New research identifies neurodevelopment-related gene deficiency

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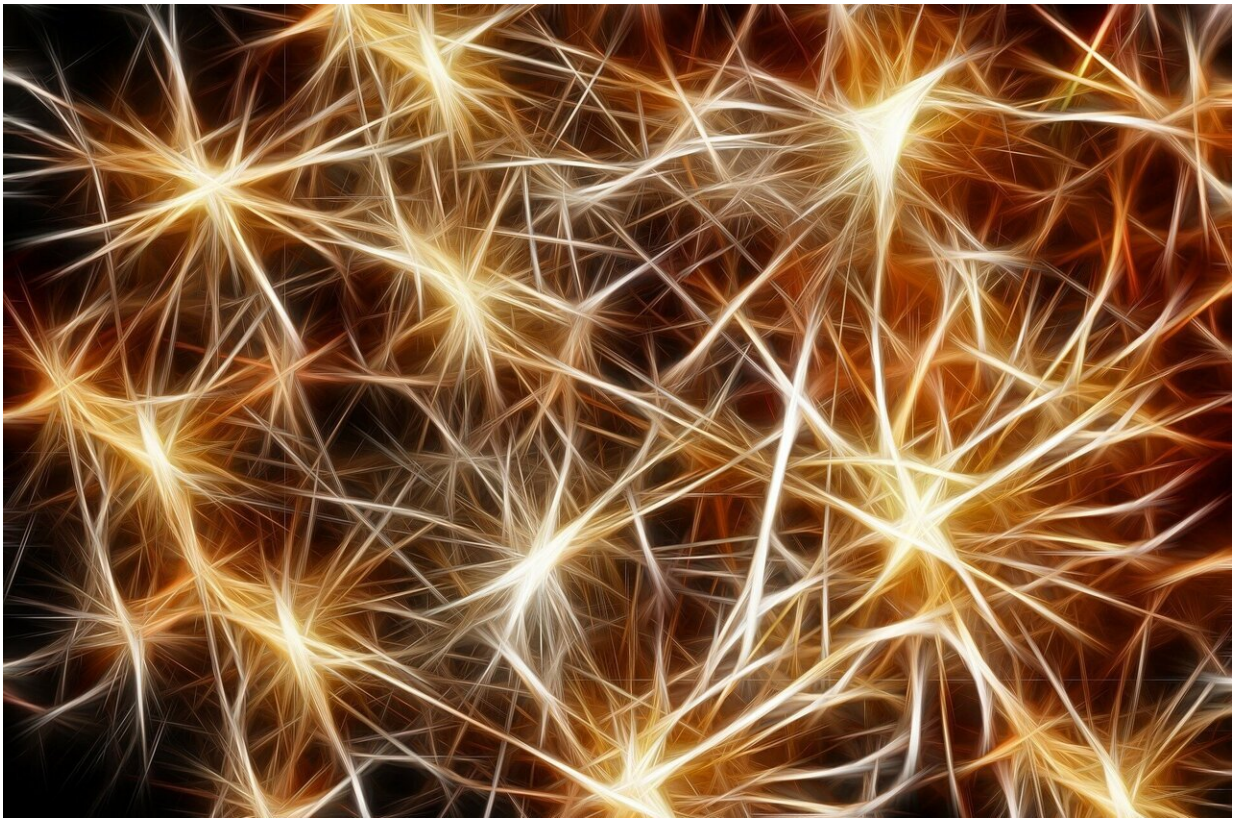

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Researchers at the Case Western Reserve University School of Medicine have identified that a gene critical to clearing up unnecessary proteins plays a role in brain development and contributes to the development of

autism spectrum disorders (ASD) and schizophrenia.

The discovery, published today in *Neuron*, provides important insight into the mechanism of both diseases—a possible step toward finding how to treat the disorders.

Cullin 3 is a core component of an E3 ubiquitin ligase responsible for the cell's clearance of proteins. Mutations of its gene CUL3 have been associated with autism and schizophrenia. However, pathologic mechanisms of CUL3 deficiency have been unclear.

"CUL3 is abundant in the brain, yet little is known of its function," said Lin Mei, the Allen C. Holmes Professor of Neurological Diseases and chair of the Department of Neurosciences at the Case Western Reserve University School of Medicine. "Here, we show that CUL3 is critical for brain development and communication between cells in the brain."

Mei, also director of the Cleveland Brain Health Initiative, is the principal investigator with research assistants Zhaoqi Dong and Wenbing Chen. (The published research is titled "CUL3 deficiency causes social deficits and anxiety-like behaviors by impairing excitation-inhibition balance through the promotion of Cap-dependent translation.")

ASD is a complicated condition that includes difficulty with communication and social interaction, obsessive interests and repetitive behaviors. It affects 1 in 59 children in the United States, according to a recent report by the Centers for Disease Control. Schizophrenia affects about 1 in 100 people worldwide. However, autism and schizophrenia remain among the most mysterious disorders.

Mei and his team studied how CUL3 mutation impacts the brain in mouse models. The researchers were able to demonstrate that altering the gene in mouse models can cause similar social problems that appear

in people with these disorders.

Normal mice would spend more time with a mouse over an inanimate object, Mei said. But CUL3-mutant mice couldn't differentiate between a mouse and an inanimate object, showing a problem with social preference.

In another test, normal mice would spend more time with an unfamiliar mouse over a familiar one. But CUL3-mutant mice couldn't remember seeing a familiar mouse, suggesting a problem of social memory. Also, CUL3-mutant mice were more anxious than normal mice.

Researchers at Beijing Normal University and the Louis Stokes Cleveland Veterans Affairs Medical Center contributed to the research.

Provided by Case Western Reserve University

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