Nemours

New Genetic Test Detects Hundreds of Harmful Mutations Among High-Risk Groups

Study Suggests Widespread Screening May Lower Morbidity and Mortality for Amish and Mennonites

New genetic testing helps detect problems in infants before symptoms arise

WILMINGTON, Del. (March 22, 2019) – Researchers at Nemours Children's Health System have developed a new low-cost genetic test that accurately identified more than 200 known disease-causing gene variations in two high-risk populations, the Old Order Amish and Old Order Mennonites of Lancaster County, Pennsylvania. The findings, published today in the *Journal of Molecular Diagnostics,* could help reduce morbidity and mortality from these rare genetic disorders, and dramatically reduce costs of care through early diagnosis of newborns.

> *"For many disorders that disproportionately occur in the Plain communities, detection of asymptomatic infants is critical to prevent the devastating effects of these diseases." -- Erin Crowgey, PhD*

"These are genetically isolated communities with a higher incidence of certain disorders," said Erin Crowgey, PhD, lead author of the study and associate director for bioinformatics at Nemours. "Robust, expanded screening and diagnostic testing in these populations for people who may carry these gene variants could potentially improve patient outcomes and reduce medical costs, through a single low-cost procedure."

The research team developed a next-generation sequencing test capable of identifying 202 known gene variants, or alleles, associated with 162 conditions found in these Amish and Mennonite communities, also known as Plain communities, to identify carriers of these variants in a simple blood test. To do so, the Clinic for Special Children (CSC), a medical home for uninsured Plain community children with genetic disorders, selected 63 patients to participate by providing blood samples for the DNA analysis.

The research team created a targeted gene panel using a custom configuration of the ArcherDX Anchored Multiplexed PCR (polymerase chain reaction) technology. In total, 309 different gene variants were detected. To assess the test's accuracy,

they used an alternate method to validate all genetic variants. For instance, they compared 48 samples with prior whole exome sequencing results, and found 100 percent agreement between the two methods.

“Due to their small number of community founders, the Plain populations over time have come to exhibit relatively high carrier rates for a small set of genetic diseases,” said Erik Puffenberger, PhD, a study author and laboratory director at CSC. “We needed a methodology for a single procedure to test individuals for all known genetic variations related to those conditions.”

The researchers note that population-wide carrier screening may help decrease morbidity and mortality, as well as treatment costs associated with genetic conditions in these high-risk groups by helping to identify asymptomatic newborns when many of these conditions are most treatable.

“For many disorders that disproportionately occur in the Plain communities, detection of asymptomatic infants is critical to prevent the devastating effects of these diseases,” said Crowgey. “Without rapid diagnosis and treatment of newborns, children can have shorter lifespans or lasting disabilities, even after intensive, lengthy, and costly medical care.”

The study authors estimate that use of this low-cost screening tool (approx. $165 per person) by Plain communities could result in hundreds of thousands of dollars health care costs savings annually.

Other members of the study team include Michael Washburn, PhD, of ArcherDX, Inc., and E. Anders Kolb, MD, of Nemours Children’s Health System.

Matthew Demczko, MD, a pediatrician who cares for Amish children at Nemours Kinder Clinic in Dover, Delaware, said: “In our ongoing study of the Delaware Amish, we’ve found that the community is aware of their increased risk for inherited disorders and knowledgeable about carrier screening. They generally perceive screening to be useful to avoid surprises and guide care decisions for their children. We hope that data from this study will help promote larger screening efforts throughout Plain communities in North America.”

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About Nemours Children’s Health System

Nemours is an internationally recognized children's health system that owns and operates the two free-standing children’s hospitals: the Nemours/Alfred I. duPont Hospital for Children in Wilmington, Del., and Nemours Children's Hospital in Orlando, Fla., along with outpatient facilities in five states, delivering pediatric primary, specialty and urgent care. Nemours also powers the world’s most-visited website for information on the health of children and teens, KidsHealth.org, and offers on-demand, online video patient visits through Nemours CareConnect. Nemours ReadingBrightstart.org is a program dedicated to preventing reading failure in young children, grounded in Nemours’ understanding that child health and learning are inextricably linked, and that reading level is a strong predictor of adult health.

Established as The Nemours Foundation through the legacy and philanthropy of Alfred I. duPont, Nemours provides pediatric clinical care, research, education, advocacy and prevention programs to families in the communities it serves.

About the Clinic for Special Children

The Clinic for Special Children is a non-profit organization located in Strasburg, Penn., which provides primary pediatric care and advanced laboratory services to those who suffer from genetic or other complex medical disorders. Founded in 1989, the organization provides services to over 1,050 active patients and is recognized as a world leader in translational and precision medicine. The organization is primarily supported through community fundraising events and donations.

About ArcherDX, Inc.

ArcherDX, Inc., is advancing molecular pathology with a robust technology platform for genetic mutation detection by next-generation sequencing. By combining patented Anchored Multiplexed PCR (AMP™) chemistry in an easy-to-use, lyophilized format and powerful bioinformatics software, the Archer® platform dramatically enhances genetic mutation identification and discovery. The company is headquartered in Boulder, Colo.

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