Atlas of Genetics and Cytogenetics
in Oncology and Haematology

OPEN ACCESS JOURNAL

INIST-CNRS

Solid Tumour Section

Short Communication

Nervous system: Astrocytoma with t(1;17)(p36;q21) SPOP/PRDM16

Jean-Loup Huret

Genetics, Dept Medical Information, University of Poitiers, CHU Poitiers Hospital, F-86021 Poitiers, France. jean-loup.huret@chu-poitiers.fr

Published in Atlas Database: September 2016
Online updated version : http://AtlasGeneticsOncology.org/Tumors/t0117p36q21ID5447.html
Printable original version : http://documents.irevues.inist.fr/bitstream/handle/2042/69012/09-2016-t0117p36q21ID5447.pdf
DOI: 10.4267/2042/69012

Abstract

Review on t(1;17)(p36;q21) SPOP/PRDM16 translocation in astrocytic tumor, with data on the genes involved.

Keywords

chromosome 1; chromosome 17; t(1;17)(p36;q21); SPOP; PRDM16, Astrocytic tumor

Clinics and pathology

Disease

A t(1;17)(p36;q21) was found in a case of astrocytoma grade I-II, but no further data is available (Yoshihara et al 2015).

Clinics

Grade I astrocytomas are pilocytic astrocytoma and subependymal giant cell astrocytoma, the latter being the most common central nervous system neoplasm in tuberous sclerosis; they are slow growing tumors; they typically occur during the first two decades of life. Grade II astrocytomas are pilomyxoid astrocytoma occurring most often in infants and very young children, diffuse astrocytoma, seen at any age, but often between ages 30-40, and pleomorphic xanthoastrocytoma, typically developing in children and young adults.

Genes involved and proteins

PRDM16 (PR domain containing 16)

Location
1p36.32

DNA / RNA
11 splice variants

Protein
1276 amino acids and smaller proteins. Contains a N-term PR domain; 7 Zinc fingers, a proline-rich domain, and 3 Zinc fingers in the C-term. Binds DNA.
Transcription activator; PRDM16 has an intrinsic histone methyltransferase activity. PRDM16 forms a transcriptional complex with CEBPB. PRDM16 plays a downstream regulatory role in mediating TGFB signaling (Bjork et al., 2010).
PRDM16 induces brown fat determination and differentiation. PRDM16 is expressed selectively in the earliest stem and progenitor hematopoietic cells, and is required for the maintenance of the hematopoietic stem cell pool during development. PRDM16 is also required for survival, cell-cycle regulation and self-renewal in neural stem cells (Chuikov et al., 2010; Kajimura et al., 2010; Aguilo et al., 2011; Chi and Cohen, 2016).

SPOP (speckle type BTB/POZ protein)

Location
17q21.33

DNA / RNA
24 splice variants

Protein

374 amino acids SPOP comprises a N-term MATH domain (**M**eprin **A**nd **T**RAF **H**omology; substrate recognition and binding), a BTB/POZ domain (**B**ric-a-brac, **T**ramtrack and **B**road complex/ **P**ox virus and **Z**inc finger; connects to the CUL3 - RBX1 (Cullin 3-RING box 1) scaffold protein), a 3-box domain (facilitating CUL3 binding and resembling to F-/SOCS-boxes) and a C-terminal nuclear localization sequence. SPOP is a E3 ubiquitin ligase adaptor protein that participates in the degradation of various substrates. AR (androgen receptor), DAXX, BMI1, BRMS1 and PDX1 are targets of SPOP. SPOP is critically involved in SETD2 (a tumor suppressor) stability. SPOP enables homology-directed DNA repair of double strand breaks, and mutant SPOP promotes genomic rearrangements within chromosomes. SPOP suppresses gastric tumorigenesis through inhibiting hedgehog/ GLI2 signaling pathway. SPOP is frequently mutated in prostate and endometrial cancers. TMPRSS2 - ERG fusions, frequently seen in prostate carcinoma, encode N-terminal-truncated ERG proteins that are resistant to the SPOP-mediated degradation. Decreased expression of SPOP is associated with poor prognosis in glioma. On the other hand, SPOP is highly expressed in clear cell renal cell carcinoma (Zhuang et al., 2009; Mani, 2014; Zeng et al., 2014; Karnes et al., 2015; Ding et al., 2015; Rider and Cramer, 2015).

References

Aguilo F, Avagyan S, Labar A, Sevilla A, Lee DF, Kumar P, Lemischka IR, Zhou BY, Snoeck HW. Prdm16 is a physiologic regulator of hematopoietic stem cells. Blood. 2011 May 12;117(19):5057-66

An J, Ren S, Murphy SJ, Dalangood S, Chang C, Pang X,

Cui Y, Wang L, Pan Y, Zhang X, Zhu Y, Wang C, Halling GC, Cheng L, Sukov WR, Karnes RJ, Vasmatzis G, Zhang Q, Zhang J, Cheville JC, Yan J, Sun Y, Huang H. Truncated ERG Oncoproteins from TMPRSS2-ERG Fusions Are Resistant to SPOP-Mediated Proteasome Degradation. Mol Cell. 2015 Sep 17;59(6):904-16

Bjork BC, Turbe-Doan A, Prysak M, Herron BJ, Beier DR. Prdm16 is required for normal palatogenesis in mice. Hum Mol Genet. 2010 Mar 1;19(5):774-89

Chi J, Cohen P. The Multifaceted Roles of PRDM16: Adipose Biology and Beyond. Trends Endocrinol Metab. 2016 Jan;27(1):11-23

Chuikov S, Levi BP, Smith ML, Morrison SJ. Prdm16 promotes stem cell maintenance in multiple tissues, partly by regulating oxidative stress. Nat Cell Biol. 2010 Oct;12(10):999-1006

Ding D, Song T, Jun W, Tan Z, Fang J. Decreased expression of the SPOP gene is associated with poor prognosis in glioma. Int J Oncol. 2015 Jan;46(1):333-41

Kajimura S, Seale P, Kubota K, Lunsford E, Frangioni JV, Gygi SP, Spiegelman BM. Initiation of myoblast to brown fat switch by a PRDM16-C/EBP-beta transcriptional complex. Nature. 2009 Aug 27;460(7259):1154-8

Mani RS. The emerging role of speckle-type POZ protein (SPOP) in cancer development. Drug Discov Today. 2014 Sep;19(9):1498-502

Rider L, Cramer SD. SPOP the mutation. Elife. 2015 Oct 27;4

Yoshihara K, Wang Q, Torres-Garcia W, Zheng S, Vegesna R, Kim H, Verhaak RG. The landscape and therapeutic relevance of cancer-associated transcript fusions. Oncogene. 2015 Sep 10;34(37):4845-54

Zeng C, Wang Y, Lu Q, Chen J, Zhang J, Liu T, Lv N, Luo S. SPOP suppresses tumorigenesis by regulating Hedgehog/Gli2 signaling pathway in gastric cancer. J Exp Clin Cancer Res. 2014 Sep 11;33:75

Zhuang M, Calabrese MF, Liu J, Waddell MB, Nourse A, Hammel M, Miller DJ, Walden H, Duda DM, Seyedin SN, Hoggard T, Harper JW, White KP, Schulman BA. Structures of SPOP-substrate complexes: insights into molecular architectures of BTB-Cul3 ubiquitin ligases. Mol Cell. 2009 Oct 9;36(1):39-50

This article should be referenced as such:

Nervous system: Astrocytoma with t(1;17)(p36;q21) SPOP/PRDM16. Nervous system: Astrocytoma with t(1;17)(p36;q21) SPOP/PRDM16. Atlas Genet Cytogenet Oncol Haematol. 2017; 21(12):470-471.