ASXL1 gene

ASXL transcriptional regulator 1

Normal Function

The *ASXL1* gene provides instructions for making a protein that is involved in a process known as chromatin remodeling. Chromatin is the complex of DNA and proteins that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. When DNA is tightly packed, gene activity (expression) is lower than when DNA is loosely packed.

Through its role in chromatin remodeling, the ASXL1 protein regulates the expression of many genes, including a group of genes known as HOX genes, which play important roles in development before birth. The ASXL1 protein can turn on (activate) or turn off (repress) HOX genes depending on when they are needed.

The ASXL1 protein may have an additional role in gene regulation by signaling to molecules to add a methyl group (a process called methylation) to an area near a gene called the promoter region, which controls gene activity. When a promoter region is methylated, gene activity is repressed, and when a promoter region is not methylated, the gene is active.

Health Conditions Related to Genetic Changes

Bohring-Opitz syndrome

More than 20 mutations in the *ASXL1* gene have been found to cause Bohring-Opitz syndrome, a condition that causes abnormal head size and shape, distinctive facial features, joint abnormalities, intellectual disability, and other signs and symptoms. Most of the *ASXL1* gene mutations that cause Bohring-Opitz syndrome create a premature stop signal in the instructions for making the ASXL1 protein, resulting in either an abnormally short, nonfunctional protein or a complete lack of ASXL1 protein. These *ASXL1* gene mutations are described as "loss-of-function" because they reduce the amount of functional ASXL1 protein available, which likely disrupts the regulation of the activity of HOX genes and other genes during development. Altered activity of HOX genes probably leads to the neurological and physical features of this condition.

Systemic mastocytosis

MedlinePlus Genetics provides information about Systemic mastocytosis

Cancers

Mutations in the *ASXL1* gene have been associated with cancerous conditions of blood-forming cells, such as acute myeloid leukemia, chronic myelomonocytic leukemia, and myelodysplastic syndrome. These mutations are somatic, which means they are acquired during a person's lifetime and are present only in cells that give rise to cancer.

The mutations associated with these conditions are likely "gain-of-function," which means that they lead to an overactive ASXL1 protein. Researchers believe that the overactive ASXL1 protein leads to poor regulation of gene activity. It is unclear how this altered gene regulation plays a role in the development of cancer, but it is likely that overactive genes promote the growth of cancers by allowing abnormal blood cells to grow and divide uncontrollably.

The *ASXL1* gene mutations involved in these cancers are different from the ones that cause Bohring-Opitz syndrome (described above). People with Bohring-Opitz syndrome are not thought to have an increased risk of developing cancer.

Other Names for This Gene

- additional sex combs like 1
- additional sex combs like 1, transcriptional regulator
- additional sex combs like transcriptional regulator 1
- KIAA0978
- putative Polycomb group protein ASXL1 isoform 1
- putative Polycomb group protein ASXL1 isoform 2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ASXL1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=171023[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ASXL1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- ASXL TRANSCRIPTIONAL REGULATOR 1; ASXL1 (https://omim.org/entry/612990)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/171023)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ASXL1[gene])

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Genomic Location

The *ASXL1* gene is found on chromosome 20 (https://medlineplus.gov/genetics/chromosome/20/).

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