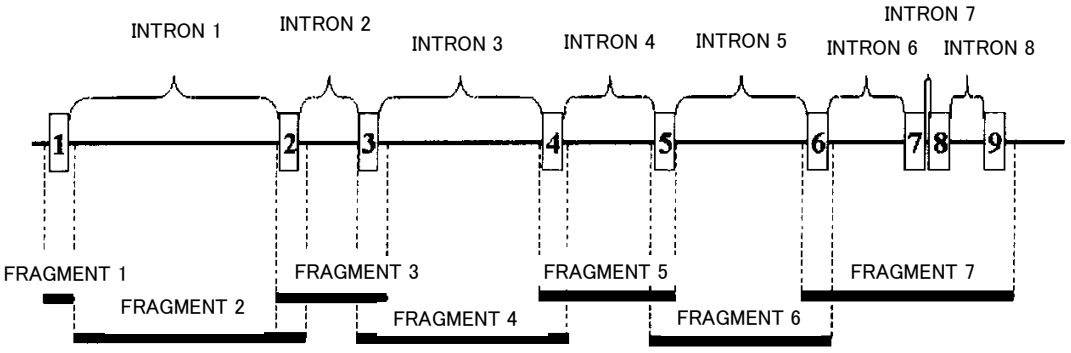

INTRON 1
INTRON 2
INTRON 3
INTRON 4
INTRON 5
INTRON 6
INTRON 7
INTRON 8
1
2
3
4
5
6
7
8
9
FRAGMENT 1
FRAGMENT 2
FRAGMENT 3
FRAGMENT 4
FRAGMENT 5
FRAGMENT 6
FRAGMENT 7

FIG. 1

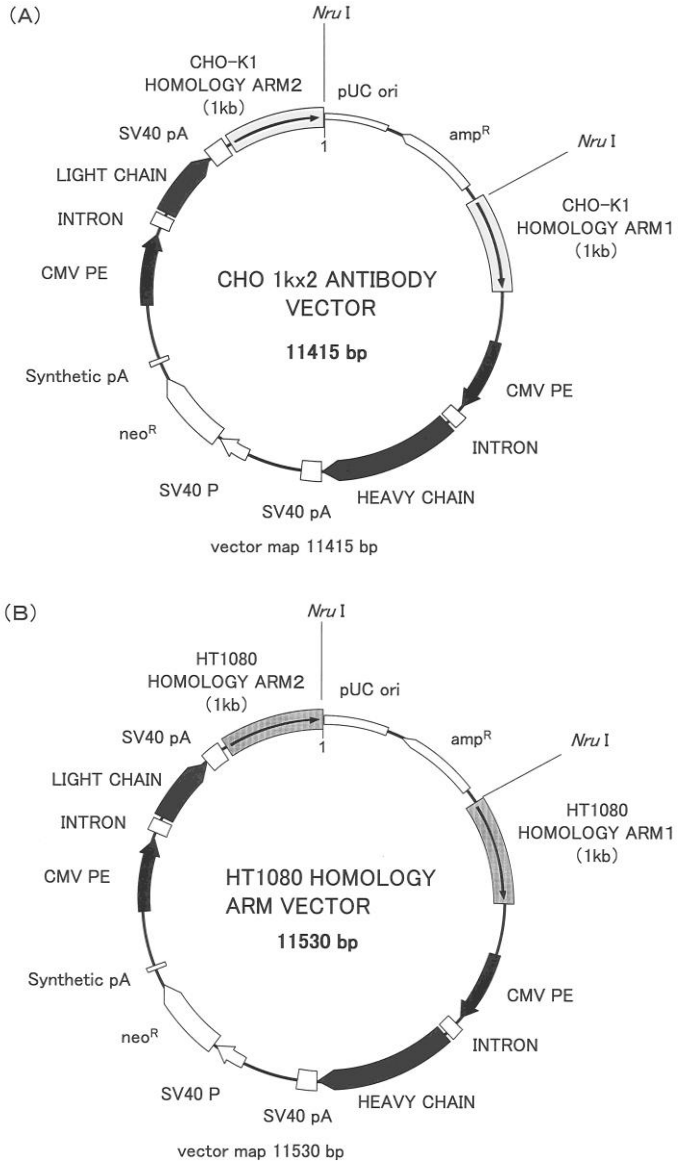

(A)
Nru I
CHO-K1
HOMOLOGY ARM2
(1kb)
pUC ori
SV40 pA
ampR
Nru I
LIGHT CHAIN
INTRON
CHO-K1
HOMOLOGY ARM1
(1kb)
CMV PE
CHO 1kx2 ANTIBODY
VECTOR
11415 bp
Synthetic pA
CMV PE
neoR
INTRON
SV40 P
HEAVY CHAIN
SV40 pA
vector map 11415 bp
(B)
Nru I
HT1080
HOMOLOGY ARM2
(1kb)
pUC ori
SV40 pA
ampR
Nru I
LIGHT CHAIN
INTRON
HT1080
HOMOLOGY ARM1
(1kb)
CMV PE
HT1080 HOMOLOGY
ARM VECTOR
11530 bp
Synthetic pA
CMV PE
neoR
INTRON
SV40 P
HEAVY CHAIN
SV40 pA
vector map 11530 bp

FIG. 2

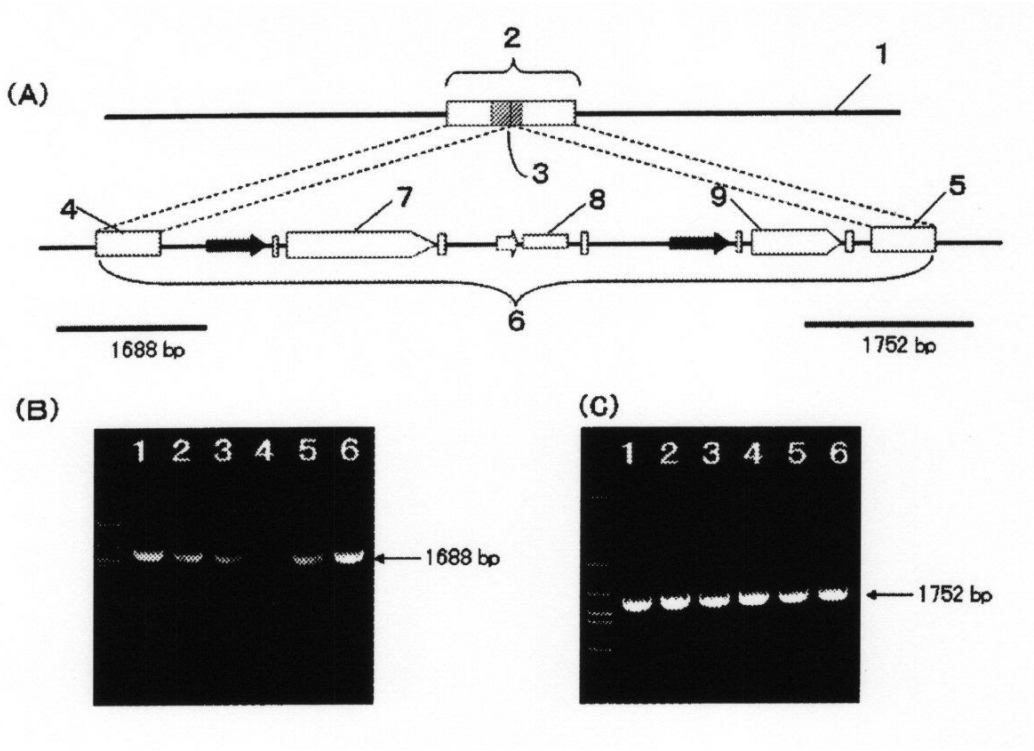

(A)
1
2
3
4
5
6
7
8
9
1688 bp
1752 bp
(B)
1 2 3 4 5 6
1688 bp
(C)
1 2 3 4 5 6
1752 bp

FIG. 3

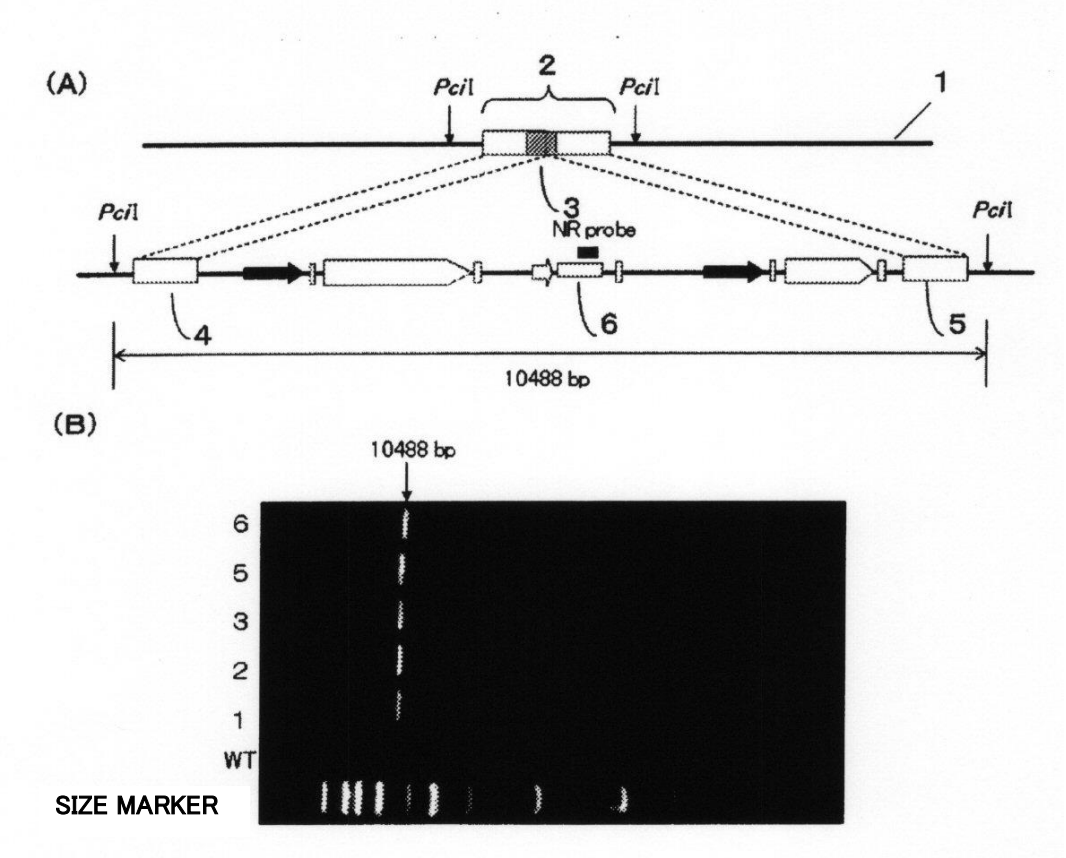

(A)
PciI
PciI
PciI
PciI
1
2
3
NR probe
4
5
6
10488 bp
(B)
10488 bp
6
5
3
2
1
WT
SIZE MARKER

FIG. 4

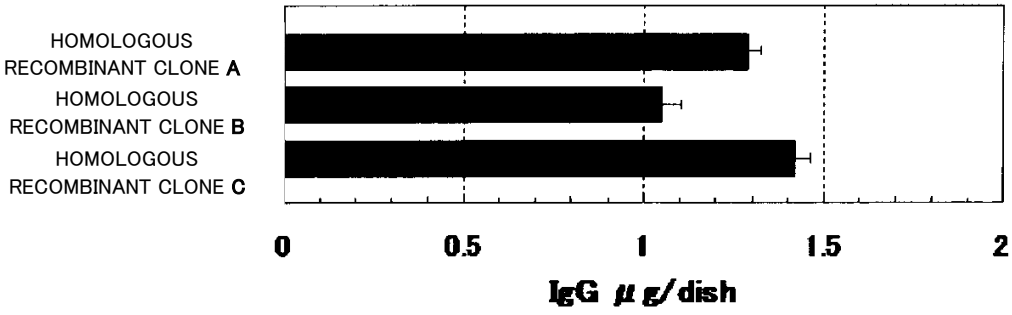

HOMOLOGOUS
RECOMBINANT CLONE A
HOMOLOGOUS
RECOMBINANT CLONE B
HOMOLOGOUS
RECOMBINANT CLONE C
0
0.5
1
1.5
2
IgG μg/dish

FIG. 5

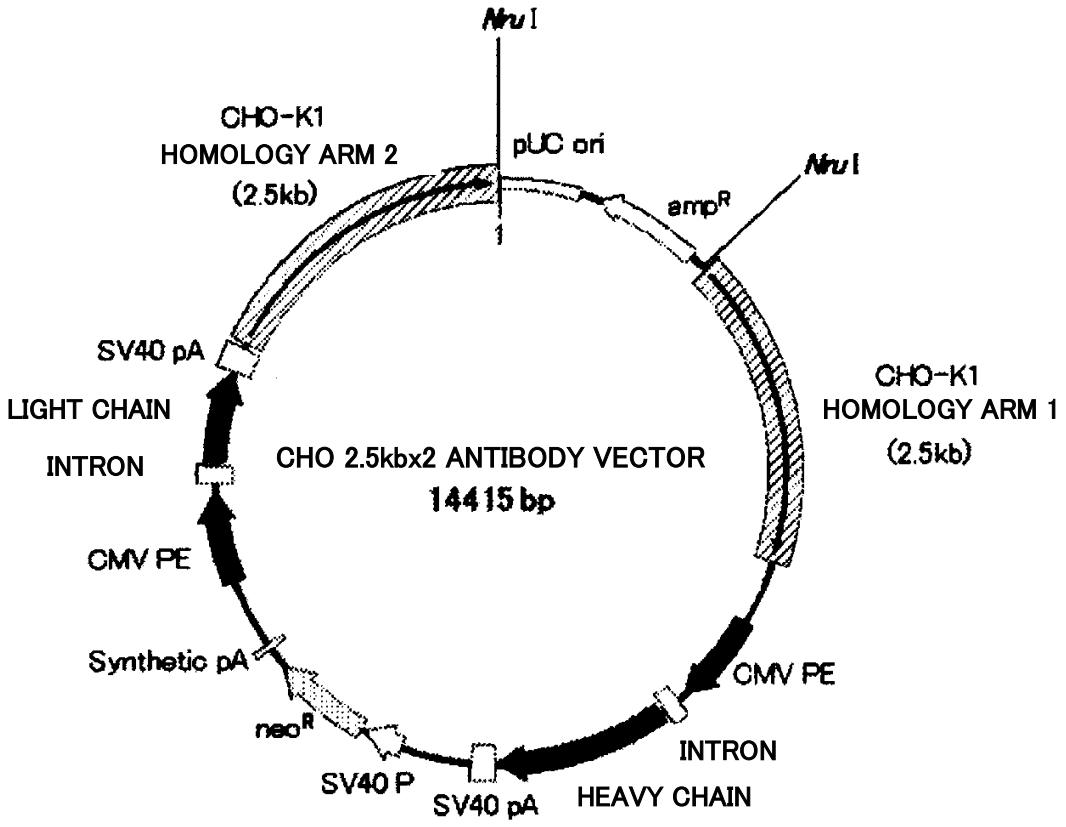

NruI
CHO-K1
HOMOLOGY ARM 2
(2.5kb)
pUC ori
ampR
NruI
1
SV40 pA
LIGHT CHAIN
INTRON
CHO 2.5kbx2 ANTIBODY VECTOR
14415 bp
CHO-K1
HOMOLOGY ARM 1
(2.5kb)
CMV PE
Synthetic pA
CMV PE
neoR
INTRON
SV40 P
SV40 pA
HEAVY CHAIN

FIG. 6

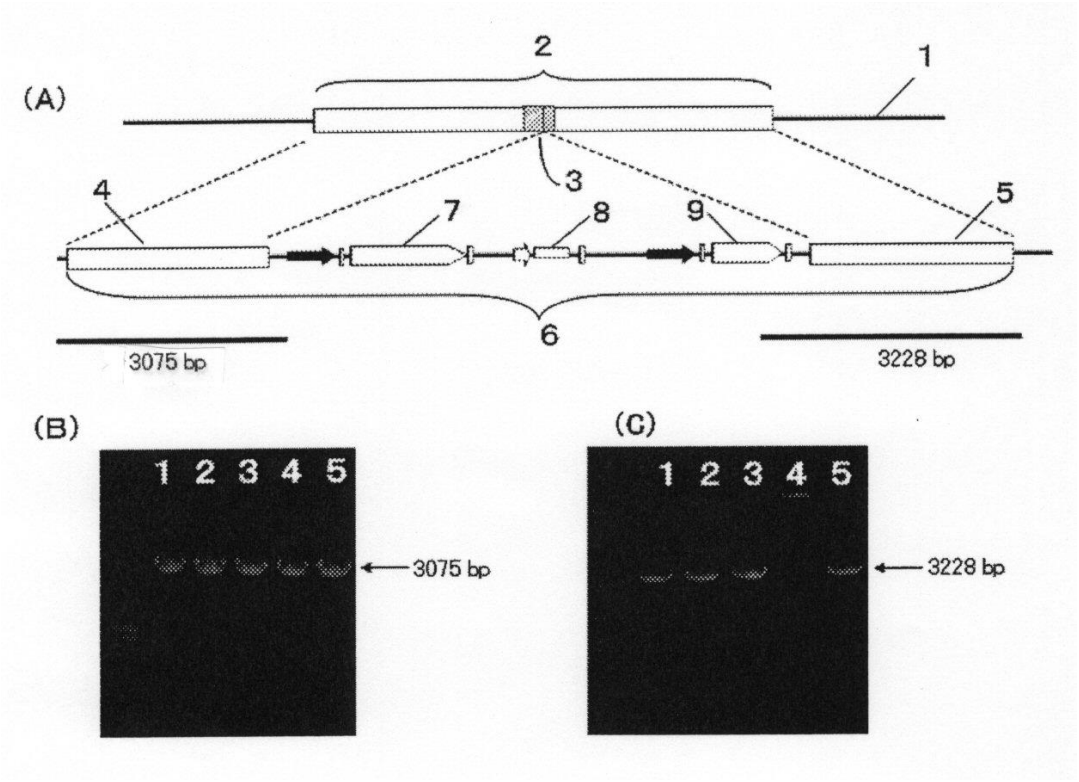

(A)
1
2
3
4
5
6
7
8
9
3075 bp
3228 bp
(B)
1 2 3 4 5
3075 bp
(C)
1 2 3 4 5
3228 bp

FIG. 7

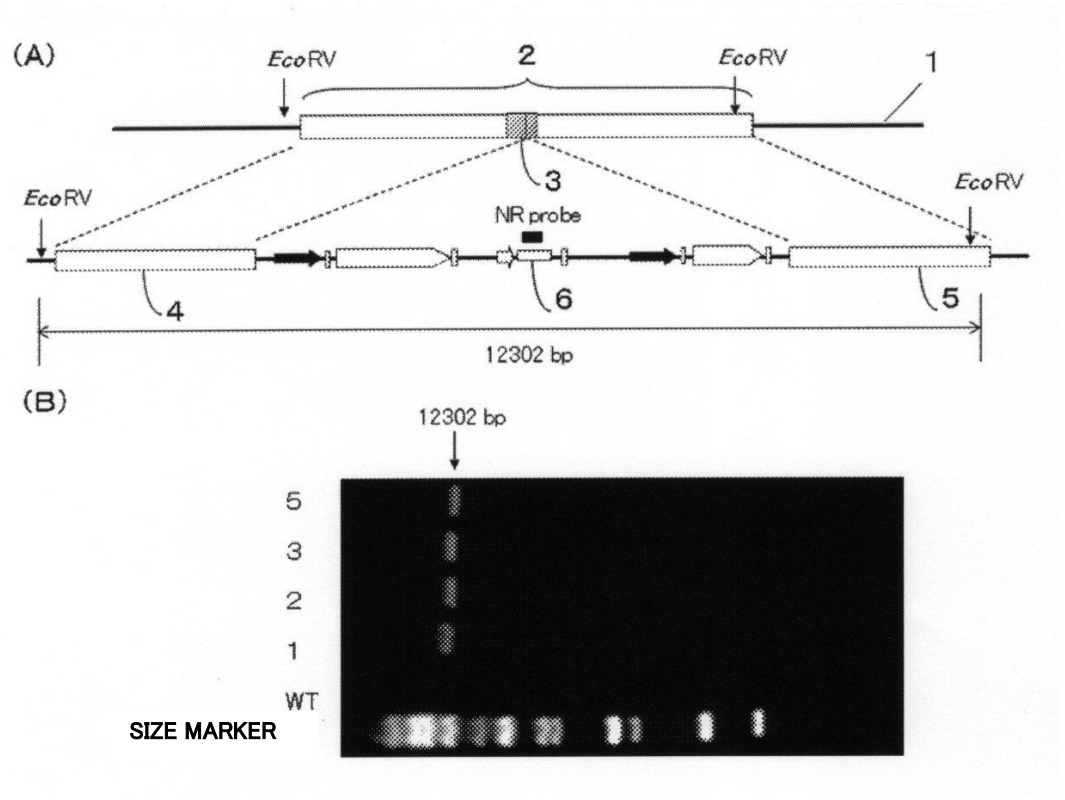

(A)
EcoRV
2
EcoRV
1
EcoRV
3
EcoRV
NR probe
4
6
5
12302 bp
(B)
12302 bp
5
3
2
1
WT
SIZE MARKER

FIG. 8

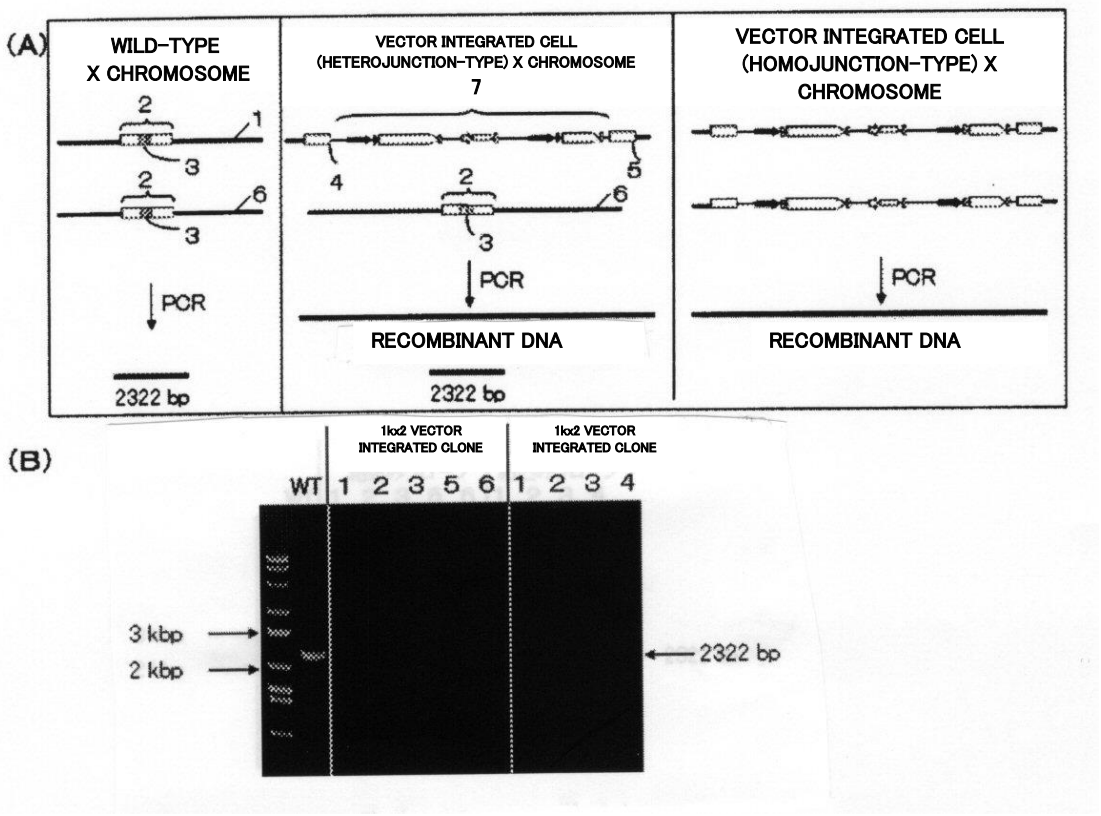

(A)
WILD-TYPE
X CHROMOSOME
VECTOR INTEGRATED CELL
(HETEROJUNCTION-TYPE) X CHROMOSOME
VECTOR INTEGRATED CELL
(HOMOJUNCTION-TYPE) X
CHROMOSOME
PCR
RECOMBINANT DNA
2322 bp
(B)
1ko2 VECTOR
INTEGRATED CLONE
WT 1 2 3 5 6 1 2 3 4
3 kbp
2 kbp
2322 bp

FIG. 9

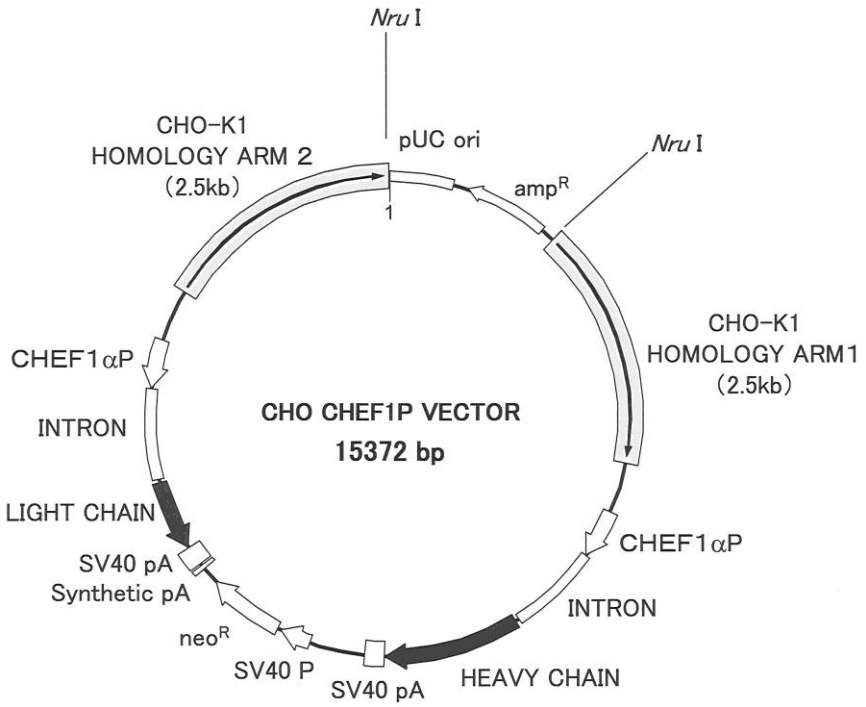

Nru I
CHO-K1
HOMOLOGY ARM 2
(2.5kb)
pUC ori
ampR
Nru I
CHO-K1
HOMOLOGY ARM1
(2.5kb)
CHEF1αP
INTRON
CHO CHEF1P VECTOR
15372 bp
LIGHT CHAIN
SV40 pA
Synthetic pA
neoR
SV40 P
SV40 pA
HEAVY CHAIN
INTRON
CHEF1αP

FIG. 10

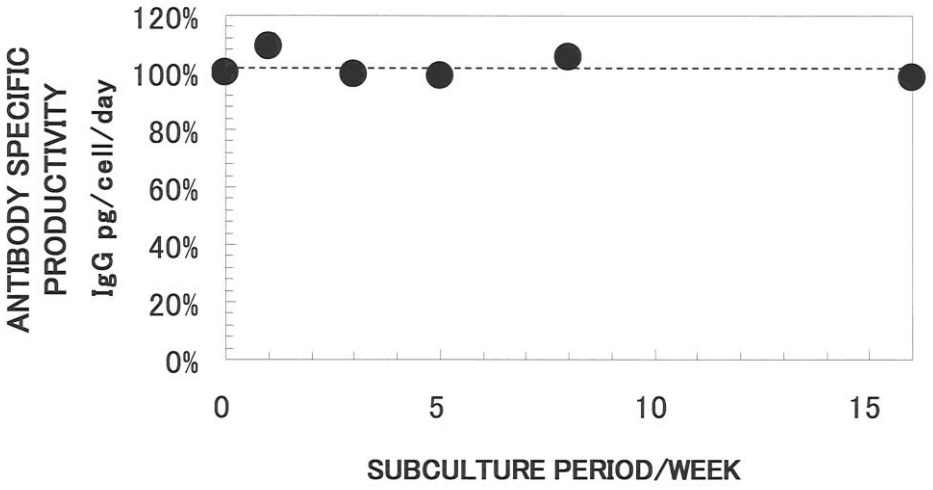

ANTIBODY SPECIFIC PRODUCTIVITY
IgG pg/cell/day
120%
100%
80%
60%
40%
20%
0%
0
5
10
15
SUBCULTURE PERIOD/WEEK

FIG. 11

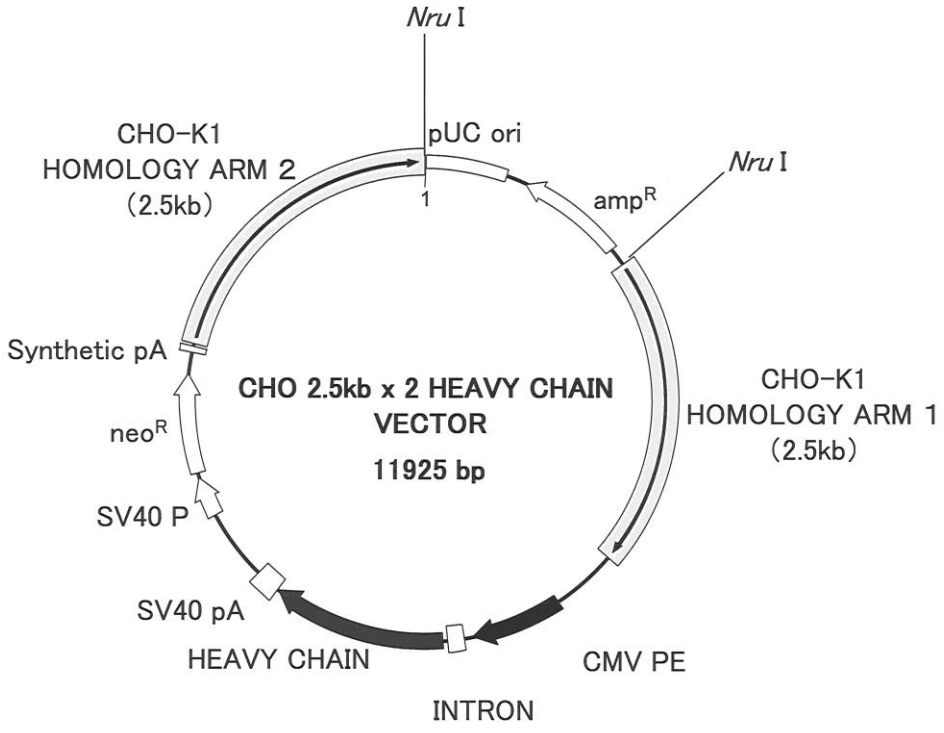

Nru I
CHO-K1
HOMOLOGY ARM 2
(2.5kb)
pUC ori
1
ampR
Nru I
Synthetic pA
CHO 2.5kb x 2 HEAVY CHAIN
VECTOR
11925 bp
CHO-K1
HOMOLOGY ARM 1
(2.5kb)
neoR
SV40 P
SV40 pA
HEAVY CHAIN
CMV PE
INTRON

FIG. 12

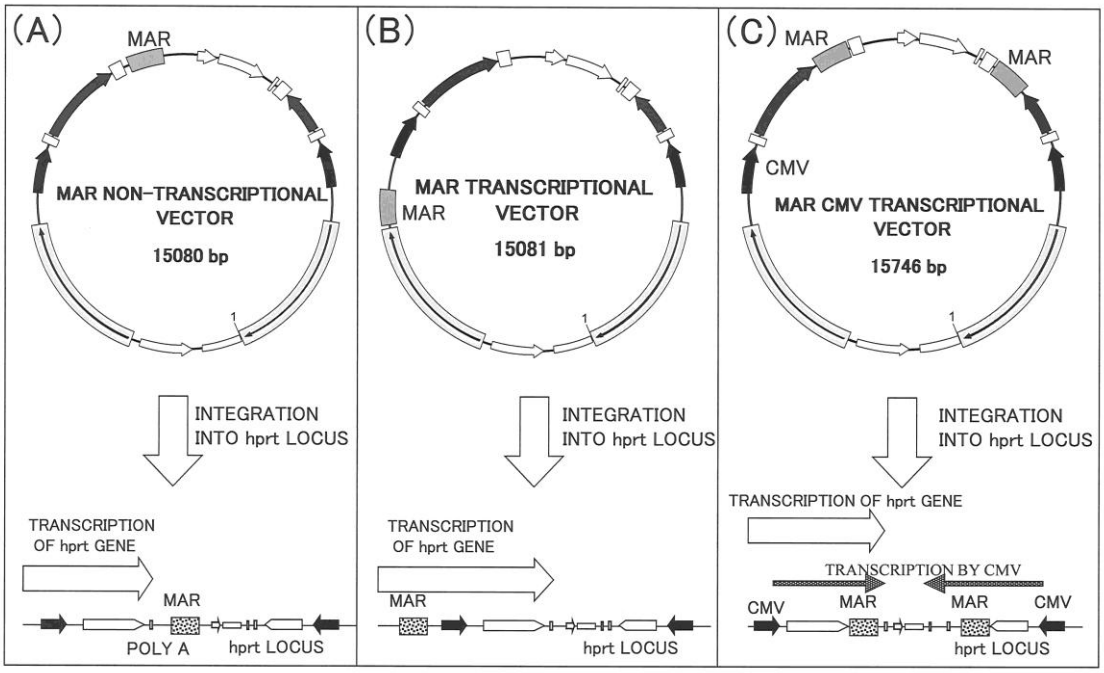

(A)
MAR
MAR NON-TRANSCRIPTIONAL VECTOR
15080 bp
INTEGRATION INTO hprt LOCUS
TRANSCRIPTION OF hprt GENE
MAR
POLY A
hprt LOCUS
(B)
MAR TRANSCRIPTIONAL VECTOR
MAR
15081 bp
INTEGRATION INTO hprt LOCUS
TRANSCRIPTION OF hprt GENE
MAR
hprt LOCUS
(C)
MAR
MAR
CMV
MAR CMV TRANSCRIPTIONAL VECTOR
15746 bp
INTEGRATION INTO hprt LOCUS
TRANSCRIPTION OF hprt GENE
TRANSCRIPTION BY CMV
CMV
MAR
MAR
CMV
hprt LOCUS

FIG. 13

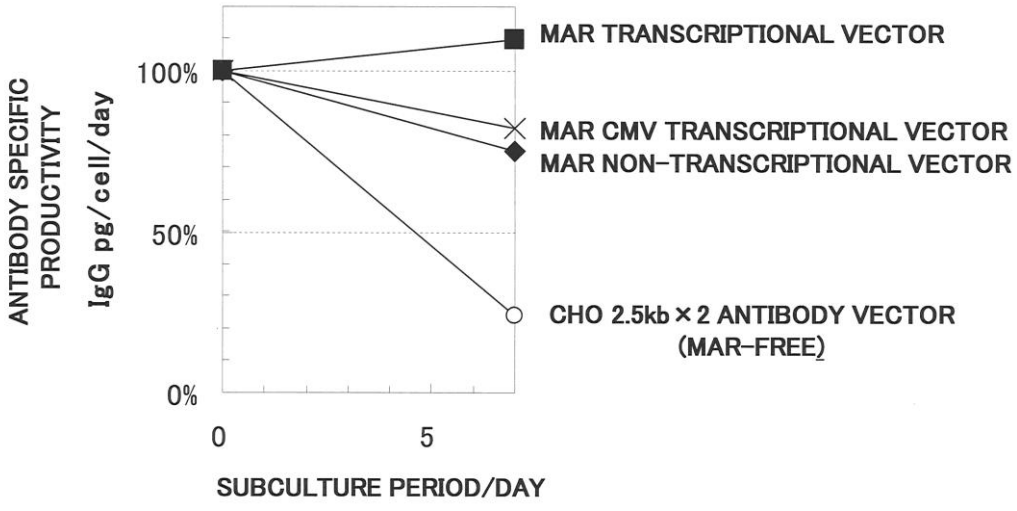

ANTIBODY SPECIFIC PRODUCTIVITY
IgG pg/cell/day
100%
50%
0%
0
5
SUBCULTURE PERIOD/DAY
MAR TRANSCRIPTIONAL VECTOR
MAR CMV TRANSCRIPTIONAL VECTOR
MAR NON-TRANSCRIPTIONAL VECTOR
CHO 2.5kb × 2 ANTIBODY VECTOR
(MAR-FREE)

FIG. 14

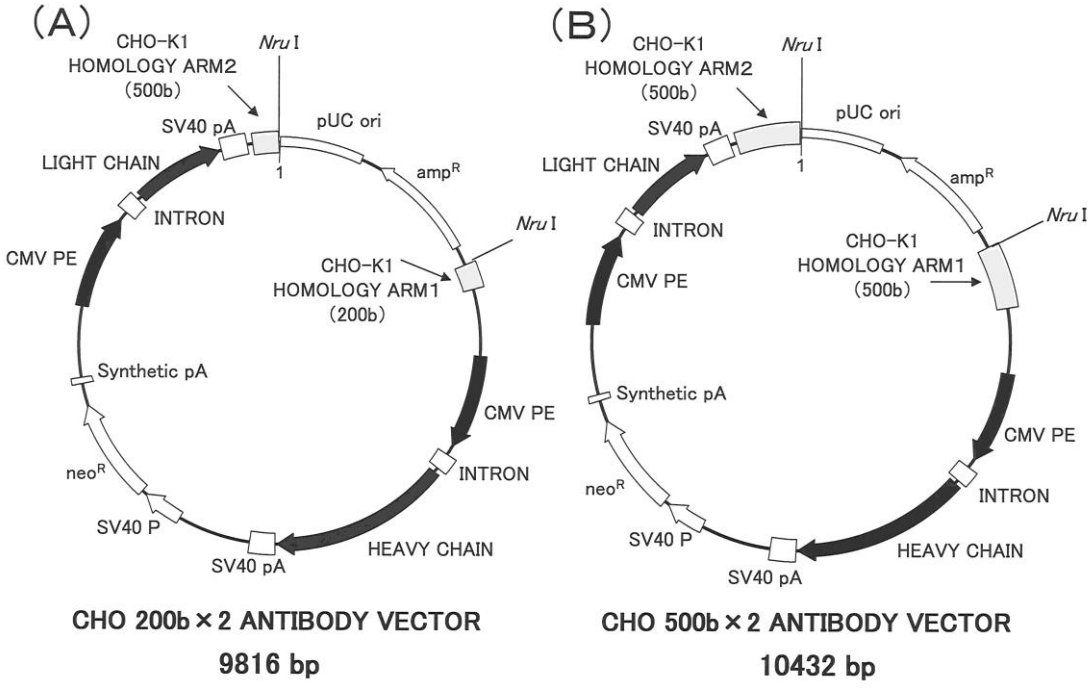

(A)
CHO-K1
HOMOLOGY ARM2
(500b)
Nru I
SV40 pA
pUC ori
LIGHT CHAIN
1
ampR
INTRON
Nru I
CMV PE
CHO-K1
HOMOLOGY ARM1
(200b)
Synthetic pA
CMV PE
INTRON
neoR
SV40 P
HEAVY CHAIN
SV40 pA
CHO 200b × 2 ANTIBODY VECTOR
9816 bp
(B)
CHO-K1
HOMOLOGY ARM2
(500b)
Nru I
SV40 pA
pUC ori
LIGHT CHAIN
1
ampR
INTRON
Nru I
CHO-K1
HOMOLOGY ARM1
(500b)
CMV PE
Synthetic pA
CMV PE
INTRON
neoR
SV40 P
HEAVY CHAIN
SV40 pA
CHO 500b × 2 ANTIBODY VECTOR
10432 bp

FIG. 15

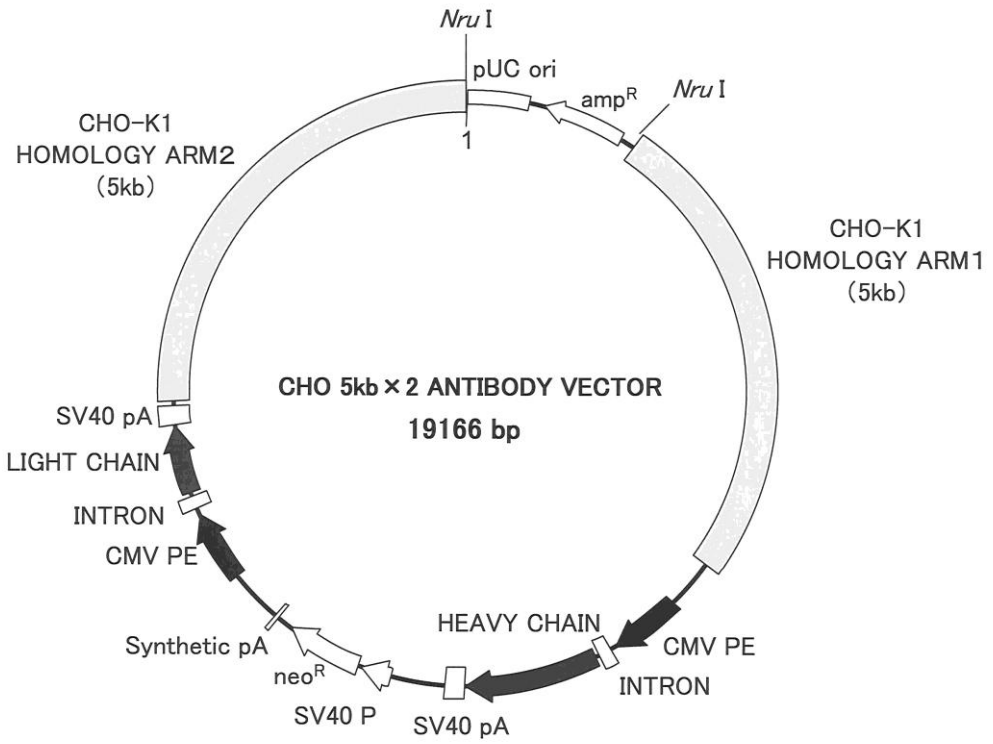

Nru I
pUC ori
ampR
Nru I
1
CHO-K1
HOMOLOGY ARM2
(5kb)
CHO-K1
HOMOLOGY ARM1
(5kb)
CHO 5kb × 2 ANTIBODY VECTOR
19166 bp
SV40 pA
LIGHT CHAIN
INTRON
CMV PE
HEAVY CHAIN
Synthetic pA
CMV PE
neoR
INTRON
SV40 P
SV40 pA

FIG. 16