SDPS-13 CELL LINE STUDY OF NUCLEOSOME-BASED BIOMARKERS IN THE DIAGNOSIS AND DETECTION OF RELAPSES IN GLIOBLASTOMA

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; 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. In addition, 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 level of expression 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.

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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 cerebrospinal fluid) 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 (Belgian Volition) addressing 13 histone-PTMs. Quantitative results of PTMs expression were normalized on quantification of total nucleosomes (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%