Fig. 1

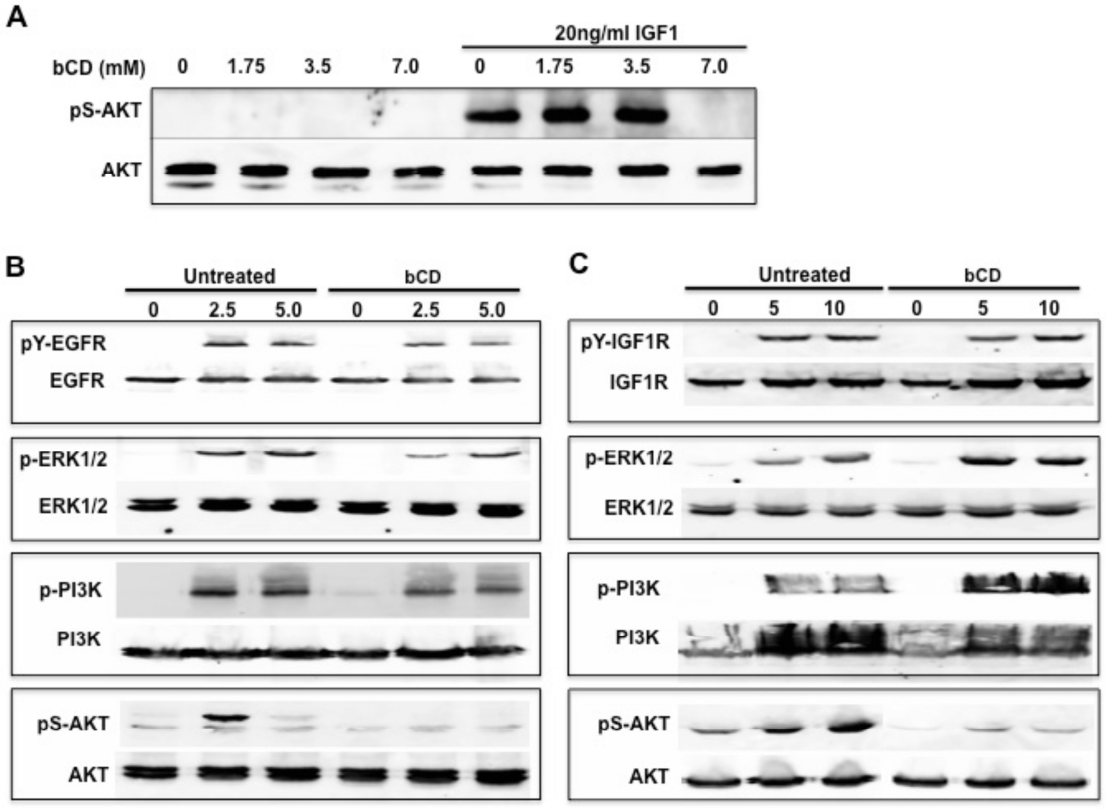

A
20ng/ml IGF1
bCD (mM) 0 1.75 3.5 7.0 0 1.75 3.5 7.0
pS-AKT
AKT
B
Untreated
bCD
0 2.5 5.0 0 2.5 5.0
pY-EGFR
EGFR
p-ERK1/2
ERK1/2
p-PI3K
PI3K
pS-AKT
AKT
C
Untreated
bCD
0 5 10 0 5 10
pY-IGF1R
IGF1R
p-ERK1/2
ERK1/2
p-PI3K
PI3K
pS-AKT
AKT

Fig. 2

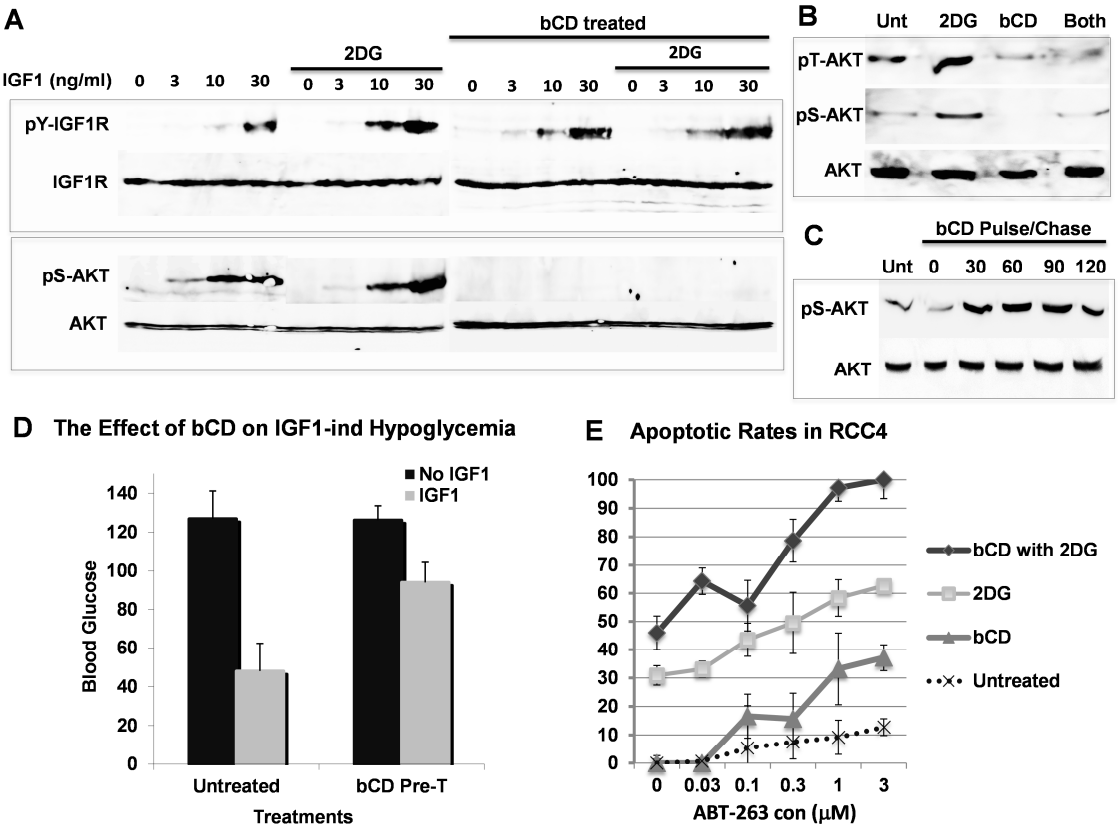
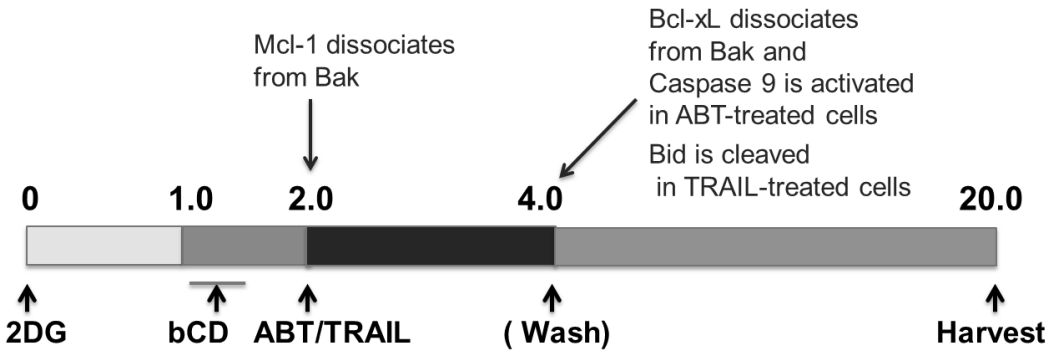

A
bCD treated
2DG
2DG
IGF1 (ng/ml) 0 3 10 30 0 3 10 30 0 3 10 30 0 3 10 30
pY-IGF1R
IGF1R
pS-AKT
AKT
B
Unt 2DG bCD Both
pT-AKT
pS-AKT
AKT
C
bCD Pulse/Chase
Unt 0 30 60 90 120
pS-AKT
AKT
D The Effect of bCD on IGF1-ind Hypoglycemia
No IGF1
IGF1
Blood Glucose
140
120
100
80
60
40
20
0
Untreated
bCD Pre-T
Treatments
E Apoptotic Rates in RCC4
100
90
80
70
60
50
40
30
20
10
0
0 0.03 0.1 0.3 1 3
ABT-263 con (μM)
bCD with 2DG
2DG
bCD
Untreated

Fig. 3



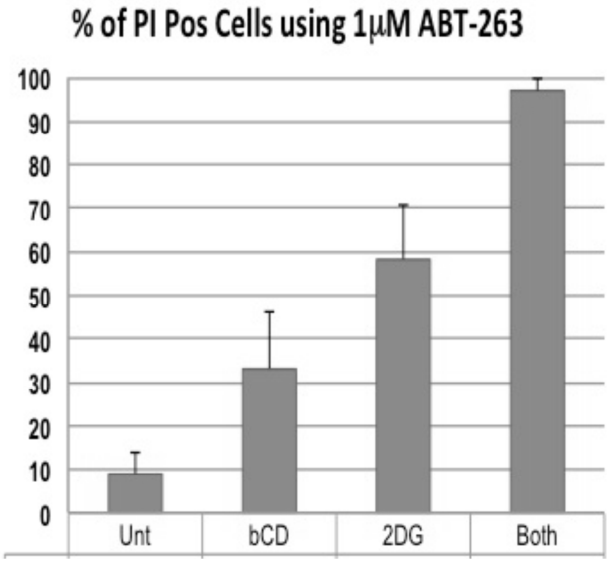
In vitro

10 mM 2DG in media containing 25mM glucose
1-1.5 hours later, add 10m M bCD at 1-1.5 hours later
2 hours from the start, add 1 mM ABT-263 w/wo zVAD , 10 ng/ml TRAIL,
or harvest cells for molecular analysis or fix cells for microscopy.
4 hours from the start, wash cells and incubated in fresh medium or fix or harvest cells
20 hours from the start, harvest cells for viability assays

In vivo

Orally administer 10mg/kg of glucose and 10mg/kg of 2-deoxyglucose
1.5 hour later, orally administer 2 mg/kg of HPBCD in PBS
2 hours from the start, add 100mg/kg of ABT-263 in 10% ethanol, 30% polyethylene glycerol & 60% Cremphor
20 hours from the start of the treatment, measure tumor size

Fig. 4



Supposing that bCD and 2DG work independently,

Expected outcome for 2DG-bCD is 72.19327

Observed Value is 97.13564

Chi Sq Test : P<0.0001

Thus bCD and 2DG work synergistically
to sensitize cells for ABT-263.

Fig. 5

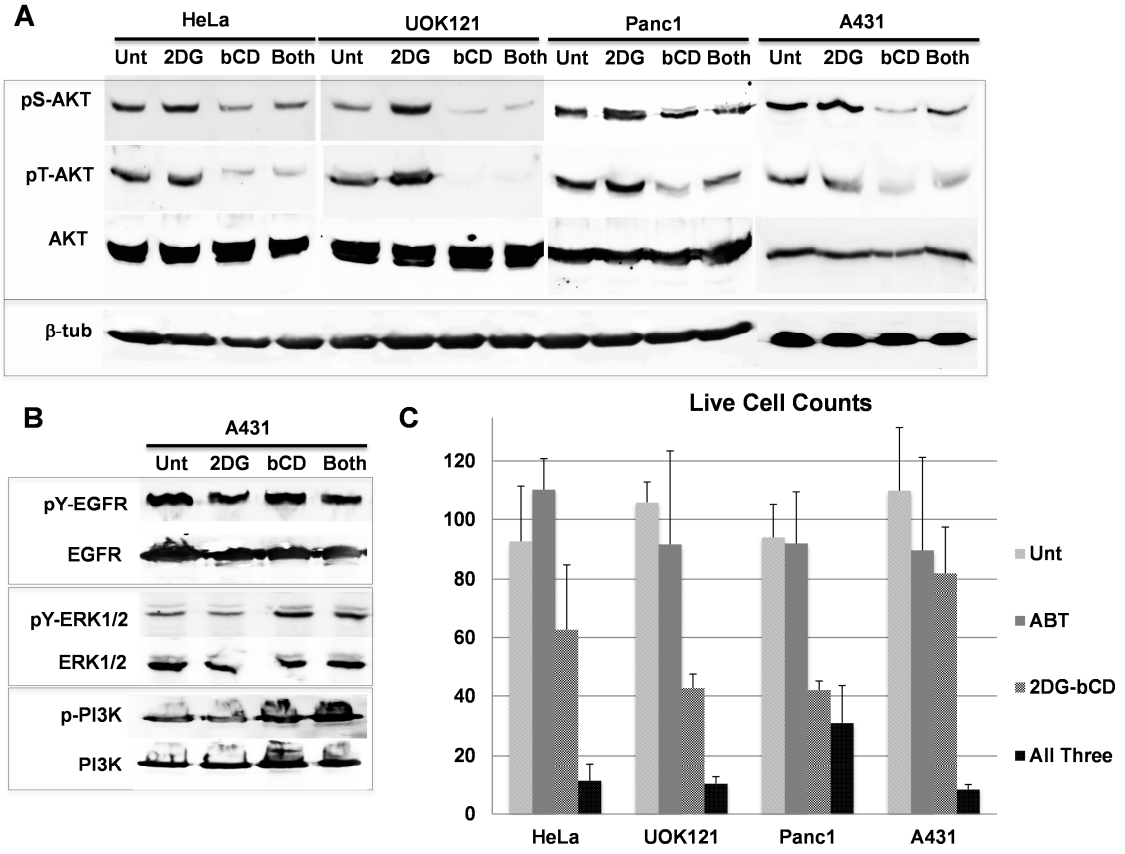

A
HeLa
UOK121
Panc1
A431
Unt 2DG bCD Both
pS-AKT
pT-AKT
AKT
β-tub
B
A431
Unt 2DG bCD Both
pY-EGFR
EGFR
pY-ERK1/2
ERK1/2
p-PI3K
PI3K
C
Live Cell Counts
120
100
80
60
40
20
0
HeLa
UOK121
Panc1
A431
Unt
ABT
2DG-bCD
All Three

Fig. 6

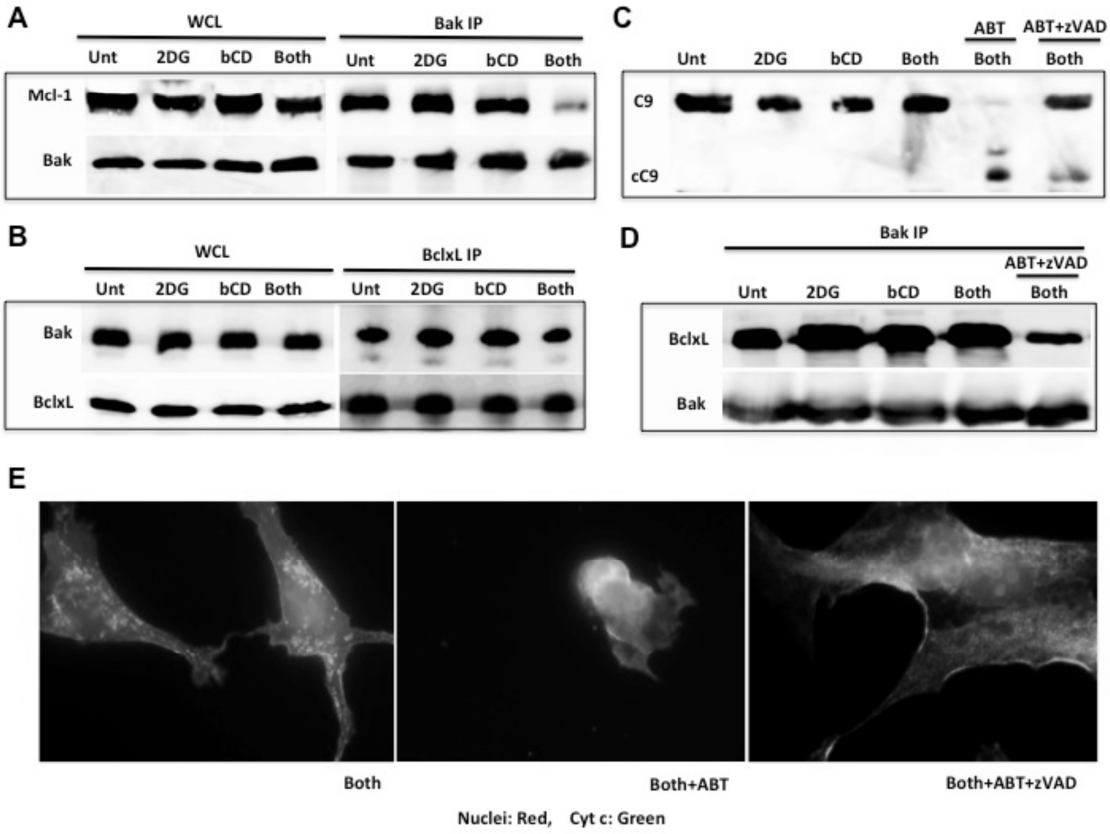

A
WCL
Bak IP
Unt
2DG
bCD
Both
Unt
2DG
bCD
Both
Mcl-1
Bak
C
ABT
ABT+zVAD
Unt
2DG
bCD
Both
Both
Both
C9
cC9
B
WCL
BclxL IP
Unt
2DG
bCD
Both
Unt
2DG
bCD
Both
Bak
BclxL
D
Bak IP
ABT+zVAD
Unt
2DG
bCD
Both
Both
BclxL
Bak
E
Both
Both+ABT
Both+ABT+zVAD
Nuclei: Red, Cyt c: Green

Fig. 7

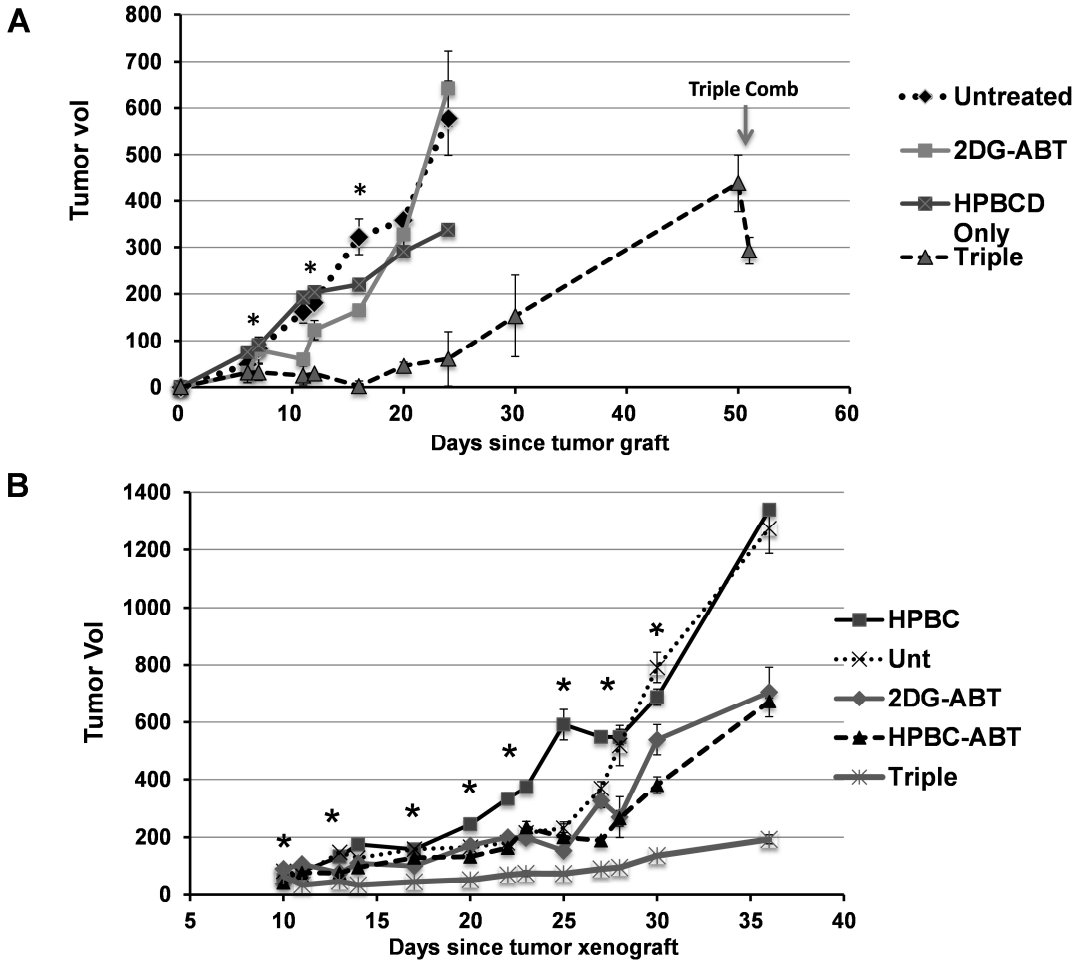

A
Tumor vol
Days since tumor graft
Triple Comb
Untreated
2DG-ABT
HPBCD Only
Triple
B
Tumor Vol
Days since tumor xenograft
HPBC
Unt
2DG-ABT
HPBC-ABT
Triple

Fig. 8

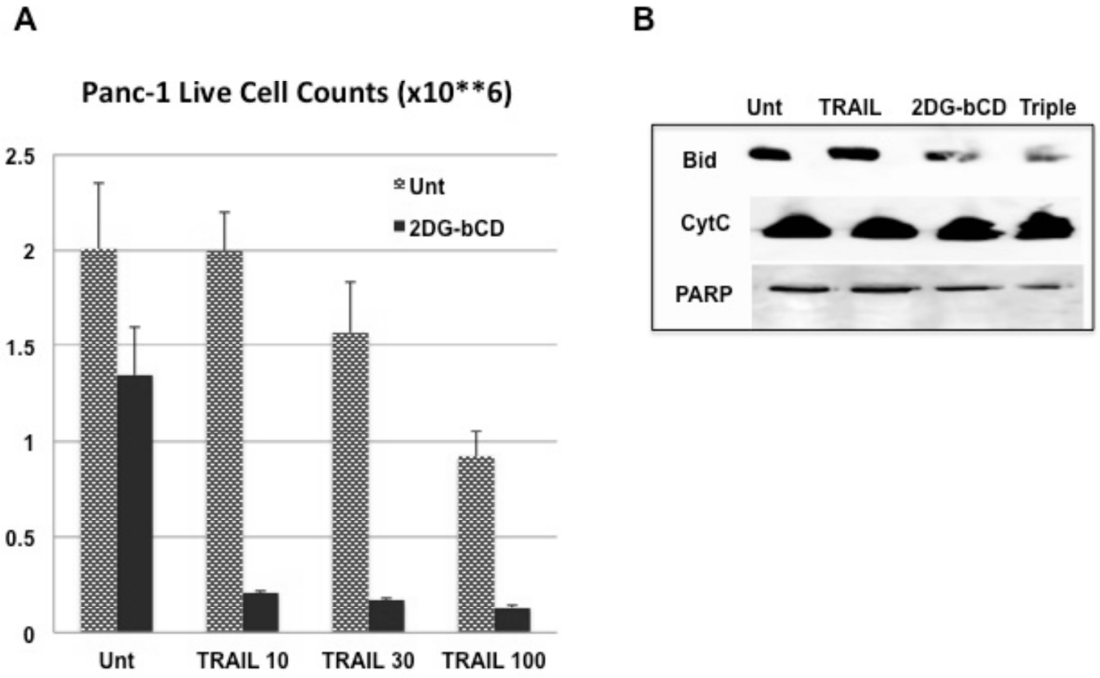
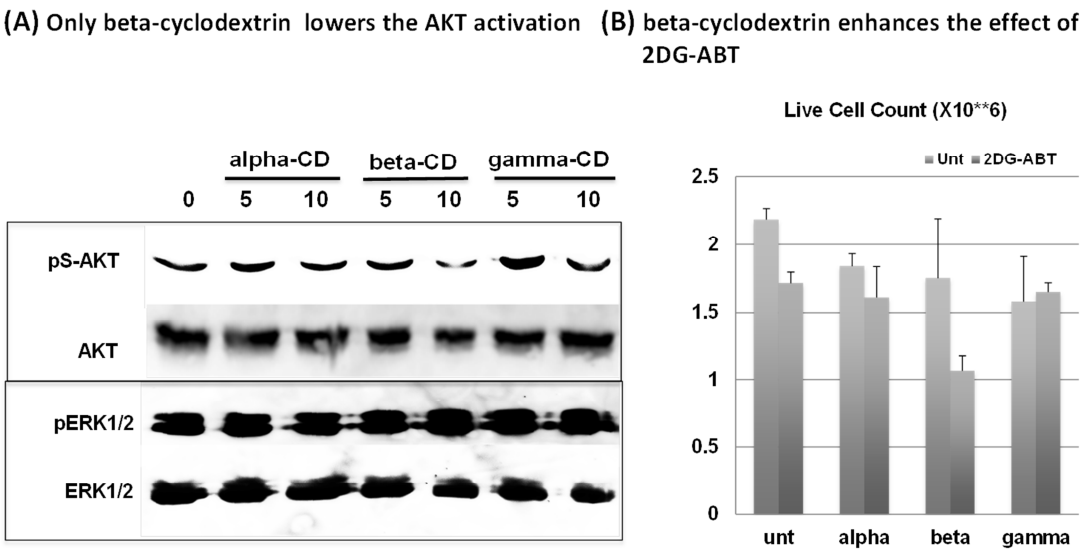

A
Panc-1 Live Cell Counts (x10**6)
2.5
2
1.5
1
0.5
0
Unt
2DG-bCD
Unt
TRAIL 10
TRAIL 30
TRAIL 100
B
Unt
TRAIL
2DG-bCD
Triple
Bid
CytC
PARP

Fig. 9


(A) Only beta-cyclodextrin lowers the AKT activation
alpha-CD
beta-CD
gamma-CD
0
5
10
5
10
5
10
pS-AKT
AKT
pERK1/2
ERK1/2
(B) beta-cyclodextrin enhances the effect of 2DG-ABT
Live Cell Count (X10**6)
Unt
2DG-ABT
2.5
2
1.5
1
0.5
0
unt
alpha
beta
gamma