Atlas of Genetics and Cytogenetics
in Oncology and Haematology

OPEN ACCESS JOURNAL

INIST-CNRS

Gene Section
Review

SEPT7 (septin 7)

Kaifee Arman, Esra Bozgeyik, Yusuf Ziya Igci, Mehri Igci

University of Gaziantep, Faculty of Medicine, Department of Medical Biology, Gaziantep, Turkey
kaifeearman786@gmail.com; gyk.esra@gmail.com; igci@gantep.edu.tr; mehriigci@gmail.com

Published in Atlas Database: January 2015
Online updated version : http://AtlasGeneticsOncology.org/Genes/SEPT7ID999ch7p14.html
Printable original version : http://documents.irevues.inist.fr/bitstream/handle/2042/62516/01-2015-SEPT7ID999ch7p14.pdf
DOI: 10.4267/2042/62516

Abstract

Review on SEPT7, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Keywords: SEPT7

Identity

Other names: CDC10, CDC3, NBLA02942, SEPT7A

HGNC (Hugo): SEPT7

Location: 7p14.2

Location (base pair): Starts at 35840596 and ends at 35946715 bp from pter (according to hg19-Feb_2009).

DNA/RNA

Description

The human SEPT7 gene (NM_001011553) is located on the positive strand of chromosome 7. It consists of an open reading frame (ORF) having 1254 nucleotides which encodes 418 amino acids, consisting of a GTP-binding motif. Its size is about 51 kDa. It has a total of 17 exons.

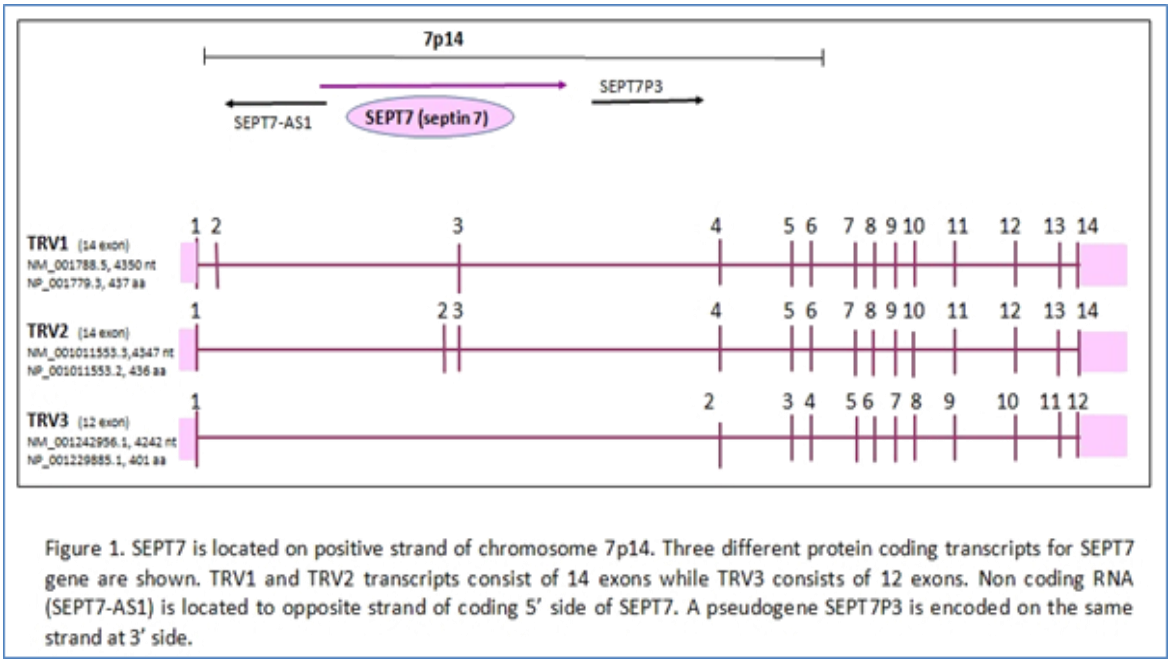

Figure 1. SEPT7 is located on positive strand of chromosome 7p14. Three different protein coding transcripts for SEPT7 gene are shown. TRV1 and TRV2 transcripts consist of 14 exons while TRV3 consists of 12 exons. Non coding RNA (SEPT7-AS1) is located to opposite strand of coding 5' side of SEPT7. A pseudogene SEPT7P3 is encoded on the same strand at 3' side.

Figure 2. Amino acid sequence of SEPT7 protein is shown. Isoform-1 encoded by SEPT7 TRV1 transcript is also shown. The different regions of this isoform like binding site, helix, domain, nucleotide binding and coiled coil are highlighted in different colours.

Transcription

Till date three transcript variants encoding different isoforms are known for SEPT7 [Figure1]. These are transcript variant 1 (accession number NM_001788), transcript variant 2 (NM_001011553) and transcript variant 3 (accession number NM_001242956). Transcript variant 1 (TV1) is known to be the longest transcript encoding the longest isoform (1).

As compared to TV1, TV2 (transcript variant 2) has no in-frame segment in the 5' coding region giving rise to an isoform (2).

It is 1 aa shorter than isoform 1. On the other hand transcript variant (3) also does not possess an in-frame segment in the 5' coding region which results in an isoform (3).

This isoform (3) is 36 aa shorter than isoform 1. In fact alternative splicing results in multiple transcript variant.

SEPT7 is linked to Papillary thyroid carcinoma (PTC).

It was found that SEPT7 mRNA expression was relatively lower expressed in follicular variant of classical type of PTC (FVPTC) as compared to classical type PTC (CVPTC) (Igci et al., 2011)

Pseudogene

There are several related pseudogenes for SEPT7 which have been identified on chromosomes 5, 7, 9, 10, 11, 14, 17 and 19. A novel septin, SEPT13 has been shown to be related to SEPT7 and represent a transcribed pseudogene of SEPT7 (Hall et al., 2005).

Protein

Description

SEPT7 belongs to the septin family that is known to be a highly conserved subfamily of GTPases and is well recognized as a novel component of the cytoskeleton. It consists of an open reading frame (ORF) having 1254 nucleotides which encodes 418 amino acids, consisting of a GTP-binding motif (Nakatsuru et al., 1994). The amino acid sequence of SEPT7 protein is shown in Figure 2. Septins are GTP-binding proteins which are known to contain all the necessary elements to perform the general GDP-to-GTP conformational switch. Sept7, the only member of the Sept7 subgroup, forms a very tight G-interface dimer in the GDP-bound state. It has been shown that the stability of the interface is dramatically decreased by exchanging GDP with a nucleoside triphosphate, which is believed to influence filament formation and dynamics via Sept7 (Zent & Wittinghofer, 2014). SEPT7 is having a molecular mass of approximately 51 kDa and has a basal isoelectric point of 8.76.

The protein encoded by this gene has a high similarity to the CDC10 protein of Saccharomyces cerevisiae. It also shows similarity to Diff 6 of Drosophila and H5 of mouse. All of these similar proteins contain a GTP-binding motif. The GTPase activity of SEPT7 is required for filament formation. It is also required for the association of centromere-associated protein E (CENPE) with the kinetochore. Multiple transcript variants are formed as a result of alternative splicing. This protein has a role in ciliogenesis and collective cell movements. The

GTPase domain of SEPT7 is unique as it contains a conserved sequence near its end - the Septin Unique Element (SUE) (Pan et al., 2007, Steels et al., 2007, Versele et al., 2004). SEPT7 has additional conserved elements that flank the GTPase domain. It possesses a polybasic region at N-terminal to the GTPase domain that has been shown to bind phosphoinositides (Casamayor & Snyder, 2003, Zhang et al., 1999). In fact, mammalian SEPT7 exist solely as 6- to 8-unit heteromeric complexes within the cell (Sellin et al., 2011).

In mammals, SEPT7 forms a complex with SEPT2, SEPT4 and SEPT6 which was first identified in brain tissue (Hsu et al., 1998). SEPT7 monomers within the unit complex interact through G-G and NC-NC interfaces, thereby pairing up with other septin members. These G-G and NC-NC interactions alternate along the unit complex, and are necessary for its formation (Sirajuddin et al., 2007). SEPT7 also shows non-septin interactions. 9% of the interactors have been identified to be non-septins for SEPT7 (Nakahira et al., 2010). SEPT7 was identified as a mutual partner with SEPT9 at a very high percentage (Nakahira et al., 2010). SEPT7 is known to be expressed in several tissues. It is therefore believed to be much more involved in processes like cell division. It does belong to the group of septins with the least members (SEPT7 and 13, only) and is found in almost all of the heterofilaments known till date. It is therefore a basic element for filament formation (Nakahira et al., 2010)

Expression

SEPT7 has cytoplasmic expression in most tissues but is always found associated to actin filaments as well as several regions through-out mitosis (Zhu et al., 2008). There are already cytoplasmic, nuclear, and overall (total) SEPT7 protein expression levels which have also been determined in PTC (Igci et al., 2014). SEPT7 was also shown to be negatively regulated by miR-30a-5p in glioma cells (Jia et al., 2013). There is very high expression of SEPT7 proteins in cerebral cortex but moderate expression in hippocampus, lateral ventricle and cerebellum of CNS. SEPT7 is also moderately expressed in gall bladder, pancreas, stomach, colon, kidney, testis, prostate, breast, thyroid gland. It has low expression in liver, small intestine, bone marrow and lung. But it has not been detected in skeletal muscles, smooth muscles and heart muscles.

Localisation

SEPT7 is distributed throughout the cytoplasm in prometaphase cells. During metaphase it is associated with the spindle. While at anaphase it is associated with the central spindle and at the cleavage furrow in anaphase cells. It has been detected at the midbody in telophase and is associated with actin stress fibers (Zhu et al., 2008).

Function

SEPT7 has cytoskeletal GTPase which is responsible for filament-forming. It is needed for normal orientation of the actin cytoskeleton. It is needed for normal progress through mitosis. It is also involved in cytokinesis. It has been revealed that septins are extremely necessary for cytokinesis in fibroblasts, but of relatively little significance in cells of the hematopoietic system by studying genetic loss of the septin subunit SEPT7 in vivo (Menon et al., 2014). SEPT7 is of utmost requirement for associating centromere-associated protein E (CENPE) with the kinetochore. It is known to play a role in ciliogenesis and collective cell movements. SEPT7 is a GTP-binding protein that is known to form hetero-oligomeric complexes as well as higher-order structures for example filaments and rings (Mostowy & Cossart, 2012). It has been shown that Septin 7 is required for axonal association of Schwann cells (Roth et al., 2013). It also helps in glucose transporter trafficking. Septin 7 regulates glucose transporter trafficking by forming a complex with CD2AP and nephrin (Wasik et al., 2012). It is known to function in gliomagenesis as well as in suppression of glioma cell growth (Jia et al., 2010).

Homology

SEPT7 is highly similar to the CDC10 (cell division cycle 10) protein of Saccharomyces cerevisiae. A novel human gene (418-amino acid product) has been cloned which shared almost 39% and 54% sequence identity with yeast CDC10 and mouse H5 proteins, respectively (Nakatsuru et al., 1994). This protein is also similar to Diff 6 of Drosophila to a good extent. Each of these known sequence homologues contains a common GTP-binding motif.

Mutations

Mutation in SEPT7 is not known to a great extent. But some works mention it. For example it has been revealed that the interaction of SEPT7 (Y318) with other known septins is regulated by mutation of a potential phosphorylation site in SEPT7 (Y318). This study has been done through mutagenic analyses (Sandrock et al., 2011).

Implicated in

Gliomagenesis

It has been demonstrated that SEPT7 has an important role in progression of cell cycle as well as growth of glioma cells (Jia et al., 2010). mRNA and protein expression of SEPT7 has been detected in human glioma samples and normal brain tissues by using several techniques such as RT-PCR, immunohistochemical staining, and western blot analysis. The overexpression of SEPT7 inhibits cell

proliferation as well as put a check on cell cycle progression in the G0/G1. It has been noticed that further knocking down the already low endogenous expression of SEPT7 in U251 xenograft tumors with siRNA accelerates growth as compared to control tumors. This particular study gives evidence that SEPT7 is primarily involved in gliomagenesis and leads to suppression of glioma cell growth (Jia et al., 2010, Xu et al., 2010). SEPT7 is targeted by MiR-30a-5p to cause glioma cell growth (Jia et al., 2013).

Papillary Thyroid Carcinoma

PTC is well known and the most common among thyroid cancers. SEPT7 protein expression has been evaluated in PTC. By using immunohistochemistry technique nuclear, cytoplasmic, and overall (total) SEPT7 protein expression levels were evaluated. There were significantly lower expressions of cytoplasmic, nuclear and overall SEPT7 expressions in FVPTC tissues as compared to benign hyperfunctioning thyroid nodules. The significantly lower SEPT7 expression in all expressional categories in FVPTC group may be a sign of different molecular signature in this type of tissue (Igci et al., 2014).

Hepatocellular carcinoma

SEPT7 has tumorigenic role in case of hepatocellular carcinoma. There is overexpression of SEPT7 in hepatocellular carcinoma. SEPT7 is post-transcriptionally downregulated by miR-127 and thus miR-127 suppresses cell growth in hepatocellular carcinoma cells by downregulating SEPT7 (Zhou et al., 2014).

Human azoospermic testes

The mRNA expression of CDC10/SEPT7 was confirmed to be stronger in spermatogenic cells of normal fertility compared with that of azoospermic testes by in situ hybridization. CDC10/SEPT7 was up-regulated in human azoospermic testes. It was performed through cDNA microarray analysis (Yang et al., 2009). It has also been found that the rate of improper SEPT7 signal was greatly increased in men with asthenozoospermia. It was figured out that the absence of a SEPT7 signal was more widespread in sperm having morphological defects of several types (Chao et al., 2010).

To be noted

Acknowledgment: Kaifee Arman is recipient of Graduate Scholarship from TUBITAK under the program 2215-Graduate Scholarship Program for International Students.

References

Casamayor A, Snyder M. Molecular dissection of a yeast septin: distinct domains are required for septin interaction, localization, and function. Mol Cell Biol. 2003 Apr;23(8):2762-77

Chao HC, Lin YH, Kuo YC, Shen CJ, Pan HA, Kuo PL. The expression pattern of SEPT7 correlates with sperm morphology. J Assist Reprod Genet. 2010 Jun;27(6):299-307

Hall PA, Jung K, Hillan KJ, Russell SE. Expression profiling the human septin gene family. J Pathol. 2005 Jul;206(3):269-78

Hsu SC, Hazuka CD, Roth R, Foletti DL, Heuser J, Scheller RH. Subunit composition, protein interactions, and structures of the mammalian brain sec6/8 complex and septin filaments. Neuron. 1998 Jun;20(6):1111-22

Igci YZ, Arslan A, Akarsu E, Erkilic S, Igci M, Oztuzcu S, Cengiz B, Gogebakan B, Cakmak EA, Demiryurek AT. Differential expression of a set of genes in follicular and classic variants of papillary thyroid carcinoma. Endocr Pathol. 2011 Jun;22(2):86-96

Igci YZ, Erkilic S, Arslan A. Septin 7 immunoexpression in papillary thyroid carcinoma: a preliminary study. Pathol Res Pract. 2014 Jul;210(7):426-31

Jia Z, Wang K, Wang G, Zhang A, Pu P. MiR-30a-5p antisense oligonucleotide suppresses glioma cell growth by targeting SEPT7. PLoS One. 2013;8(1):e55008

Jia ZF, Huang Q, Kang CS, Yang WD, Wang GX, Yu SZ, Jiang H, Pu PY. Overexpression of septin 7 suppresses glioma cell growth J Neurooncol 2010 Jul;98(3):329-40

Menon MB, Sawada A, Chaturvedi A, Mishra P, Schuster-Gossler K, Galla M, Schambach A, Gossler A, Förster R, Heuser M, Kotlyarov A, Kinoshita M, Gaestel M. Genetic deletion of SEPT7 reveals a cell type-specific role of septins in microtubule destabilization for the completion of cytokinesis PLoS Genet 2014 Aug 14;10(8):e1004558

Mostowy S, Cossart P. Septins: the fourth component of the cytoskeleton Nat Rev Mol Cell Biol 2012 Feb 8;13(3):183-94

Nakahira M, Macedo JN, Seraphim TV, Cavalcante N, Souza TA, Damalio JC, Reyes LF, Assmann EM, Alborghetti MR, Garratt RC, Araujo AP, Zanchin NI, Barbosa JA, Kobarg J. A draft of the human septin interactome PLoS One 2010 Nov 2;5(11):e13799

Nakatsuru S, Sudo K, Nakamura Y. Molecular cloning of a novel human cDNA homologous to CDC10 in Saccharomyces cerevisiae Biochem Biophys Res Commun 1994 Jul 15;202(1):82-7

Pan F, Malmberg RL, Momany M. Analysis of septins across kingdoms reveals orthology and new motifs BMC Evol Biol 2007 Jul 1;7:103

Roth AD, Liazoghli D, Perez De Arce F, Colman DR. Septin 7: actin cross-organization is required for axonal association of Schwann cells Biol Res 2013;46(3):243-9

Sandrock K, Bartsch I, Bläser S, Busse A, Busse E, Zieger B. Characterization of human septin interactions Biol Chem 2011 Aug;392(8-9):751-61

Sellin ME, Sandblad L, Stenmark S, Gullberg M. Deciphering the rules governing assembly order of mammalian septin complexes Mol Biol Cell 2011 Sep;22(17):3152-64

Sirajuddin M, Farkasovsky M, Hauer F, Kühlmann D, Macara IG, Weyand M, Stark H, Wittinghofer A. Structural insight into filament formation by mammalian septins Nature 2007 Sep 20;449(7160):311-5

Steels JD, Estey MP, Froese CD, Reynaud D, Pace-Asciak C, Trimble WS. Sept12 is a component of the mammalian sperm tail annulus Cell Motil Cytoskeleton 2007 Oct;64(10):794-807

Versele M, Gullbrand B, Shulewitz MJ, Cid VJ, Bahmanyar S, Chen RE, Barth P, Alber T, Thorner J. Protein-protein interactions governing septin heteropentamer assembly and septin filament organization in Saccharomyces cerevisiae Mol Biol Cell 2004 Oct;15(10):4568-83

Wasik AA, Polianskyte-Prause Z, Dong MQ, Shaw AS, Yates JR 3rd, Farquhar MG, Lehtonen S. Septin 7 forms a complex with CD2AP and nephrin and regulates glucose transporter trafficking Mol Biol Cell 2012 Sep;23(17):3370-9

Xu S, Jia ZF, Kang C, Huang Q, Wang G, Liu X, Zhou X, Xu P, Pu P. Upregulation of SEPT7 gene inhibits invasion of human glioma cells Cancer Invest 2010 Mar;28(3):248-58

Yang B, Yuan JL, Gao XK, Qin WJ, Liu F, Shao C, Liu HL, Kang FX. [Expression of cell cycle molecules in human azoospermic testes] Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi 2009 May;25(5):393-5

Zent E, Wittinghofer A. Human septin isoforms and the GDP-GTP cycle Biol Chem 2014 Feb;395(2):169-80

Zhang J, Kong C, Xie H, McPherson PS, Grinstein S, Trimble WS. Phosphatidylinositol polyphosphate binding to the mammalian septin H5 is modulated by GTP Curr Biol 1999 Dec 16-30;9(24):1458-67

Zhou J, Lu S, Yang S, Chen H, Shi H, Miao M, Jiao B. MicroRNA-127 post-transcriptionally downregulates Sept7 and suppresses cell growth in hepatocellular carcinoma cells Cell Physiol Biochem 2014;33(5):1537-46

Zhu M, Wang F, Yan F, Yao PY, Du J, Gao X, Wang X, Wu Q, Ward T, Li J, Kioko S, Hu R, Xie W, Ding X, Yao X. Septin 7 interacts with centromere-associated protein E and is required for its kinetochore localization J Biol Chem 2008 Jul 4;283(27):18916-25

This article should be referenced as such:

Arman K, Bozgeyik E, Igci YZ, Igci M. SEPT7 (septin 7). Atlas Genet Cytogenet Oncol Haematol. 2016; 20(2) :81-85.