

# PPP2R5D-RELATED NEURODEVELOPMENTAL DISORDER

## FACT SHEET FOR HEALTHCARE PROVIDERS



### BACKGROUND

**PPP2R5D-related neurodevelopmental disorder**, also called Jordan's syndrome, is a genetic condition characterized by mild to profound neurodevelopmental delay. Affected individuals also have hypotonia, macrocephaly, speech impairment, developmental delay in gross motor skills, and prominent forehead. Other common clinical signs include autism spectrum disorder, seizures, and ophthalmologic abnormalities, as well as additional skeletal, endocrine, cardiac, and genital anomalies. There is wide variability in how severely individuals may be affected.

23 individuals with Jordan's syndrome have been reported in the literature to date, ranging in age from 22 months to 53 years. total of 170 cases have been identified in 30 different countries according to the advocacy organization Jordan's Guardian Angels. It's estimated that over 250,000 individuals worldwide are affected but remain undiagnosed.

### DIAGNOSIS

PPP2R5D-related neurodevelopmental disorder is diagnosed by identification of a heterozygous (single) pathogenic variant in the PPP2R5D gene upon molecular genetic testing.

A diagnosis of PPP2R5D-related neurodevelopmental disorder should be considered if the following suggestive findings are appreciated:

- Macrocephaly
- Generalized hypotonia of infancy
- Mild to profound neurodevelopmental delays
- Autism spectrum disorder
- Epilepsy
- Megalencephaly on brain MRI
- Nonspecific brain MRI findings including mild-to-moderate ventricular dilatation, hydrocephalus, and others

### GENETIC TESTING

Genetic testing for variants in PPP2R5D became available in 2014. Strategies for diagnostic genetic testing include:

- A developmental delay, macrocephaly, autism spectrum disorder, or epilepsy multigene panel that includes PPP2R5D and other possible causative genes.
- Comprehensive clinical exome sequencing or genome sequencing.

### GENETIC INHERITANCE

PPP2R5D-related neurodevelopmental disorder is inherited in an autosomal dominant manner, meaning each pregnancy of an affected individual has a 50% chance of inheriting their pathogenic variant in the PPP2R5D gene. Most cases of Jordan's syndrome reported to date are due to de novo genetic changes, meaning they were not inherited from a parent. For parents of an affected individual, the recurrence risk for future pregnancies is estimated at 1% due to the possibility of parental germline mosaicism.

### MANAGEMENT

Individuals diagnosed with PPP2R5D-related neurodevelopmental disorder should have nutrition, neurologic, neuropsychiatric, ophthalmologic, cardiac, gastrointestinal, and developmental evaluations and/or surveillance. Families should also have a consultation with a clinical geneticist and/or genetic counselor.

The following management recommendations may be appropriate:

- Referral for an early intervention program or evaluation for an individualized education plan
- Physical therapy for mobility
- Occupational therapy for fine motor skills
- Feeding therapy
- Alternative means of communication for individuals with expressive language difficulties
- Therapies for social or behavioral concerns
- Consultation with a developmental pediatrician

## SIMILAR DISORDERS

The PPP2R5D gene encodes a subunit of an enzyme called protein phosphatase 2A (PP2A). Pathogenic variants in other genes associated with this enzyme such as PPP2R1A and PPP2R5C cause similar clinical features.

## RESOURCES FOR AFFECTED INDIVIDUALS AND CLINICIANS

### Jordan's Guardian Angels

Email: [info@jordansguardianangels.org](mailto:info@jordansguardianangels.org)

1-720-725-1727

[jordansguardianangels.org](http://jordansguardianangels.org)

*Jordan's Guardian Angels (JGA) is a nonprofit organization that connects families with Jordan's syndrome, creates awareness of the syndrome, and funds research aiming to understand and develop therapies related to variants in this gene.*

### Simons Searchlight

[simonssearchlight.org](http://simonssearchlight.org)

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