

Figure S1. Loss of KDM5D expression in CDDP-resistant neuroblastoma cell lines. (A) Viability of IMR-32 and IMR-32^{CDDP}, SK-N-F1 and SK-N-F1^{CDDP} cells after 72 h treatment with CDDP. SK-N-F1 has 27.02 μ M and CDDP-resistant SK-N-F1^{CDDP} has IC₅₀ 38.02 μ M. IMR-32 has IC₅₀ 25.29 μ M and CDDP-resistant IMR-32^{CDDP} has IC₅₀ 43.61 μ M. Data shown are representative from one measurement of two independent experiments. (B) KDM5D expression of mRNA in the CDDP-sensitive IMR-32 and the CDDP-resistant IMR-32^{CDDP}. KDM5D expression was lost in CDDP-resistant IMR-32^{CDDP} cell line. Treatment with 20 μ M CDDP significantly decreased KDM5D expression levels in IMR-32 depending on the incubation time (P<0.01; P<0.001). (C) KDM5D expression of mRNA in the CDDP-sensitive SK-N-F1 and the CDDP-resistant SK-N-F1^{CDDP}. KDM5D expression was lost in CDDP-resistant SK-N-F1^{CDDP} cell line. Treatment with 20 μ M CDDP significantly decreased KDM5D level in SK-N-F1 depending on the incubation time (P<0.001). (D) Protein expression levels of KDM5D in the CDDP-sensitive IMR-32 and CDDP-resistant IMR-32^{CDDP}. KDM5D expression was lost in CDDP-resistant IMR-32^{CDDP} cell line. Treatment with 20 μ M CDDP significantly decreased KDM5D protein expression levels in IMR-32 depending on the incubation time (P<0.01; P<0.001). (E) Protein expression levels of KDM5D in the CDDP-sensitive SK-N-F1 and the CDDP-resistant SK-N-F1^{CDDP}. KDM5D expression was lost in CDDP-resistant SK-N-F1^{CDDP} cell line. Treatment with 20 μ M CDDP significantly decreased KDM5D protein expression levels in SK-N-F1 depending on the incubation time (P<0.001). Data are shown as mean \pm standard deviation from two independent experiments. Statistical significance was determined using one-way (B-E) and two-way ANOVA (A) with Tukey's post-hoc test. **P<0.01; ***P<0.001.

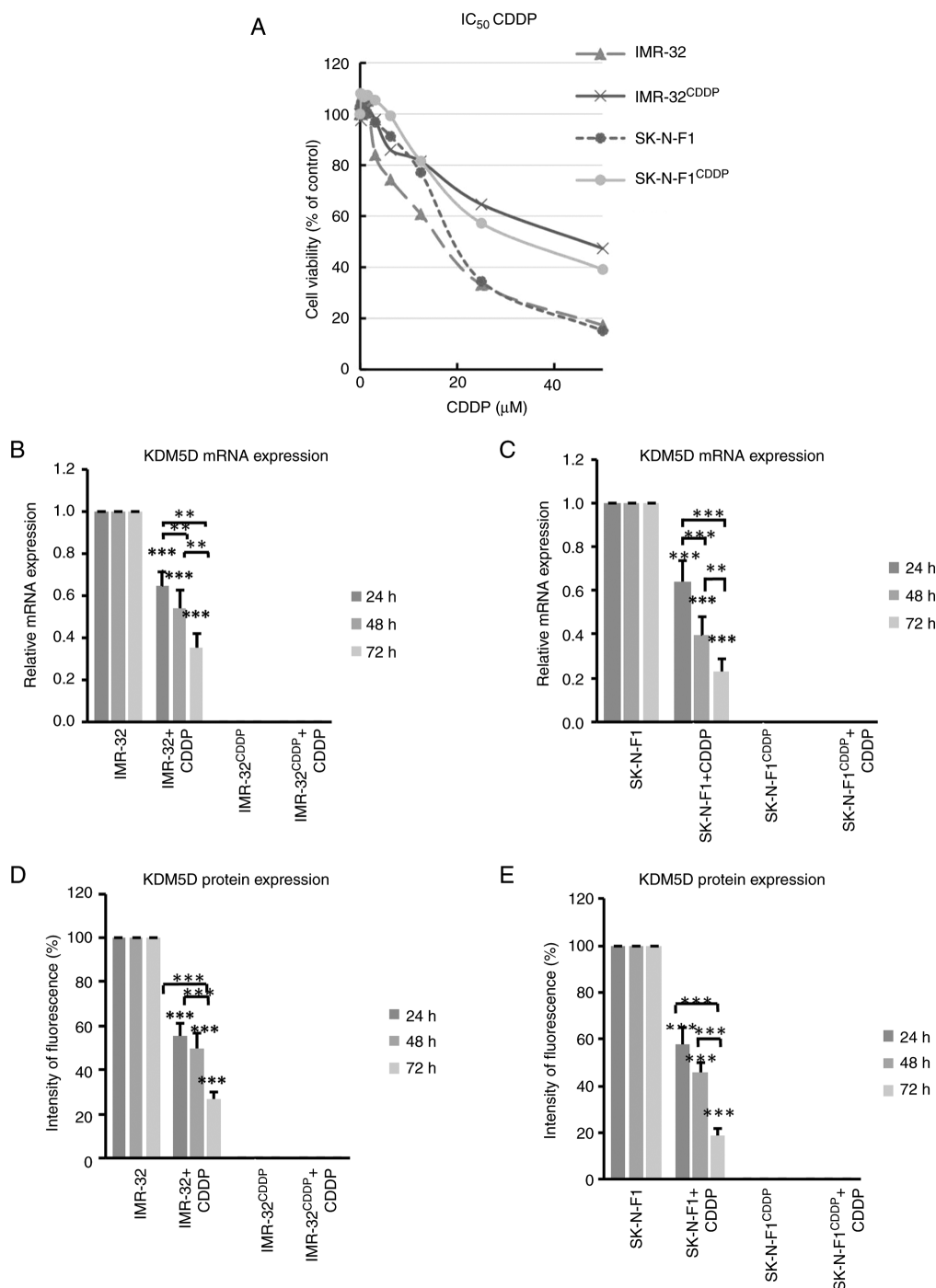


Figure S2. Representative cytometric density dot plots in UKF-NB-3 corresponding to the quantitative data shown in Fig. 1C. Each panel represents the samples used in the experiment: (A) UKF-NB-3 after 24 h of incubation, (B) UKF-NB-3 with CDDP after 24 h of incubation, (C) UKF-NB-3 after 48 h of incubation, (D) UKF-NB-3 with CDDP after 48 h of incubation, (E) UKF-NB-3 after 72 h of incubation and (F) UKF-NB-3 with CDDP after 72 h of incubation. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. CD, cisplatin; NB3, UKF-NB-3.

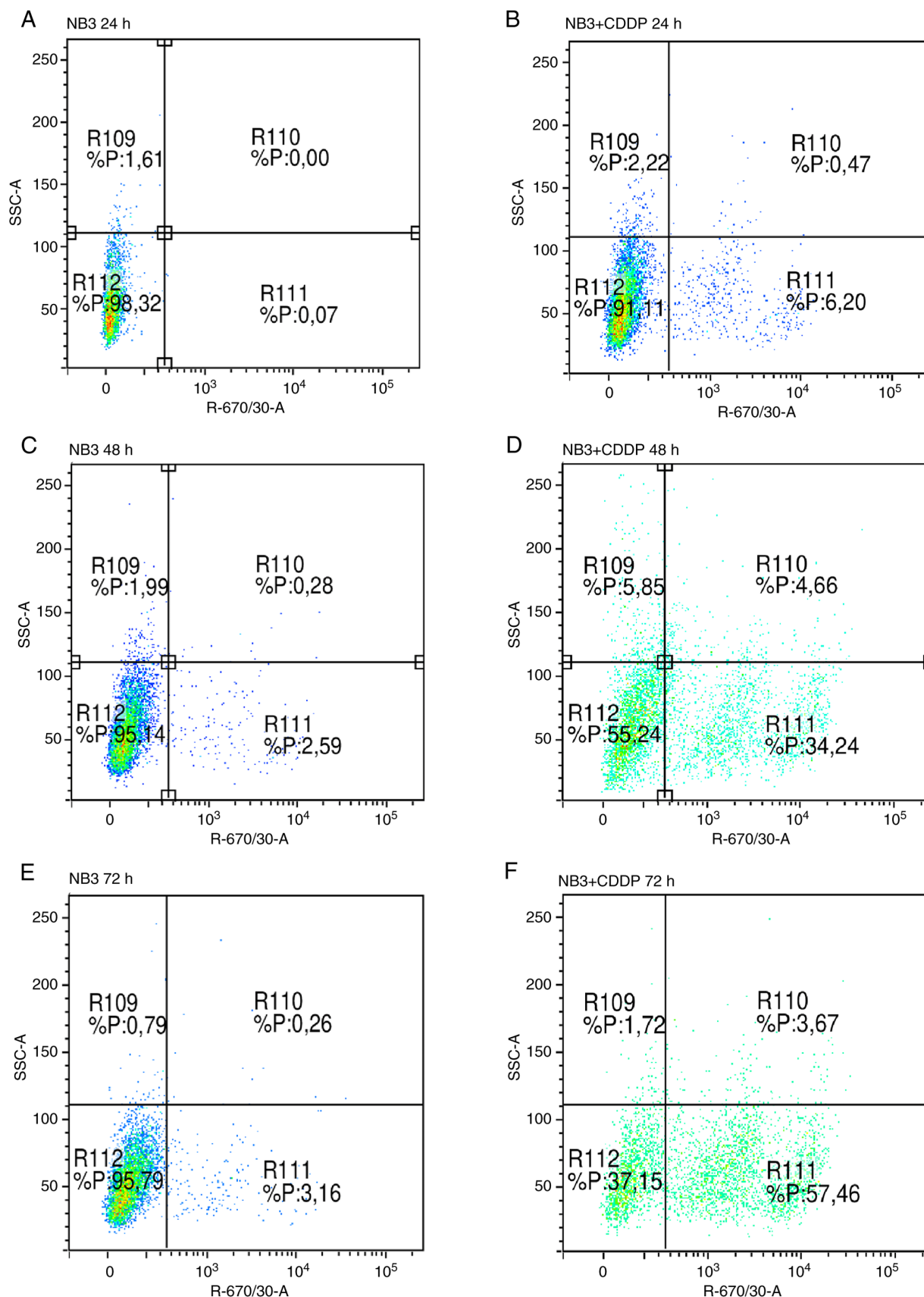


Figure S3. Representative cytometric density dot plots in UKF-NB-3^{CDDP} corresponding to the quantitative data shown in Fig. 1C. Each panel represents the samples used in the experiment: (A) UKF-NB-3 CDDP after 24 h of incubation, (B) UKF-NB-3 CDDP with CDDP after 24 h of incubation, (C) UKF-NB-3 CDDP after 48 h of incubation, (D) UKF-NB-3 CDDP with CDDP after 48 h of incubation, (E) UKF-NB-3 CDDP after 72 h of incubation and (F) UKF-NB-3 CDDP with CDDP after 72 h of incubation. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. NB3, UKF-NB-3.

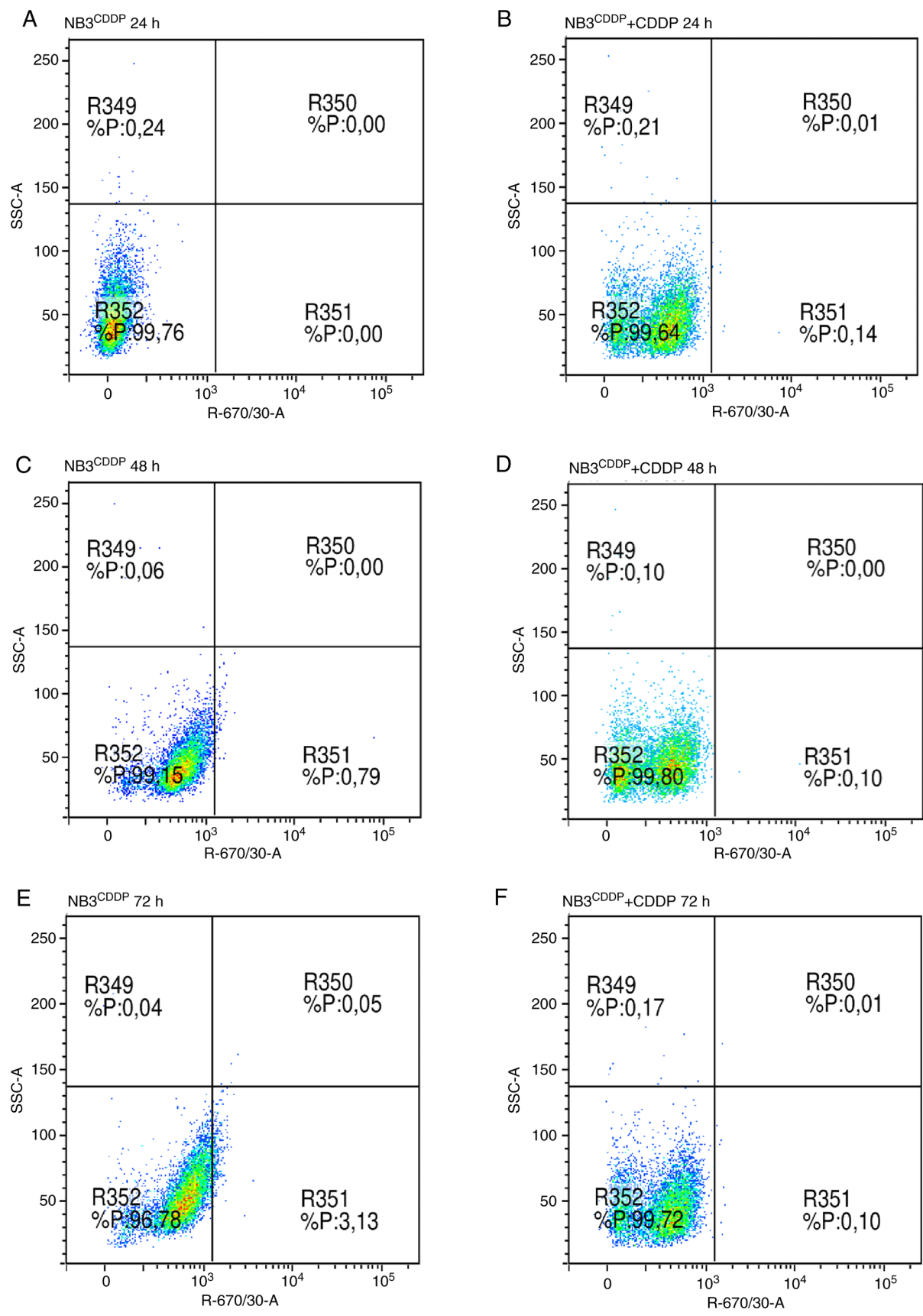


Figure S4. Representative cytometric density dot plots in IMR-32 corresponding to the quantitative data shown in Fig. S1C. Each panel represents the samples used in the experiment: (A) IMR-32 after 24 h of incubation, (B) IMR-32 with CDDP after 24 h of incubation, (C) IMR-32 after 48 h of incubation, (D) IMR-32 with CDDP after 48 h of incubation, (E) IMR-32 after 72 h of incubation and (F) IMR-32 with CDDP after 72 h of incubation. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations.

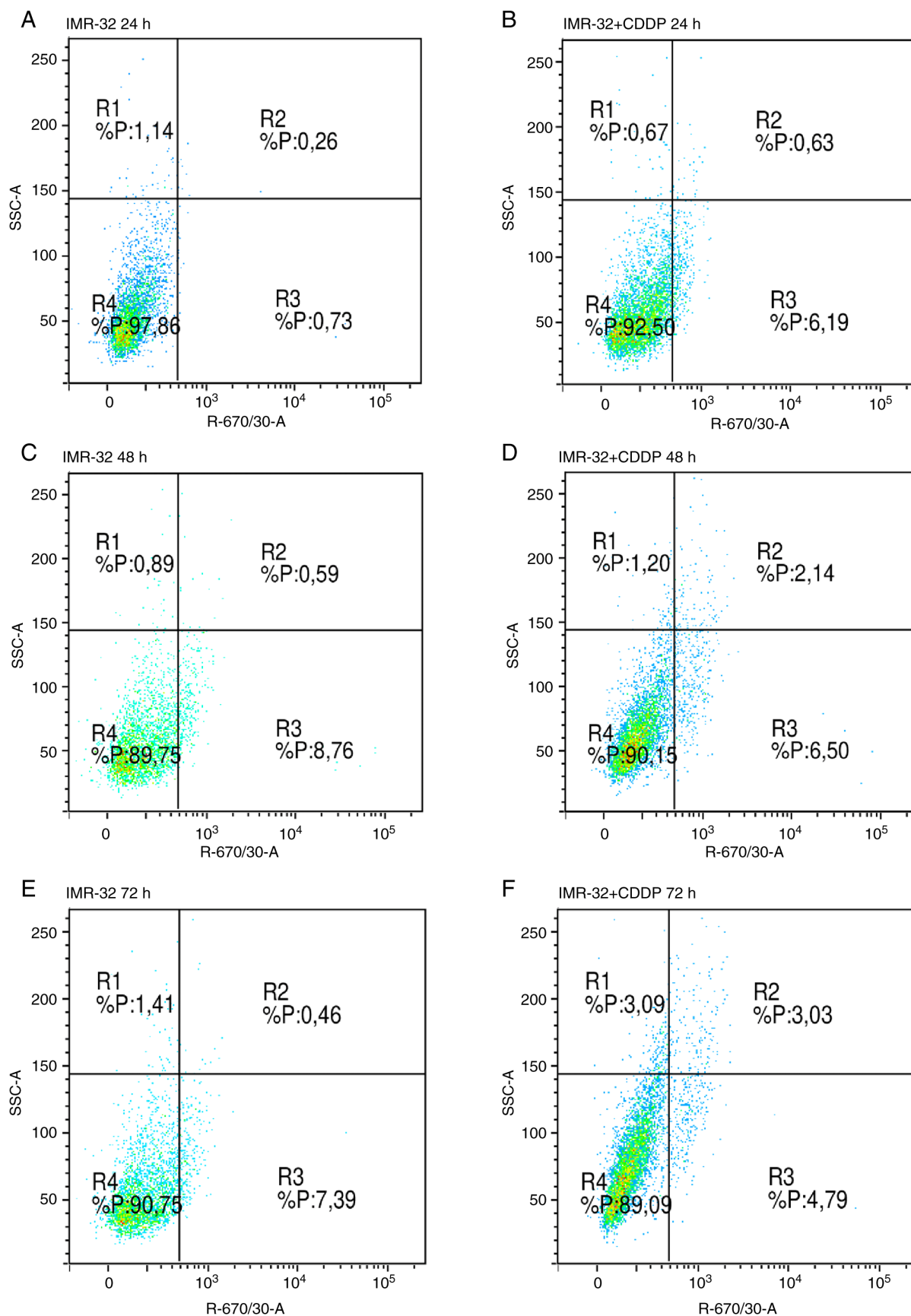


Figure S5. Representative cytometric density dot plots in IMR-32^{CDDP} corresponding to the quantitative data shown in Fig. S1C. Each panel represents the samples used in the experiment: (A) IMR-32 CDDP after 24 h of incubation, (B) IMR-32 CDDP with CDDP after 24 h of incubation, (C) IMR-32 CDDP after 48 h of incubation, (D) IMR-32 CDDP with CDDP after 48 h of incubation, (E) IMR-32 CDDP after 72 h of incubation and (F) IMR-32 CDDP with CDDP after 72 h of incubation. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations.

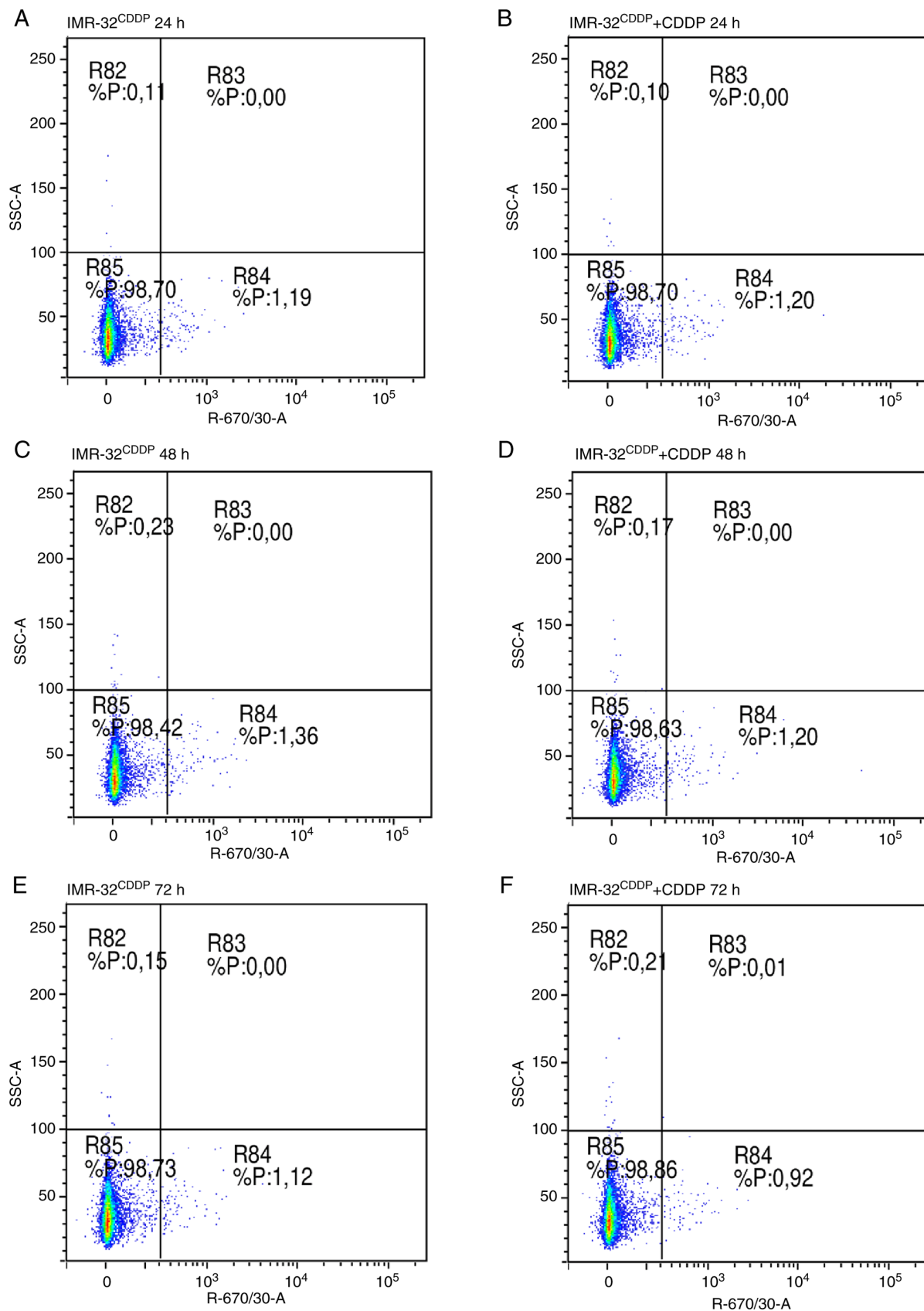


Figure S6. Representative cytometric density dot plots in SK-N-F1 corresponding to the quantitative data shown in Fig. S1E. Each panel represents the samples used in the experiment: (A) SK-N-F1 after 24 h of incubation, (B) SK-N-F1 with CDDP after 24 h of incubation, (C) SK-N-F1 after 48 h of incubation, (D) SK-N-F1 with CDDP after 48 h of incubation, (E) SK-N-F1 after 72 h of incubation and (F) SK-N-F1 with CDDP after 72 h of incubation. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations.

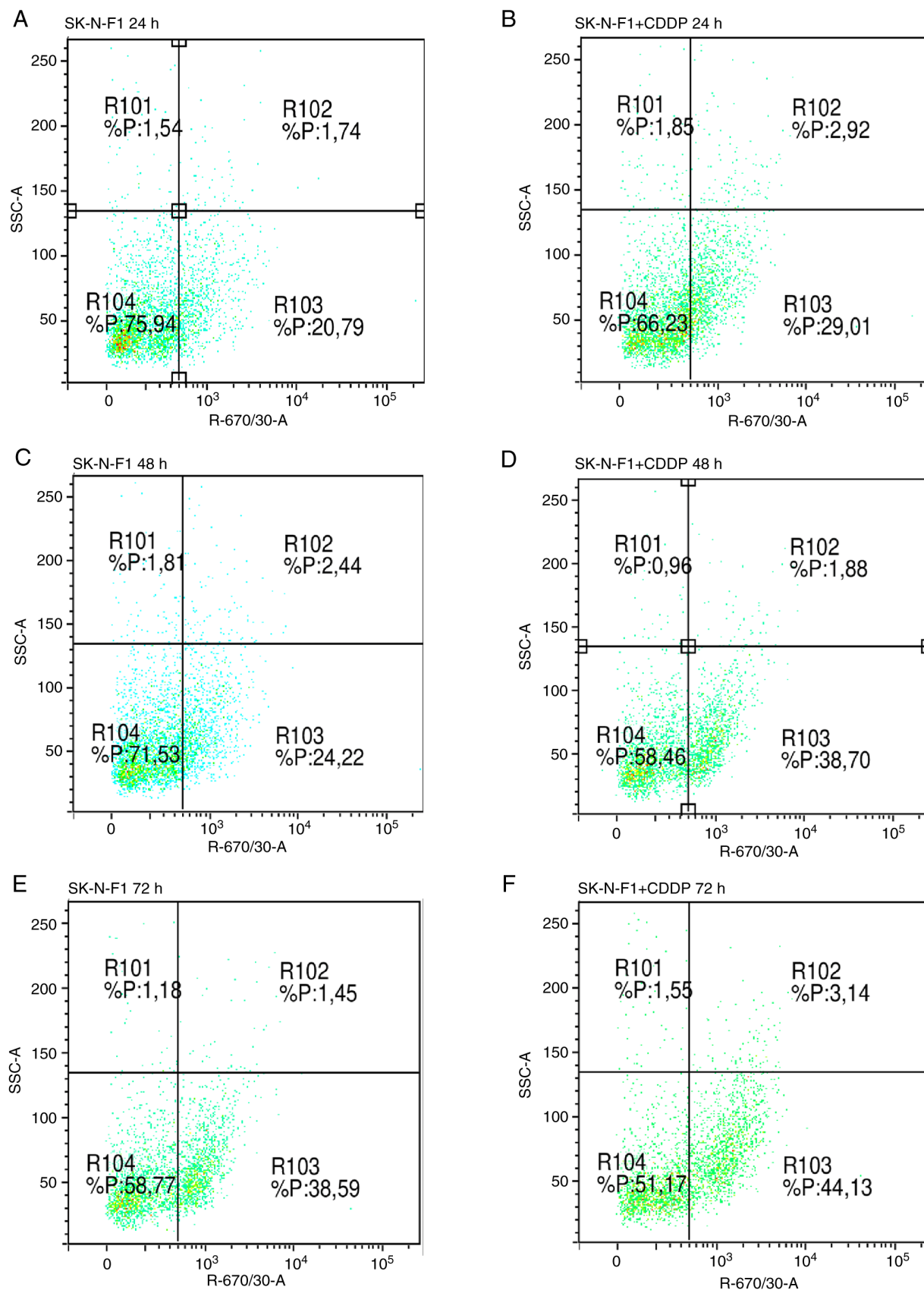


Figure S7. Representative cytometric density dot plots in SK-N-F1^{CDDP} corresponding to the quantitative data shown in Fig. 1SE. Each panel represents the samples used in the experiment: (A) SK-N-F1 CDDP after 24 h of incubation, (B) SK-N-F1 CDDP with CDDP after 24 h of incubation, (C) SK-N-F1 CDDP after 48 h of incubation, (D) SK-N-F1 CDDP with CDDP after 48 h of incubation, (E) SK-N-F1 CDDP after 72 h of incubation and (F) SK-N-F1 CDDP with CDDP after 72 h of incubation. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations.

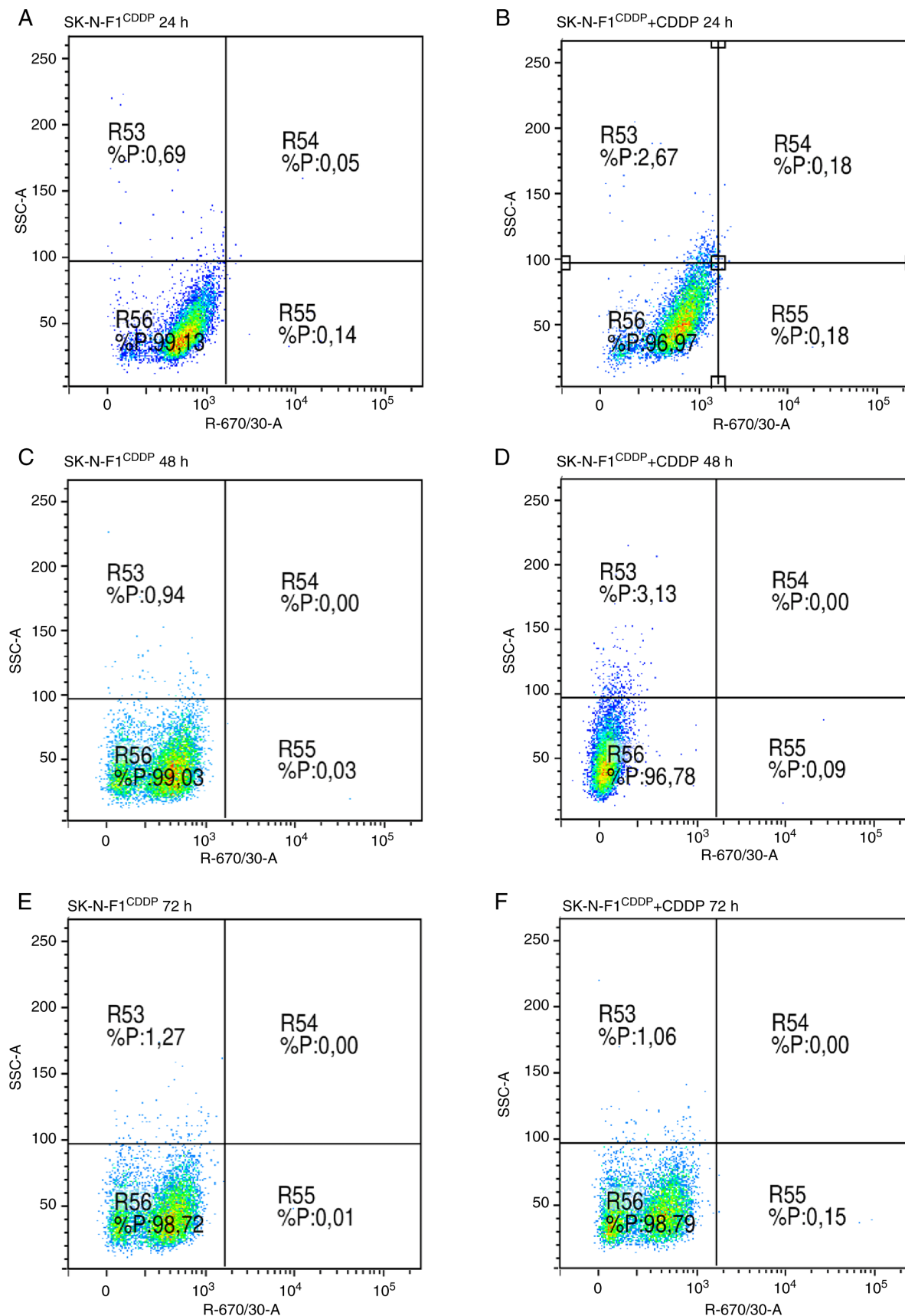


Figure S8. Verification of silencing and overexpression of KDM5D. (A) Western blot analysis of KDM5D levels in UKF-NB-3 cells transfected with siKDM5D #1 (12.5 nM) or siKDM5D #2 (25 nM) compared with control NC. (B) Western blot analysis of KDM5D levels in UKF-NB-3 cells transfected with the KDM5D ORF-clone plasmid pCMV-3Tag1, expressing the KDM5D gene (pl-KDM5D #1, 8 ng/ μ l or pl-KDM5D #2, 16 ng/ μ l). Data are presented as mean \pm standard deviation from three independent experiments. Statistical significance was determined using one-way ANOVA with Tukey's post hoc test. ***P<0.001. CTR, control; si, short interfering RNA; pl, ORF-clone plasmid.

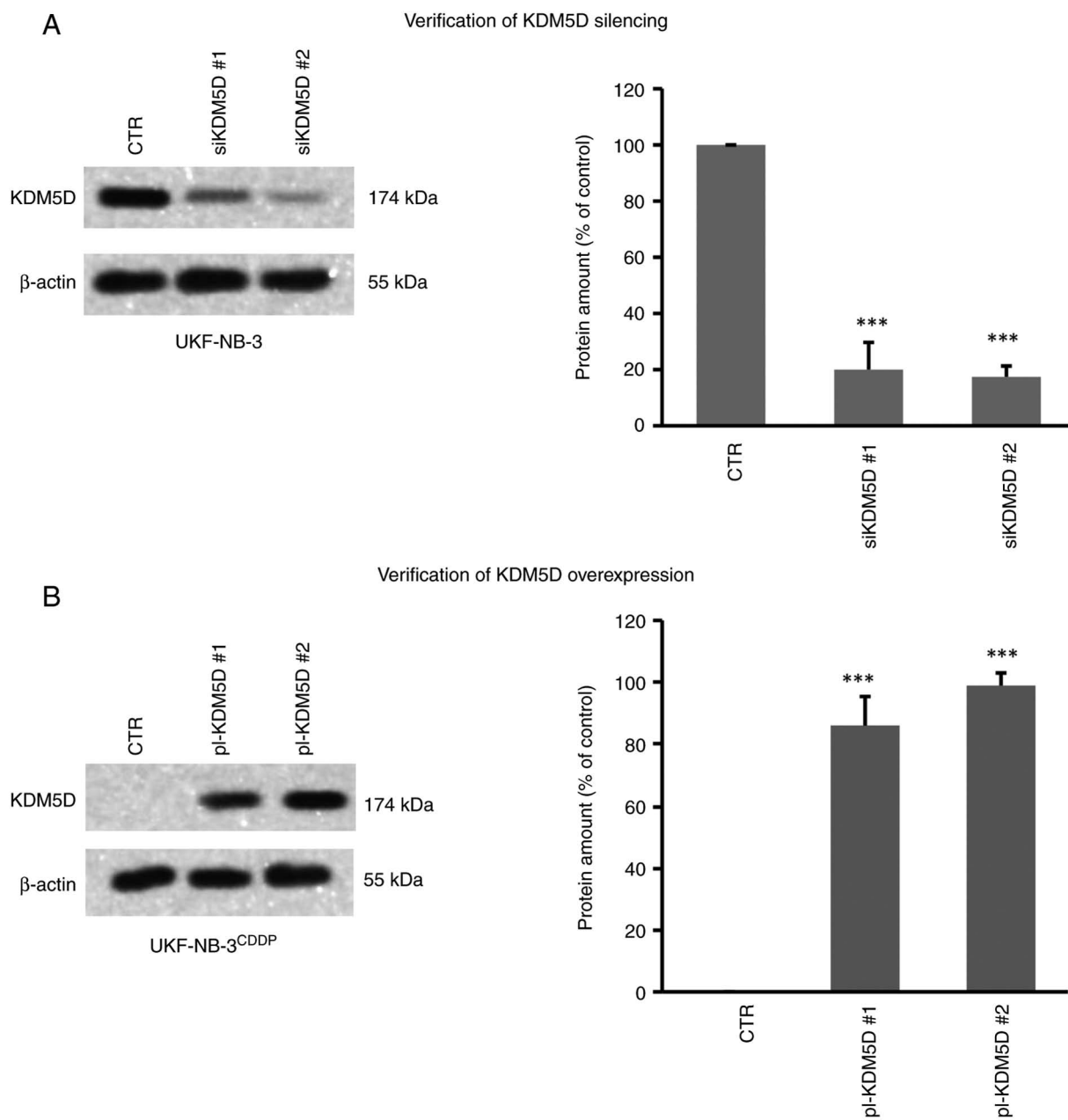


Figure S9. Representative cytometric density dot plots in UKF-NB-3 corresponding to the quantitative data shown in Fig. 2B. Each panel represents the samples used in the experiment: (A) UKF-NB-3 CTR, (B) UKF-NB-3 NC#1, (C) UKF-NB-3 NC#2, (D) UKF-NB-3 siKDM5D#1 and (E) UKF-NB-3 siKDM5D#2. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. CD, cisplatin; NB3, sensitive cell line UKF-NB-3; NC, negative control; si, short interfering.

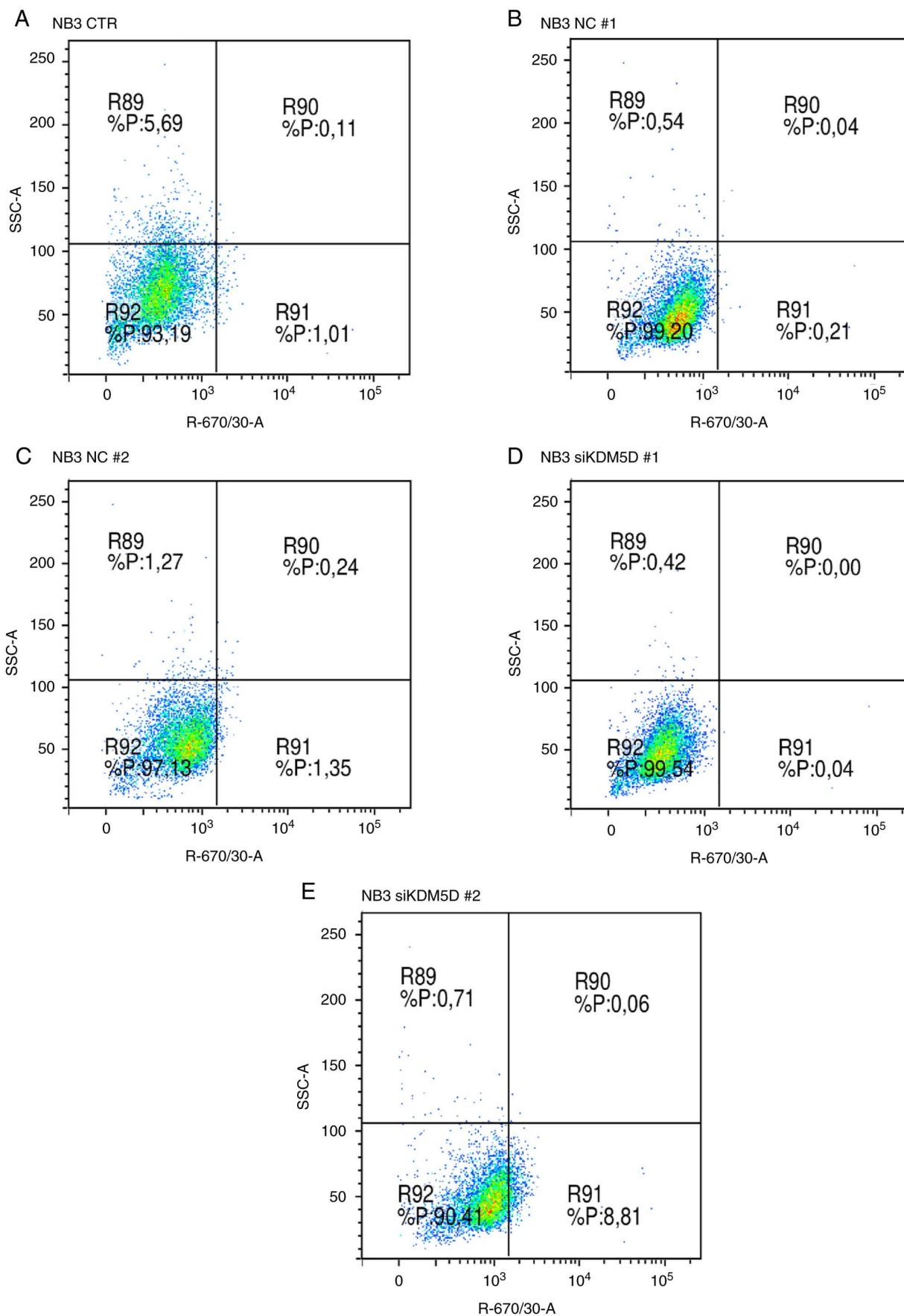


Figure S10. Representative cytometric density dot plots in UKF-NB-3 corresponding to the quantitative data shown in Fig. 2D. Each panel represents the samples used in the experiment: (A) UKF-NB-3 NC, (B) UKF-NB-3 NC with CDDP, (C) UKF-NB-3 siKDM5D and (D) UKF-NB-3 siKDM5D with CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. CD, cisplatin; NB3, sensitive cell line UKF-NB-3; NC, negative control; si, short interfering.

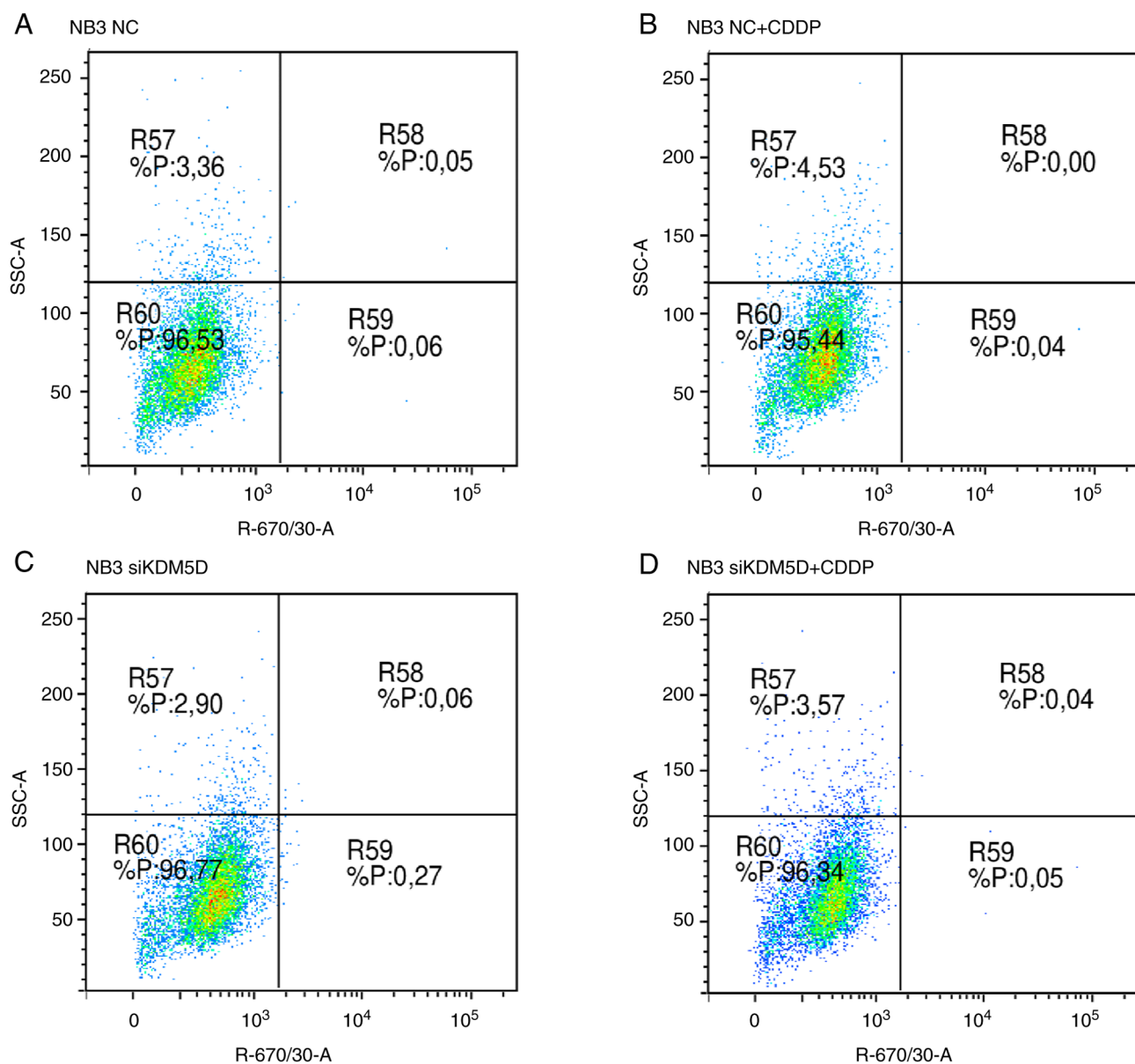


Figure S11. Representative cytometric density dot plots in UKF-NB-3^{CDDP} corresponding to the quantitative data shown in Fig. 2F. Each panel represents the samples used in the experiment: (A) UKF-NB-3 NC (B) UKF-NB-3 NC with CDDP, (C) UKF-NB-3 siKDM5D and (D) UKF-NB-3 siKDM5D with CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-H3k4me3 antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. CD, cisplatin; NB3, sensitive cell line UKF-NB-3; NC, negative control; si, short interfering.

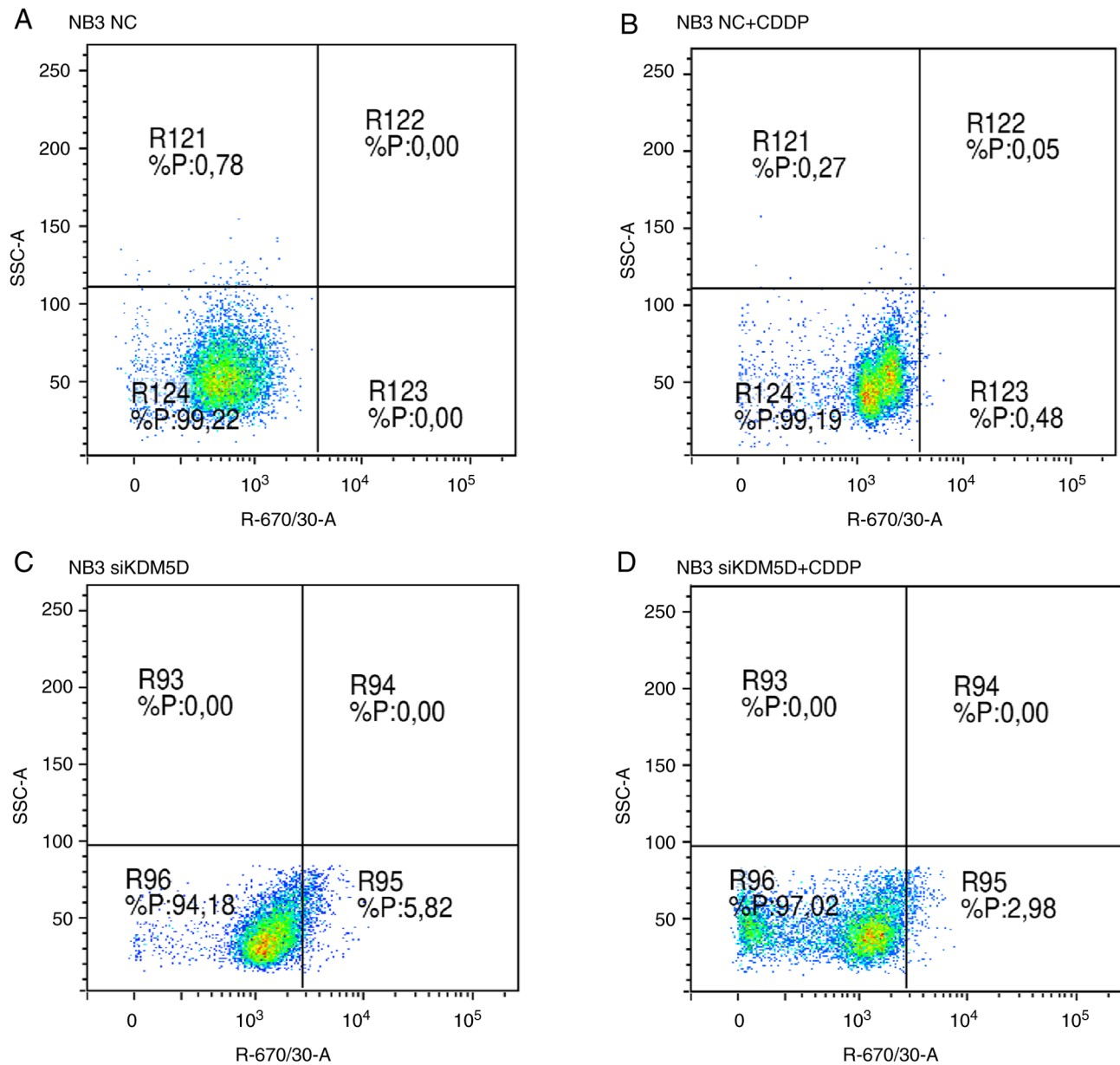


Figure S12. Representative cytometric density dot plots corresponding to the quantitative data shown in Fig. 3A. Each panel represents the samples used in the experiment: (A) UKF-NB-3 CDDP CTR, (B) UKF-NB-3 CDDP mock#1, (C) UKF-NB-3 CDDP mock#2, (D) UKF-NB-3 CDDP pl-KDM5D#1 and (E) UKF-NB-3 CDDP pl-KDM5D#2. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. NB3, cell line UKF-NB-3; mock, control cells with control plasmid; pl, ORF-clone plasmid.

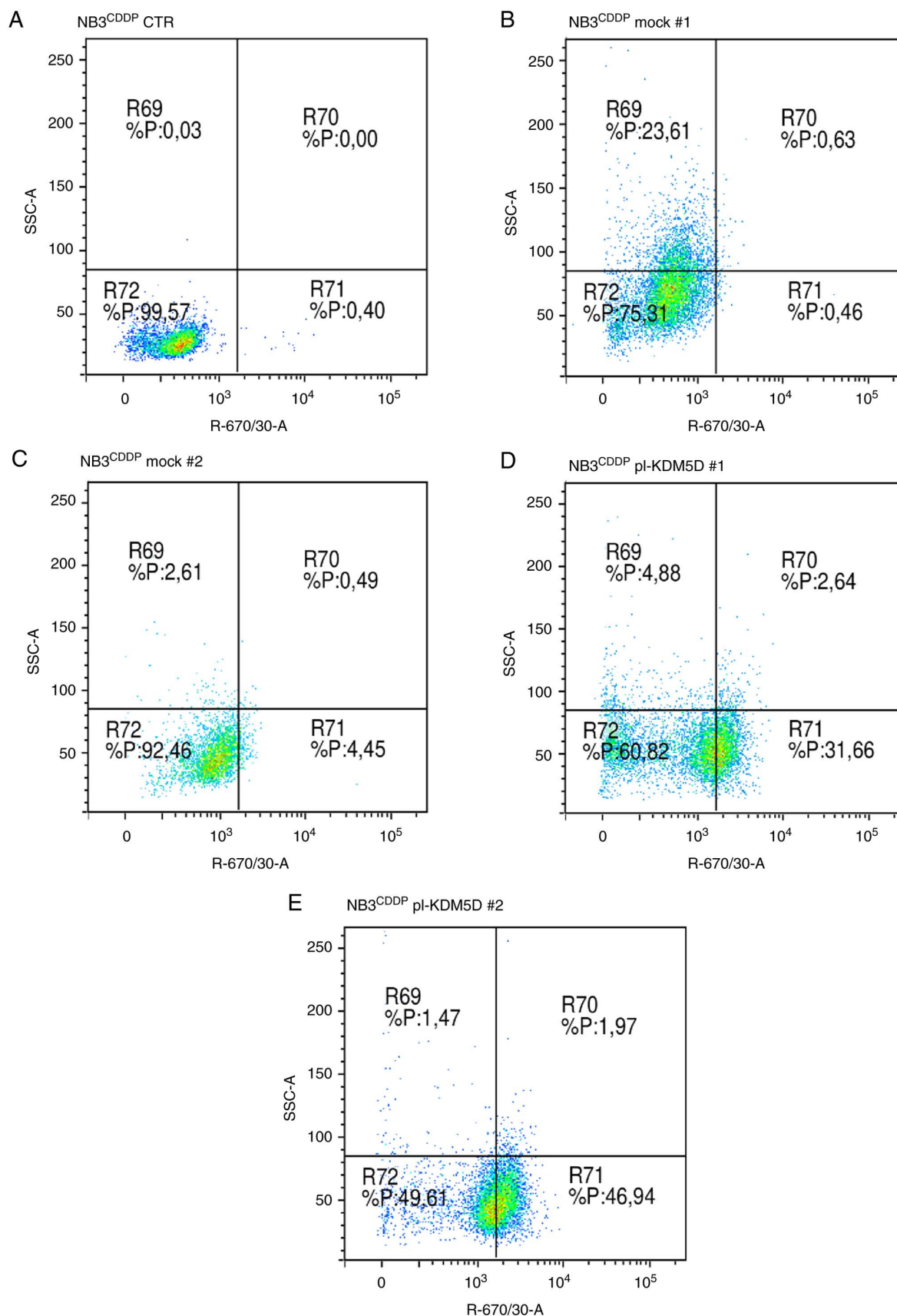


Figure S13. Representative cytometric density dot plots in UKF-NB-3^{CDDP} corresponding to the quantitative data shown in Fig. 3C. Each panel represents the samples used in the experiment: (A) UKF-NB-3 CDDP mock, (B) UKF-NB-3 CDDP mock with CDDP, (C) UKF-NB-3CDDP pl-KDM5D and (D) UKF-NB-3 CDDP pl-KDM5D with CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-KDM5D antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations NB3, cell line UKF-NB-3; mock, control cells with control plasmid; pl, ORF-clone plasmid.

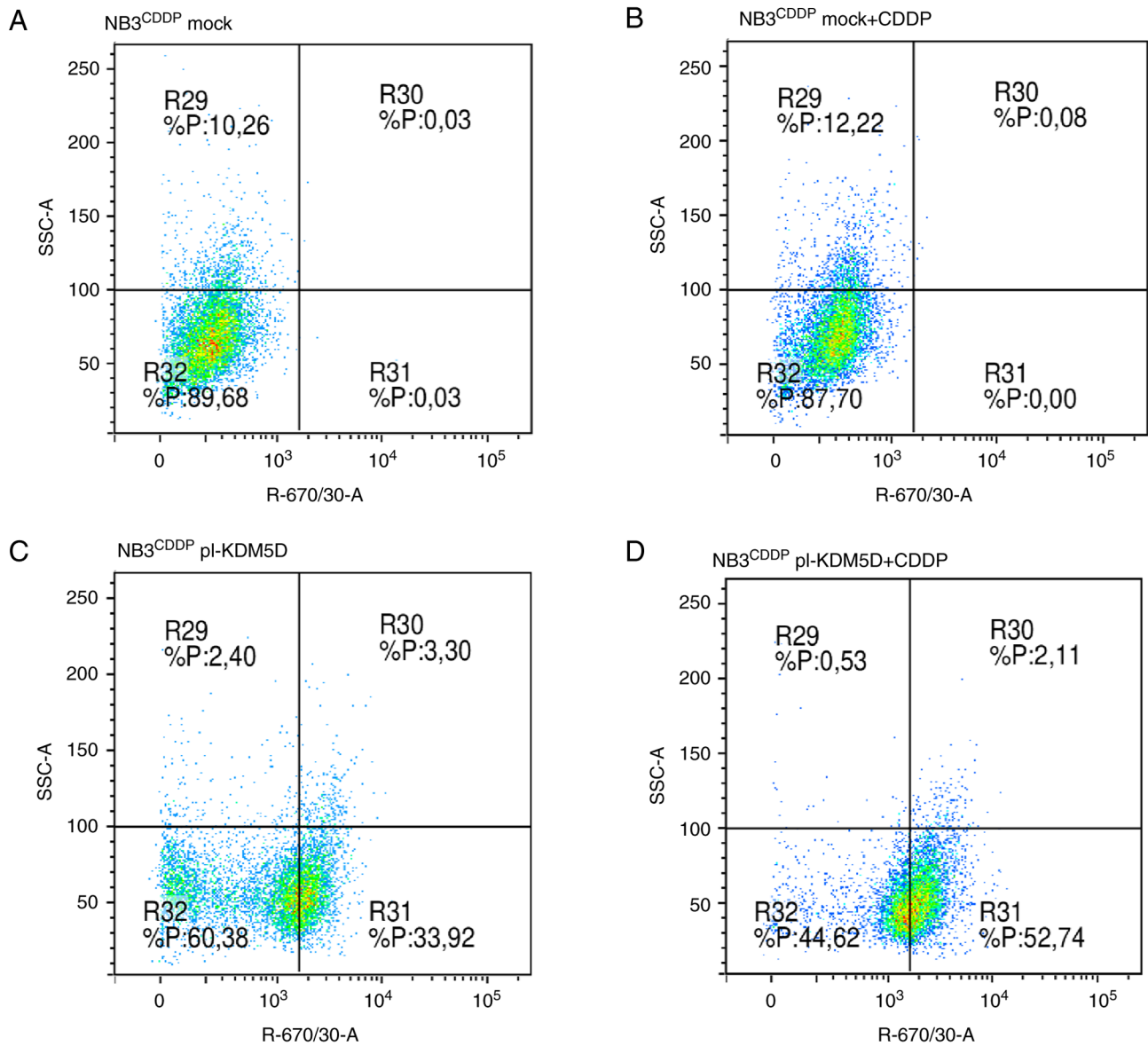


Figure S14. Representative cytometric density dot plots in UKF-NB-3^{CDDP} corresponding to the quantitative data shown in Fig. 3E. Each panel represents the samples used in the experiment: (A) UKF-NB-3 CDDP mock, (B) UKF-NB-3 CDDP mock with CDDP, (C) UKF-NB-3CDDP pI-KDM5D and (D) UKF-NB-3 CDDP pI-KDM5D with CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-H3k4me3 antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. NB3, cell line UKF-NB-3; mock, control cells with control plasmid; pl, ORF-clone plasmid.

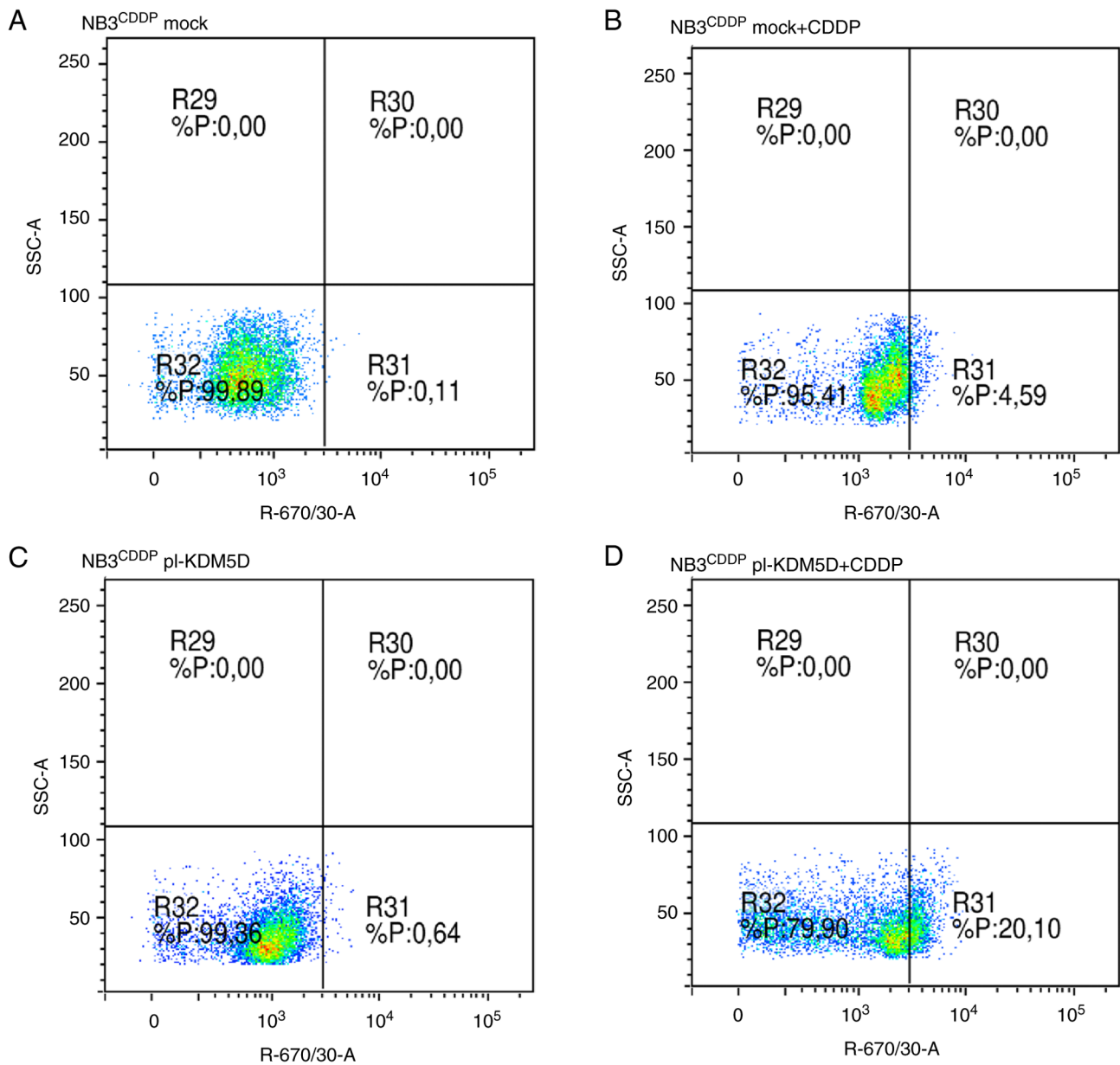


Figure S15. Viability after incubation with CDDP (24 h) and KDM5D silencing in UKF-NB-3 decrease depending on the concentration ($P < 0.05$; $P < 0.01$), decrease was smaller compared with NC ($P < 0.05$; $P < 0.01$). Data are shown as mean \pm standard deviation from three independent experiments. Statistical significance was determined using two-way ANOVA with Tukey's post hoc test. * $P < 0.05$; ** $P < 0.01$. NC, negative control; si, short interfering; CTR, control.

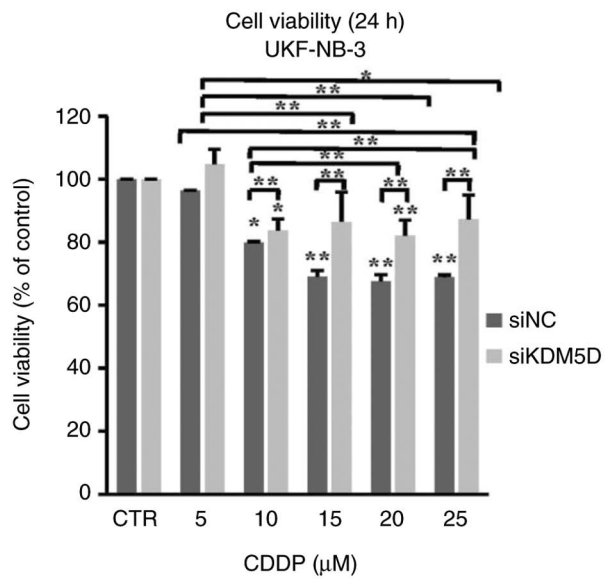


Figure S16. KDM5D expression affects cell sensitivity to CDDP in UKF-NB-3 and UKF-NB-3^{CDDP}. (A) Cell viability after incubation with CDDP (24 h) and inhibition of KDM5s with KDOAM-25 (48 h) in UKF-NB-3 is not affected even after treatment with increasing concentrations of CDDP compared with controls without KDOAM-25, in which cell viability decreased ($P < 0.001$). (B) Cell viability after incubation with CDDP (24 h) and inhibition of KDM5s with KDOAM-25 (48 h) in UKF-NB-3^{CDDP} is not affected even after treatment with increasing concentrations of CDDP compared with controls without KDOAM-25, in which cell viability decreased ($P < 0.01$). (C) Cell viability after incubation with CDDP (48 h) and inhibition of KDM5s with KDOAM-25 (48 h) in UKF-NB-3 is not affected even after treatment with increasing concentrations of CDDP compared with controls without KDOAM-25, in which cell viability decreased ($P < 0.001$). (D) Cell viability after incubation with CDDP (48 h) and inhibition of KDM5s with KDOAM-25 (48 h) in UKF-NB-3^{CDDP}. CDDP treatment does not affect cell viability in control or inhibited cells. Data are shown as mean \pm standard deviation from three independent experiments. Statistical significance was determined using two-way ANOVA with Tukey's post hoc test. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. CTR, control.

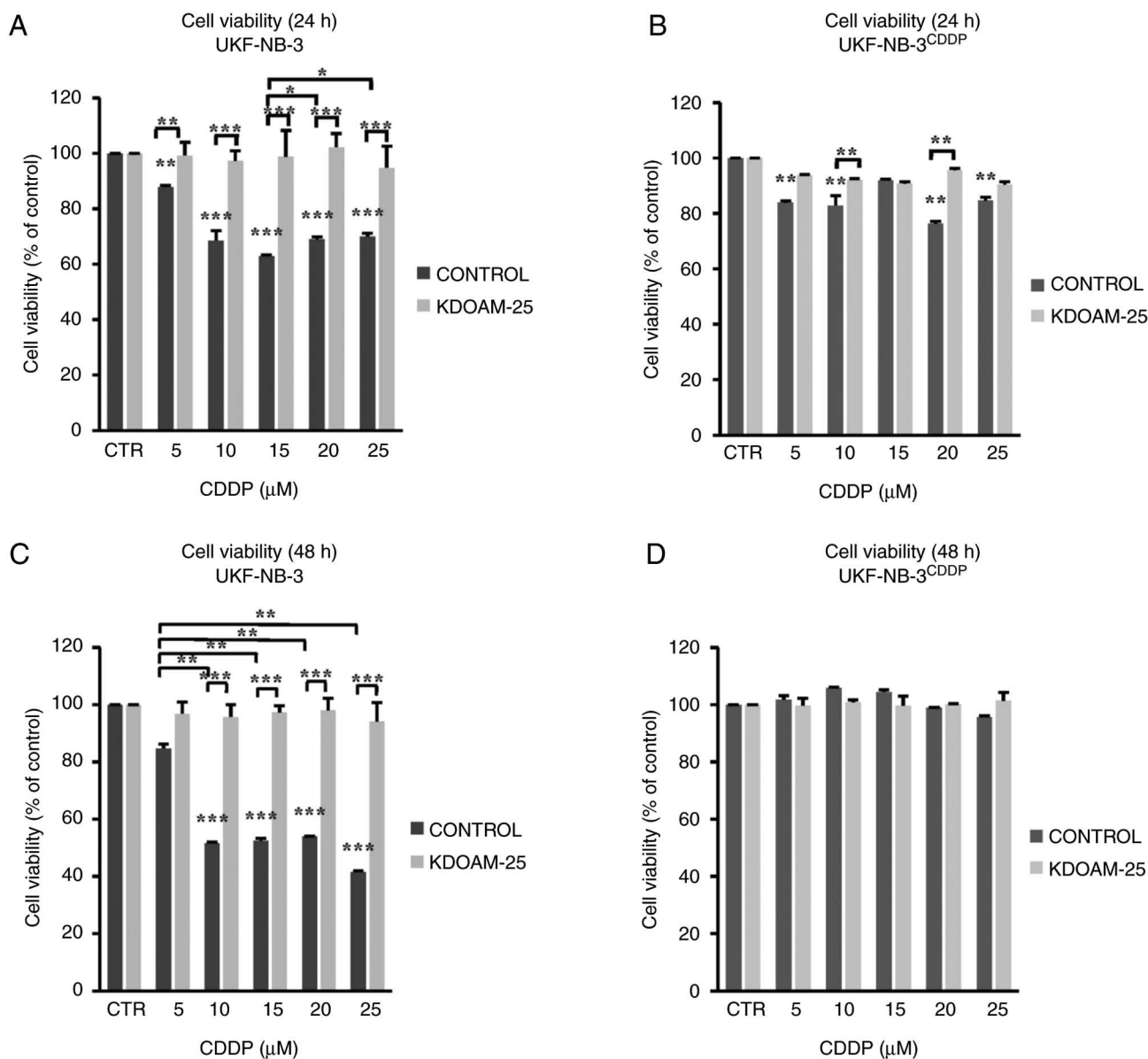


Figure S17. Cell viability after incubation with CDDP (24 h) and transfection with plasmid carrying gene KDM5D (48 h) in UKF-NB-3^{CDDP} does not affect cell viability in control or transfected cells. Data are shown as mean \pm standard deviation from three independent experiments. Statistical significance was determined using two-way ANOVA with Tukey's post hoc test. CTR, control; pl, ORF-clone plasmid.

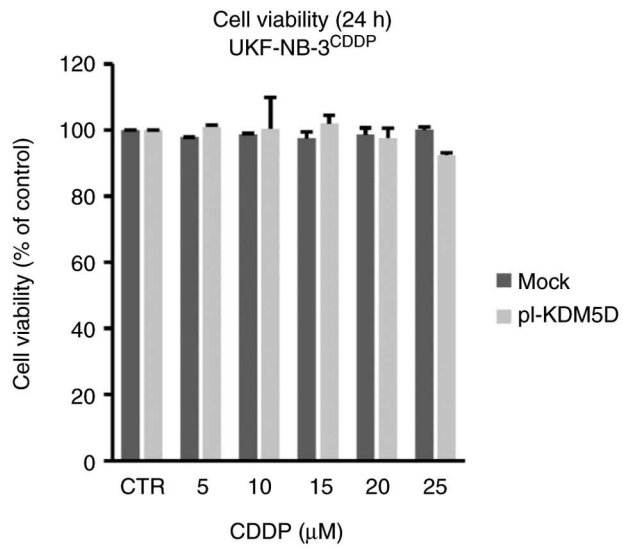


Figure S18. Western blot analysis of expression of KDM5D, caspase-3, cleaved caspase-3, PARP and CUL4A in UKF-NB-3 and UKF-NB-3^{CDDP}. (A) Representative western blotting images of KDM5D, caspase-3, cleaved caspase-3, PARP and CUL4A levels in UKF-NB-3 and UKF-NB-3^{CDDP} cells and their treatment with CDDP. (B) Graphical analysis of western blotting data. Data are shown as mean \pm standard deviation from two independent experiments. Statistical significance was determined using one-way ANOVA with Tukey's post hoc test. *P<0.05; **P<0.01; ***P<0.001. CTR, control; NC, non-coding; si, short interfering; pl, ORF-clone plasmid.

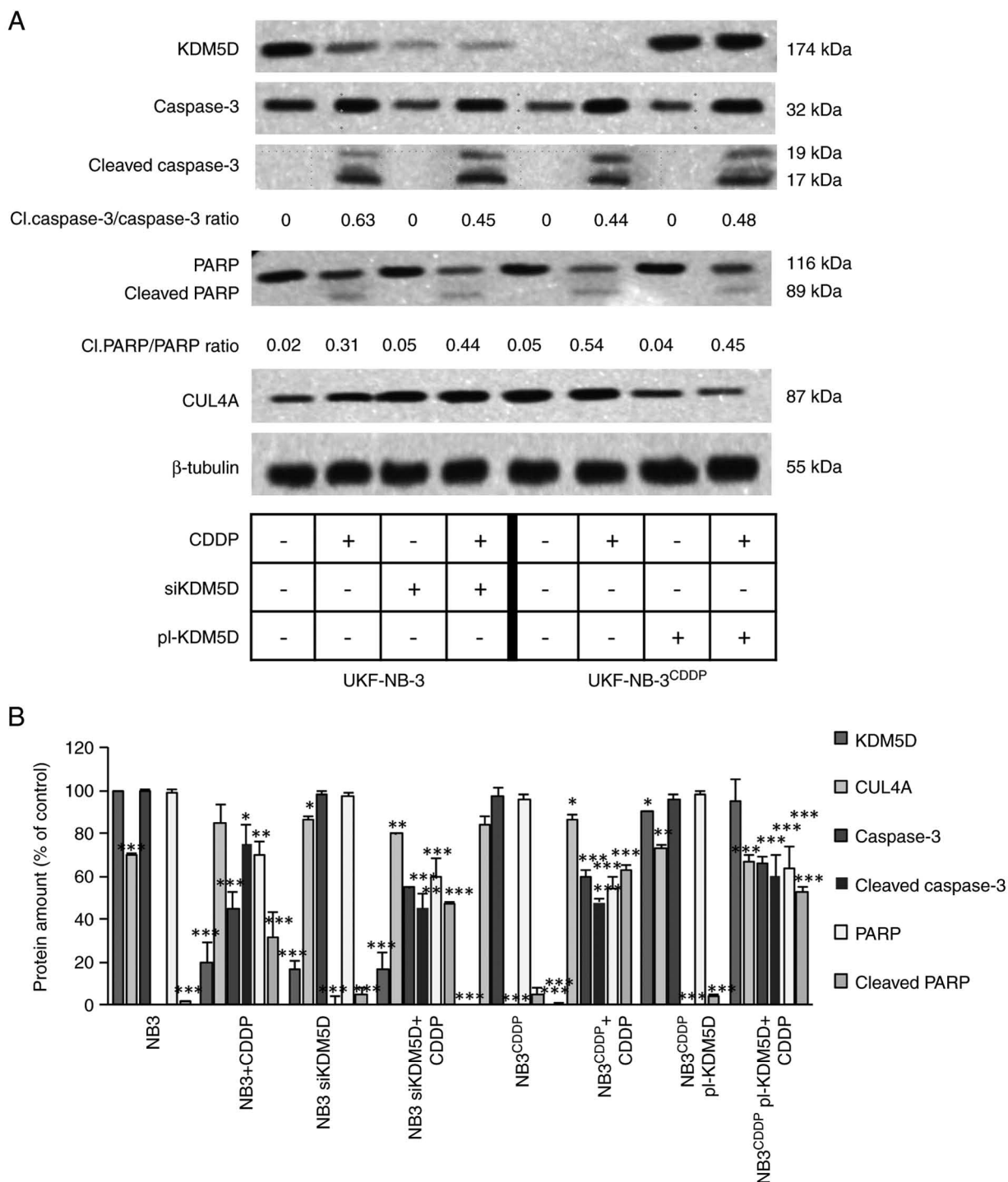


Figure S19. Representative cytometric density dot plots in UKF-NB-3 corresponding to the quantitative data shown in Fig. 5A. Each panel represents the samples used in the experiment: (A) UKF-NB-3 CTR, (B) UKF-NB-3 with CDDP, (C) UKF-NB-3 NC, (D) UKF-NB-3 NC with CDDP, (E) UKF-NB-3 siKDM5 and (F) UKF-NB-3 siKDM5D with CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-caspase-3 antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. NB3, cell line UKF-NB-3; NC, negative control; si, short interfering RNA.

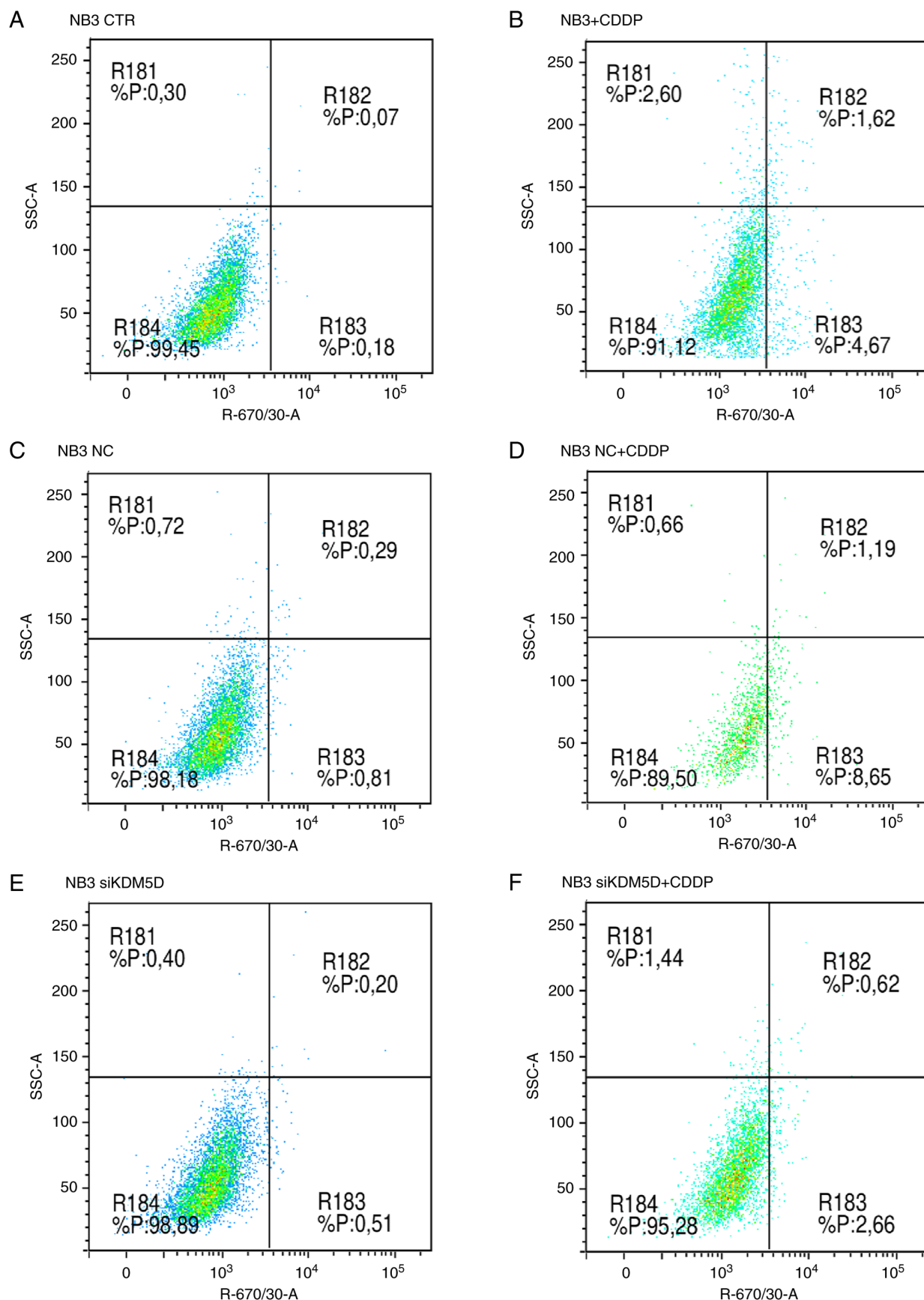


Figure S20. Flow cytometry analysis of cleaved caspase-3 in CDDP sensitive cell line UKF-NB-3 and CDDP resistant cell line UKF-NB-3^{CDDP}. In sensitive cell line, the KDM5s pan-inhibitor did not significantly change the level of cleaved caspase-3 even after CDDP treatment (48 h), but significantly decreased the amount of cleaved caspase-3 compared with control after CDDP treatment ($P < 0.001$). In resistant cell line, the KDM5s pan-inhibitor did not significantly change the level of cleaved caspase-3 even after CDDP treatment. Data are shown as mean \pm standard deviation from three independent experiments. Statistical significance was determined using two-way ANOVA with Tukey's post hoc test $***P < 0.001$. CTR, control.

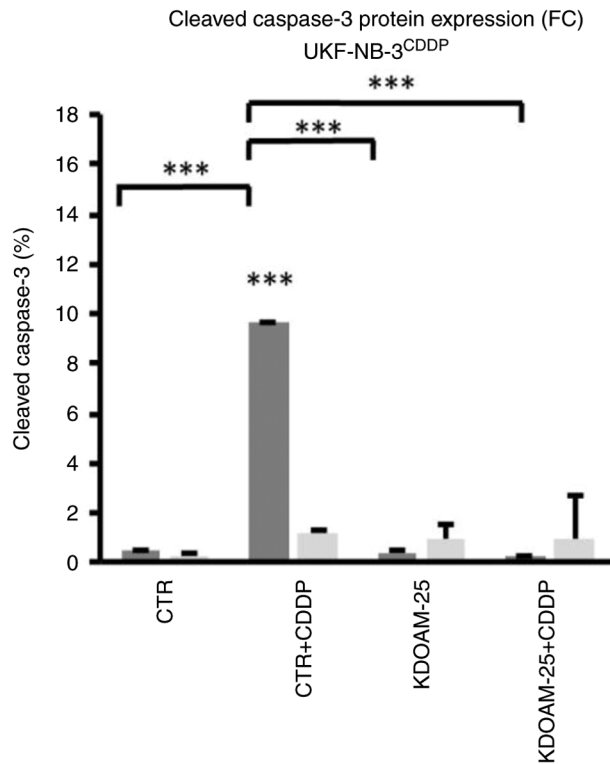


Figure S21. Representative cytometric density dot plots in UKF-NB-3 corresponding to the quantitative data shown in Fig. S20. Each panel represents the samples used in the experiment: (A) UKF-NB-3 CTR, (B) UKF-NB-3 with CDDP, (C) UKF-NB-3 with KDOAM-25 and (D) UKF-NB-3 with KDOAM-25 and CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-caspase-3 antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. NB3, cell line UKF-NB-3; CTR, control.

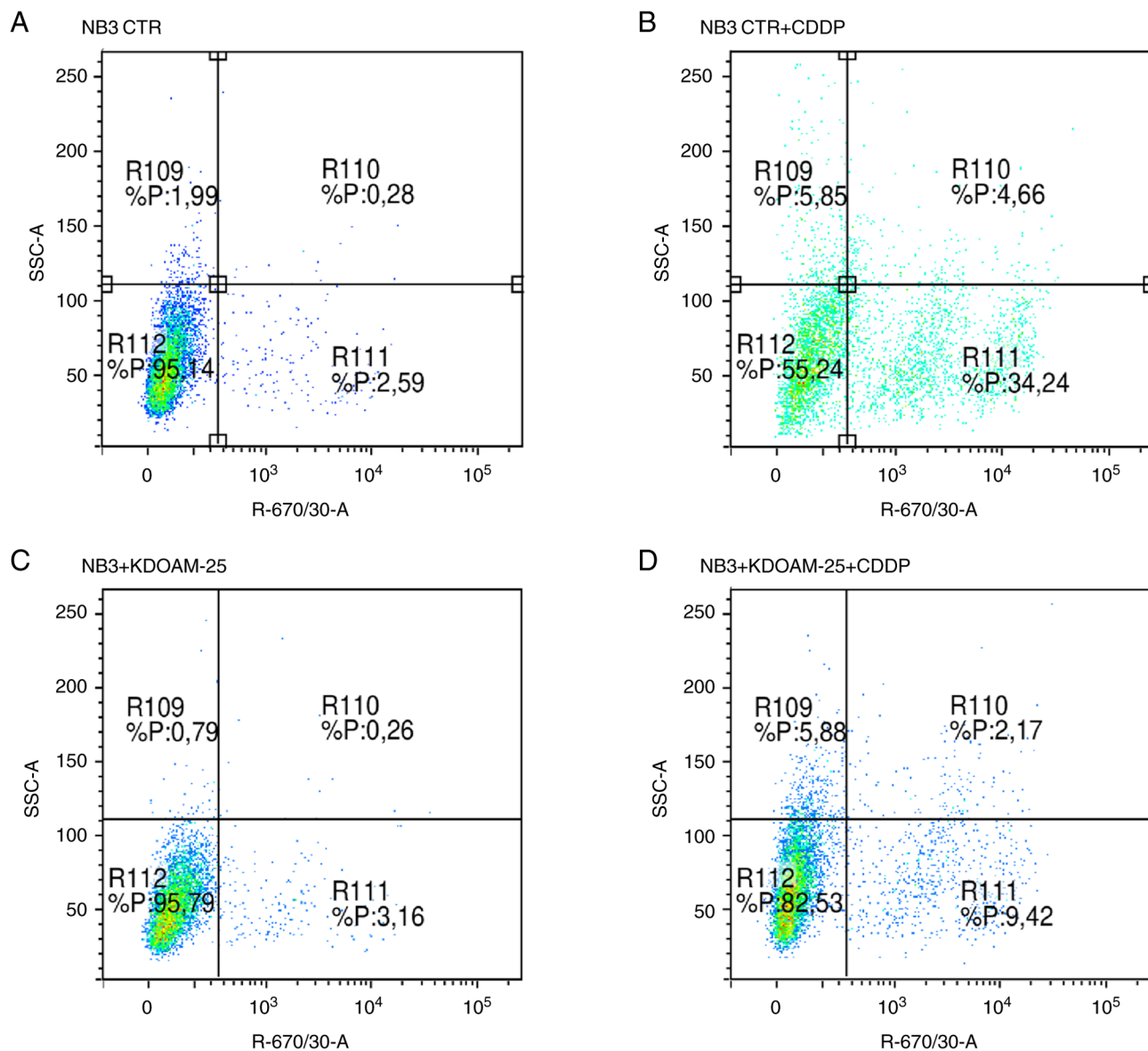


Figure S22. Representative cytometric density dot plots in UKF-NB-3^{CDDP} corresponding to the quantitative data shown in Fig. S20. Each panel represents the samples used in the experiment: (A) UKF-NB-3^{CDDP} CTR, (B) UKF-NB-3^{CDDP} with CDDP, (C) UKF-NB-3^{CDDP} with KDOAM-25 and (D) UKF-NB-3^{CDDP} with KDOAM-25 and CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-caspase-3 antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. NB3, cell line UKF-NB-3; CTR, control.

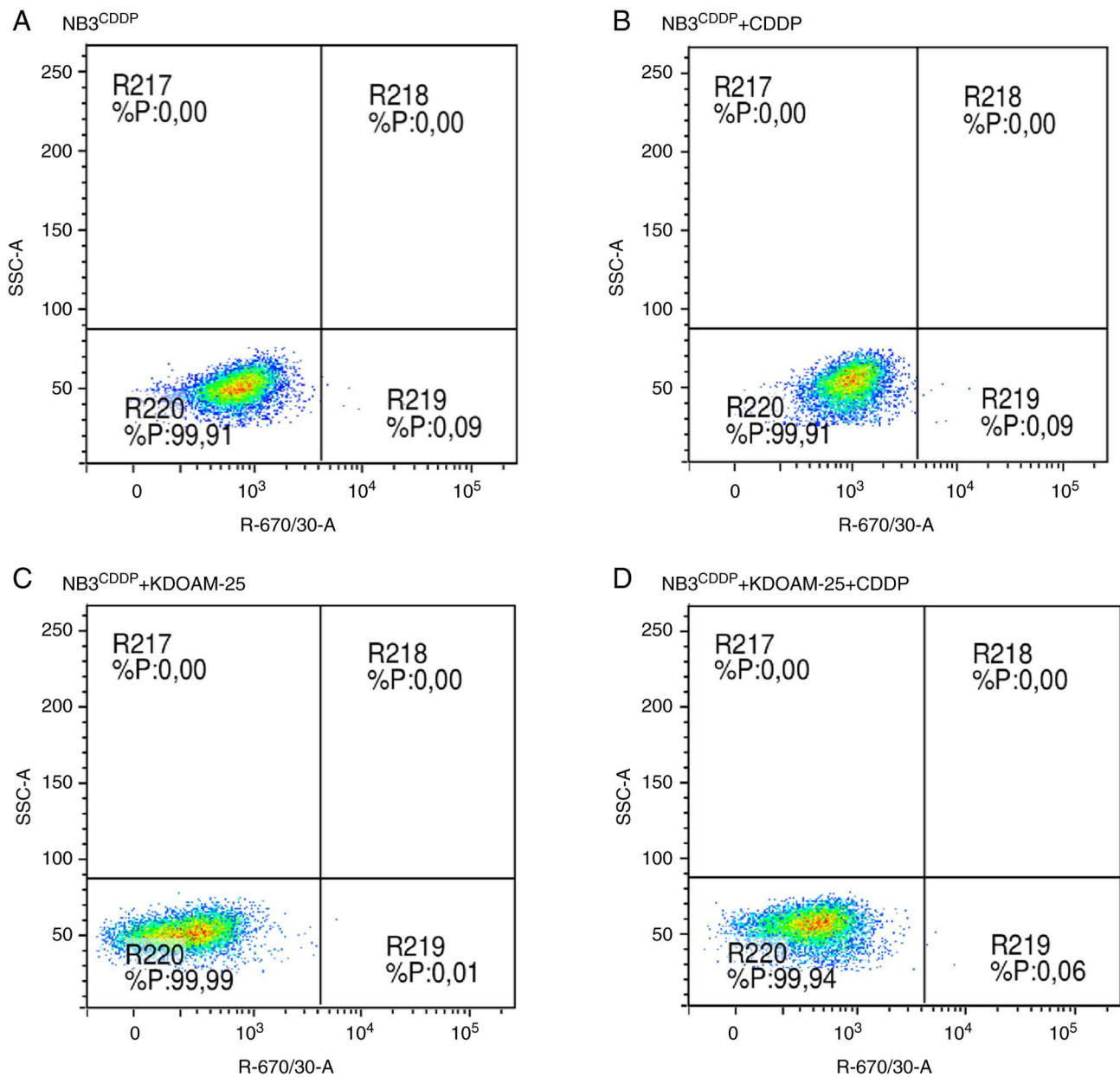


Figure S23. Representative cytometric density dot plots in UKF-NB-3^{CDDP} corresponding to the quantitative data shown in Fig. 5B. Each panel represents the samples used in the experiment: (A) UKF-NB-3^{CDDP} CTR, (B) UKF-NB-3^{CDDP} with CDDP, (C) UKF-NB-3^{CDDP} mock, (D) UKF-NB-3^{CDDP} mock with CDDP, (E) UKF-NB-3^{CDDP} pl-KDM5D and (F) UKF-NB-3^{CDDP} pl-KDM5D with CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-caspase-3 antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. NB3, cell line UKF-NB-3; mock, control cells with control plasmid; pl, ORF-clone plasmid.

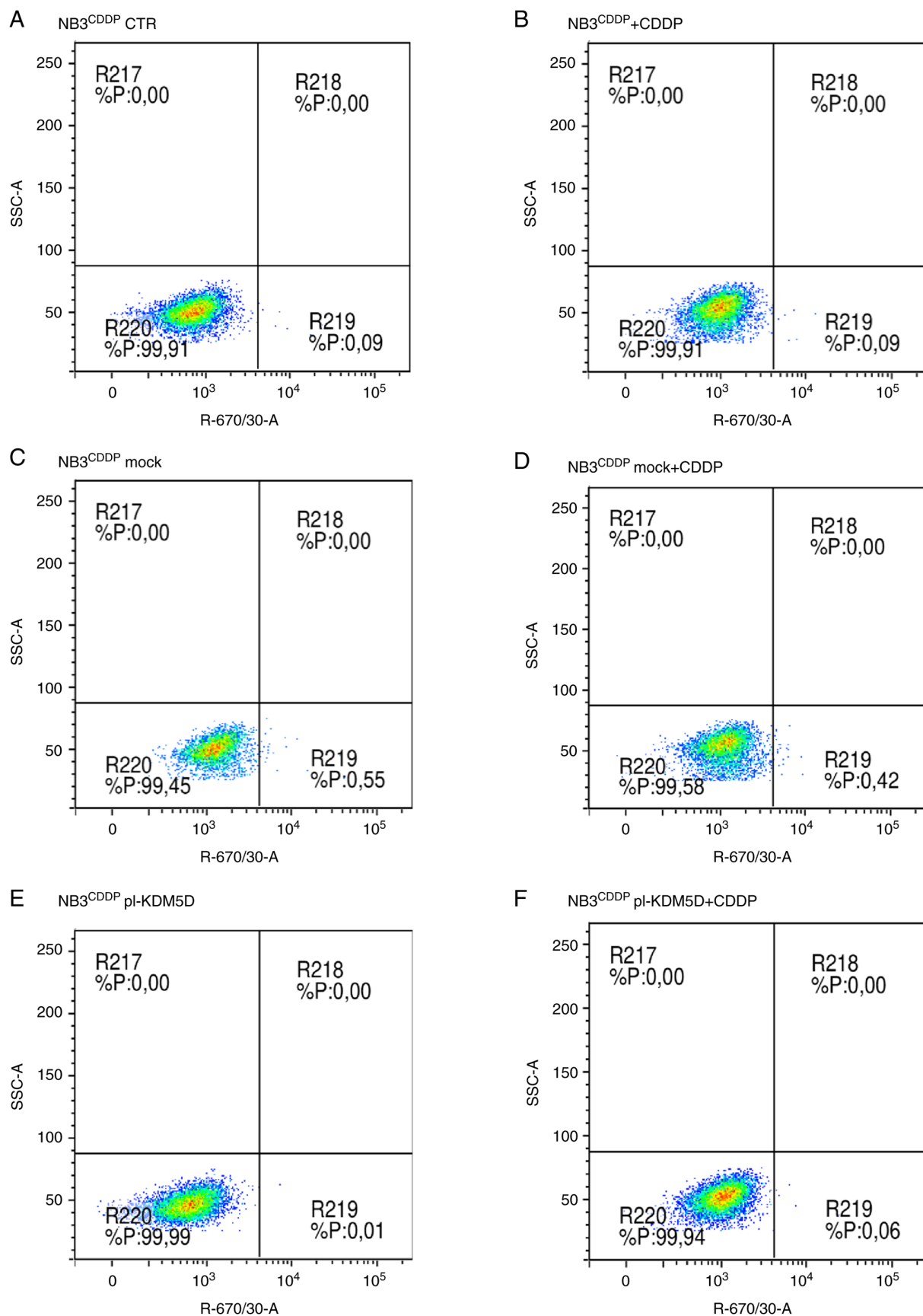
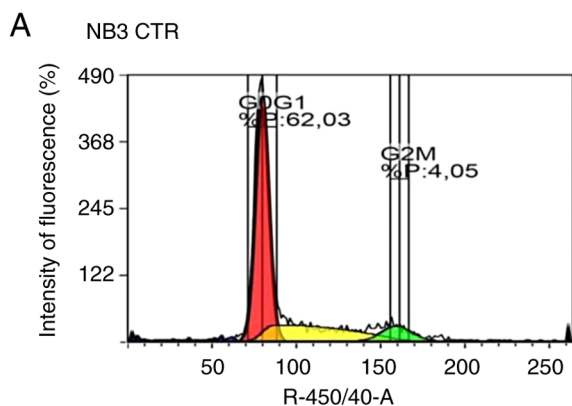
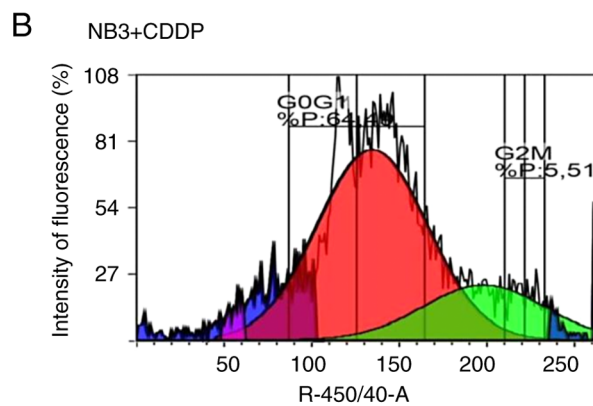


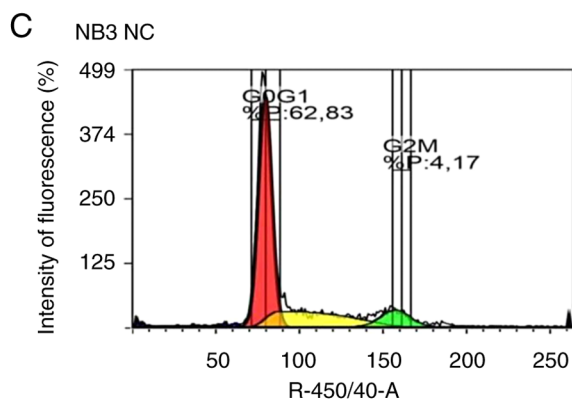
Figure S24. Flow cytometry histograms show cell cycle of UKF-NB-3 in (A) control, (B) cells after CDDP treatment (48 h), (C) cells transfected with noncoding RNA (NC) (48 h), (D) NC after CDDP treatment (48 h), (E) cells transfected with siKDM5D (si) (48 h), (F) si after CDDP treatment (48 h). Histograms are representative from one measurement from three independent experiments. CTR, control; NC, non-coding RNA; si, short interfering; pl, ORF-clone plasmid; NB3, cell line UKF-NB-3.



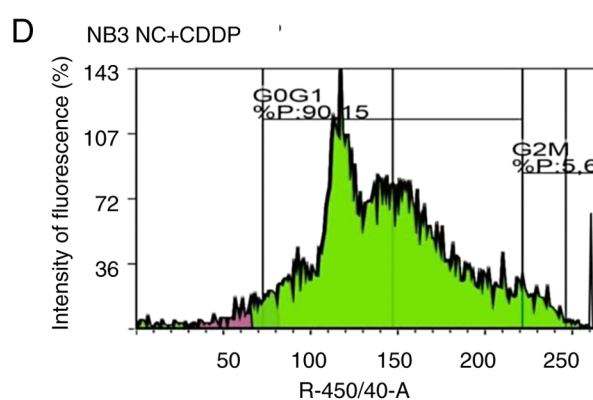
Description	Dean Jett Fox
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S (% of cell cycle)	27.66
G2M (% of cell cycle)	6.93



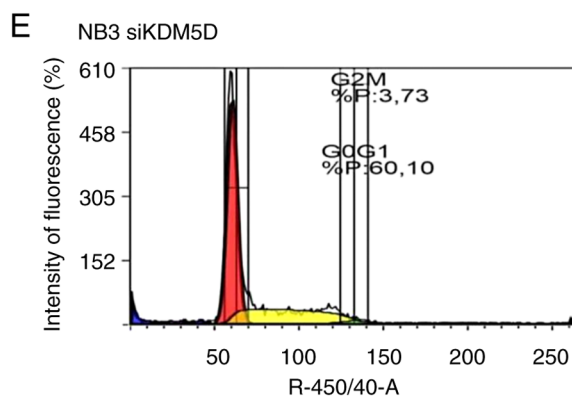
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S (% of cell cycle)	-13.66
G2M (% of cell cycle)	33.82



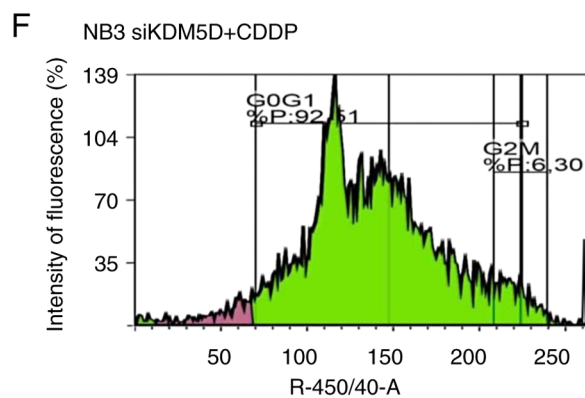
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Chi squared	275.83
G0G1 (% of cell cycle)	65.13
S (% of cell cycle)	25.83
G2M (% of cell cycle)	9.04



Description	Dean Jett Fox
Chi squared	-1.00
G0G1 (% of cell cycle)	0.04
S (% of cell cycle)	99.93
G2M (% of cell cycle)	0.04

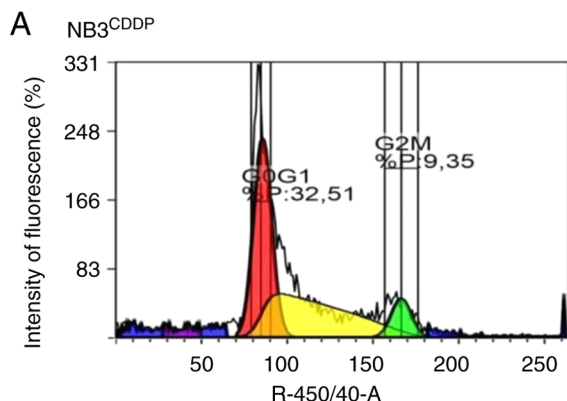


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G2M (% of cell cycle)	2.20

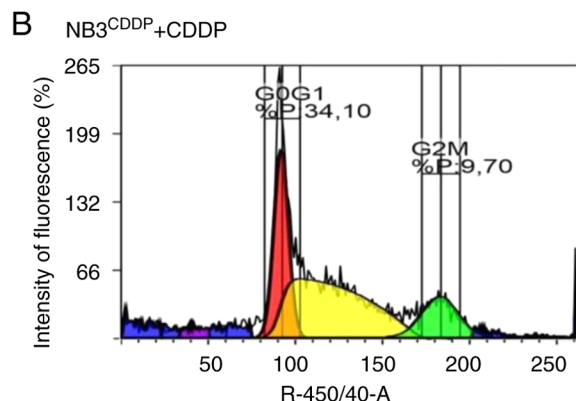


Description	Dean Jett Fox
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S (% of cell cycle)	0.00
G2M (% of cell cycle)	100.00

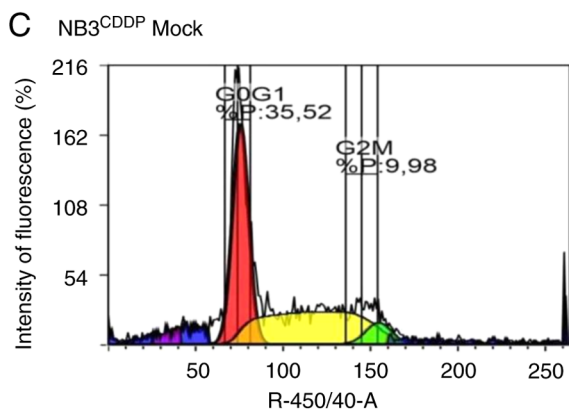
Figure S25. Flow cytometry histograms showed cell cycle of UKF-NB-3^{CDDP} in (A) control, (B) cells after CDDP treatment (48 h), (C) cells transfected with control plasmid (mock) (48 h), (D) mock after CDDP treatment (48 h), (E) cells transfected with plasmid with KDM5D (pl-KDM5D) (48 h), (F) pl-KDM5D after CDDP treatment (48 h). Histograms are representative from one measurement from three independent experiments. NB3, cell line UKF-NB-3; CTR, control; NC, non-coding RNA; si, short interfering RNA; pl, ORF-clone plasmid.



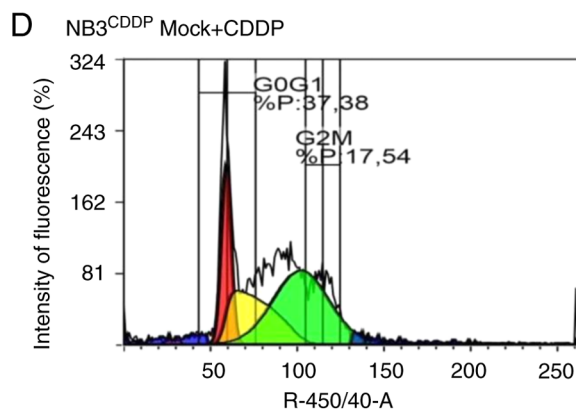
Description	Dean Jett Fox
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G0G1 (% of cell cycle)	42.20
S (% of cell cycle)	49.48
G2M (% of cell cycle)	8.31



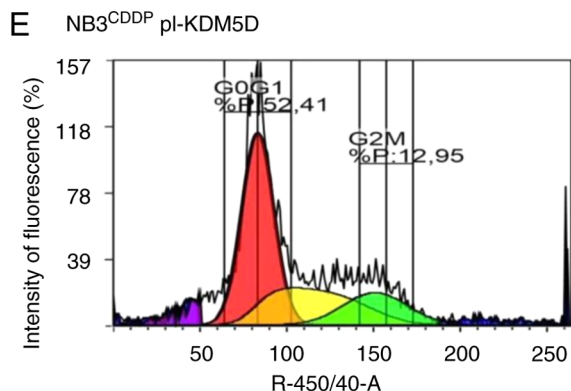
Description	Dean Jett Fox
Chi squared	682.70
G0G1 (% of cell cycle)	25.51
S (% of cell cycle)	56.57
G2M (% of cell cycle)	17.91



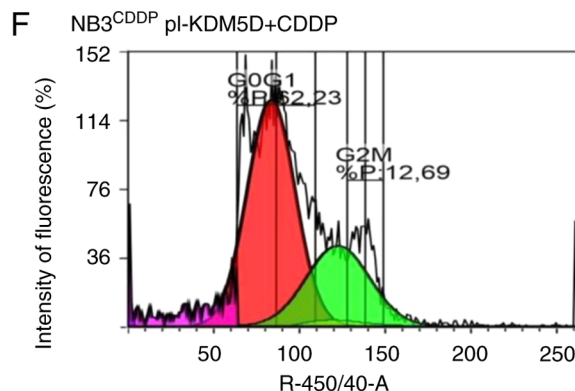
Description	Dean Jett Fox
Chi squared	854.51
G0G1 (% of cell cycle)	47.49
S (% of cell cycle)	50.73
G2M (% of cell cycle)	1.79



Description	Dean Jett Fox
Chi squared	694.17
G0G1 (% of cell cycle)	19.32
S (% of cell cycle)	35.39
G2M (% of cell cycle)	45.30



Description	Dean Jett Fox
Chi squared	1180.27
G0G1 (% of cell cycle)	53.94
S (% of cell cycle)	35.82
G2M (% of cell cycle)	10.24



Description	Dean Jett Fox
Chi squared	1308.96
G0G1 (% of cell cycle)	67.68
S (% of cell cycle)	1.85
G2M (% of cell cycle)	30.47

Figure S26. Analysis of cell proliferation and cell migration by xCELLigence. (A) Analysis of cell migration by xCELLigence showing significance in UKF-NB-3 and UKF-NB-3^{CDDP}. Monitoring of cell migration by xCELLigence after transfection of siKDM5D or plasmid with KDM5D in neuroblastoma cell line UKF-NB3 and UKF-NB-3^{CDDP}. (B) Analysis of cell proliferation by xCELLigence showing significance in UKF-NB-3 and UKF-NB-3^{CDDP}. Monitoring of cell proliferation by xCELLigence after transfection of siKDM5D or plasmid with KDM5D in neuroblastoma cell line UKF-NB3 and UKF-NB-3^{CDDP}. (C) Analysis of cell proliferation by xCELLigence in neuroblastoma cell line IMR-32. Monitoring of cell proliferation by xCELLigence after transfection of siKDM5D in neuroblastoma cell line IMR-32. (D) Analysis of cell proliferation by xCELLigence in neuroblastoma cell line SK-N-F1. Monitoring of cell proliferation by xCELLigence after transfection of siKDM5D in neuroblastoma cell line SK-N-F1. (E) Western blotting verification of KDM5D silencing in UKF-NB-3 cells transfected with siKDM5D within 7 days. Data are shown as mean \pm standard deviation from two independent experiments. Statistical significance was determined using one-way ANOVA with Tukey's post hoc test. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. NC, non-coding RNA; si, short interfering; Mock, control cells with control plasmid; pl, ORF-clone plasmid; NB3, cell line UKF-NB-3; NC, non-coding RNA; si, short interfering RNA.

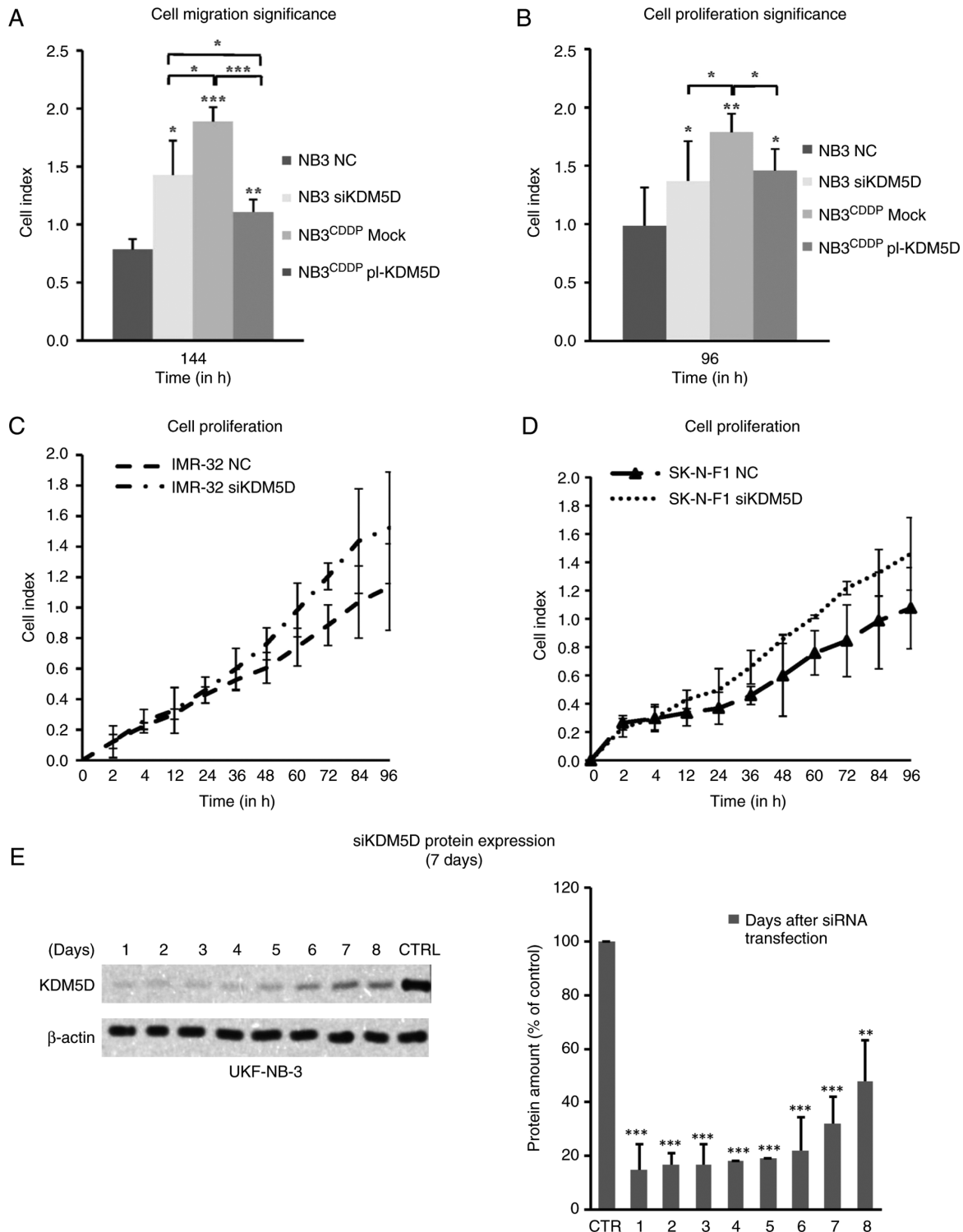


Figure S27. Representative cytometric density dot plots in UKF-NB-3 corresponding to the quantitative data shown in Fig. 7A and B. Each panel represents the samples used in the experiment: (A) UKF-NB-3 CTR, (B) UKF-NB-3 with CDDP, (C) UKF-NB-3 NC, (D) UKF-NB-3 NC with CDDP, (E) UKF-NB-3 siKDM5D and (F) UKF-NB-3 siKDM5D with CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-CUL4A antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. CTR, control; NB3, cell line UKF-NB-3; NC, non-coding; si, short interfering.

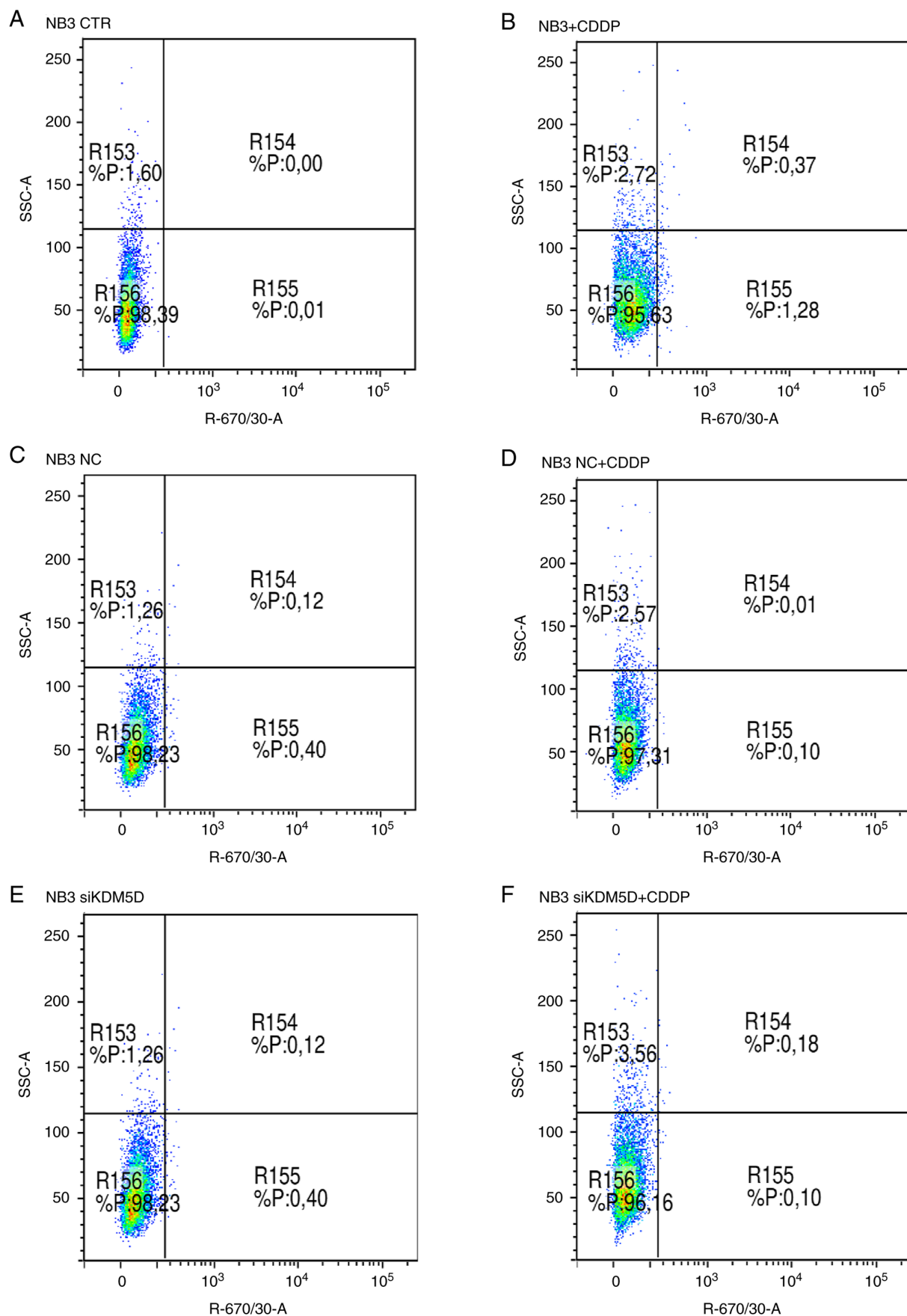


Figure S28. Representative cytometric density dot plots in UKF-NB-3^{CDDP} corresponding to the quantitative data shown in Fig. 7C. Each panel represents the samples used in the experiment: (A) UKF-NB-3 CDDP CTR, (B) UKF-NB-3 CDDP with CDDP, (C) UKF-NB-3 CDDP mock, (D) UKF-NB-3 CDDP mock with CDDP, (E) UKF-NB-3 CDDP pl-KDM5D and (F) UKF-NB-3 CDDP pl-KDM5D with CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-CUL4A antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. CTR, control; control cells with control plasmid; pl, ORF-clone plasmid.

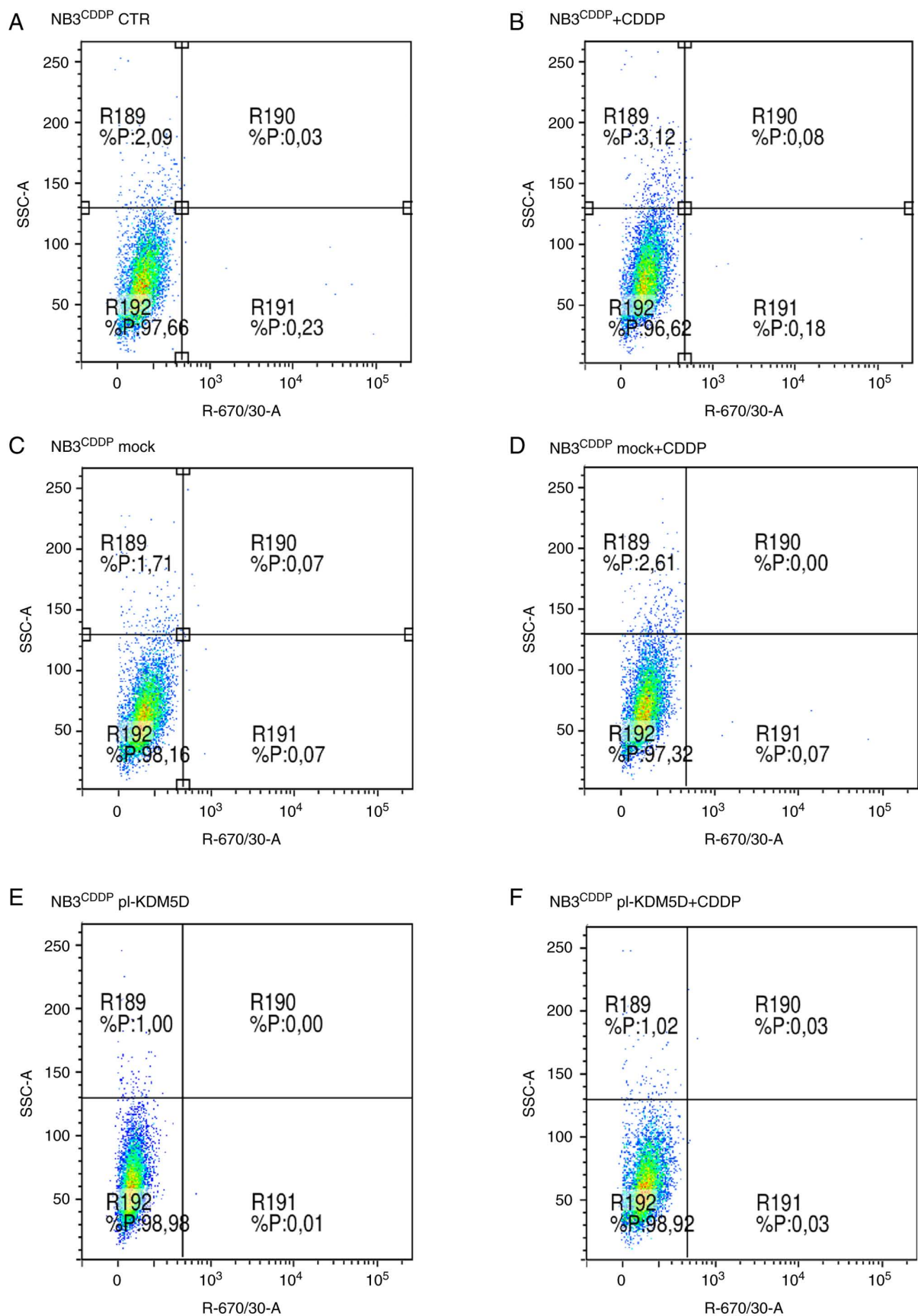


Figure S29. Protein level of CUL4A in UKF-NB-3 and UKF-NB-3^{CDDP} after treatment with (KDM5s pan-inhibitor) KDOAM-25 and after CDDP treatment. Data are shown as mean \pm standard deviation from three independent experiments. Statistical significance was determined using two-way ANOVA with Tukey's post hoc test. **P<0.01; ***P<0.001. CTR, control.

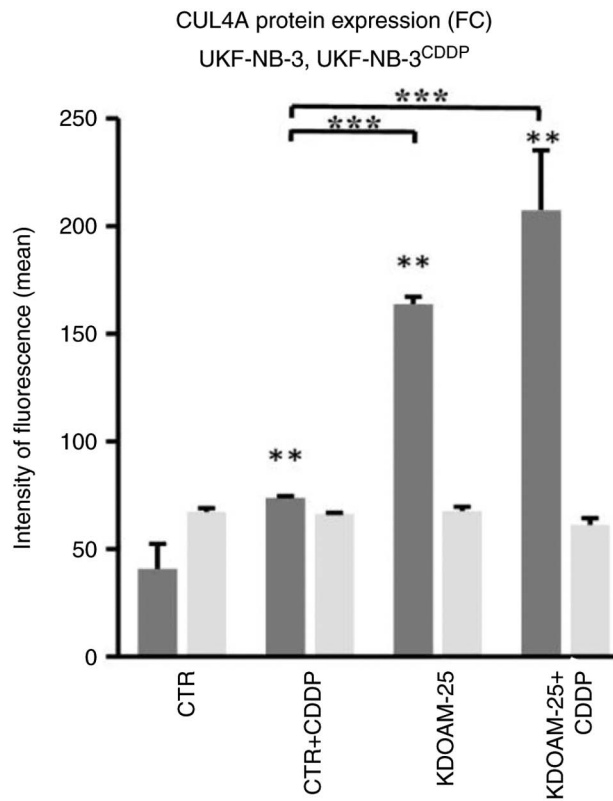


Figure S30. Representative cytometric density dot plots in UKF-NB-3 corresponding to the quantitative data shown in Fig. 7C. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-CUL4A antibody. (A) UKF-NB-3 CTR, (B) UKF-NB-3 with CDDP, (C) UKF-NB-3 with KDOAM-25 and (D) UKF-NB-3 with KDOAM-25 and CDDP. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. CTR, control; NB3, cell line UKF-NB-3.

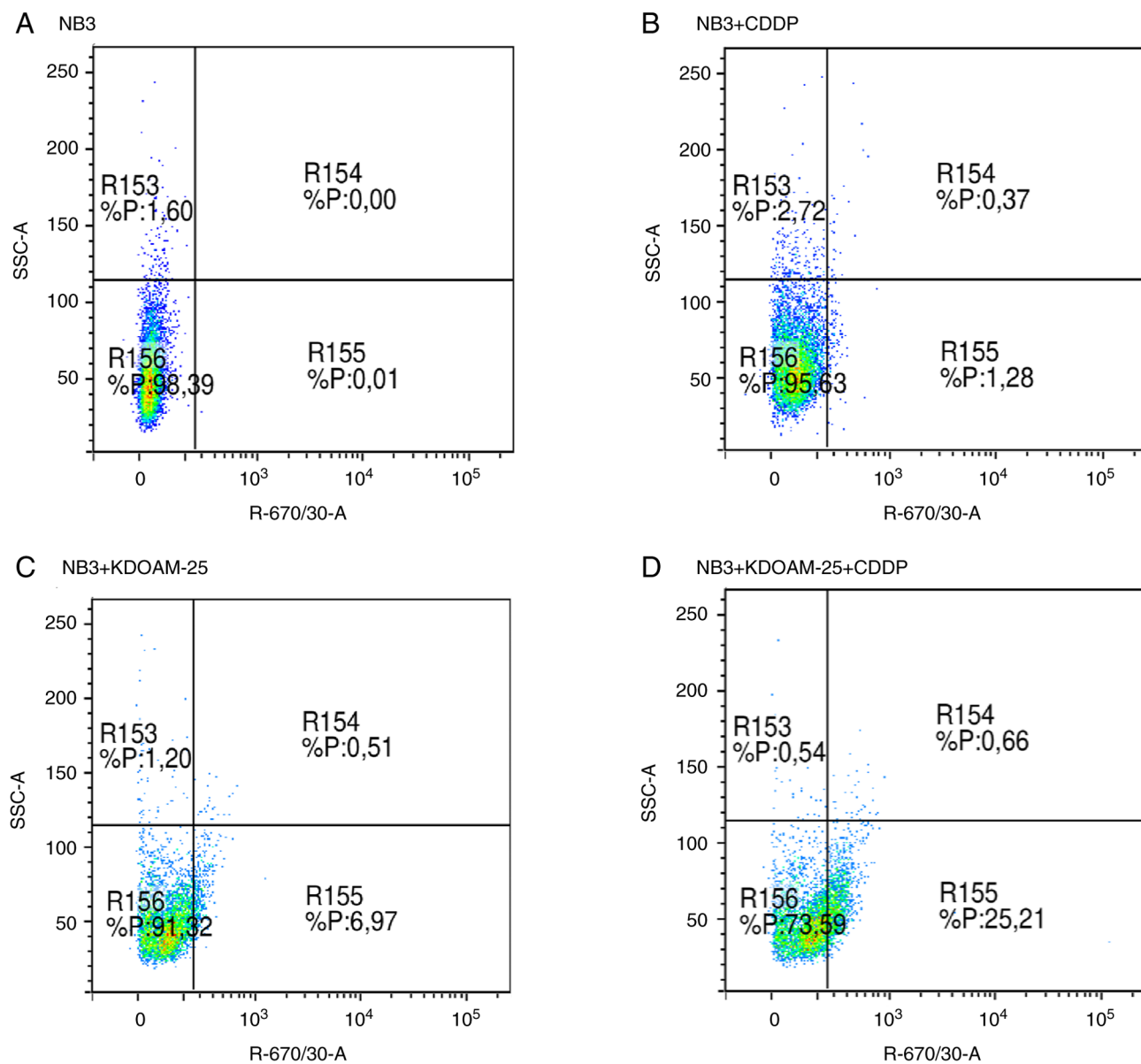


Figure S31. Representative cytometric density dot plots in UKF-NB-3^{CDDP} corresponding to the quantitative data shown in Fig. 7C. Each panel represents the samples used in the experiment: (A) UKF-NB-3^{CDDP} CTR, (B) UKF-NB-3^{CDDP} with CDDP, (C) UKF-NB-3^{CDDP} with KDOAM-25 and (D) UKF-NB-3^{CDDP} with KDOAM-25 and CDDP. Each panel illustrates fluorescence intensity distribution of Alexa Fluor 647 and anti-CUL4A antibody. Gating and quadrant percentages indicate relative proportions of positive and negative cell populations. CTR, control; NB3, cell line UKF-NB-3.

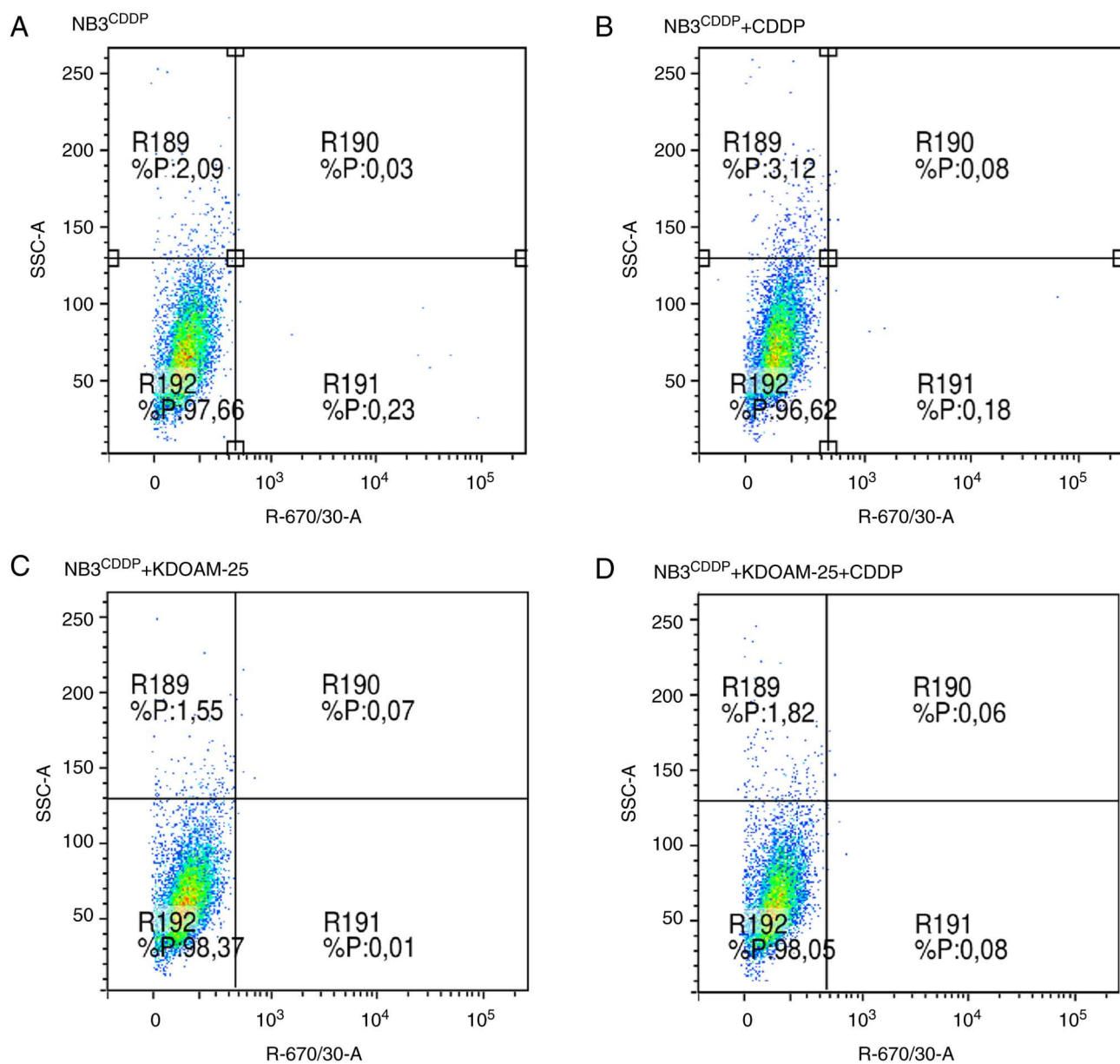


Figure S32. Kaplan-Meier curves analyzing KDM5D expression data and overall survival of patients in two different neuroblastoma datasets: Tumor Neuroblastoma by Kocak (649; custom; ag44kcwlf) in (A) male patients with stages 1, 2, 3 and 4S; (B) male patients with stage 4 and (C) all INSS in male patients; Tumor Neuroblastoma by Oberthuer (251; custom; amexp255) in (D) male patients with stages 1, 2, 3 and 4S and (E) male patients with stage 4 and (F) all INSS in male patients via the R2: Genomics Analysis and Visualization Platform. Statistical significance of survival differences was determined using the log-rank (Mantel-Cox) test. INSS, International Neuroblastoma Staging System.

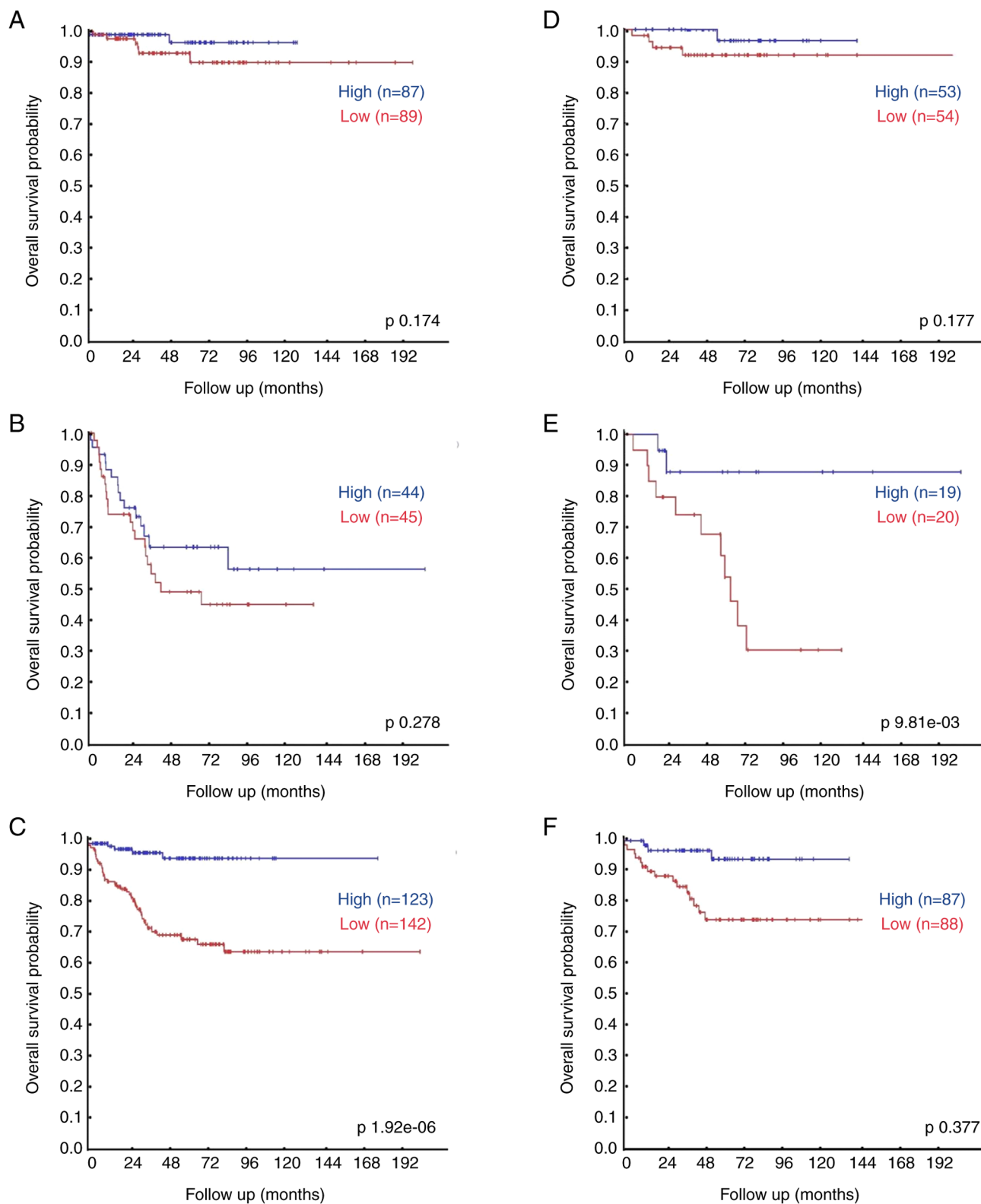


Figure S33. Kaplan-Meier curves analyzing CUL4A expression data and overall survival of patients in two different neuroblastoma datasets: Tumor Neuroblastoma by Kocak (649; custom; ag44kewolf) in (A) male patients with stages 1, 2, 3 and 4S, (B) male patients with stage 4 and (C) all INSS in male patients; Tumor Neuroblastoma by Oberthuer (251; custom; amexp255) in (D) male patients with stages 1, 2, 3 and 4S and (E) male patients with stage 4 and (F) all INSS in male patients via the R2: Genomics Analysis and Visualization Platform. Statistical significance of survival differences was determined using the log-rank (Mantel-Cox) test. INSS, International Neuroblastoma Staging System.

