DHCR7 Gene

Subjects: Genetics & Heredity
Contributor: Vivi Li

7-Dehydrocholesterol Reductase: The DHCR7 gene provides instructions for making an enzyme called 7-dehydrocholesterol reductase.

Keywords: genes

1. Normal Function

This enzyme is responsible for the final step in cholesterol production in many types of cells. Specifically, 7-dehydrocholesterol reductase converts a molecule called 7-dehydrocholesterol to cholesterol.

Cholesterol is a waxy, fat-like substance that is produced in the body and obtained from foods that come from animals (particularly egg yolks, meat, poultry, fish, and dairy products). It has important functions both before and after birth. Cholesterol plays a critical role in embryonic development by interacting with signaling proteins that control early development of the brain, limbs, genital tract, and other structures. It is also a structural component of cell membranes and myelin, the fatty covering that insulates nerve cells. Additionally, cholesterol is used to make certain hormones and is important for the production of acids used in digestion (bile acids).

2. Health Conditions Related to Genetic Changes

2.1 Smith-Lemli-Opitz Syndrome

More than 200 mutations that cause Smith-Lemli-Opitz syndrome have been identified in the *DHCR7* gene. Smith-Lemli-Opitz syndrome is a developmental disorder characterized by distinctive facial features, small head size (microcephaly), intellectual disability or learning problems, and behavioral problems. The most common mutation, which is written as IVS8-1G>C, alters a single DNA building block (nucleotide) in the *DHCR7* gene. This change interferes with the normal processing of 7-dehydrocholesterol reductase, resulting in an abnormally short, nonfunctional enzyme.

Most of the known *DHCR7* mutations change single amino acids in 7-dehydrocholesterol reductase. These mutations reduce the ability of this enzyme to convert 7-dehydrocholesterol to cholesterol. Other mutations insert or delete nucleotides in the *DHCR7* gene or lead to the production of an abnormally short enzyme; these mutations eliminate the activity of the enzyme. Without functional 7-dehydrocholesterol reductase, cells are unable to produce enough cholesterol. In addition, toxic byproducts of cholesterol production (such as 7-dehydrocholesterol) can build up in the blood and other tissues. The combination of low cholesterol levels and an accumulation of harmful substances likely disrupts the growth and development of many body systems. It is not completely understood, however, how either abnormality leads to the specific features of Smith-Lemli-Opitz syndrome.

3. Other Names for This Gene

- 7-DHC reductase
- D7SR
- delta-7-dehydrocholesterol reductase
- DHCR7_HUMAN
- sterol delta-7-reductase

References

1. Bianconi SE, Cross JL, Wassif CA, Porter FD. Pathogenesis, Epidemiology,Diagnosis and Clinical Aspects of Smith-Lemli-Opitz Syndrome. Expert Opin Orphan Drugs. 2015 Mar;3(3):267-280.
2. Correa-Cerro LS, Porter FD. 3beta-hydroxysterol Delta7-reductase and theSmith-Lemli-Opitz syndrome. Mol Genet Metab. 2005 Feb;84(2):112-26.
3. Jira PE, Waterham HR, Wanders RJ, Smeitink JA, Sengers RC, Wevers RA.Smith-Lemli-Opitz syndrome and the DHCR7 gene. Ann Hum Genet. 2003 May;67(Pt3):269-80. Review.
4. Nowaczyk MJ, Martin-Garcia D, Aquino-Perna A, Rodriguez-Vazquez M, McCaugheyD, Eng B, Nakamura LM, Waye JS. Founder effect for the T93M DHCR7 mutation inSmith-Lemli-Opitz syndrome. Am J Med Genet A. 2004 Mar 1;125A(2):173-6.
5. Nowaczyk MJ, Waye JS. The Smith-Lemli-Opitz syndrome: a novel metabolic way ofunderstanding developmental biology, embryogenesis, and dysmorphology. ClinGenet. 2001 Jun;59(6):375-86. Review.
6. Porter FD. RSH/Smith-Lemli-Opitz syndrome: a multiple congenitalanomaly/mental retardation syndrome due to an inborn error of cholesterolbiosynthesis. Mol Genet Metab. 2000 Sep-Oct;71(1-2):163-74. Review.
7. Tulenko TN, Boeze-Battaglia K, Mason RP, Tint GS, Steiner RD, Connor WE,Labelle EF. A membrane defect in the pathogenesis of the Smith-Lemli-Opitzsyndrome. J Lipid Res. 2006 Jan;47(1):134-43.
8. Waterham HR, Hennekam RC. Mutational spectrum of Smith-Lemli-Opitz syndrome.Am J Med Genet C Semin Med Genet. 2012 Nov 15;160C(4):263-84. doi:10.1002/ajmg.c.31346.
9. Waye JS, Krakowiak PA, Wassif CA, Sterner AL, Eng B, Nakamura LM, Nowaczyk MJ,Porter FD. Identification of nine novel DHCR7 missense mutations in patients withSmith-Lemli-Opitz syndrome (SLOS). Hum Mutat. 2005 Jul;26(1):59.
10. Yu H, Patel SB. Recent insights into the Smith-Lemli-Opitz syndrome. ClinGenet. 2005 Nov;68(5):383-91. Review. Erratum in: Clin Genet. 2005 Dec;68(6):570.
