Advances in Liquid Biopsy for Glioblastoma Diagnosis and Monitoring through Nucleosome Epigenetic Modifications Tracking

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Glioblastoma: Challenges & Unmet Needs

- Glioblastoma (GBM) is the most aggressive primary brain tumor in adults.
- Standard management includes surgery, radiotherapy, and chemotherapy
- High relapse rate and poor prognosis (median survival ~15 months).

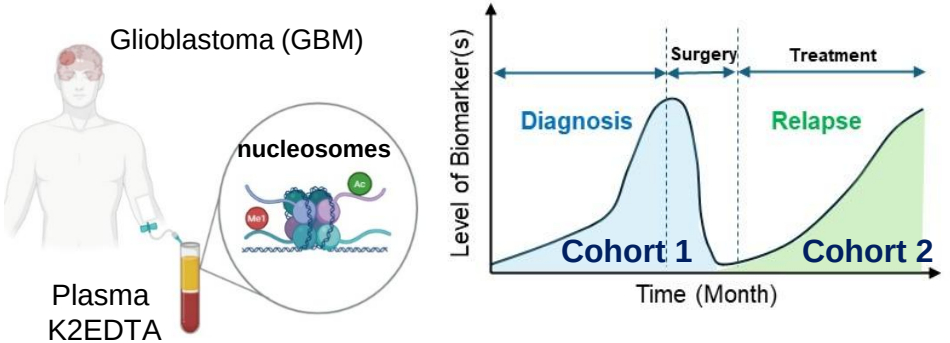
➢ **Major gap**: ***No circulating biomarkers validated*** **for GBM.**

Our Goal : Develop a liquid biopsy approach

- Develop a liquid biopsy approach for the diagnostic, the patient follow-up and early relapse detection of glioblastoma

➢ **Investigating circulating nucleosomes and their epigenetic marks as new Biomarkers.**

Methods :



Circulating H3.1 nucleosomes and their epigenetic marks (PTMs) levels were analyzed, using the Nu.Q® Immunoassays (Belgian Volition), in K2EDTA plasma from two independent cohorts including :

- **Cohort 1:** 67 samples from GBM patients collected at diagnosis and 99 samples from Healthy Donors
- **Cohort 2:** Multiple samples from 4 GBM patients collected longitudinally from diagnosis (pre-therapy; D-1) and throughout treatment, with a total of 21 samples assessed.

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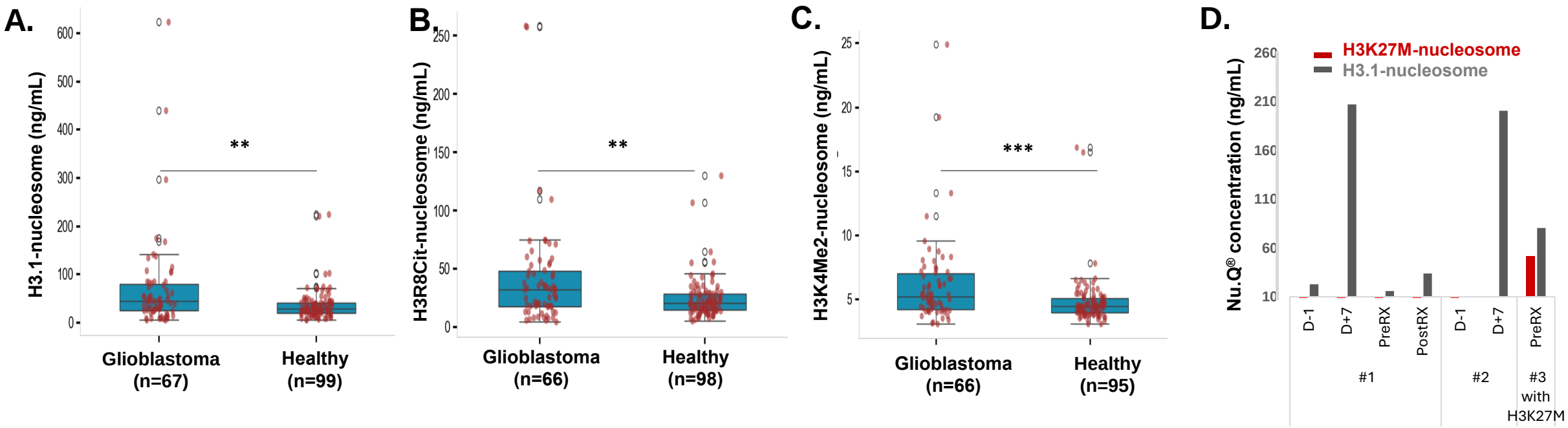
Results at diagnosis : Epigenetic Profiling of Circulating Nucleosomes Enables GBM Detection



Box plot from Nu.Q® quantification (expressed as ng/mL) showing a significant increase of (**A**) the H3.1- (**B**) H3R8Cit-, (**C**) H3K4Me2-nucleosome levels, in GBM samples (n=66-67) compared to healthy samples (n=95 - 99). (**D**) Mutation in H3K27 is detectable in the plasma of GBM patient #3 (confirmed to be carrying this mutation by tissue biopsy) by the specific Nu.Q®H3K27M. p-values were determined by Mann–Whitney (*p<0.05; ** p<0.01; *** p<0.001).

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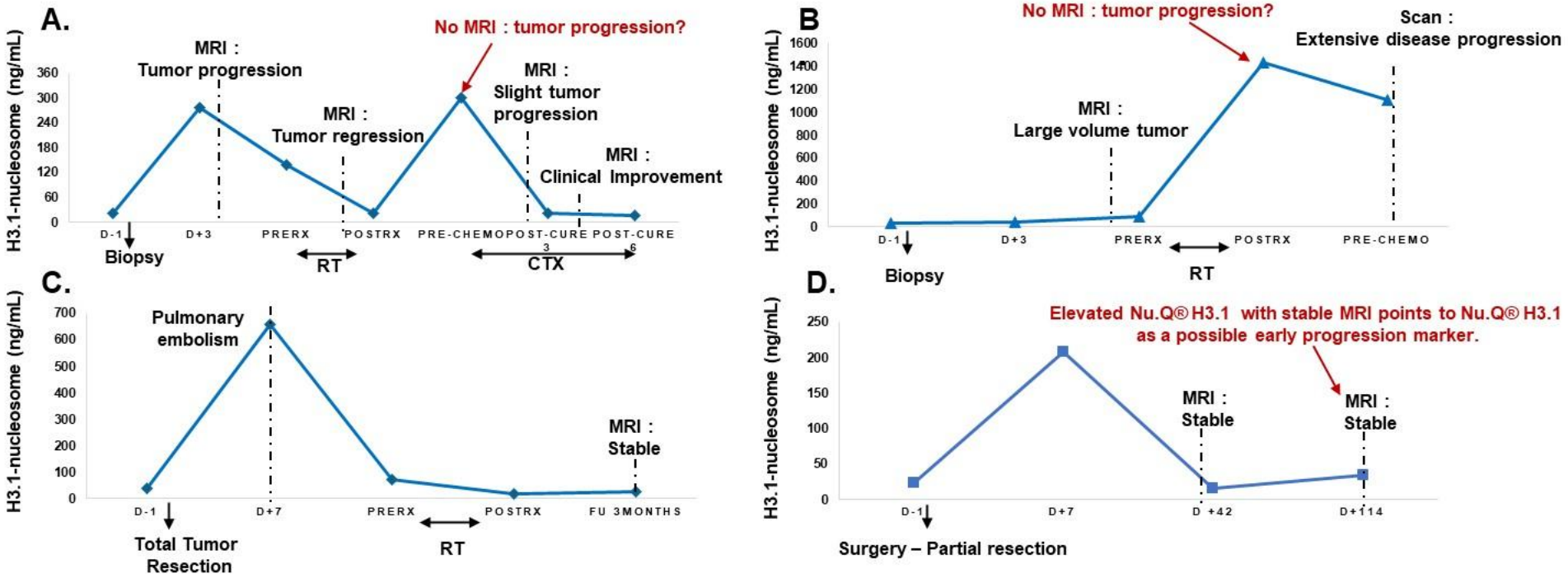
Results Monitoring : Nu.Q®H3.1 Mirrors the Clinical Course of GBM Patients



Samples from four GBM patients were analyzed at the diagnosis (pre-therapy; D-1) and throughout treatment, with a total of 21 samples assessed. Nucleosome levels were subsequently analyzed using the Nu.Q® H3.1 immunoassay and H3.1-nucleosome concentration (ng/mL) have been reported in graphical form. Results were then compared with Magnetic Resonance Imaging (MRI) reports. *RT (radiotherapy); CTX (Chemotherapy); FU (Follow-up); D (Days).*

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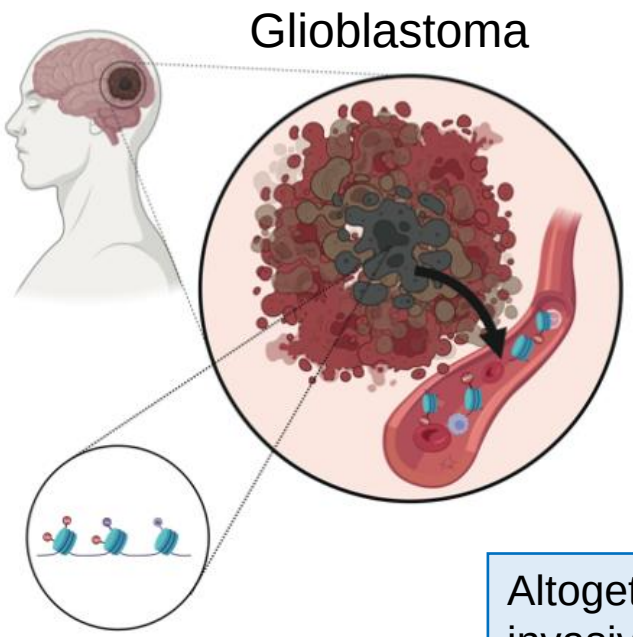
Conclusions



- ✓ Histone mutation (H3K27M) in brain-GBM cells can be detected in blood samples using Nu.Q® Immunoassay (Nu.Q®H3K27M)
- ✓ High H3.1-nucleosome levels and the presence of H3K27M-nucleosomes in plasma from GBM patients suggest that nucleosomes cross the blood-brain barrier.
- ✓ The use of Nu.Q® PTMs tests on the GBM samples suggests that epigenetic markers may be useful for glioblastoma detection
- ✓ Circulating nucleosome levels mirrors the clinical course of GBM Patients

Altogether, our findings suggest that Nu.Q® immunoassays could serve as reliable, minimally invasive biomarkers for the **detection** and **monitoring** of disease progression in GBM patients

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