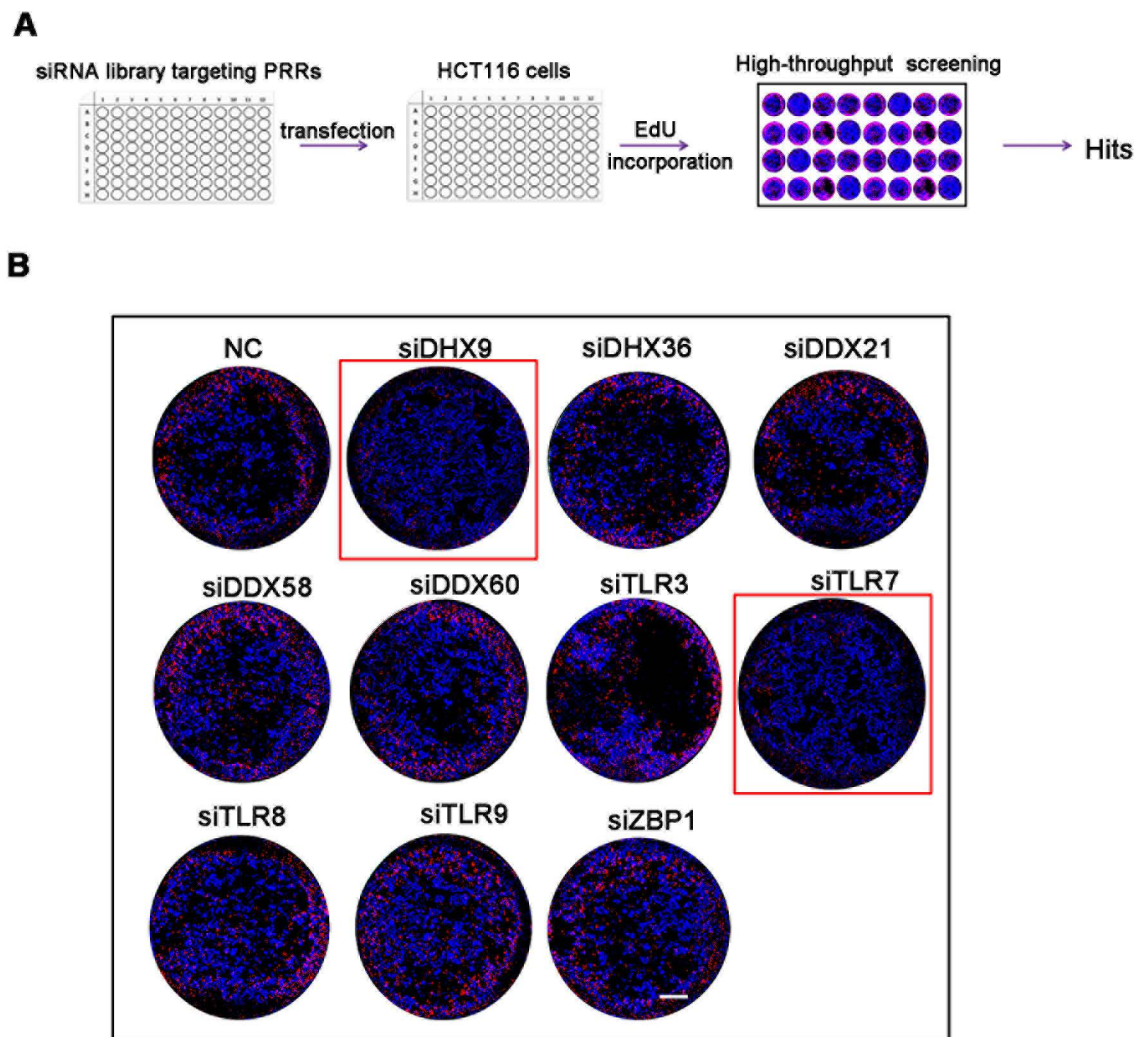


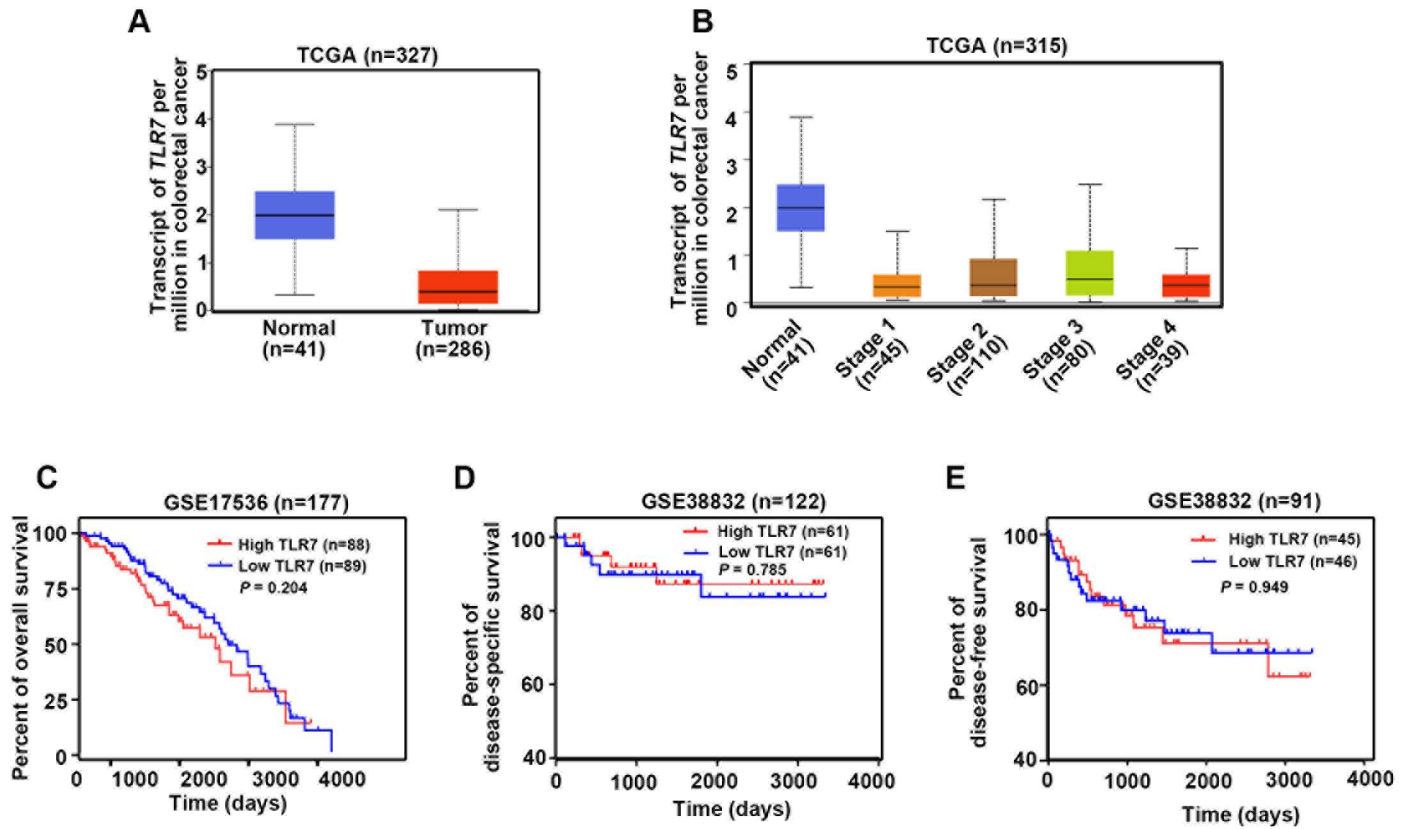
## Supplementary Figure. 1



### Supplementary Figure 1. Oncogenic nucleic acid sensing PRRs are screened with high-throughput system.

(A) Flowchart of high-throughput siRNA library screening via EdU incorporation assay. (B) Representative images of EdU proliferation assay in HCT116 cells transfected with NC siRNA or siRNA against nucleic acid sensing PRRs. EdU (red), DAPI (blue), scale bar: 500  $\mu\text{m}$  (40 $\times$ ).

## Supplementary Figure 2

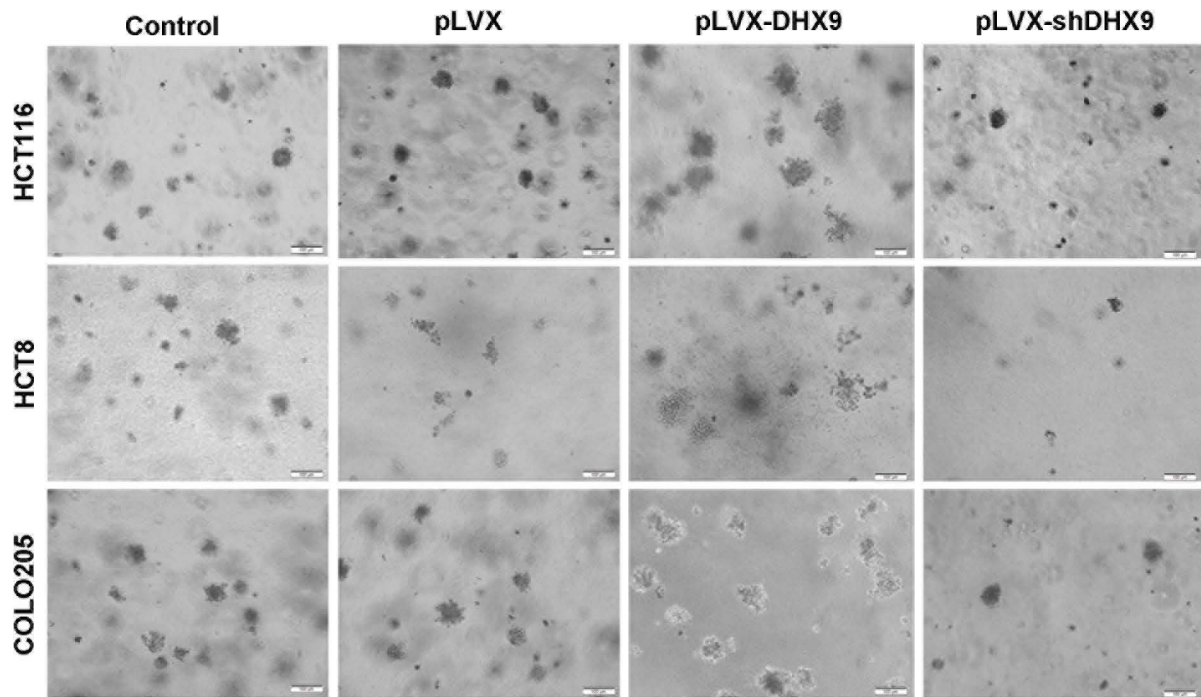


### Supplementary Figure 2. TLR7 expression and its correlation with prognosis in patients with colorectal cancer.

(A) The mRNA levels of TLR7 in CRC tissues and normal adjacent tissues in TCGA database obtained through UALCAN (<http://ualcan.path.uab.edu/index.html>). (B) TLR7 mRNA expression in different CRC stages and normal tissues from the TCGA Dataset via UALCAN. (C) Relationship of TLR7 expression with overall survival in patients with CRC in the cohort of GSE17536 database, log-rank test. (D) The disease-specific survival of patients with low or high TLR7 expression obtained from GSE38832 database, log-rank test. (E) Association of TLR7 expression with disease-free survival of CRC patients in GSE38832 dataset, log-rank test was used.

## Supplementary Figure. 3

A

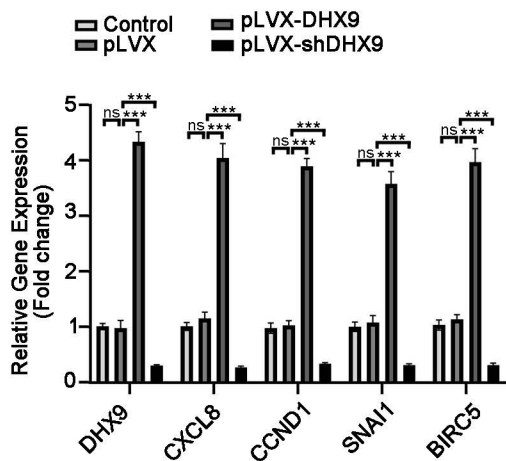


### Supplementary Figure 3. DHX9 enhances the colony-forming capacity in CRC cells.

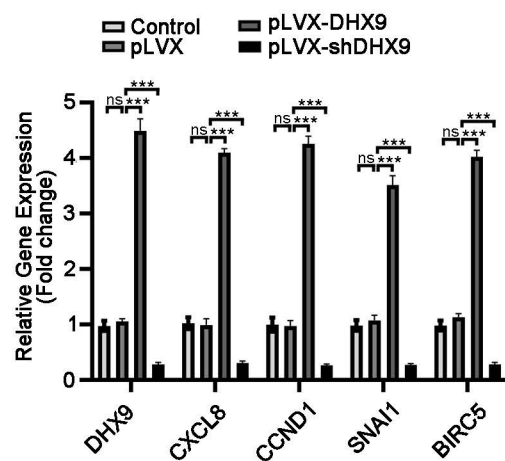
(A) CRC cells with untreated, vector-transfected, stably expressing DHX9-encoding constructs or shRNAs against DHX9 were subjected to soft agar assay. Representative images of colonies were shown. Scale bar: 100 µm.

## Supplementary Figure 4

**A**



**B**

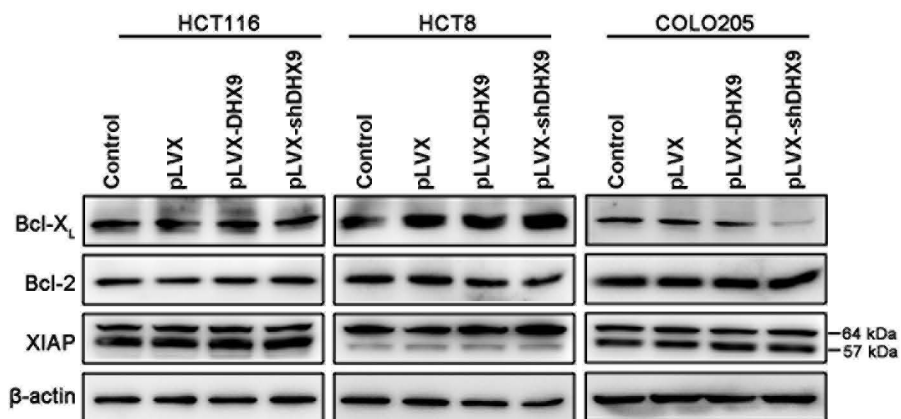


**Supplementary Figure 4. The expression profile of NF-κB-target genes in DHX9-overexpressed or -depleted colorectal cancer cells**

(A-B) NF-κB-target genes were validated in DHX9-overexpressed or -depleted HCT8 (A) and COLO205 (B) cells using RT-qPCR assay. Data were represented as mean  $\pm$  SEM. ns, not significant; \*\*\*,  $P < 0.001$ , one-way ANOVA with post hoc intergroup comparison by Tukey's test

## Supplementary Figure 5

A

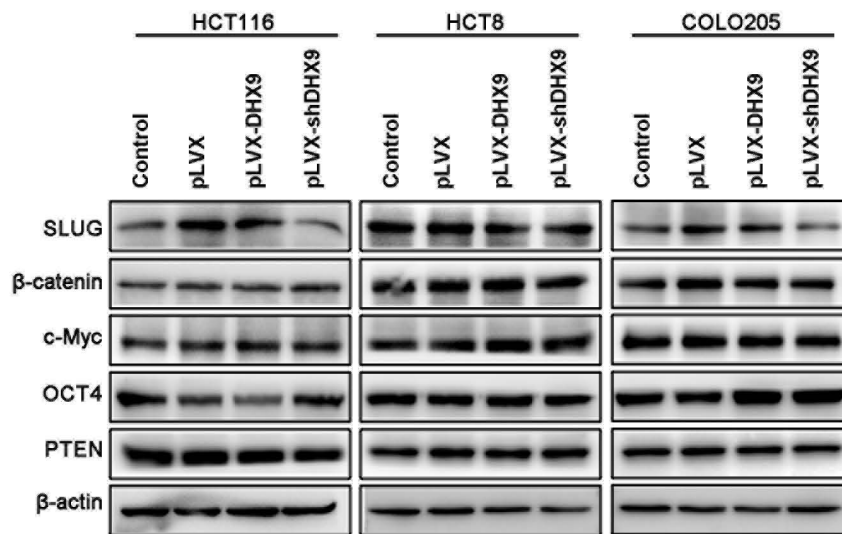


**Supplementary Figure 5. DHX9 effects on the expression levels of apoptosis-related proteins.**

**(A)** Western blotting assay was used to detect the expression levels of indicated apoptosis-related proteins.

## Supplementary Figure 6

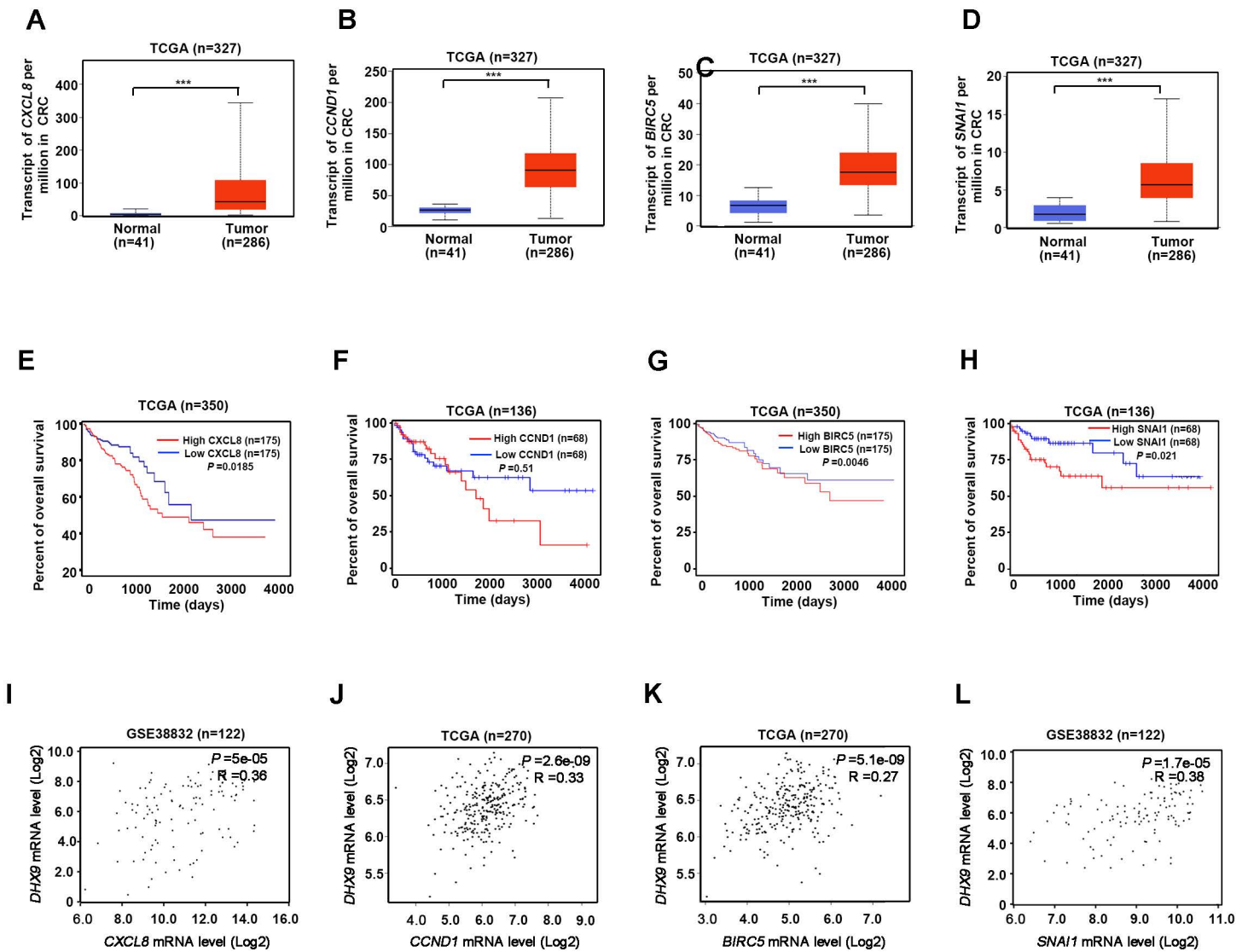
A



**Supplementary Figure 6. DHX9 effects on the expression levels of stemness-related proteins.**

(A) The expression levels of stemness-related proteins were examined with Western blotting assay.

## Supplementary Figure 7

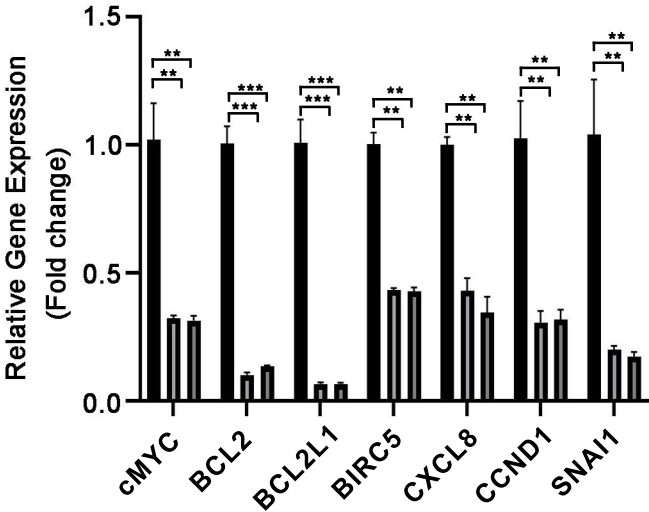


### Supplementary Figure 7. NF-κB-target genes predict poor prognosis of colorectal cancer.

(A-D) The mRNA levels of NF-κB-target genes including *CXCL8* (A), *CCND1* (B), *BIRC5* (C) and *SNAI1* (D) in CRC tissues and normal adjacent tissues in TCGA database obtained through UALCA. \*\*\*,  $P < 0.001$ ; Student's  $t$  test. (E-H) Overall survival of CRC patients based on the expression of *CXCL8* (E), *CCND1* (F), *BIRC5* (G) or *SNAI1* (H) in TCGA database using web tool SurvExpress (<http://bioinformatica.mty.itesm.mx:8080/Biomatec/SurvivaX.jsp>) or GEPIA (<http://gepia.cancer-pku.cn>), log-rank test. (I-J) Correlation of *DHX9* mRNA expression with the mRNA levels of *CXCL8* (I), *CCND1* (J), *BIRC5* (K) or *SNAI1* (L) in GSE38832 or TCGA dataset were shown.

# Supplementary Figure 8

**A**



**B**

