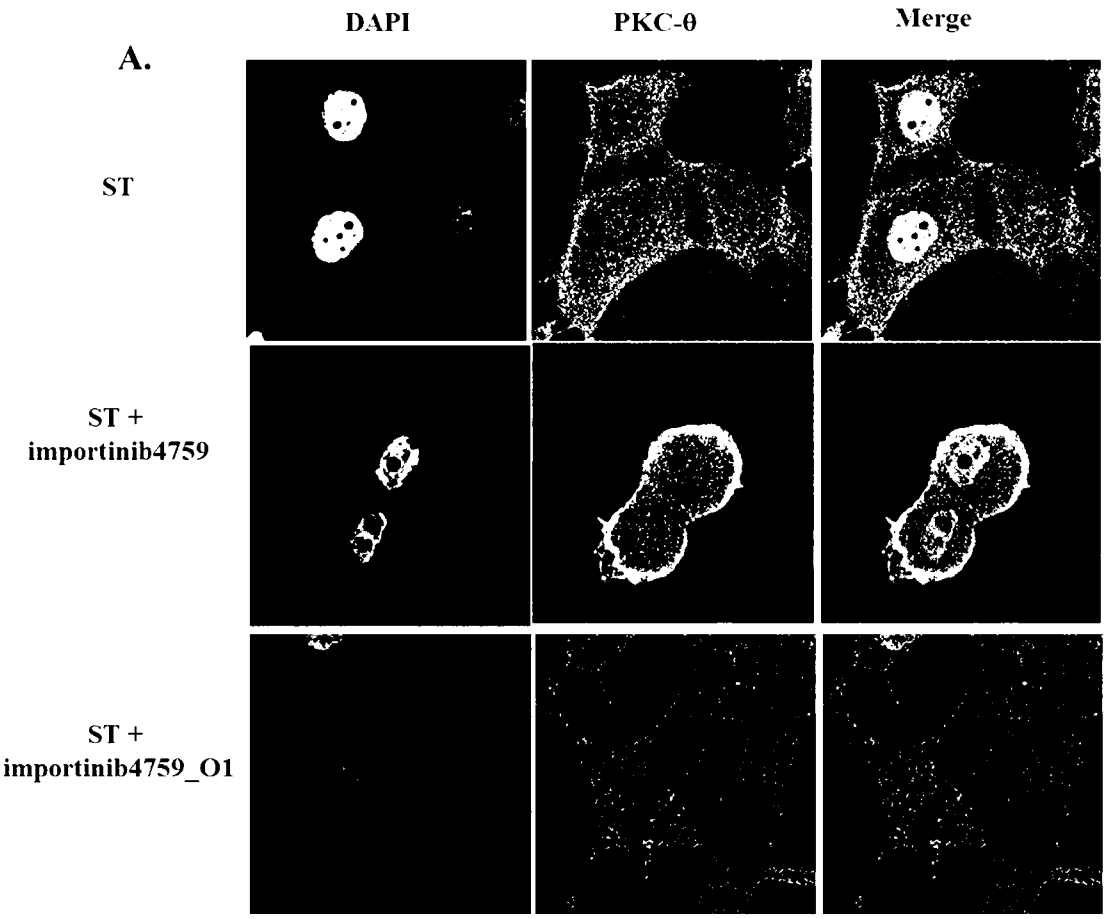

A.
DAPI
PKC-θ
Merge
ST
ST +
importinib4759
ST +
importinib4759_O1

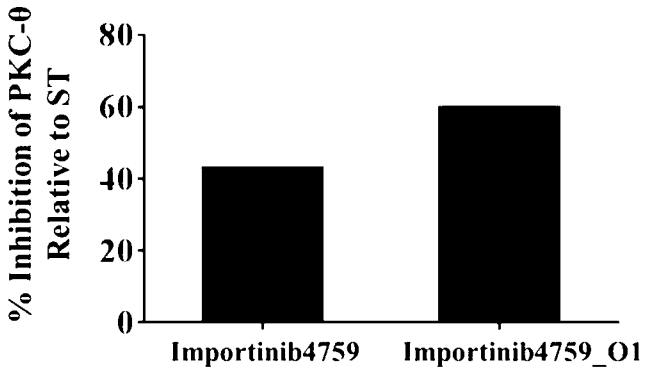

B.
% Inhibition of PKC-θ
Relative to ST
80
60
40
20
0
Importinib4759
Importinib4759_O1

Figure 1

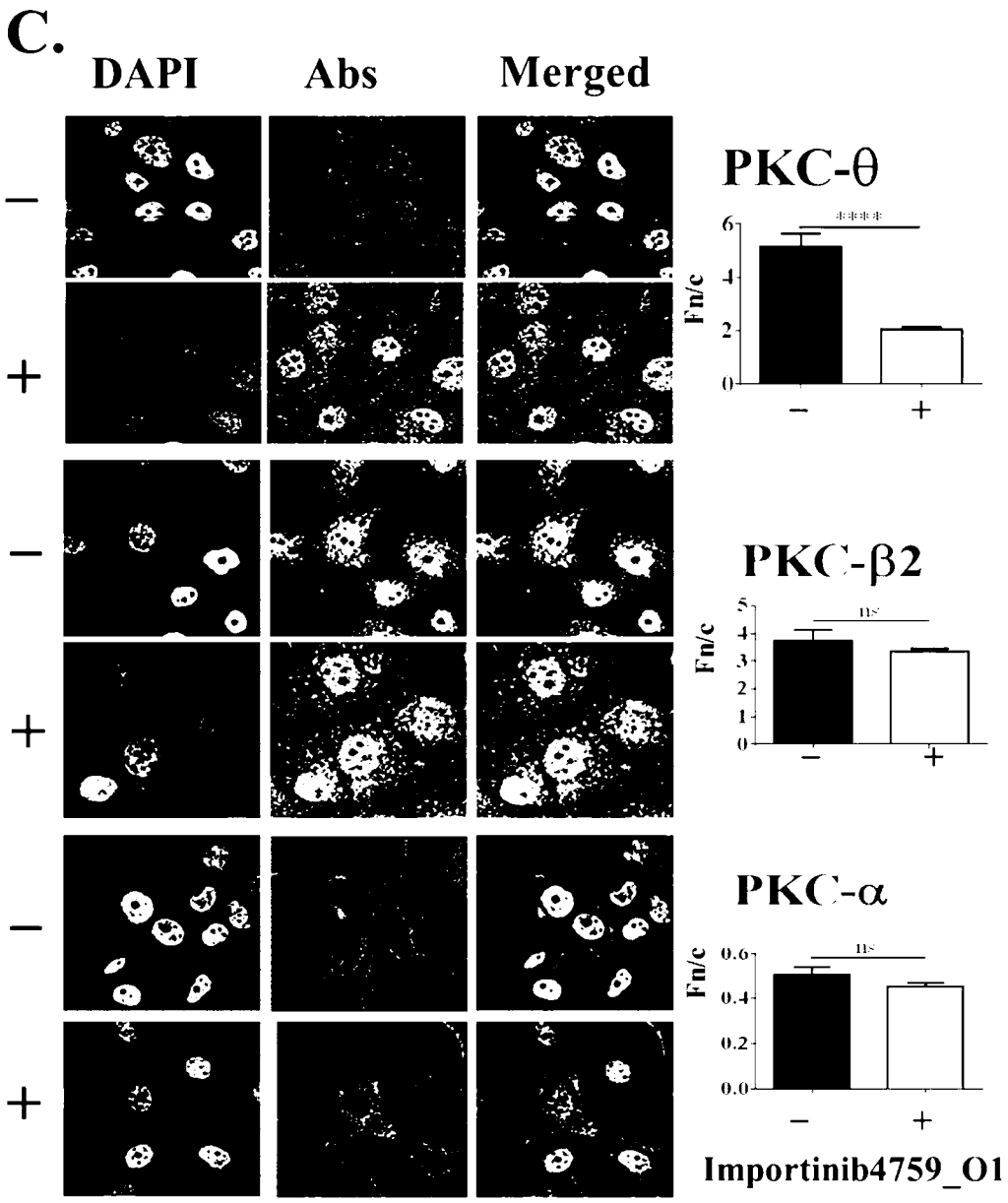


Figure 1 continued

D.

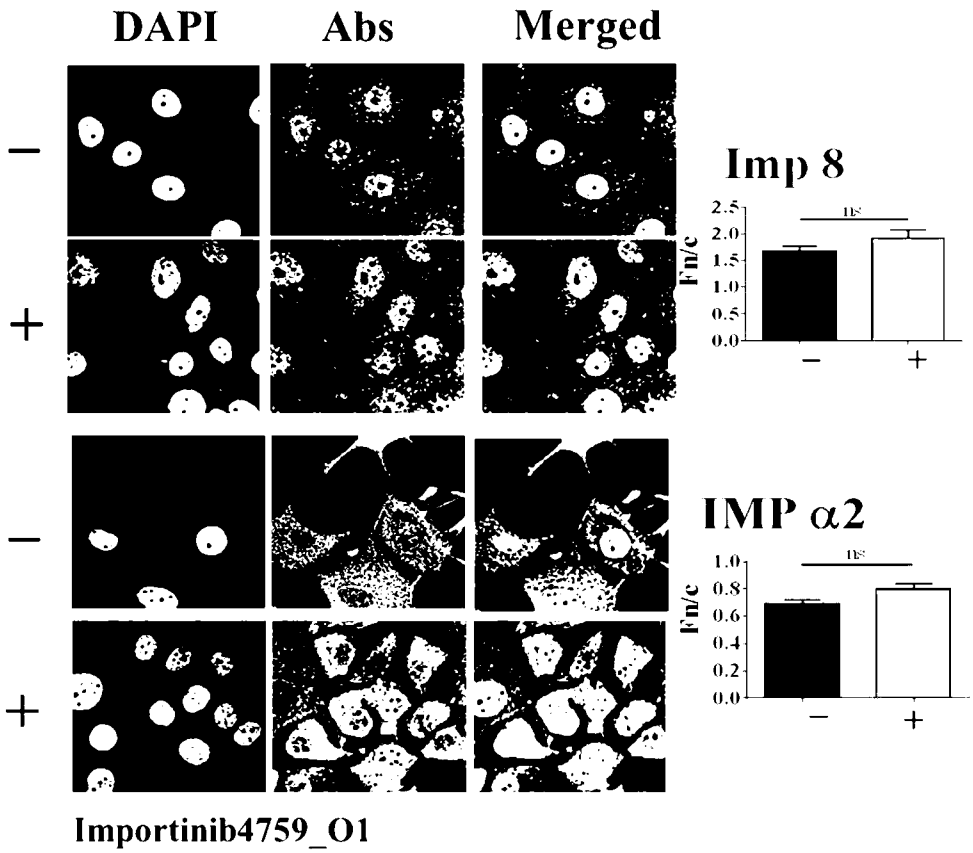
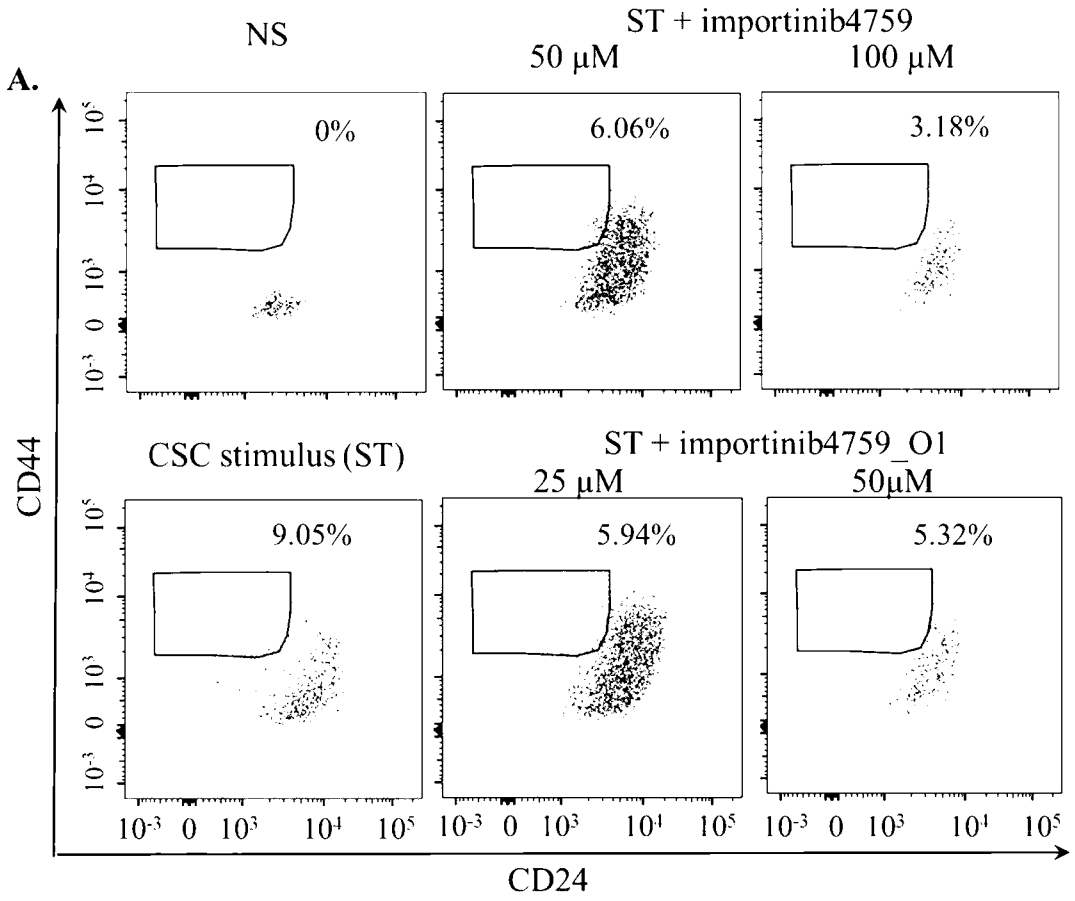


Figure 1 continued


A.
NS
ST + importinib4759
50 μM
100 μM
0%
6.06%
3.18%
CSC stimulus (ST)
ST + importinib4759_O1
25 μM
50μM
9.05%
5.94%
5.32%
CD44
CD24

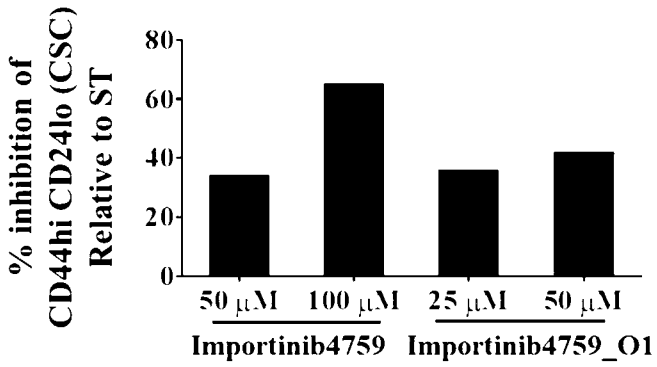

B.
% inhibition of CD44hi CD24lo (CSC) Relative to ST
80
60
40
20
0
50 μM
100 μM
25 μM
50 μM
Importinib4759
Importinib4759_O1

Figure 2

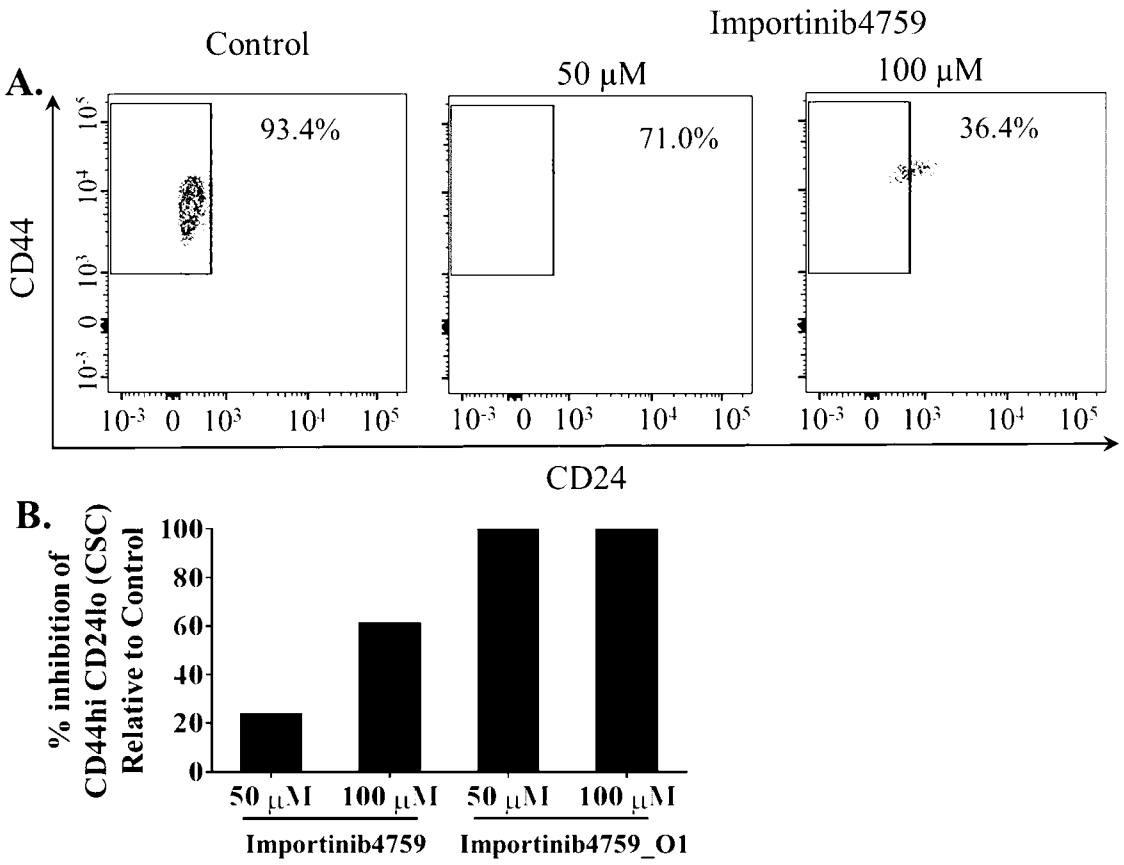

A.
Control
Importinib4759
50 μM
100 μM
93.4%
71.0%
36.4%
CD44
CD24
B.
% inhibition of CD44hi CD24lo (CSC) Relative to Control
100
80
60
40
20
0
50 μM
100 μM
50 μM
100 μM
Importinib4759
Importinib4759_O1

Figure 3

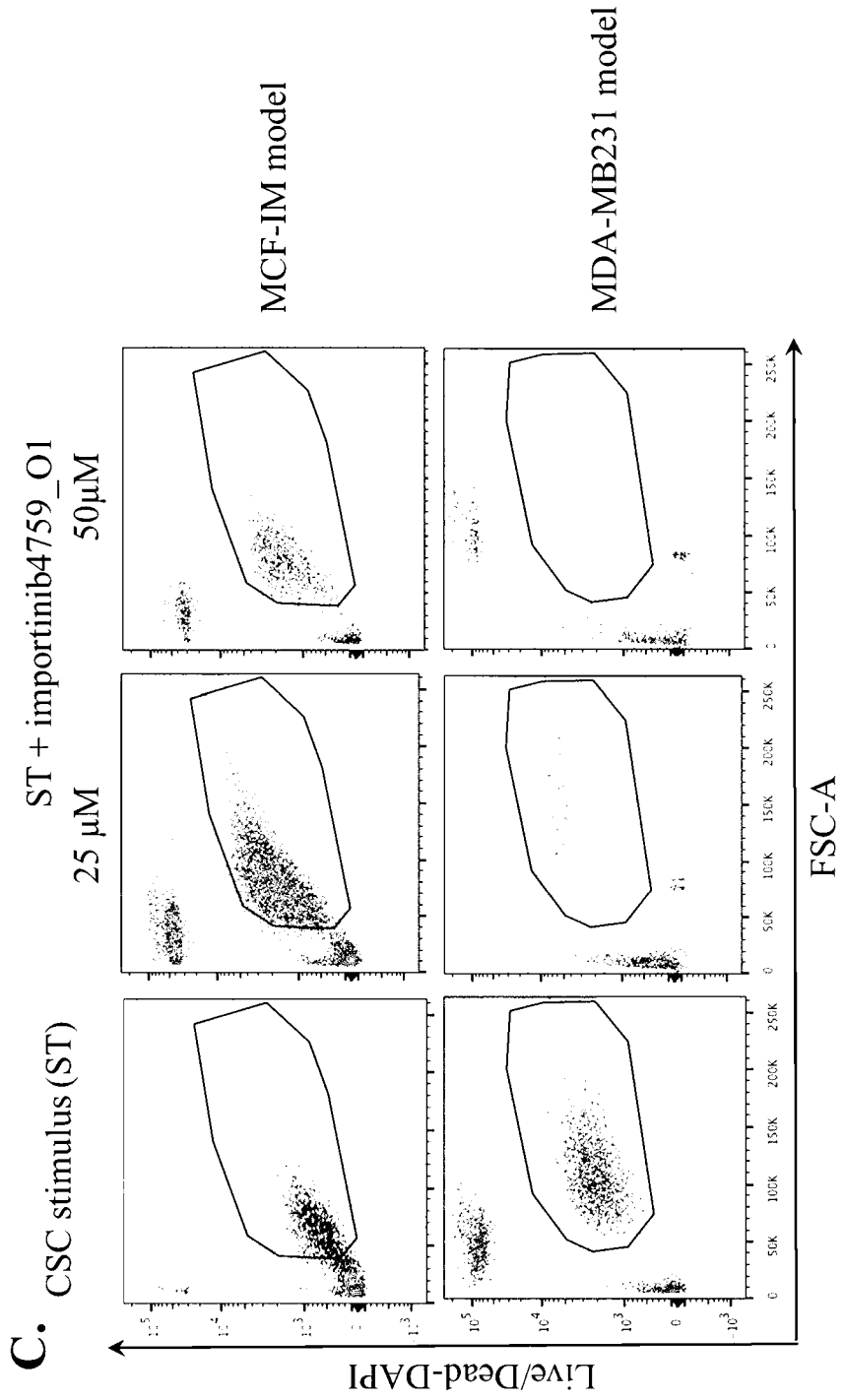


Figure 3 continued

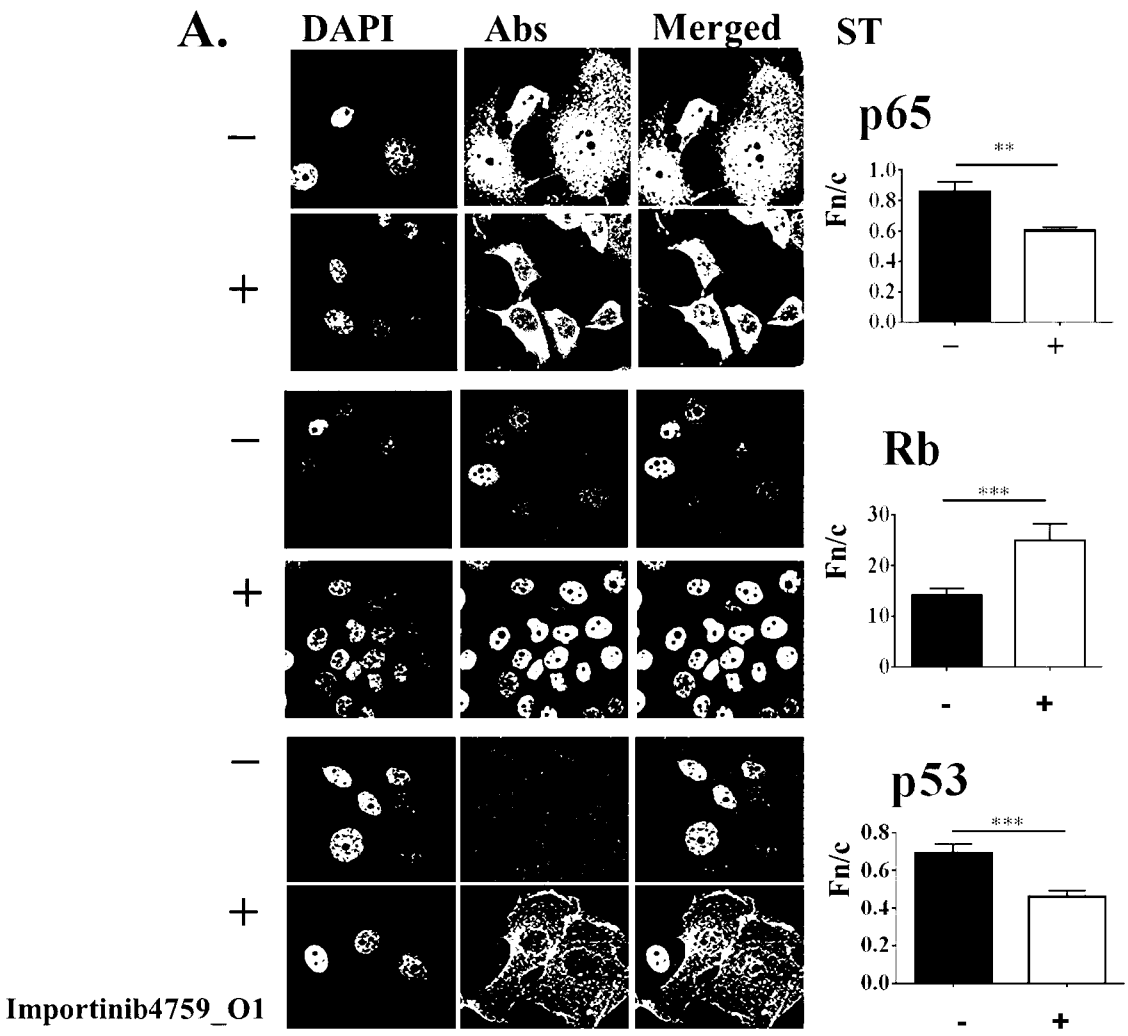

A.
DAPI
Abs
Merged
ST
p65
Rb
p53
Fn/c
**
***
***
1.0
0.8
0.6
0.4
0.2
0.0
30
20
10
0
-
+
Importinib4759_O1

Figure 4

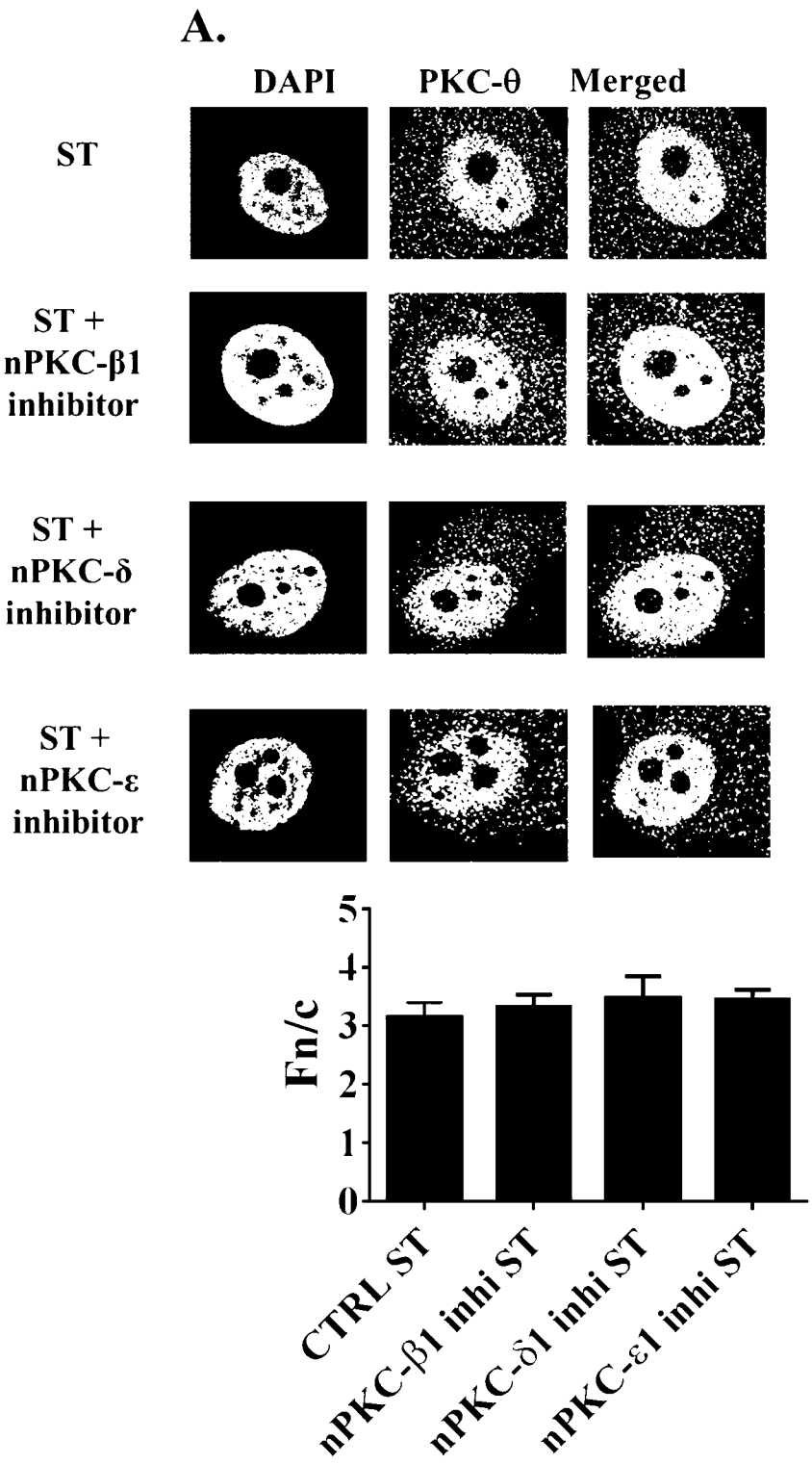

A.
DAPI
PKC-θ
Merged
ST
ST + nPKC-β1 inhibitor
ST + nPKC-δ inhibitor
ST + nPKC-ε inhibitor
Fn/c
0
1
2
3
4
5
CTRL ST
nPKC-β1 inhi ST
nPKC-δ1 inhi ST
nPKC-ε1 inhi ST

Figure 5

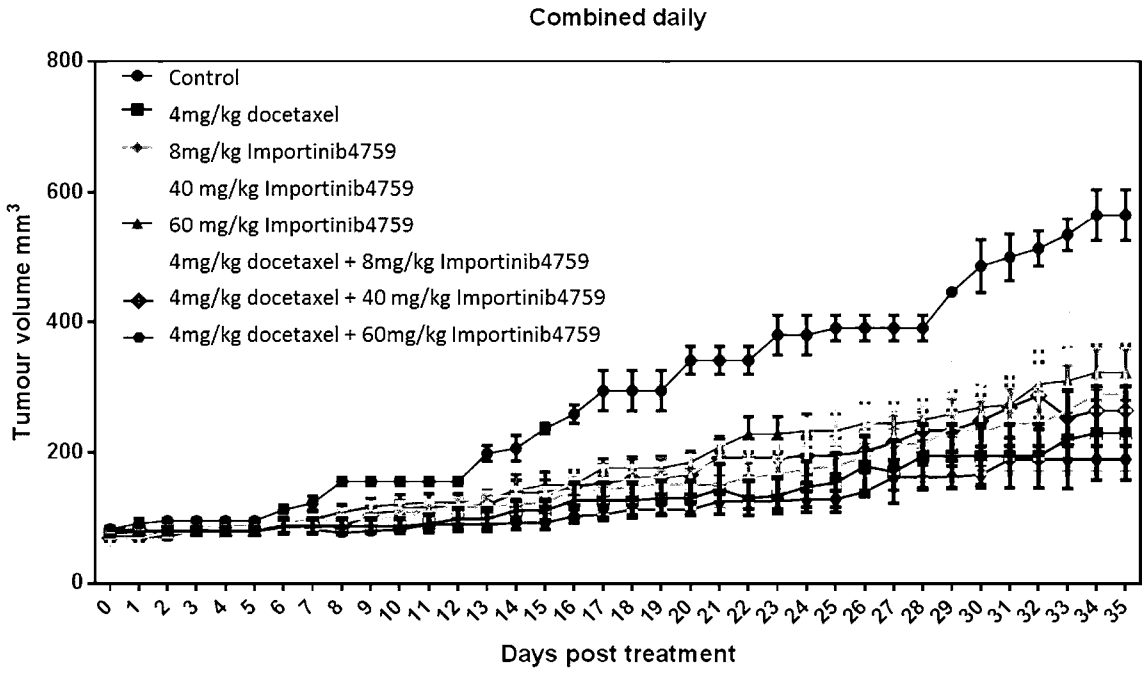

Combined daily
Control
4mg/kg docetaxel
8mg/kg Importinib4759
40 mg/kg Importinib4759
60 mg/kg Importinib4759
4mg/kg docetaxel + 8mg/kg Importinib4759
4mg/kg docetaxel + 40 mg/kg Importinib4759
4mg/kg docetaxel + 60mg/kg Importinib4759
Tumour volume mm3
Days post treatment
0
200
400
600
800
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35

Figure 6

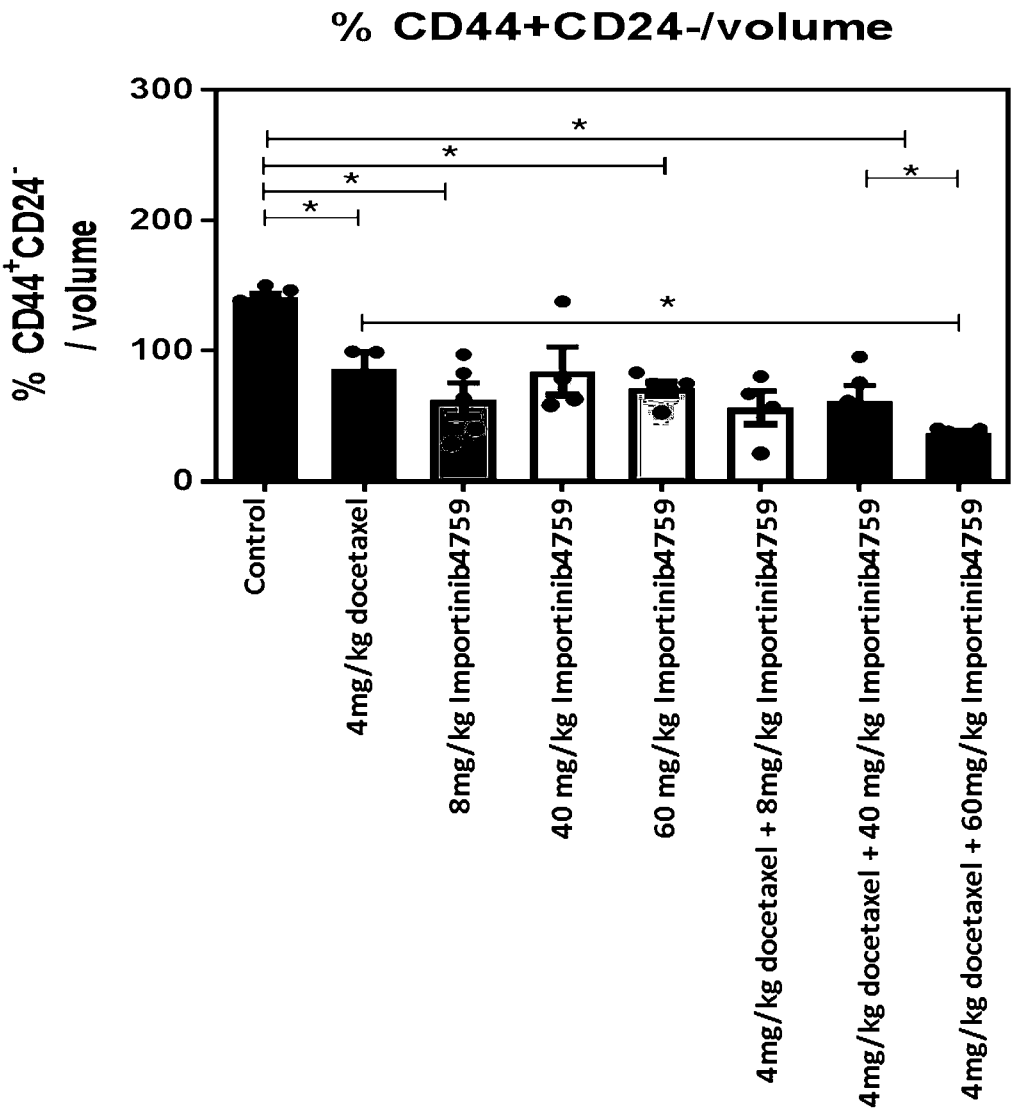

% CD44+CD24-/volume
% CD44+CD24- / volume
300
200
100
0
*
*
*
*
*
*
Control
4mg/kg docetaxel
8mg/kg Importinib4759
40 mg/kg Importinib4759
60 mg/kg Importinib4759
4mg/kg docetaxel + 8mg/kg Importinib4759
4mg/kg docetaxel + 40 mg/kg Importinib4759
4mg/kg docetaxel + 60mg/kg Importinib4759

Figure 7

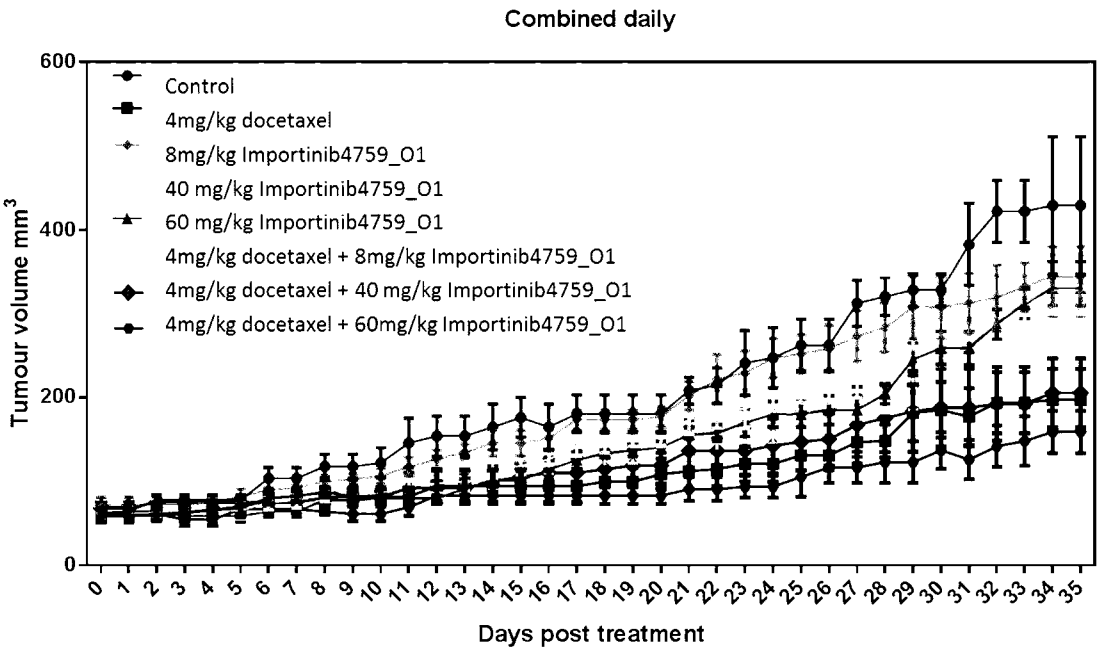

Combined daily
Control
4mg/kg docetaxel
8mg/kg Importinib4759_O1
40 mg/kg Importinib4759_O1
60 mg/kg Importinib4759_O1
4mg/kg docetaxel + 8mg/kg Importinib4759_O1
4mg/kg docetaxel + 40 mg/kg Importinib4759_O1
4mg/kg docetaxel + 60mg/kg Importinib4759_O1
Tumour volume mm3
600
400
200
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35
Days post treatment

Figure 8

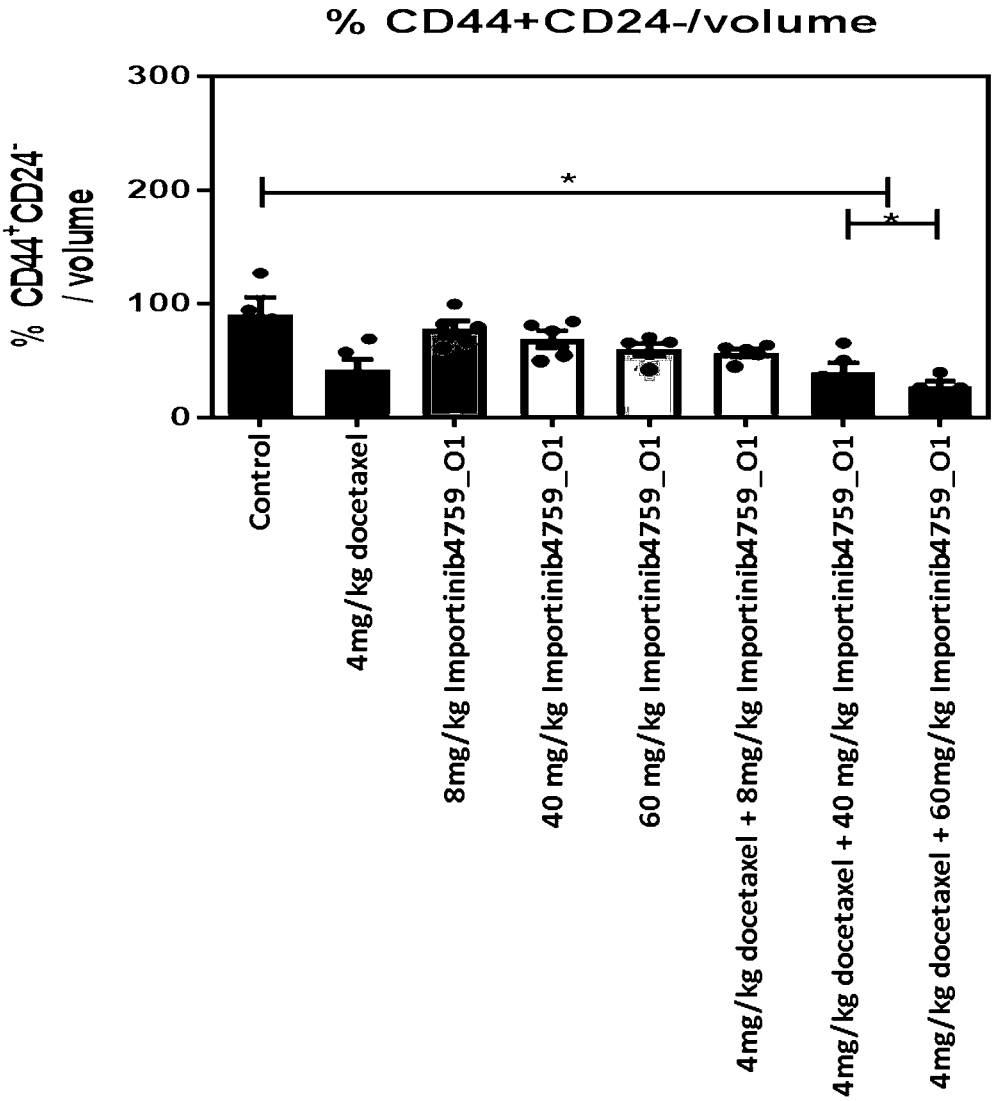

% CD44+CD24-/volume
% CD44+CD24-/volume
300
200
100
0
*
*
Control
4mg/kg docetaxel
8mg/kg Importinib4759_O1
40 mg/kg Importinib4759_O1
60 mg/kg Importinib4759_O1
4mg/kg docetaxel + 8mg/kg Importinib4759_O1
4mg/kg docetaxel + 40 mg/kg Importinib4759_O1
4mg/kg docetaxel + 60mg/kg Importinib4759_O1

Figure 9

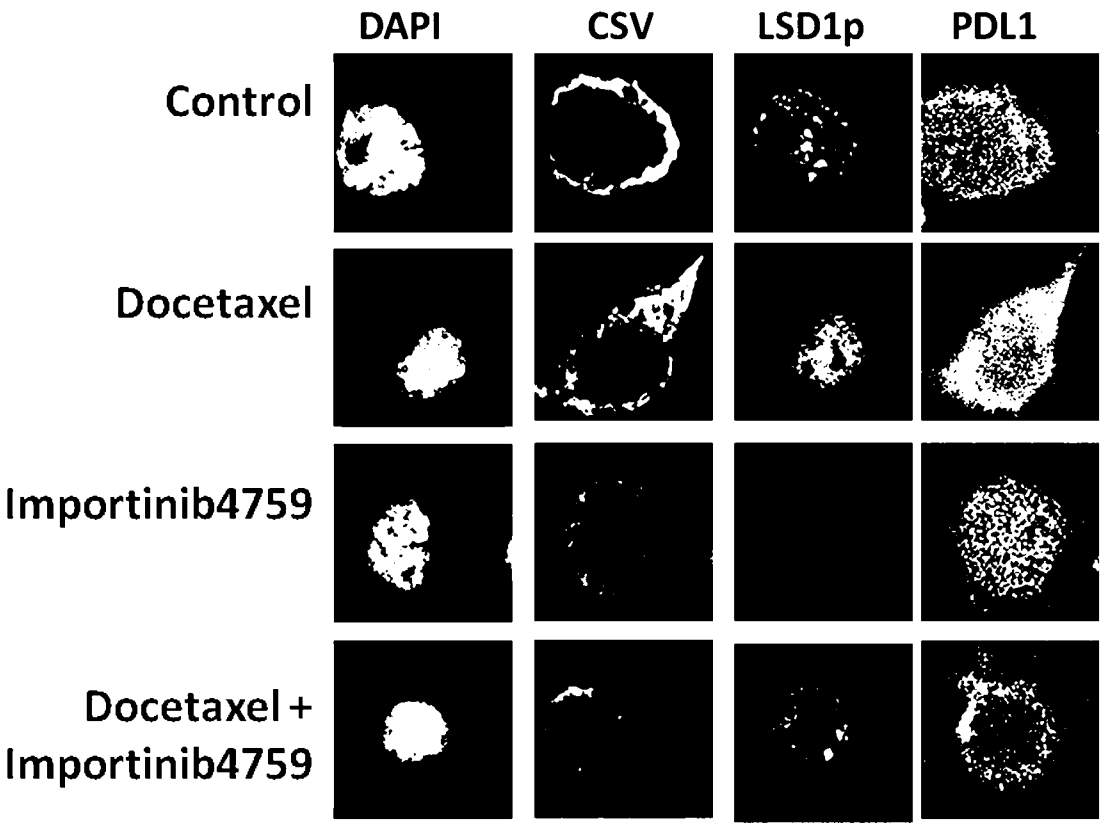

DAPI
CSV
LSD1p
PDL1
Control
Docetaxel
Importinib4759
Docetaxel +
Importinib4759

Figure 10

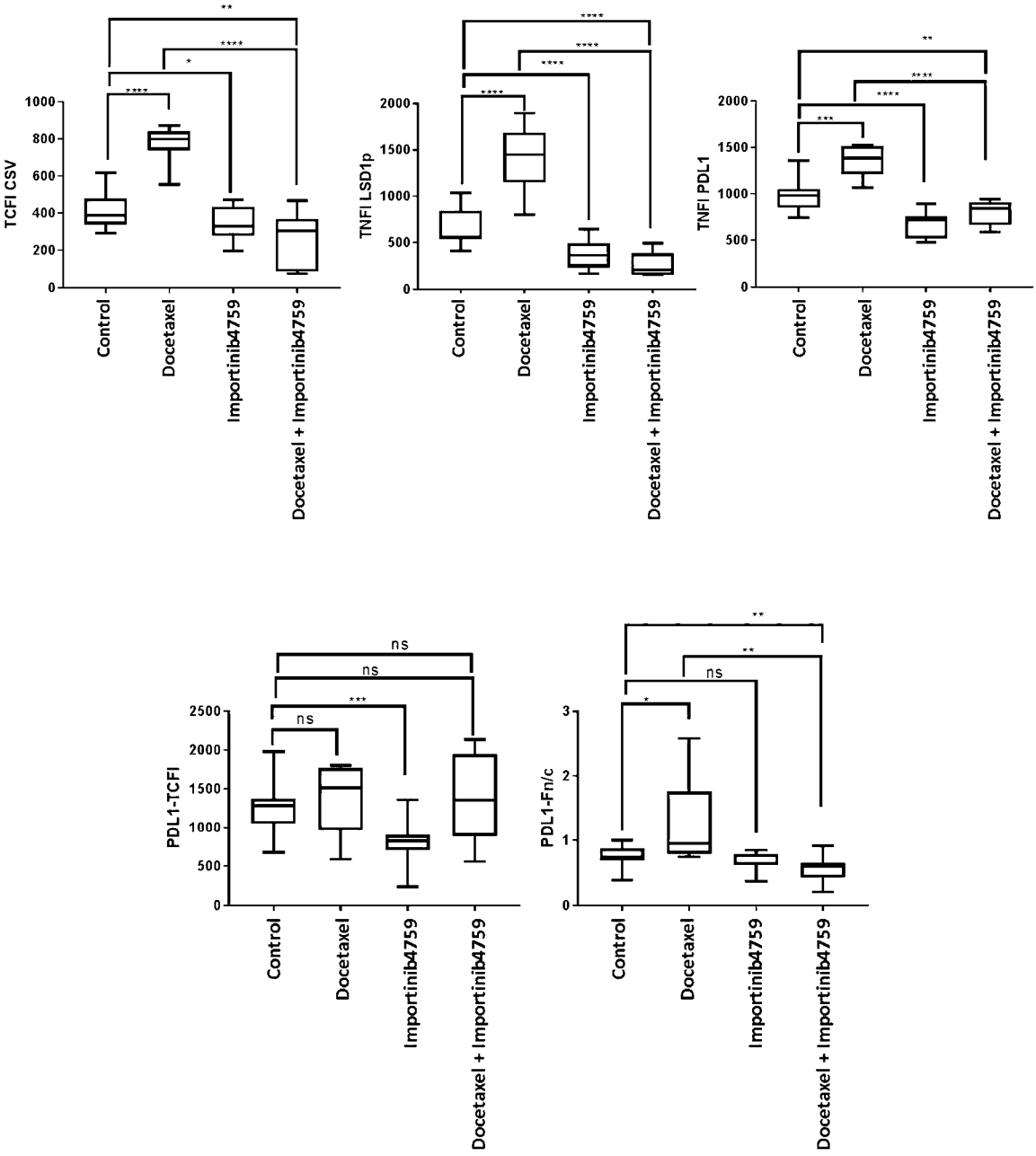

TCFI CSV
TNFI LSD1p
TNFI PDL1
PDL1-TCFI
PDL1-Fn/c
Control
Docetaxel
Importinib4759
Docetaxel + Importinib4759
ns

Figure 11

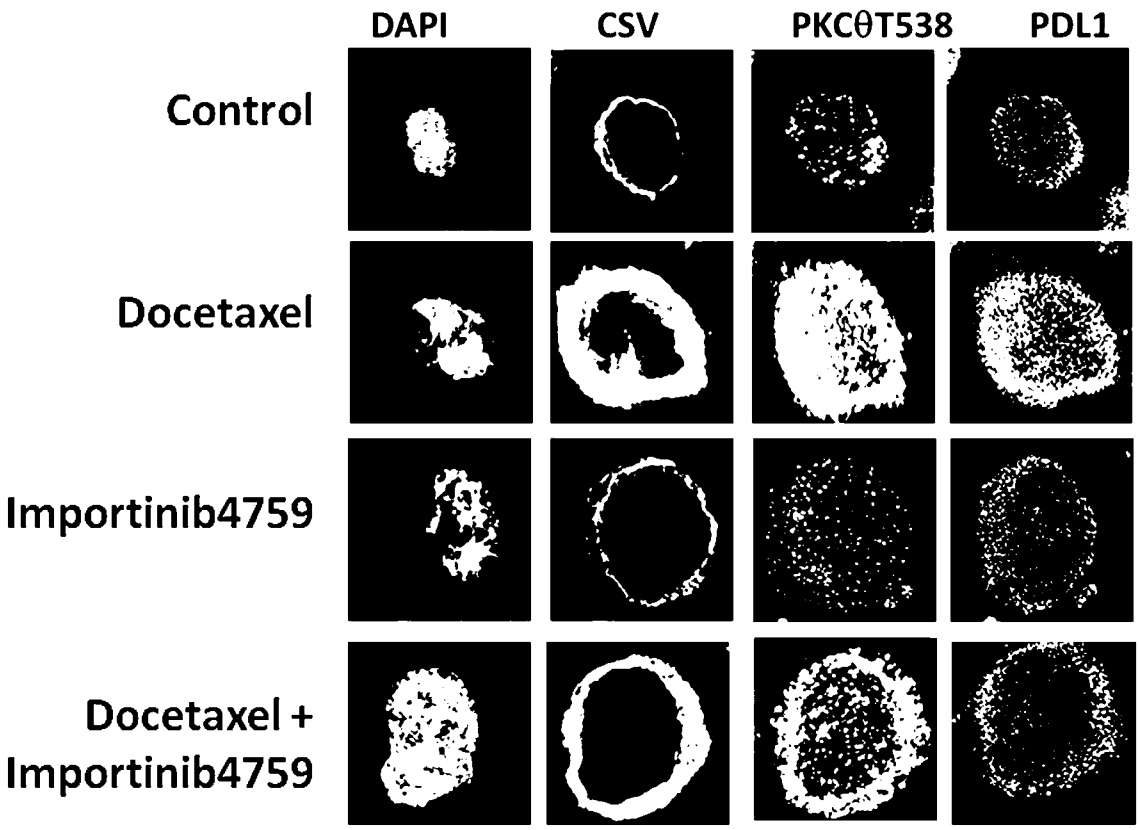

DAPI
CSV
PKCθT538
PDL1
Control
Docetaxel
Importinib4759
Docetaxel +
Importinib4759

Figure 12

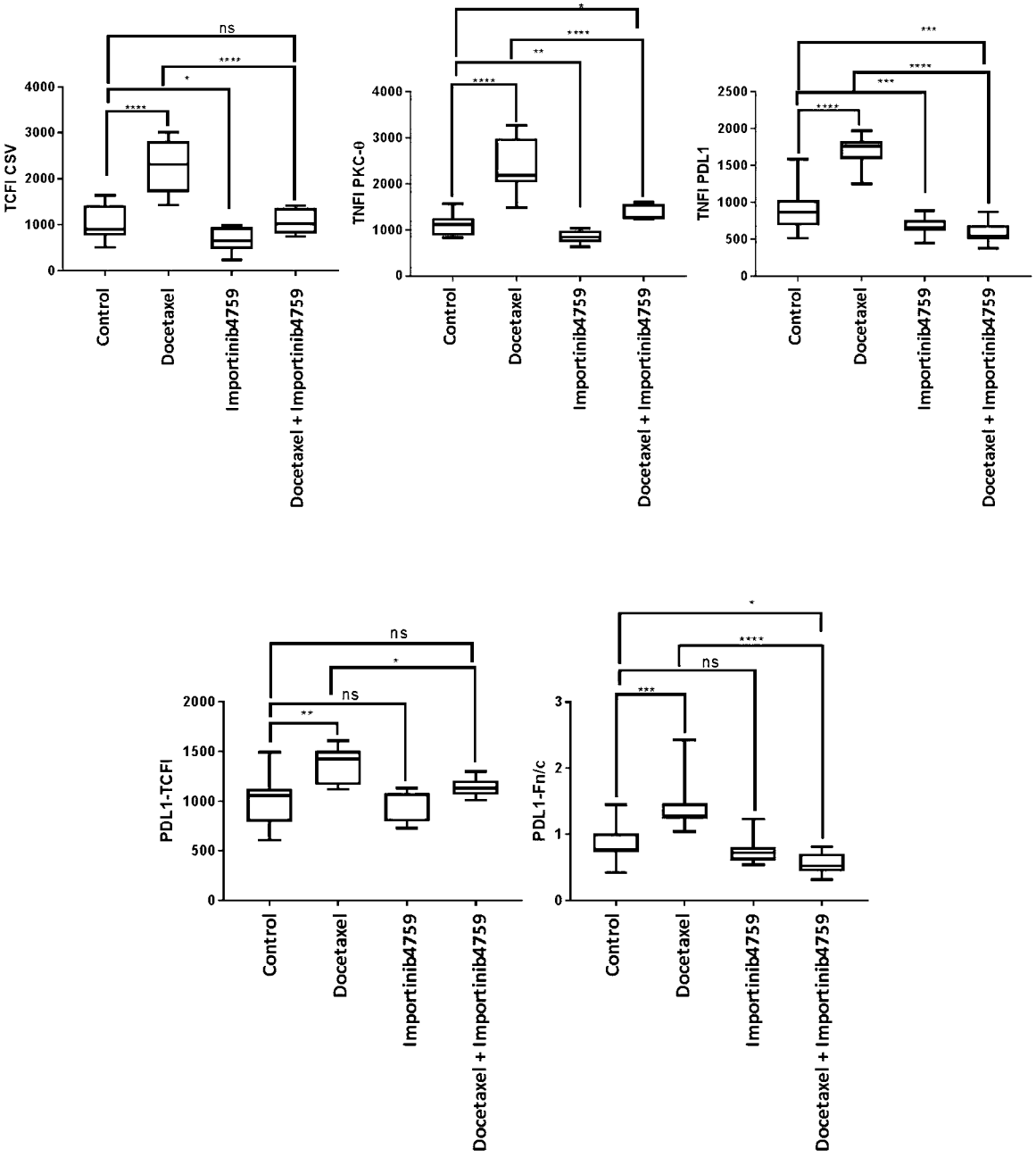

TCFI CSV
TNFI PKC-θ
TNFI PDL1
PDL1-TCFI
PDL1-Fn/c
Control
Docetaxel
Importinib4759
Docetaxel + Importinib4759
ns

Figure 13

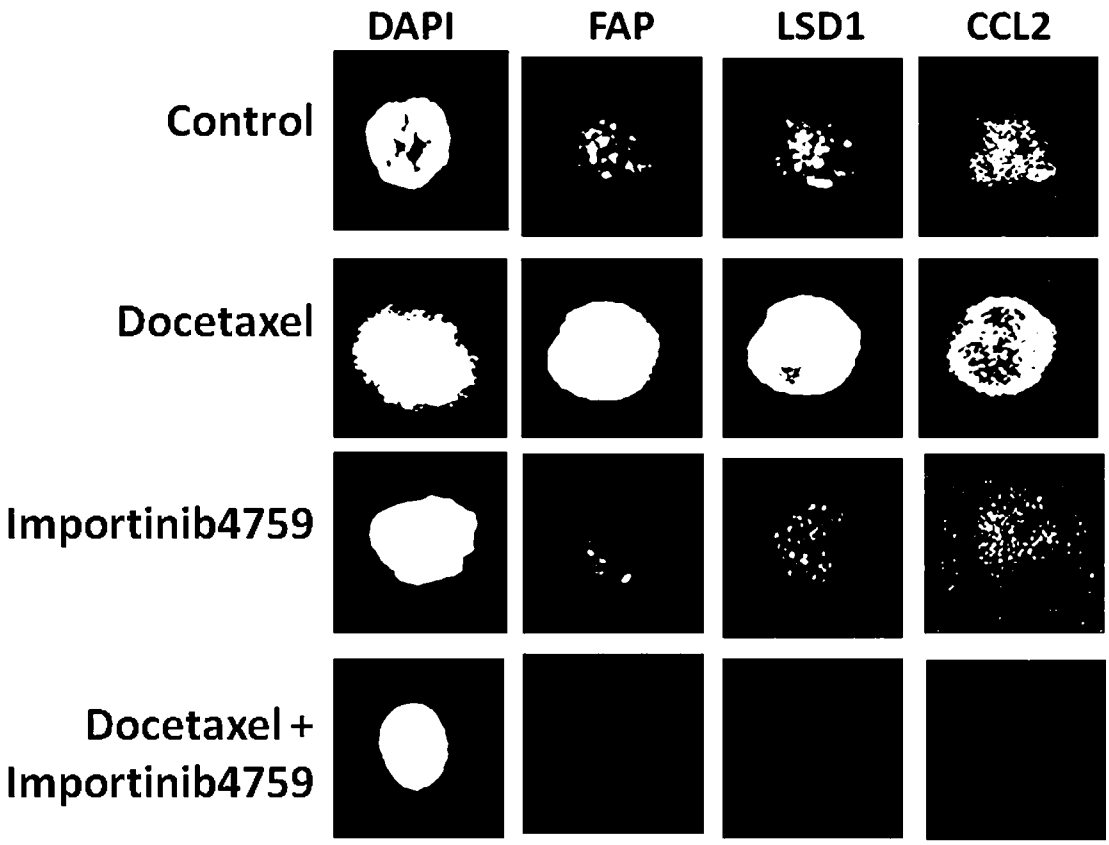

DAPI
FAP
LSD1
CCL2
Control
Docetaxel
Importinib4759
Docetaxel +
Importinib4759

Figure 14

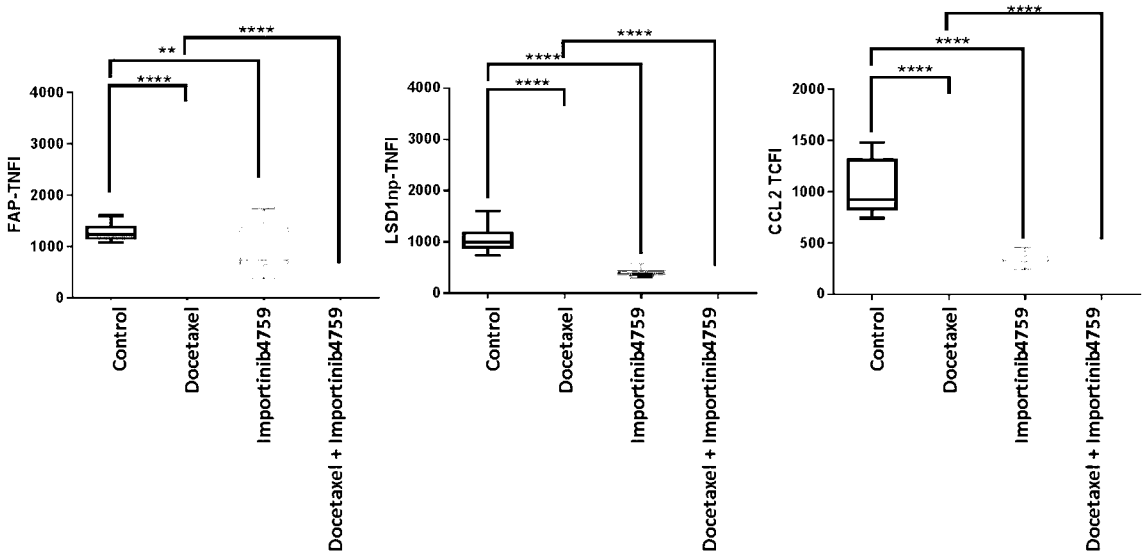

FAP-TNFI
LSD1np-TNFI
CCL2 TCFI
Control
Docetaxel
Importinib4759
Docetaxel + Importinib4759
****
**

Figure 15

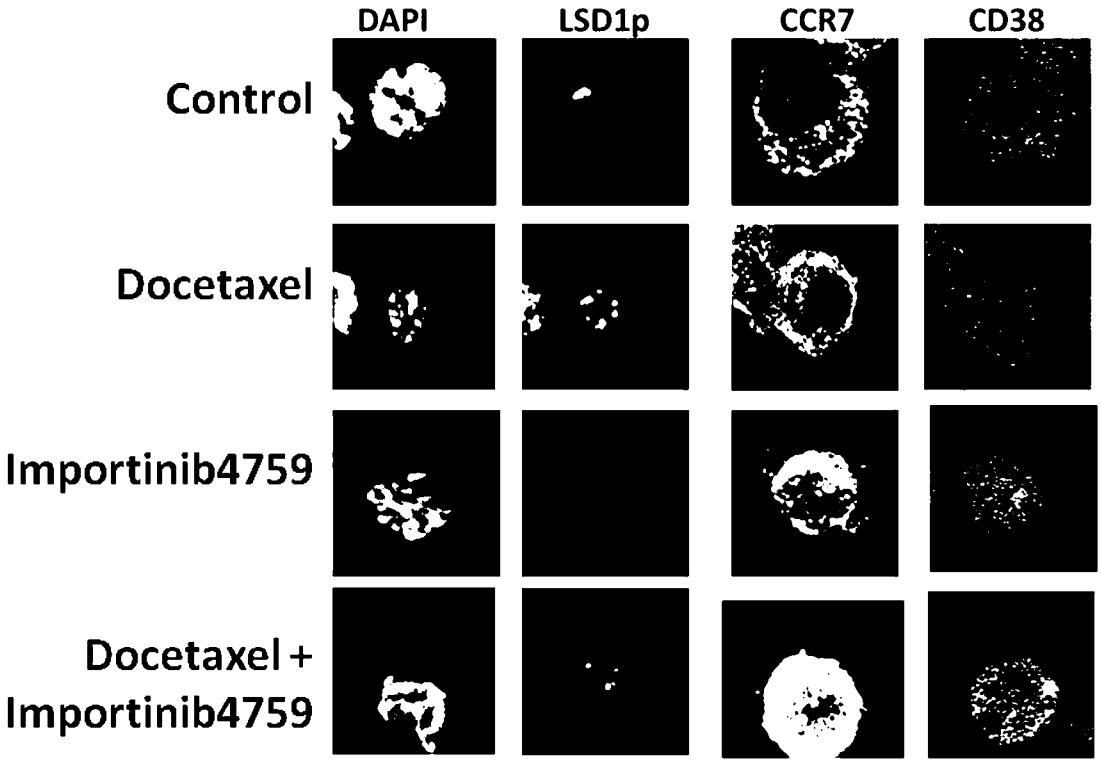

DAPI
LSD1p
CCR7
CD38
Control
Docetaxel
Importinib4759
Docetaxel +
Importinib4759

Figure 16

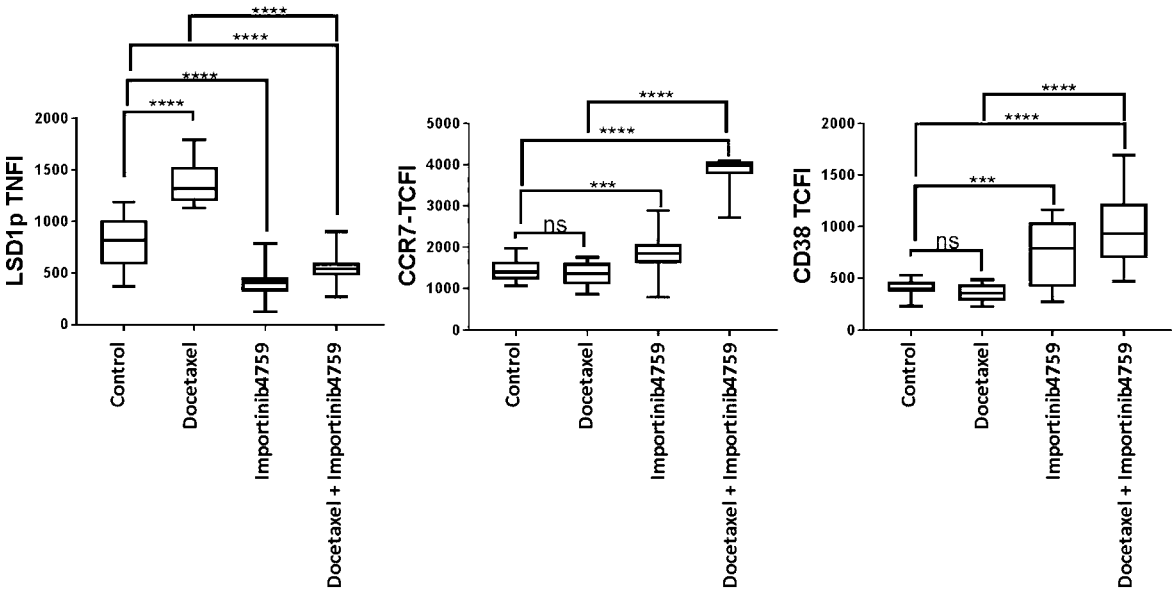

LSD1p TNFI
2000
1500
1000
500
0
****
****
****
****
Control
Docetaxel
Importinib4759
Docetaxel + Importinib4759
CCR7-TCFI
5000
4000
3000
2000
1000
0
****
****
***
ns
Control
Docetaxel
Importinib4759
Docetaxel + Importinib4759
CD38 TCFI
2000
1500
1000
500
0
****
****
***
ns
Control
Docetaxel
Importinib4759
Docetaxel + Importinib4759

Figure 17