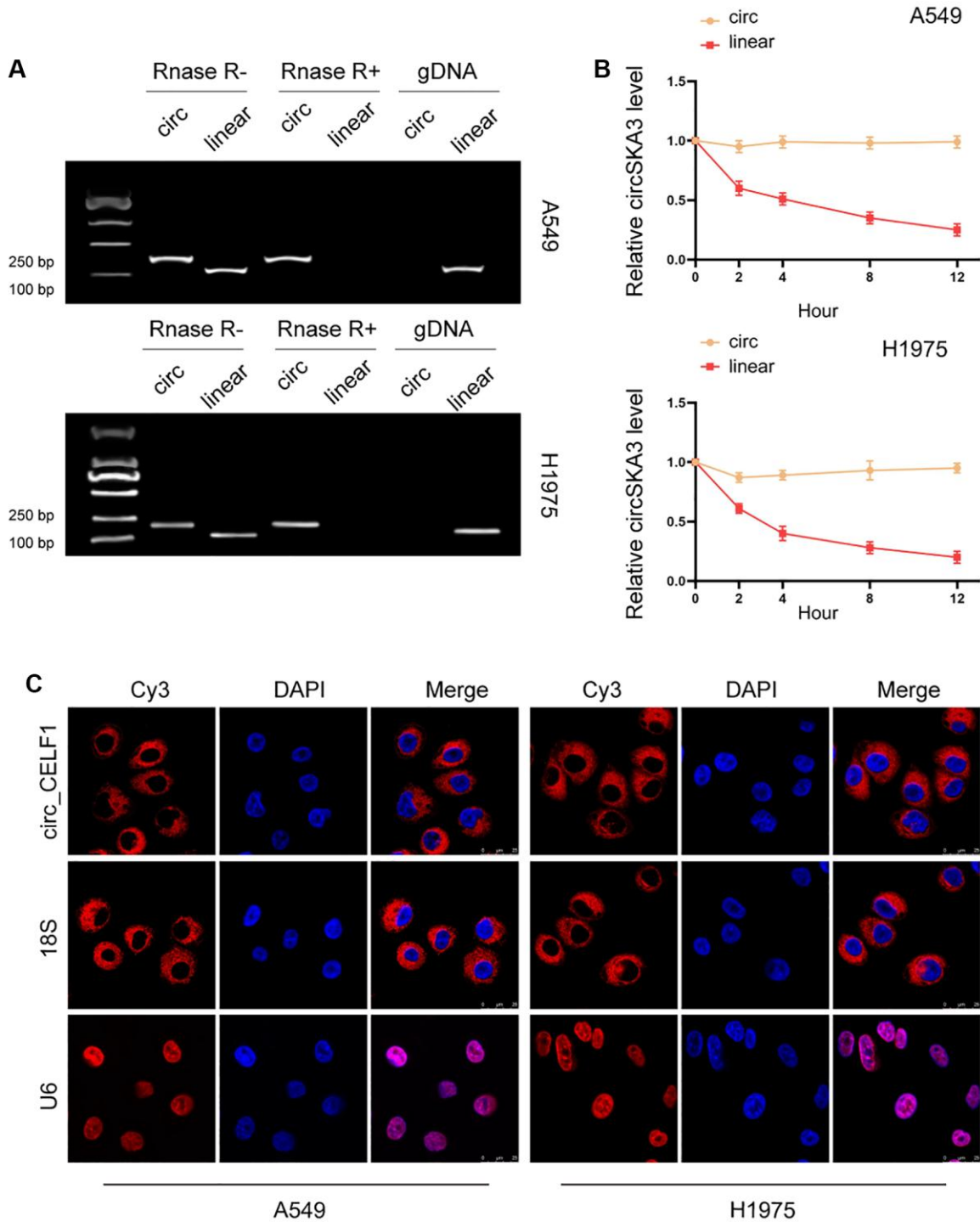
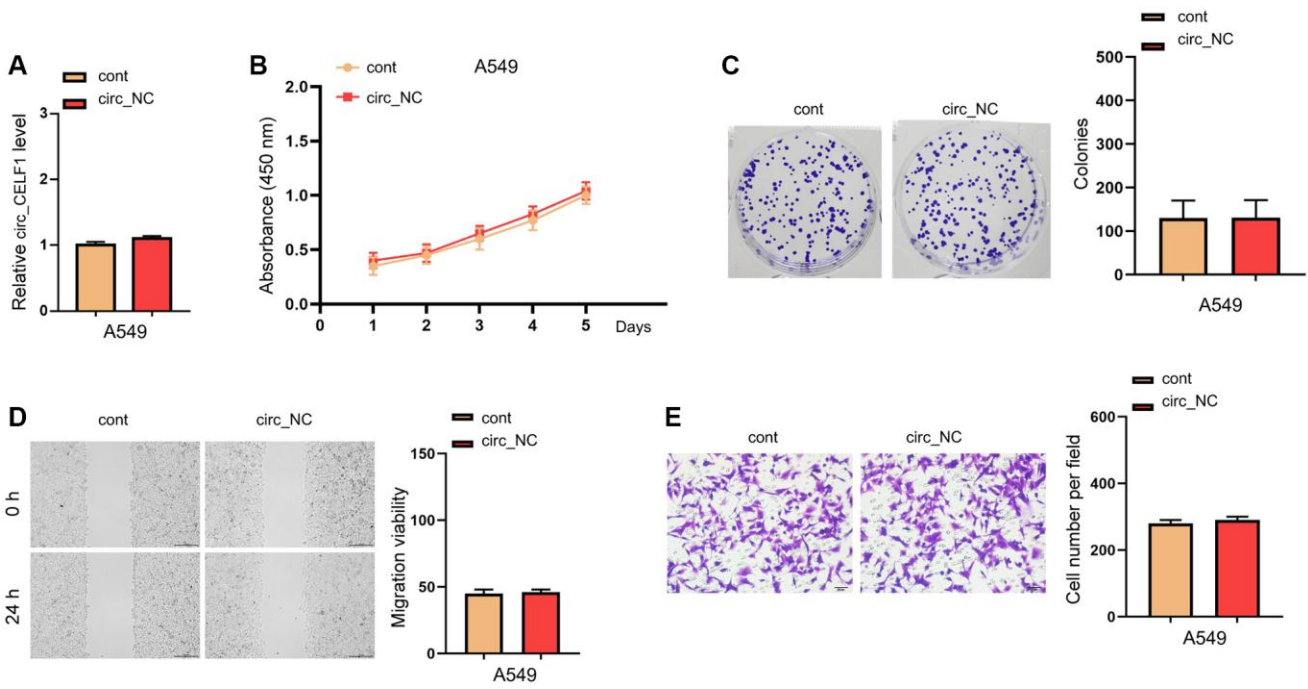


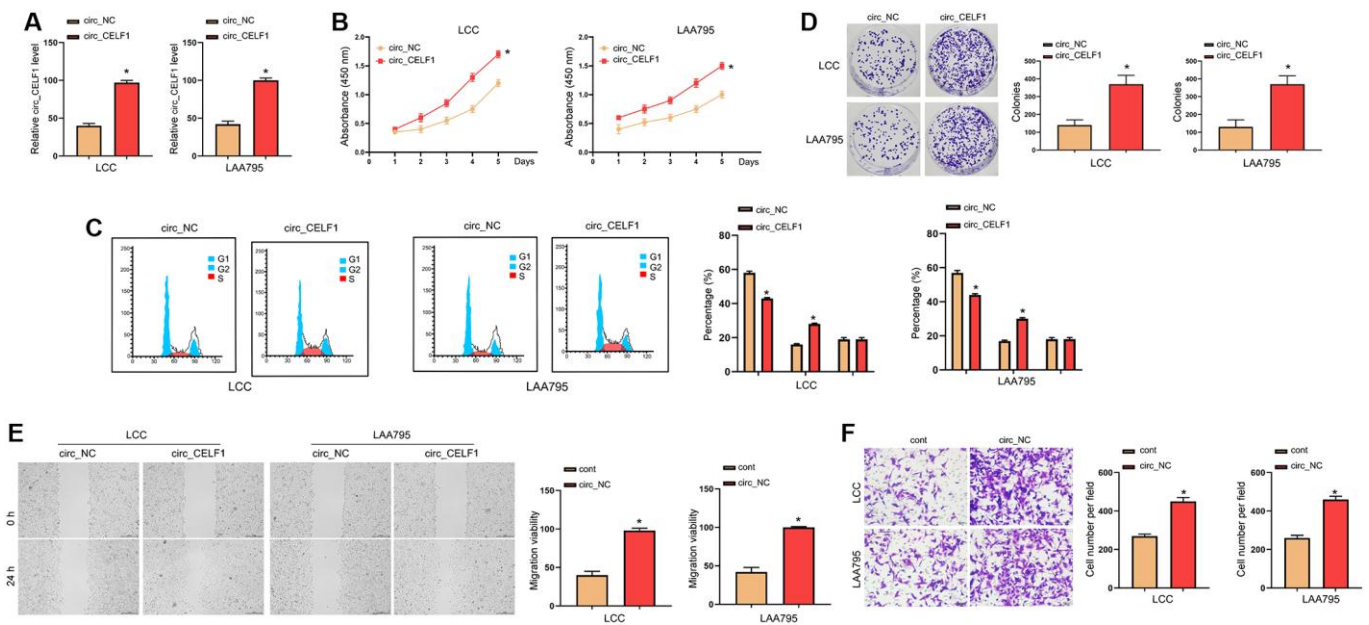
SUPPLEMENTARY FIGURES



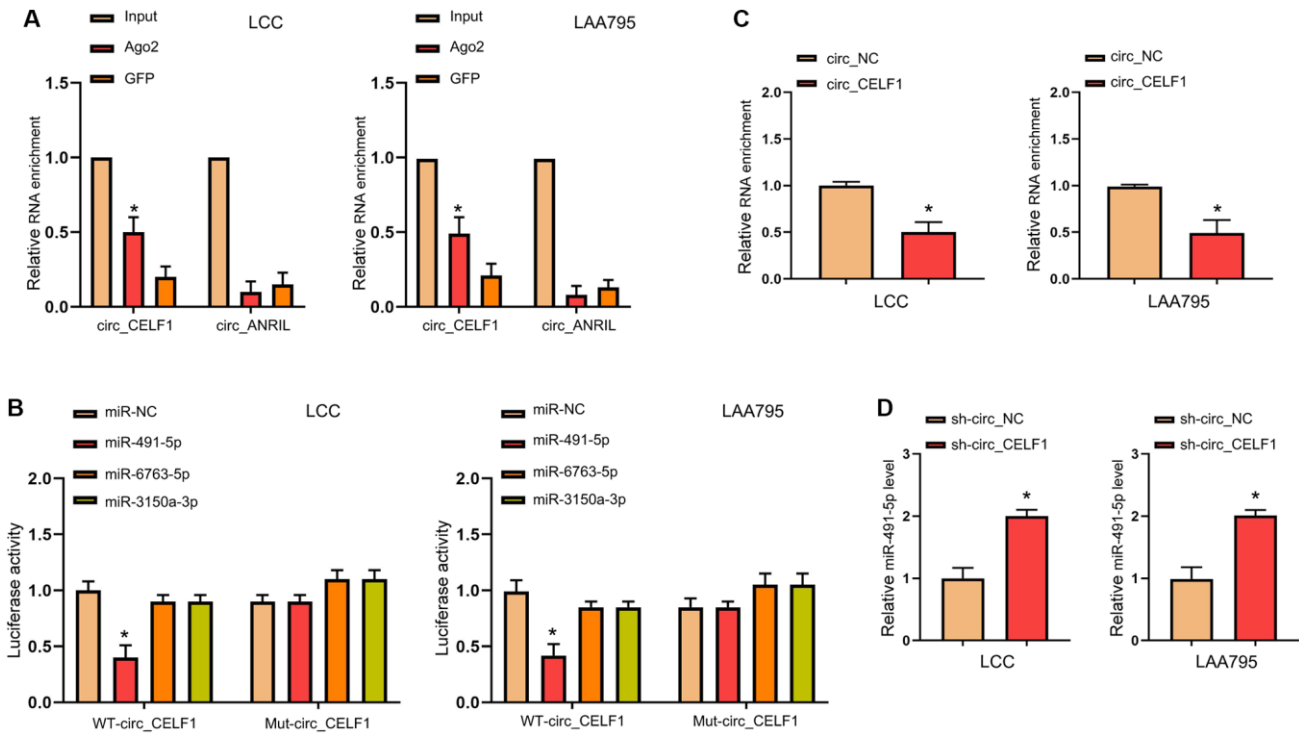
**Supplementary Figure 1. Identification of circ\_CELF1.** (A) The circular and linear form of CELF1 expression was measured by agarose gel electrophoresis assays and qRT-PCR in A549 and H1975 cells in the presence or absence of Rnase R treatment. (B, C) RNA level of circ\_CELF1 under actinomycin D treatment.  $n = 5$ ,  $^*P < 0.05$ .



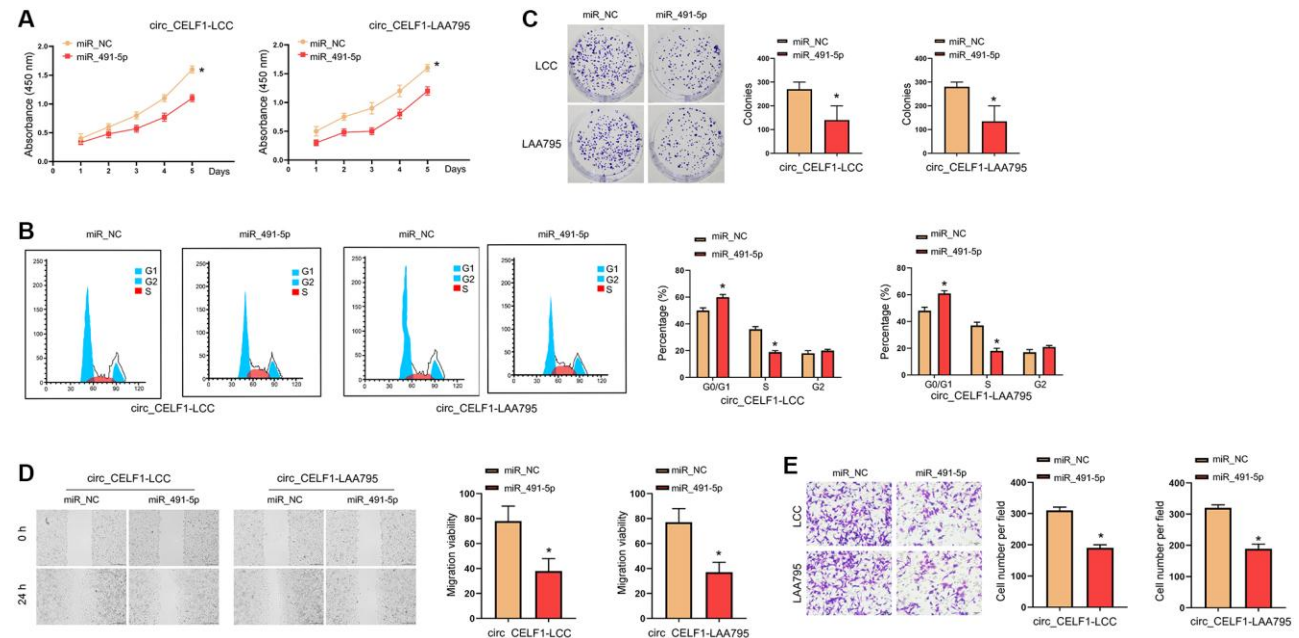
**Supplementary Figure 2. Transfection of negative control circRNA do not induces the progression of NSCLC cells *in vitro*.** (A) The qRT-PCR was performed to confirm the level of circ\_CELF1 in NSCLC cells.  $n = 5$ ,  $*P < 0.05$ . (B) CCK-8 assay was performed to detect the cell viability on A549 cells.  $n = 6$ ,  $*P < 0.05$ . (C) The clone formation assay on A549 cells.  $n = 3$ ,  $*P < 0.05$ . (D) The wound healing assay was performed on A549 cells.  $n = 3$ ,  $*P < 0.05$ . (E) The ability of invasion was explored on A549 cells by Transwell.  $n = 4$ ,  $*P < 0.05$ .



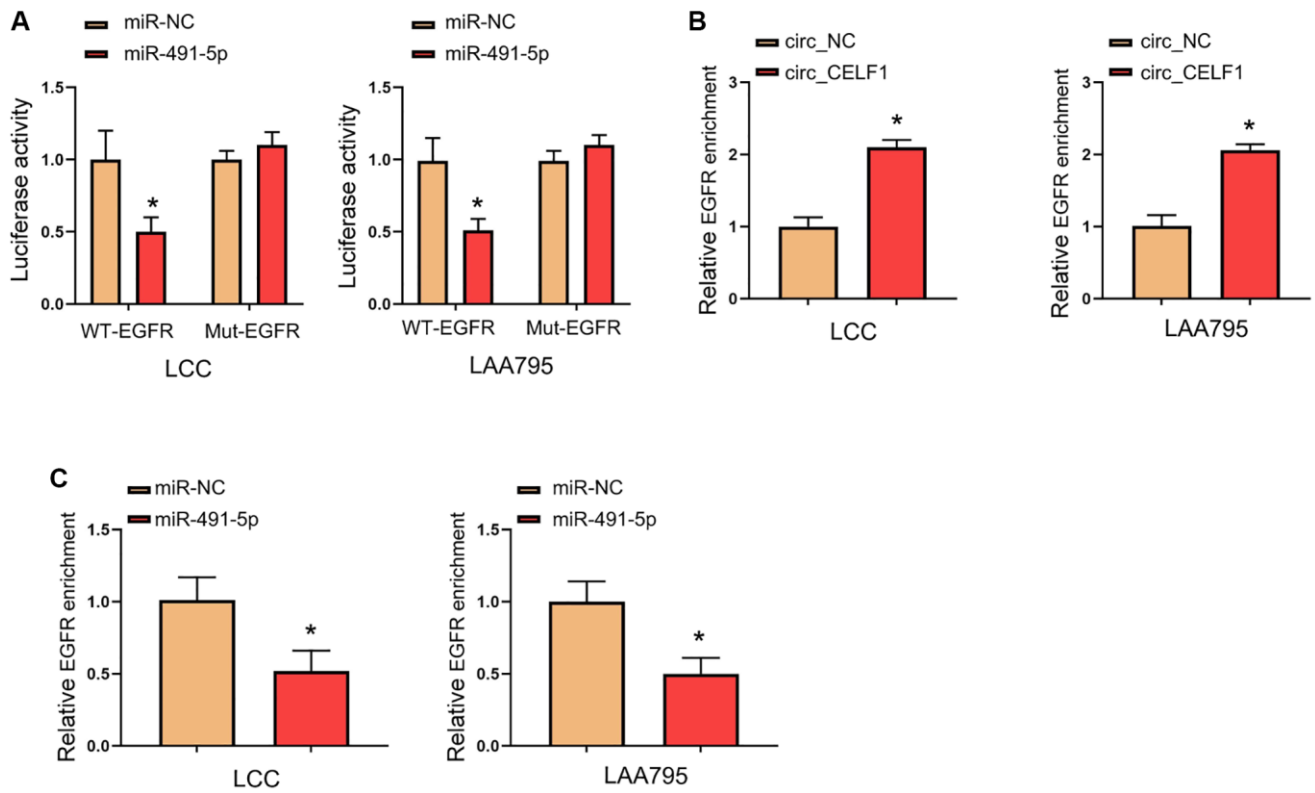
**Supplementary Figure 3. Forced expression of circ\_CELF1 induces the progression of LCC and LAA795 cells *in vitro*.** (A) The qRT-PCR was performed to confirm the transfection efficiency of circ\_CELF1 in LCC and LAA795 cells.  $*P < 0.05$ . (B) CCK-8 assay was performed to detect the cell viability on LCC and LAA795 cells.  $n = 6$ ,  $*P < 0.05$ . (C) The cell cycle was analyzed on LCC and LAA795 cells.  $n = 3$ ,  $*P < 0.05$ . (D) The clone formation assay on LCC and LAA795 cells.  $n = 3$ ,  $*P < 0.05$ . (E) The wound healing assay was performed on LCC and LAA795 cells.  $n = 3$ ,  $*P < 0.05$ . (F) The ability of invasion was explored on LCC and LAA795 cells by Transwell.  $n = 4$ ,  $*P < 0.05$ .



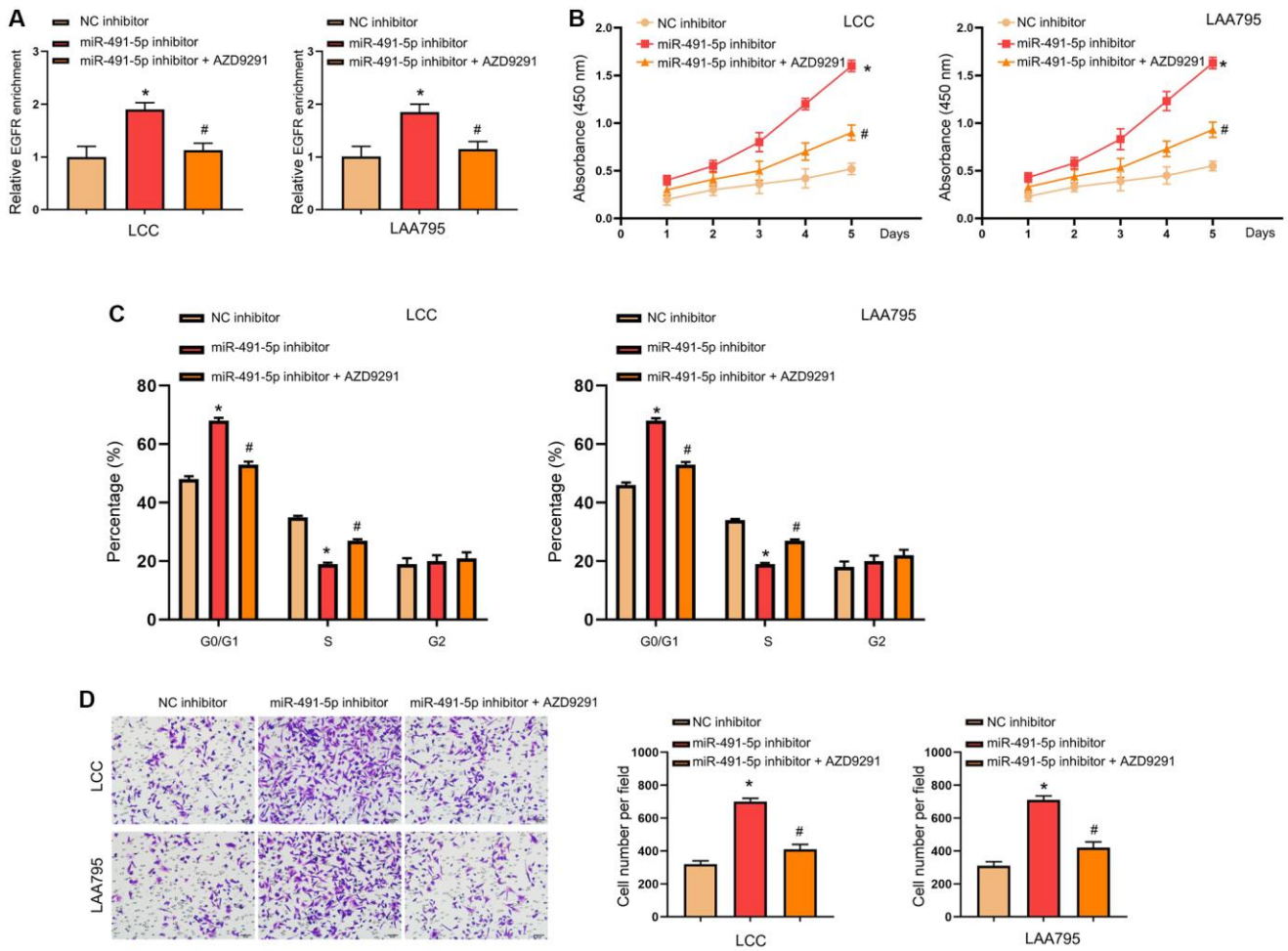
**Supplementary Figure 4. circ\_CELF1 binds miR-491-5p in LCC and LAA795 cells.** (A) AGO2 RIP experiments were performed using an antibody against Ago2 on extracts from LCC and LAA795 cells.  $n = 3$ ,  $*P < 0.05$ . (B) The luciferase activity of WT- circ\_CELF1 or mutant circ\_CELF1 in LCC and LAA795 cells after co-transfection with miR-491-5p, miR-6763-5p, and miR-3150a-3p.  $n = 3$ ,  $*P < 0.05$ . (C-D) The expression of miR-491-5p in LCC and LAA795 cells was explored by RT-PCR under downregulation of circ\_CELF1.  $n = 4$ ,  $*P < 0.05$ .



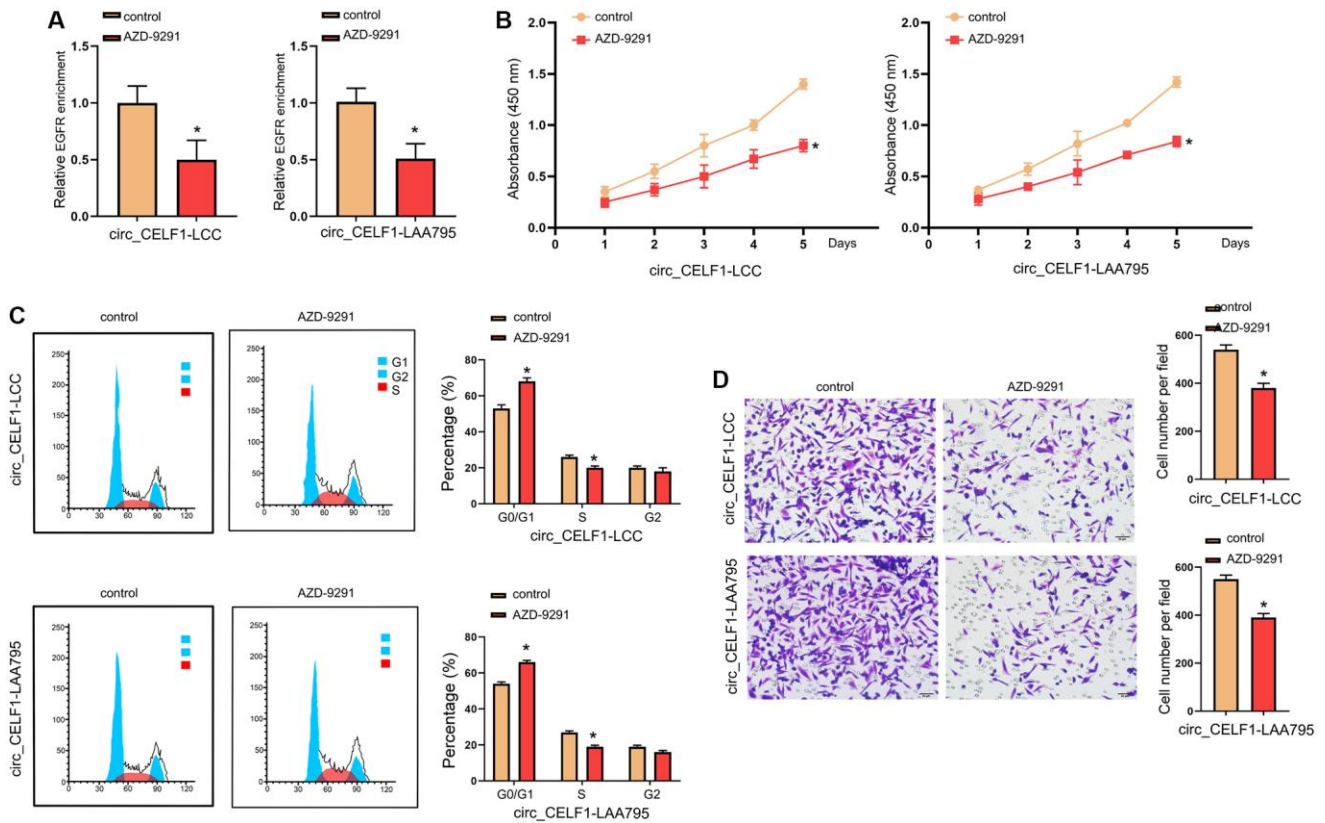
**Supplementary Figure 5. Forced expression of miR-491-5p remits the cell progression in stabled circ\_CELF1 expression LCC and LAA795 cells.** (A) CCK-8 assay was performed to detect the effect of miR-491-5p on overexpression of circ\_CELF1 LCC and LAA795 cells.  $n = 6$ ,  $*P < 0.05$ . (B) The cell cycle was explored on overexpression of circ\_CELF1 LCC and LAA795 cells after miR-491-5p transfection by flow cytometry.  $n = 6$ ,  $*P < 0.05$ . (C) The clone formation assay was performed on overexpression of circ\_CELF1 LCC and LAA795 cells.  $n = 5$ ,  $*P < 0.05$ . (D) Wound healing assay was used to confirm the migration ability.  $n = 5$ ,  $*P < 0.05$ . (E) The migration and invasion ability was explored by Transwell.  $n = 6$ ,  $*P < 0.05$ ,  $**P < 0.01$ .



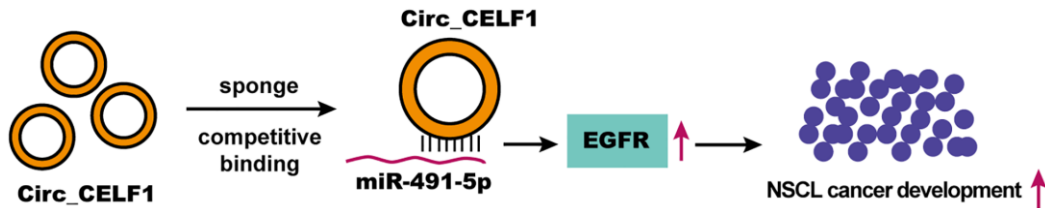
**Supplementary Figure 6. EGFR is a target of miR-491-5p in LCC and LAA795 cells.** (A) Luciferase assay confirmed the relationship between EGFR and miR-491-5p (lower).  $n = 3$ ,  $*P < 0.05$ . (B, C) The expression of EGFR was detected in LCC and LAA795 cells after transfection with circ\_CELF1 or miR-491-5p was detected by RT-PCR assay.  $n = 3$ ,  $*P < 0.05$ .



**Supplementary Figure 7. EGFR blockage prevents LCC and LAA795 cell progression induced by miR-491-5p inhibition.** (A) The expression level of EGFR was confirmed by RT-PCR assay. (B) CCK-8 assay was performed to detect cell viability in LCC and LAA795 cells. (C) The cell cycle was explored in LCC and LAA795 cells after miR-491-5p inhibitor transfection and AZD-9291 treatment by flow cytometry. (D) The invasion ability was explored by Transwell.  $n = 4$ , \* $P < 0.05$  vs. NC inhibitor, # $P < 0.05$  vs. miR-491-5p inhibitor.



**Supplementary Figure 8. Inhibition of EGFR prevents cell progression in stabled circ\_CELF1 expressed LCC and LAA795 cells.** (A) The knockdown efficiency of AZD-9291 was confirmed by qRT-PCR.  $n = 4$ ,  $*P < 0.05$ . (B) CCK-8 assay was performed to detect the effect of MK-1775 in NSCLC cells.  $n = 4$ ,  $*P < 0.05$ . (C) The cell cycle was explored in NSCLC cells after miR-491-5p transfection by flow cytometry.  $n = 4$ ,  $*P < 0.05$ . (D) The invasion ability was explored by Transwell.  $n = 4$ ,  $*P < 0.05$ .



**Supplementary Figure 9. Schematic illustration of circ\_CELF1/miR-491-5p/EGFR regulatory network in NSCLC cells.**