

Supplementary information

Supplementary Figure 1. Gene ontology (GO) enrichment analysis of differentially expressed genes (DEGs).

Supplementary Figure 2. The effects of PD-L1 overexpression on p-p38, p-JNK, p-AKT and p-NF- κ B proteins levels were verified by Western Blotting in PC9 and HCC827 cells.

Supplementary Figure 3. A. The effects of PD-L1 overexpression on EGFR downstream signaling pathway activation were verified by Western Blotting in EGFR-wild type H1299 cells. B. The protein levels of p-ERK, ERK, apoptosis and autophagy-related proteins were assessed by Western Blotting. H1299 PD-L1 cells were pretreated with MER/ERK pathway inhibitor PD98059. C. H1299 cells as in (B) were immunostained with antibodies against LC3B (scale bar, 20 μ m). D. Apoptotic rate was measured using Annexin V/7-AAD staining in cells as in (B). E-G. The viability of cells as in (B) was assessed by colony formation assay (E), EDU assay (F) and CCK-8 assay (G) (scale bar, 150 μ m). H, I. Cell migration and invasion of H1299 PD-L1 and vector cells were measured by Transwell assay. The different cells were pretreated with gefitinib, pemetrexed or combined treatment for 72 h (scale bar, 150 μ m; magnification, 20 $\times$). J. Wound-healing assay comparing the cell migration differences among H1299 PD-L1 and vector cells under gefitinib, pemetrexed or combined treatment for 24 h (scale bar, 750 μ m). The analyses were repeated three times. Data were presented as mean $\pm$ SD. * p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001

Supplementary Figure 4. A. PC9 PD-L1 and vector cells were treated with different

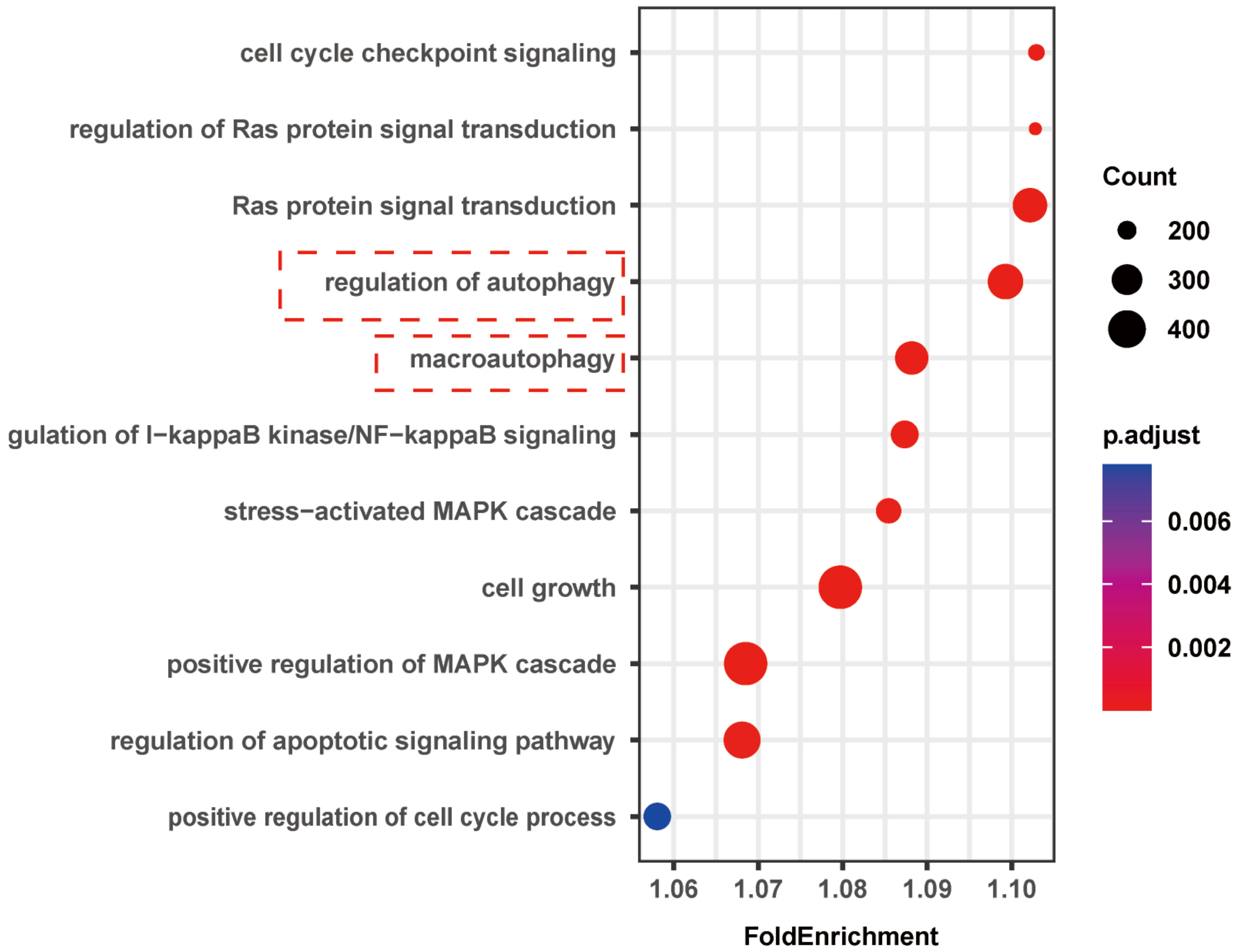
combinations of concentrations of gefitinib and pemetrexed for 72 h, and the CI values of gefitinib-pemetrexed combination therapy were calculated. B. HCC827 PD-L1 and vector cells were treated with different combinations of concentrations of gefitinib and pemetrexed for 72 h, and the CI values of gefitinib-pemetrexed combination therapy were calculated. CI, Combination index.

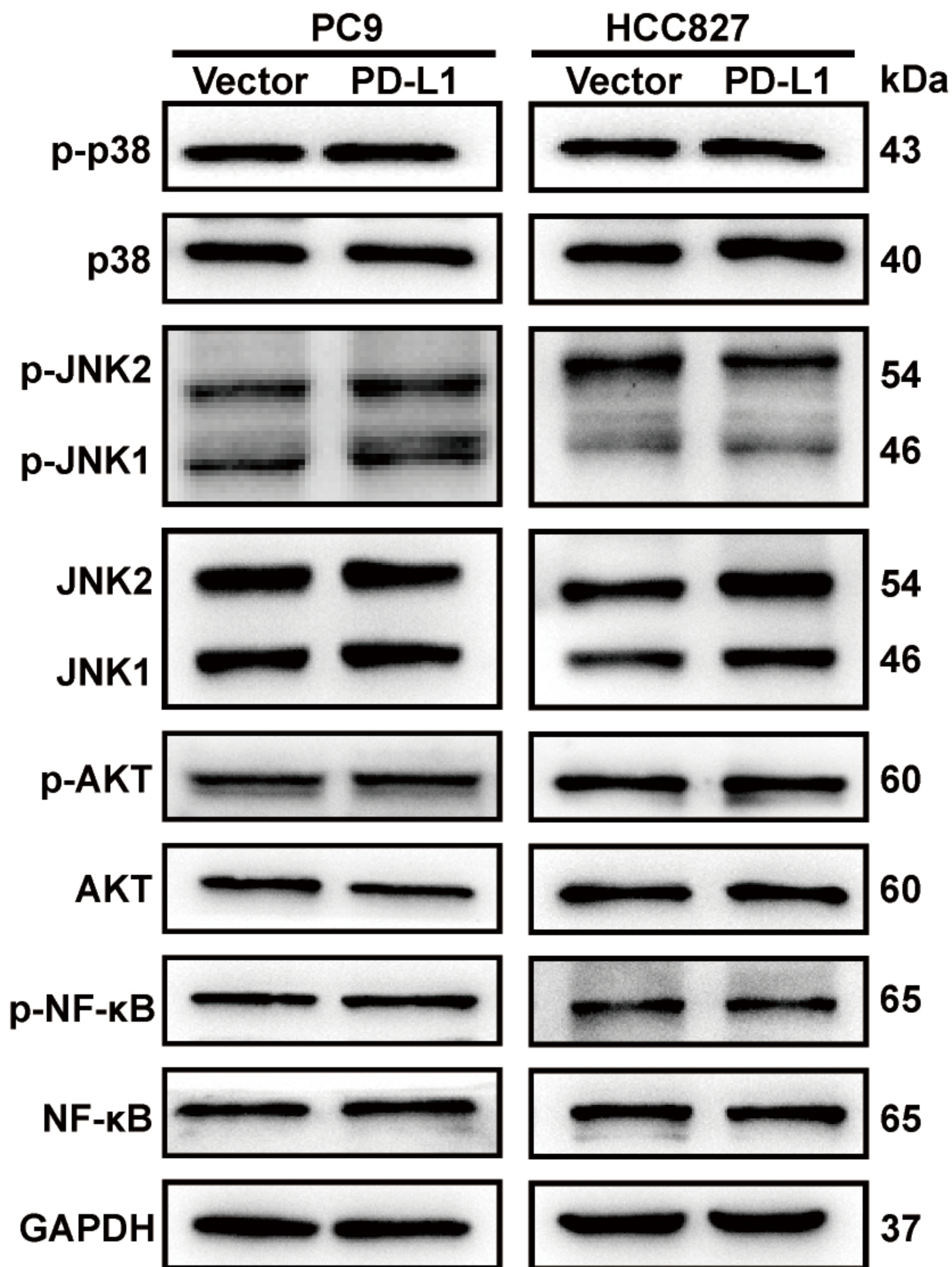
Supplementary Table 1. Univariate and multivariate analysis for ORR in EGFR–TKIs monotherapy cohort.

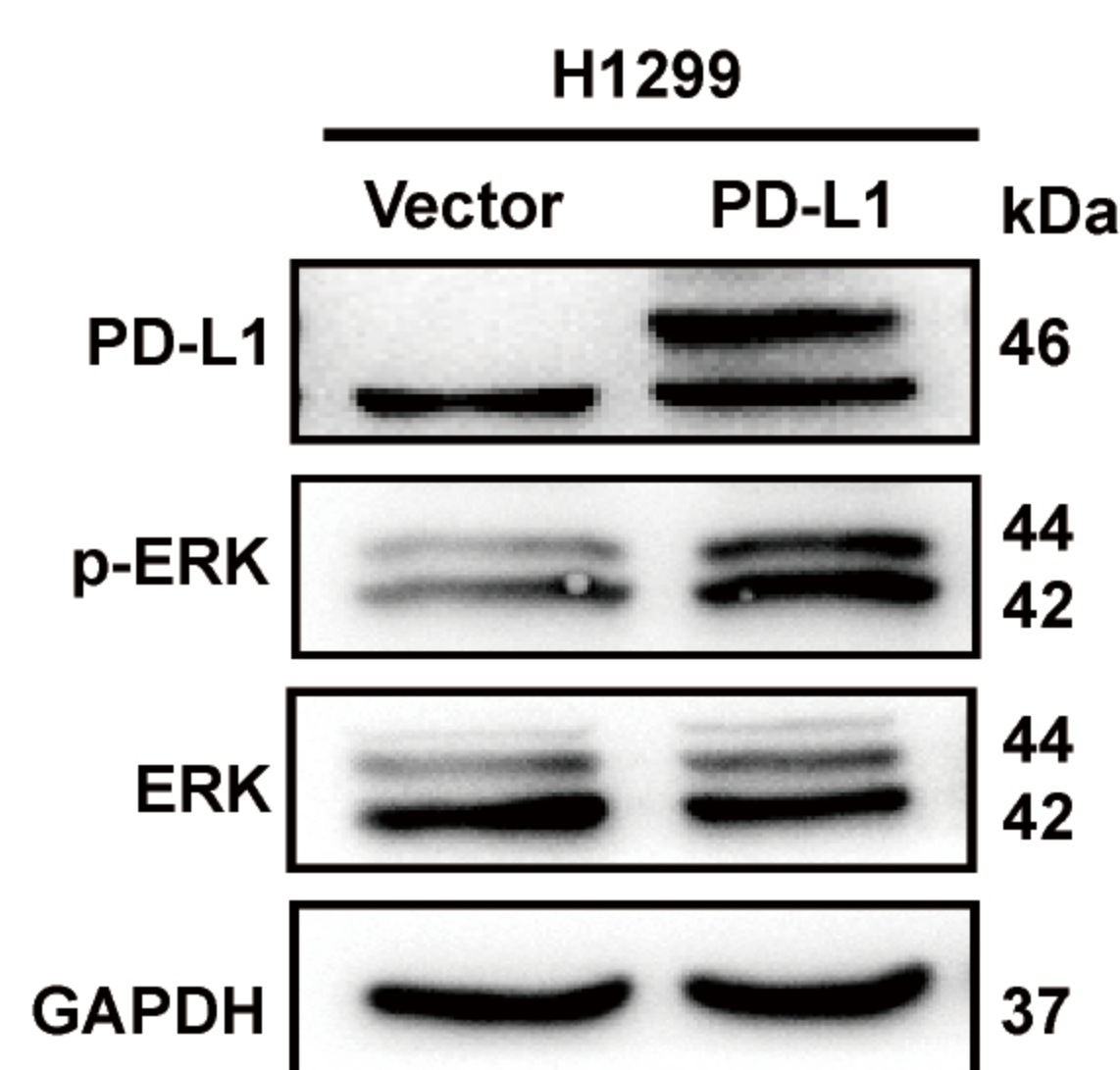
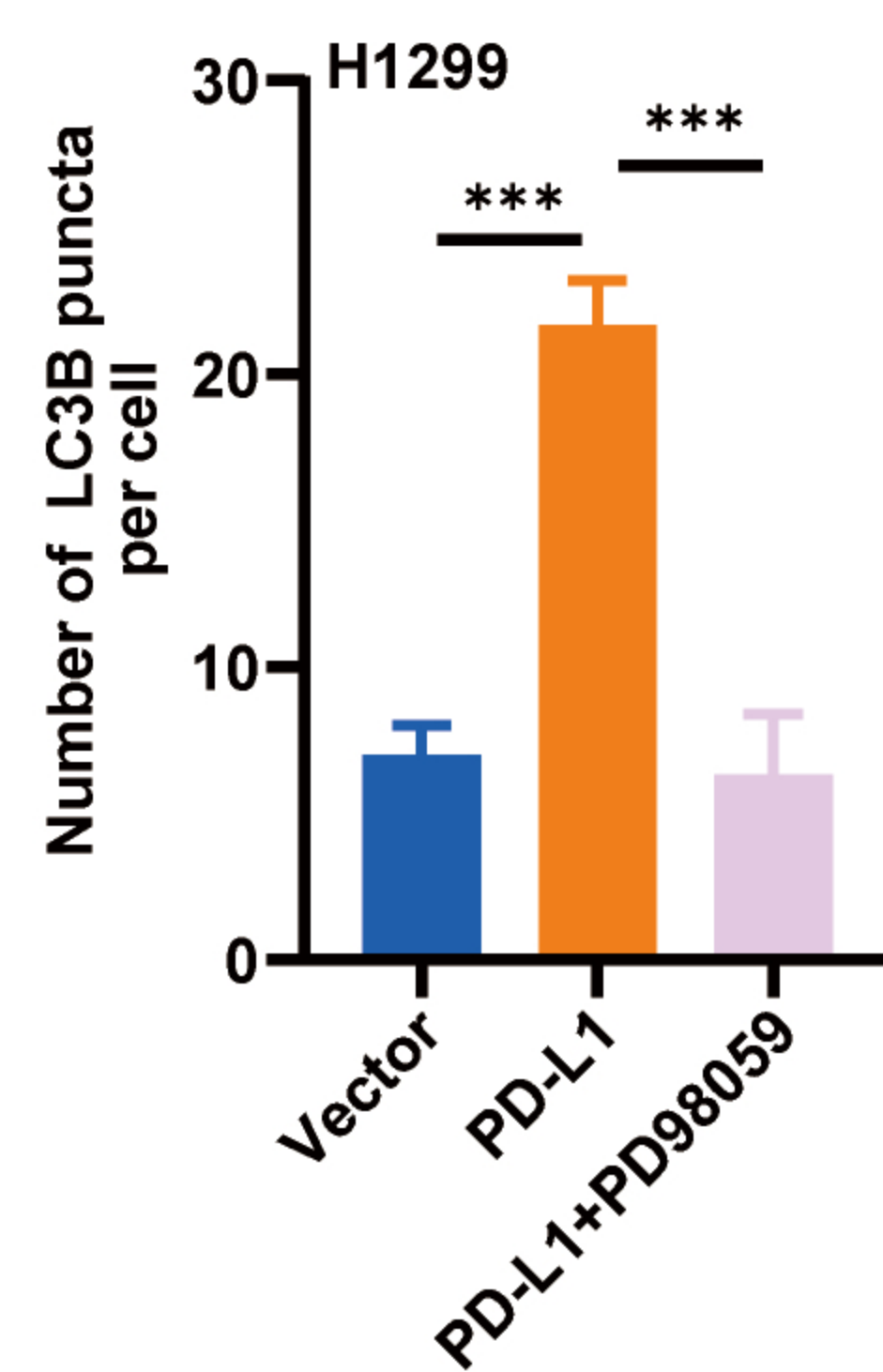
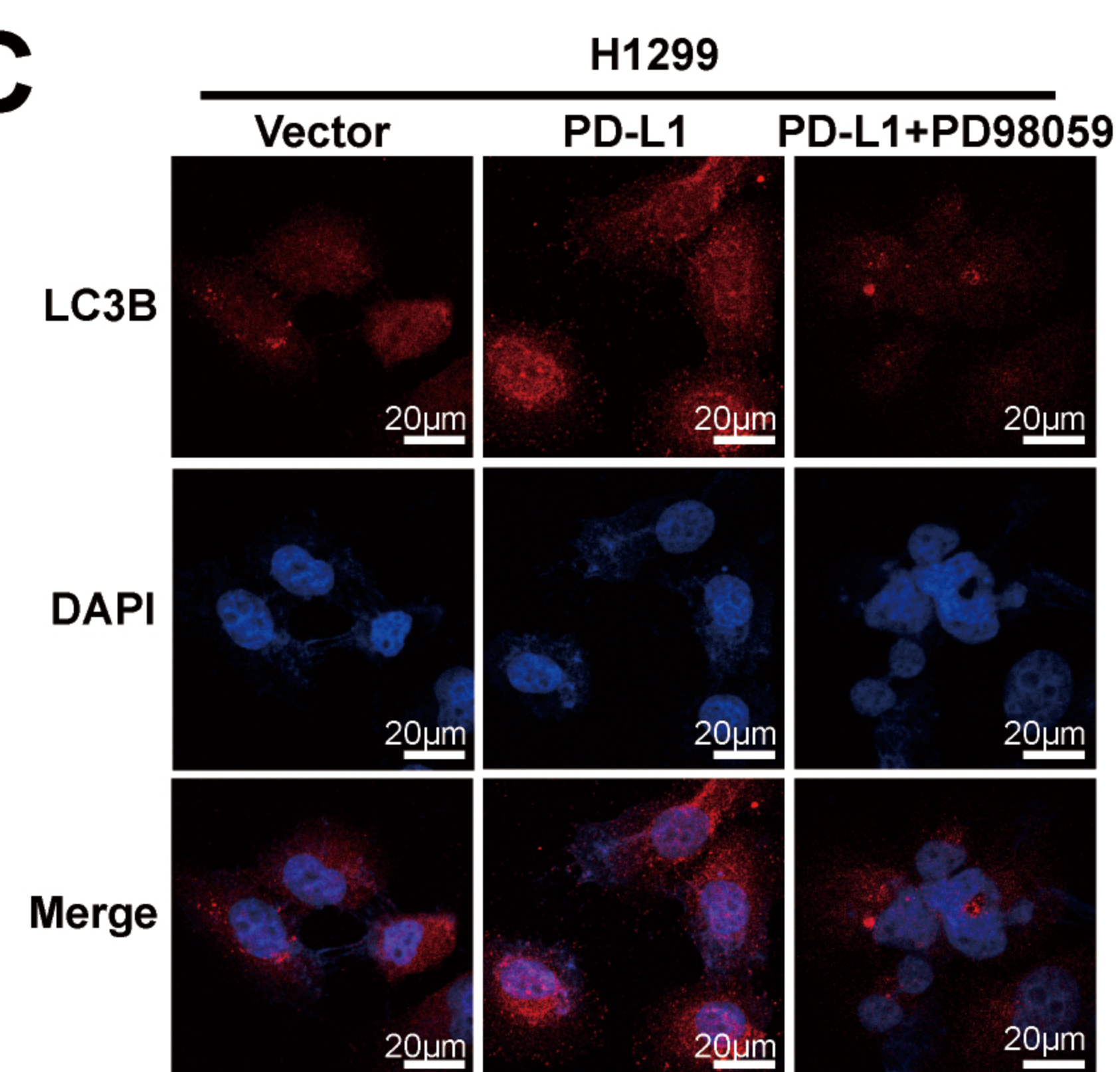
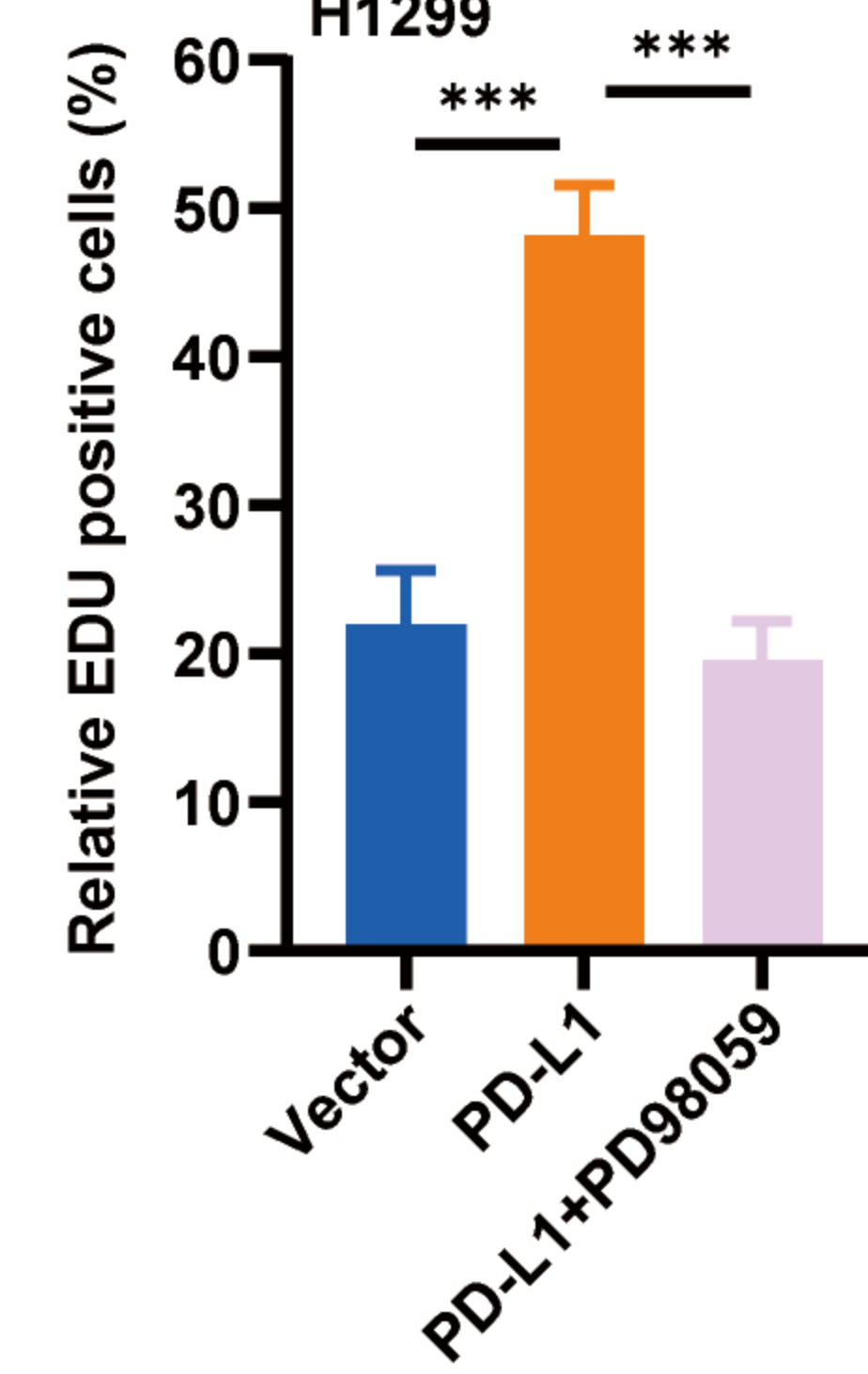
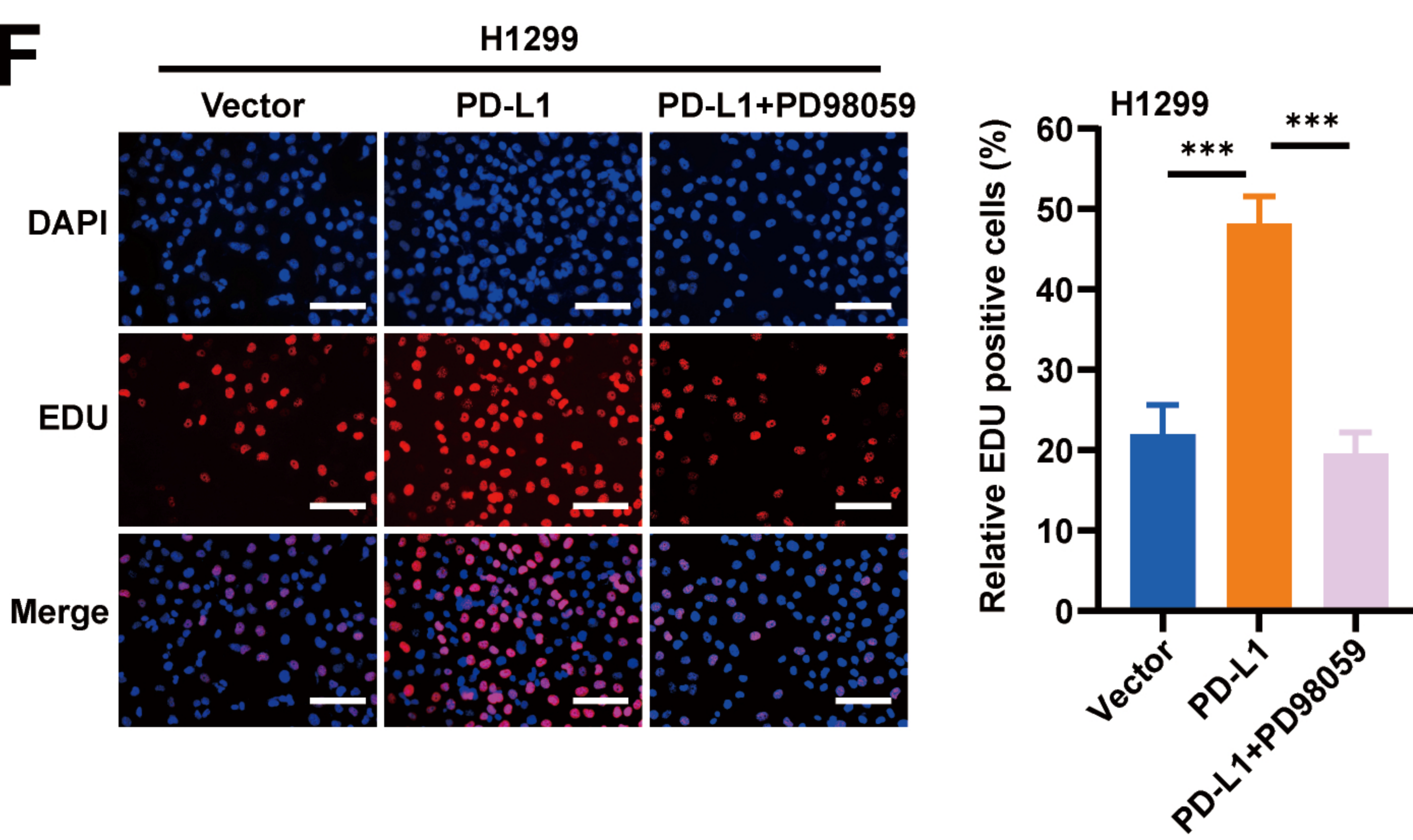
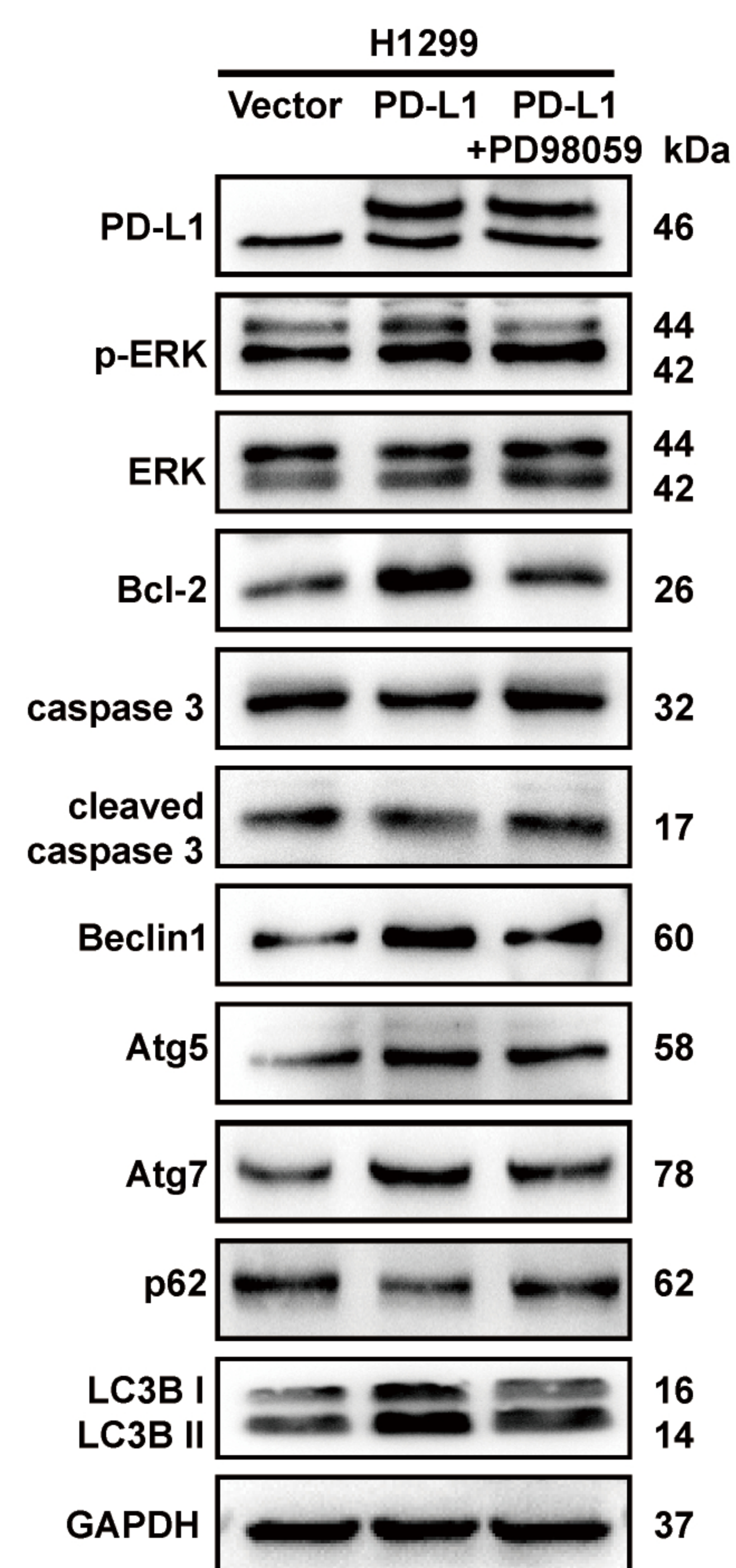
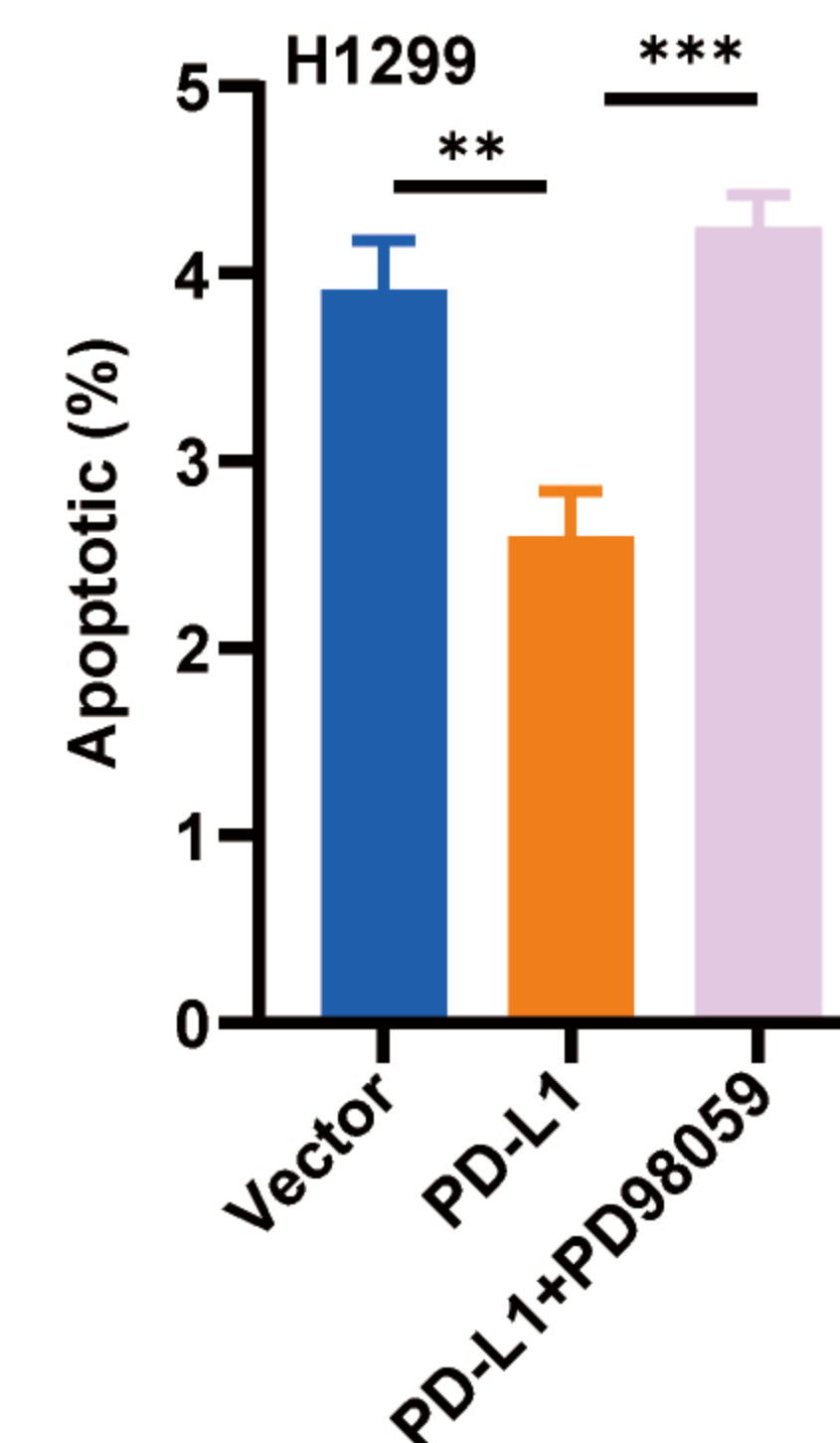
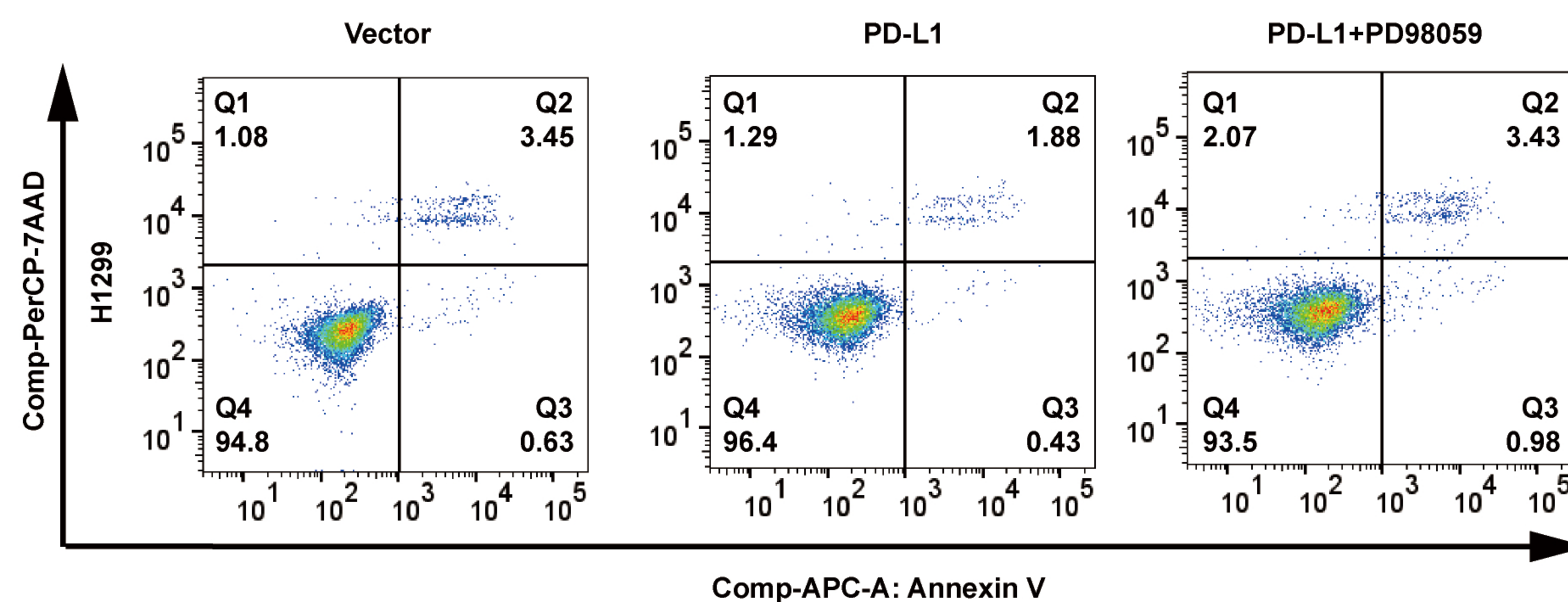
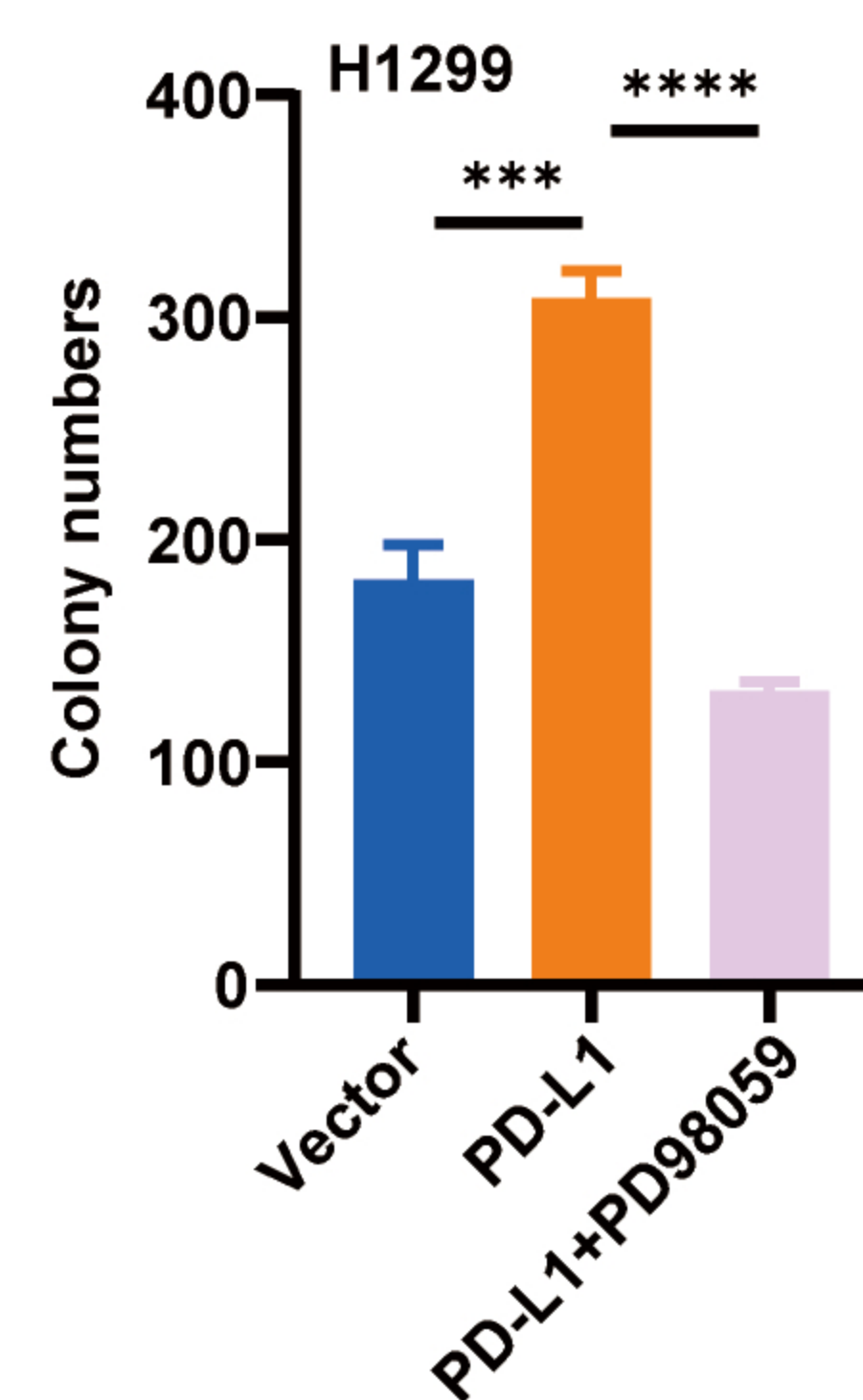
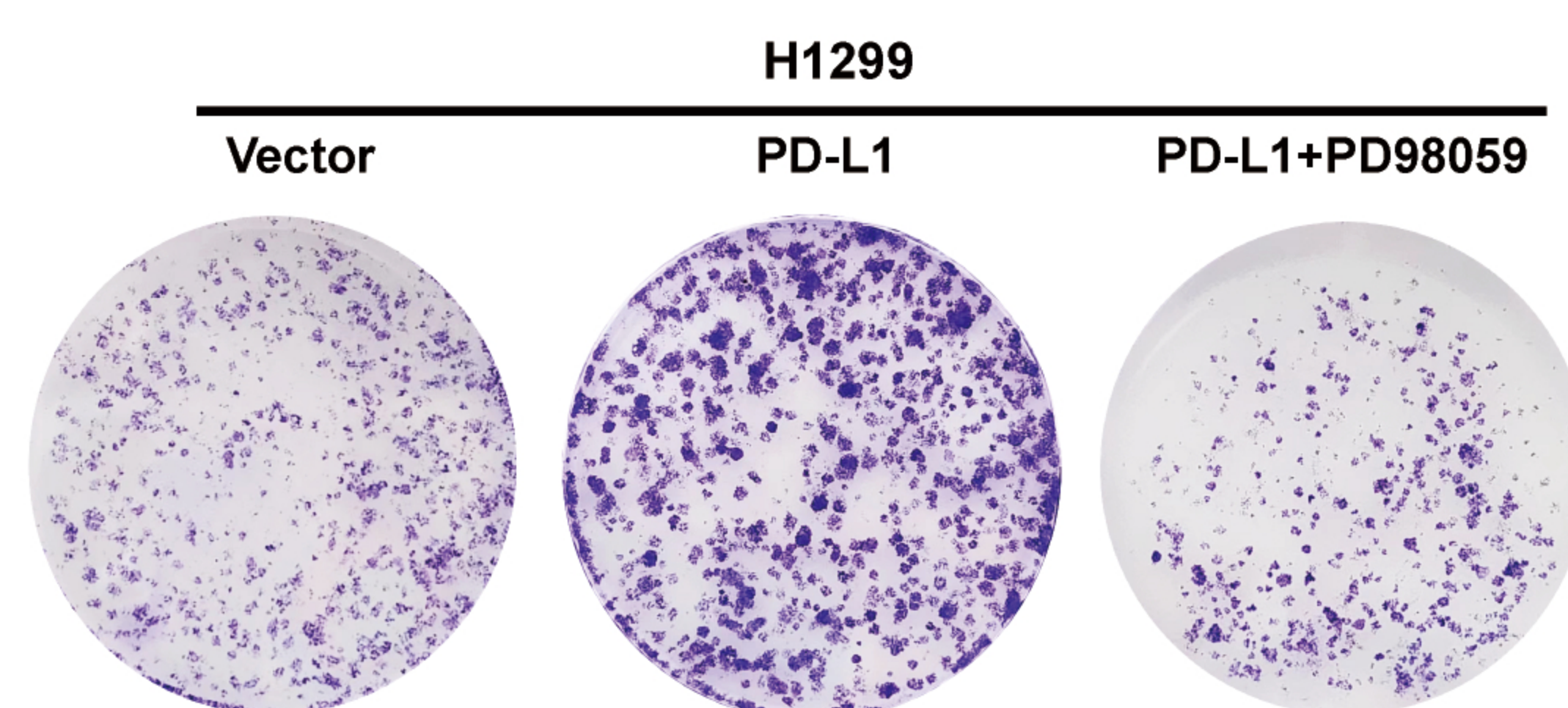
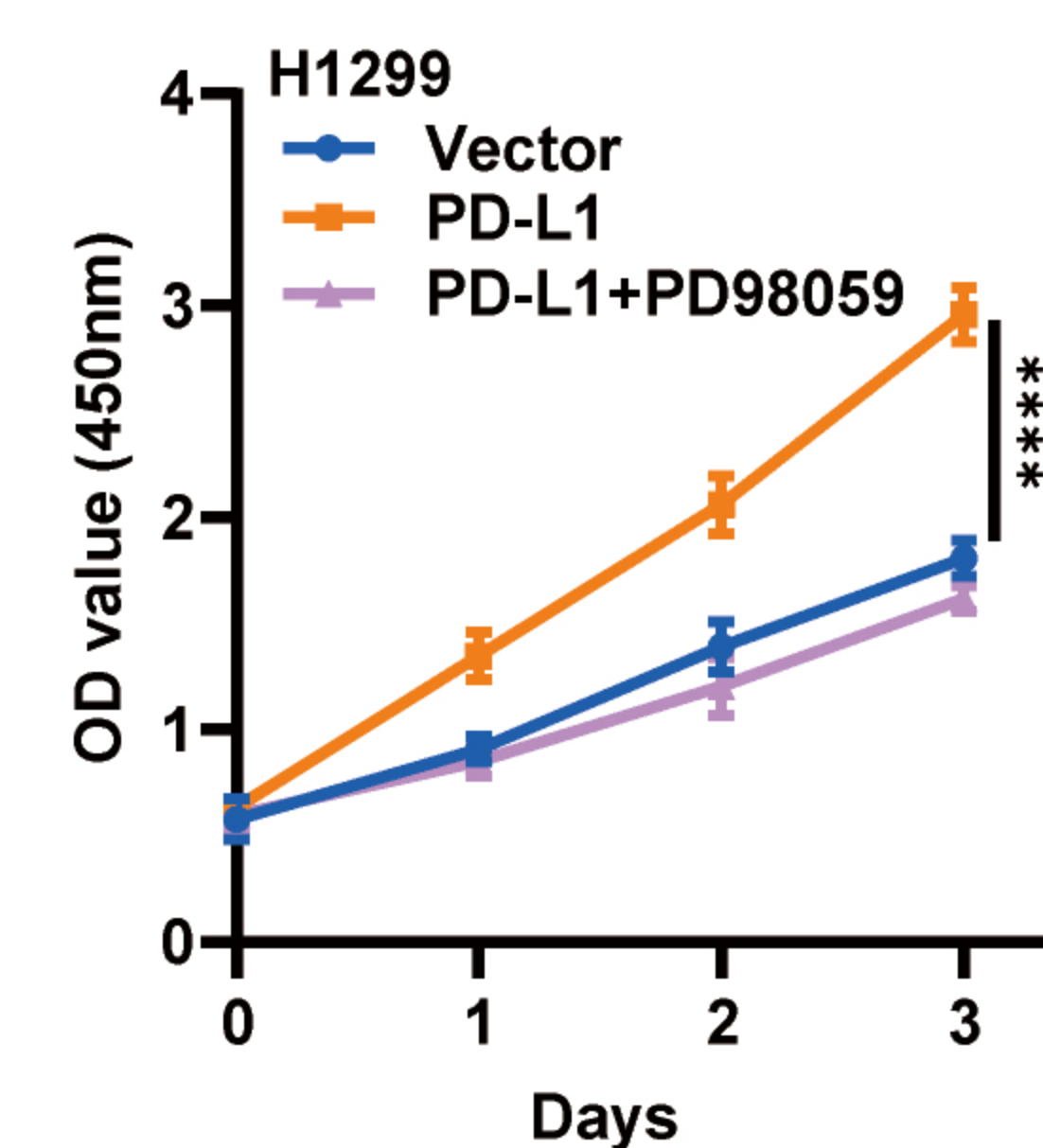
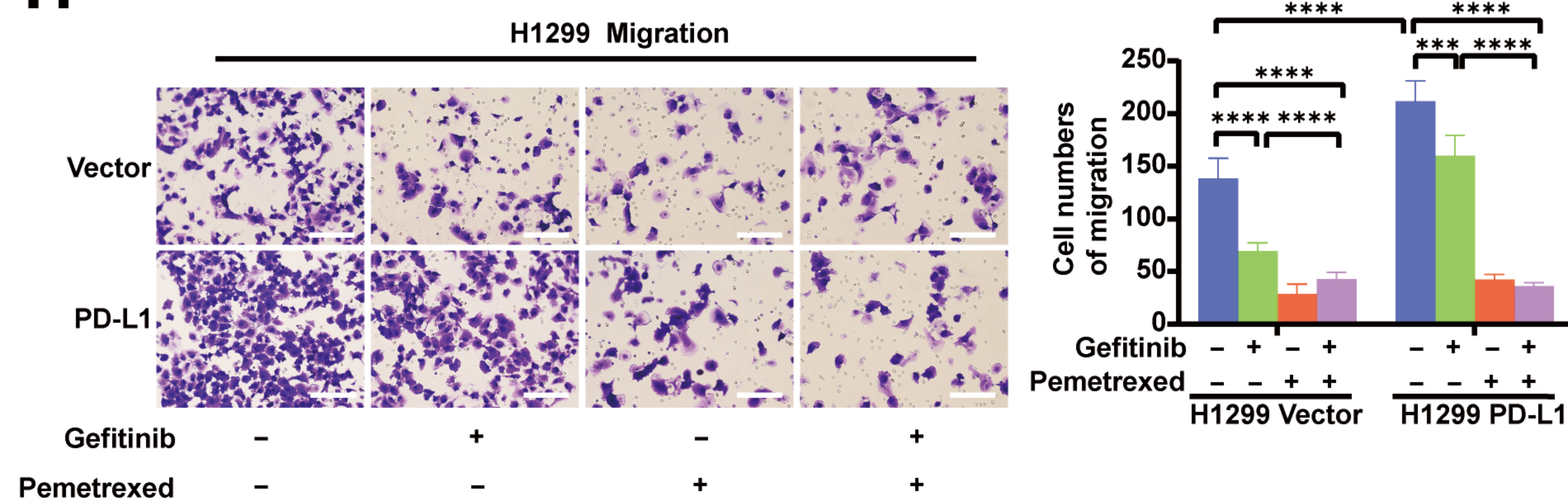
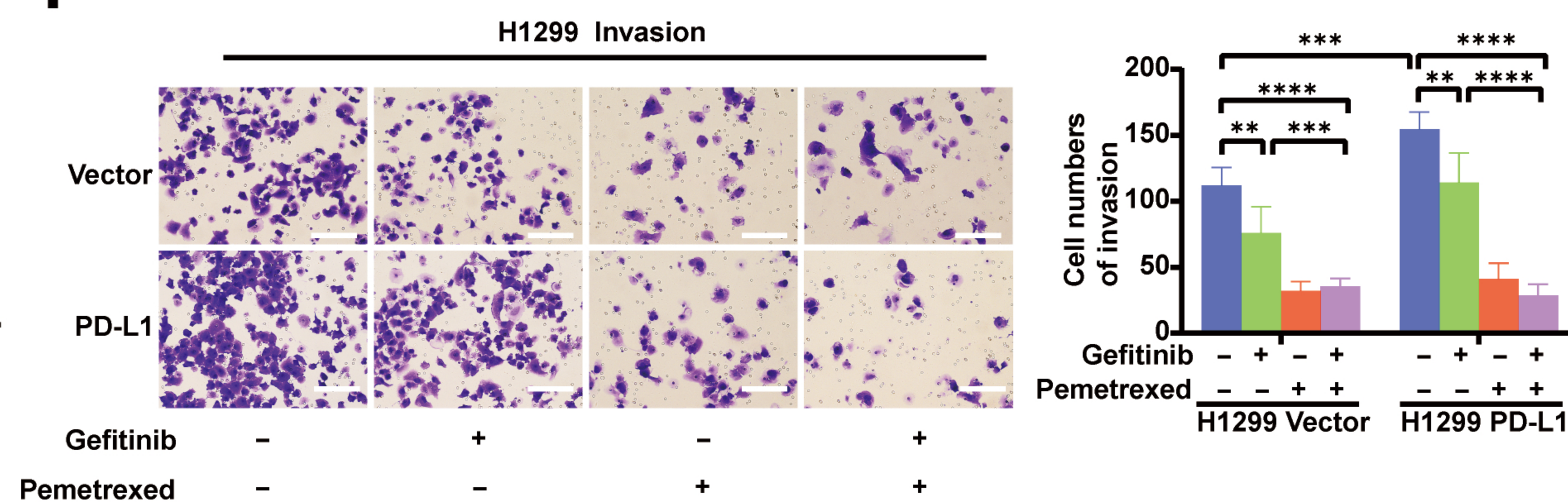
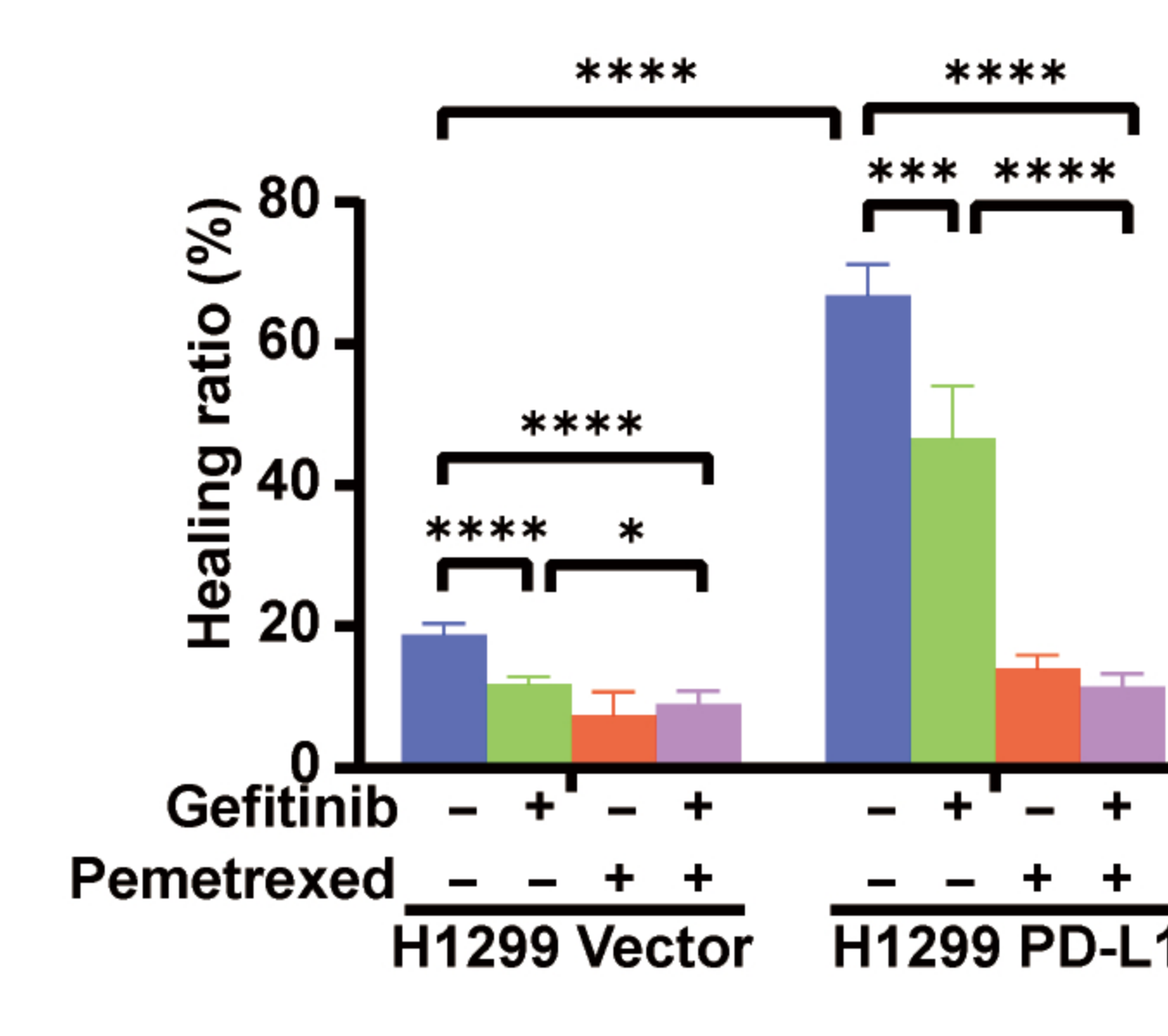
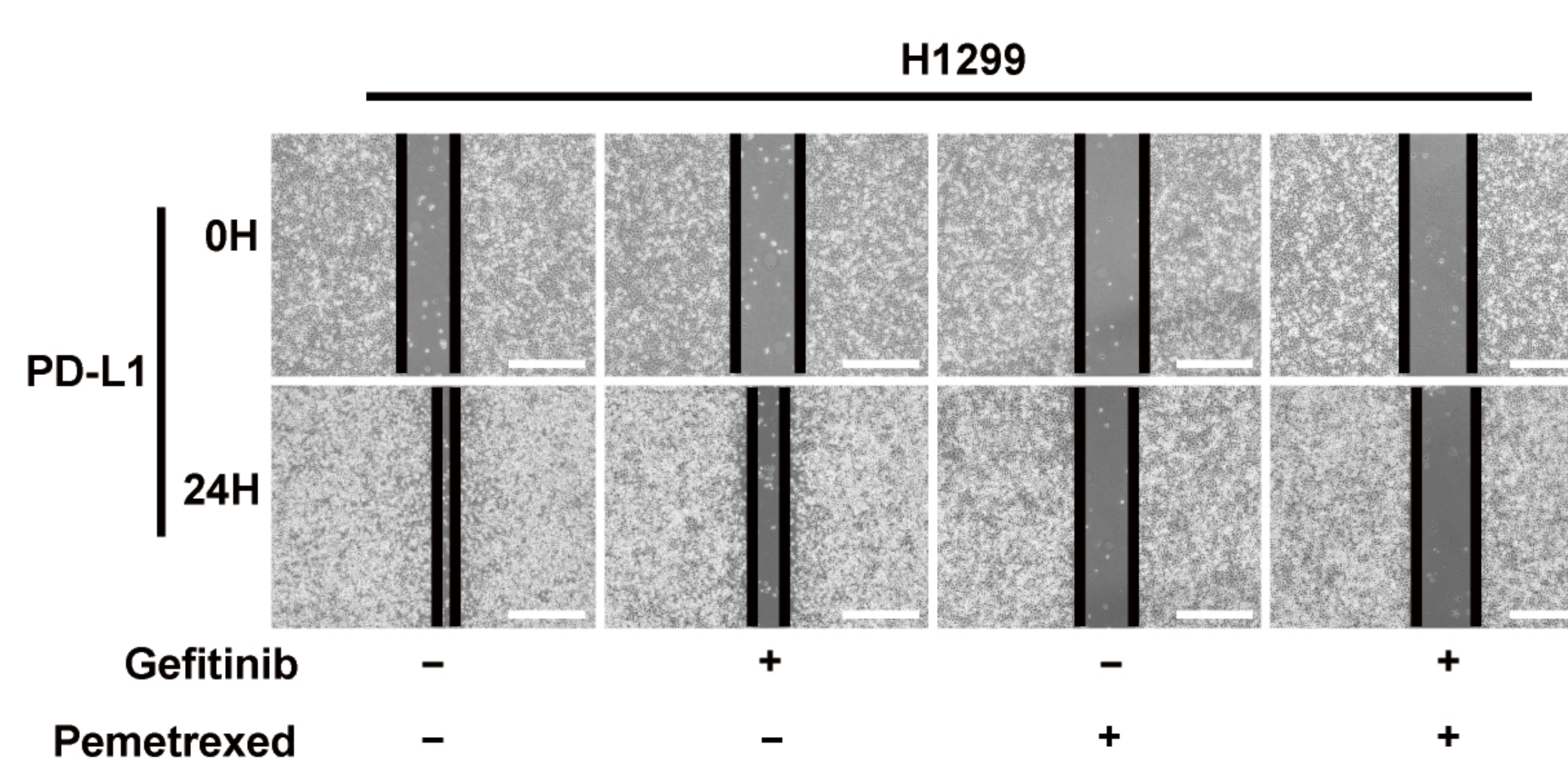
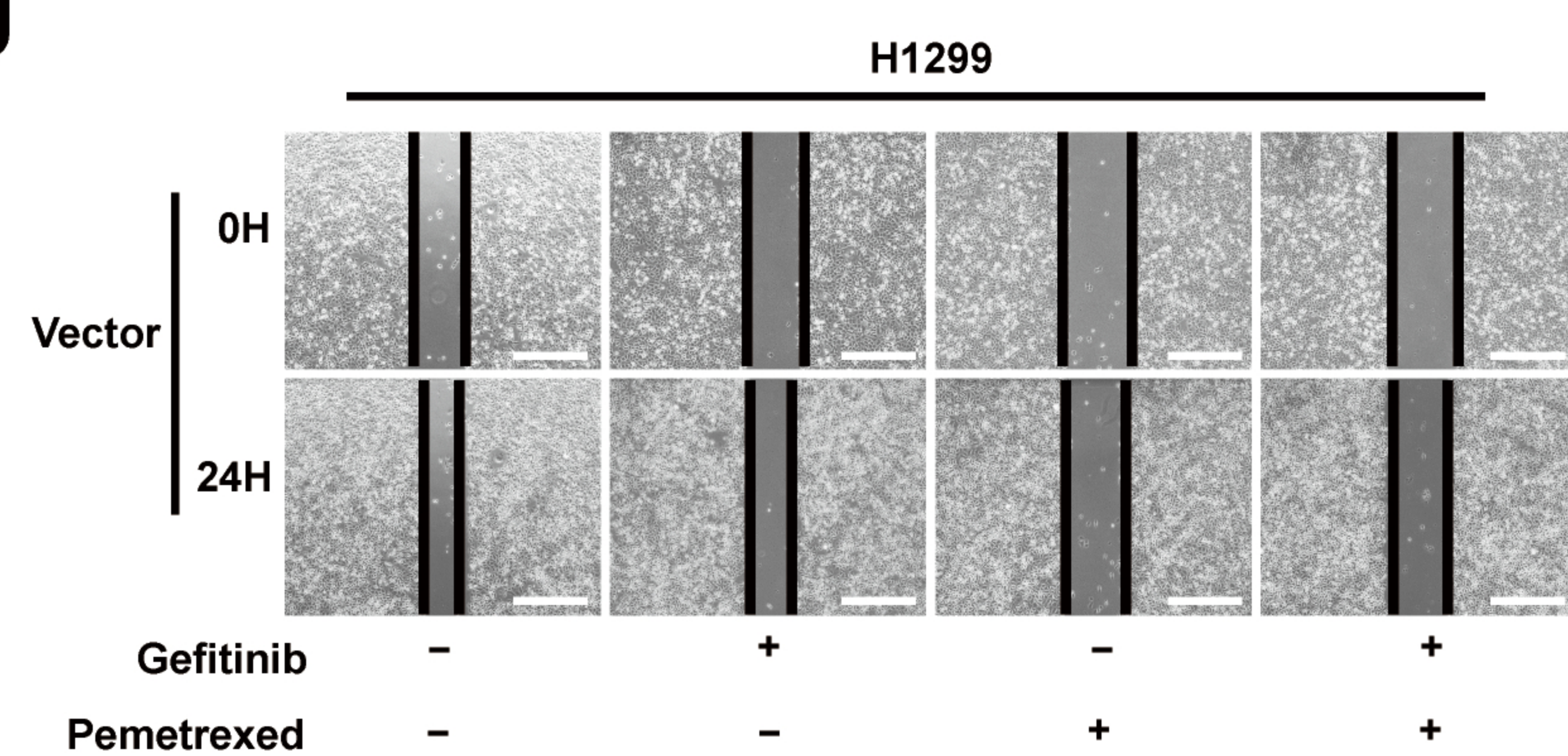
Characteristics	Objective responses (complete and partial) (n)	Patients (n)	ORR (%)	Univariate analysis		Multivariate analysis	
				Odds ratio (95% CI)	<i>p</i>	Odds ratio (95 % CI)	<i>p</i>
Sex							
male	13	32	40.6	0.489	0.147	0.324	0.125
female	21	36	58.3	(0.186-1.286)		(0.077-1.367)	
Age							
< 60	16	34	47.1	0.790	0.628	1.141	0.813
≥ 60	18	34	52.9	(0.305-2.048)		(0.383-3.400)	
Smoking history							
no	23	45	51.1	1.140	0.798	0.567	0.469
yes	11	23	47.8	(0.417-3.117)		(0.122-2.636)	
TNM stage							
III	8	11	72.7	3.179	0.112	3.626	0.112
IV	26	57	45.6	(0.764-13.228)		(0.741-17.737)	
PD-L1status							
negative	16	22	72.7	4.148	0.012*	4.170	0.017*
positive	18	46	39.1	(1.368-12.580)		(1.294-13.437)	

Abbreviations: ORR, Objective response rate; CI, confidence interval. **p* < 0.05

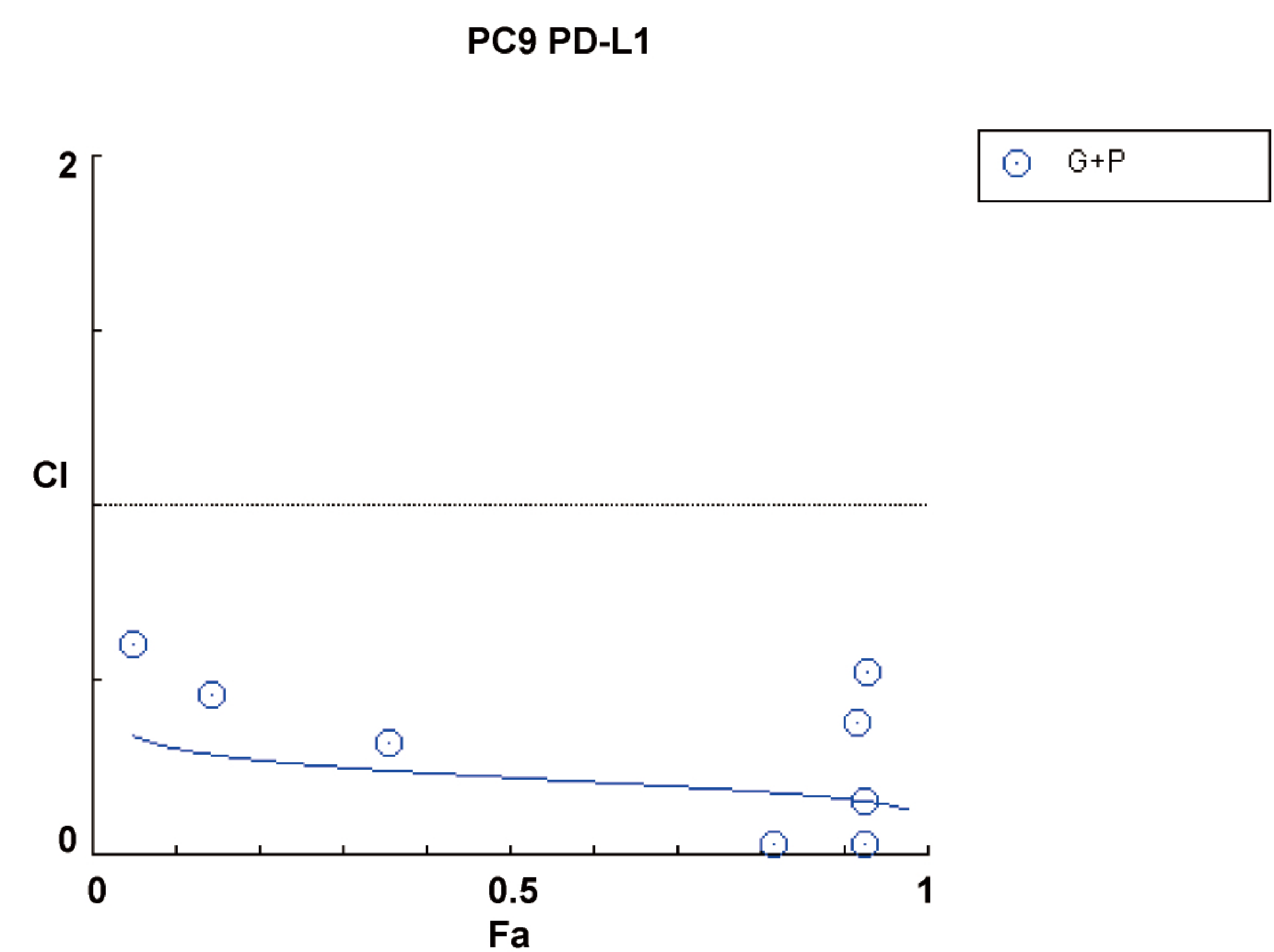
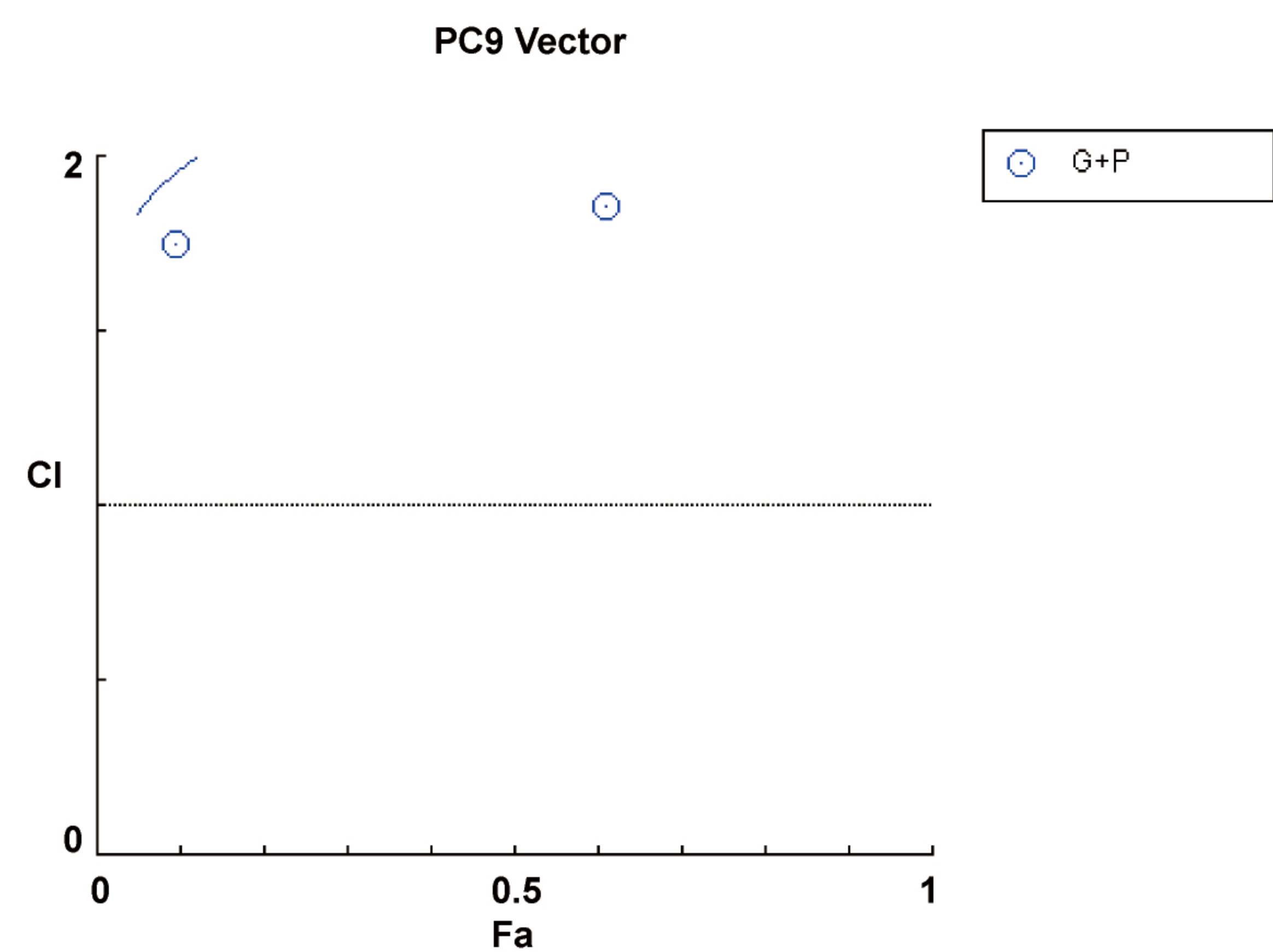
GO Pathway Enrichment





A**C****F****B****D****E****G****H****I****J**

A



B

