Advances in liquid biopsy for glioblastoma diagnosis and monitoring through nucleosome epigenetic modifications tracking

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Abstract

Background:

Glioblastoma (GBM) represents one of the most aggressive forms of brain cancer. Currently, GBM is diagnosed and monitored through neuroimaging and histopathological analysis. However, overall survival has remained stagnant in recent decades, largely due to treatment failures and the lack of biomarkers for relapse detection, creating an urgent need for innovative biomarkers for both diagnostic and monitoring purposes. Liquid biopsies using nucleosomes-containing-histone post-translational modifications (PTMs) have the potential to become valuable biomarkers for detecting and monitoring GBM, as they offer a non-invasive approach to detect tumor-related alterations, such as genetic mutations or epigenetic changes.

Objectives

Our aim is to develop a non-invasive epigenetic-based biomarker for the early detection, monitoring of treatment response and identification of relapse in GBM patients with the ultimate goal of improving diagnosis and patient management.

Methods:

K2EDTA plasma from GBM patients (n=10) and healthy donors (n=10) were subjected to Nu.Q®Capture-MassSpectrometry (MS) method. Then, retrospective plasma samples from GBM patients at diagnosis (n = 68) were compared to age-matched healthy donors (n = 68) using quantitative Nu.Q® Immunoassays targeting distinct epigenetic features on circulating nucleosomes such as : H3R8cit, H3K4Me2, H3K9Me1,H3K9Me3, as well as the global level of nucleosomes with the Nu.Q® H3.1 assay. Additionally, longitudinal samples from 10 patients undergoing treatment for GBM were analyzed using the same panel of Nu.Q® Immunoassays.

Results:

The Nu.Q®Capture-MS analysis revealed a dysregulated methylation pattern at lysine 9 of the histone H3 (H3K9) in GBM samples compared to healthy ($p<0.05$). Subsequently, the results reveal significantly elevated levels of circulating H3.1-nucleosomes, as well as some PTMs-nucleosomes in GBM patients compared to healthy donors. Additionally, the pattern of circulating nucleosome and their associated PTMs in GBM patients undergoing treatment highlighted the potential use of these new biomarkers to monitor treatment response and/or disease progression.

Conclusion:

Given their elevated levels in patient samples, our findings support the use of circulating nucleosomes as a promising biomarker for GBM detection. Additionally, the study highlights the critical role of epigenetic modifications on circulating nucleosomes in assessing tumor progression and therapeutic response, contributing to advancements in liquid biopsy approaches.

Do you have any conflicts of interest?

Yes, I have a conflict of interest.

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