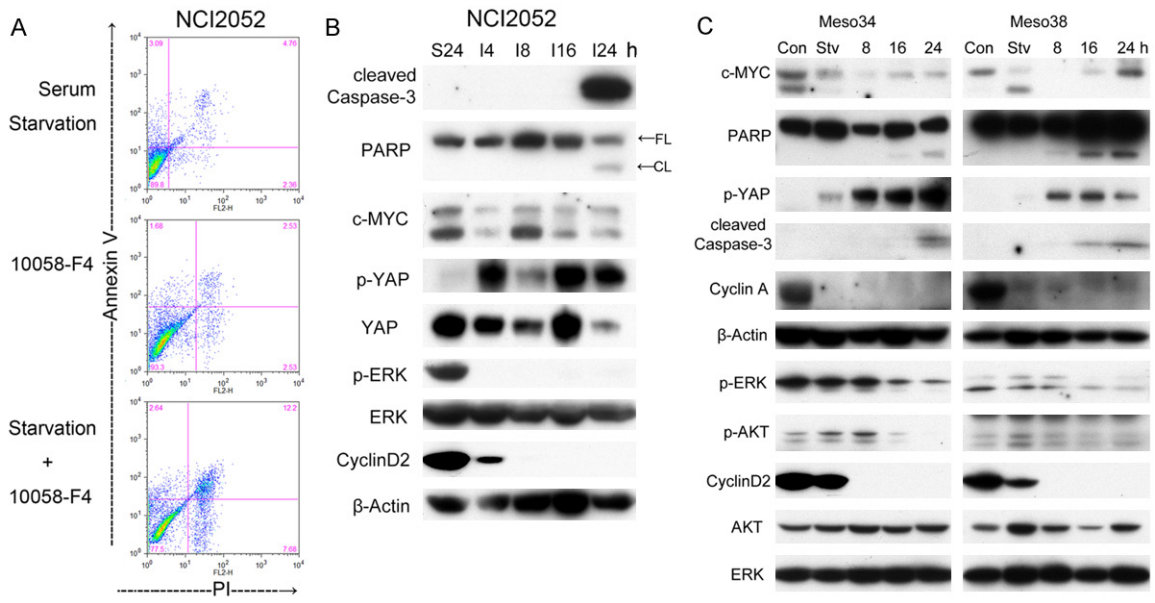


Figure S1. MYC inhibitor 10058-F4 triggers apoptosis in MM cells under serum starvation conditions. A. MM cell line NCI-2052 was treated with 10058-F4 plus serum starvation. Membrane integrity was monitored by FACS. B. Western blot analysis was performed to assess activation of caspase-3, inactivation of YAP, and expression of cyclin D2 in NCI-2052 and in (C) Meso34 and Meso38 cells.

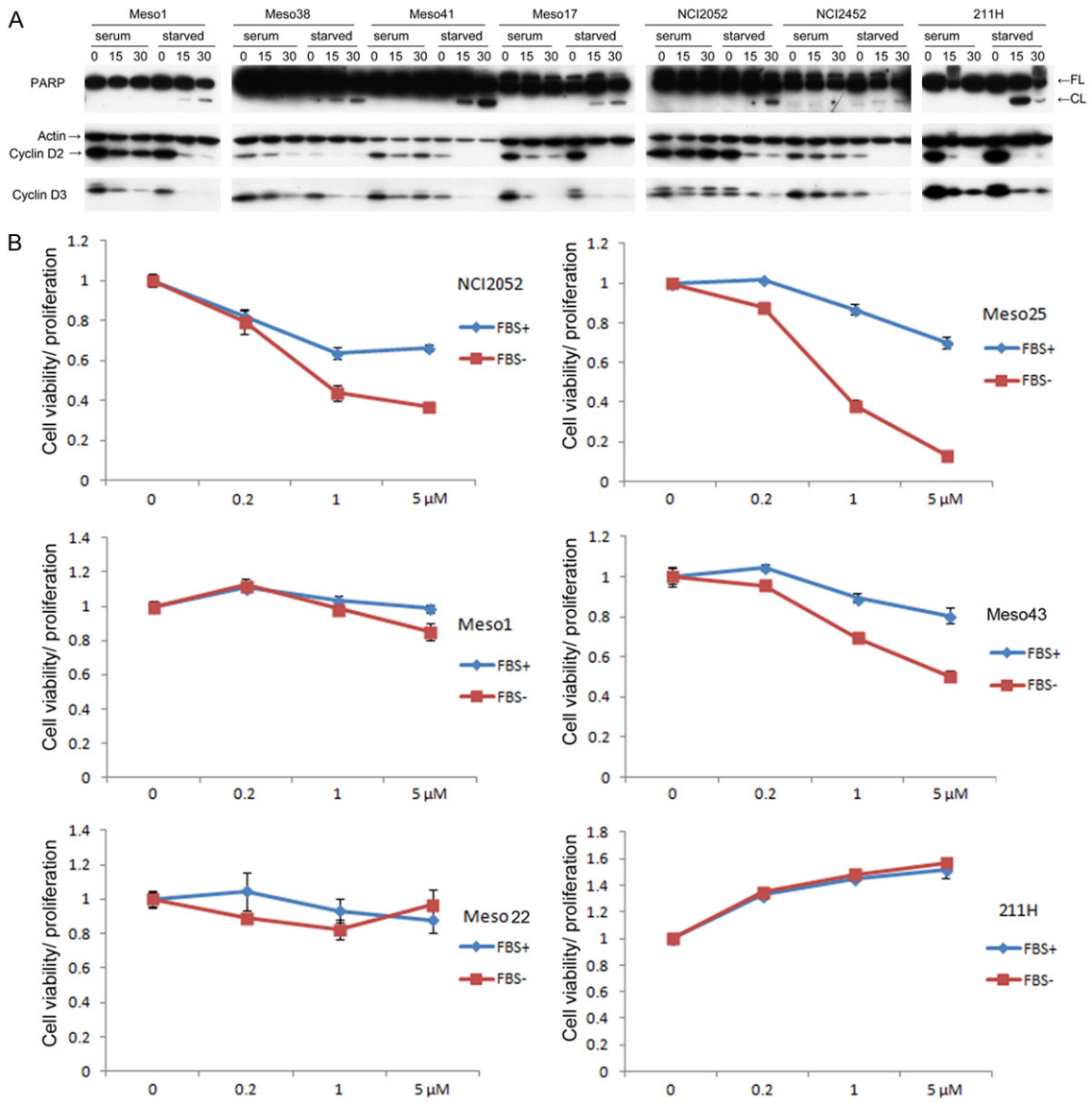
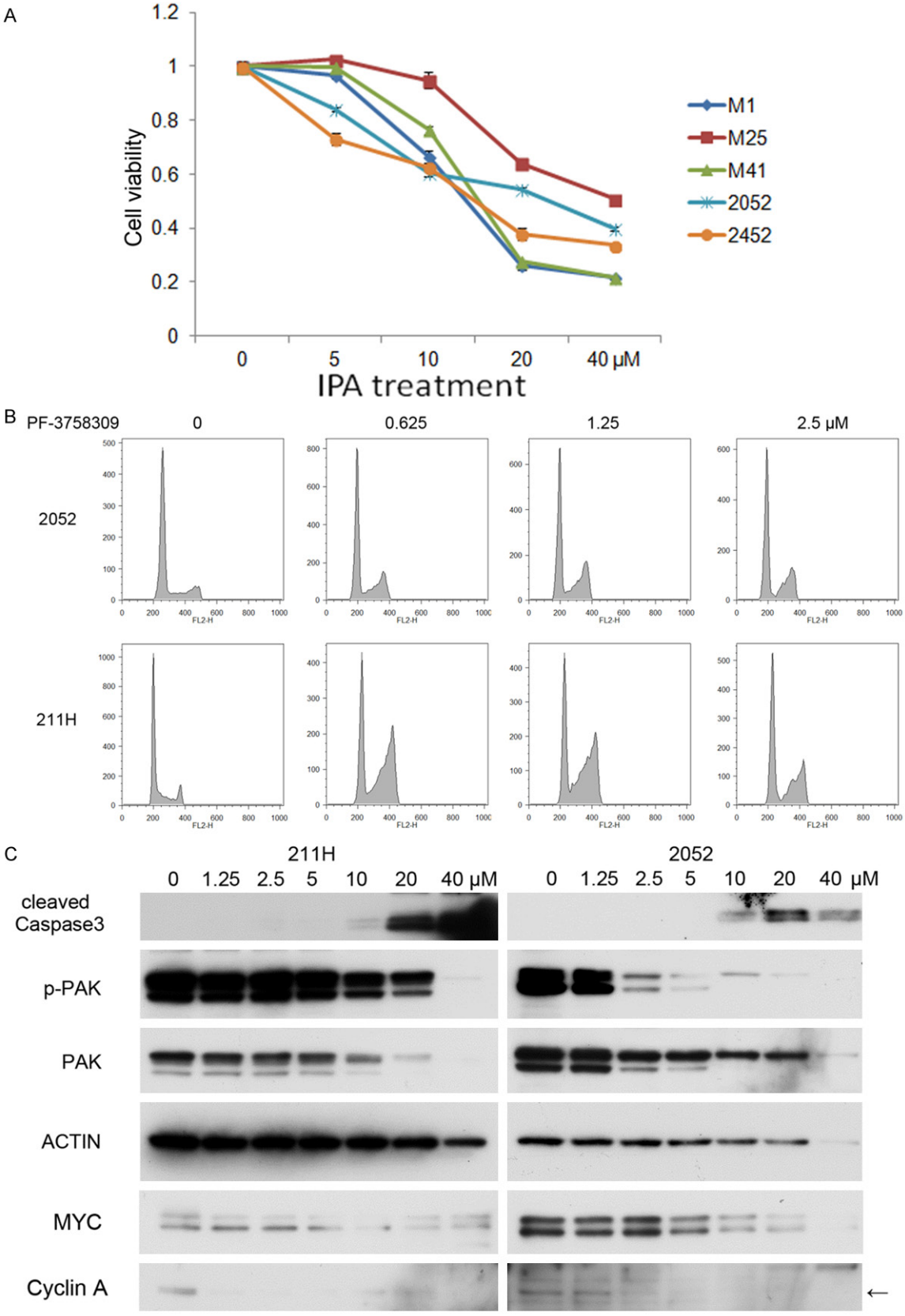


Figure S2. MYC inhibitor 10074-G5 and BRD4/MYC inhibitor JQ1 induces cell death under serum starvation conditions. A. MM cells were treated with 10074-G5 at 40 μM for 24 h under normal or serum-depleted culture conditions. Immunoblotting was performed to evaluate the expression of Cyclin D2, D3 as well as PARP cleavage. B. MM cells were treated with BRD4 inhibitor JQ1 at the indicated concentration for 36 h, with or without serum. MTS assay was performed to evaluate cell viability.


A
Cell viability
1.2
1
0.8
0.6
0.4
0.2
0
0
5
10
20
40 μM
IPA treatment
M1
M25
M41
2052
2452
B
PF-3758309
0
0.625
1.25
2.5 μM
2052
211H
FL2-H
C
211H
2052
0 1.25 2.5 5 10 20 40 μM
cleaved Caspase3
p-PAK
PAK
ACTIN
MYC
Cyclin A

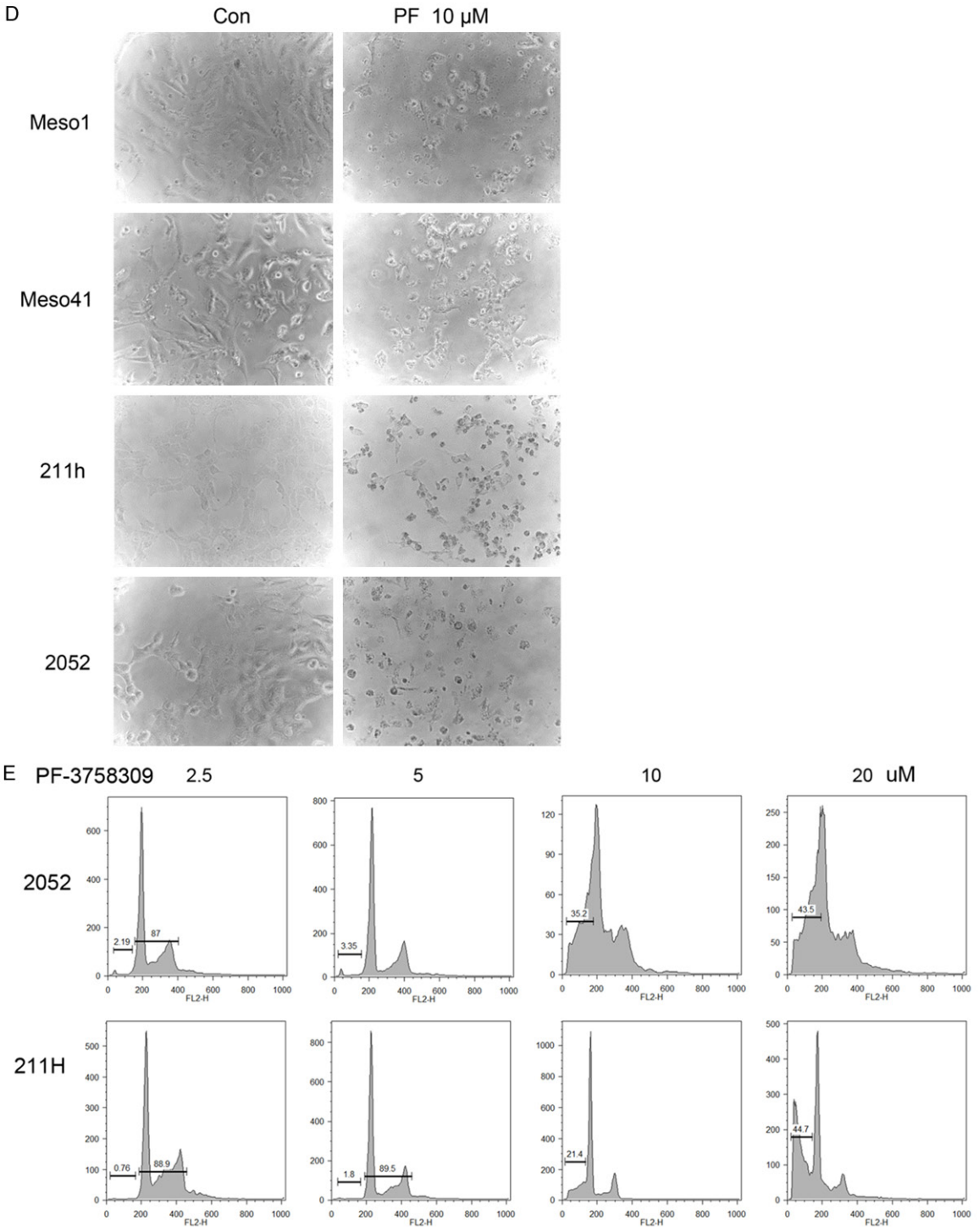


Figure S3. PAK inhibitors reduces viability of MM cells. A. Meso1, Meso25, Meso41, NCI-2052, NCI-2452 lines were treated with IPA-3 at the indicated concentration, and MTS activity was measured after 24 h. B. NCI-2052 and MSTO211H cells were treated with PF3758309 at the indicated concentrations for 20 h, and cell cycles were analyzed by FACS. C. PF3758309 induces apoptosis in a dose dependent manner. Cells were treated with PF3758309 at the indicated concentrations for 24 h, and the caspase3 cleavage was shown by western blotting. D. NCI2052 and MSTO211H cells treated with 10 μM PF3758309, and cell morphology was assessed 20 h after treatment. E. sub-G1 populations were visualized by FACS.

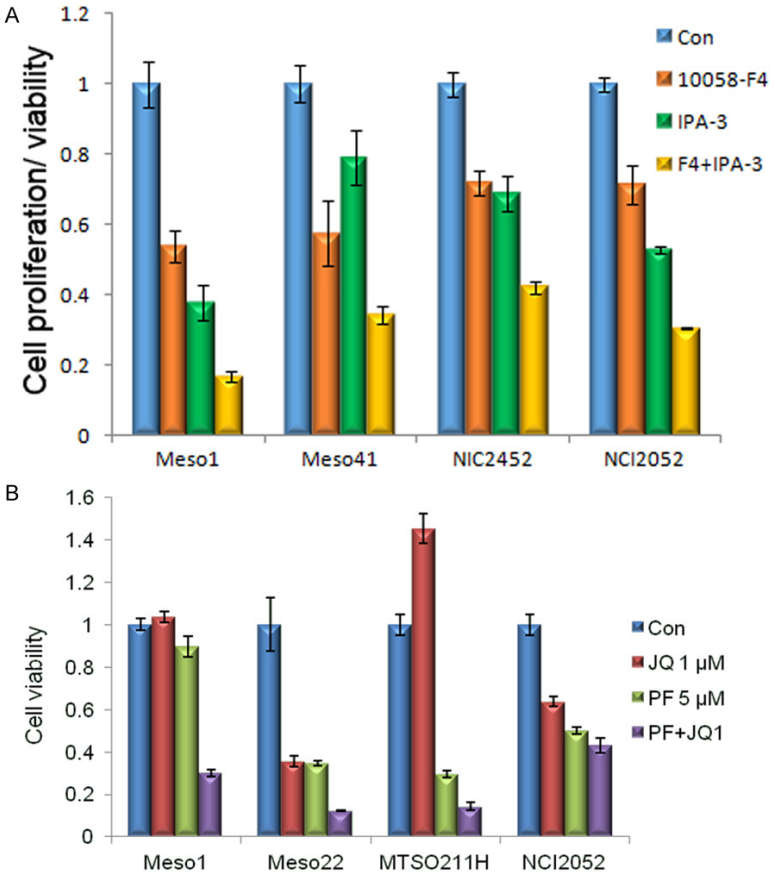
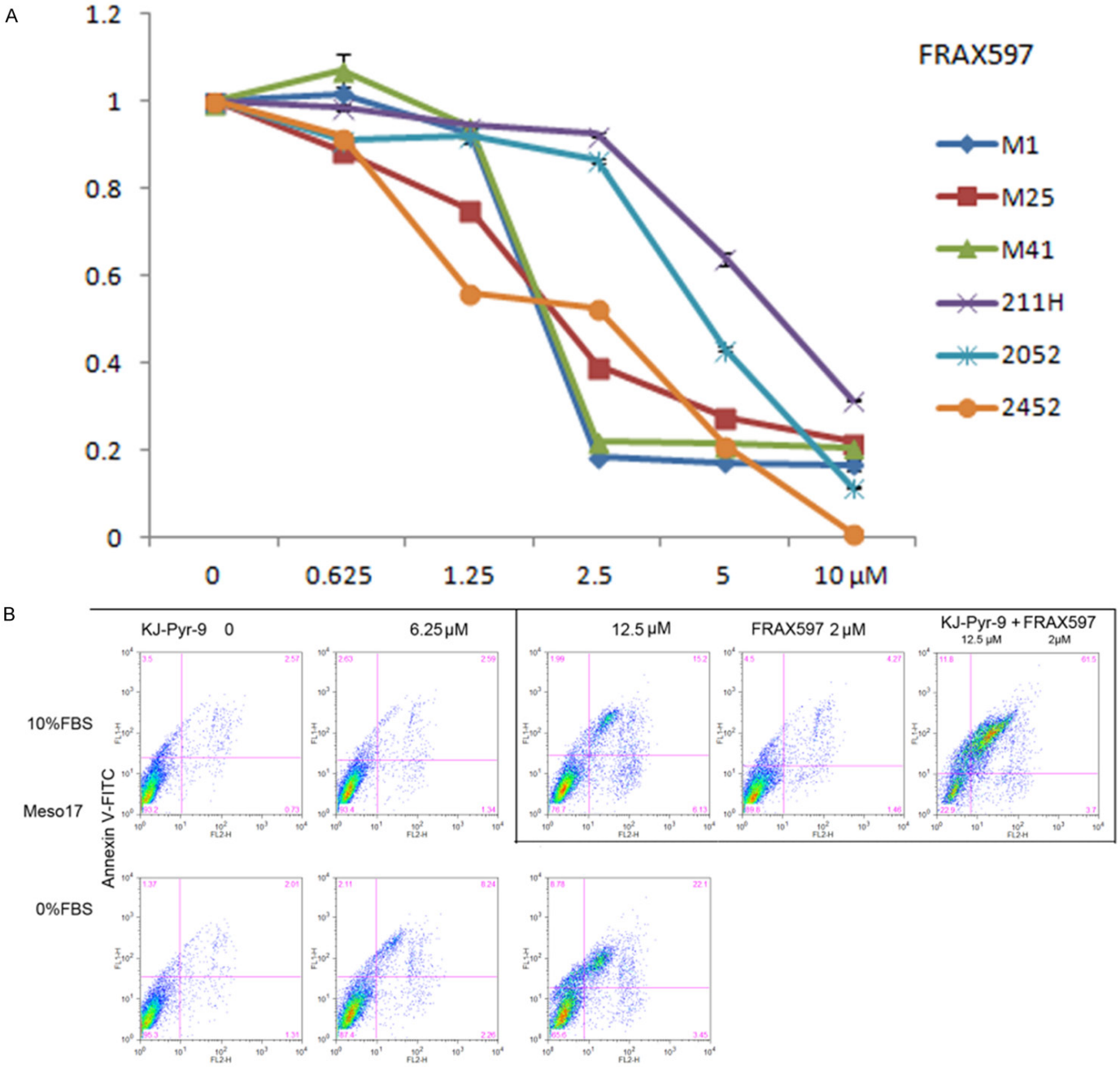
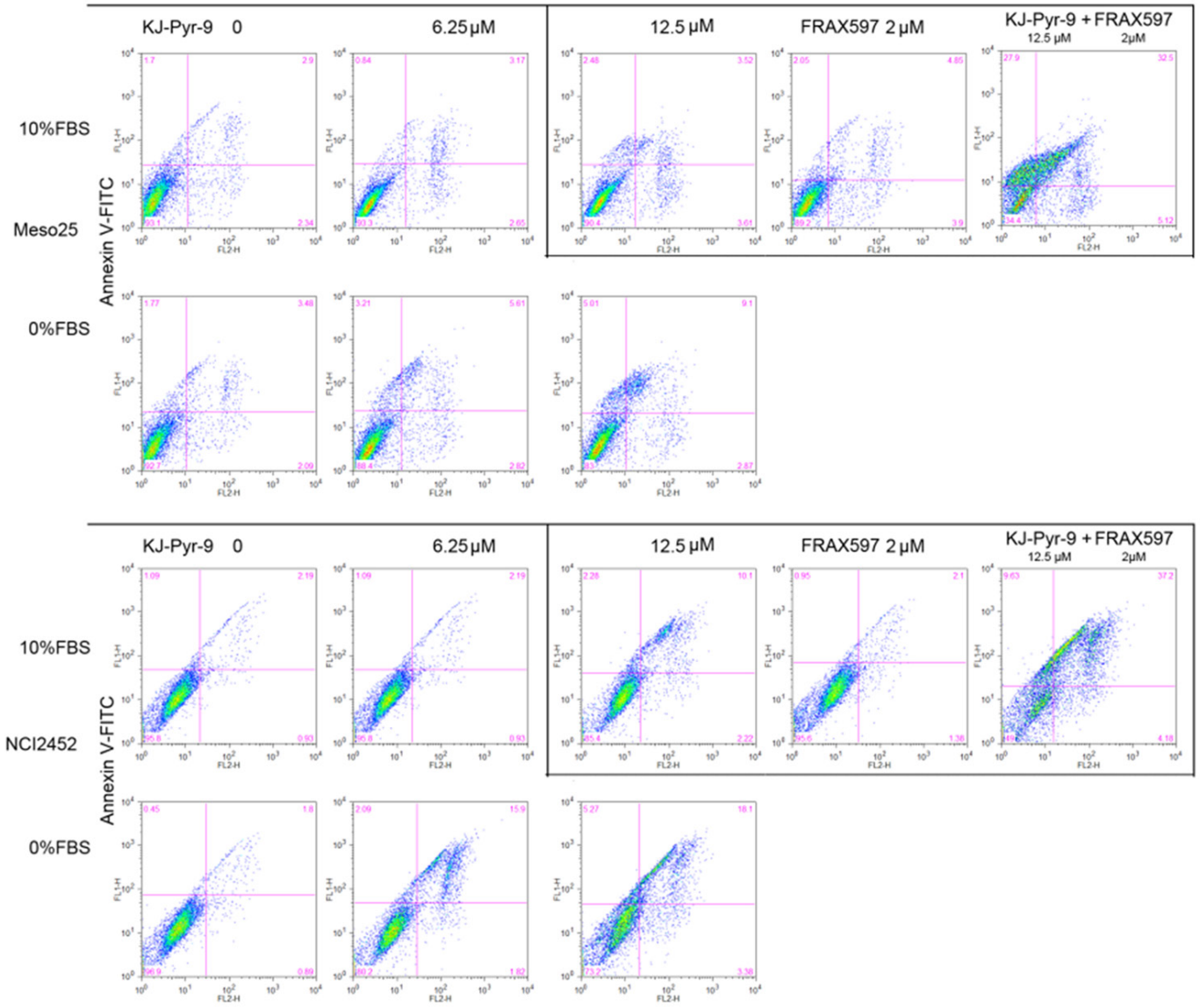


Figure S4. Different MYC inhibitors cooperate with different PAK inhibitors to suppress cell viability. A. MST assay of cell proliferation/viability when cells are treated the 40 μM 10058-F4 and 15 μM IPA-3, either alone or in combination for 24 h. B. MM cells were treated with BRD4/MYC inhibitor JQ1 either alone or in combination with PF3758309. Cell viability was measured after 24 h.


A
1.2
1
0.8
0.6
0.4
0.2
0
0
0.625
1.25
2.5
5
10 μM
FRAX597
M1
M25
M41
211H
2052
2452
B
KJ-Pyr-9 0
6.25 μM
12.5 μM
FRAX597 2 μM
KJ-Pyr-9 + FRAX597
12.5 μM
2μM
10%FBS
Meso17
0%FBS
Annexin V-FITC
FL2-H


KJ-Pyr-9 0
6.25 μM
12.5 μM
FRAX597 2 μM
KJ-Pyr-9 + FRAX597
12.5 μM
2μM
10%FBS
Meso25
0%FBS
Annexin V-FITC
FL2-H
KJ-Pyr-9 0
6.25 μM
12.5 μM
FRAX597 2 μM
KJ-Pyr-9 + FRAX597
12.5 μM
2μM
10%FBS
NCI2452
0%FBS
Annexin V-FITC
FL2-H

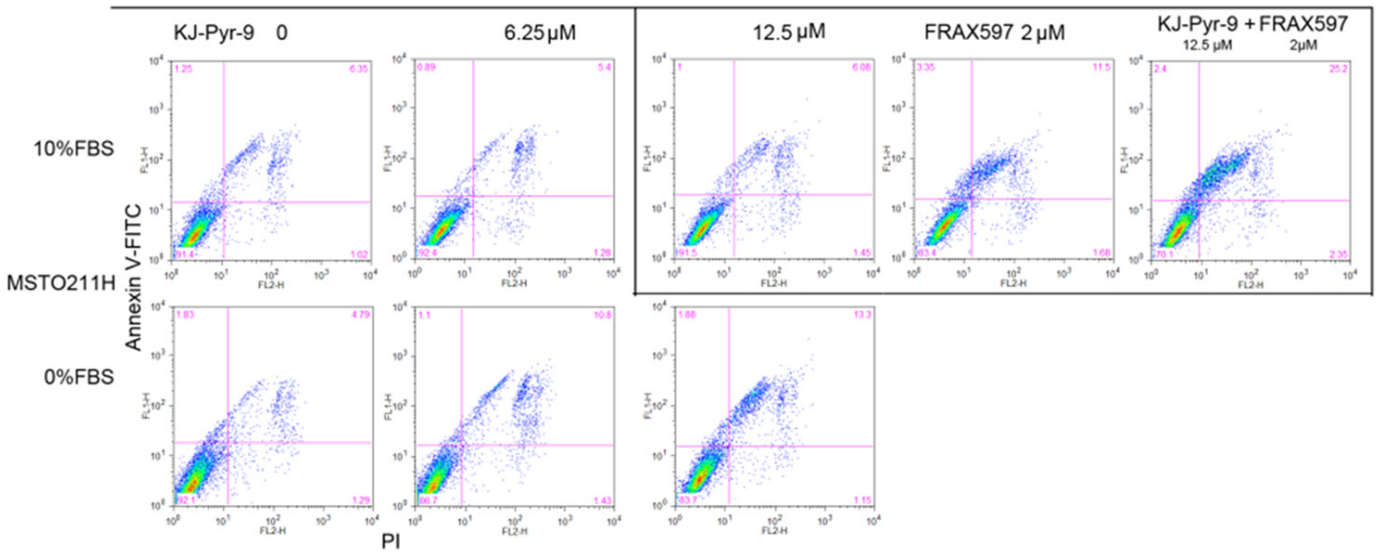


Figure S5. A novel MYC inhibitor KJ-Pyr-9 boosts FRAX597- induced apoptosis in MM cells. A. MM cells were added with PAK inhibitor PRAX597 at the indicated concentration and MTS activity was measured after 48hr. B. AnnexinV/PI staining of MM cells when treated with KJ-Pyr-9 alone or in combination with FRAX597, or under serum starvation conditions.