PHF8 gene

PHD finger protein 8

Normal Function

The *PHF8* gene provides instructions for making a protein that is found in the cell nucleus, particularly in brain cells before and just after birth. The PHF8 protein is part of a group known as zinc finger proteins, which contain one or more short regions called zinc finger domains. These regions include a specific pattern of protein building blocks (amino acids) and one or more charged atoms of zinc (zinc ions). The folded configuration of the zinc finger domain stabilizes the protein and allows it to attach (bind) to other molecules.

The PHF8 protein contains a specific zinc finger domain called a PHD domain, which binds to complexes called chromatin, the network of DNA and proteins (called histones) that packages DNA into chromosomes. Binding with the PHF8 protein is part of the process that changes the structure of chromatin (chromatin remodeling) to alter how tightly regions of DNA are packaged. Chromatin remodeling is one way gene activity (expression) is regulated; when DNA is tightly packed genes tend to be turned off, compared to when DNA is loosely packed and genes are usually turned on. While the PHF8 protein is bound to chromatin, another domain of the PHF8 protein, called Jumonji C (JmjC), removes molecules called methyl groups from histones. Removing these methyl groups (demethylation) causes the chromatin to become loosely packed and increases the expression of specific genes.

Health Conditions Related to Genetic Changes

X-linked intellectual disability, Siderius type

At least four mutations in the *PHF8* gene have been found to cause X-linked intellectual disability, Siderius type. This condition is characterized by mild to moderate intellectual disability, and it occurs only in males. Affected boys often have an opening in the lip (cleft lip) with an opening in the roof of the mouth (cleft palate). Most *PHF8* gene mutations lead to an abnormally short protein that gets transported out of the cell's nucleus. Outside of the nucleus, the PHF8 protein cannot interact with chromatin to regulate gene expression. Other mutations impair the protein's ability to remove methyl groups from histones within chromatin, leading to a decrease in gene expression.

While the exact disease mechanism is unknown, it is likely that impaired protein function

or a lack of PHF8 protein in the nucleus of brain cells before birth prevents chromatin remodeling, altering the normal expression of genes involved in intellectual function and formation of structures along the midline of the skull. This altered gene expression leads to intellectual disability and cleft lip and palate found in males with X-linked intellectual disability, Siderius type.

Other Names for This Gene

- histone lysine demethylase PHF8
- JHDM1F
- jumonji C domain-containing histone demethylase 1F
- KIAA1111
- PHF8_HUMAN
- ZNF422

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PHF8 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=23133[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28PHF8%5BTIAB%5D%29+OR+%28PHD+finger+protein+8%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- PHD FINGER PROTEIN 8; PHF8 (https://omim.org/entry/300560)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/23133)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=PHF8[gene])

References

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Genomic Location

The *PHF8* gene is found on the X chromosome (https://medlineplus.gov/genetics/chromosome/x/).

Last updated June 1, 2015