H19

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H19, imprinted maternally expressed transcript

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1. Introduction

The *H19* gene provides instructions for making a molecule called a noncoding RNA. (RNA is a chemical cousin of DNA.) Unlike many genes, the *H19* gene does not contain instructions for making a protein. The function of the noncoding RNA produced from the gene is unknown, but researchers believe that it may act as a tumor suppressor, keeping cells from growing and dividing too fast or in an uncontrolled way. The *H19* gene is highly active in various tissues before birth and appears to play an important role in early development.

People inherit one copy of most genes from their mother and one copy from their father. Both copies are typically active, or "turned on," in cells. However, the activity of the *H19* gene depends on which parent it was inherited from. Only the copy inherited from a person's mother (the maternally inherited copy) is active; the copy inherited from the father (the paternally inherited copy) is not active. This parent-specific difference in gene activation is caused by a phenomenon called genomic imprinting.

H19 is part of a cluster of genes on the short (p) arm of chromosome 11 that undergoes genomic imprinting. Another gene in this cluster, *IGF2*, is also involved in growth and development. A nearby region of DNA known as imprinting center 1 (IC1) or the H19 differentially methylated region (H19 DMR) controls the parent-specific genomic imprinting of both the *H19* and *IGF2* genes. The IC1 region undergoes a process called methylation, which is a chemical reaction that attaches small molecules called methyl groups to certain segments of DNA. Methylation, which occurs during the formation of an egg or sperm cell, is a way of marking or "stamping" the parent of origin. The IC1 region is normally methylated only on the paternally inherited copy of chromosome 11.

2. Health Conditions Related to Genetic Changes

2.1. Beckwith-Wiedemann Syndrome

Beckwith-Wiedemann syndrome, a condition characterized by overgrowth and other signs and symptoms that affect many parts of the body, can result from changes that affect the IC1 region. In some people with this condition, the maternally inherited copy of the IC1 region is methylated along with the paternally inherited copy. Because the IC1 region controls the genomic imprinting of the *H19* and *IGF2* genes, this abnormality disrupts the regulation of both genes. Specifically, abnormal methylation of the IC1 region leads to a loss of *H19* gene activity and increased *IGF2* gene activity in many tissues. A loss of *H19* gene activity, which normally restrains growth, and an increase in *IGF2* gene activity, which promotes growth, together lead to overgrowth in people with Beckwith-Wiedemann syndrome.

In a few cases, Beckwith-Wiedemann syndrome has been caused by deletions of a small amount of DNA from the IC1 region. Like abnormal methylation, these deletions alter the activity of the *H19* and *IGF2* genes.

2.2. Russell-Silver syndrome

Changes in methylation of the IC1 region are also responsible for some cases of Russell-Silver syndrome, a disorder characterized by slow growth before and after birth. The changes are different than those seen in Beckwith-Wiedemann syndrome and have the opposite effect on growth.

In Russell-Silver syndrome, the paternally inherited copy of the IC1 region often has too few methyl groups attached (hypomethylation). Hypomethylation of the IC1 region leads to increased activity of the *H19* gene and a loss of *IGF2* gene activity in many tissues. An increase in *H19* gene activity, which restrains growth, and a loss of *IGF2* gene activity, which normally promotes growth, together lead to poor growth and short stature in people with Russell-Silver syndrome.

2.3. Wilms Tumor

Changes in methylation of the IC1 region have also been found in some cases of Wilms tumor, a rare form of kidney cancer that occurs almost exclusively in children.

In some people with Wilms tumor, the maternally inherited copy of the IC1 region is methylated along with the paternally inherited copy. Abnormal methylation of the IC1 region leads to a loss of *H19* gene activity and increased *IGF2* gene activity in kidney cells. A loss of *H19* gene activity, which normally restrains cell growth, and an increase in *IGF2* gene activity, which promotes cell growth, together lead to uncontrolled cell growth and tumor development in people with Wilms tumor. As this mechanism is similar to the one that causes Beckwith-Wiedemann syndrome (described above), it is thought that individuals with Wilms tumor caused by changes in IC1 methylation may later be diagnosed with Beckwith-Wiedemann syndrome.

In most cases, abnormal methylation of IC1 and subsequent changes in *H19* and *IGF2* gene activity are somatic, which means that they are acquired during a person's lifetime and present only in the some tissues. Rarely, these changes are germline, which means they are present in all of the body's cells.

3. Other Names for This Gene

- D11S813E
- H19, imprinted maternally expressed transcript (non-protein coding)
- LINC00008
- MGC4485
- PRO2605

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