The landscape of PDGFRA mutation in Chinese patients with glioma

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Next-generation sequencing (NGS) with 131-gene profiling was performed to analyze postoperative tissue from 4294 Chinese adult glioma patients from 2019 to 2023.

Somatic mutations and copy number variations in tumor samples were detected using the NGS method according to standard operating procedures (SOP).

We screened for PDGFRA mutations and calculated mutation frequencies and evaluated other co-mutations.

Background

- Glioma originated from the intracranial glial cells, represents the most aggressive subtype of brain tumors, with few treatments available.
- Platelet-derived growth factor receptor alpha (PDGFRA) is the second most frequently mutated tyrosine kinase receptor in glioblastoma (GBM).
- Mutations in PDGFRA are potential therapeutic targets. Here, we explore the PDGFRA mutation profile in Chinese adult glioma patients.

Methods

- Next-generation sequencing (NGS) with 131-gene profiling was performed to analyze postoperative tissue from 4294 Chinese adult glioma patients from 2019 to 2023.
- Somatic mutations and copy number variations in tumor samples were detected using the NGS method according to standard operating procedures (SOP).
- We screened for PDGFRA mutations and calculated mutation frequencies and evaluated other co-mutations.

Results

- PDGFRA mutations were observed in 185 of 4294 tumor samples (4.3%). The extracellular domain accounted for the majority of mutations (62.78%), followed by the tyrosine kinase domain (27.82%) and the transmembrane domain (9.40%).
- The main mutation hotspot was found to be in exon 5/6/7, accounting for 42.48% of the mutations. The most common mutations identified were p.C235Y (5.26%), p.Y288C (4.51%), and p.E229K (4.14%). The most common tyrosine kinase domain mutation is p.D842Y (1.82%) of exon 18 (9.39%), while p.D842V (1.12%) is also frequently observed, which should be noted that the PDGFRA mutation pattern in gliomas differs from that observed in solid tumors.
- The majority of the samples analyzed exhibited both PDGFRA mutation and PDGFRA amplification, with a small percentage (3.28%) showing PDGFRA fusion, specifically KIT-PDGFRA fusion.

Fig. 1 Main distribution of PDGFRA mutations

Figures

- Fig. 1 Main distribution of PDGFRA mutations

Conclusions

- The incidence of PDGFRA mutation in glioma patients is 4.3%.
- This type of mutation is mostly found in the non-tyrosine kinase domain.
- Investigating the PDGFRA map and PDGFRA inhibitors has significant exploratory value.