

Fig. S1. Genome-wide distribution of hyper and hypomethylated DMRs between GSC lines and the control group.

NB **NSC** **GBM**
GSC **Xenograft**

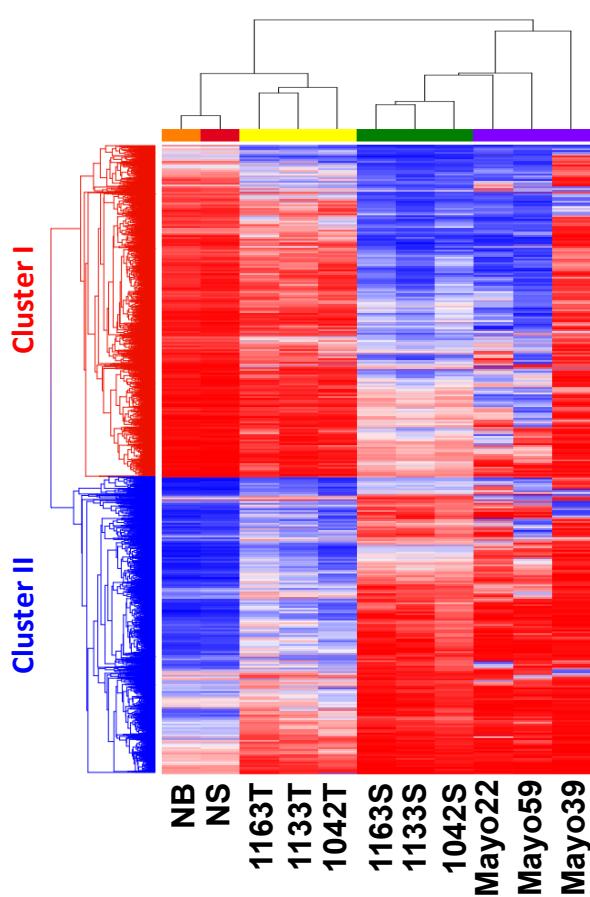
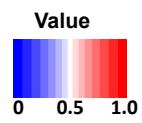


Fig. S2. Supervised cluster analysis of DNA methylation using DMRs between control group and GSCs.

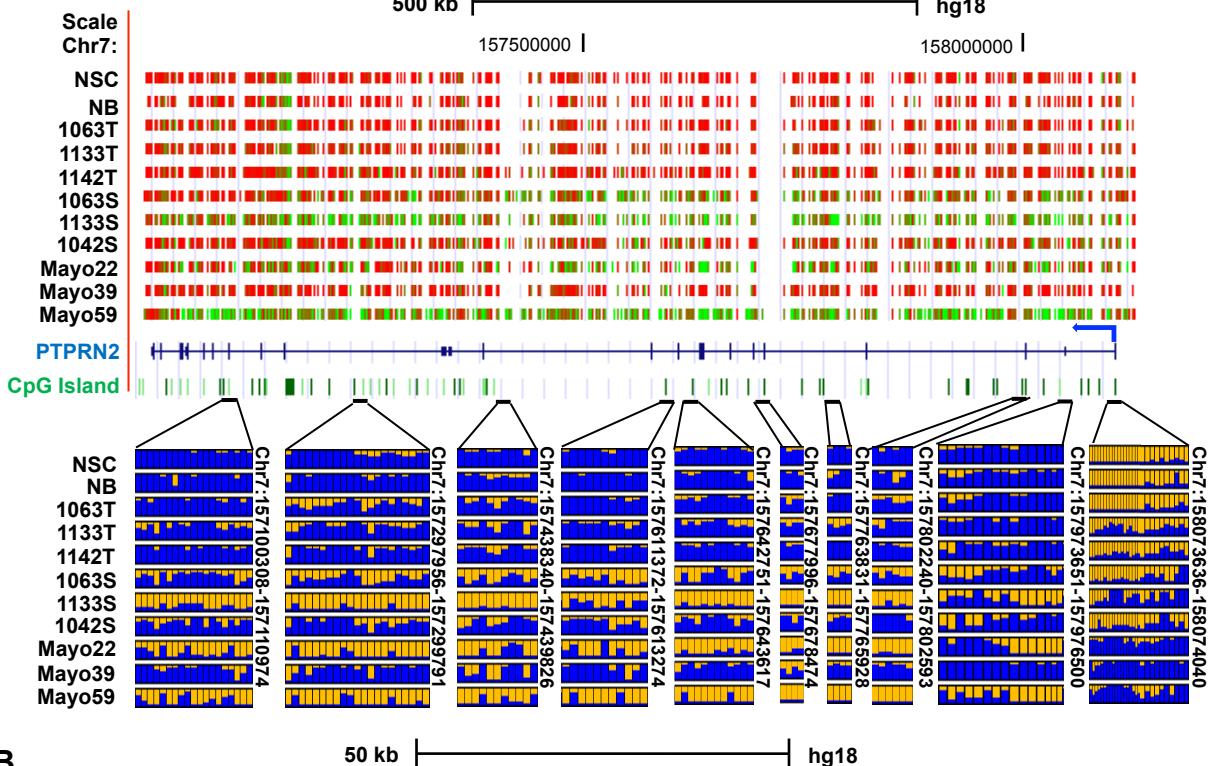
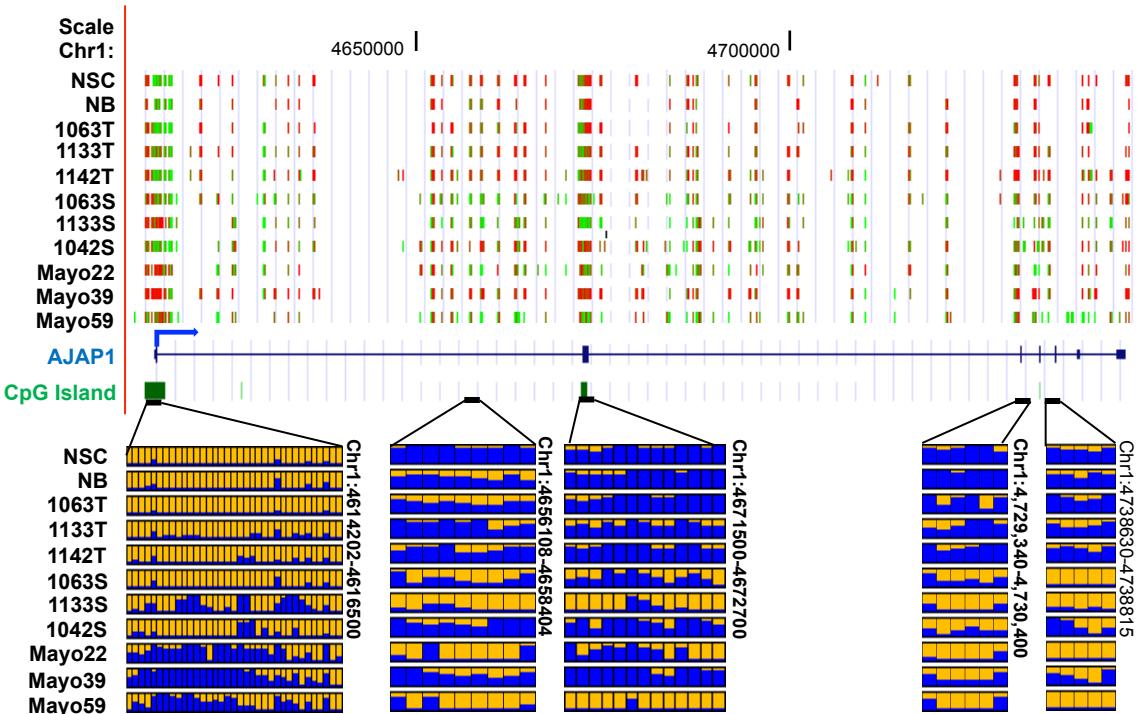
A**B**

Fig. S3. The observation of promoter hypermethylation and gene body hypomethylation in *PTPRN2* (A) and *AJAP1* (B). In each figure, the upper panel shows a UCSC genome browser snapshot illustrating the RRBS results of *PTPRN2* (A) and *AJAP1* (B); the lower panels illustrate the DNA methylation profiles of multiple DMRs located in the 5'-end and gene body of *PTPRN2* (A) and *AJAP1* (B).

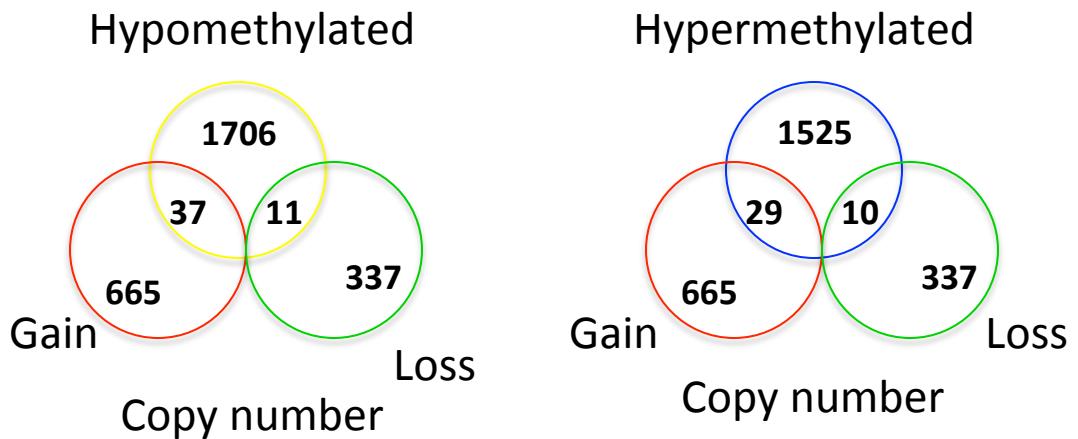


Fig. S4. Venn diagrams displaying the overlaps between genes consistently affected by genetic and epigenetic alterations in GSCs. The DMRs in Fig. S2 were compared with genomic loci associated with copy alterations (gain or loss) in GSCs.

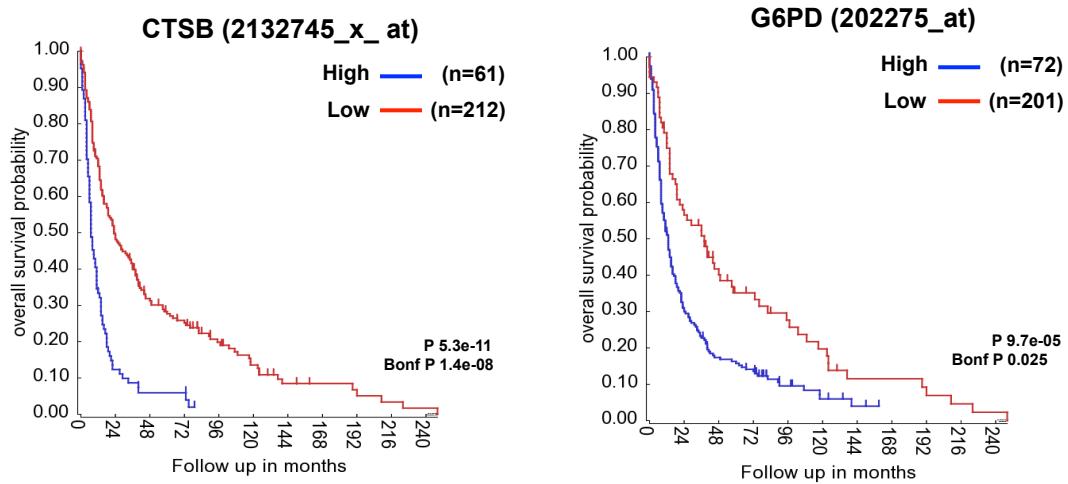


Fig. S5. Kaplan-Meier analysis of overall survival for *CTSB* and **G6PD** using the French dataset with the log-rank test p value indicated. The survival plot was downloaded from R2 microarray analysis and visualization platform. Patients with higher gene expression are highlighted in blue, whereas patients with lower expression are highlighted in red.

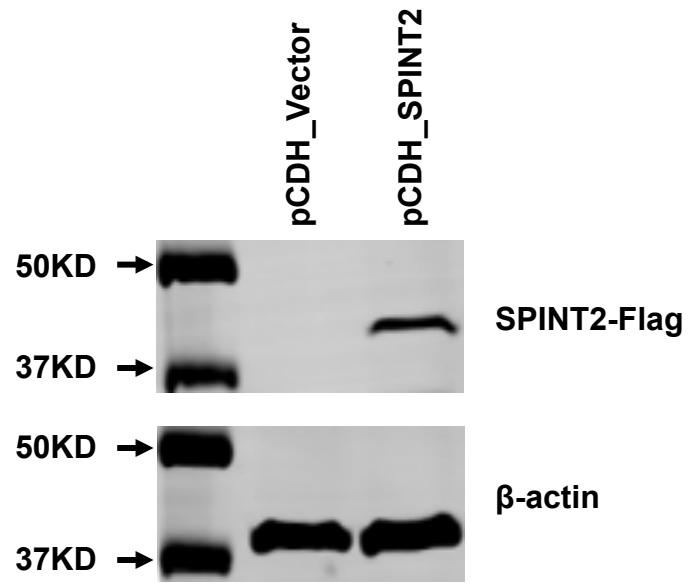


Fig. S6. Immunoblot analysis of Flag-tagged SPINT2 fusion protein expression in pCDH-*SPINT2* stable cell line. The protein lysates were prepared from pCDH vector and pCDH-*SPINT2* stable cell lines, respectively, and analyzed by immunoblot using anti-Flag M2 antibody. The results confirm SPINT2 expression in pCDH-*SPINT2* stable U87G cell line.