SETBP1 haploinsufficiency disorder

Description

SETBP1 haploinsufficiency disorder is a condition that involves speech and language problems, intellectual disability, and distinctive facial features.

In people with SETBP1 haploinsufficiency disorder, problems with vocabulary and the production of speech (expressive language skills) are generally more severely affected than the ability to understand speech (receptive language skills). About 80 percent of affected children have a condition called childhood apraxia of speech, in which they have difficulty with the mouth movements needed to speak. Speech development may be limited to a few words or no speech. Affected individuals often communicate using gestures or by mimicking the expressions of others.

Individuals with SETBP1 haploinsufficiency disorder have intellectual disability that can range from mild to moderate. They may also have neurodevelopment problems, such as attention-deficit/hyperactivity disorder (ADHD) or autistic behaviors that affect communication and social interaction. Affected individuals may have weak muscle tone (hypotonia); delayed development of motor skills, such as sitting, standing, and walking; or recurrent seizures (epilepsy).

Distinctive facial features in people with SETBP1 haploinsufficiency disorder can include a long face, a high forehead, eyebrows that grow together in the middle (synophrys), short eye openings (short palpebral fissures), skin folds covering the inner corner of the eyes (epicanthal folds), droopy eyelids (ptosis), puffiness of the skin around the eyes (periorbital fullness), small nostrils, a high nasal bridge, a broad tip of the nose, a thin upper lip, a high arch in the roof of the mouth (high-arched palate), and a small chin.

Frequency

The exact prevalence of SETBP1 haploinsufficiency disorder is unknown, although it is thought to be a rare disorder. At least 45 affected individuals have been described in the scientific literature.

Causes

SETBP1 haploinsufficiency disorder is caused by variants (also called mutations) in the *SETBP1* gene. This gene provides instructions for making a protein that attaches (binds) to certain regions of DNA to increase gene activity (expression). The SETBP1 protein is

found throughout the body, but protein levels are highest during brain development before birth. During this time, nerve cells grow and divide (proliferate) and move (migrate) to their proper location in the brain. The SETBP1 protein is thought to control the activity of genes involved in these developmental processes.

SETBP1 gene variants that cause SETBP1 haploinsufficiency disorder prevent the production of any functional SETBP1 protein from one copy of the gene. It is unclear how the loss of SETBP1 protein leads to the specific features of SETBP1 haploinsufficiency disorder. A shortage of this protein probably impairs the expression of certain genes in the brain, disrupting development. Abnormalities in certain brain regions likely underlie the speech, intellectual, and behavioral problems that can occur in SETBP1 haploinsufficiency disorder.

Learn more about the gene associated with SETBP1 haploinsufficiency disorder

- SETBP1

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) variants 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

- Mental retardation, autosomal dominant 29
- MRD29
- SETBP1 disorder
- SETBP1 LoF syndrome
- SETBP1 loss of function syndrome
- SETBP1 related developmental delay
- SETBP1-related disorder
- SETBP1-related intellectual disability

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Intellectual disability, autosomal dominant 29 (https://www .ncbi.nlm.nih.gov/gtr/conditions/C4015141/)

Genetic and Rare Diseases Information Center

- Intellectual developmental disorder, autosomal dominant 29 (https://rarediseases.info.nih.gov/diseases/13379/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- INTELLECTUAL DEVELOPMENTAL DISORDER, AUTOSOMAL DOMINANT 29; MRD29 (https://omim.org/entry/616078)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SETBP1+disorder%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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