PPP2R5D-related intellectual disability

Description

PPP2R5D-related intellectual disability is a neurological disorder characterized by moderate to severe developmental delay and intellectual disability. Affected individuals have weak muscle tone (hypotonia); delayed development of motor skills, such as sitting, standing, and walking; and delayed speech development. Recurrent seizures (epilepsy) and autism spectrum disorder, which is characterized by impaired communications and social interaction, can also occur in affected individuals. Most people with *PPP2R5D*-related intellectual disability have an unusually large head size (macrocephaly), and some have other unusual facial features, including a prominent forehead (frontal bossing), widely spaced eyes (hypertelorism), and eyes that slant downward (downslanting palpebral fissures).

Frequency

PPP2R5D-related intellectual disability is a rare disorder. At least 20 individuals with this condition have been described in the medical literature.

Causes

Mutations in the *PPP2R5D* gene have been found to cause *PPP2R5D*-related intellectual disability. This gene provides instructions for making a protein called B56-delta (B56δ). The B56δ protein is one piece of an enzyme called protein phosphatase 2A (PP2A), which removes phosphate groups, consisting of clusters of oxygen and phosphorus atoms, from certain proteins. This process, called dephosphorylation, helps control whether the protein is turned on or off. PP2A enzymes containing the B56δ protein are found mainly in the brain, where they are thought to play roles in the normal development and function of nerve cells (neurons).

PPP2R5D gene mutations are thought to result in the production of an altered B56δ protein. Although the effects of these variations are unclear, researchers suspect that they change or impair the activity of the PP2A enzyme. Abnormal or reduced PP2A enzyme activity is thought to disrupt signaling pathways in neurons, impairing their normal development and functioning, which may underlie intellectual disability and other neurological features of *PPP2R5D*-related intellectual disability.

Learn more about the gene associated with PPP2R5D-related intellectual disability

- PPP2R5D

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of this condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- Autosomal dominant mental retardation 35

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Intellectual disability-macrocephaly-hypotonia-behavioral abnormalities syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4225354/)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22PPP2R5D-related intell ectual disability%22)

Catalog of Genes and Diseases from OMIM

- HOUGE-JANSSENS SYNDROME 1; HJS1 (https://omim.org/entry/616355)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Intellectual+Disability%5BTIA B%5D%29+AND+%28%28PPP2R5D%5BTIAB%5D%29+OR+%28B56delta%5BTIA B%5D%29%29+OR+%28%28protein+phosphatase+2A%29+AND+%28intellectual+ disability%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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