SBDS Gene

Subjects: Genetics & Heredity
Contributor: Karina Chen

SBDS, ribosome maturation factor

Keywords: genes

1. Normal Function

The *SBDS* gene provides instructions for making a protein that is critical for building ribosomes. Ribosomes are cellular structures that process the cell's genetic instructions to create proteins. Each ribosome is made up of two parts (subunits) called the large subunit and the small subunit. The SBDS protein helps prepare the large subunit so it can assemble into the ribosome by helping remove another protein (called eIF6) that blocks the interaction of the large subunit with the small subunit.

Research suggests that the SBDS protein may be involved in other cellular processes, such as ensuring proper cell division, aiding cell movement, protecting cells from stress, and processing RNA, a molecule that is a chemical cousin of DNA. More research is needed to clarify the protein's role in these processes.

2. Health Conditions Related to Genetic Changes

2.1. Shwachman-Diamond syndrome

More than 80 mutations in the *SBDS* gene have been identified in people with Shwachman-Diamond syndrome. This condition causes problems related to impaired function of the bone marrow and pancreas. Affected individuals also have skeletal abnormalities and a higher-than-average chance of developing a blood cell cancer called acute myeloid leukemia or a related bone marrow disorder called myelodysplastic syndrome.

Many of the *SBDS* gene mutations involved in Shwachman-Diamond syndrome result from an exchange of genetic material between the *SBDS* gene and a very similar, but nonfunctional, piece of DNA called a pseudogene, which is located close to the *SBDS* gene on chromosome 7. This type of DNA exchange is called a gene conversion. The genetic material from the pseudogene contains errors that, when introduced into the *SBDS* gene, disrupt the way the gene's instructions are used to make a protein.

The two most common mutations in people with Shwachman-Diamond syndrome result from exchanges between the *SBDS* gene and the nearby pseudogene. One of these mutations, written as 258+2T>C, changes a single DNA building block (nucleotide) in a region of the gene known as intron 2. This mutation, which is called a splice-site mutation, prevents the production of functional SBDS protein. Other splice-site mutations in the *SBDS* gene can also cause Shwachman-Diamond syndrome. The other common mutation, written as 183_184delTAinsCT, changes two nucleotides in the *SBDS* gene. This genetic change introduces a premature stop signal in the instructions for making the SBDS protein. It is unclear whether this mutation results in an abnormally shortened protein or prevents any protein from being made.

The features of Shwachman-Diamond syndrome result when mutations reduce the amount or impair the function of the SBDS protein. Researchers are unsure how a reduction of functional SBDS protein causes the condition. They suspect a shortage of SBDS protein impairs ribosome formation, which may reduce the production of other proteins and alter developmental processes. It is unclear whether disruption of other cellular functions contribute to the features of Shwachman-Diamond syndrome.

3. Other Names for This Gene

- CGI-97
- FLJ10917

- SBDS ribosome assembly guanine nucleotide exchange factor
- SBDS, ribosome assembly guanine nucleotide exchange factor
- SBDS_HUMAN
- Sdol1
- SDS
- Shwachman-Bodian-Diamond syndrome
- SWDS
- YLR022c

References

1. Austin KM, Gupta ML Jr, Coats SA, Tulpule A, Mostoslavsky G, Balazs AB,Mulligan RC, Daley G, Pellman D, Shimamura A. Mitotic spindle destabilization andgenomic instability in Shwachman-Diamond syndrome. J Clin Invest. 2008Apr;118(4):1511-8. doi: 10.1172/JCI33764.
2. Ball HL, Zhang B, Riches JJ, Gandhi R, Li J, Rommens JM, Myers JS.Shwachman-Bodian Diamond syndrome is a multi-functional protein implicated incellular stress responses. Hum Mol Genet. 2009 Oct 1;18(19):3684-95. doi:10.1093/hmg/ddp316.
3. Boocock GR, Marit MR, Rommens JM. Phylogeny, sequence conservation, andfunctional complementation of the SBDS protein family. Genomics. 2006Jun;87(6):758-71.
4. Boocock GR, Morrison JA, Popovic M, Richards N, Ellis L, Durie PR, Rommens JM.Mutations in SBDS are associated with Shwachman-Diamond syndrome. Nat Genet. 2003Jan;33(1):97-101.
5. Calamita P, Miluzio A, Russo A, Pesce E, Ricciardi S, Khanim F, Cheroni C,Alfieri R, Mancino M, Gorrini C, Rossetti G, Peluso I, Pagani M, Medina DL,Rommens J, Biffo S. SBDS-Deficient Cells Have an Altered Homeostatic Equilibrium due to Translational Inefficiency Which Explains their Reduced Fitness andProvides a Logical Framework for Intervention. PLoS Genet. 2017 Jan5;13(1):e1006552. doi: 10.1371/journal.pgen.1006552.
6. Dror Y. Shwachman-Diamond syndrome. Pediatr Blood Cancer. 2005Dec;45(7):892-901. Review.
7. Finch AJ, Hilcenko C, Basse N, Drynan LF, Goyenechea B, Menne TF, GonzálezFernández A, Simpson P, D'Santos CS, Arends MJ, Donadieu J, Bellanné-Chantelot C,Costanzo M, Boone C, McKenzie AN, Freund SM, Warren AJ. Uncoupling of GTPhydrolysis from eIF6 release on the ribosome causes Shwachman-Diamond syndrome.Genes Dev. 2011 May 1;25(9):917-29. doi: 10.1101/gad.623011.
8. Ganapathi KA, Austin KM, Lee CS, Dias A, Malsch MM, Reed R, Shimamura A. Thehuman Shwachman-Diamond syndrome protein, SBDS, associates with ribosomal RNA.Blood. 2007 Sep 1;110(5):1458-65.
9. Orelio C, Kuijpers TW. Shwachman-Diamond syndrome neutrophils have alteredchemoattractant-induced F-actin polymerization and polarization characteristics. Haematologica. 2009 Mar;94(3):409-13. doi: 10.3324/haematol.13733.
10. Savchenko A, Krogan N, Cort JR, Evdokimova E, Lew JM, Yee AA, Sánchez-PulidoL, Andrade MA, Bochkarev A, Watson JD, Kennedy MA, Greenblatt J, Hughes T,Arrowsmith CH, Rommens JM, Edwards AM. The Shwachman-Bodian-Diamond syndromeprotein family is involved in RNA metabolism. J Biol Chem. 2005 May13;280(19):19213-20.
11. Shammas C, Menne TF, Hilcenko C, Michell SR, Goyenechea B, Boocock GR, DuriePR, Rommens JM, Warren AJ. Structural and mutational analysis of the SBDS proteinfamily. Insight into the leukemia-associated Shwachman-Diamond Syndrome. J BiolChem. 2005 May 13;280(19):19221-9.
12. Shimamura A. Shwachman-Diamond syndrome. Semin Hematol. 2006 Jul;43(3):178-88.Review.
13. Weis F, Giudice E, Churcher M, Jin L, Hilcenko C, Wong CC, Traynor D, Kay RR, Warren AJ. Mechanism of eIF6 release from the nascent 60S ribosomal subunit. Nat Struct Mol Biol. 2015 Nov;22(11):914-9. doi: 10.1038/nsmb.3112.
14. Woloszynek JR, Rothbaum RJ, Rawls AS, Minx PJ, Wilson RK, Mason PJ, Bessler M,Link DC. Mutations of the SBDS gene are present in most patients withShwachman-Diamond syndrome. Blood. 2004 Dec 1;104(12):3588-90.