Protein capicua homolog is a protein that in humans is encoded by the CIC gene.

The protein encoded by this gene is an ortholog of the Drosophila melanogaster capicua gene, and is a member of the high mobility group (HMG)-box superfamily of transcriptional repressors. This protein contains a conserved HMG domain that is involved in DNA binding and nuclear localization, and a conserved C-terminus. Studies suggest that the N-terminal region of this protein interacts with Atxn1 (GeneID:6310), to form a transcription repressor complex, and in vitro studies suggest that polyglutamine-expansion of ATXN1 may alter the repressor activity of this complex. Mutations in this gene have been associated with olidodendrogliomas (PMID:21817013). In addition, translocation events resulting in gene fusions of this gene with both DUX4 (GeneID:100288687) and FOXO4 (GeneID:4303) have been associated with round cell sarcomas. There are multiple pseudogenes of this gene found on chromosomes 1, 4, 6, 7, 16, 20, and the Y chromosome. Alternative splicing results in multiple transcript variants encoding different isoforms. [provided by RefSeq, Feb 2015]

CIC-rearranged sarcoma is a high-grade sarcoma, most often harboring CIC:: DUX4 fusion, and is characterized by a distinct round cell histology, co-expression of ETV4 and WT1, and a specific DNA methylation class. Satomi et al. reported a brain tumor with ATXN1:: DUX4 that had an indistinguishable phenotype and DNA methylation profile from CIC-rearranged sarcoma. A 40-year-old man presented with a 5 cm hemorrhagic mass in the right frontal lobe of the cerebrum. The tumor was resected and histologically showed a dense proliferation of relatively monomorphic round cells with multifocal myxoid changes. Immunohistochemically, the tumor was diffusely positive for ETV4, WT1, and DUX4. Through classic histomorphology and immune profile, the tumor was provisionally diagnosed as CIC-rearranged sarcoma. However, no CIC fusions or mutations were identified using CIC break-apart fluorescence in situ hybridization (FISH) or FoundationOne CDx. Despite multiple surgeries and adjuvant chemoradiation therapy, the patient succumbed 16 months after presentation. RNA exome sequencing detected an in-frame intraexonic ATXN1 (exon 9):: DUX4 (exon 1) fusion, which was validated by reverse transcription-polymerase chain reaction and ATXN1 FISH assay. Upon DNA methylation analysis, the tumor matched with CIC-rearranged sarcoma both by the Deutsche Krebsforschungszentrum classifier and t-distributed stochastic neighbor embedding. Along with a recent report of a similar pediatric brain tumor, the present case suggests that ATXN1::DUX4 is a recurrent alternative molecular event in the sarcoma type that is presently defined by CIC rearrangement, which prompts an expansion of the tumor concept [1].

1)
Satomi K, Ohno M, Kubo T, Honda-Kitahara M, Matsushita Y, Ichimura K, Narita Y, Ichikawa H, Yoshida A. Central nervous system sarcoma with ATXN1::DUX4 fusion expands the concept of CIC-rearranged sarcoma. Genes Chromosomes Cancer. 2022 Jun 17. doi: 10.1002/gcc.23080. Epub ahead of print. PMID: 35715887.