More Than 10% of Healthy People Have Monogenic Risk Variants

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Investigators conducting studies on genomic sequencing in healthy newborns and adults say they have found genetic results revealing far more variants associated with diseases than previously anticipated, along with previously unrecognized, but related, clinical features of genetic conditions.

The National Institutes of Health (NIH) compiles information on more than 1200 health conditions with a genetic basis. A gene variant or mutation can be inherited from a parent or acquired during the course of a person's life. A genetic variation can make a gene function improperly and may influence the risk of developing certain disorders. Some individuals with a genetic predisposition to disease may go on to develop disease while others with the same variant will never get the disease.

Investigators from Brigham and Women's Hospital and Boston Children's Hospital working on the Genomes2People Research Program recently announced news on findings from their BabySeq and MedSeq Projects. In these 2 randomized clinical trials, the study team has worked to analyze the genomes of infants and adults for approximately 5000 disease-associated genes to identify monogenic disease risk variants—mutations associated with diseases thought to be caused by variants in a single gene. These monogenic diseases include rare diseases such as hereditary cancer syndromes, hereditary cardiac syndromes, and metabolic disorders that can have life-threatening complications.

In research presented at the recent 2018 American Society for Human Genetics meeting, BabySeq and MedSeq investigators say they have found that searching for unanticipated genetic results in newborns and adults can reveal far more variants associated with diseases than previously thought. In addition, they can detect previously unrecognized, but related, clinical features of genetic conditions.

These findings come following the team's genome or exome sequencing on a total of 269 individuals. They found unanticipated risk variants in 16 of 110 adults (14.5%) and in 18 of 159 infants (11.3%). Upon further examination on these study participants, the investigators discovered clinical features suggestive of a previously unrecognized genetic condition in 4 of the adult cases and 4 of the newborn cases,

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including 3 cases with highly effective interventions.

“These results are unexpected and exciting, suggesting that if we examine enough well-established, disease-associated genes, we will unearth monogenic risk variants in more than 10 percent of purportedly healthy individuals,” the projects’ principal investigator Robert Green, MD, MPH, said in a recent statement. “And, if on the basis of these genetic clues, we carefully examine those individuals, we find that a quarter of them have previously unrecognized features of underlying disease—something that we might never have realized had we not performed genetic sequencing.”

Additional presentations made by the team at the recent meeting included The Impact of Newborn Genomic Sequencing on Families: Findings from the BabySeq Project and Analysis of Actionable Adult-Onset Disease Risk Findings in Newborn Genomic Sequencing. The BabySeq Project is funded by a 5-year $25 million grant from the National Institute of Child Health and Human Development and the National Human Genome Research Institute. MedSeq is also funded by the NIH.

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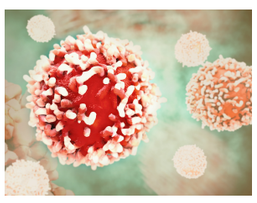

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