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Telomere profiling : toward glioblastoma personalized medicine

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Despite a standard of care combining surgery, radiotherapy (RT) and Temozolomide chemotherapy, average. Glioblastoma patient survival is still less than one year. However, recent advances in molecular signalization profiling in glioblastoma have provided new targets for personalized medicine development and new irradiation techniques, such as carbon ion Hadrontherapy, are now available. The latter technology leads to a higher biological response, while minimizing adverse effects on healthy tissues in comparison with RT. As carbon ion Hadrontherapy access is restricted to RT resistant patient, photon irradiation resistance biomarkers are needed. Long telomeres and high TA have widely been associated with photon radio-resistance in other cancers. Moreover, telomere protection, function and length also depend on the Shelterin protein complex (TRF1, TRF2, TPP1, POT1, TIN2, hRAP1). We thus decided to evaluate an enlarged telomeric status (TL, telomerase catalytic subunit (hTERT) and the shelterin component expression level as a potential radioresistance biomarker in a panel of 11 glioblastoma-derived cell lines. In addition, nothing was known about the role of telomeres in carbon ion response. We have thus evaluated this telomeric status after both types of irradiations. We report a significant correlation between TL, basal POT1 expression level and photon radioresistance and a significant variation in TERT, TERF1 and POT1 expression after photon irradiation. Strikingly, all of these correlations were lost when considering carbon irradiation. We thus propose (i) a model of telomeric damage implications in cell response to both irradiations, (ii) to assess POT1 expression level or TL on tumor biopsy to identify radioresistant patients.

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