Figure S1. Maps of Tet-On plasmids and validation of STAT1 overexpression. (A-C) Structural diagrams of (A) the empty vector, and (B) STAT1α- and (C) STAT1β-overexpression plasmids. (D) Validation of the overexpression of STAT1 by western blotting after lentiviral infection of empty vector pLenti-tet-on-GFP (Vector), pLenti-tet-on-STAT1α-GFP (oe-STAT1α) and pLenti-tet-on-STAT1β-GFP (oe-STAT1β) in SK3R-PTX, OV3R-PTX and A2780-PTX cells. In order to induce the gene expression, all cells were treated with 8 μg/ml doxycycline for 4 days of transduction. GFP, green fluorescent protein; oe, overexpression vector; PTX, paclitaxel.

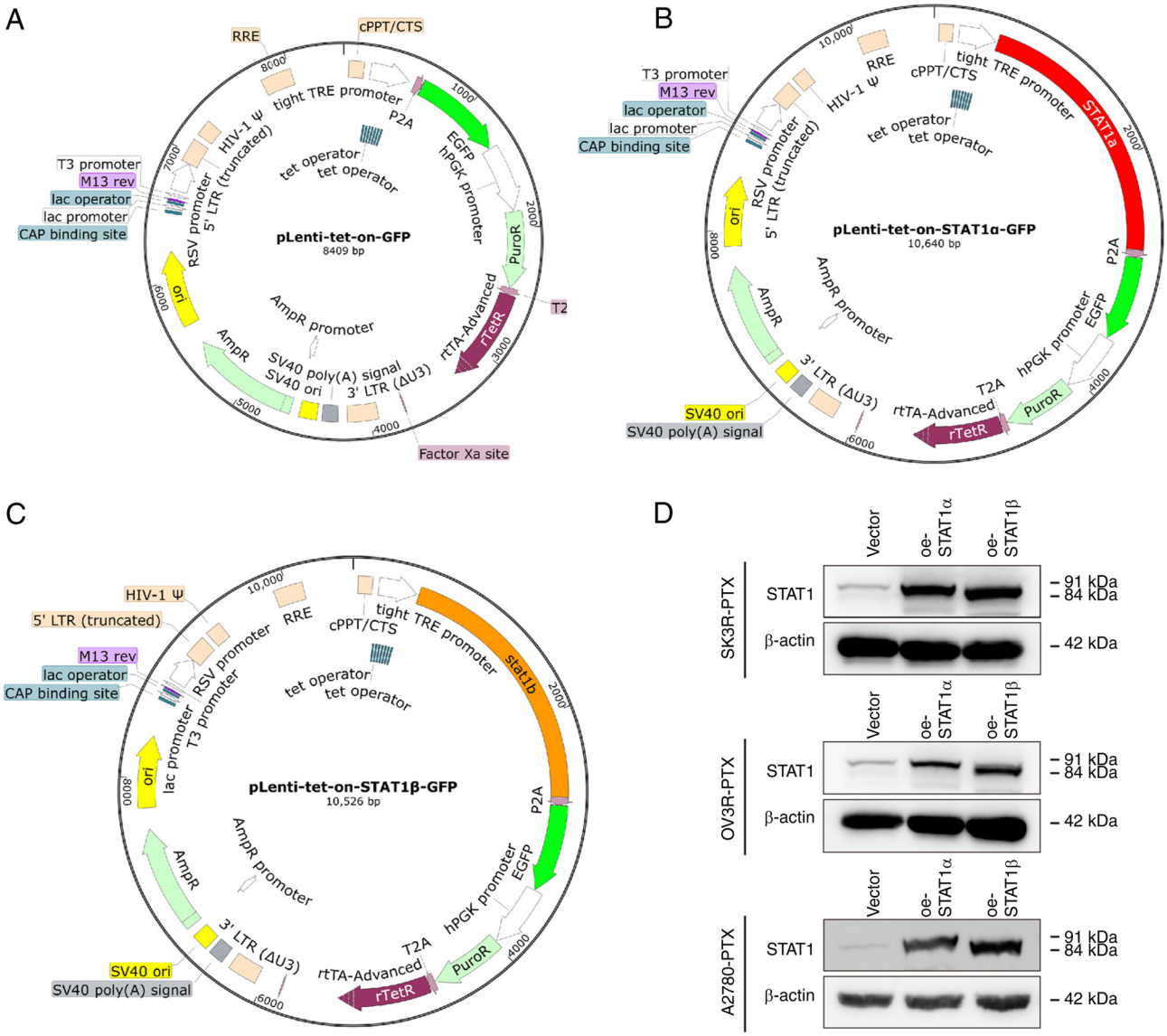

Figure S2. Analysis of altered expression of TF genes. (A) Classification of TF genes with significantly altered expression. (B) Heatmap of the top 20 upregulated and the top 20 downregulated TF genes in A2780-PTX cells compared with A2780 cells. (C) GO term analysis of TF genes with significantly altered expression. GO, Gene Ontology; TF, transcription factor; p.adjust, adjusted P-value; PTX, paclitaxel.

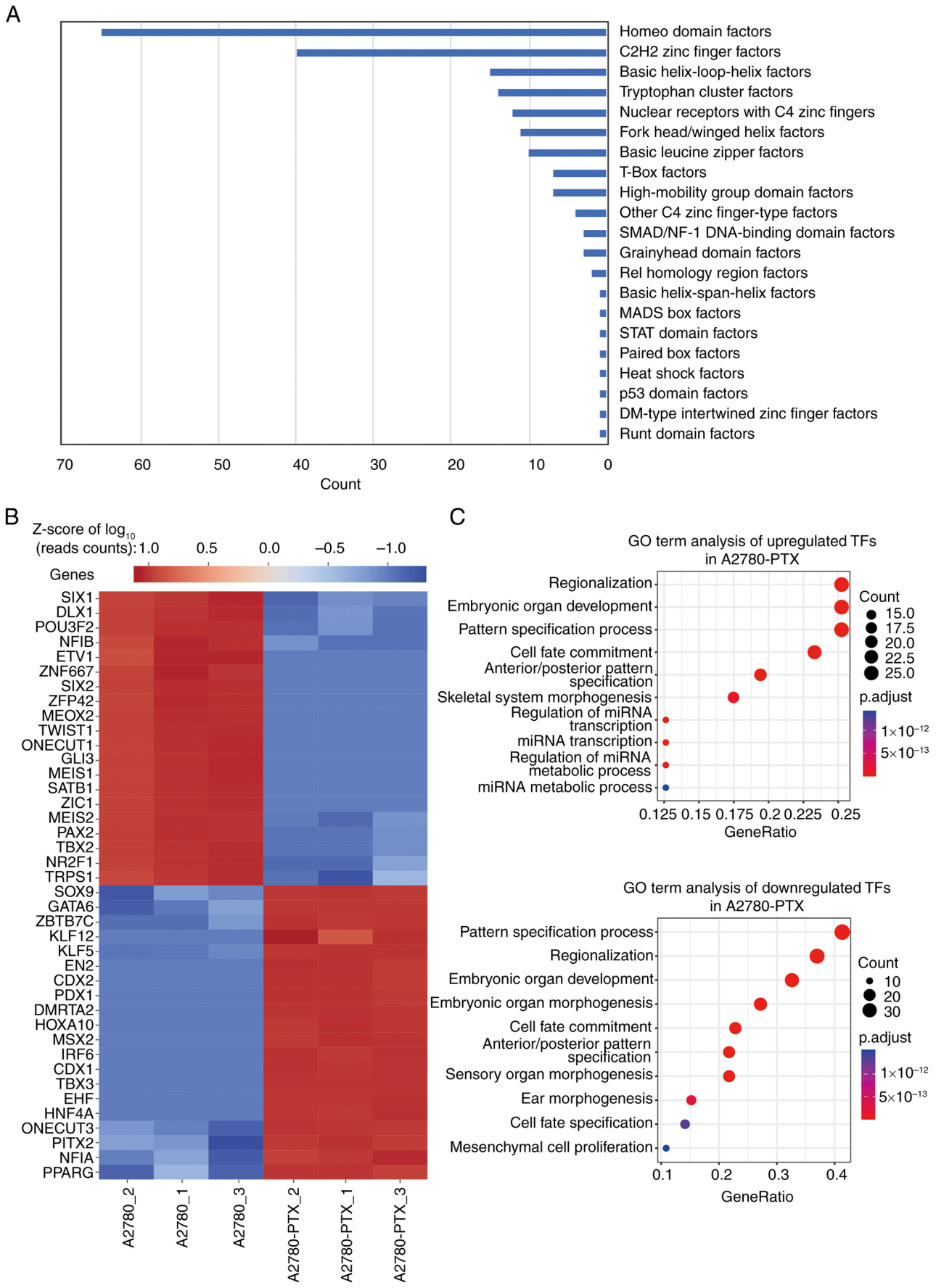

Figure S3. Validation of STAT1 expression in Tet-On STAT1-overexpressing cells. PTX-resistant cells were infected with lentivirus containing pLenti-tet-on-GFP (vector), pLenti-tet-on-STAT1α-GFP or pLenti-tet-on-STAT1β-GFP plasmids, followed by Dox treatment (8 μg/ml) for 4 days (right three columns). (A) SK3R-PTX cells. (B) OV3R-PTX cells. (C) A2780-PTX cells. Dox-induced STAT1 expression (green dots) in PTX-resistant ovarian cancer cells was detected by immunofluorescence microscopy and images were captured. Scale bar, 100 μm. Dox, doxycycline; GFP, green fluorescent protein; oe, overexpression vector; PTX, paclitaxel.

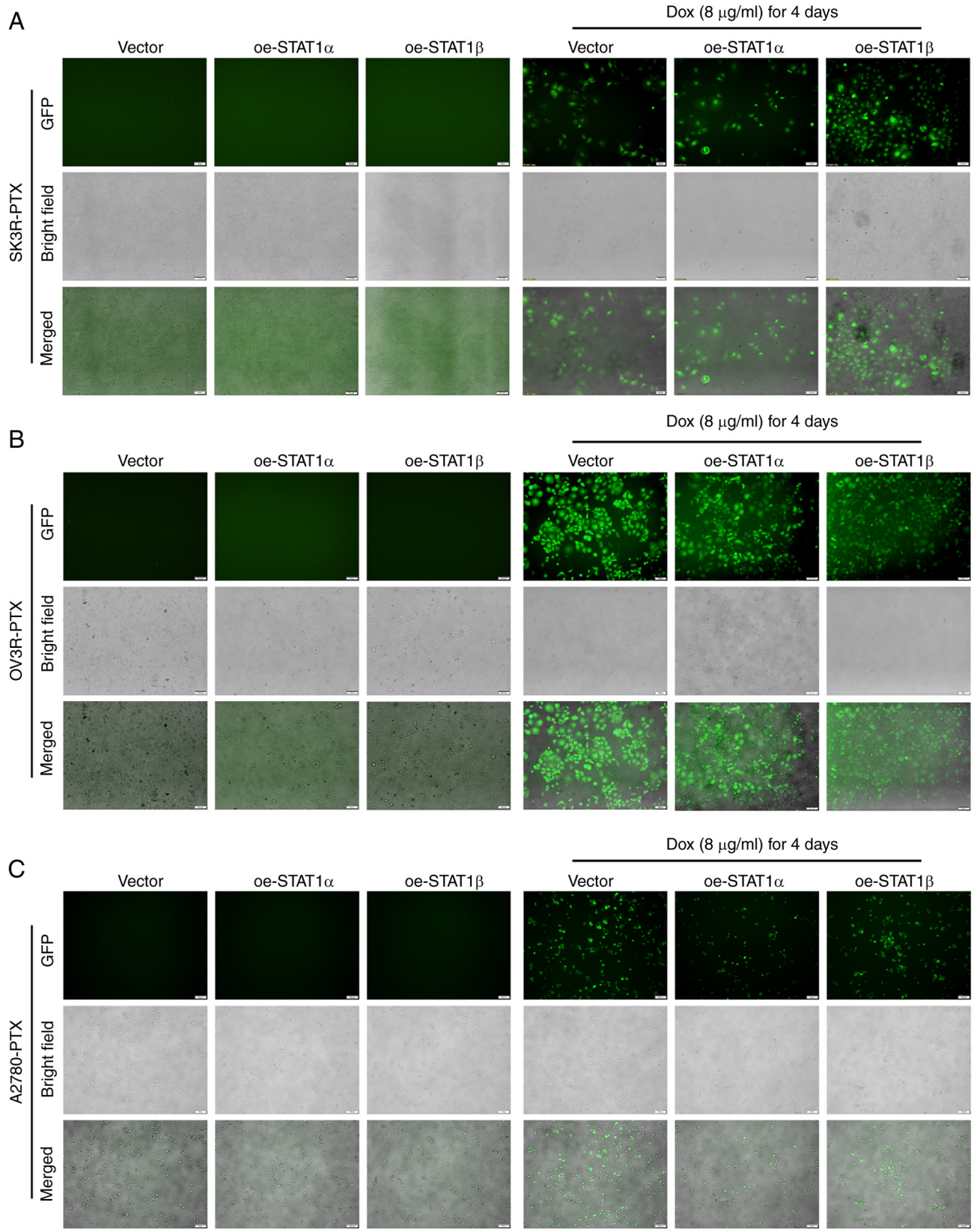

Figure S4. Detection of STAT1α and STAT1β mRNA expression in PTX-sensitive cells (SK-OV-3, OVCAR-3 and A2780 cells) and their counterpart PTX-resistant cells (SK3R-PTX, OV3R-PTX and A2780-PTX cells) by reverse transcription-quantitative PCR. (A) STAT1α/β expression in three PTX-sensitive cell lines. (B) STAT1α/β expression in three PTX-resistant cell lines. STAT1α was the major transcript of STAT1 expressed in both PTX-sensitive and PTX-resistant cells. Expression values were normalized using β-actin as an internal reference. Differences were analyzed using Student's t-test. Data are presented as the mean ± SD (n=3). ****P<0.0001. PTX, paclitaxel.

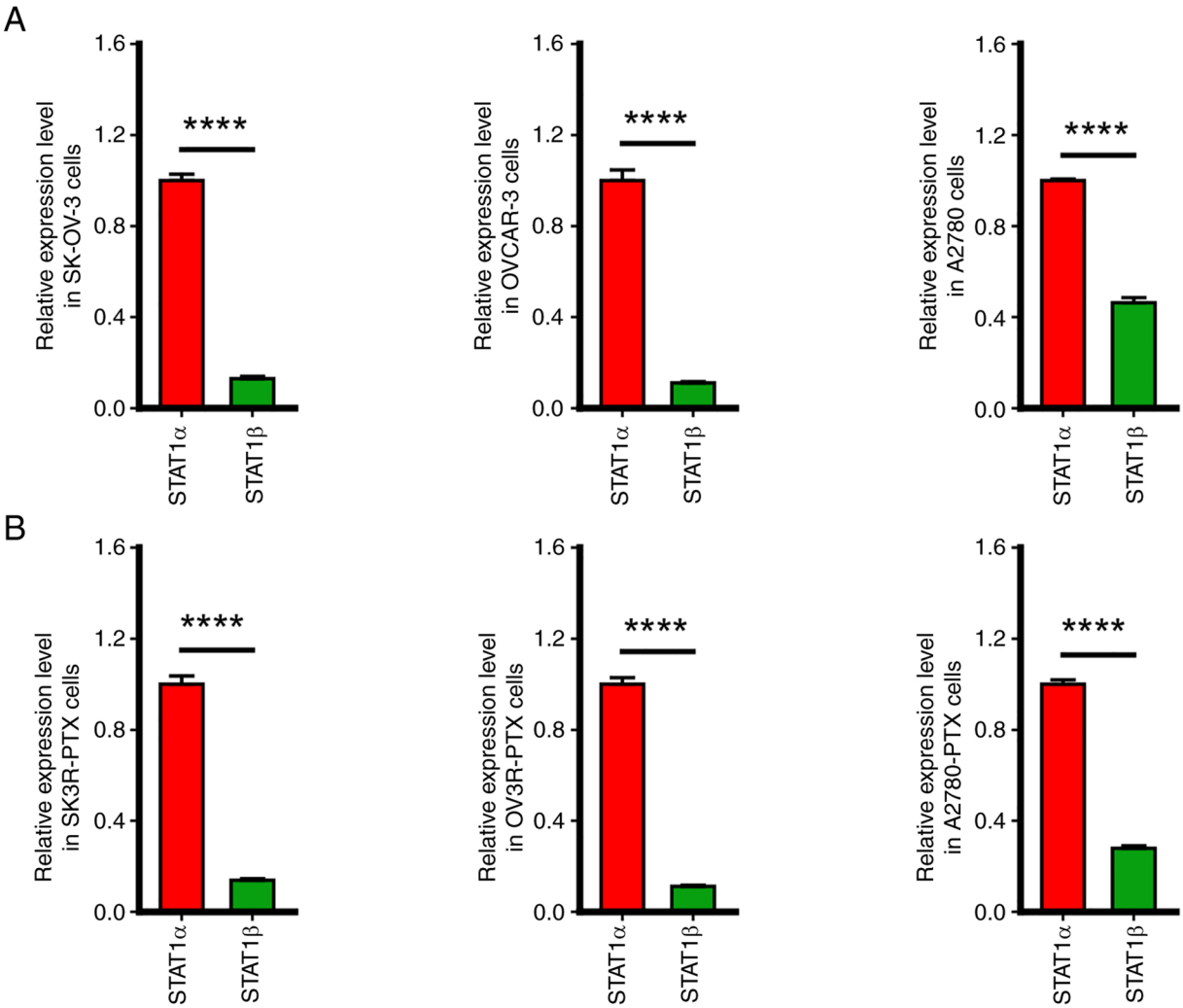

Figure S5. Effect of PTX on CASP8, FAS and STAT1 expression in time-course and dose-dependent experiments. (A) CASP8, FAS, total STAT1, STAT1α and STAT1β mRNA expression in SK-OV-3 cells after treatment with 0.001, 0.01 and 0.1 μM PTX for 6, 12, 18 and 24 h was detected by reverse transcription-quantitative PCR. Expression values for each group were normalized using β-actin as an internal reference. Differences among multiple groups were analyzed by one-way ANOVA followed by Tukey's Honestly Significant Difference test. Data are presented as the mean ± SD (n=3). *P<0.05; **P<0.01; ***P<0.001 vs. 6-h group. (B) Results of linear trend test for changes in (A). The vertical coordinate indicates the concentration of PTX, and the horizontal coordinate indicates the genes. The color of the bubble represents the slope of the change trend, while the size of the bubble represents the statistical significance. *P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. CASP8, caspase-8; FAS, Fas cell surface death receptor; ns, not significant; PTX, paclitaxel.

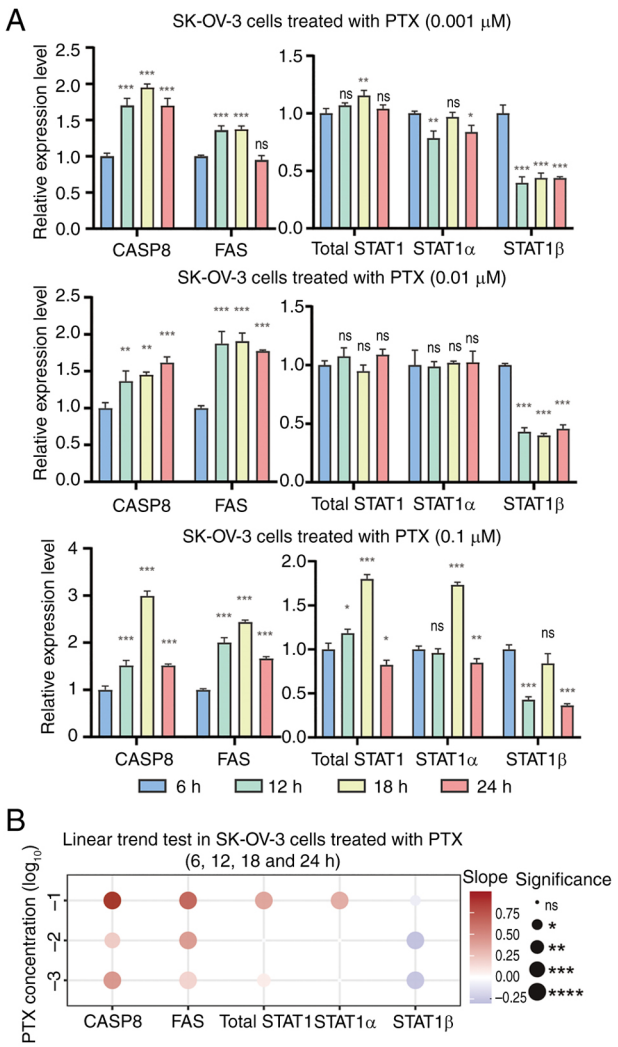

Figure S6. Validation of STAT1 mRNA expression after lentiviral infection and doxycycline induction in PTX-resistant cells. (A) Detection of STAT1 mRNA expression in oe-STAT1α- and oe-STAT1β-lentivirus-infected SK3R-PTX cells by RT-qPCR. (B) Detection of STAT1 mRNA expression in oe-STAT1α- and oe-STAT1β-lentivirus-infected OV3R-PTX cells by RT-qPCR. (C) Detection of STAT1 mRNA expression in oe-STAT1α- and oe-STAT1β-lentivirus-infected A2780-PTX cells by RT-qPCR. Expression values were normalized using β-actin as an internal reference. Differences were analyzed using Student's t-test. Data are presented as the mean ± SD (n=3). ***P<0.001; ****P<0.0001. oe, overexpression vector; PTX, paclitaxel; RT-qPCR, reverse transcription-quantitative PCR.

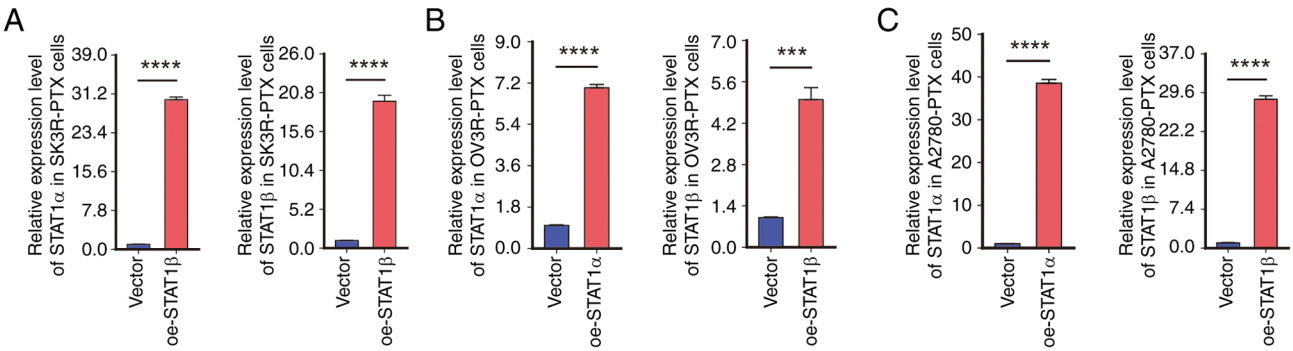

Figure S7. Prediction of STAT1 binding sites in the promoter regions of CASP8 and FAS. Chromatin immunoprecipitation-sequencing data of STAT1 were downloaded from the Gene Expression Omnibus database (GSM320736). Data analysis revealed that STAT1 could directly bind to DNA on the promoter of CASP8 and FAS. Q-value, false discovery rate-adjusted P-value; CASP8, caspase-8; Chr, chromosome; FAS, Fas cell surface death receptor; IP, immunoprecipitation; UTR, untranslated region.

Gene	Chr	Start	End	Location	IP group	Control group	Fold change	Difference	Q-value
CASP8	chr2	201800245	201800397	Intron	20	6	3.538724942	14	0.020314
CASP8	chr2	201801460	201802147	3' UTR	222	26	8.728854857	196	$1.69X10^{-38}$
CASP8	chr2	201805068	201805550	Promoter	95	57	1.680894347	38	0.007046
CASP8	chr2	201806206	201807175	Promoter	105	73	1.457122035	32	0.036961
CASP8	chr2	201830393	201831842	Promoter	208	90	2.336681866	118	$6.43X10^{-11}$
FAS	chr10	90739885	90741954	Promoter	702	165	4.269443436	537	$1.00X10^{-77}$
FAS	chr10	90753166	90753472	Intron	43	5	9.572708609	38	$1.00X10^{-7}$