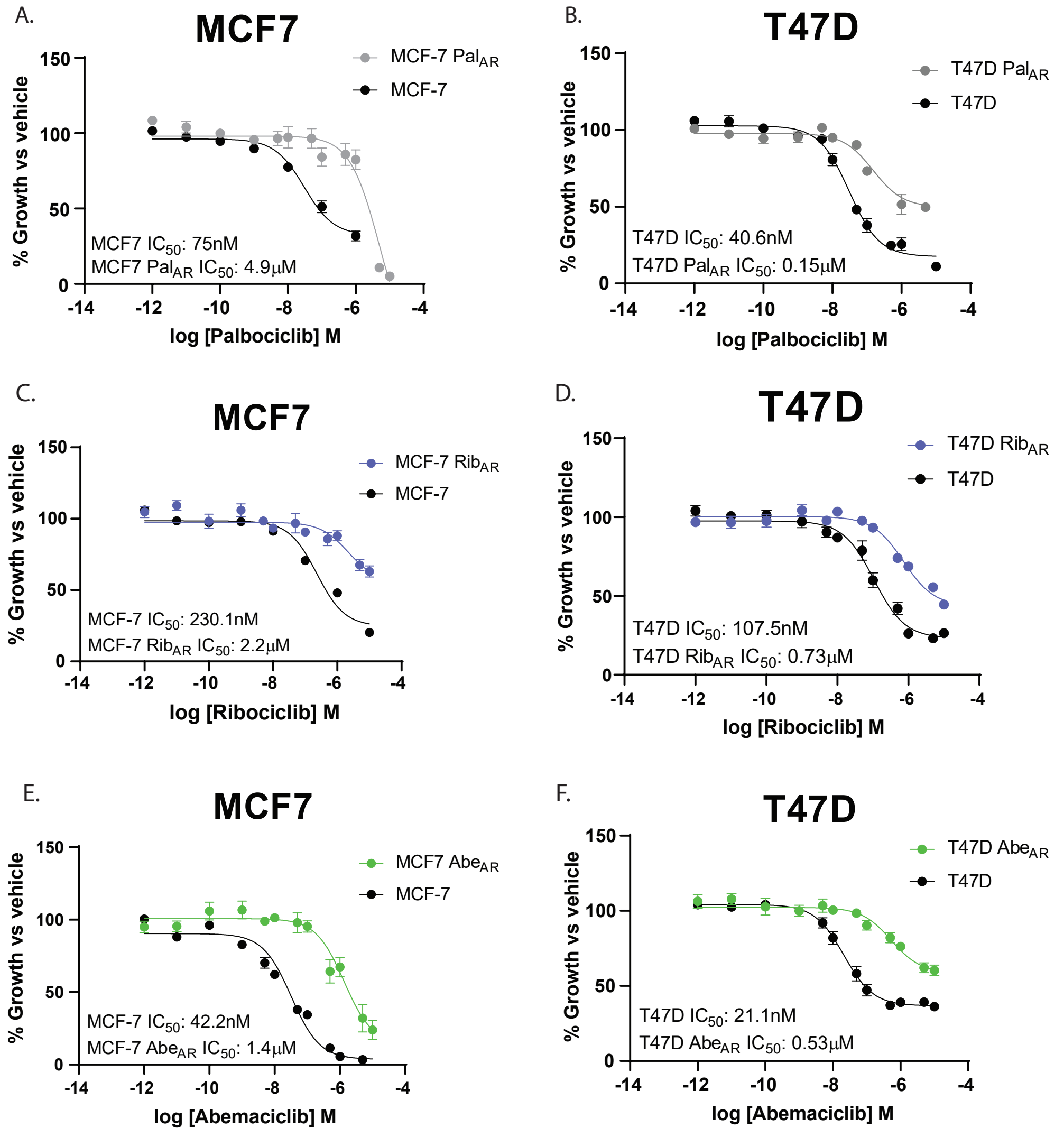
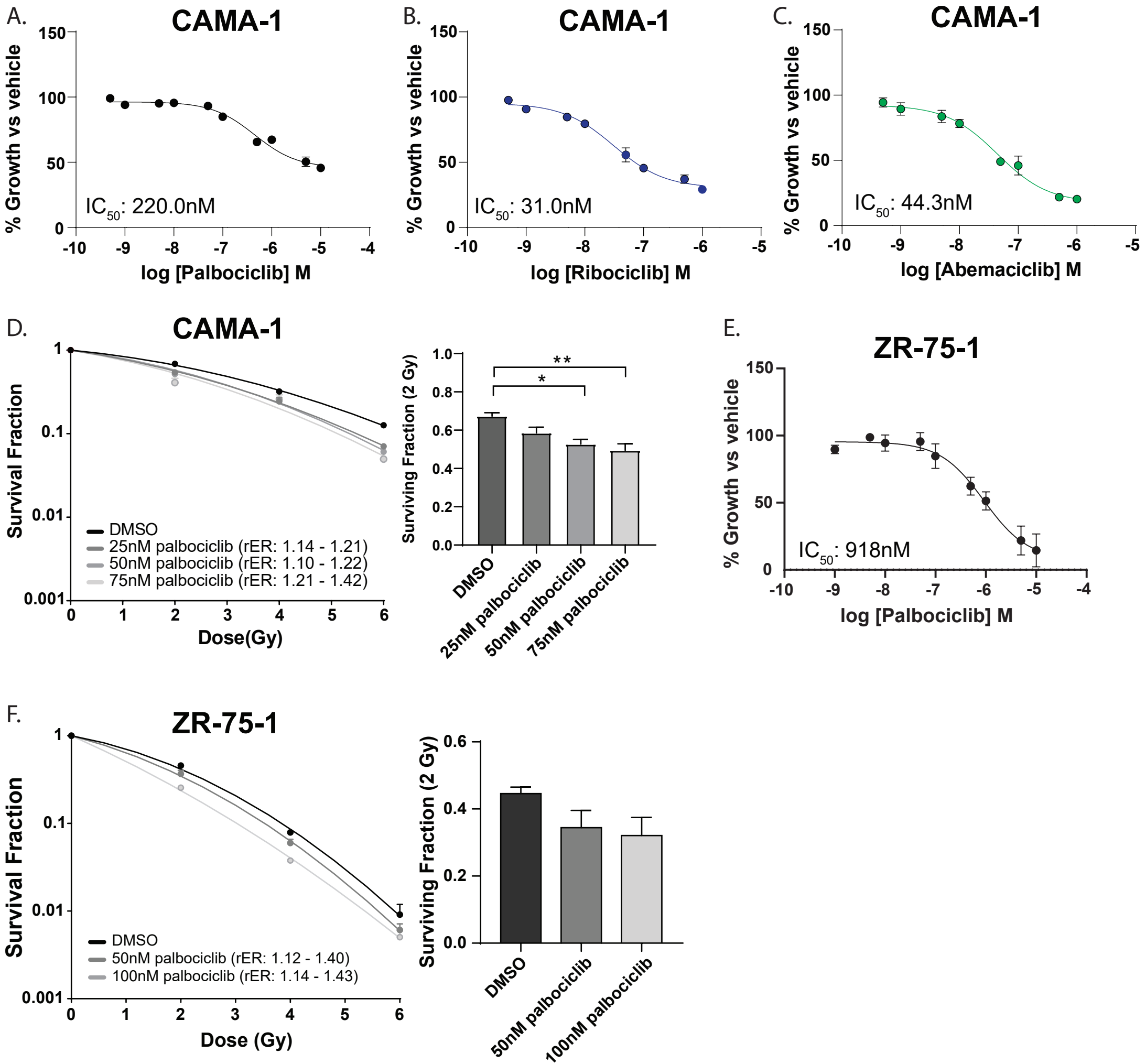


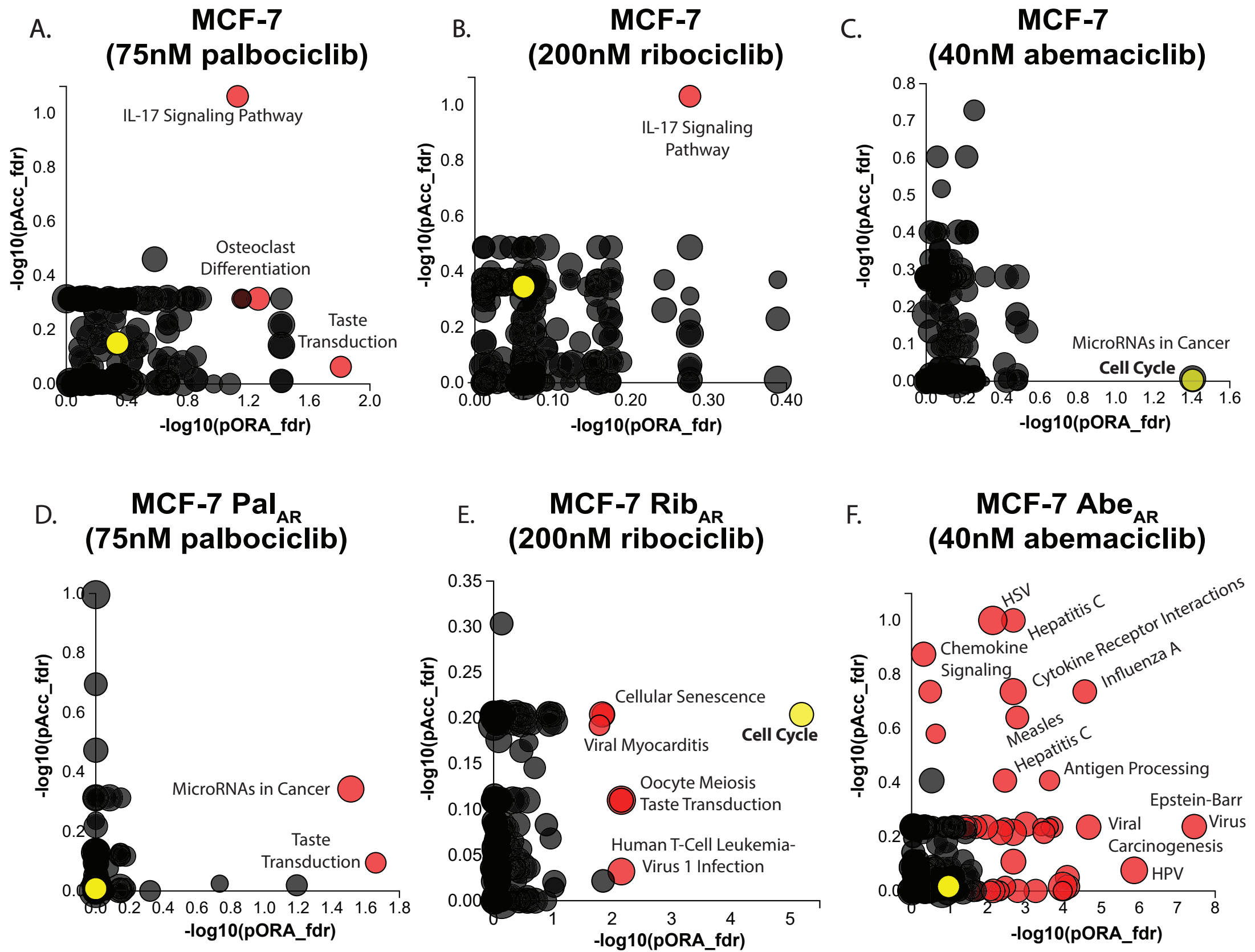
# Supplemental Figure 1



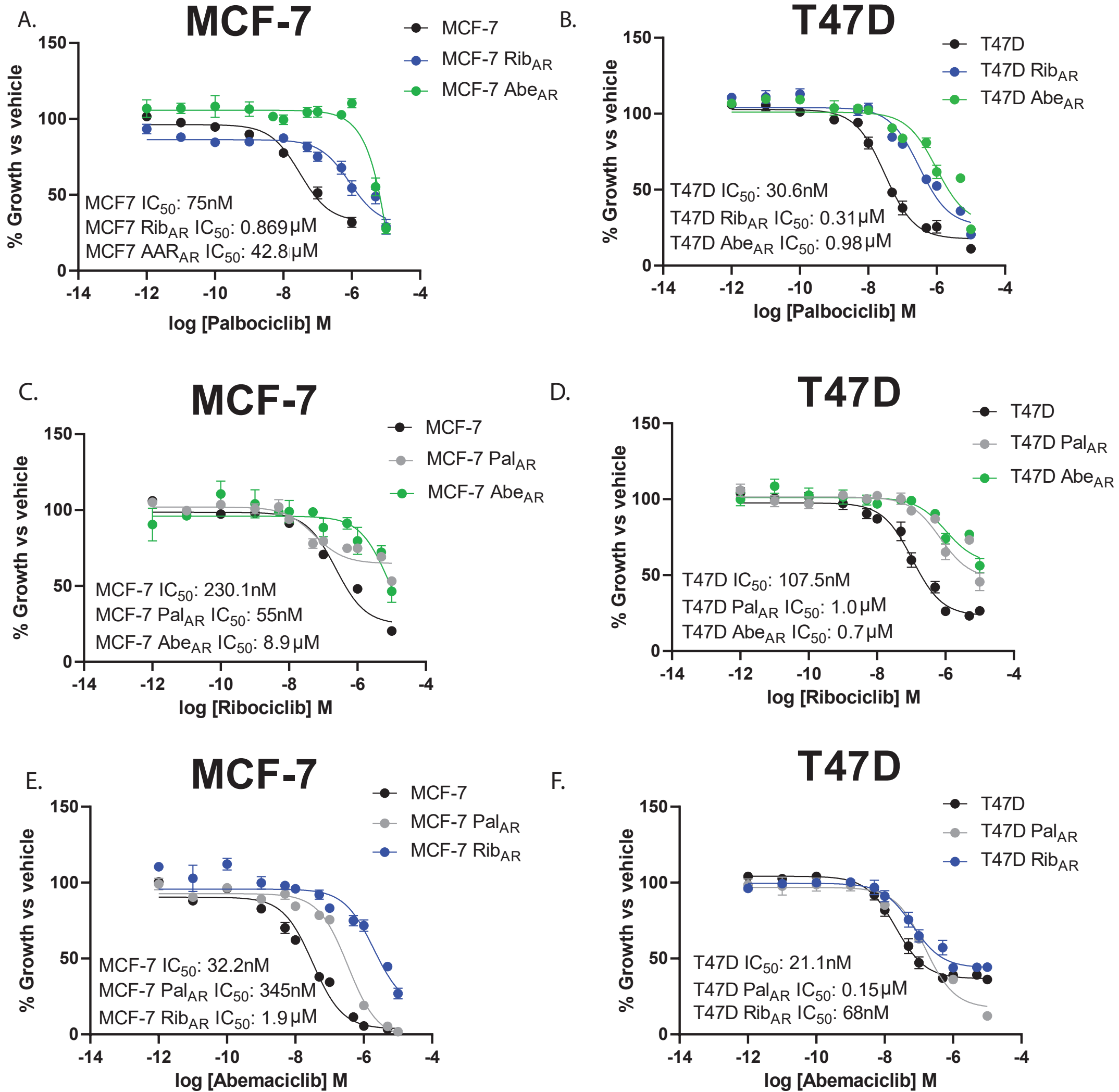
# Supplemental Figure 2



# Supplemental Figure 3

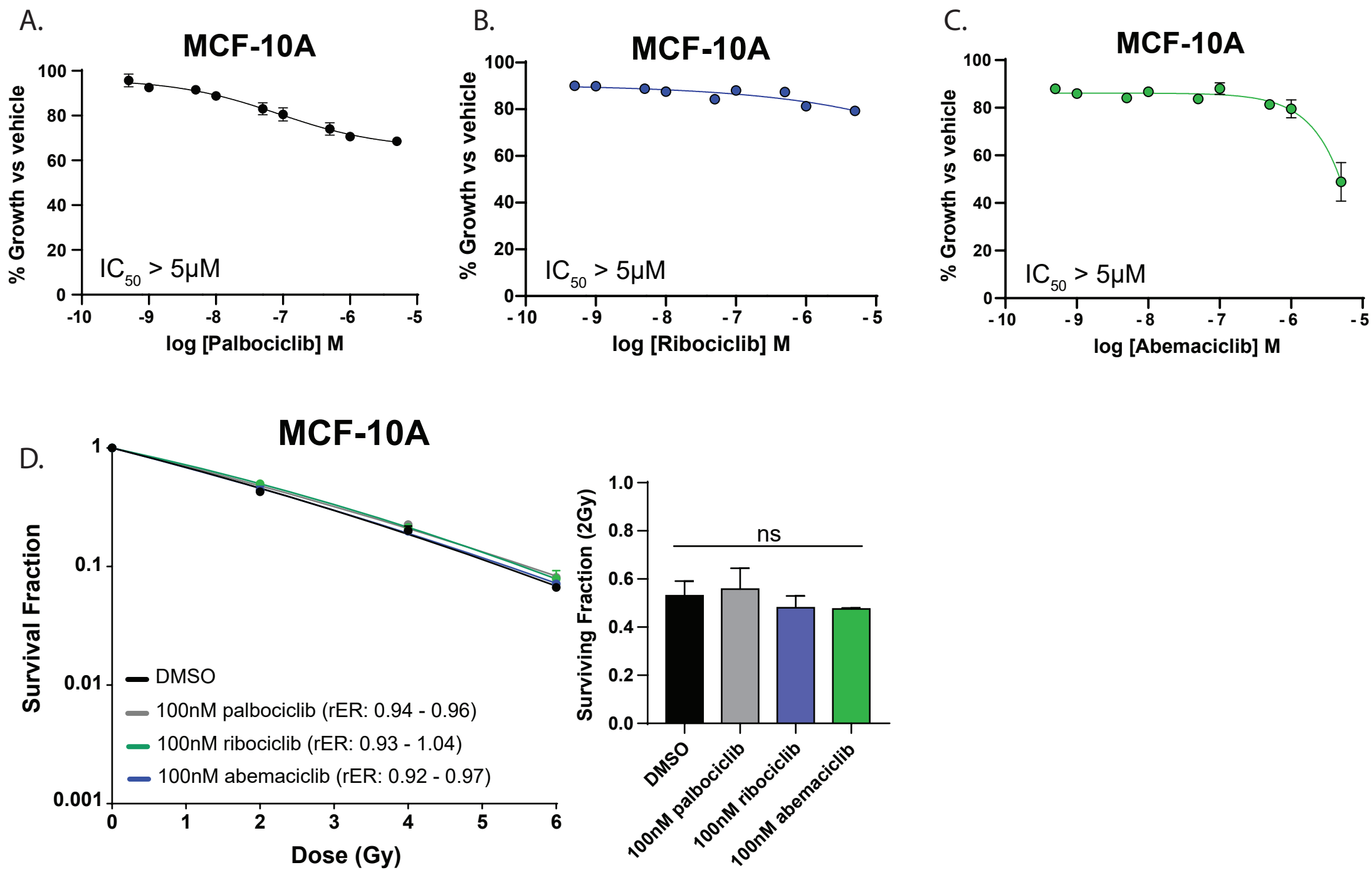


# Supplemental Figure 4



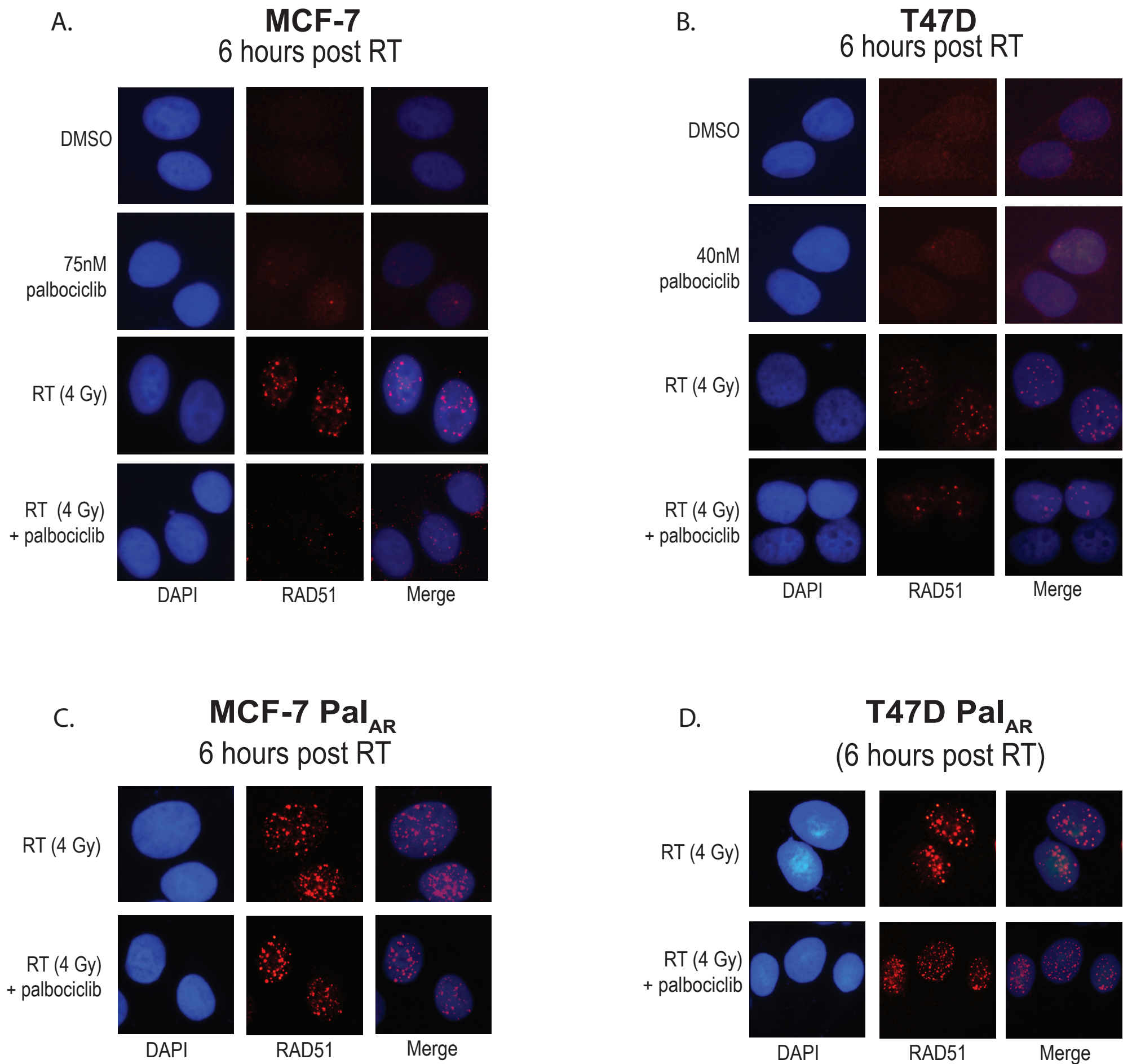


# Supplemental Figure 5



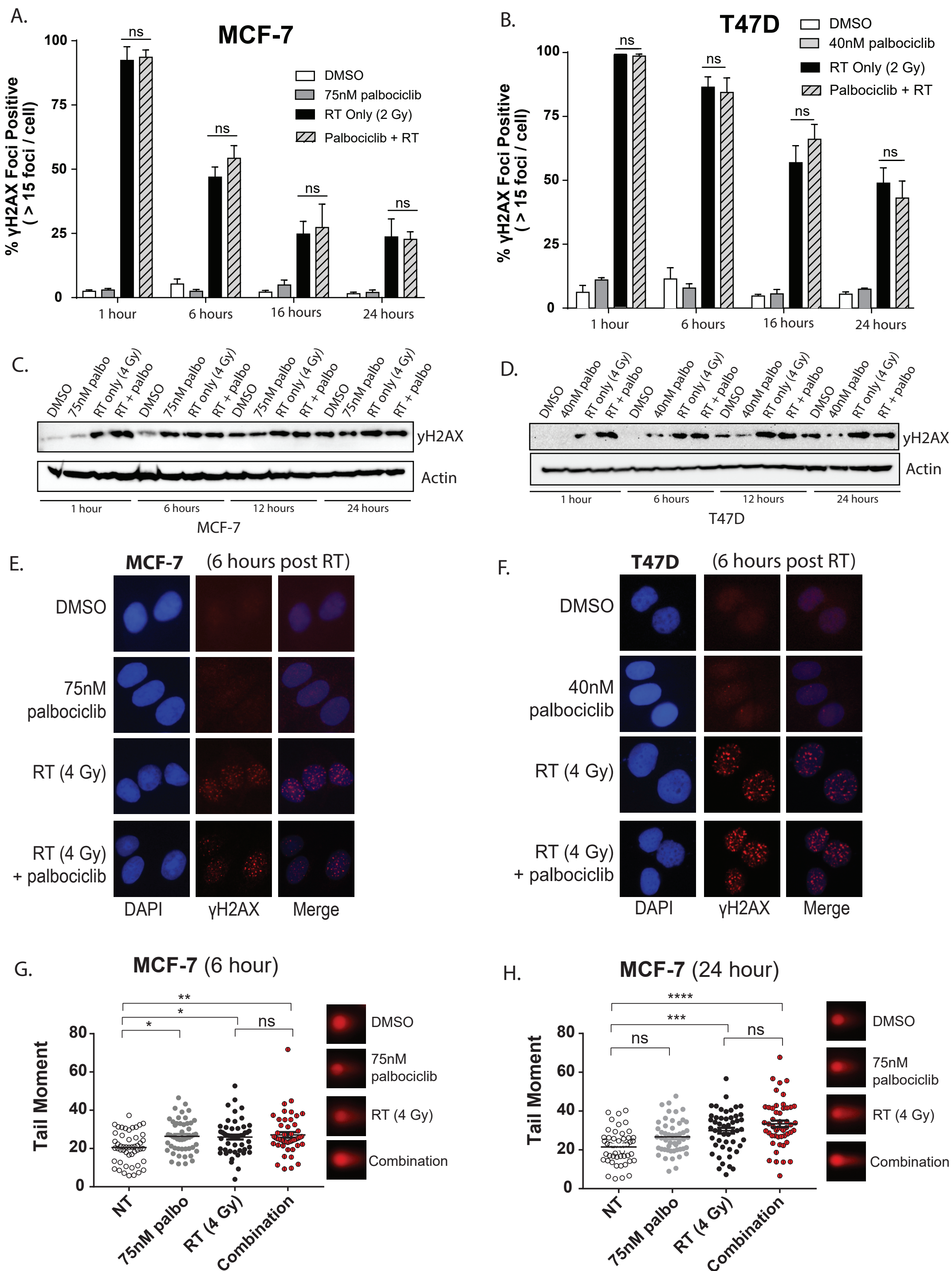


# Supplemental Figure 7



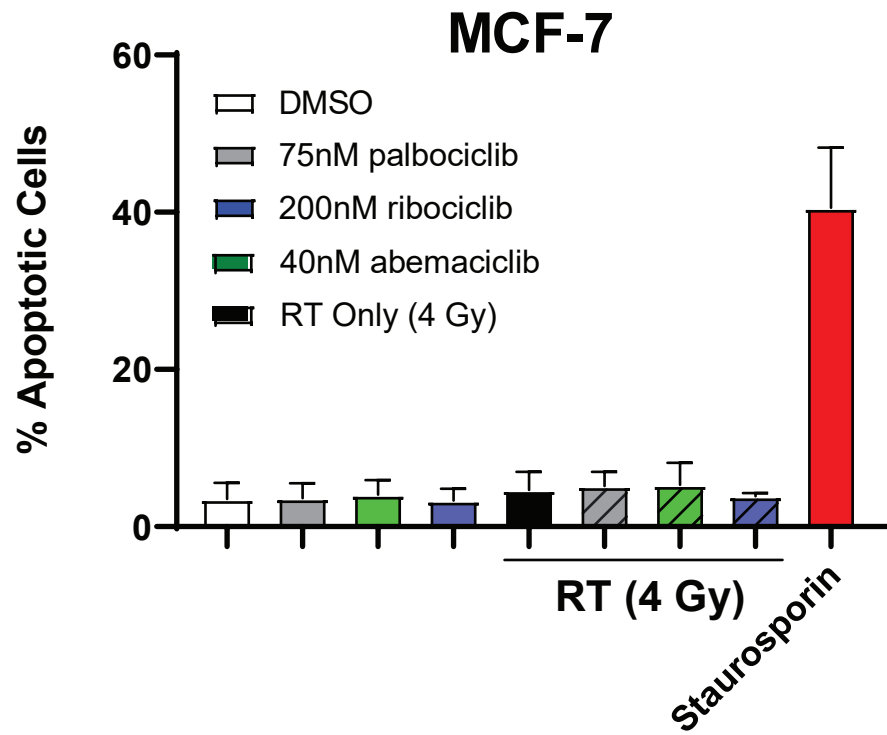


# Supplemental Figure 8

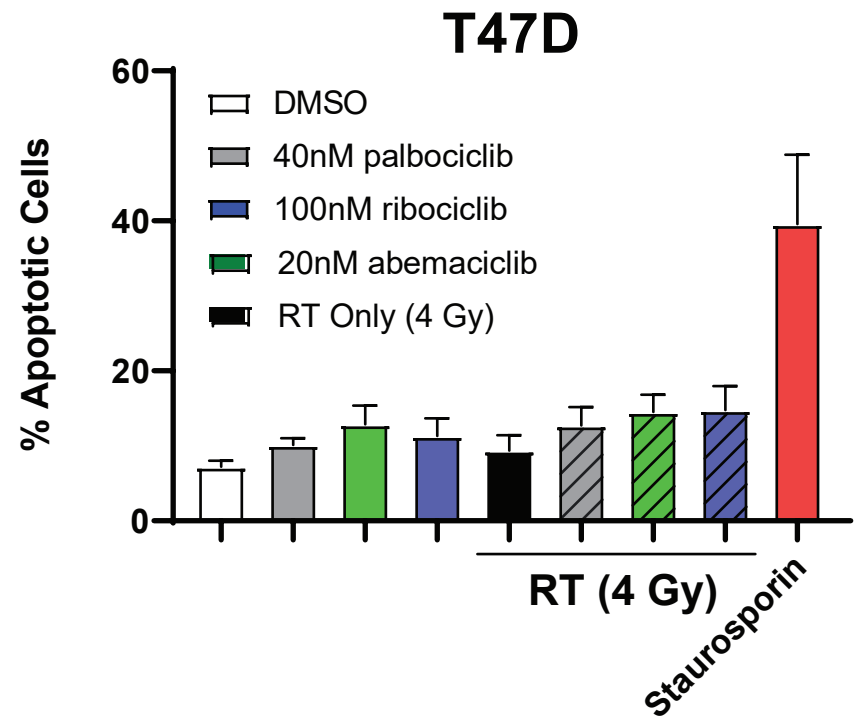


# Supplemental Figure 9

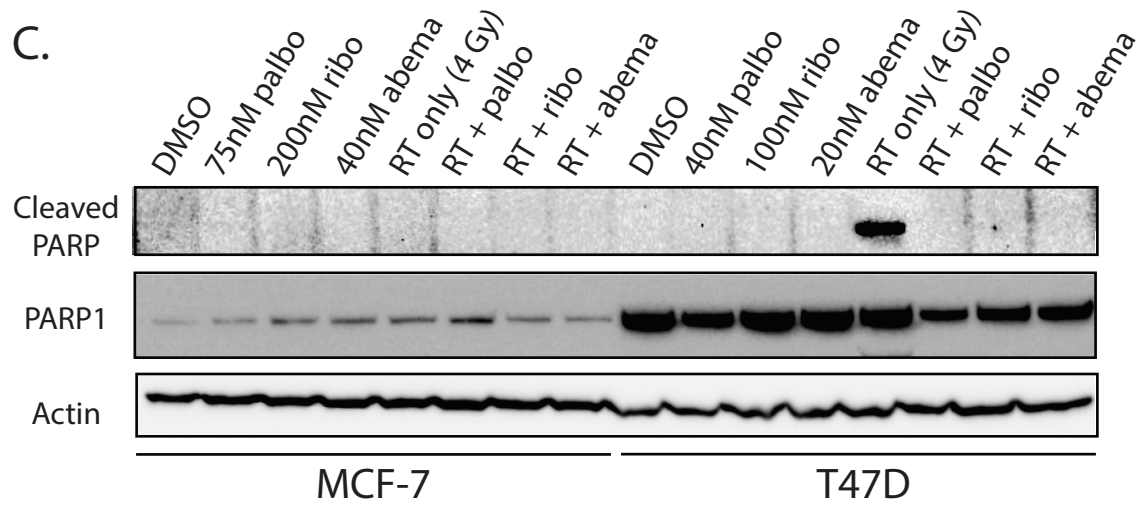
A.



B.



C.



# Supplemental Table 1

A. **MCF-7 Clonogenic Survival Assay (Palbociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
50 nM palbociclib	1.22 ± 0.06	0.70 ± 0.12
75 nM palbociclib	1.31 ± 0.06	0.67 ± 0.14
100 nM palbociclib	1.52 ± 0.14	0.53 ± 0.08

B. **T47D Clonogenic Survival Assay (Palbociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
1 nM palbociclib	1.23 ± 0.15	0.99 ± 0.14
10 nM palbociclib	1.29 ± 0.13	0.54 ± 0.11
25 nM palbociclib	1.50 ± 0.13	0.29 ± 0.05

**MCF-7 Clonogenic Survival Assay (Ribociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
50 nM ribociclib	1.20 ± 0.05	0.88 ± 0.04
75 nM ribociclib	1.33 ± 0.02	0.69 ± 0.10
100 nM ribociclib	1.58 ± 0.11	0.64 ± 0.02

**T47D Clonogenic Survival Assay (Ribociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
10 nM ribociclib	1.20 ± 0.12	0.85 ± 0.13
25 nM ribociclib	1.28 ± 0.11	0.78 ± 0.15
50 nM ribociclib	1.58 ± 0.07	0.57 ± 0.15

**MCF-7 Clonogenic Survival Assay (Abemaciclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
50 nM abemaciclib	1.34 ± 0.05	0.78 ± 0.05
75 nM abemaciclib	1.51 ± 0.15	0.80 ± 0.09
100 nM abemaciclib	1.59 ± 0.13	0.44 ± 0.06

**T47D Clonogenic Survival Assay (Abemaciclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
10 nM abemaciclib	1.31 ± 0.11	0.88 ± 0.22
25 nM abemaciclib	1.38 ± 0.23	0.74 ± 0.20
50nM abemaciclib	1.81 ± 0.26	0.69 ± 0.11

C. **CAMA-1 Clonogenic Survival Assay (Palbociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
25nM palbociclib	1.17 ± 0.04	0.92 ± 0.13
50nM palbociclib	1.16 ± 0.06	0.72 ± 0.05
75nM palbociclib	1.30 ± 0.09	0.51 ± 0.10

D. **ZR-75-1 Clonogenic Assay (Palbociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
50 nM palbociclib	1.21 ± 0.15	0.81 ± 0.14
100 nM palbociclib	1.27 ± 0.14	0.47 ± 0.16



# Supplemental Table 2

A. **MCF-7 Pal<sub>AR</sub> Clonogenic Assay (Palbociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
100nM palbociclib	1.03 ± 0.07	0.95 ± 0.04
500nM palbociclib	0.95 ± 0.05	0.82 ± 0.13

B. **T47D Pal<sub>AR</sub> Clonogenic Assay (Palbociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
100nM palbociclib	0.90 ± 0.07	0.75 ± 0.17
250nM palbociclib	0.92 ± 0.08	0.70 ± 0.32

C. **MCF-7 Rib<sub>AR</sub> Clonogenic Assay (Ribociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
100nM ribociclib	0.97 ± 0.11	0.75 ± 0.19
500nM ribociclib	1.03 ± 0.04	0.85 ± 0.06

D. **T47D Rib<sub>AR</sub> Clonogenic Assay (Ribociclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
100nM ribociclib	1.08 ± 0.07	0.47 ± 0.11
250nM ribociclib	1.01 ± 0.11	0.33 ± 0.13

E. **MCF-7 Abe<sub>AR</sub> Clonogenic Assay (Abemaciclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
100nM abemaciclib	0.96 ± 0.08	0.85 ± 0.08
500nM abemaciclib	0.92 ± 0.11	0.81 ± 0.26

F. **T47D Abe<sub>AR</sub> Clonogenic Assay (Abemaciclib)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
100nM abemaciclib	1.06 ± 0.06	0.95 ± 0.16
250nM abemaciclib	1.10 ± 0.06	0.58 ± 0.15

# Supplemental Table 3

A. **MCF-10A Clonogenic Assay**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
100nM palbociclib	0.95 ± 0.01	0.47 ± 0.13
100nM ribociclib	0.99 ± 0.08	0.87 ± 0.09
100nM abemaciclib	0.95 ± 0.02	0.54 ± 0.03

# Supplemental Table 4

**MCF-7 Clonogenic Assay (6 hour pretreatment)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
50 nM palbociclib	1.33 ± 0.05	0.81 ± 0.10
75 nM palbociclib	1.37 ± 0.17	0.66 ± 0.06
100 nM palbociclib	1.57 ± 0.02	0.64 ± 0.11

B. **MCF-7 Clonogenic Assay (24 hour pretreatment)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
50 nM palbociclib	1.29 ± 0.07	0.74 ± 0.16
75 nM palbociclib	1.33 ± 0.11	0.67 ± 0.16
100 nM palbociclib	1.48 ± 0.20	0.59 ± 0.10

# Supplemental Table 5

A. **MCF-7 Clonogenic Assay (NU7441, AZD7762)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
75nM palbociclib	1.35 ± 0.11	0.83 ± 0.07
500nM NU7441	1.97 ± 0.71	0.99 ± 0.19
NU7441 + palbo	2.70 ± 0.87	0.85 ± 0.04
100nM AZD7762	1.60 ± 0.29	0.24 ± 0.05
AZD7762 + palbo	1.36 ± 0.13	0.28 ± 0.04

B. **MCF-7 Clonogenic Assay (siNT, siRAD51, siXRCC6)**

Treatment	Enhancement Ratio	Cytotoxicity
siNT	1.0	1.0
siNT + 75nM palbo	1.33 ± 0.11	0.79 ± 0.18
siXRCC6	1.44 ± 0.26	0.36 ± 0.20
siXRCC6 + palbo	2.08 ± 0.34	0.15 ± 0.15
siRAD51	1.69 ± 0.51	0.09 ± 0.05
siRAD51 + palbo	1.87 ± 0.58	0.04 ± 0.03

C. **T47D Clonogenic Assay (NU7441)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
10nM palbociclib	1.29 ± 0.17	1.26 ± 0.15
500nM NU7441	2.22 ± 0.70	1.03 ± 0.60
NU7441 + palbo	2.51 ± 0.09	1.28 ± 0.36

D. **MCF7 Pal<sub>AR</sub> Clonogenic Assay (NU7441)**

Treatment	Enhancement Ratio	Cytotoxicity
DMSO	1.0	1.0
75nM palbociclib	0.89 ± 0.08	0.82 ± 0.06
500nM NU7441	1.67 ± 0.19	0.91 ± 0.09
NU7441 + palbo	1.88 ± 0.24	0.89 ± 0.09

# Supplemental Table 6

MCF-7 Xenografts (FTV)			Combination		
Day	RT	Palbo	Expected	Observed	Ratio
9	0.822	0.795	0.654	0.671	0.974
26	0.584	0.704	0.411	0.373	1.103
38	0.558	0.699	0.390	0.358	1.090
61	0.505	0.674	0.340	0.323	1.055
77	0.499	0.759	0.379	0.286	1.326