**Supplementary material**

**S1.** **Targeted mass spectrometry for histone tail analysis**. Analysis of histone tail post-translational modification states in pediatric glioma specimens. Using targeted mass spectrometry of the histone H3 and H4 N-terminal tail, quantitation of histone post-translational modifications (me1, me2, me3, ac) and unmodified peptide on lysine (K) residues was performed.

**S2.** **Table of results from targeted histone tail mass spectroscopy** (Microsoft Excel format). Statistically significant differences in histone post translational modifications are observed in glioma cell lines by H3.3K27M mutation status (Independent-sample t test, two-tailed).

**S3.** **H3.3K27M, H3.1K27me3, and H3.3K27me3 peptide abundance in cell lines**. Targeted mass spectroscopy reveals differences in H3.3K27M, H3.1K27me3, and H3.3K27me3 peptide abundance in pediatric glioma and adult glioma cells, and normal human astrocytes. Of note, loss of H3.1K27 and H3.3K27 trimethylation is observed in H3.3K27M cell lines.

**S4.** **H3.3K27M mutation is associated with distinct histone modification states** (Microsoft Excel format). Statistically significant differences in histone post translational modifications are observed in glioma tissues by H3.3K27M mutant status (Independent-sample t test, two-tailed).

**S5.** **Modification states along short peptides** (Microsoft Excel format). Distinct combinations of histone peptide modification states with H3.3K27M mutation status in tissues (Independent-sample t test, two-tailed).

**S6.** **Radiation treatment is associated with changes in histone modification states *in* *vitro*** (Microsoft Excel format). Statistically significant differences in histone post translational modification states are observed in NHA, U87, SF8628, and DIPG007 cells treated with radiation (one-way ANOVA).

**S7.** **Bromodomain inhibition with JQ1** **is associated with changes in histone modification states *in vitro***. Unsupervised analysis of histone tail modification profiles of glioma cell lines (SF8628, DIPG007 and U87) and normal astrocytes (NHA) reveals clustering by cell line and treatment condition.

**S8.** **Peptide modification states observed after bromodomain inhibition with *in vitro***. (Microsoft Excel format). Statistically significant differences in histone post translational modification states are observed in NHA, U87, SF8628, and DIPG007 cells after bromodomain inhibition with JQ1 (Independent-sample t test, two-tailed).