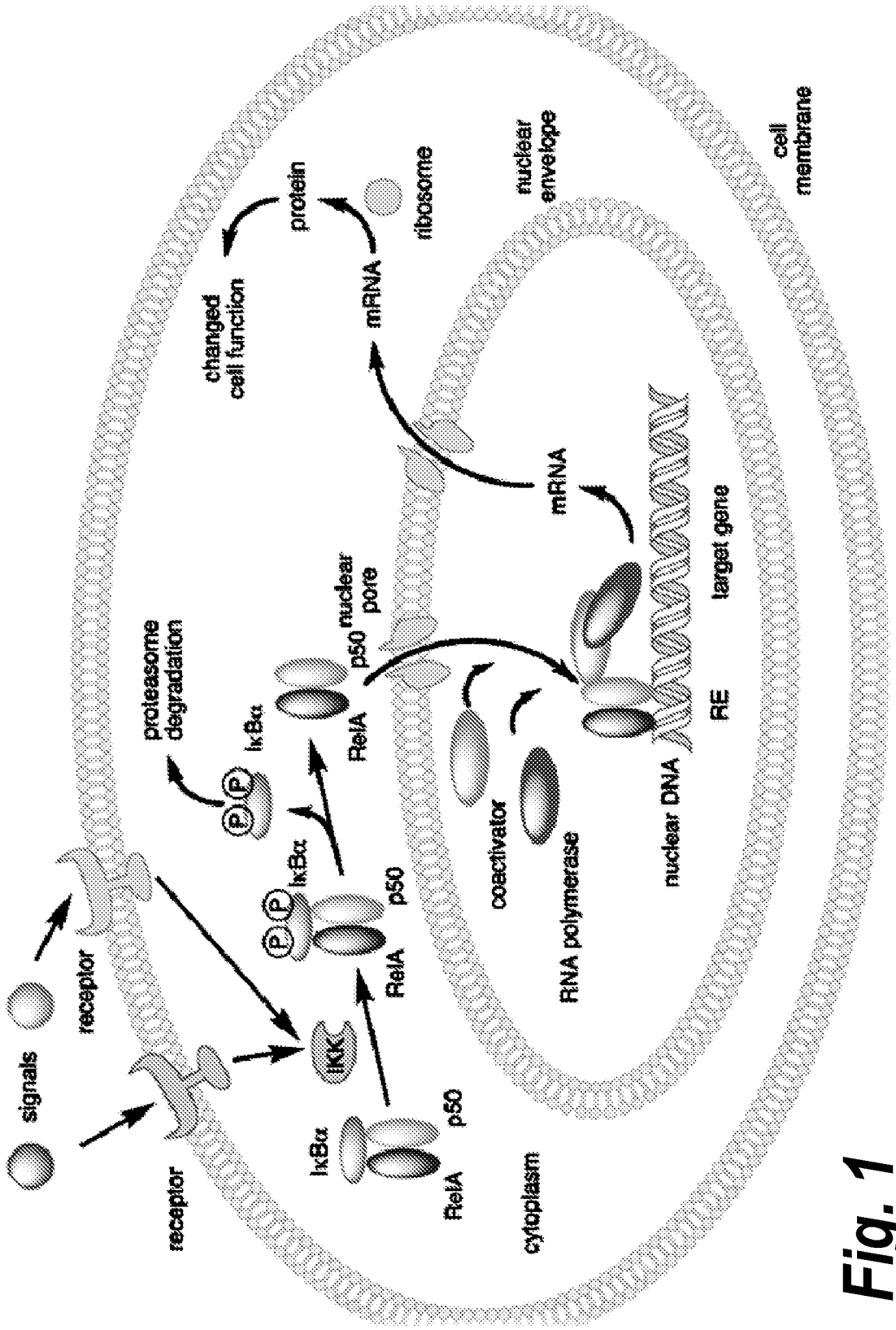

signals
receptor
receptor
IKK
IκBα
RelA
p50
P
P
IκBα
RelA
p50
P
P
IκBα
proteasome degradation
RelA
p50
nuclear pore
changed cell function
protein
ribosome
mRNA
nuclear envelope
cell membrane
mRNA
coactivator
RNA polymerase
nuclear DNA
RE
target gene
cytoplasm

Fig. 1

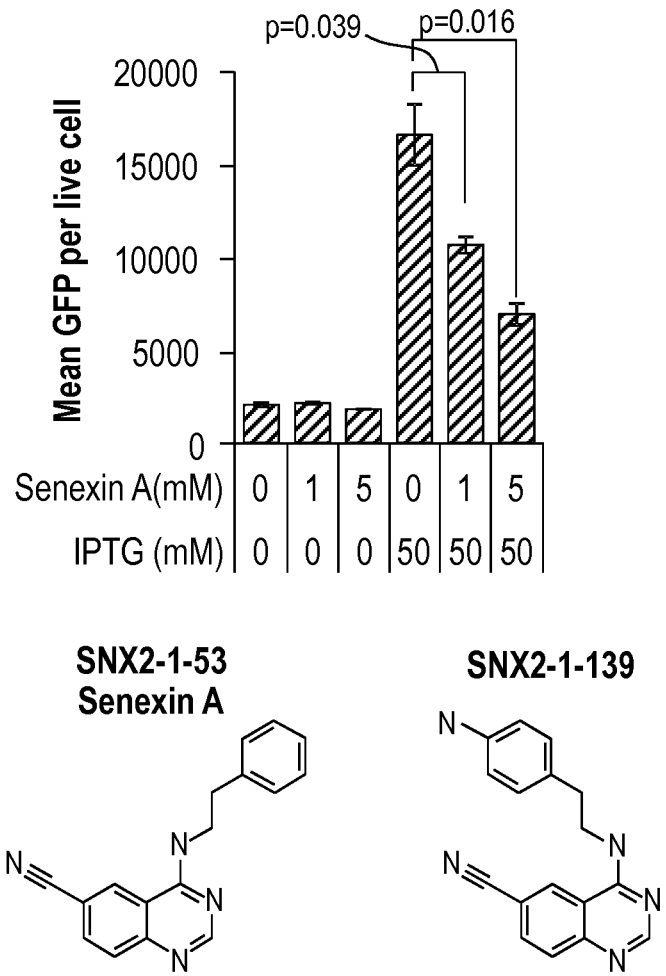

p=0.039
p=0.016
Mean GFP per live cell
20000
15000
10000
5000
0
Senexin A(mM) 0 1 5 0 1 5
IPTG (mM) 0 0 0 50 50 50
SNX2-1-53
Senexin A
SNX2-1-139

Fig. 2

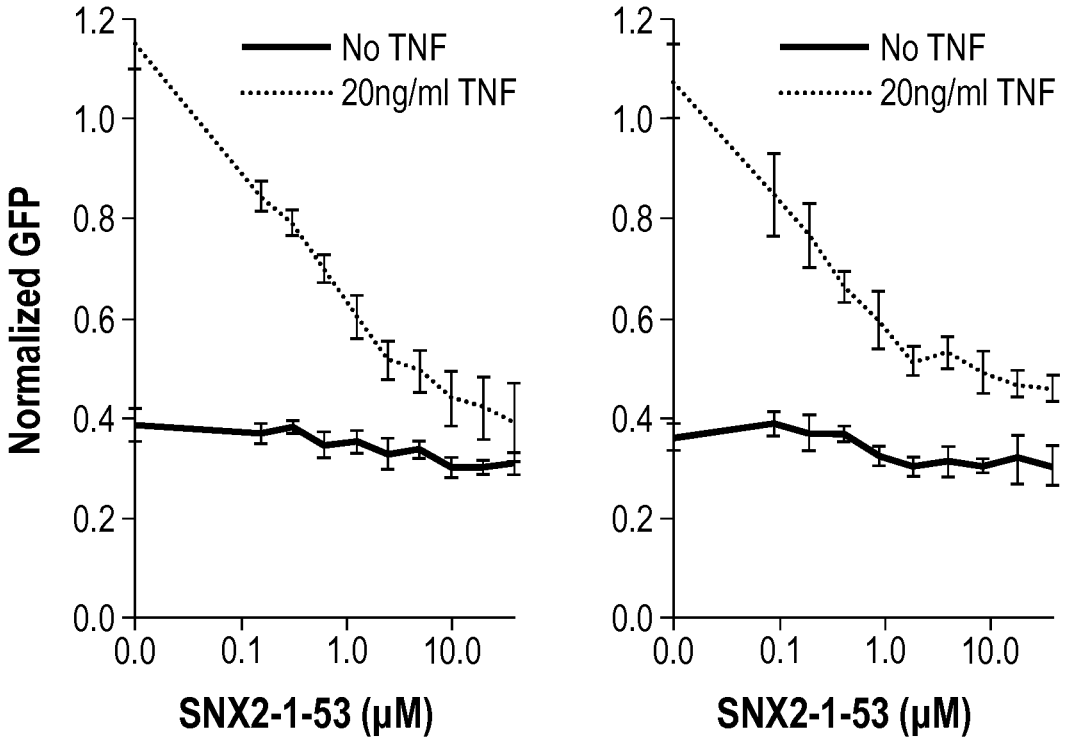

Normalized GFP
1.2
1.0
0.8
0.6
0.4
0.2
0.0
No TNF
20ng/ml TNF
0.0
0.1
1.0
10.0
SNX2-1-53 (μM)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
No TNF
20ng/ml TNF
0.0
0.1
1.0
10.0
SNX2-1-53 (μM)

Fig. 3

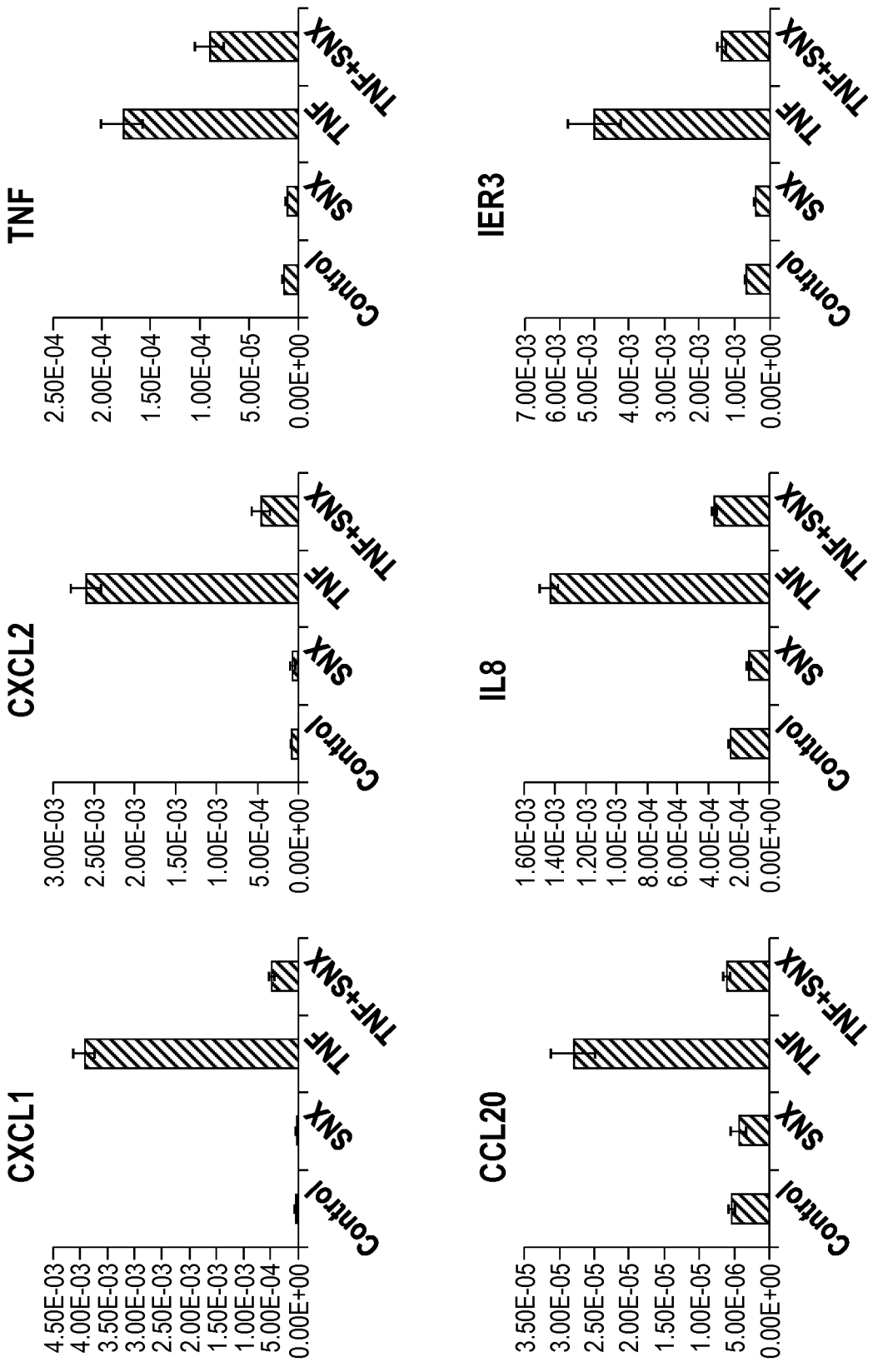

TNF
2.50E-04
2.00E-04
1.50E-04
1.00E-04
5.00E-05
0.00E+00
Control
SNX
TNF
TNF+SNX
IER3
7.00E-03
6.00E-03
5.00E-03
4.00E-03
3.00E-03
2.00E-03
1.00E-03
0.00E+00
CXCL2
3.00E-03
2.50E-03
2.00E-03
1.50E-03
1.00E-03
5.00E-04
0.00E+00
IL8
1.60E-03
1.40E-03
1.20E-03
1.00E-03
8.00E-04
6.00E-04
4.00E-04
2.00E-04
0.00E+00
CXCL1
4.50E-03
4.00E-03
3.50E-03
3.00E-03
2.50E-03
2.00E-03
1.50E-03
1.00E-03
5.00E-04
0.00E+00
CCL20
3.50E-05
3.00E-05
2.50E-05
2.00E-05
1.50E-05
1.00E-05
5.00E-06
0.00E+00

Fig. 4

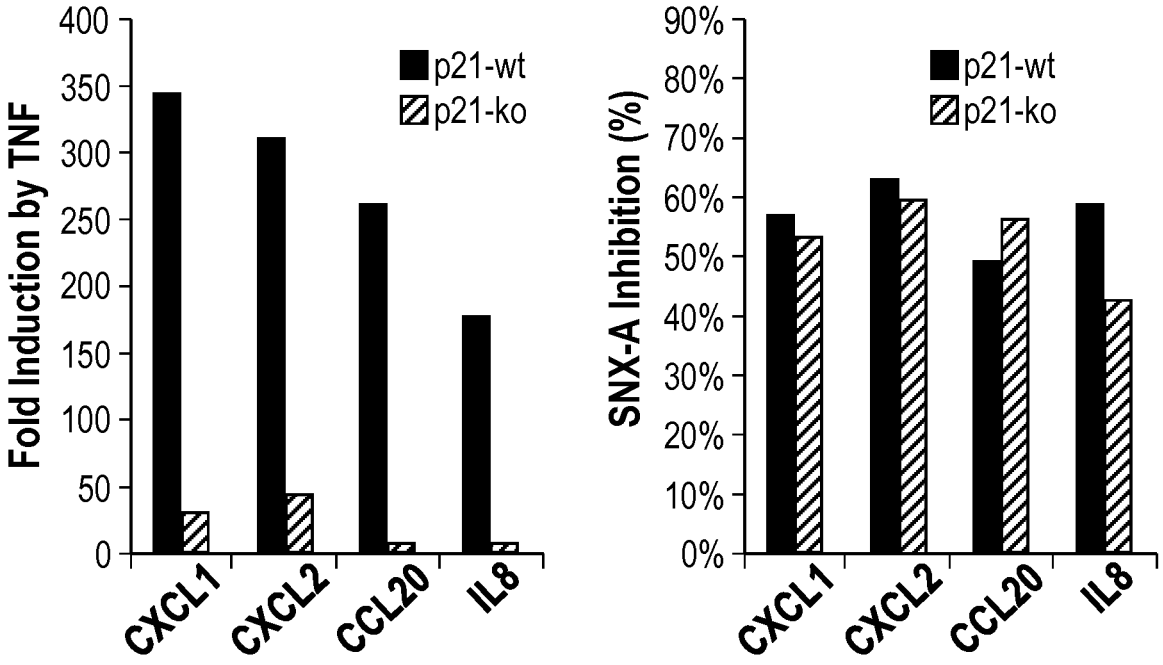

Fold Induction by TNF
400
350
300
250
200
150
100
50
0
p21-wt
p21-ko
CXCL1
CXCL2
CCL20
IL8
SNX-A Inhibition (%)
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
p21-wt
p21-ko
CXCL1
CXCL2
CCL20
IL8

Fig. 5

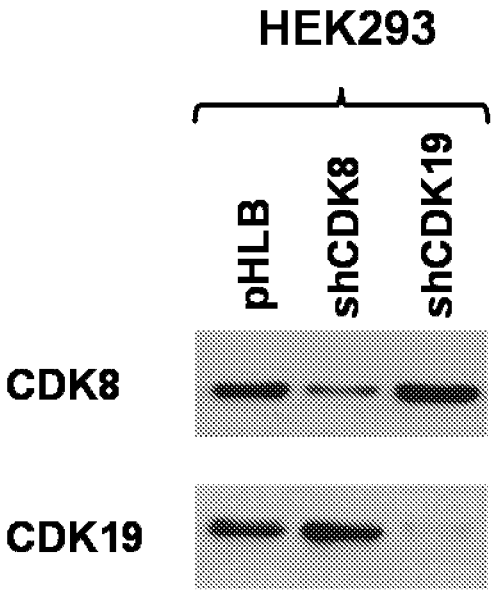


Fig. 6

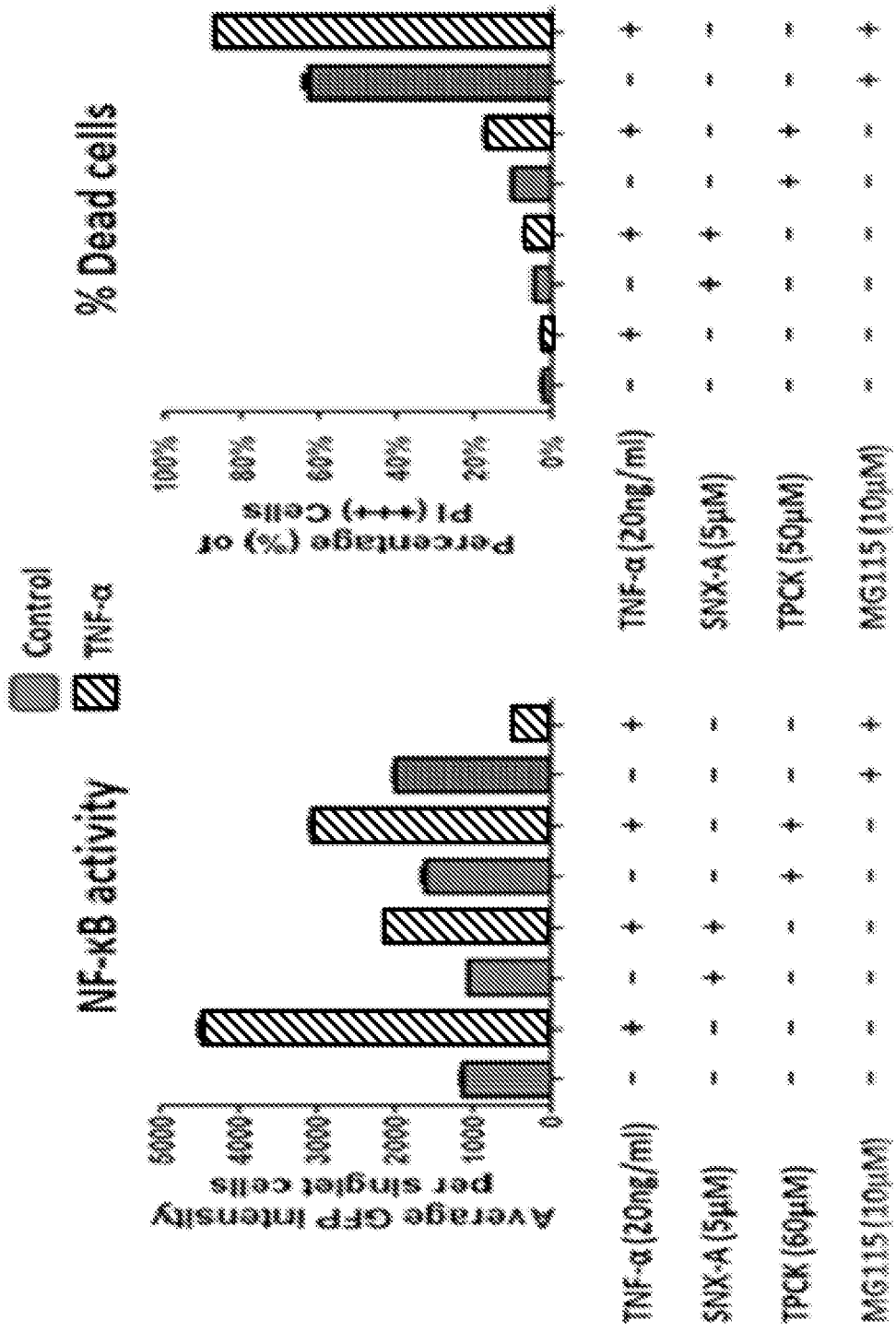

NF-κB activity
Control
TNF-α
Average GFP intensity per singlet cells
5000
4000
3000
2000
1000
0
% Dead cells
Percentage (%) of PI (++) Cells
100%
80%
60%
40%
20%
0%
TNF-α (20ng/ml)
SNX-A (5μM)
TPCK (60μM)
MG115 (10μM)
TNF-α (20ng/ml)
SNX-A (5μM)
TPCK (50μM)
MG115 (10μM)

Fig. 7

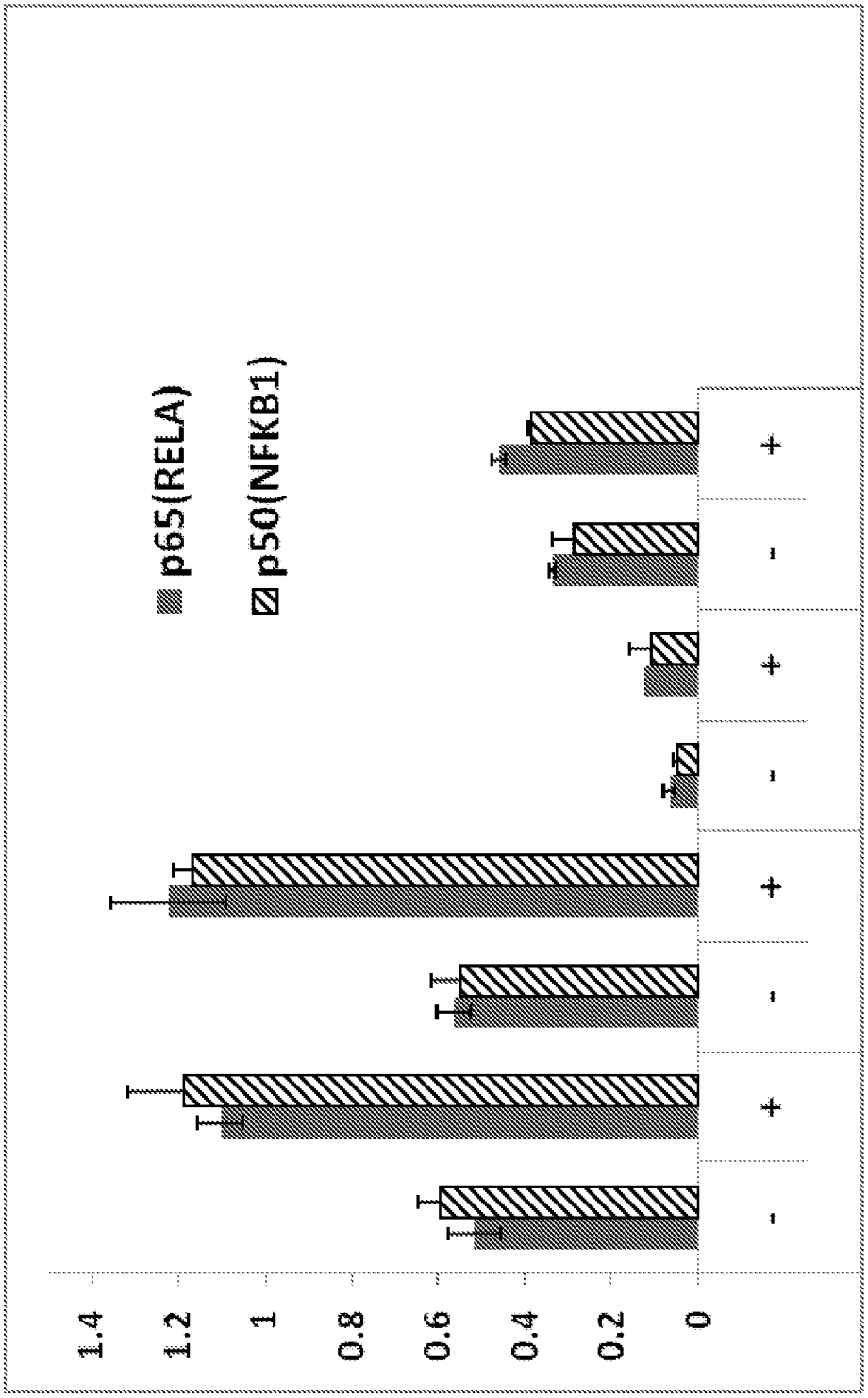
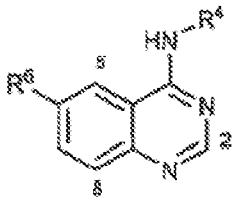
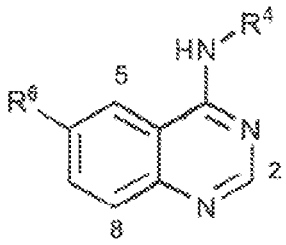

p65(RELA)
p50(NFKB1)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Control
Senexin A
TPCK
MG115
-
+
-
+
-
+
-
+

Fig. 8



Cmpd No	R^6	R^4	IC_{50} (μM)
1	CN	$(CH_2)_2Ph$	1.8
2	Cl	$(CH_2)_2Ph$	4.7
3	I	$(CH_2)_2Ph$	10.9
4	CF_3	$(CH_2)_2Ph$	12.7
5	F	$(CH_2)_2Ph$	3.9
6	NHAc	$(CH_2)_2Ph$	na
7	NO_2	$(CH_2)_2Ph$	2.9
8	CN	$(CH_2)_2CH_3$	6.0
9	CN	CH_2Ph	3.3
10	CN	$CH_2CH(CH_3)_2$	5.3
11	CN	$(CH_2)_3Ph$	4.7
12	CN	CH_2-2,4-$(OMe)_2C_6H_4$	13.7
13	CN	CH_2-3-$NO_2C_6H_5$	9.6
14	CN	CH_2-2-napthyl	1.8
15	CN	CH_2-3,5-$(CF_3)_2C_6H_4$	na
16	CN	CH_2-4-$CF_3C_6H_5$	6.5
17	CN	CH_2-2,4-$F_2C_6H_4$	3.0
18	CN	CH_2-3,4-$F_2C_6H_4$	3.0
19	CN	$CH(CH_3)Ph$	9.4

Fig. 9A



Cmpd No	R^6	R^4	IC_{50}(μM)
20	CN	CH_2-4-Cl-benzyl	0.6
21	CN	CH_2-4-F-benzyl	1.07
22	CN	CH_2-2-F-4-Br-benzyl	1.96
23	CN	CH_2-4-Nitro-benzyl	2.57
24	CN	CH_2-2-Cl-benzyl	3.51
25	CN	CH_2-4-Cl-2-F-benzyl	1.17
26	CN	$(CH_2)_2$-2-Naphthalen-2-yl	1.03
27	CN	CH_2-4-methoxy-benzyl	2.65
28	CN	CH_2-2,4-dichlorobenzyl	1.20
29	CN	CH_2-2-F,4-Cl-benzyl	1.36
30	CN	$(CH_2)_2$-2-naphthyl	1.14
31	CN	CH_2-4-methoxybenzyl	2.34
32	CN	CH_2-2,3,4-trifluorobenzyl	1.90
33	CN	CH_2-3-acetamidobenzyl	0.90
34	CN	CH_2-3-aminobenzyl	2.21
35	CN	$(CH_2)_2$-4-hydroxybenzyl	2.17
36	CN	$(CH_2)_2$-4-aminobenzyl	0.73
37	CN	$(CH_2)_2$-4-methylbenzyl	2.09
38	CN	$(CH_2)_2$-4-methoxybenzyl	1.03
39	CN	$(CH_2)_2$-4-F-benzyl	1.38
40	CN	CH_2-4-methylbenzyl	1.69
41	CN	$(CH_2)_2$-4-Cl-benzyl	2.17
42	CN	$(CH_2)_2$-4-dimethylaminobenzyl	1.18
43	CN	CH_2-3-naphthyl	0.95
44	methoxy	CH_2-benzyl	11
45	trifluoromethyl	CH_2-CH-$(CH_3)_2$	12.8
46	morpholino	n-propyl	> 100
47	NC(=O)benzyl	n-propyl	> 100

Fig. 9B