carriers," said Dr. Strom, lead investigator of the study. "Comprehensive mutation analysis using DNA sequencing and exon deletions/duplications is therefore important to resolve apparent homozygosity (the false appearance that the patient inherited the same mutations from each parent) for novel and rare mutations, some of which are currently found in recommended testing panels."

In "Identification of cystic fibrosis (CF) variants by PCR/oligonucleotide ligation (OLA) assay,(3)" Quest Diagnostics' scientists analyzed one million specimens in the Quest Diagnostics database in order to identify rare genetic variants that are potential sources of testing error. The investigators, led by Victoria Pratt, Ph.D., FACMG, chief director, Molecular Genetics, Quest Diagnostics Nichols Institute, identified eleven instances of "allele drop-out," or failure to detect a targeted mutation, for an aberrancy rate of less than 0.01%. "We concluded that the recognition and enumeration of such variants along with clinical information in CF testing is valuable in avoiding false-positive and false-negative results," Dr. Pratt said.

In addition, Quest Diagnostics, participated in a study coordinated by the Centers for Disease Control and Prevention's Genetic Testing Reference Material Coordination (GeT-RM) to develop a set of genomic DNA reference materials for CF mutations not currently included in a 23-mutation test panel recommended for carrier screening by the American College of Medical Genetics (ACMG) and the American College of Obstetricians and Gynecologists (ACOG). These additional mutations are currently offered in half of the nearly dozen commercially available test panels on the CF testing market, which has grown significantly since ACMG/ACOG made their first CFTR mutation screening recommendation in 2001.

"Accurate characterization of CF mutations is essential to promoting uniform standards and quality screening. Yet, the surge in CF testing demand caused by ACMG/ACOG's promotion of broader population screening has outpaced scientific efforts to characterize several mutations commonly found on test panels used in clinical practice and research," said Dr. Pratt, investigator of "Development of genomic reference materials for cystic fibrosis testing.(4)" "The establishment of genomic DNA reference materials will promote CF testing accuracy across the U.S. lab industry and may be expected to advance CF research and development."

Quest Diagnostics and Genetic Screening

Quest Diagnostics is one of the leading providers of pre- and post-natal and carrier genetic screening. In March 2009, the company announced that it operates one of only three laboratories approved by the state of New York to perform microarray-based comparative genomic hybridization (aCGH) postnatal testing, using its ClariSure aCGH postnatal test, for copy-number chromosomal abnormalities implicated in mental retardation, birth defects, and autism spectrum and developmental disorders. The company also provides a broad-based population screening technology designed to help determine whether parents are carriers of the genetic mutation that causes Fragile X syndrome, the most common form of inherited mental retardation. In 2002, the company launched its CF Complete test, which enables physicians to identify rare mutations that cause CF by sequencing the complete coding sequence of the cystic fibrosis gene.

About Quest Diagnostics

Quest Diagnostics is the world's leading provider of diagnostic testing, information and services that patients and doctors need to make better healthcare decisions. The company offers the broadest access to diagnostic testing services through its network of laboratories and patient service centers, and provides interpretive consultation through its extensive medical and scientific staff. Quest Diagnostics is a pioneer in developing innovative diagnostic tests and advanced healthcare information technology solutions that help improve patient care. Additional company information

is available at www.questdiagnostics.com.

(1) Grody W: Cystic fibrosis testing comes of age. J Mol Diagn 2009, 173-175

(2) Hanta FM, Reburying A, Pang M, Redman JOB, Sun W, Strom CM: Apparent homozygosity of a novel frame shift mutation in the CFTR gene because of a large deletion. J Mol Diagn 2009, 253-256

(3) Schwartz KM, Pike-Buchanan LL, Muralidharan K, Redman JB, Wilson JA, Jarvis M, Cura MG, Pratt VM: Identification of cystic fibrosis (CF) variants by PCR/oligonucleotide ligation (OLA) assay. J Mol Diagn 2009, 211-215

(4) Pratt VM, Caggana M, Bridges C, Buller AM, DiAntonio L, Highsmith WE, Holtegaard LM, Muralidharan K, Rohlfs EM, Tarleton J, Toji L, Barker SD, Kalman LV: Development of genomic reference materials for cystic fibrosis testing. J Mol Diagn 2009, 186-193

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