

IT'S TIME TO PAINT A BETTER PICTURE OF HIGH GRADE GLIOMA^a

CHALLENGES POSED BY TUMOR HETEROGENEITY

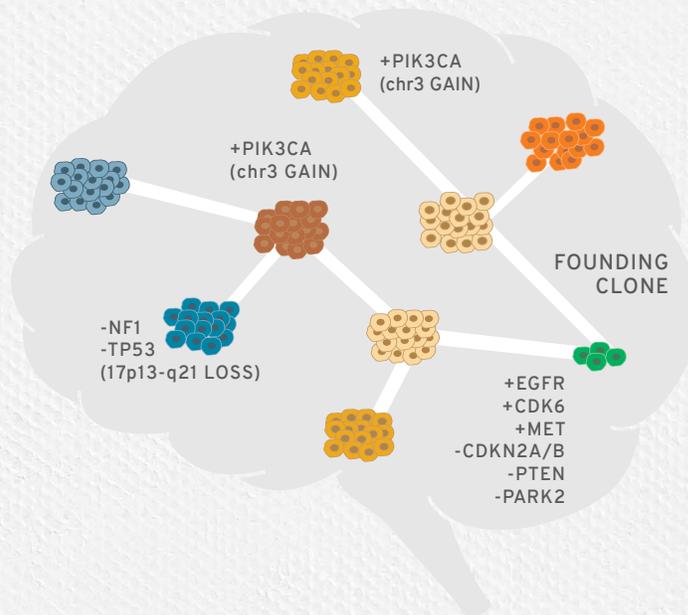


High grade glioma is complex by its very nature. The name glioblastoma multiforme (Grade 4 glioma, also called glioblastoma) reflects the heterogenic nature of the disease, and a challenge that treatments face.

Heterogeneity hinders effective treatment of high grade glioma

The aggressive nature of high grade glioma and its relative therapeutic resistance are due in part to heterogeneity, both in the microenvironment and within individual tumors.^{1,2} Intratumoral heterogeneity is complex in that molecular variations in cells and variation in the microenvironment of the disease process differ not only from patient to patient and from tumor to tumor, but also between subtypes within the same tumor.^{3,4}

TUMOR EVOLUTION



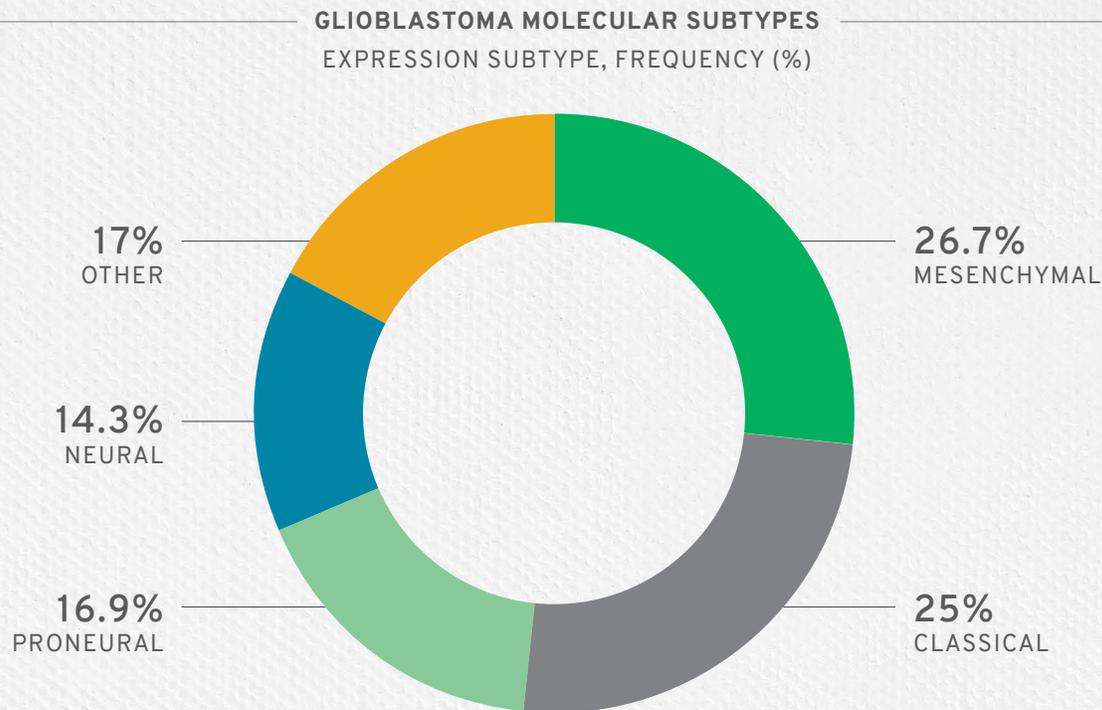
Although every tumor derives from a unique founder clone, it is likely that the diverse subpopulations of cancer cells that develop within that single tumor may be a leading cause of treatment resistance, ultimately leading to treatment failure and the recurrence of the malignancy.³

^aHigh grade glioma includes grade 3 (anaplastic astrocytoma, anaplastic oligodendroglioma, anaplastic ependymoma) and grade 4 (glioblastoma) gliomas, as defined by World Health Organization criteria.

Glioblastoma subtypes

Even though molecular subgroups are defined based on dominant characteristics, tumors often contain cells from multiple subgroups. This confounds the effectiveness of treatment.²

Based on gene expression profiles, glioblastoma can be stratified into four molecular types, each of which corresponds to a different spatial region of the tumor; these include mesenchymal, classical (or proliferative), proneural, and neural.⁴



The multiple levels of heterogeneity inherent in high grade glioma contribute to the difficulty in developing targeted and effective therapies.⁴

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Tumor heterogeneity must be overcome to be potentially successful in managing high grade glioma. Research efforts are needed to provide more treatment options. Go to FUTUREofGLIOMA.com for informative videos featuring prominent experts in neuro-oncology discussing the challenges of high grade glioma.

References: 1. Abedalthagafi M, Barakeh D, Foshay KM. *NPJ Precis Oncol.* 2018;2(27):1-8. 2. Ho IAW, Shim WSN. *Biomed Res Int.* 2017;2017:9634172. doi:10.1155/2017/9634172. 3. Inda MM, Bonavia R, Seoane J. *Cancers (Basel).* 2014;6(1):226-239. 4. Lombardi MY, Assem M. In: De Vleeschouwer S, ed. *Glioblastoma*. Brisbane, Australia; Codon Publications; 2017: Chapter 1.