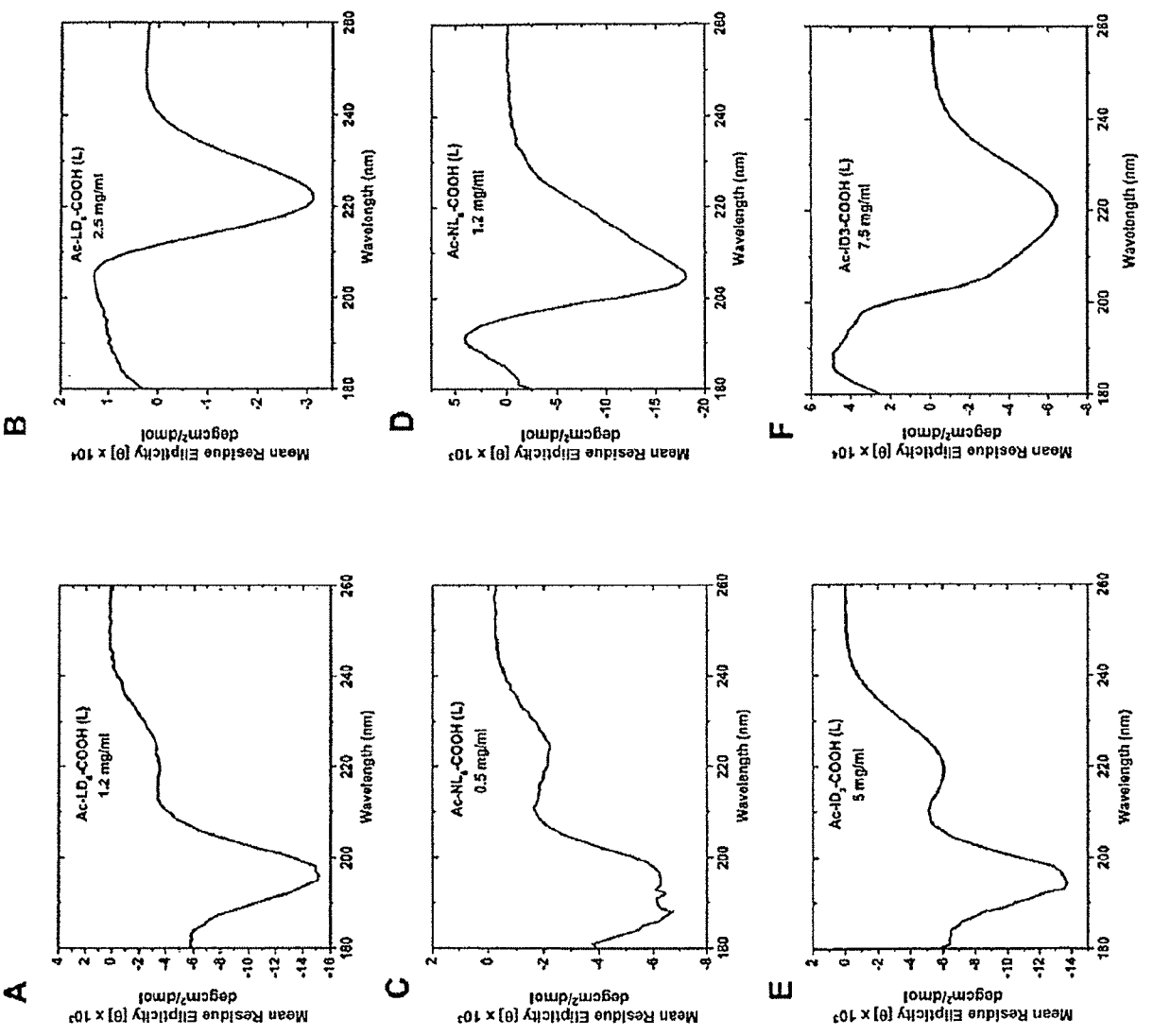

A
Ac-LD4-COOH (L)
1.2 mg/ml
Mean Residue Ellipticity [θ] x 10³
degcm²/dmol
Wavelength (nm)
B
Ac-LD4-COOH (L)
2.5 mg/ml
Mean Residue Ellipticity [θ] x 10⁴
degcm²/dmol
Wavelength (nm)
C
Ac-NL4-COOH (L)
0.5 mg/ml
Mean Residue Ellipticity [θ] x 10³
degcm²/dmol
Wavelength (nm)
D
Ac-NL4-COOH (L)
1.2 mg/ml
Mean Residue Ellipticity [θ] x 10³
degcm²/dmol
Wavelength (nm)
E
Ac-4D3-COOH (L)
5 mg/ml
Mean Residue Ellipticity [θ] x 10³
degcm²/dmol
Wavelength (nm)
F
Ac-4D3-COOH (L)
7.5 mg/ml
Mean Residue Ellipticity [θ] x 10⁴
degcm²/dmol
Wavelength (nm)

Figure 1

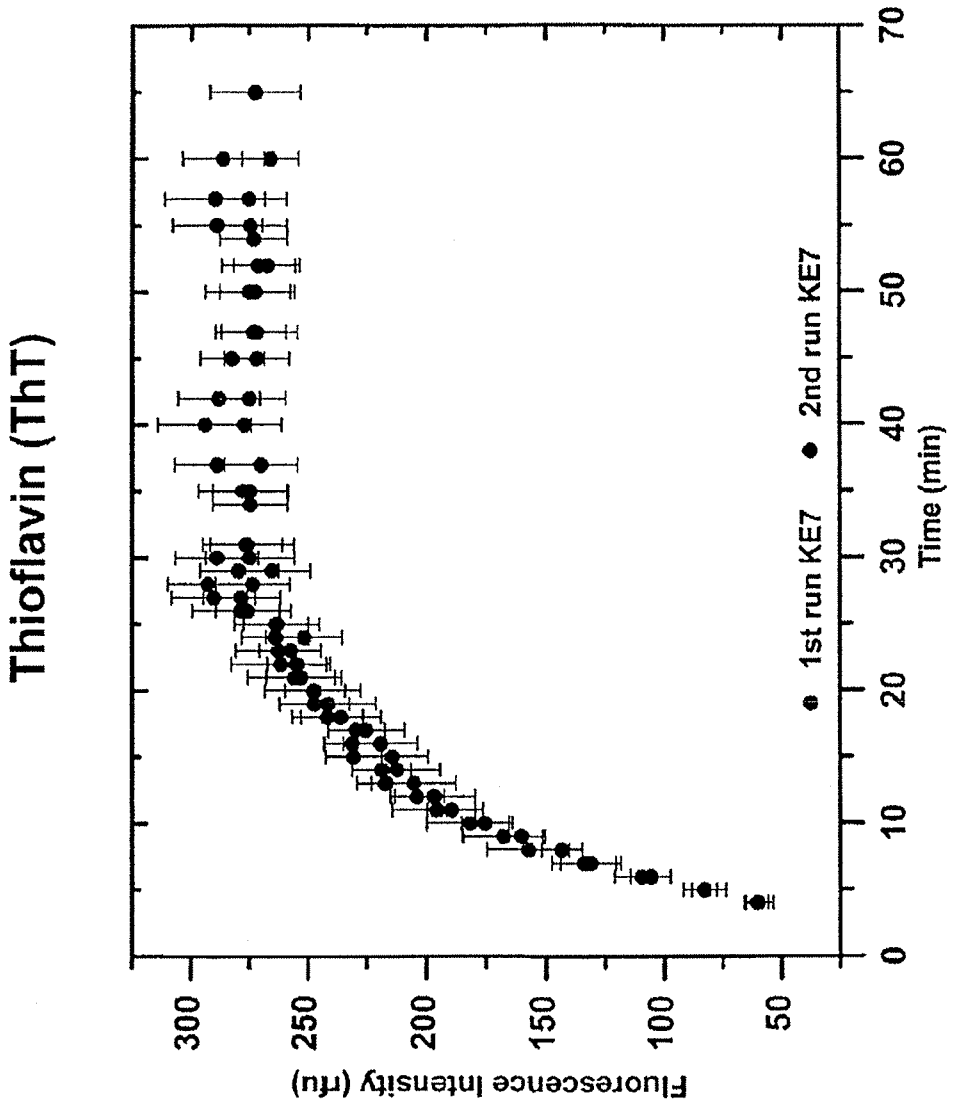

Thioflavin (ThT)
Fluorescence Intensity (rfu)
300
250
200
150
100
50
0
10
20
30
40
50
60
70
Time (min)
1st run KE7
2nd run KE7

Figure 2

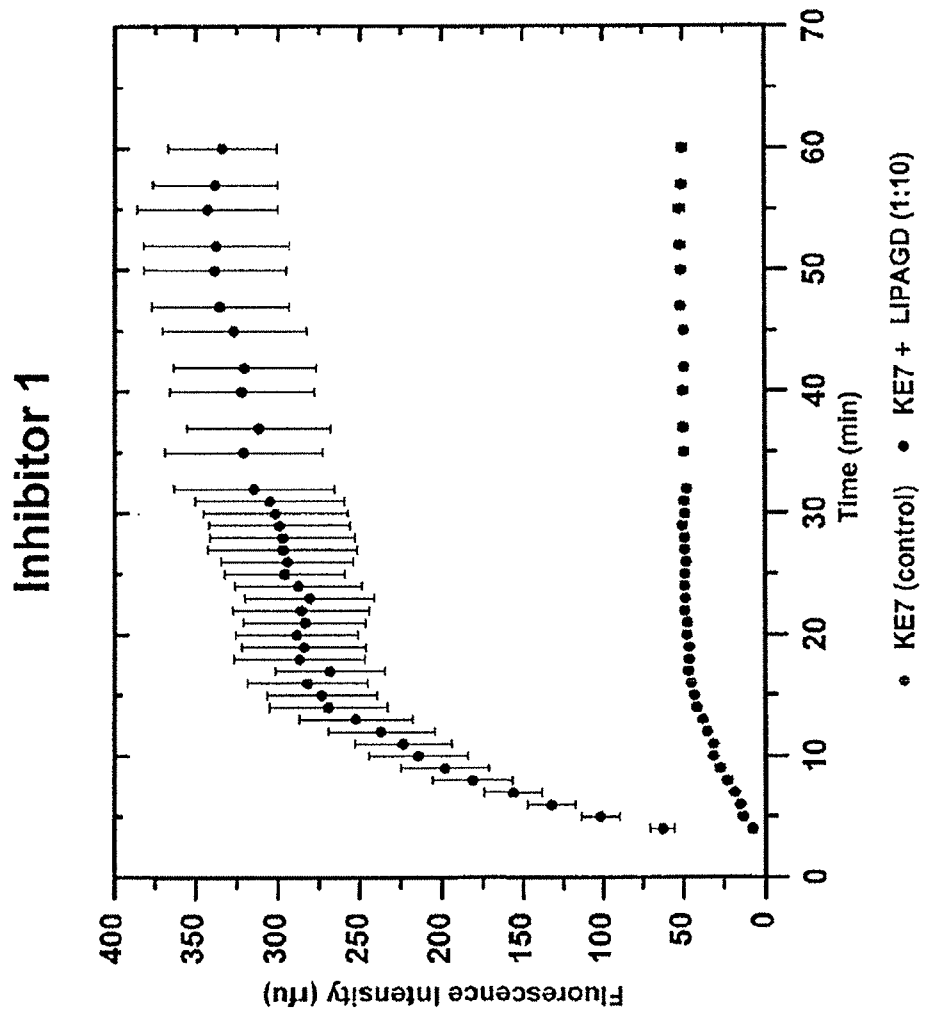

Inhibitor 1
Fluorescence Intensity (rfu)
400
350
300
250
200
150
100
50
0
0
10
20
30
40
50
60
70
Time (min)
KE7 (control)
KE7 + LIPAGD (1:10)

Figure 3

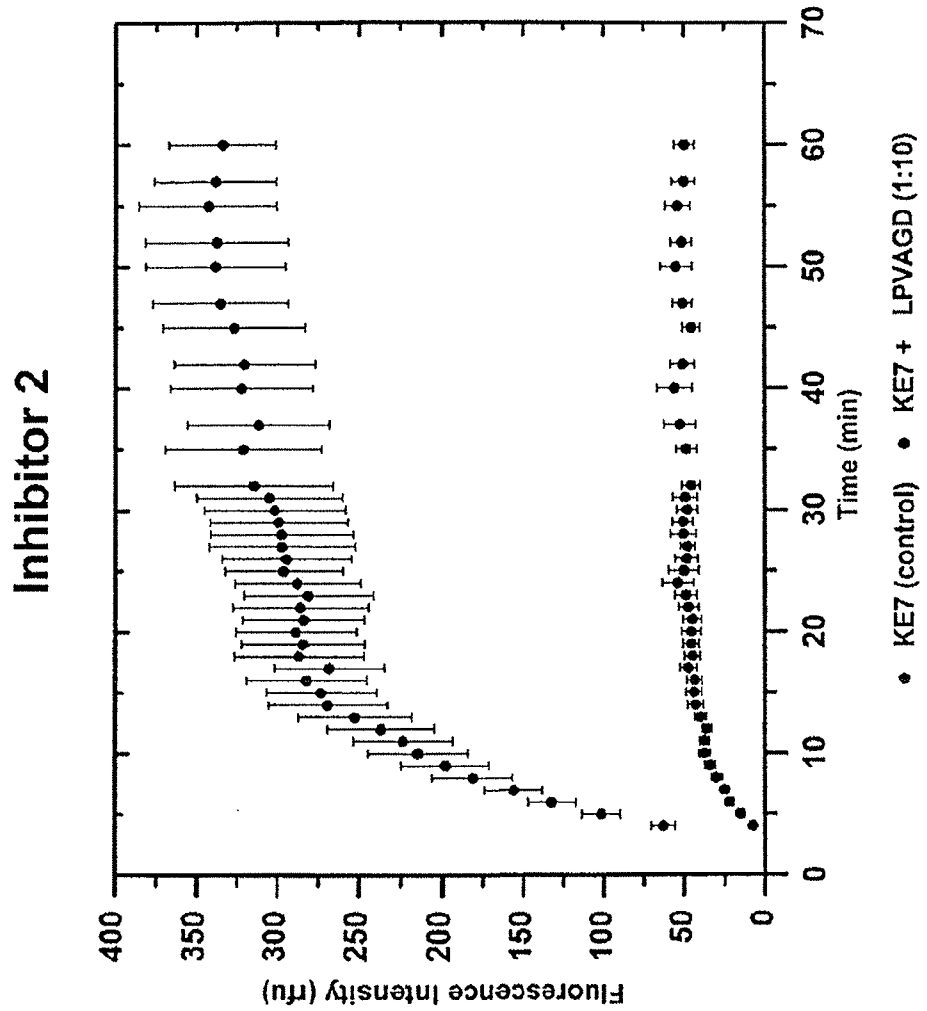

Inhibitor 2
Fluorescence Intensity (rfu)
400
350
300
250
200
150
100
50
0
0
10
20
30
40
50
60
70
Time (min)
KE7 (control)
KE7 + LPVAGD (1:10)

Figure 4

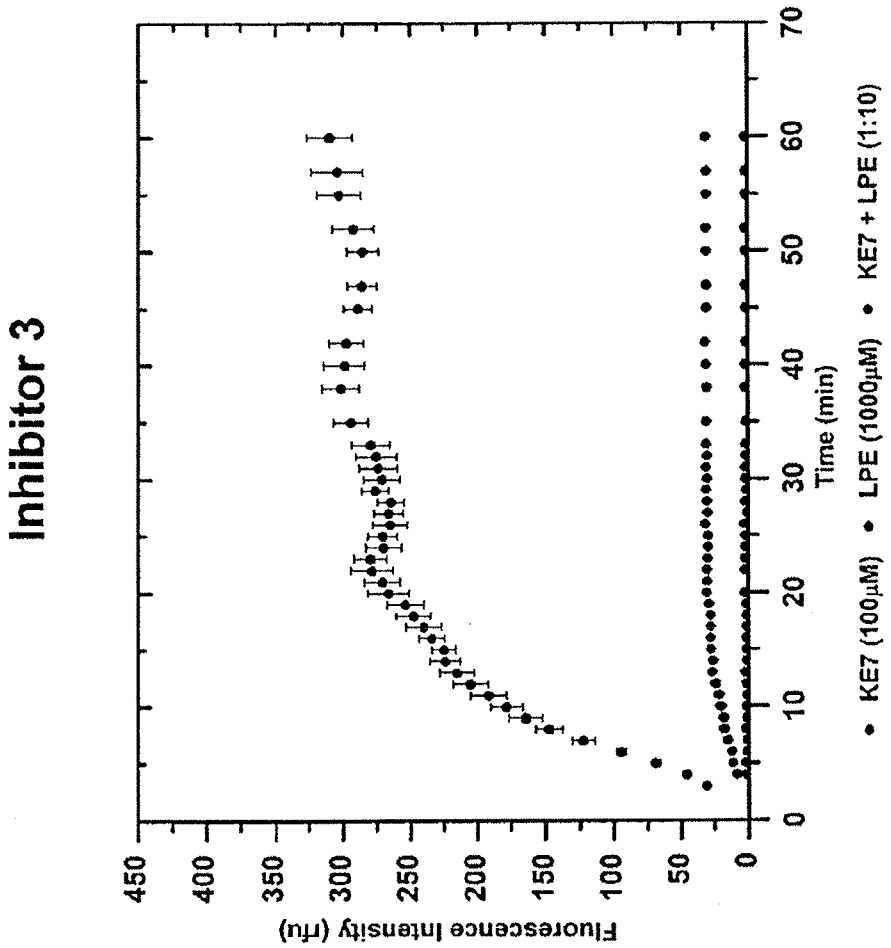

Inhibitor 3
Fluorescence Intensity (rfu)
450
400
350
300
250
200
150
100
50
0
0
10
20
30
40
50
60
70
Time (min)
KE7 (100µM)
LPE (1000µM)
KE7 + LPE (1:10)

Figure 5

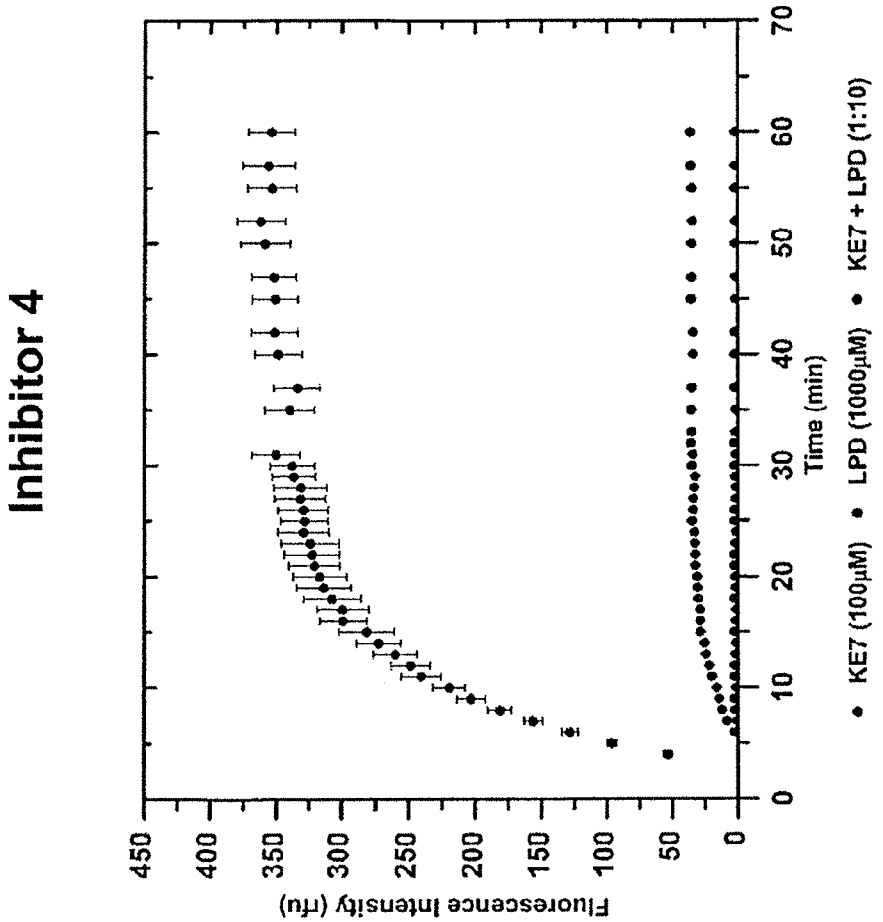

Inhibitor 4
Fluorescence Intensity (rfu)
450
400
350
300
250
200
150
100
50
0
0
10
20
30
40
50
60
70
Time (min)
KE7 (100µM)
LPD (1000µM)
KE7 + LPD (1:10)

Figure 6

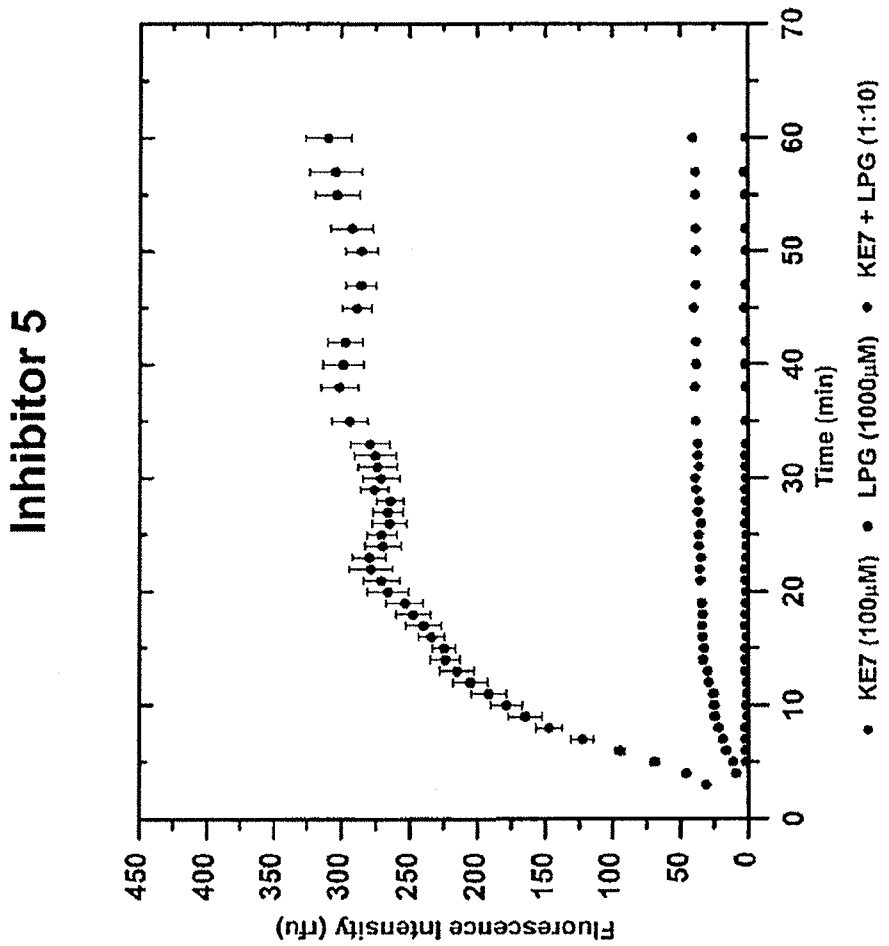

Inhibitor 5
Fluorescence Intensity (rfu)
450
400
350
300
250
200
150
100
50
0
0
10
20
30
40
50
60
70
Time (min)
KE7 (100µM)
LPG (1000µM)
KE7 + LPG (1:10)

Figure 7

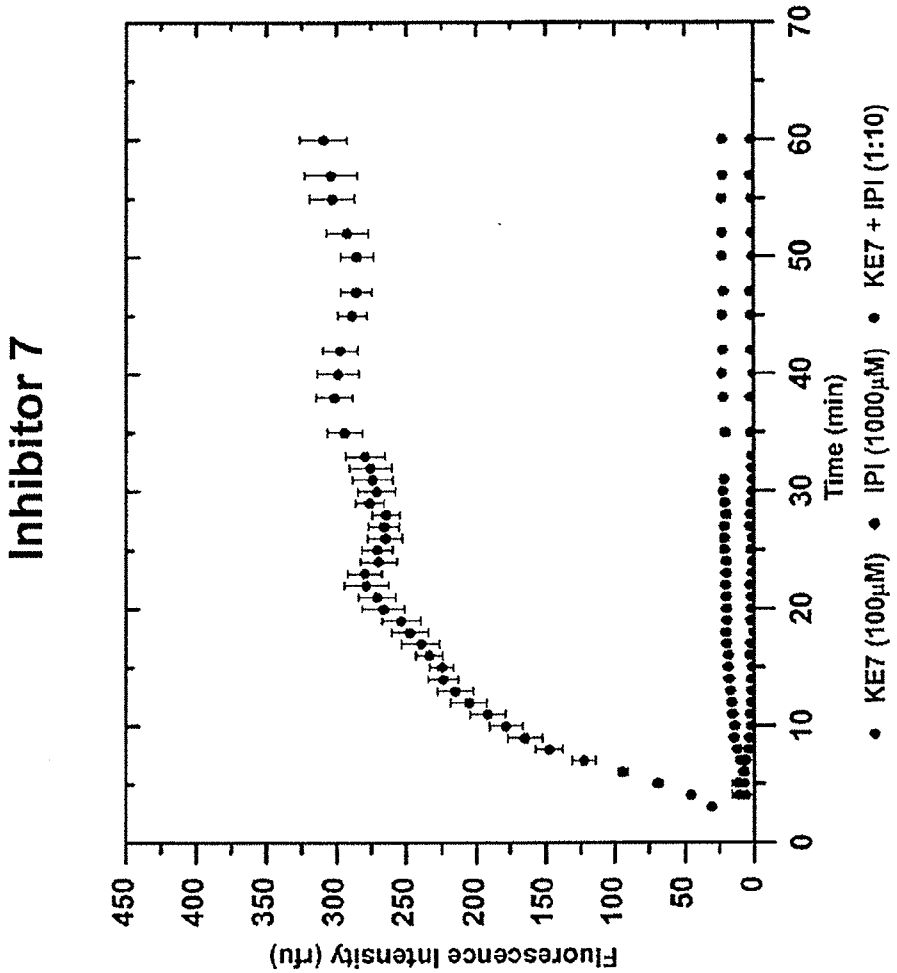

Inhibitor 7
Fluorescence Intensity (rfu)
0
50
100
150
200
250
300
350
400
450
0
10
20
30
40
50
60
70
Time (min)
KE7 (100μM)
IPI (1000μM)
KE7 + IPI (1:10)

Figure 8

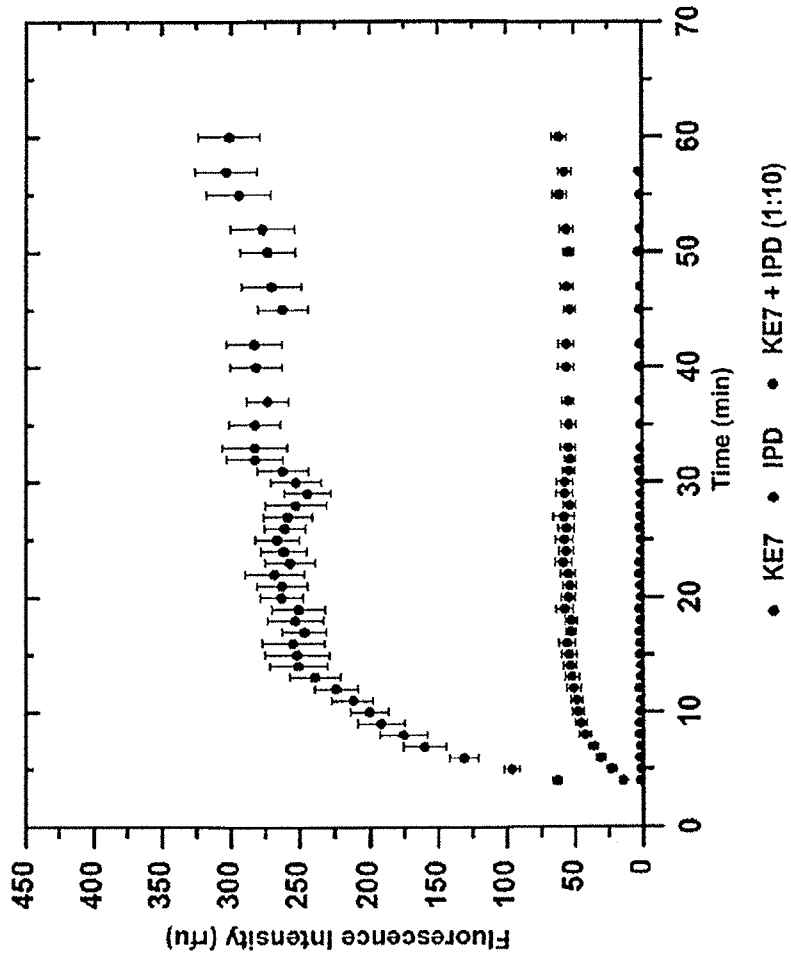

Inhibitor 8
Fluorescence Intensity (rfu)
Time (min)
KE7
IPD
KE7 + IPD (1:10)

Figure 9

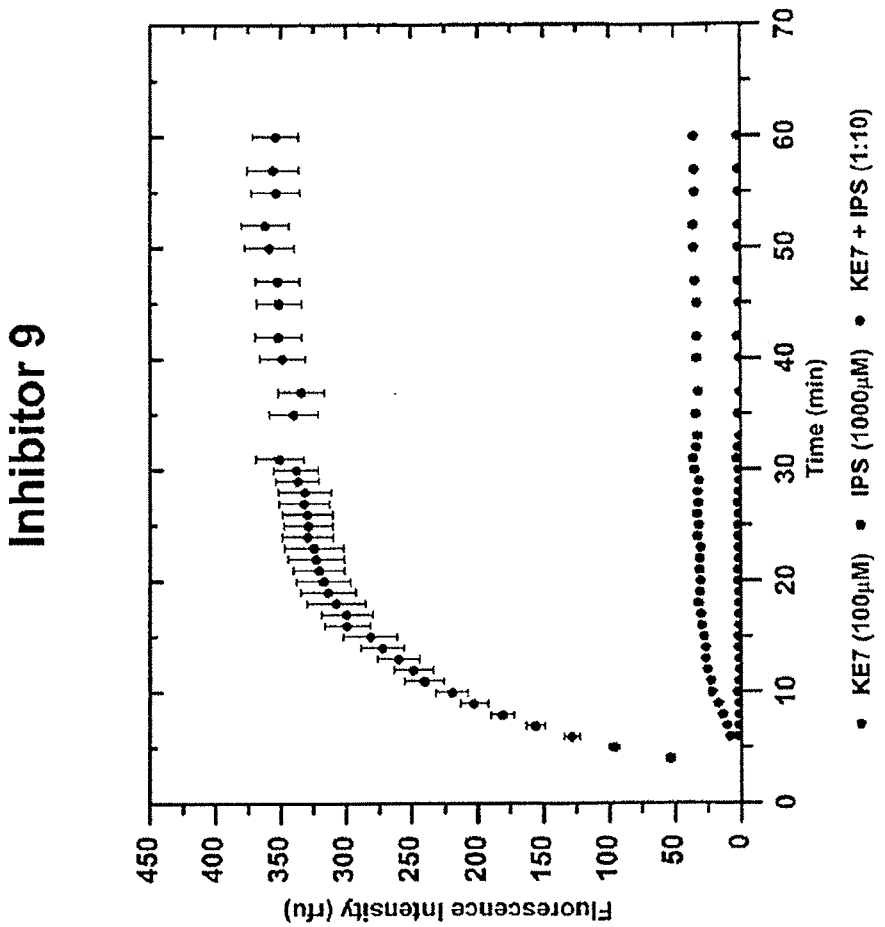

Inhibitor 9
Fluorescence Intensity (rfu)
450
400
350
300
250
200
150
100
50
0
0
10
20
30
40
50
60
70
Time (min)
KE7 (100µM)
IPS (1000µM)
KE7 + IPS (1:10)

Figure 10

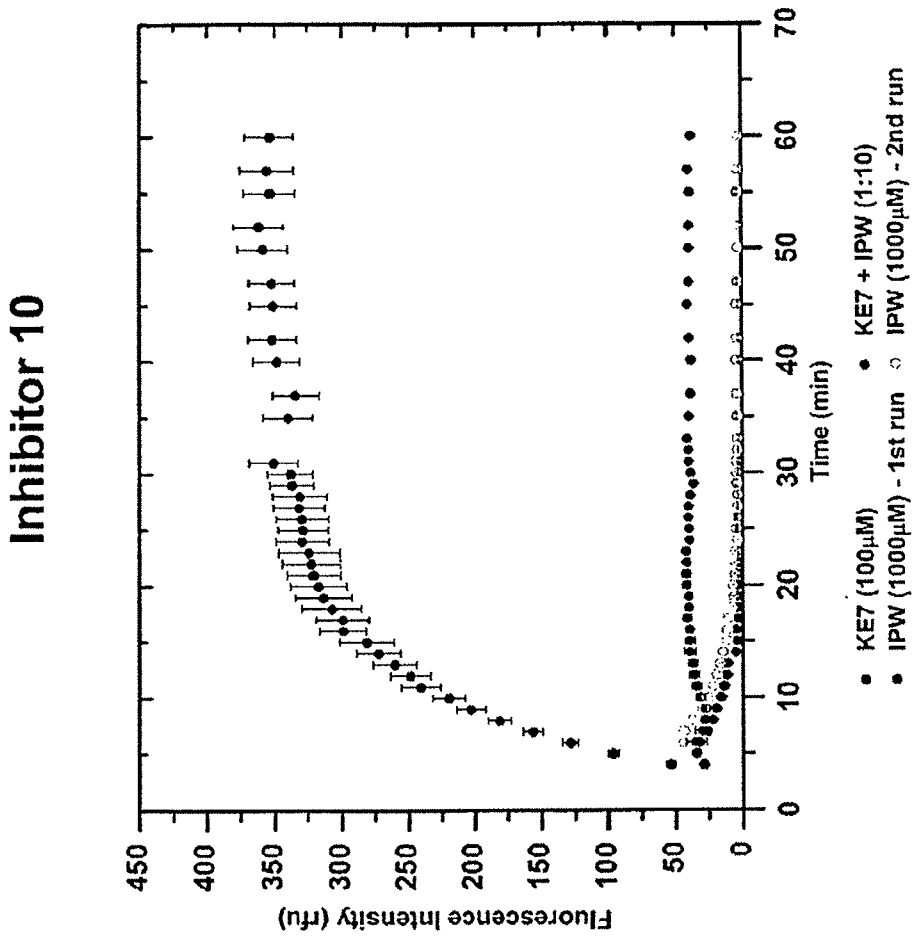

Inhibitor 10
Fluorescence Intensity (rfu)
Time (min)
KE7 (100µM)
KE7 + IPW (1:10)
IPW (1000µM) - 1st run
IPW (1000µM) - 2nd run

Figure 11

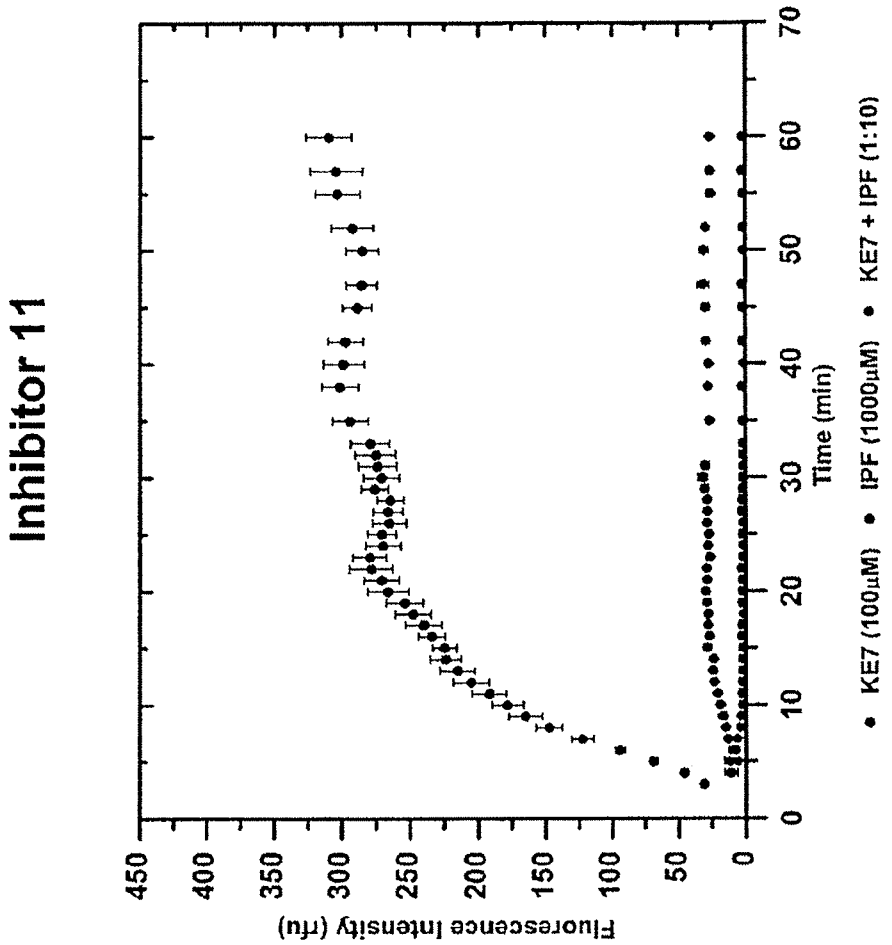

Inhibitor 11
Fluorescence Intensity (rfu)
Time (min)
KE7 (100µM)
IPF (1000µM)
KE7 + IPF (1:10)

Figure 12

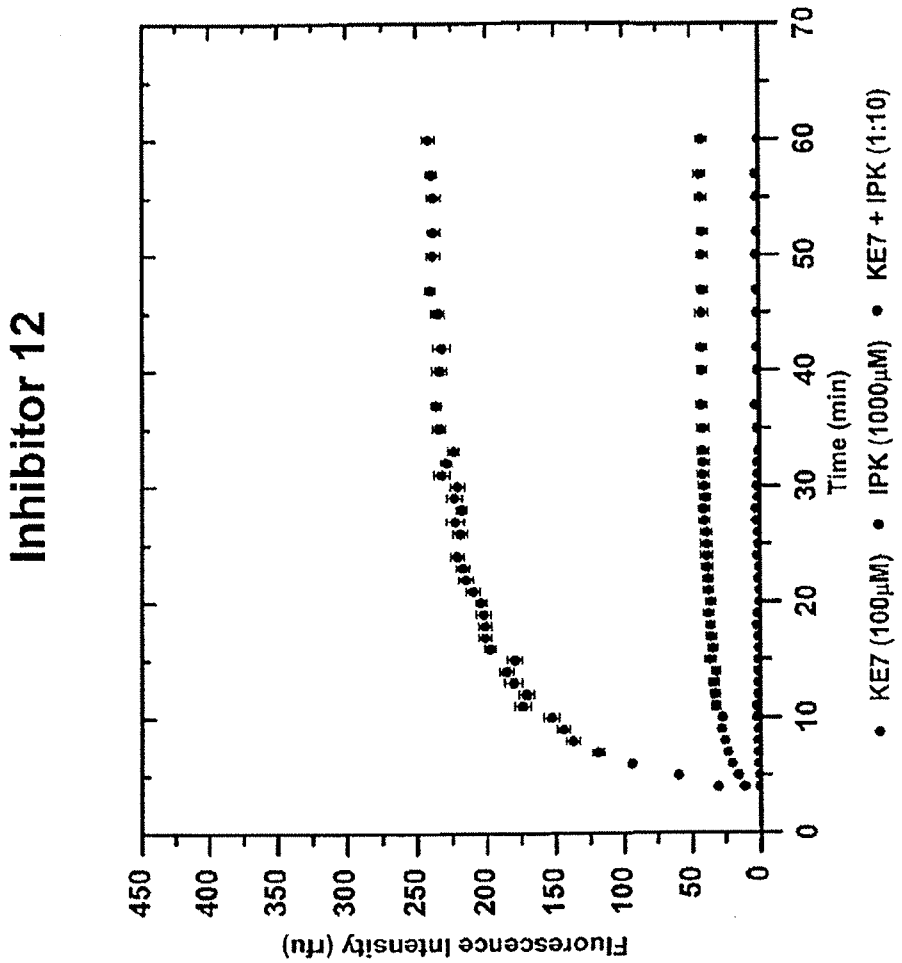

Inhibitor 12
Fluorescence Intensity (rfu)
450
400
350
300
250
200
150
100
50
0
0
10
20
30
40
50
60
70
Time (min)
KE7 (100µM)
IPK (1000µM)
KE7 + IPK (1:10)

Figure 13

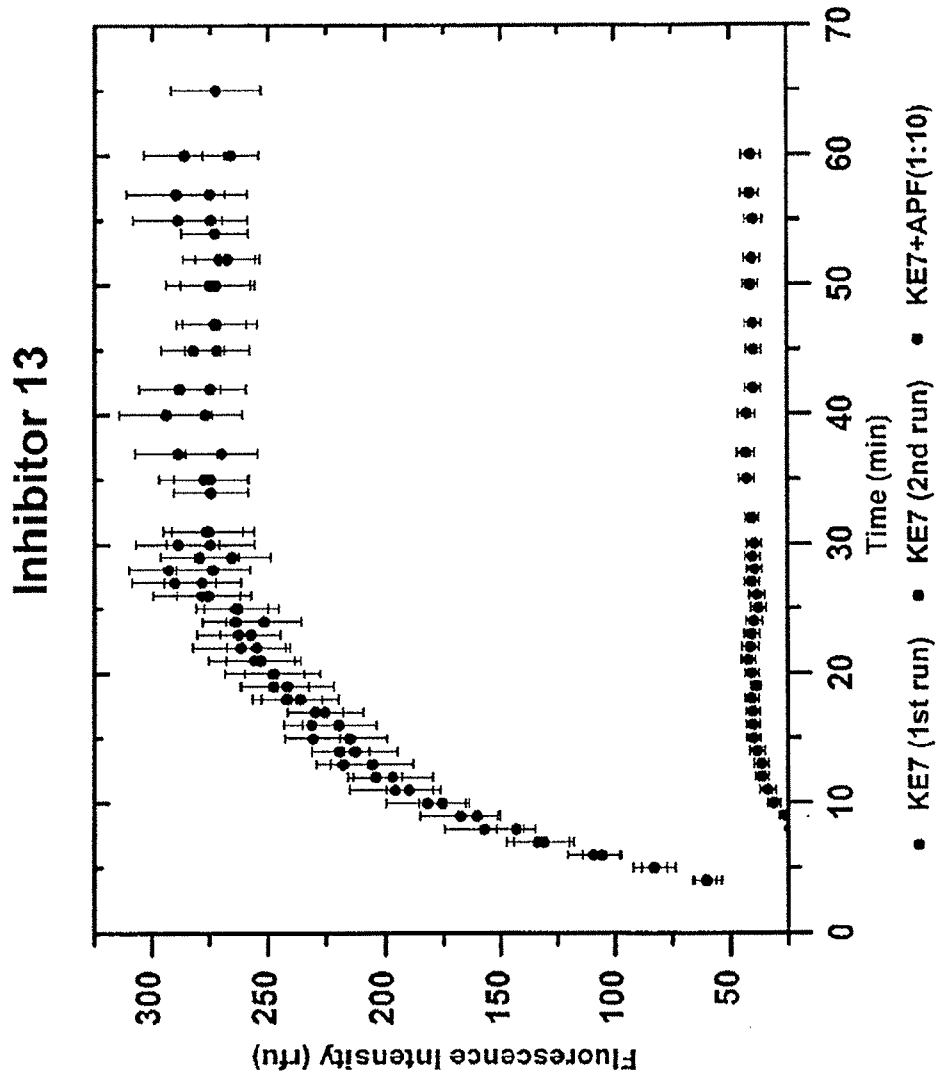

Inhibitor 13
Fluorescence Intensity (rfu)
300
250
200
150
100
50
0
10
20
30
40
50
60
70
Time (min)
KE7 (1st run)
KE7 (2nd run)
KE7+APF(1:10)

Figure 14

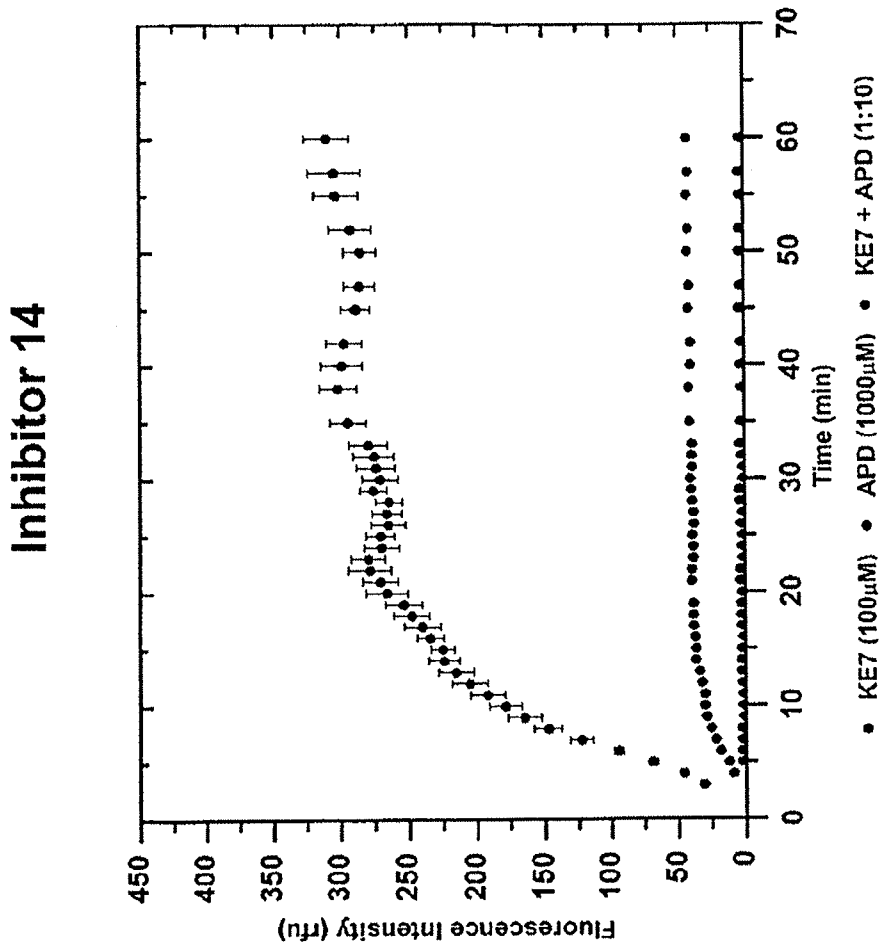

Inhibitor 14
Fluorescence Intensity (rfu)
450
400
350
300
250
200
150
100
50
0
0
10
20
30
40
50
60
70
Time (min)
KE7 (100µM)
APD (1000µM)
KE7 + APD (1:10)

Figure 15

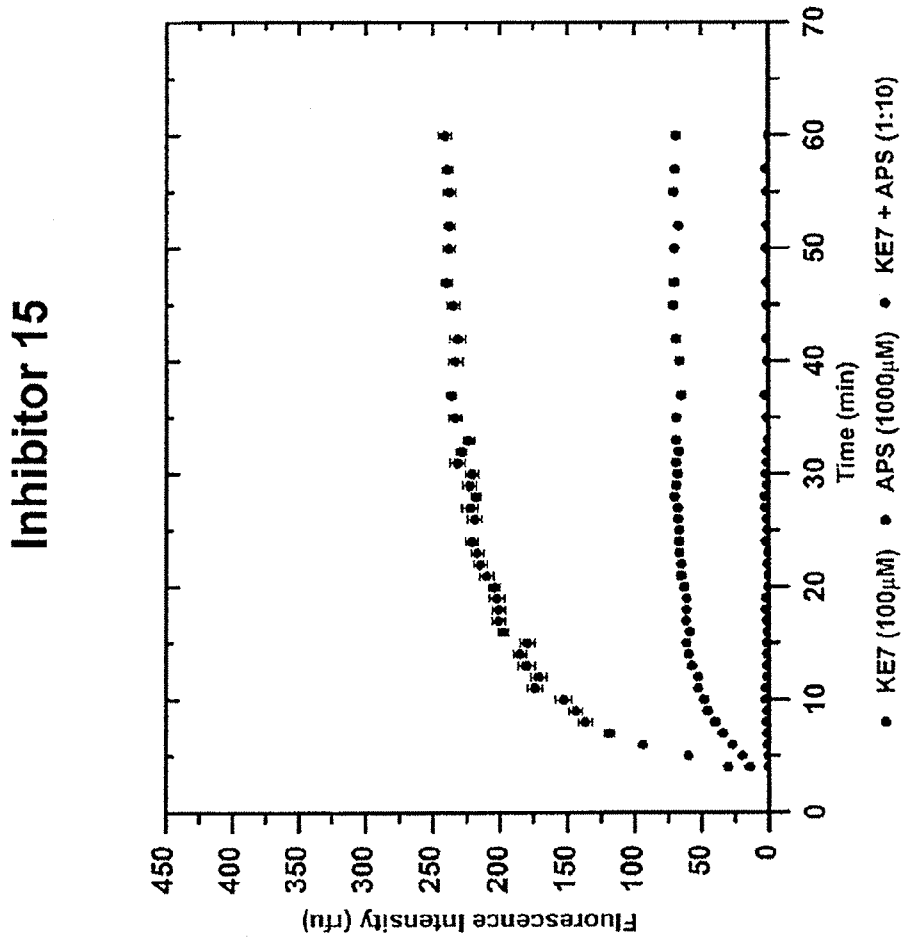

Inhibitor 15
Fluorescence Intensity (rfu)
Time (min)
KE7 (100μM)
APS (1000μM)
KE7 + APS (1:10)

Figure 16

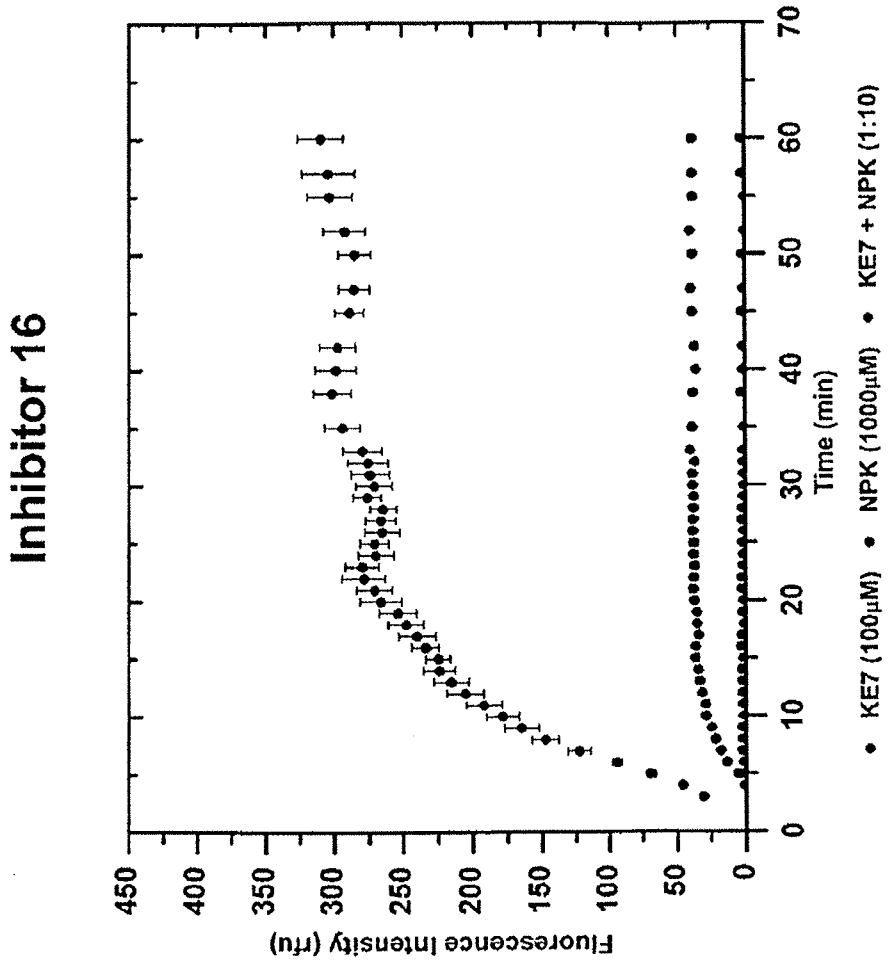

Inhibitor 16
Fluorescence Intensity (rfu)
Time (min)
KE7 (100µM)
NPK (1000µM)
KE7 + NPK (1:10)

Figure 17

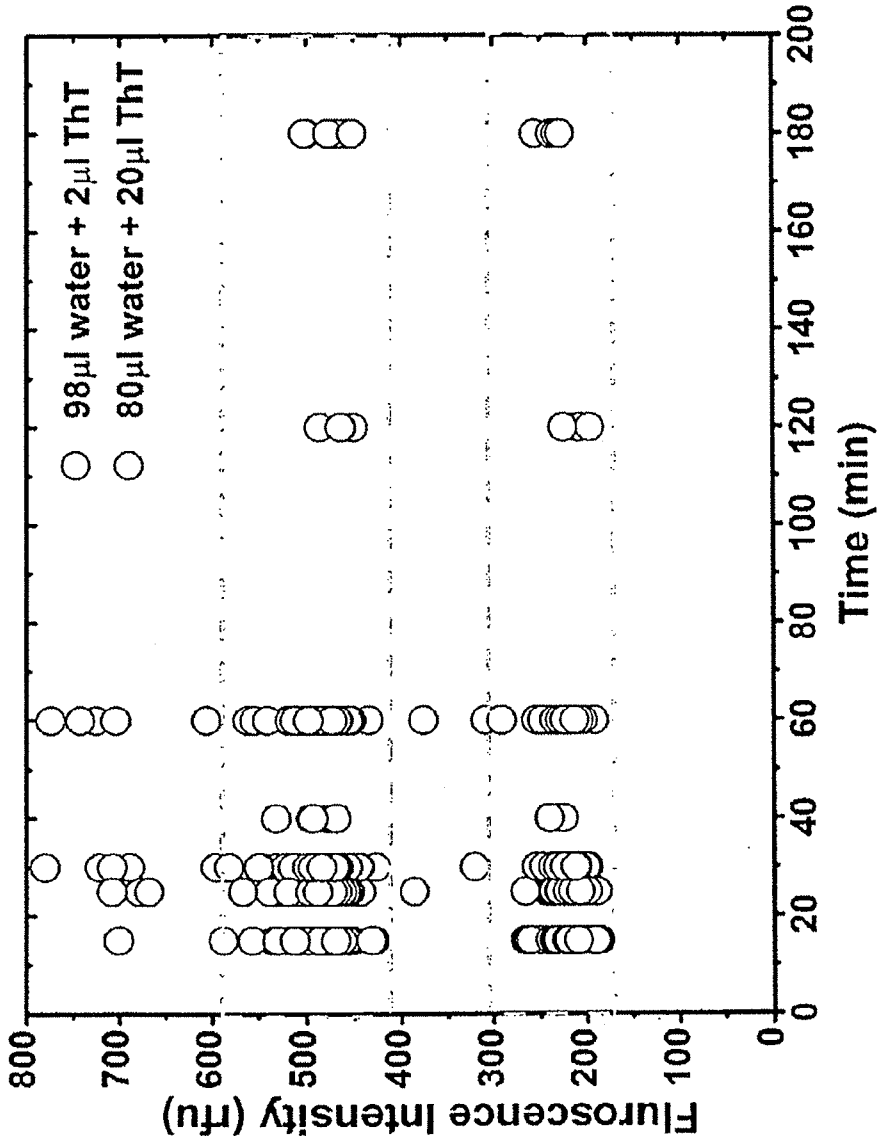

98µl water + 2µl ThT
80µl water + 20µl ThT
Fluorescence Intensity (rfu)
Time (min)
0
100
200
300
400
500
600
700
800
0
20
40
60
80
100
120
140
160
180
200

Figure 18

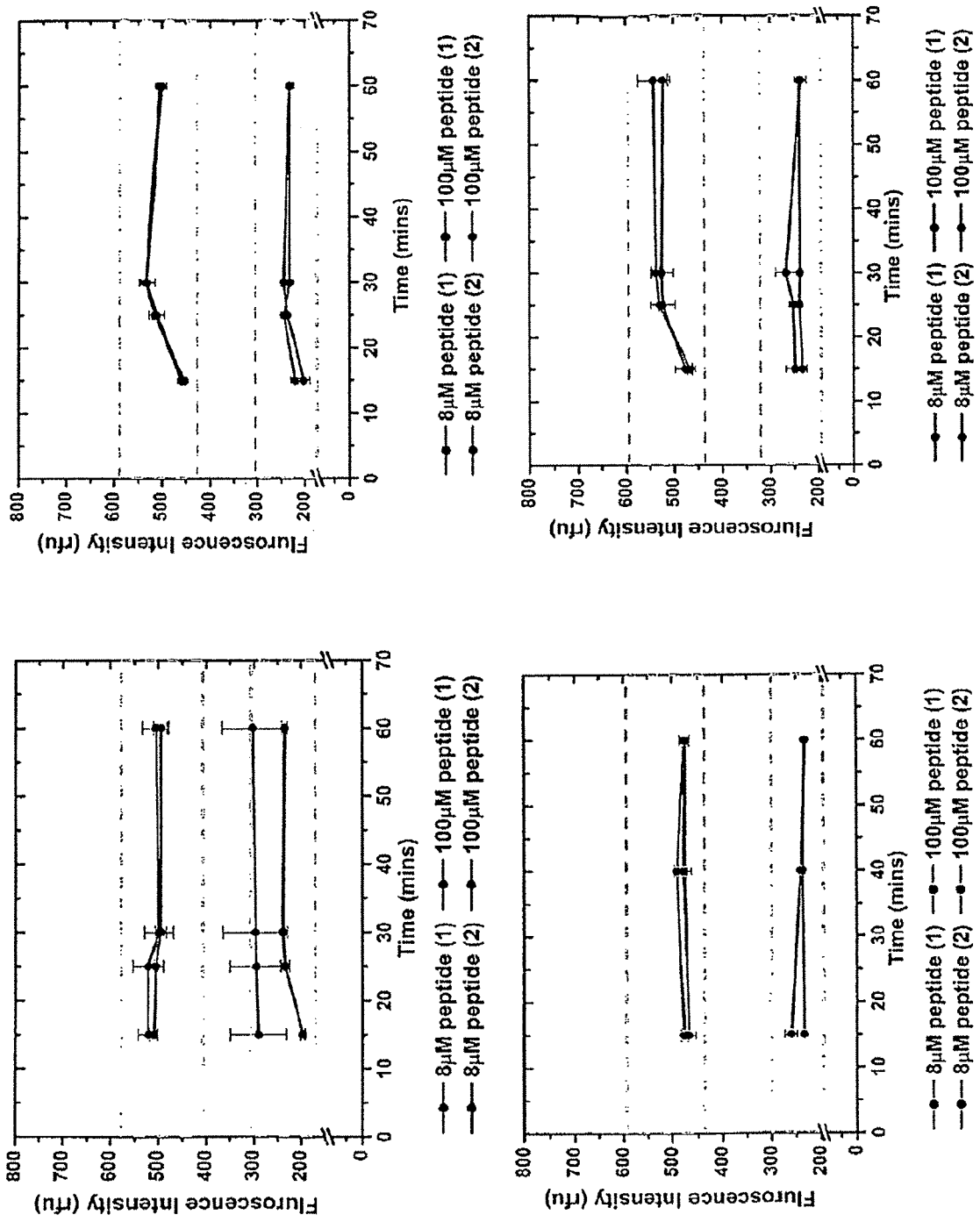

Fluorescence Intensity (rfu)
Time (mins)
8μM peptide (1)
100μM peptide (1)
8μM peptide (2)
100μM peptide (2)

Figure 19

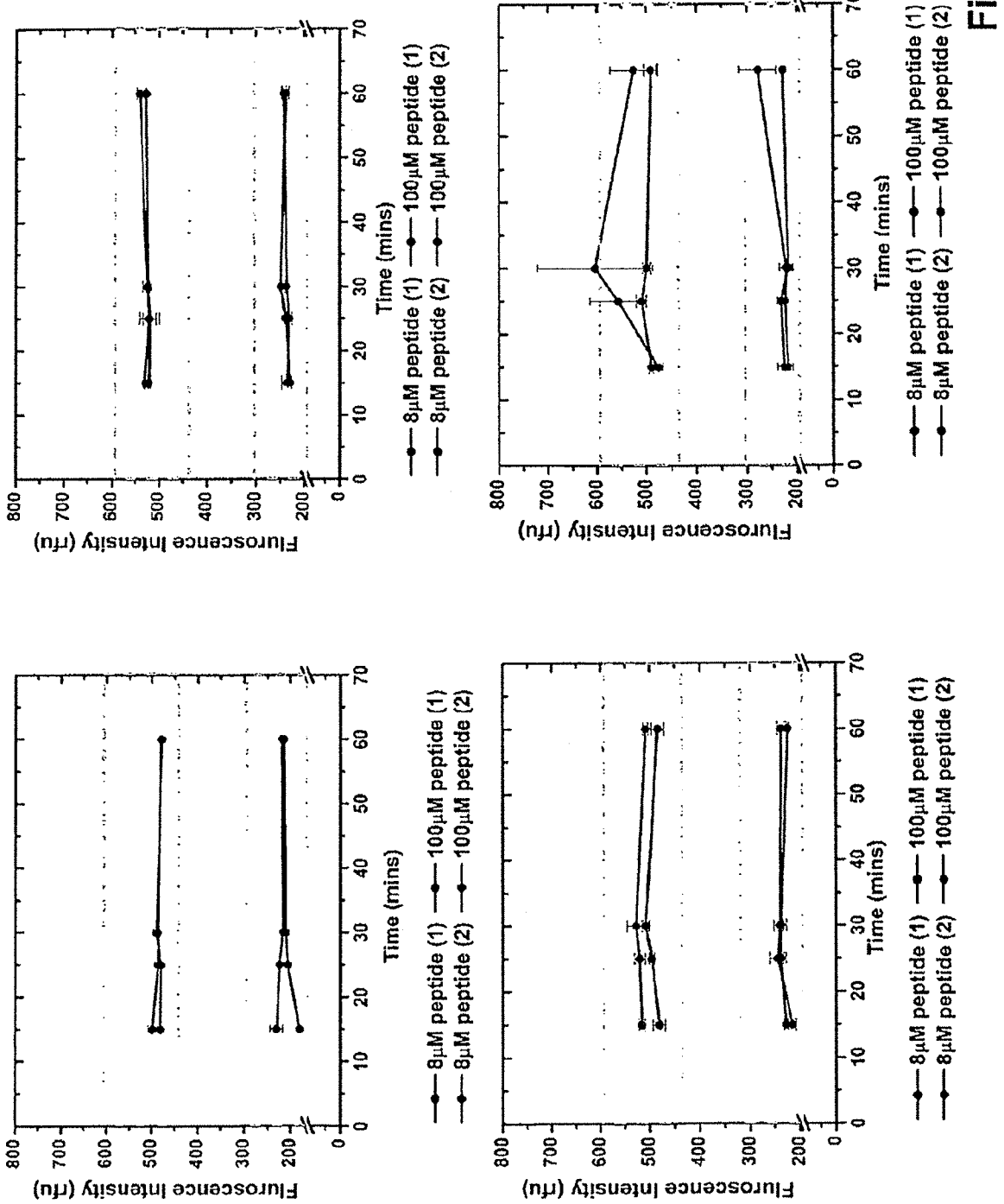

Fluorescence Intensity (rfu)
Time (mins)
8μM peptide (1)
100μM peptide (1)
8μM peptide (2)
100μM peptide (2)

Figure 20

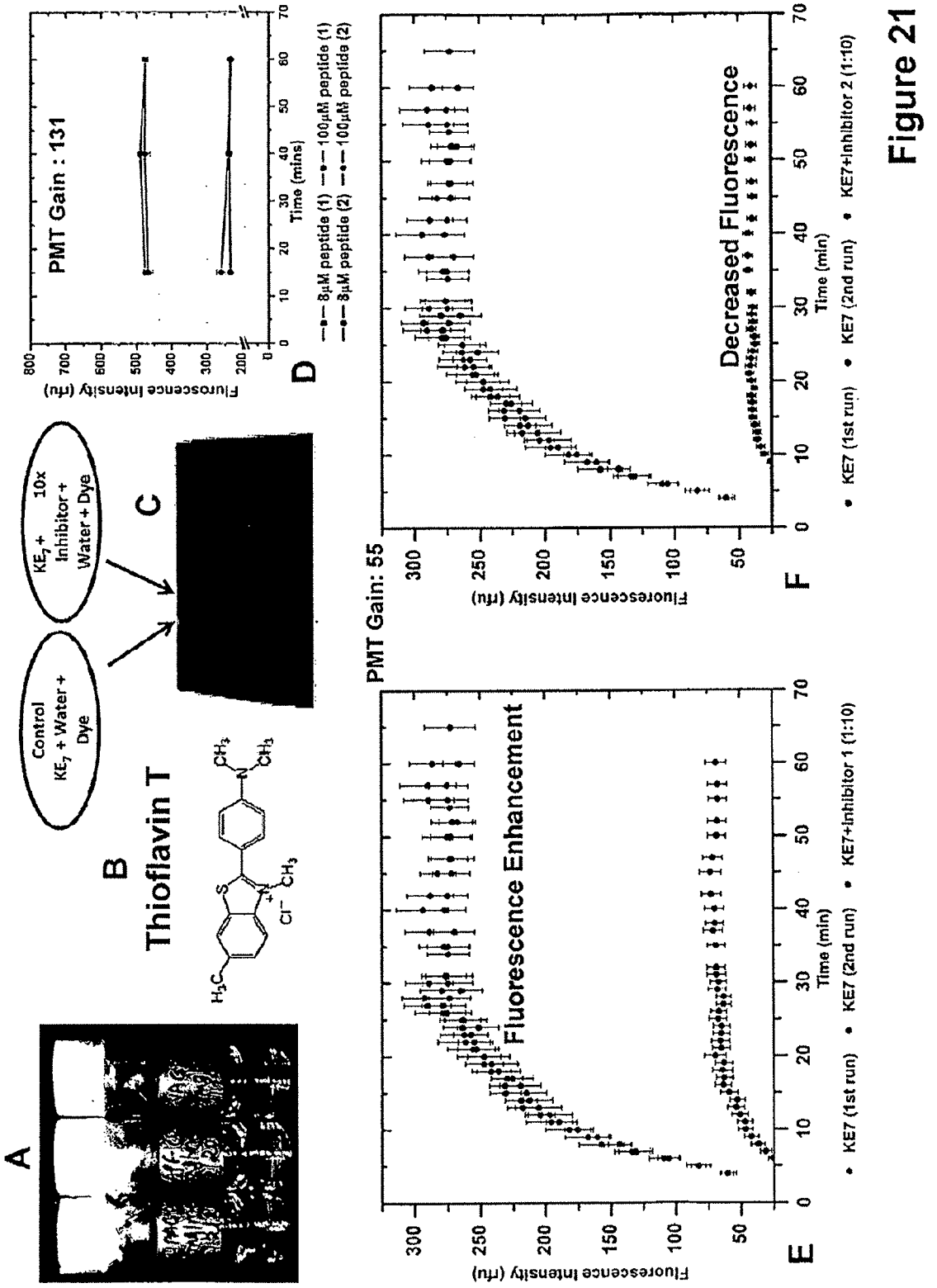

A
B
Thioflavin T
Control
KE7 + Water + Dye
KE7 + 10x Inhibitor + Water + Dye
C
D
PMT Gain : 131
Fluorescence Intensity (rfu)
Time (mins)
8μM peptide (1)
100μM peptide (1)
8μM peptide (2)
100μM peptide (2)
PMT Gain: 55
Decreased Fluorescence
Fluorescence Enhancement
Time (min)
KE7 (1st run)
KE7 (2nd run)
KE7+inhibitor 1 (1:10)
KE7+inhibitor 2 (1:10)
E
F

Figure 21

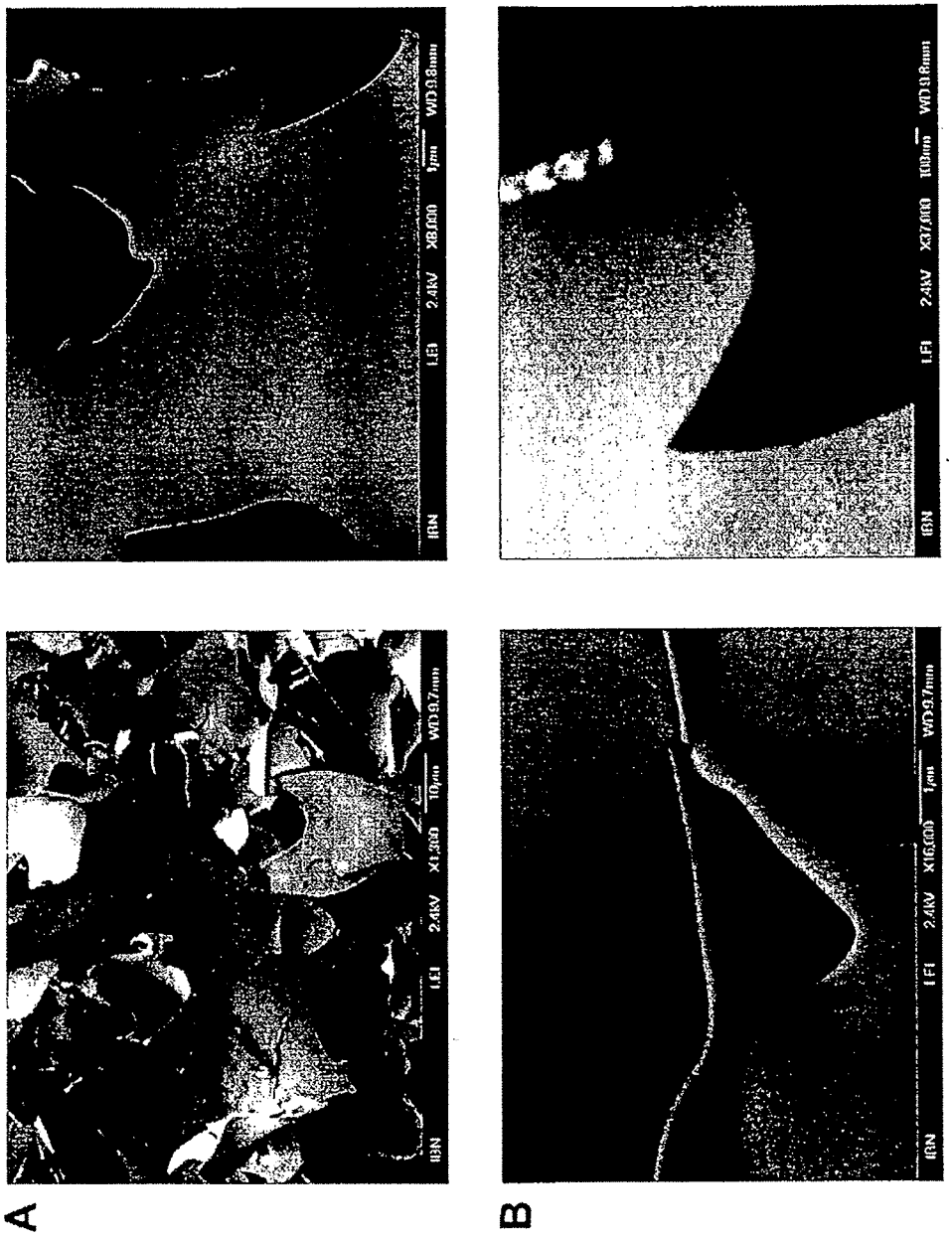


Figure 22

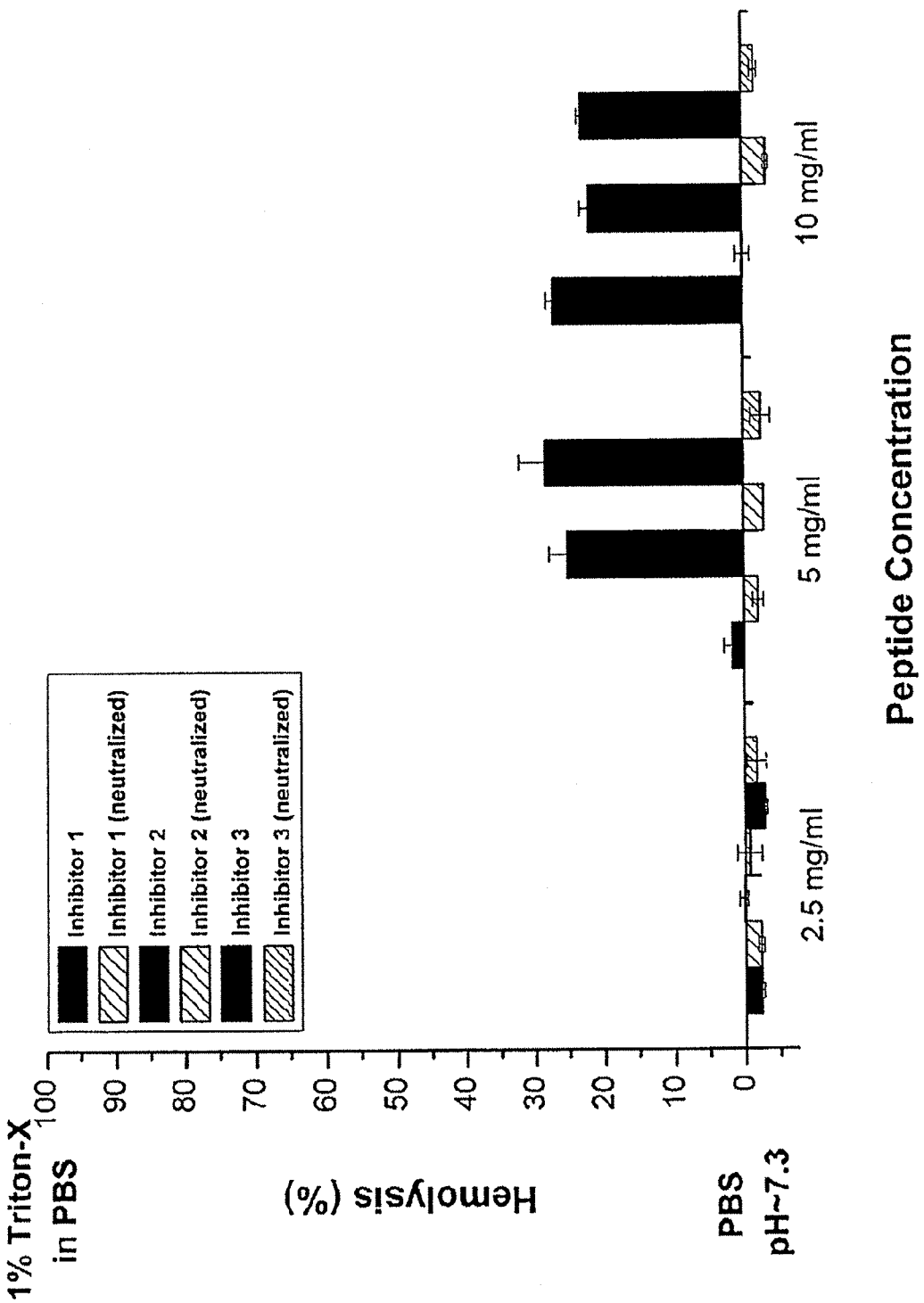

1% Triton-X in PBS
PBS pH~7.3
Hemolysis (%)
Peptide Concentration
2.5 mg/ml
5 mg/ml
10 mg/ml
Inhibitor 1
Inhibitor 1 (neutralized)
Inhibitor 2
Inhibitor 2 (neutralized)
Inhibitor 3
Inhibitor 3 (neutralized)
0
10
20
30
40
50
60
70
80
90
100

Figure 23

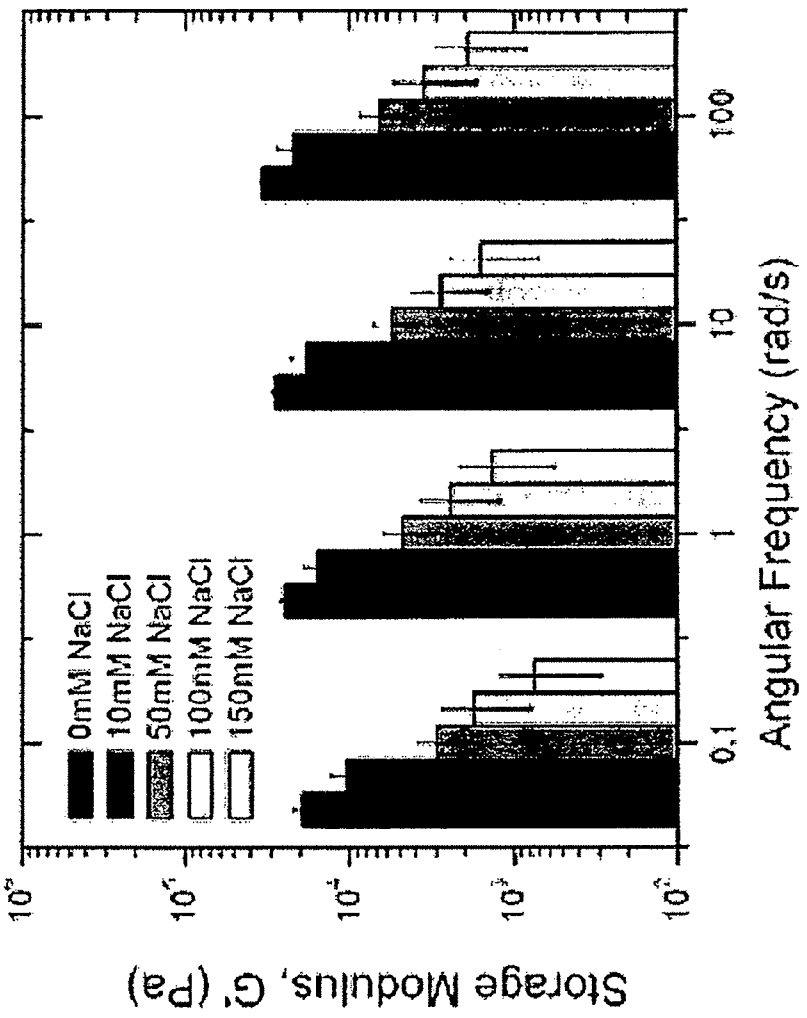
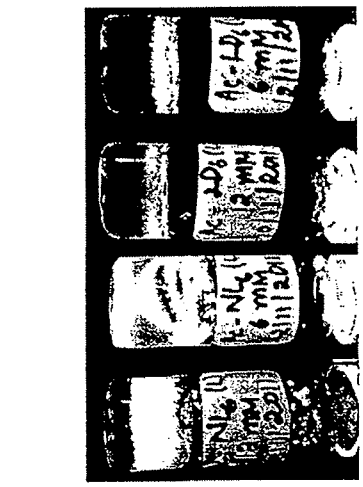

Storage Modulus, G' (Pa)
Angular Frequency (rad/s)
0mM NaCl
10mM NaCl
50mM NaCl
100mM NaCl
150mM NaCl
0.1
1
10
100

Figure 24



B

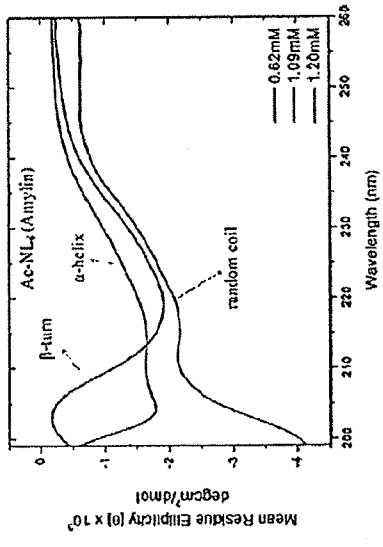

A
Mean Residue Ellipticity [θ] x 10³
degcm²/dmol
Ac-NL4 (Amylin)
β-turn
α-helix
random coil
0.62mM
1.09mM
1.20mM
Wavelength (nm)
200
210
220
230
240
250
260
0
-1
-2
-3
-4

Figure 25

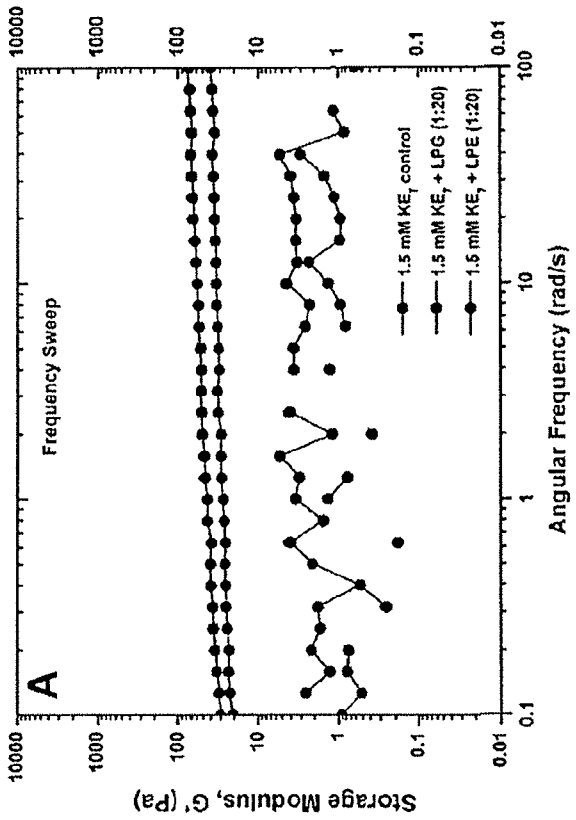

A
Frequency Sweep
Storage Modulus, G' (Pa)
Angular Frequency (rad/s)
1.5 mM KE2 control
1.5 mM KE2 + LPG (1:20)
1.5 mM KE2 + LPE (1:20)
B
Amplitude Sweep
Storage Modulus, G' (Pa)
Oscillation Strain (%)
1.5 mM KE2 control
1.5 mM KE2 + LPG (1:20)
1.5 mM KE2 + LPE (1:20)

Figure 26

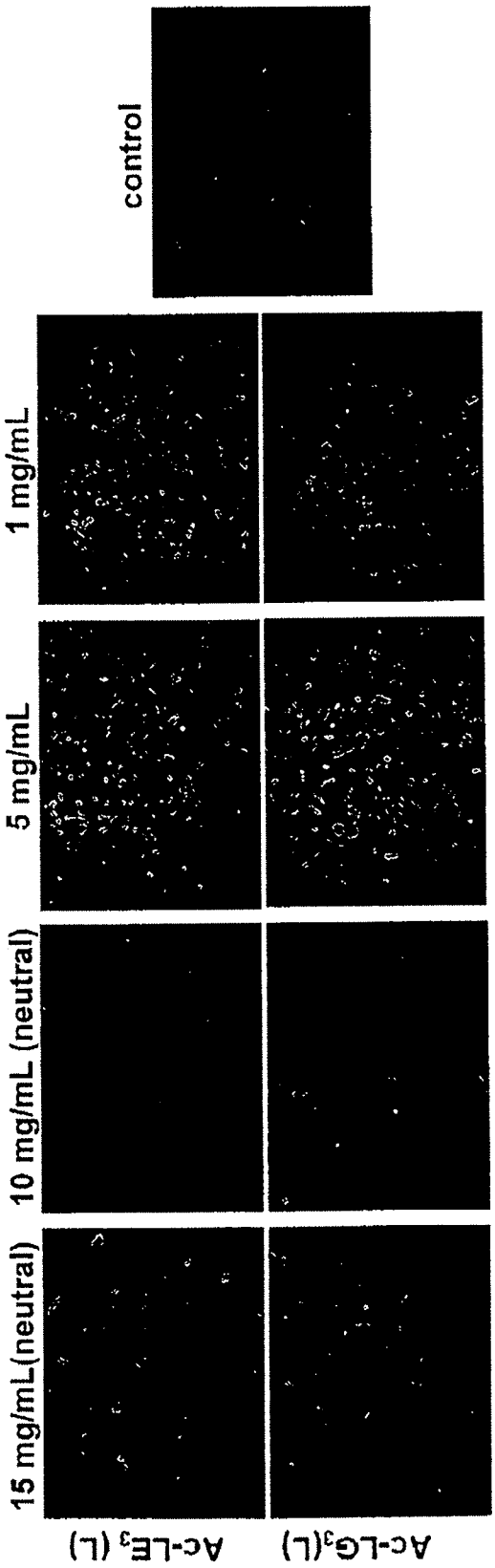

control
1 mg/mL
5 mg/mL
10 mg/mL (neutral)
15 mg/mL(neutral)
Ac-LG3(L)
Ac-LE3 (L)

Figure 27

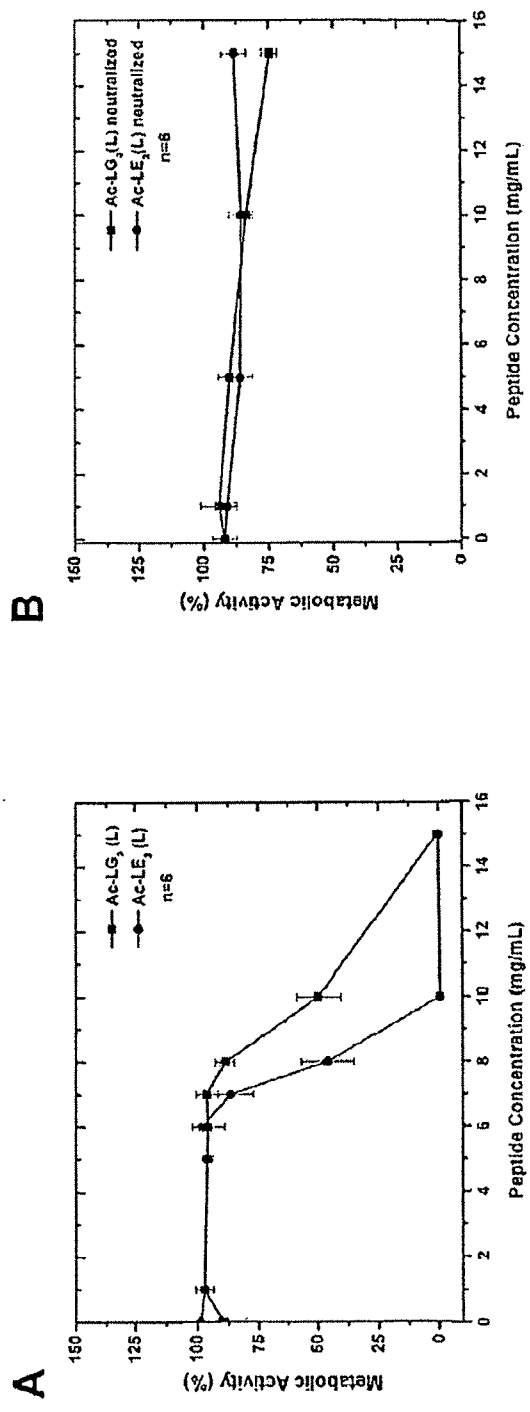

A
Metabolic Activity (%)
Peptide Concentration (mg/mL)
Ac-LG3 (L)
Ac-LE2 (L)
n=6
B
Metabolic Activity (%)
Peptide Concentration (mg/mL)
Ac-LG3 (L) neutralized
Ac-LE2 (L) neutralized
n=6

Figure 28

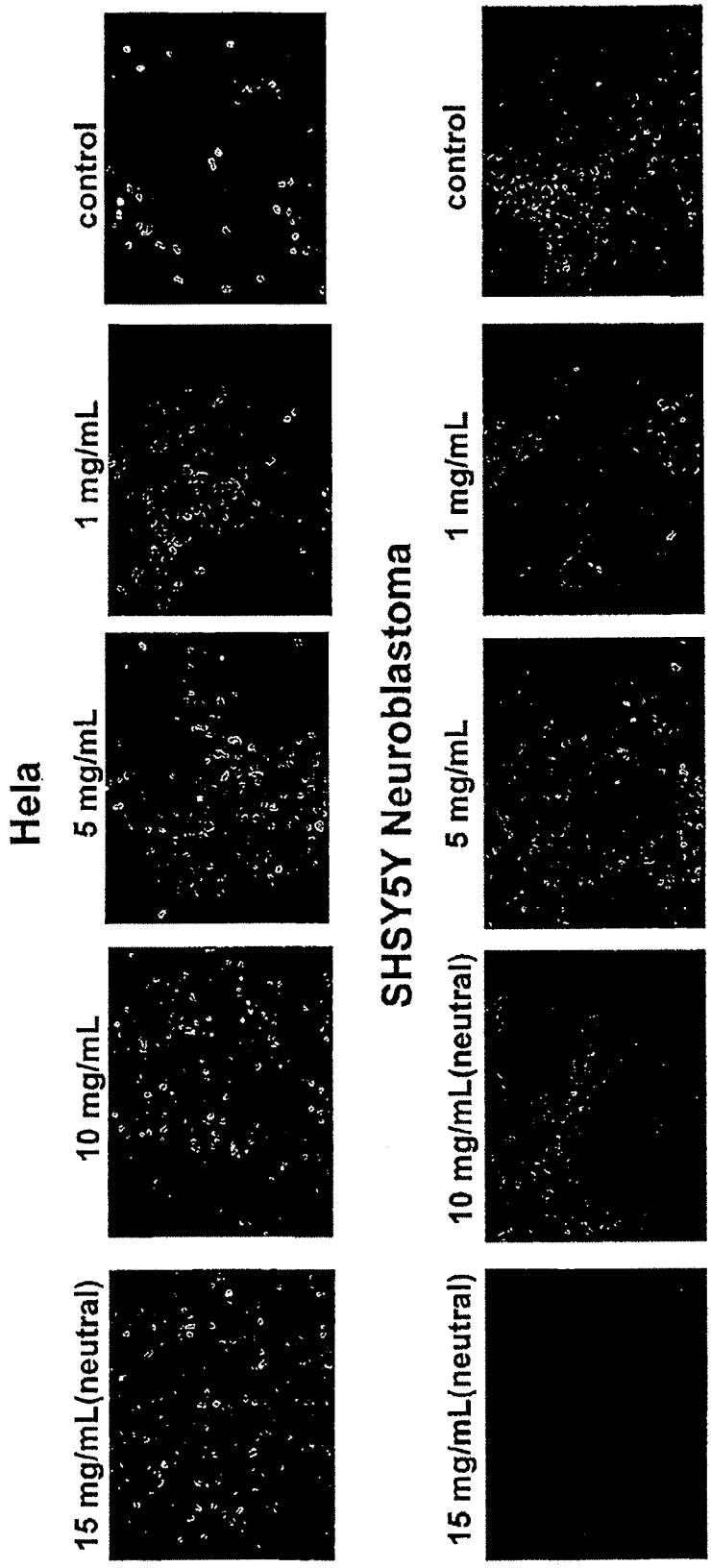

Hela
control
1 mg/mL
5 mg/mL
10 mg/mL
15 mg/mL(neutral)
SHSY5Y Neuroblastoma
control
1 mg/mL
5 mg/mL
10 mg/mL(neutral)
15 mg/mL(neutral)

Figure 29

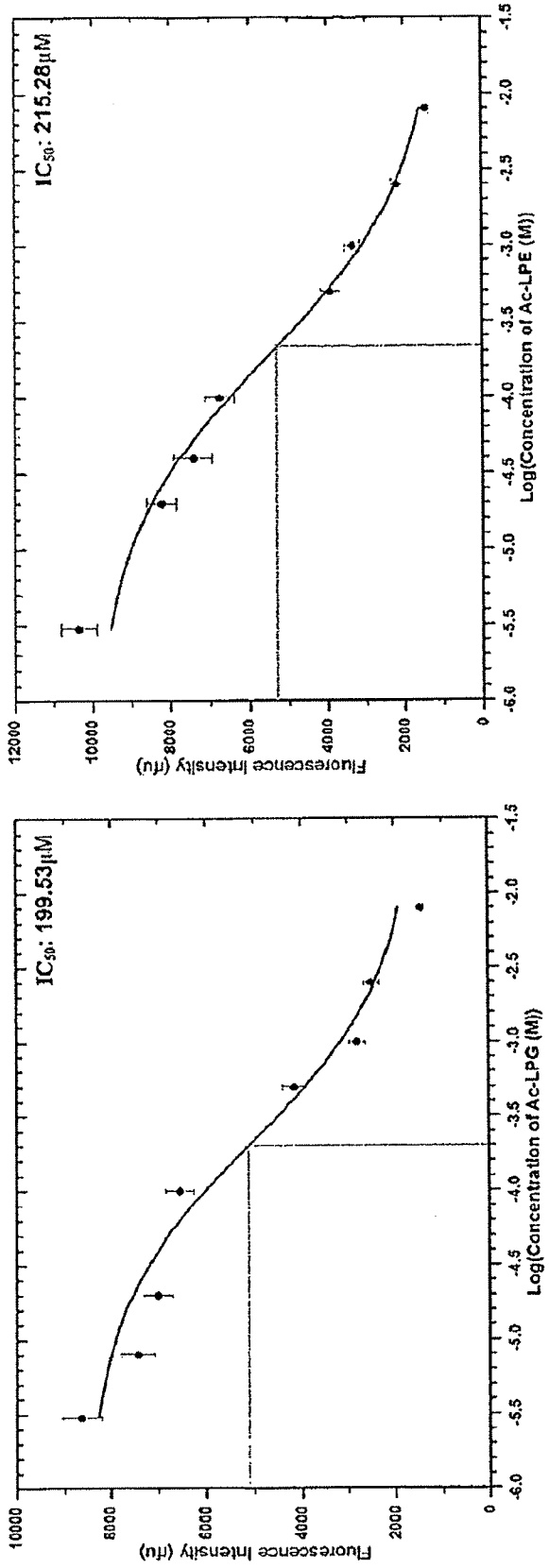
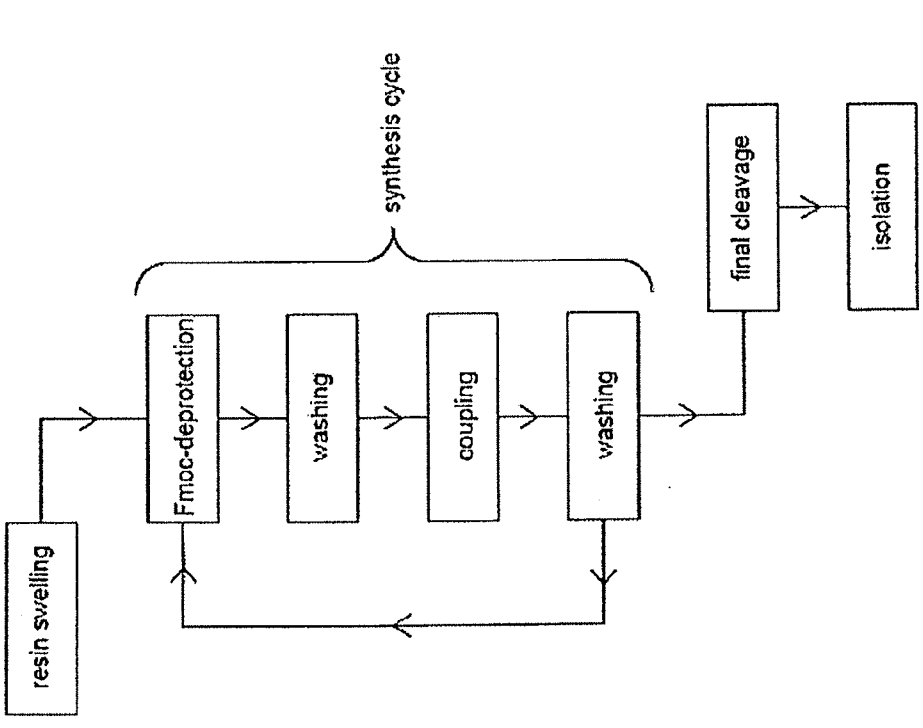
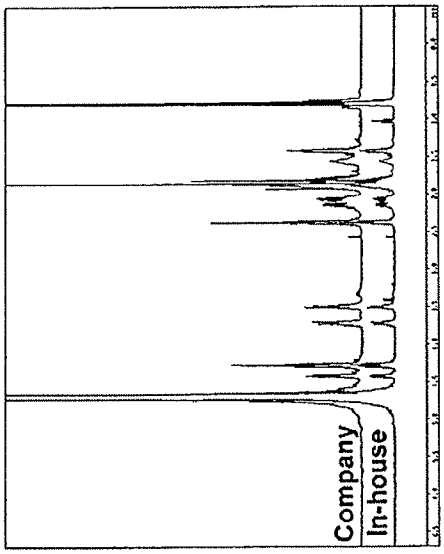
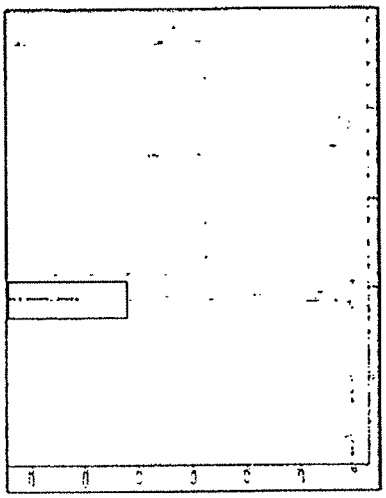

IC50: 215.28μM
Fluorescence Intensity (rfu)
Log(Concentration of Ac-LPE (M))
IC50: 199.53μM
Fluorescence Intensity (rfu)
Log(Concentration of Ac-LPG (M))

Figure 30





^{1}H NMR of Inhibitor



LC-MS of Inhibitor

Figure 31

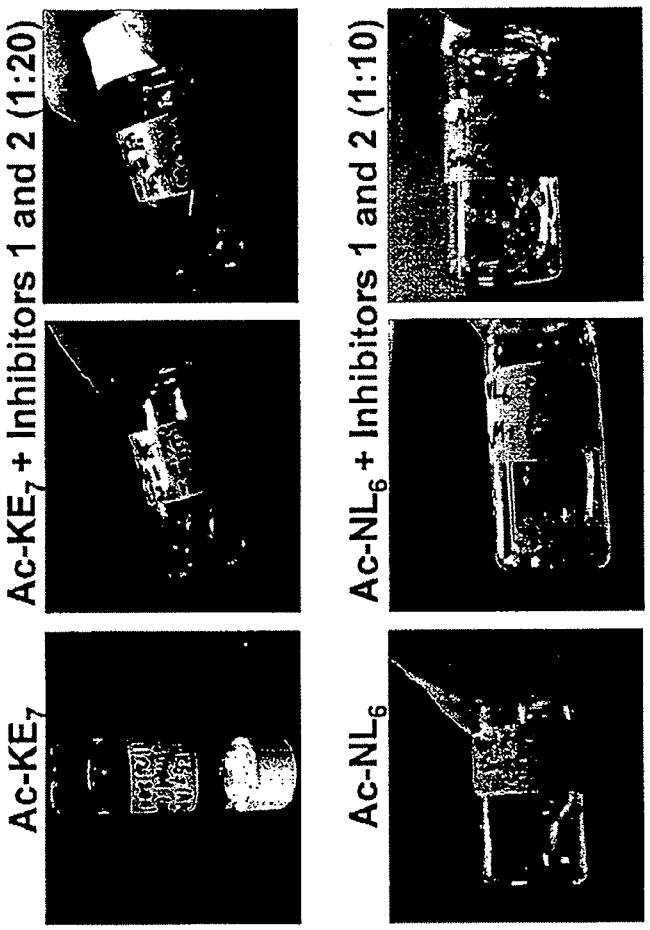

A
Ac-KE7
Ac-KE7 + Inhibitors 1 and 2 (1:20)
Ac-NL6
Ac-NL6 + Inhibitors 1 and 2 (1:10)
B
FESEM

Figure 32

SEQUENCE LISTING

<110> Agency for Science, Technology and Research

<120> Anti-amyloidogenic, alpha-helix breaking ultra-small peptide therapeutics

<130> A32079PCT

<150> SG 201104978-0
<151> 2011-07-07

<160> 61

<170> PatentIn version 3.5

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<223> Synthetic Peptide

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<222> (1)..(1)
<223> BLOCKED (N-terminal Protecting Group)

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<400> 2

Leu Ile Val Ala Gly Glu Glu
1 5

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1 5

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1 5

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<223> BLOCKED (N-terminal Protecting Group)

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Leu Ile Val Ala Ala Asp
1 5

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Ile Ile Ile Lys
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Ile Pro Asn
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Ala Pro Ala
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Ile Pro Leu
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<400> 32

Leu Pro Leu
1

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Ala Pro Phe
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<210> 34
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Lys Pro Ala
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Leu Pro Asp
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Leu Pro Glu
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Ile Pro Lys
1

<210> 38
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<400> 38

Ala Pro Asp
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<210> 39
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<400> 39

Ile Pro Phe
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<210> 40
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Ile Pro Ser
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Ile Pro Trp
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<400> 42

Ala Pro Ser
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Asn Pro Lys
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Leu Ile Pro Ala Gly Asp
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<400> 46

Leu Pro Val Ala Gly Asp
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Leu Pro Glu
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<400> 48

Leu Pro Asp
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Leu Pro Gly

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Leu Pro Leu
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<400> 51

Ile Pro Ile
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<400> 52

Ile Pro Asp
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Ile Pro Ser
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Ile Pro Trp
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Ile Pro Phe
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Ile Pro Lys
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Ala Pro Phe
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Ala Pro Asp
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<210> 59

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Ala Pro Ser
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Asn Pro Lys
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<400> 61

Asn Phe Gly Ala Ile Leu
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