***Supplementary Figure legends***

**Supplementary Figure 1.** Immunohistochemical (IHC) analysis was performed on tissue sections from paraffin-embedded 85 GBM specimens with anti-FOXM1 antibody and anti-MTDH antibody. The representative pictures of FOXM1 and MTDH’s distribution and abundance were shown. 5 Normal Brain (NB) were used as negative control. Pictures were all taken by 200X magnification.

**Supplementary Figure 2**. The FOXM1 and MTDH protein expression in the same normal brain and four glioblastoma frozen tissues as Supplementary Figure 1 were detected by Western blotting.

**Supplementary Figure 3.** The FOXM1 and MTDH protein expression in several gliomas frozen samples were detected by immuno-florescence double staining. Scale bars, 20μm. The co-localized cells in every 100 cells were calculated.

**Supplementary Figure 4.** Mascot analysis showed that MTDH peptides were identified in the FOXM1 IP complex.

**Supplementary Figure 5.** **a.** 293T cells were transfected with Flag-tagged FOXM1 or HA-tagged MTDH. Cell extracts were subjected to IP using an anti-Flag antibody, followed by IB with an anti-HA or anti-Flag antibody. **b.** Left panel, total cell extracts of T98G, U87 and MD11 were subjected to IP by using an anti-FOXM1 antibody followed by IB with an anti-MTDH or anti-FOXM1antibody. Right panel, total cell extracts of T98G, U87 and MD11 were subjected to IP by using an anti-MTDH antibody followed by IB with an anti-FOXM1 or anti-MTDH antibody.

**Supplementary Figure 6.** Protein level of Cdh1 and APC were detected by Western blotting in T98G and U87 cells that stably expressing 2 independent MTDH shRNA or control shRNA.

**Supplementary Figure 7.** Immunofluorescence staining for MTDH (Alexa 596), FOXM1 (Alexa 488) and nuclei (DAPI, blue) was performed in NHA cells that were transfected with HA-tagged-ubiquitin together with the indicating plasmids. Scale bar represents 20μM.

**Supplementary Figure 8.** The nucleus extracts of T98G and U87 cells were subjected to IP by using an anti-FOXM1 antibody(left) or anti-MTDH antibody(right), followed by IB with an anti-MTDH antibody or anti-FOXM1 antibody. IP with IgG was used as negative control.

**Supplementary Figure 9. a**. Protein level of VEGF, MMP-2, skp2 and cdc25B were compared in T98G, U87 and MD11 cells stably knocking down MTDH or FOXM1 and their control cells by Western blotting. **b**. Cell cycle changes were determined by Flow cytometry analysis in T98G, U87 and MD11 cells that stably knocking down MTDH or FOXM1 and the control cells. **c**. Left panel, the angiogenesis and invasive ability of T98G, U87 and MD11 cells that stably knocking down MTDH or FOXM1 and the control cells were compared by HUVEC tube formation assay and Transwell invasion assay. Scale bar represents 20μM. Right panel, quantification data of HUVEC tube formation assay and Transwell invasion assay shown in the left, Error bars±s.d.

**Supplementary Figure 10**. MTDH inhibition abolished tumorigenesis in vivo by destabilizing FOXM1.

**a.** the angiogenesis and invasive ability of T98G, U87 and MD11 cells that stably expressed the indicated plasmids and the control cells were compared by HUVEC tube formation assay and Transwell invasion assay. Scale bar represents 20μM.

 **b.** Module of MTDH stabilizes FOXM1 and enhances FOXM1 transcriptional activity. Left, in normal cells which has little or none MTDH expression, most of cytoplasmic FOXM1 were recognized by cdh1 and quickly subjected to the APC/C induced proteasome degradation. Limited amount of nuclear FOXM1 were required for driving G2/M transition, indicating that directly targeting FOXM1 in cancer therapy may lead to the cytotoxic effect of normal cells. Right, in cancer cells, excessive MTDH interacts with FOXM1 by competing cdh1 away, leading FOXM1 aberrantly accumulated in the cells. Also, MTDH enhances the transcriptional activity of FOXM1 in the nucleus. Both events boosted the amount and activity of FOXM1, which promotes the downstream oncogenic events.

**Supplementary Figure 11.** MTDH inhibition induced increased sensitivity of glioma cells to TMZ.

1. MTDH stably knocked down U87 and MD11 cells and their parental cells were

treated with 20μM TMZ or DMSO for 5 days. Cell viability were tested as each indicated time point. Error bars±s.d.

1. MTDH stably knocked down U87 and MD11 cells and their parental cells were

treated with indicated concentrations of TMZ for 24 hours and survival fraction were tested. Error bars±s.d.

1. Indicated MD 11 cells were treated with different concentrations of TMZ for 8 hours. Rad51 and Chk2 level was determined by western blot.

**Supplementary Figure 12.** Immunohistochemical (IHC) analysis was performed on tissue sections from paraffin-embedded mouse in vivo tumor specimens with anti-MMP-2 antibody and anti-CD31 antibody. The representative pictures of MMP-2 and CD31’s distribution and abundance were shown. Pictures were all taken by 200X or 400X magnification.

**Supplementary Figure 13.** a. 293T cells were transfected with indicated plasmids and promoters for 24 hours and the luciferase activity were tested. Scale bar represents 20μM. b. U87 and MD11 cells were transfected with indicated plasmids and after 24 hours the expression of VEGF, MMP-2, Skp-2, cdc25B were tested. c. Cell cycle of U87 and MD11 transfected with indicated plasmids and their parental cells were tested. d. The *in vitro* tube formation capacity of U87 and MD11 transfected with indicated plasmids and their parental cells were calculated. Error bars±s.d.

**Supplementary Figure 14.** a. The VEGF, MMP-2, Skp2 and Cdc25B protein levels were compared among the indicated plasmid-transfected and control cells. b. The VEGF, MMP-2, Skp2 and Cdc25B mRNA levels were compared among the indicated plasmid-transfected and control cells. c. Cell cycle of MD11 cells transfected with indicated plasmids and their parental cells were tested d. Changes in tube formation, and cell invasion among the cells indicated above were compared. Values are presented as means±s.d for triplicate samples.

**Supplementary Figure 15.** The FOXM1 and MTDH co-localization in MD11 cells induced xenograft was detected by immuno-florescence double staining. Scale bars, 200μm.