Bloom syndrome

Description

Bloom syndrome is an inherited disorder characterized by short stature, a skin rash that develops after exposure to the sun, and a greatly increased risk of cancer.

People with Bloom syndrome are usually smaller than 97 percent of the population in both height and weight from birth, and they rarely exceed 5 feet tall in adulthood.

Affected individuals have skin that is sensitive to sun exposure, and they usually develop a butterfly-shaped patch of reddened skin across the nose and cheeks. A skin rash can also appear on other areas that are typically exposed to the sun, such as the back of the hands and the forearms. Small clusters of enlarged blood vessels (telangiectases) often appear in the rash; telangiectases can also occur in the eyes. Other skin features include patches of skin that are lighter or darker than the surrounding areas (hypopigmentation or hyperpigmentation respectively). These patches appear on areas of the skin that are not exposed to the sun, and their development is not related to the rashes.

People with Bloom syndrome have an increased risk of cancer. They can develop any type of cancer, but the cancers arise earlier in life than they do in the general population, and affected individuals often develop more than one type of cancer.

Individuals with Bloom syndrome have a high-pitched voice and distinctive facial features including a long, narrow face; a small lower jaw; and prominent nose and ears. Other features can include learning disabilities, an increased risk of diabetes, chronic obstructive pulmonary disease (COPD), and mild immune system abnormalities leading to recurrent infections of the upper respiratory tract, ears, and lungs during infancy. Men with Bloom syndrome usually do not produce sperm and as a result are unable to father children (infertile). Women with the disorder generally have reduced fertility and experience menopause at an earlier age than usual.

Frequency

Bloom syndrome is a rare disorder. Only a few hundred affected individuals have been described in the medical literature, about one-third of whom are of Central and Eastern European (Ashkenazi) Jewish background.

Causes

Mutations in the *BLM* gene cause Bloom syndrome. The *BLM* gene provides instructions for making a member of a protein family called RecQ helicases. Helicases are enzymes that attach (bind) to DNA and unwind the two spiral strands (double helix) of the DNA molecule. This unwinding is necessary for several processes in the cell nucleus, including copying (replicating) DNA in preparation for cell division and repairing damaged DNA. Because RecQ helicases help maintain the structure and integrity of DNA, they are known as the "caretakers of the genome."

When a cell prepares to divide to form two cells, the DNA that makes up the chromosomes is copied so that each new cell will have two copies of each chromosome, one from each parent. The copied DNA from each chromosome is arranged into two identical structures, called sister chromatids, which are attached to one another during the early stages of cell division. Sister chromatids occasionally exchange small sections of DNA during this time, a process known as sister chromatid exchange. Researchers suggest that these exchanges may be a response to DNA damage during the copying process. The BLM protein helps to prevent excess sister chromatid exchanges and is also involved in other processes that help maintain the stability of the DNA during the copying process.

BLM gene mutations result in the absence of functional BLM protein. As a result, the frequency of sister chromatid exchange is about 10 times higher than average. Exchange of DNA between chromosomes derived from the individual's mother and father are also increased in people with *BLM* gene mutations. In addition, chromosome breakage occurs more frequently in affected individuals. All of these changes are associated with gaps and breaks in the genetic material that impair normal cell activities and cause the health problems associated with this condition. Without the BLM protein, the cell is less able to repair DNA damage caused by ultraviolet light, which results in increased sun sensitivity. Genetic changes that allow cells to divide in an uncontrolled way lead to the cancers that occur in people with Bloom syndrome.

Learn more about the gene associated with Bloom syndrome

- BLM

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Bloom's syndrome
- Bloom-Torre-Machacek syndrome

- Congenital telangiectatic erythema

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Bloom syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0005859/)

Genetic and Rare Diseases Information Center

- Bloom syndrome (https://rarediseases.info.nih.gov/diseases/915/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Bloom syndrome%22)

Catalog of Genes and Diseases from OMIM

- BLOOM SYNDROME; BLM (https://omim.org/entry/210900)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Bloom+Syndrome%5BMAJR%5D%29+AND+%28Bloom+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

References

- Amor-Gueret M. Bloom syndrome, genomic instability and cancer: the SOS-likehypothesis. Cancer Lett. 2006 May 8;236(1):1-12. doi:10.1016/j.canlet.2005.04.023. Epub 2005 Jun 13. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15950375)
- Arora H, Chacon AH, Choudhary S, McLeod MP, Meshkov L, Nouri K, Izakovic J. Bloom syndrome. Int J Dermatol. 2014 Jul;53(7):798-802. doi: 10.1111/ijd.12408. Epub 2014 Mar 6. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24602044)
- Atlas of Genetics and Cytogenetics in Oncology and Haematology (http://atlasgeneticsoncology.org/Kprones/BLOID10002.html)

- Cheok CF, Bachrati CZ, Chan KL, Ralf C, Wu L, Hickson ID. Roles of the Bloom'ssyndrome helicase in the maintenance of genome stability. Biochem Soc Trans. 2005Dec;33(Pt 6):1456-9. doi: 10.1042/BST0331456. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16246145)
- German J, Sanz MM, Ciocci S, Ye TZ, Ellis NA. Syndrome-causing mutations ofthe BLM gene in persons in the Bloom's Syndrome Registry. Hum Mutat. 2007Aug;28(8):743-53. doi: 10.1002/humu.20501. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17407155)
- Guo RB, Rigolet P, Ren H, Zhang B, Zhang XD, Dou SX, Wang PY, Amor-Gueret M,Xi XG. Structural and functional analyses of disease-causing missense mutationsin Bloom syndrome protein. Nucleic Acids Res. 2007;35(18):6297-310. doi: 10.1093/nar/gkm536. Epub 2007 Sep 18. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17878217) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2094094/)
- Kaneko H, Kondo N. Clinical features of Bloom syndrome and function of thecausative gene, BLM helicase. Expert Rev Mol Diagn. 2004 May;4(3):393-401. doi:10.1586/14737159.4.3.393. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15137905)
- Liu Y, West SC. More complexity to the Bloom's syndrome complex. Genes Dev.2008 Oct 15;22(20):2737-42. doi: 10.1101/gad.1732808. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18923071) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2751278/)
- Ouyang KJ, Woo LL, Ellis NA. Homologous recombination and maintenance ofgenome integrity: cancer and aging through the prism of human RecQ helicases. Mech Ageing Dev. 2008 Jul-Aug;129(7-8):425-40. doi: 10.1016/j.mad.2008.03.003. Epub 2008 Mar 15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18430459)
- Singh DK, Ahn B, Bohr VA. Roles of RECQ helicases in recombination based DNArepair, genomic stability and aging. Biogerontology. 2009 Jun;10(3):235-52. doi: 10.1007/s10522-008-9205-z. Epub 2008 Dec 15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19083132) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2713741/)
- Wu L. Role of the BLM helicase in replication fork management. DNA Repair(Amst). 2007 Jul 1;6(7):936-44. doi: 10.1016/j.dnarep.2007.02.007. Epub 2007 Mar23. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17363339)

Last updated April 1, 2015