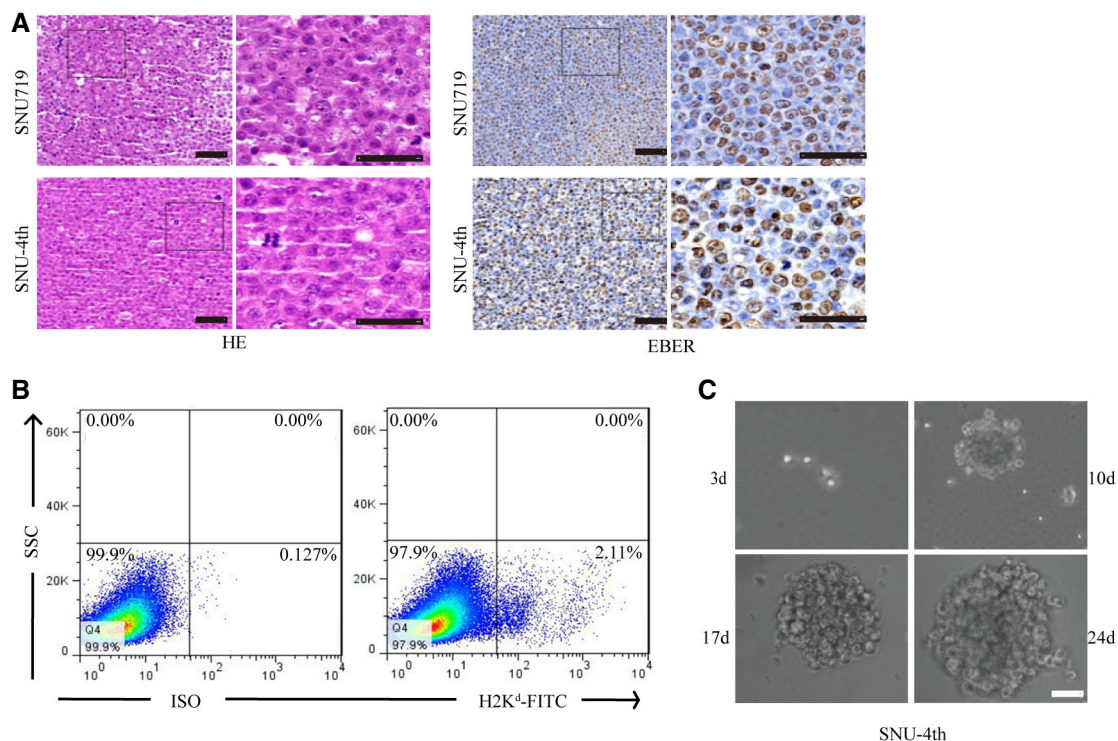


## Expanded View Figures



**Figure EV1. Isolation of SNU-4th cells from fourth passage xenograft treated with 5-Fu.**

- A Representative images showing H&E staining (left) and EBER-1 ISH staining (right) of the parental cell line SNU719 and SNU-4th cells.  
 B H2K<sup>d</sup>-positive mouse cells were removed from freshly isolated SNU-4th cells by flow cytometry.  
 C Compared with parental SNU719 cells, SNU-4th single cell could grow as a tumour sphere.

Data information: Scale bars = 100  $\mu$ m.

**Figure EV2. Stable transfection of circLMP2A in SNU-4th cells.**

- A ROC curves for the discrimination of patients with high or low expression of circLMP2A. The black arrow indicates the cut-off value (left).  
 B Fluorescence microscopy showing the expression of GFP-labelled plasmids in SNU-4th, SNU719 and YCCEL1 cells.  
 C The linear LMP2A mRNA levels were detected by real-time PCR.  
 D Northern blots for the detection of circLMP2A in SNU719 and YCCEL1 cells (circLMP2A over-expressing stable transfectants) treated with or without RNase R digestion. Please note that the image was assembled from different blots (indicated by the black lines). The red arrow indicates the size of circLMP2A (429 bp).  
 E The back-spliced sequence of circLMP2A from the over-expression system was validated by Sanger sequencing. The red arrow indicates the "head-to-tail" splicing sites of circLMP2A.  
 F The expression of circLMP2A was detected in xenograft tissues from *in vivo* tumorigenicity experiments using RT-qPCR.

Data information: Results are presented as the mean  $\pm$  SD,  $n = 3$  biological replicates, scale bar = 100  $\mu$ m, \* $P < 0.05$ , Student's t-test.

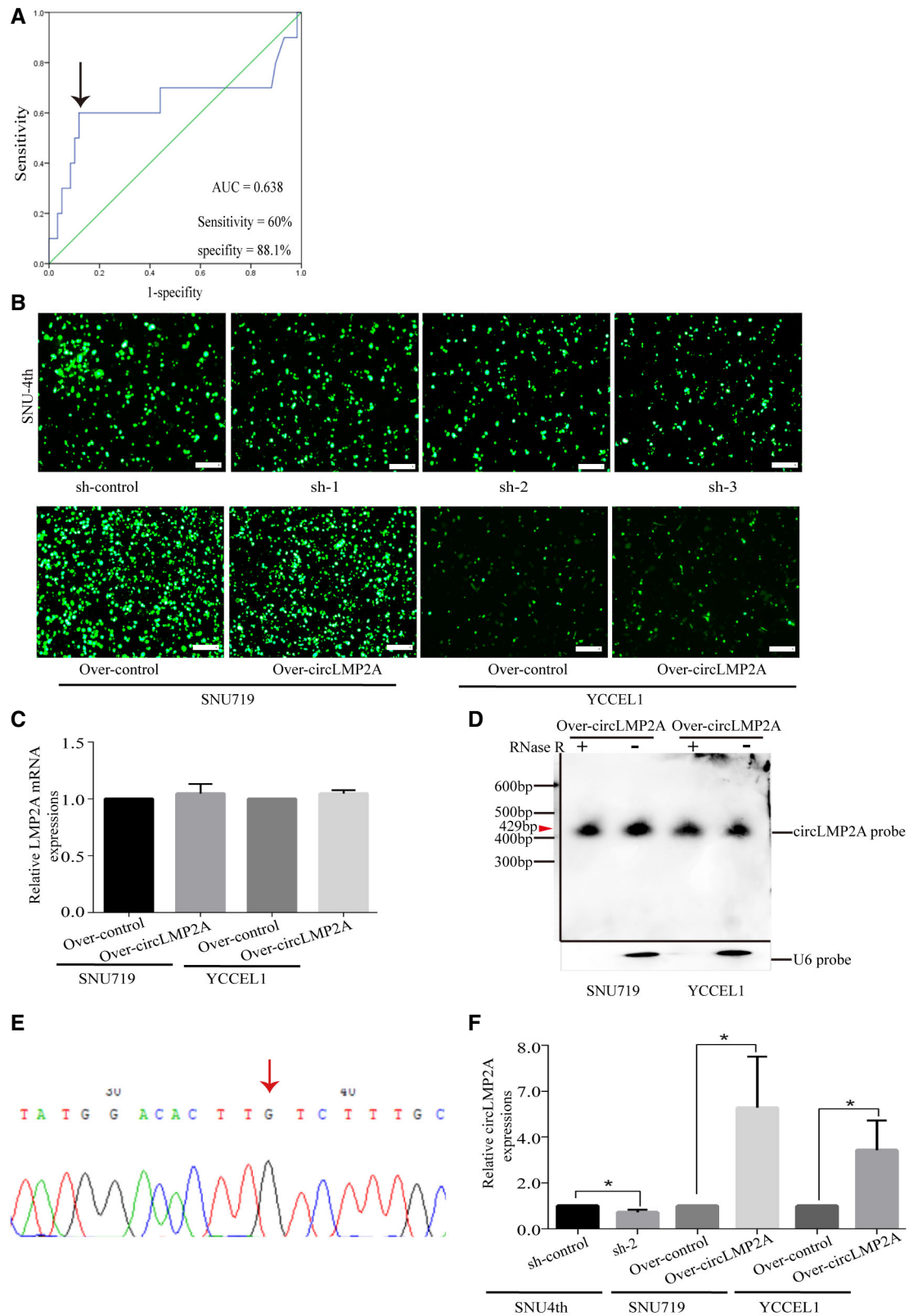
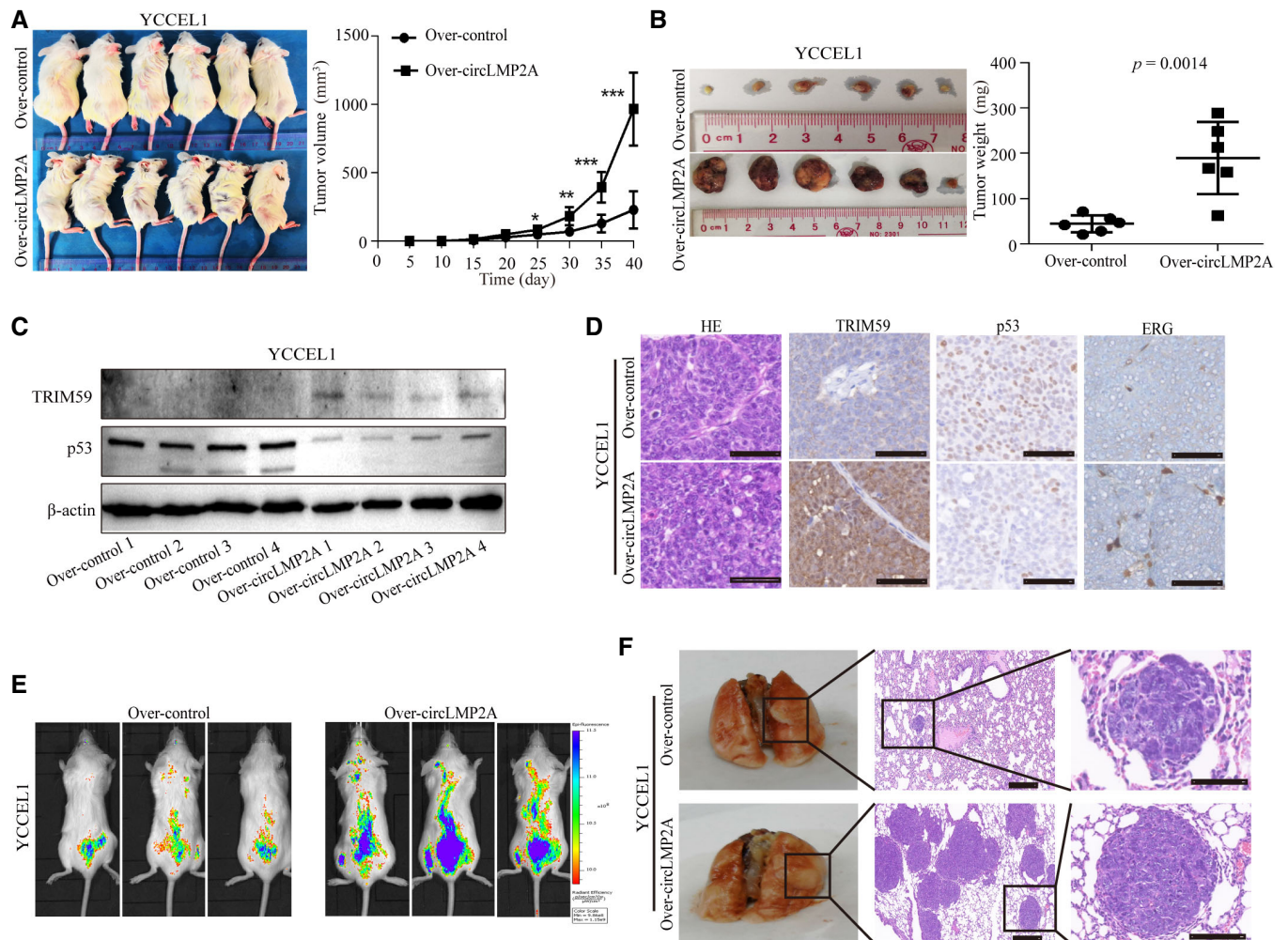


Figure EV2.



**Figure EV3. Forced expression of circLMP2A promoted tumour growth, angiogenesis and metastasis *in vivo*.**

A, B Subcutaneously established tumour xenografts in NOD/SCID mice. Tumour volume (A) and tumour weight (B) of the xenografts were significantly increased by over-expression of circLMP2A.

C WB analysis of the expression of TRIM59 and p53 in tumour xenografts.

D The expression of TRIM59, p53 and ERG was measured using IHC in tumour xenografts.

E, F Representative images of bioluminescence (E) and lung metastases (F) are presented to measure the metastatic colonies.

Data information: Results are presented as the mean  $\pm$  SD, six mice per group, biological replicates, scale bars = 50  $\mu$ m, \* $P$  < 0.05; \*\* $P$  < 0.01; \*\*\* $P$  < 0.001, Student's *t*-test. Source data are available online for this figure.

**Figure EV4. Inhibition of miR-3908 expression induces the stemness phenotype of SNU719 and YCCEL1 cells.**

A, B Suppression of miR-3908 expression promoted the formation of tumour spheres in SNU719 (A) and YCCEL1 (B) cells, and miR-3908 could impair the promoting function of circLMP2A on sphere formation.

C, D Real-time PCR showed that miR-3908 inhibitors elevated the expression levels of EMT-related markers, stemness markers and drug resistance genes in SNU719 (C) and YCCEL1 cells (D), and miR-3908 could weaken the upregulation effect of circLMP2A on EMT-related markers, stemness markers and drug resistance genes.

E WB revealed the upregulation effect of miR-3908 inhibitors on EMT-related markers, stemness markers and drug resistance genes in SNU719 and YCCEL1 cells, and miR-3908 could attenuate the upregulation effect of circLMP2A on EMT-related markers, stemness markers and drug resistance genes.

F, G The colony formation assay indicated that miR-3908 inhibitors enhanced colony formation of SNU719 (F) and YCCEL1 (G) cells, and miR-3908 could impair the promoting function of circLMP2A on colony formation.

H, I miR-3908 inhibitors promoted the migratory and invasive capabilities of SNU719 (H) and YCCEL1 (I) cells, and miR-3908 could attenuate the promoting function of circLMP2A on migration and invasion.

J Kaplan–Meier survival curve analysis showing the correlation between TRIM59 expression and overall survival.  $n = 69$ ,  $P = 0.391$ , log-rank test.

Data information: Results are presented as the mean  $\pm$  SD,  $n = 3$  biological replicates, scale bars = 100  $\mu$ m, \* $P$  < 0.05; \*\* $P$  < 0.01; \*\*\* $P$  < 0.001, Student's *t*-test. Source data are available online for this figure.



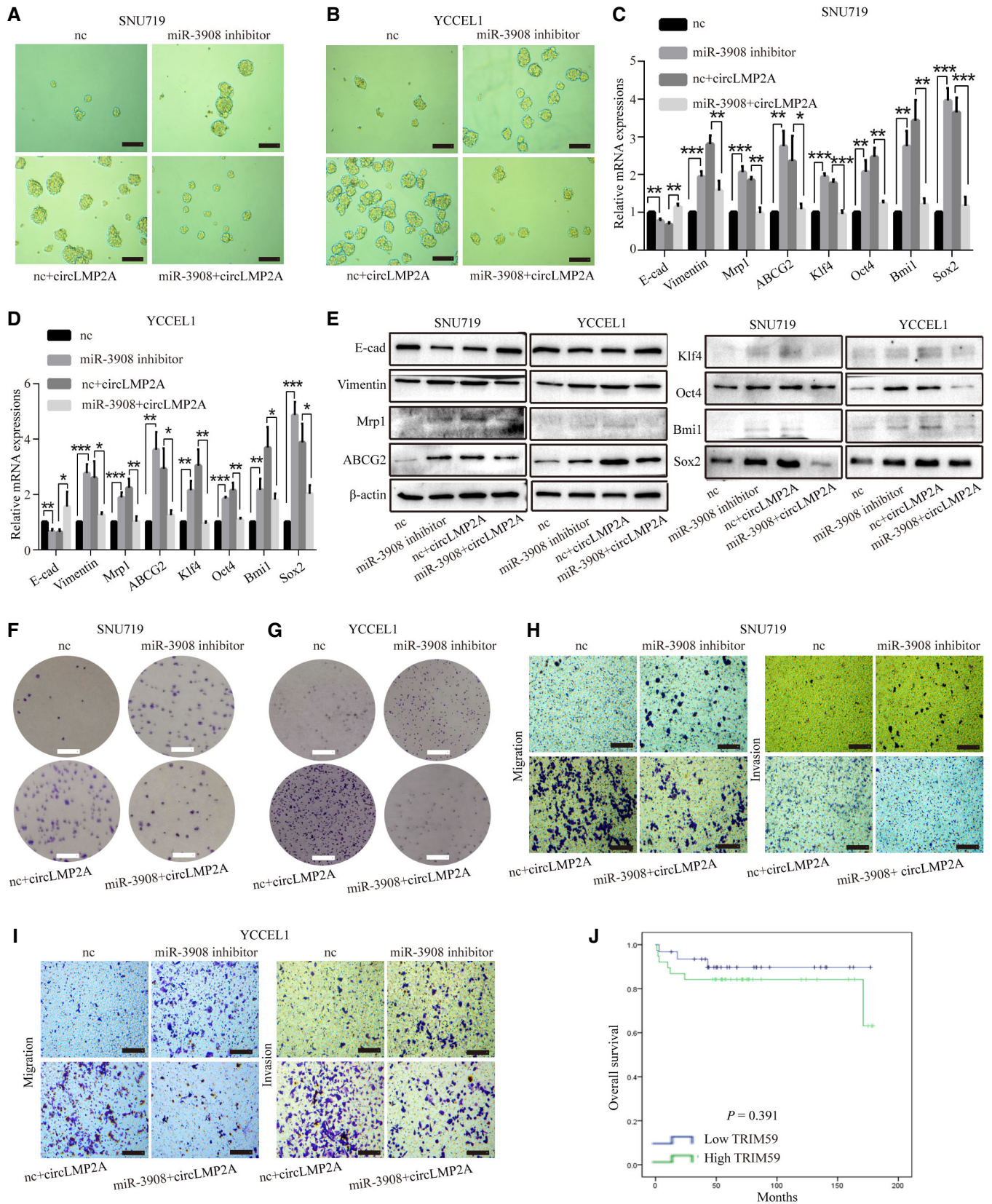
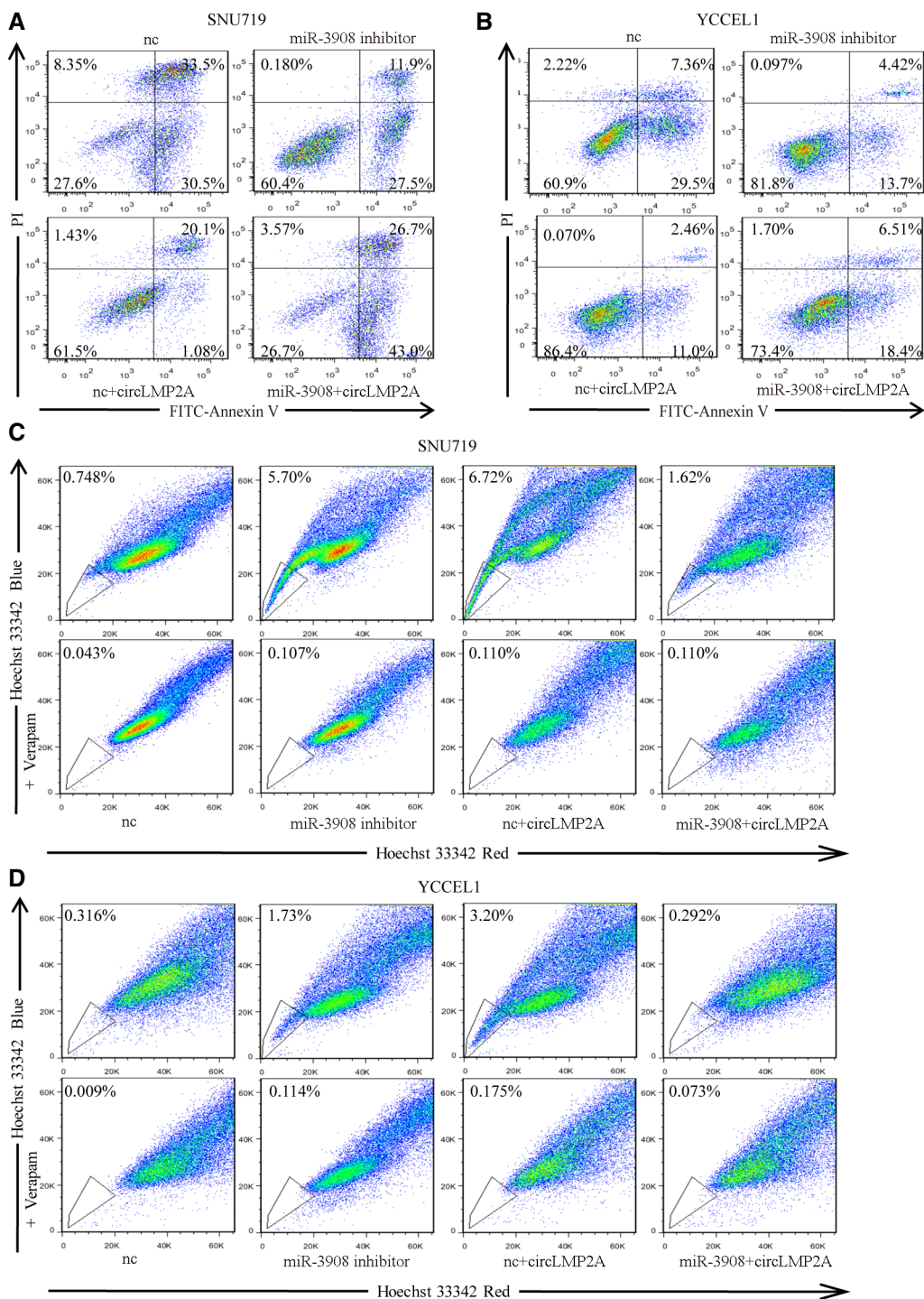


Figure EV4.



**Figure EV5. miR-3908 inhibitors decrease cell apoptosis and increase the ratio of SP cells in SNU719 and YCCEL1 cells.**

A, B miR-3908 inhibitors decreased the rate of apoptosis in SNU719 (A) and YCCEL1(B) cells, and miR-3908 could attenuate the inhibitory function of circLMP2A on cell apoptosis.

C, D miR-3908 inhibitors elevated the percentage of SP cells in SNU719 (C) and YCCEL1 (D) cells, and miR-3908 could reverse the upregulation effect of circLMP2A on SP cells.