**Supplementary Table 1.** Patient's demographics and tumor characteristics and association of ZEB1/2 level with clinicopathological features in lung tumor population

| Characteristics | No. of patients, N=45 (%) | P value |
|---|---|---|
| Patients Parameter | | |
| Age (years) | | 0.112 |
| Average [range] | 50 [30-81] | |
| <55 | 20 (44.4) | |
| ⩾55 | 25 (55.6) | |
| Gender | | 0.0381 |
| Male | 35 (77.7) | |
| Female | 10 (22.3) | |
| Tumor Characteristics | | |
| Tumor size (cm) | | 0.002** |
| <4 | 10 (22.2) | |
| ⩾4 | 35 (77.8) | |
| Differentiation | | 0.126 |
| Poor | 30 (66.7) | |
| Well-moderate | 15 (33.3) | |
| Lymph node metastasis | | 0.014* |
| N- | 30 (66.7) | |
| N+ | 15 (33.3) | |
| Distant metastasis | | 0.024* |
| M- | 38 (84.4) | |
| M+ | 7 (15.6) | |
| Level of ZEB1 | | |
| Protein level | N=45 (Figure 2B) | |
| High | 38 (84.4) | 0.005** |
| median | 5 (11.1) | 0.061 |
| low | 2 (4.5) | 0.142 |
| mRNA level | N=45 (Figure 2A) | |
| High | 36 (80.0) | 0.002** |
| median | 7 (15.6) | 0.053 |
| Low | 2 (4.3) | 0.083 |
| Level of ZEB2 | | |
| Protein level | N=45 (Figure 2B) | |
| High | 37 (82.2) | 0.004** |
| median | 6 (13.3) | 0.071 |
| low | 2 (4.5) | 0.122 |
| mRNA level | N=45 (Figure 2A) | |
| High | 37 (82.2) | 0.002** |
| median | 5 (11.1) | 0.083 |
| low | 3 (6.7) | 0.107 |

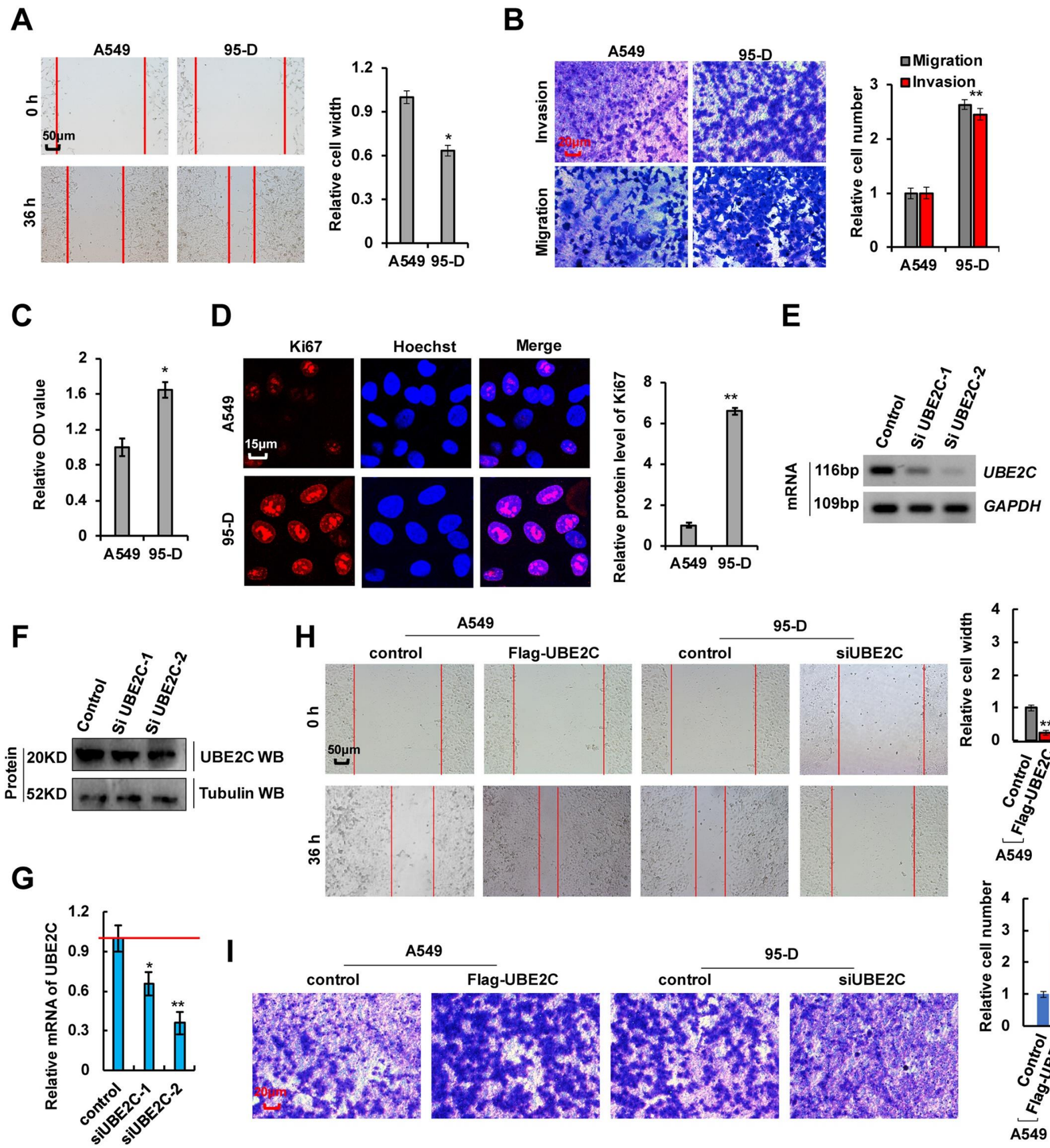
Differences between experimental groups were assessed by Student's t-test or one-way analysis

of variance. Data represent mean ± SD. *$p<0.05$; **$p<0.01$.

**Supplementary Table 2** The candidate miRNAs targeting UBE2C were predicted using a combination of three databases: miRbase, miRanda and TargetScan.

| miRBase predicted targeting | | |
|---|---|---|
| hsa-miR-5088-5p | hsa-miR-140-3p.2 | hsa-miR-134-3p |
| hsa-miR-3127-5p | hsa-miR-32-3p | hsa-miR-320c |
| hsa-miR-3918 | hsa-miR-4775 | hsa-miR-320b |
| hsa-miR-6742-3p | | hsa-miR-4429 |
| hsa-miR-661 | TargetScan-7.1 predicted targeting | hsa-miR-320d |
| hsa-miR-6721-5p | hsa-miR-1972 | hsa-miR-320a |
| hsa-miR-5189-5p | hsa-miR-5585-3p | hsa-miR-548e-5p |
| hsa-miR-548e-5p | hsa-miR-1285-3p | hsa-miR-302a-5p |
| hsa-miR-6860 | hsa-miR-1268a | hsa-miR-3682-5p |
| hsa-miR-1285-3p | hsa-miR-1268b | hsa-miR-657 |
| hsa-miR-612 | hsa-miR-5585-5p | hsa-miR-3665 |
| hsa-miR-5787 | hsa-miR-548e-5p | hsa-miR-6811-5p |
| hsa-miR-4505 | hsa-miR-4699-5p | hsa-miR-6511b-5p |
| hsa-miR-4438 | hsa-miR-5585-3p | hsa-miR-578 |
| hsa-miR-8080 | hsa-miR-5708 | hsa-miR-4748 |
| hsa-miR-4457 | hsa-miR-1225-3p | hsa-miR-329-5p |
| hsa-miR-4801 | hsa-miR-548s | hsa-miR-4464 |
| hsa-miR-4731-3p | hsa-miR-4452 | hsa-miR-6869-5p |
| hsa-miR-3148 | hsa-miR-6739-3p | hsa-miR-8081 |
| hsa-miR-651-3p | | hsa-miR-1251-3p |
| hsa-miR-4521 | miRanda predicted targeting | hsa-miR-631 |
| hsa-miR-6502-3p | hsa-miR-525-5p | hsa-miR-3661 |
| hsa-miR-8080 | hsa-miR-520a-5p | hsa-miR-4299 |
| hsa-miR-4719 | hsa-miR-3180-5p | hsa-miR-138-5p |
| hsa-miR-1185-2-3p | hsa-miR-193b-5p | hsa-miR-6842-3p |
| hsa-let-7f-2-3p | hsa-miR-3170 | hsa-miR-3652 |
| hsa-miR-1185-1-3p | hsa-miR-6855-5p | hsa-miR-4430 |
| hsa-miR-1284 | hsa-miR-6742-5p | hsa-miR-4505 |
| hsa-miR-337-3p | hsa-miR-6796-5p | hsa-miR-5787 |
| hsa-miR-4311 | hsa-miR-491-5p | hsa-miR-3064-5p |
| hsa-miR-583 | hsa-miR-4447 | hsa-miR-6504-5p |
| hsa-miR-1276 | hsa-miR-4472 | hsa-miR-8073 |
| hsa-miR-577 | hsa-miR-3151-5p | hsa-miR-221-5p |
| | | hsa-miR-5088-5p |

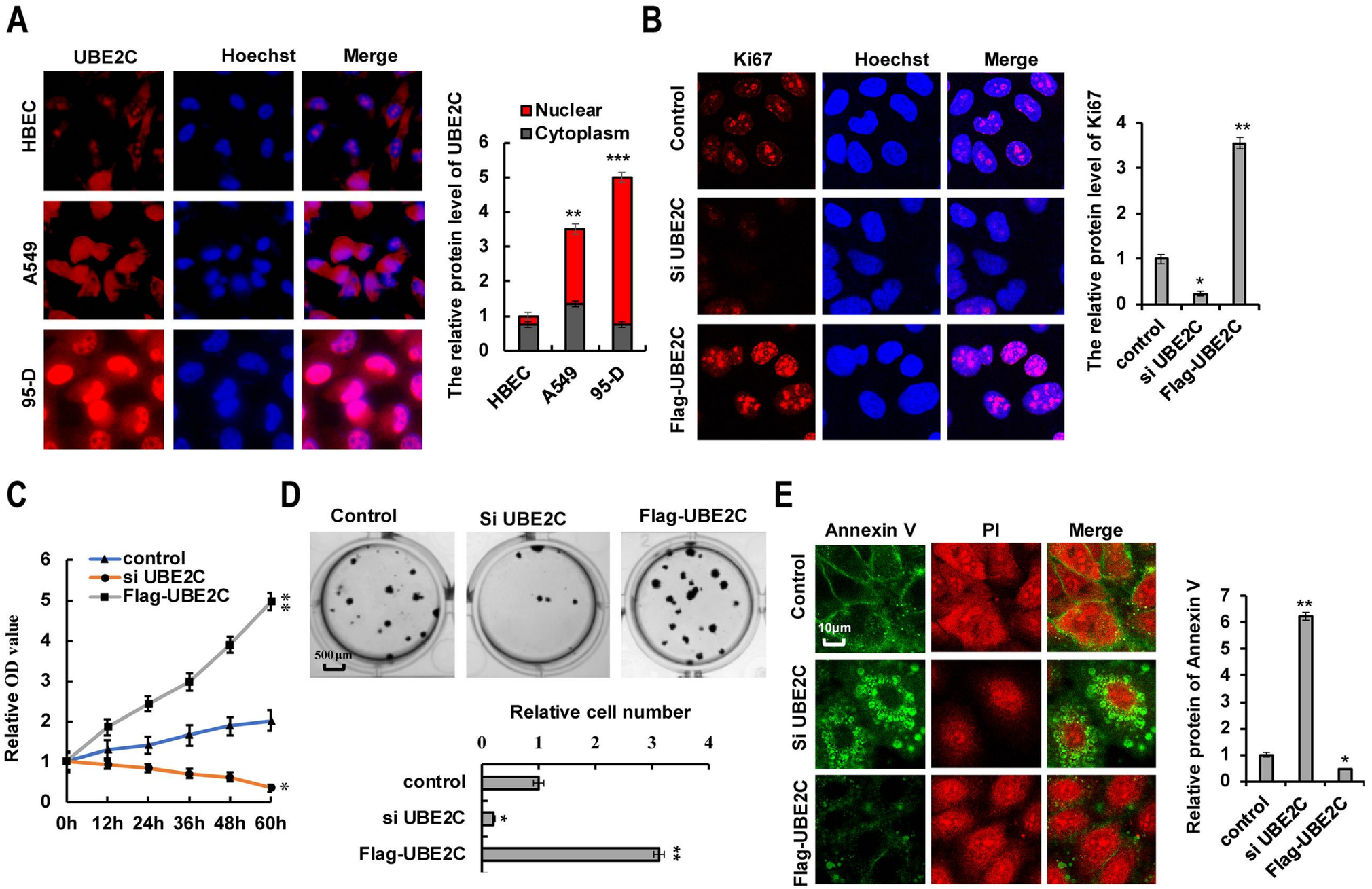
## Supplementary Figures




(22 ×22.3 cm, 300 dpi)

**Supplementary Figure 1**

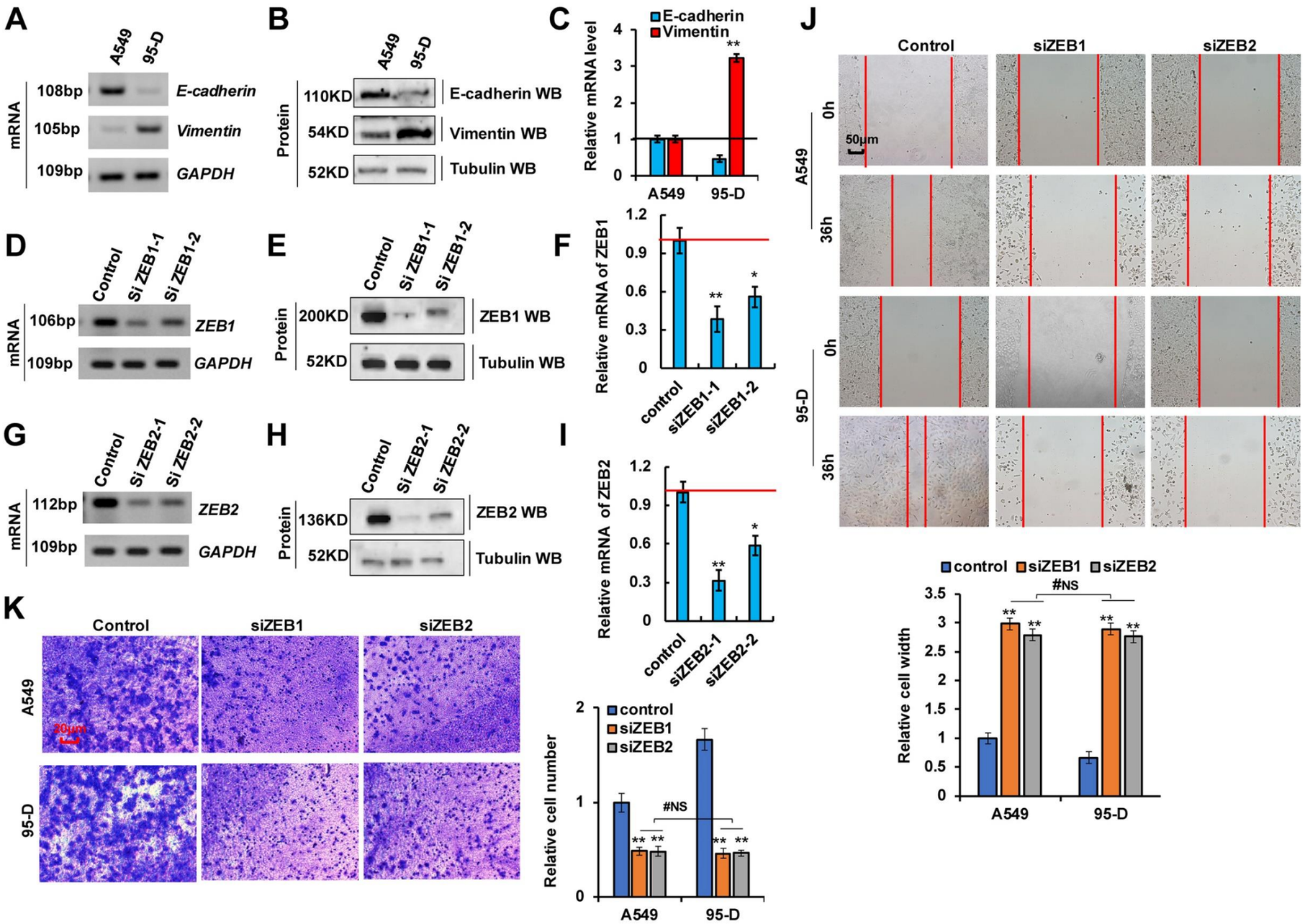
**(A, B)** the cellular migration and invasion growth was analyzed by scratch assay (**A**) and transwell assay (**B**) in the A549 and 95-D cells. **(C)** In vitro proliferation assay by CCK8 assay demonstrating that the cellular proliferation was increased in 95-D cells than A549 cells. **(D)** Ki67 were analyzed by immunofluorescent staining in A549 and 95-D cells. (*p<0.05, **p<0.01 *vs* control group correspond to two–tailed Student's tests). **(E-G)** A549 cells were transfected with siUBE2C-1 or siUBE2C-2. The mRNA and protein levels of UBE2C were analyzed by RT-PCR (**E**), immunoblotting (**F**) and RT-qPCR (**G**) assays. (*p<0.05, **p<0.01, ANOVA with Bonferroni correction). **(H, I)** Scratch assay (**H**) and transwell assay (**I**) indicated that cellular migration and invasion growth was increased in 95-D cells than in A549 cells. (*p<0.05, **p<0.01 *vs* control group correspond to two–tailed Student's tests). Results were presented as mean ± SD, and the error bars represent the SD of three independent experiments. (**p<0.01 *vs* control group correspond to two–tailed Student's tests).




(22 ×14.5 cm, 300 dpi)

**Supplementary Figure 2**

**(A)** the protein of UBE2C was analyzed by immunofluorescent staining in the HBEC, A549 and 95-D cells. (**p<0.01, ***p<0.001 *vs* control group correspond to two–tailed Student's tests). (**B-E**) A549 cells were transfected with UBE2C or siUBE2C, respectively. **(B, C)** the protein of Ki67 was analyzed by immunofluorescent staining (**B**) and the cellular growth was analyzed by MTT assay (**C**). **(D)** Colony formation density was analyzed by colony formation assay. **(E)** Annexin V was analyzed by immunofluorescent staining. (*p<0.05, **p<0.01, ANOVA with Bonferroni correction). Results were presented as mean ± SD, and the error bars represent the SD of three independent experiments.

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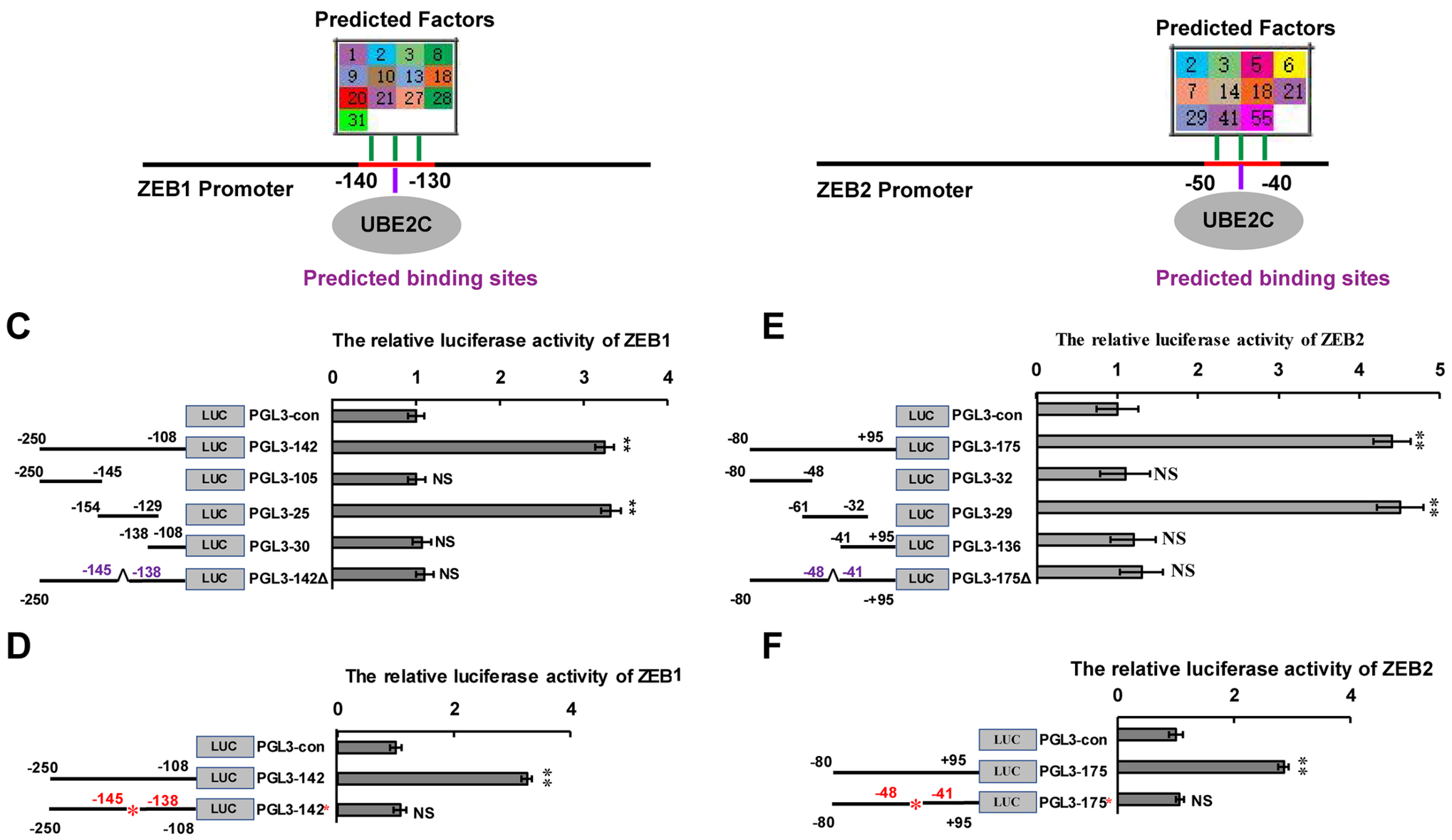
**Supplementary Figure 3**

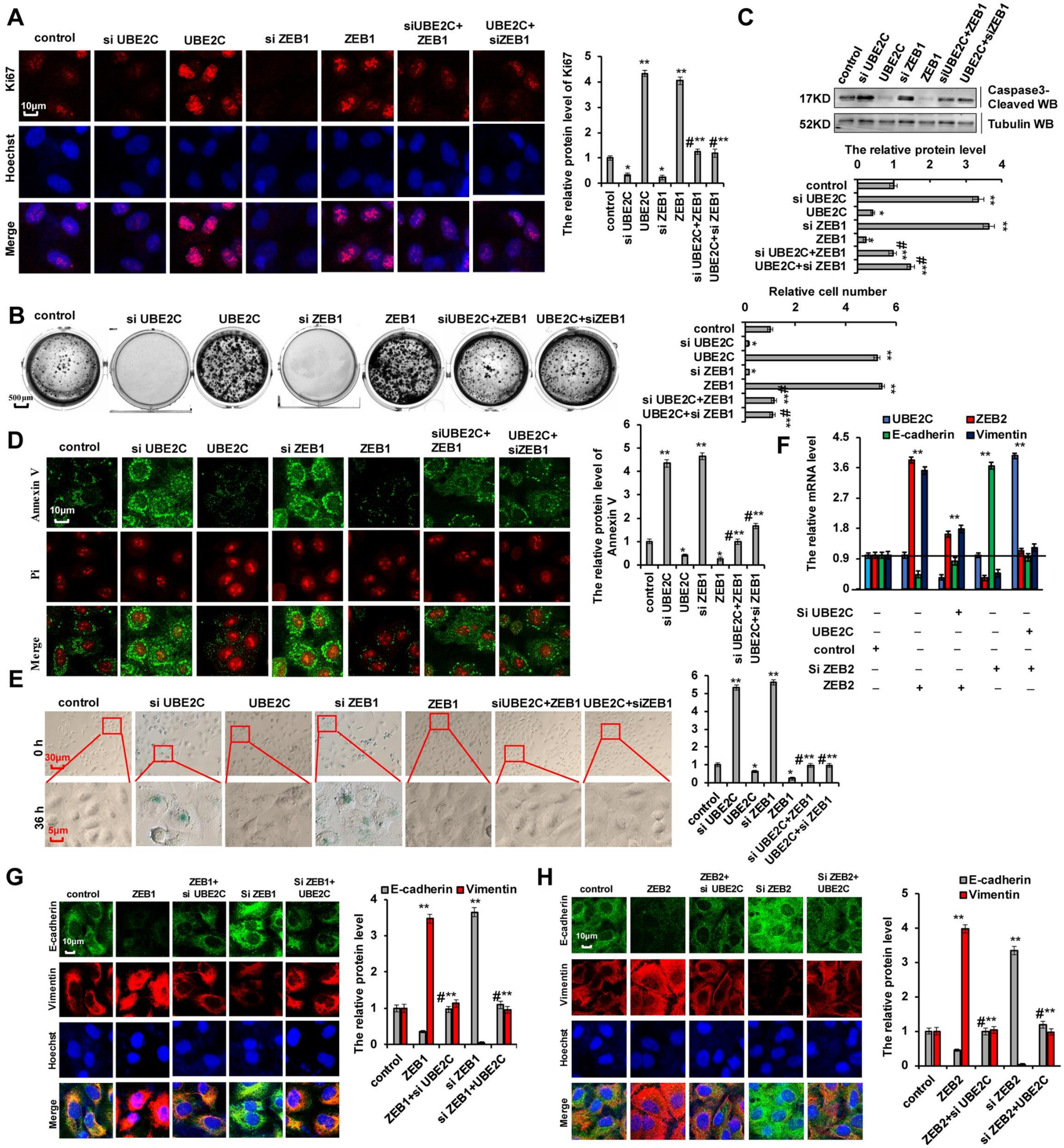
**(A-C)** the mRNA and protein expression levels of E-cadherin and Vimentin were analyzed by RT-PCR (**A**), immunoblotting (**B**) and RT-qPCR (**C**) in A549 and 95-D cells, respectively. (**p<0.01 *vs* control group correspond to two–tailed Student's tests). **(D-I)** A549 cells were transfected with siZEB1/2-1 or siZEB1/2-2. The mRNA and protein levels of ZEB1 and ZEB2 were analyzed by RT-PCR (**D, G**), immunoblotting (**E, H**) and RT-qPCR (**F, I**) assay. (*p<0.05, **p<0.01, ANOVA with Bonferroni correction). **(J, K)** A549 and 95-D cells were transfected with siZEB1 or siZEB2, respectively. Cell migration growth was analyzed by scratch assay **(J)**. Cellular invasion ability was analyzed by Trans-well assay **(K)**. (**p<0.01 *vs* control group correspond to two–tailed Student's tests). Results were presented as mean ± SD, and the error bars represent the SD of three independent experiments.




(22 ×14.0 cm, 300 dpi)

**Supplementary Figure 4**

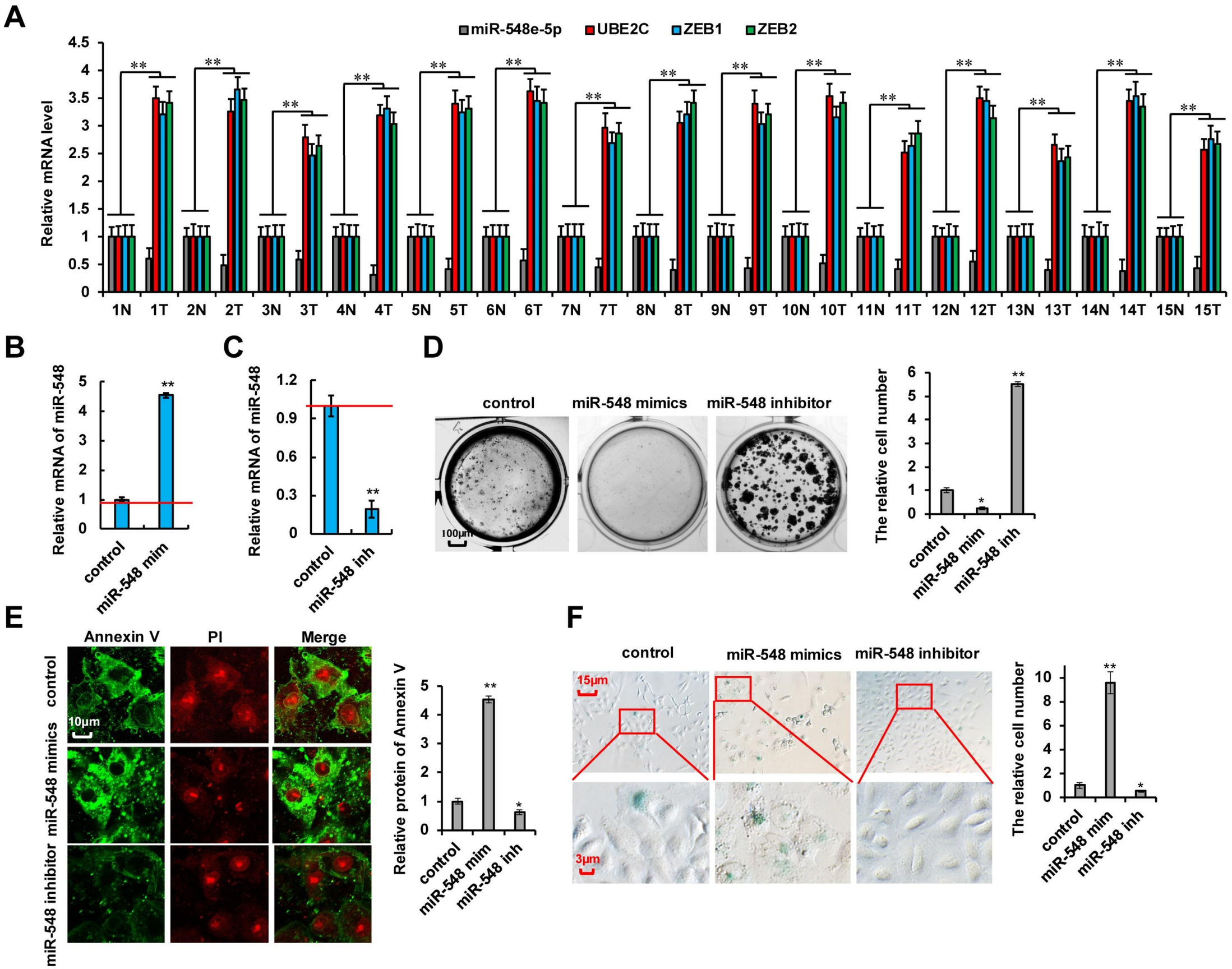
**(A, B)** the diagram of PROMO analysis for ZEB1 (**A**) and ZEB2 (**B**). **(C, D)** the activities of different fragments of ZEB1 promoter (pGL3-basic, pGL3-142, pGL3-105, pGL3-25, pGL3-30, pGL3-142Δ and pGL3-142*) were measured by luciferase reporter gene assay in A549 cells. **(E, F)** the activities of different fragments of ZEB2 promoter (pGL3-basic, pGL3-175, pGL3-32, pGL3-29, pGL3-136, pGL3-175Δ and pGL3-175*) were measured by luciferase reporter gene assay in A549 cells. Results were presented as mean ± SD, and the error bars represent the SD of three independent experiments. (**p<0.01, ANOVA with Bonferroni correction).




(22 ×23.4 cm, 300 dpi)

**Supplementary Figure 5**

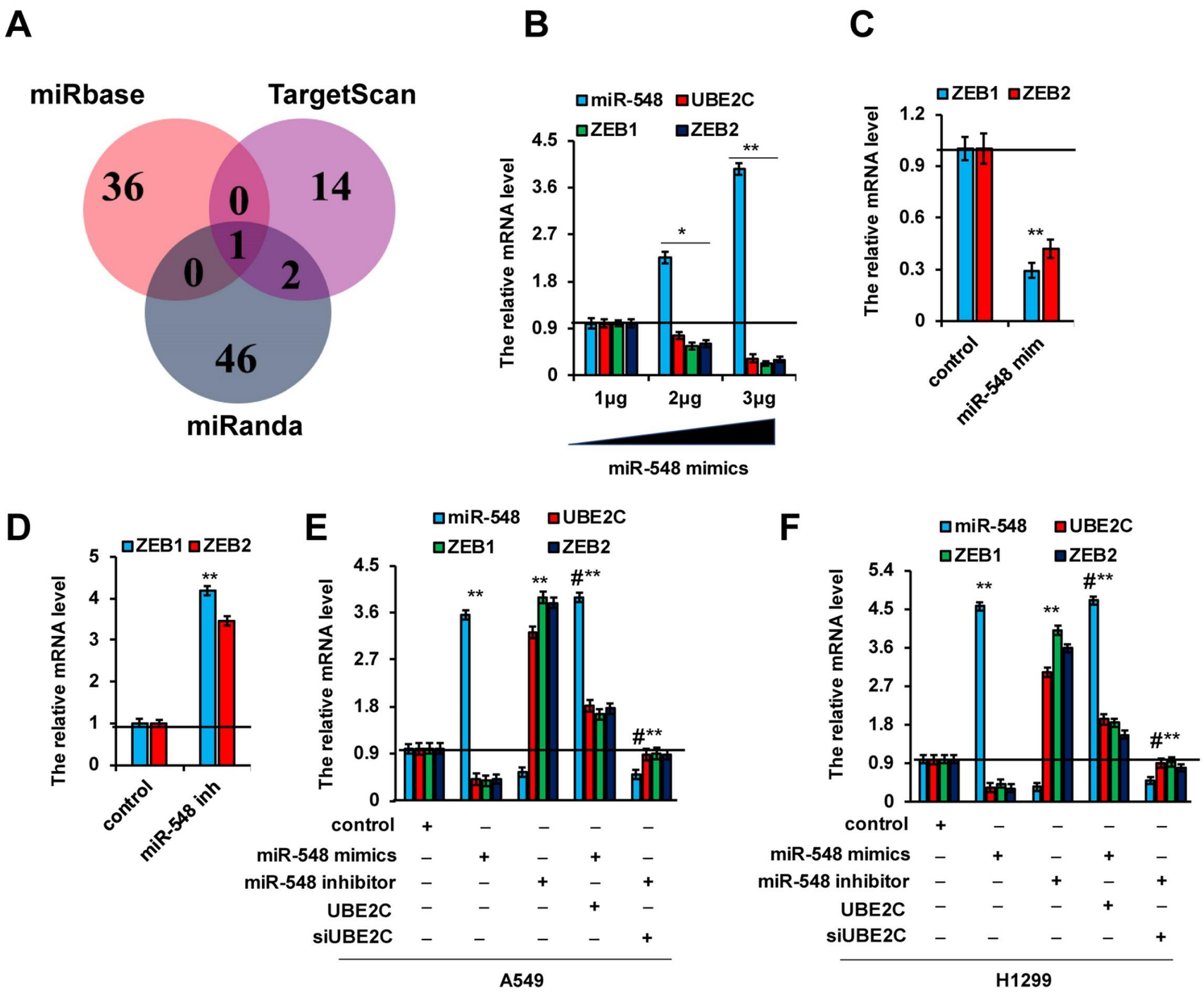
**(A-E)** A549 cells were transfected with UBE2C or siUBE2C. ZEB1 or siZEB1 were used for upregulating or downregulating the protein level of UBE2C target genes, respectively. **(A)** Ki67 was analyzed by immunofluorescent staining. **(B)** Colony formation density was analyzed by colony formation assay. **(C)** Cleaved Caspase-3 was analyzed by immunoblotting assay. **(D)** Annexin V was analyzed by immunofluorescent staining. **(E)** Cell senescence was analyzed by SA-β-gal staining. **(F-H)** A549 cells were transfected with UBE2C or siUBE2C. ZEB1 or ZEB2 were used for upregulated the protein level of UBE2C target genes, respectively. **(F)** the mRNA levels of UBE2C, ZEB2, E-cadherin and vimentin were analyzed by RT-qPCR. **(G, H)** the protein expression levels of EMT-related molecules E-cadherin and Vimentin were analyzed by immunofluorescent staining. Results were presented as mean ± SD, and the error bars represent the SD of three independent experiments. (*p<0.05, **p<0.01, ANOVA with Bonferroni correction).




(22 ×17.2 cm, 300 dpi)

**Supplementary Figure 6**

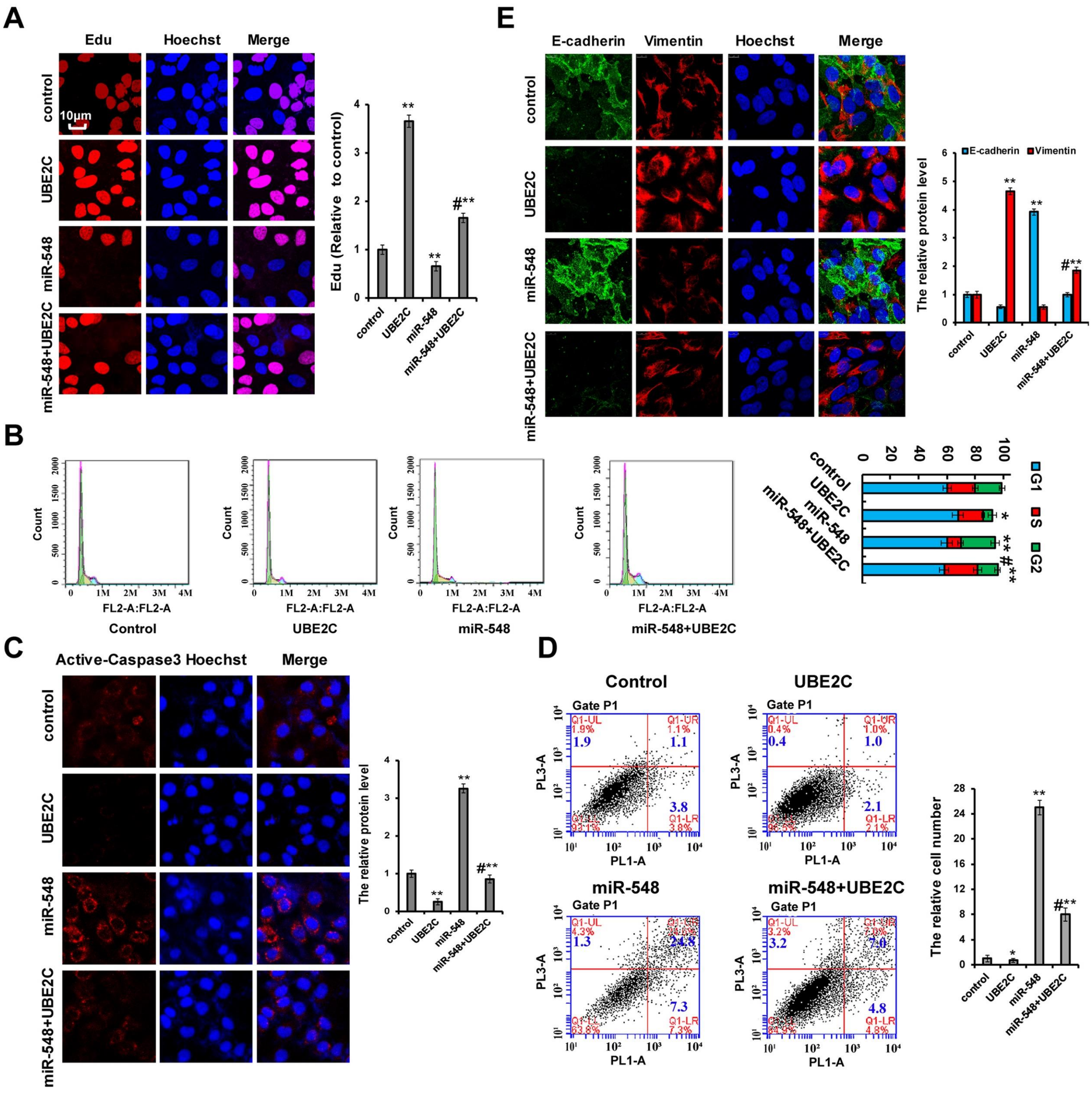
**(A)** RT-qPCR assay showed that the mRNA levels of UBE2C, ZEB1 and ZEB2 were increased but the mRNA level of miR-548e-5p (miR-548) was decreased in human lung cancer tissues compared with their normal adjacent lung tissues in the same individual patients (n=15). **(B-F)** A549 cells were transfected with miR-548e-5p-mimics and miR-548e-5p inhibitor. **(B, C)** the mRNA level of miR-548e-5p was analyzed by RT-qPCR assay. **(D)** Colony formation density was analyzed by colony formation assay. **(E)** the protein of Annexin V was analyzed by immunofluorescent staining. **(F)** Cell senescence was analyzed by SA-β-gal staining. Results were presented as mean ± SD, and the error bars represent the SD of three independent experiments. (*p<0.05, **p<0.01 *vs* control group correspond to two–tailed Student's tests).




(22 ×17.6 cm, 300 dpi)

**Supplementary Figure 7**

**(A)** Three bioinformatic softwares (miRbase, miRanda and TargetScan) were used to identify the potential regulatory miRNAs targeting UBE2C. **(B)** RT-qPCR result shows that miR-548e-5p (miR-548) dose-dependently decreased the mRNA levels of UBE2C, ZEB1 and ZEB2 in A549 cells. **(C, D)** A549 cells were transfected with miR-548e-5p-mimics (**C**) and miR-548e-5p inhibitor (**D**). The mRNA levels of ZEB1 and ZEB2 were analyzed by RT-qPCR. (*p<0.05, **p<0.01 *vs* control group correspond to two–tailed Student's tests). **(E, F)** A549 (**E**) or H1299 (**F**) cells were transfected with miR-548e-5p mimics or miR-548e-5p inhibitor. UBE2C or siUBE2C were used for upregulating or downregulating the protein level of miR-548e-5p target genes, respectively. The mRNA levels of miR-548e-5p, UBE2C, ZEB1 and ZEB2 were analyzed by RT-qPCR. (*p<0.05, **p<0.01, ANOVA with Bonferroni correction). Results were presented as mean ± SD, and the error bars represent the SD of three independent experiments.




(22 ×22.2 cm, 300 dpi)

**Supplementary Figure 8**

A549 cells were transfected with miR-548e-5p-mimics, UBE2C or co-transfected with miR-548e-5p-mimics and UBE2C. **(A)** Edu was analyzed by immunofluorescent staining. **(B)** Cell cycle profile was analyzed by cell flow cytometry. **(C)** Active-Caspase3 was analyzed by immunofluorescent staining. **(D)** Apoptosis was analyzed by cell flow cytometry. (**E**) E-cadherin and Vimentin were analyzed by immunofluorescent staining. Results were presented as mean ± SD, and the error bars represent the SD of three independent experiments. (*p<0.05, **p<0.01, ANOVA with Bonferroni correction).