TRAF7

TNF receptor associated factor 7

Tumor necrosis factor (TNF; see MIM 191160) receptor-associated factors, such as TRAF7, are signal transducers for members of the TNF receptor superfamily (see MIM 191190). TRAFs are composed of an N-terminal cysteine/histidine-rich region containing zinc RING and/or zinc finger motifs; a coiled-coil (leucine zipper) motif; and a homologous region that defines the TRAF family, the TRAF domain, which is involved in self-association and receptor binding.

Genetic aberrations (TRAF7, KLF4, AKT1, and SMO) and the effects of genetic aberrations on the expression of immune checkpoint inhibitory molecules (PD-L1, IDO, and TDO2) in skull base meningiomas are still unclear.

Genetic alterations in the four genes were identified in 92 skull base meningiomas by Sanger sequencing. The expression differences in immune checkpoints between mutant and wild-type (WT) tumors were determined by immunohistochemistry (IHC) and Western blot (WB).

The four mutations were not concurrently detected in the patients with skull base meningiomas. Among the tumors from the KLF4-mutated group, almost half were petroclival meningiomas. KLF4- and TRAF7-mutated tumors were predominantly secretory meningiomas. SMO-mutated tumors exhibited higher calcification, and half of these tumors were observed in the brain midline. Receiver operating characteristic curve analysis indicated that tumor volume can predict KLF4 and TRAF7 mutation status with high sensitivity and specificity, respectively. The IHC and WB analyses indicated that PD-L1, IDO, and TDO2 levels in tumors with TRAF7 mutations were significantly higher than those in WT tumors. Meanwhile, there was a significant difference in TDO2 between tumors with AKT1 mutations and WT tumors. Specifically, TRAF7 mutations could play a key role in skull base meningiomas by regulating the expression of inhibitory immune checkpoints and thus suppressing immune responses.

Checkpoint inhibitors may be potential strategies for targeted immunotherapies of these mutant meningiomas [1].

In a genomic analysis of 300 meningiomas, lead to the discovery of mutations in TRAF7, a proapoptotic E3 ubiquitin ligase, in nearly one-fourth of all meningiomas. Mutations in TRAF7 commonly occurred with a recurrent mutation (K409Q) in KLF4, a transcription factor known for its role in inducing pluripotency, or with AKT1(E17K), a mutation known to activate the PI3K pathway. SMO mutations, which activate Hedgehog signaling, were identified in ~5% of non-NF2 mutant meningiomas. These non-NF2 meningiomas were clinically distinctive-nearly always benign, with chromosomal stability, and originating from the medial skull base. In contrast, meningiomas with mutant NF2 and/or chromosome 22 loss were more likely to be atypical, showing genomic instability, and localizing to the cerebral and cerebellar hemispheres [2].

Unclassified

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