Chromosomal instability

Chromosomal instability (CIN) is a type of genomic instability in which chromosomes are unstable, such that either whole chromosomes or parts of chromosomes are duplicated or deleted. More specifically, CIN refers to the increase in the rate of addition or loss of entire chromosomes or sections of them.

Reports have demonstrated that chromosomal instability, driven in part by gene mutations maintaining overall genomic stability, is found in subsets of adult-type diffusely infiltrating diffuse gliomas of all histologic and molecular grades, with resulting in elevated overall copy number burden, chromothripsis, and poor clinical Glioma prognosis. Still, relatively few studies have examined the effect of this process, due in part to the difficulty of routinely measuring CIN clinically.

Richardson et al. reviewed the underlying mechanisms of CIN, the relationship between chromosomal instability and malignancy, the prognostic significance and treatment potential in various cancers, systemic disease, and more specifically, infiltrating diffuse glioma subtypes. While still in the early stages of discovery compared to other solid tumor types in which CIN is a known driver of malignancy, the presence of CIN as an early factor in gliomas may in part explain the ability of these tumors to develop resistance to standard therapy, while also providing a potential molecular target for future therapies [1].

Data suggest that CIN and Microsatellite instability (MSI) contribute to the genomic instability in Glioblastomas via independent pathways. Since MSI was significantly more frequent in relapses, it might play a role in the malignant progression of Glioblastoma [2].

Impaired regulation of Aurora-B/AIM-1 expression in human cells causes chromosomal abnormality and instability, Aurora-B/AIM-1 was highly expressed in high-grade gliomas and its expression was well correlated with histological malignancy and clinical outcomes. The modification of the level of Aurora-B/AIM-1 expression might be a new target for glioma therapy.

Loss of genetic material on chromosome 14q may play an important role in the molecular genetic glioblastoma pathogenesis. The chromosomal regions at D14S65 on 14q31-32.3 and from D14S63 to D14S74 on 14q21-24.1 may harbor novel tumor suppressor genes associated with glioblastoma. [3].

1)
Richardson TE, Walker JM, Abdullah KG, McBrayer SK, Viapiano MS, Mussa ZM, Tsankova NM, Snuderl M, Hatanpaa KJ. Chromosomal instability in adult-type diffuse gliomas. Acta Neuropathol Commun. 2022 Aug 17;10(1):115. doi: 10.1186/s40478-022-01420-w. PMID: 35978439.
2)
Martinez R, Schackert HK, Plaschke J, Baretton G, Appelt H, Schackert G. Molecular mechanisms associated with chromosomal and microsatellite instability in sporadic glioblastoma multiforme. Oncology. 2004;66(5):395-403. doi: 10.1159/000079488. PMID: 15331927.

3)

Hu J, Jiang C, Ng HK, Pang JC, Tong CY. [A preliminary study of loss of heterozygosity on chromosome 14 in glioblastoma]. Zhonghua Yi Xue Yi Chuan Xue Za Zhi. 2001 Oct;18(5):347-50. Chinese. PMID: 11592040.