The analysis of FGFR-gene family alterations in glioma Y. Li¹, T. han², W. sun², Y. lu³, G. lu², W. deng³, R. ding⁴, F. bu⁴

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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.

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

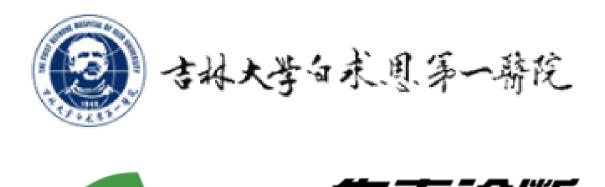
Table 1: FGFR-gene family alterations in glioma

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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.





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