FIG 1-A

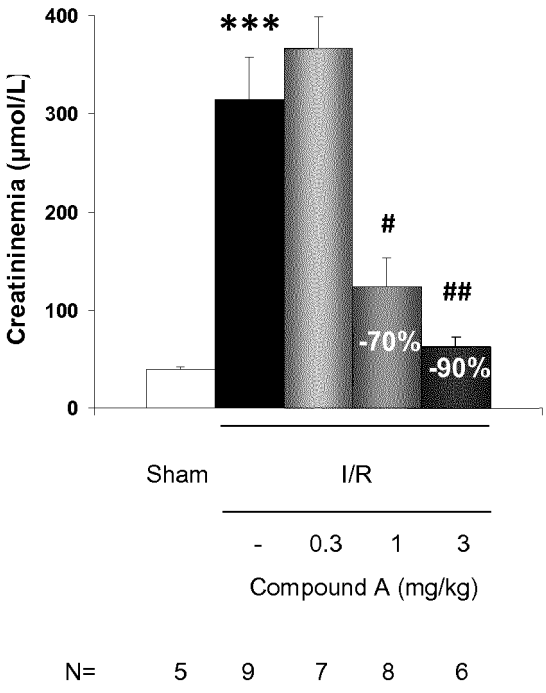


FIG 1-B

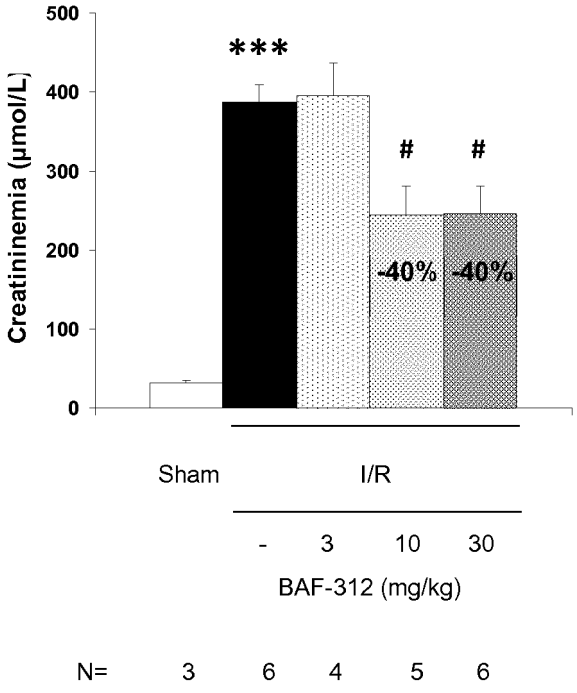


FIG 1-C

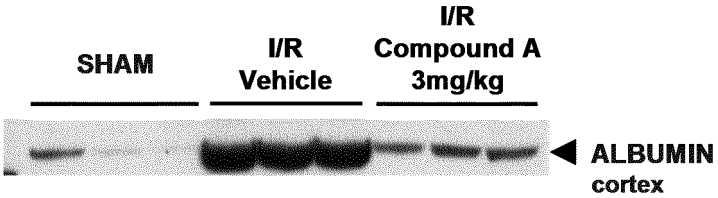


FIG 1-D

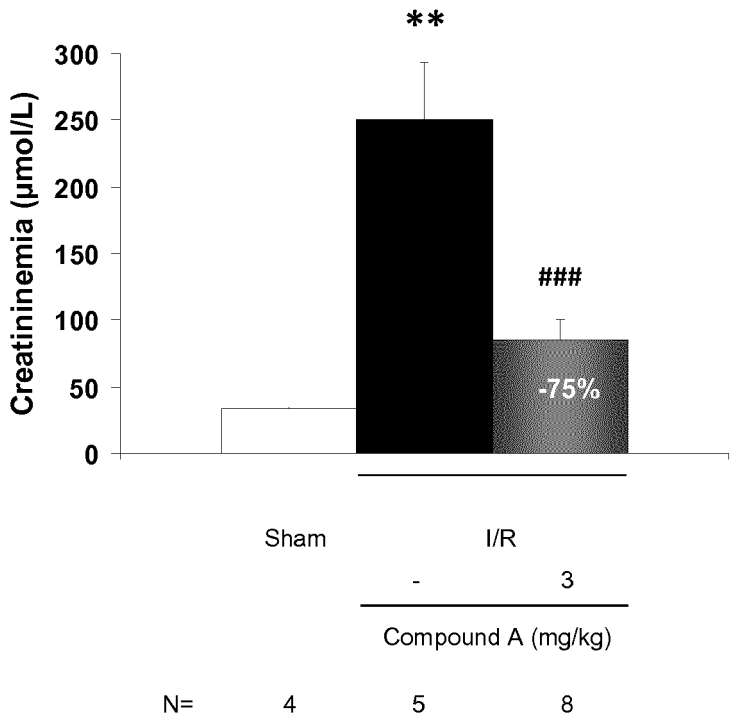

**
###
-75%
Creatininemia (µmol/L)
300
250
200
150
100
50
0
Sham
I/R
-
3
Compound A (mg/kg)
N=
4
5
8

FIG 2

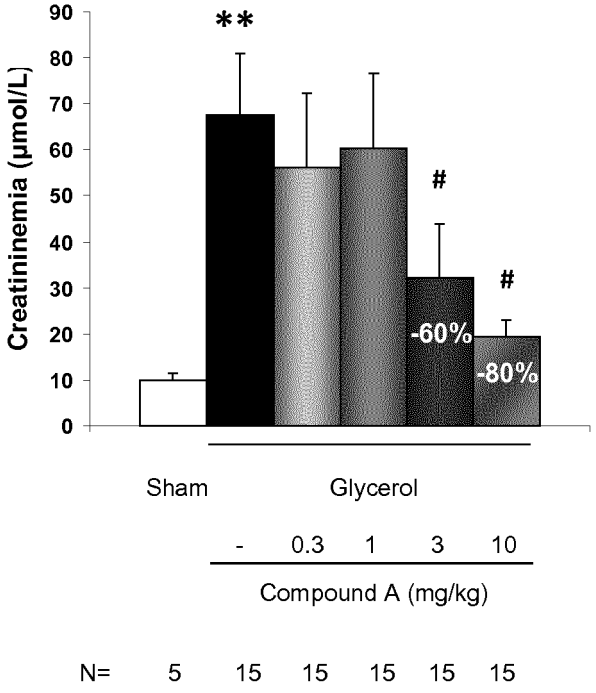

Creatininemia (µmol/L)
90
80
70
60
50
40
30
20
10
0
**
#
#
-60%
-80%
Sham
Glycerol
-
0.3
1
3
10
Compound A (mg/kg)
N=
5
15
15
15
15
15

FIG 3-A

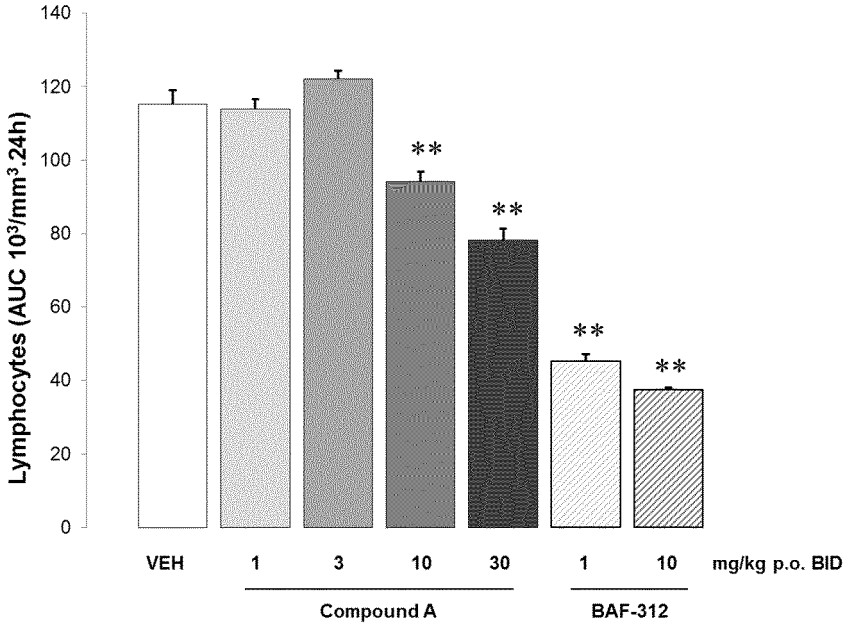


FIG 3-B- Single oral administration

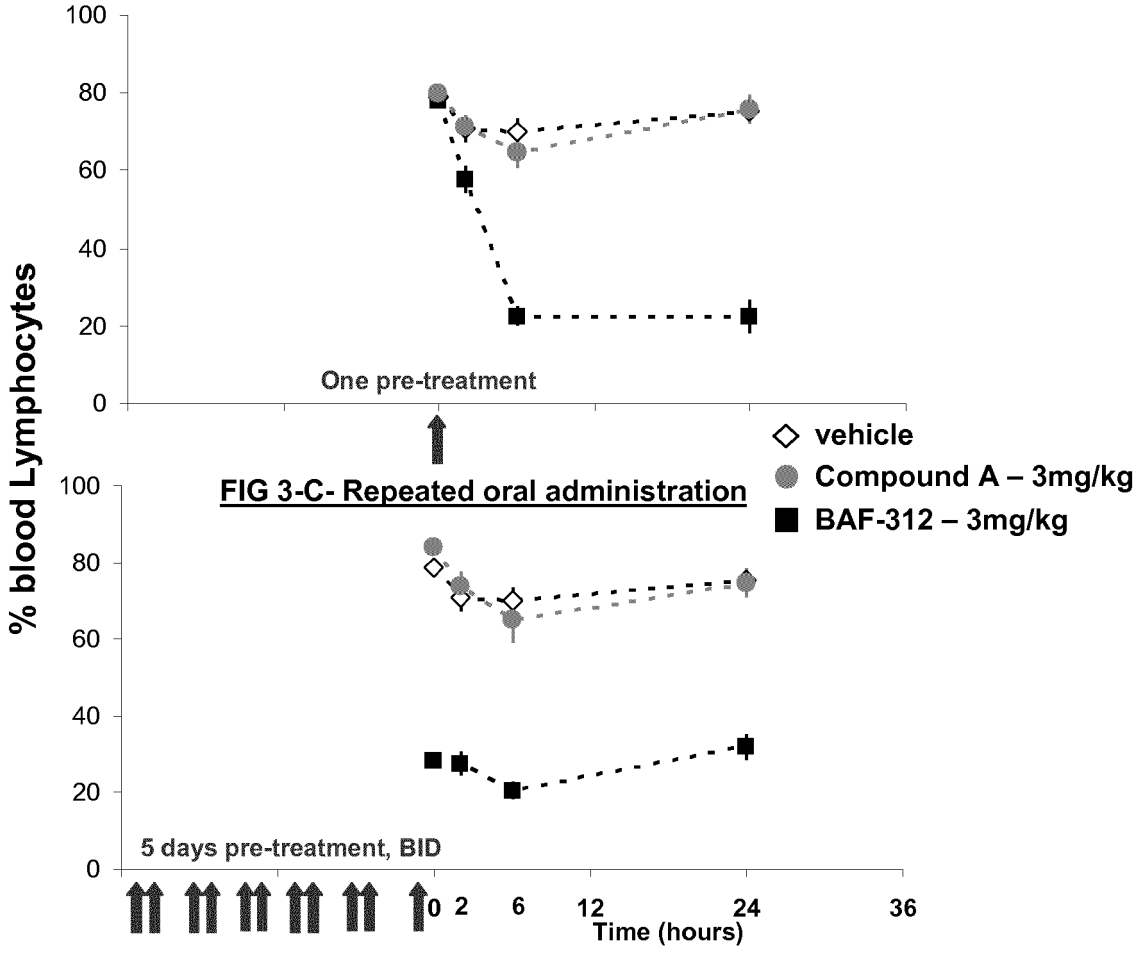


FIG 3-C- Repeated oral administration

FIG 3-D

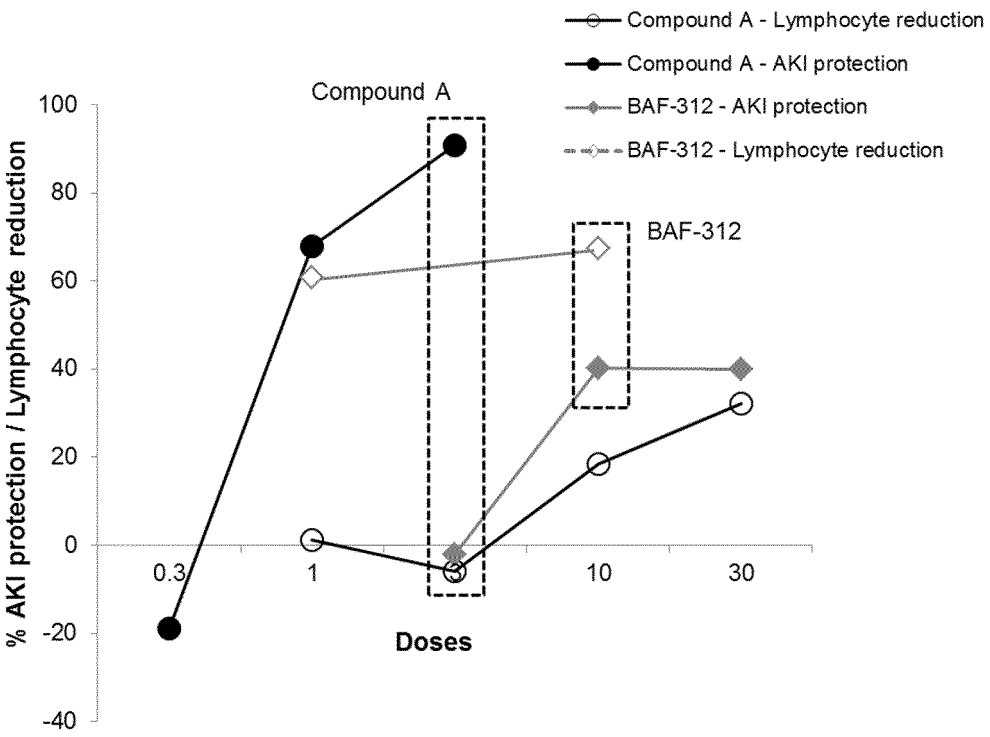

Compound A - Lymphocyte reduction
Compound A - AKI protection
BAF-312 - AKI protection
BAF-312 - Lymphocyte reduction
Compound A
BAF-312
100
80
60
40
20
0
-20
-40
% AKI protection / Lymphocyte reduction
0.3
1
10
30
Doses

FIG 4

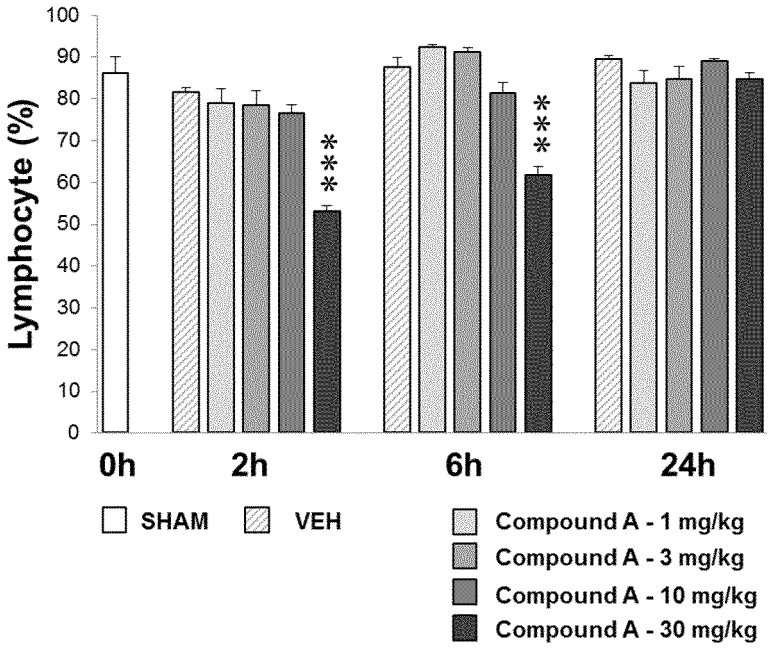

Lymphocyte (%)
100
90
80
70
60
50
40
30
20
10
0
0h
2h
6h
24h
***
***
SHAM
VEH
Compound A - 1 mg/kg
Compound A - 3 mg/kg
Compound A - 10 mg/kg
Compound A - 30 mg/kg

FIG 5-A

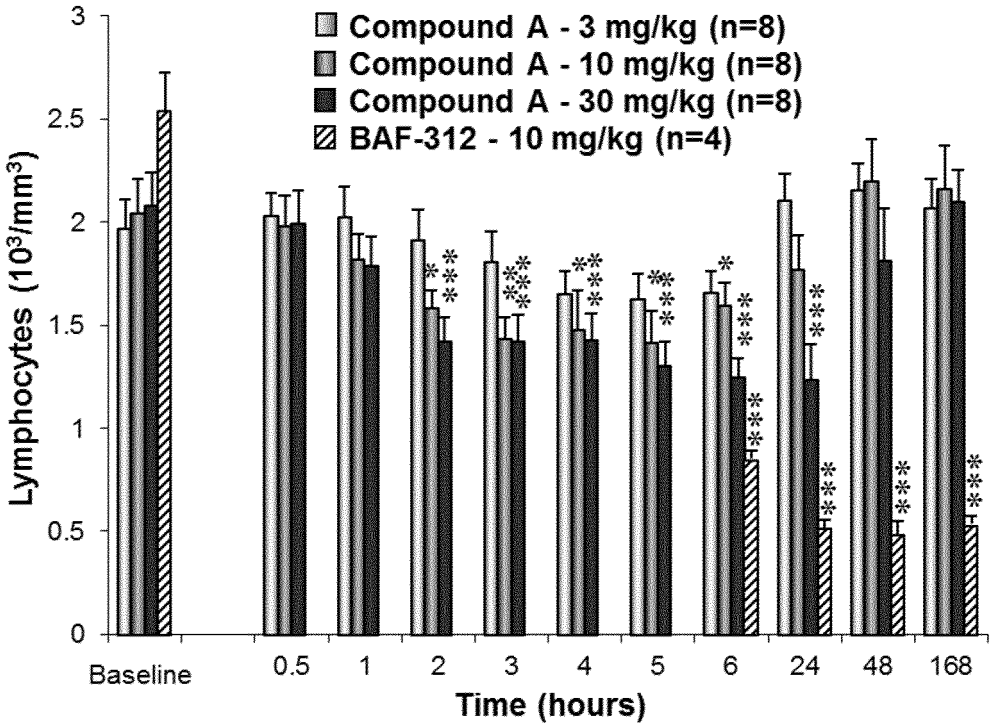

Compound A - 3 mg/kg (n=8)
Compound A - 10 mg/kg (n=8)
Compound A - 30 mg/kg (n=8)
BAF-312 - 10 mg/kg (n=4)
Lymphocytes (10³/mm³)
Time (hours)
Baseline
0.5
1
2
3
4
5
6
24
48
168

FIG 5-B

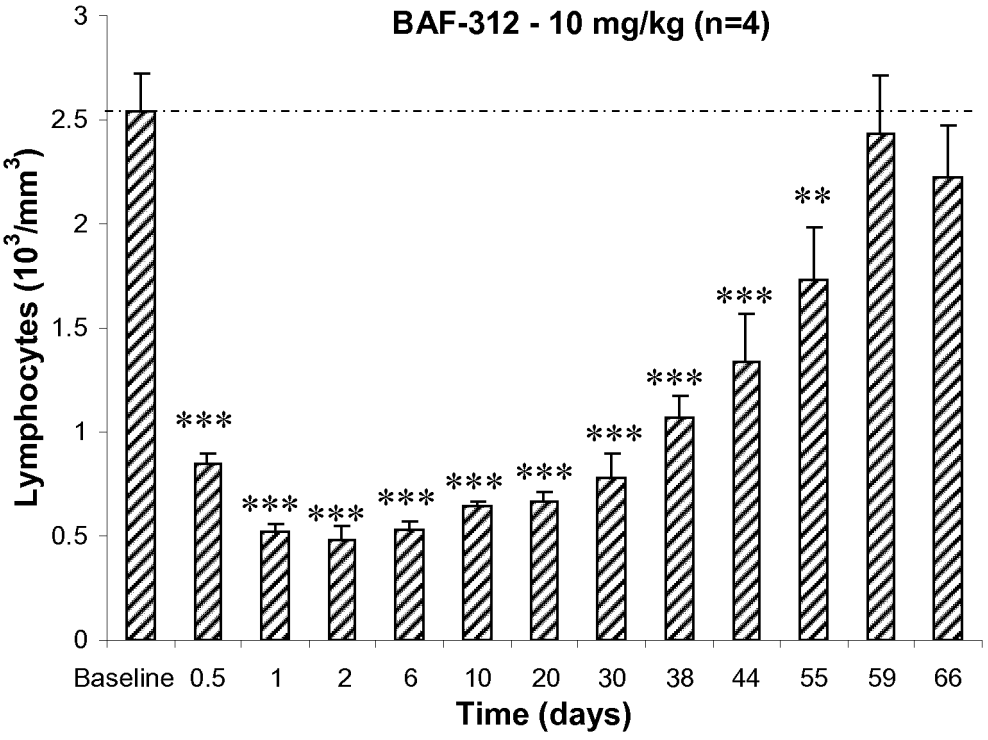

BAF-312 - 10 mg/kg (n=4)
Lymphocytes (10³/mm³)
Time (days)
Baseline
0.5
1
2
6
10
20
30
38
44
55
59
66

FIG 6-A

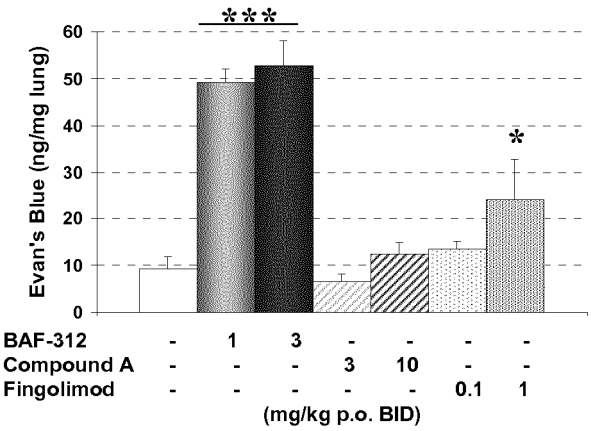


FIG 6-B

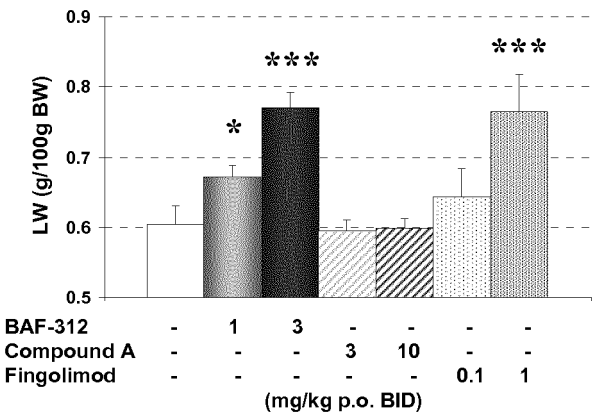


FIG 6-C

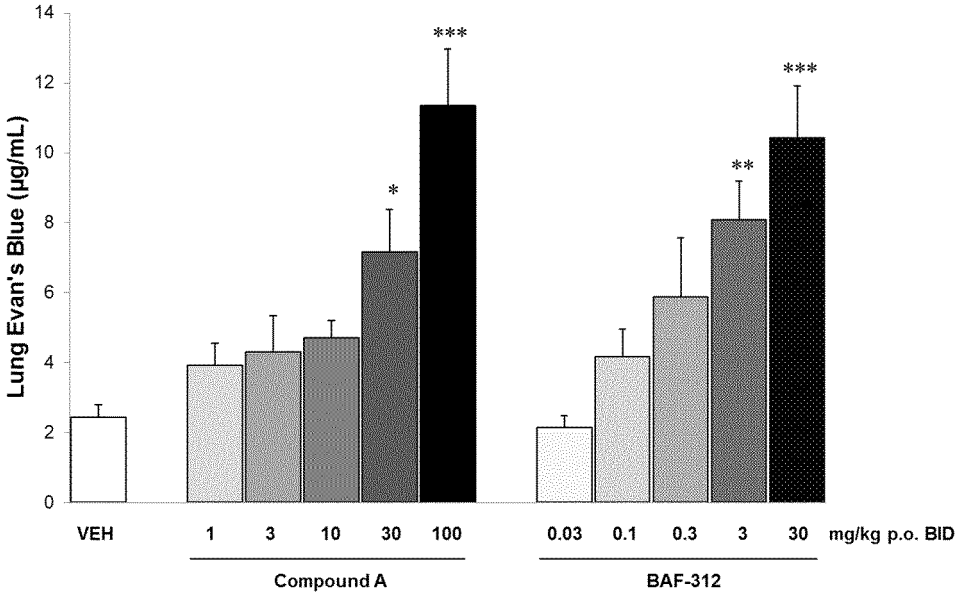


FIG 7

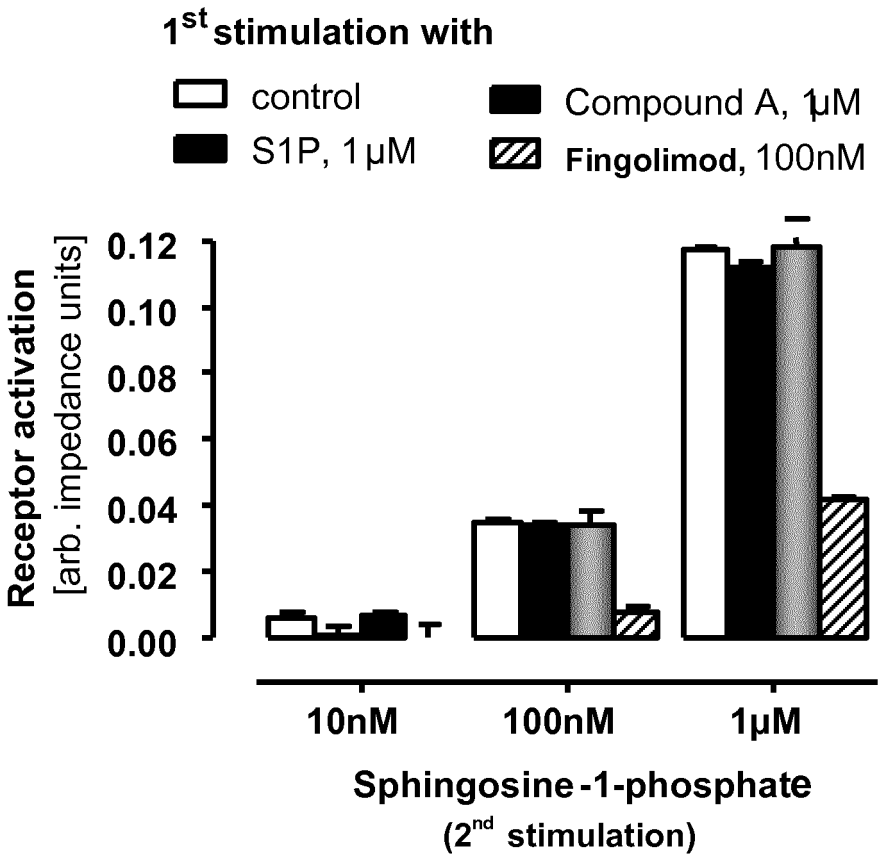

1st stimulation with
control
S1P, 1 µM
Compound A, 1µM
Fingolimod, 100nM
Receptor activation
[arb. impedance units]
0.12
0.10
0.08
0.06
0.04
0.02
0.00
10nM
100nM
1µM
Sphingosine-1-phosphate
(2nd stimulation)

FIG 8-A

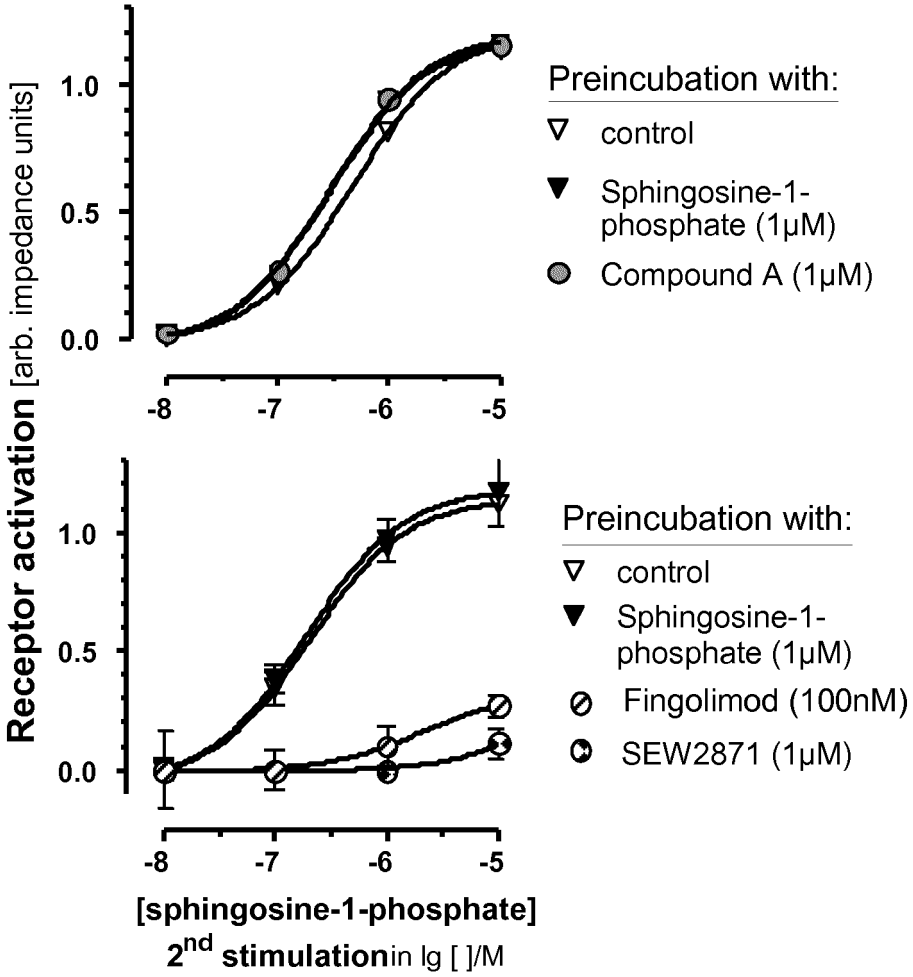

Receptor activation [arb. impedance units]
1.0
0.5
0.0
-8
-7
-6
-5
Preincubation with:
control
Sphingosine-1-phosphate (1µM)
Compound A (1µM)
Preincubation with:
control
Sphingosine-1-phosphate (1µM)
Fingolimod (100nM)
SEW2871 (1µM)
[sphingosine-1-phosphate]
2nd stimulation in lg [ ]/M

FIG 8-B

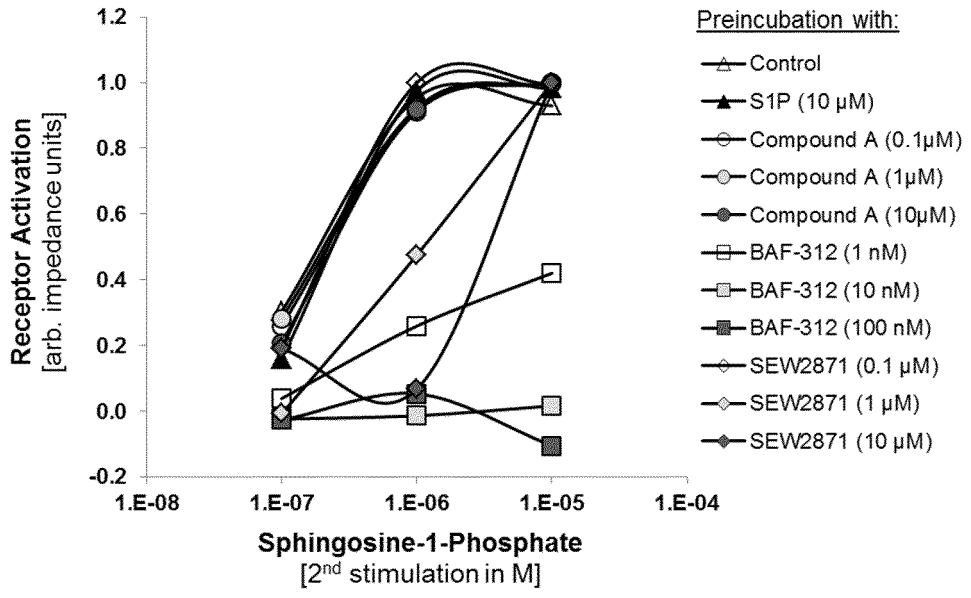

Receptor Activation [arb. impedance units]
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
1.E-08
1.E-07
1.E-06
1.E-05
1.E-04
Sphingosine-1-Phosphate [2nd stimulation in M]
Preincubation with:
Control
S1P (10 µM)
Compound A (0.1µM)
Compound A (1µM)
Compound A (10µM)
BAF-312 (1 nM)
BAF-312 (10 nM)
BAF-312 (100 nM)
SEW2871 (0.1 µM)
SEW2871 (1 µM)
SEW2871 (10 µM)

FIG 9-A

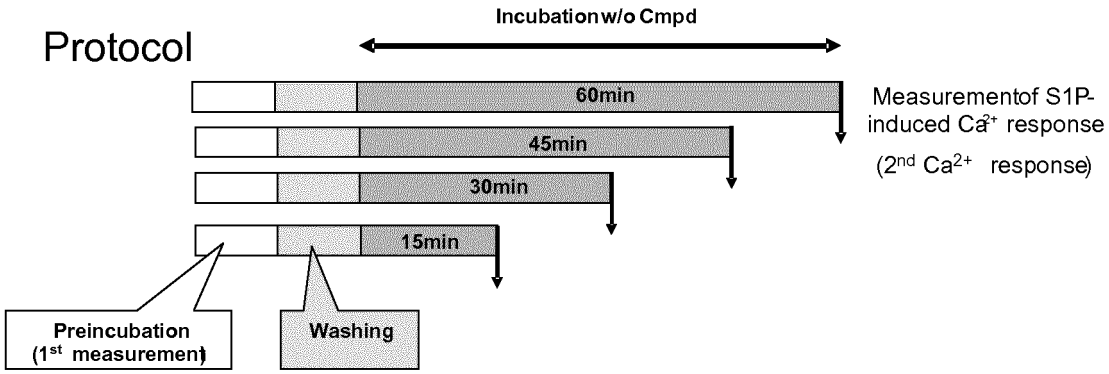

Protocol
Incubation w/o Cmpd
60min
45min
30min
15min
Measurement of S1P-induced Ca2+ response
(2nd Ca2+ response)
Preincubation (1st measurement)
Washing

FIG 9-B

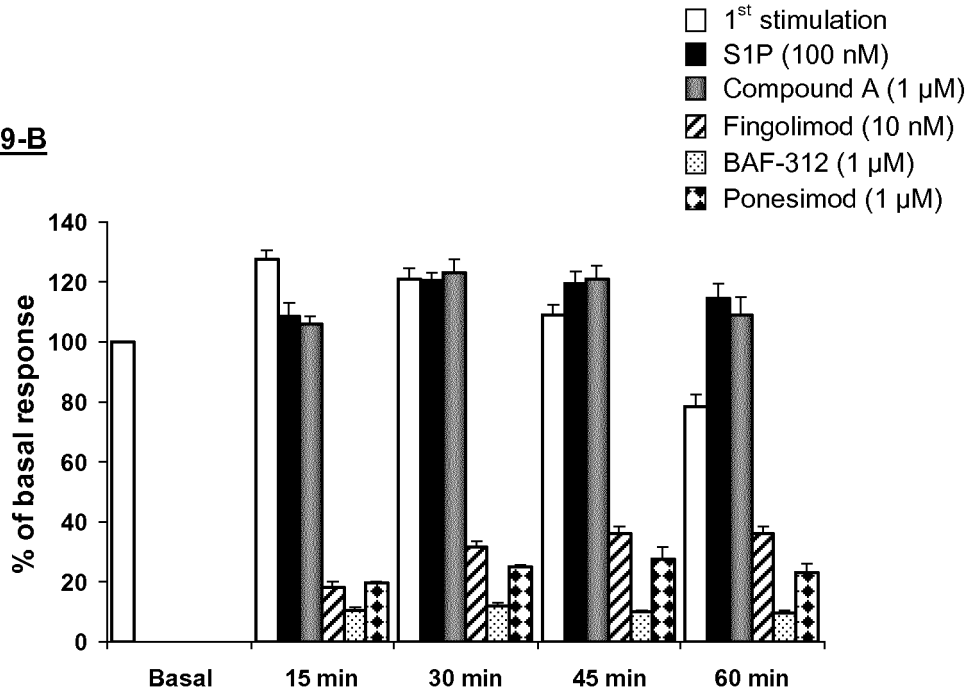

1st stimulation
S1P (100 nM)
Compound A (1 µM)
Fingolimod (10 nM)
BAF-312 (1 µM)
Ponesimod (1 µM)
% of basal response
140
120
100
80
60
40
20
0
Basal
15 min
30 min
45 min
60 min

FIG 10-A

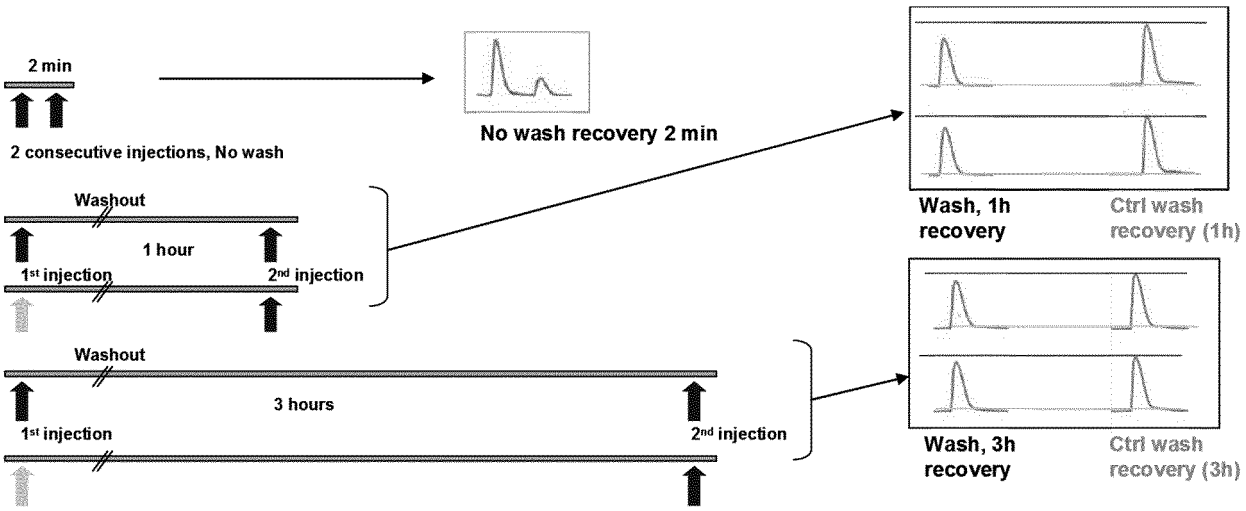


FIG 10-B 1 hour washout 3 hours washout

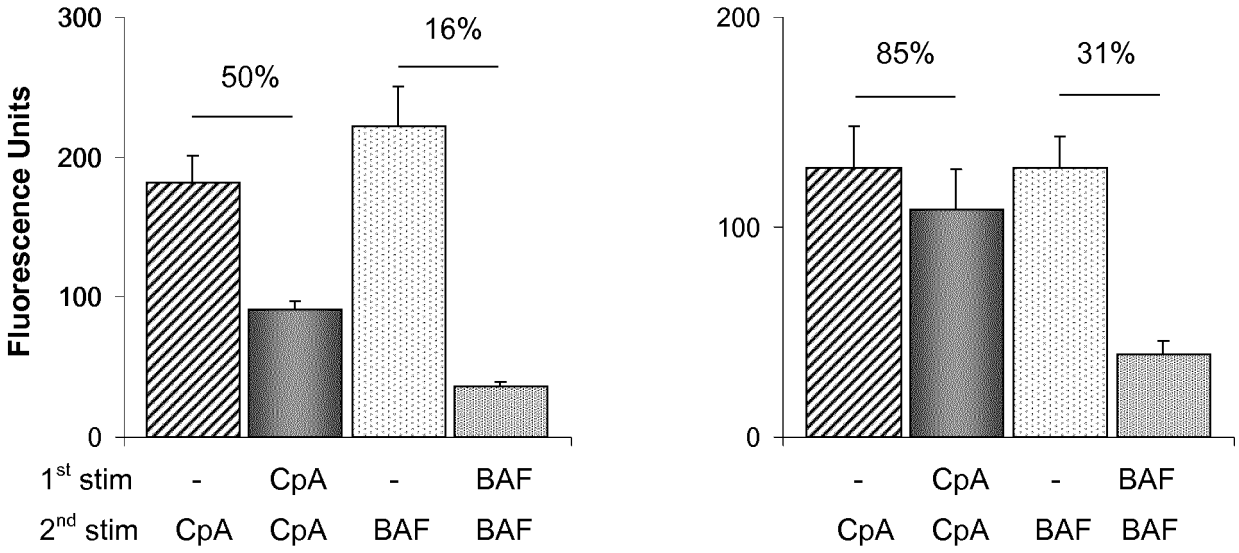
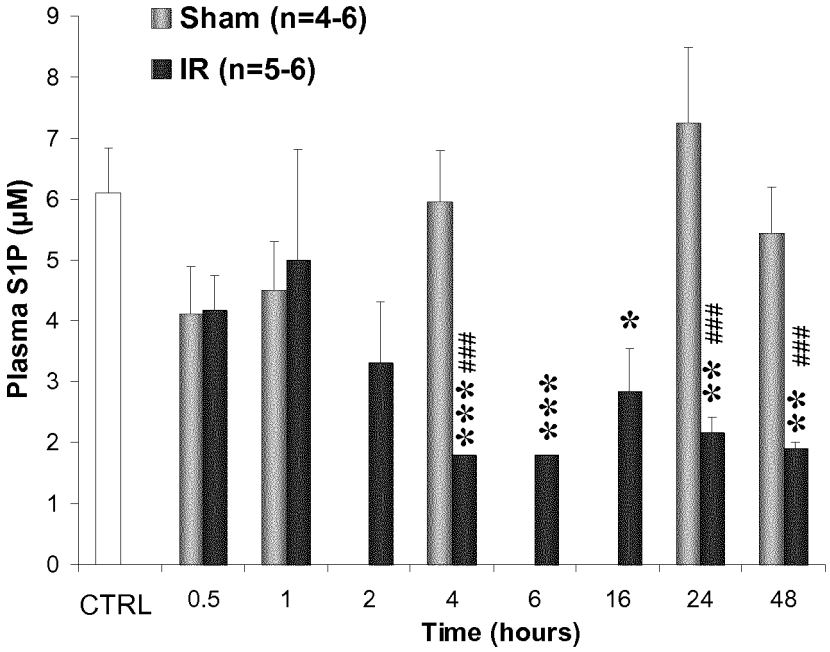


FIG 11


Sham (n=4-6)
IR (n=5-6)
Plasma S1P (µM)
0
1
2
3
4
5
6
7
8
9
CTRL
0.5
1
2
4
6
16
24
48
Time (hours)
*
**
***
###