CUL3-RELATED NEURODEVELOPMENTAL DISORDER

Information for patients, families, and healthcare providers

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OVERVIEW

CUL3-related neurodevelopmental disorder, also referred to as CUL3-related syndrome or neurodevelopmental disorder with or without autism or seizures (NEDAUS), is a rare genetic condition caused by changes (pathogenic variants) in the CUL3 gene. This autosomal dominant disorder can lead to a range of neurodevelopmental and health concerns, which vary from person to person.

Changes in the CUL3 gene can also cause another condition called pseudohypoaldosternoism type IIE (PHA2E). However, PHA2E is associated with variants affecting specific regions of the gene (intron 8, exon 9, and intron 9), whereas CUL3-related neurodevelopmental disorder is thought to result from variants in other regions. The information provided here pertains only to CUL3-related neurodevelopmental disorder.

SIGNS & SYMPTOMS

The following is a list of clinical features that are associated with this disorder. While not exhaustive, it is based on current medical literature and patient surveys. It is important to note that CUL3-related neurodevelopmental disorder has a wide range of characteristics, with symptoms differing among individuals in both presence and severity.

DEVELOPMENTAL / BEHAVIORAL

- Speech & language delays
- Gross & fine motor delays
- Intellectual disability
- Autism spectrum disorder
- Attention-deficit/hyperactivity disorder
- Anxiety

NEUROLOGICAL

- Hypotonia
- Seizures
- Brain imaging anomalies
- Dystonia, tremor, spasms

FEEDING & GROWTH

- Fetal growth restriction
- Feeding difficulties
- Digestive issues (GERD, constipation, diarrhea)
- Difficulty gaining weight / growth faltering

OTHER

- Congenital heart abnormalities
- Hand & foot abnormalities
- Skeletal abnormalities

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TREATMENT

Research on CUL3-related neurodevelopmental disorder is still in its early stages, and currently, there are no medications designed to treat the condition. However, a genetic diagnosis can help individuals and families make informed decisions about monitoring and managing symptoms.

SPECIALIST REFERRALS

Since CUL3-related neurodevelopmental disorder can affect multiple areas of development and health, individuals may benefit from evaluations and/or care by various specialists. Depending on a person's specific needs, doctors may recommend referrals to:

- **Genetics** - To confirm the diagnosis and discuss potential implications.
- **Developmental Pediatrics** - To track progress over time and provide guidance.
- **Cardiology** - To evaluate and monitor for congenital heart defects.
- **Neurology** - To conduct neurological assessments, which may include an electroencephalogram (EEG) or brain imaging, and to manage movement disorders or seizures.
- **Endocrinology** - To assess growth concerns.
- **Psychology** - To perform developmental and behavioral assessments that help to understand cognitive, social, and emotional needs.
- **Other Specialists** - To address additional medical concerns as needed, such as sleep disorders, digestive issues, or immune function.

ONGOING SUPPORT & THERAPY

Individuals with CUL3-related neurodevelopmental disorder may benefit from a range of therapies that support their development, independence, and overall well-being. A multidisciplinary approach can help address challenges in motor skills, communication, learning, and daily living activities.

- Physical therapy
- Occupational therapy
- Speech language therapy
- Emotional & behavioral therapy

Early and consistent intervention with therapies, combined with educational support through an Individualized Education Plan (IEP), may help to enhance quality of life. Regular reassessments help ensure therapy plans remain aligned with evolving needs and goals over time.

FUTURE DIRECTIONS

Research on CUL3-related neurodevelopmental disorder is ongoing, and we remain optimistic about future discoveries that will deepen our understanding. To learn more about research opportunities or patient advocacy, please contact CUL3 Support & Awareness at info@cul3.org.

FOR MORE INFORMATION

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For more information on CUL3-related neurodevelopmental disorder, please refer to the following sources.

SIMONS SEARCHLIGHT

https://www.simonssearchlight.org/research/what-we-study/cul3/

MEDLINEPLUS

https://medlineplus.gov/genetics/condition/cul3-related-neurodevelopmental-disorder/

SELECT PUBLISHED RESEARCH ARTICLES

van der Laan, L., Silva, A., Kleinendorst, L., ..., Sadikovic, B., van Haelst, M. M., & Henneman, P. (2025). CUL3-related neurodevelopmental disorder: Clinical phenotype of 20 new individuals and identification of a potential phenotype-associated episignature. Human Genetics and Genomics Advances.

Blackburn, P. R., Ebstein, F., Hsieh, T.-C., Motta, M., Radio, F. C., Herkert, J. C., Rinne, T., Thiffault, I., Rapp, M., Alders, M., Maas, S., Gerard, B., Smol, T., Vincent-Delorme, C., Cogné, B., Isidor, B., Vincent, M., Bachmann-Gagescu, R., Rauch, A., ... Wang, T. (2024). Loss-of-function variants in CUL3 cause a syndromic neurodevelopmental disorder. Annals of Neurology.

Lin, P., Yang, J., Wu, S., Ye, T., Zhuang, W., Wang, W., & Tan, T. (2023). Current trends of high-risk gene Cul3 in neurodevelopmental disorders. Frontiers in Psychiatry.