

Additional data file 2:

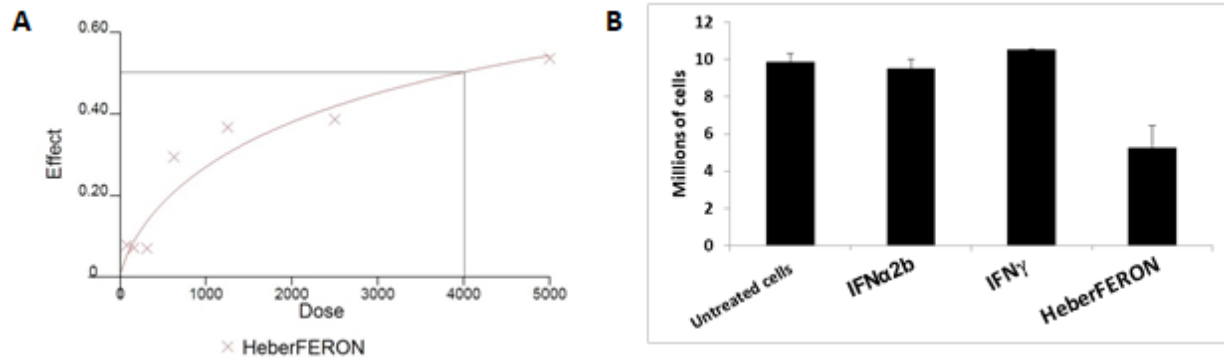


Figure S1. Dose-Effect HeberFERON Curves and cell counts. (A) The cells were treated with HeberFERON at different concentrations for 72 h and cell viability was assessed by the MTT assay. The relationship between concentration in IU/mL (Dose) and Effect (0-0.6, meaning 0-60% of cell proliferation inhibition) is plotted. IC₅₀ was calculated as the concentration required to achieve a 50% (0.5) effect. (B) Cell counts with Trypan blue (0.4%) was performed in duplicated cultures treated with HeberFERON at IC₅₀ or their equivalent dose for IFNα₂b or IFNγ. The average and standard deviations of millions of cells are shown.

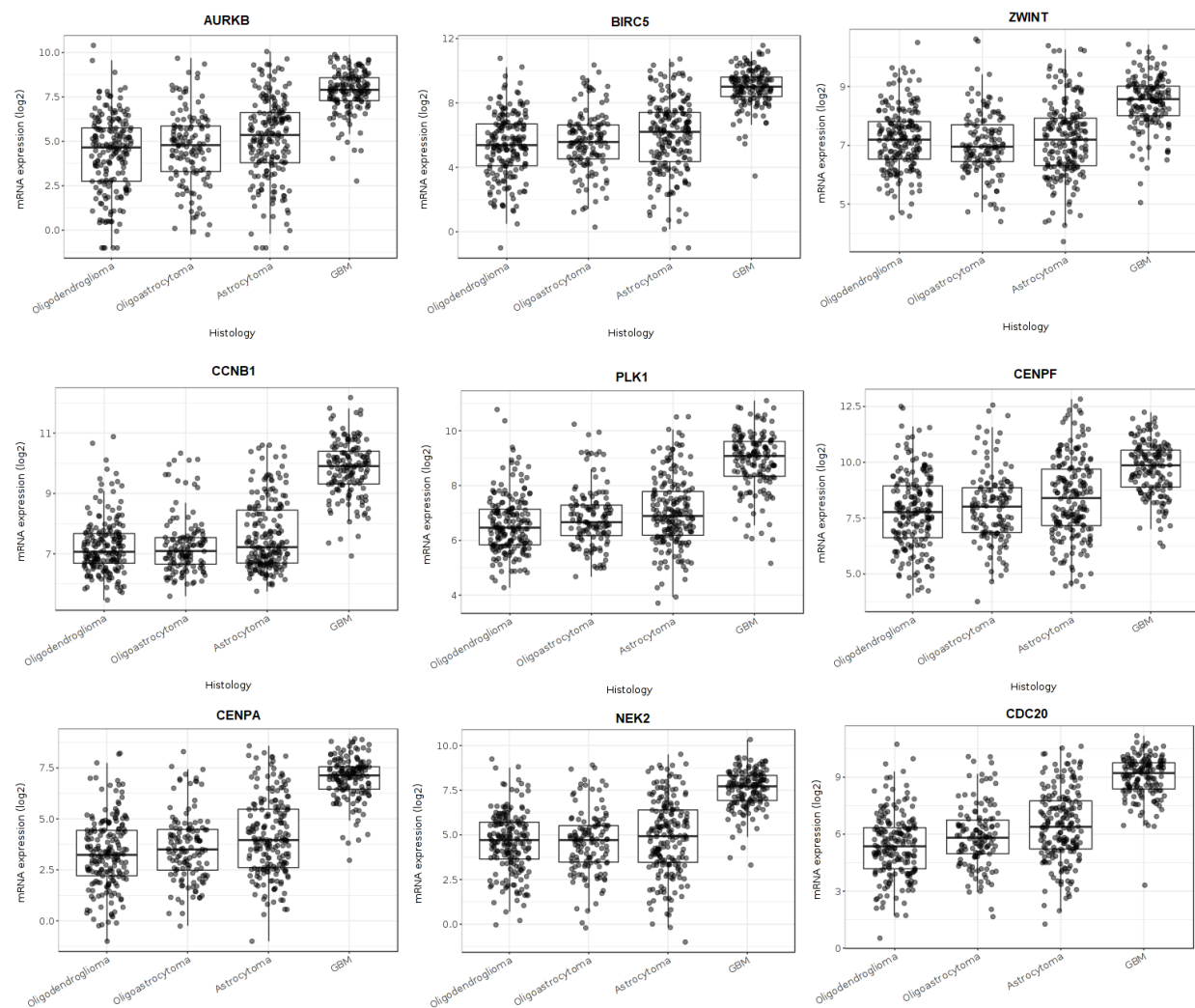


Figure S2: Expression profiles of FOXM1 regulated genes and CDC20 in brain tumors by GlioVis.

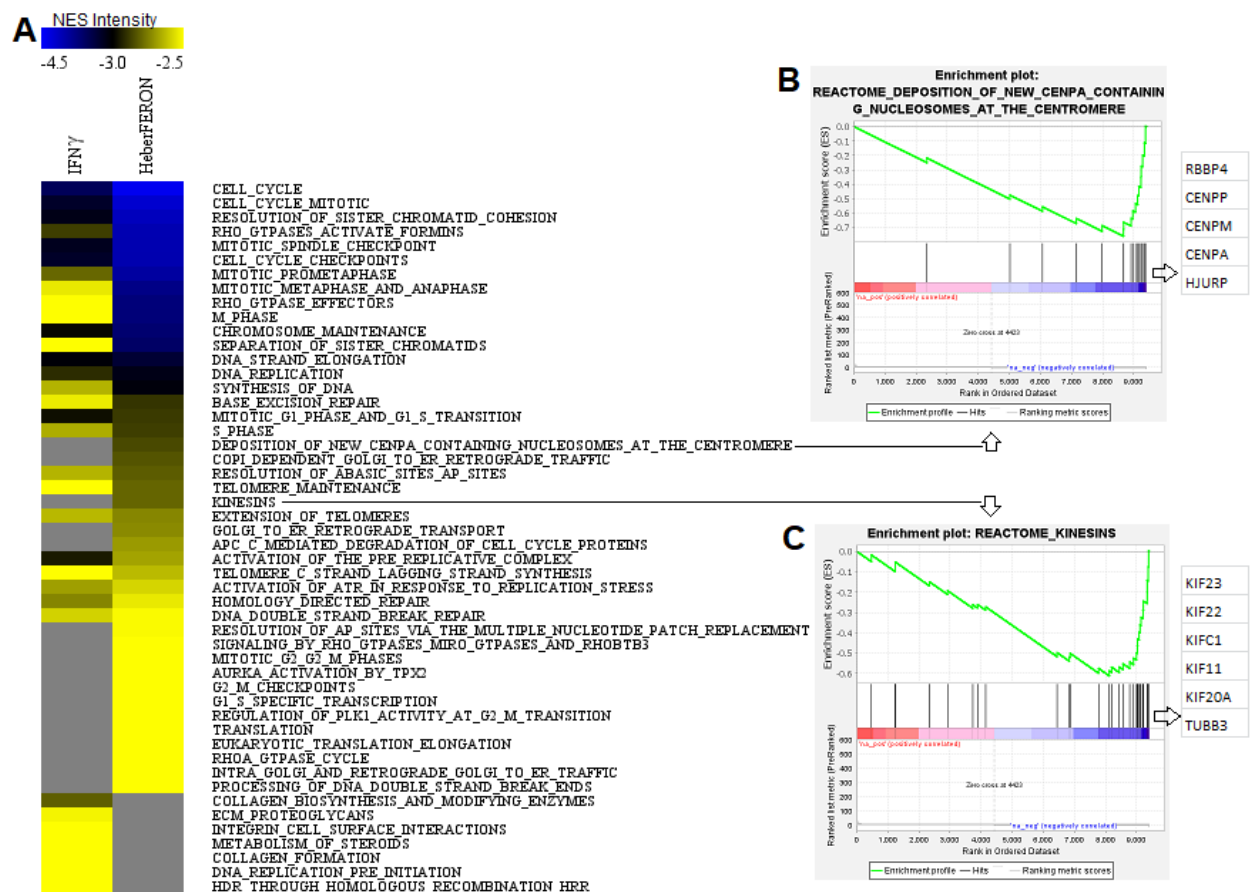


Figure S3: Results of Gene Set Enrichment Analysis (GSEA). A) Heatmap of the NES of Reactome pathways resulting from GSEA analysis. The two columns correspond to IFN γ and HeberFERON. Reactome Pathways ordered by NES for HeberFERON. Identification of signaling distinctively regulated (inhibited) by this combination of IFNs $\alpha 2b$ and γ . B/C) Two enrichment plots for Pathways present only under HeberFERON: “Deposition of new CENPA containing nucleosomes at the centromere”(B) and “Kinesins” (C). The most relevant genes for the enrichment significance are listed to the right of each Enrichment Plot.

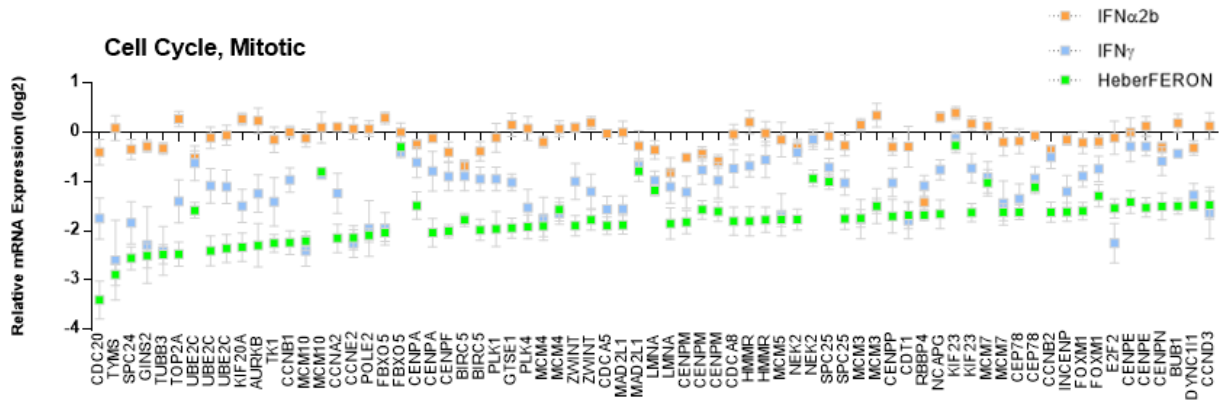


Figure S4: Cell cycle gene expression plot. $\log_2$ expression (mean + SD) relative to averaged controls at probe level are plotted. Orange, blue and green bars correspond to $\text{IFN}\alpha 2b$, $\text{IFN}\gamma$ and HeberFERON expression values, respectively. The top 50 genes (71 probes) from the CES of Reactome mitotic cell cycle pathway are shown ordered by the rank metric score.

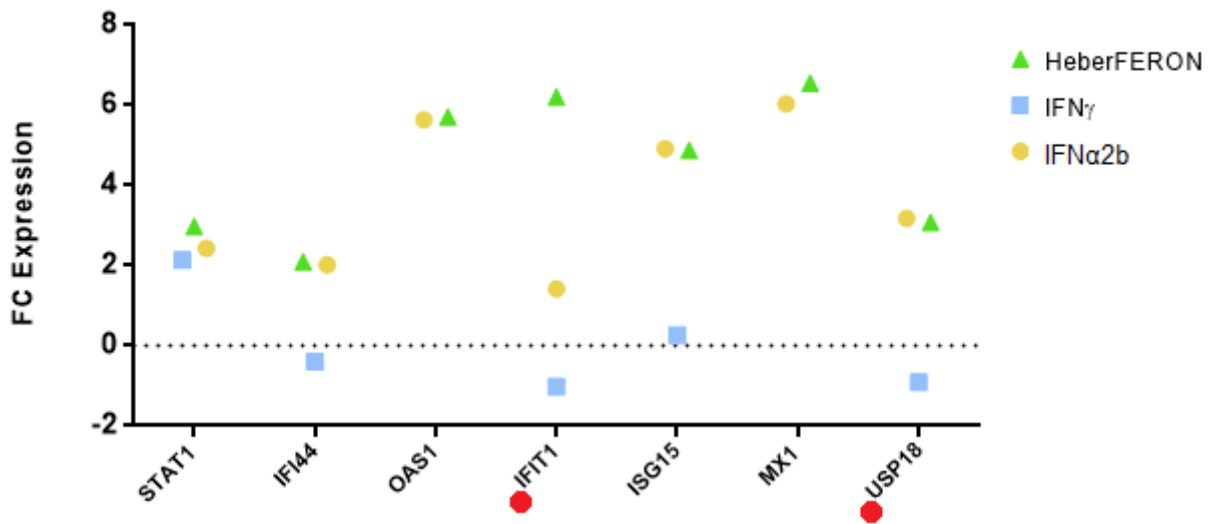


Figure S5: Fold changes of genes from a molecular signature associated to poor prognosis in the Proneural GBM subtype. Orange, blue and green dots represents expression values in samples treated with $\text{IFN}\alpha 2b$, $\text{IFN}\gamma$ and HeberFERON,

respectively. Red dots highlight genes whose expression is favorable for the disease outcome.