

ARID1B Gene

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AT-rich interaction domain 1B

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1. Normal Function

The *ARID1B* gene provides instructions for making a protein that forms 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 proteins that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression is regulated during development; when DNA is tightly packed, gene expression is 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. The ARID1B protein and other SWI/SNF subunits are thought to act as tumor suppressors, which keep cells from growing and dividing too rapidly or in an uncontrolled way.

The ARID1B subunit is able to attach (bind) to DNA and is thought to help target SWI/SNF complexes to the chromatin location that needs to be remodeled.

2. Health Conditions Related to Genetic Changes

2.1. Coffin-Siris Syndrome

At least 69 mutations in the *ARID1B* gene have been found to cause Coffin-Siris syndrome. This condition is characterized by delayed development, abnormalities of the fifth (pinky) fingers or toes, and characteristic facial features that are described as coarse. Most *ARID1B* gene mutations involved in Coffin-Siris syndrome lead to an abnormally short, nonfunctional protein. As a result, affected individuals have half the normal amount of functional ARID1B protein. Although it is unclear how these changes affect SWI/SNF complexes, researchers suggest that *ARID1B* gene 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. People with Coffin-Siris syndrome do not appear to have an increased risk of cancer (see below).

2.2. Autism Spectrum Disorder

At least 13 *ARID1B* gene mutations have been identified in people with autism spectrum disorder (ASD), a varied condition characterized by impaired social skills, communication problems, and repetitive behaviors. Some affected individuals also have other features, including intellectual disability, severe speech problems, and brain malformations. The *ARID1B* gene mutations associated with ASD result in a reduced amount of the ARID1B protein or impair the protein's function in chromatin remodeling. These changes likely affect the control of gene expression and interfere with normal brain development, but the specific relationship between the mutations and ASD is unknown.

2.3. Other Disorders

Mutations in the *ARID1B* gene can cause intellectual disability without other hallmark features of Coffin-Siris syndrome (described above). As in Coffin-Siris syndrome, the gene mutations that cause intellectual disability lead to an abnormally short, nonfunctional protein, and affected individuals have half the normal amount of ARID1B protein. It is unclear why

some people with an *ARID1B* gene mutation develop intellectual disability and others have the additional features of Coffin-Siris syndrome.

2.4. Cancers

Mutations in the *ARID1B* gene are involved in several types of cancer, including breast cancer, a childhood cancer of nerve tissue called neuroblastoma, and a type of blood cancer called diffuse large B-cell lymphoma. These mutations are somatic, which means they are acquired during a person's lifetime and are present only in tumor cells. The mechanism by which mutations in the *ARID1B* gene contribute to cancer is unknown, although it is thought that changes in SWI/SNF complexes are involved. These changes may impair normal cell differentiation, which leads to the overgrowth of certain cell types, causing cancer. Alternatively, abnormal SWI/SNF complexes may disrupt the regulation of genes that help control the growth and division of cells, which leads to cancer. It is likely that other genetic changes in addition to *ARID1B* gene mutations are necessary for cancer development.

3. Other Names for This Gene

- 6A3-5
- ARI1B_HUMAN
- ARID domain-containing protein 1B
- AT rich interactive domain 1B (SWI1-like)
- AT-rich interactive domain-containing protein 1B
- BAF250B
- BRG1-associated factor 250b
- BRG1-binding protein ELD/OSA1
- BRIGHT
- DAN15
- ELD (eyelid)/OSA protein
- ELD/OSA1
- KIAA1235
- MRD12
- OSA2
- P250R

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