

Technology Offer

CITED4 as prognostic marker in oligodendroglial tumors

Reference no.: TO 0021

The challenge

Cancer of the central nervous system (CNS), is a complex disease and, despite of improved treatments, it still represents a leading cause of death in the world. The prognosis for most patients with cancer of the CNS, particular with brain tumours, remains poor. The establishment of tumor grade is a key determinant in the choice of a therapeutic approach and in prognosis. Presently there are no tumor markers available that are useful for diagnosis of CNS tumors including oligodendroglial tumors.

The technology

Loss of heterozygosity (LOH) on chromosome arms 1p and 19q is frequent in oligodendroglial tumors and associated with sensitivity to radio- and chemotherapy as well as favorable prognosis. Using micro-array-based expression profiling researchers at the German Cancer Research Center (DKFZ) found that oligodendroglial tumors with LOH 1p/19q showed significantly lower expression of the CBP/p300-interacting transactivator with glutamic acid/aspartic acid-rich carboxyl-terminal domain 4 gene (CITED4) at 1p34.2 as compared to gliomas without LOH 1p/19q. Mutational analysis showed no mutations in the CITED4 coding sequence. However, LOH 1p/19q and low expression of CITED4 transcripts were closely associated with hypermethylation of the CITED4 promoter. Treatment of CITED4 hypermethylated glioma cells with 5-aza-2'-deoxycytidine and trichostatine A markedly increased CITED4 expression. Furthermore, CITED4 hypermethylation was a significant predictor of longer survival in patients with oligodendroglial tumors. Taken together, the results suggest CITED4 as a putative tumor suppressor gene that is epigenetically silenced in the majority of oligodendroglial tumors with LOH 1p/19q and represents a powerful prognostic marker.

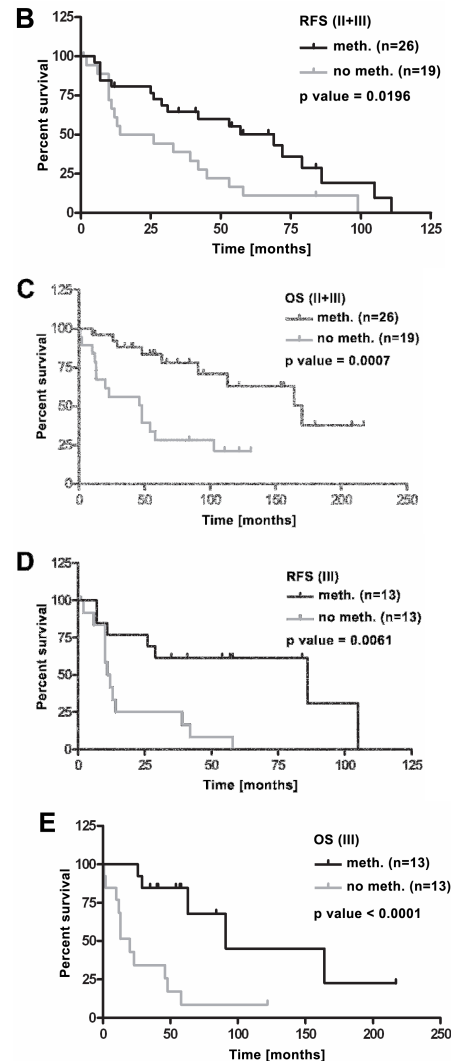


Figure 1: Significant correlations (log rank tests) of CITED4 promoter hypermethylation with progression-free survival (B, D) and overall survival (C, E) in patients with oligodendroglial tumors. Shown are Kaplan-Meier survival curves obtained for 45 patients (B,C), including 19 patients with WHO grade II and 26 patients with WHO grade III tumors, as well as in the subgroup of 26 patients with WHO grade III tumors (D,E).

Commercial Use

In-licensing opportunity for the development of diagnostic tools and therapeutics in the field of oligodendroglial tumors. Cooperation for further development is also sought.

Patent situation

An European priority patent application is pending.

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