**Supplementary Figures**

**Additional supporting data is presented as four supplementary figures and the corresponding figure legends.**

**Supplementary Fig. S1: INSECT analysis and KANSL2 expression in stem cells.** SOX2/OCT4 cis regulatory module (CRM) *in silico* search performed over the KANSL2 gene for both, human (Ensembl ID ENSG00000139620) (A-B) and mouse (Ensembl ID ENSMUSG00000022992) (C-D) using the INSECT tool. OCT4 (*POU5F1*) was selected as the master transcriptional factor of the CRM having a SOX2 biding site in the same orientation (i.e. direct or reverse) at a maximum distance of 4 bp. The search of the SOX2/OCT4 motif was performed by using the Position Weight Matrix (PWM) referred to the Jaspar Sox2/Oct4 TFBS (ID MA0143.1). This Jaspar Motif is composed of contiguous occurrences for the SOX2 and OCT4 sites. In order to allow for a spacing distance > 0 bp between the two motifs and to use the assumption of independence among the sites during the construction of this PWM, we divided it into its SOX2 and OCT4 submotifs and used them as the PWM inputs in INSECT as was reported previously (20). E. Relative expression (qRT-PCR analysis) of POUF51, and KANSL2 mRNAs in hESC H9 and Neural Progenitors (NP) cells. F. Relative expression (qRT-PCR analysis) of *Kansl2*, and *Oct4*, *Nanog*, *Sox2* and *Cdx2* mRNAs in murine P19 and embryonic body cells.

**Supplementary Fig. S2: KANSL2 down regulation inhibits GBM derived tumor growth.** A, RT-qPCR analysis of KD-K2-1 and KD-K2-2 LN299 cells showing significantly suppressed *KANSL2* mRNA levels compared to NT. Results are expressed as mean ± SEM from three independent measurements. \*, P≤0.05; \*\*\*, P≤0.0005. B, Western blot analysis of 20 μg of total proteins from LN299 described in A) using a specific antibody against KANSL2 showing decreased KANSL2 protein level. The level of GAPDH expression was used as a loading control. Average fold decrease of KANSL2 protein accumulation is shown above. C-E, NOD*scid* mice were injected subcutaneously with 1x106 LN229 cells stably expressing control shRNA (NT) or two different KANSL2 shRNA (KD-K2-1 or KD-K2-2). C. Average tumor volume ± SEM is plotted against time (in days). \*P≤0.05, \*\*P≤0.005, \*\*\*P≤0.0005. D, Final tumor weight at 9 days after subcutaneous injection. \*\*\*P≤0.0005. E, Representative photographs of tumors excised from mice.

**Supplementary Fig. S3: Reduced acetylation on H4K16 in KD-KANSL2 cells.** Western blot of AcH4K16 levels in KD-K2-1 and KD-K2-2 U87MG and T98 cells. Histones were normalized using an antibody for non-modified histone 3 (H3). GBM, glioblastoma; NT, non-targeting; KD-K2-1, shRNA KANSL2-1 and KD-K2-2, shRNA KANSL2-2.

**Supplementary Fig. S4:** **Higher self-renewal capacity of sorted G03 patient-derived cell.** A, significant differences in stem cell frequencies was observed between the patient-derived G03 cell line CD133+/+ (1/27.3) and CD133-/- (1/110.1) cells calculated using online Extreme Limiting Dilutions Assay (ELDA) analysis program (p: 0.0007). C, cell proliferation was measured by MTT assay of dissociated cells. Patient-derived G03 CD133+/+ cells showed significantly higher relative cell number after 3 days. \*\*, P ≤ 0.005. Results are expressed as mean ± SEM of one representative experiment.