KDM6A gene

lysine demethylase 6A

Normal Function

The *KDM6A* gene provides instructions for making an enzyme called lysine-specific demethylase 6A that is found in many organs and tissues of the body. Lysine-specific demethylase 6A functions as a histone demethylase. Histone demethylases are enzymes that modify proteins called histones. Histones are structural proteins that attach (bind) to DNA and give chromosomes their shape. By removing a molecule called a methyl group from histones (a process called demethylation), histone demethylases control (regulate) the activity of certain genes. Lysine-specific demethylase 6A appears to regulate certain genes that are important for development.

Lysine-specific demethylase 6A is also believed to act as a tumor suppressor, which means it normally helps prevent cells from growing and dividing in an uncontrolled way.

Health Conditions Related to Genetic Changes

Kabuki syndrome

Many variants (also known as mutations) in the *KDM6A* gene have been identified in people with Kabuki syndrome, a disorder characterized by distinctive facial features, intellectual disability, and abnormalities affecting other parts of the body.

Most of the *KDM6A* gene variants associated with Kabuki syndrome remove (delete) genetic material in the *KDM6A* gene sequence or result in a premature stop signal that leads to an abnormally short lysine-specific demethylase 6A enzyme. As a result of these changes, the enzyme is nonfunctional. A lack of functional lysine-specific demethylase 6A enzyme disrupts its role in histone demethylation and impairs proper regulation of certain genes in many of the body's organs and tissues, resulting in the abnormalities of development and function characteristic of Kabuki syndrome.

Although lysine-specific demethylase 6A is believed to act as a tumor suppressor, a loss of this enzyme's function does not seem to increase cancer risk in people with Kabuki syndrome.

Bladder cancer

Some gene variants are acquired during a person's lifetime and are present only in

certain cells. These changes, which are called somatic variants, are not inherited. Somatic variants in the *KDM6A* gene have been found in some cases of bladder cancer. Bladder cancer is a disease in which certain cells in the bladder become abnormal and multiply uncontrollably to form a tumor. Bladder cancer may cause blood in the urine, pain during urination, frequent urination, the feeling to of needing to urinate without being able to, or lower back pain.

Bladder cancer is generally divided into two types, non-muscle invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC), based on where in the bladder the tumor is located. About half of NMIBC tumors have *KDM6A* gene variants. These *KDM6A* gene variants change single protein building blocks (amino acids) in the enzyme, which appears to impair the enzyme's role in histone demethylation. As a result, regulation of certain genes in bladder cells is disrupted, which likely leads to uncontrolled cell division and the formation of bladder cancer.

Cancers

Somatic variants in the *KDM6A* gene have been identified in cancers of the breast, esophagus, colon, kidney, and brain, and cancers of blood-forming cells called myeloid leukemia and multiple myeloma. Most of these variants result in an abnormally short, nonfunctional lysine-specific demethylase 6A enzyme that cannot perform its role as a tumor suppressor, resulting in the development of cancer.

Other Names for This Gene

- bA386N14.2
- bA386N14.2 (ubiquitously transcribed X chromosome tetratricopeptide repeat protein (UTX))
- histone demethylase UTX
- KABUK2
- KDM6A_HUMAN
- lysine (K)-specific demethylase 6A
- lysine-specific demethylase 6A
- ubiquitously transcribed tetratricopeptide repeat protein X-linked
- ubiquitously-transcribed TPR gene on the X chromosome
- ubiquitously-transcribed TPR protein on the X chromosome
- UTX

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of KDM6A (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7403[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28KDM6A%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+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- LYSINE DEMETHYLASE 6A; KDM6A (https://omim.org/entry/300128)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7403)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=KDM6A[gene])

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Genomic Location

The *KDM6A* gene is found on the X chromosome (https://medlineplus.gov/genetics/chromosome/x/).

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