GGAAACGGGCCACAGTTCTA
TCAGCTTTAGCCTTGGCCTT
TCTCGACCACGTAATGTGCC
TCTCAGTTGTGATGGACGGC
ACAACTTTGGTATCGTGGAAGG
GCCATCACGCCACAGTTTC
GAGAGGGTGTGAAGGGGGA
AAGGAGAAAAACCAGGCCCC
CTACCAGAGAGGCAACAGGC
CTTTACCCACCAACCCCTCC
TCAGCCGTAGAAGCTGAACTC
TGGTAGTCAAGAGACCTCCGT
CGTTCGACCAAGTAACGCTGA
CTCCCAGAAGCCTACCCGAG
GAGCAGTTCCCGTCAATCC
GCATTTCGCAGTTCCTGTCT
CTGAGGACCCATGACTCCTCTTTC
GGAAGTCTGGATCCTCCTGGTACT

Supplementary table 1, primers for RT-Q-PCR and ChIP to detect indicated genes



**Supplementary Figure 1. A**, biological progression was compared in SLP2 high-expressed tissues and lower ones by gene set enrichment analysis. **B**, immunoblot analysis of baseline expression of SLP2 in normal gastric cells and GC cells. **C** and **D**, immunoblot and RT-Q-PCR analysis of efficiencies of 3 small interference RNA targeting SLP2 in MGC803 cell. Data presented as means  $\pm$  SEM from three independent experiments. **E**, indicated cells were stained with propidium iodide followed by DNA content analysis. **F**, proliferation rates of Scr or siRNAs targeting SLP2 transfected MGC803 cells measured by CCK8. 5000 indicated cells

were plated in 96 well culture-plates. Data presented as means  $\pm$  SEM from five independent experiments. \*\*\**p*<0.001, two-way ANOVA test. **G**, colony formation of Scr or siRNAs targeting SLP2 transfected MGC803 cells. 200 indicated cells were plated in 6 well culture-plates. Data presented as means  $\pm$  SEM from three independent experiments. \*\**p*<0.01, \*\*\**p*<0.001, one-way ANOVA test. **H**, sgRNA targeting SLP2 or control sgRNA without target was transfected and DNA was extracted. PCR products were incubated with Cruiser<sup>TM</sup> Detecase and then subjected to southern blot. **I**, sgRNA transfected cell was cloned by limiting dilutions and clones were randomly picked. By PCR and DNA sequencing, 3 clones with frame shift mutation were selected for further studies. **J** and **K**, immunoblot and RT-Q-PCR analysis of efficiencies of SLP2 overexpression in AGS cells. Data presented as means  $\pm$  SEM from three independent experiments.



**Supplementary Figure 2. A**, analysis of potential proteins interacted with SLP2 based on String database. **B** and **C**, analysis of correlation between SLP2 and PHB mRNA levels in GEO and TCGA database.



**Supplementary Figure 3. A**, immunoblot ananlysis of indicated protein in SLP2 knocked-down cells. **B**, analysis of potential posttranscriptional modification sites of PHB in PTMfunc database. **C**, analysis of potential E3 ubiquitin ligases binding to PHB. **D**, total cell lysates from MGC803 cell were precipitated with anti-SLP2 and subjected to immunoblot with anti-SLP2 and anti-SKP2 antibody.



**Supplementary Figure 4. A**, representative images of PHB staining in GC and paired normal tissues. **B**, Kaplan-Meier tumor-free survival curves for GC patients with different PHB expression. **C**, immunoblot analysis of baseline expression of SLP2 in normal gastric cells and GC cells. and **D**, RT-Q-PCR analysis of efficiencies of 3 small interference RNA targeting PHB in MGC803 cells. Data presented as means  $\pm$  SEM from three independent experiments. **E**, immunonlot analysis of efficiencies of 3 siRNAs targeting PHB in MGC803 cells. **F**, proliferation rates of Scr or siRNAs targeting PHB transfected MGC803 cells measured by CCK8. 5000 indicated cells were plated in 96 well culture-plates. Data presented as means  $\pm$  SEM from five independent experiments. **\*\***p<0.001, two-way ANOVA test. **G**, colony formation of

Scr or siRNAs targeting PHB transfected MGC803 cells. 500 indicated cells were plated in 6 well culture-plates. Data presented as means  $\pm$  SEM from three independent experiments. \*\*p<0.01, one-way ANOVA test. **H**, tumors derived from hind limbs of NCG mice 50 days after subcutaneous injection of indicated cells. **I**, tumor weight was determined 50 days after transplantation. Data are presented as means  $\pm$  SEM; n = 10 for each group. \*p<0.001, Mann-Whitney test. **J**, immunoblot analysis of indicated proteins in Scr or siRNAs targeting PHB transfected MGC803 cells.



**Supplementary Figure 5. A** and **B**, position frequency matrix (PFM) analysis of ELK1 binding sites. **C**, sequence logo for ELK1 binding sites in plus strand derived from Jaspar database. **D**, potential binding site of ELK1 in plus strand of SLP2 promoter predicted in Jaspar database. **E**, sequence logo for ELK1 binding sites in reverse complementary strand derived from Jaspar database. **F**, potential binding site of ELK1 in reverse complementary strand of SLP2 promoter predicted in Jaspar database. **G**, diagrammatic sketch of sites for SLP2 promoter amplification primers. **H**, an expression vector for triple flag-tagged SLP2 were transfected into AGS cells and total cell lysates were subjected to immunoblot to detect exogenous and endogenous SLP2 levels. **I** and **J**, enrichment of potential genes regulated by ELK1 in PHB highly

expressed tissues. **K**, mRNA levels of SLP2 and PHB measured by RT-Q-PCR in indicated cells. Data presented as means  $\pm$  SEM from three independent experiments. \*\*p<0.01, \*\*\*p<0.001, one-way ANOVA test. **L**, protein expression levels of SLP2 and PHB measured by immunoblot in indicated cells.



**Supplementary Figure 6. A**, proliferation rates of DMSO and Sorafenib (10µM) treated MGC803 cells measured by CCK8 assay, 5000 indicated cells were plated in 96 culture-plates. Data are presented as means  $\pm$  SEM from five independent experiments. The *p* values were determined using a two-way ANOVA test. \*\*\**p*<0.001, **B**, 500 indicated cells were plated in 6 well culture-plates and the colonies were stained with giemsa for quantification. Data presented as means  $\pm$  SEM from three independent experiments. \*\*\**p*<0.001, one-way ANOVA test. **C**, tumors derived from hind limbs of NCG mice 50 days after subcutaneous injection of MGC803 cells treated with or without Sorafenib. **D**, MGC803 cells (1×10<sup>6</sup>) were transplanted into NCG mice, and tumor growth was monitored after the indicated times. Data are presented as means  $\pm$  SEM; n = 10 tumors for each group. \*\**p*<0.001, Mann-Whitney test.