

BTK gene

Bruton tyrosine kinase

Normal Function

The *BTK* gene provides instructions for making a protein called Bruton tyrosine kinase (BTK), which is essential for the development and maturation of B cells. B cells are specialized white blood cells that help protect the body against infection. These cells can mature into cells that produce special proteins called antibodies or immunoglobulins. Antibodies attach to specific foreign particles and germs, marking them for destruction. The BTK protein transmits important chemical signals that instruct B cells to mature and produce antibodies.

Health Conditions Related to Genetic Changes

Isolated growth hormone deficiency

A few mutations in the *BTK* gene have been found to cause isolated growth hormone deficiency type III, a condition characterized by slow growth, short stature, and a weakened immune system. Mutations that cause this condition lead to production of a nonfunctional version of the BTK protein. People with isolated growth hormone deficiency are prone to infections because they produce very few B cells and have a shortage of antibodies (agammaglobulinemia). A lack of the BTK protein is likely responsible for the immune system symptoms, but how a shortage of BTK protein causes short stature in affected individuals is unclear.

X-linked agammaglobulinemia

More than 600 different mutations in the *BTK* gene have been found to cause X-linked agammaglobulinemia (XLA). Most of these mutations result in the absence of the BTK protein. Other mutations change a single protein building block (amino acid), which probably leads to the production of an abnormal BTK protein that is quickly broken down in the cell. The absence of functional BTK protein blocks B cell development and leads to a lack of antibodies, causing an increased susceptibility to infections in people with XLA.

Some people with XLA have large DNA deletions that remove one end of the *BTK* gene and all of a neighboring gene known as *TIMM8A*. Mutations in *TIMM8A* cause deafness-dystonia-optic neuropathy (DDON) syndrome, which is characterized by hearing loss,

vision problems, a decline in intellectual function (dementia), and involuntary muscle tensing (dystonia) or difficulty coordinating movements (ataxia). Individuals with large DNA deletions that include the *BTK* gene and the *TIMM8A* gene have the signs and symptoms of both XLA and DDON syndrome.

Other Names for This Gene

- AGMX1
- AT
- ATK
- BPK
- Bruton agammaglobulinemia tyrosine kinase
- Bruton's tyrosine kinase
- BTK_HUMAN
- dominant-negative kinase-deficient Bruton's tyrosine kinase
- IMD1
- MGC126261
- MGC126262
- PSCTK1
- tyrosine-protein kinase BTK
- XLA

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of BTK ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=695\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=695[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28BTK%5BTIAB%5D%29+OR+%28Bruton+agammaglobulinemia+tyrosine+kinase%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+1080+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- BRUTON AGAMMAGLOBULINEMIA TYROSINE KINASE; BTK (<https://omim.org/entry/300300>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/695>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=BTK\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=BTK[gene]))

References

- Alatzoglou KS, Dattani MT. Genetic causes and treatment of isolated growth hormone deficiency-an update. *Nat Rev Endocrinol*. 2010 Oct;6(10):562-76. doi:10.1038/nrendo.2010.147. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20852587>)
- Broides A, Yang W, Conley ME. Genotype/phenotype correlations in X-linked agammaglobulinemia. *Clin Immunol*. 2006 Feb-Mar;118(2-3):195-200. doi:10.1016/j.clim.2005.10.007. Epub 2005 Nov 16. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16297664>)
- Conley ME, Farmer DM, Dobbs AK, Howard V, Aiba Y, Shurtleff SA, Kurosaki T. A minimally hypomorphic mutation in Btk resulting in reduced B cell numbers but no clinical disease. *Clin Exp Immunol*. 2008 Apr;152(1):39-44. doi:10.1111/j.1365-2249.2008.03593.x. Epub 2008 Jan 28. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18241230>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2384053/>)
- Jyonouchi H, Geng L, Toruner GA, Vinekar K, Feng D, Fitzgerald-Bocarsly P. Monozygous twins with a microdeletion syndrome involving BTK, DDP1, and two other genes; evidence of intact dendritic cell development and TLR responses. *Eur J Pediatr*. 2008 Mar;167(3):317-21. doi: 10.1007/s00431-007-0493-0. Epub 2007 May 23. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17520285>)
- Maas A, Hendriks RW. Role of Bruton's tyrosine kinase in B cell development. *Dev Immunol*. 2001;8(3-4):171-81. doi: 10.1155/2001/28962. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11785667>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2276078/>)
- Richter D, Conley ME, Rohrer J, Myers LA, Zahradka K, Kelecic J, Sertic J, Stavljenic-Rukavina A. A contiguous deletion syndrome of X-linked agammaglobulinemia and sensorineural deafness. *Pediatr Allergy Immunol*. 2001 Apr;12(2):107-11. doi: 10.1034/j.1399-3038.2001.0129999107.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11338284>)
- Sediva A, Smith CI, Asplund AC, Hadac J, Janda A, Zeman J, Hansikova H, Dvorakova L, Mrazova L, Velbri S, Koehler C, Roesch K, Sullivan KE, Futatani T, Ochs HD. Contiguous X-chromosome deletion syndrome encompassing the BTK, TIMM8A, TAF7L, and DRP2 genes. *J Clin Immunol*. 2007 Nov;27(6):640-6. doi:10.1007/s10875-007-9123-x. Epub 2007 Sep 12. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17851739>)
- Smith CIE, Berglof A. X-Linked Agammaglobulinemia. 2001 Apr 5 [updated 2016 Aug 4]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. *GeneReviews*(R) [Internet]. Seattle (WA):

University of Washington, Seattle; 1993-2024. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1453/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301626>)

- Valiaho J, Smith CI, Vihinen M. BTKbase: the mutation database for X-linked agammaglobulinemia. *Hum Mutat.* 2006 Dec;27(12):1209-17. doi: 10.1002/humu.20410. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16969761>)
- Wit JM, Kiess W, Mullis P. Genetic evaluation of short stature. *Best Pract Res Clin Endocrinol Metab.* 2011 Feb;25(1):1-17. doi: 10.1016/j.beem.2010.06.007. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21396571>)

Genomic Location

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

Last updated February 1, 2012