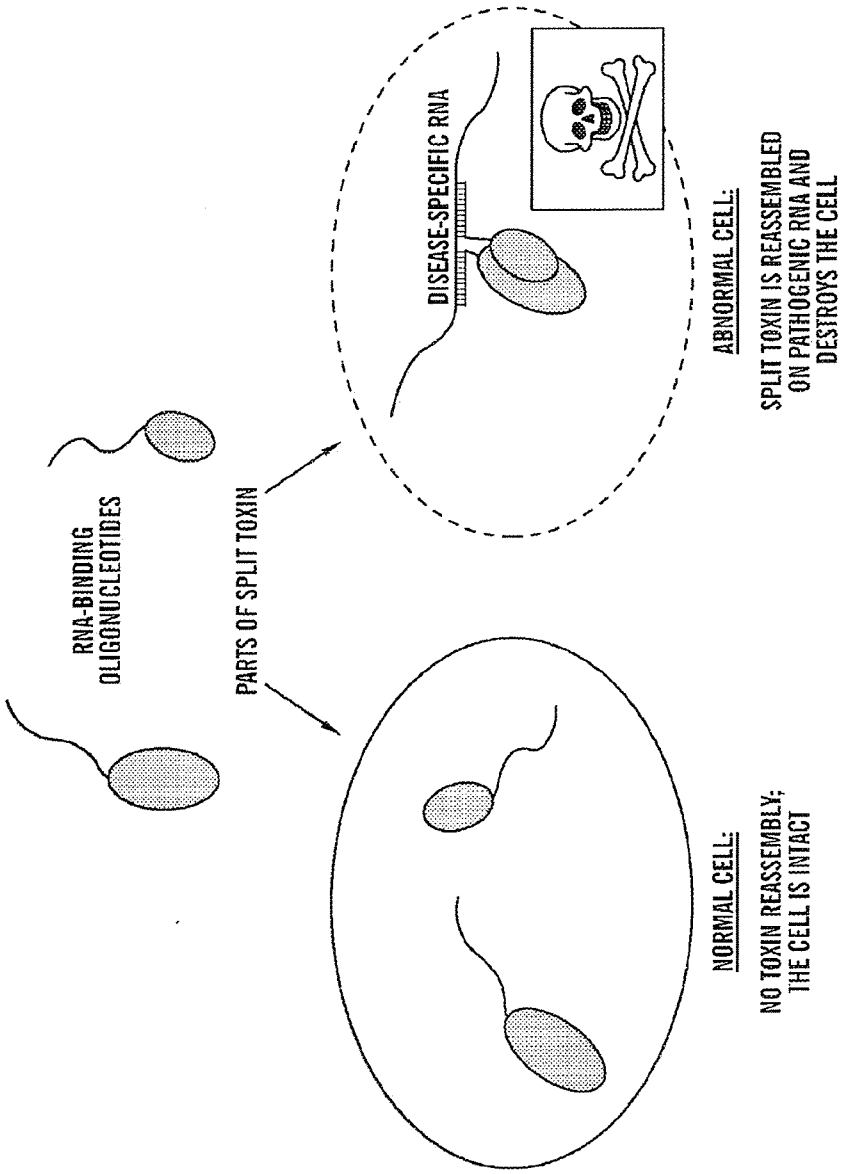
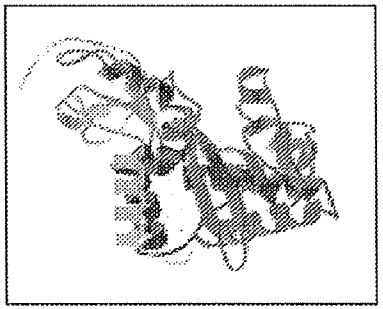
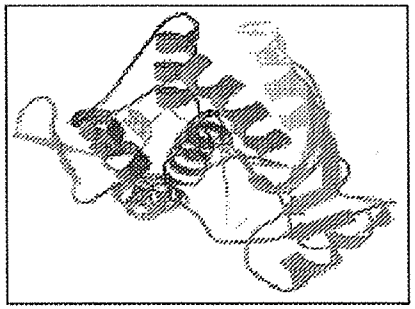

RNA-BINDING
OLIGONUCLEOTIDES
PARTS OF SPLIT TOXIN
DISEASE-SPECIFIC RNA
ABNORMAL CELL:
SPLIT TOXIN IS REASSEMBLED
ON PATHOGENIC RNA AND
DESTROYS THE CELL
NORMAL CELL:
NO TOXIN REASSEMBLY;
THE CELL IS INTACT

*FIG. 1*



Misna *et al., 1993*

*FIG. 2A*



Weston *et al., 1994*

*FIG. 2B*

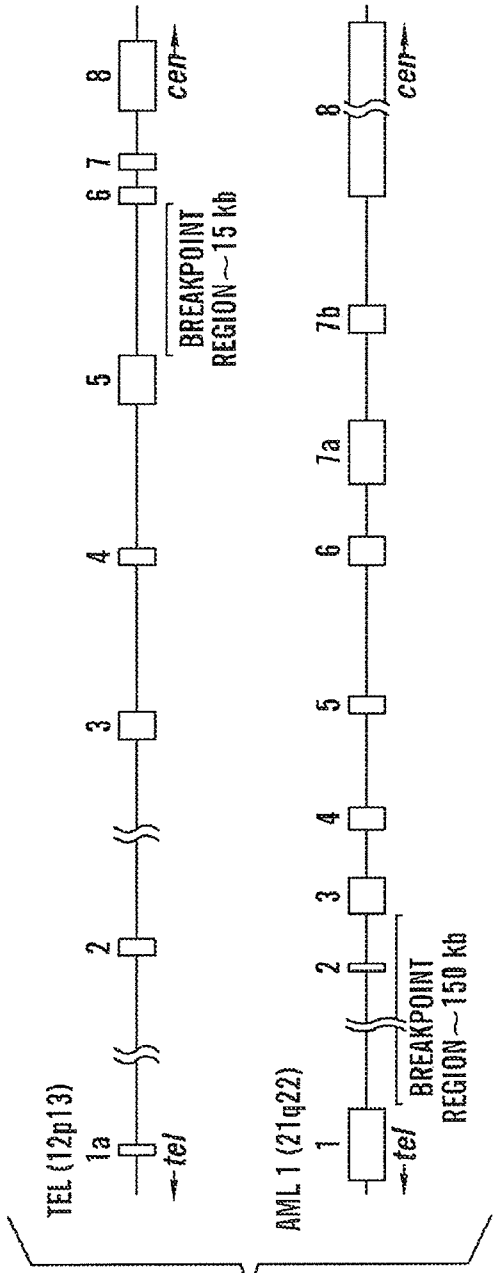

TEL (12p13)
1a
2
3
4
5
6 7
8
tel
cen
BREAKPOINT
REGION ~ 15 kb
AML 1 (21q22)
1
2
3
4
5
6
7a
7b
8
tel
cen
BREAKPOINT
REGION ~ 150 kb

FIG. 3A

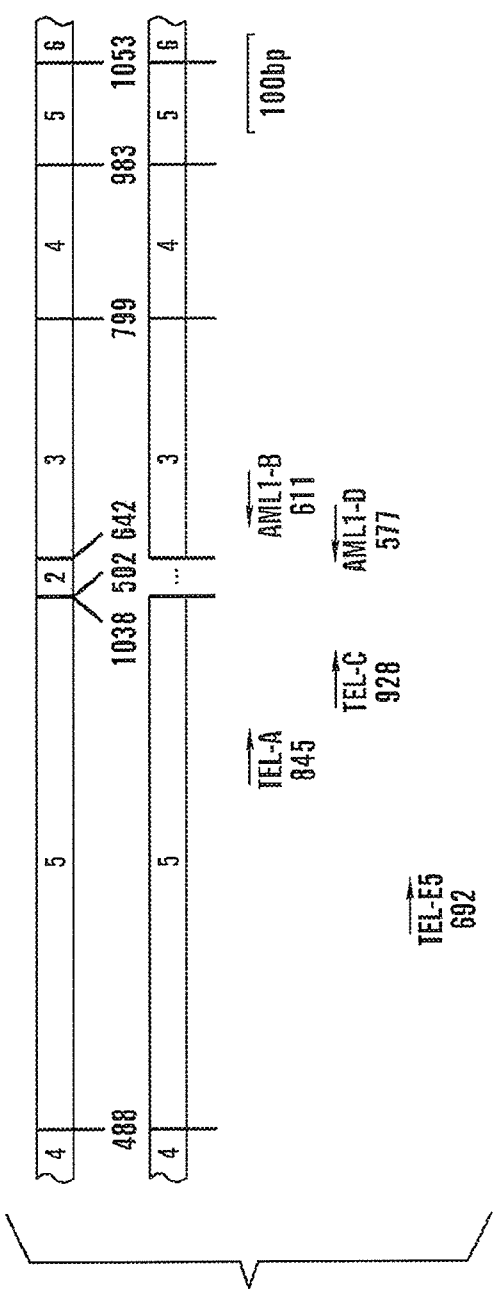

4
5
6
488
1038
502
642
799
983
1053
100bp
TEL-A
845
TEL-C
928
TEL-E5
692
AML1-B
611
AML1-D
577

FIG. 3B

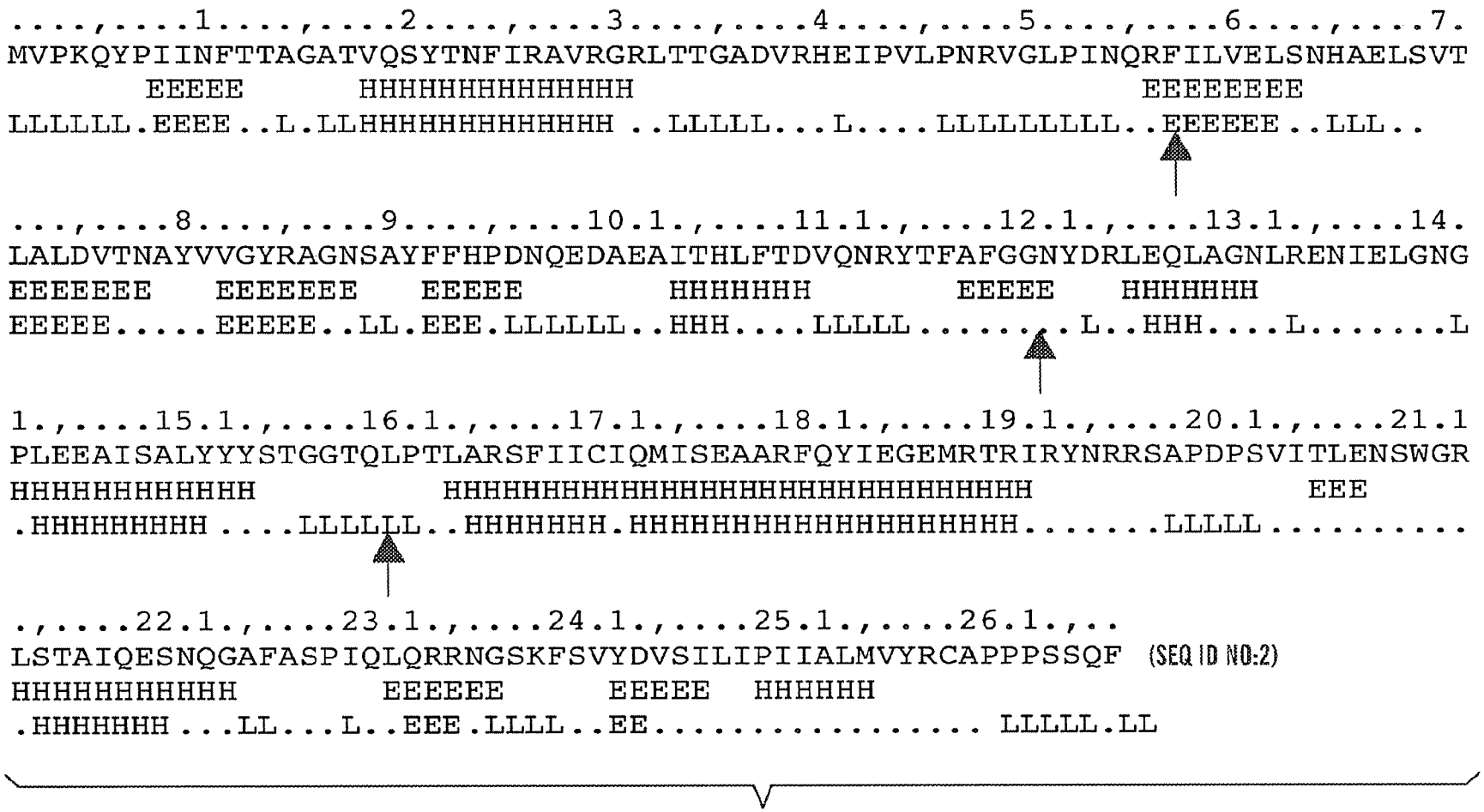

...,....1....,....2....,....3....,....4....,....5....,....6....,....7.
MVPKQYPIINFTTAGATVQSYTNFIRAVRGRLTTGADVRHEIPVLPNRVGLPINQRFILVELSNHAELSVT
EEEEE HHHHHHHHHHHHHH EEEEEEEE
LLLLLL.EEEE..L.LLHHHHHHHHHHHHH ..LLLLL...L....LLLLLLLLL..EEEEEE..LLL..
...,....8....,....9....,....10.1.,....11.1.,....12.1.,....13.1.,....14.
LALDVTNAYVVGYRAGNSAYFFHPDNQEDAEAITHLFTDVQNRYTFAFGGNYDRLEQLAGNLRENIELGNG
EEEEEEE EEEEEEE EEEEE HHHHHHH EEEEE HHHHHHH
EEEEE.....EEEEE..LL.EEE.LLLLLL..HHH....LLLLL.....L..HHH....L.....L
1.,....15.1.,....16.1.,....17.1.,....18.1.,....19.1.,....20.1.,....21.1
PLEEAISALYYYSTGGTQLPTLARSFIICIQMISEAARFQYIEGEMRTRIRYNRRSAPDPSVITLENSWGR
HHHHHHHHHHHH HHHHHHHHHHHHHHHHHHHHHHHHHHHH EEE
.HHHHHHHHH....LLLLLL..HHHHHHH.HHHHHHHHHHHHHHHHHH.....LLLLL.....
.,....22.1.,....23.1.,....24.1.,....25.1.,....26.1.,..
LSTAIQESNQGAFASPIQLQRRNGSKFSVYDVSILIPIIALMVYRCAPPPSSQF (SEQ ID NO:2)
HHHHHHHHHHH EEEEEE EEEEE HHHHHH
.HHHHHHH...LL...L..EEE.LLLL..EE..... LLLLL.LL

*FIG. 4*

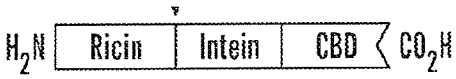



*FIG. 5A*

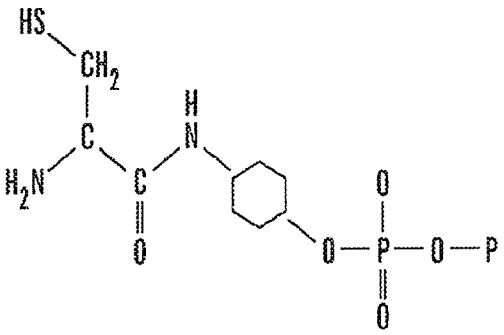



*FIG. 5B*

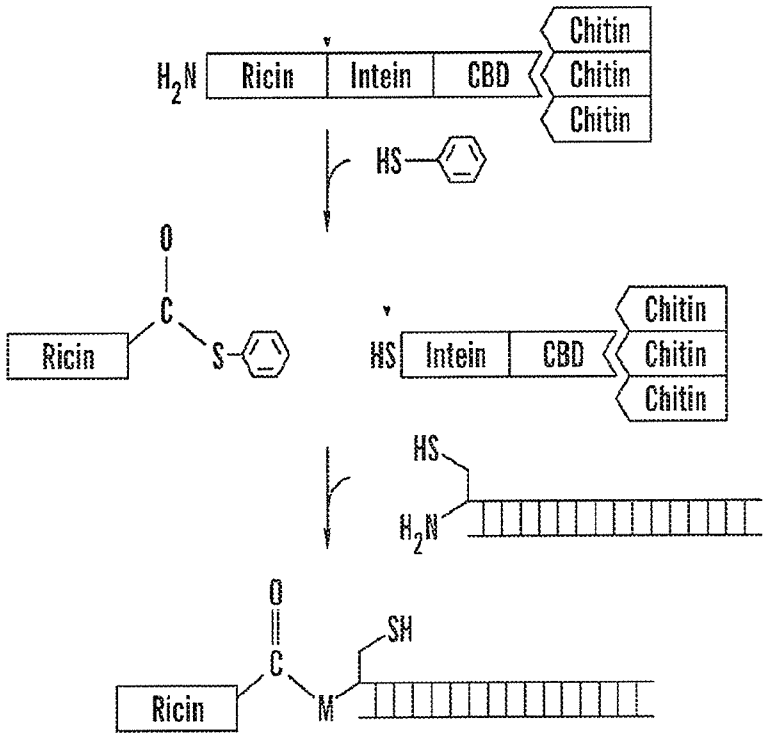



*FIG. 5C*

S78496
Breakpoint
↓

**attgggagaa tagcag** aatg catacttgga atgaatcctt ctagagacgt ccac (SEQ ID NO:4)

TEL or ETV exon 5 AML1 or RUNX1 exon 2

*FIG. 6*



MIFPKQYPIINFTTAGATVQSYTNFIRAVRGRLTTGADVRHEIPVLPN**R**VGL↓PINQRFIL
VELSNHAELSVTLAL**D**VT**N**A***Y******V***VGYRAGNSAYFFHPDNQEDAEAITHLFTDVQNRYTF
AFG↓ ***G*****N*****Y***DRLEQLAGNL**R**ENIELGNGPLEEAISALYYYSTGG↓TQLPTLARSFIICIQMIS
***E***AA***R***FQYIEGEMRTRIRYNRRSAPDPSVITL***EN***S***W***G**R**LSTAIQESNQGAFASPIQLQRRN
GSKFSVYDVSILIPIIALMVY**R**CAPPPSSQF (SEQ ID NO:3)

*FIG. 7A*

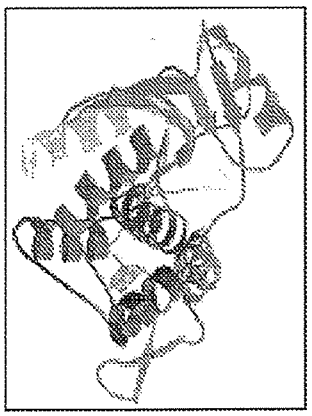


FIG. 7C

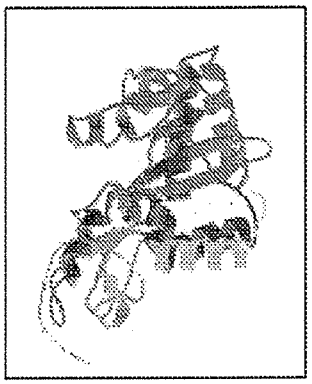


FIG. 7B

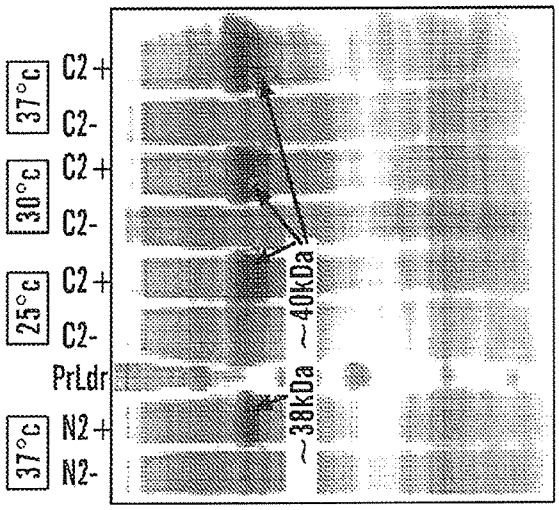

37°C
N2+
N2-
PrLdr
25°C
C2+
C2-
30°C
C2+
C2-
37°C
C2+
C2-
~38kDa
~40kDa

FIG. 9

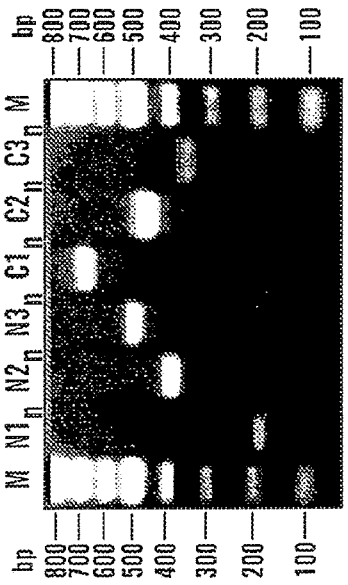

bp
800
700
600
500
400
300
200
100
M
N1n
N2n
N3n
C1n
C2n
C3n
M

FIG. 8

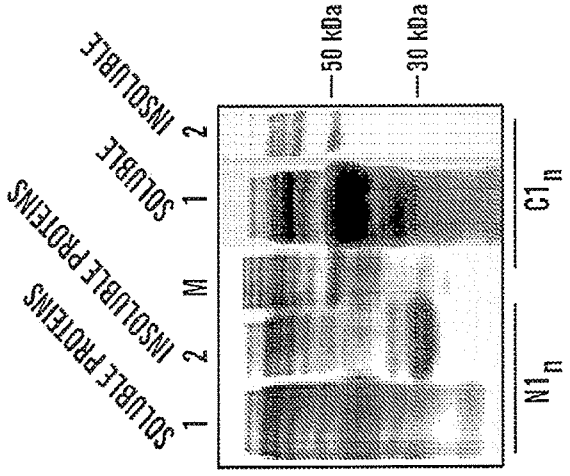



FIG. 10A

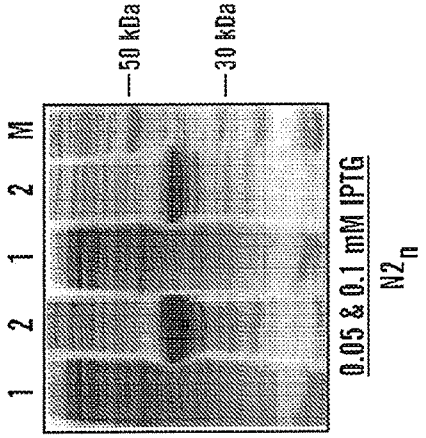



FIG. 10B

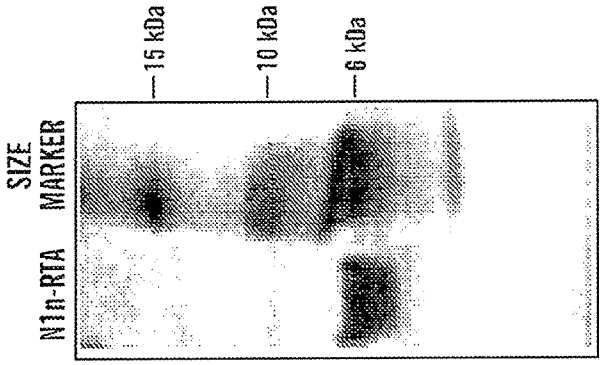



FIG. 11

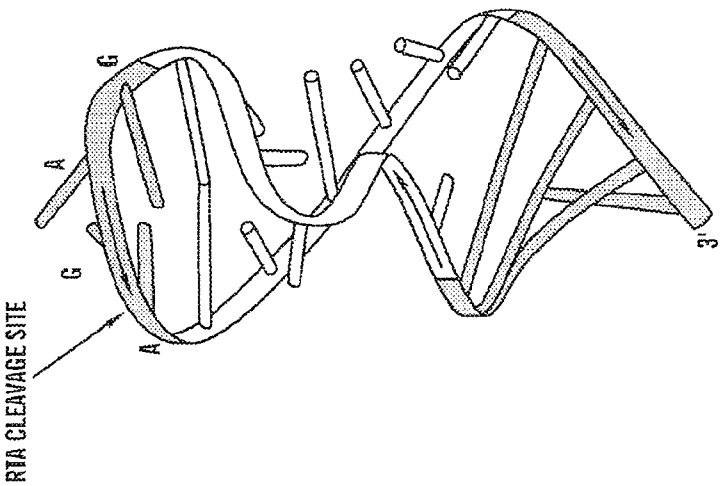



FIG. 12A

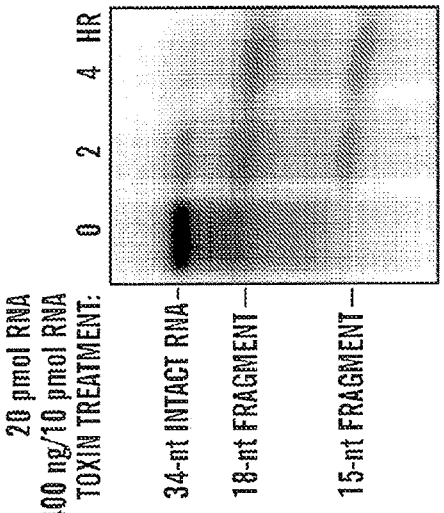



FIG. 12B

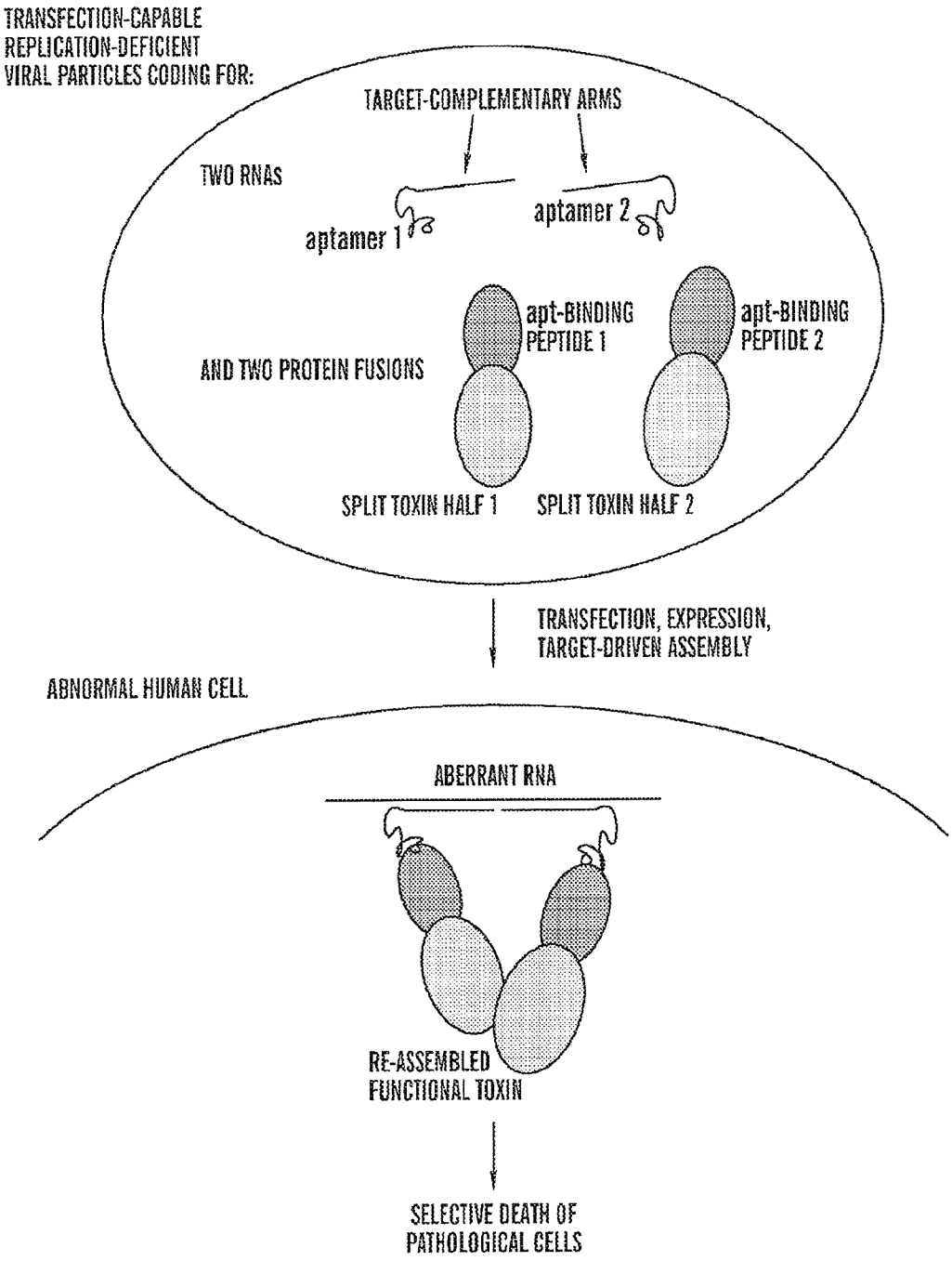

TRANSFECTION-CAPABLE
REPLICATION-DEFICIENT
VIRAL PARTICLES CODING FOR:
TARGET-COMPLEMENTARY ARMS
TWO RNAs
aptamer 1
aptamer 2
apt-BINDING PEPTIDE 1
apt-BINDING PEPTIDE 2
AND TWO PROTEIN FUSIONS
SPLIT TOXIN HALF 1
SPLIT TOXIN HALF 2
TRANSFECTION, EXPRESSION,
TARGET-DRIVEN ASSEMBLY
ABNORMAL HUMAN CELL
ABERRANT RNA
RE-ASSEMBLED
FUNCTIONAL TOXIN
SELECTIVE DEATH OF
PATHOLOGICAL CELLS

*FIG. 13*

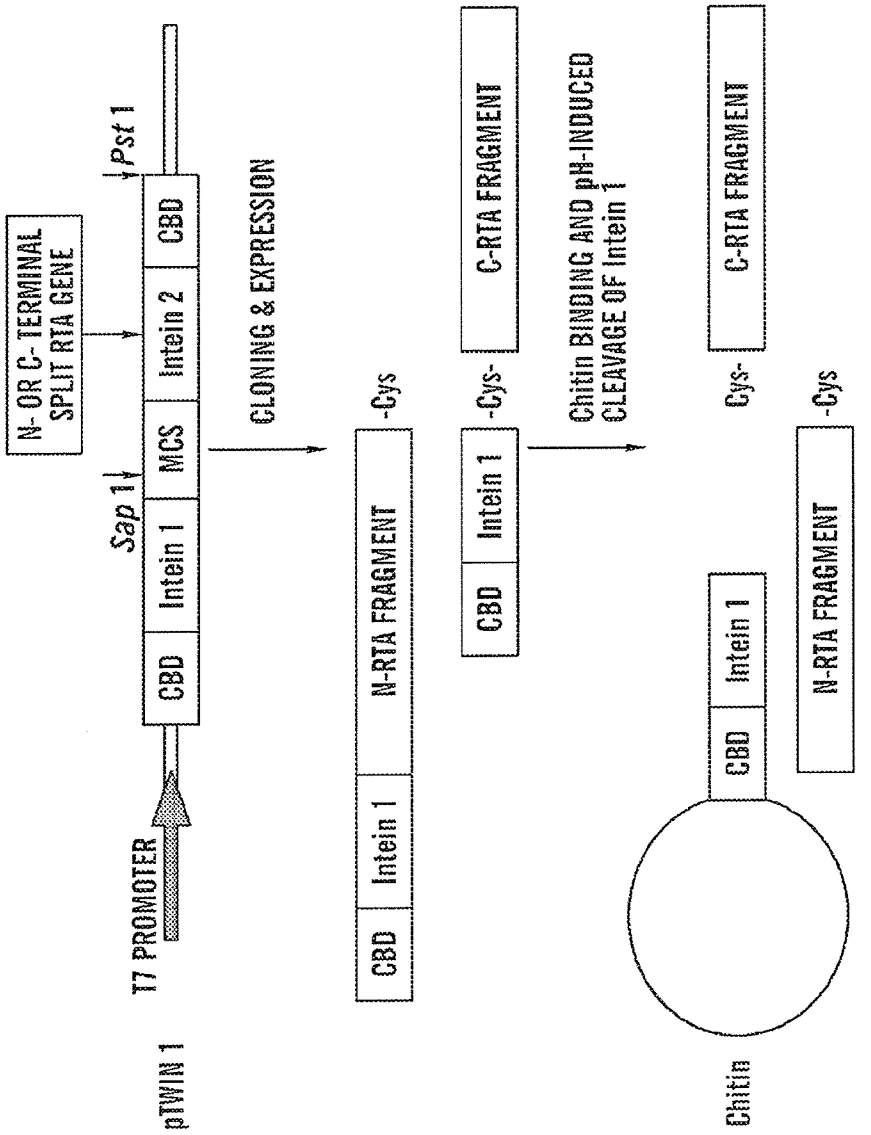

pTWIN 1
T7 PROMOTER
CBD
Intein 1
Sap 1
MCS
Intein 2
CBD
Pst 1
N- OR C- TERMINAL SPLIT RTA GENE
CLONING & EXPRESSION
CBD
Intein 1
N-RTA FRAGMENT
-Cys
CBD
Intein 1
-Cys-
C-RTA FRAGMENT
Chitin BINDING AND pH-INDUCED CLEAVAGE OF Intein 1
Chitin
CBD
Intein 1
N-RTA FRAGMENT
-Cys
Cys-
C-RTA FRAGMENT

*FIG. 14*