Coffin-Siris Syndrome

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Coffin-Siris syndrome is a condition that affects several body systems. Although there are many variable signs and symptoms, hallmarks of this condition include developmental disability, abnormalities of the fifth (pinky) fingers or toes, and characteristic facial features.

genetic conditions

1. Introduction

Most affected individuals have mild to severe intellectual disability or delayed development of speech and motor skills such as sitting and walking. Another feature of Coffin-Siris syndrome is underdevelopment (hypoplasia) of the tips of the fingers or toes, or hypoplasia or absence of the nails. These abnormalities are most common on the fifth fingers or toes. In addition, most affected individuals have facial features described as coarse. These typically include a wide nose with a flat nasal bridge, a wide mouth with thick lips, and thick eyebrows and eyelashes. Affected individuals can have excess hair on other parts of the face and body (hirsutism), but scalp hair is often sparse. There is a range of facial features seen in people with Coffin-Siris syndrome, and not all affected individuals have the typical features. In addition, people with this condition may have an abnormally small head (microcephaly).

Additionally, some infants and children with Coffin-Siris syndrome have frequent respiratory infections, difficulty feeding, and an inability to gain weight at the expected rate (failure to thrive). Other signs and symptoms that may occur in people with this condition include short stature, low muscle tone (hypotonia), and abnormally loose (lax) joints. Abnormalities of the eyes, brain, heart, and kidneys may also be present.

2. Frequency

Coffin-Siris syndrome is a rare condition that is diagnosed in females more frequently than in males. Approximately 140 cases have been reported in the medical literature.

3. Causes

Coffin-Siris syndrome is caused by mutations in the *ARID1A*, *ARID1B*, *SMARCA4*, *SMARCB1*, or *SMARCE1* gene. Each of these genes provides instructions for making one piece (subunit) of several different SWI/SNF protein complexes. SWI/SNF complexes regulate gene activity (expression) by a process known as chromatin remodeling.

Chromatin is the network of DNA and protein that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly regions of DNA are packaged. Chromatin remodeling is one way gene expression is regulated during development; when DNA is tightly packed, gene expression is often lower than when DNA is loosely packed.

Through their ability to regulate gene activity, SWI/SNF complexes are involved in many processes, including repairing damaged DNA; copying (replicating) DNA; and controlling the growth, division, and maturation (differentiation) of cells.

Although it is unclear what effect mutations in these genes have on SWI/SNF complexes, researchers suggest that the mutations result in abnormal chromatin remodeling. Disturbance of this process alters the activity of many genes and disrupts several cellular processes, which could explain the diverse signs and symptoms of Coffin-Siris syndrome.

3.1. The Genes Associated with Coffin-Siris Ayndrome

- ARID1A
- ARID1B
- SMARCA4
- SMARCB1
- SMARCE1

4. Inheritance

Coffin-Siris syndrome appears to follow an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell is sufficient to cause the disorder. However, the condition is not usually inherited from an affected parent, but occurs from new (de novo) mutations in the gene that likely occur during early embryonic development.

5. Other Names for This Condition

- dwarfism-onychodysplasia
- fifth digit syndrome
- mental retardation with hypoplastic fifth fingernails and toenails
- short stature-onychodysplasia

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