The analysis of *STAG2* variants in Chinese adult patients with glioma

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Poster NO.:#1797

BACKGROUND

- Gliomas are the most frequently occurring primary tumor of the central nervous system, of which HGG is an aggressive form with no effective therapy. So far, standard therapy in the adult setting includes maximal safe surgical resection followed by adjuvant temozolomide and radiation therapy (RT).
- Stromal Antigen-2 (STAG2) is a component of the cohesion complex that is required for DNA replication, the cohesion of the sister chromatids, and transcriptional regulation. Inactivating mutations in *STAG2* can lead to aneuploidy and chromosomal instability in cancer. Within glioblastoma, approximately 4-6% of tumors harbor *STAG2* mutations, according to large-scale genomic databases. At present, cell line trials have reported that glioblastomas carrying *STAG2* mutations are sensitive to PARP inhibitors.
- To explore the possibility of more targeted drugs in glioma, herein, we explore *STAG2* mutation profiles in Chinese adult gliomas.

METHODS

Tumor specimens from 915 Chinese clinical glioma patients were analyzed using the 131-gene profiling, including all the exons of the *STAG2* gene, flanking intronic regions. *STAG2* mutations were detected by following the standard operating procedure (SOP).

RESULTS

- A total of 67 *STAG2* aberrations, including mutations, amplification, and deletion were detected in 50/915 adult glioma patients. Loss of function (LOF) mutations, including frameshift, nonsense, splicing was more (43/67, 71.6%) observed, and 26.9% are missense mutations.
- *STAG2* mutations were more frequently observed in IDH wild-type glioma (7.3%, 43/590) than IDH mutation glioma (2.15%, 7/325). There was a significant difference in the frequency of IDH wild-type and IDH-mutant gliomas with *STAG2* mutations (7.3% vs. 2.15%, P=0.001217).36/43 cases of clinical staging are grade IV and others are unknown.
- Pathway enrichment analysis was performed, and both GO and KEGG enrichment revealed no significant differences in the functions or biological processes between *STAG2* mutation and wild type.

Fig. 1 Pathway enrichment analysis processes between *STAG2* mutation and wild type

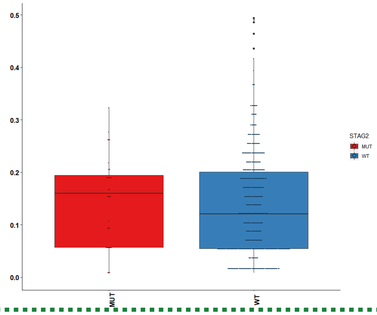
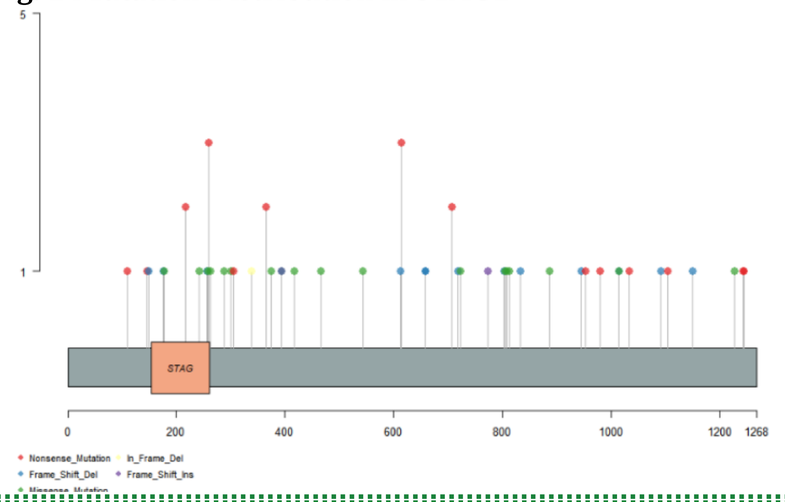


Fig. 2 Mutation Distribution in *STAG2*



CONCLUSIONS

- In our Chinese patients, STAG2 gene mutations mostly occur in IDH wild-type gliomas and may be a molecular marker of IDH wild-type glioma. PARP inhibitors may be a potential treatment option for IDH wild-type gliomas accompanying STAG2 mutation..

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