DNMT3A overgrowth syndrome

Description

DNMT3A overgrowth syndrome is a disorder characterized by faster than normal growth before and after birth, subtle differences in facial features, and intellectual disability.

Individuals with *DNMT3A* overgrowth syndrome are often longer than normal at birth and are taller than their peers throughout life. Many affected individuals become overweight in late childhood or adolescence. They may also have an abnormally large head size (macrocephaly).

The characteristic facial appearance of individuals with *DNMT3A* overgrowth syndrome includes a round face; thick, horizontal eyebrows; and narrowed openings of the eyes (narrowed palpebral fissures). Additionally, the upper front teeth are often larger than normal.

Intellectual disability in *DNMT3A* overgrowth syndrome ranges from mild to severe. Individuals may have features of autism spectrum disorder, which are characterized by impaired communication and socialization skills.

Individuals with *DNMT3A* overgrowth syndrome may have other signs and symptoms, including a rounded upper back that also curves to the side (kyphoscoliosis), heart defects, flat feet (pes planus), weak muscle tone (hypotonia), or joints that are loose and very flexible (hypermobile joints). Psychological disorders such as depression, anxiety, or obsessive-compulsive disorder can also occur in this disorder.

Frequency

The prevalence of *DNMT3A* overgrowth syndrome is unknown. More than 20 affected individuals have been described in the medical literature.

Causes

As its name suggests, mutations in the *DNMT3A* gene cause *DNMT3A* overgrowth syndrome. The *DNMT3A* gene provides instructions for making an enzyme called DNA methyltransferase 3 alpha. This enzyme is involved in DNA methylation, which is the addition of methyl groups, consisting of one carbon atom and three hydrogen atoms, to DNA molecules. DNA methylation is important in many cellular functions. These include regulating gene activity and certain chemical reactions and controlling the processing of

chemicals that relay signals in the nervous system (neurotransmitters). DNA methyltransferase 3 alpha is particularly important for establishing DNA methylation patterns during development before birth.

Some *DNMT3A* gene mutations that cause *DNMT3A* overgrowth syndrome lead to a decrease in normal enzyme function. As a result, there is a reduction in DNA methylation, particularly affecting DNA methylation before birth. It is unclear how other mutations affect protein function. Decreased DNA methylation likely disrupts the normal regulation of important developmental genes, although how these change cause the specific features of *DNMT3A* overgrowth syndrome is unknown.

Learn more about the gene associated with DNMT3A overgrowth syndrome

- DNMT3A

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.

In some cases, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- Tatton-Brown-Rahman syndrome
- TBRS

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Tatton-Brown-Rahman overgrowth syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4014545/)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- TATTON-BROWN-RAHMAN SYNDROME; TBRS (https://omim.org/entry/615879)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28DNMT3A+overgrowth+syndrome%29+OR+%28Tatton-Brown-Rahman+syndrome%29%29+AND+%22last+3600+days%22%5Bdp%5D)

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Last updated April 1, 2019