IDH1 gDNA sequences detected in liquid biopsies from GBM patients.

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Abstract

BACKGROUND. Diffuse gliomas are the most common malignant primary tumors, and Glioblastoma (WHO grade IV) is the most frequent diffuse glioma with a median patient survival of 15 months after diagnosis. Temozolomide (TMZ) and radiotherapy is currently the first-line of treatment for this disease, however, survival remains poor among these patients because of resistance to TMZ. The identification and validation of biomarkers for prosgnostic and responsed to therapy values, using minimally invasive approaches, along the course of the disease, will significalntly improve the management of these tumors. In this sense, the use of liquid biopsies would allow to for the monitoring of tumor changes in real time. Thereby, glioma cell extracellular vesicles (EVs) containing mRNA, gDNA or proteins, can cross the Blood Brain Barrier reaching the peripheral blood, from where they can be isolated and their cargo analysed. Somatic mutations at codon 132 of the isocitrate dehydrogenase 1 gene (IDH1) have been identified in approximately 12% of glioblastomas. This subgroup of patients display better prognostic, with improved overall survival. Our group have recently detected IDH1 gDNA sequences within EVs isolated from either tumor cells or EVs isolated from peripheral blood of athymic mice xenografted with cancer-initiating cells. RESULTS AND CONCLUSION. We have studied the IDH1 sequence of EVs-isolated gDNA of peripheral blood samples from patients diagnosed with different degree of gliomas, together with controls. The results were validated by analysing the IDH1 sequence within the counterpart paraffin-embedded solid tumor specimens. Here we show a proof of concept for the use of the IDH1 mutations within peripheral blood EVs, as a prognostic biomarker via a minimally invasive technique.

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