**Figure S1.** The transfection efficiencies of shZNF280A and shCtrl in HCT116 and RKO cells were evaluated through observing the fluorescence of GFP on lentivirus vector.

**Figure S2.** (A) The volcano plot of gene expression profiling in RKO cells with or without ZNF280A knockdown. Green dots represented the downregulated DEGs, red dots represented the upregulated DEGs. (B-E) The quality of all the microarray data was assessed in several ways. (F, G) Results showed cell cycle control of chromosomal replication as one of the most enriched pathways and cancer as one of the most enriched diseases.

**Figure S3.** (A) The expression of RPS14 in CRC cells was analyzed by qPCR. (B) The transfection efficiencies in RKO cells were evaluated through observing the fluorescence of GFP on lentivirus vector. (C, D) The expression of ZNF280A and RPS14 of the indicated cells were e analyzed by qPCR and WB. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

**Figure S4.** Subcellular localization analysis indicated that there was a great possibility of interaction between ZNF280A and SYVN1.

**Table S1.** All the antibodies used in WB and IHC.

**Table S2.** Primers used in qPCR.

**Table S3.** The target sequences and shRNA sequences.

**Table S4.** Relationship between ZNF280A expression and tumor characteristics in patients with colorectal cancer analyzed by Spearman rank correlation analysis.

**Table S5.** The ligases were predicted by using UbiBrowser.