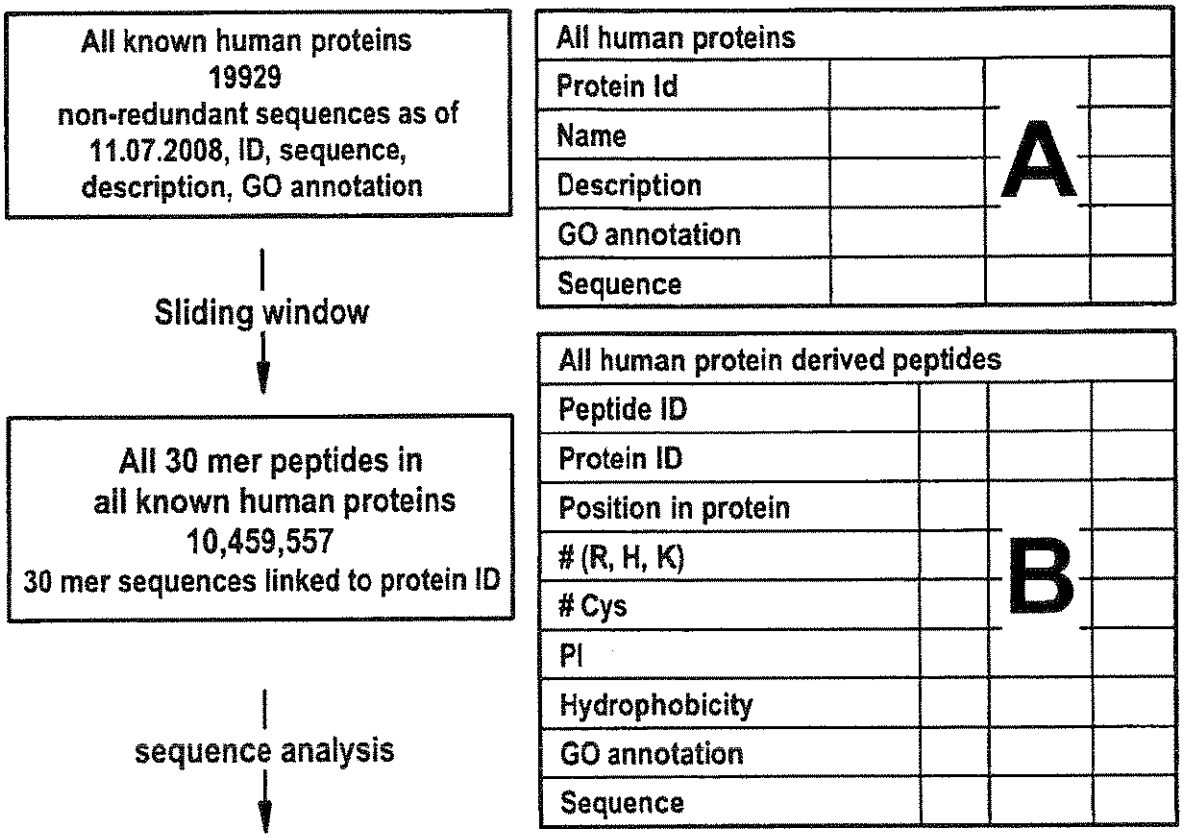
Fig. 1



Step	Filter	#	Rationale for filter
1	None (all peptides)	10,459,557	All human peptides
2	(H+K+R) >= 10	227,307	Fits search ‚pattern'
3	2 + GO ‚extracellular'	8630	Visible, exposed
4	3 + IEP >= 12.53	1000	Poly-cation effects?
5	3 + Phob >= -25.4	1000	Membrane effects?
6	Intersect 4 and 5	91	Combined effects
7	6 + nonred. ProtID	29	Combine clusters
8	3 + similarity to TAT> 6	135	CPP prediction
9	8 + nonred. ProtID	10	Combine clusters
10	3 + nonred. ProtID	583	Combine clusters
11	10 + subj. Description	~ 60	Membrane/lipids/bactericidal

C

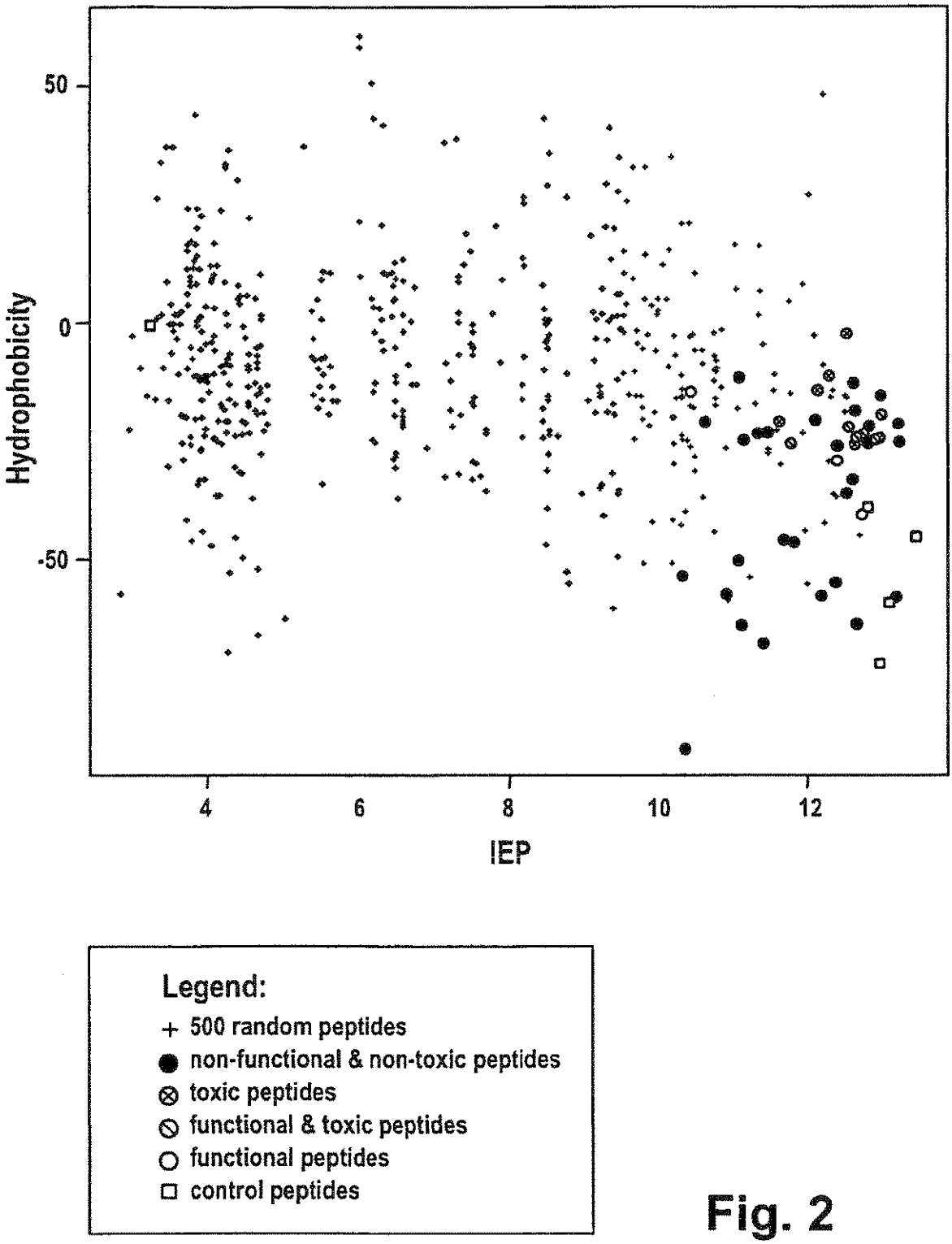

50
0
-50
Hydrophobicity
4
6
8
10
12
IEP
Legend:
+ 500 random peptides
● non-functional & non-toxic peptides
⊗ toxic peptides
⊘ functional & toxic peptides
○ functional peptides
□ control peptides

Fig. 2

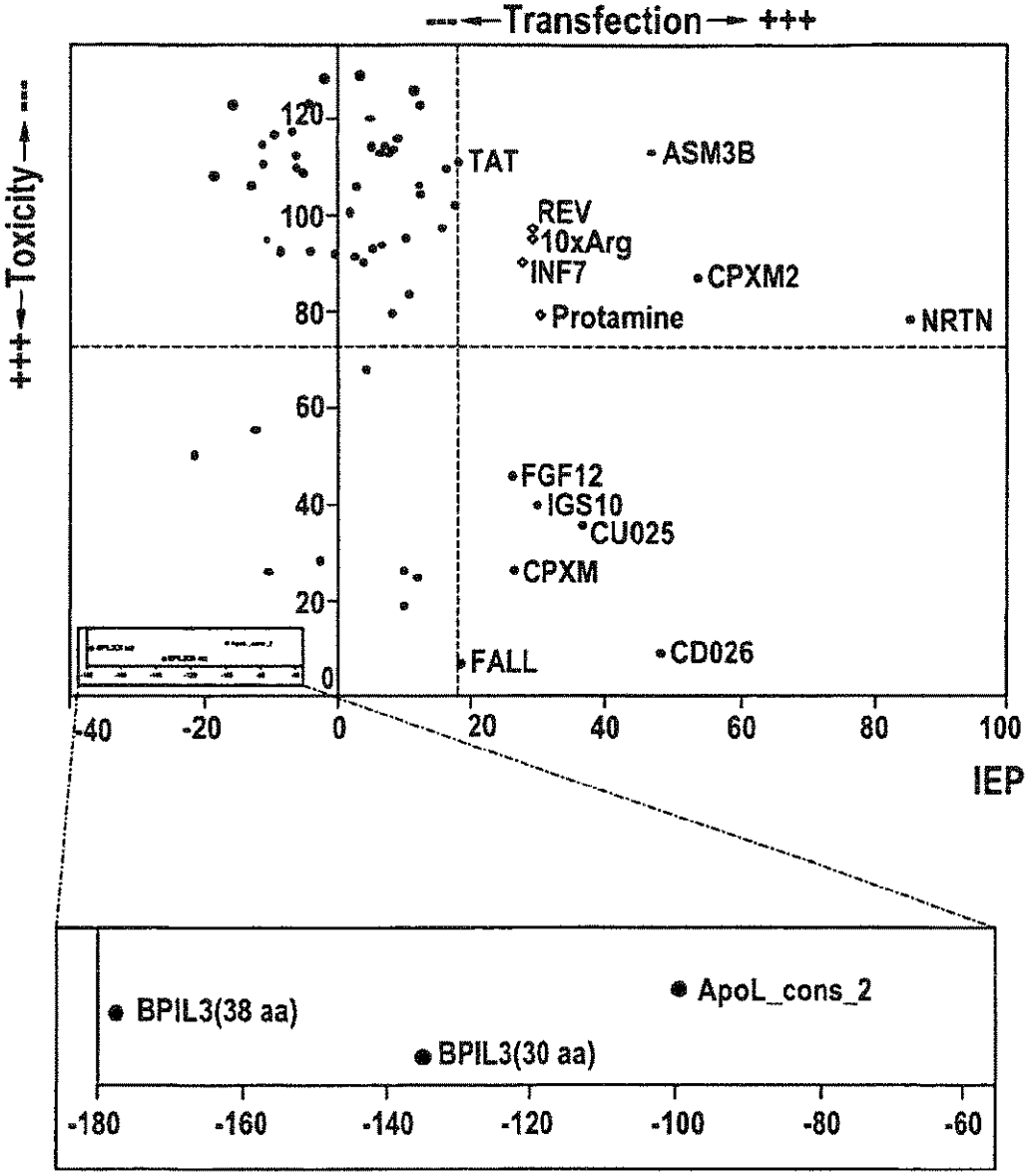

---←Transfection→ +++
+++←Toxicity→ ---
120
100
80
60
40
20
0
TAT
ASM3B
REV
10xArg
INF7
CPXM2
Protamine
NRTN
FGF12
IGS10
CU025
CPXM
FALL
CD026
-40
-20
0
20
40
60
80
100
IEP
BPIL3(38 aa)
ApoL_cons_2
BPIL3(30 aa)
-180
-160
-140
-120
-100
-80
-60

Fig. 3

Fig. 4

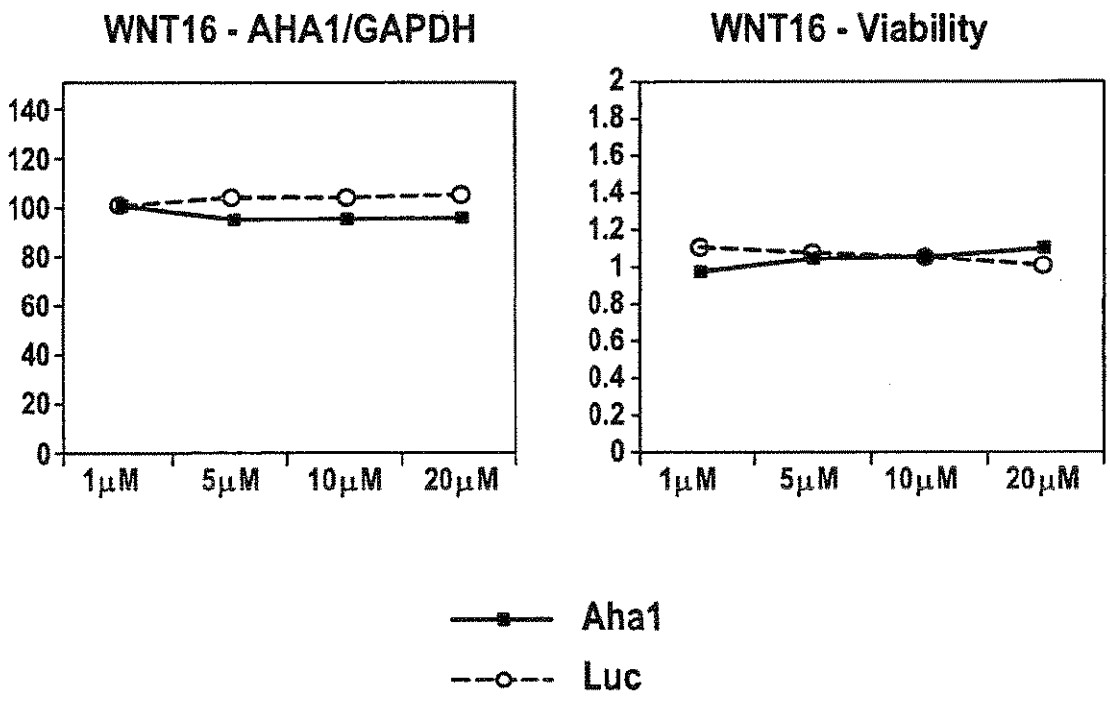

WNT16 - AHA1/GAPDH
140
120
100
80
60
40
20
0
1µM
5µM
10µM
20µM
WNT16 - Viability
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
1µM
5µM
10µM
20µM
Aha1
Luc

Fig. 5

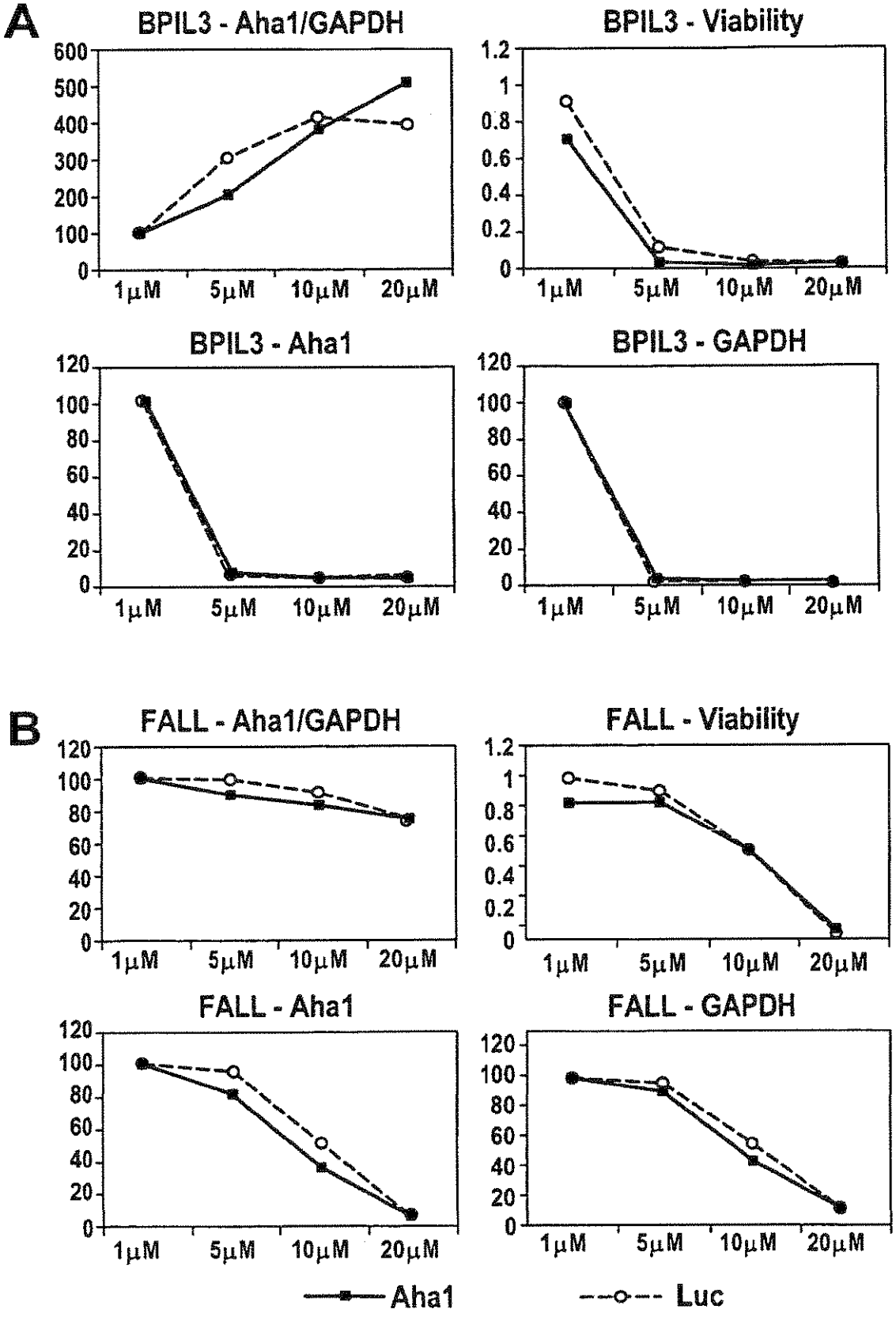

A
BPIL3 - Aha1/GAPDH
BPIL3 - Viability
BPIL3 - Aha1
BPIL3 - GAPDH
B
FALL - Aha1/GAPDH
FALL - Viability
FALL - Aha1
FALL - GAPDH
1µM
5µM
10µM
20µM
Aha1
Luc

Fig. 6

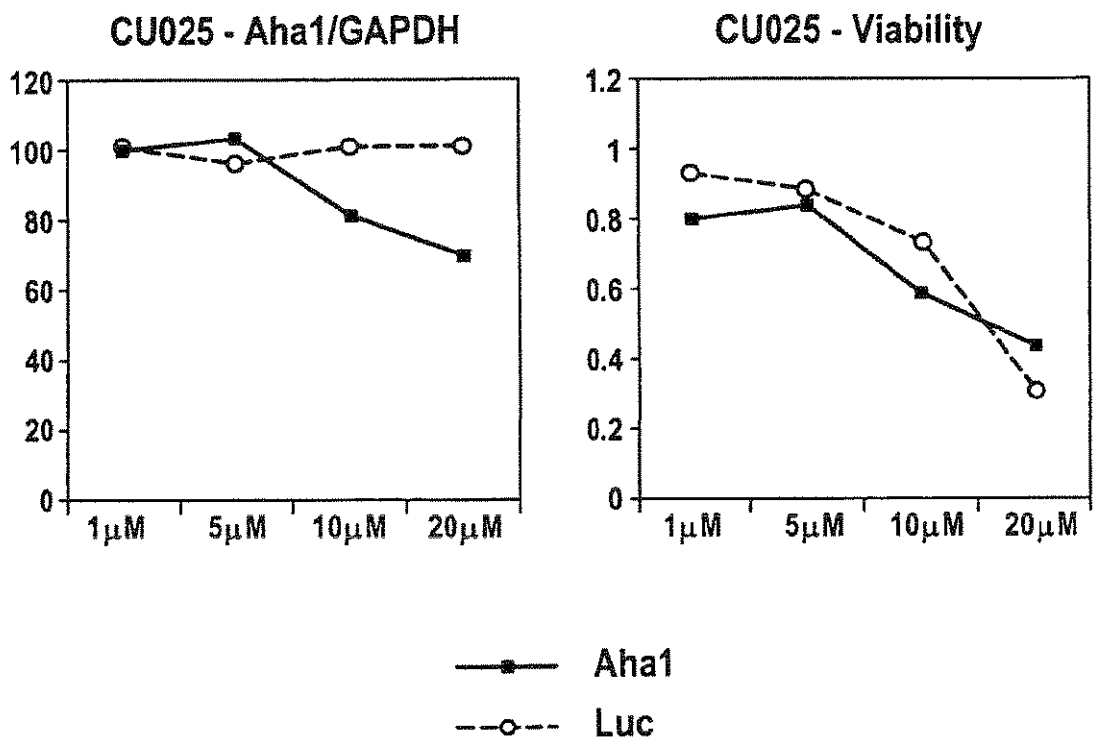

CU025 - Aha1/GAPDH
120
100
80
60
40
20
0
1μM
5μM
10μM
20μM
CU025 - Viability
1.2
1
0.8
0.6
0.4
0.2
0
1μM
5μM
10μM
20μM
Aha1
Luc

Fig. 7

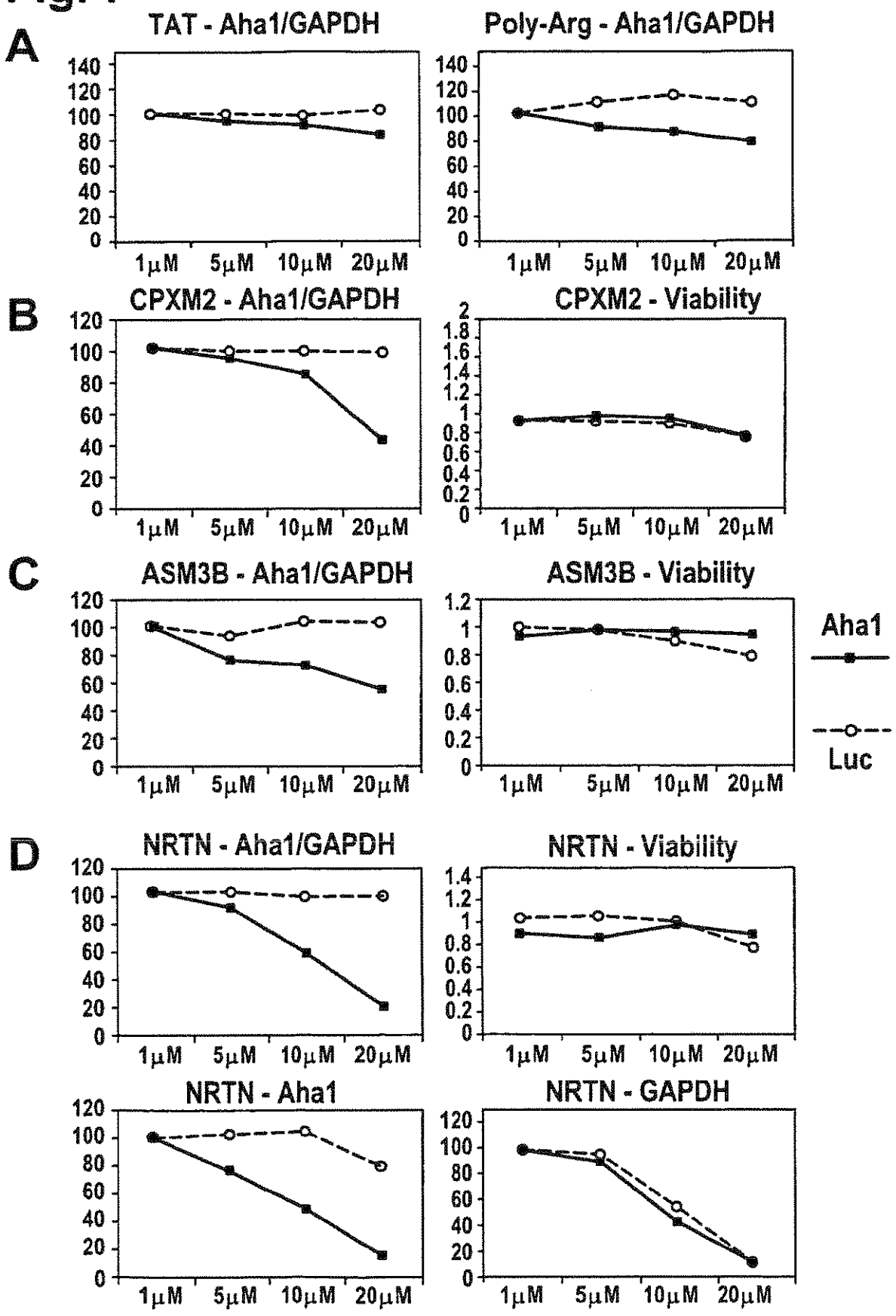

A
TAT - Aha1/GAPDH
Poly-Arg - Aha1/GAPDH
B
CPXM2 - Aha1/GAPDH
CPXM2 - Viability
C
ASM3B - Aha1/GAPDH
ASM3B - Viability
Aha1
Luc
D
NRTN - Aha1/GAPDH
NRTN - Viability
NRTN - Aha1
NRTN - GAPDH
1µM 5µM 10µM 20µM

Fig. 8

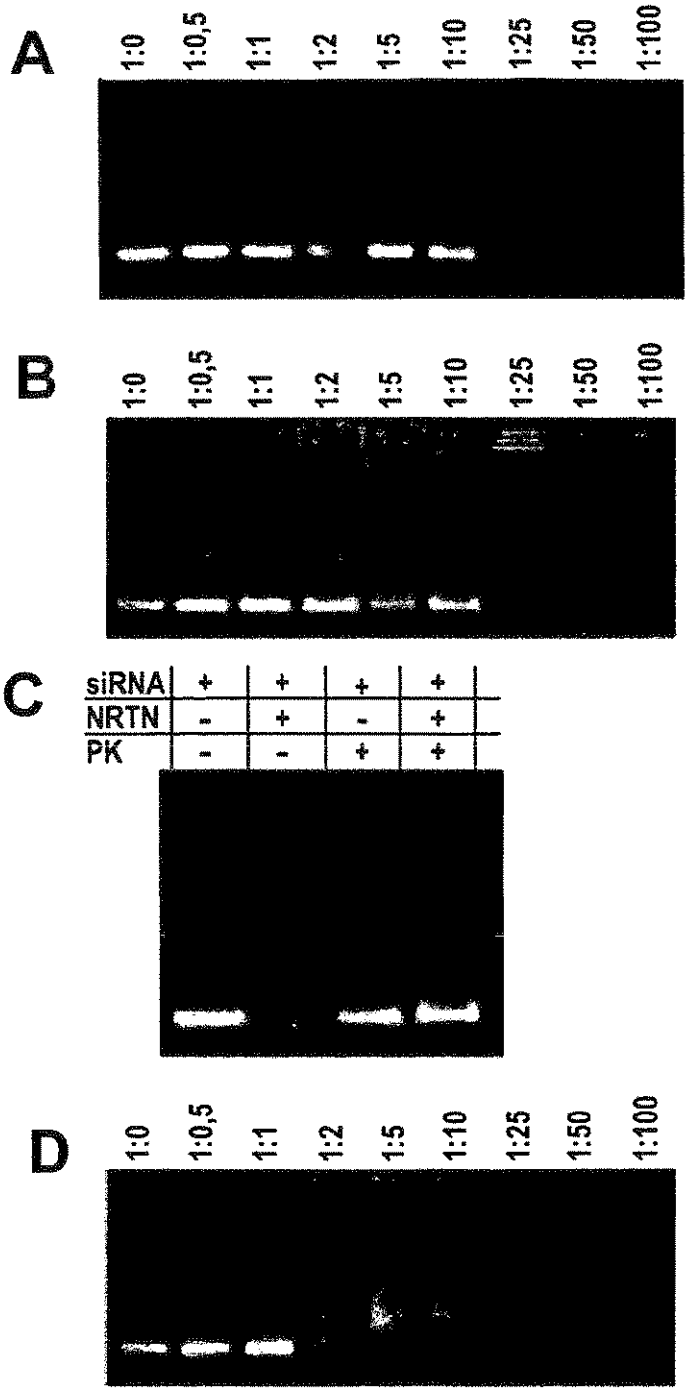

A
1:0
1:0,5
1:1
1:2
1:5
1:10
1:25
1:50
1:100
B
1:0
1:0,5
1:1
1:2
1:5
1:10
1:25
1:50
1:100
C
siRNA + + + +
NRTN - + - +
PK - - + +
D
1:0
1:0,5
1:1
1:2
1:5
1:10
1:25
1:50
1:100

Fig. 9

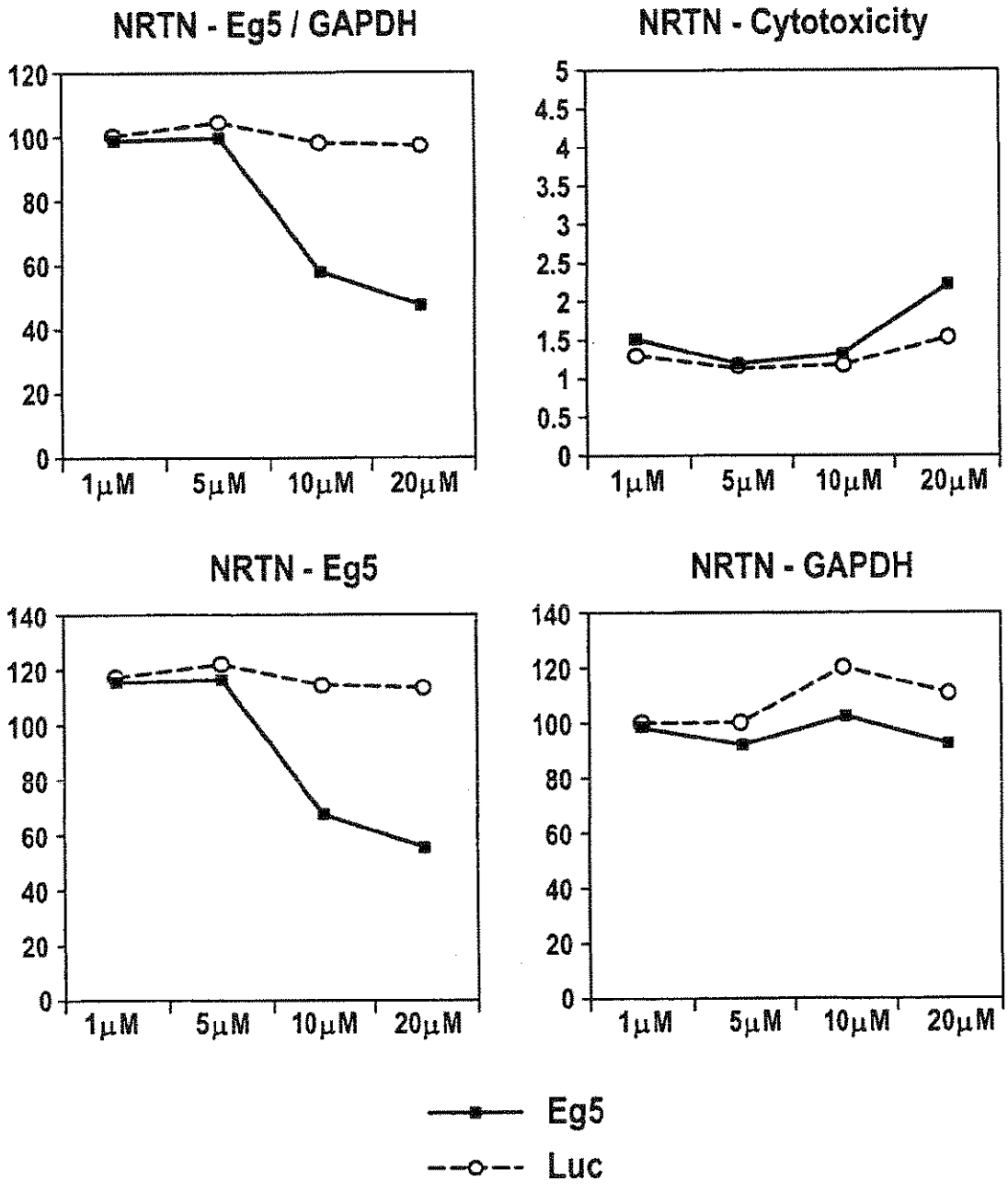

NRTN - Eg5 / GAPDH
120
100
80
60
40
20
0
1µM
5µM
10µM
20µM
NRTN - Cytotoxicity
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1µM
5µM
10µM
20µM
NRTN - Eg5
140
120
100
80
60
40
20
0
1µM
5µM
10µM
20µM
NRTN - GAPDH
140
120
100
80
60
40
20
0
1µM
5µM
10µM
20µM
Eg5
Luc

Fig. 10

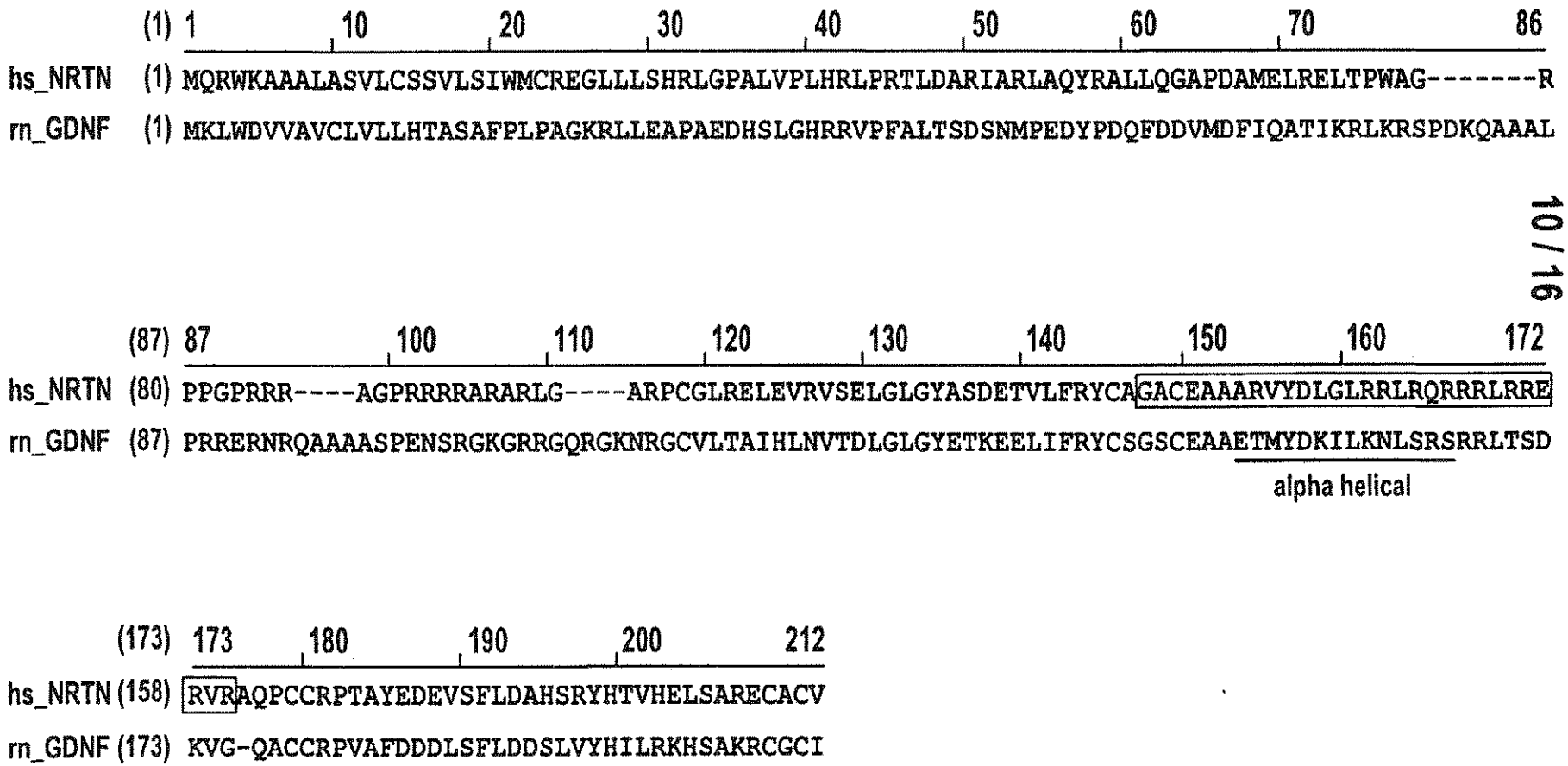

(1) 1 10 20 30 40 50 60 70 86
hs_NRTN (1) MQRWKAAALASVLCSSVLSIWMCREGLLLSHRLGPALVPLHRLPRTLDARIARLAQYRALLQGAPDAMELRELTPWAG-------R
rn_GDNF (1) MKLWDVVAVCLVLLHTASAFPLPAGKRLLEAPAEDHSLGHRRVPFALTSDSNMPEDYPDQFDDVMDFIQATIKRLKRSPDKQAAAL
(87) 87 100 110 120 130 140 150 160 172
hs_NRTN (80) PPGPRRR----AGPRRRRARARLG----ARPCGLRELEVRVSELGLGYASDETVLFRYCAGACEAAARVYDLGLRRLRQRRRLRRE
rn_GDNF (87) PRRERNRQAAAASPENSRGKGRRGQRGKNRGCVLTAIHLNVTDLGLGYETKEELIFRYCSGSCEAAETMYDKILKNLSRSRRLTSD
alpha helical
(173) 173 180 190 200 212
hs_NRTN (158) RVRAQPCCRPTAYEDEVSFLDAHSRYHTVHELSARECACV
rn_GDNF (173) KVG-QACCRPVAFDDDLSFLDDSLVYHILRKHSAKRCGCI

Fig. 11

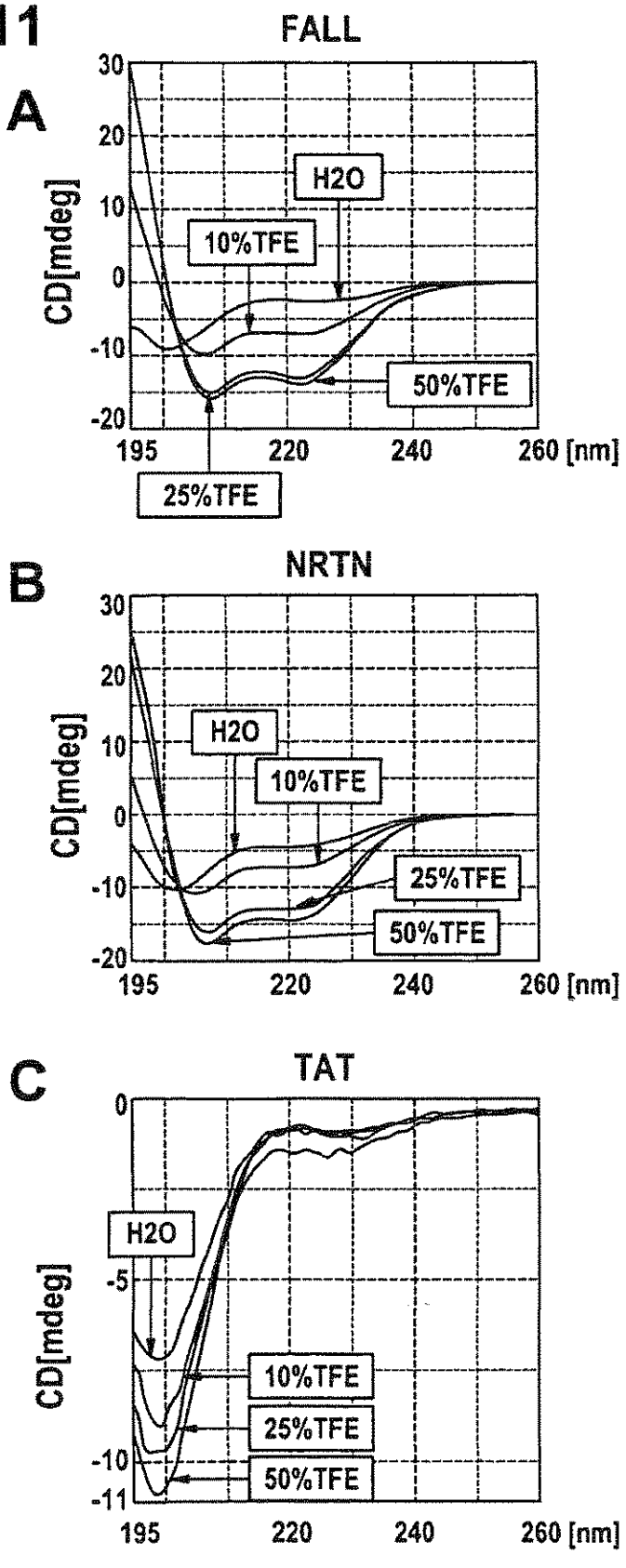
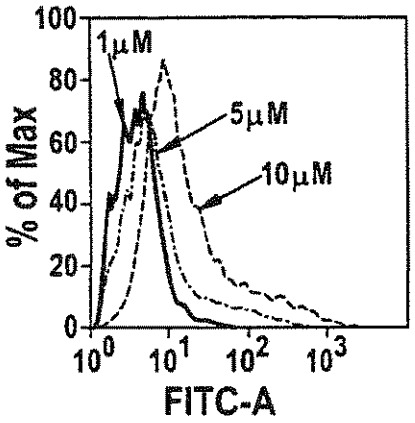

A
FALL
CD[mdeg]
30
20
10
0
-10
-20
H2O
10%TFE
50%TFE
25%TFE
195
220
240
260 [nm]
B
NRTN
CD[mdeg]
30
20
10
0
-10
-20
H2O
10%TFE
25%TFE
50%TFE
195
220
240
260 [nm]
C
TAT
CD[mdeg]
0
-5
-10
-11
H2O
10%TFE
25%TFE
50%TFE
195
220
240
260 [nm]

Fig. 12

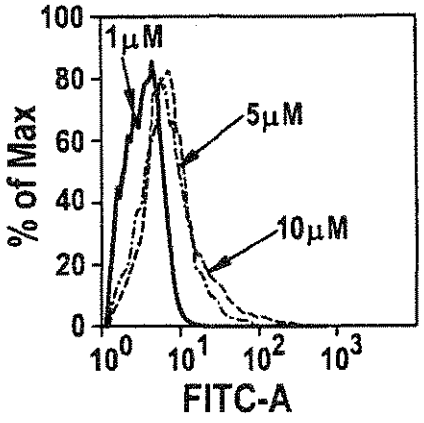
a



Viable/FITC-A subset

	WELL ID	Geom. Mean, FITC-A	Count
---	MCF7 CF-TAT 10μM	17,26	9157
---	MCF7 CF-TAT 5 μM	7,20	8509
—	MCF7 CF-TAT 1μM	4,06	7327

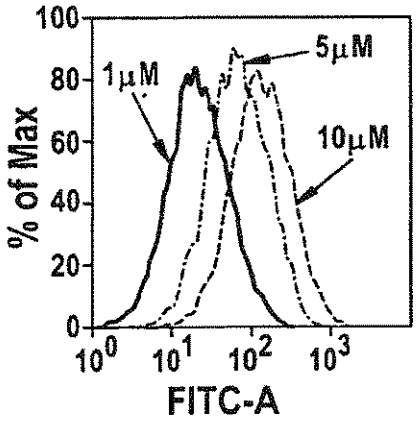
b



Viable/FITC-A subset

	WELL ID	Geom. Mean, FITC-A	Count
---	MCF7 CF-WNT 16 10μM	8,54	8973
---	MCF7 CF-WNT 16 5μM	6,61	8778
—	MCF7 CF-WNT 16 1μM	3,57	7148

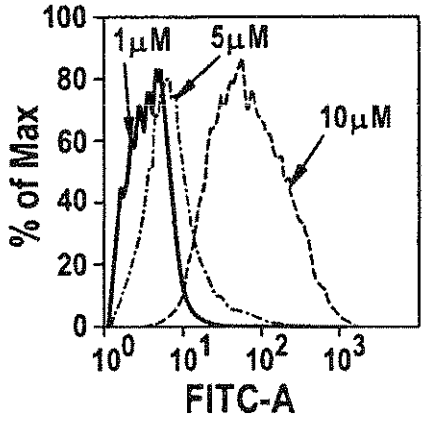
c



Viable/FITC-A subset

	WELL ID	Geom. Mean, FITC-A	Count
---	MCF7 CF-FALL 10μM	123,23	9079
---	MCF7 CF-FALL 5μM	68,55	9146
—	MCF7 CF-FALL 1μM	22,41	9085

d



Viable/FITC-A subset

	WELL ID	Geom. Mean, FITC-A	Count
---	MCF7 CF-NRTN 10μM	70,23	9132
---	MCF7 CF-NRTN 5μM	7,44	8942
—	MCF7 CF-NRTN 1μM	3,87	7362

Fig. 13

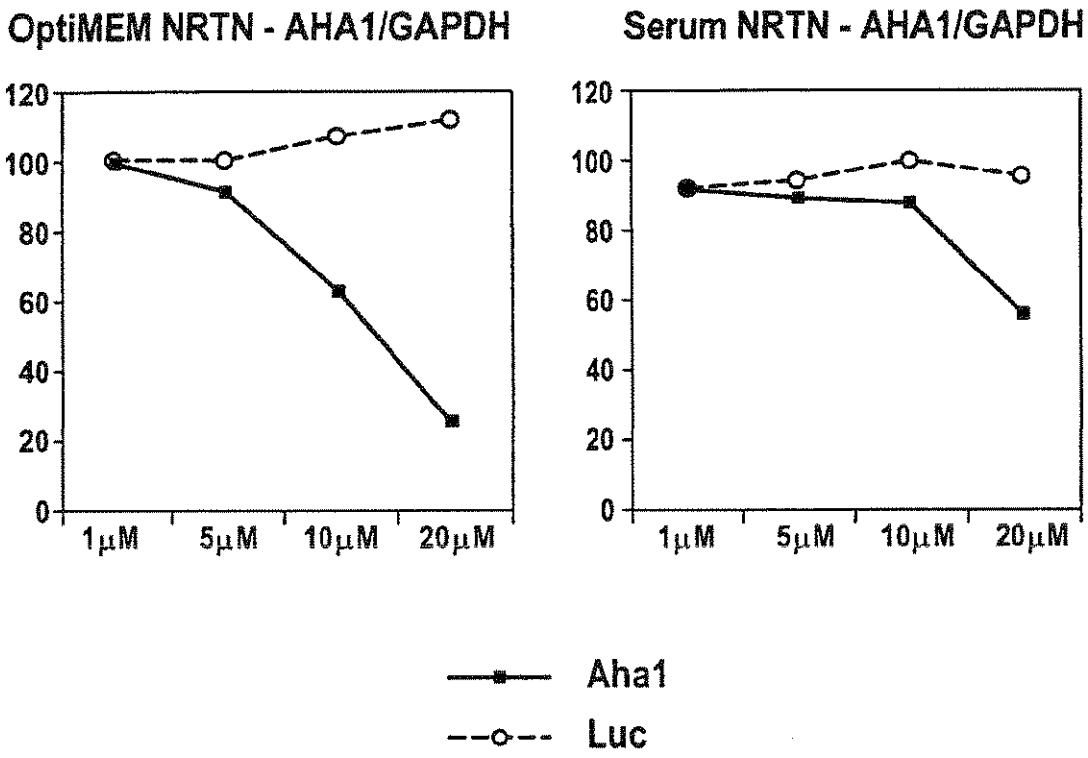
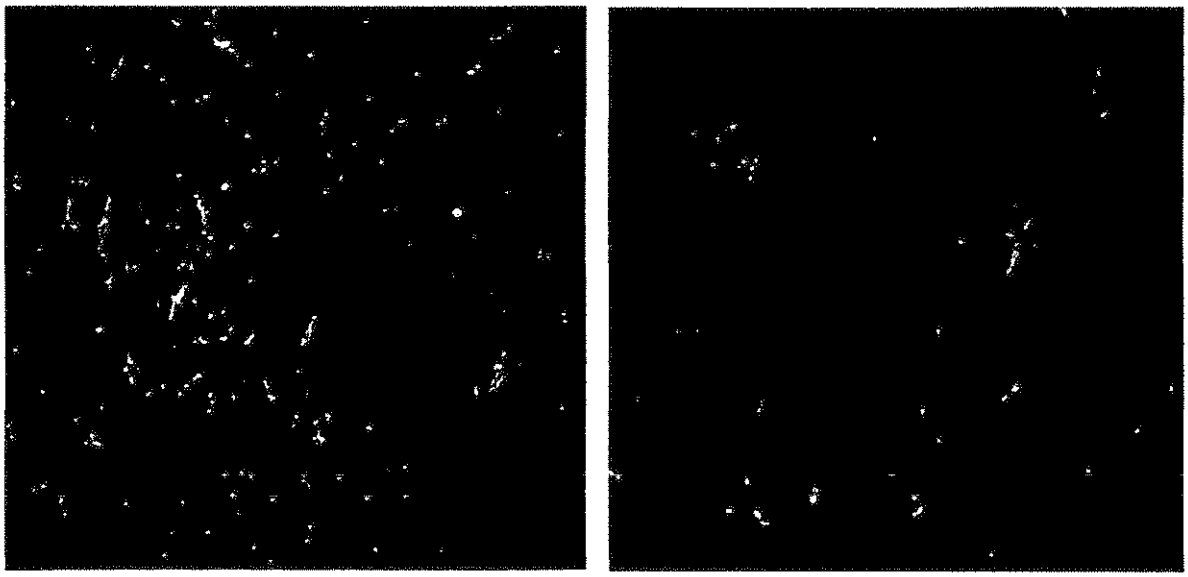
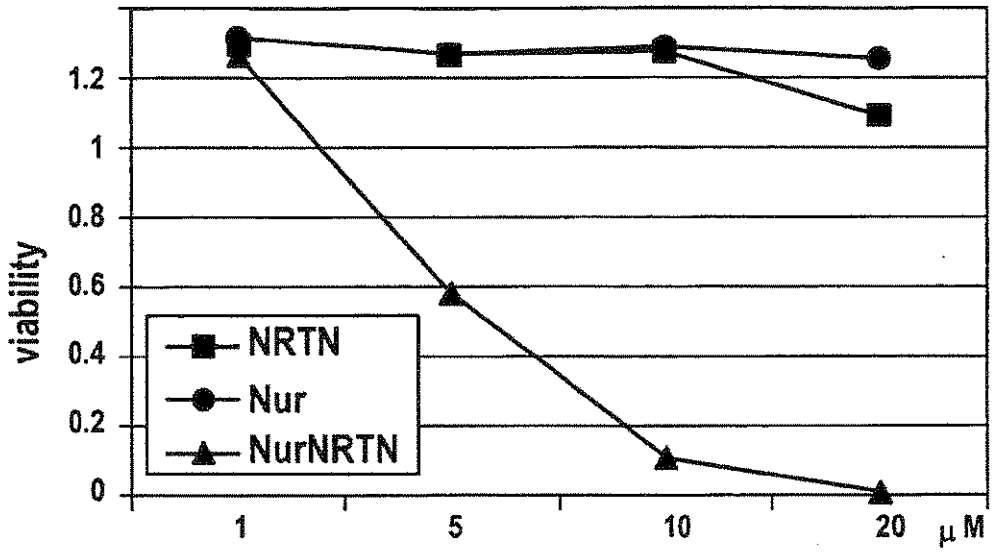

OptiMEM NRTN - AHA1/GAPDH
Serum NRTN - AHA1/GAPDH
120
100
80
60
40
20
0
1µM
5µM
10µM
20µM
Aha1
Luc

Fig. 14



FITC-NRTN NRTN-FITC

Fig. 15



Nor/Nur ● FSRSLHSLLVDL

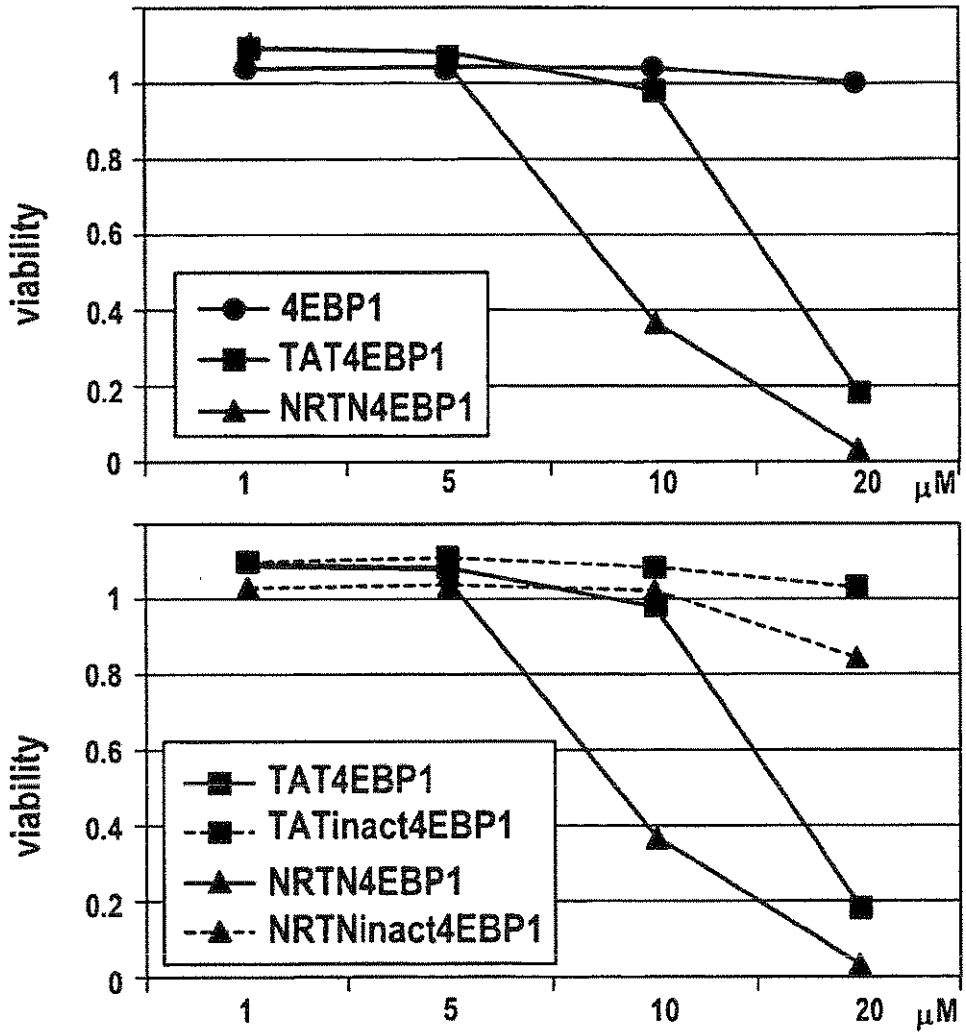
NRTN ■ GAAEAAARVYDLGLRRLRQRRRLRRERVRA

NurNRTN ▲ FSRSLHSLLYDLGLRRLRQRRRLRRERVRA

BCL2-conversion functionalitiy

CPP functionalitiy

Fig. 16




```
4EBP1                                          GTRIIYDRKFLMECRNSPVT
inact4EBP1                                     GTRIIGDGKFGMECRNSPVT
TAT4EBP1                            YGRKKRRQRRRGTRIIYDRKFLMECRNSPVT
TATinact4EBP1                       YGRKKRRQRRRGTRIIGDGKFGMECRNSPVT
NRTN4EBP1          GAAEAAARVYDLGLRRLRQRRRLRRERVRAGTRIIYDRKFLMECRNSPVT
NRTNinact4EBP1     GAAEAAARVYDLGLRRLRQRRRLRRERVRAGTRIIGDGKFGMECRNSPVT
                   ^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^
                   CPP functionalitiy                  4EBP1 functionalitiy
```