



CYLD gene

CYLD lysine 63 deubiquitinase

Normal Function

The *CYLD* gene provides instructions for making a protein that helps regulate nuclear factor-kappa-B. Nuclear factor-kappa-B is a group of related proteins that help protect cells from self-destruction (apoptosis) in response to certain signals. In regulating the action of nuclear factor-kappa-B, the CYLD protein allows cells to respond properly to signals to self-destruct when appropriate, such as when the cells become abnormal. By this mechanism, the CYLD protein acts as a tumor suppressor, which means that it helps prevent cells from growing and dividing too fast or in an uncontrolled way.

Health Conditions Related to Genetic Changes

Brooke-Spiegler syndrome

At least 20 *CYLD* gene mutations have been identified in individuals with Brooke-Spiegler syndrome. This condition is characterized by multiple noncancerous (benign) tumors that develop in structures associated with the skin (skin appendages), such as sweat glands and hair follicles. People with Brooke-Spiegler syndrome may develop several types of skin appendage tumors, including growths called spiradenomas, trichoepitheliomas, and cylindromas. Spiradenomas are tumors of the sweat glands. Trichoepitheliomas arise from the hair follicles. While previously thought to derive from sweat glands, cylindromas are now generally believed to begin in hair follicles.

People with Brooke-Spiegler syndrome are born with a mutation in one of the two copies of the *CYLD* gene in each cell. This mutation prevents the cell from making functional CYLD protein from the altered copy of the gene. However, enough protein is usually produced from the other, normal copy of the gene to regulate cell growth effectively. For tumors to develop, a second mutation or deletion of genetic material involving the other copy of the *CYLD* gene must occur in certain cells during a person's lifetime. These genetic changes are called somatic mutations and are not inherited.

When both copies of the *CYLD* gene are mutated in a particular cell, that cell cannot produce any functional CYLD protein. The loss of this protein impairs the regulation of nuclear factor-kappa-B, allowing the cell to grow and divide in an uncontrolled way to form a tumor. In people with Brooke-Spiegler syndrome, second *CYLD* mutations typically occur in different types of cells in the skin over an affected person's lifetime, leading to the growth of multiple types of skin appendage tumors.

Familial cylindromatosis

More than 30 *CYLD* gene mutations have been identified in individuals with familial cylindromatosis. People with this disorder typically develop large numbers of cylindromas.

As in Brooke-Spiegler syndrome, people with familial cylindromatosis are born with one mutated copy of the *CYLD* gene in each cell, and a second mutation or deletion of genetic material involving the other copy of the *CYLD* gene must occur in certain cells during a person's lifetime.

When both copies of the *CYLD* gene are mutated in particular hair follicle cells, those cells cannot produce any functional CYLD protein. The loss of this protein allows the cells to grow and divide in an uncontrolled way to form cylindromas.

Multiple familial trichoepithelioma

At least 22 mutations in the *CYLD* gene have been identified in individuals with multiple familial trichoepithelioma. People with this disorder typically develop large numbers of trichoepitheliomas.

As in Brooke-Spiegler syndrome and familial cylindromatosis, people with *CYLD*-related multiple familial trichoepithelioma are born with one mutated copy of the *CYLD* gene in each cell, and a second mutation or deletion of genetic material involving the other copy of the *CYLD* gene must occur in certain cells during a person's lifetime.

When both copies of the *CYLD* gene are mutated in particular hair follicle cells, those cells cannot produce any functional CYLD protein. The loss of this protein allows the cells to grow and divide in an uncontrolled way to form trichoepitheliomas.

Some researchers consider familial cylindromatosis, multiple familial trichoepithelioma, and Brooke-Spiegler syndrome to be different forms of the same disorder. It is unclear why mutations in the *CYLD* gene cause different types of skin appendage tumors in each of these conditions, or why the tumors are generally confined to the skin in these disorders.

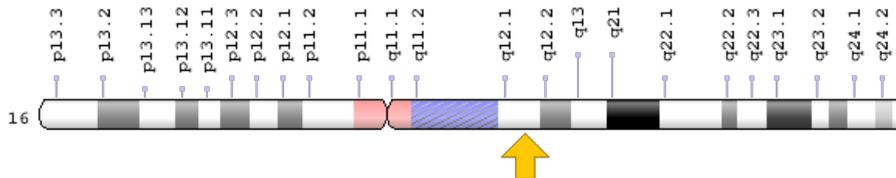
Cancers

Somatic mutations and reduced activity (expression) of the *CYLD* gene have also been identified in certain cancerous tumors. These cancers include multiple myeloma, which starts in cells of the bone marrow, and cancers of the kidney, liver, uterus, and colon. These genetic changes likely impair the tumor suppressor function of the CYLD protein, allowing cells to grow and divide in an uncontrolled way and become cancerous.

Chromosomal Location

Cytogenetic Location: 16q12.1, which is the long (q) arm of chromosome 16 at position 12.1

Molecular Location: base pairs 50,742,026 to 50,801,935 on chromosome 16 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- BRSS
- CDMT
- CYLD1
- CYLD_HUMAN
- CYLDI
- cylindromatosis (turban tumor syndrome)
- EAC
- HSPC057
- KIAA0849
- MFT
- MFT1
- SBS
- TEM
- USPL2

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database (2000): Activation of the NF-KB Signaling Cascade
<https://www.ncbi.nlm.nih.gov/books/NBK6169/#A63402>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CYLD%5BTIAB%5D%29+OR+%28cylindromatosis%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+720+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- CYLD GENE
<http://omim.org/entry/605018>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/CYLDID40232ch16q12.html>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=CYLD%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:2584
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:1540>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/1540>
- UniProt
<https://www.uniprot.org/uniprot/Q9NQC7>

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Reviewed: June 2012
Published: June 11, 2019

Lister Hill National Center for Biomedical Communications
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