## **Telomeric repeat amplification protocol**

Telomeric repeat amplification protocol (TRAP) is a fast and sensitive PCR-based assay for detection and measurement of telomerase activity. Since its introduction, the TRAP assay has been widely used in cancer and aging studies.

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, we 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, we discovered that the TMM is not fixed and can change with glioma progression.

Conclusions: This study suggests that the TMM 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 TMM. An accurate understanding of the TMM in glioma is expected to provide important information for establishing cancer management strategies<sup>1)</sup>

## 1)

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