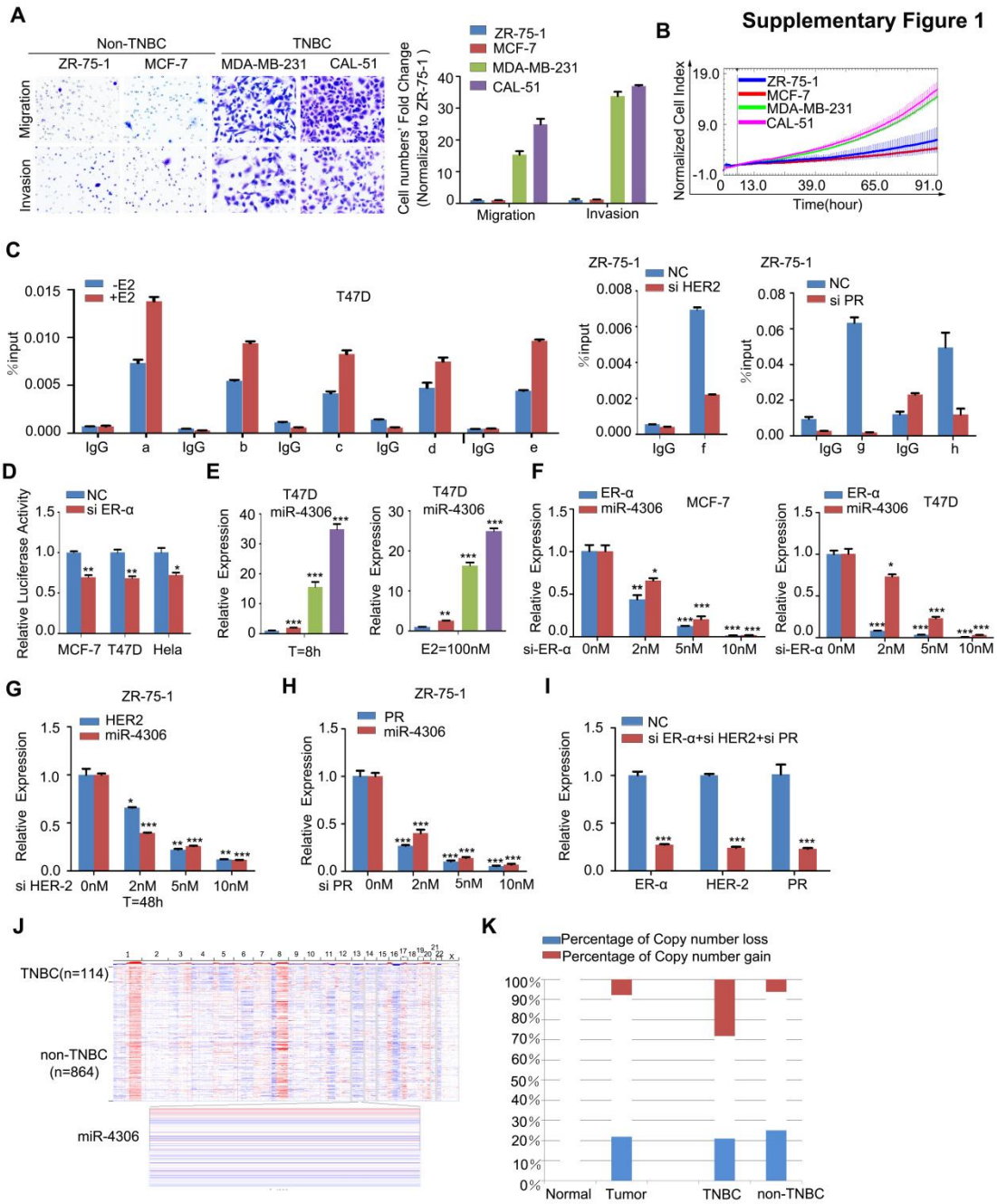
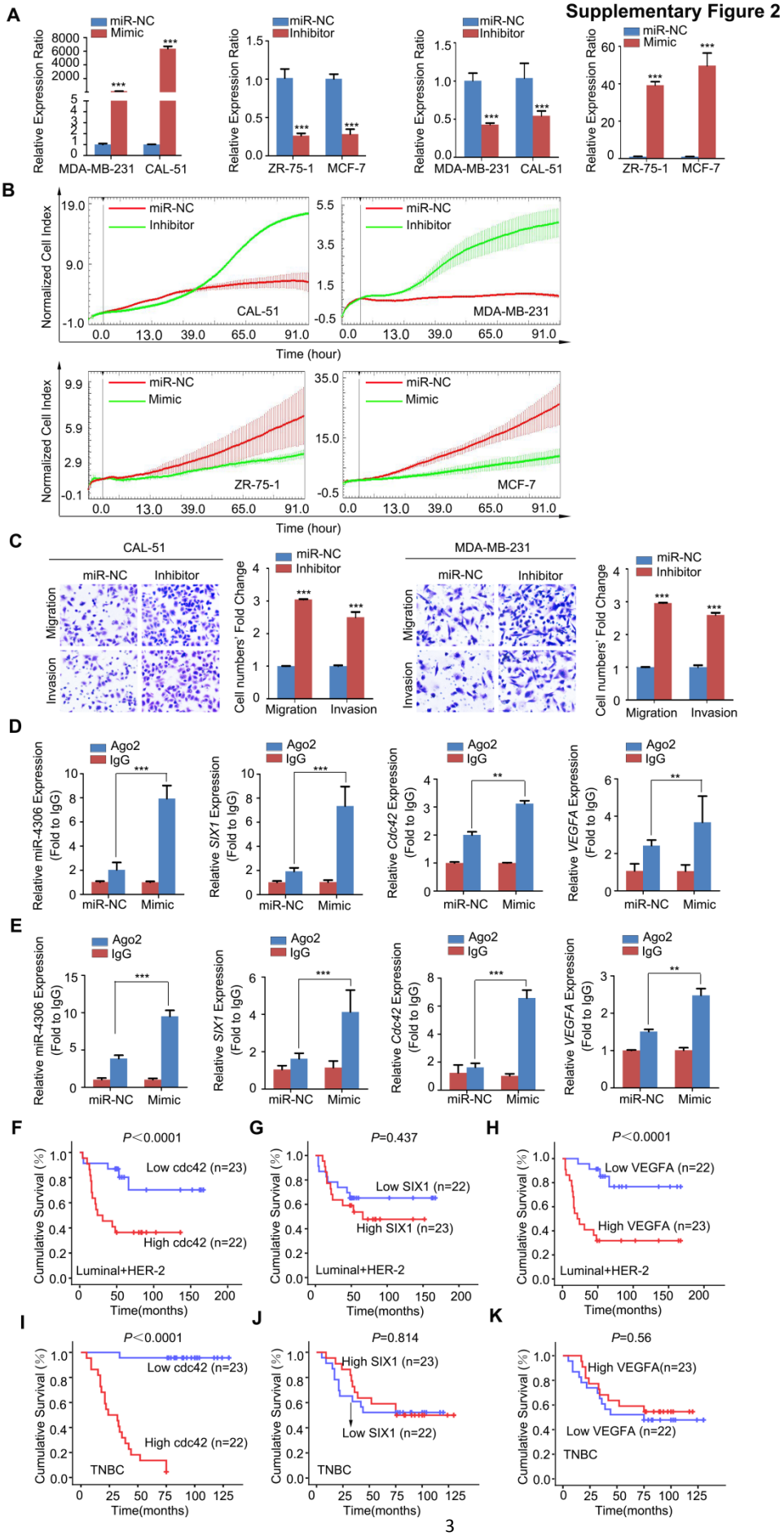


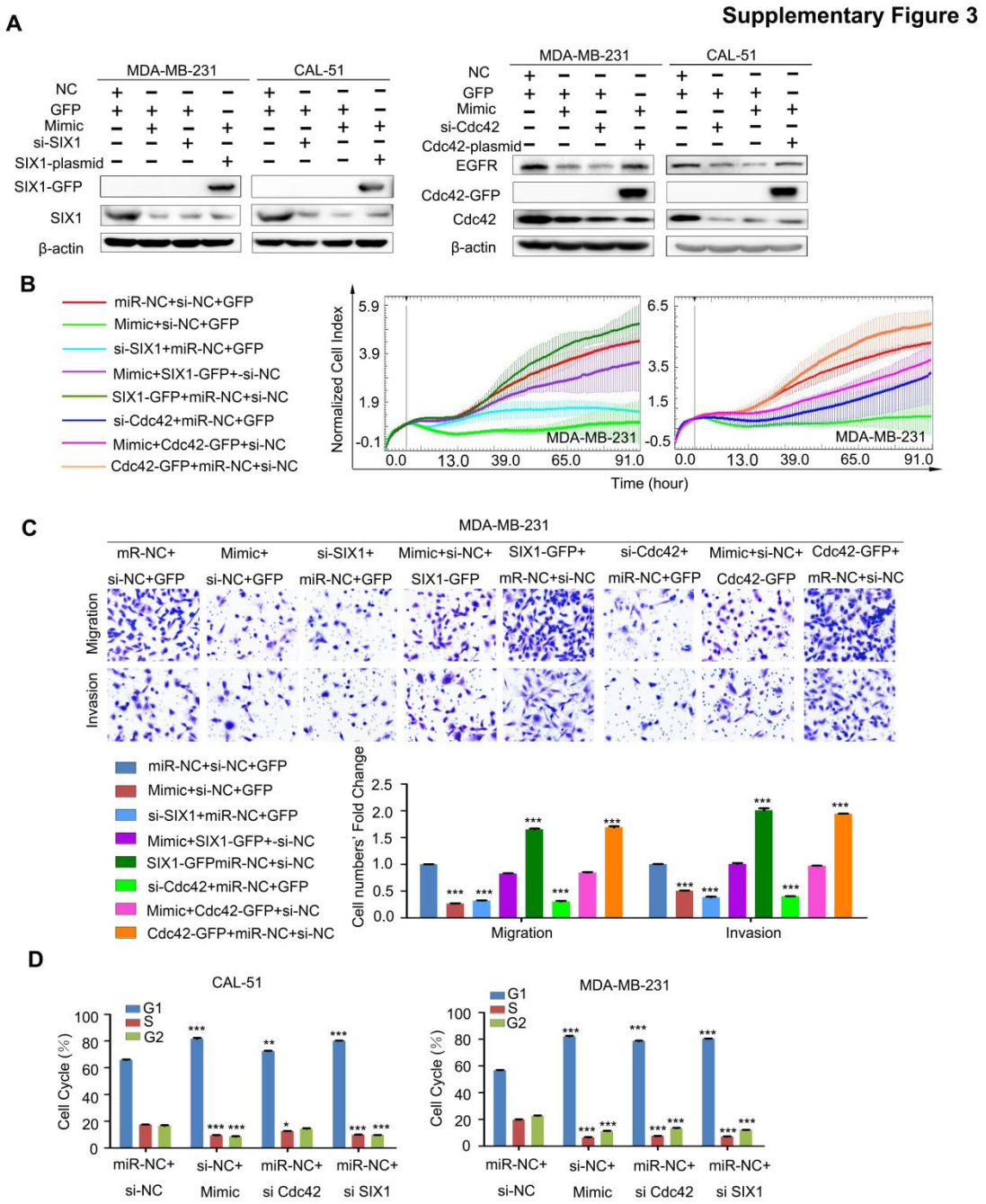
Supplementary Figure 1. (A) Analysis of migration and invasion in the four breast cancer cell lines by transwell assays. The quantitative data are shown in the histograms, and the photographs are representative of the migrated/invaded cells. Original magnification, ×100. (B) Analysis of proliferation in the four breast cancer cell lines with the xCELLigence Real-Time Cell Analyzer (RTCA)-MP system. (C) ChIP assays were performed with ER-α/HER2/PR antibody. IgG served as the negative control. (D) Relative luciferase activity of reporter constructs miR-4306 promoter in cells. Luciferase reporter activity was normalized to Renilla luciferase activity. (E-H) qPCR analysis of miR-4306 levels in cells. (E)T47D cells treated with different concentrations of E2 (0

μM, 10 μM, 50 μM, and 100 μM) for 8 h, or with 100 μM E2 for different times (0 h, 2 h, 4 h, and 8 h). (F) MCF-7/T47D cells were treated with different concentrations of ER-α siRNA (0 nM, 2 nM, 5 nM, and 10 nM) for 48 h. (G) ZR-75-1 cells were treated with different concentrations of HER2 siRNA (0 nM, 2 nM, 5 nM and 10 nM) for 48 h. (H) ZR-75-1 cells were treated with different concentrations of PR siRNA (0 nM, 2 nM, 5 nM and 10 nM) for 48 h. (I) qPCR analysis of ER-α/HER2/PR levels after simultaneous ER-α, HER2, and PR knockdown in ZR-75-1 cells. (J and K analysis data from TCGA) (J) Top: Landscape of the genomic copy number alterations in 114 TNBC and 864 non-TNBC tissues. Bottom: Segmentation data for the location of miR-4306 on chromosome 13. Copy number gains are shown in shades of red, and copy number losses are shown in shades of blue. (K) Percentages of cancer samples with significant copy number alterations to miR-4306 (> 25% of specimens).The data are representative of three independent experiments. The error bars represent the SEM. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$; two-tailed unpaired Student's t-test.

Supplementary Figure 2

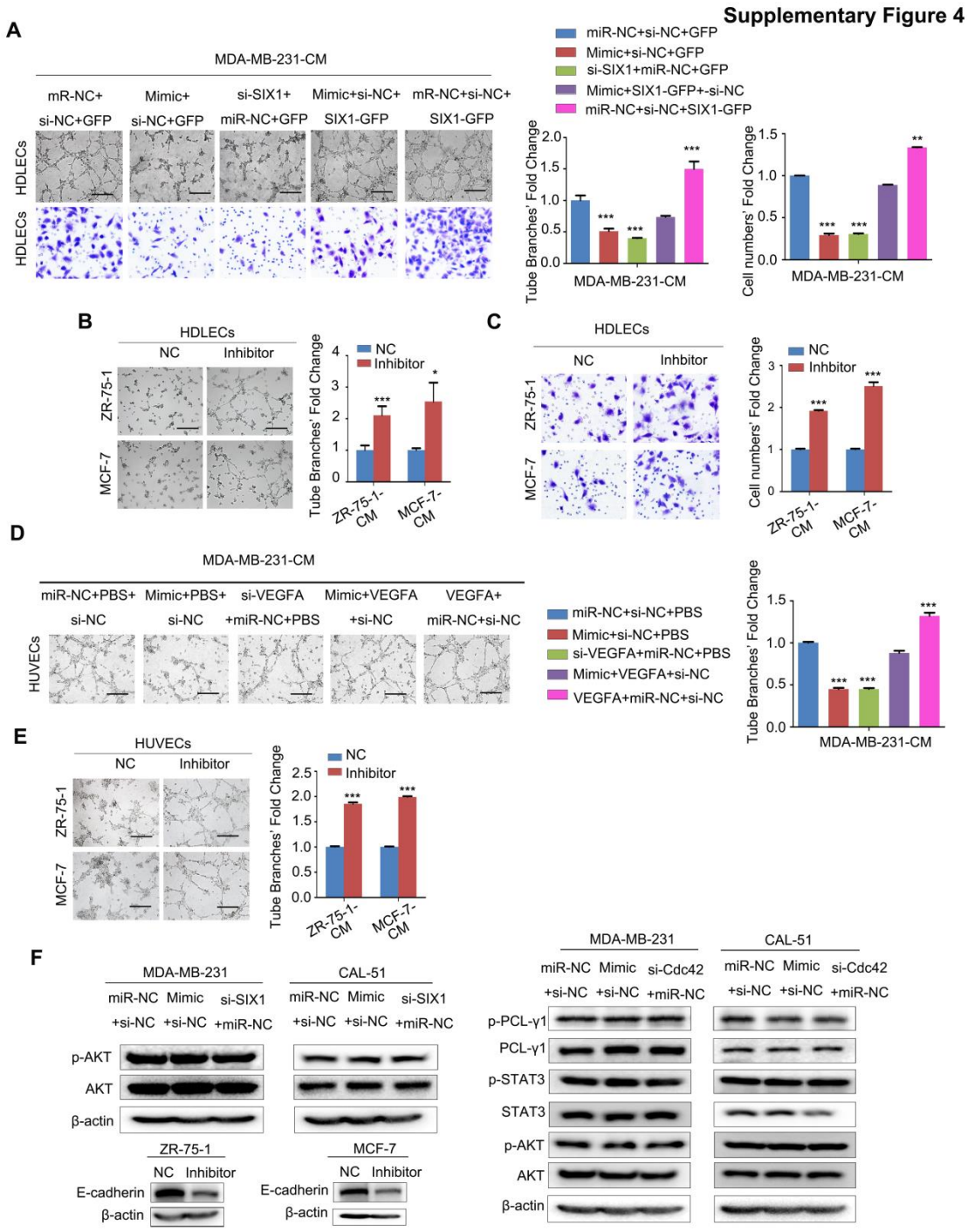


Supplementary Figure 2. (A) qPCR analysis of miR-4306 expression in cells transfected with mimic or cells transfected with inhibitor. (B-C) cells transfected with miR-4306 mimic (Mimic) or miRNA mimic control (miR-NC) and cells transfected with miR-4306 inhibitor (Inhibitor) or miRNA inhibitor control (miR-NC). (B) After transfection for 24 h, the xCELLigence Real-Time Cell Analyzer (RTCA)-MP system was used to analyze the effects of miR-4306 on cell proliferation. (C) After transfection for 48 h, transwell assays were performed to analyze the effects of miR-4306 on cell migration and invasion. The quantitative data are shown in the histograms, and the photographs are representative of the migrated/invaded cells. Original magnification, ×100. The data are representative of three independent experiments. The error bars represent the SEM. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$; two-tailed unpaired Student's t-test. (D-E) RIP assays were performed with Ago2 antibody. IgG served as the negative control. The association between SIX1/Cdc42/VEGFA, miR-4306 and Ago2 was ascertained by analyzing CAL-51(D) and MDA-MB-231(E) cell lysates using RNA immunoprecipitation with an Ago2 antibody. (F-K) Kaplan-Meier curves for breast cancer patients with low versus high expression levels of SIX1/Cdc42/VEGFA; log-rank test.



Supplementary Figure 3. (A-D) MDA-MB-231 and CAL-51 cells were transfected with miR-4306 mimic or Cdc42/SIX1 siRNA or cotransfected miR-4306 mimic and the Cdc42/SIX1 plasmid. (A) Western blot analysis showing SIX1, Cdc42 and EGFR expression. (B) The xCELLigence Real-Time Cell Analyzer (RTCA)-MP system was used to analyze growth ability after transfection for 24 h. (C) Transwell assays were used to analyze migration and invasion abilities after transfection for 48 h. The quantitative data are shown in the histograms, and the photographs are representative of the migrated/invaded cells. Original magnification, ×100. (D)

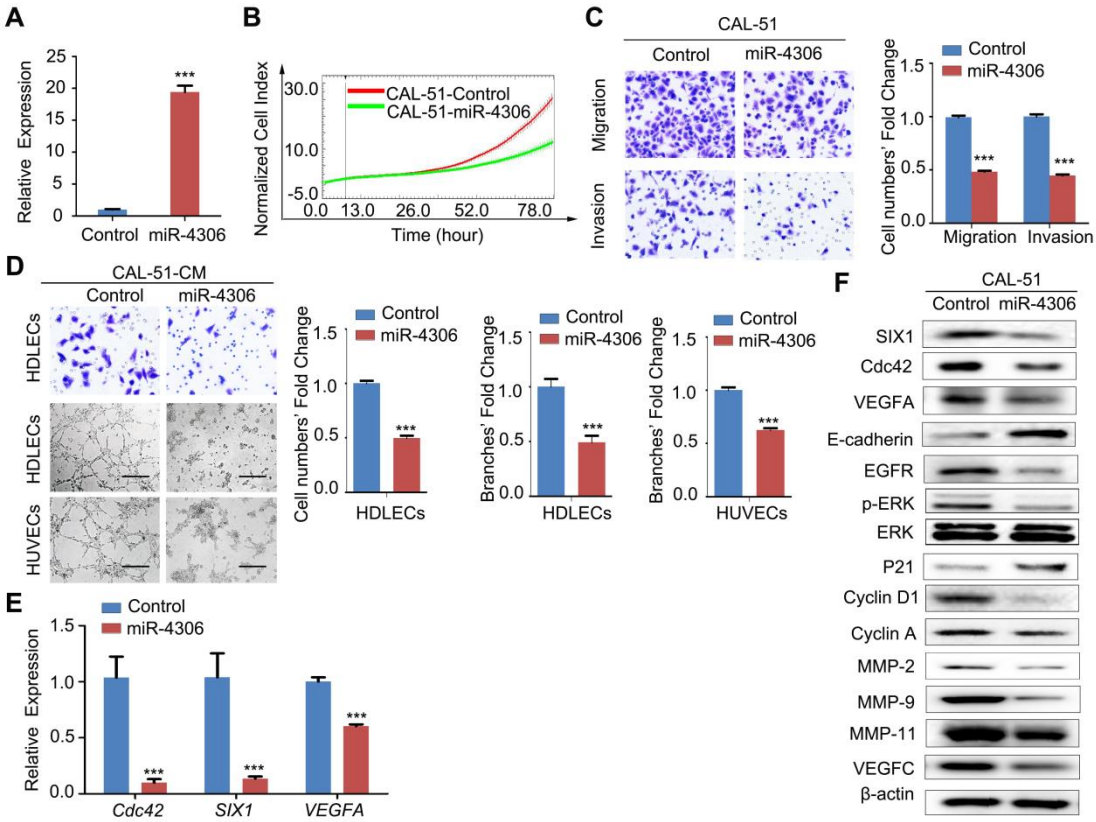
CAL-51/MDA-MB-231 cells were transfected with miR-4306 mimic, Cdc42/SIX1 siRNA or control for 48 h. Flow cytometry analysis showing the effects of miR-4306 mimic or Cdc42/SIX1 knockdown on the cell cycle. The data are representative of three independent experiments. The error bars represent the SEM. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$; two-tailed unpaired Student's *t*-test.



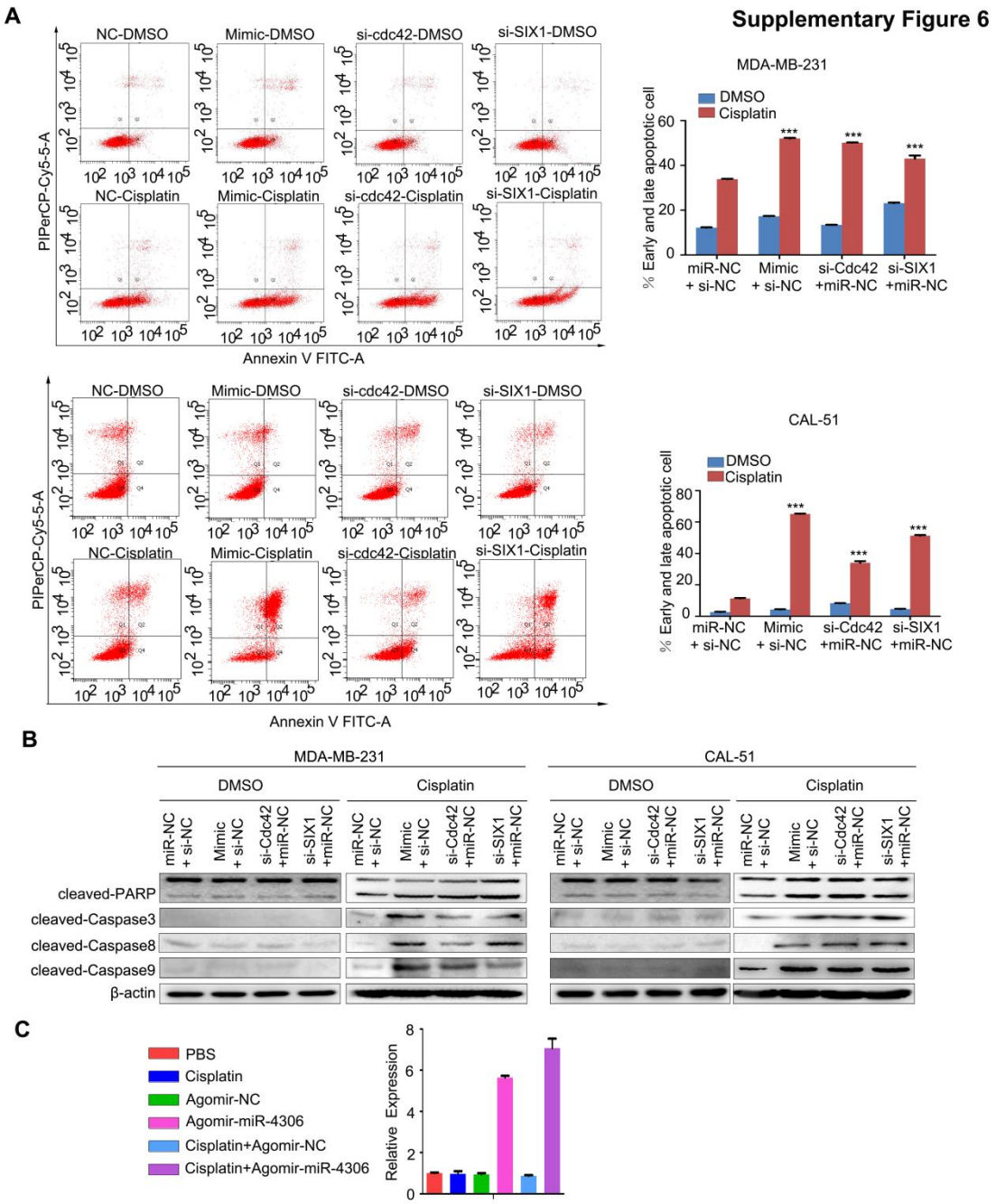
Supplementary Figure 4. MDA-MB-231 and CAL-51 cells were transfected with miR-4306 mimic or SIX1/VEGFA siRNA or cotransfected miR-4306 mimic and the SIX1 plasmid/VEGFA.

(A) Representative images of HDLECs cultured with conditioned medium from miR-4306-overexpressing cells, SIX1-silenced cells, miR-4306- SIX1-overexpressing, miR-4306-SIX1-overexpressing and control cells. Matrigel tube formation assay (scale bar: 20μm) and migration assay (original magnification, ×100). (B-C) MCF-7 and ZR-75-1 cells were transfected with miR-4306 inhibitor and controls. (B) Matrigel tube formation assay. Scale bar: 20μm. (C) Migration assay. Original magnification, ×100. Representative images of HDLECs cultured with conditioned medium from miR-4306 inhibitor cells and control cells. (D) Matrigel tube formation assay. Representative images of HUVECs cultured with conditioned medium from miR-4306 inhibitor cells and control cells. Scale bar: 20 μm. (E) Matrigel tube formation assay. Representative images of HUVECs cultured with conditioned medium derived from miR-4306-overexpressing cells, VEGFA-silenced cells, miR-4306-overexpressing cells with added VEGFA and control cells. Scale bar: 20 μm. (F) Western blot analysis showing E-cadherin expression levels in miR-4306 inhibitor-treated cells. The data are representative of three independent experiments. The error bars represent the SEM. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$; two-tailed unpaired Student's *t*-test.

Supplementary Figure 5



Supplementary Figure 5. (A) CAL-51 cells were stably infected with lentiviral vectors expressing control (Control) or miR-4306 (lenti-miR-4306), and the miR-4306 levels were analyzed via qPCR. (B) The xCELLigence Real-Time Cell Analyzer (RTCA)-MP system was used to perform a growth analysis; the results show that proliferation ability was decreased in lenti-miR-4306 cells compared to that in control cells. (C) Transwell assays were used to show that motility was lower in lenti-miR-4306 cells than in control cells. (D) Matrigel tube formation assay and migration assay. Representative images of HDLECs/HUVECs cultured with conditioned medium from miR-4306-overexpressing cells and control cells. Scale bar: 20 μm. (E) qPCR analysis of Cdc42, SIX1, and VEGFA levels in lenti-miR-4306 cells and control cells. The data are representative of three independent experiments. The error bars represent the SEM. ***$P < 0.001$; two-tailed unpaired Student's *t*-test. (F) Western blot analysis of protein levels in lenti-miR-4306 cells compared to those in control cells.



Supplementary Figure 6. MDA-MB-231 and CAL-51 cells were transfected with miR-4306 mimic, Cdc42/SIX1 siRNA or control. (A) Flow cytometry analysis of Annexin V/PI cells after the indicated cells were treated with cisplatin (20 μg/ml) for 24 h. The results are expressed as percentages of the total cells. (B) Western blot analysis of apoptosis-related protein levels after the indicated cells were treated with cisplatin (20 μg/ml) for 24 h. (C) qPCR analysis of miR-4306 levels in tumors from the PBS, cisplatin, agomir control, miR-4306 agomir, cisplatin and agomir control, and cisplatin and miR-4306 agomir groups. The data are representative of three independent experiments. The error bars represent the SEM. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$;

two-tailed unpaired Student's *t*-test.