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BIOM-30. CELL LINE STUDY OF NUCLEOSOME-BASED BIOMARKERS IN THE DIAGNOSIS AND DETECTION OF RELAPSES IN GLIOBLASTOMA

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Currently, glioblastoma (GBM) diagnosis and monitoring rely on neuroimaging and histopathological confirmation. However, overall survival has not improved in last decades due to therapeutic failure and to a lack of biomarkers for relapses' detection. Liquid biopsies (i.e. blood or CSF) using nucleosomes-containing-histone post-translational modifications (PTMs) have the potential to become valuable biomarkers for diagnosis and monitoring GBM. Four glioblastoma cell lines (SF-126, U-87MG, U-118MG, and U-138MG) compared to a healthy microglia cell line (HMC3) and other solid cancer cell lines including pancreas (MIA-PaCa-2), liver (HepG2), and cervix/uterus (HeLa) have been analyzed to identify their epigenetic profile. Nucleosomes were extracted and analyzed with the Nu.Q® Discover immunoassays platform addressing 13 histone-PTMs. Quantitative results of PTMs expression were normalized on quantification of total H3.1-nucleosomes. The immunoassay identified three candidate biomarkers compared to control cell lines (n = 4): citrullinated-histone-H3 (H3R8Cit) (control = 4.68%; GBM = 13.88%; $p < 0.05$), phosphorylation of H3S10 (H3S10Ph) (control = 2.31%; GBM = 5.57%; $p < 0.05$), and a trend in H3K4Me2 elevation (control = 0.43%; GBM = 1.07%; $p = 0.066$) in GBM cell lines (n = 4). These results were confirmed by western blot. Moreover, principal component analysis revealed a segregation between GBM and control cells, mainly driven by these three PTMs. Moreover, to demonstrate the capacity of the Nu.Q® assays to quantitatively monitor PTMs, GBM cell line SF-126 (n = 3) was treated with an EZH2 inhibitor (responsible of H3K27 methylation) (iEZH2). After 24 hours and 48 hours of exposure, the expression level

of H3K27Me3 –expressed as ratio of total nucleosomes– was decreased by 32% (control = 14.67%±0.58%; iEZH2= 10.00%±1.73%; p< 0.05) and 41% (control = 15.33%±1.53%; iEZH2= 9.00%±0.00%; p< 0.05), respectively. Those results were also confirmed by western blot analysis. In conclusion, we identified three specific *in vitro* epigenetic-based marks of GBM and demonstrated that the Nu.Q® technology is a valuable tool to monitor the degree of PTMs expression.