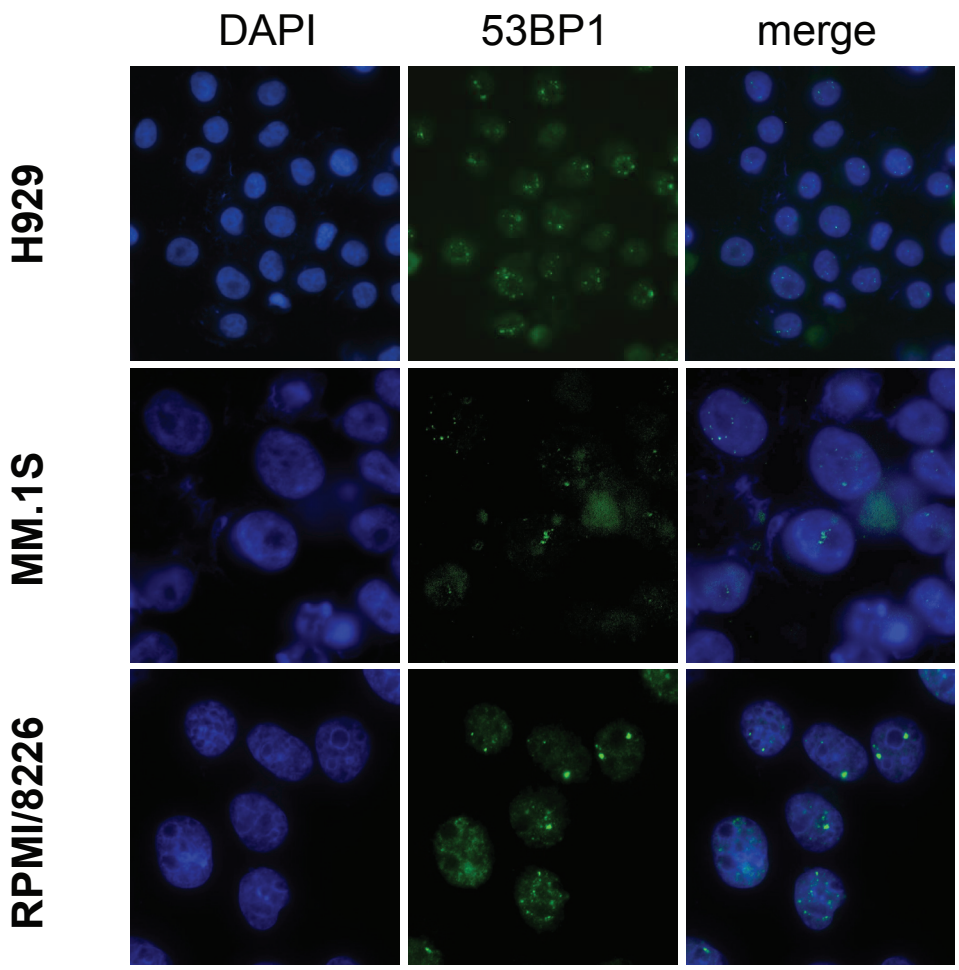
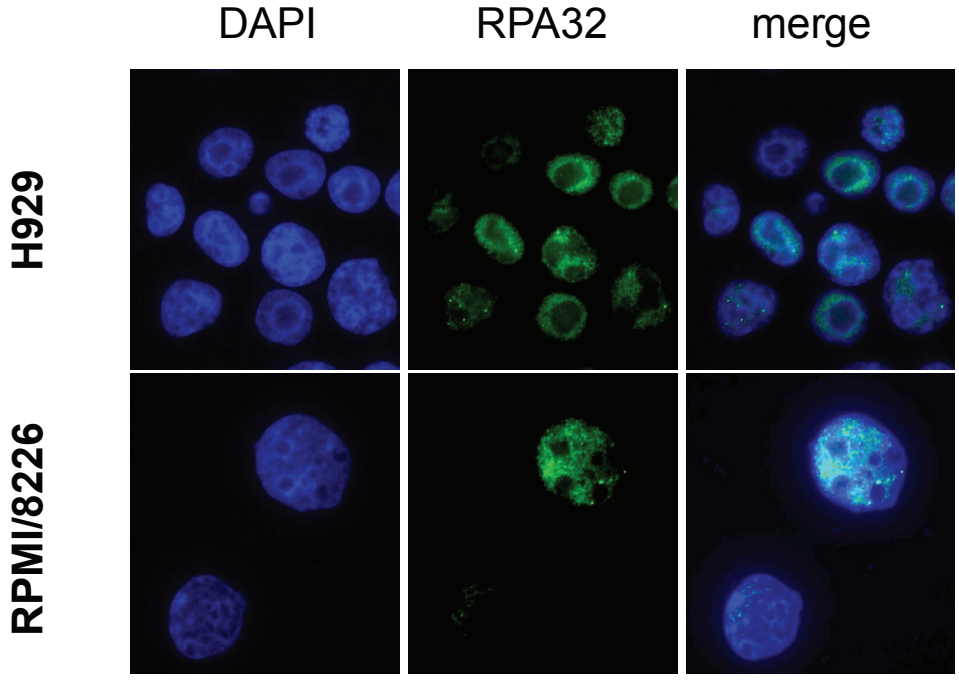
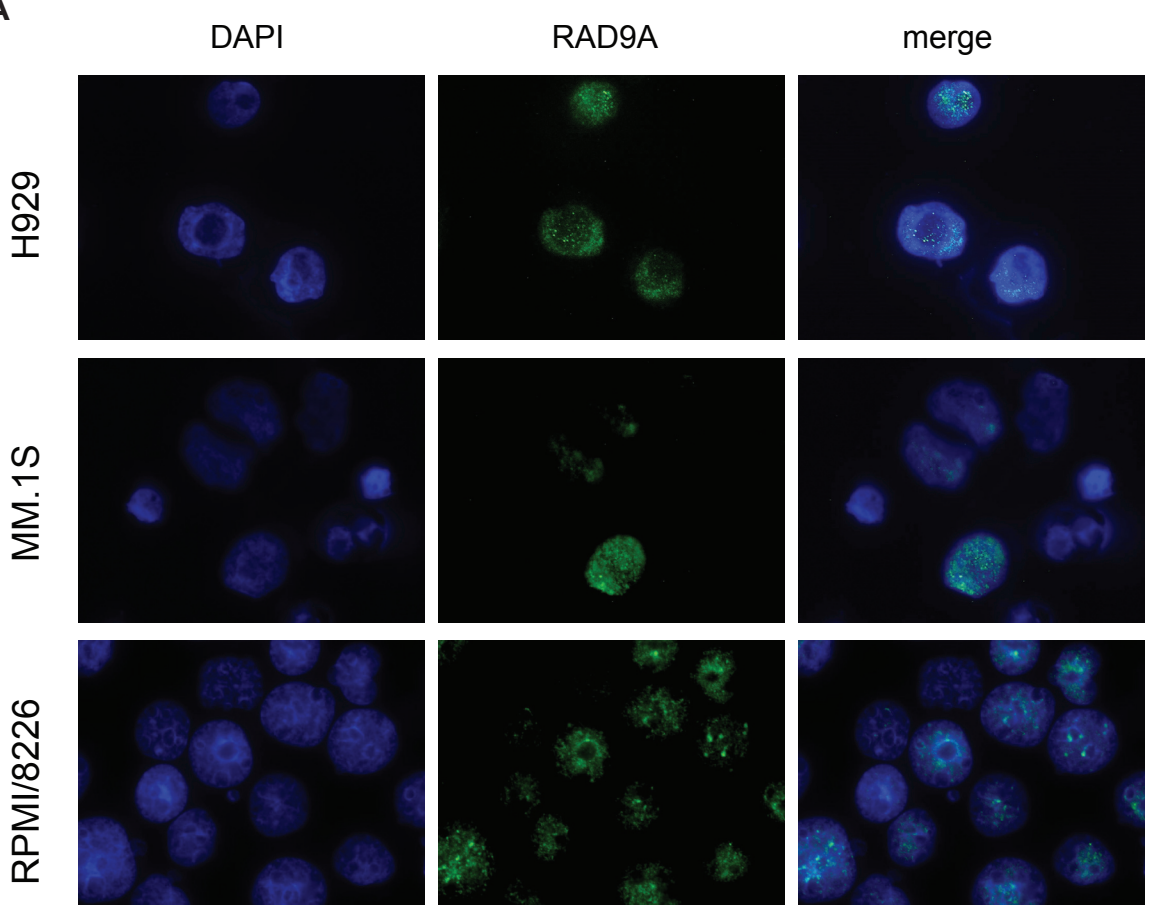
A


DAPI
53BP1
merge
H929
MM.1S
RPMI/8226

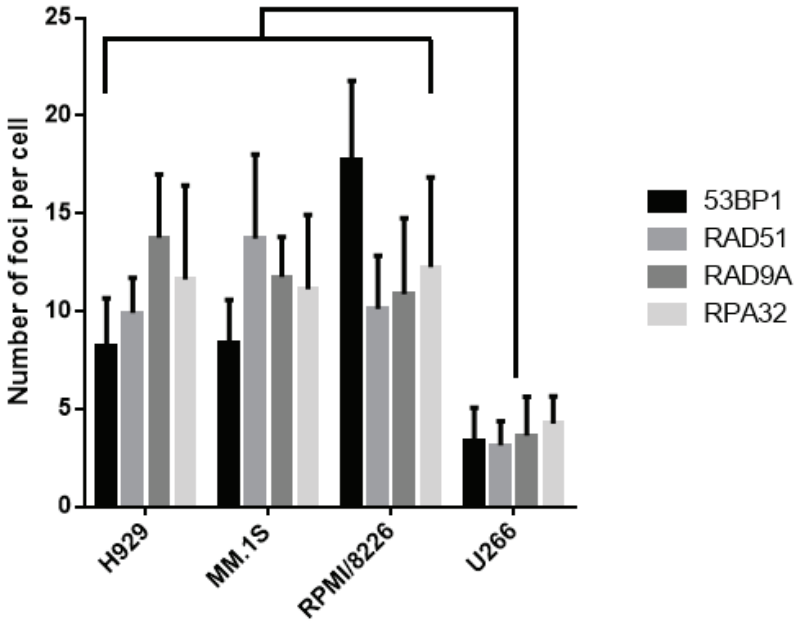
B

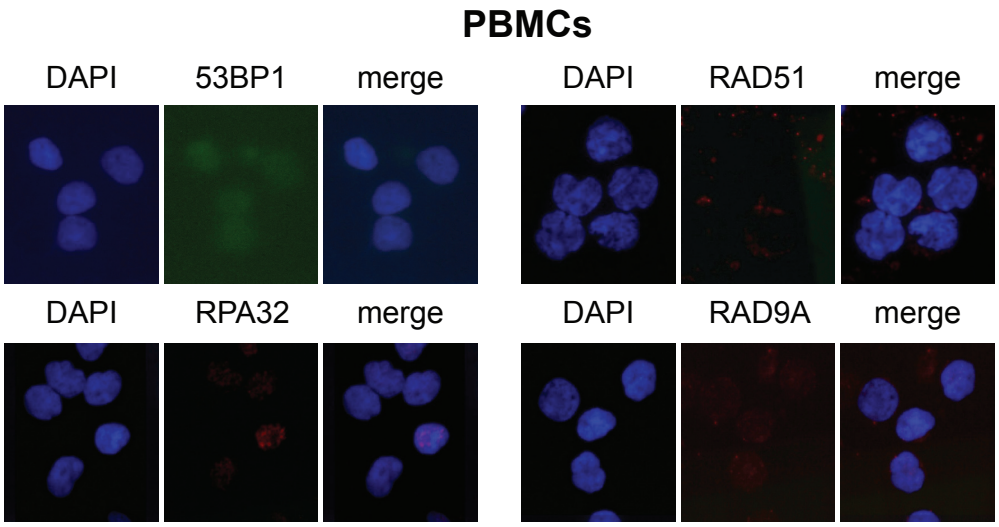

DAPI
RPA32
merge
H929
RPMI/8226

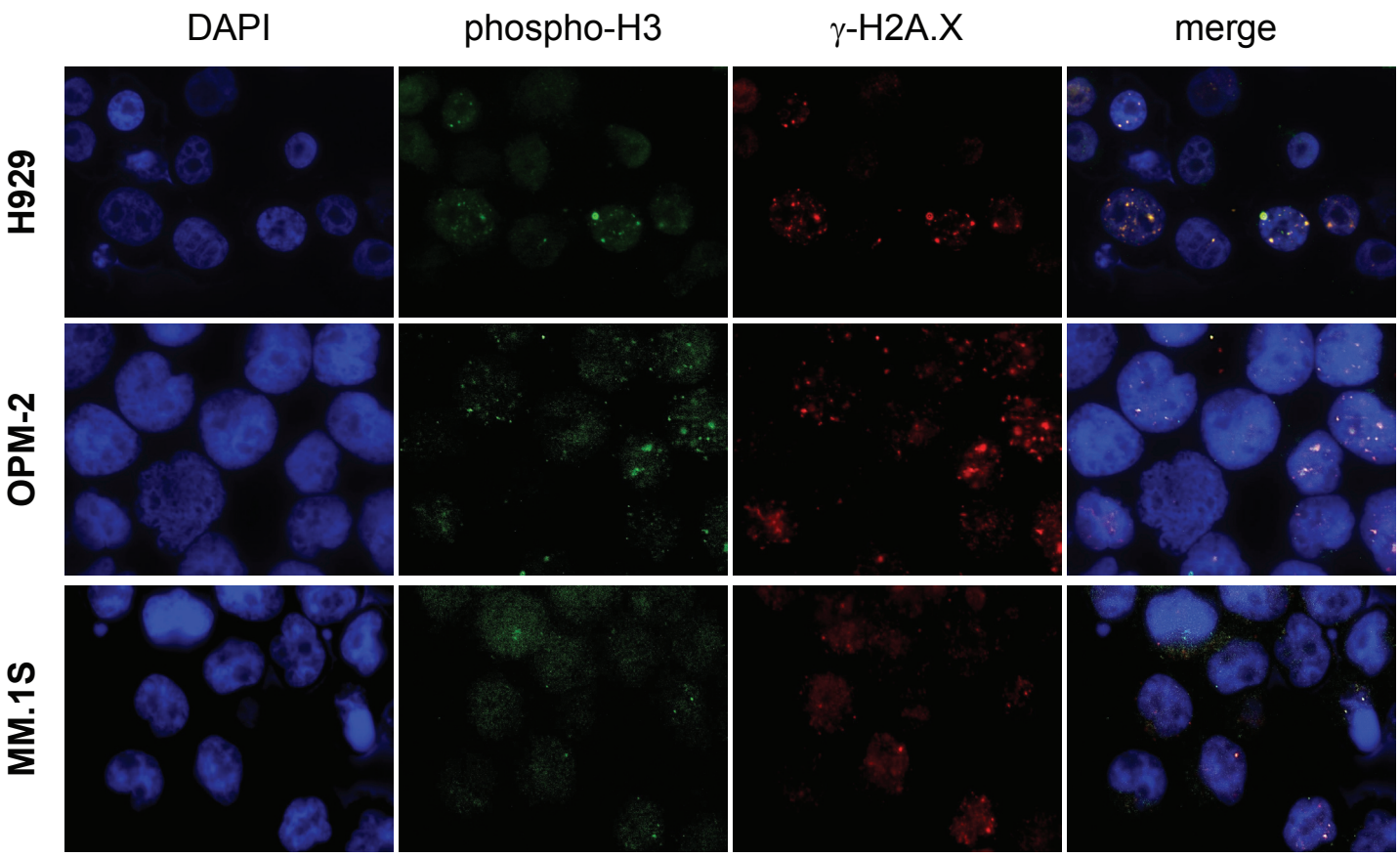
A

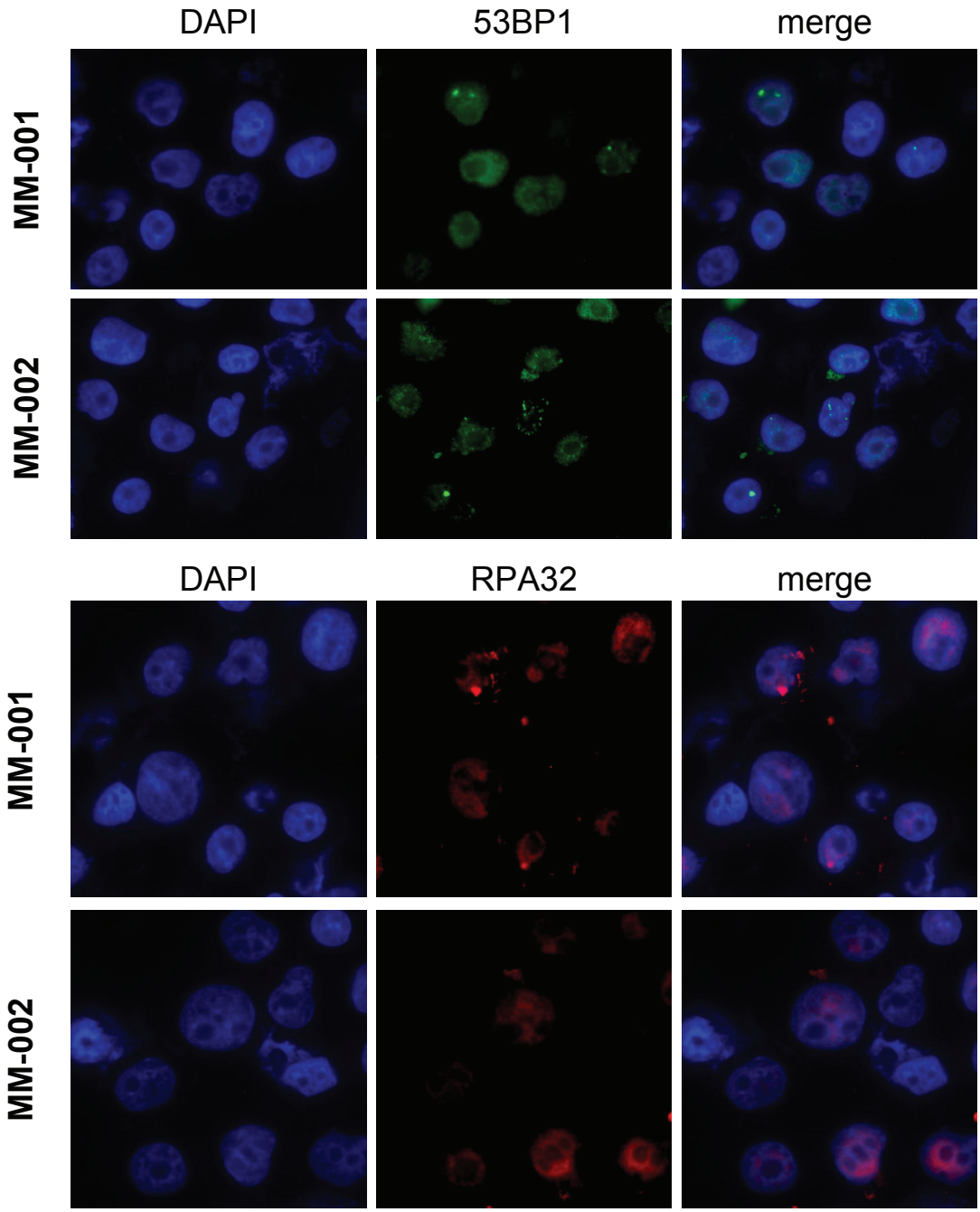

DAPI
RAD9A
merge
H929
MM.1S
RPMI/8226

B

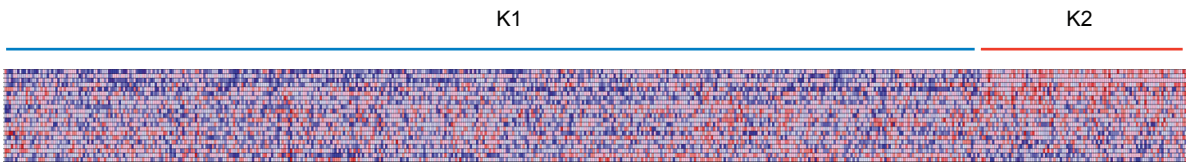

Number of foci per cell
25
20
15
10
5
0
H929
MM.1S
RPMI/8226
U266
53BP1
RAD51
RAD9A
RPA32


PBMCs
DAPI
53BP1
merge
DAPI
RAD51
merge
DAPI
RPA32
merge
DAPI
RAD9A
merge

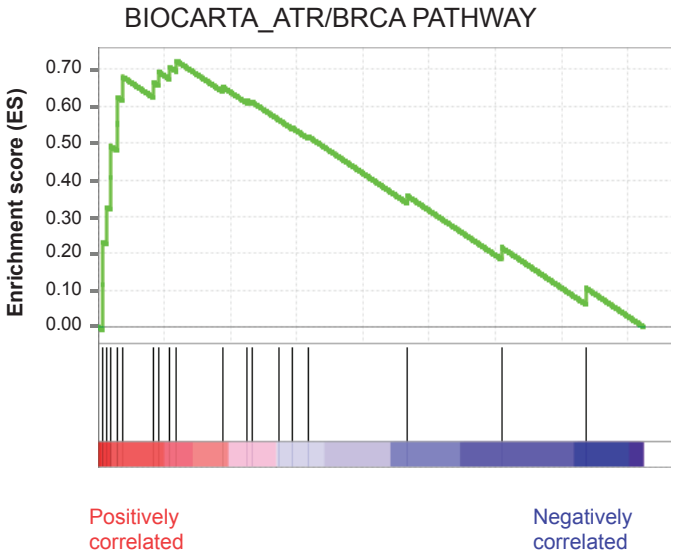

DAPI
phospho-H3
γ-H2A.X
merge
H929
OPM-2
MM.1S


DAPI
53BP1
merge
MM-001
MM-002
DAPI
RPA32
merge
MM-001
MM-002

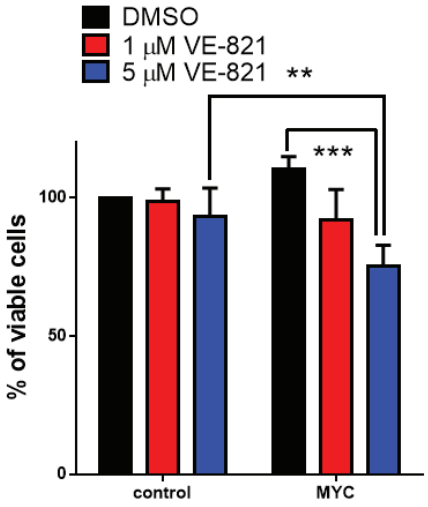
A


K1
K2

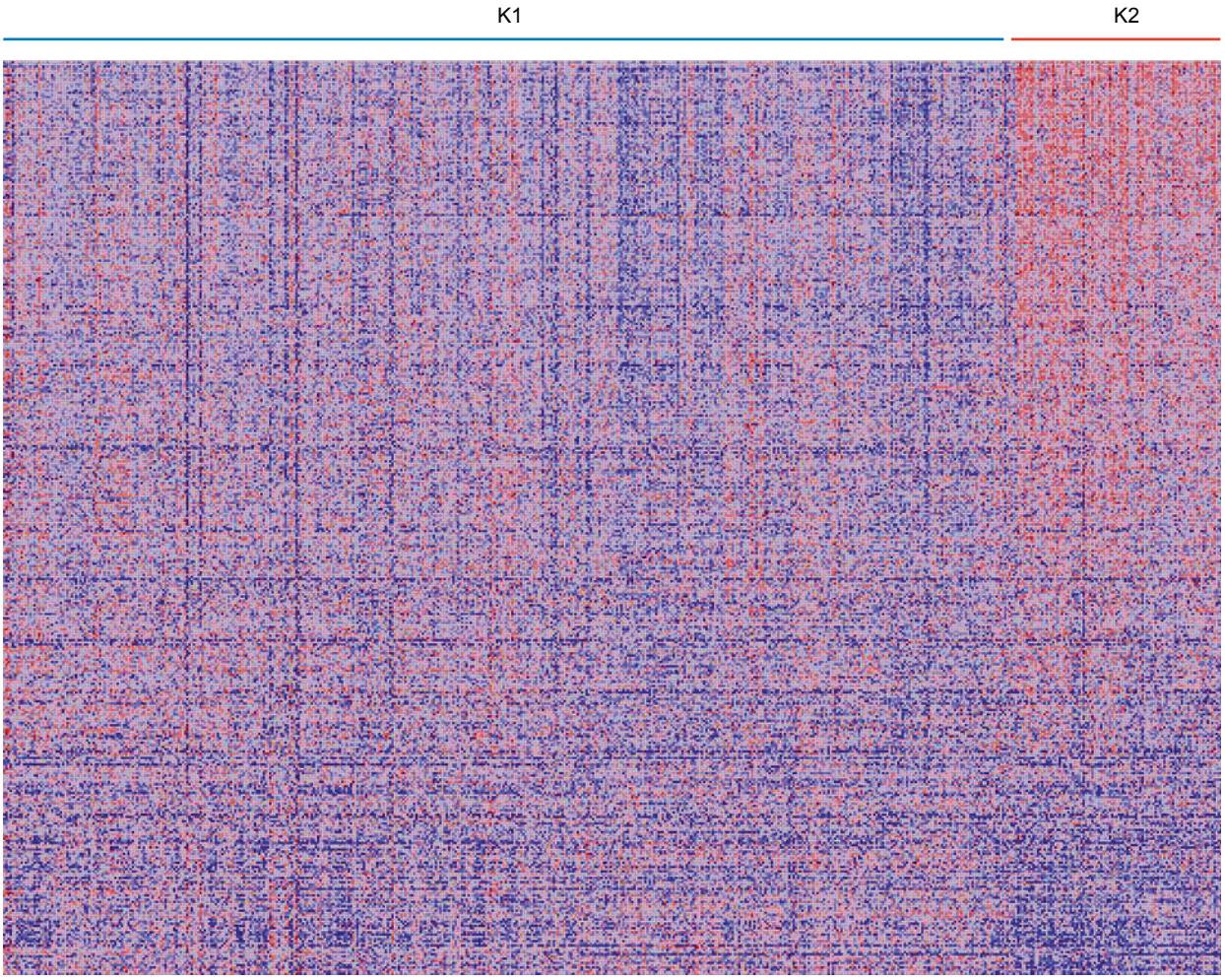
B


BIOCARTA_ATR/BRCA PATHWAY
Enrichment score (ES)
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
Positively correlated
Negatively correlated

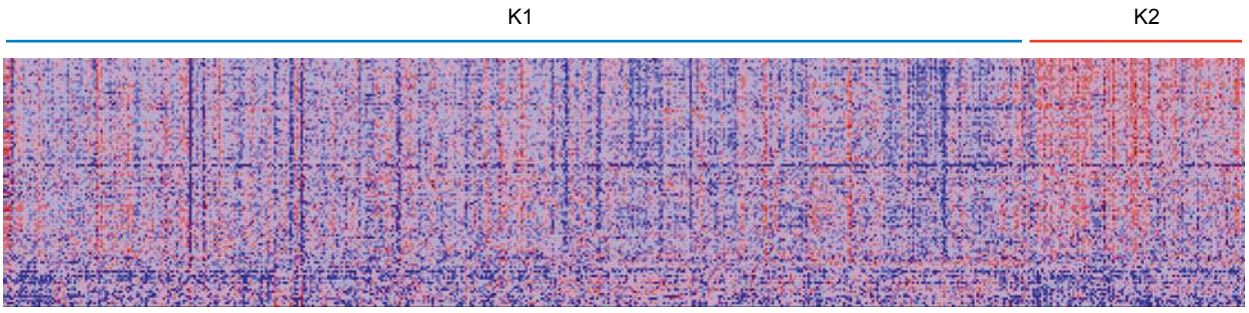
C


DMSO
1 μM VE-821
5 μM VE-821 **
***
% of viable cells
100
50
0
control
MYC

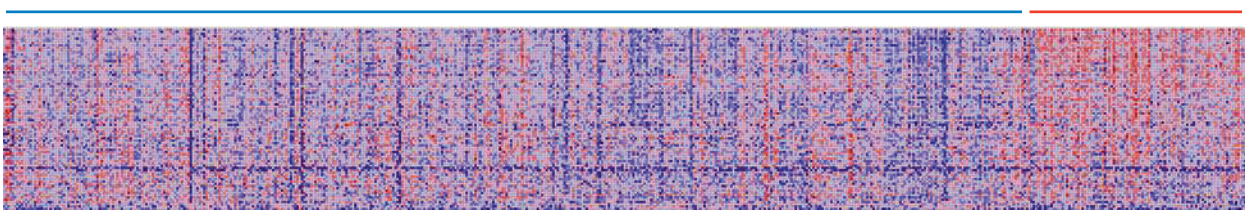
A

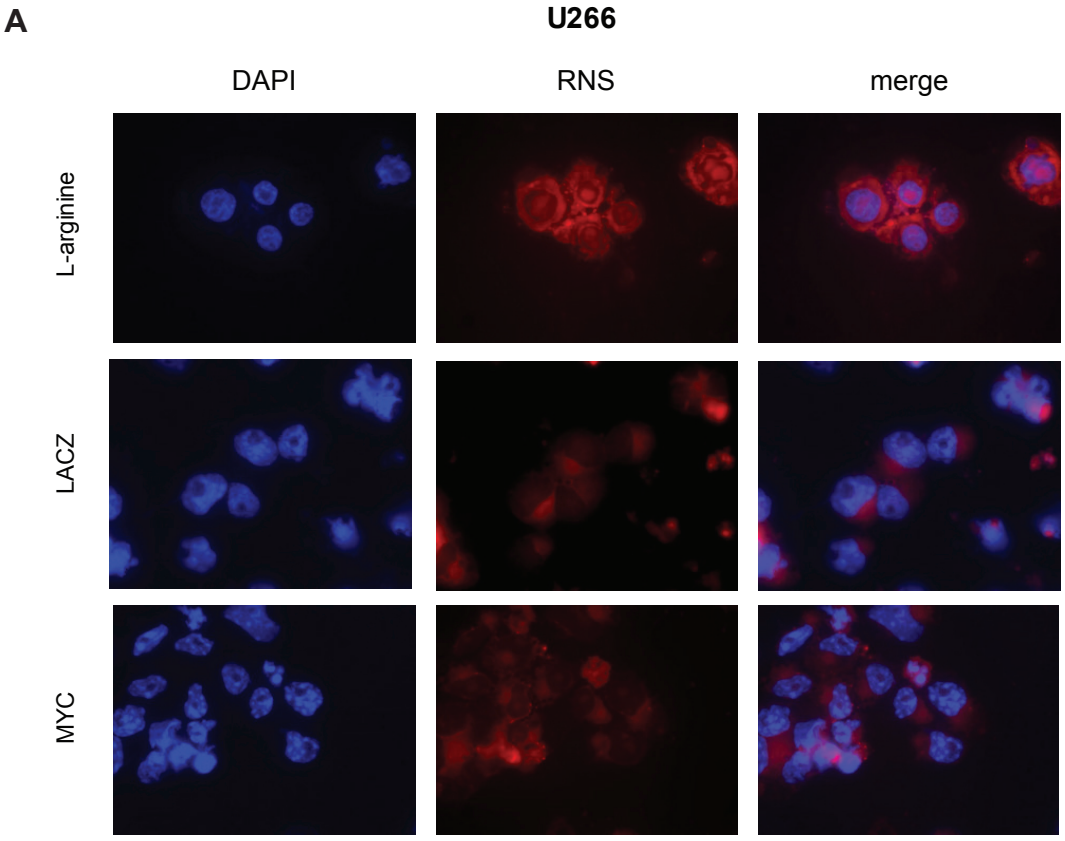


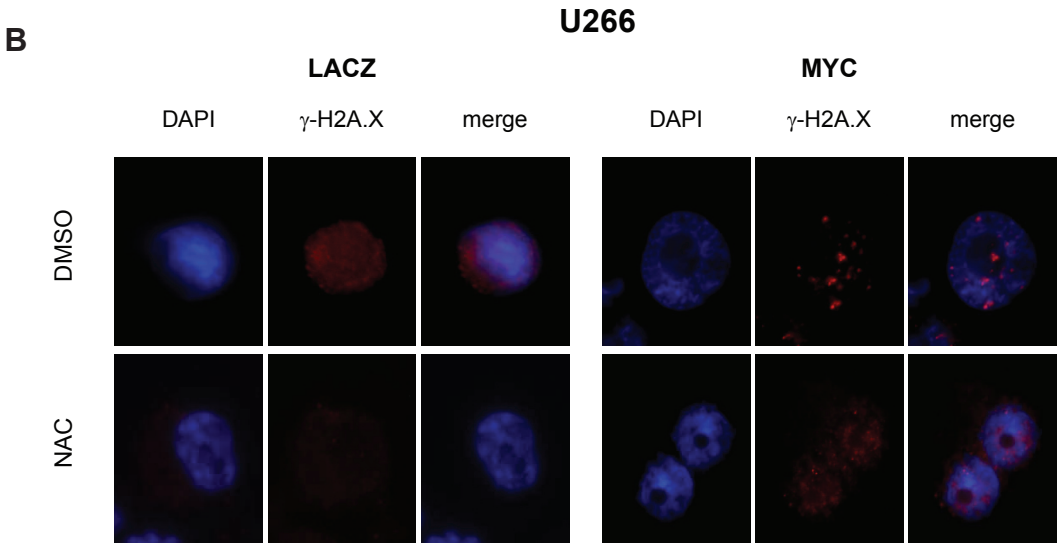
B

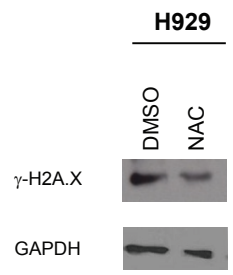


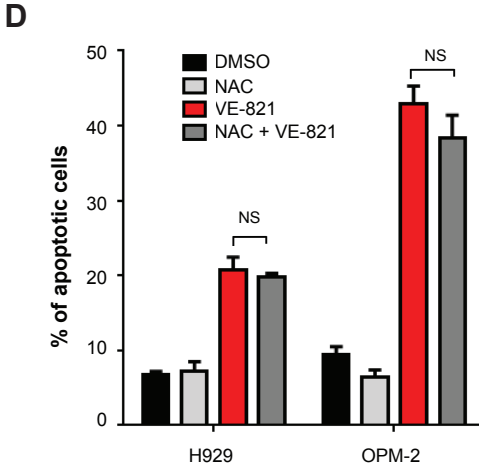
C

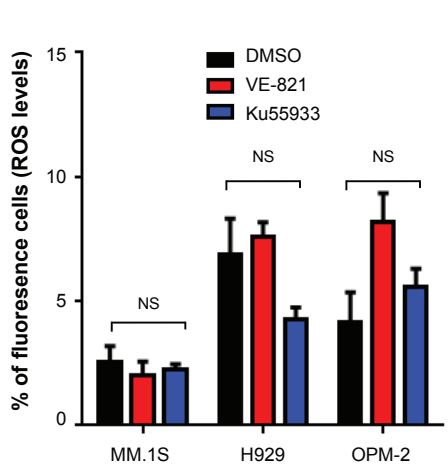


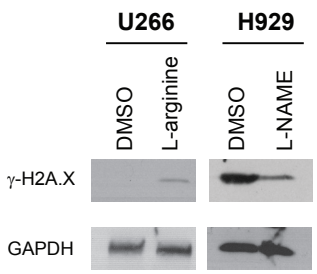

A
U266
DAPI
RNS
merge
L-arginine
LACZ
MYC

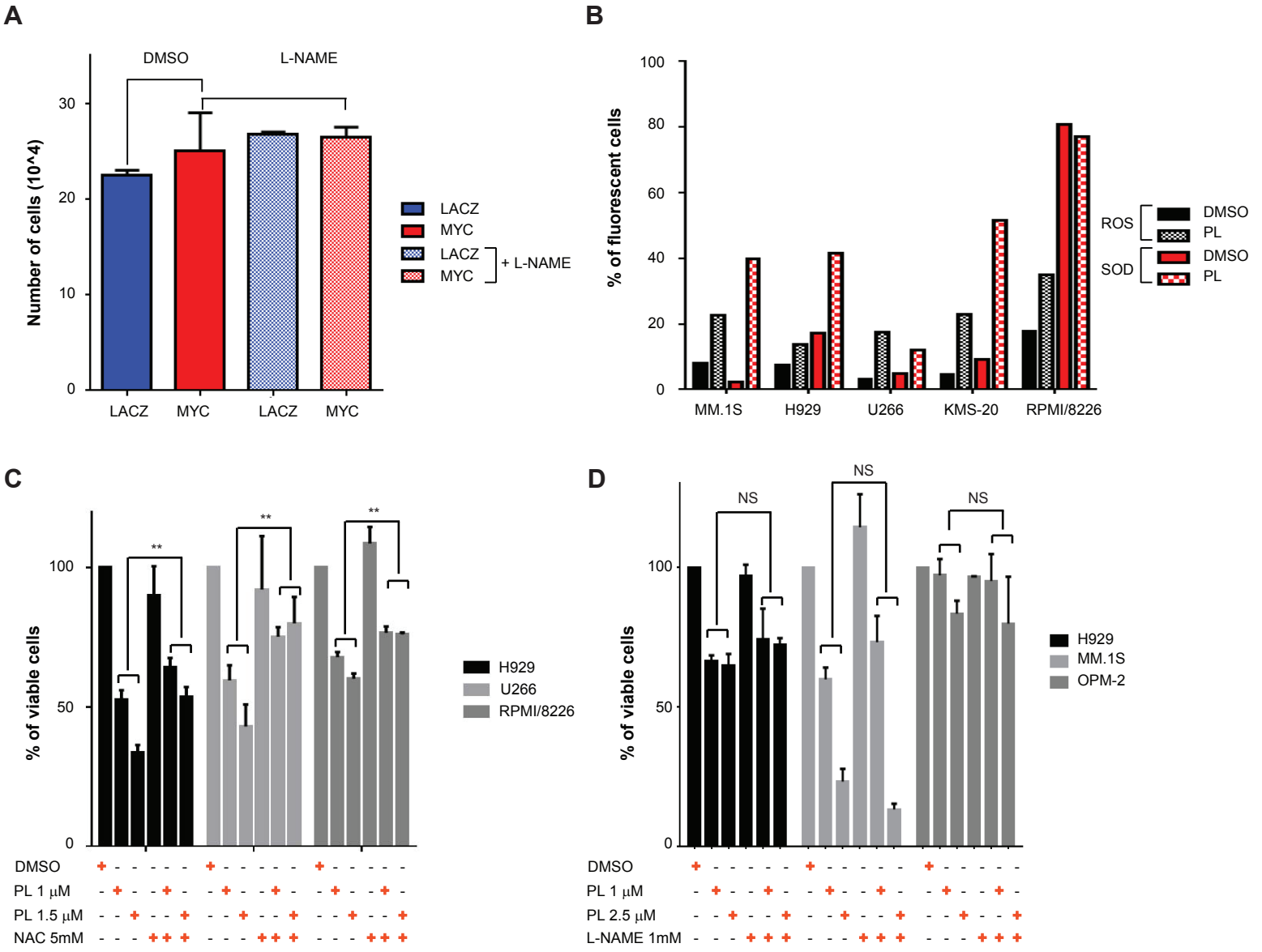

B
U266
LACZ
MYC
DAPI
γ-H2A.X
merge
DAPI
γ-H2A.X
merge
DMSO
NAC

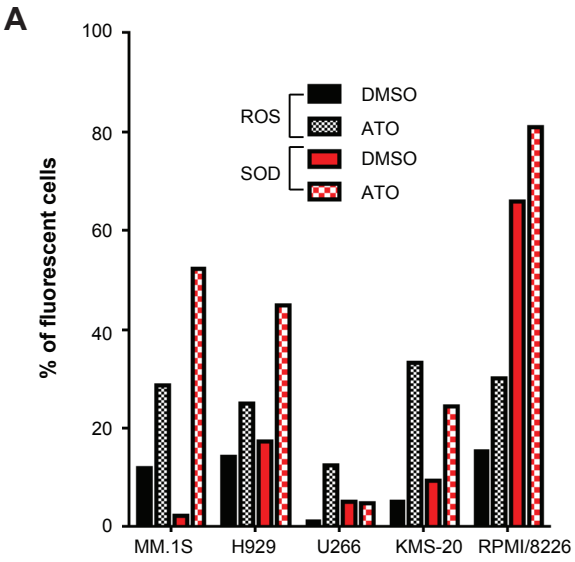

C
H929
DMSO
NAC
γ-H2A.X
GAPDH

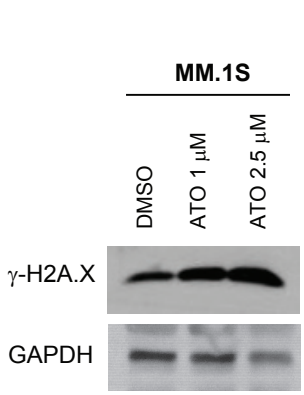

D
% of apoptotic cells
50
40
30
20
10
0
DMSO
NAC
VE-821
NAC + VE-821
NS
NS
H929
OPM-2

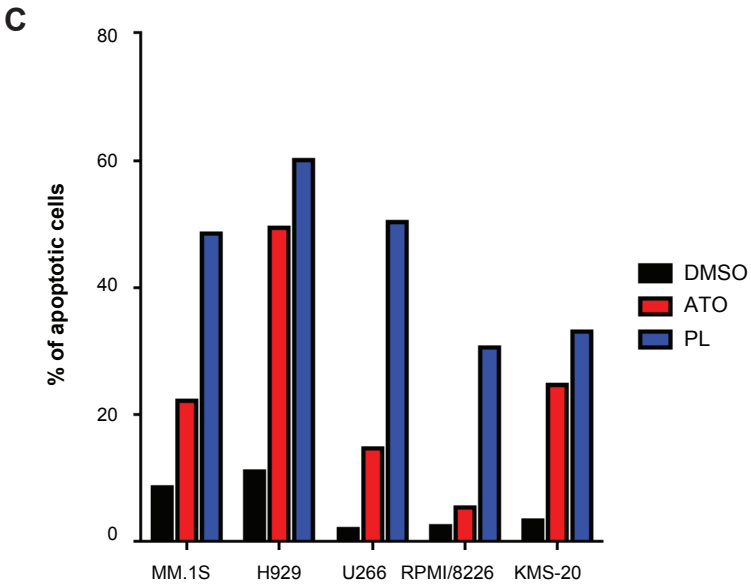

E
% of fluoresence cells (ROS levels)
15
10
5
0
DMSO
VE-821
Ku55933
NS
NS
NS
MM.1S
H929
OPM-2

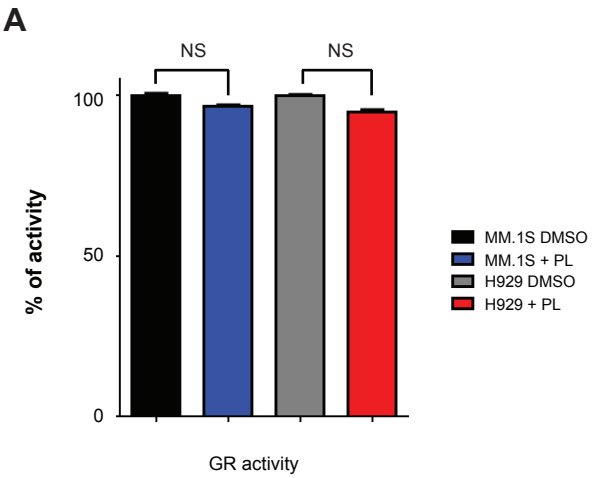

F
U266
H929
DMSO
L-arginine
DMSO
L-NAME
γ-H2A.X
GAPDH

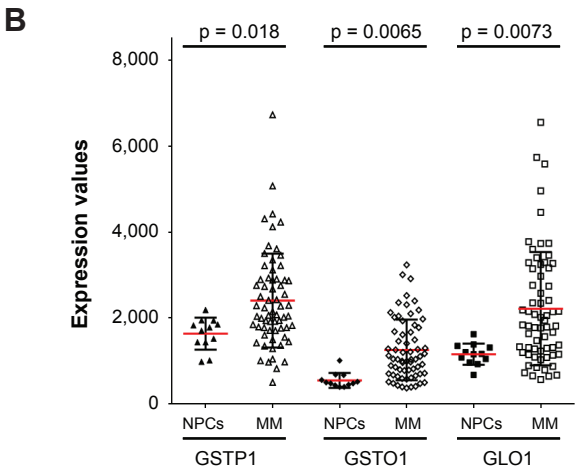

A
DMSO
L-NAME
Number of cells (10^4)
30
20
10
0
LACZ
MYC
LACZ
MYC
LACZ
MYC
+ L-NAME
B
% of fluorescent cells
100
80
60
40
20
0
MM.1S
H929
U266
KMS-20
RPMI/8226
ROS
DMSO
PL
SOD
DMSO
PL
C
% of viable cells
100
50
0
**
**
**
H929
U266
RPMI/8226
DMSO
PL 1 μM
PL 1.5 μM
NAC 5mM
D
% of viable cells
100
50
0
NS
NS
NS
H929
MM.1S
OPM-2
DMSO
PL 1 μM
PL 2.5 μM
L-NAME 1mM

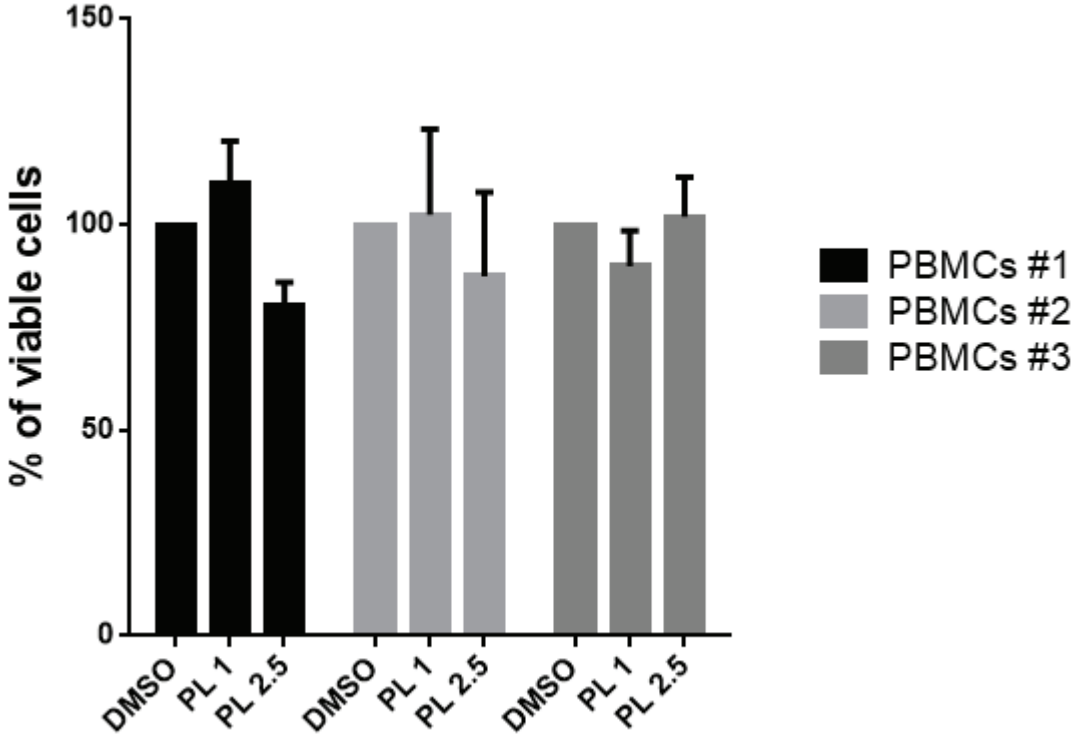

A
100
80
60
40
20
0
% of fluorescent cells
ROS
DMSO
ATO
SOD
DMSO
ATO
MM.1S
H929
U266
KMS-20
RPMI/8226

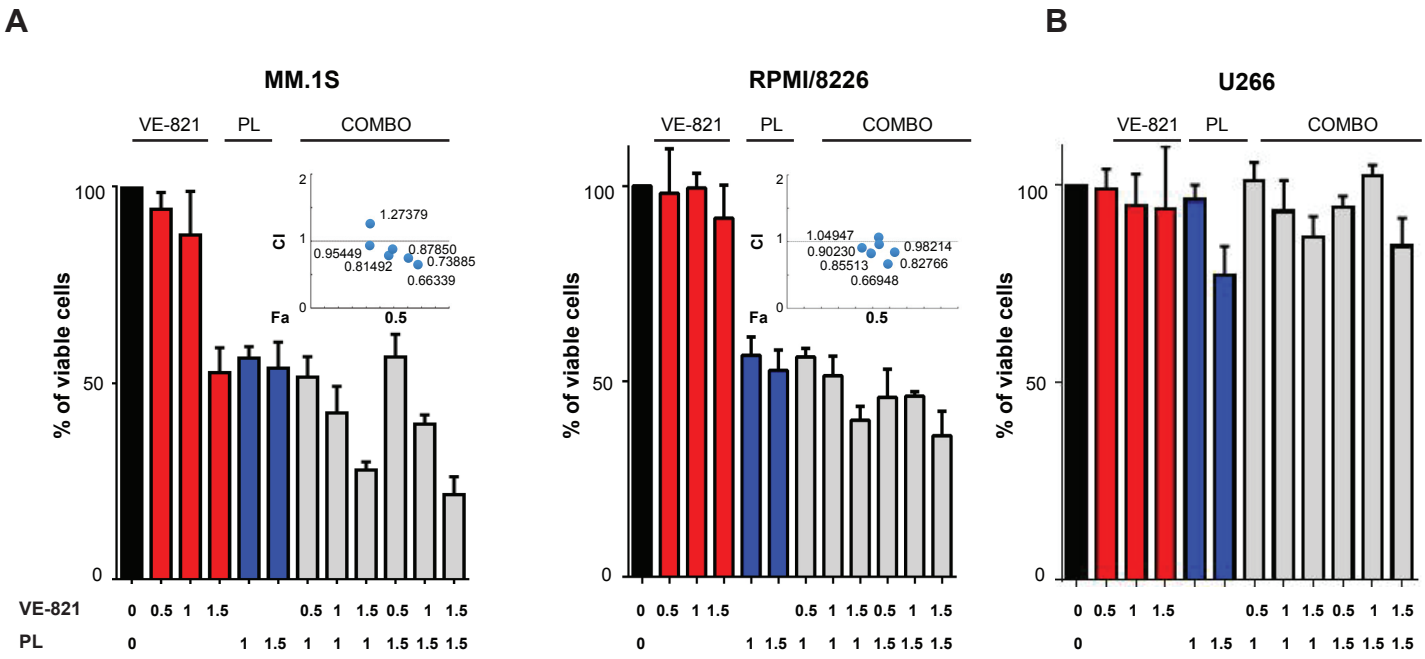

B
MM.1S
DMSO
ATO 1 μM
ATO 2.5 μM
γ-H2A.X
GAPDH


C
80
60
40
20
0
% of apoptotic cells
MM.1S
H929
U266
RPMI/8226
KMS-20
DMSO
ATO
PL

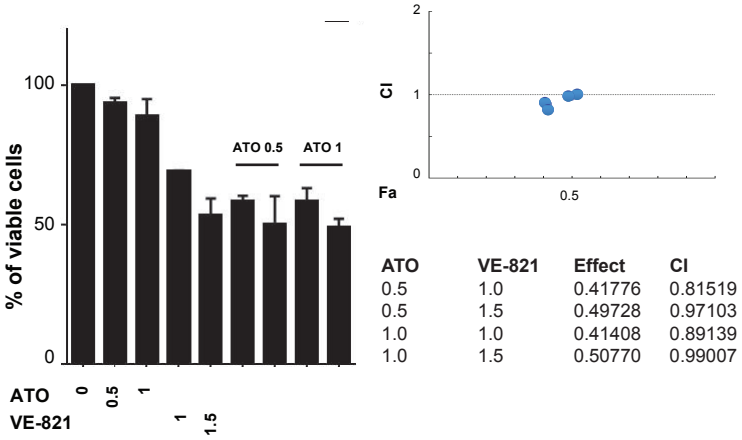

A
NS
NS
100
50
0
% of activity
GR activity
MM.1S DMSO
MM.1S + PL
H929 DMSO
H929 + PL


B
p = 0.018
p = 0.0065
p = 0.0073
8,000
6,000
4,000
2,000
0
Expression values
NPCs
MM
NPCs
MM
NPCs
MM
GSTP1
GSTO1
GLO1


150
100
50
0
% of viable cells
DMSO
PL 1
PL 2.5
DMSO
PL 1
PL 2.5
DMSO
PL 1
PL 2.5
PBMCs #1
PBMCs #2
PBMCs #3

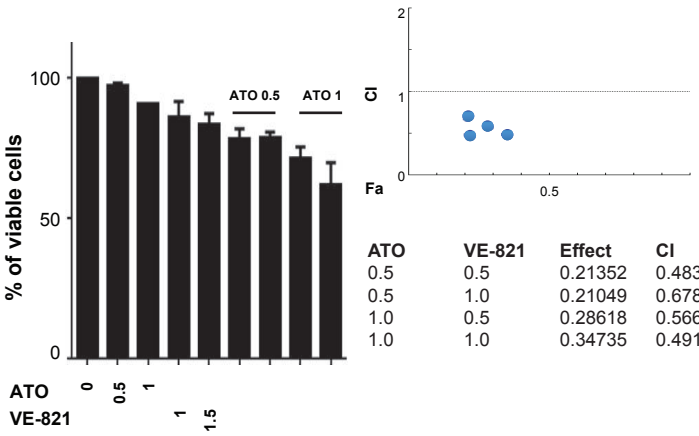

A
B
MM.1S
RPMI/8226
U266
VE-821
PL
COMBO
% of viable cells
100
50
0
CI
Fa
0.5
1.27379
0.95449
0.87850
0.81492
0.73885
0.66339
1.04947
0.90230
0.98214
0.85513
0.82766
0.66948
VE-821 0 0.5 1 1.5 0.5 1 1.5 0.5 1 1.5
PL 0 1 1.5 1 1 1 1.5 1.5 1.5

MM.1S



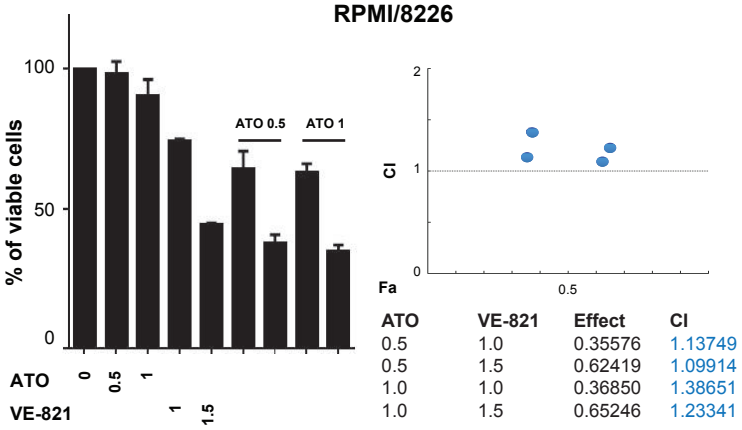
ATO	VE-821	Effect	CI
0.5	1.0	0.41776	0.81519
0.5	1.5	0.49728	0.97103
1.0	1.0	0.41408	0.89139
1.0	1.5	0.50770	0.99007

H929



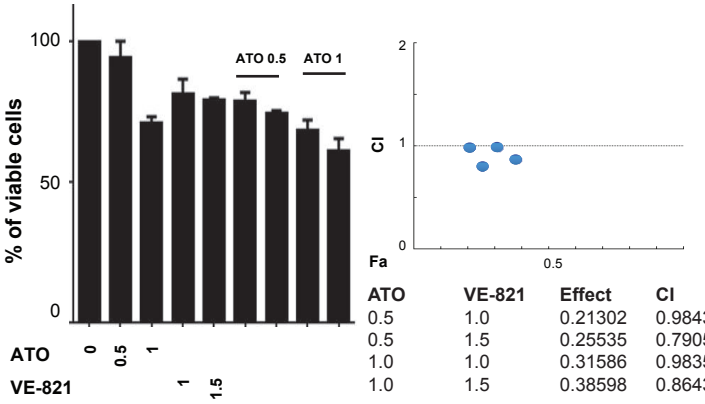
ATO	VE-821	Effect	CI
0.5	0.5	0.21352	0.48356
0.5	1.0	0.21049	0.67895
1.0	0.5	0.28618	0.56656
1.0	1.0	0.34735	0.49149

RPMI/8226



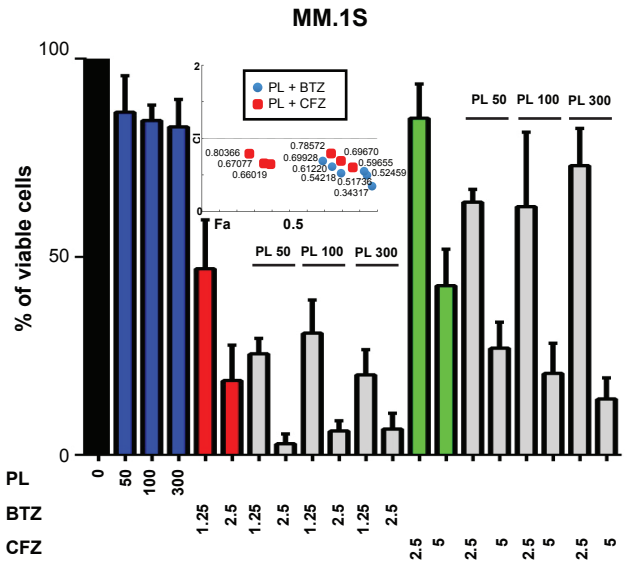
ATO	VE-821	Effect	CI
0.5	1.0	0.35576	1.13749
0.5	1.5	0.62419	1.09914
1.0	1.0	0.36850	1.38651
1.0	1.5	0.65246	1.23341

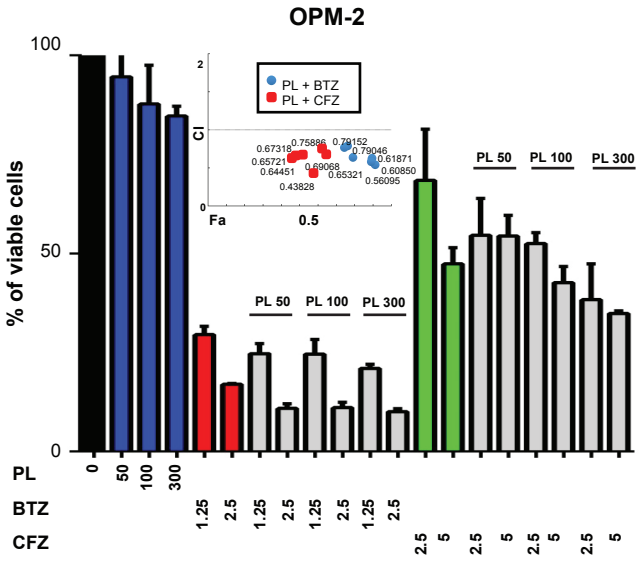
KMS-20



ATO	VE-821	Effect	CI
0.5	1.0	0.21302	0.98438
0.5	1.5	0.25535	0.79052
1.0	1.0	0.31586	0.98355
1.0	1.5	0.38598	0.86433

A



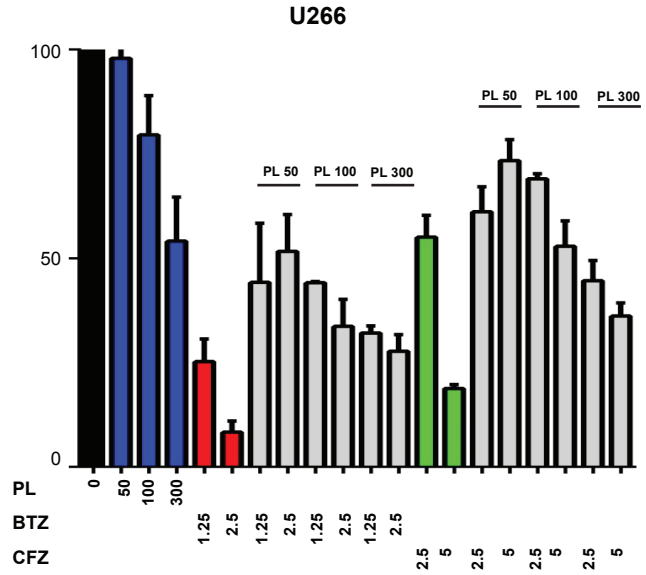


B

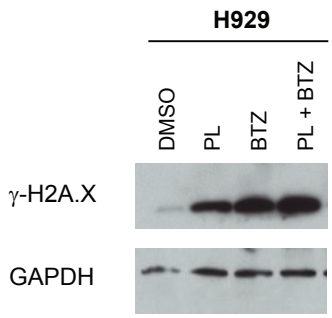
U266

BTZ (nM)	PL (nM)	Effect	CI
1.25	50	0.55746	1.72570
1.25	100	0.48332	2.22177
1.25	300	0.55854	2.51657
2.5	50	0.66327	2.59862
2.5	100	0.67887	2.61600
2.5	300	0.72243	2.73544

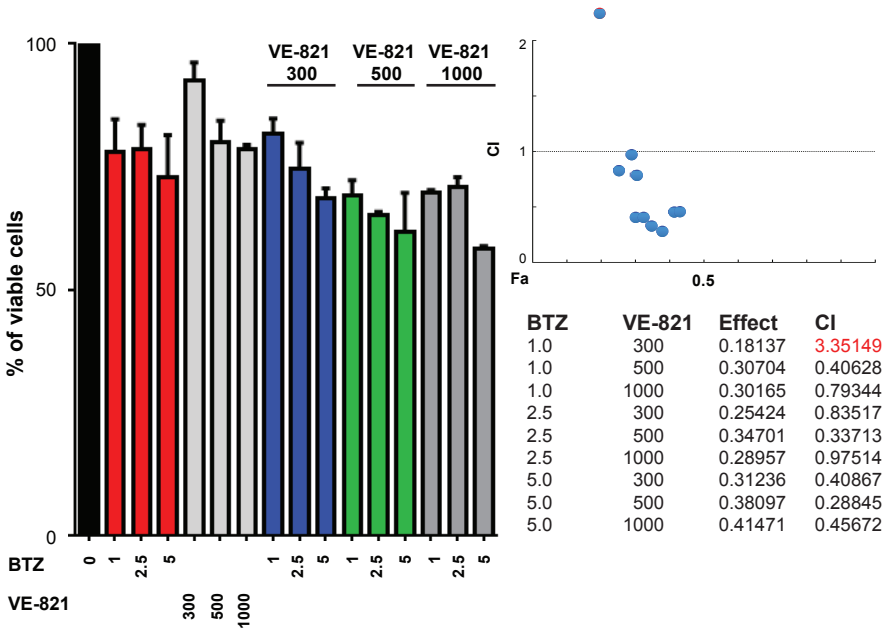
CFZ (nM)	PL (nM)	Effect	CI
2.5	50	0.38879	1.35524
2.5	100	0.26583	2.10934
2.5	300	0.30965	3.14531
5	50	0.47142	2.12826
5	100	0.55329	2.00876
5	300	0.63855	1.49490



C

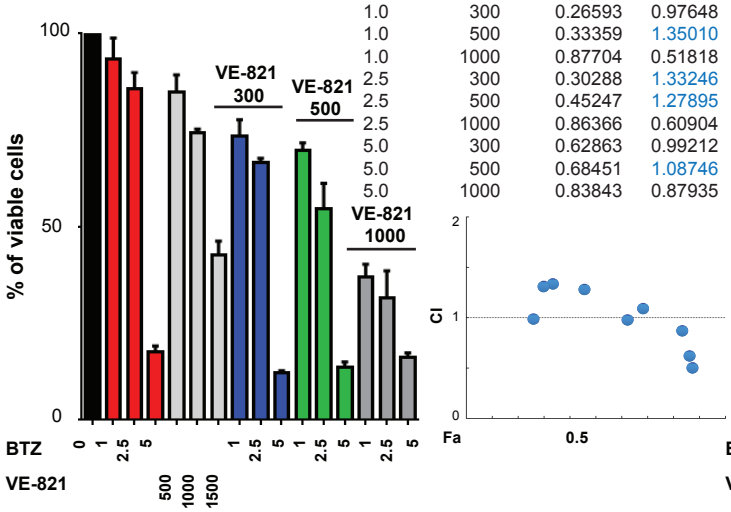


RPMI/8226



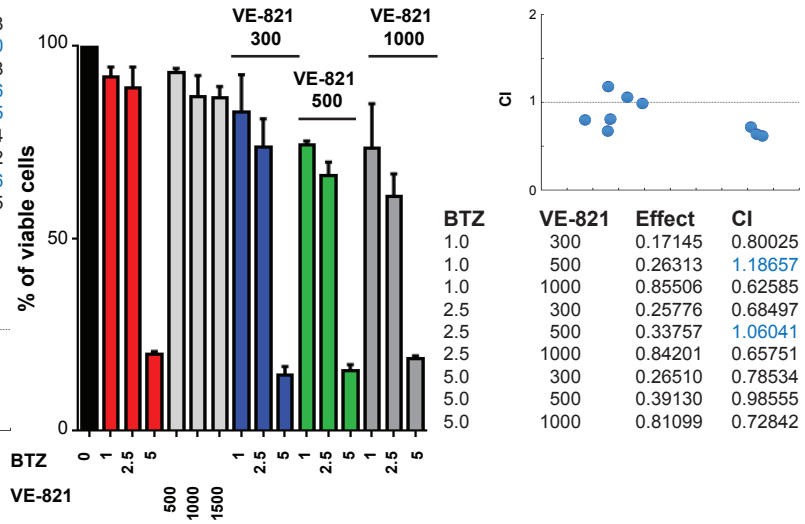
BTZ	VE-821	Effect	CI
1.0	300	0.18137	3.35149
1.0	500	0.30704	0.40628
1.0	1000	0.30165	0.79344
2.5	300	0.25424	0.83517
2.5	500	0.34701	0.33713
2.5	1000	0.28957	0.97514
5.0	300	0.31236	0.40867
5.0	500	0.38097	0.28845
5.0	1000	0.41471	0.45672

MM.1S



BTZ	VE-821	Effect	CI
1.0	300	0.26593	0.97648
1.0	500	0.33359	1.35010
1.0	1000	0.87704	0.51818
2.5	300	0.30288	1.33246
2.5	500	0.45247	1.27895
2.5	1000	0.86366	0.60904
5.0	300	0.62863	0.99212
5.0	500	0.68451	1.08746
5.0	1000	0.83843	0.87935

H929



BTZ	VE-821	Effect	CI
1.0	300	0.17145	0.80025
1.0	500	0.26313	1.18657
1.0	1000	0.85506	0.62585
2.5	300	0.25776	0.68497
2.5	500	0.33757	1.06041
2.5	1000	0.84201	0.65751
5.0	300	0.26510	0.78534
5.0	500	0.39130	0.98555
5.0	1000	0.81099	0.72842