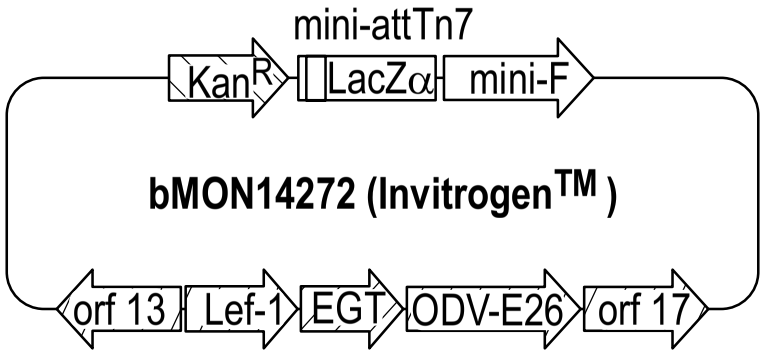


FIG. 1A

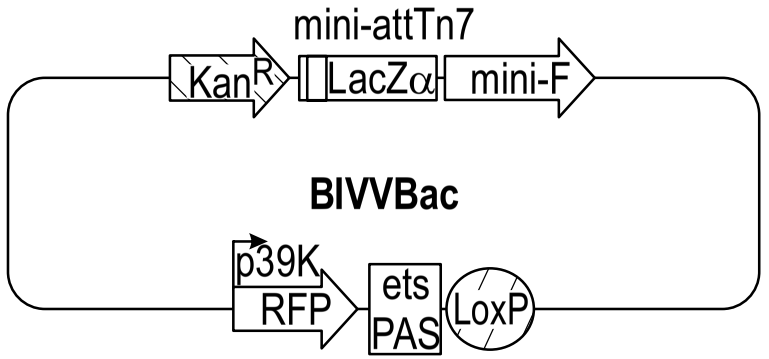


FIG. 1C

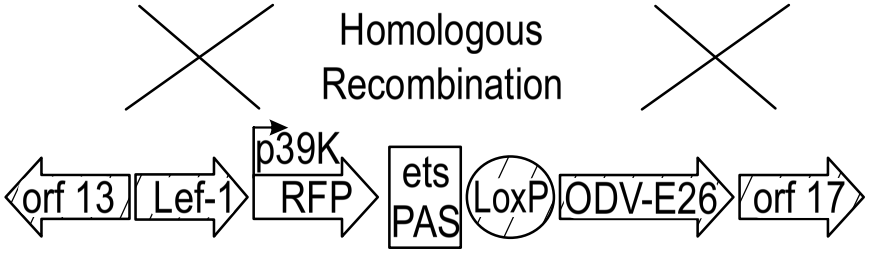


FIG. 1B



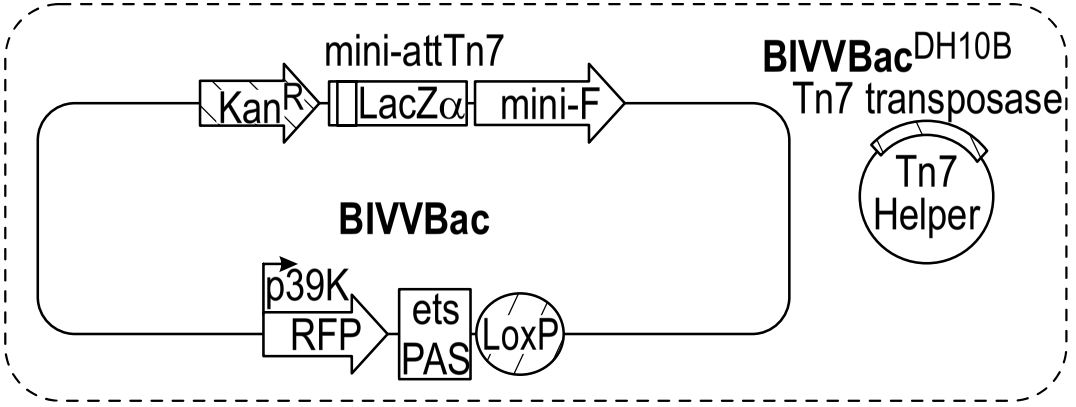


FIG. 1D

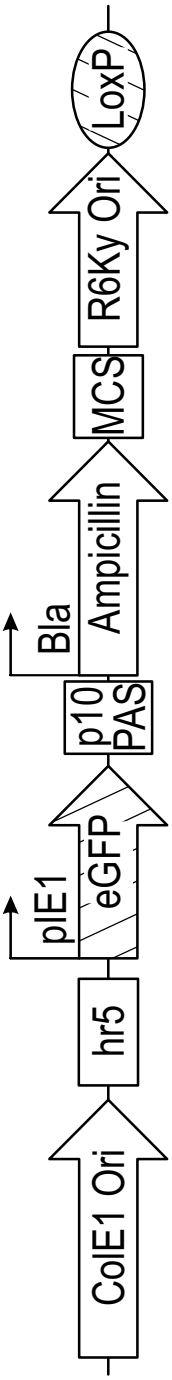

ColE1 Ori
hr5
pIE1
eGFP
p10
PAS
Bla
Ampicillin
MCS
R6Ky Ori
LoxP

FIG. 2A

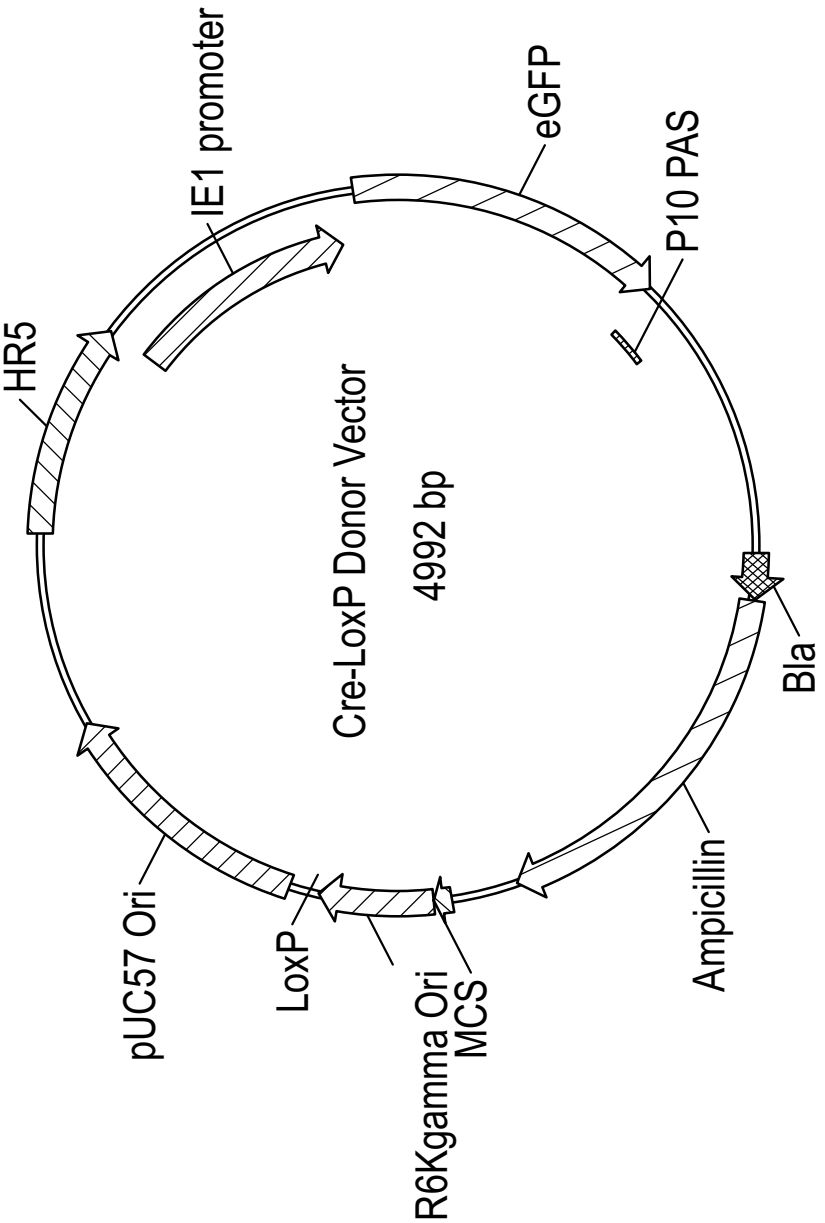

HR5
IE1 promoter
eGFP
P10 PAS
Cre-LoxP Donor Vector
4992 bp
Bla
Ampicillin
pUC57 Ori
LoxP
R6Kgamma Ori
MCS

FIG. 2B

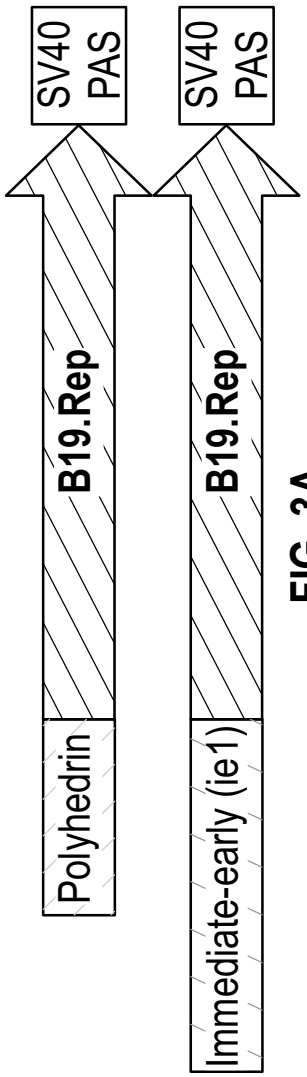

SV40
PAS
SV40
PAS
B19.Rep
B19.Rep
Polyhedrin
Immediate-early (ie1)

FIG. 3A

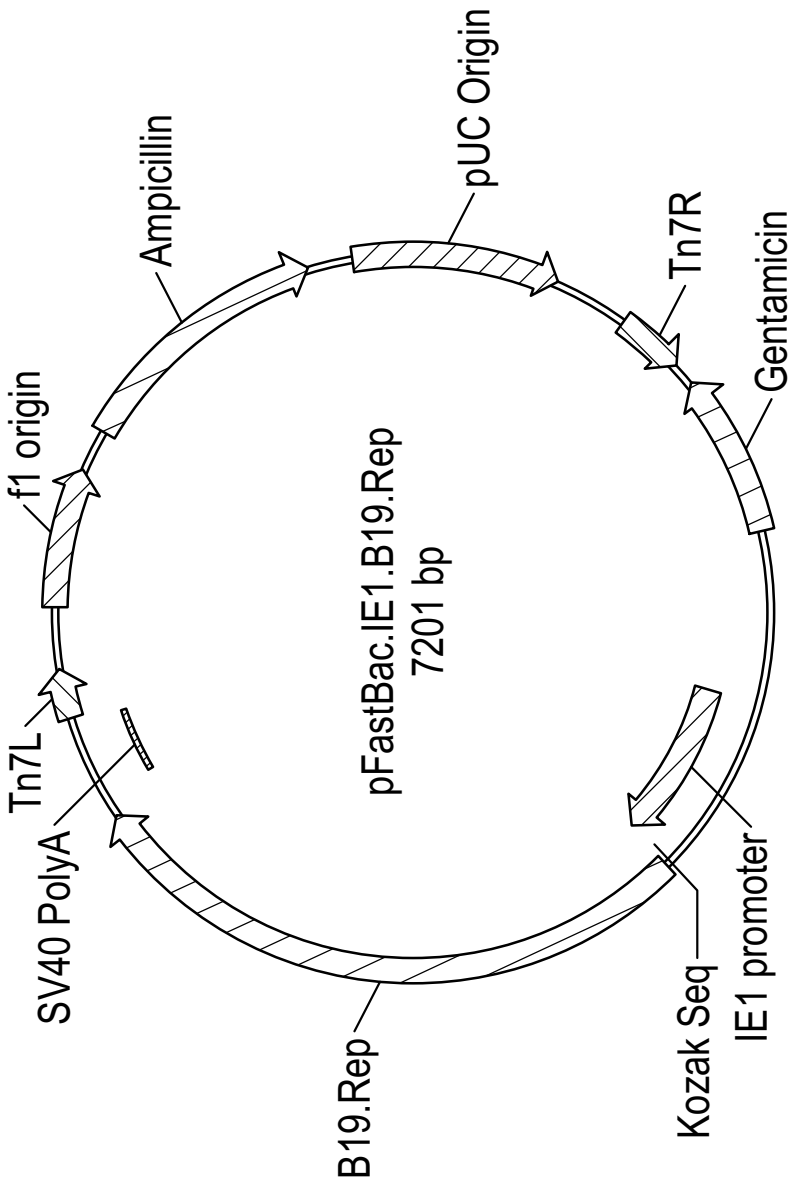

Ampicillin
pUC Origin
Tn7R
Gentamicin
f1 origin
pFastBac.IE1.B19.Rep
7201 bp
Tn7L
SV40 PolyA
B19.Rep
Kozak Seq
IE1 promoter

FIG. 3B

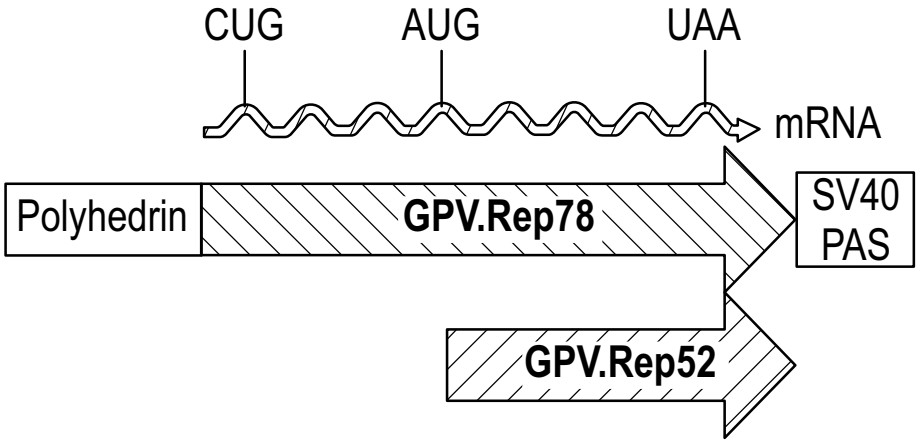

CUG
AUG
UAA
mRNA
Polyhedrin
GPV.Rep78
SV40
PAS
GPV.Rep52

FIG. 3C

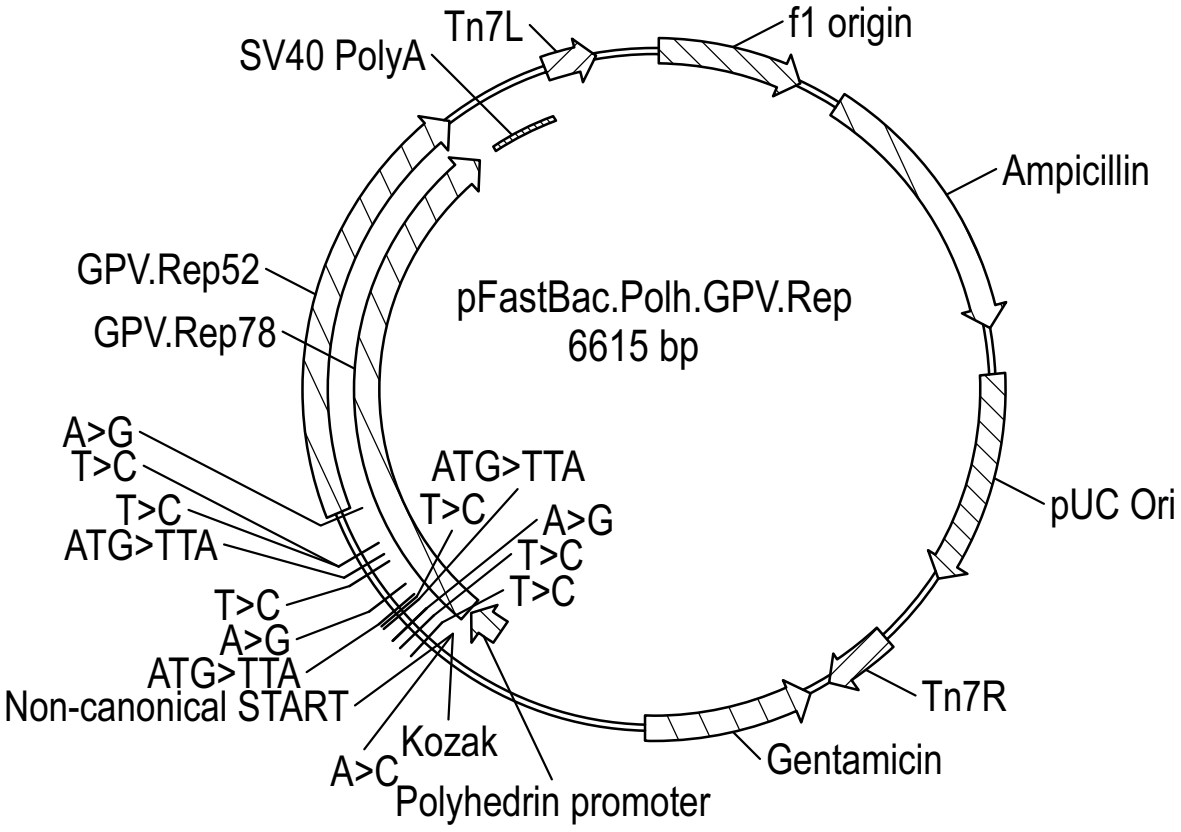

Tn7L
f1 origin
SV40 PolyA
Ampicillin
GPV.Rep52
GPV.Rep78
pFastBac.Polh.GPV.Rep
6615 bp
A>G
T>C
T>C
ATG>TTA
ATG>TTA
T>C
A>G
T>C
T>C
T>C
A>G
ATG>TTA
Non-canonical START
A>C
Kozak
Polyhedrin promoter
pUC Ori
Tn7R
Gentamicin

FIG. 3D

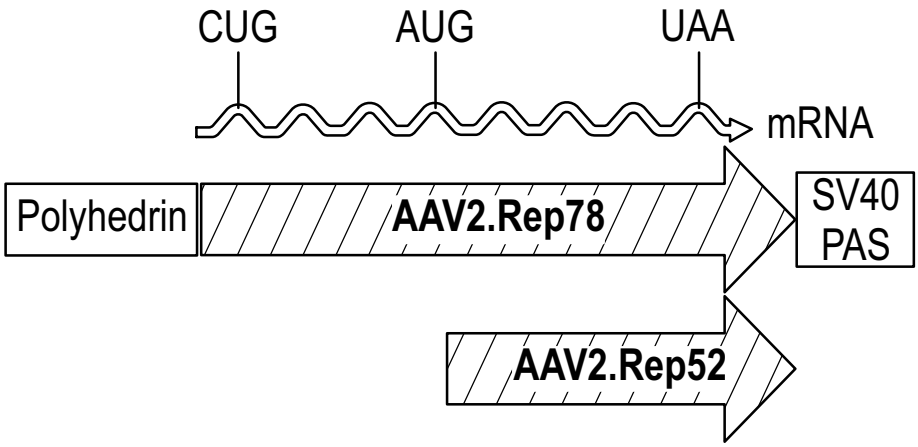

CUG
AUG
UAA
mRNA
Polyhedrin
AAV2.Rep78
SV40
PAS
AAV2.Rep52

FIG. 3E

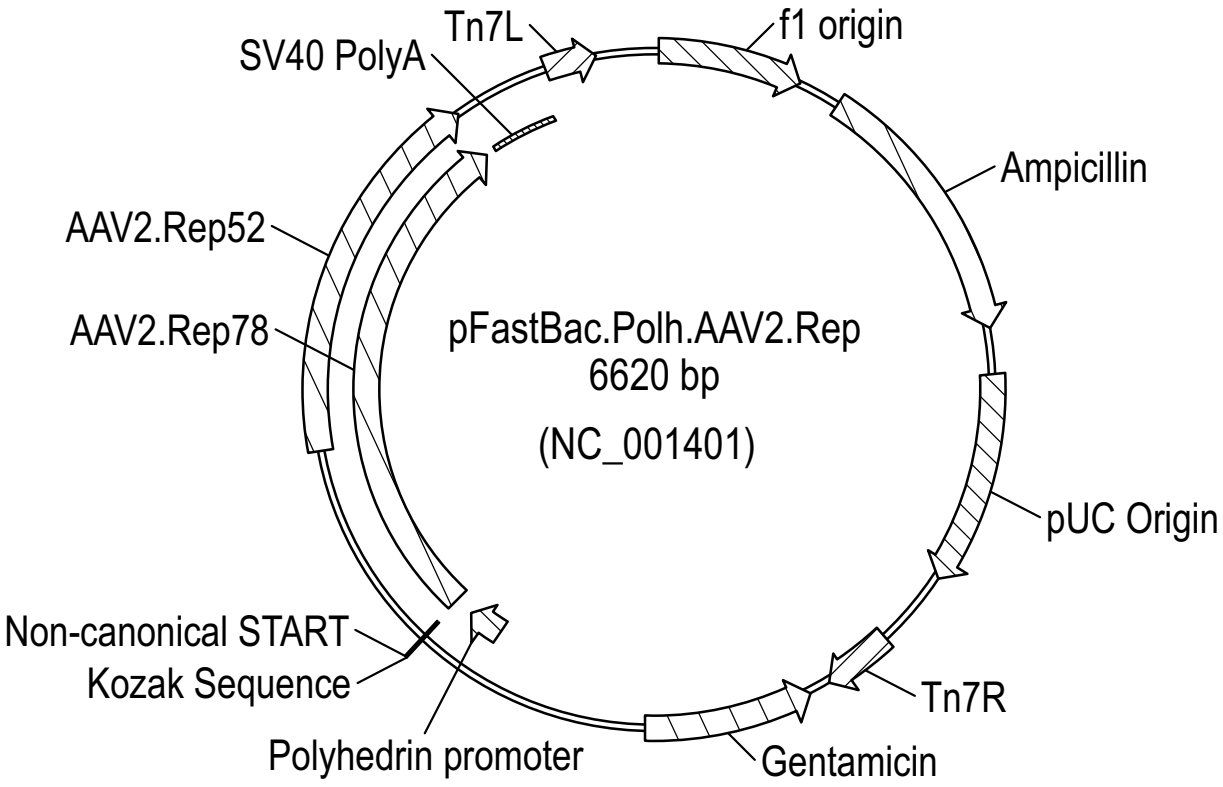

Tn7L
f1 origin
SV40 PolyA
Ampicillin
AAV2.Rep52
AAV2.Rep78
pFastBac.Polh.AAV2.Rep
6620 bp
(NC_001401)
pUC Origin
Non-canonical START
Kozak Sequence
Tn7R
Polyhedrin promoter
Gentamicin

FIG. 3F

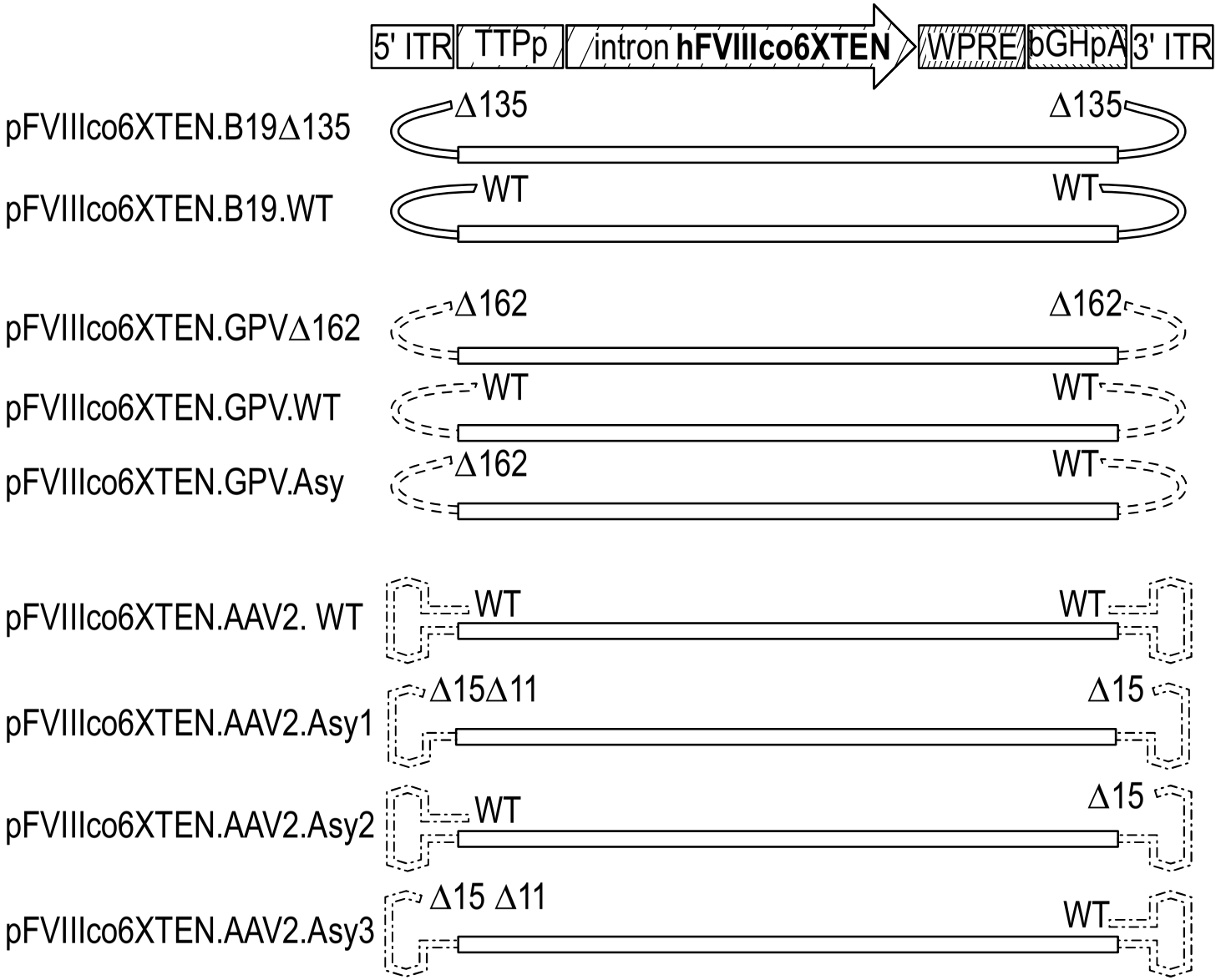

5' ITR
TTPp
intron hFVIIIco6XTEN
WPRE
bGHpA
3' ITR
pFVIIIco6XTEN.B19Δ135
Δ135
Δ135
pFVIIIco6XTEN.B19.WT
WT
WT
pFVIIIco6XTEN.GPVΔ162
Δ162
Δ162
pFVIIIco6XTEN.GPV.WT
WT
WT
pFVIIIco6XTEN.GPV.Asy
Δ162
WT
pFVIIIco6XTEN.AAV2. WT
WT
WT
pFVIIIco6XTEN.AAV2.Asy1
Δ15Δ11
Δ15
pFVIIIco6XTEN.AAV2.Asy2
WT
Δ15
pFVIIIco6XTEN.AAV2.Asy3
Δ15 Δ11
WT

FIG. 4A

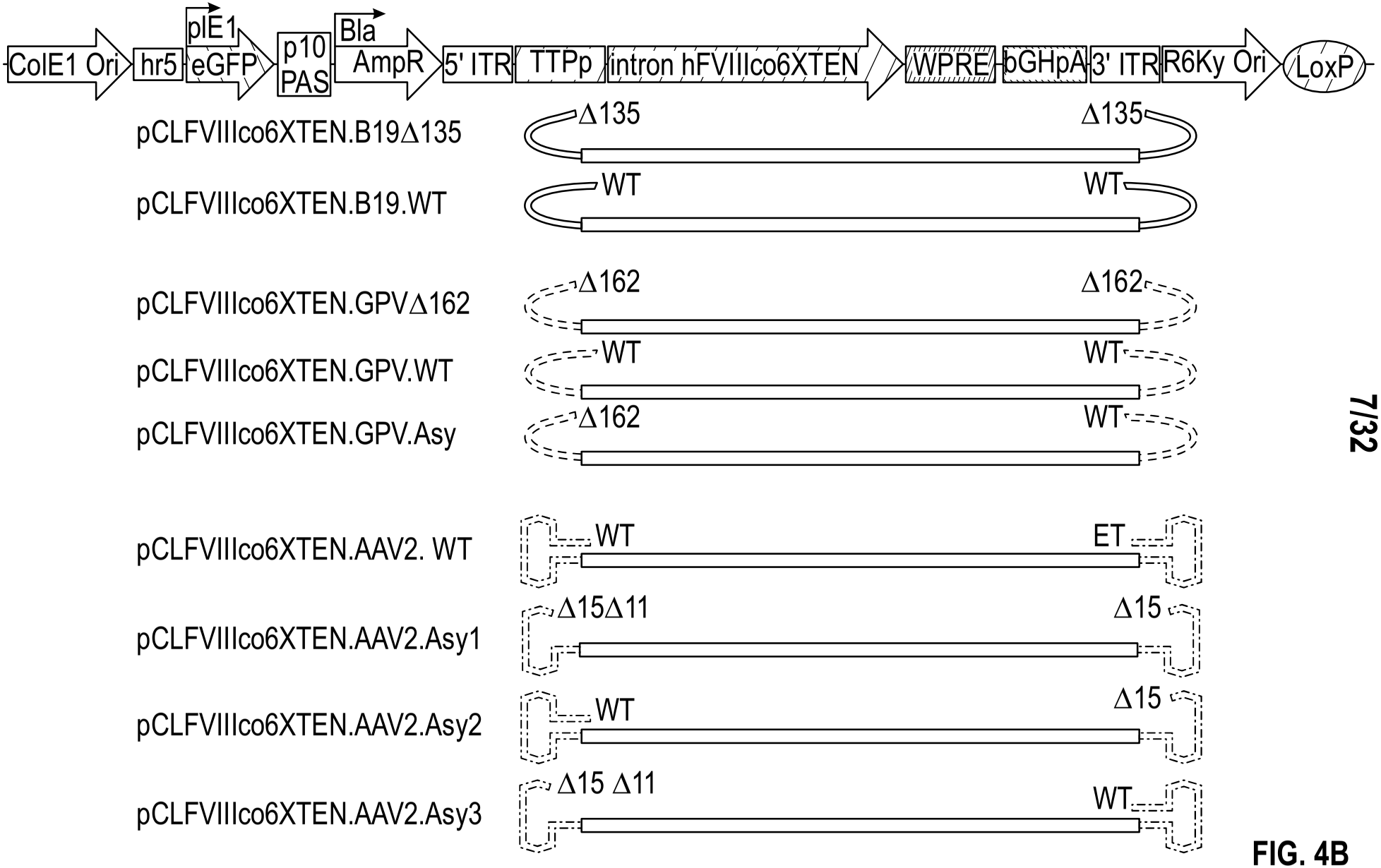

ColE1 Ori
hr5
pIE1
eGFP
p10
PAS
Bla
AmpR
5' ITR
TTPp
intron hFVIIIco6XTEN
WPRE
bGHpA
3' ITR
R6Ky Ori
LoxP
pCLFVIIIco6XTEN.B19Δ135
Δ135
Δ135
pCLFVIIIco6XTEN.B19.WT
WT
WT
pCLFVIIIco6XTEN.GPVΔ162
Δ162
Δ162
pCLFVIIIco6XTEN.GPV.WT
WT
WT
pCLFVIIIco6XTEN.GPV.Asy
Δ162
WT
pCLFVIIIco6XTEN.AAV2. WT
WT
ET
pCLFVIIIco6XTEN.AAV2.Asy1
Δ15Δ11
Δ15
pCLFVIIIco6XTEN.AAV2.Asy2
WT
Δ15
pCLFVIIIco6XTEN.AAV2.Asy3
Δ15 Δ11
WT

FIG. 4B

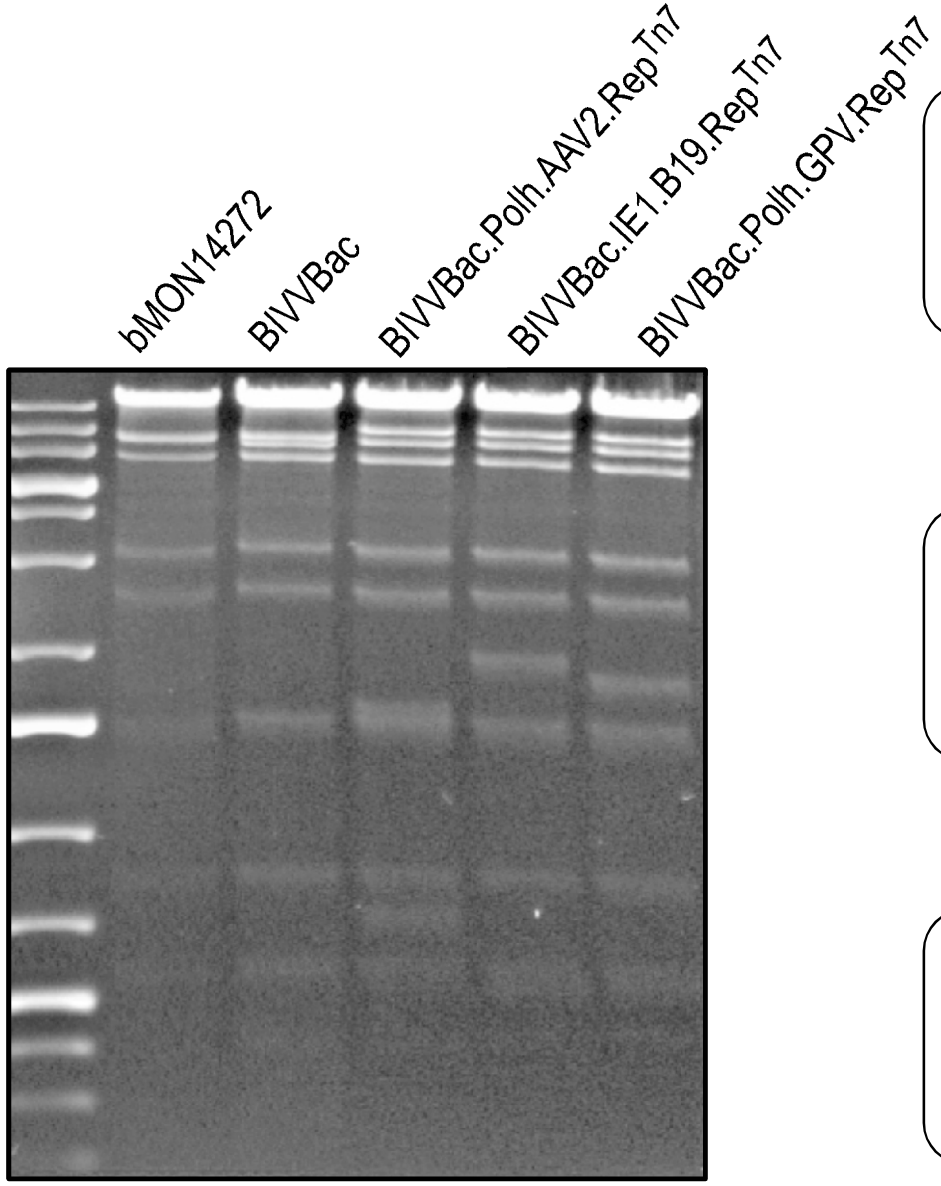


FIG. 5A

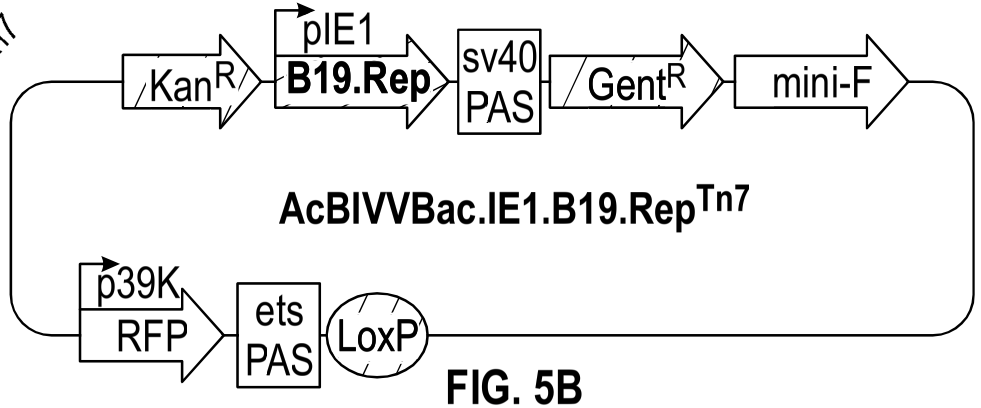


FIG. 5B

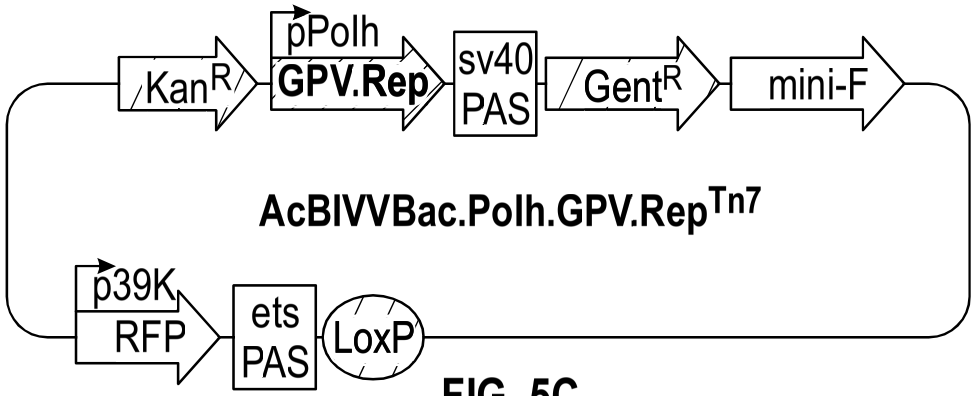


FIG. 5C

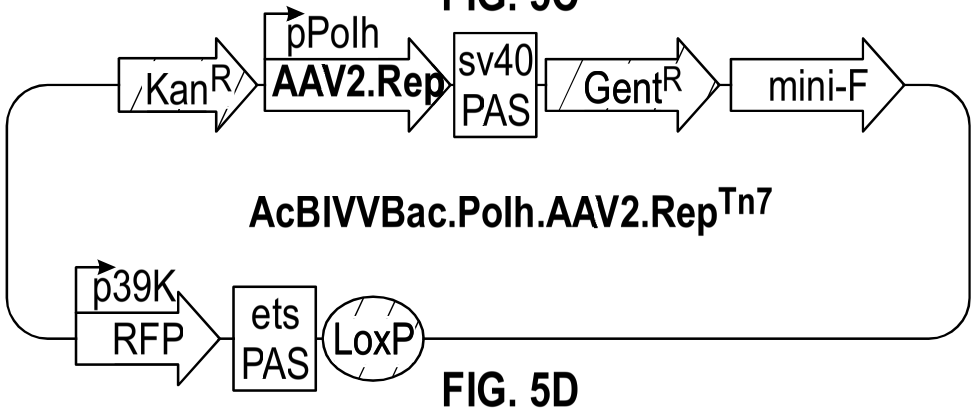


FIG. 5D

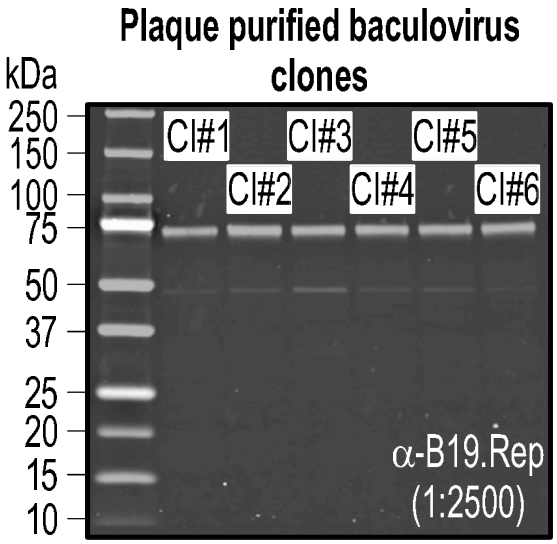


FIG. 5E

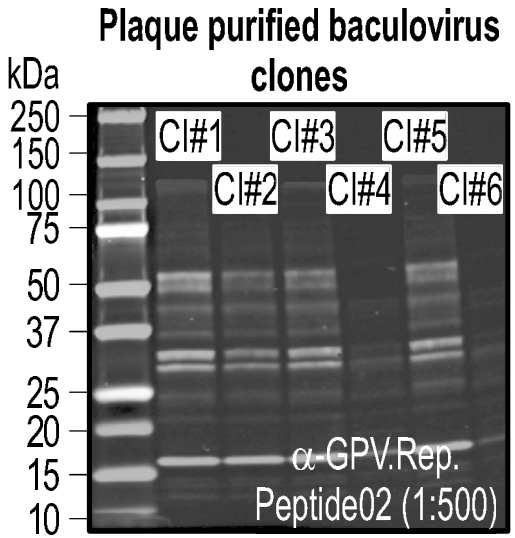


FIG. 5F

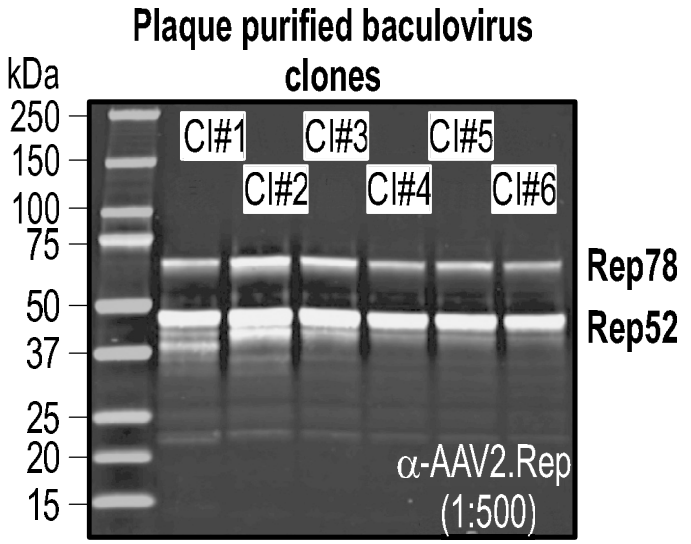


FIG. 5G

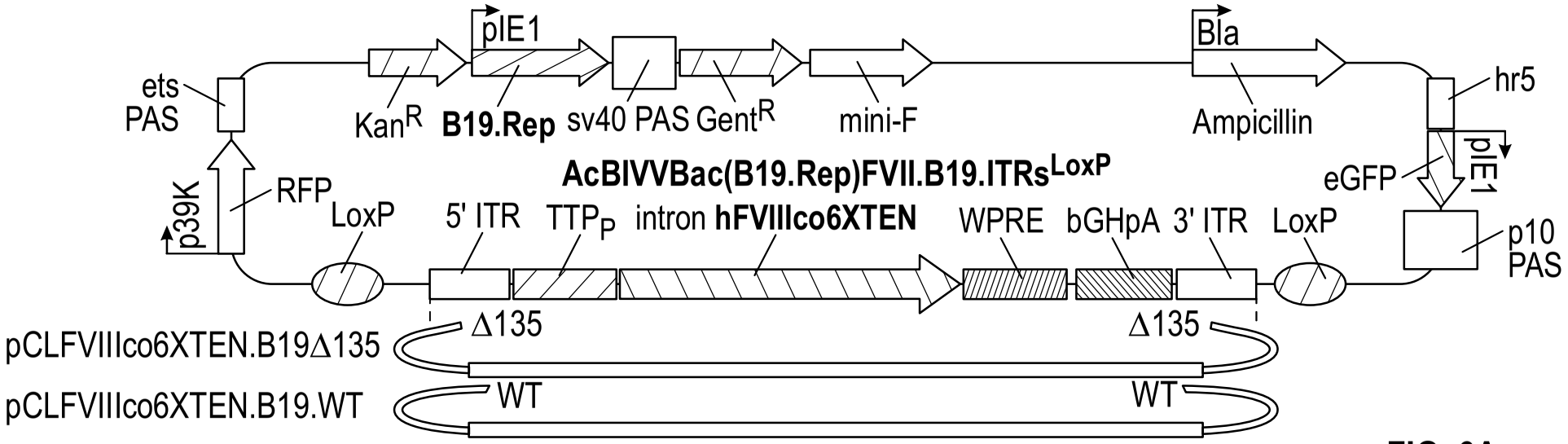

pIE1
Bla
ets
PAS
Kan^R
B19.Rep
sv40 PAS
Gent^R
mini-F
Ampicillin
hr5
pIE1
eGFP
AcBIVVBac(B19.Rep)FVII.B19.ITRs^LoxP
p39K
RFP
LoxP
5' ITR
TTP_P
intron hFVIIIco6XTEN
WPRE
bGHpA
3' ITR
LoxP
p10
PAS
Δ135
Δ135
pCLFVIIIco6XTEN.B19Δ135
WT
WT
pCLFVIIIco6XTEN.B19.WT

FIG. 6A

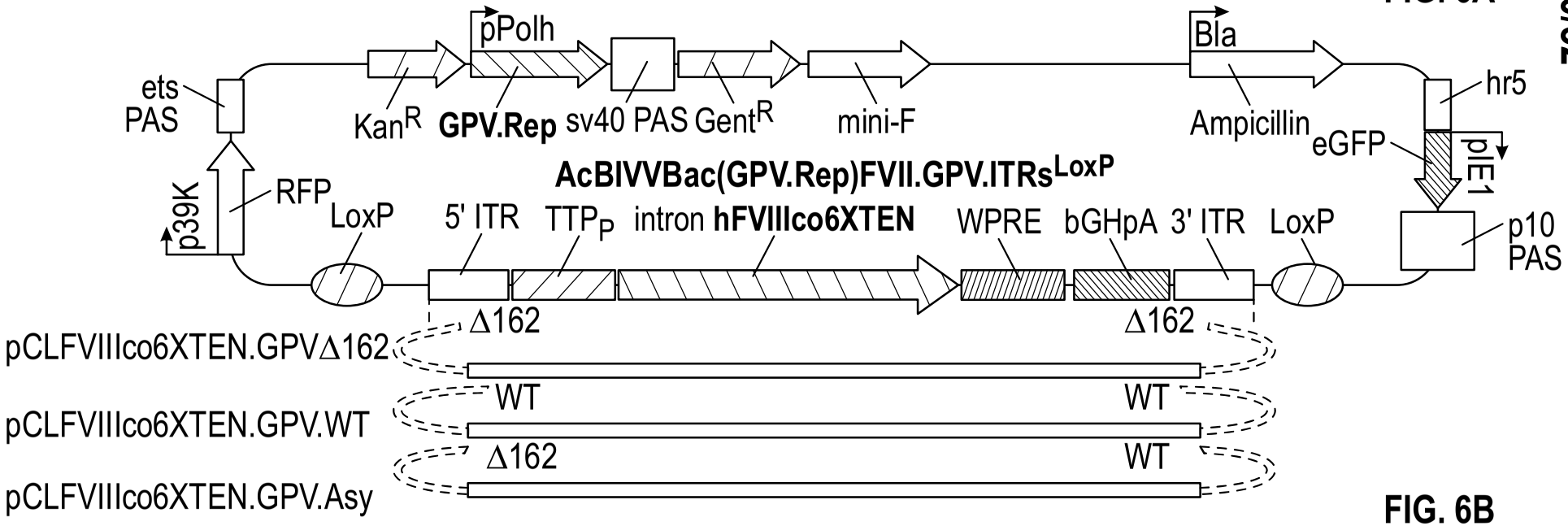

pPolh
Bla
ets
PAS
Kan^R
GPV.Rep
sv40 PAS
Gent^R
mini-F
Ampicillin
hr5
eGFP
pIE1
AcBIVVBac(GPV.Rep)FVII.GPV.ITRs^LoxP
p39K
RFP
LoxP
5' ITR
TTP_P
intron hFVIIIco6XTEN
WPRE
bGHpA
3' ITR
LoxP
p10
PAS
Δ162
Δ162
pCLFVIIIco6XTEN.GPVΔ162
WT
WT
pCLFVIIIco6XTEN.GPV.WT
Δ162
WT
pCLFVIIIco6XTEN.GPV.Asy

FIG. 6B

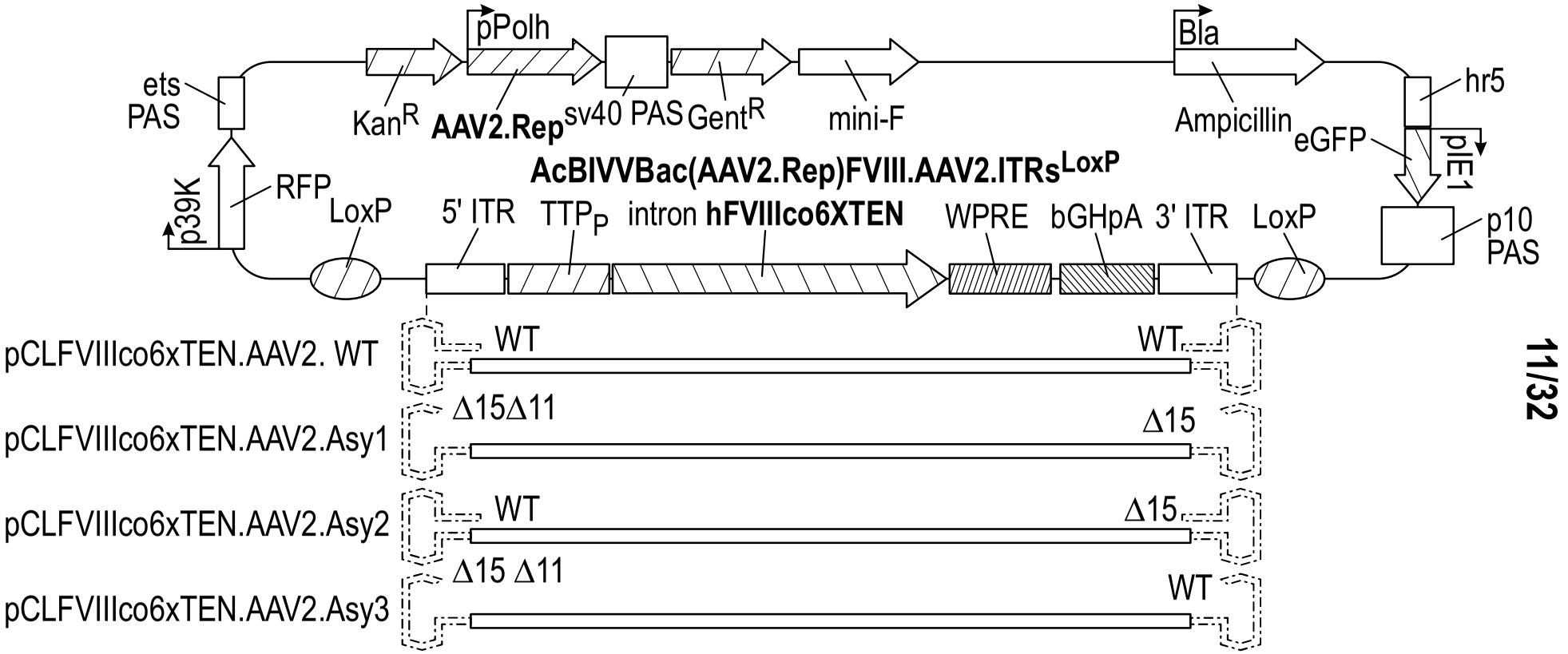

ets PAS
pPolh
Kan^R
AAV2.Rep
sv40 PAS
Gent^R
mini-F
Bla
Ampicillin
hr5
eGFP
pIE1
p39K
RFP
LoxP
AcBIVVBac(AAV2.Rep)FVIII.AAV2.ITRs^LoxP
5' ITR
TTP_P
intron hFVIIIco6XTEN
WPRE
bGHpA
3' ITR
LoxP
p10 PAS
pCLFVIIIco6xTEN.AAV2. WT
WT
WT
pCLFVIIIco6xTEN.AAV2.Asy1
Δ15Δ11
Δ15
pCLFVIIIco6xTEN.AAV2.Asy2
WT
Δ15
pCLFVIIIco6xTEN.AAV2.Asy3
Δ15 Δ11
WT

FIG. 6C

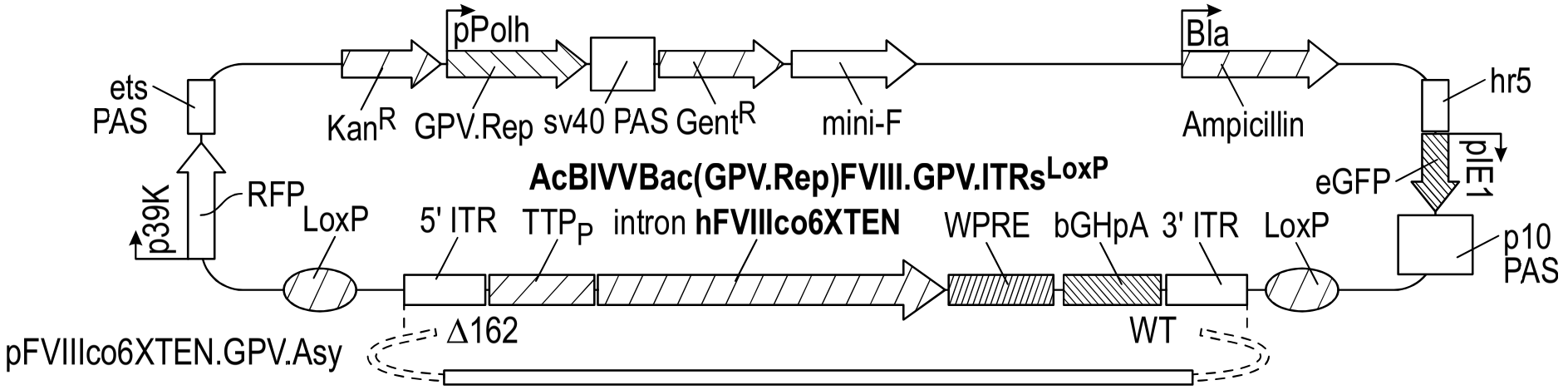


FIG. 7A

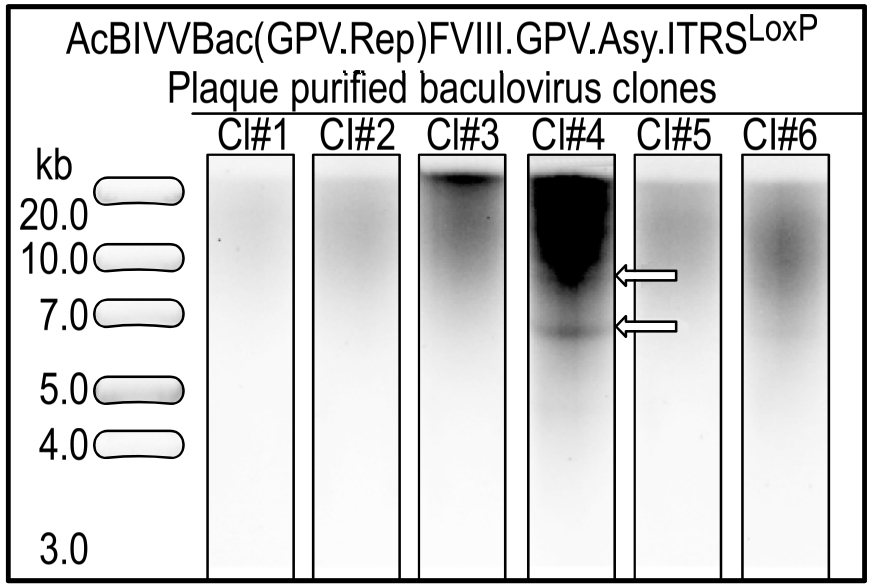


FIG. 7B

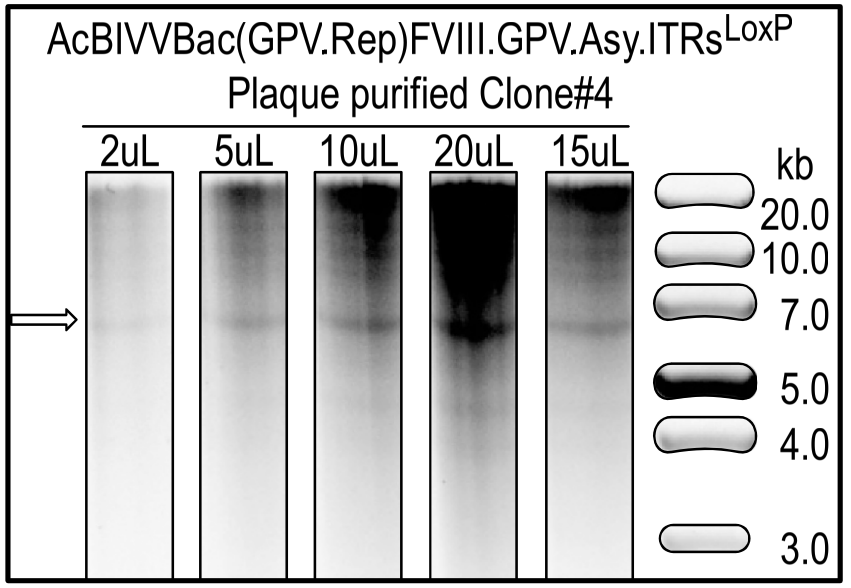


FIG. 7C

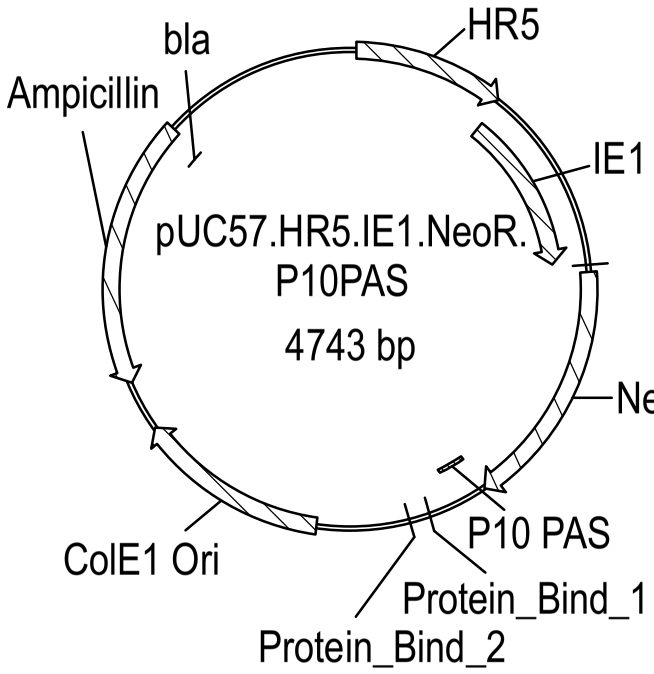

bla
Ampicillin
HR5
IE1
pUC57.HR5.IE1.NeoR.
P10PAS
4743 bp
NeoR
P10 PAS
ColE1 Ori
Protein_Bind_1
Protein_Bind_2

FIG. 8A

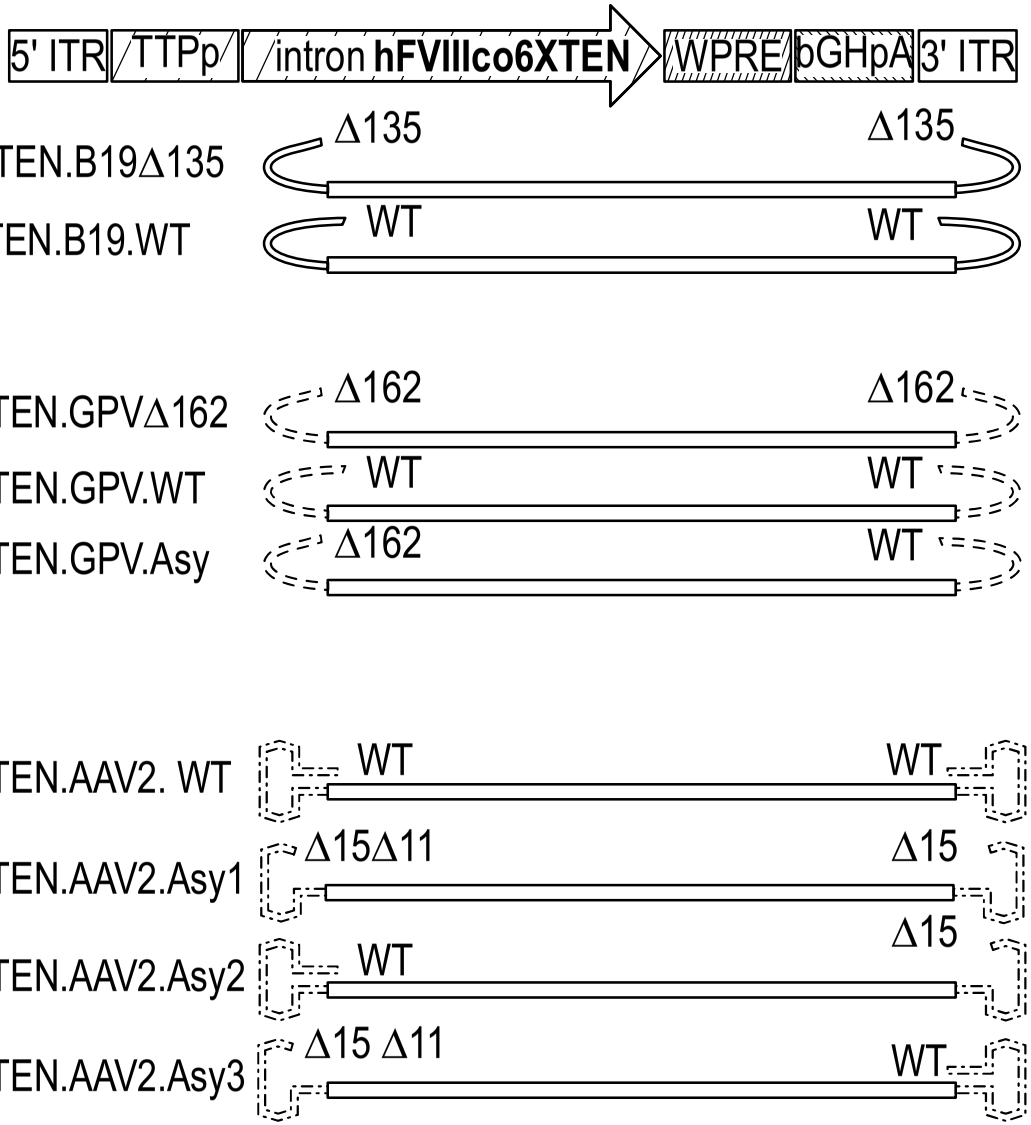

5' ITR
TTPp
intron hFVIIIco6XTEN
WPRE
bGHpA
3' ITR
Sf.FVIIIco6XTEN.B19Δ135
Δ135
Δ135
Sf.FVIIIco6xTEN.B19.WT
WT
WT
Sf.FVIIIco6XTEN.GPVΔ162
Δ162
Δ162
Sf.FVIIIco6XTEN.GPV.WT
WT
WT
Sf.FVIIIco6XTEN.GPV.Asy
Δ162
WT
Sf.FVIIIco6XTEN.AAV2. WT
WT
WT
Sf.FVIIIco6XTEN.AAV2.Asy1
Δ15Δ11
Δ15
Sf.FVIIIco6XTEN.AAV2.Asy2
Δ15
WT
Sf.FVIIIco6XTEN.AAV2.Asy3
Δ15 Δ11
WT

FIG. 8B

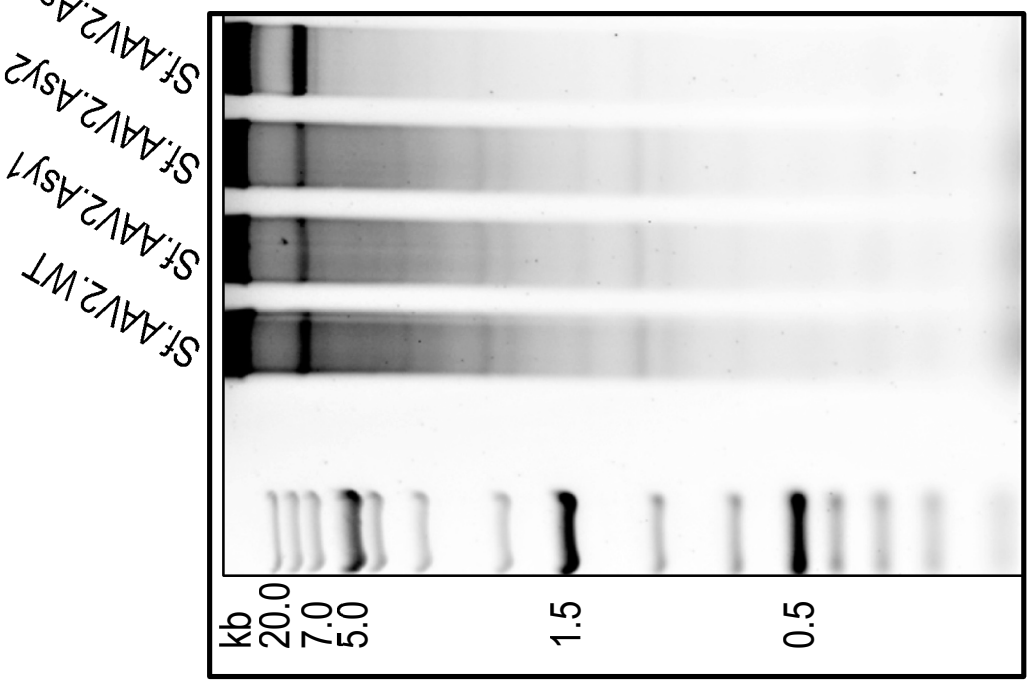


FIG. 9C

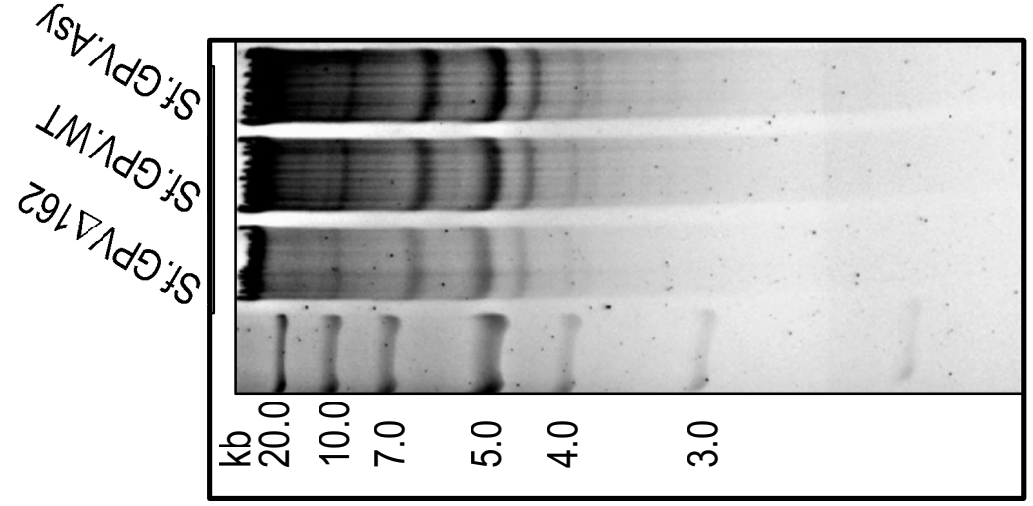


FIG. 9B

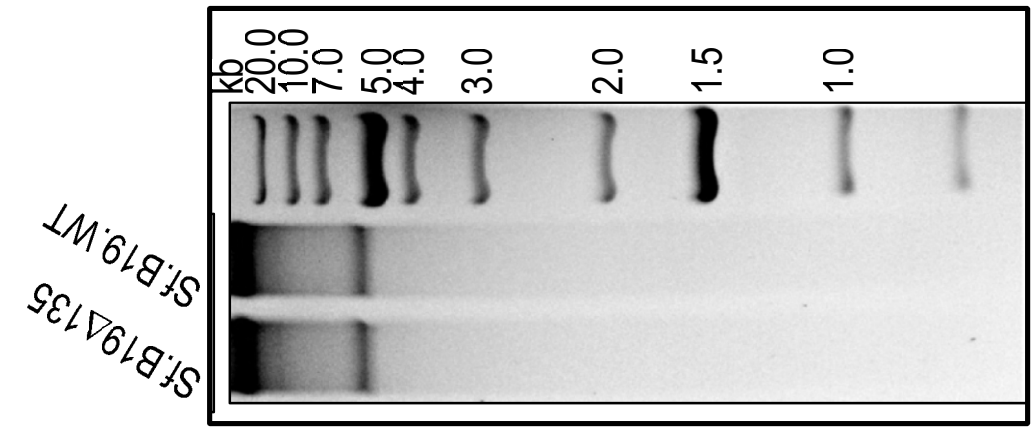


FIG. 9A

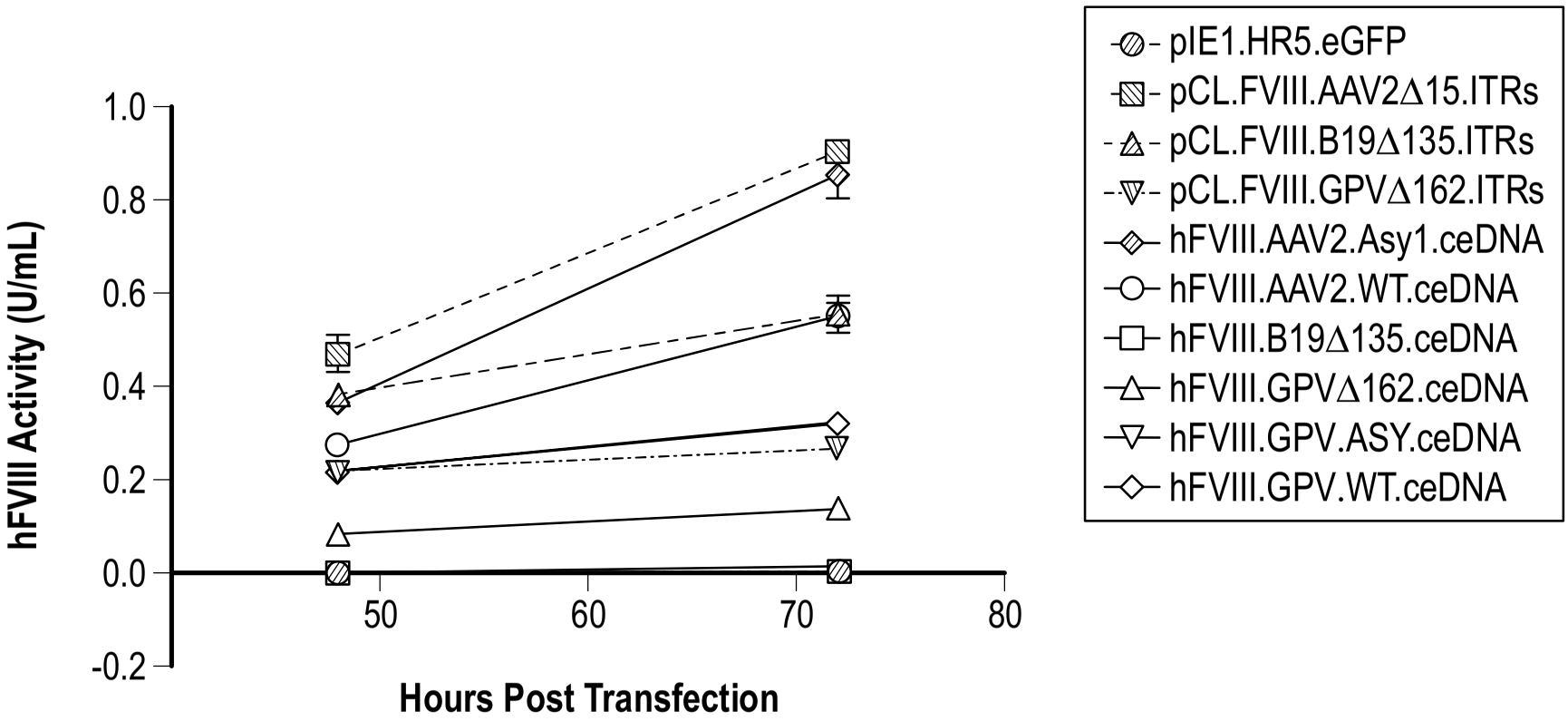

hFVIII Activity (U/mL)
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
50
60
70
80
Hours Post Transfection
pIE1.HR5.eGFP
pCL.FVIII.AAV2Δ15.ITRs
pCL.FVIII.B19Δ135.ITRs
pCL.FVIII.GPVΔ162.ITRs
hFVIII.AAV2.Asy1.ceDNA
hFVIII.AAV2.WT.ceDNA
hFVIII.B19Δ135.ceDNA
hFVIII.GPVΔ162.ceDNA
hFVIII.GPV.ASY.ceDNA
hFVIII.GPV.WT.ceDNA

FIG. 10

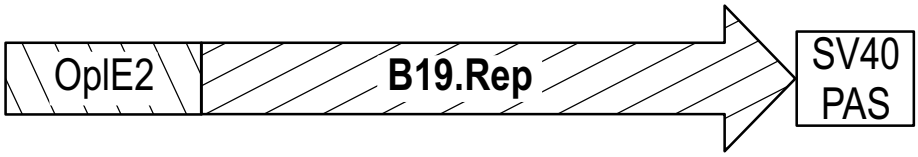


FIG. 11A

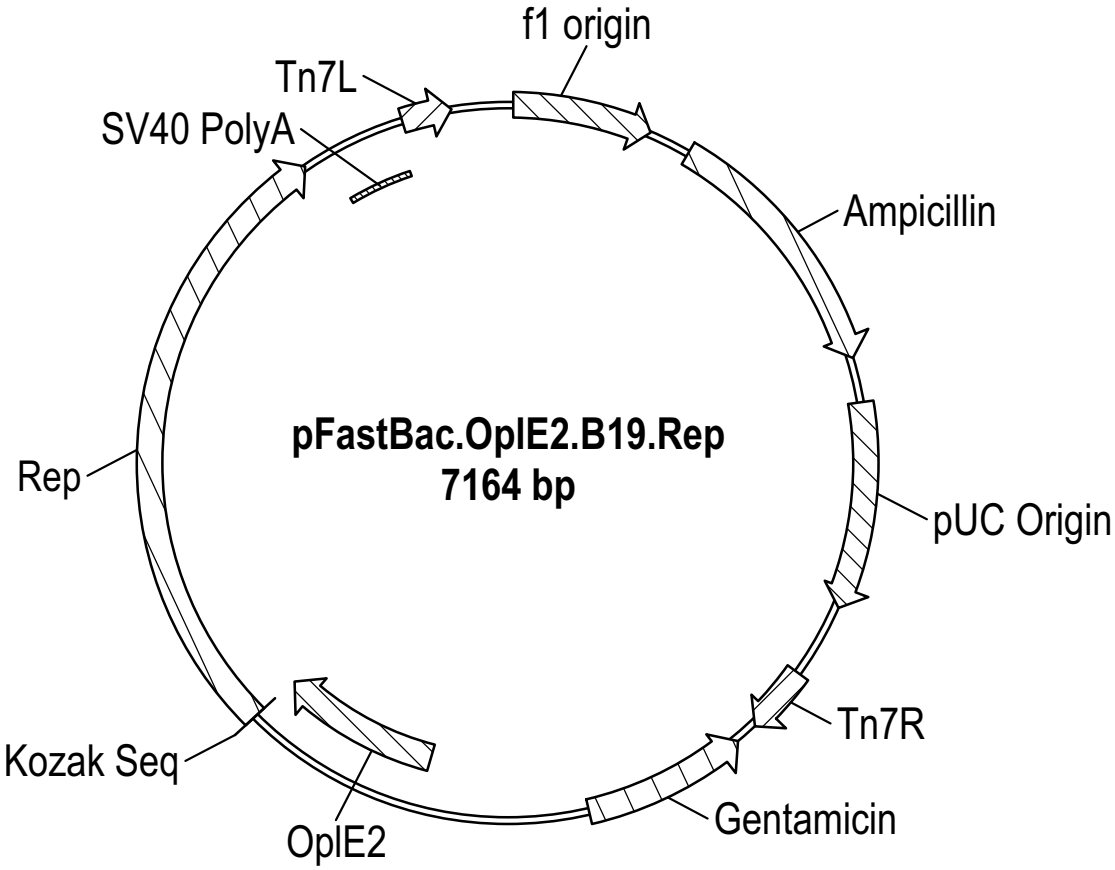


FIG. 11B

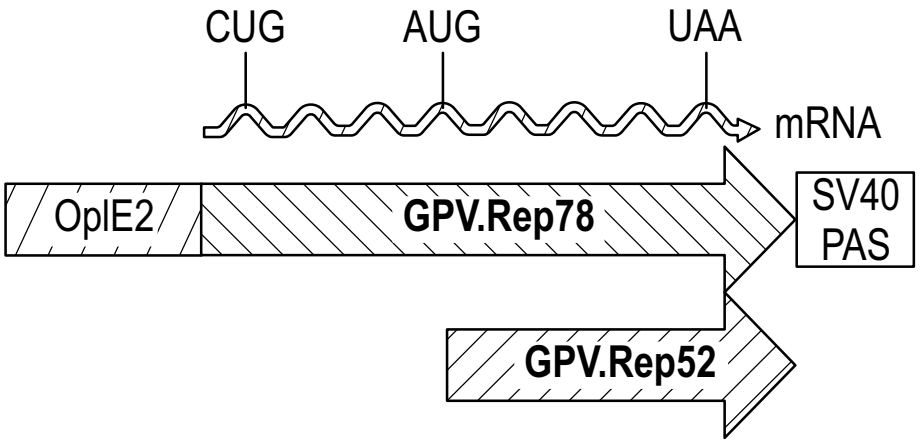


FIG. 11C

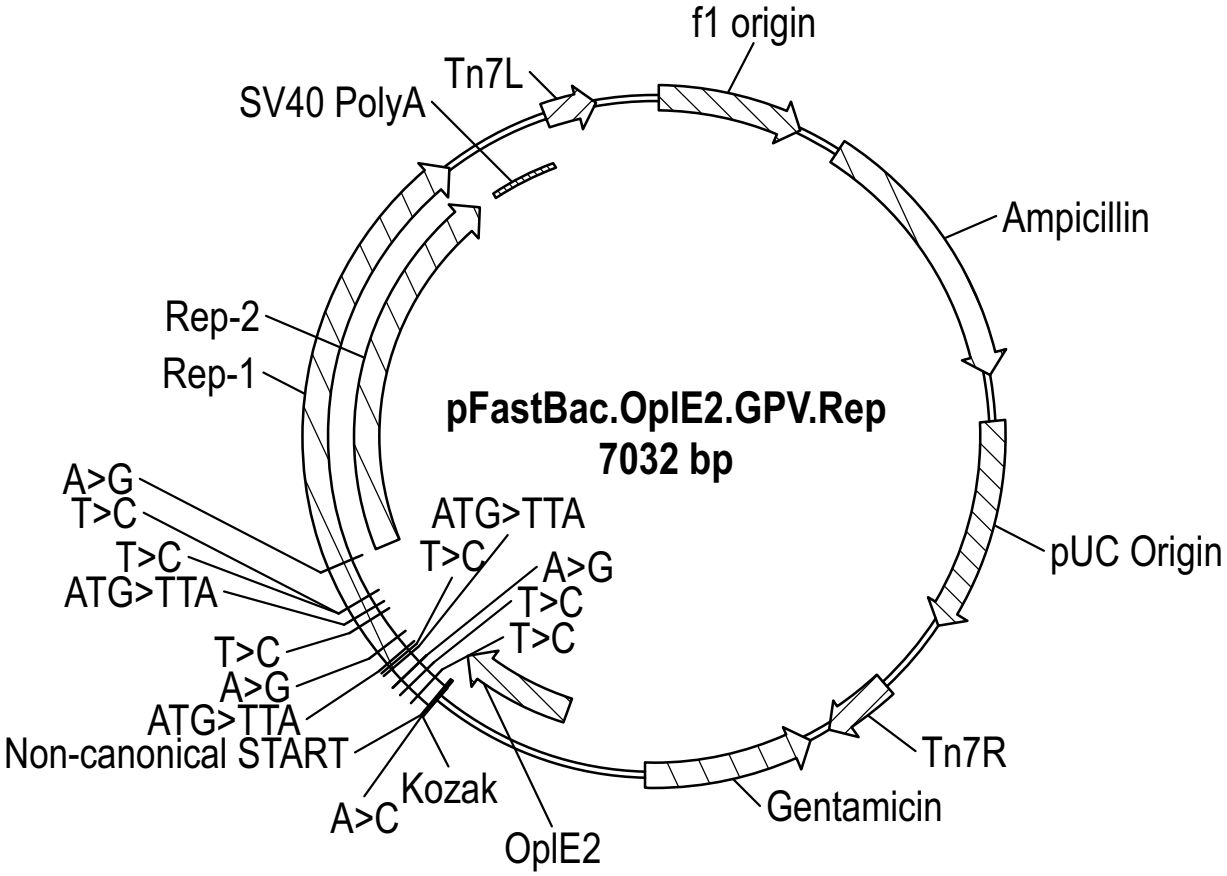


FIG. 11D

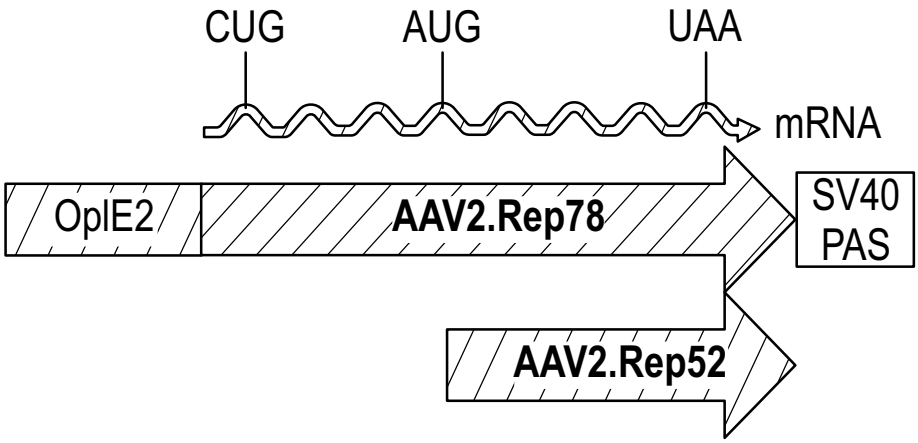


FIG. 11E

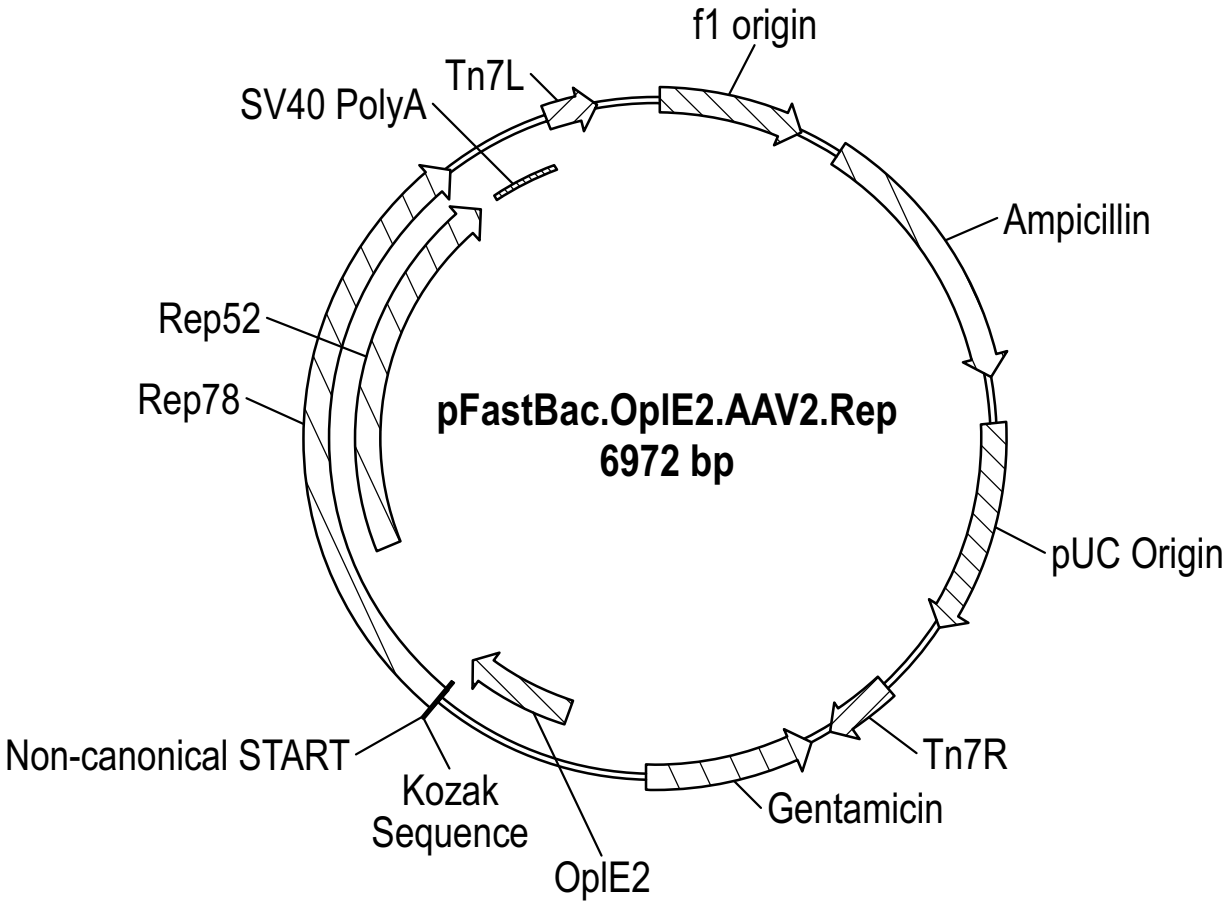


FIG. 11F

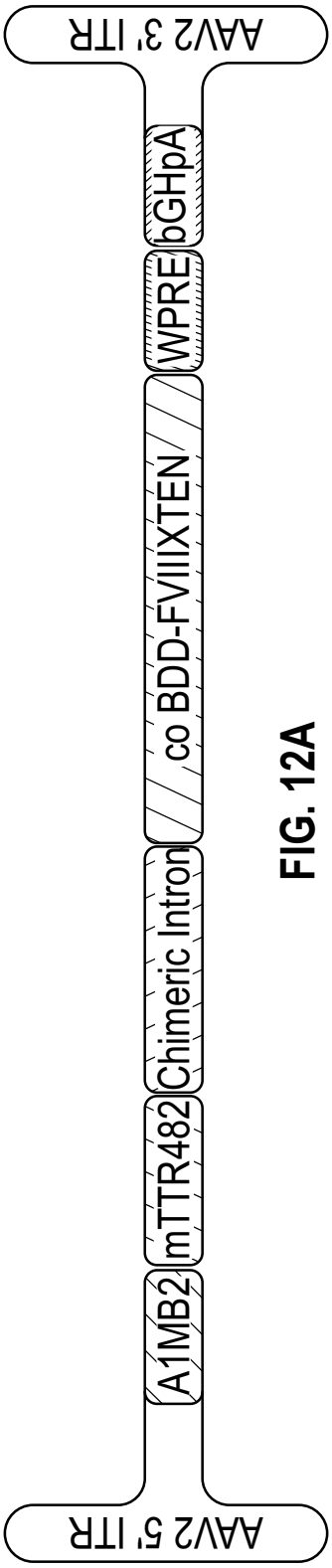


FIG. 12A

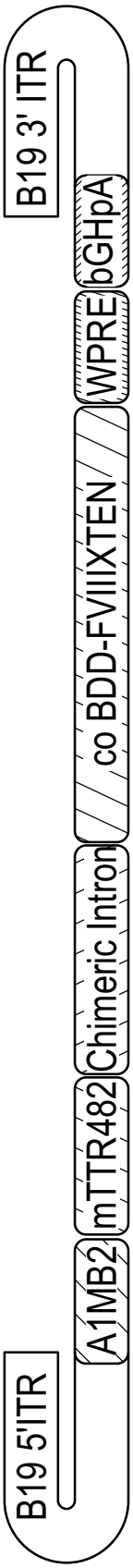


FIG. 12B

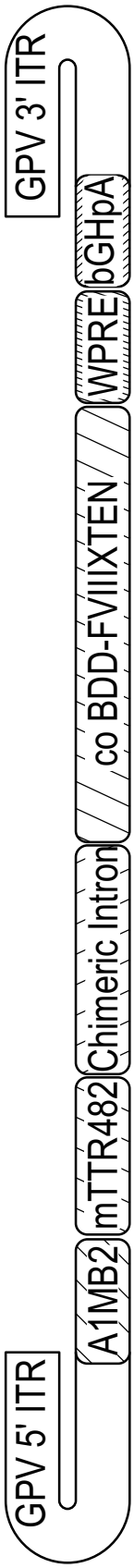


FIG. 12C

One BAC:

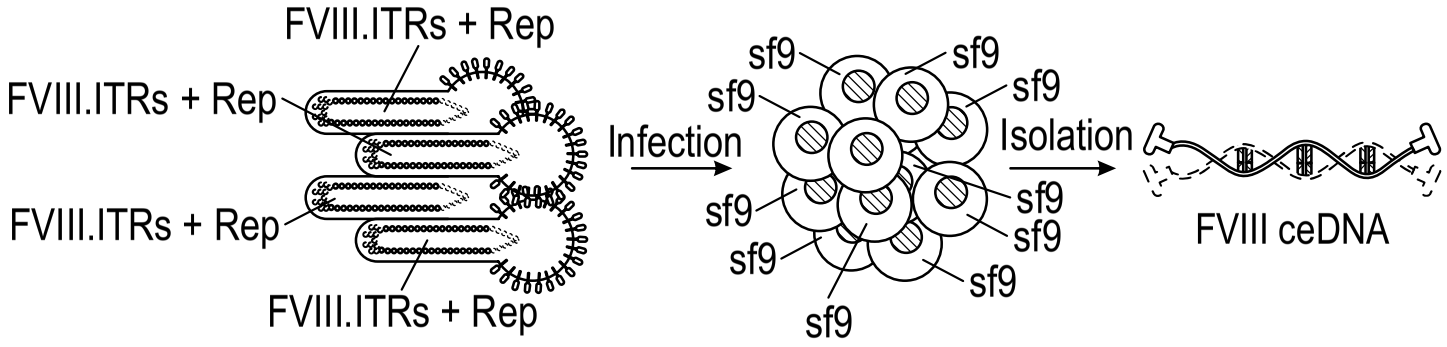


FIG. 13A

Two BAC:

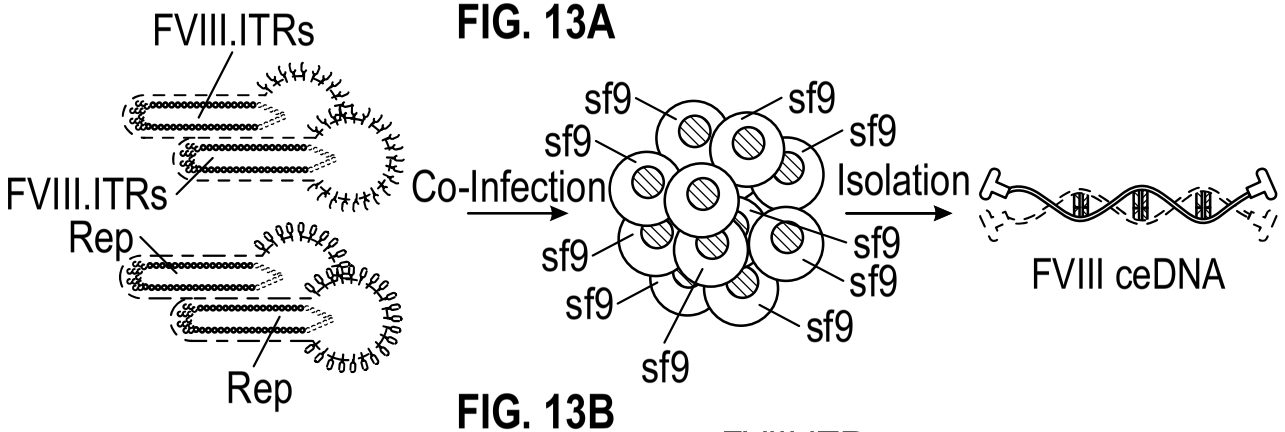


FIG. 13B

Stable Cell Line:

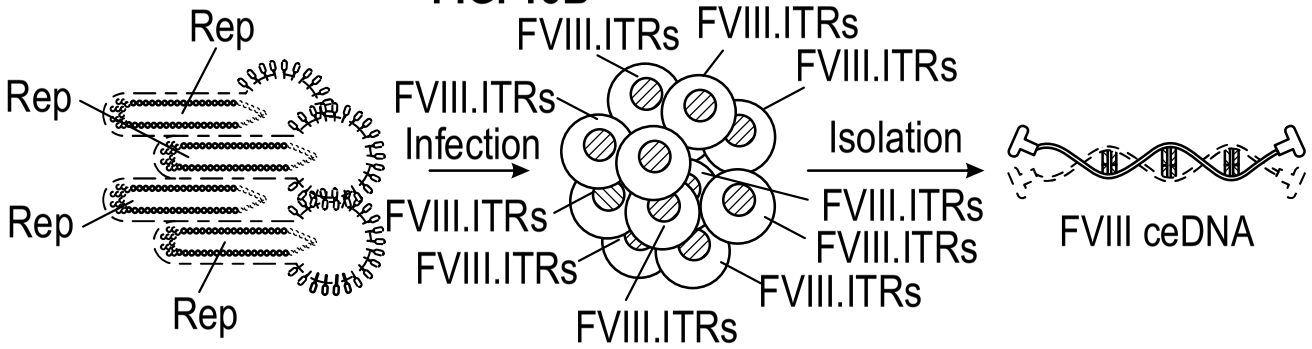


FIG. 13C

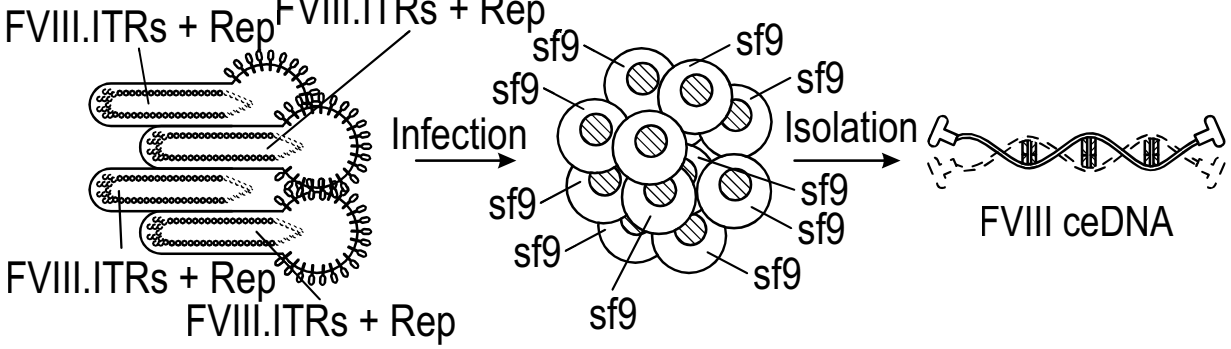


FIG. 14A

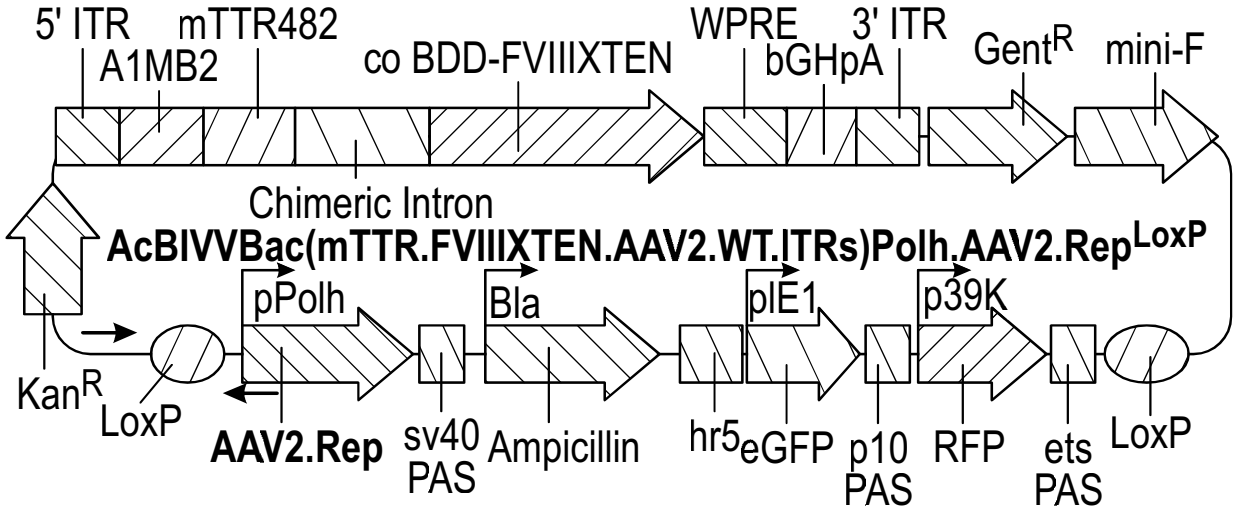


FIG. 14B

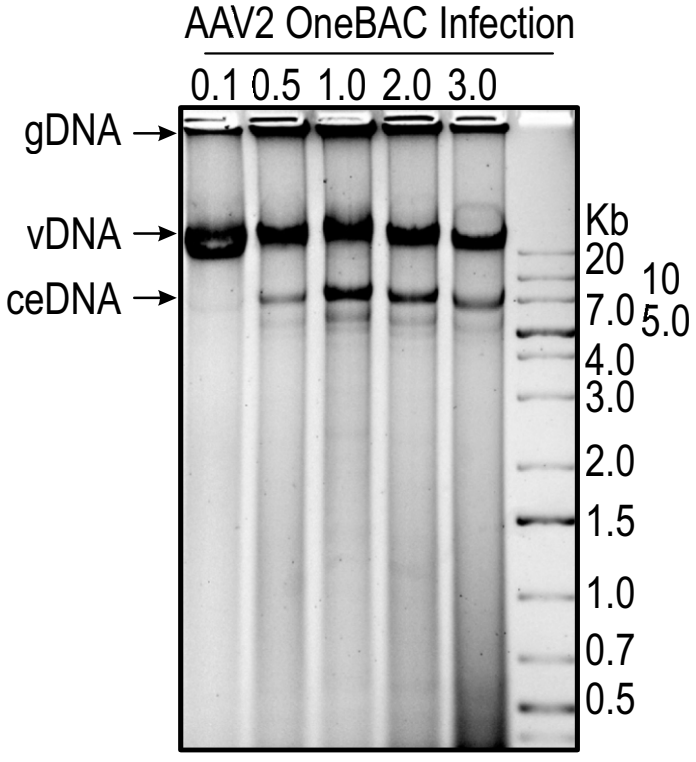


FIG. 14C

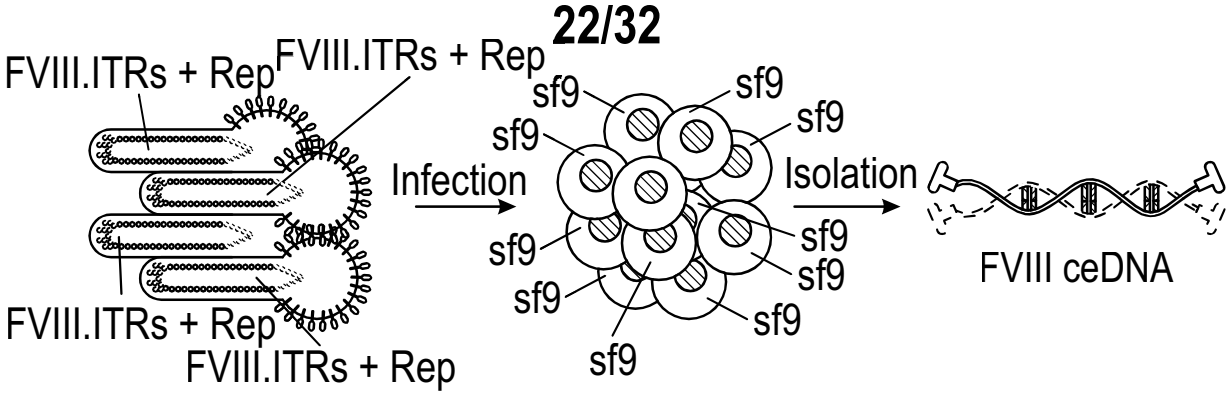


FIG. 15A

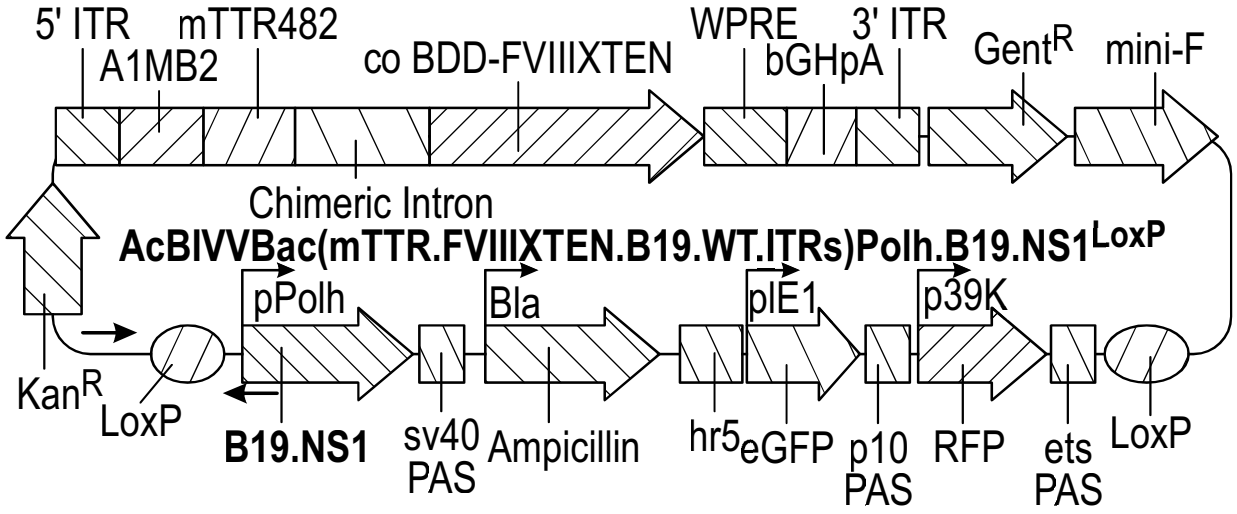


FIG. 15B

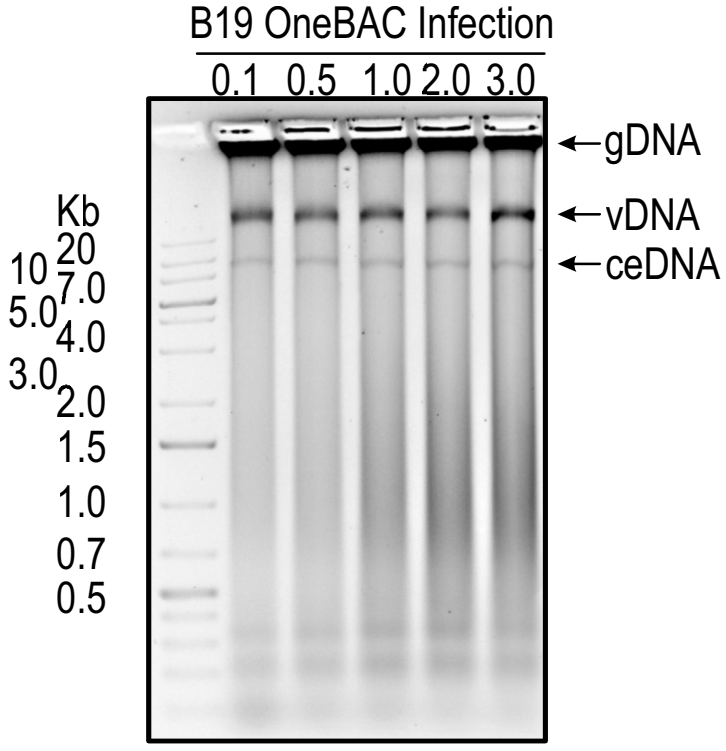


FIG. 15C

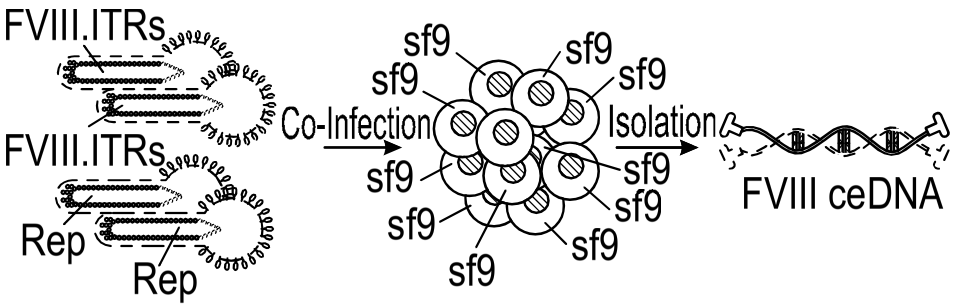


FIG. 16A

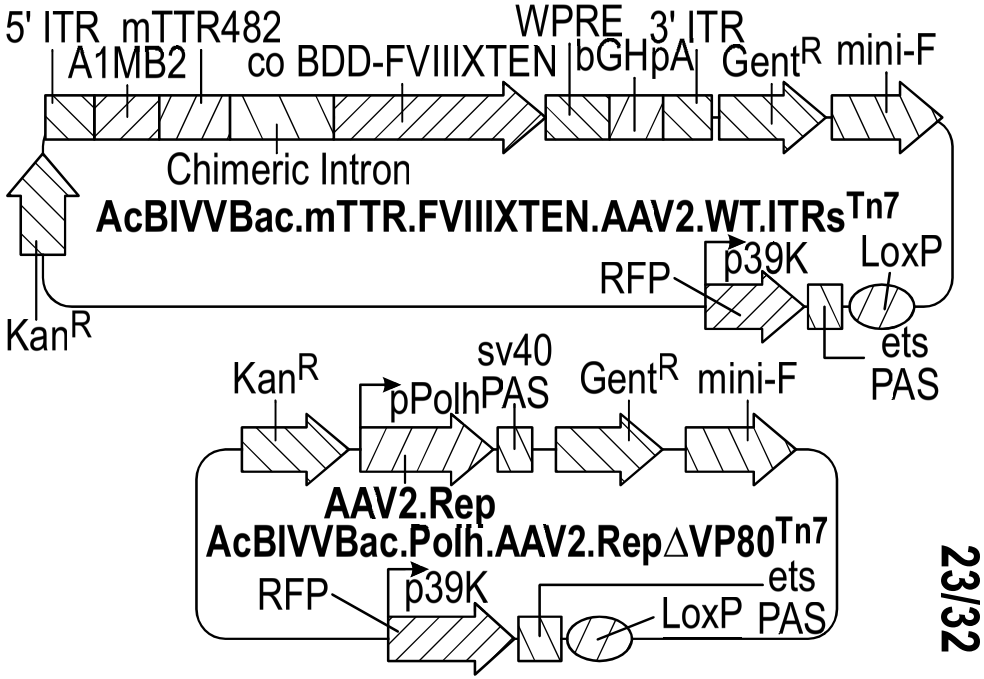


FIG. 16B

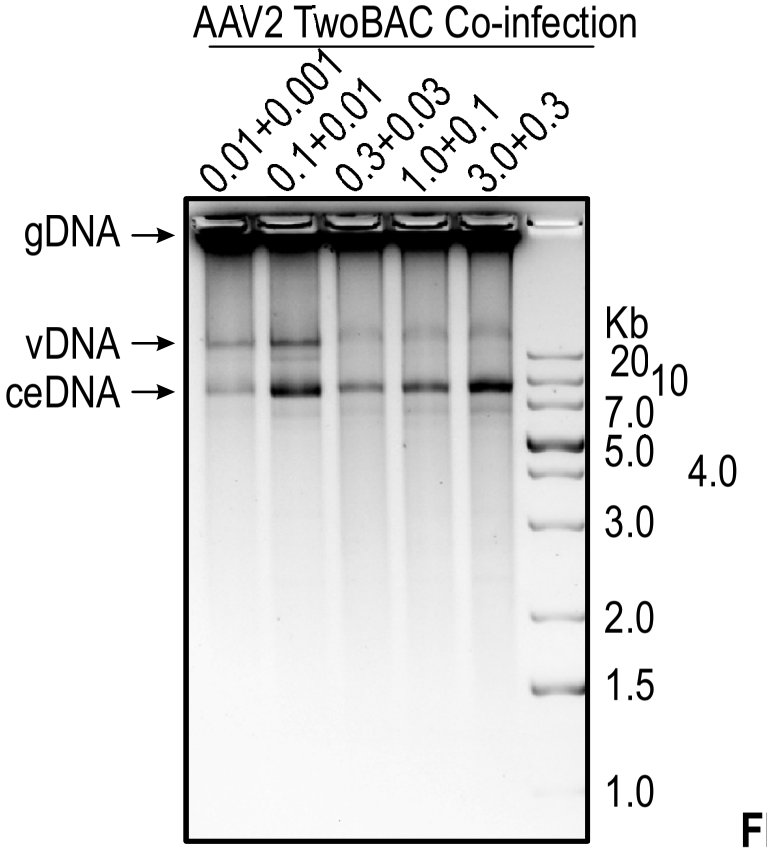


FIG. 16C

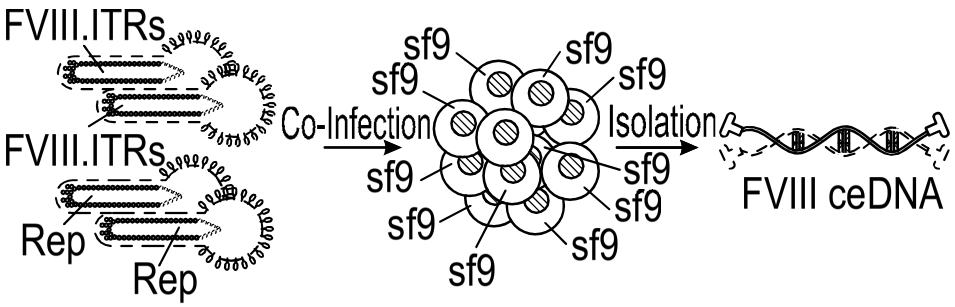


FIG. 17A

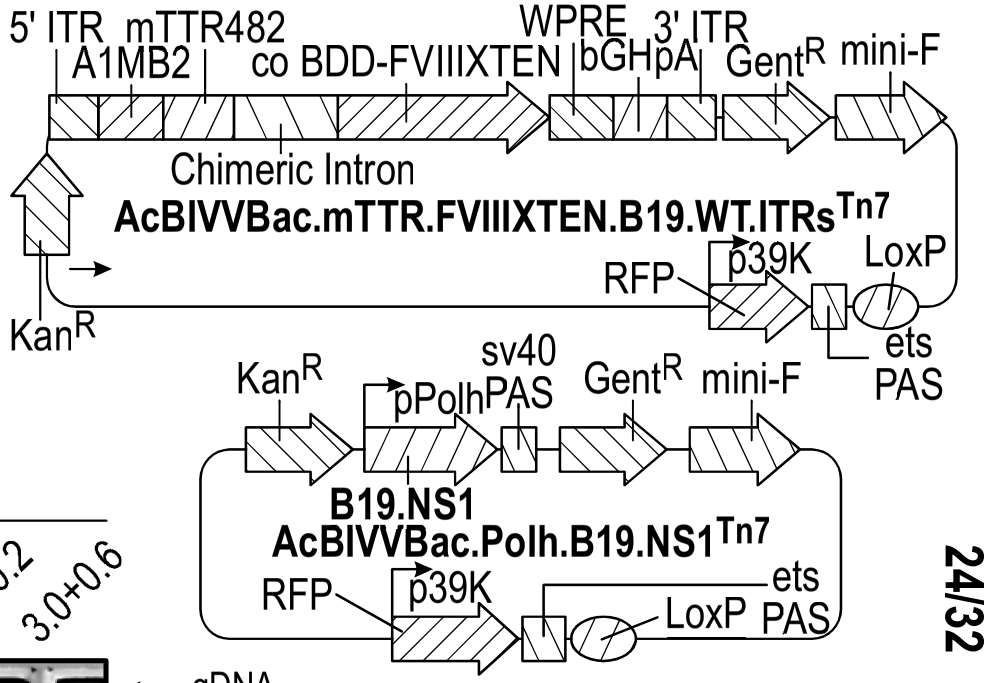


FIG. 17B

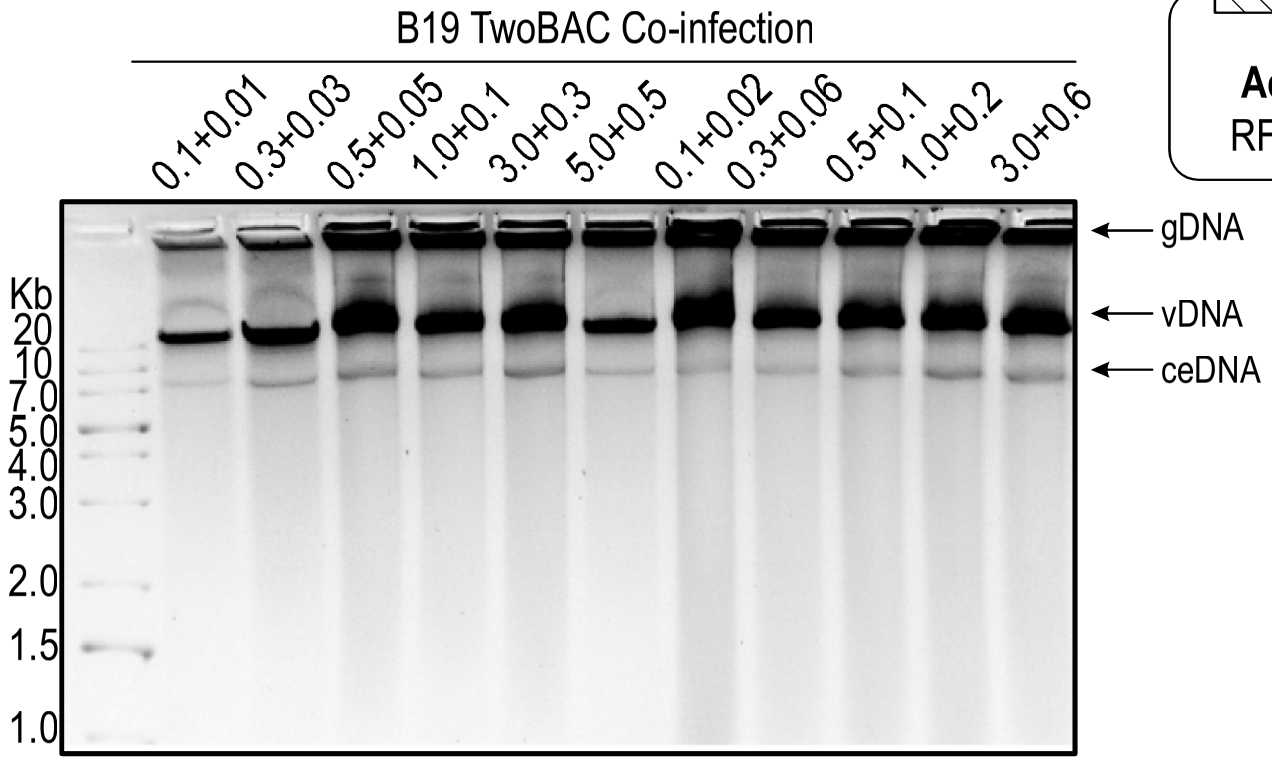


FIG. 17C

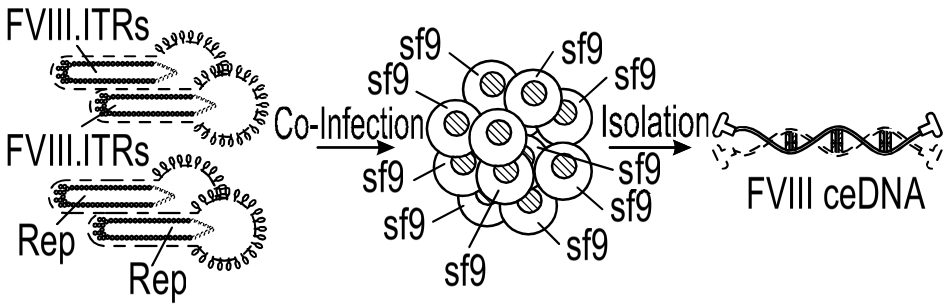


FIG. 18A

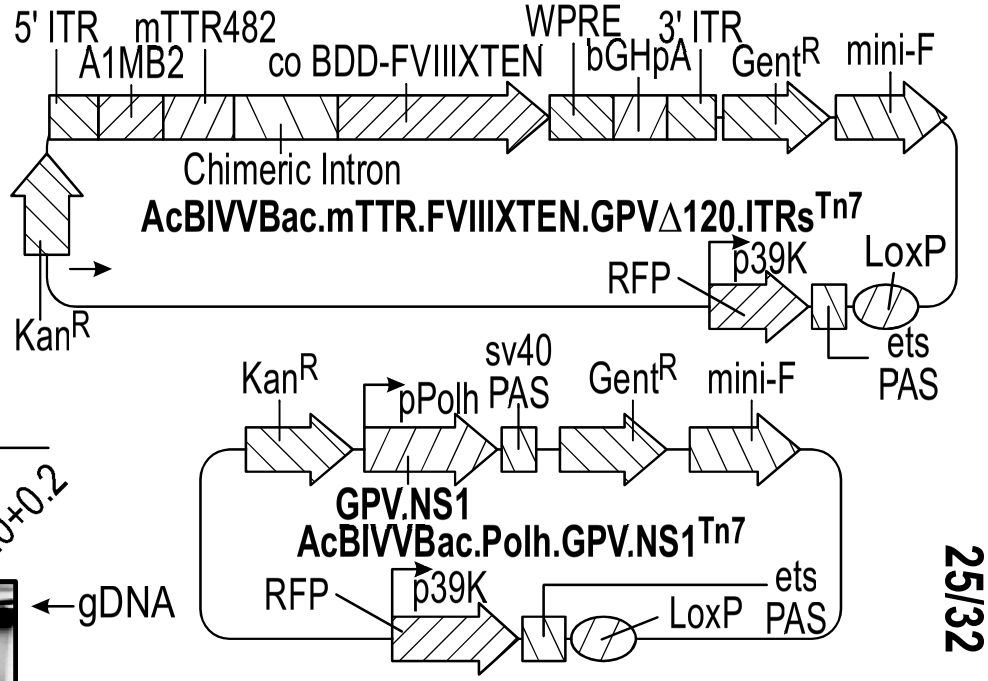


FIG. 18B

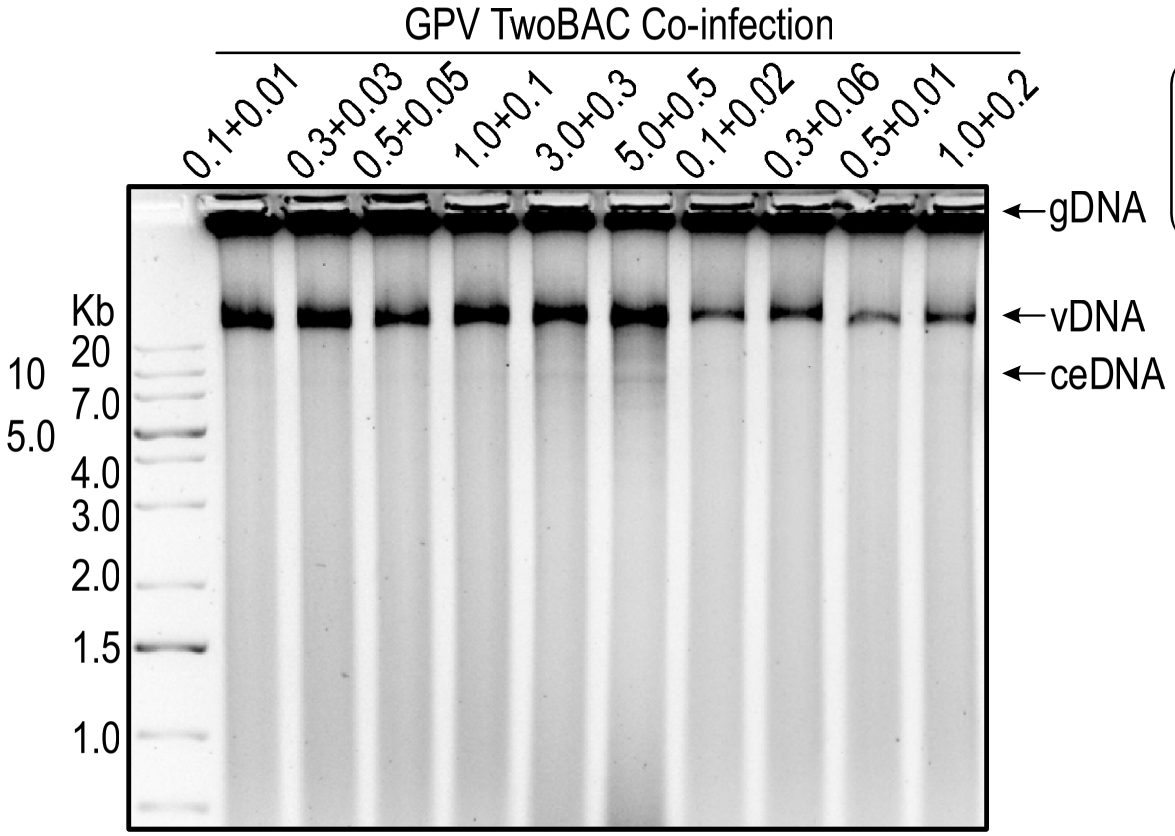


FIG. 18C

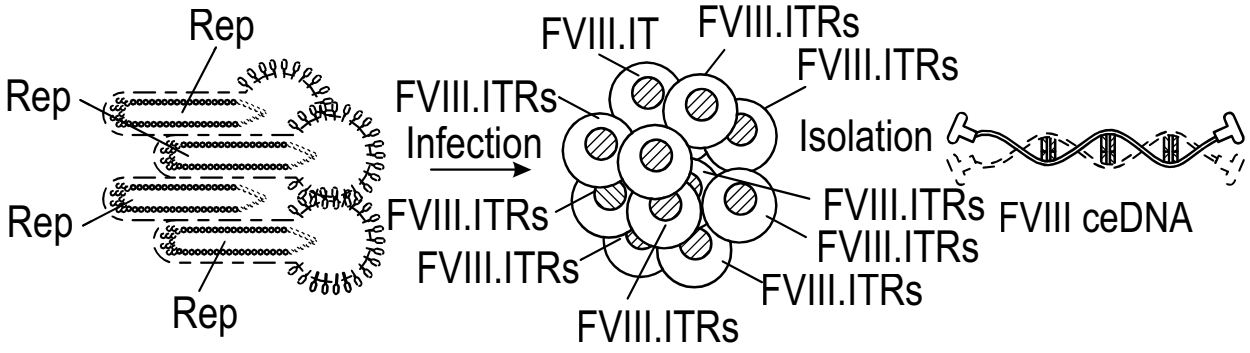


FIG. 19A

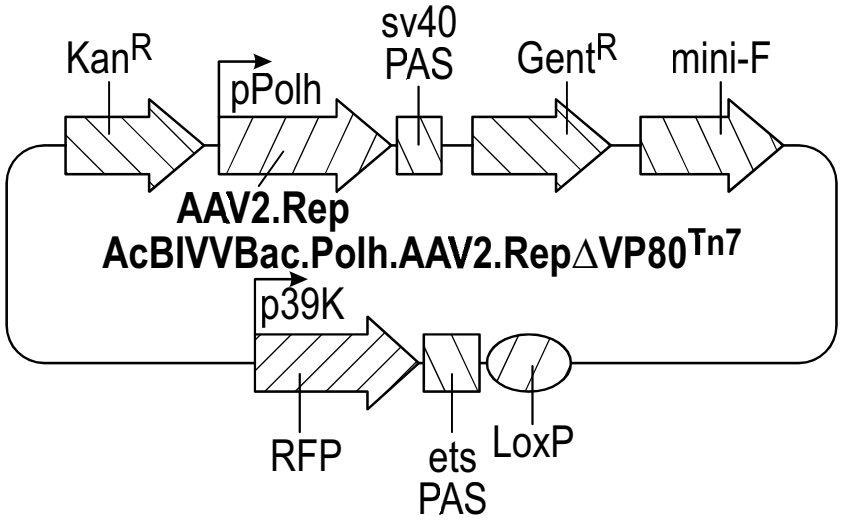


FIG. 19B

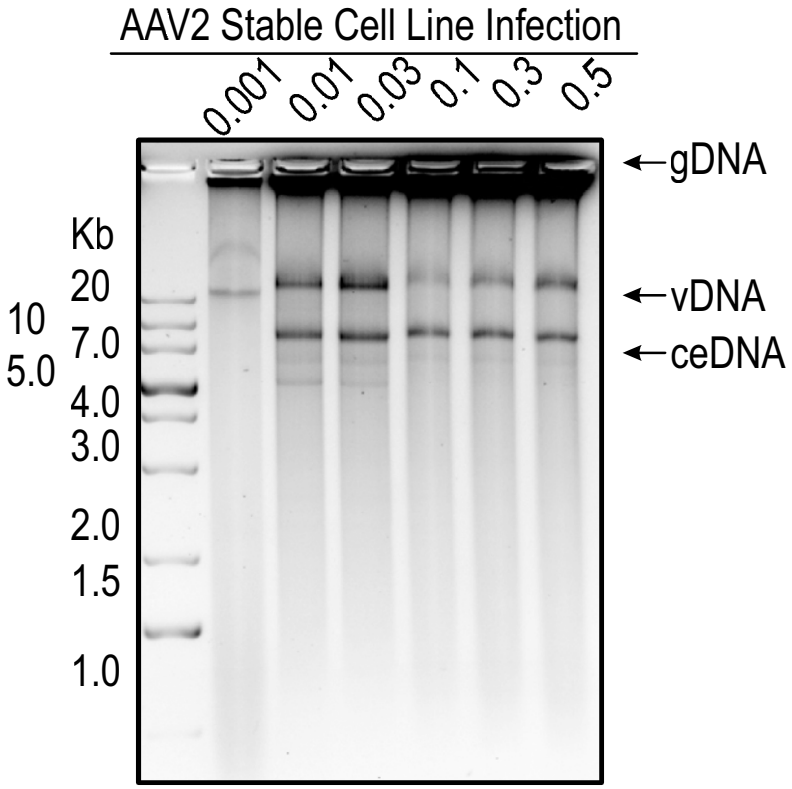


FIG. 19C

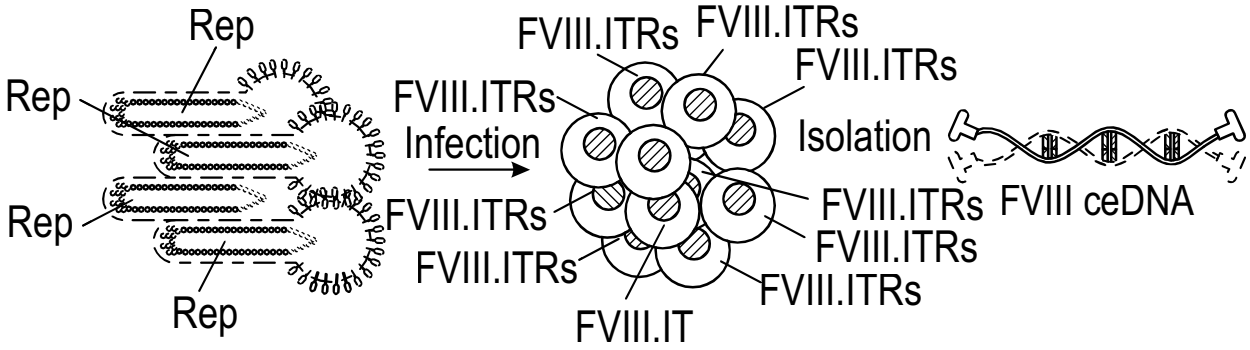


FIG. 20A

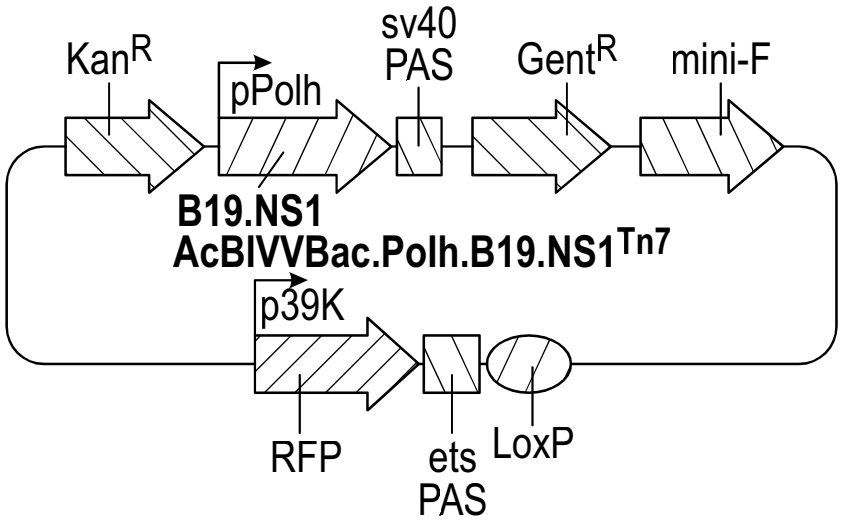


FIG. 20B

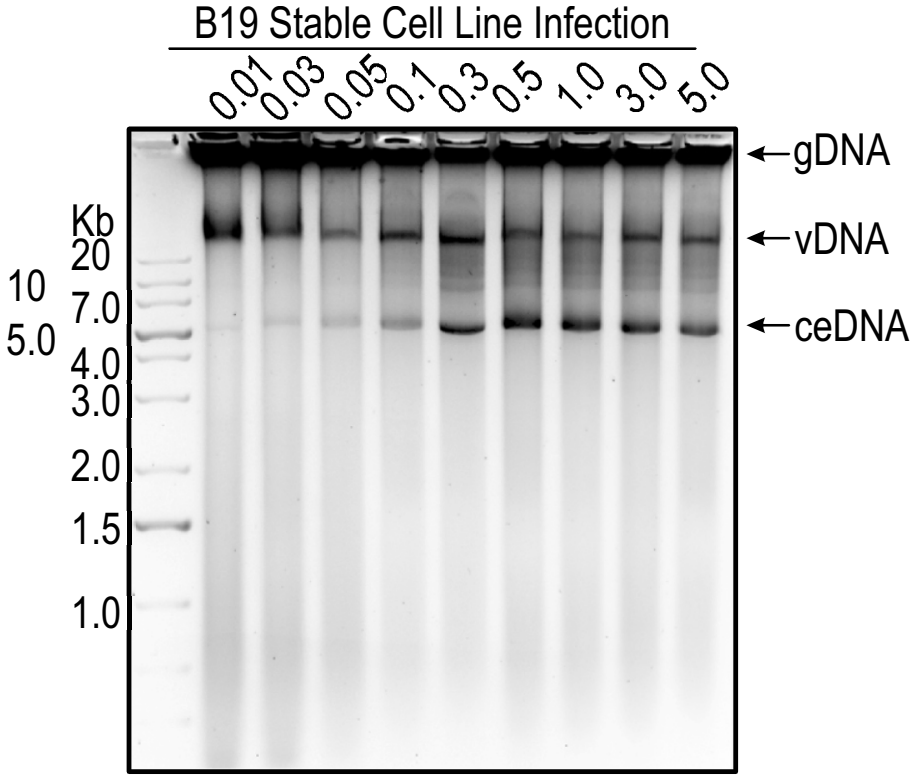


FIG. 20C

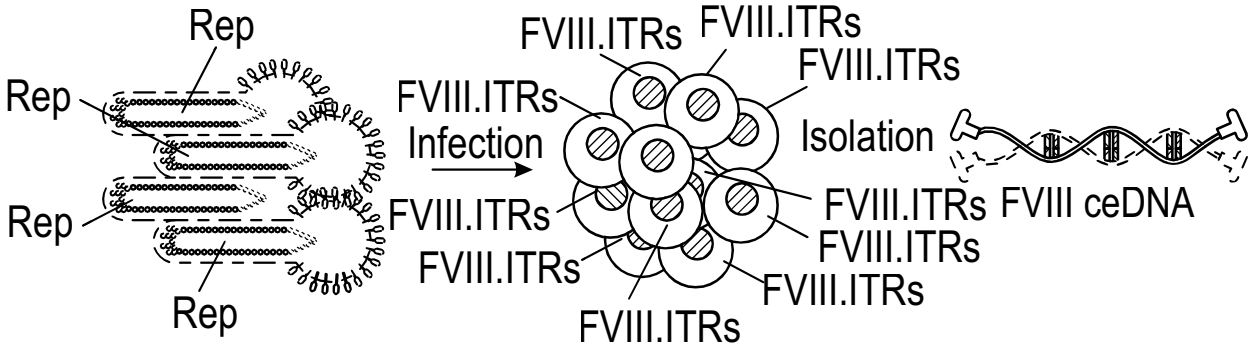


FIG. 21A

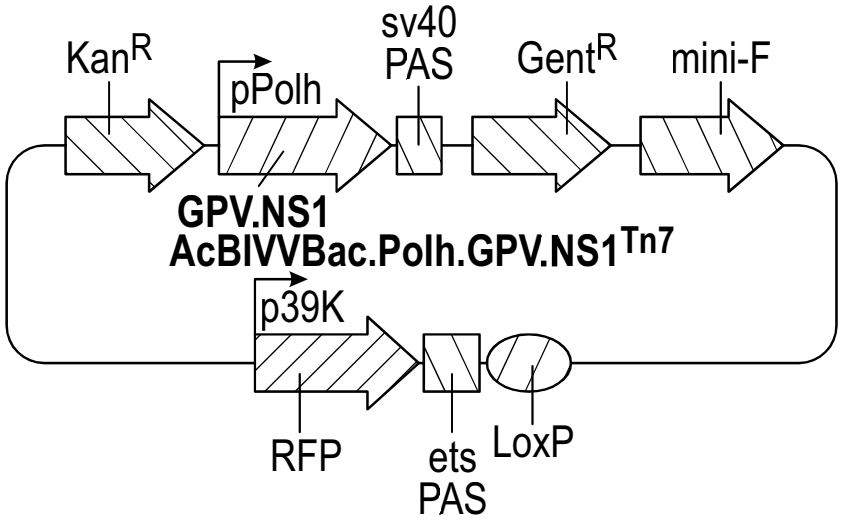


FIG. 21B

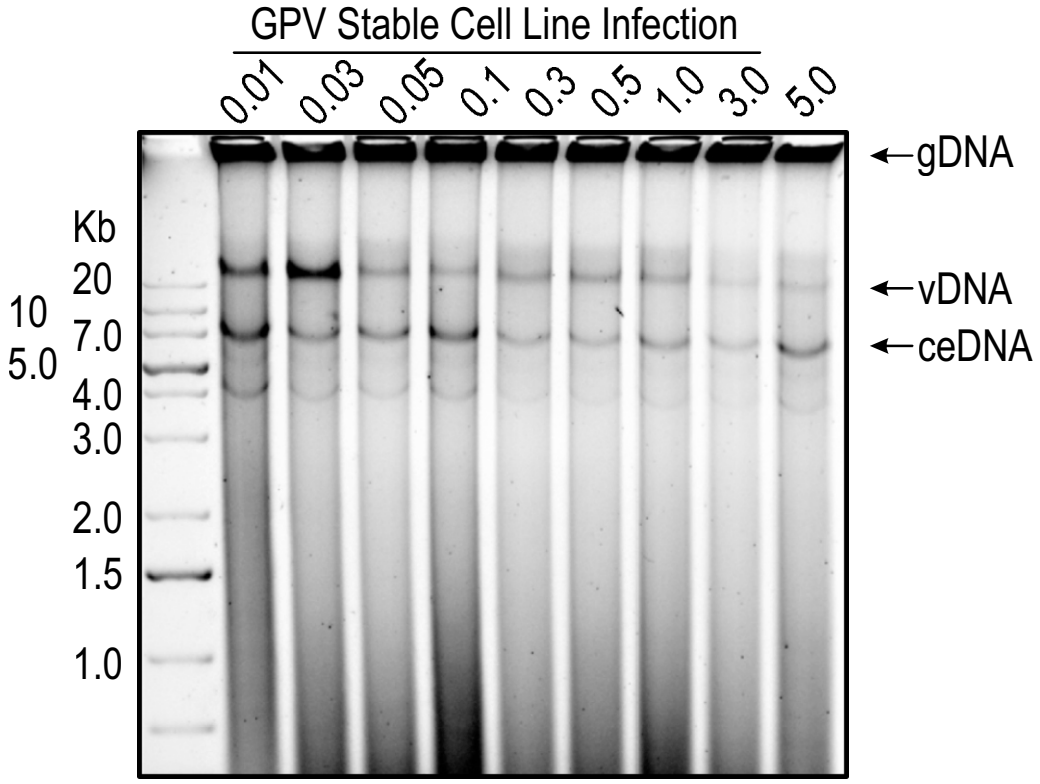


FIG. 21C

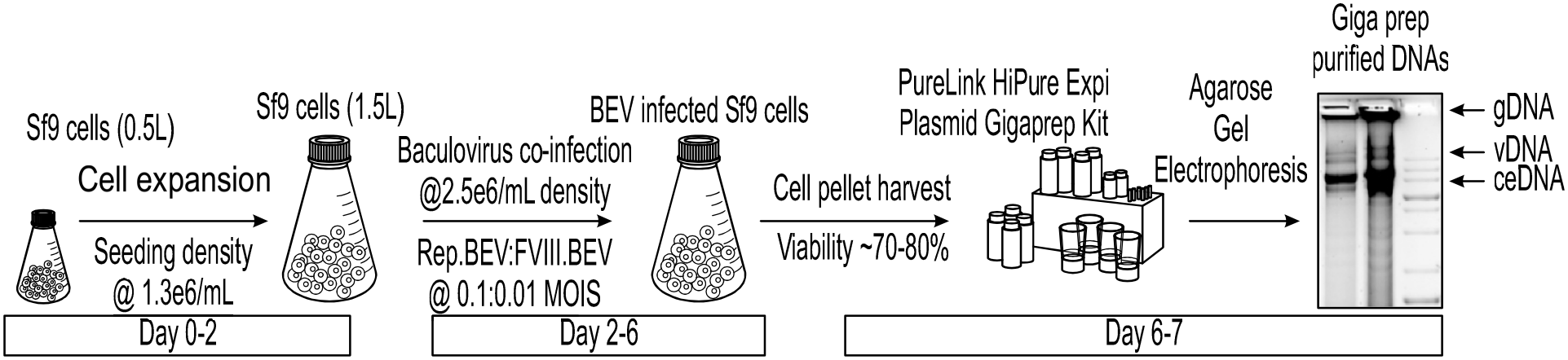


FIG. 22A

FIG. 22B

FIG. 22C

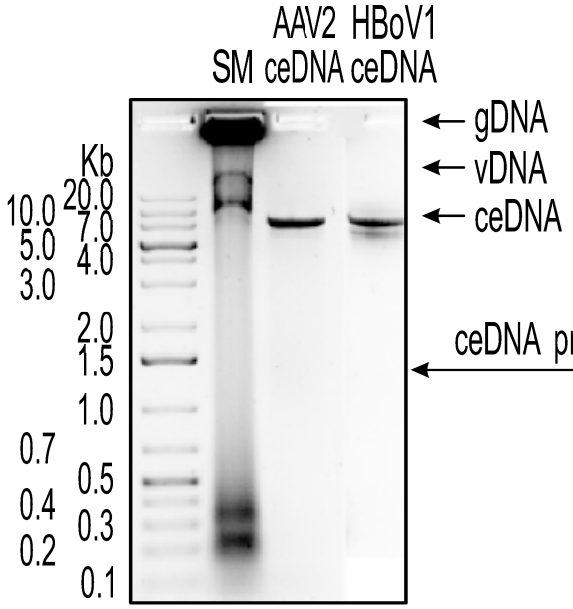


FIG. 22E

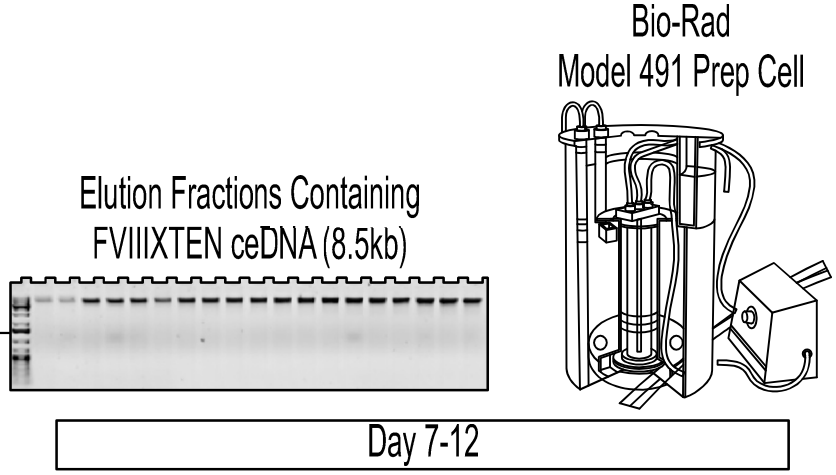


FIG. 22D

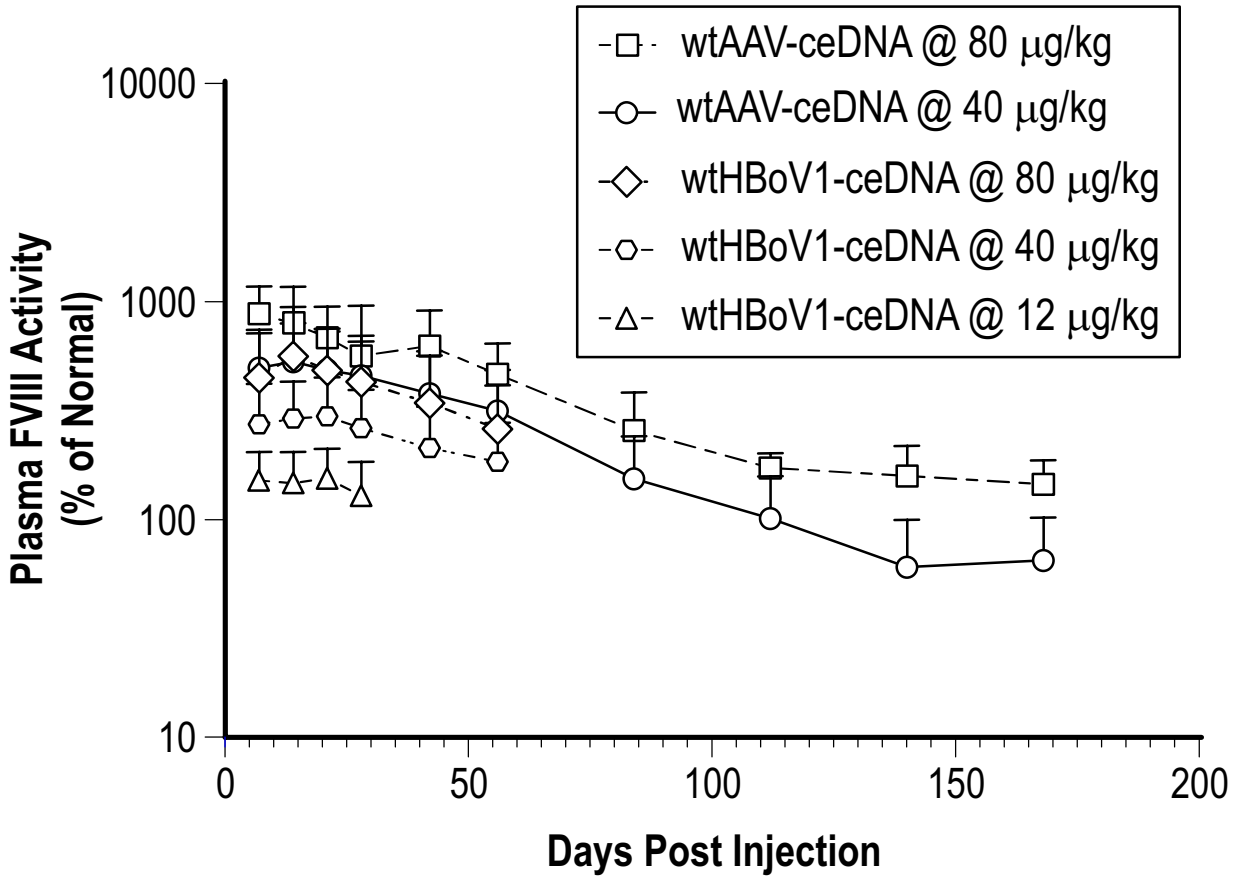

wtAAV-ceDNA @ 80 μg/kg
wtAAV-ceDNA @ 40 μg/kg
wtHBoV1-ceDNA @ 80 μg/kg
wtHBoV1-ceDNA @ 40 μg/kg
wtHBoV1-ceDNA @ 12 μg/kg
Plasma FVIII Activity (% of Normal)
10000
1000
100
10
0
50
100
150
200
Days Post Injection

FIG. 23

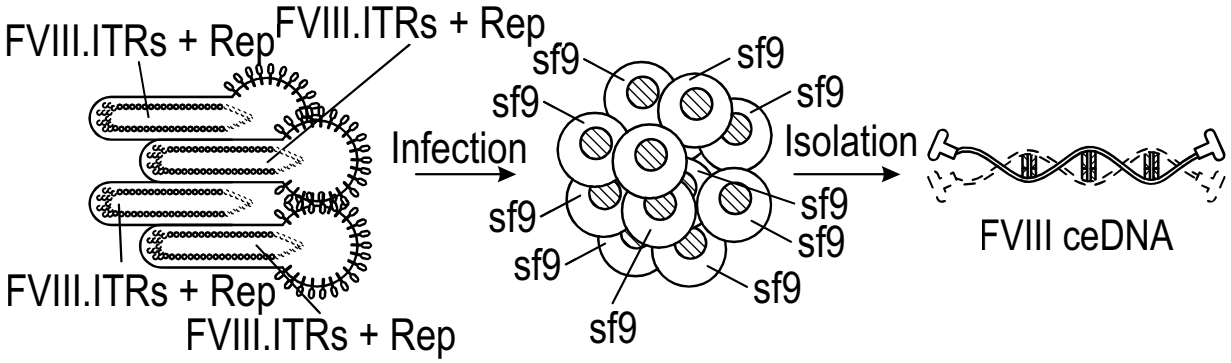


FIG. 24A

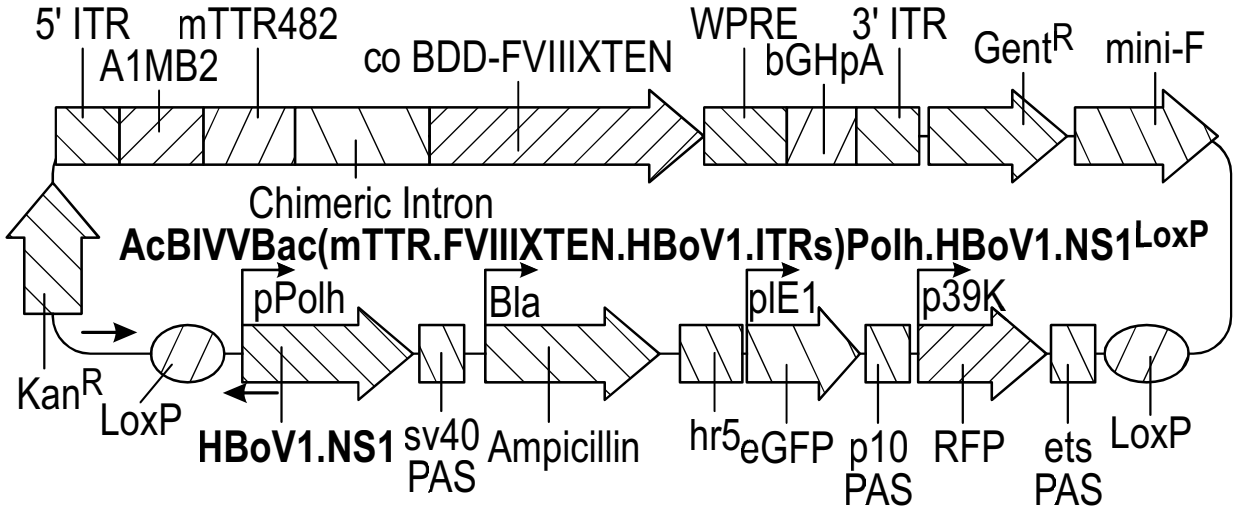


FIG. 24B

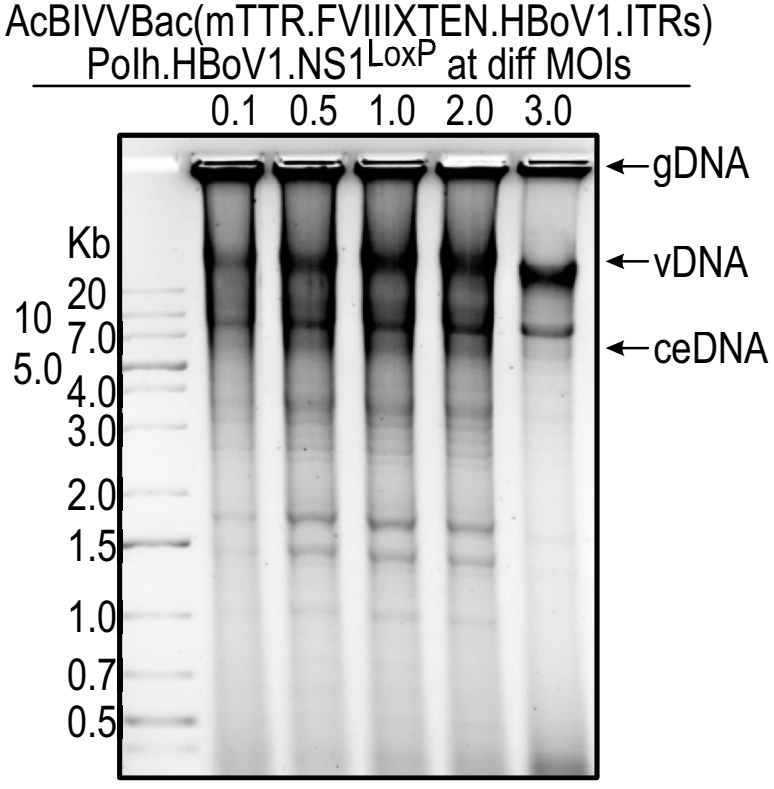


FIG. 24C

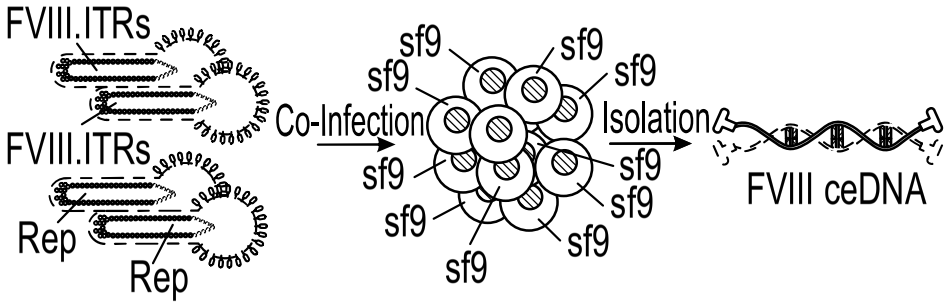


FIG. 25A

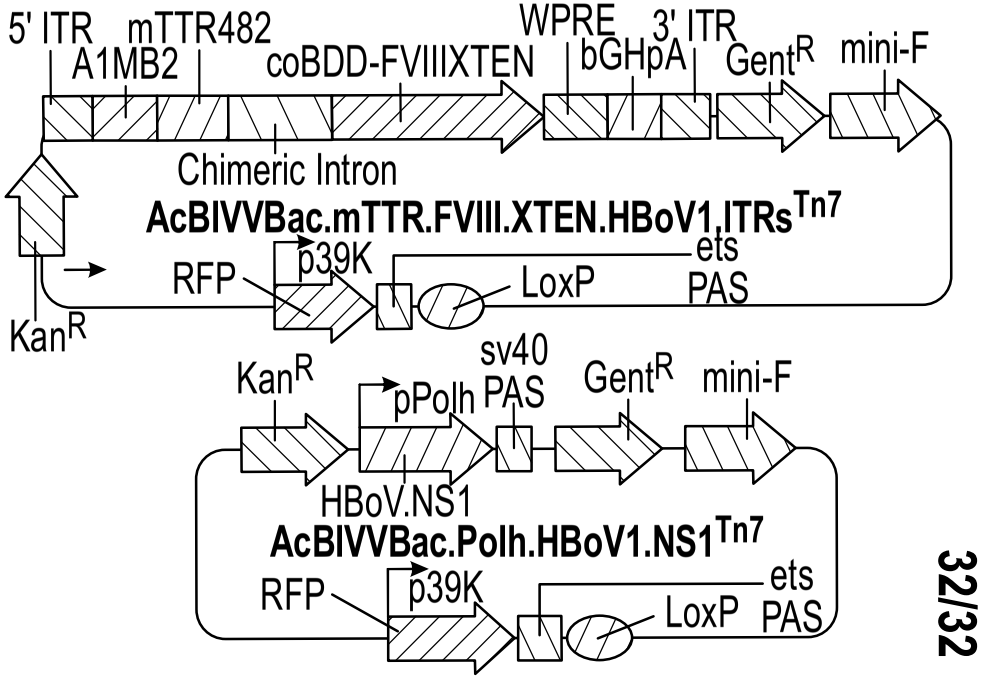


FIG. 25B

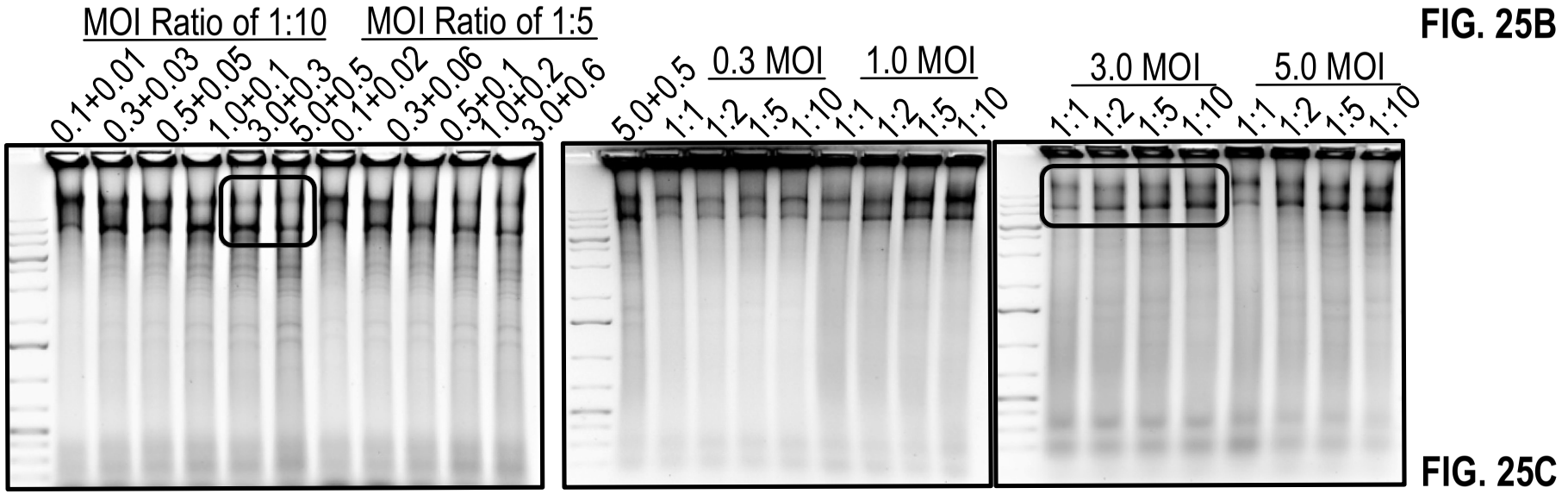


FIG. 25C