Figure S1. Characterization of bazedoxifene. (A) Surface plasmon resonance (SPR) analysis of bazedoxifene binding to IL-6Rα was immobilized on a CM5 sensor chip, and bazedoxifene was injected into the flow cells. (B) T-200 BIA evaluation software was used to subtract references and determine the steady-state K_D. IL-6Rα, interleukin 6 receptor α.

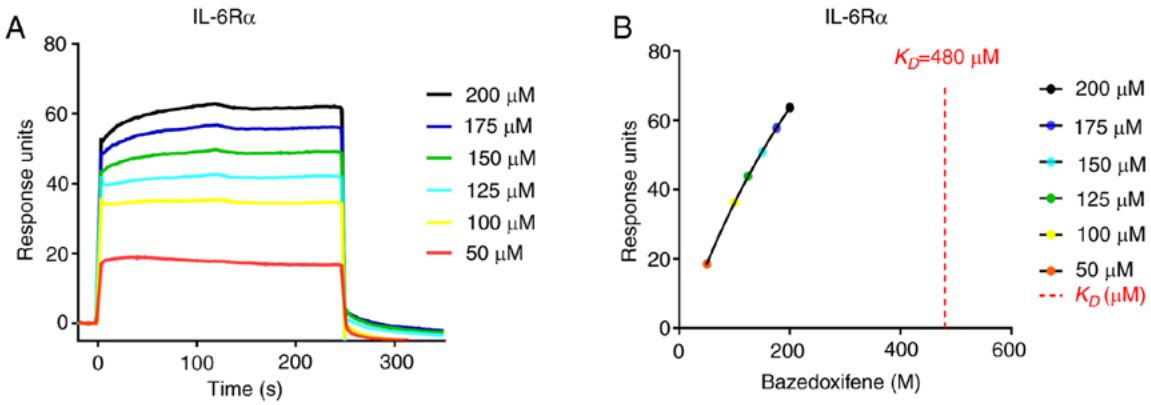


Figure S2. Bazedoxifene, paclitaxel and their combination inhibit cell viability and proliferation of ovarian cancer cells. (A) A2780 and TOV112D cells were treated with bazedoxifene at the indicated concentrations in triplicate for 48 h and processed for MTT assay to analyse cell viability (*P<0.05, **P<0.01, ***P<0.001). (B) A2780 and TOV112D cells were treated with bazedoxifene (B), paclitaxel (P) and their combination (B+P) at the indicated concentration in triplicate for 48 h and processed for MTT assay to analyse cell viability (*P<0.05, **P<0.01, ***P<0.001). (C) Colony formation assay revealed that bazedoxifene combined with paclitaxel significantly reduced the colony growth of A2780 and TOV112D cells. Data are representative of results obtained from three independent proliferation assay, and three replicates were analysed in each assay (*P<0.05, **P<0.01, ***P<0.001). CI, combination index.

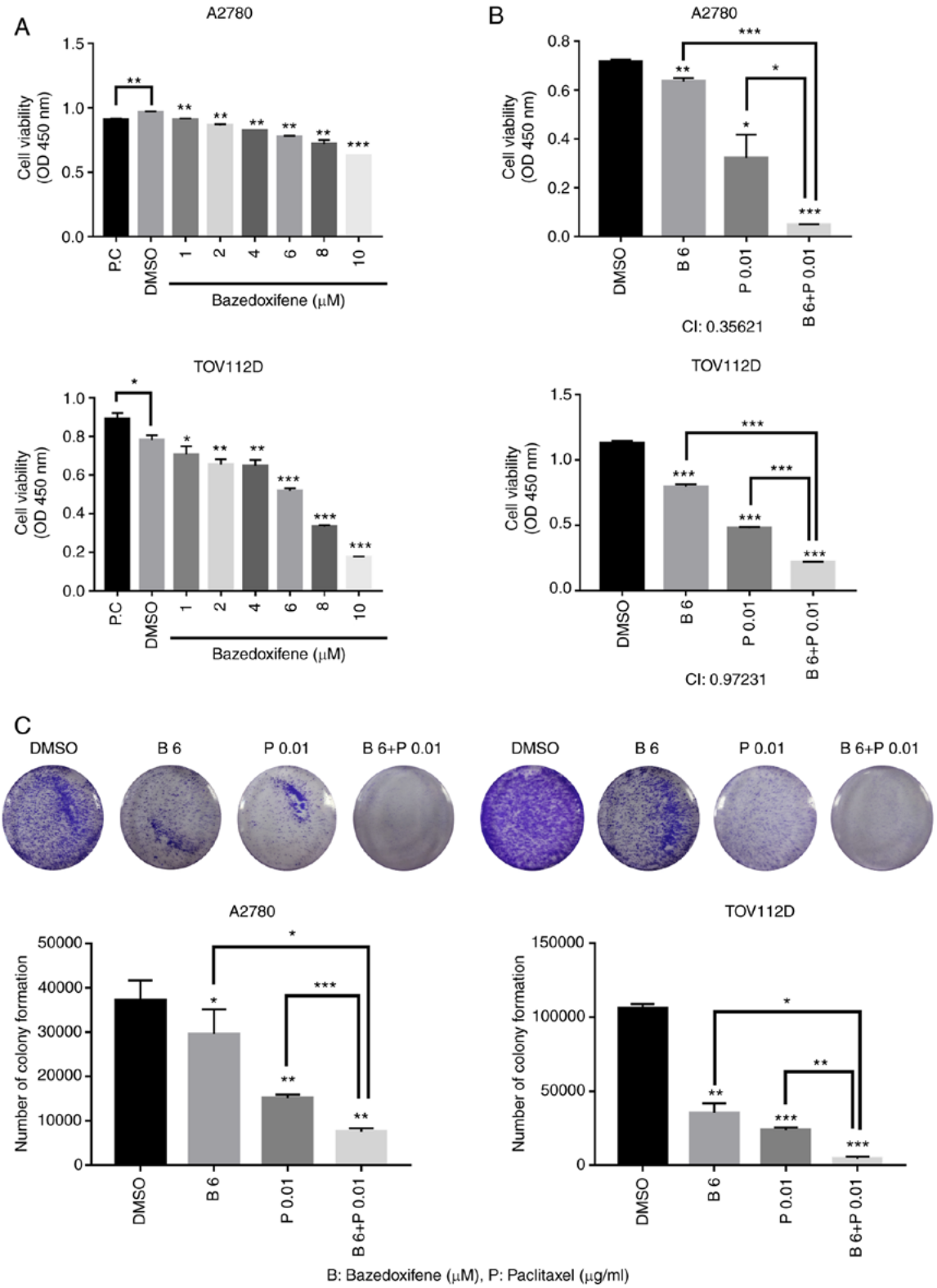


Figure S3. Bazedoxifene and paclitaxel or their combination inhibit the migration and invasion of ovarian cancer cells. (A) A2780 and TOV112D cells were treated with bazedoxfiene (B), paclitaxel (P) or their combination (B+P) and allowed to migrate to the scratched area for 48 h. Yellow coloured lines indicate a gap in the scratched area. The percentage of the migrating area in the wound-healing assay was quantified in A2780 and TOV112D cells (*P<0.05, **P<0.01, ***P<0.001). (B) Matrigel invasion assay was used to determine invasion after 48 h in A2780 and TOV112D cells treated with bazedoxfiene (B), paclitaxel (P) or their combination (B+P). Bars indicate mean ± standard deviation of three independent experiments performed in triplicate (*P<0.05, **P<0.01, ***P<0.001).

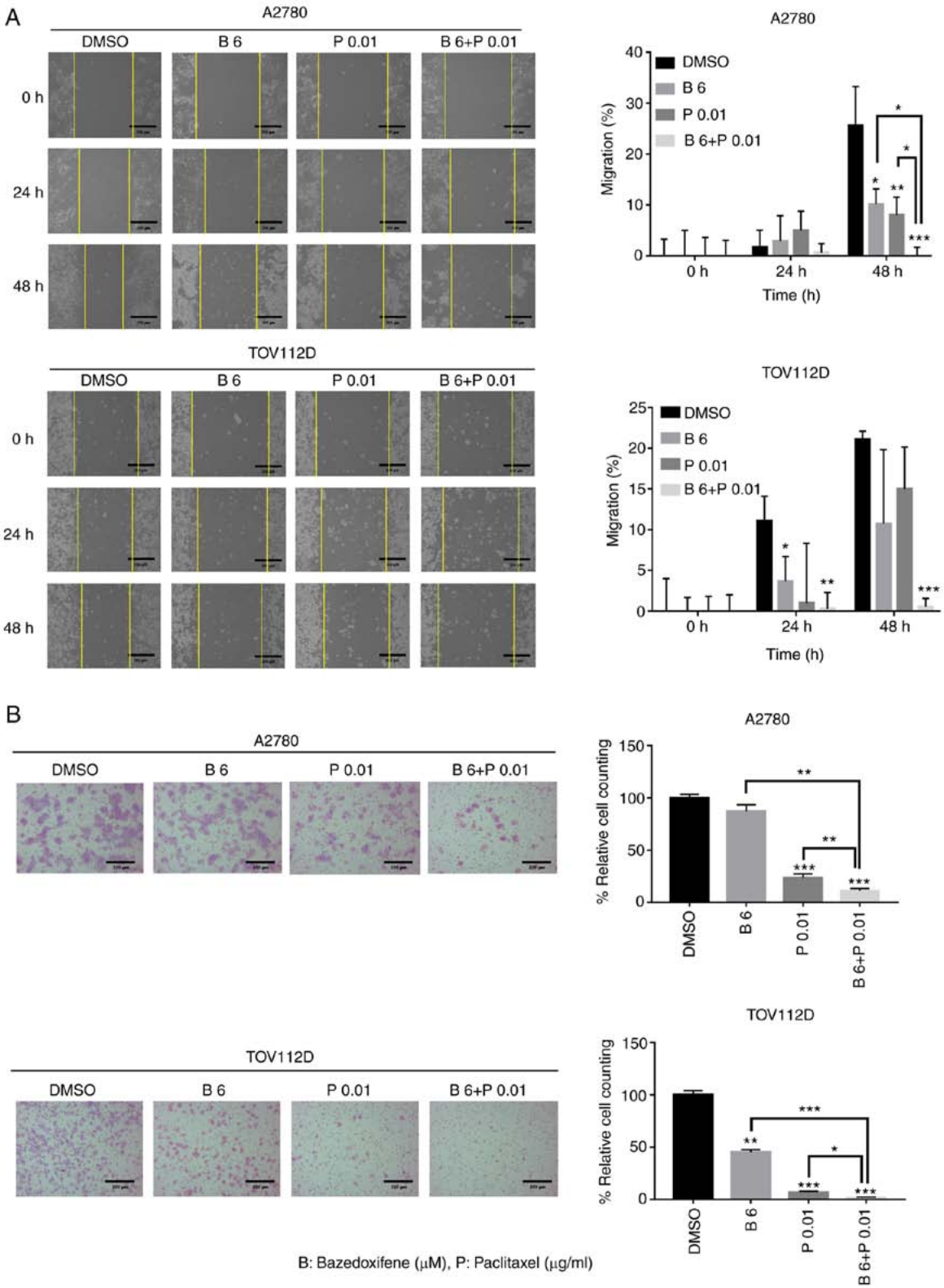


Figure S4. Bazedoxifene has no significant effect on the migration of ovarian cancer cells transfected with siSTAT3. (A and B) The inhibitory effect of bazedoxifene on the migration of OVCA433 (A) and SKOV3 (B) cells after transfection with siNC or siSTAT3-4 (*P<0.05, **P<0.01, ***P<0.001; NS, not significant). STAT3, signal transducer and activator of transcription 3; NC, negative control.

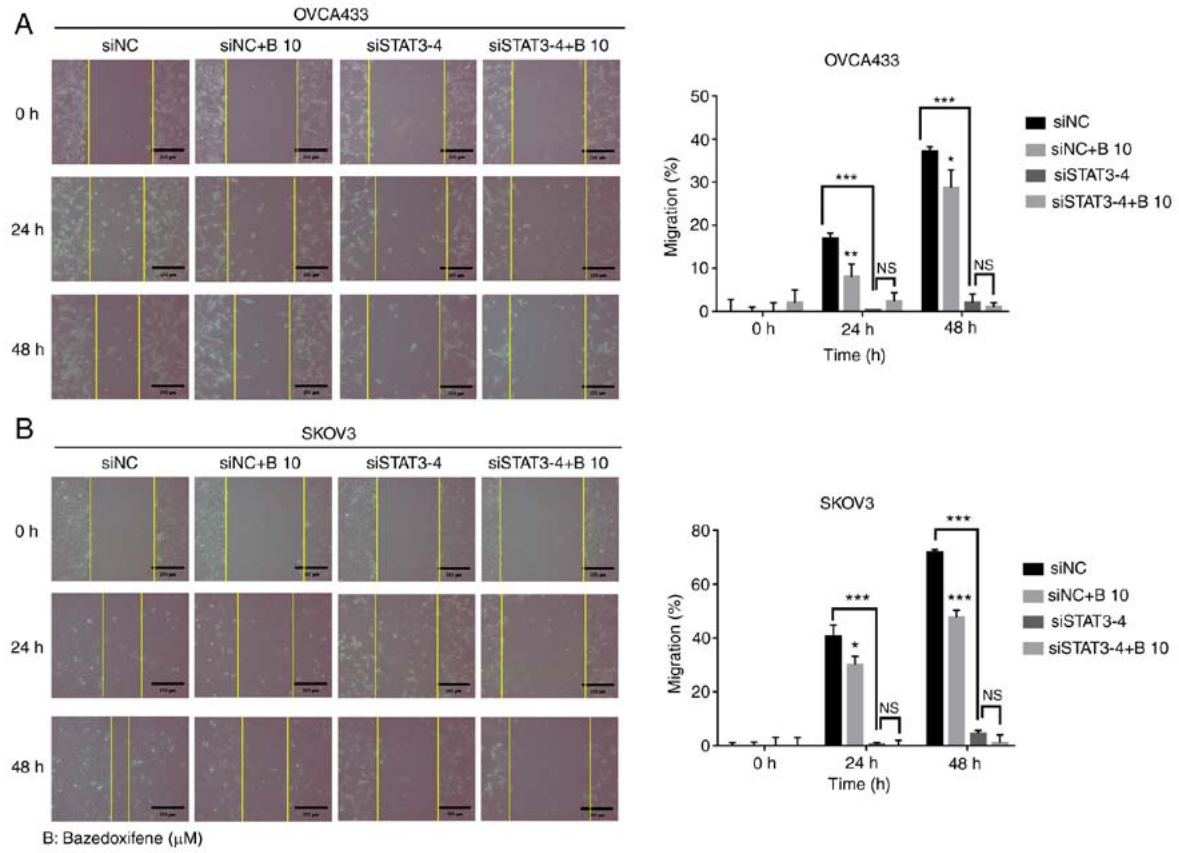


Figure S5. The whole western blot analysis for Fig. 4A-D. (A) The whole western blot membrane and expression levels of estrogen receptors (ERα and ERβ), and phosphorylated (p)-STAT3 were confirmed in A2780, OVCA433, SKOV3 and TOV112D cells. (B) The whole western blot membrane and decreased expression levels of p-STAT3 in A2780 and TOV112D cells after treatment with bazedoxifene and IL-6 for 6 h at each concentration. (C) The whole western blot membrane and decreased expression levels of p-STAT3 and ERα in OVCA433 and SKOV3 cells after treatment with bazedoxifene for 6 h at each concentration. (D) The whole western blot membrane and expression of p-STAT3 and STAT3 was confirmed after treatment with siSTAT3 for 48 h in OVCA433 and SKOV3 cell lines (*P<0.05 identified by two-way ANOVA vs. DMSO+IL-6 or siNC). STAT3, signal transducer and activator of transcription 3; NC, negative control.

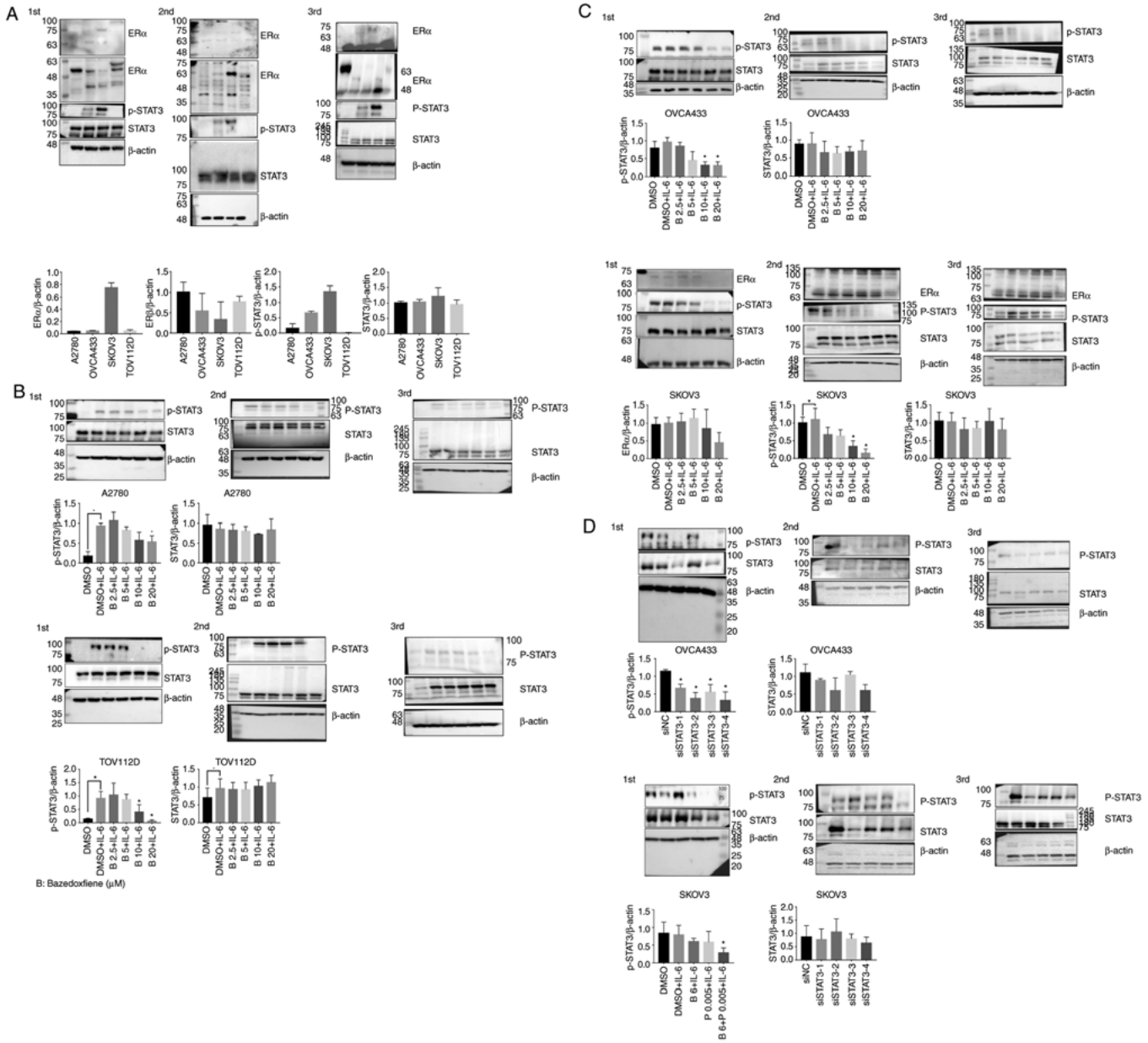


Figure S6. The whole western blot for ovarian cancer OVCA433 cells in Fig. 5A. (A) The whole western blot membrane by western blotting in OVCA433 cells. (B) Levels of phosphorylated (p)-GP130, GP130, p-STAT3, STAT3, p-Akt, Akt, p-p38 MAPK, p38 MAPK, p-ERK1/2, and ERK1/2 analysed by western blotting in OVCA433 cells. Data are presented as mean ± SD from three independent experiments (*P<0.05, **P<0.01, ***P<0.001 as identified by two-way ANOVA vs. DMSO+IL-6). STAT3, signal transducer and activator of transcription 3; GP130, glycoprotein 130; IL, interleukin.

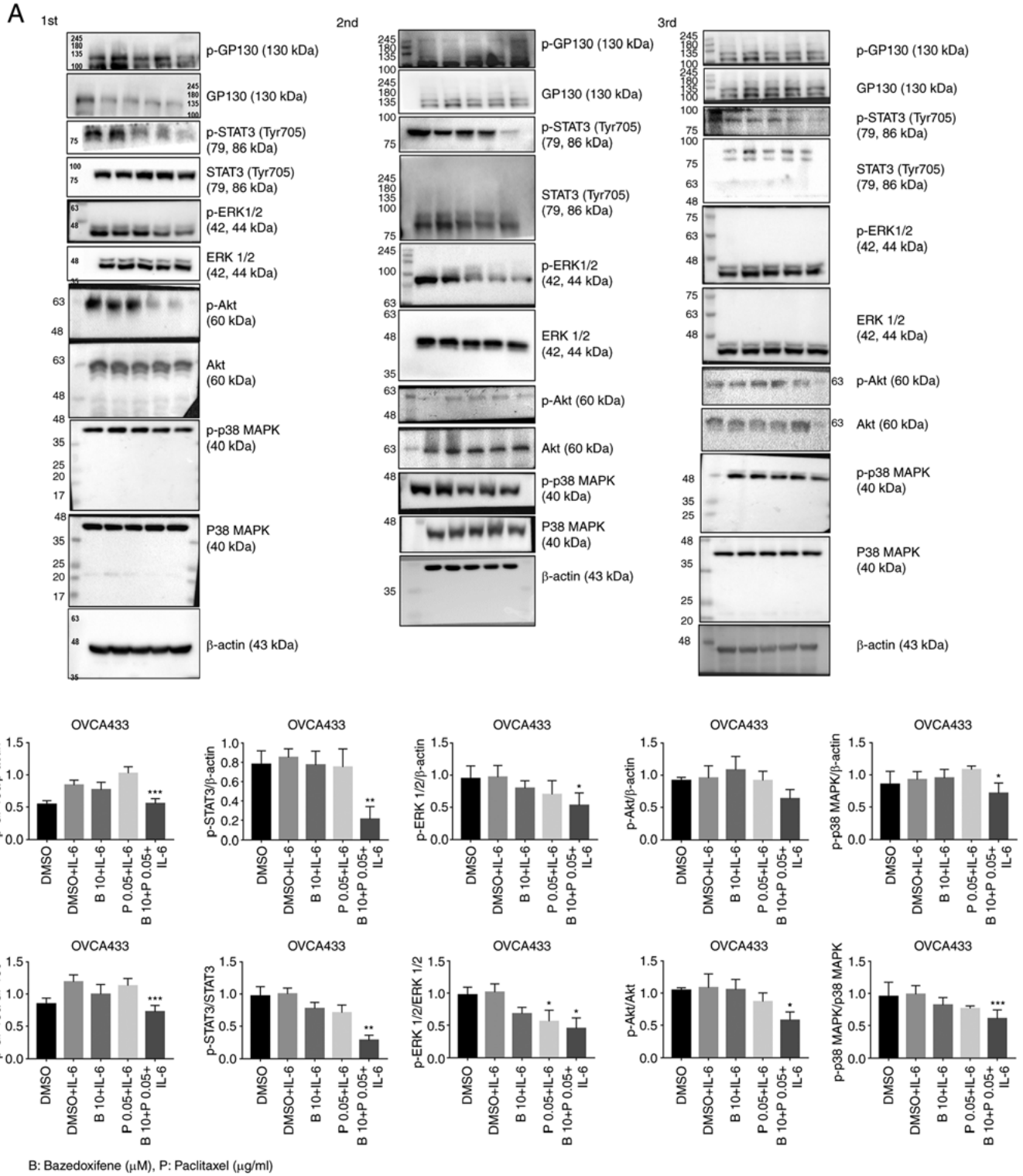


Figure S7. The whole western blot for SKOV3 in Fig. 5A. (A) The whole western blot membrane by western blotting in SKOV3 cells. (B) Levels of phosphorylated (p)-GP130, GP130, p-STAT3, STAT3, p-Akt, Akt, p-p38 MAPK, p38 MAPK, p-ERK1/2, and ERK1/2 analysed by western blotting in SKOV3 cells. Data are presented as mean ± SD from three independent experiments (*P<0.05, **P<0.01 as identified by two-way ANOVA vs. DMSO+IL-6). STAT3, signal transducer and activator of transcription 3; GP130, glycoprotein 130; IL, interleukin.

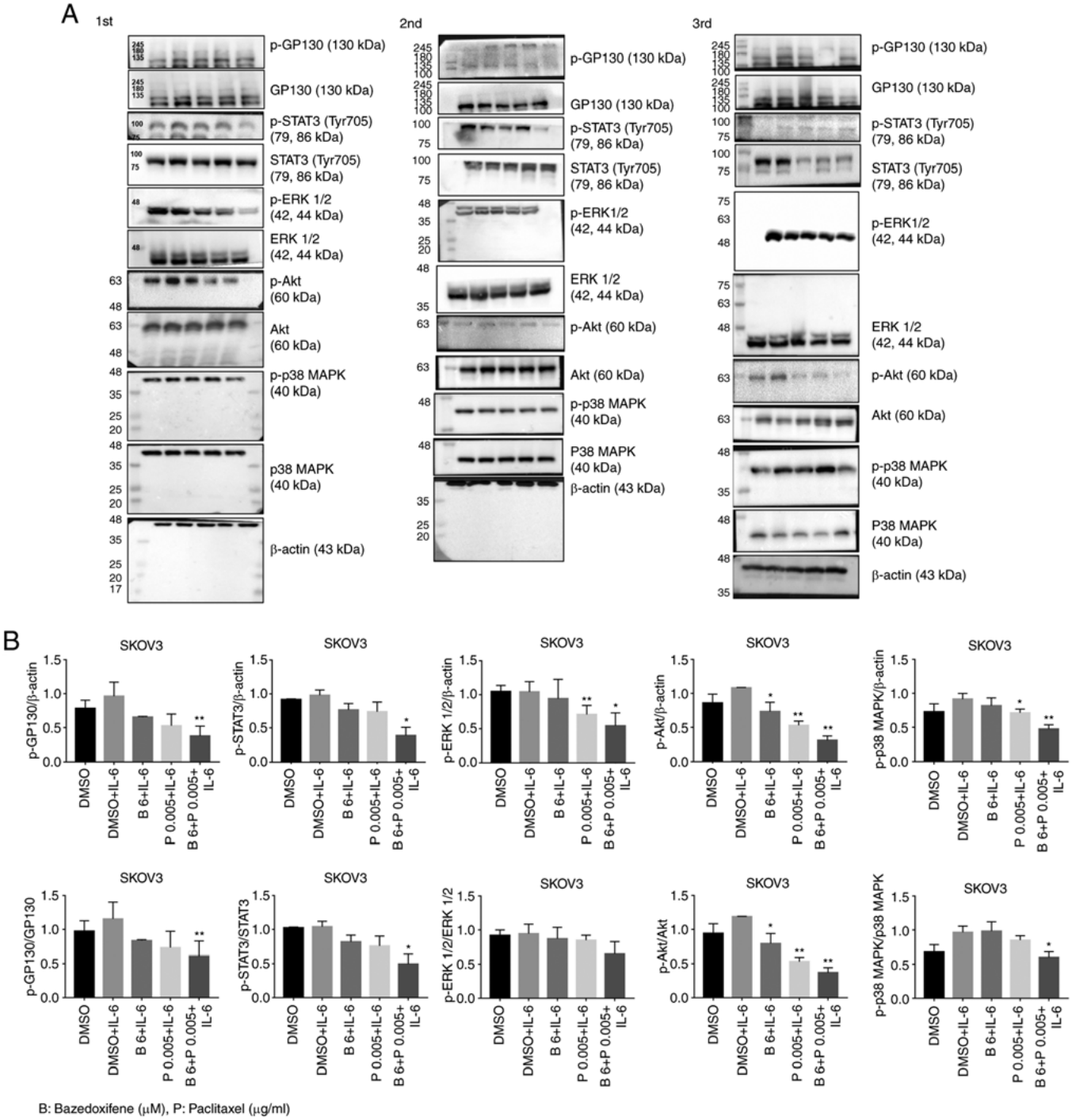


Figure S8. Combined treatment of bazedoxifene and paclitaxel inhibits the expression of phosphorylated (p)-GP130, p-STAT3, p-ERK1/2 and EMT-related proteins in A2780 and TOV112D cells. (A) Combined bazedoxifene and paclitaxel decreased the expression of p-GP130, p-STAT3 and p-ERK1/2 in ovarian cancer A2780 and TOV112D cells. (B) The effect of combined bazedoxifene and paclitaxel on the expression of N-cadherin, E-cadherin, β-catenin, Vimentin, Snail, Twist, and claudin-1 (EMT markers) in A2780 and TOV112D cells. STAT3, signal transducer and activator of transcription 3; GP130, glycoprotein 130; EMT, epithelial-mesenchymal transition.

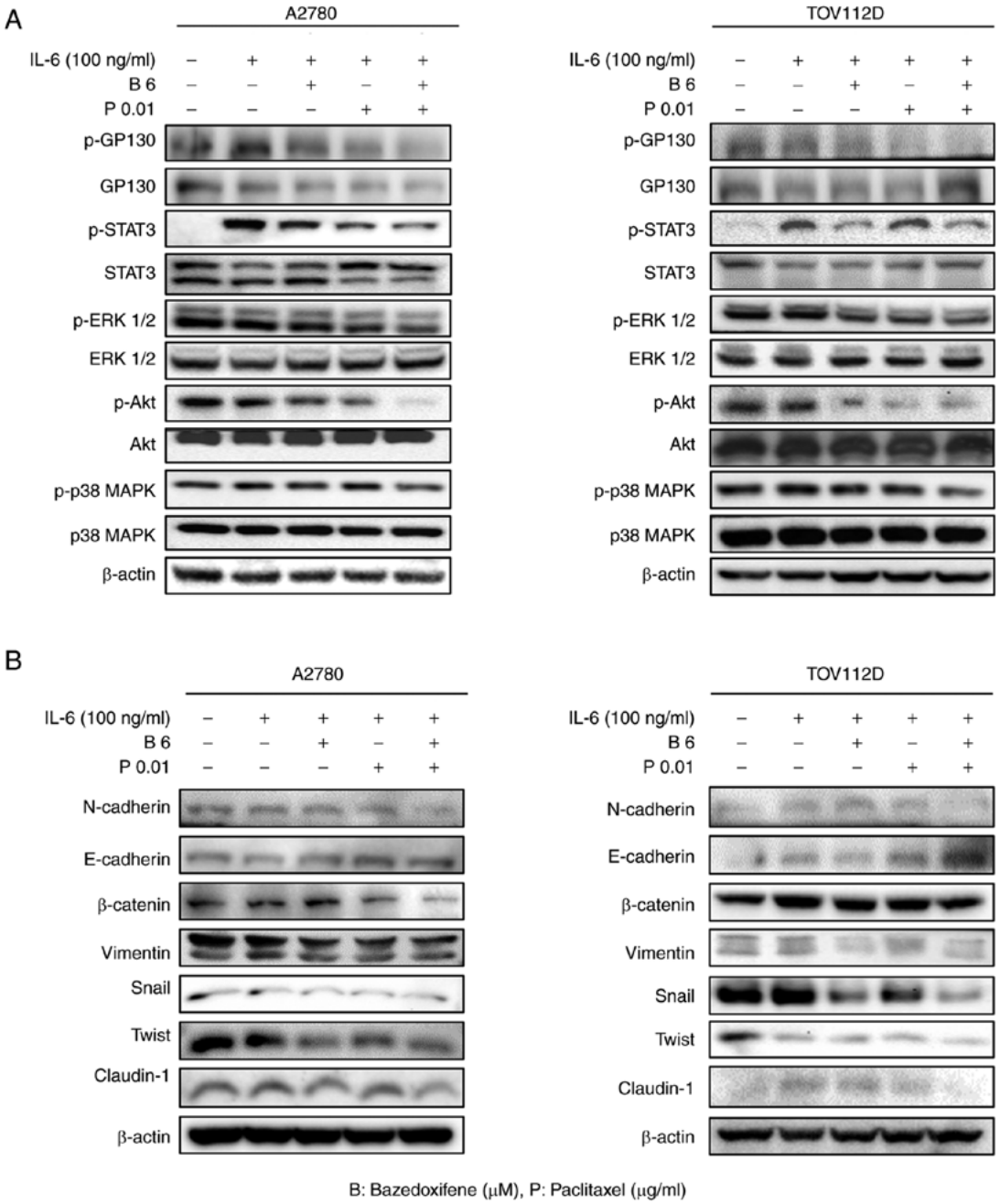


Figure S9. The whole western blot for A2780 cells in Fig. S8A. (A) The whole western blot membrane by western blotting in ovarian cancer A2780 cells. (B) Levels of phosphorylated (p)-GP130, GP130, p-STAT3, STAT3, p-Akt, Akt, p-p38 MAPK, p38 MAPK, p-ERK1/2, and ERK1/2 as analysed by western blotting in A2780 cells. Data are presented as mean ± SD form three independent experiments (*P<0.05, **P<0.01, as identified by two-way ANOVA vs. DMSO+IL-6). STAT3, signal transducer and activator of transcription 3; GP130, glycoprotein 130; IL, interleukin.

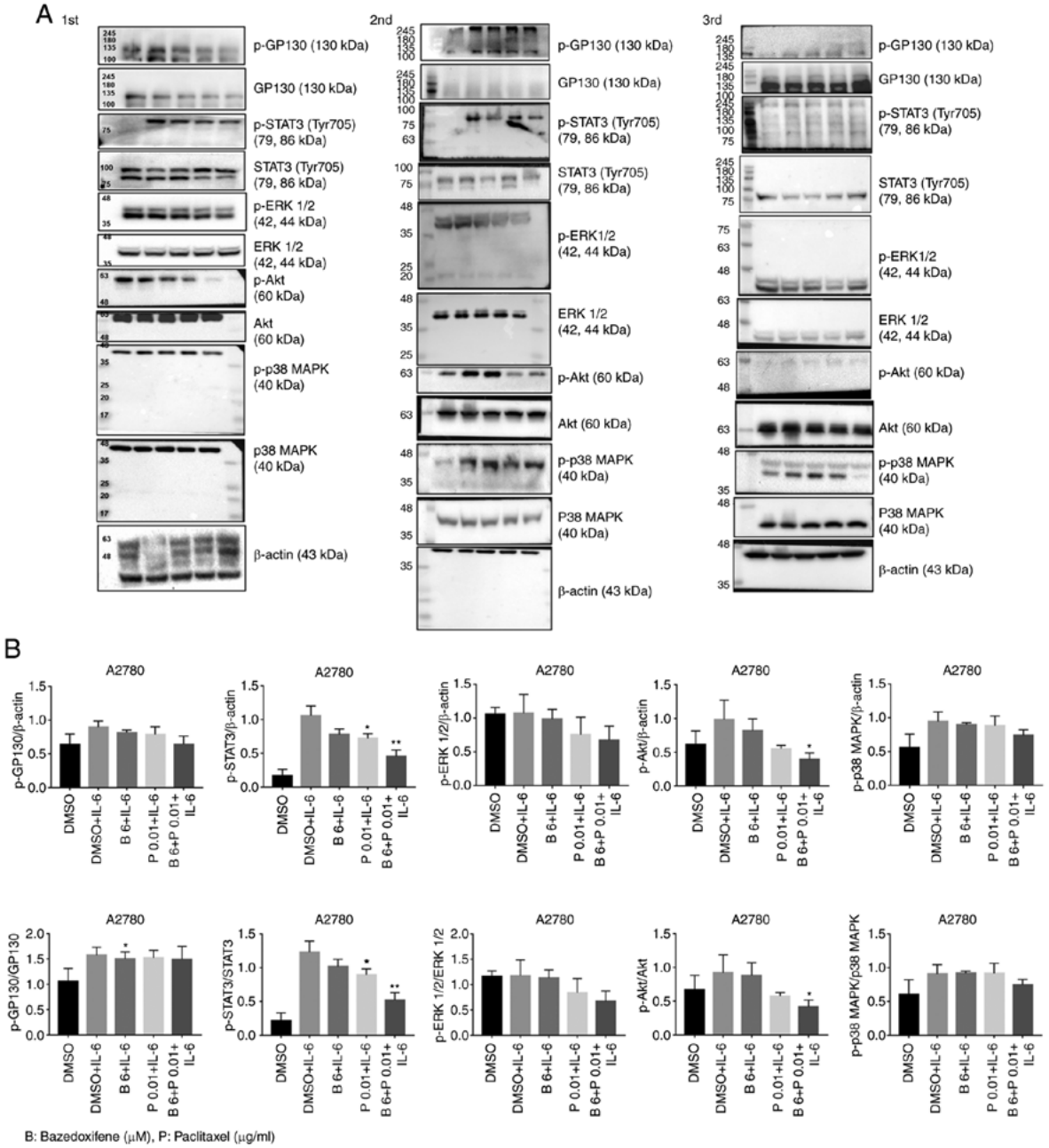


Figure S10. The whole western blot for TOV112D in Fig. S8A. (A) The whole western blot membrane by western blotting in ovarian cancer TOV112D cells. (B) Levels of phosphorylated (p)-GP130, GP130, p-STAT3, STAT3, p-Akt, Akt, p-p38 MAPK, p38 MAPK, p-ERK1/2, and ERK1/2 as analysed by western blotting in TOV112D cells. Data are presented as mean ± SD from three independent experiments ($^{*}P<0.05$, $^{**}P<0.01$, as identified by two-way ANOVA vs. DMSO+IL-6). STAT3, signal transducer and activator of transcription 3; GP130, glycoprotein 130; IL, interleukin.

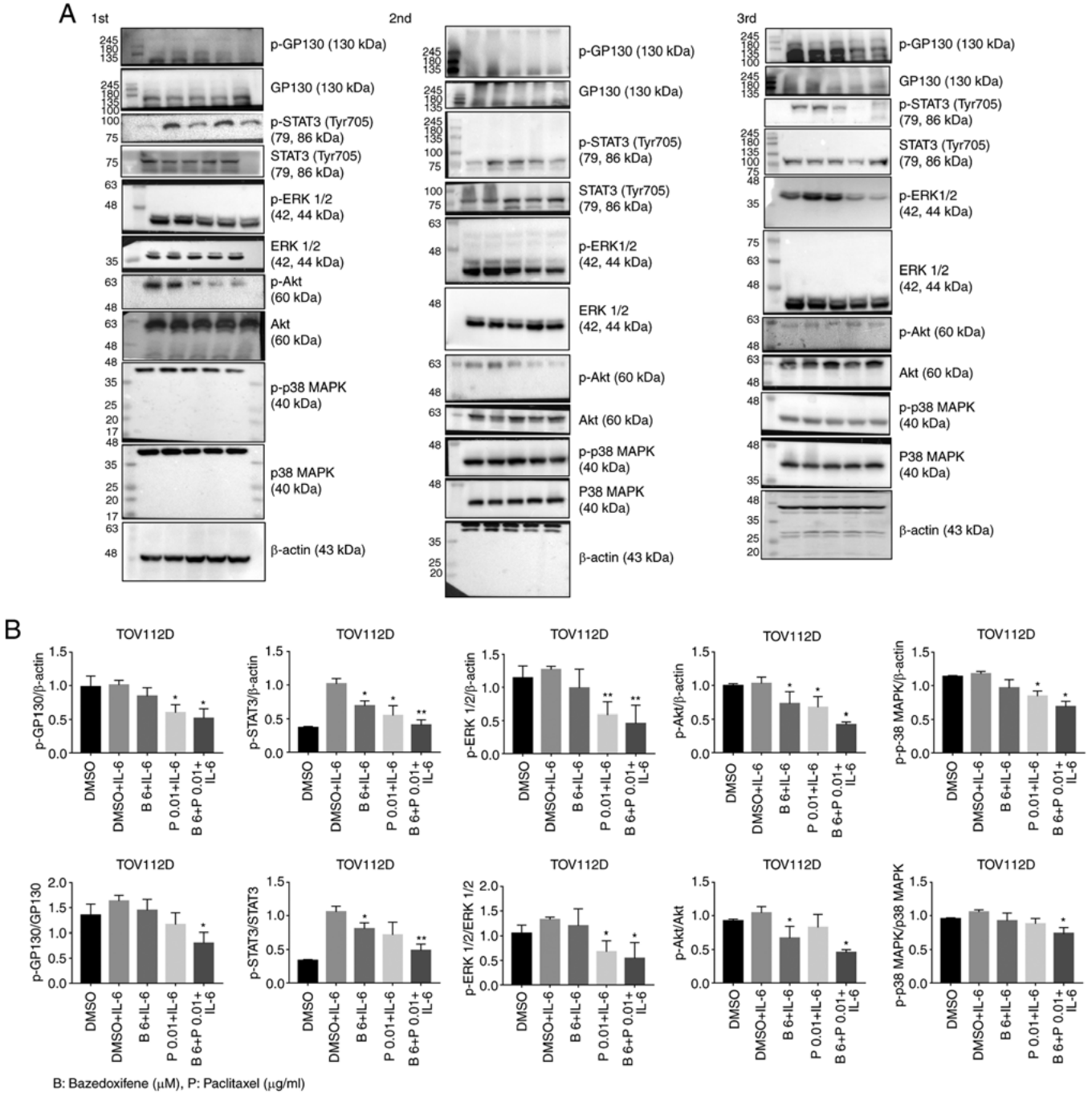


Figure S11. The whole western blot for OVCA433 in Fig. 5B. (A) The whole western blot membrane by western blotting in OVCA433 cells. (B) Levels of N-cadherin, E-cadherin, β-catenin, Vimentin, Snail, Twist, and claudin-1 as analysed by western blotting in OVCA433 cells. Data are presented as mean ± SD from three independent experiments ($^{*}P<0.05$, $^{**}P<0.01$ identified by two-way ANOVA vs. DMSO+IL-6).

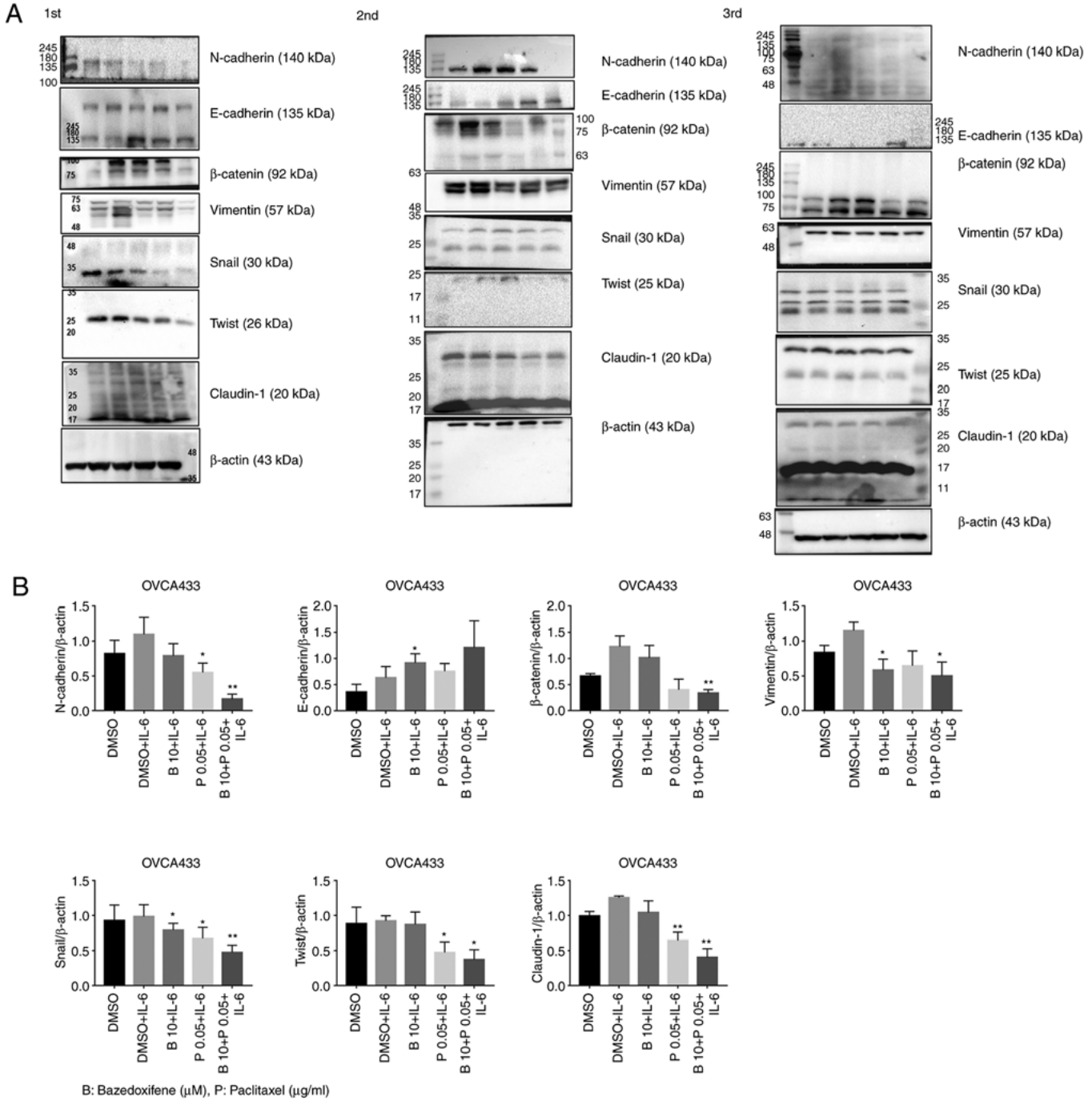
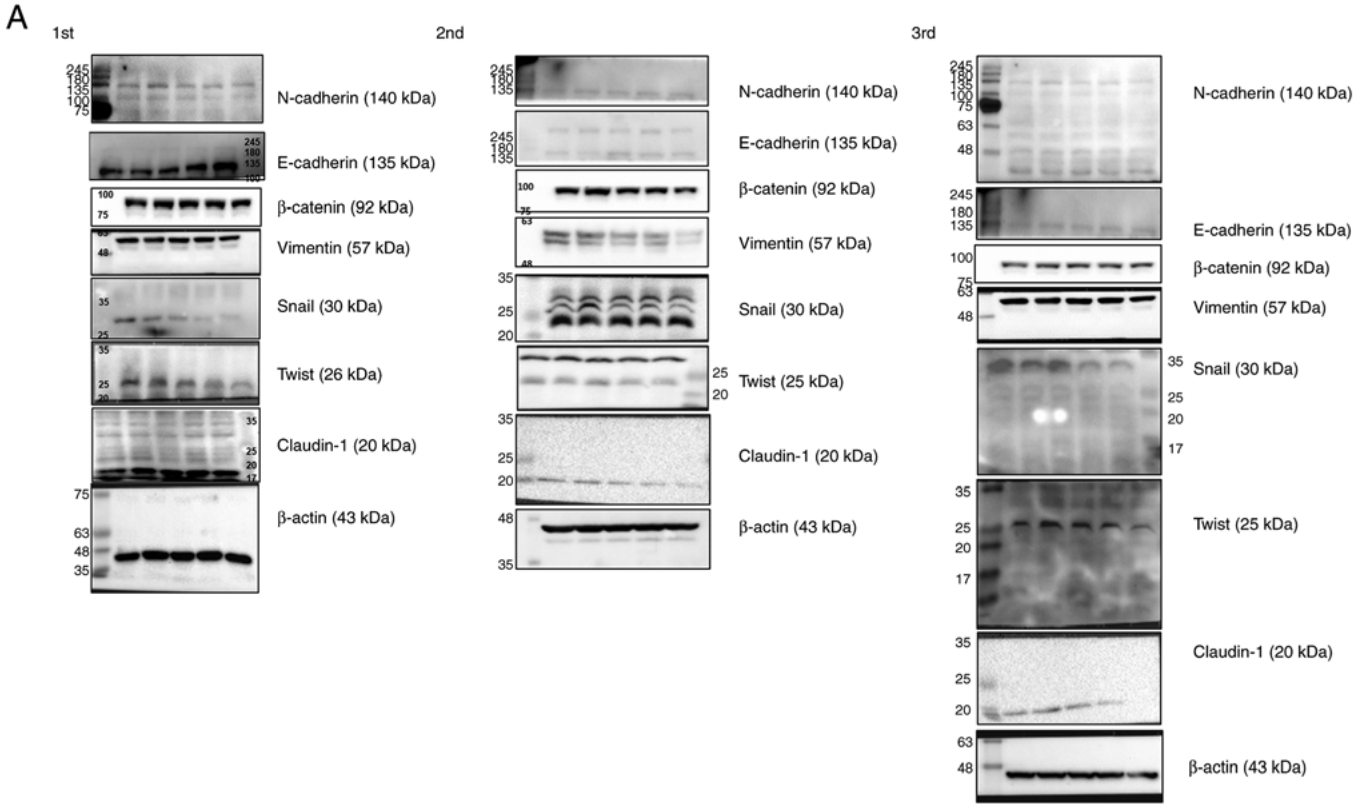
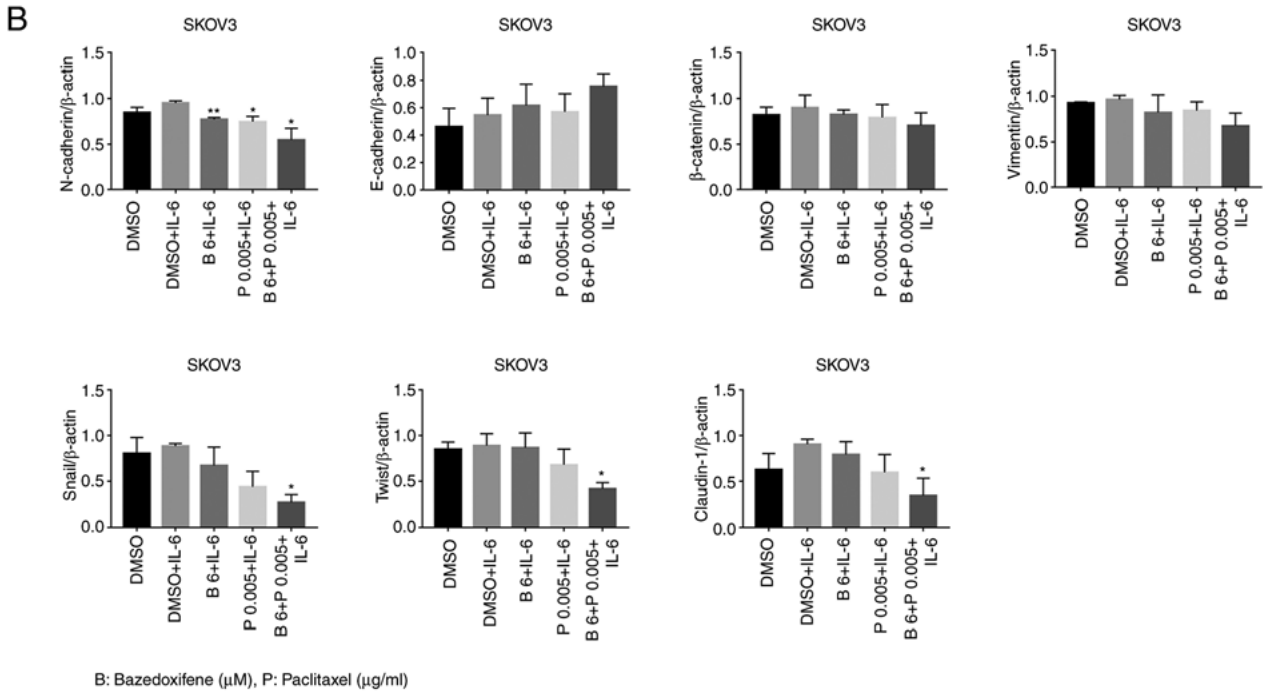


Figure S12. The whole western blot for SKOV3 in Fig. 5B. (A) The whole western blot membrane by western blotting in SKOV3 cells. (B) Levels of N-cadherin, E-cadherin, β-catenin, Vimentin, Snail, Twist, and claudin-1 as analysed by western blotting in SKOV3 cells. Data are presented as mean ± SD from three independent experiments ($^{*}P<0.05$, $^{**}P<0.01$ identified by two-way ANOVA vs. DMSO+IL-6).





B: Bazedoxifene (μM), P: Paclitaxel (μg/ml)

Figure S13. The whole western blot for A2780 in Fig. S8B. (A) The whole western blot membrane by western blotting in ovarian cancer A2780 cells. (B) Levels of N-cadherin, E-cadherin, β-catenin, vimentin, Snail, Twist, and claudin-1 as analysed by western blotting in A2780 cells. Data are presented as mean ± SD from three independent experiments (*P<0.05, **P<0.01, as identified by two-way ANOVA vs. DMSO+IL-6). IL, interleukin.

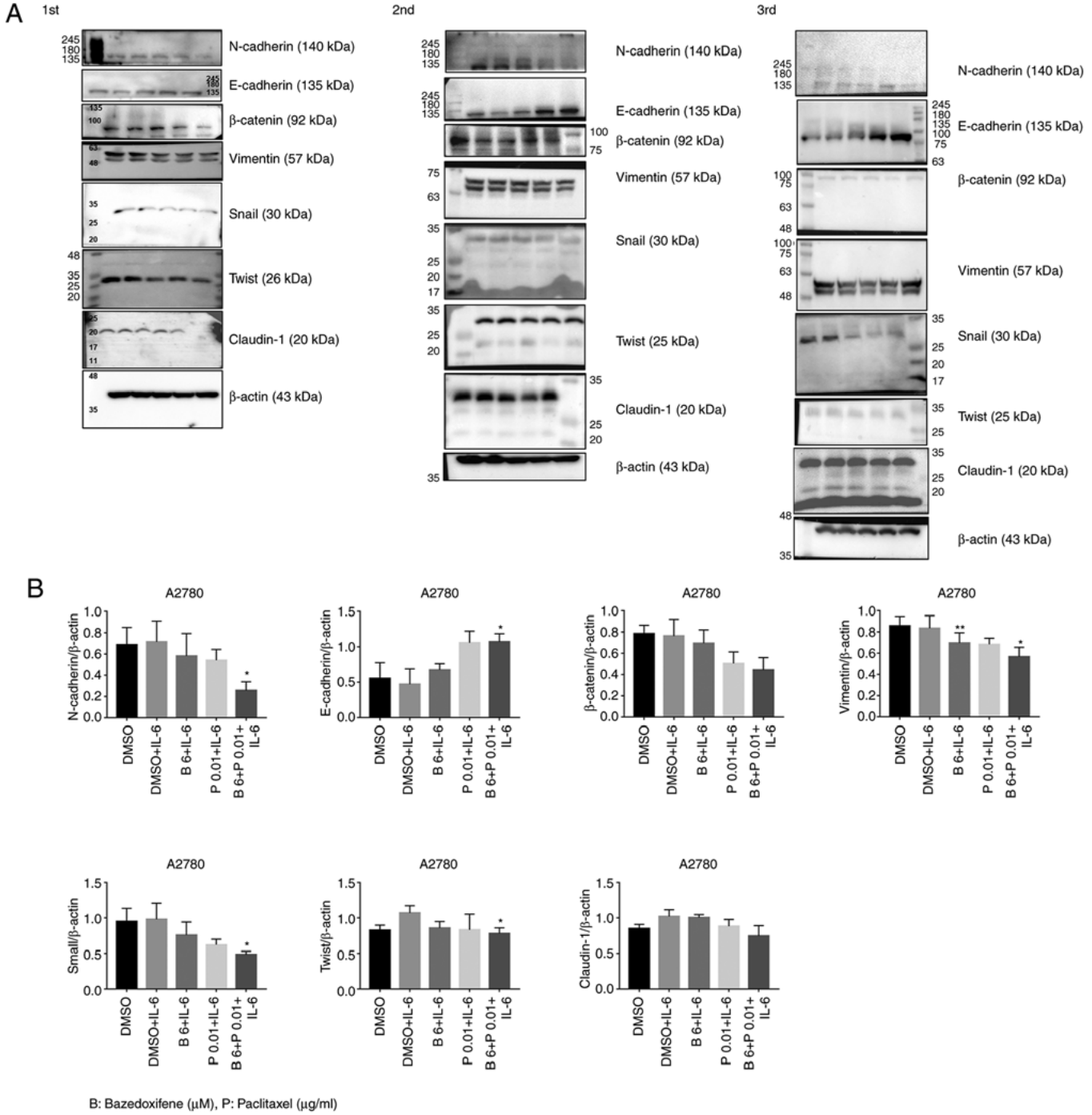


Figure S14. The whole western blot for TOV112D in Fig. S8B. (A) The whole western blot membrane by western blotting in ovarian cancer TOV112D cells. (B) Levels of N-cadherin, E-cadherin, β-catenin, Vimentin, Snail, Twist, and claudin-1 as analysed by western blotting in TOV112D cells. Data are presented as mean ± SD from three independent experiments (*P<0.05, **P<0.01, as identified by two-way ANOVA vs. DMSO+IL-6). IL, interleukin.

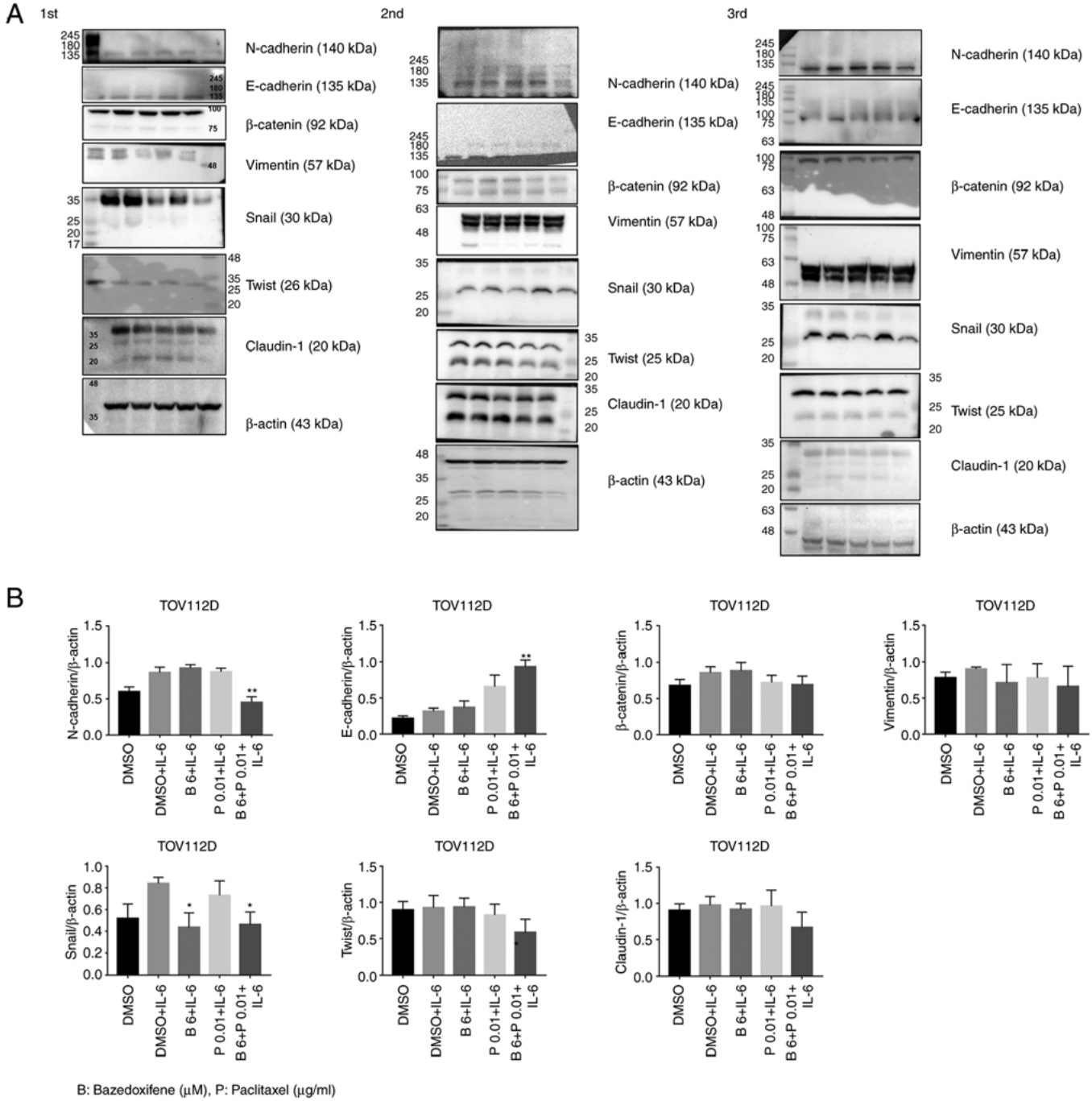


Figure S15. The whole western blot for OVCA433 cells in Fig. 6. (A) The whole western blot membrane by western blotting in Fig. 6A. (B) Levels of cyclin D1, CDK4, CDK6, $p21^{WAF1}$, and $p27^{KIPLas}$ analysed by western blotting in ovarian cancer OVCA433 cells. (C) The whole western blot membrane by western blotting in Fig. 6B. (D) Levels of Mcl-1, Bcl-xl, Bcl-2, and Bax analysed by western blotting in OVCA433 cells. Data are presented as mean ± SD from three independent experiments ($^{*}P<0.05$, $^{**}P<0.01$, as identified by two-way ANOVA vs. DMSO).

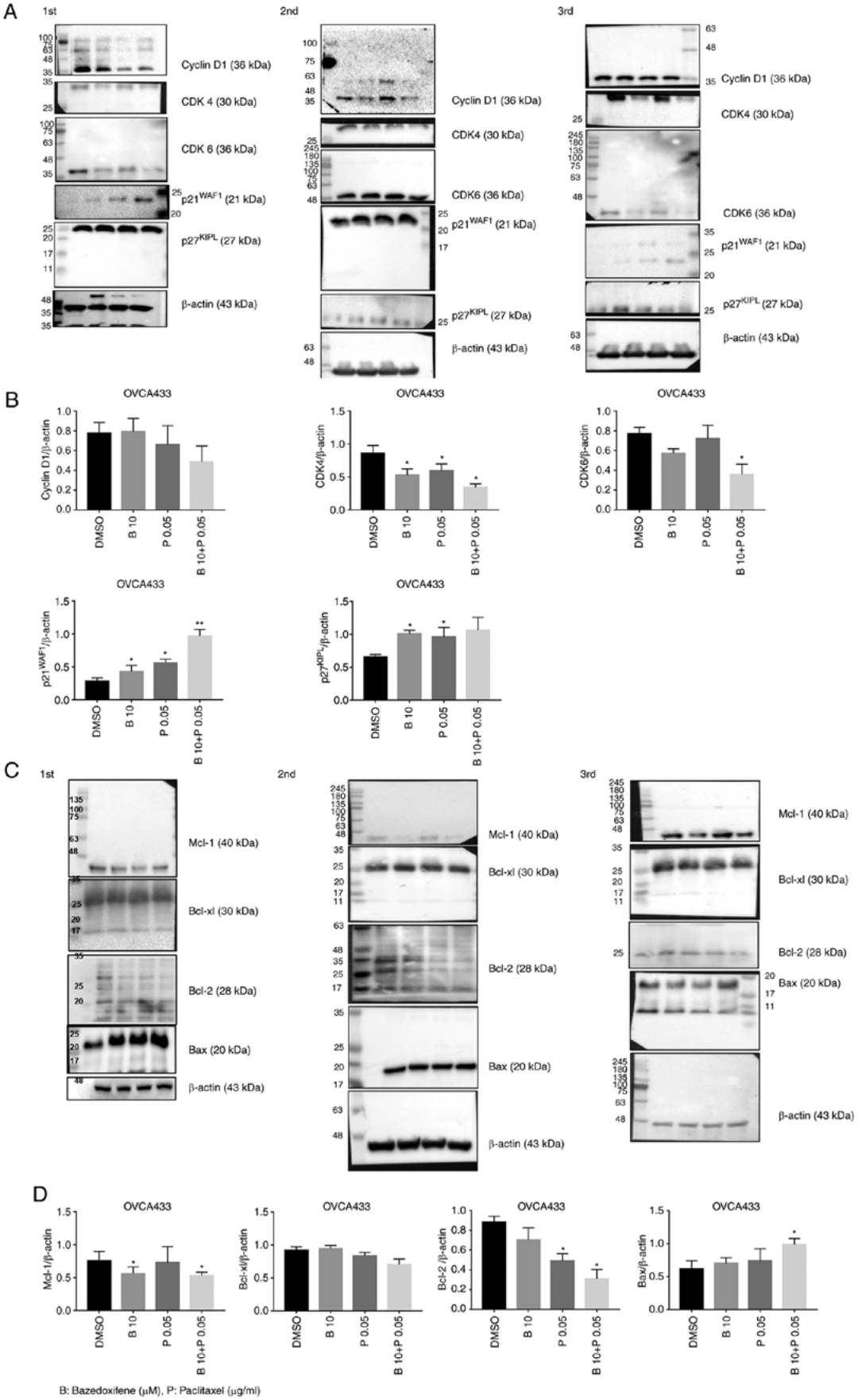


Figure S16. The whole western blot for SKOV3 in Fig. 6. (A) The whole western blot membrane by western blotting in Fig. 6A. (B) Levels of cyclin D1, CDK 4, CDK 6, $p21^{WAF1}$, and $p27^{KIPL}$ as analysed by western blotting in SKOV3 cells. (C) The whole western blot membrane by western blotting in Fig. 6B. (D) Levels of Mcl-1, Bcl-xl, Bcl-2, and Bax analysed by western blotting in SKOV3 cells. Data are presented as mean ± SD form three independent experiments ($^{*}P<0.05$, $^{**}P<0.01$, as identified by two-way ANOVA vs. DMSO).

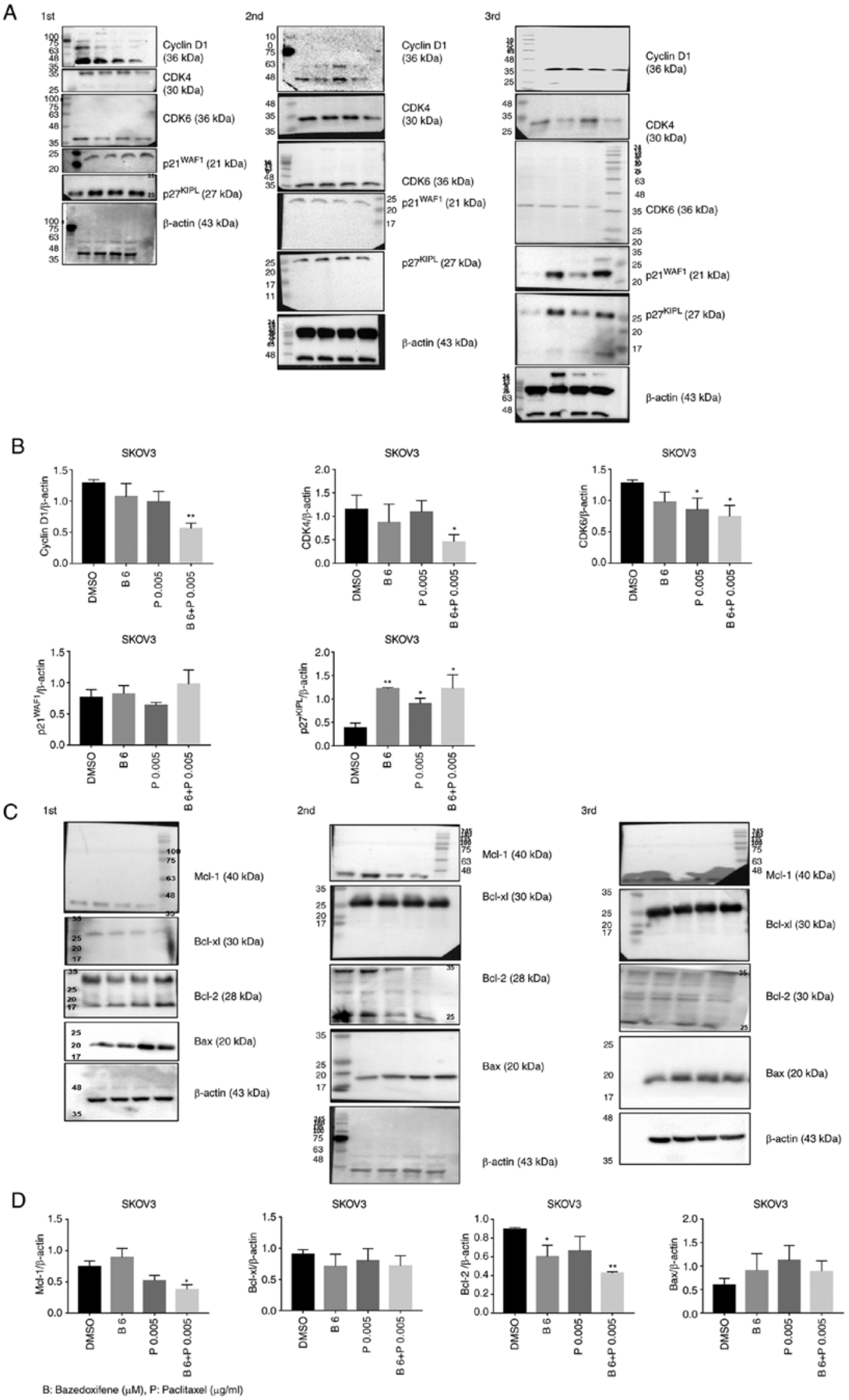


Figure S17. (A and B) Ovarian cancer A2780 and TOV112D cells were treated with bazedoxifene (B) or/and paclitaxel (P/B+P) in triplicate for 48 h to detect cell apoptosis using FITC Annexin V apoptosis Kit (*P<0.05, **P<0.01, ***P<0.001).

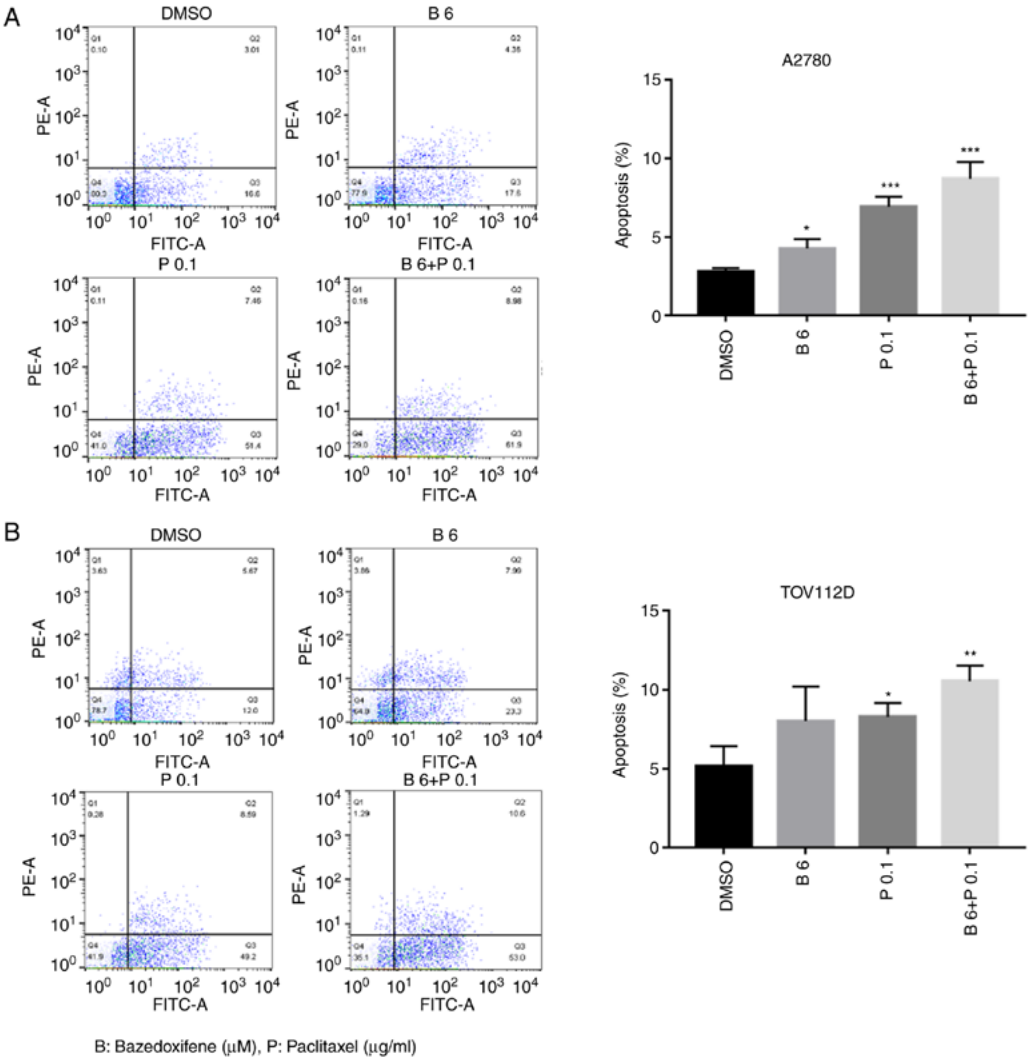


Figure S18. The whole western blot for Fig. 7G. (A) The whole western blot membrane by western blotting in the OVCA433 tumours *in vivo*. (B) Levels of phosphorylated (p)-GP130, GP130, p-STAT3, STAT3, p-ERK 1/2, and ERK 1/2 as analysed by western blotting in vivo. Data are presented as mean ± SD from three independent experiments (*P<0.05, **P<0.01, ***P<0.001, as identified by two-way ANOVA vs. Vehicle). STAT3, signal transducer and activator of transcription 3; GP130, glycoprotein 130.

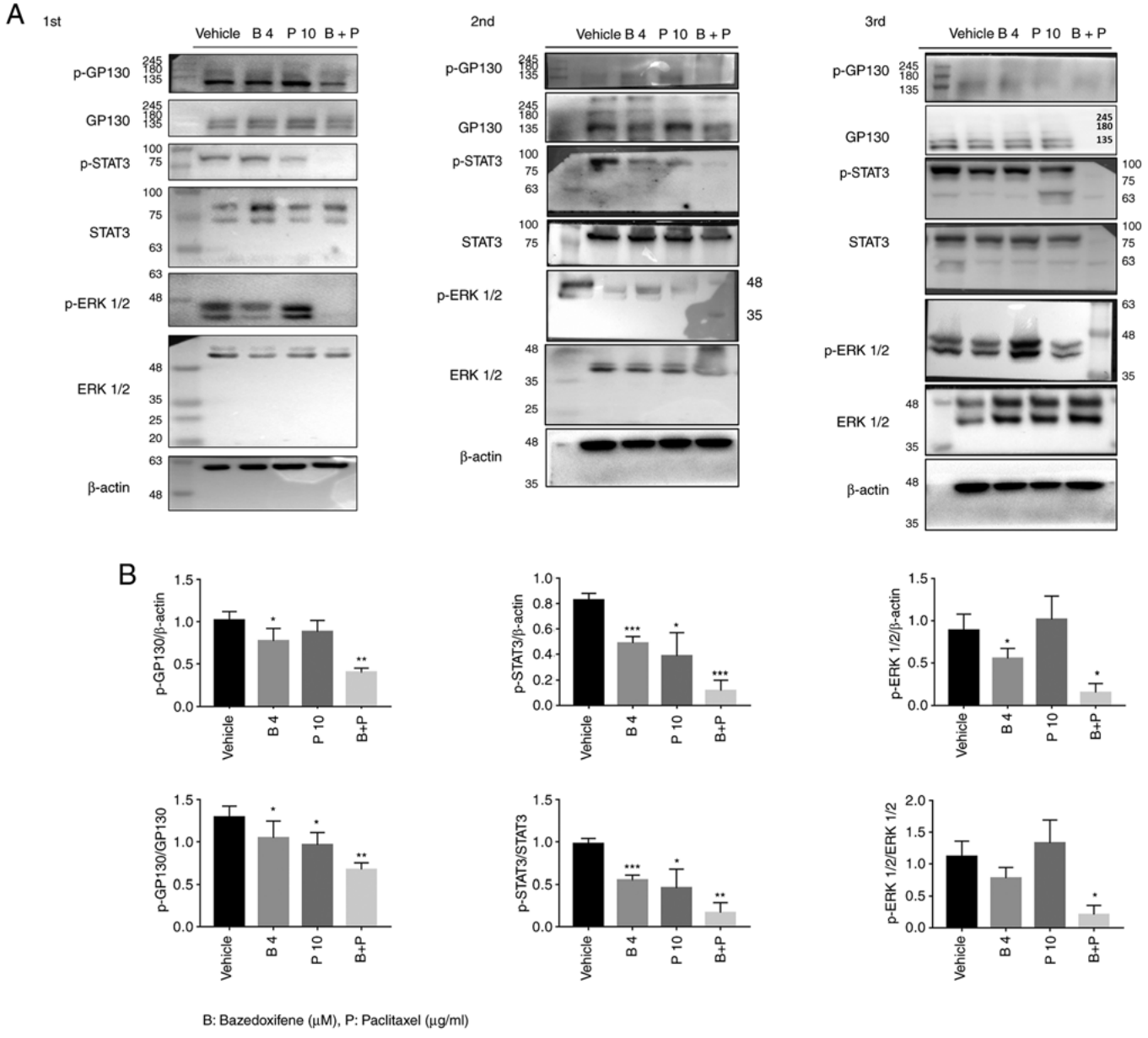


Figure S19. The whole western blot for Fig. 7H. (A) The whole western blot membrane by western blotting in the OVCA433 tumours *in vivo*. (B) Levels of N-cadherin, E-cadherin, β-catenin, vimentin, Snail, Twist, and claudin-1 as analysed by western blotting *in vivo*. Data are presented as mean ± SD from three independent experiments (*P<0.05, **P<0.01, as identified by two-way ANOVA vs. Vehicle).

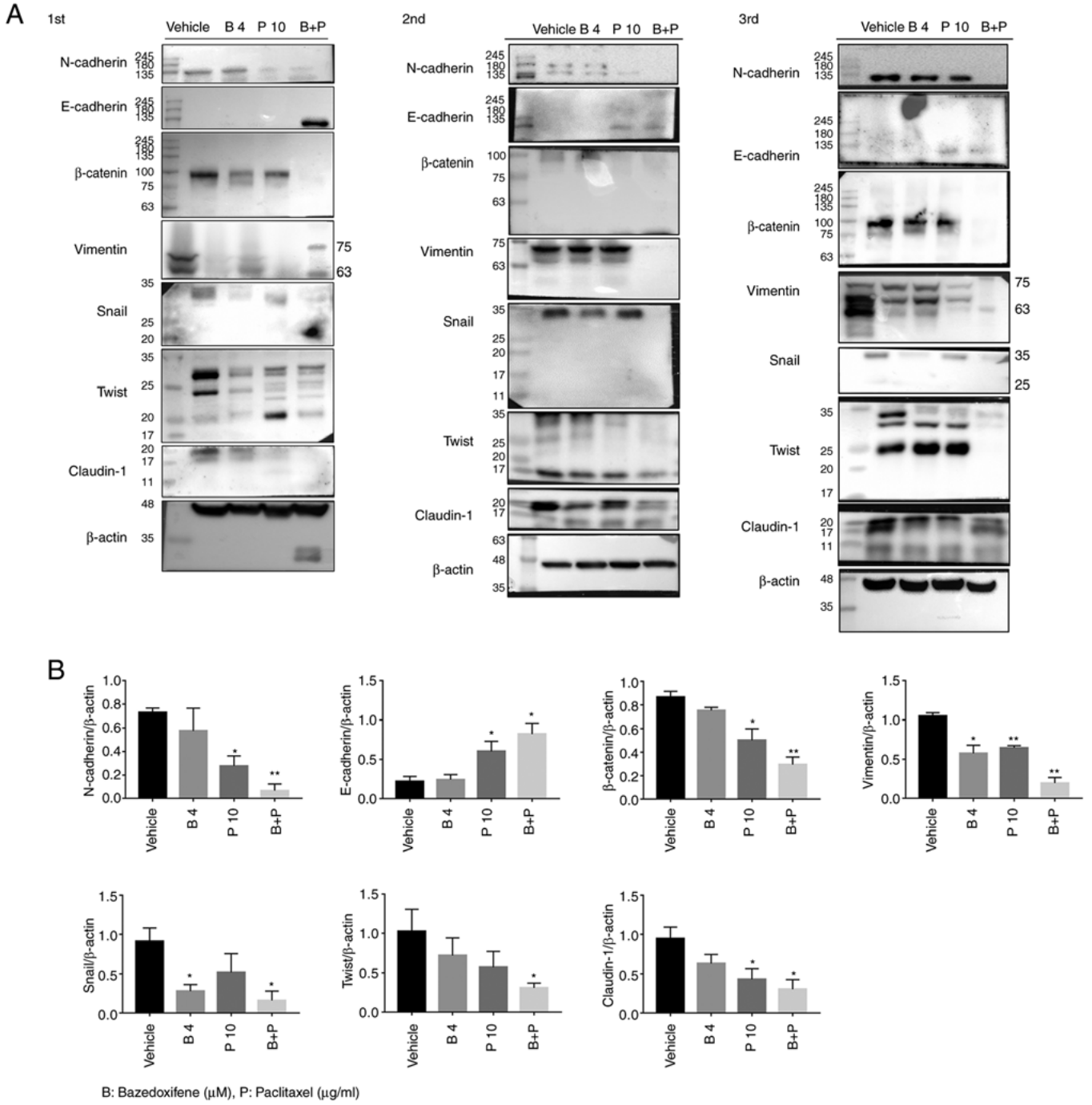


Table SI. siRNA primer sequences used in the present study.

No.	siRNA name	Duplex sequence
1	STAT3-1	Sense 5'ACAGGAUGGCCCAAUGGAAUU3' Antisense 5'UUCCAUUGGGCCAUCCUGUUU3'
2	STAT3-2	Sense 5'CCAACAAUCCCAAGAAUGUUU3' Antisense 5'ACAUUCUUGGGAUUGUUGGUU3'
3	STAT3-3	Sense 5'AACAUUCUGGGCACAAACAUU3' Antisense 5'UGUUUGUGCCCAGAAUGUUUU3'
4	STAT3-4	Sense 5'GCAAGAUCUGAAUGGAAACUU3' Antisense 5'GUUUCCAUUCAGAUCUUGCUU3'
5	Negative control	Sense 5'CCUCGUGCCGUUCCAUCAGGUAGUU3' Antisense 5'CUACCUGAUGGAACGGCACGAGGUU3'

STAT3, signal transducer and activator of transcription 3.