NSD1 Gene

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nuclear receptor binding SET domain protein 1

genes

1. Introduction

The *NSD1* gene provides instructions for making a protein that functions as a histone methyltransferase. Histone methyltransferases are enzymes that modify structural proteins called histones, which attach (bind) to DNA and give chromosomes their shape. By adding a molecule called a methyl group to histones (a process called methylation), histone methyltransferases control (regulate) the activity of certain genes and can turn them on and off as needed. The NSD1 enzyme controls the activity of genes involved in normal growth and development, although most of these genes have not been identified.

2. Health Conditions Related to Genetic Changes

2.1. Sotos syndrome

More than 380 mutations in the *NSD1* gene have been identified in people with Sotos syndrome. The most common mutation in the Japanese population deletes genetic material from the region of chromosome 5 that contains the *NSD1* gene. In most other populations, mutations within the gene itself are more frequent. These mutations include insertions or deletions of a small amount of DNA and changes in single DNA building blocks (base pairs) that make up the gene. Most mutations prevent one copy of the *NSD1* gene from making any enzyme or lead to the production of an abnormally small, nonfunctional version of the enzyme. Research suggests that a reduced amount of the NSD1 enzyme disrupts the normal activity of genes involved in growth and development. However, it remains unclear exactly how a shortage of this enzyme during development leads to overgrowth, learning disabilities, and the other signs and symptoms of Sotos syndrome.

2.2. Cancers

A change involving the *NSD1* gene is associated with a blood cancer called childhood acute myeloid leukemia. This change occurs when part of chromosome 5 breaks off and reattaches to part of chromosome 11. This change is acquired during a person's lifetime and is present only in cancer cells. This type of genetic change, called a somatic mutation, is not inherited. The rearrangement of genetic material involved in childhood acute myeloid

leukemia, known as a translocation, abnormally fuses the *NSD1* gene on chromosome 5 with the *NUP98* gene on chromosome 11. Research shows that the fused *NUP98-NSD1* gene turns on genes that promote the growth of immature blood cells and blocks processes that would turn the genes off. The resulting overgrowth of these immature cells leads to development of acute myeloid leukemia.

A different type of alteration involving the *NSD1* gene is associated with a cancer of nerve tissue called neuroblastoma and a type of brain cancer called glioma. This alteration, known as promoter hypermethylation, turns off the production of the NSD1 enzyme. Researchers speculate that without NSD1, the activity of one or more genes involved in cell growth and division is uncontrolled. As a result, the cells can grow and divide unchecked, leading to the development of cancer.

3. Other Names for This Gene

- androgen receptor-associated coregulator 267
- ARA267
- histone-lysine N-methyltransferase, H3 lysine-36 and H4 lysine-20 specific
- NR-binding SET domain containing protein
- NSD1_HUMAN
- nuclear receptor-binding Su-var, Enhancer of zeste and Trithorax domain protein 1
- SOTOS1

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