Effect of Copy-Number Variation in Disease Elucidated

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There is considerable variation in the phenotypes associated with recurrent copy-number variants, with multiple, large copy-number variants compounding to result in severe clinical presentation, according to a study published online Sept. 12 in the *New England Journal of Medicine*.

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Multiple, large copy-number variants compound, resulting in severe clinical presentation

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WEDNESDAY, Sept. 12 (HealthDay News) -- There is considerable variation in the phenotypes associated with recurrent copy-number variants, with multiple, large copy-number variants compounding to result in severe clinical presentation, according to a study published online Sept. 12 in the *New England Journal of Medicine*.

Santhosh Girirajan, M.B., B.S., Ph.D., from the University of Washington in Seattle, and colleagues used array comparative genomic hybridization to analyze the genomes of 2,312 children known to carry a copy-number variant associated with intellectual disability and congenital abnormalities.

The researchers found that 10.1 percent of affected children carried a second large copy-number variant as well as the primary genetic lesion. There were seven genomic disorders in which the affected children were more likely to carry multiple copy-number variants than controls, each defined by a specific copy-number variant. Two factors, the number of copy-number variants and whether the variants were inherited or de novo, could distinguish syndromic disorders from those with extreme phenotypic heterogeneity. Compared with controls, children with two large copy-number variants of unknown clinical significance were eight times as likely to have developmental delay. For affected children, inherited copy-number variation tended to occur together with a second-site large copy-number variation. Disorders of phenotypic heterogeneity were significantly more likely among boys than girls, and mothers rather than fathers were significantly more likely to transmit the second-site copy number variant to their children.

"Our study represents a step toward deconvoluting the effect of copy-number variants in disease and understanding, more broadly, the causes of neurologic disease," the authors write. "Our analysis shows that the phenotypic variation of at least seven genomic disorders may be partially explained by the presence of additional large variants."

Several authors disclosed financial ties to the biotechnology industry.

Abstract
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