Molecular and cellular heterogeneity: the hallmark of glioblastoma.
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Abstract
There has been increasing awareness that glioblastoma, which may seem histopathologically similar across many tumors, actually represents a group of molecularly distinct tumors. Emerging evidence suggests that cells even within the same tumor exhibit wide-ranging molecular diversity. Parallel to the discoveries of molecular heterogeneity among tumors and their individual cells, intense investigation of the cellular biology of glioblastoma has revealed that not all cancer cells within a given tumor behave the same. The identification of a subpopulation of brain tumor cells termed "glioblastoma cancer stem cells" or "tumor-initiating cells" has implications for the management of glioblastoma. This focused review will therefore summarize emerging concepts on the molecular and cellular heterogeneity of glioblastoma and emphasize that we should begin to consider each individual glioblastoma to be an ensemble of molecularly distinct subclones that reflect a spectrum of dynamic cell states.

KEYWORDS: 2-HG = 2-hydroxyglutarate; G-CIMP = glioma CpG island methylator phenotype; H3K27Ac = histone H3 Lysine27 acetylation; IDH1; RTK = receptor tyrosine kinase; SCNA = somatic copy number alteration; TCGA = The Cancer Genome Atlas; TIC = tumor-initiating cell; genomic; glioblastoma; glioma; heterogeneity

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