

ATRX loss

ATRX loss is a hallmark of astrocytic tumors. Furthermore, ATRX loss defines a subgroup of astrocytic tumors with a favorable prognosis.

In gliomas, TERT expression and TERT promoter mutation are considered to reliably indicate telomerase activation, while ATRX mutation and/or loss indicates an alternative lengthening of telomeres (ALT). However, these relationships have not been extensively validated in tumor tissues.

Telomerase repeated amplification protocol (TRAP) and C-circle assays were used to profile and characterize the telomere maintenance mechanism (TMM) cross-sectionally (n = 412) and temporally (n = 133) across glioma samples. WES, RNA-seq, and NanoString analyses were performed to identify and validate the genetic characteristics of the TMM groups.

Kim et al. showed through the direct measurement of telomerase activity and Alternative lengthening of telomeres (ALT) in a large set of glioma samples that the TMM in glioma cannot be defined solely by the combination of telomerase activity and ALT, regardless of TERT expression, TERT promoter mutation, and ATRX loss. Moreover, they observed that a considerable proportion of gliomas lacked both telomerase activity and ALT. This telomerase activation-negative and ALT negative group exhibited evidence of slow growth potential. By analyzing a set of longitudinal samples from a separate cohort of glioma patients, they discovered that the telomere maintenance mechanism is not fixed and can change with glioma progression.

This study suggests that the telomere maintenance mechanism is dynamic and reflects the plasticity and oncogenicity of tumor cells. Direct measurement of telomerase enzyme activity and evidence of ALT should be considered when defining telomere maintenance mechanism. An accurate understanding of the telomere maintenance mechanism in glioma is expected to provide important information for establishing cancer management strategies ¹⁾

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Kim S, Chowdhury T, Yu HJ, Kahng JY, Lee CE, Choi SA, Kim KM, Kang H, Lee JH, Lee ST, Won JK, Kim KH, Kim MS, Lee JY, Kim JW, Kim YH, Kim TM, Choi SH, Phi JH, Shin YK, Ku JL, Lee S, Yun H, Lee H, Kim D, Kim K, Hur JK, Park SH, Kim SK, Park CK. The telomere maintenance mechanism spectrum and its dynamics in gliomas. Genome Med. 2022 Aug 11;14(1):88. doi: 10.1186/s13073-022-01095-x. PMID: 35953846.

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