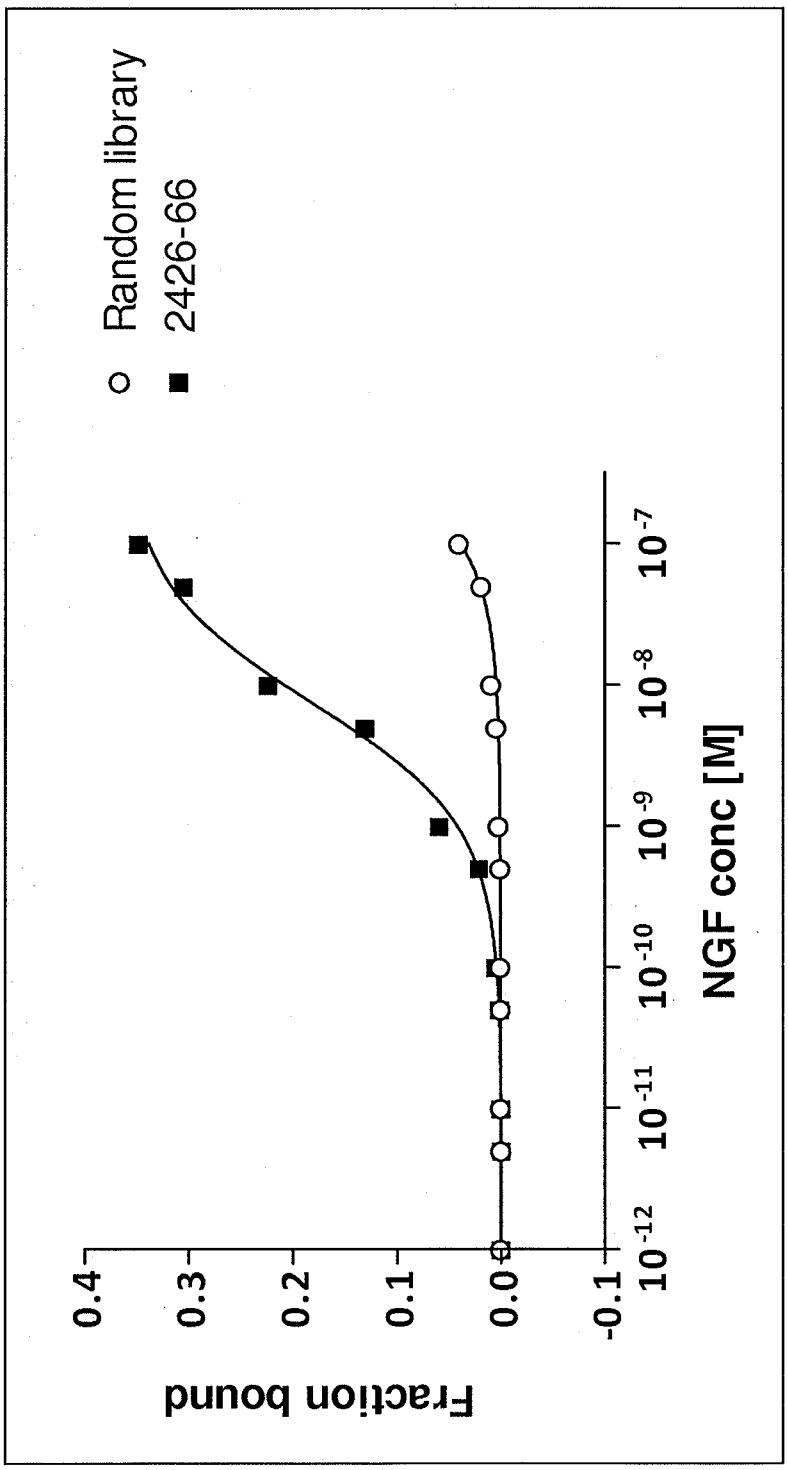

Random library
2426-66
Fraction bound
0.4
0.3
0.2
0.1
0.0
-0.1
10^{-12}
10^{-11}
10^{-10}
10^{-9}
10^{-8}
10^{-7}
NGF conc [M]

FIG. 1

FIG. 2A

Row (A)

	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
A	0	92	0	0	61	0	0	75	2	1	0	0	0	1	0	0	0	1	96	13	0	0	3	0	0	20	0	1
Z	23	0	99	1	0	2	3	2	0	97	97	2	0	0	0	99	99	87	0	13	0	0	1	94	93	0	89	7
G	17	7	0	98	38	97	96	20	10	0	2	97	99	98	96	0	0	7	2	71	0	1	89	0	0	71	0	62
C	57	0	0	0	0	0	0	0	86	0	0	0	0	0	0	0	0	0	0	0	97	93	0	0	0	0	0	6
T											•							•										

Consensus	B	A	Z	G	R	G	G	R	S	Z	W	G	G	G	G	Z	Z	W	A	D	C	C	G	Z	Z	R	Z	G

indicates the frequency at which A is observed in the 2426-66 aptamer family at each of the 28 conserved positions
Row (Z) indicates the frequency at which Z is observed in the 2426-66 aptamer family at each of the 28 conserved positions
Row (G) indicates the frequency at which G is observed in the 2426-66 aptamer family at each of the 28 conserved positions
Row (C) indicates the frequency at which C is observed in the 2426-66 aptamer family at each of the 28 conserved positions
Row (T) indicates the only two conserved Z positions that can be replaced with T with no loss of β-NGF binding activity (•)

Row (Consensus) is the consensus sequence for the aptamer with the BzdU substitution, where:

Z = modified U
B = any nucleotide other than A
R = A or G
S = C or G
W = Z or T
D = any nucleotide other than C

FIG. 2B

	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
A	0	92	0	0	0	51	0	0	0	75	2	0	1	0	0	0	1	0	0	0	0	1	96	13	0	0	0	3	0	0	0	20	0	1
Z	23	0	0	99	1	0	1	2	3	2	0	1	97	97	2	0	0	0	0	99	99	87	0	13	0	0	0	1	94	93	0	0	89	7
G	17	7	1	0	98	38	0	97	96	20	10	6	0	2	97	99	98	96	3	0	0	7	2	71	0	0	1	89	0	0	1	71	0	62
C	57	0	0	0	0	0	0	0	0	0	86	0	0	0	0	0	0	0	0	0	0	0	0	0	0	97	93	0	0	0	0	0	0	6
-	0	0	98	0	0	0	97	0	0	0	0	91	0	0	0	0	0	3	95	0	0	3	0	0	97	1	2	4	4	6	96	6	8	20

Consensus	B	A	-	Z	G	R	-	G	G	R	S	-	Z	Z	G	G	G	G	-	Z	Z	Z	A	D	-	C	C	G	Z	Z	-	R	Z	G

Row (A) indicates the frequency at which A is observed in the 2426-66 aptamer family at each of the 34 conserved positions
Row (Z) indicates the frequency at which Z is observed in the 2426-66 aptamer family at each of the 34 conserved positions
Row (G) indicates the frequency at which G is observed in the 2426-66 aptamer family at each of the 34 conserved positions
Row (C) indicates the frequency at which C is observed in the 2426-66 aptamer family at each of the 34 conserved positions
Row (-) indicates the frequency at which a deletion is observed in the 2426-66 aptamer family at each of the 34 conserved positions

Row (Consensus) is the consensus sequence for the aptamer with the BzdU substitution, where:

Z = modified U
B = C, G or Z
R = A or G
S = C or G
D = A, G or Z

FIG. 3

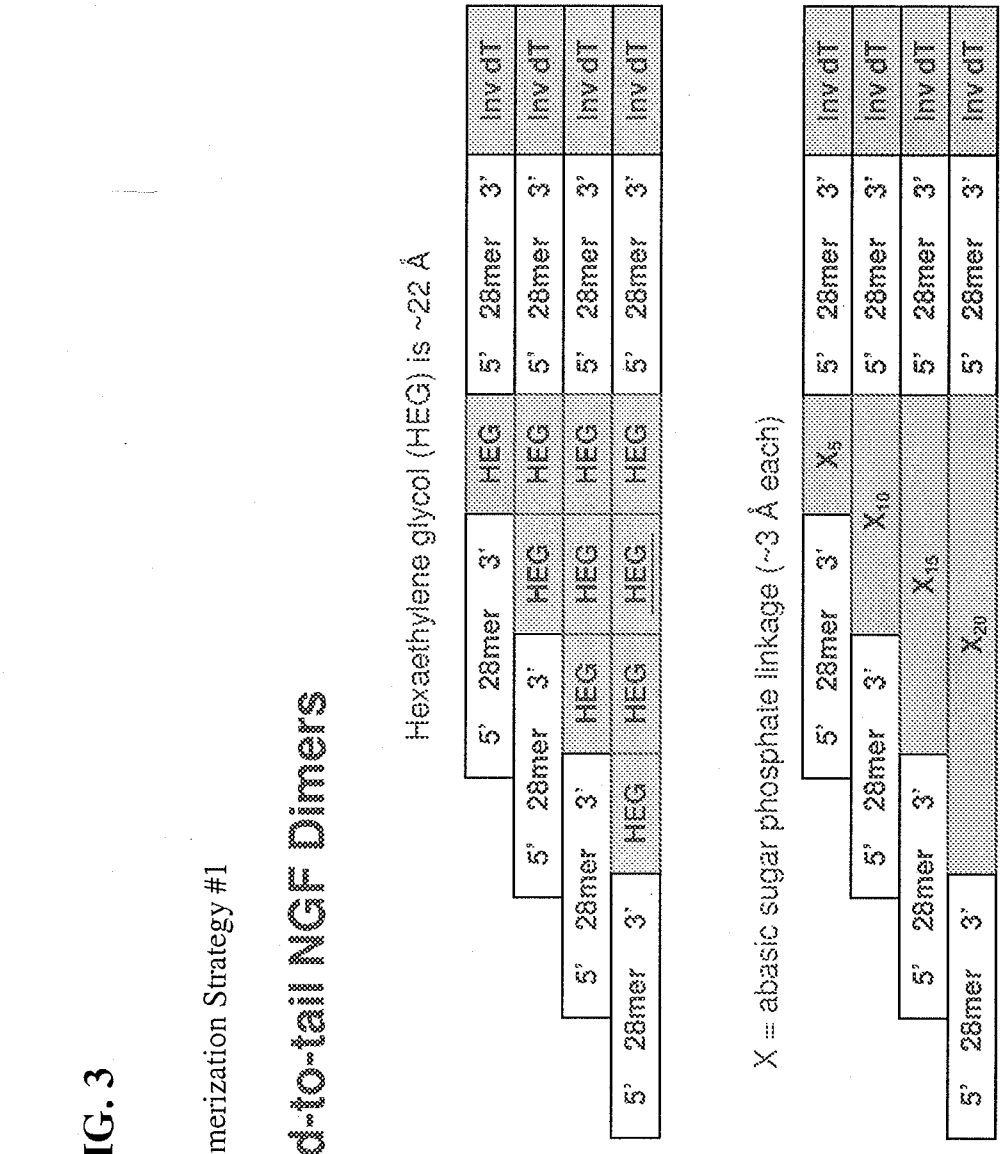
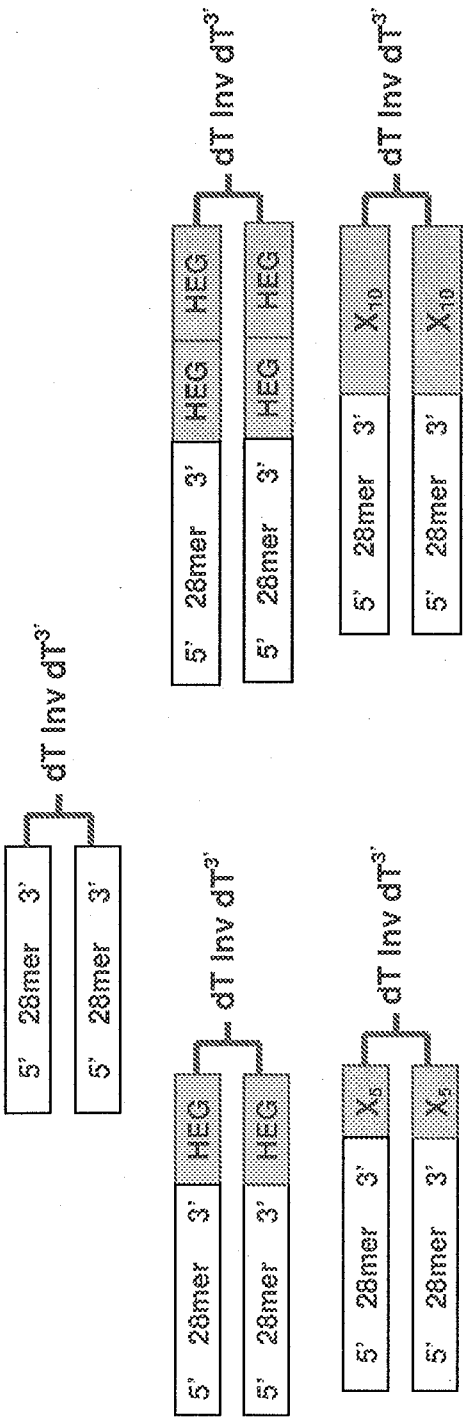

Dimerization Strategy #1
Head-to-tail NGF Dimers
Hexaethylene glycol (HEG) is ~22 Å
5' 28mer 3'
HEG
Inv dT
X = abasic sugar phosphate linkage (~3 Å each)
X5
X10
X15
X20

FIG. 4

Dimerization Strategy #2



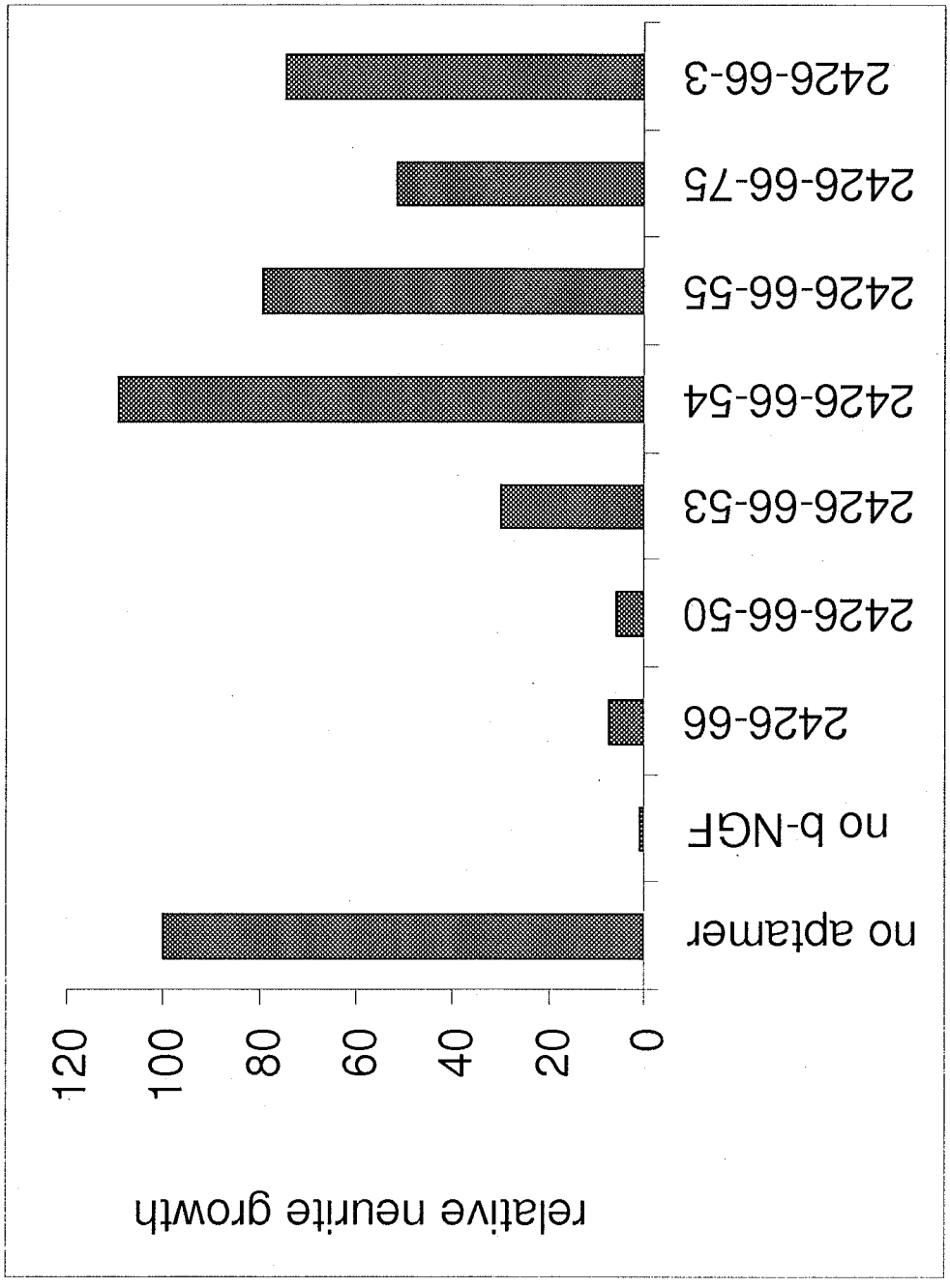

relative neurite growth
120
100
80
60
40
20
0
no aptamer
no b-NGF
2426-66
2426-66-50
2426-66-53
2426-66-54
2426-66-55
2426-66-75
2426-66-3

FIG. 5

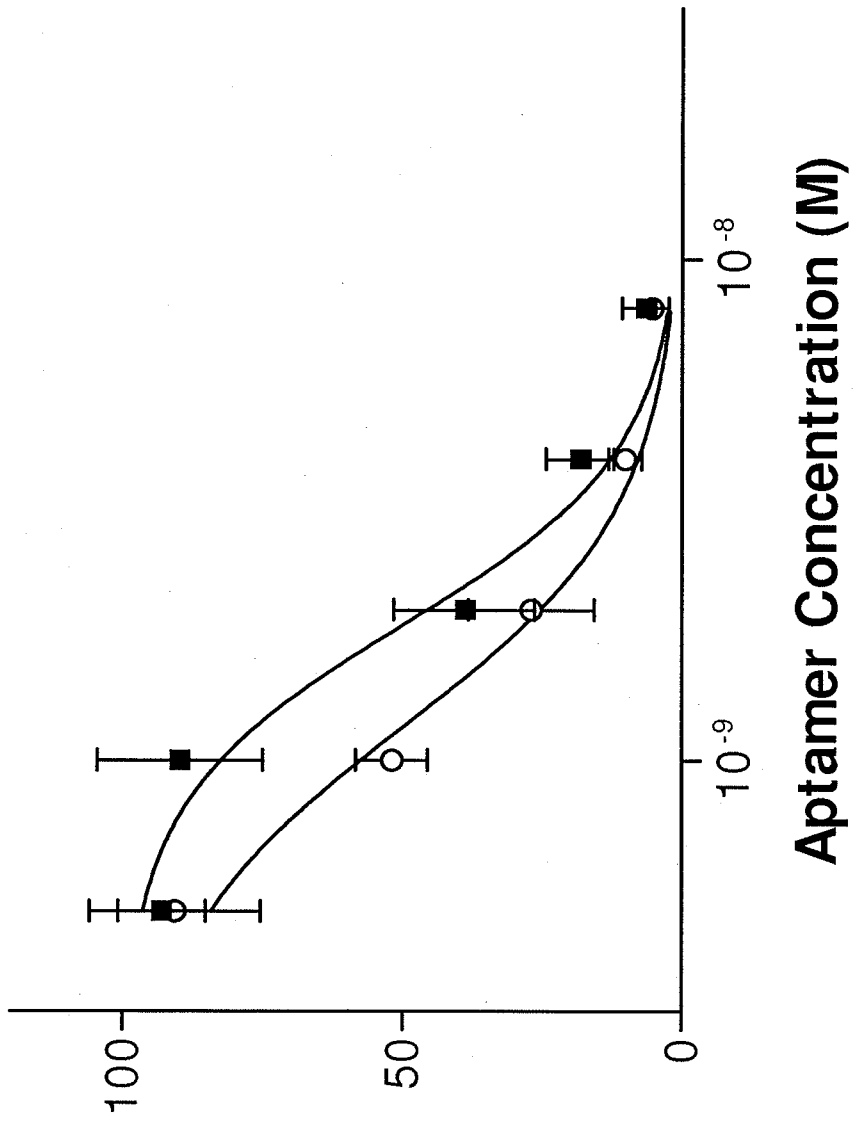

relative neurite growth
100
50
0
10^{-9}
10^{-8}
Aptamer Concentration (M)

FIG. 6

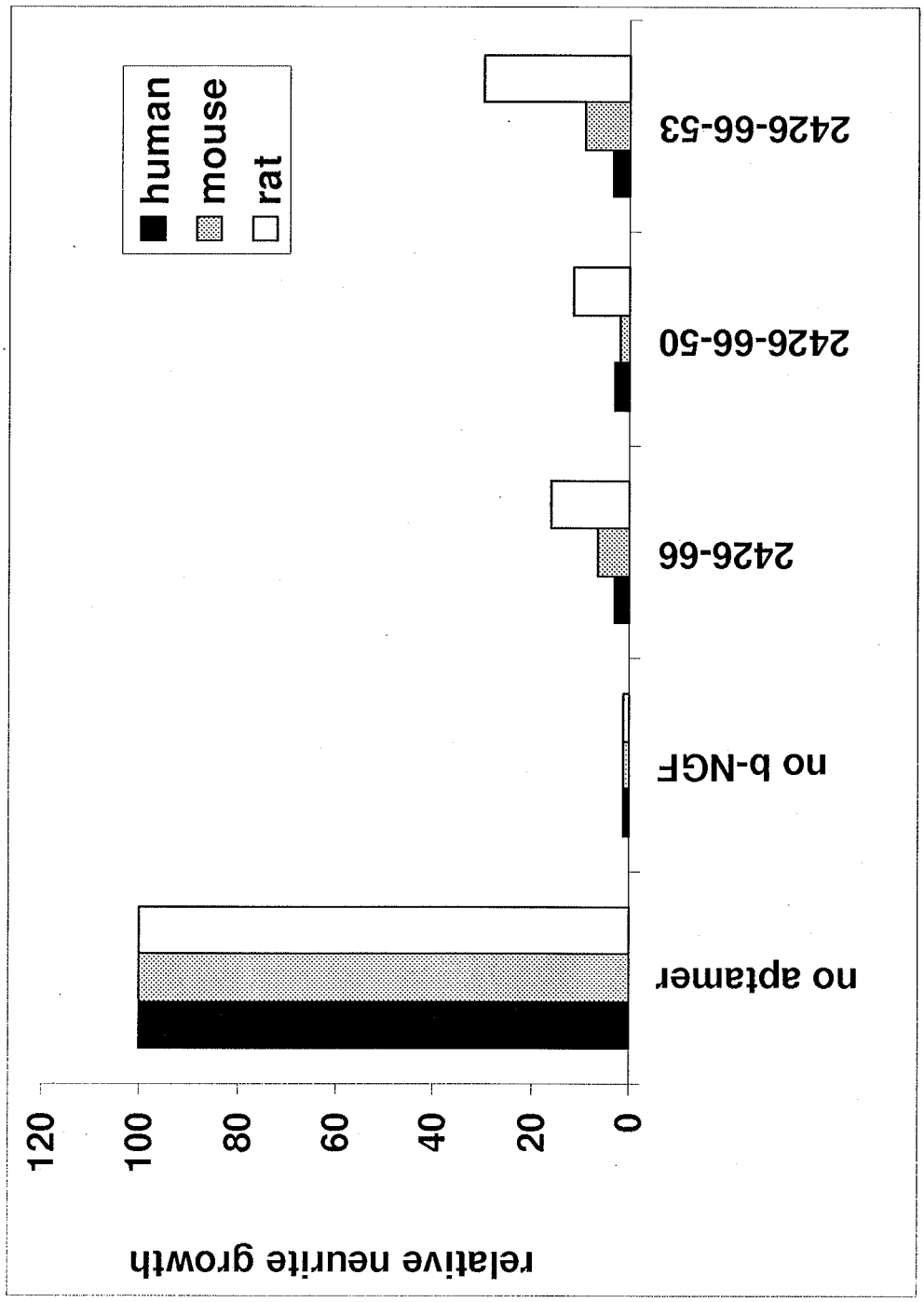

relative neurite growth
120
100
80
60
40
20
0
human
mouse
rat
no aptamer
no b-NGF
2426-66
2426-66-50
2426-66-53

FIG. 7

FIG. 8

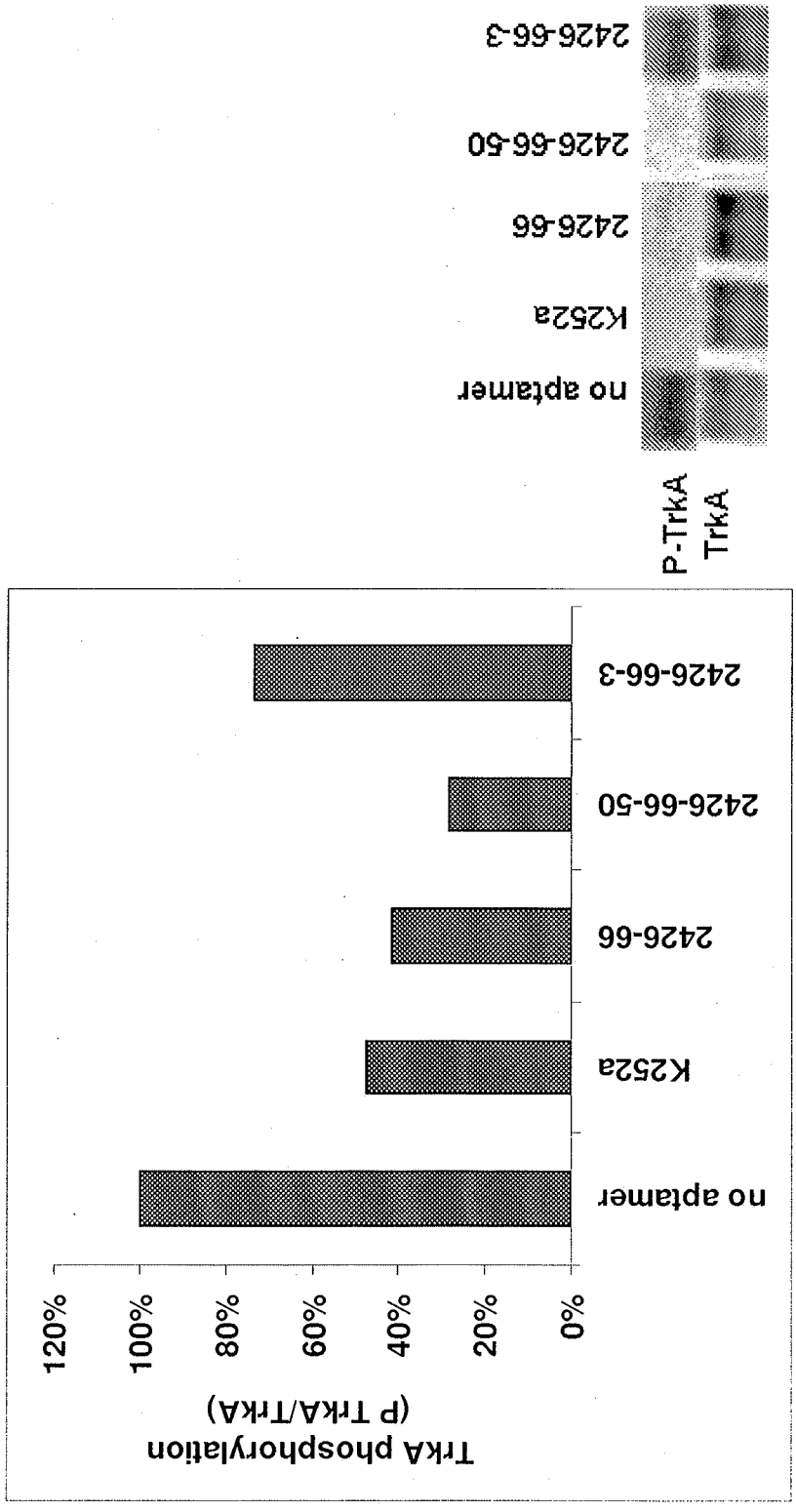

TrkA phosphorylation
(P TrkA/TrkA)
120%
100%
80%
60%
40%
20%
0%
no aptamer
K252a
2426-66
2426-66-50
2426-66-3
P-TrkA
TrkA
no aptamer
K252a
2426-66
2426-66-50
2426-66-3

FIG. 9

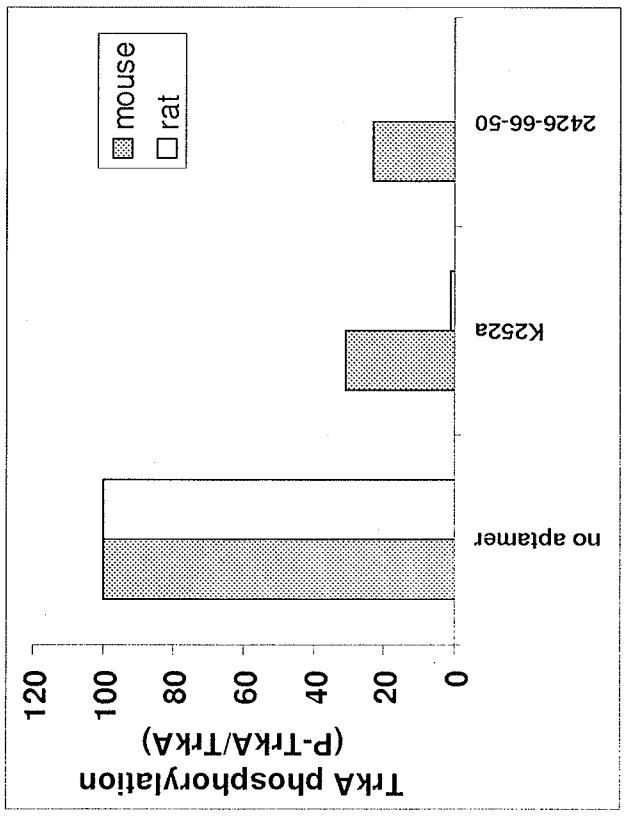
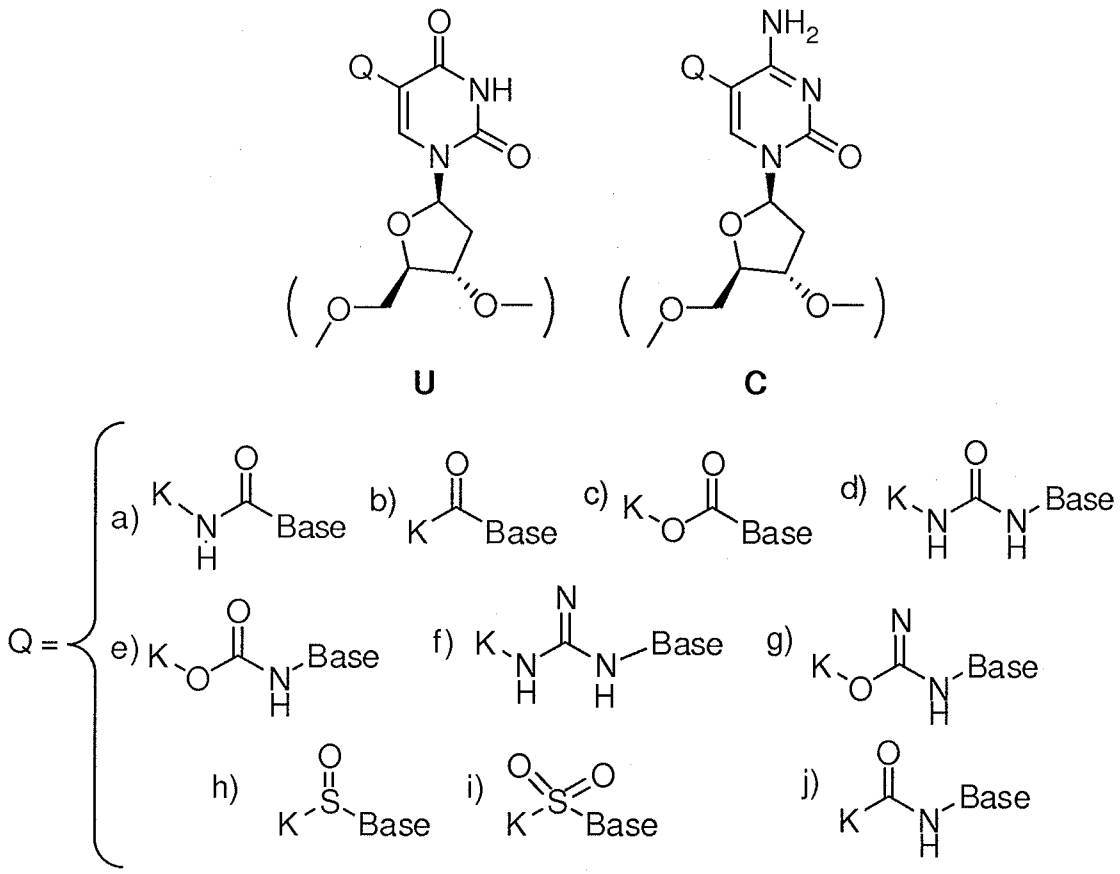

TrkA phosphorylation
(P-TrkA/TrkA)
120
100
80
60
40
20
0
mouse
rat
no aptamer
K252a
2426-66-50
P-TrkA
TrkA
Mouse
no aptamer
K252a
2426-66-50
Rat
no aptamer
K252a
2426-66-50

FIG. 10



Base = Uridine (U) or Cytidine(C) (attachment is to the 5-position)
K = R' group plus $(CH_2)_n$ connecting group, where n = 0-3

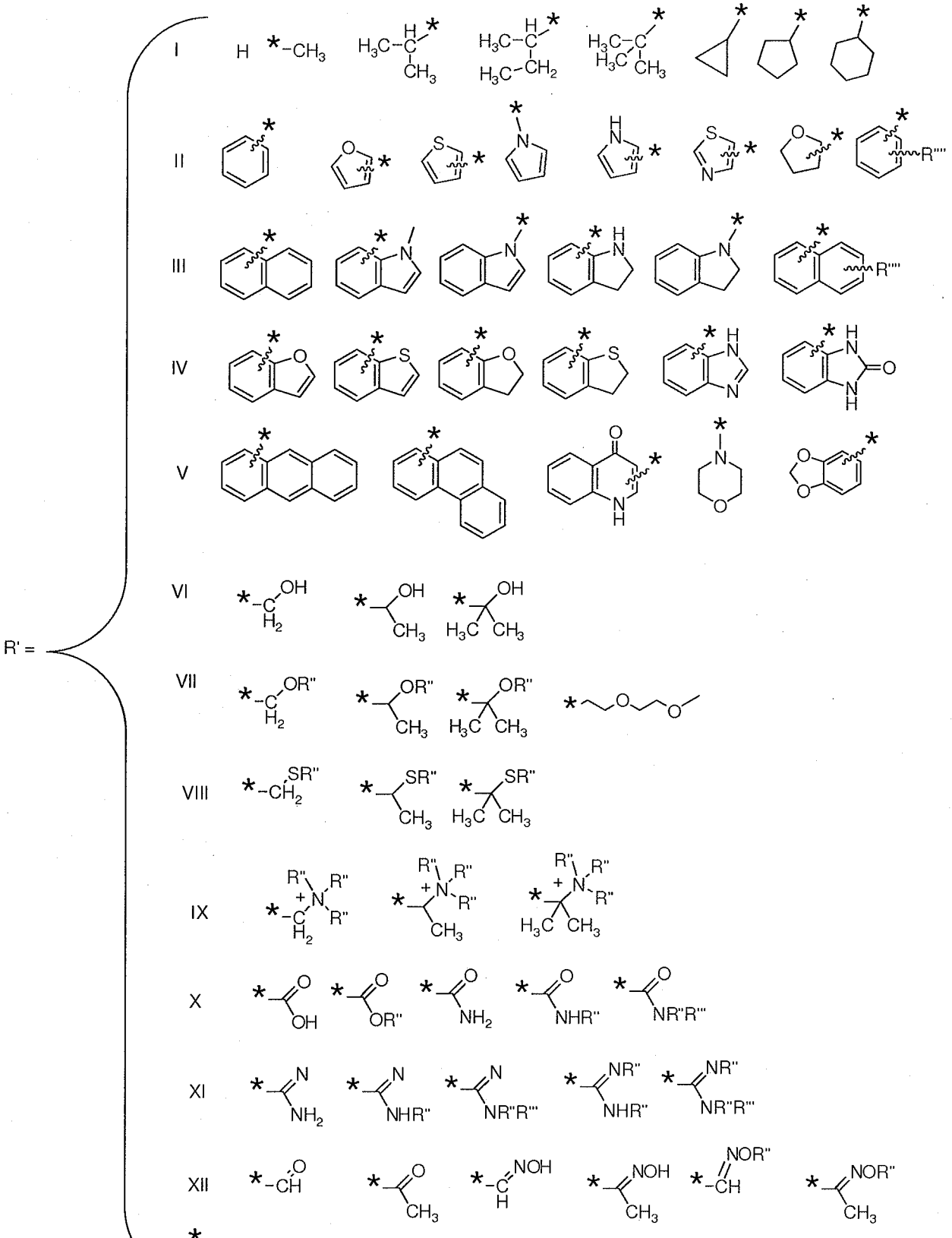


FIG. 10 continued

FIG. 10 continued

wherein

R"" is selected from the group consisting of a branched or linear lower alkyl (C1-C20); halogen (F, Cl, Br, I); nitrile (CN); boronic acid (BO_2H_2); carboxylic acid (COOH); carboxylic acid ester (COOR"); primary amide ($CONH_2$); secondary amide (CONHR"); tertiary amide (CONR"R'"); sulfonamide (SO_2NH_2); N-alkylsulfonamide (SONHR");

wherein

R", R'" are independently selected from a group consisting of a branched or linear lower alkyl (C1-C2)); phenyl (C6H5); an R"" substituted phenyl ring (R""C6H4); wherein R"" is defined above; a carboxylic acid (COOH); a carboxylic acid ester (COOR""); wherein R"" is a branched or linear lower alkyl (C1-C20); and cycloalkyl; wherein R" = R'" = (CH2)n;

wherein n =2-10.

FIG. 11

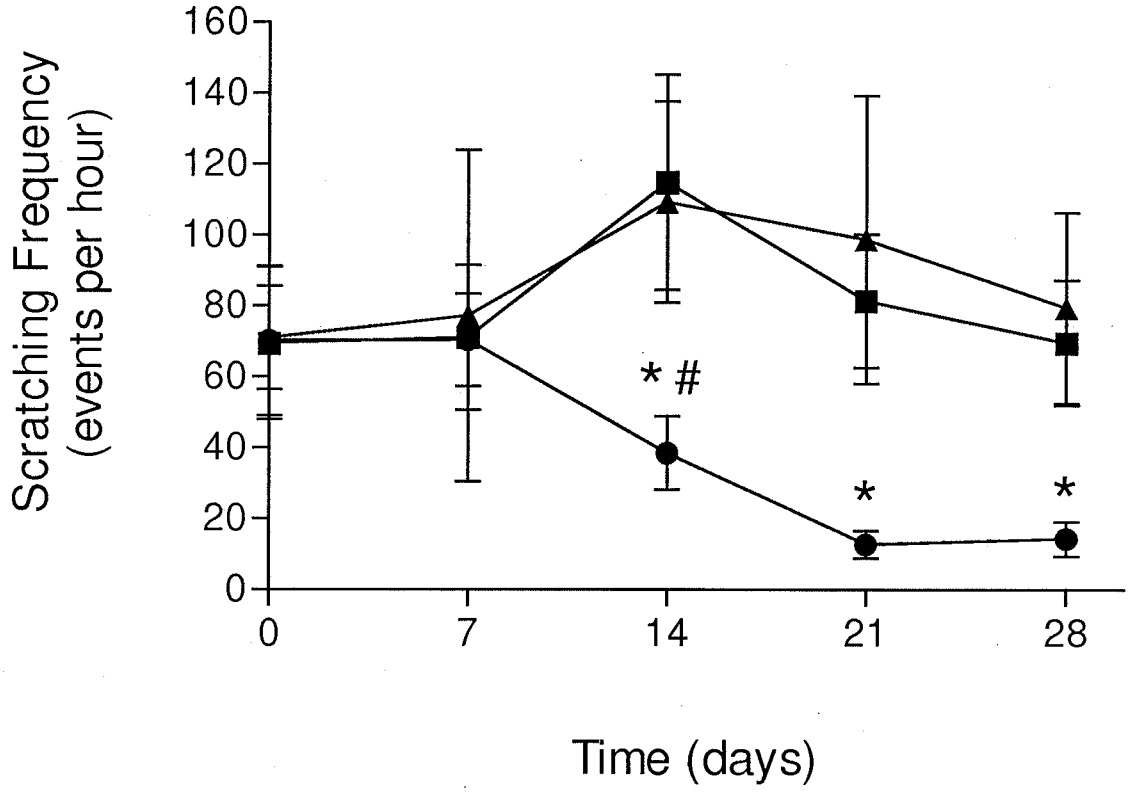

Scratching Frequency
(events per hour)
160
140
120
100
80
60
40
20
0
0
7
14
21
28
* #
*
*
Time (days)

FIG. 12

