The analysis of FGFR-gene family alterations in glioma

Y. Li[1], T. han[2], W. sun[2], Y. lu[3], G. lu[2], W. deng[3], R. ding[4], F. bu[4]

[1] Department of neurooncology, The First Hospital of Jilin University, Changchun, China, [2] 2The Medical Department, Jiangsu Simcere Diagnostics Co., Ltd., Nanjing, China, Nanjing, China, [3] Department of biological information, Jiangsu Simcere Diagnostics Co., Ltd., Nanjing, China, Nanjing, China, [4] The State Key Lab of Translational Medicine and Innovative Drug Development, Jiangsu Simcere Diagnostics Co., Ltd., Nanjing, China, Nanjing, China

Poster NO.:#1664

BACKGROUND

- Fibroblast growth factor (FGFR) alterations are implicated across a range of solid tumors, promoting oncogenesis as a result of amplification, mutations, and structural variations. The *FGFR* gene family consists of four highly conserved transmembrane tyrosine kinase receptors (FGFR1–4). FGFR signaling influences angiogenesis and tumor cell migration, differentiation, proliferation, and survival.
- Recently, the cIMPACT-NOW released update 4 and update research, which considered *FGFR* alterations as a marker in brain tumor classification and prognosis. FGFR inhibitors have presented good clinical trial data in CNS tumors.
- Therefore, the features of *FGFR*-gene family alterations in Chinese gliomas are of great interest.

METHODS

- Tumor specimens from 993 glioma patients were analyzed using the 131-gene profiling.
- *FGFR* variants including mutations, amplification, and fusion were detected by following the standard operating procedure(SOP). The molecular characteristics, *FGFR* mutation types, and frequency were also evaluated.

RESULTS

- A total of 116 *FGFR* variants, including mutations, fusions, and gene amplification were identified. The majority of the *FGFR* variants were mutations (62.1%), amplification and fusion being observed in similar frequencies(17.2%, 20.7%).
- *FGFR1* alterations were slightly more than in *FGFR2-4*. Interestingly, we observed more amplification events in *FGFR1* (66.7%, 13/20), more fusion in *FGFR3* (75%, 18/24), no amplification in *FGFR2*, only mutations in *FGFR4*. In addition to *FGFR-TACC* fusion, 4 novel *FGFR* fusions retaining the intact kinase domain were detected, including *FGFR3-KCNB1*, *FGFR3-POC1A*, *FGFR2-CEACAM1* (Intergenic), *FGFR3-WASF2*(Intergenic).
- *FGFR* variants were more common in *IDH* wild-type and H3 mutant than in *IDH*-mutant gliomas (P=0.003461, P=0.002304). Pathway enrichment (GO, KEGG) analysis was performed, revealed no significant differences between *FGFR* mutation and wild type.

Table 1: FGFR-gene family alterations in glioma

Gene	Vraiant type	frequencies
FGFR1	fusion	0.109
FGFR1	CNV	0.283
FGFR1	somatic	0.609
FGFR2	fusion	0.063

Countinued Table 1:

Gene	Vraiant type	frequencies
FGFR2	somatic	0.938
FGFR3	fusion	0.514
FGFR3	somatic	0.371
FGFR3	CNV	0.200
FGFR4	somatic	1

CONCLUSIONS

- We report the prevalence of FGFR variants was 9.1% in in Chinese glioma patients, including mutations, gene amplifications, and novel FGFR fusions. Moreover, targeting FGFR pathway in gliomas with FGFR alterations may be a therapeutic strategy.

吉林大学白求恩第一医院

先声诊断 Simcere

Contact e-mail: 13943188080@163.com