Identification of a molecular cause of a neurodevelopmental disorder

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Video Abstract

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Abstract

The brain is the most complex biological structure known. All thoughts, movements, and behaviors are coordinated in this control center, where information is processed and transmitted in the form of electrical impulses and chemical signals. It perhaps comes as no surprise then, that alterations in this function can lead to neurological and psychiatric disorders. Now, a new study has pinpointed specific regions of a gene expressed in brain cells that appear to be associated with conditions such as developmental delay and intellectual disability. Neurodevelopmental disorders present early in life and are caused by impairments of growth, development, and function of the brain and central nervous system. With conditions including autism, attention deficit disorder, and schizophrenia, these disorders are characterized by deficits in cognitive, social, or personal functioning. Recent advances in high-resolution genetic screening methods have highlighted the prevalence of genetic anomalies associated with these conditions. For example, DLG2 -- a gene expressed in the brains of humans and mice -- plays an important role in complex cognitive and learning tasks in both species. But a lack of precise characterization of such genes has hindered our understanding of this link. Using genetic testing, an international team of researchers found that two pediatric patients exhibiting global developmental delay and intellectual disability both showed a partial deletion of the DLG2 gene. They then took a so-called 'multi-omics' approach – integrating genomic, transcriptomic, and epigenomic data from large, international databases to further understand these deletions. This led to the identification of two novel promoters and coding-exons in fetal brain tissue that appear to be especially important in neurodevelopmental disorders. When they consulted genetic databases for individuals bearing DLG2 deletions, they found that these exons were missing in 88% of patients with these conditions. This study provides elegant progress into understanding the molecular cause of neurodevelopmental disorders and improves fundamental knowledge about the DLG2 gene.