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

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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

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 (Meprin And TRAF Homology; substrate recognition and binding), a BTB/POZ domain (Bric-a-brac, Tramtrack and Broad complex/Pox virus and Zinc 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.

References


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