Supplementary Table S1. Primers used in this study

Gene (homo sapiens)	Forward (5'-3')	Reverse (5'-3')	Application
HCP5	TCTCCTTCTGCCCATCACTTG	AACCCTCCTCCTGCTGTTCTC	qRT-PCR
GAPDH	GGGAAACTGTGGCGTGAT	GAGTGGGTGTCGCTGTTGA	qRT-PCR
LMNB1(LaminB1)	GAAAAAGACAACTCTCGTCGCA	GTAAGCACTGATTTCCATGTCCA	qRT-PCR
MSH5	TCCAGCTCTTTCGGGACATT	AGGACTTGTGGGGAGTAACG	qRT-PCR
YBX1(YB1)	GGACAAGAAGGTCATCGCAAC	TCTCCATCTCCTACACTGCGA	qRT-PCR
ILF2	GGGGAACAAAGTCGTGGAAAG	CCAGTTTCGTTGGTCAGCA	qRT-PCR
MSH5 promoter	TTTCTTTCTCCCTCATAACCCCAC	AAGTAAGACCTAAATGAGCGGTGT	ChIP-qPCR
HCP5 Sense	GGGAAGCTTACTATAGAATATTAAATTCC (XhoI)	GGCCTCGAGCTCAGATTCTCCCCAGACGC (HindIII)	*in vitro* transcription
HCP5 Antisense	GGGAAGCTTCTCAGATTCTCCCCAGACGC (XhoI)	GGCCTCGAGACTATAGAATATTAAATTCC (HindIII)	*in vitro* transcription

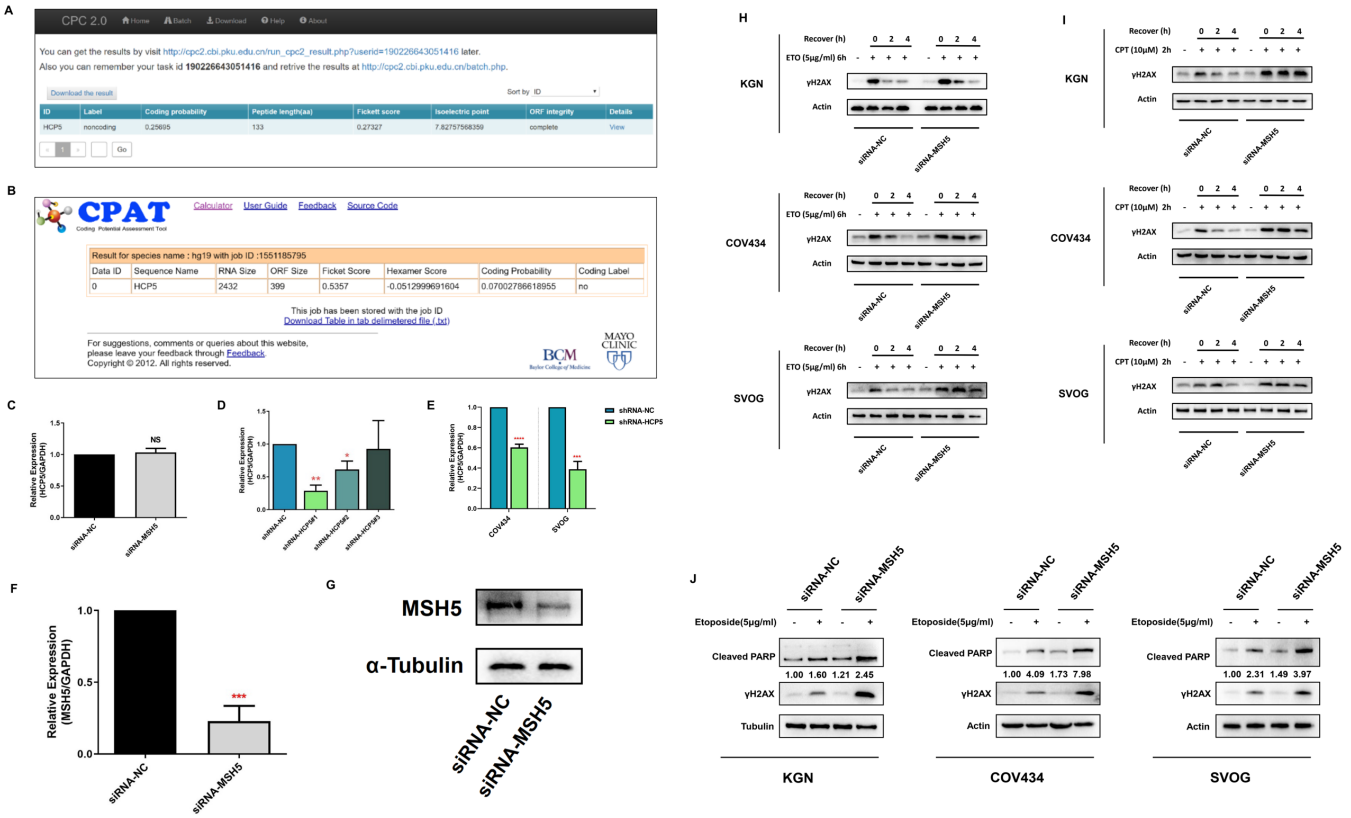
Supplementary Table S2. SiRNA used in this study

siRNAs	Sense (5'-3')
siRNA-MSH5 Mix	CCUCUUCCUCUCUUCCAUUTT
	CCUCACAGUUCGAGCACUUTT
	CCUGGGCUUUAAGAAAUUUTT
siRNA-ILF2#1	CUUUGUACCACAUAUCCCATT
siRNA-ILF2#2	GAACUCCAUUUGGAUAUCATT

Supplementary Table S3. Antibodies used in this study

Antibody	Supplier	Catalog#	Application
MSH5	Abcam	ab130484	WB
Phospho-Histone H2A.X (Ser139)	Cell Signaling Technology	9718S	WB/IF
PARP (Cleaved Asp214, Asp215)	Invitrogen	44-698G	WB
YB1	Cell Signaling Technology	4202	WB/IF
Lamin B1	Abcam	ab133741	WB
ILF2/NF45	Santa Cruz	sc-365068	WB
Phospho-YB1 (Ser102)	Cell Signaling Technology	2900S	WB
GAPDH	Proteintech	60004-1-Ig	WB
α-Tubulin	Proteintech	66031-1-Ig	WB
β-Actin	Proteintech	66009-1-Ig	WB
YB1	Abcam	Ab76149	ChIP/RIP
RNA polymerase II	Sigma-Aldrich	05-623-25UG	ChIP
ILF2	Abcam	ab154791	RIP
YB1	Abcam	Ab12148	coIP
Fibrillarin (FBL)	Abcam	ab4566	IF

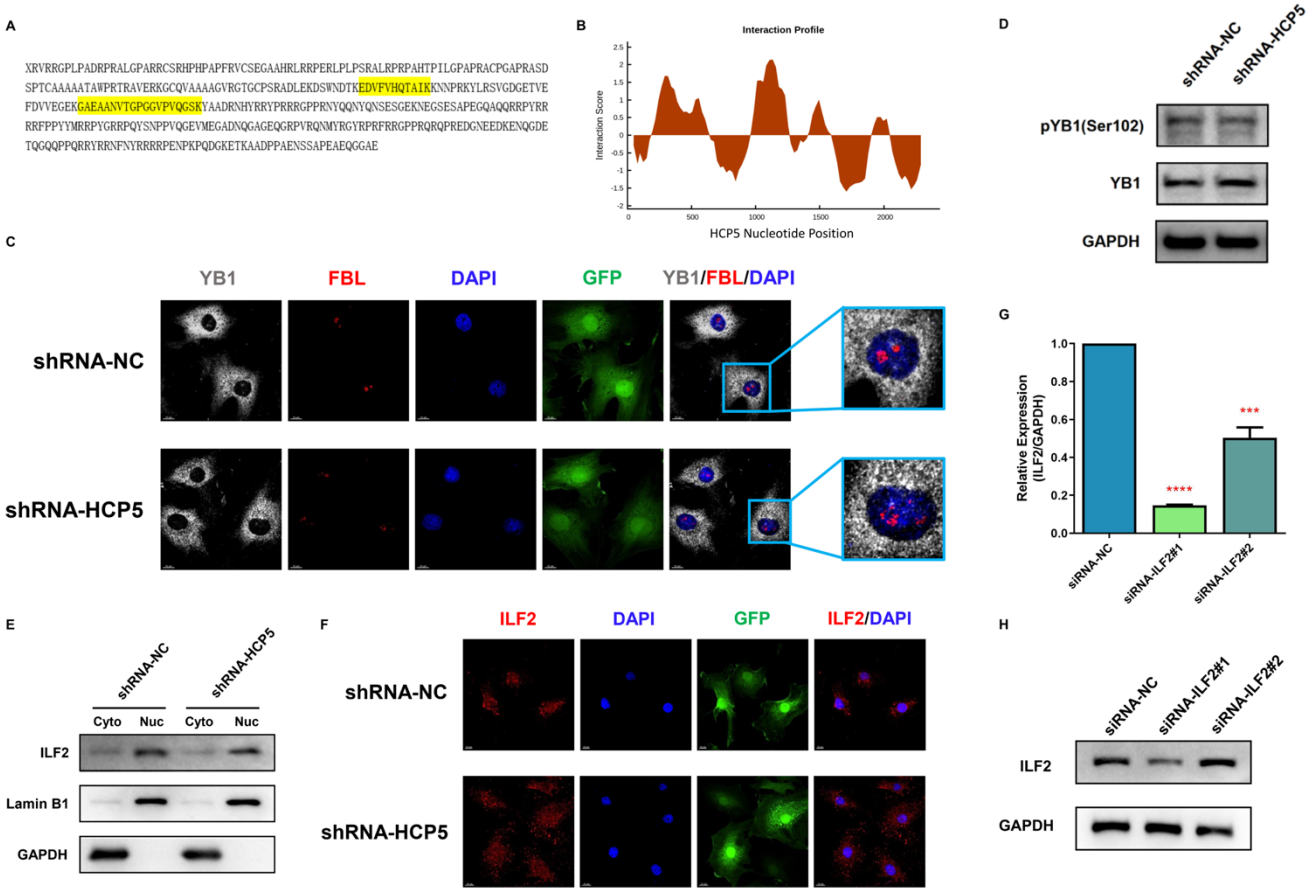
Supplementary Figure S1



Supplementary Figure S1.

(A) Coding probability of HCP5 was assessed by Coding Potential Calculator (CPC2). (B) Coding probability of HCP5 was assessed by Coding-Potential Assessment Tool (CPAT). (C) The qRT-PCR indicated that HCP5 levels were not affected by siRNA-mediated knockdown of MSH5 in KGN cells. Results are expressed as the mean ± SD (n=3). Two-tailed Student's t-test. (D, E) The qRT-PCR detected the expression of HCP5 after knockdown of HCP5 mediated by three specific shRNAs in KGN(D), COV434 and SVOG cells (E). Results are expressed as the mean ± SD (n=3). *P < 0.05, **P < 0.01 and ***P < 0.001. Two-tailed Student's t-test. (F) The qRT-PCR detected the levels of MSH5 mRNA after knockdown of MSH5 mediated by siRNA. Results are expressed as the mean ± SD (n=3). ***P < 0.001. Two-tailed Student's t-test. (G) Western blot detected the levels of MSH5 protein after knockdown of MSH5 mediated by siRNA. (H) After exposed to ETO for 6 h, the γH2AX levels were detected by western blot in MSH5-knockdown and negative control KGN, COV434 and SVOG cells. Data shown represent three independent experiments. (I) After exposed to CPT for 2 h, the γH2AX levels were detected by western blot in MSH5-knockdown and negative control KGN, COV434 and SVOG cells. Data shown represent three independent experiments. (J) Silencing of MSH5 enhanced the cleavage of PARP and formation of γH2AX caused by treatment with Etoposide in KGN, COV434 and SVOG cells. Data shown represent three independent experiments.

Supplementary Figure S2



Supplementary Figure S2.

(A) Two HCP5-binding peptides identified by MS were highlighted in the amino acid sequence of YB1 protein. (B) The *cat*RAPID fragments module prediction of the interaction profile between HCP5 and YB1 protein. (C) Co-localization of YB1 protein and the nucleolar marker Fibrillarin (FBL) was confirmed by immunofluorescence assay after HCP5 silencing. (D) Western blot detected the phosphorylation levels of YB1 protein at Ser102. (E) Subcellular localization of ILF2 protein was detected by western blot after HCP5 knockdown in KGN cells. Lamin B1 was used as nuclear control. GAPDH was used as cytoplasmic control. (F) Subcellular localization of ILF2 protein was confirmed by immunofluorescence assay after HCP5 silencing. (G) The qRT-PCR detected the expression of ILF2 mRNA after knockdown of ILF2 mediated by two specific siRNAs. Results are expressed as the mean ± SD (n=3). ***P < 0.001 and ****P < 0.0001. Two-tailed Student's t-test. (H) Western blot detected the levels of ILF2 protein after knockdown of ILF2 mediated by two specific siRNAs.