G00002

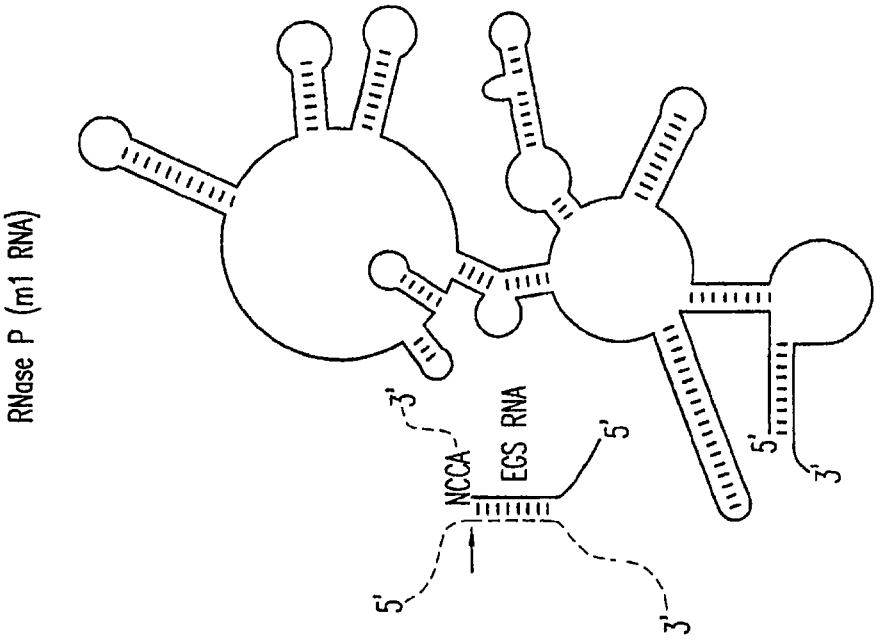


FIG. 1B

163163

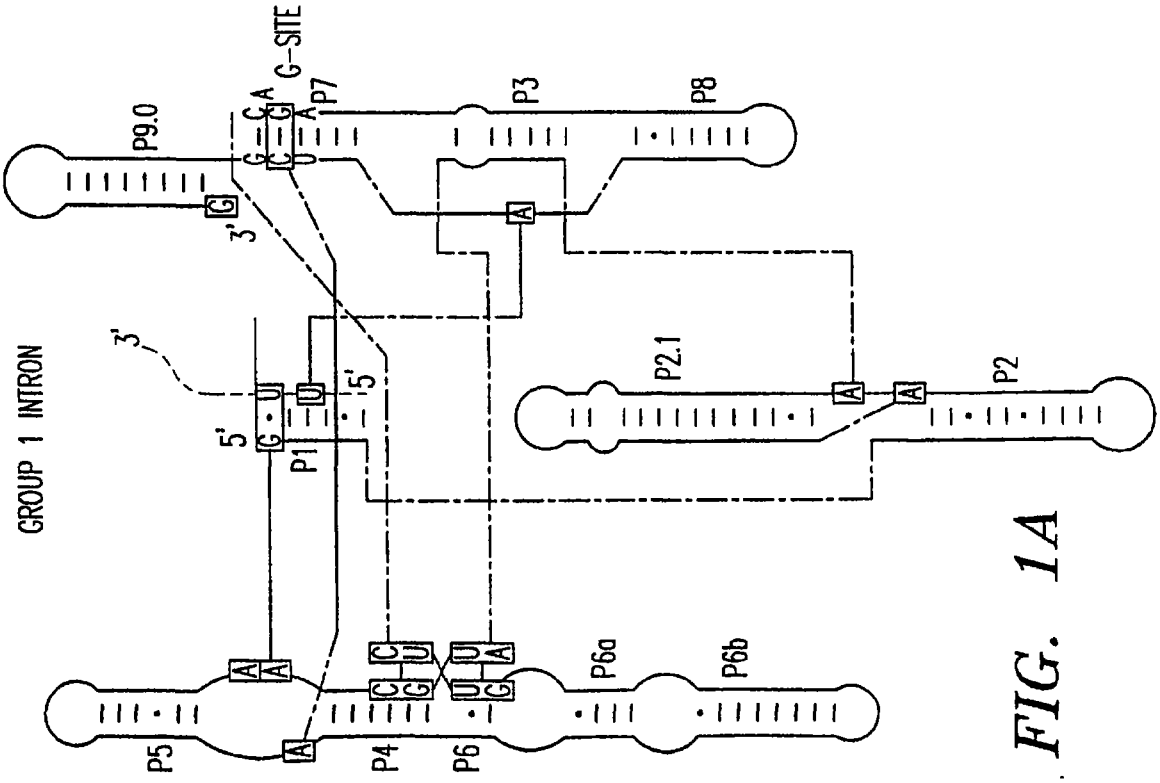


FIG. 1A

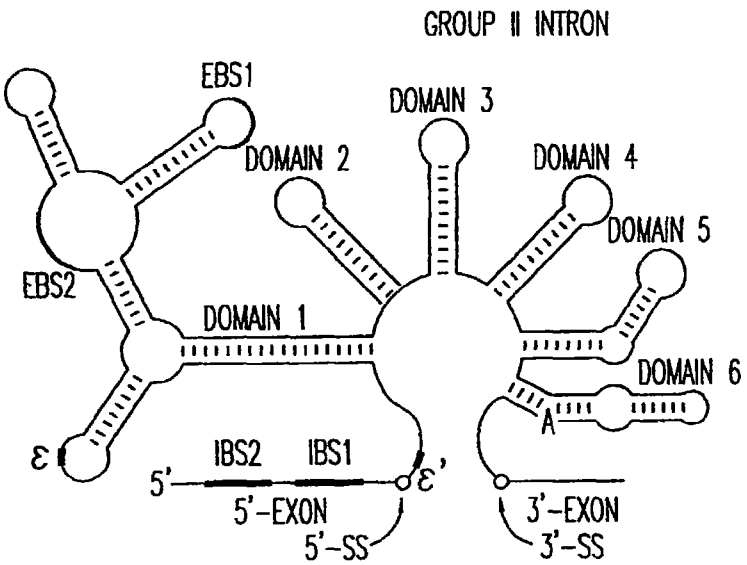


FIG. 1C

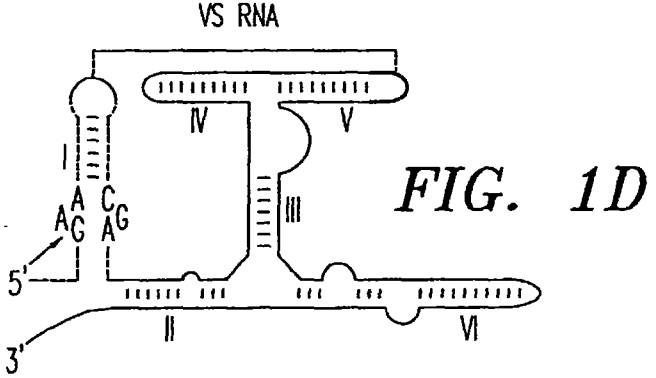


FIG. 1D

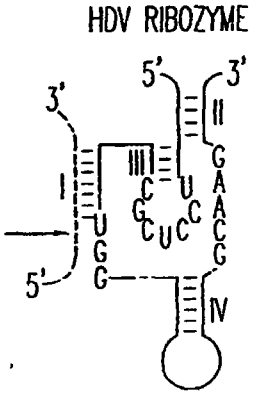


FIG. 1E

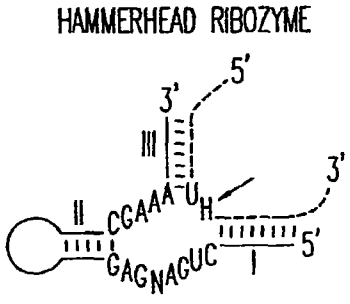


FIG. 1F

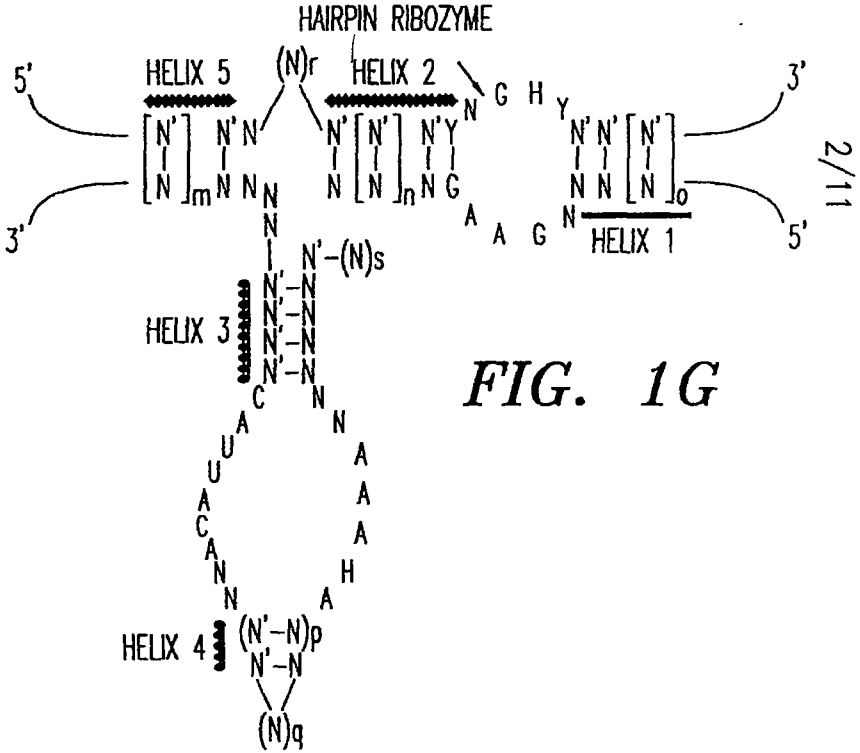


FIG. 1G

12 SEP 2002
PCT/US99/09027

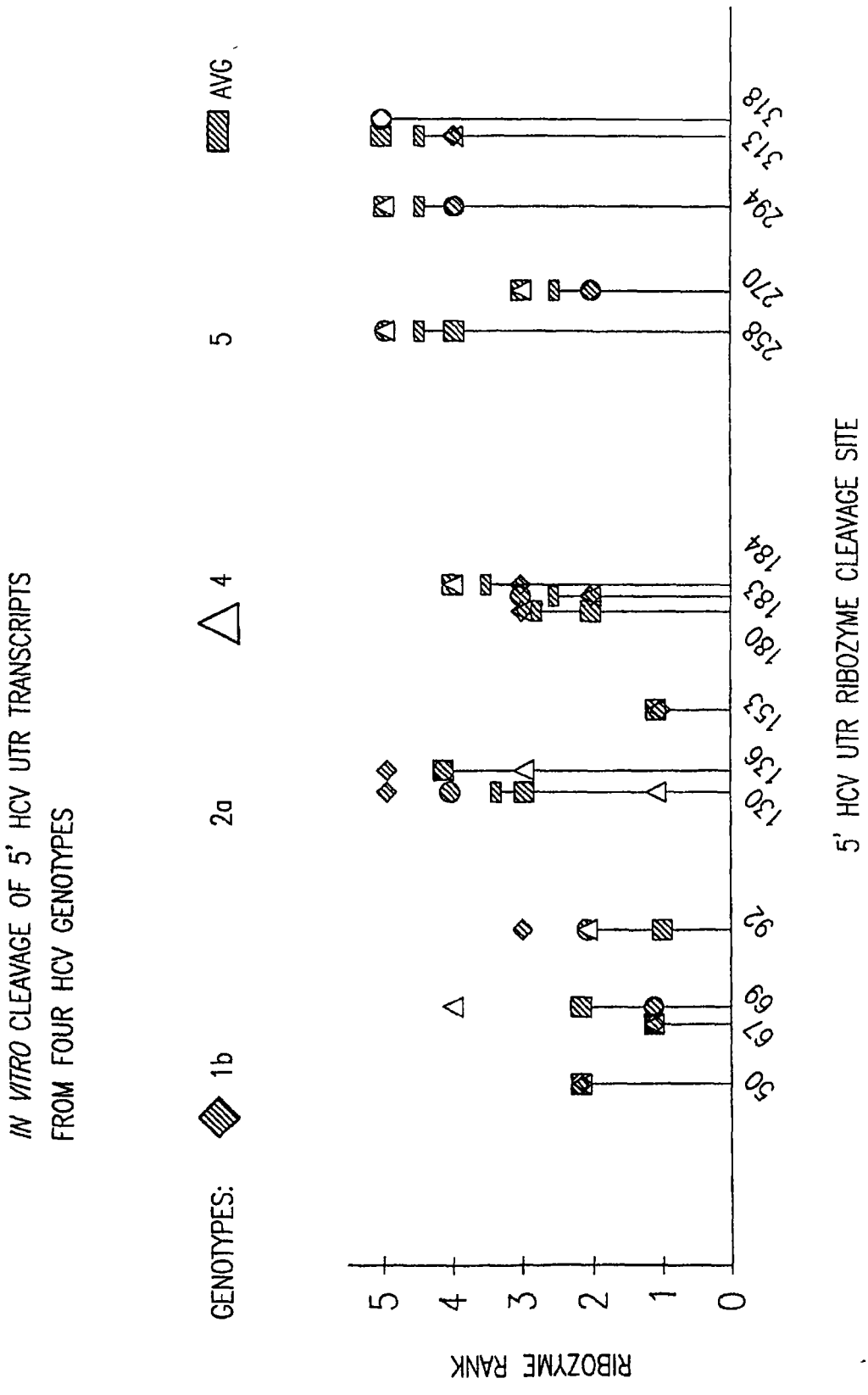

IN VITRO CLEAVAGE OF 5' HCV UTR TRANSCRIPTS
FROM FOUR HCV GENOTYPES
GENOTYPES:
1b
2a
4
5
AVG
RIBOZYME RANK
5
4
3
2
1
0
50
67
69
92
130
136
153
180
183
184
258
270
294
313
318
5' HCV UTR RIBOZYME CLEAVAGE SITE

FIG. 2

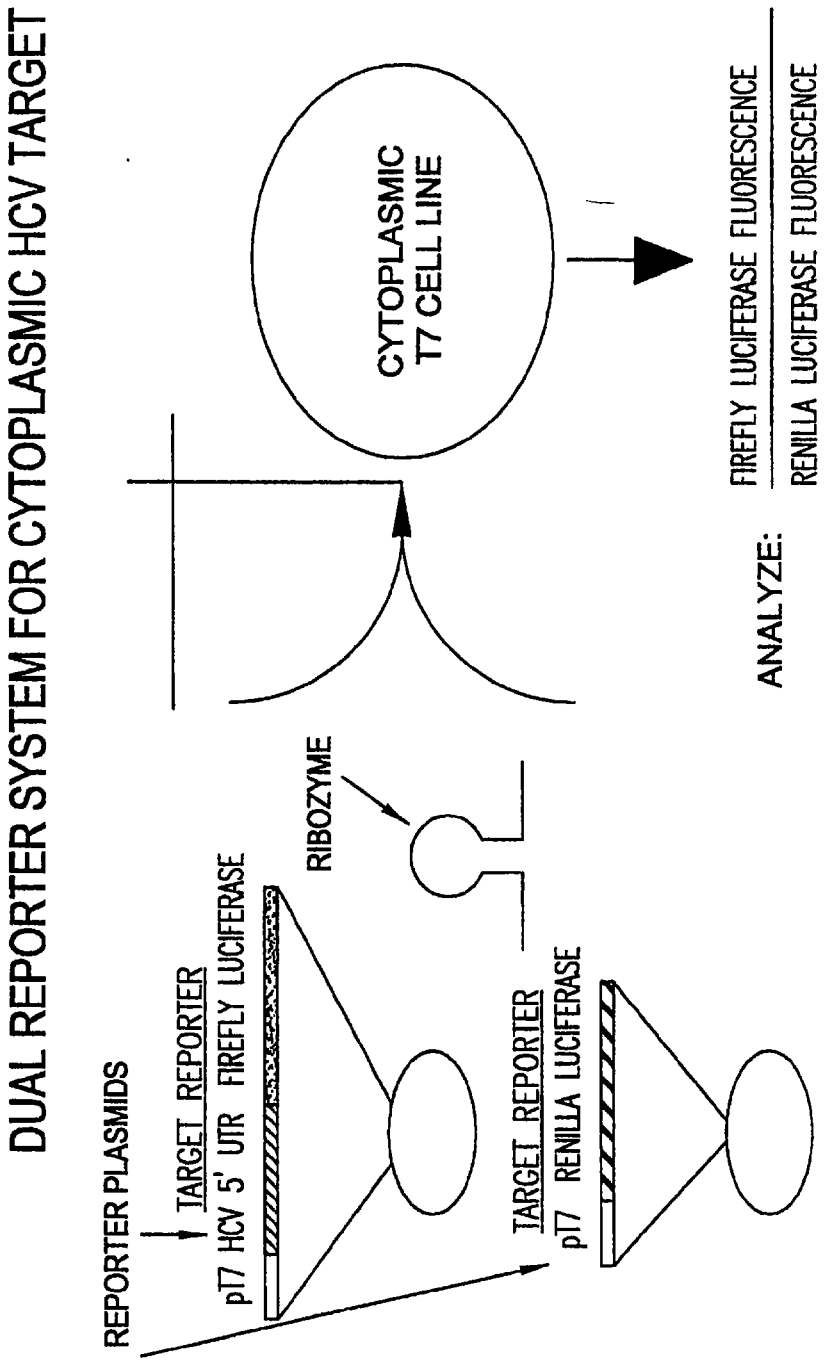

DUAL REPORTER SYSTEM FOR CYTOPLASMIC HCV TARGET
REPORTER PLASMIDS
TARGET REPORTER
pT7 HCV 5' UTR FIREFLY LUCIFERASE
RIBOZYME
TARGET REPORTER
pT7 RENILLA LUCIFERASE
CYTOPLASMIC
T7 CELL LINE
ANALYZE:
FIREFLY LUCIFERASE FLUORESCENCE
RENILLA LUCIFERASE FLUORESCENCE

FIG. 3

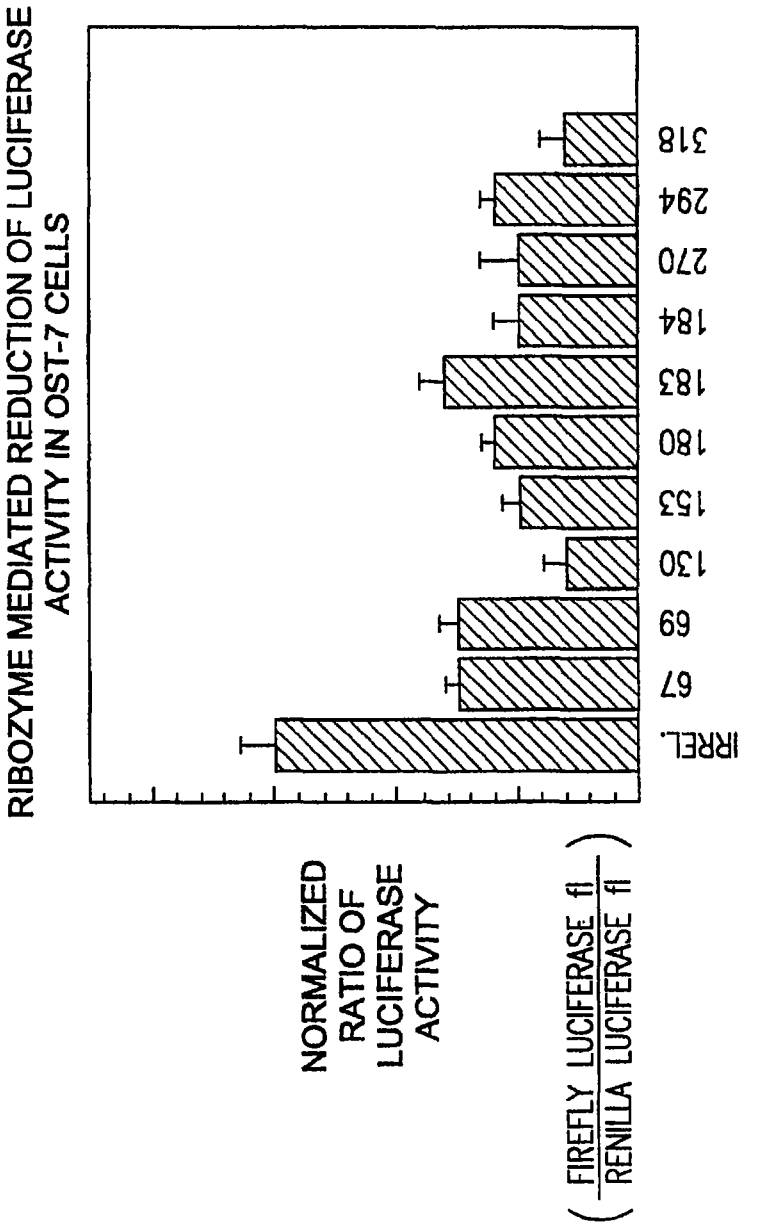

RIBOZYME MEDIATED REDUCTION OF LUCIFERASE ACTIVITY IN OST-7 CELLS
NORMALIZED RATIO OF LUCIFERASE ACTIVITY
(FIREFLY LUCIFERASE fl / RENILLA LUCIFERASE fl)
IRREL.
67
69
130
153
180
183
184
270
294
318
5' HCV UTR RIBOZYME SITE

FIG. 4

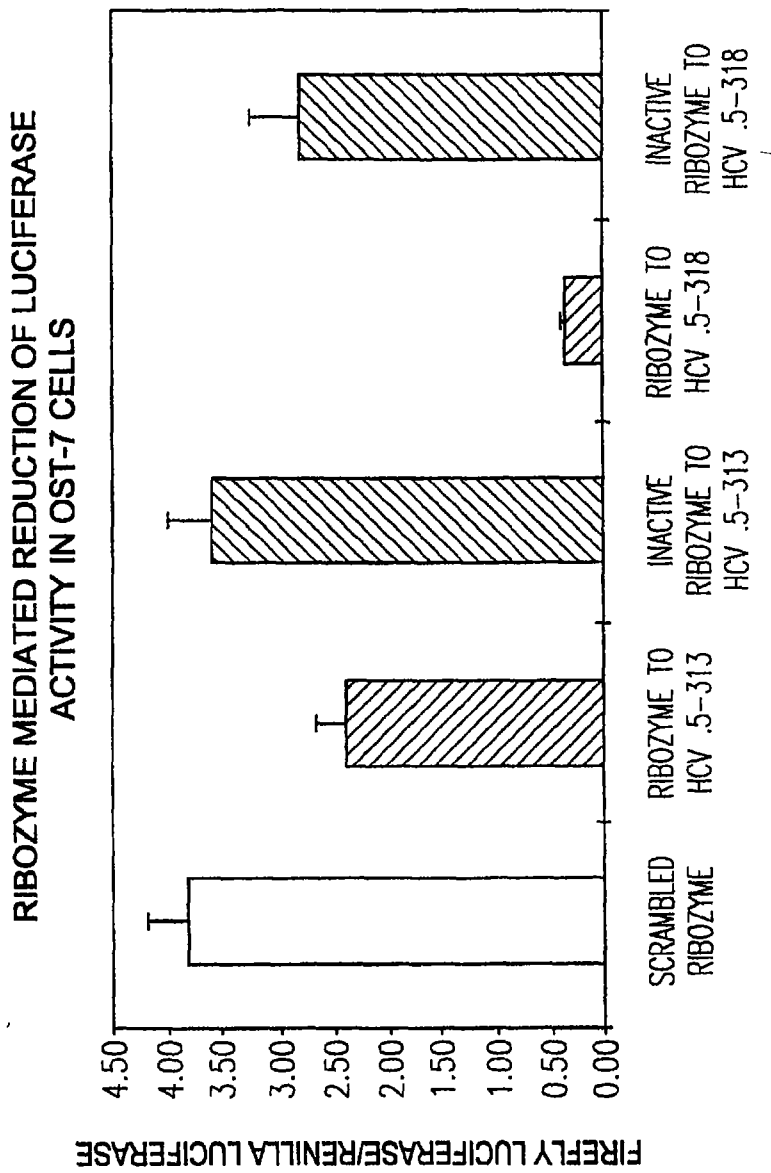
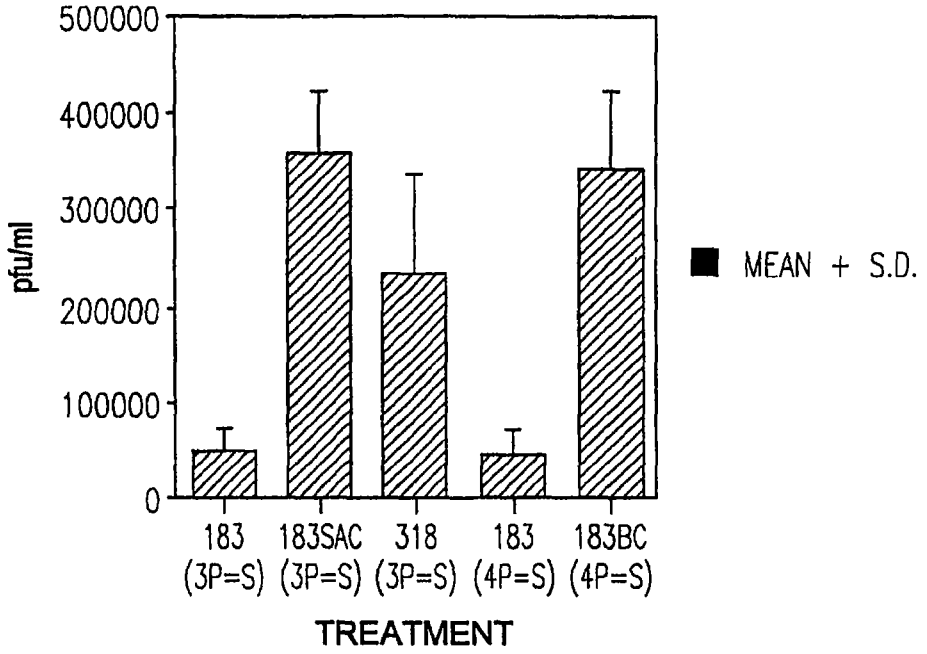

RIBOZYME MEDIATED REDUCTION OF LUCIFERASE ACTIVITY IN OST-7 CELLS
FIREFLY LUCIFERASE/RENILLA LUCIFERASE
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
SCRAMBLED RIBOZYME
RIBOZYME TO HCV .5-313
INACTIVE RIBOZYME TO HCV .5-313
RIBOZYME TO HCV .5-318
INACTIVE RIBOZYME TO HCV .5-318

FIG. 5

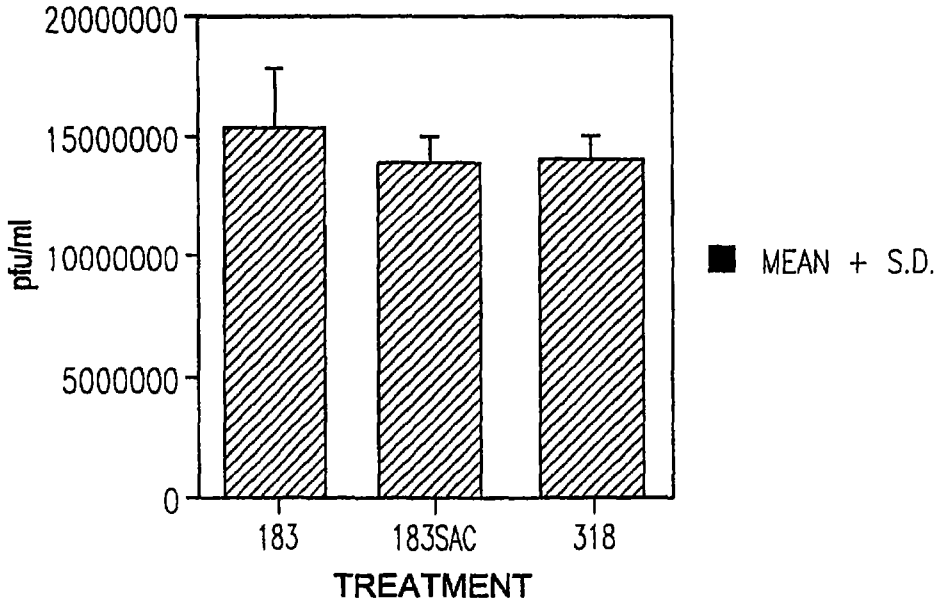
INHIBITION OF HCV-POLIO VIRUS RIBOZYMES



P=S–PHOSPHOROTHIOATE INTERNUCLEOTIDE LINKAGES AT THE 5' END
SAC–SCRAMBLED CONTROL
BC–RIBOZYME WITH INACTIVATED CORE

FIG. 6A

NO INHIBITION OF WILD TYPE POLIO VIRUS



SAC–SCRAMBLE CONTROL

FIG. 6B

HAMMERHEAD RIBOZYMES TARGETED AGAINST HCV RNA
183 HH (7/4) Ribozyme
183 HH (7/3) Ribozyme
183 HH (6/4) Ribozyme
183 HH (6/3) Ribozyme
Uppercase=ribonucleotides
Lowercase=2'O -methylnucleotides
U=2'-C-Allyl
s=phosphorothioatelinkages
iH=Inverted abasic moiety

FIG. 7

INHIBITION OF HCV-POLIO VIRUS USING RIBOZYMES OF VARYING LENGTHS

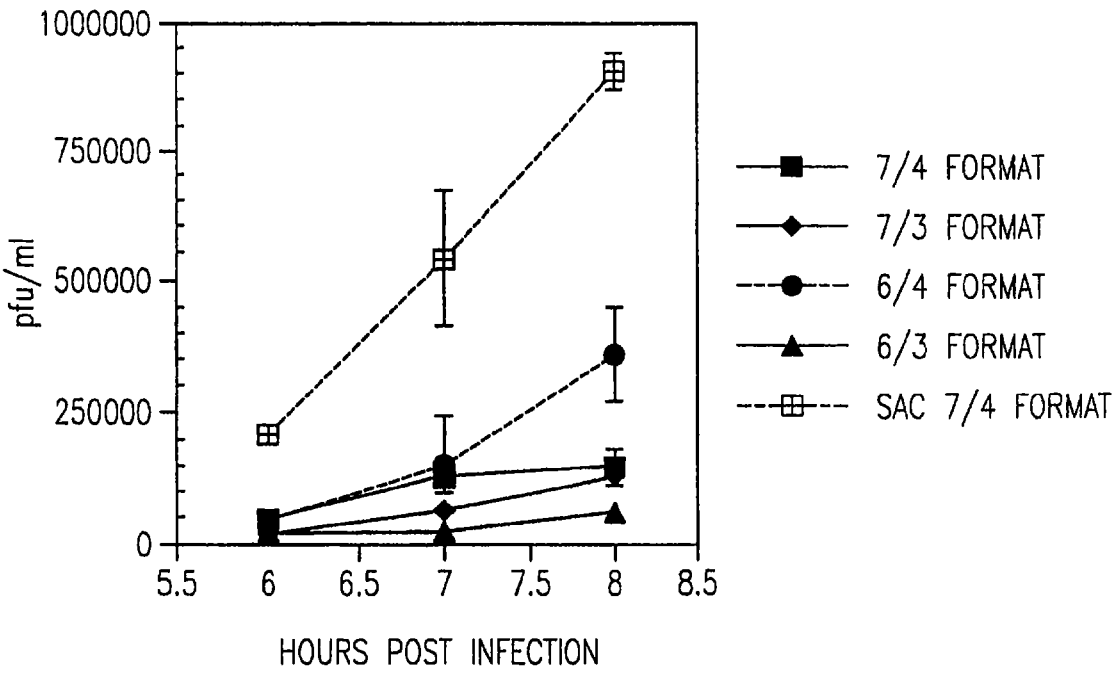


FIG. 8

SAC-SCRAMBLE CONTROL

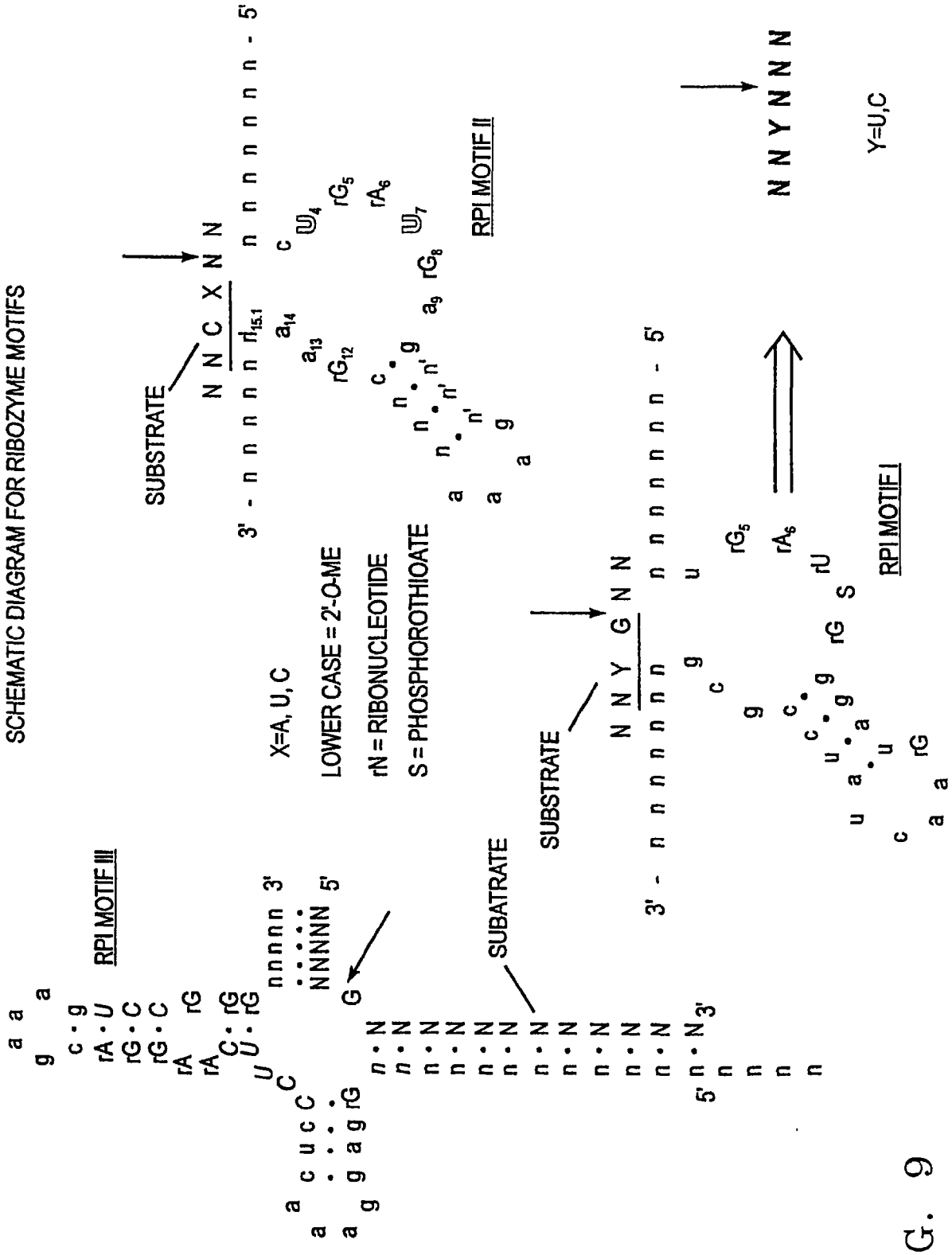

SCHEMATIC DIAGRAM FOR RIBOZYME MOTIFS
RPI MOTIF III
RPI MOTIF II
RPI MOTIF I
SUBSTRATE
SUBATRATE
SUBSTRATE
X=A, U, C
LOWER CASE = 2'-O-ME
rN = RIBONUCLEOTIDE
S = PHOSPHOROTHIOATE
Y=U,C
N N C X N N
N N Y G N N
N N Y N N N

FIG. 9

SYNERGISTIC EFFECT OF HCV RIBOZYME AND INTERFERON

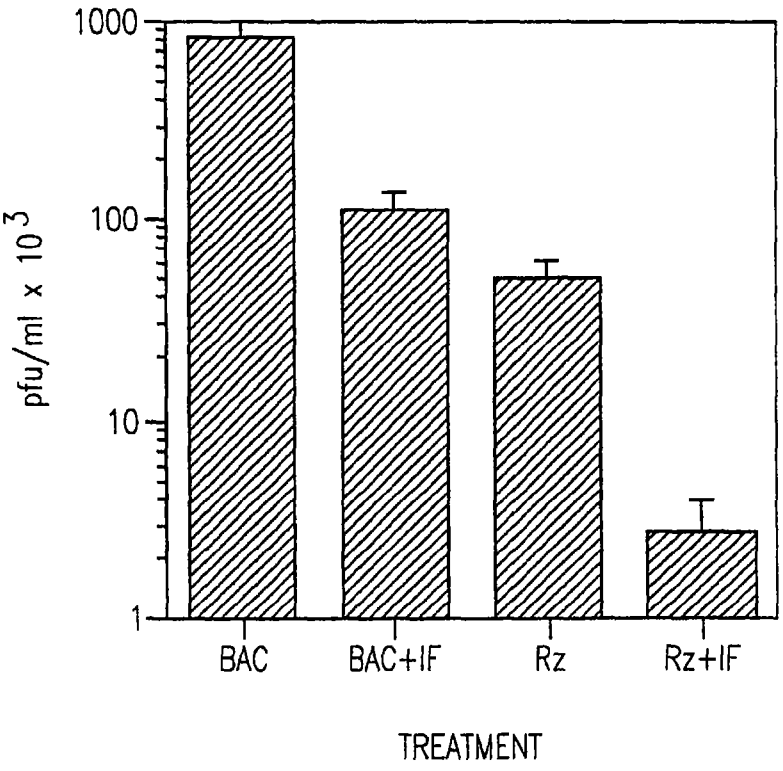


FIG. 10