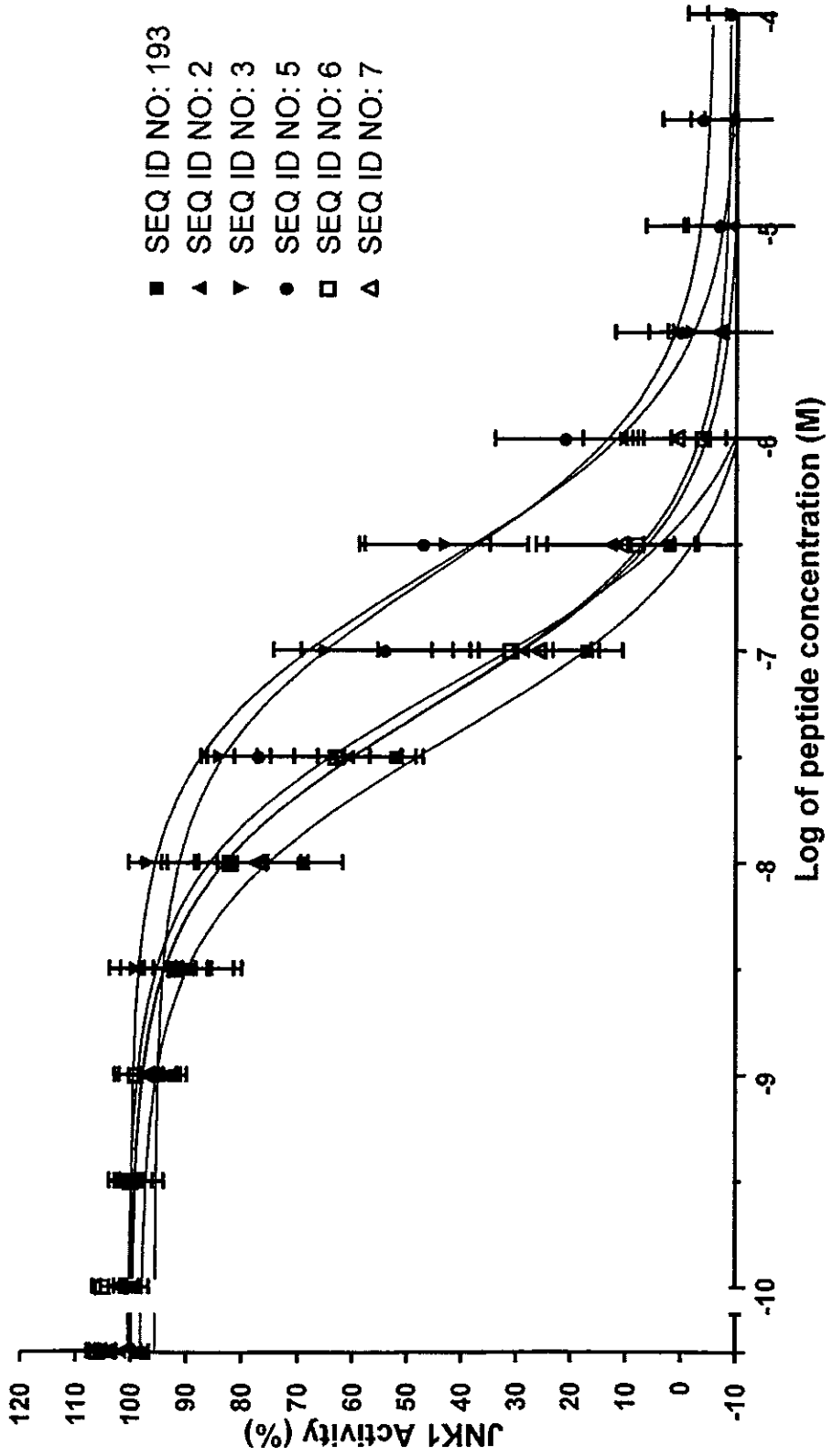

SEQ ID NO: 193
SEQ ID NO: 2
SEQ ID NO: 3
SEQ ID NO: 5
SEQ ID NO: 6
SEQ ID NO: 7
JNK1 Activity (%)
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Log of peptide concentration (M)
-4
-5
-6
-7
-8
-9
-10

Fig. 1a

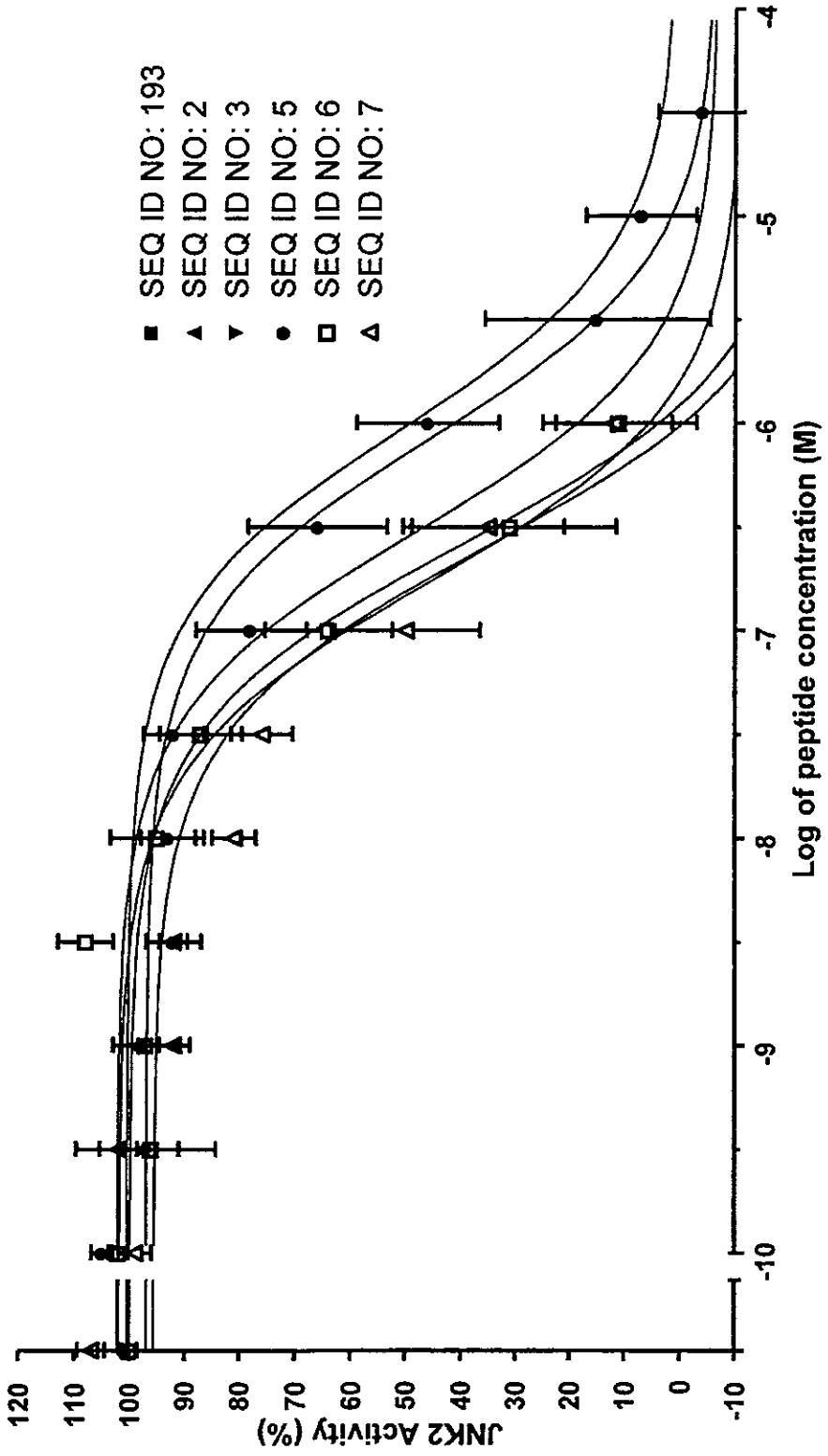

SEQ ID NO: 193
SEQ ID NO: 2
SEQ ID NO: 3
SEQ ID NO: 5
SEQ ID NO: 6
SEQ ID NO: 7
JNK2 Activity (%)
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Log of peptide concentration (M)
-4
-5
-6
-7
-8
-9
-10

Fig. 1b

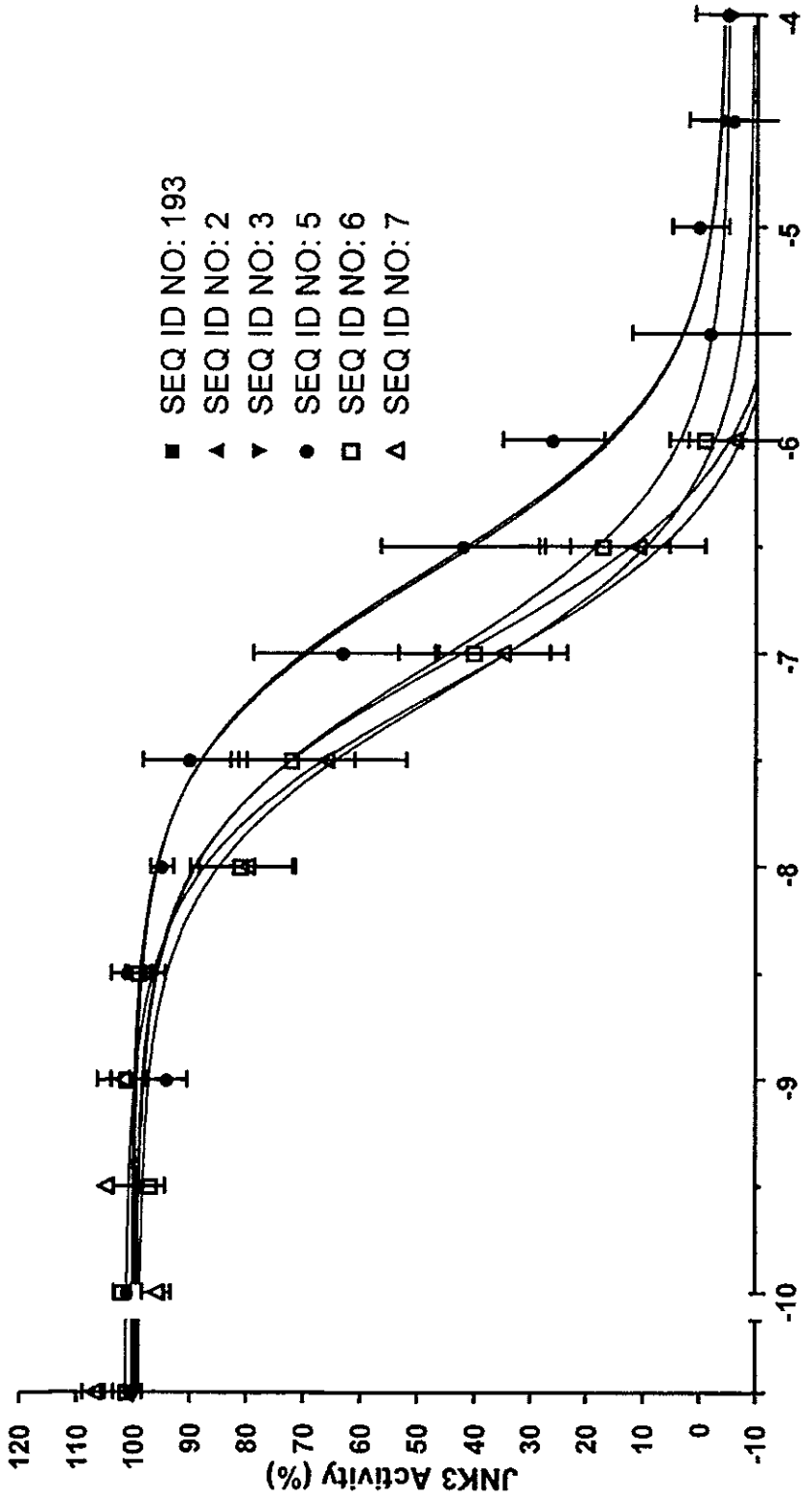

SEQ ID NO: 193
SEQ ID NO: 2
SEQ ID NO: 3
SEQ ID NO: 5
SEQ ID NO: 6
SEQ ID NO: 7
JNK3 Activity (%)
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-4
-5
-6
-7
-8
-9
-10

Fig. 1c

SEQ ID NO:	Sequence														hJNK1			hJNK2			hJNK3		
															IC50	SEM	n	IC50	SEM	n	IC50	SEM	n
193	NH2	R	P	K	R	P	T	T	L	N	L	F	CONH2		39,52	0,57	2	183,85	50,45	2	67,68	13,92	2
2	NH2	r	P	K	R	P	T	T	L	N	L	F	CONH2		65,55	26,03	3	423,53	241,45	3	103,32	36,53	3
3	NH2	R	P	k	R	P	T	T	L	N	L	F	CONH2		311,63	99,86	4	1213,53	437,87	4	359,47	161,02	4
5	NH2	R	P	K	R	P	T	T	L	n	L	F	CONH2		347,55	174,17	4	1501,88	701,33	4	387,15	179,51	4
6	NH2	R	P	K	R	P	T	T	L	r	L	F	CONH2		90,50	29,63	4	358,75	105,28	4	119,50	39,82	4
7	NH2	R	P	K	R	P	T	T	L	N	L	f	CONH2		69,53	21,75	4	278,18	51,43	4	88,97	26,72	4

Fig. 2

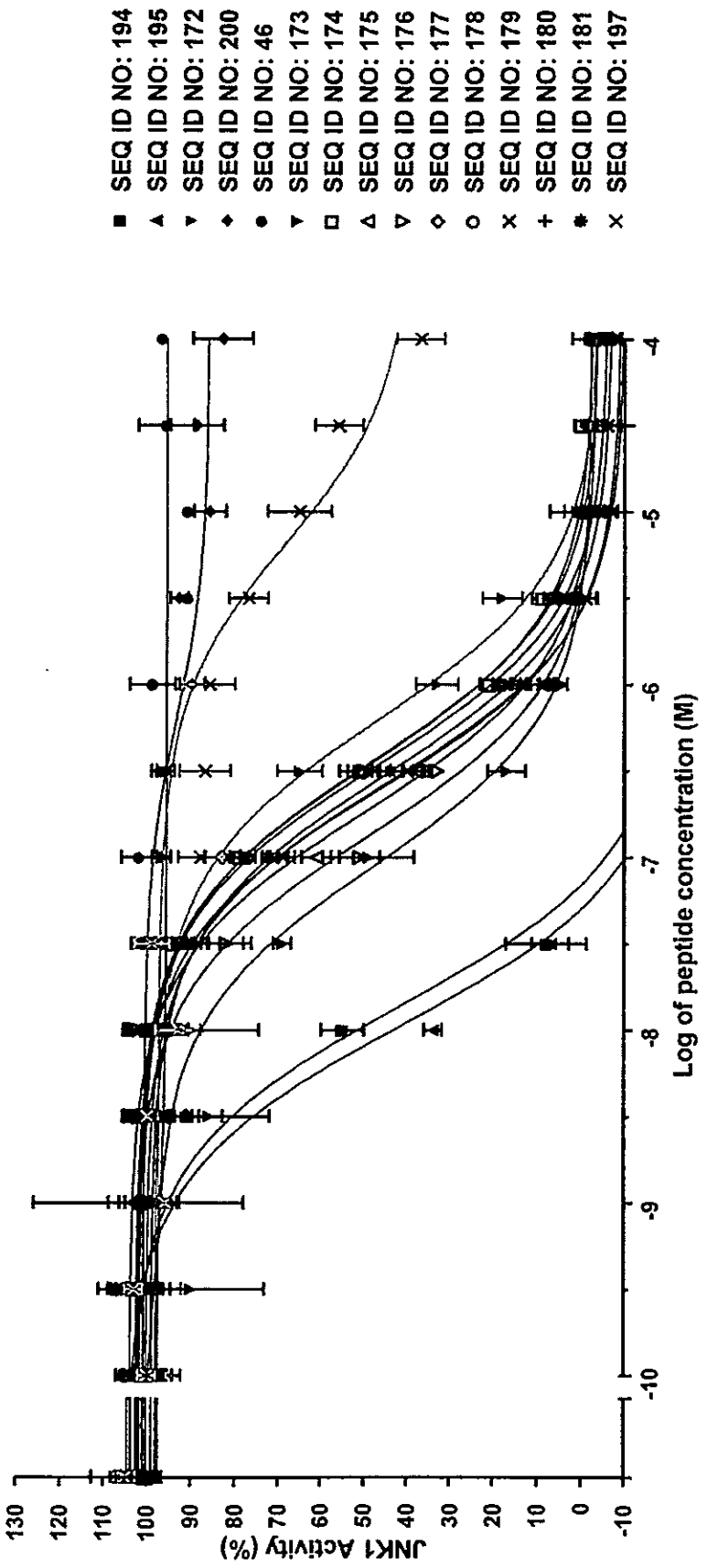

SEQ ID NO: 194
SEQ ID NO: 195
SEQ ID NO: 172
SEQ ID NO: 200
SEQ ID NO: 46
SEQ ID NO: 173
SEQ ID NO: 174
SEQ ID NO: 175
SEQ ID NO: 176
SEQ ID NO: 177
SEQ ID NO: 178
SEQ ID NO: 179
SEQ ID NO: 180
SEQ ID NO: 181
SEQ ID NO: 197
JNK1 Activity (%)
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Log of peptide concentration (M)
-4
-5
-6
-7
-8
-9
-10

Fig. 3a

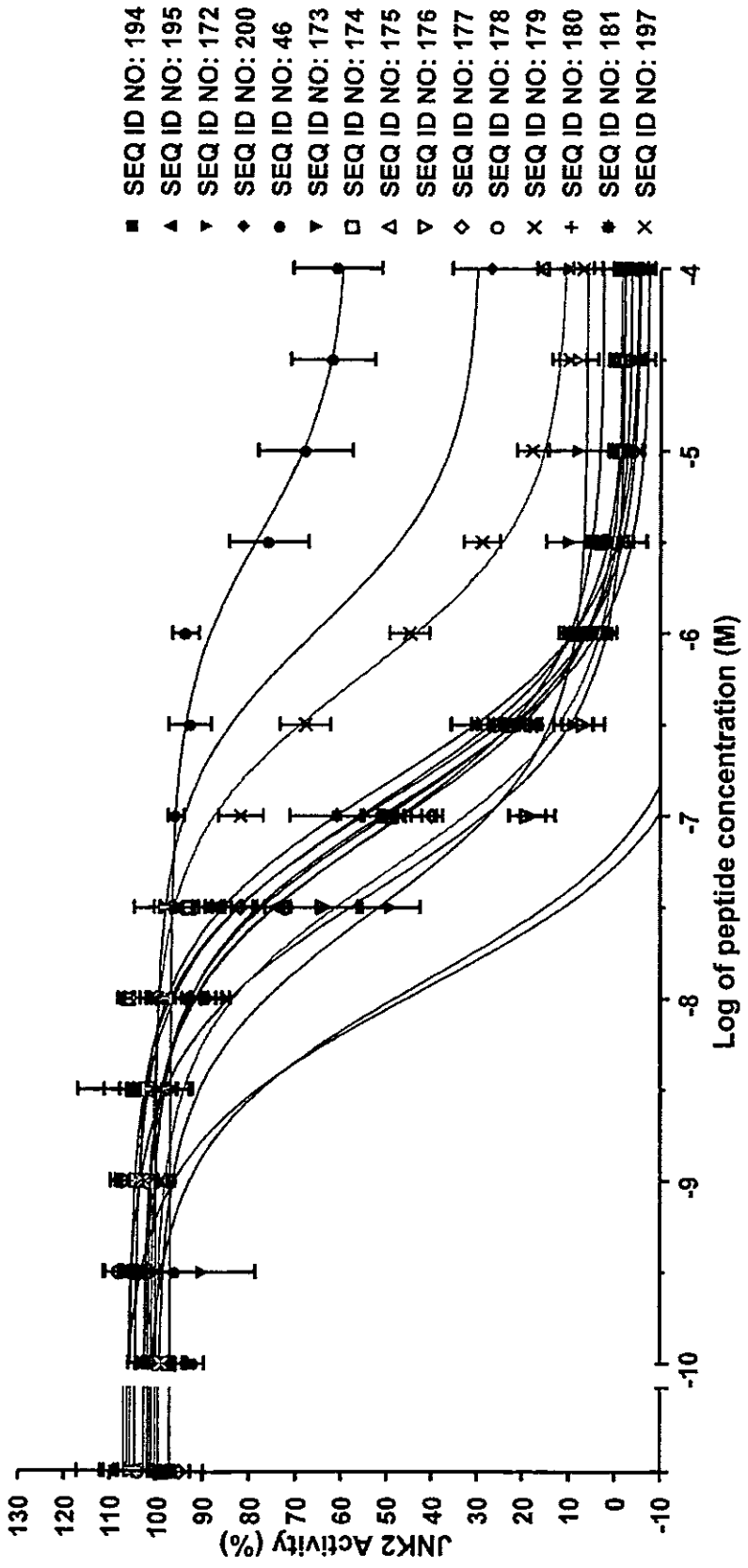

SEQ ID NO: 194
SEQ ID NO: 195
SEQ ID NO: 172
SEQ ID NO: 200
SEQ ID NO: 46
SEQ ID NO: 173
SEQ ID NO: 174
SEQ ID NO: 175
SEQ ID NO: 176
SEQ ID NO: 177
SEQ ID NO: 178
SEQ ID NO: 179
SEQ ID NO: 180
SEQ ID NO: 181
SEQ ID NO: 197
JNK2 Activity (%)
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-4
-5
-6
-7
-8
-9
-10
Log of peptide concentration (M)

Fig. 3b

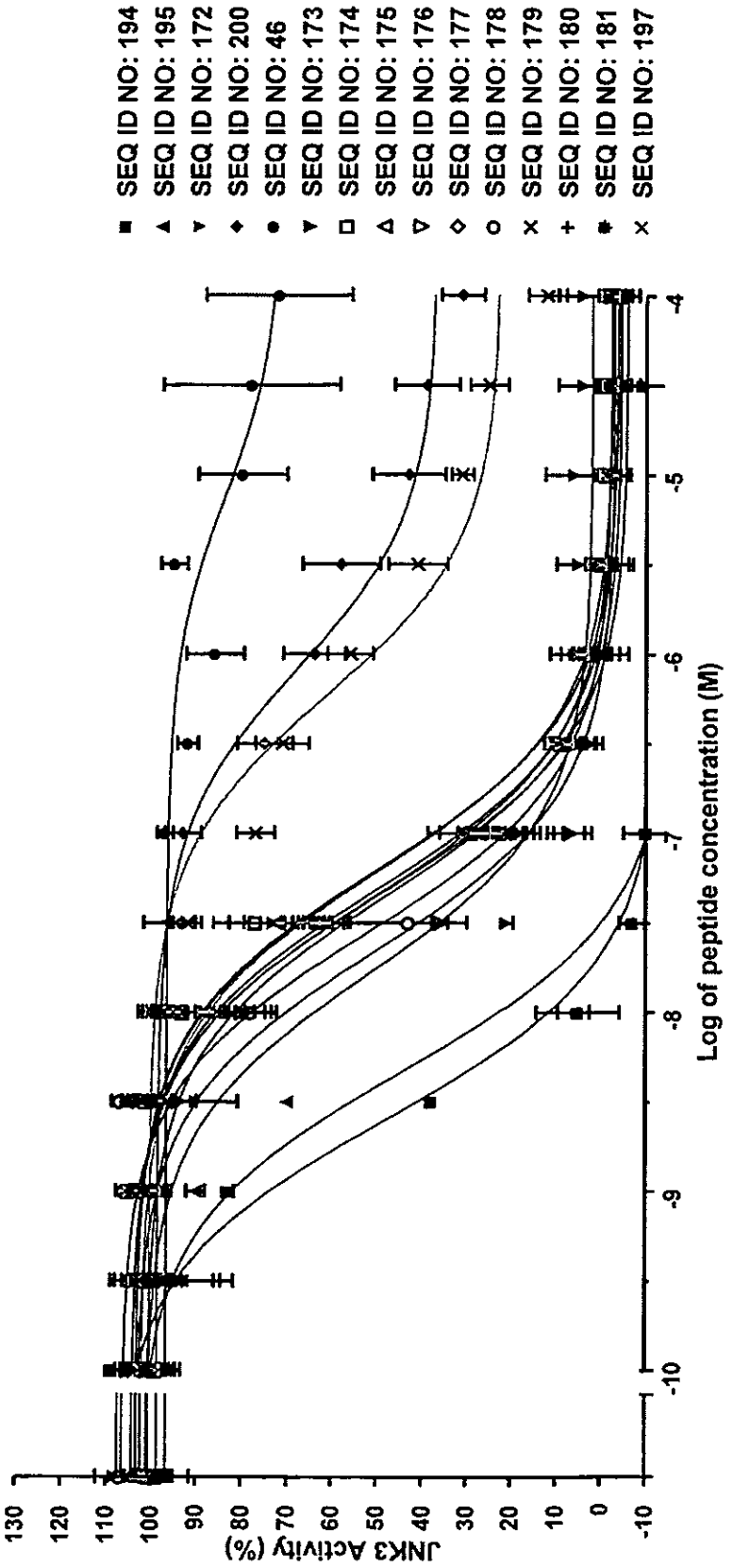

SEQ ID NO: 194
SEQ ID NO: 195
SEQ ID NO: 172
SEQ ID NO: 200
SEQ ID NO: 46
SEQ ID NO: 173
SEQ ID NO: 174
SEQ ID NO: 175
SEQ ID NO: 176
SEQ ID NO: 177
SEQ ID NO: 178
SEQ ID NO: 179
SEQ ID NO: 180
SEQ ID NO: 181
SEQ ID NO: 197
JNK3 Activity (%)
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Log of peptide concentration (M)
-4
-5
-6
-7
-8
-9
-10

Fig. 3c

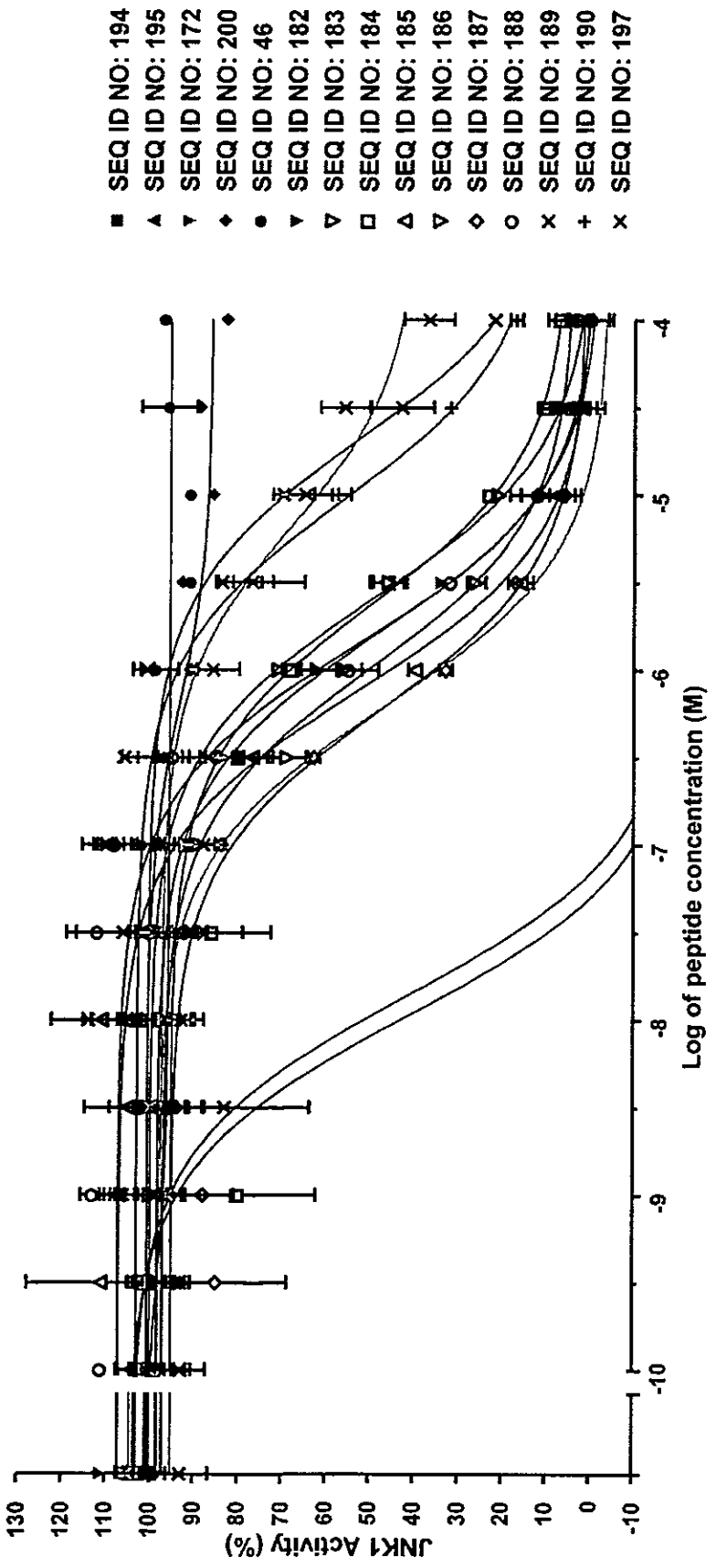

SEQ ID NO: 194
SEQ ID NO: 195
SEQ ID NO: 172
SEQ ID NO: 200
SEQ ID NO: 46
SEQ ID NO: 182
SEQ ID NO: 183
SEQ ID NO: 184
SEQ ID NO: 185
SEQ ID NO: 186
SEQ ID NO: 187
SEQ ID NO: 188
SEQ ID NO: 189
SEQ ID NO: 190
SEQ ID NO: 197
JNK1 Activity (%)
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Log of peptide concentration (M)
-4
-5
-6
-7
-8
-9
-10

Fig. 3d

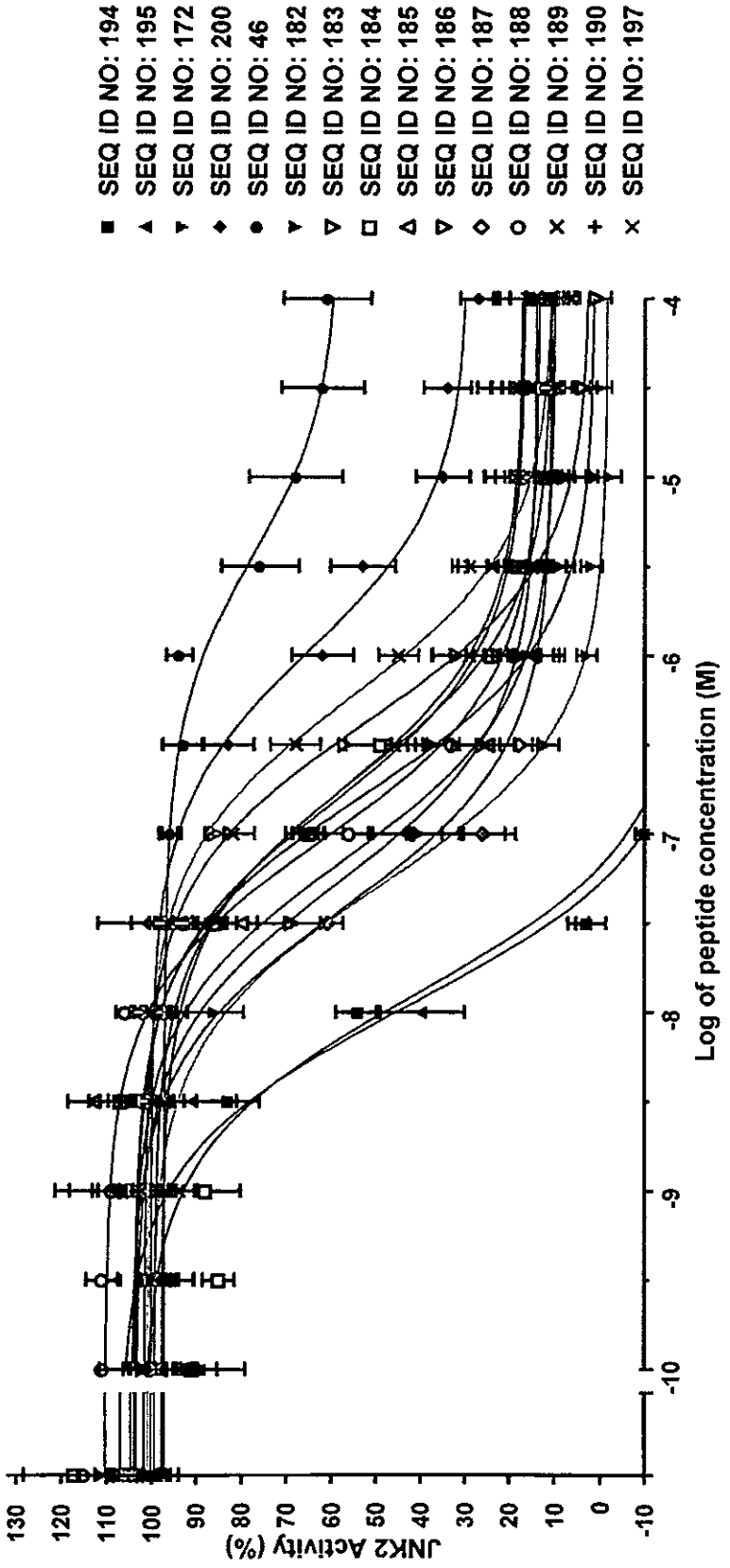

SEQ ID NO: 194
SEQ ID NO: 195
SEQ ID NO: 172
SEQ ID NO: 200
SEQ ID NO: 46
SEQ ID NO: 182
SEQ ID NO: 183
SEQ ID NO: 184
SEQ ID NO: 185
SEQ ID NO: 186
SEQ ID NO: 187
SEQ ID NO: 188
SEQ ID NO: 189
SEQ ID NO: 190
SEQ ID NO: 197
JNK2 Activity (%)
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Log of peptide concentration (M)
-4
-5
-6
-7
-8
-9
-10

Fig. 3e

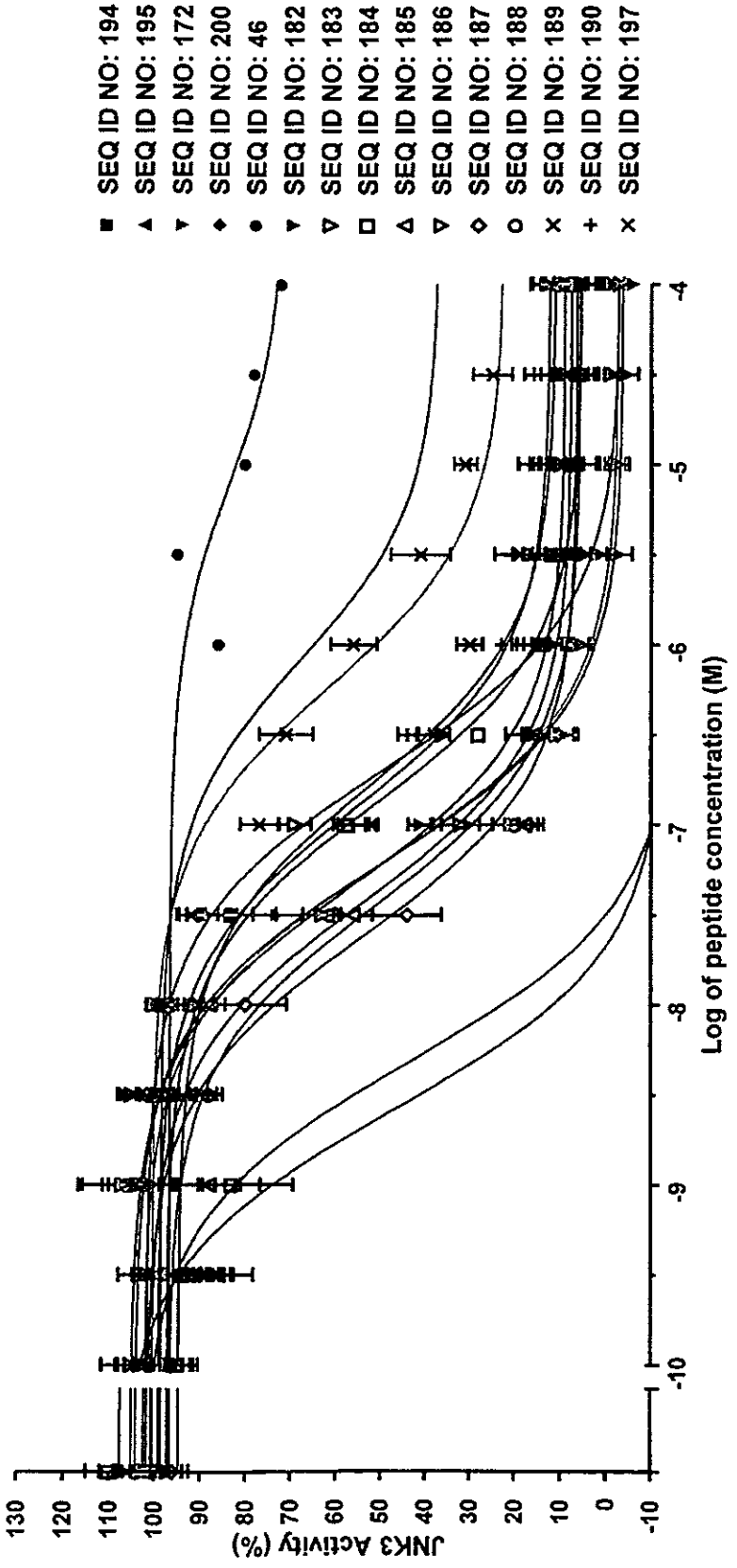

SEQ ID NO: 194
SEQ ID NO: 195
SEQ ID NO: 172
SEQ ID NO: 200
SEQ ID NO: 46
SEQ ID NO: 182
SEQ ID NO: 183
SEQ ID NO: 184
SEQ ID NO: 185
SEQ ID NO: 186
SEQ ID NO: 187
SEQ ID NO: 188
SEQ ID NO: 189
SEQ ID NO: 190
SEQ ID NO: 197
JNK3 Activity (%)
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Log of peptide concentration (M)
-4
-5
-6
-7
-8
-9
-10

Fig. 3f

SEQ ID NO:		Sequence		hJNK1			hJNK2			hJNK3		
				IC50	SEM	n	IC50	SEM	n	IC50	SEM	n
196	NH2	G R K K R R Q R R R P P R P K R P T T L N L F P Q V P R S Q D	CONH2	42,20	8,17	8	8,43	2,01	6	5,22	0,71	6
197	CONH2	G r k k r r q r r r p p r r p k r p t t l n l f p q v p r s q d	NH2	24358,50	10019,91	8	801,77	114,66	11	1294,24	255,51	11
194	NH2	G R K K R R Q R R R P P K R P T T L N L F P Q V P R S Q D	CONH2	13,99	0,06	2	12,70	0,48	2	2,59	0,08	2
195	NH2	G R K K R R Q R R R P T T L N L F P Q V P R S Q D	CONH2	10,77	1,83	2	11,26	0,56	2	4,92	0,27	2
172	NH2	r K K R r Q R R r R P k R P a T L N L f	CONH2	722,49	124,58	7	54,66	13,04	7	102,32	47,81	7
200	NH2	r K K R r Q R R r R P k A A a A A N A f	CONH2	NA	NA	6	3324,00	2468,99	6	3820,81	3190,08	6
46	NH2	r K K R r Q R R r	CONH2	NA	NA	3	5340,33	1803,08	3	8130,86	5323,73	3
173	NH2	r K K R r Q R R r R P k R P T T L r L f	CONH2	88,36	4,02	2	30,03	0,16	2	16,76	2,03	2
174	NH2	r K K R r Q R R r R P T T L N L f	CONH2	333,73	36,46	3	120,13	4,53	3	63,12	6,04	3
175	NH2	r K K R r Q R r R P T T L N L f	CONH2	185,30	18,10	3	82,30	9,26	3	60,60	8,01	3
176	NH2	r K K R r Q R R r R P k R P T T L N L w	CONH2	131,17	12,28	3	40,33	4,60	3	22,38	1,60	3
177	NH2	r K K R r Q R R r R P k R P T D L N L f	CONH2	355,10	34,02	3	87,20	7,12	3	45,38	6,70	3
178	NH2	r K K R r Q R R r R P T T L r L w	CONH2	329,33	12,26	3	108,60	42,64	3	30,41	5,81	3
179	NH2	r K K R r Q R r R P T T L r L w	CONH2	249,47	22,35	3	122,11	20,73	3	45,66	3,79	3
180	NH2	r K K R r Q R R r R P T D L r L w	CONH2	265,20	34,65	3	117,65	10,58	3	46,99	8,21	3
181	NH2	r K K R r Q R r R P T D L r L w	CONH2	293,70	9,79	3	160,22	40,13	3	47,56	5,77	3
182	NH2	r K K R r Q R R r R P a T L N L f	CONH2	1677,50	34,50	2	168,40	20,80	2	59,36	2,35	2
183	NH2	r K K R r Q R r R P a T L N L f	CONH2	2588,00	494,00	2	427,30	25,00	2	199,20	3,90	2
184	NH2	r K K R r Q R r K R P a T L N L f	CONH2	2426,00	128,00	2	205,95	8,25	2	129,45	9,65	2
185	NH2	r K K R r Q R R r R P k R P s T L N L f	CONH2	765,65	78,15	2	72,09	2,85	2	35,52	6,34	2
186	NH2	r K K R r Q R R r R P k R P q T L N L f	CONH2	1021,30	100,70	2	52,59	2,73	2	44,24	4,80	2
187	NH2	r K K R r Q R R r R P k R P k T L N L f	CONH2	594,45	40,45	2	37,88	5,47	2	25,41	8,95	2
188	NH2	r K K R r Q R R r G K R K A L K L f	CONH2	1421,00	98,00	2	98,14	27,26	2	36,12	2,46	2
189	NH2	r K K R r Q R R r G K R K A L r L f	CONH2	22270,00	5090,00	2	175,60	1,30	2	127,72	31,88	2
190	NH2	r K K R r Q R R r R K A L r L f	CONH2	8969,50	2070,50	2	148,20	9,70	2	159,35	13,45	2

Fig. 4

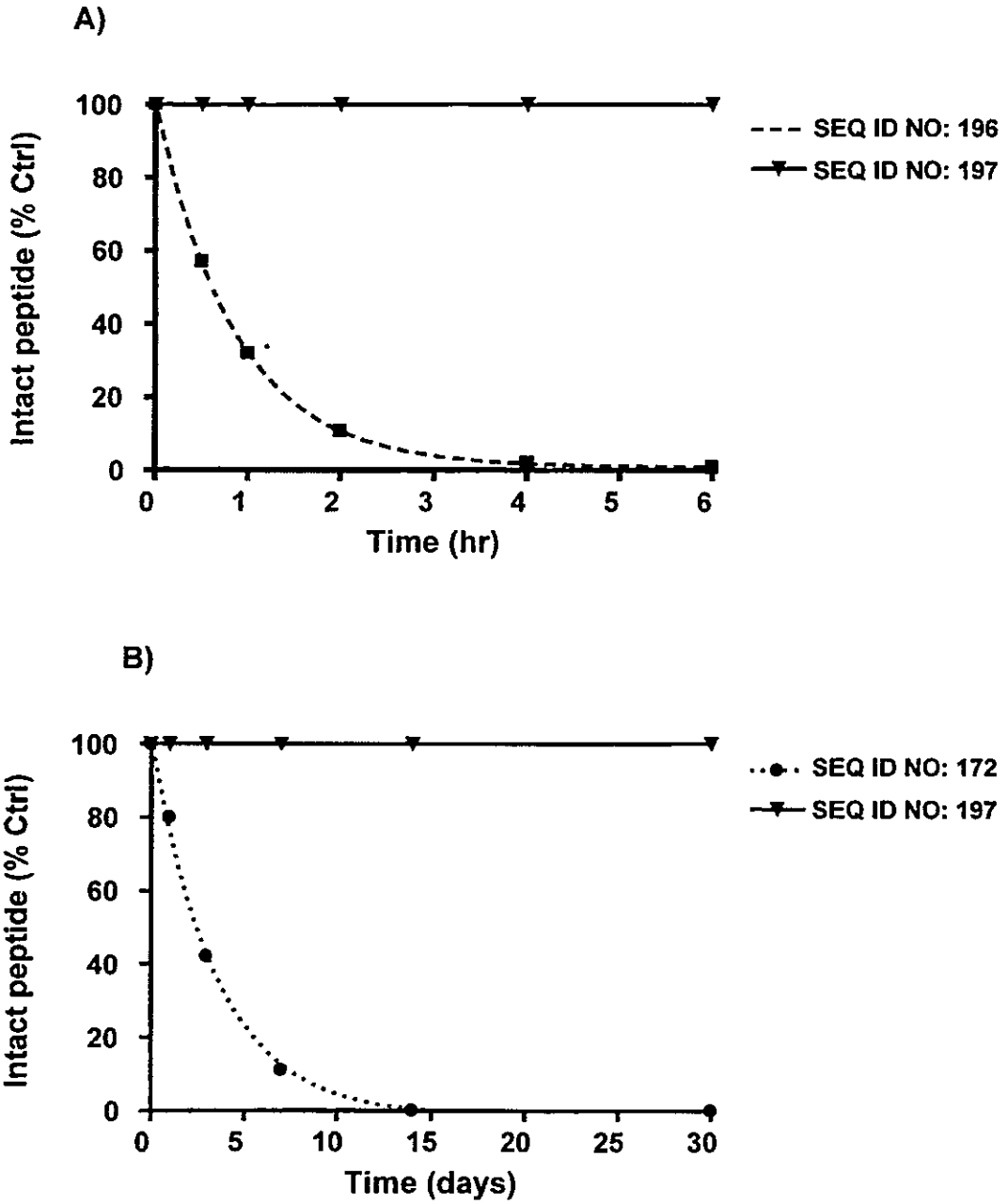

A)
Intact peptide (% Ctrl)
100
80
60
40
20
0
0
1
2
3
4
5
6
Time (hr)
SEQ ID NO: 196
SEQ ID NO: 197
B)
Intact peptide (% Ctrl)
100
80
60
40
20
0
0
5
10
15
20
25
30
Time (days)
SEQ ID NO: 172
SEQ ID NO: 197

Fig. 5

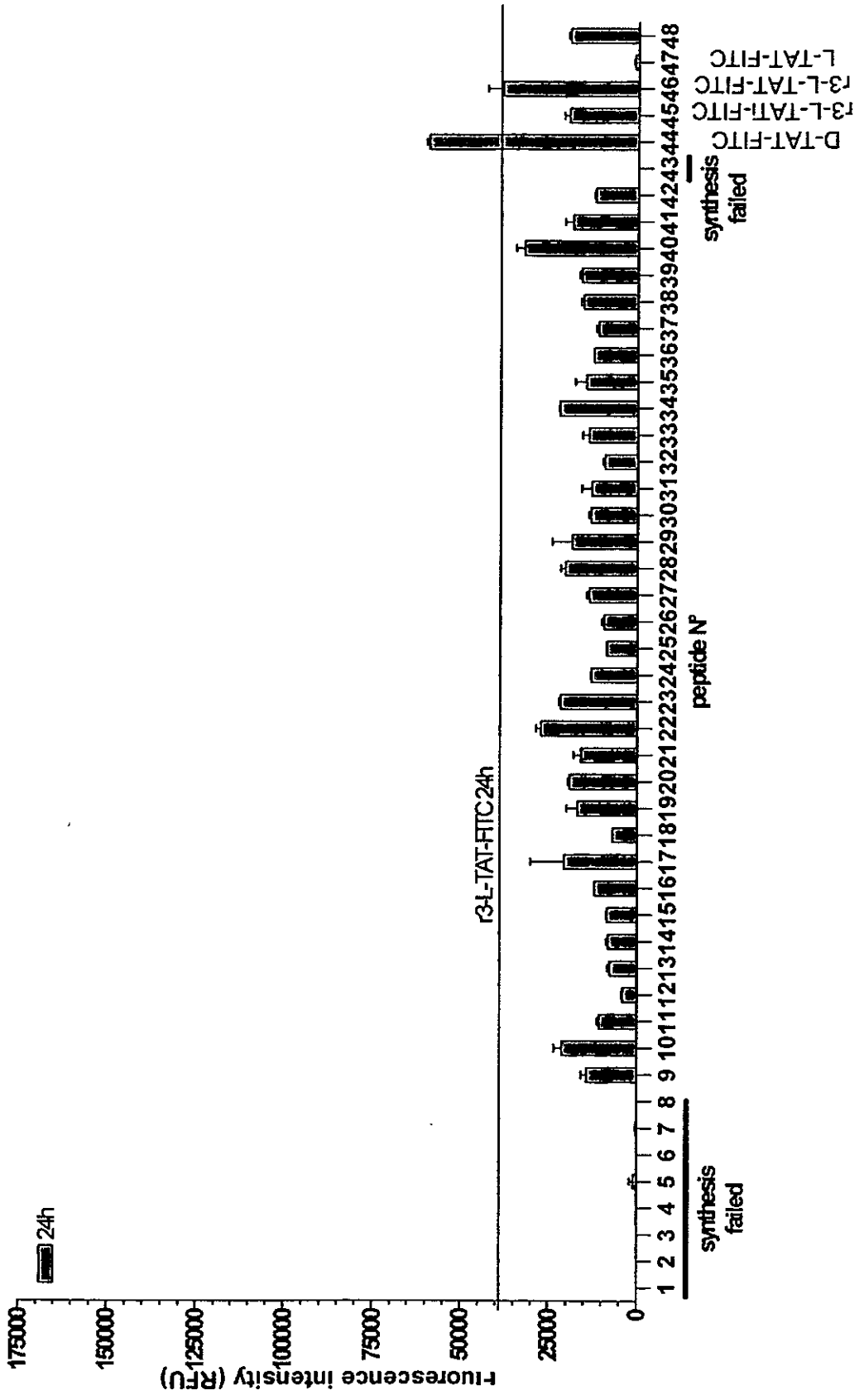

24h
fluorescence intensity (RFU)
175000
150000
125000
100000
75000
50000
25000
0
r3-L-TAT-FITC 24h
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48
peptide N°
synthesis failed
synthesis failed
D-TAT-FITC
r3-L-TAT-FITC
r3-L-TAT-FITC
L-TAT-FITC

Fig. 6a

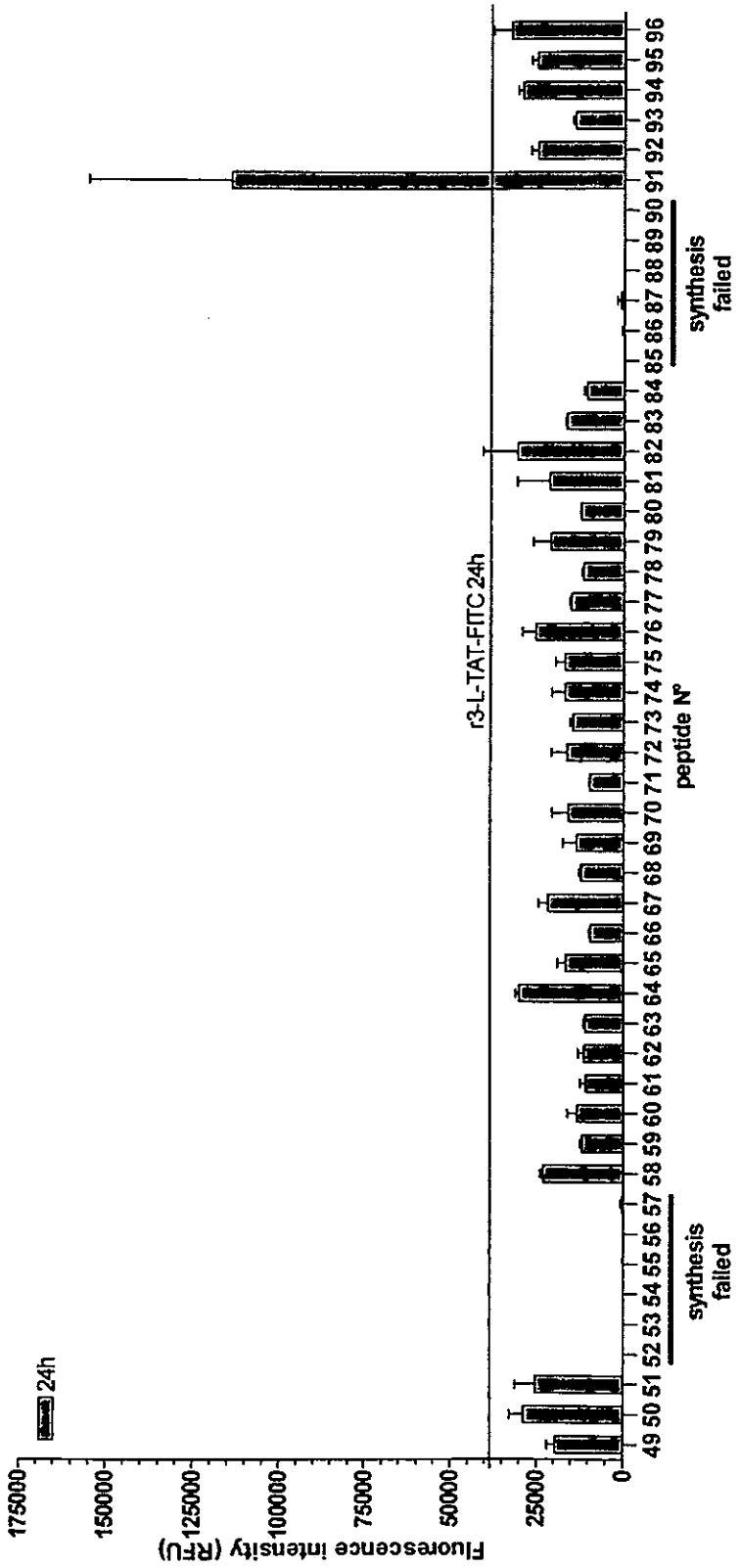

24h
Fluorescence intensity (RFU)
175000
150000
125000
100000
75000
50000
25000
0
r3-L-TAT-FITC 24h
peptide N°
49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96
synthesis failed
synthesis failed

Fig. 6b

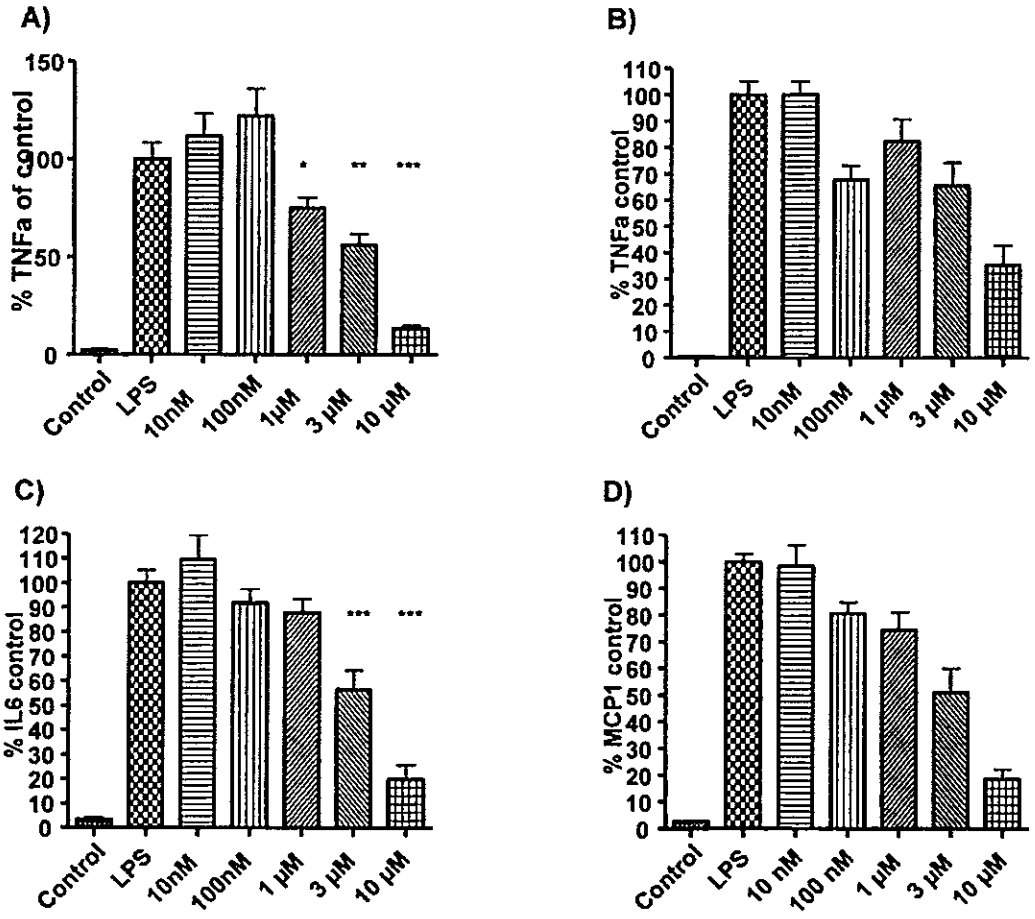

A)
% TNFa of control
150
100
50
0
*
**
***
Control
LPS
10nM
100nM
1µM
3 µM
10 µM
B)
% TNFa control
110
100
90
80
70
60
50
40
30
20
10
0
Control
LPS
10nM
100nM
1 µM
3 µM
10 µM
C)
% IL6 control
120
110
100
90
80
70
60
50
40
30
20
10
0
***
***
Control
LPS
10nM
100nM
1 µM
3 µM
10 µM
D)
% MCP1 control
110
100
90
80
70
60
50
40
30
20
10
0
Control
LPS
10 nM
100 nM
1 µM
3 µM
10 µM

Fig. 7

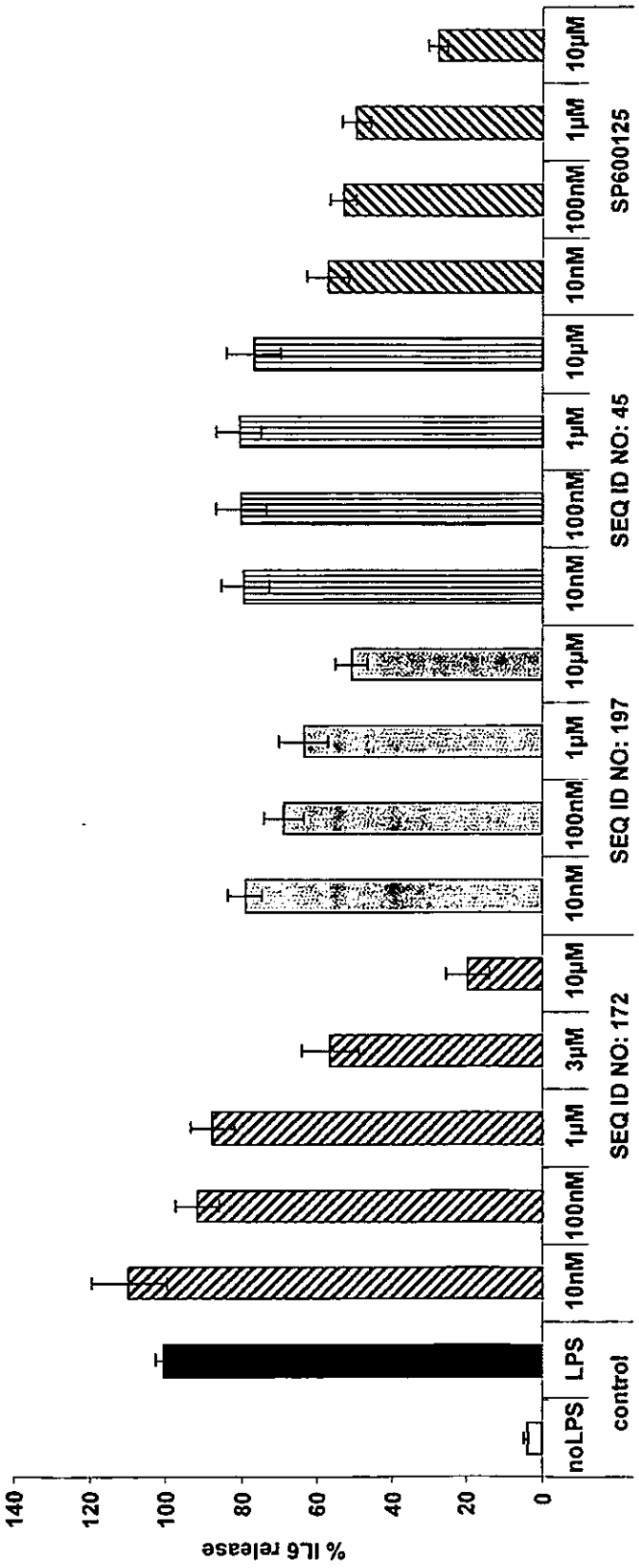

% IL6 release
0
20
40
60
80
100
120
140
noLPS
LPS
10nM
100nM
1µM
3µM
10µM
10nM
100nM
1µM
10µM
10nM
100nM
1µM
10µM
10nM
100nM
1µM
10µM
control
SEQ ID NO: 172
SEQ ID NO: 197
SEQ ID NO: 45
SP600125

Fig. 8

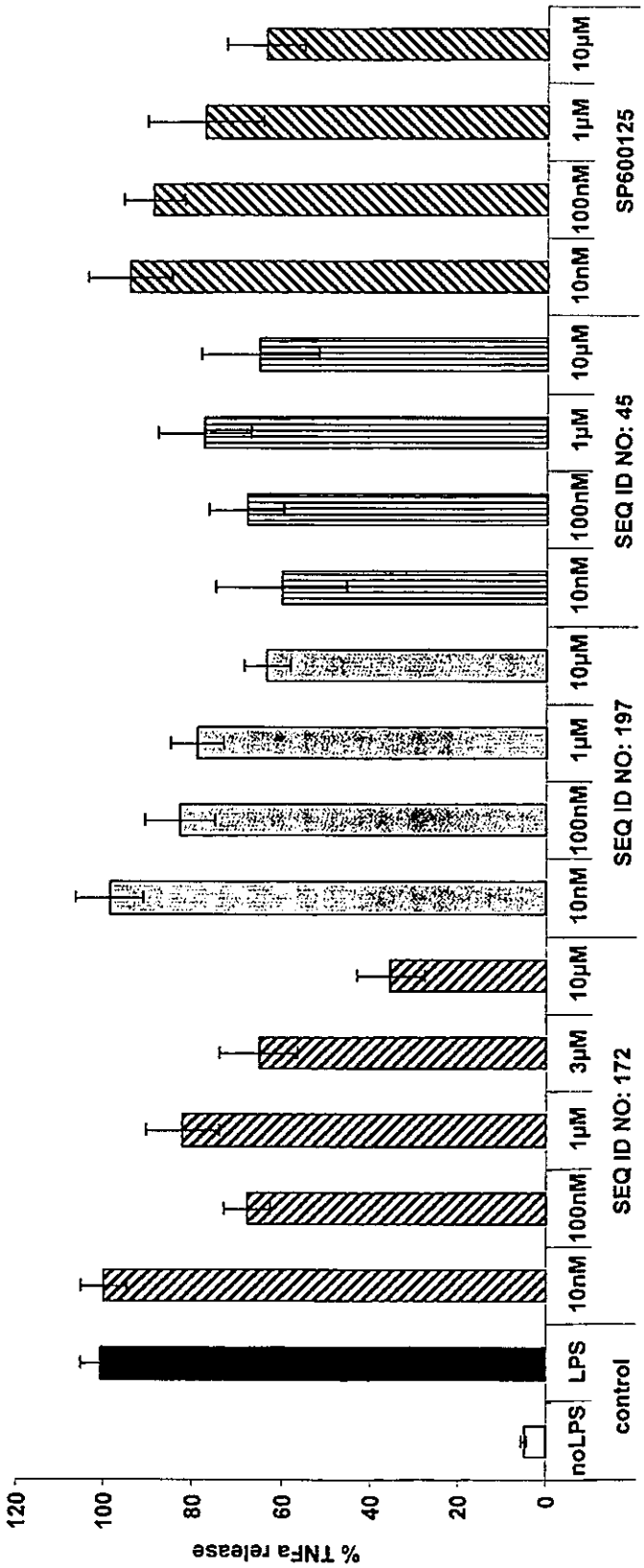

% TNFa release
120
100
80
60
40
20
0
noLPS
LPS
10nM
100nM
1µM
3µM
10µM
control
SEQ ID NO: 172
SEQ ID NO: 197
SEQ ID NO: 45
SP600125

Fig. 9

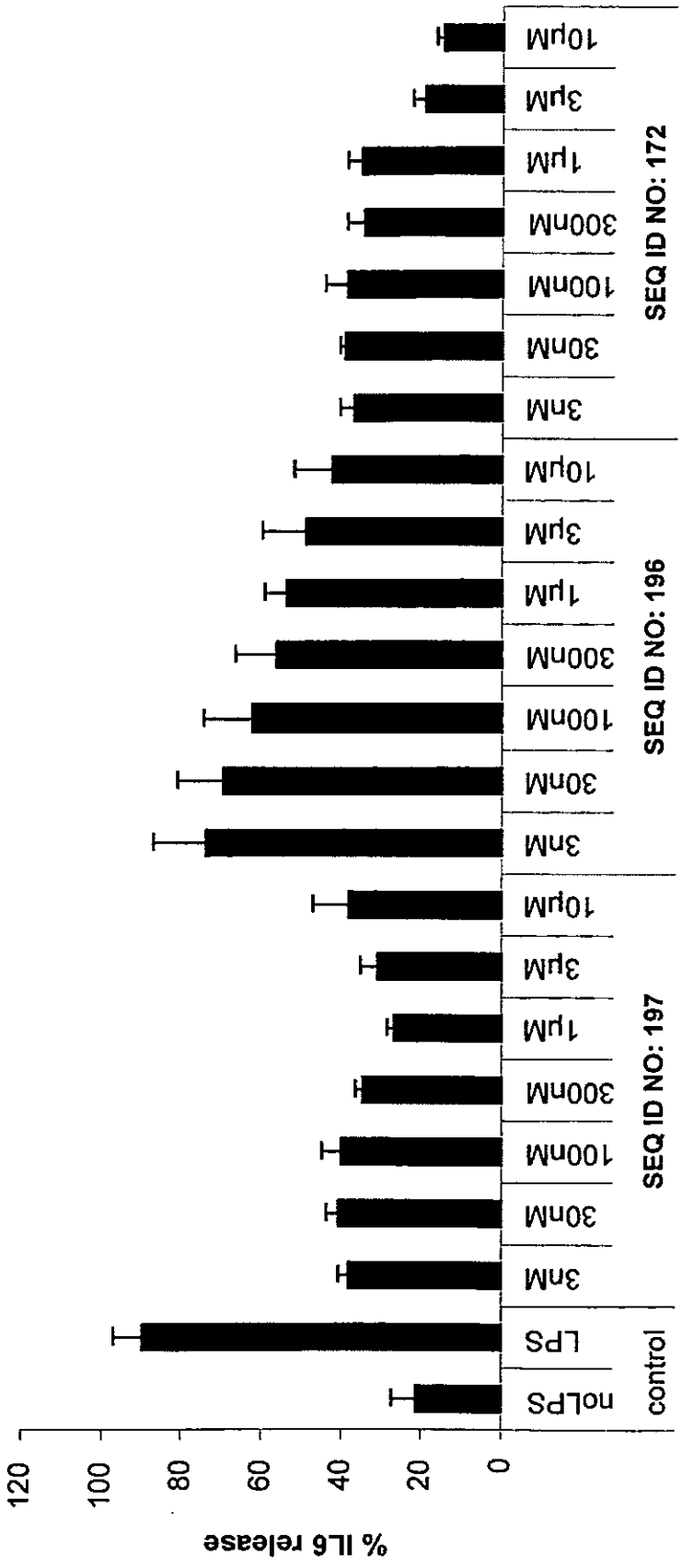

% IL6 release
120
100
80
60
40
20
0
control
noLPS
LPS
3nM
30nM
100nM
300nM
1µM
3µM
10µM
SEQ ID NO: 197
3nM
30nM
100nM
300nM
1µM
3µM
10µM
SEQ ID NO: 196
3nM
30nM
100nM
300nM
1µM
3µM
10µM
SEQ ID NO: 172

Fig. 10

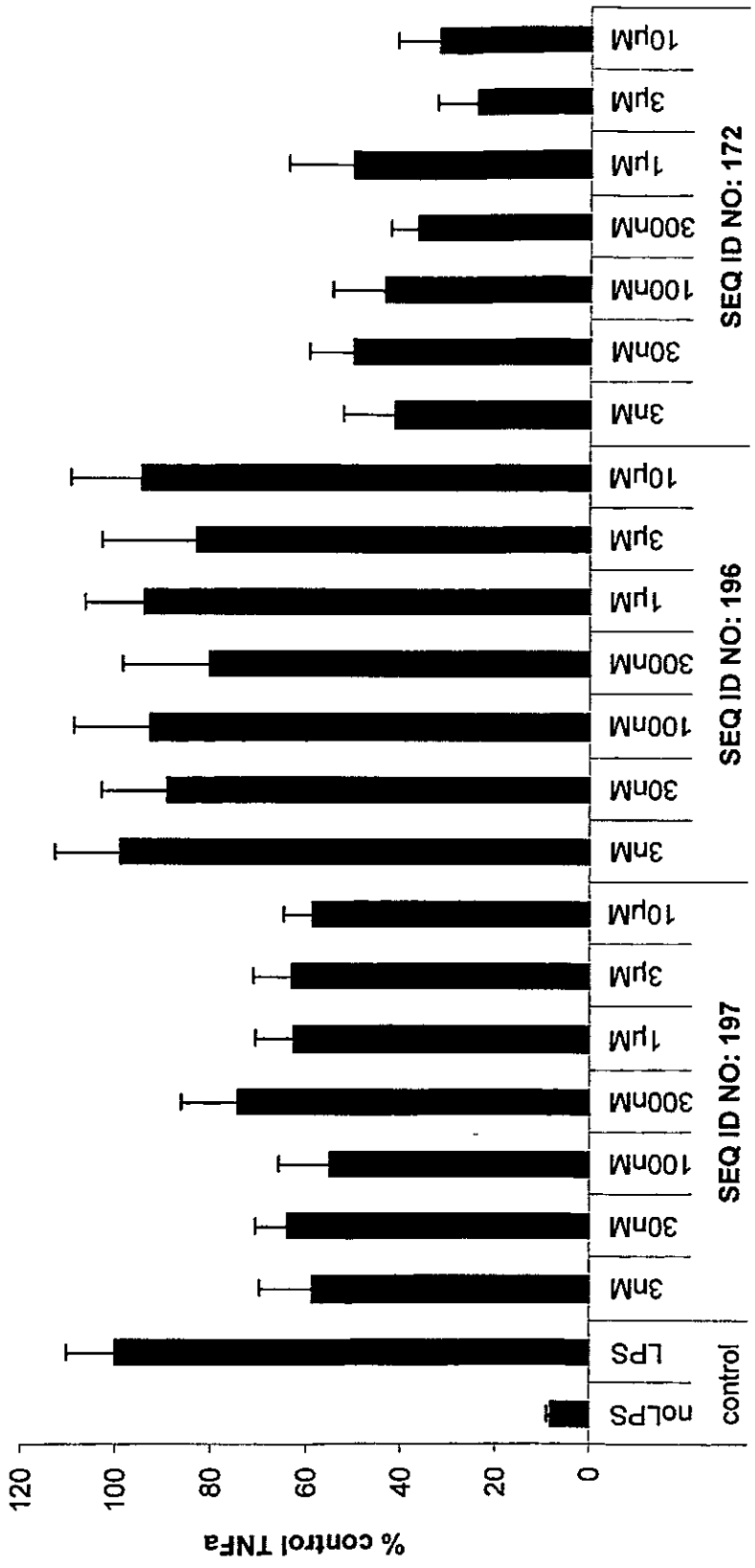

% control TNFa
120
100
80
60
40
20
0
control
noLPS
LPS
SEQ ID NO: 197
3nM
30nM
100nM
300nM
1µM
3µM
10µM
SEQ ID NO: 196
3nM
30nM
100nM
300nM
1µM
3µM
10µM
SEQ ID NO: 172
3nM
30nM
100nM
300nM
1µM
3µM
10µM

Fig. 11

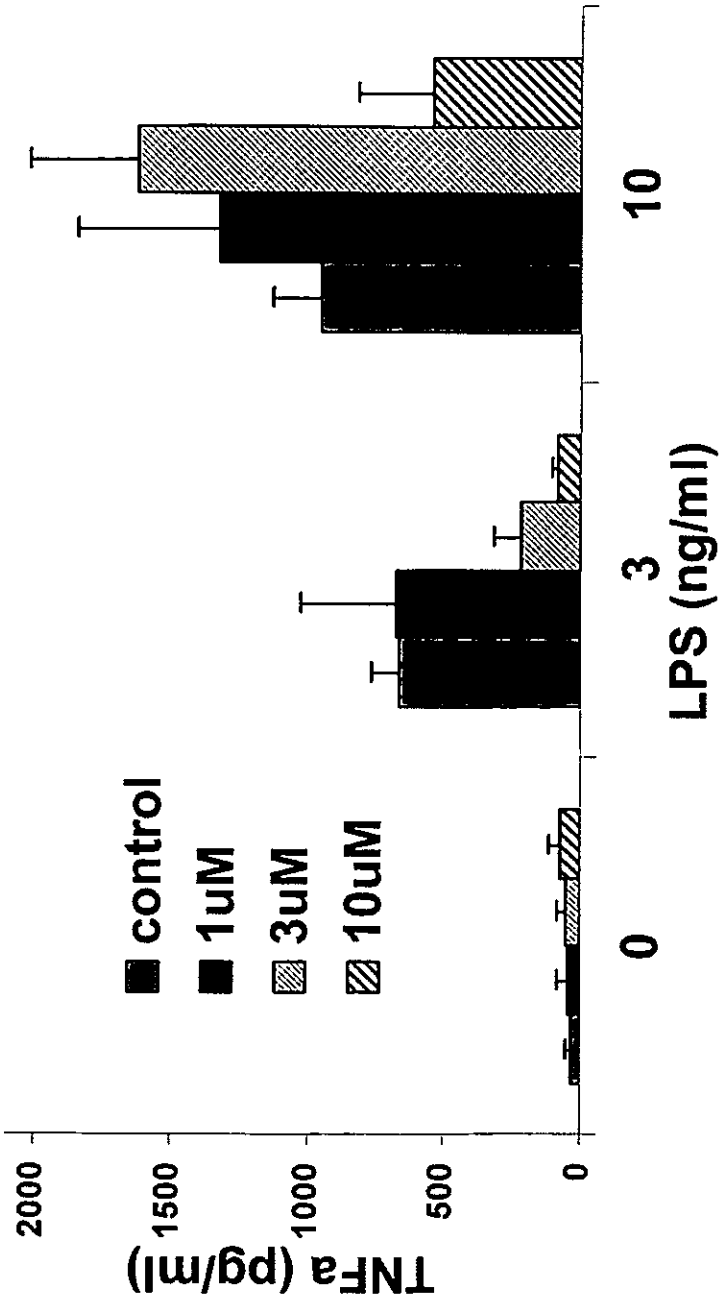

TNFa (pg/ml)
2000
1500
1000
500
0
control
1uM
3uM
10uM
0
3
10
LPS (ng/ml)

Fig. 12

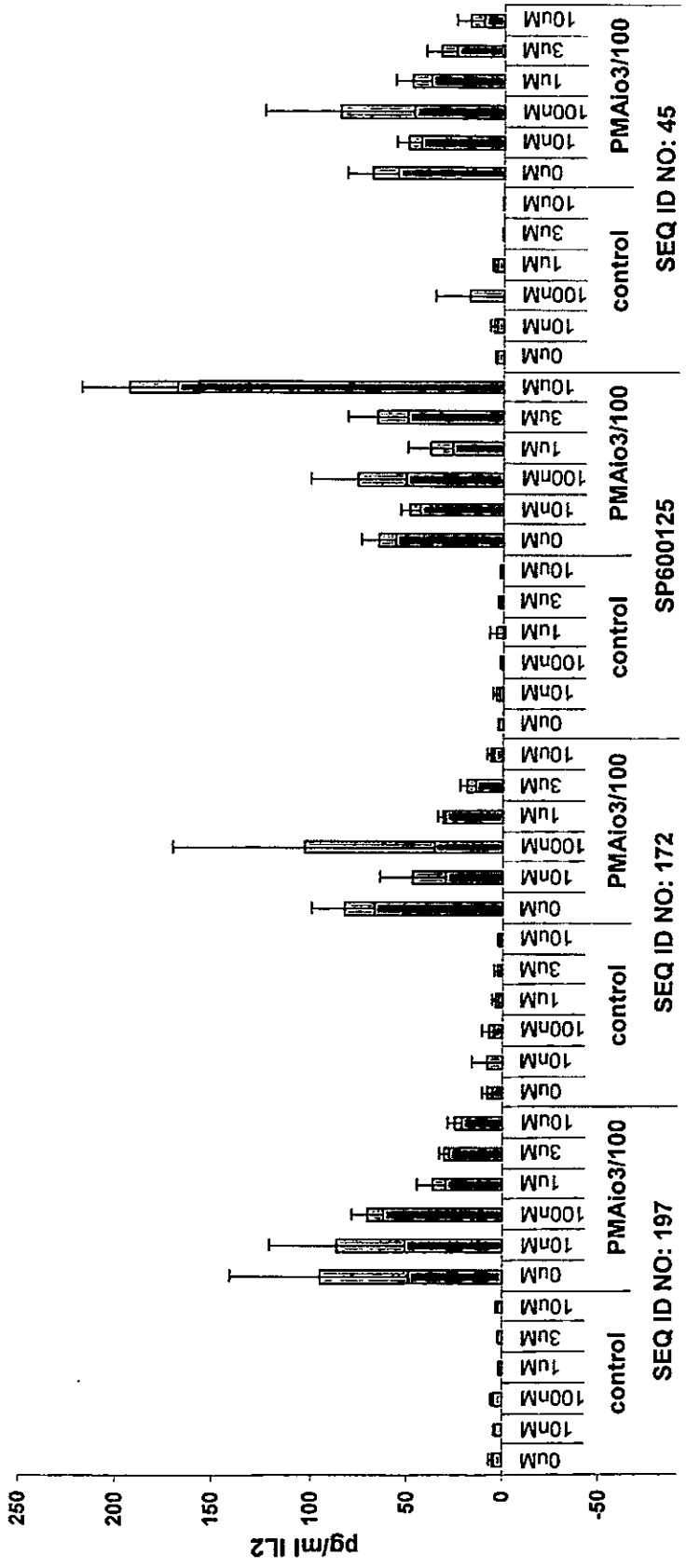

pg/ml IL2
250
200
150
100
50
0
-50
SEQ ID NO: 197
SEQ ID NO: 172
SP600125
SEQ ID NO: 45
PMAio3/100
control
0uM
10nM
100nM
1uM
3uM
10uM

Fig. 13

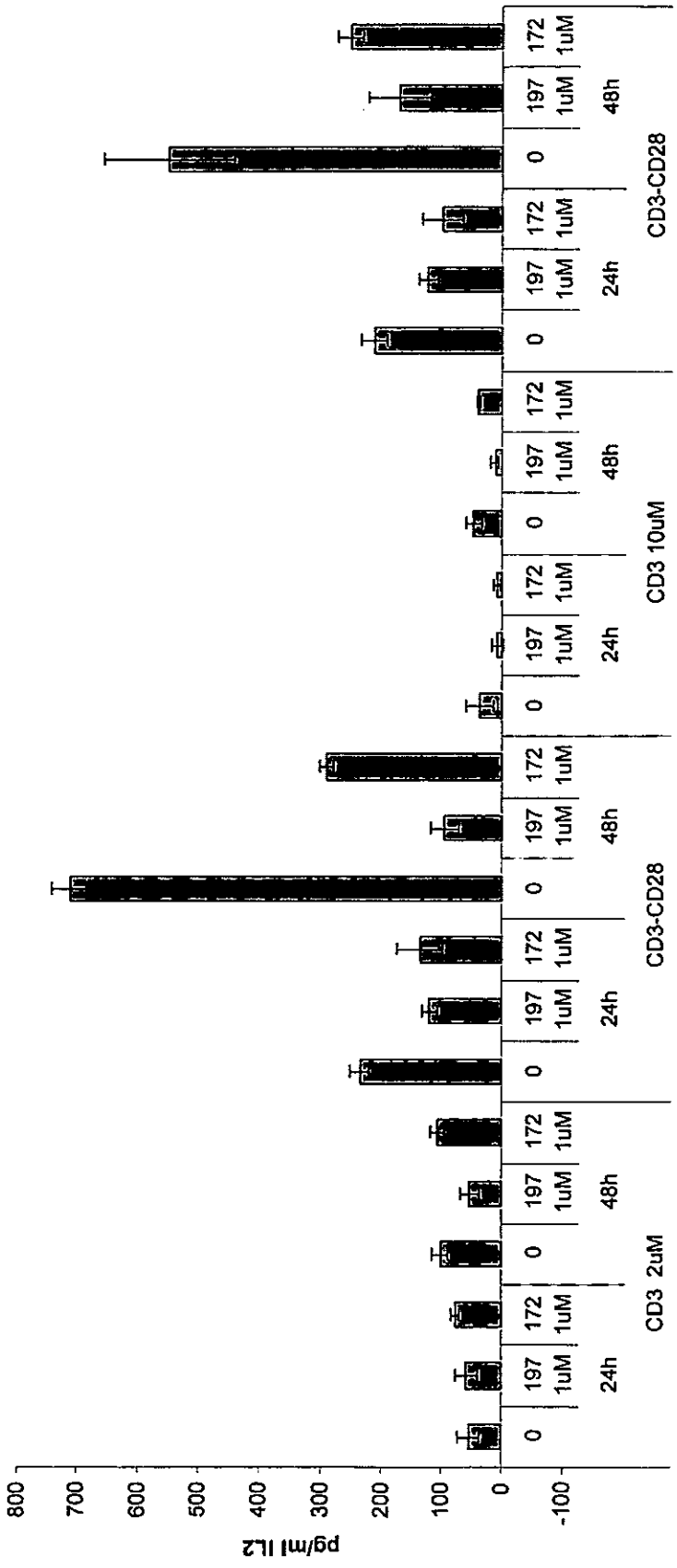

pg/ml IL2
800
700
600
500
400
300
200
100
0
-100
CD3 2uM
CD3-CD28
CD3 10uM
CD3-CD28
24h
48h
0
197 1uM
172 1uM

Fig. 14

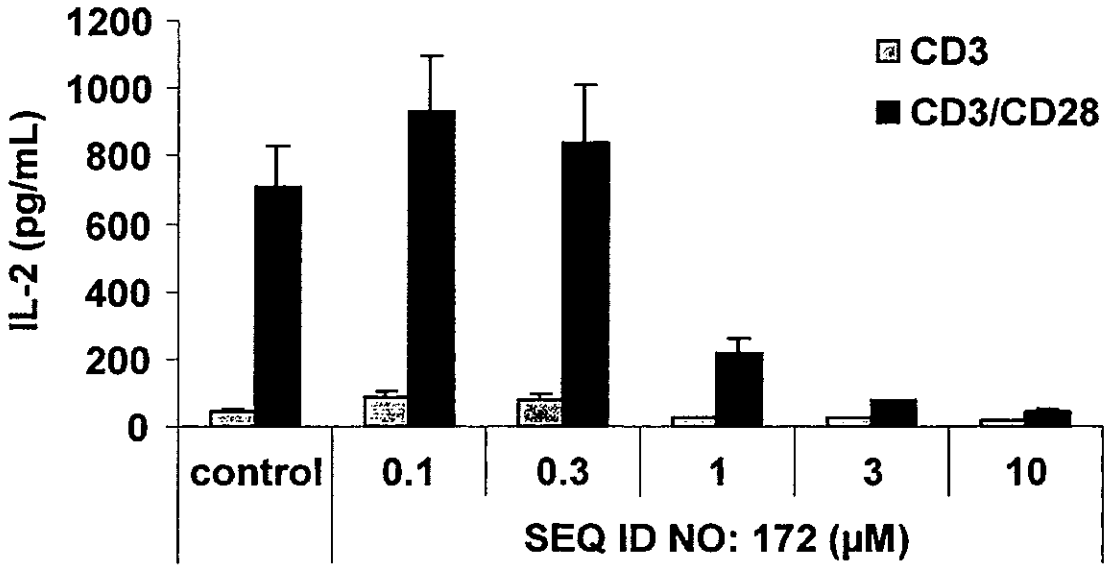

1200
1000
800
600
400
200
0
IL-2 (pg/mL)
CD3
CD3/CD28
control
0.1
0.3
1
3
10
SEQ ID NO: 172 (µM)

Fig. 15

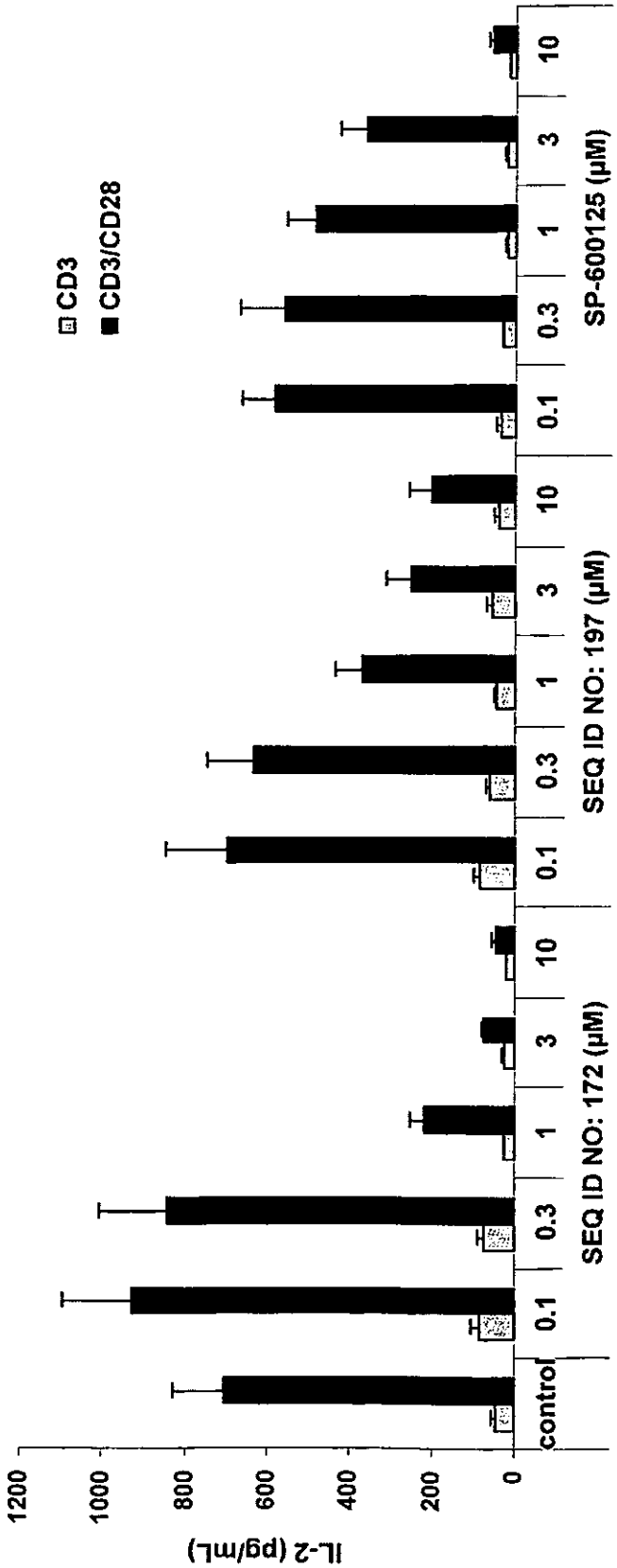

CD3
CD3/CD28
IL-2 (pg/mL)
1200
1000
800
600
400
200
0
control
0.1
0.3
1
3
10
SEQ ID NO: 172 (µM)
0.1
0.3
1
3
10
SEQ ID NO: 197 (µM)
0.1
0.3
1
3
10
SP-600125 (µM)

Fig. 16

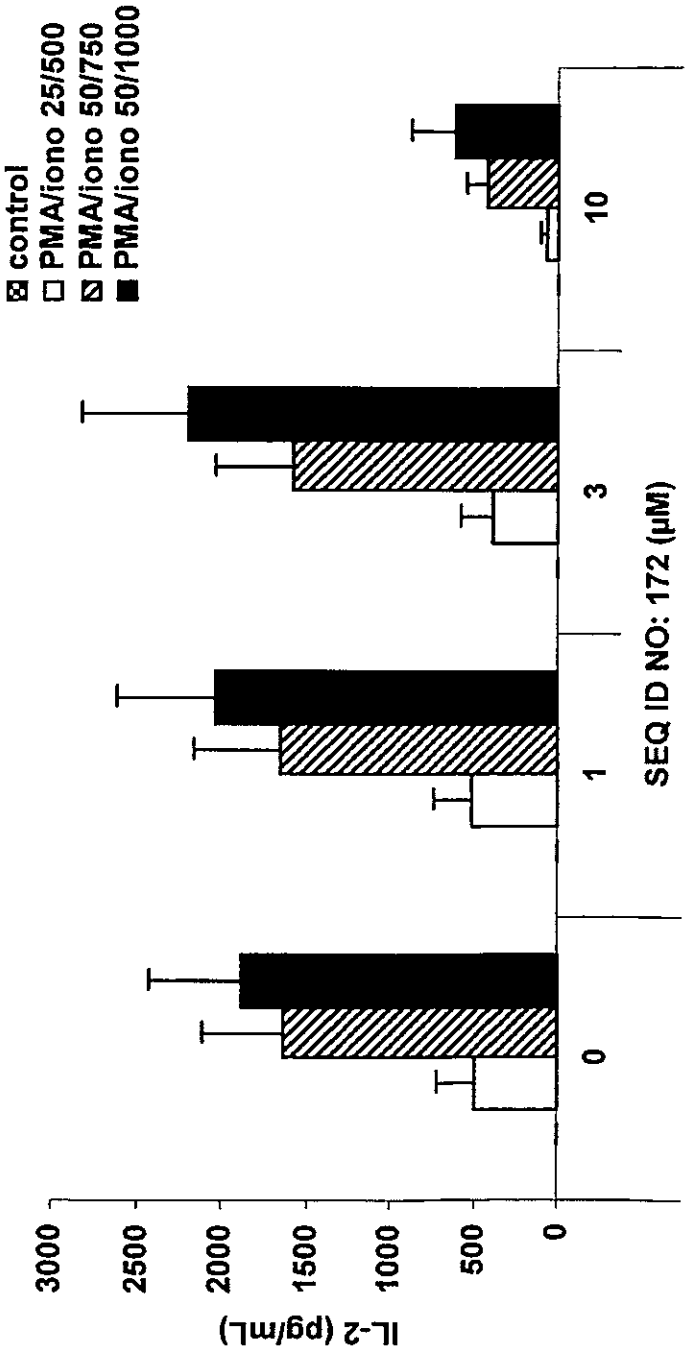

control
PMA/iono 25/500
PMA/iono 50/750
PMA/iono 50/1000
IL-2 (pg/mL)
3000
2500
2000
1500
1000
500
0
0
1
3
10
SEQ ID NO: 172 (µM)

Fig. 17

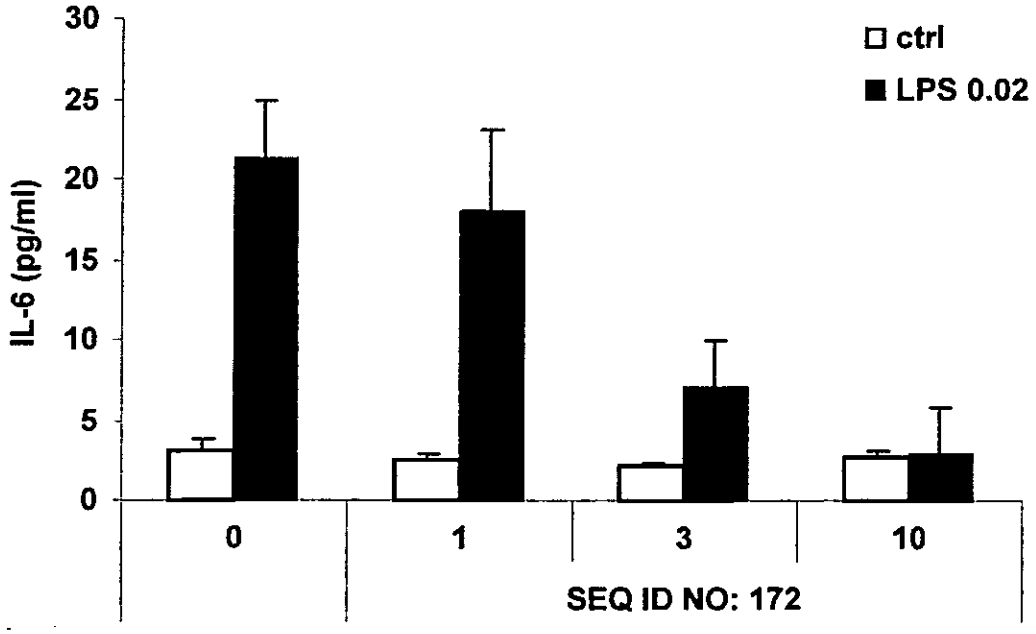


Fig. 18

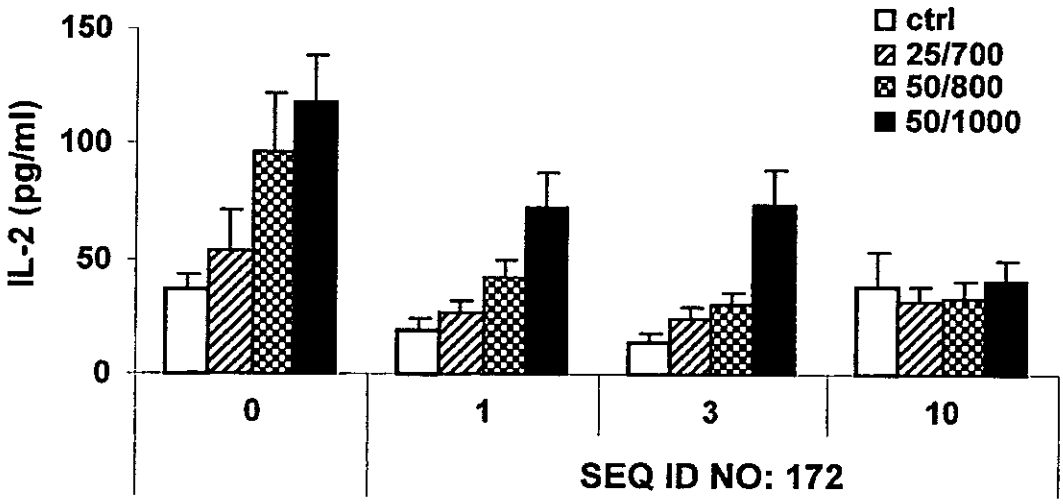

150
100
50
0
IL-2 (pg/ml)
ctrl
25/700
50/800
50/1000
0
1
3
10
SEQ ID NO: 172

Fig. 19

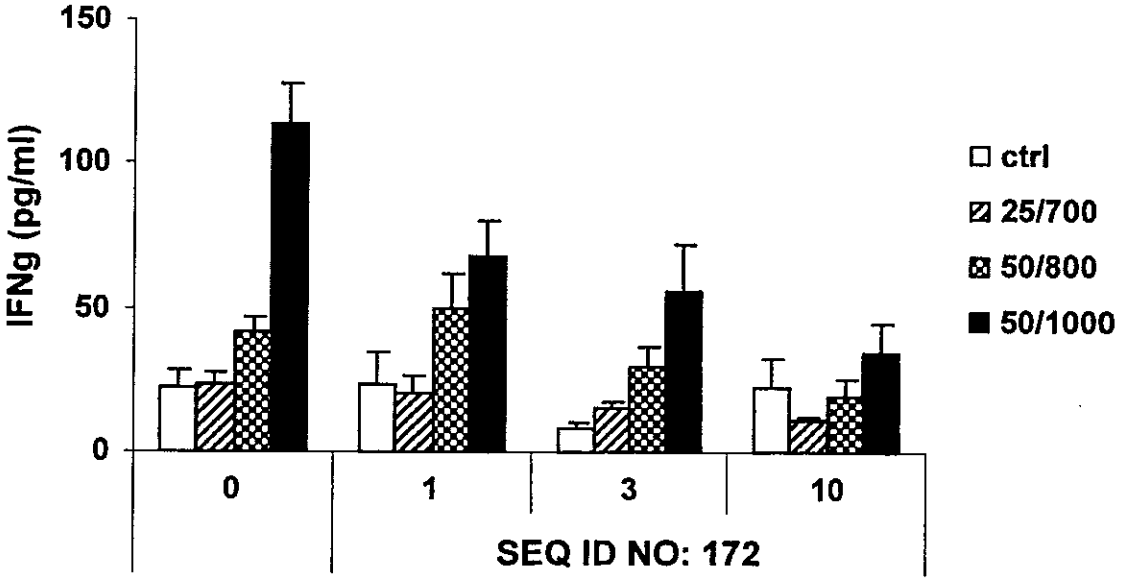

150
100
50
0
IFNg (pg/ml)
0
1
3
10
SEQ ID NO: 172
ctrl
25/700
50/800
50/1000

Fig. 20

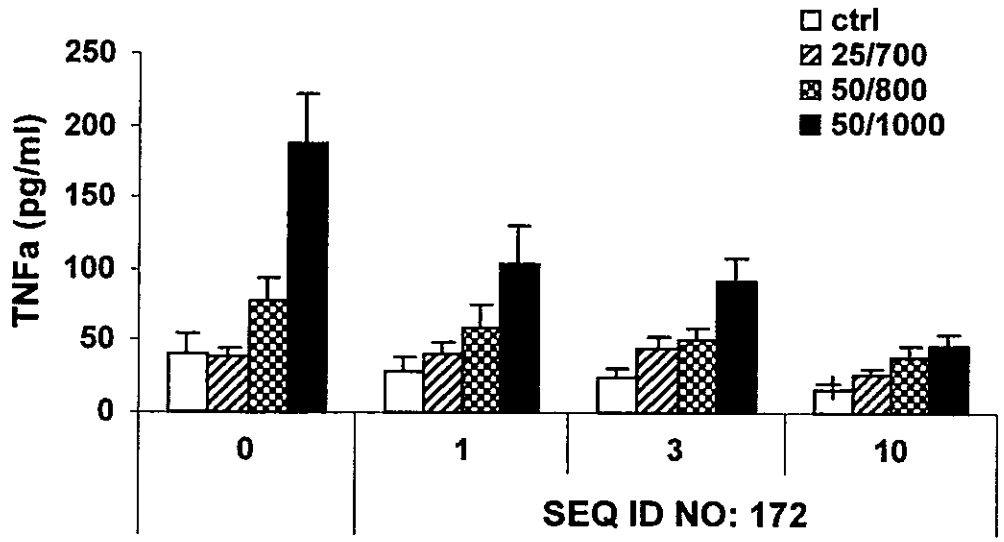

ctrl
25/700
50/800
50/1000
TNFa (pg/ml)
250
200
150
100
50
0
0
1
3
10
SEQ ID NO: 172

Fig. 21

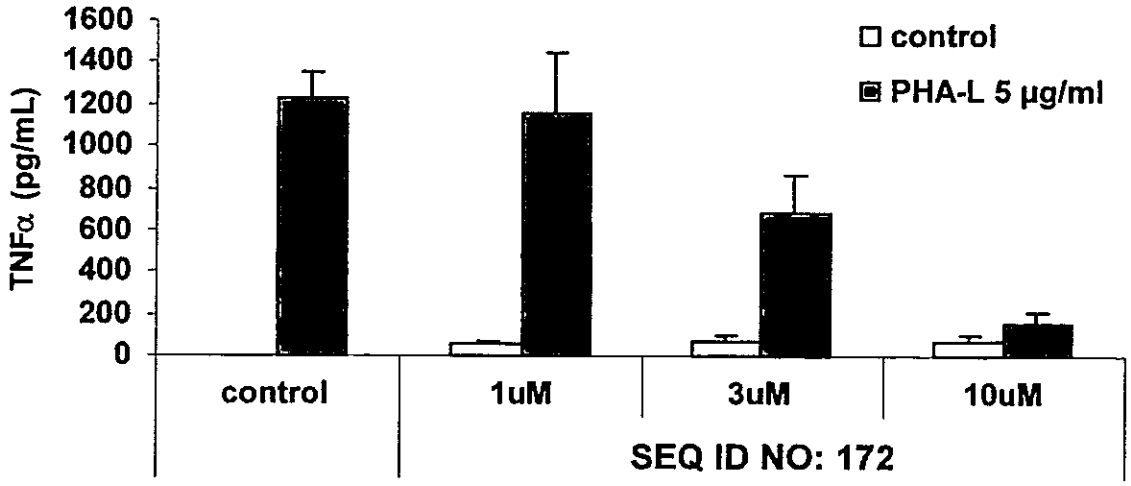

1600
1400
1200
1000
800
600
400
200
0
TNFα (pg/mL)
control
PHA-L 5 µg/ml
control
1uM
3uM
10uM
SEQ ID NO: 172

Fig. 22

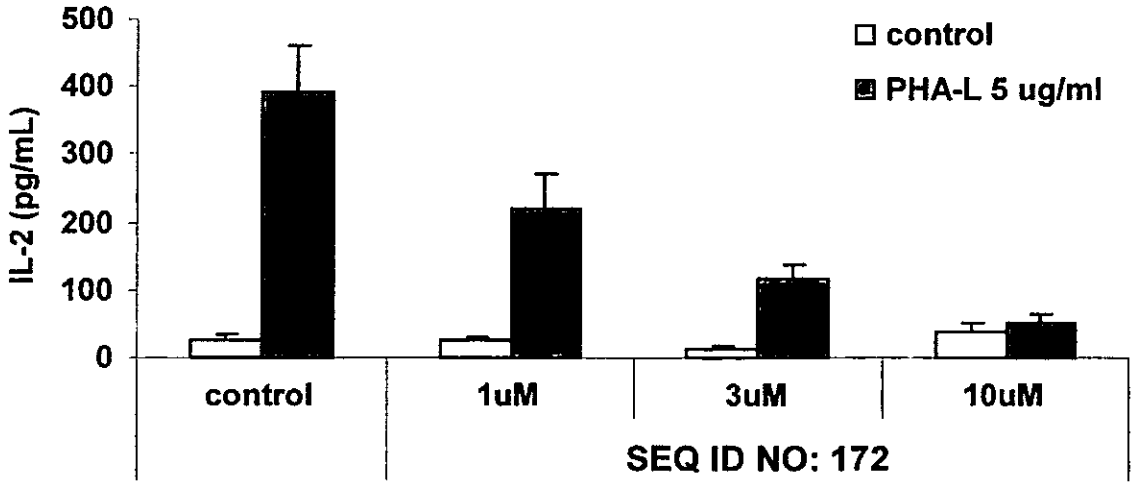

500
400
300
200
100
0
IL-2 (pg/mL)
control
PHA-L 5 ug/ml
control
1uM
3uM
10uM
SEQ ID NO: 172

Fig. 23

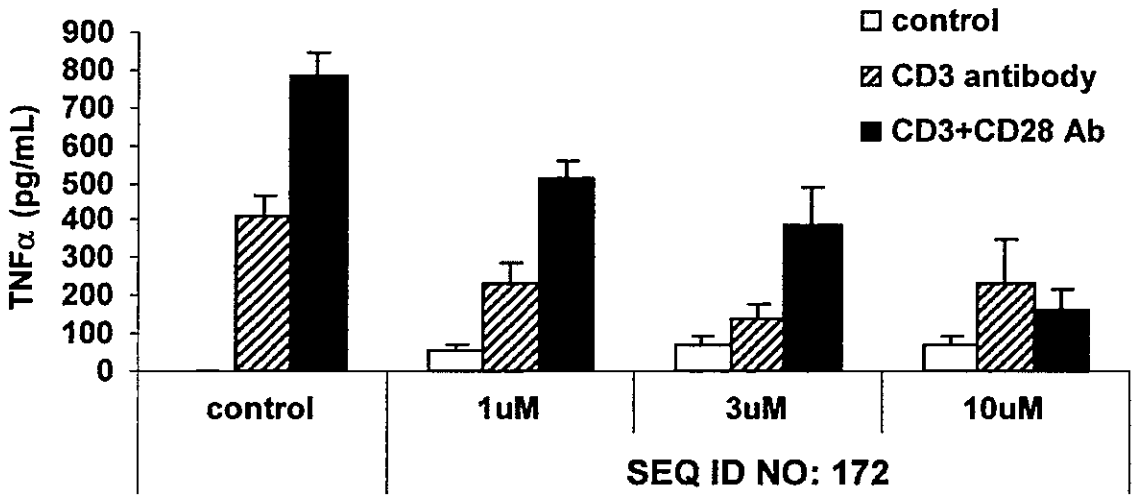

900
800
700
600
500
400
300
200
100
0
TNFα (pg/mL)
control
CD3 antibody
CD3+CD28 Ab
control
1uM
3uM
10uM
SEQ ID NO: 172

Fig. 24