# SEPTIN9 Gene

Subjects: Genetics & Heredity
Contributor: Karina Chen

septin 9

Keywords: genes

## 1. Normal Function

The *SEPTIN9* gene provides instructions for making a protein called septin-9, which is part of a group of proteins called septins. Septins are involved in a process called cytokinesis, which is the step in cell division when the fluid inside the cell (cytoplasm) divides to form two separate cells. The septin-9 protein also seems to act as a tumor suppressor, which means that it regulates cell growth and keeps cells from dividing too fast or in an uncontrolled way.

The *SEPTIN9* gene seems to be turned on (active) in cells throughout the body. Approximately 15 slightly different versions (isoforms) of the septin-9 protein may be produced from this gene. Some types of cells make certain isoforms, while other cell types produce other isoforms. However, the specific distribution of these isoforms in the body's tissues is not well understood. Septin-9 isoforms interact with other septin proteins to perform some of their functions.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Hereditary neuralgic amyotrophy

A few *SEPTIN9* gene mutations have been identified in individuals with hereditary neuralgic amyotrophy, a disorder characterized by episodes of severe pain and muscle wasting (amyotrophy) in the shoulders and arms. The most common mutation results in the replacement of the protein building block (amino acid) arginine with the amino acid tryptophan at position 88 in the septin-9 protein sequence, written as Arg88Trp or R88W. This mutation has appeared in several unrelated families from different parts of the world. Duplication of genetic material within the *SEPTIN9* gene has also been identified in affected individuals.

Changes in the *SEPTIN9* gene may alter the sequence of amino acids in certain septin-9 isoforms in ways that interfere with their function. These mutations may also change the distribution of septin-9 isoforms and their interactions with other septin proteins in some of the body's tissues. This change in the functioning of septin proteins seems to particularly affect the network of nerves controlling movement and sensation in the shoulders and arms (brachial plexus), but the reason for this is unknown.

Because many of the triggers for episodes of hereditary neuralgic amyotrophy also affect the immune system, researchers believe that an autoimmune reaction may be involved in this disorder. However, the relation between *SEPTIN9* gene mutations and immune function is unclear. Autoimmune disorders occur when the immune system malfunctions and attacks the body's own tissues and organs. An autoimmune attack on the nerves in the brachial plexus likely results in the signs and symptoms of hereditary neuralgic amyotrophy.

### 2.2. Cancers

Alterations in the activity (expression) of the *SEPTIN9* gene are associated with certain cancers. The altered gene expression may enhance several cancer-related events such as cell division (proliferation), cell movement, and the development of new blood vessels (angiogenesis) that nourish a growing tumor. Increased production of particular isoforms of the septin-9 protein has been associated with breast and prostate cancers. Altered *SEPTIN9* gene expression has also been found in many other cancers, including tumors of the ovary, pancreas, lung, kidney, liver, thyroid and esophagus.

## 3. Other Names for This Gene

- AF17q25
- FLJ75490
- KIAA0991
- MLL septin-like fusion
- MSF
- MSF1
- NAPB
- Ov/Br septin
- ovarian/breast septin
- PNUTL4
- SEPT9
- SEPT9_HUMAN
- SeptD1
- septin 9 isoform a
- septin 9 isoform b
- septin 9 isoform c
- septin 9 isoform d
- septin 9 isoform e
- septin 9 isoform f
- septin D1
- SINT1

### References


1. Gonzalez ME, Makarova O, Peterson EA, Privette LM, Petty EM. Up-regulation of SEPT9_v1 stabilizes c-Jun-N-terminal kinase and contributes to itspro-proliferative activity in mammary epithelial cells. Cell Signal. 2009Apr;21(4):477-87. doi: 10.1016/j.cellsig.2008.11.007.
2. Gonzalez ME, Peterson EA, Privette LM, Loffreda-Wren JL, Kalikin LM, Petty EM.High SEPT9_v1 expression in human breast cancer cells is associated withoncogenic phenotypes. Cancer Res. 2007 Sep 15;67(18):8554-64.
3. Hannibal MC, Ruzzo EK, Miller LR, Betz B, Buchan JG, Knutzen DM, Barnett K,Landsverk ML, Brice A, LeGuern E, Bedford HM, Worrall BB, Lovitt S, Appel SH,Andermann E, Bird TD, Chance PF. SEPT9 gene sequencing analysis reveals recurrentmutations in hereditary neuralgic amyotrophy. Neurology. 2009 May19;72(20):1755-9. doi: 10.1212/WNL.0b013e3181a609e3.
4. Hoque R, Schwendimann RN, Kelley RE, Bien-Willner R, Sivakumar K. Painfulbrachial plexopathies in SEPT9 mutations: adverse outcome related to comorbidstates. J Clin Neuromuscul Dis. 2008 Jun;9(4):379-84. doi:10.1097/CND.0b013e318166ee89.
5. Klein CJ, Wu Y, Cunningham JM, Windebank AJ, Dyck PJ, Friedenberg SM, KleinDM, Dyck PJ. SEPT9 mutations and a conserved 17q25 sequence in sporadic andhereditary brachial plexus neuropathy. Arch Neurol. 2009 Feb;66(2):238-43. doi:10.1001/archneurol.2008.585.
6. Kuhlenbäumer G, Hannibal MC, Nelis E, Schirmacher A, Verpoorten N, Meuleman J,Watts GD, De Vriendt E, Young P, Stögbauer F, Halfter H, Irobi J, Goossens D,Del-Favero J, Betz BG, Hor H, Kurlemann G, Bird TD, Airaksinen E, Mononen T,Serradell AP, Prats JM, Van Broeckhoven C, De Jonghe P, Timmerman V, Ringelstein EB, Chance PF. Mutations in SEPT9 cause hereditary neuralgic amyotrophy. NatGenet. 2005 Oct;37(10):1044-6.
7. Laccone F, Hannibal MC, Neesen J, Grisold W, Chance PF, Rehder H. Dysmorphicsyndrome of hereditary neuralgic amyotrophy associated with a SEPT9 genemutation--a family study. Clin Genet. 2008 Sep;74(3):279-83. doi:10.1111/j.1399-0004.2008.01022.x.
8. Landsverk ML, Ruzzo EK, Mefford HC, Buysse K, Buchan JG, Eichler EE, Petty EM,Peterson EA, Knutzen DM, Barnett K, Farlow MR, Caress J, Parry GJ, Quan D,Gardner KL, Hong M, Simmons Z, Bird TD, Chance PF, Hannibal MC. Duplicationwithin the SEPT9 gene associated with a founder effect in North American familieswith hereditary neuralgic amyotrophy. Hum Mol Genet. 2009 Apr 1;18(7):1200-8.doi: 10.1093/hmg/ddp014.
9. McDade SS, Hall PA, Russell SE. Translational control of SEPT9 isoforms isperturbed in disease. Hum Mol Genet. 2007 Apr 1;16(7):742-52.

10. Scott M, Hyland PL, McGregor G, Hillan KJ, Russell SE, Hall PA. Multimodality expression profiling shows SEPT9 to be overexpressed in a wide range of humantumours. Oncogene. 2005 Jul 7;24(29):4688-700.
11. Scott M, McCluggage WG, Hillan KJ, Hall PA, Russell SE. Altered patterns oftranscription of the septin gene, SEPT9, in ovarian tumorigenesis. Int J Cancer. 2006 Mar 1;118(5):1325-9.
12. Sudo K, Ito H, Iwamoto I, Morishita R, Asano T, Nagata K. SEPT9 sequencealternations causing hereditary neuralgic amyotrophy are associated with altered interactions with SEPT4/SEPT11 and resistance to Rho/Rhotekin-signaling. HumMutat. 2007 Oct;28(10):1005-13.
13. van Alfen N, Hannibal MC, Chance PF, van Engelen BGM. Hereditary NeuralgicAmyotrophy – RETIRED CHAPTER, FOR HISTORICAL REFERENCE ONLY. 2008 Feb 27 [updated2012 Dec 6]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, StephensK, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2020. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1395/

---