PTPRZ1-MET fusion transcript

Receptor protein tyrosine kinase type Z1 (PTPRZ1)-MET proto-oncogene receptor tyrosine kinase (MET) (ZM) fusion has been identified as a biomarker for secondary glioblastoma (sGlioblastoma) that is involved in glioma progression, but the mechanism of gliomagenesis and pathology of ZM-negative sGlioblastoma has remained to be fully elucidated. A whole-transcriptome signature is thus required to improve the outcome prediction for patients with sGlioblastoma without ZM fusion.

In a study, whole-transcriptome sequencing on 42 sGlioblastoma samples with or without ZM fusion from the Chinese Glioma Genome Atlas database identified mRNAs with differential expression between patients with and without ZM fusion and the most significant survival-associated genes were identified. A 6-gene signature was identified as a novel prognostic model reflecting survival probability in patients with ZM-negative sGlioblastoma. Clinical characteristics in patients with a high or low risk score value were analyzed with the Kaplan-Meier method and a two-sided log-rank test. In addition, ZM-negative sGlioblastoma patients with a high risk score exhibited an increase in immune cells, NF-κB-induced pathway activation and a decrease in endothelial cells compared with those with a low risk score. The present study demonstrated the potential use of a next-generation sequencing-based cancer gene signature in patients with ZM-negative sGlioblastoma, indicating possible clinical therapeutic strategies for further treatment of such patients [1)].

Glioma patients harboring ZM could benefit from MET inhibitors. According to the remarkable role of ZM as a driver of glioma progression and indicator of MET inhibitor sensitivity, it is necessary to detect this alteration even when it presents in glioma with relatively fewer copies.

Early detection could be performed with a high-sensitive method of reverse transcriptase PCR. The hyperactivations of MET signaling driving glioma progression might be contributed by a ligand-independent activation enabled by the protein structure modification of extracellular domain of MET in ZM fusions [2)].

1)
Chen BS, Wang KY, Yu SQ, Zhang CB, Li GZ, Wang ZL, Bao ZS. Whole-transcriptome sequencing profiling identifies functional and prognostic signatures in patients with PTPRZ1-MET fusion-negative secondary glioblastoma multiforme. Oncol Lett. 2020 Nov;20(5):187. doi: 10.3892/ol.2020.12049. Epub 2020 Sep 3. PMID: 32952656; PMCID: PMC7479526.
2)
Huang R, Liu Y, Wang K, Wang Z, Zhang C, Zhang W, Zhao Z, Li G, Huang L, Chang Y, Zeng F, Jiang T, Hu H. High-sensitive clinical diagnostic method for PTPRZ1-MET and the characteristic protein structure contributing to ligand-independent MET activation. CNS Neurosci Ther. 2021 Feb 28. doi: 10.1111/cns.13627. Epub ahead of print. PMID: 33645009.