**SUPPLEMENTARY FIGURE LEGENDS**

**Supplementary Figure S1.** **SET is deregulated in CRC patients and induces proliferation and colonosphere formation in DLD-1, SW620 and HCT-116 cells.** (**A**) Western blot analysis of SET expression in CRC patients with paired normal colonic mucosa and tumor samples; \* SET overexpression; N: normal mucosa; T: tumor sample. (**B**) MTS assays showing proliferation in CRC cells after SET silencing. (**C**) Colonosphere formation and (**D**) evaluation of the number of cells per colonosphere after SET silencing. (**E**) Validation of the SET silencing by real-time PCR and western blot; \* *P* < 0.05; \*\* *P* < 0.01.

**Supplementary Figure S2.** **SET modulation in CRC cells ectopically expressing PP2A.** (**A**)PP2A and (**B**) MTS assays after SET silencing. (**C**) Caspase 3/7 assays in SW480, HT-29 and LS513 cells after transfection with SET, PP2A or with both SET and PP2A. (**D**) Validation of SET overexpression by real time PCR (2-ΔΔCt) and western blot; \* *P* < 0.05; \*\* *P* < 0.01.

**Supplementary Figure S3. Effect of SET silencing in the sensitivity of CRC cells to 5-FU alone or combined with oxaliplatin.** (**A**)MTS, (**B**) caspase 3/7 assays and (**C**) drug concentration curves to evaluate the effect of SET silencing in the sensitivity to oxaliplatin and 5-FU in SW480, HT-29 and LS513 cells; \* *P* < 0.05; \*\* *P* < 0.01.

**Supplementary Figure S4. Effects of FTY720 in SW480, HT-29 and LS513 cells ectopically expressing SET and treated with 5-FU alone or combined with oxaliplatin.** (**A**)MTS, (**B**) caspase 3/7 assays, (**C**) cell cycle analysis and (**D**) drug concentration curves to evaluate the effect of SET overexpression in the sensitivity to oxaliplatin and 5-FU in SW480, HT-29 and LS513 cells;\* *P* < 0.05; \*\* *P* < 0.01.

**Supplementary Figure S5.** Immunohistochemical detection of SET expression in patients with metastatic colorectal cancer showingSET negative (**A**) and positive (**B**) stainings. The line in A and B shows 25 µm. Magnification x400.(**C**) Kaplan-Meier analyses of overall and progression-free survival and in the subgroups of patients younger (*N* = 113) and older than 70 years (*N* = 117).

**Supplementary Figure S6.** (**A**) Kaplan-Meier analyses of overall and progression-free survival and in the subgroups of patients with KRAS wild type (*N* = 136) and KRAS mutated (*N* = 102).(**B**) Predictive value of response to treatment by SET deregulation in those patients who received oxaliplatin-based chemotherapy (*N*= 101).