

Circulating VDPVs Detected

Country	Number of cases	Virus type	Duration
<hr/>			
Egypt	32	Type 2	1982~1993
Hispaniola	17	Type 1	2000~2001
Philippines	3	Type 1	2001

Long-term Carriers

Developed Countries

OPV → IPV → no polio virus
no immunization

Many Developing Countries

OPV  no immunization

Low cost anti-PV drugs

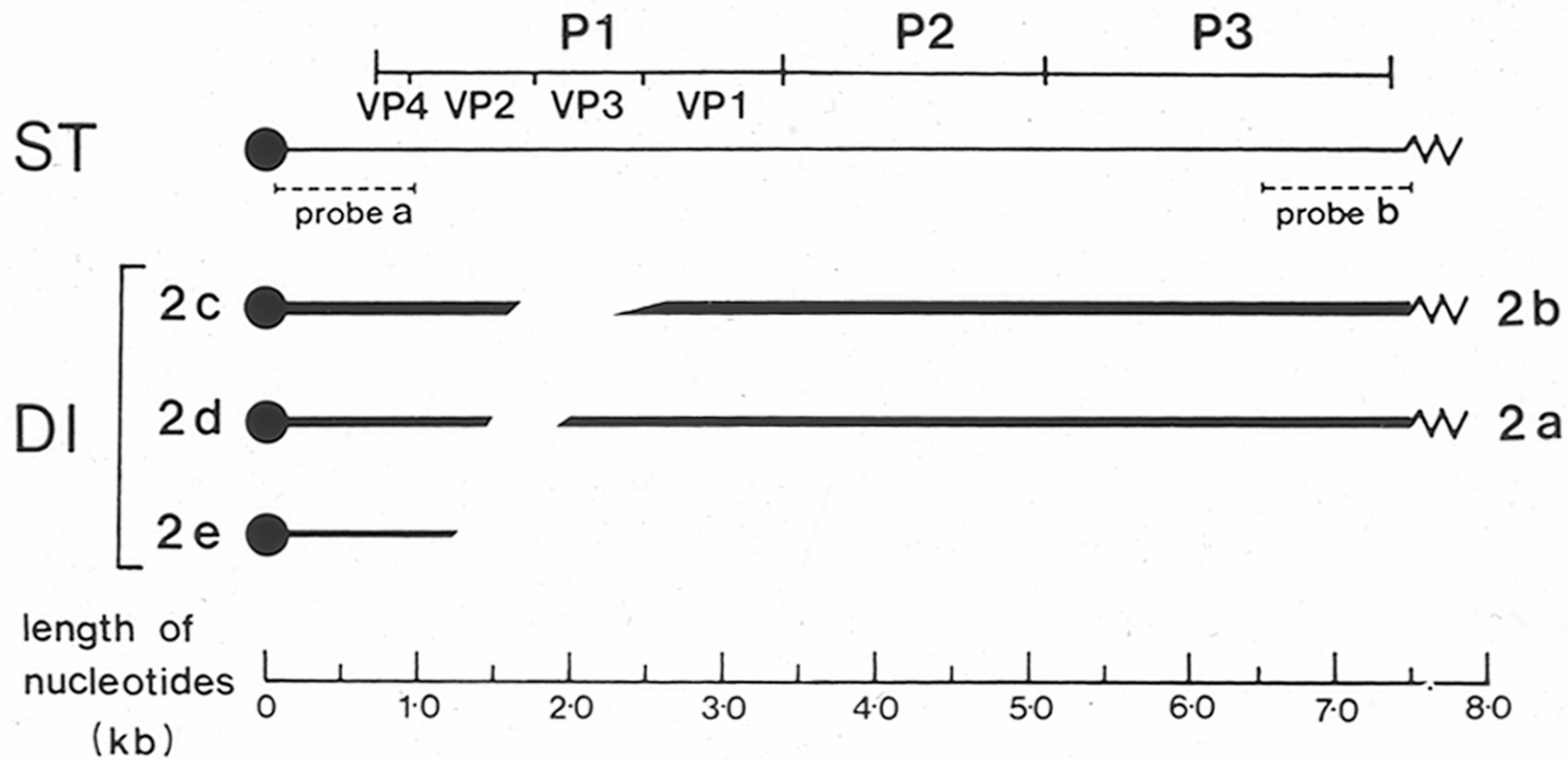
New OPV with high genetic stability

RATE OF MUTATION

Replication of ssRNA genomes ---- $10^{-3} \sim 10^{-4}$

Replication of dsDNA genomes---- $10^{-8} \sim 10^{-11}$

Holland et al. (1982) Science 215:1577



1,2

1225 2111
 --- CCU GAU GCA CTG CGG GAC AUG GGA CUC UUU UUC ACG UUU CUG UUC UGU GGA UCC AUG AUG ---
 Pro Asp Ala Leu Arg Asp Met Gly Leu Phe Phe Thr Phe Leu Phe Cys Gly Ser Met Met

GGC CAA AAU AUG ---885 b--- GGA UCC CUG AAG
 Gly Gln Asn Met Gly Ser Leu Lys

30-1

1737 2425
 --A GCC CCU AUG UGC UGU GAG UUC AAU GGA UUC C AGC GUG CGC UUG AUG CGA GAU ACC ACA CA--
 Ala Pro Met Cys Cys Glu Phe Asn Gly Phe Ser Var Arg Leu Met Arg Asp Thr Thr

A AGA AAC AAU ACC ---687 b--- GCG UGU AAU GAC UUU
 Leu Arg Asn Ile Thr Ala Cys Asn Asp Phe

30-2

2654 2706
 -CU GGG GCC ACA AAU CCA CUA GUC CCU UCU G GC AUA GAG UCU UUC UUC GCG CGG GGU GCA U--
 Gly Ala Thr Asn Pro Leu Val Pro Ser Gly Ile Glu Ser Phe Phe Ala Arg Gly Ala

AU ACA GUG CAA ACC ---51 b--- AGG UCA GAG UCU A
 Asp Thr Val Gln Thr Arg Ser Glu Ser Ser

39

1315 2528
 --- AAC GCC UCC AAA UUC CAC CAG GGG GCA CUA ACG GUG GGG GCG GCA ACG UCU AGA GAC GCU ---
 Asn Ala Ser Lys Phe His Gln Gly Ala Leu Thr Val Gly Ala Ala Thr Ser Arg Asp Ala

GGG GUA UUC GCC ---1212b--- ACA GUC CGU GAA
 Gly Val Phe Ala Thr Val Arg Glu

209

1686 2002
 --A UUA AAU UUU GCU AGU GAG UCC UCC CCA GA C GAU CCC AUA CUC UGC CUG UCA CUC UCU CC--
 Leu Asn Phe Ala Ser Glu Ser Ser Pro Asp Asp Pro Ile Leu Cys Leu Ser Leu Ser

G AUU CCA AUC ACC ---315 b--- AAA CCA CAU ACA GA
 Glu Ile Pro Ile Thr Lys Pro His Thr Asp

25

1475 2385
 -AC CAG ACA UCA CCU GCC CGU AGG UUC UGC C AG AUG GAC AUC CUU GGU UUU GUG UCA GCG U--
 Gln Thr Ser Pro Ala Arg Arg Phe Cys Gln Met Asp Ile Leu Gly Phe Val Ser Ala

CG CUG GAU UAC CUC ---909 b--- UCG ACA CCC AGA G
 Pro Val Asp Tyr Leu Ser Thr Pro Arg Glu

16

1581 2563
 --G ACC AAC AAC UGU GCU ACA CUG GUA CUC CC A AAC ACU GAA GCC AGU GGA CCA GCA CAC UC--
 Thr Asn Asn Cys Ala Thr Leu Val Leu Pro Asn Thr Glu Ala Ser Gly Pro Ala His

U UAC GUG AAC UCC ---981 b--- AGA GAC GCU CUC CC
 Pro Tyr Val Asn Ser Arg Asp Ala Leu Pro

11

1633 2396
 --- GAU AGU AUG GUA AAG CAC AAU AAU UGG GGA CUU GGU UUU GUG UCA GCG UGU AAU GAC UUC ---
 Asp Ser Met Val Lys His Asn Asn Trp Gly Leu Gly Phe Val Ser Ala Cys Asn Asp Phe

AUU GCA AUA UUA ---762 b--- GAG AUG GAC AUC
 Ile Ala Ile Leu Glu Met Asp Ile

17

1639 2519
 --- AUG GUA AAG CAC AAU AAU UGC GGA AUU GCA GUC CGU GAA ACG GUG GGG GCG GCA ACG UCU ---
 Met Val Lys His Asn Asn Trp Gly Ile Ala Val Arg Glu Thr Val Gly Ala Ala Thr Ser

AUA UUA CCA UUG ---879 b--- AUU GAC AAC ACA
 Ile Leu Pro Leu Ile Asp Asn Thr

13,213

1662 2479
 --A AUU GCA AUA UUA CCA UUG GCC CCA UUA AA G GGG UUA GGU CAG AUG CUU GAA AGC AUG AU--
 Ile Ala Ile Leu Pro Leu Ala Pro Leu Lys Gly Leu Gly Gln Met Leu Glu Ser Met

U UUU GCU AGU GAG ---816 b--- AAA GCG CUA GCA CA
 Asn Phe Ala Ser Glu Lys Ala Leu Ala Gln

14,15

1664 2445
 -UU GCA AUA UUA CCA UUG GCC CCA UUA AAU U AU ACC ACA CAU AUA GAG CAA AAA GCG CUA G--
 Ala Ile Leu Pro Leu Ala Pro Leu Asn Tyr Thr Thr His Ile Glu Gln Lys Ala Leu

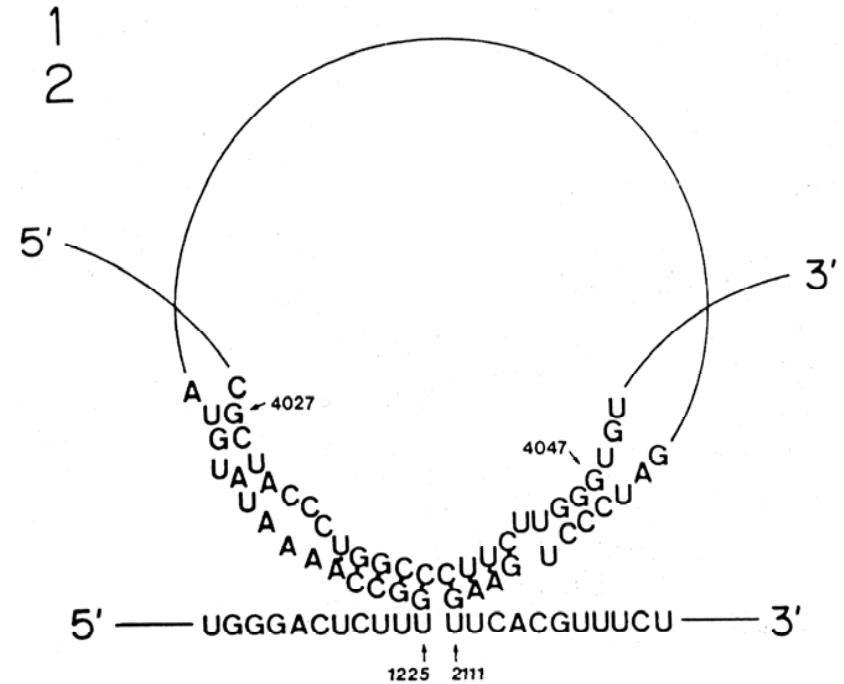
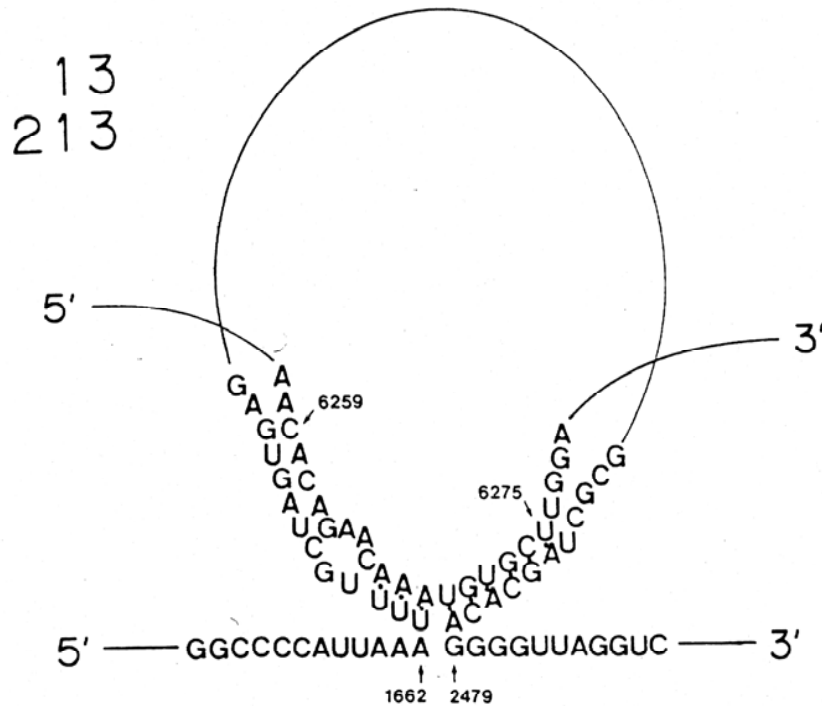
UU GCU AGU GAG UCC ---780 b--- GCG UUG AUG CGA G
 Phe Ala Ser Glu Ser Arg Leu Met Arg Asp

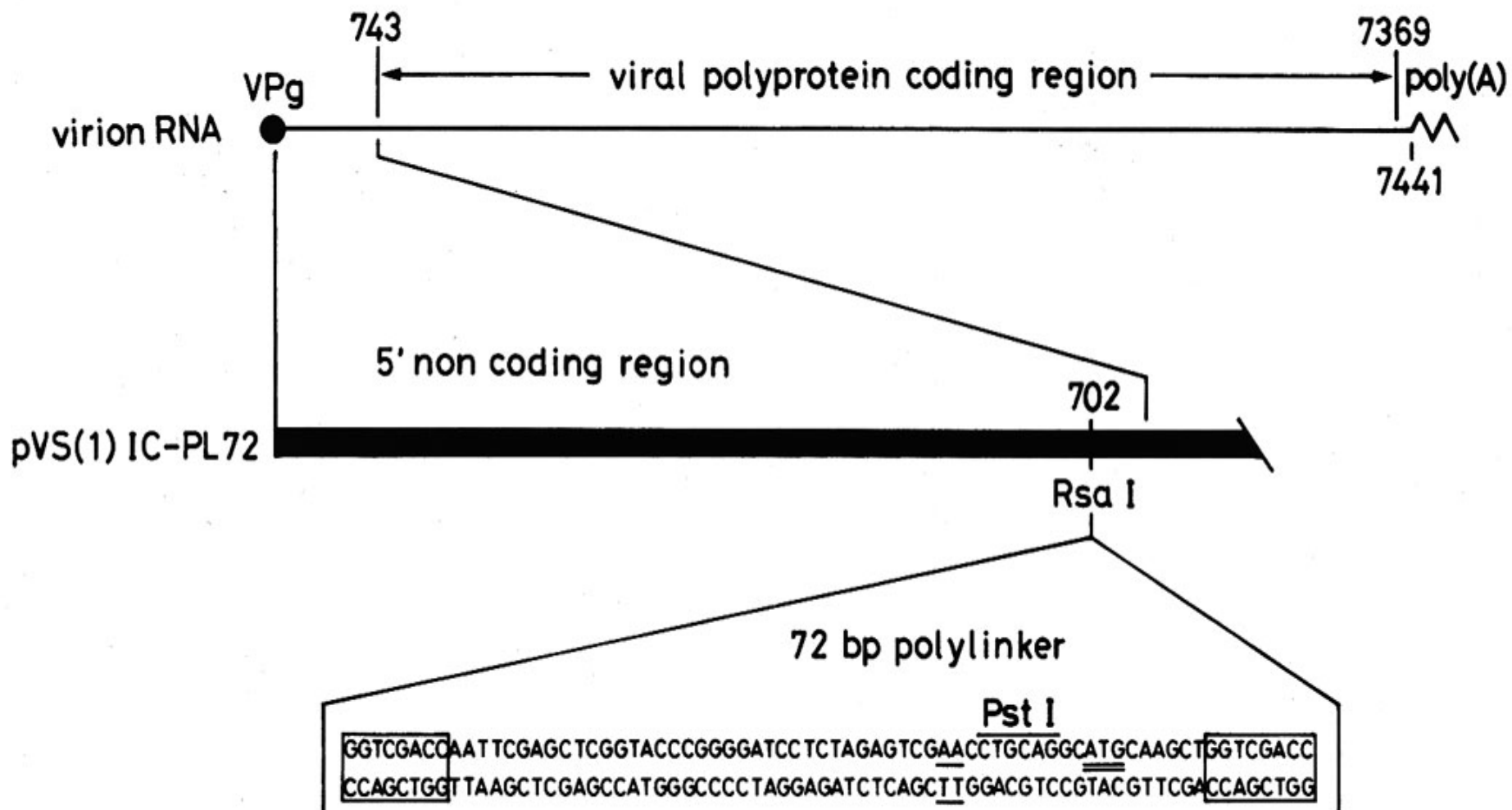
H

1619 2337
 -AC UCC CUC UCG AUA GAU AGU AUG GUA AAG C GC GUC UUC UAC CAA ACC AGA AUA GUC GUC C--
 Ser Leu Ser Ile Asp Ser Met Val Lys Arg Val Phe Tyr Gln Thr Arg Ile Val Val

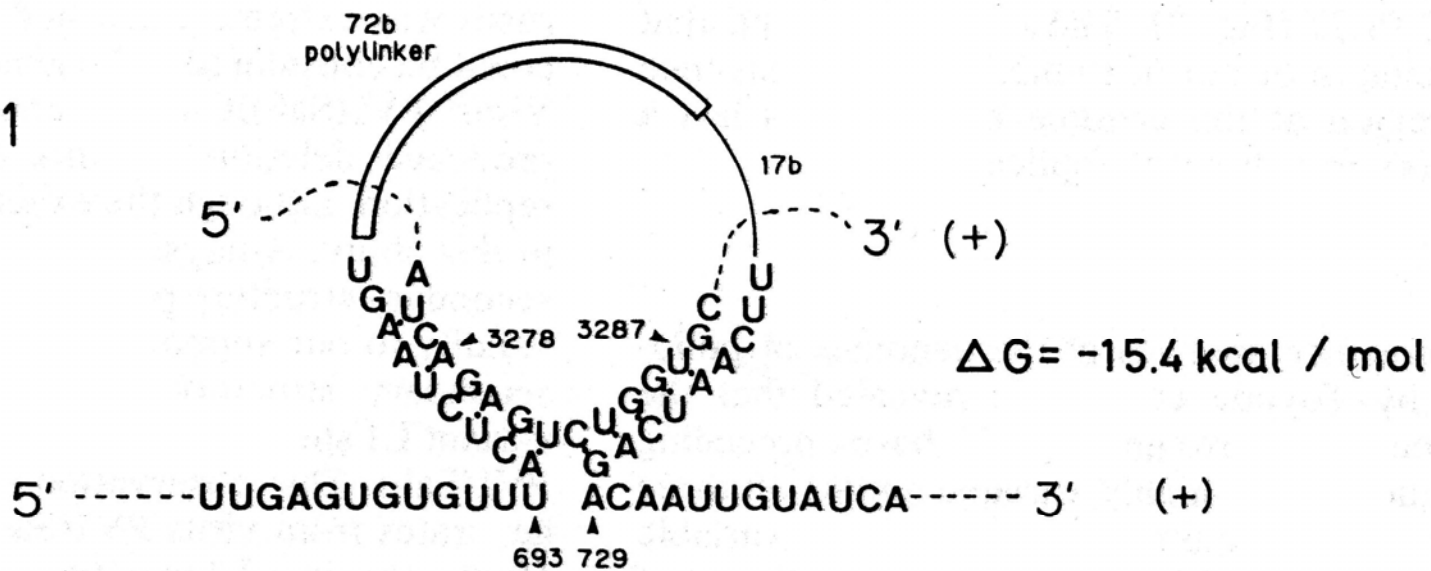
AC AAU AAU UGG GGA ---717 b--- GGC GGA UAC AUC A
 His Asn Asn Trp Gly Gly Gly Tyr Ile Ser

Supporting a Sequence-loop Model

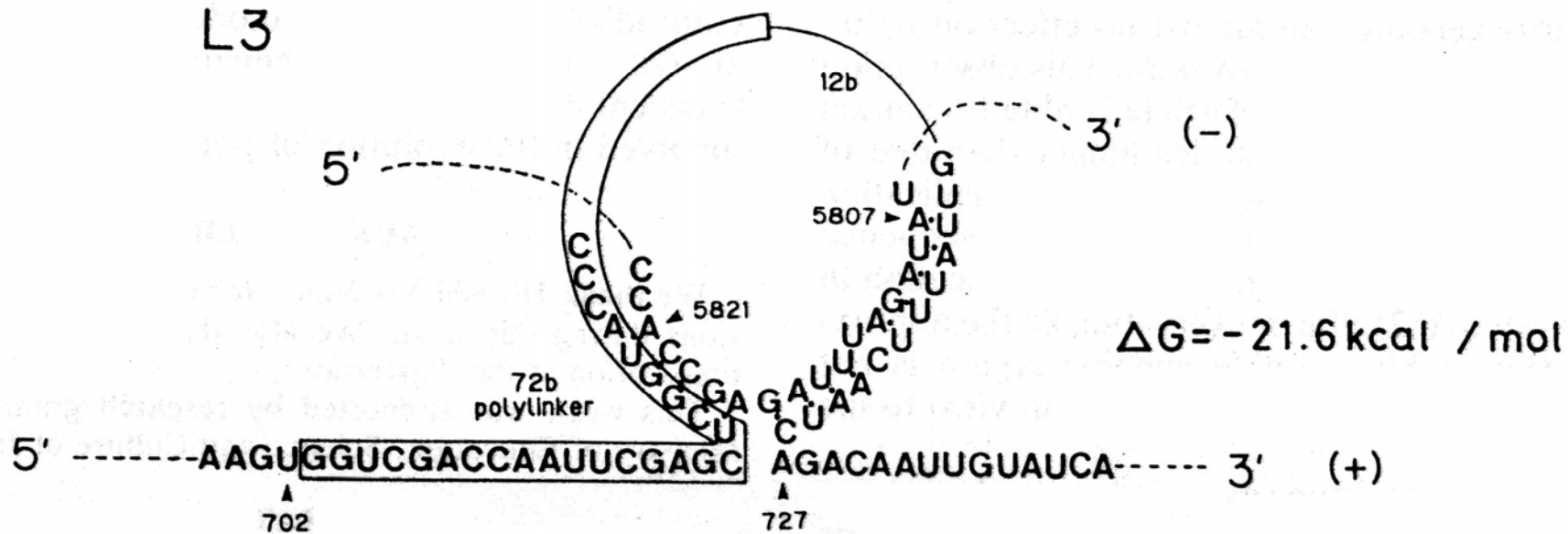




L1

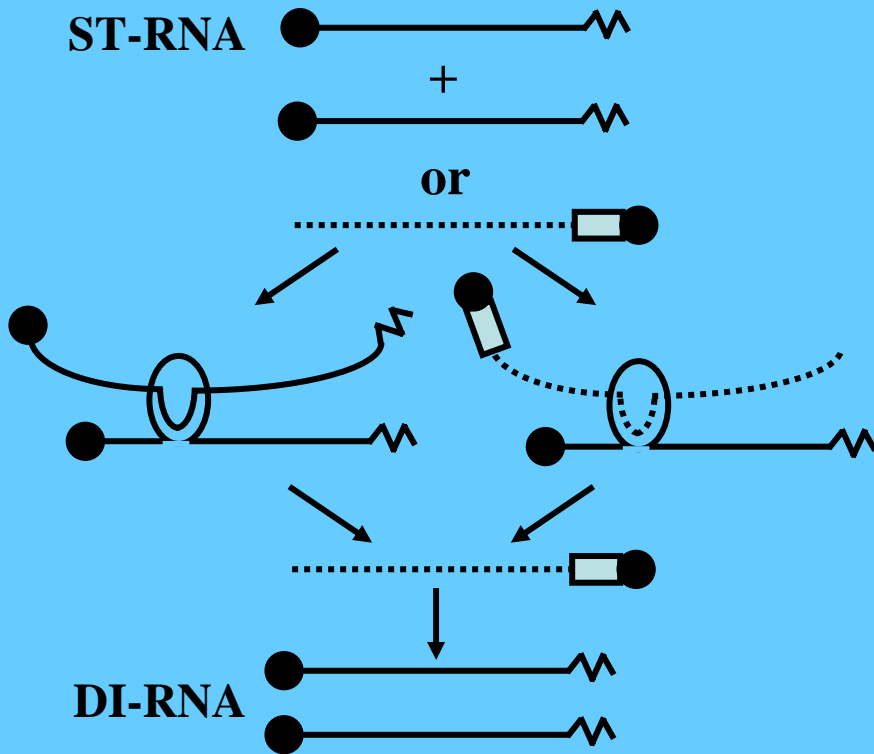


L3



Supporting a Sequence-loop Model

Generation of DI particles

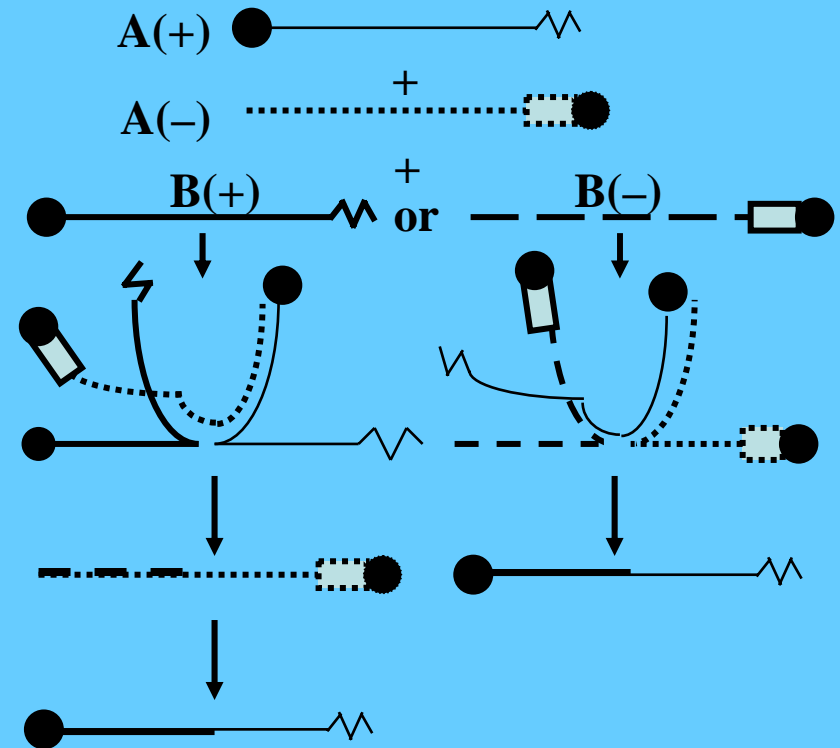


ST-RNA: RNA of Standard virus

DI-RNA: RNA of DI particle

● : VPg ♪ : polyA □ : polyU

Generation of recombinants



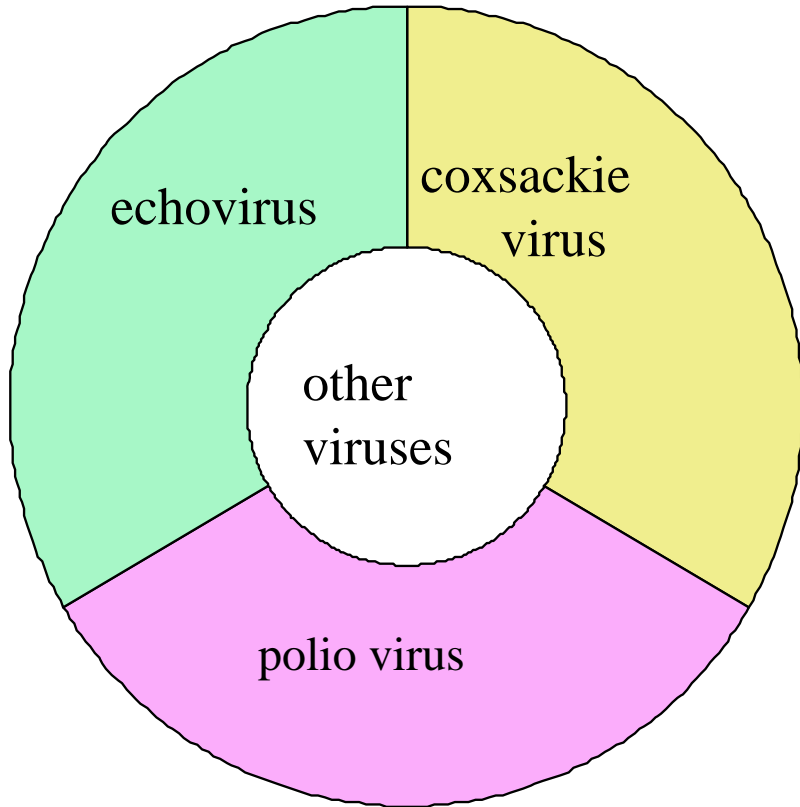
A(+): + Strand of strain A

A(-): - Strand of strain A

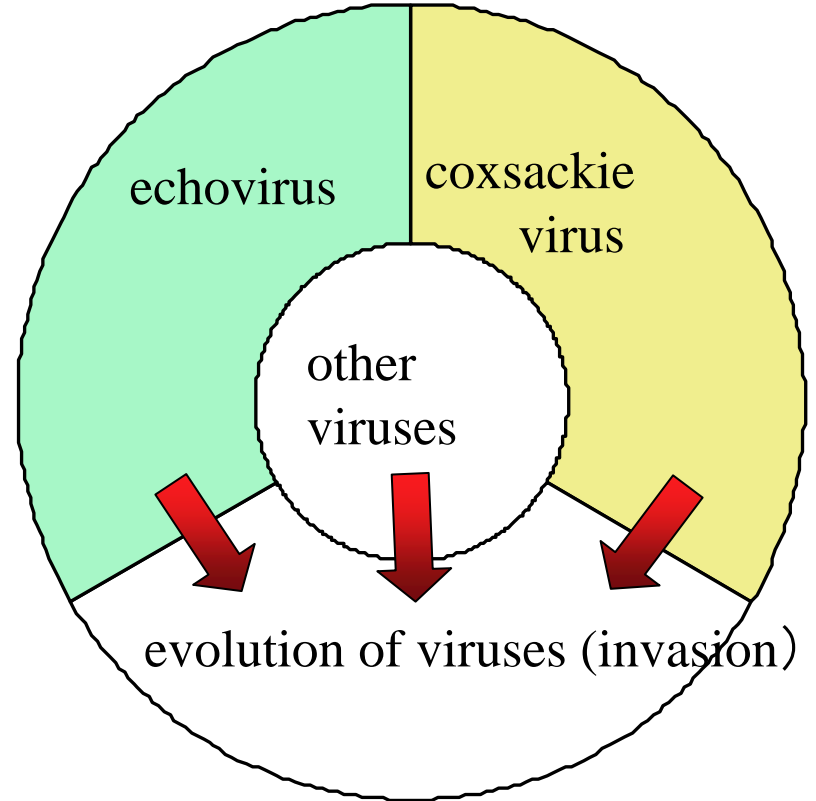
B(+): + Strand of strain B

B(-): - Strand of strain B

World power relationships of enteroviruses



Modern world



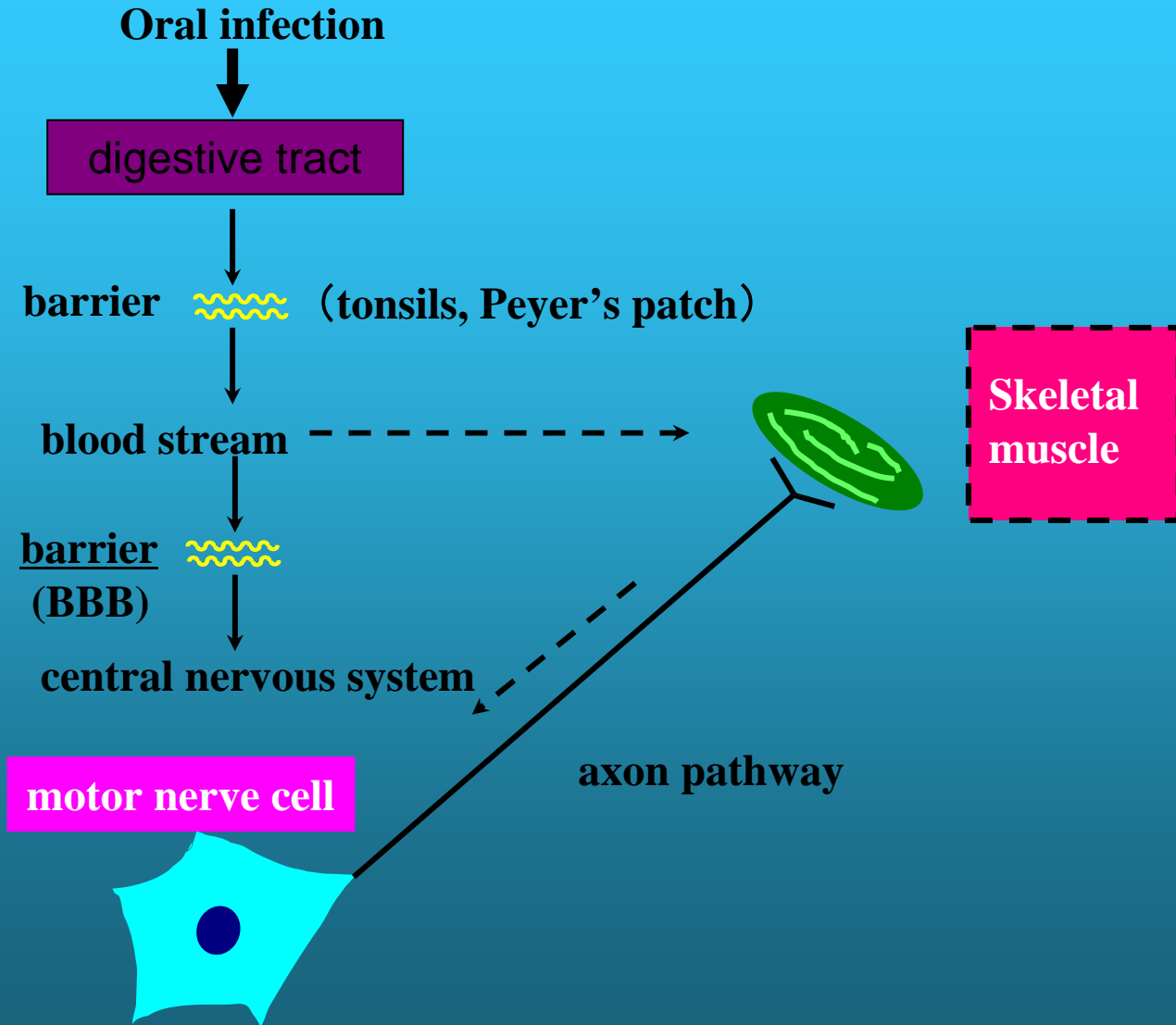
After polio virus eradication

Pathogenic microbes

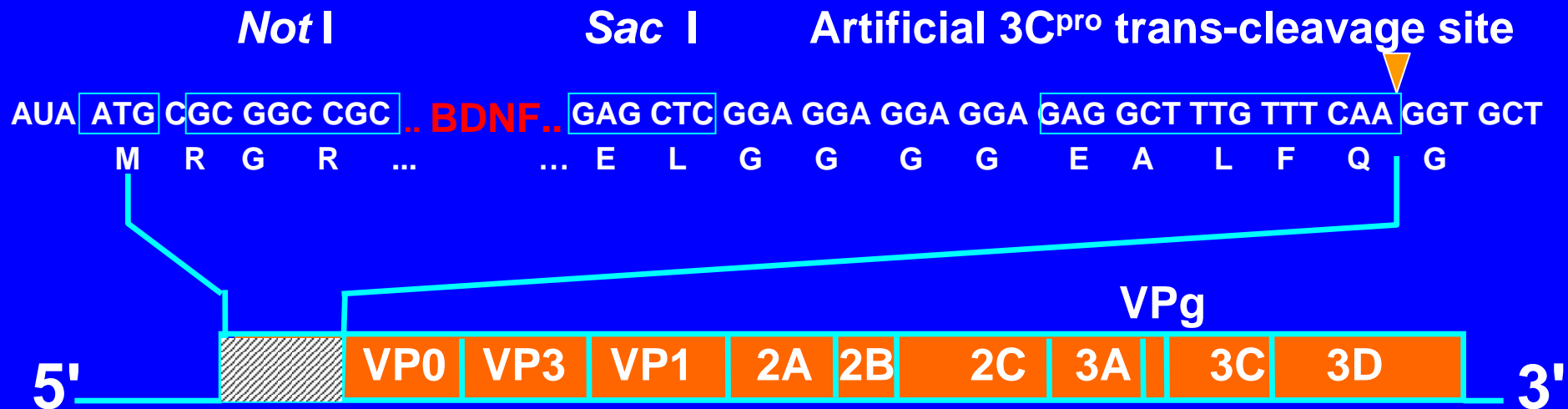
Effective microbes

Other microbes

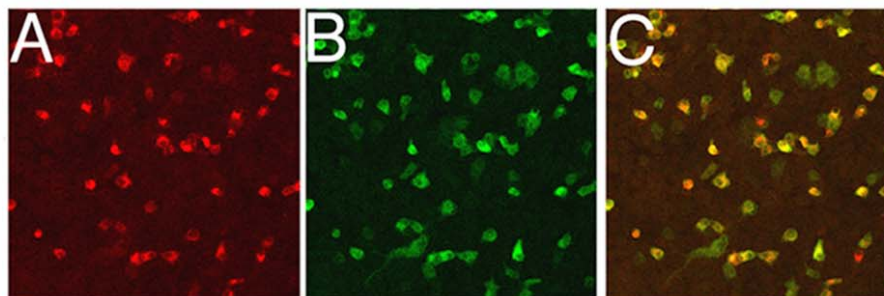
Replication of polio virus and dissemination



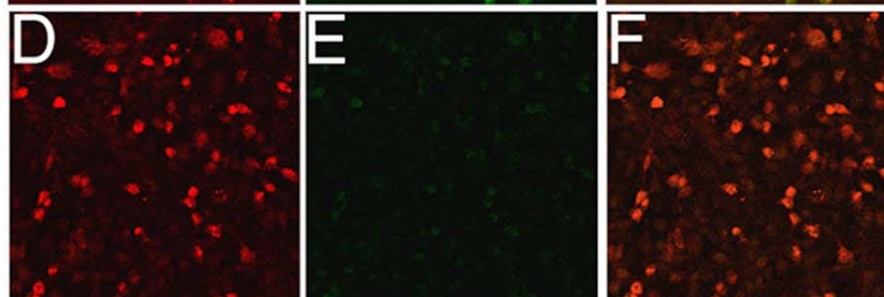
Schematic Structure of Polio Virus Vector for Expression of BDNF



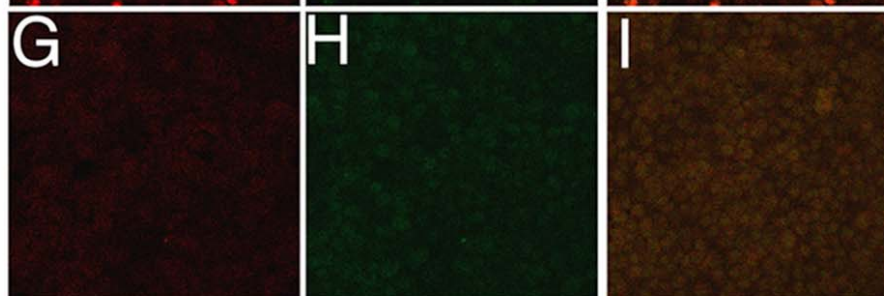
Mah/BDNF

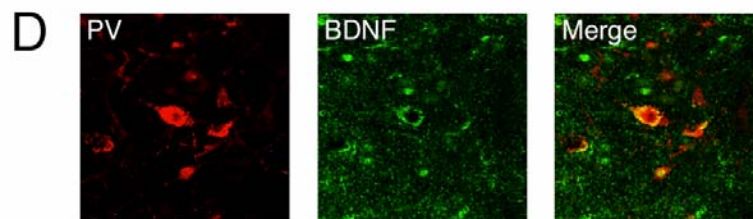
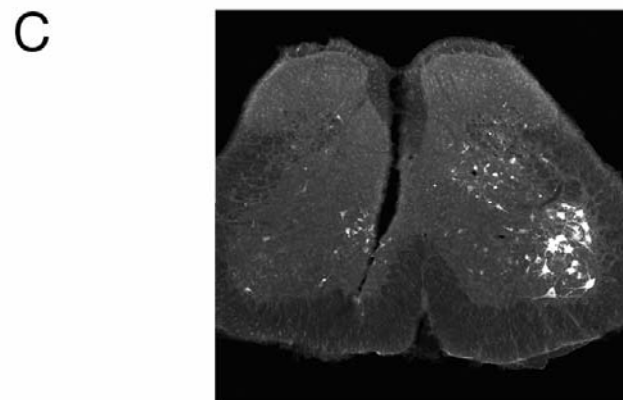
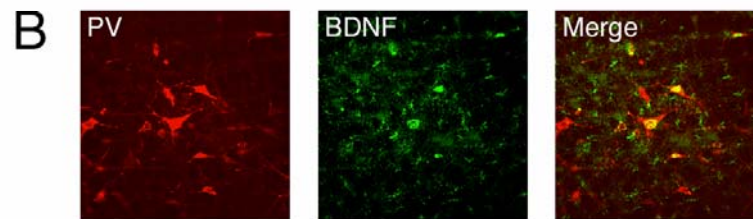
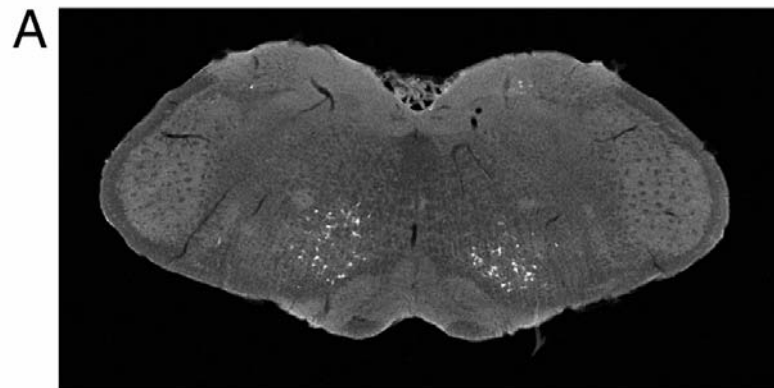


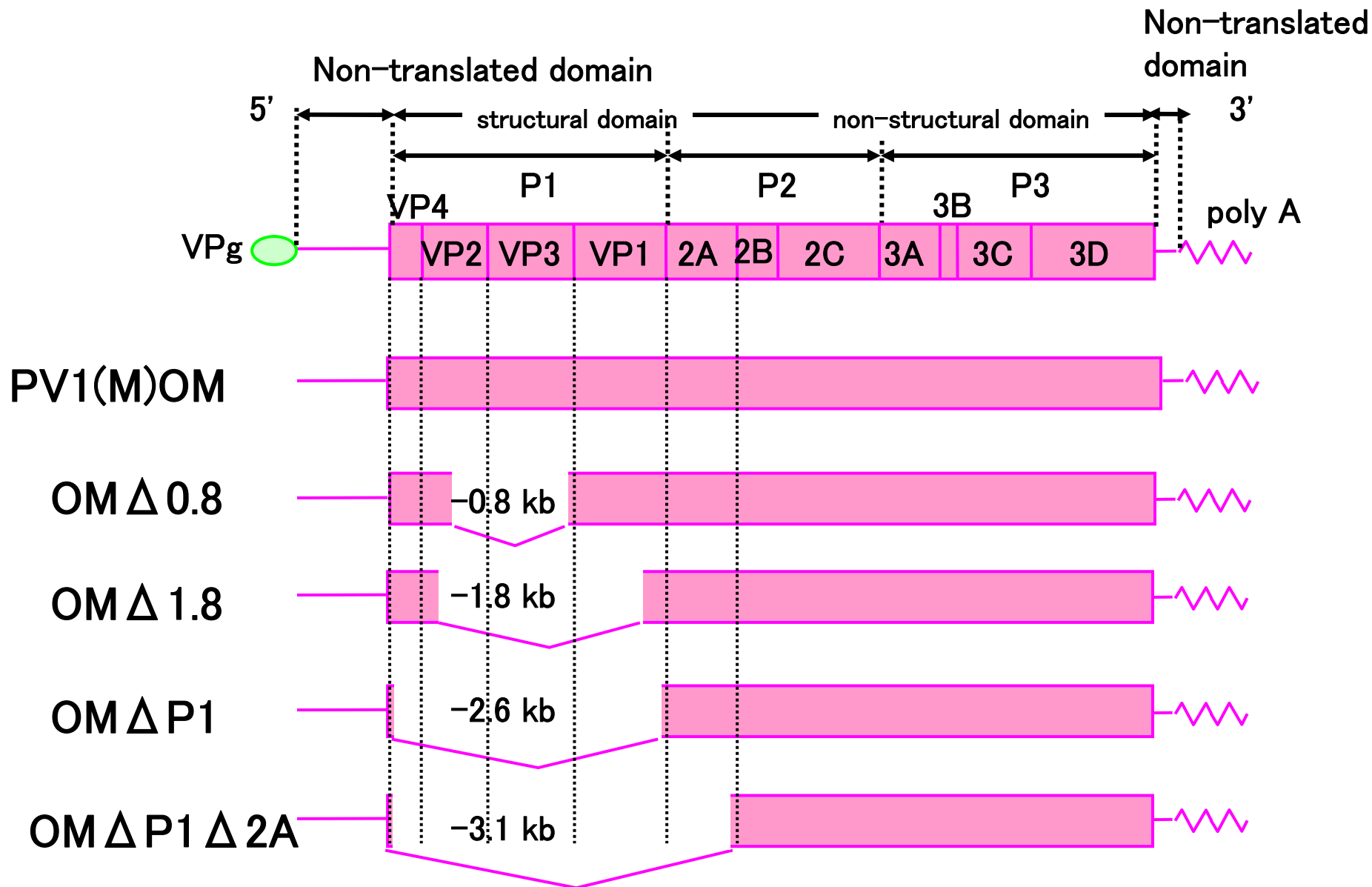
PV1/Mahoney



Mock

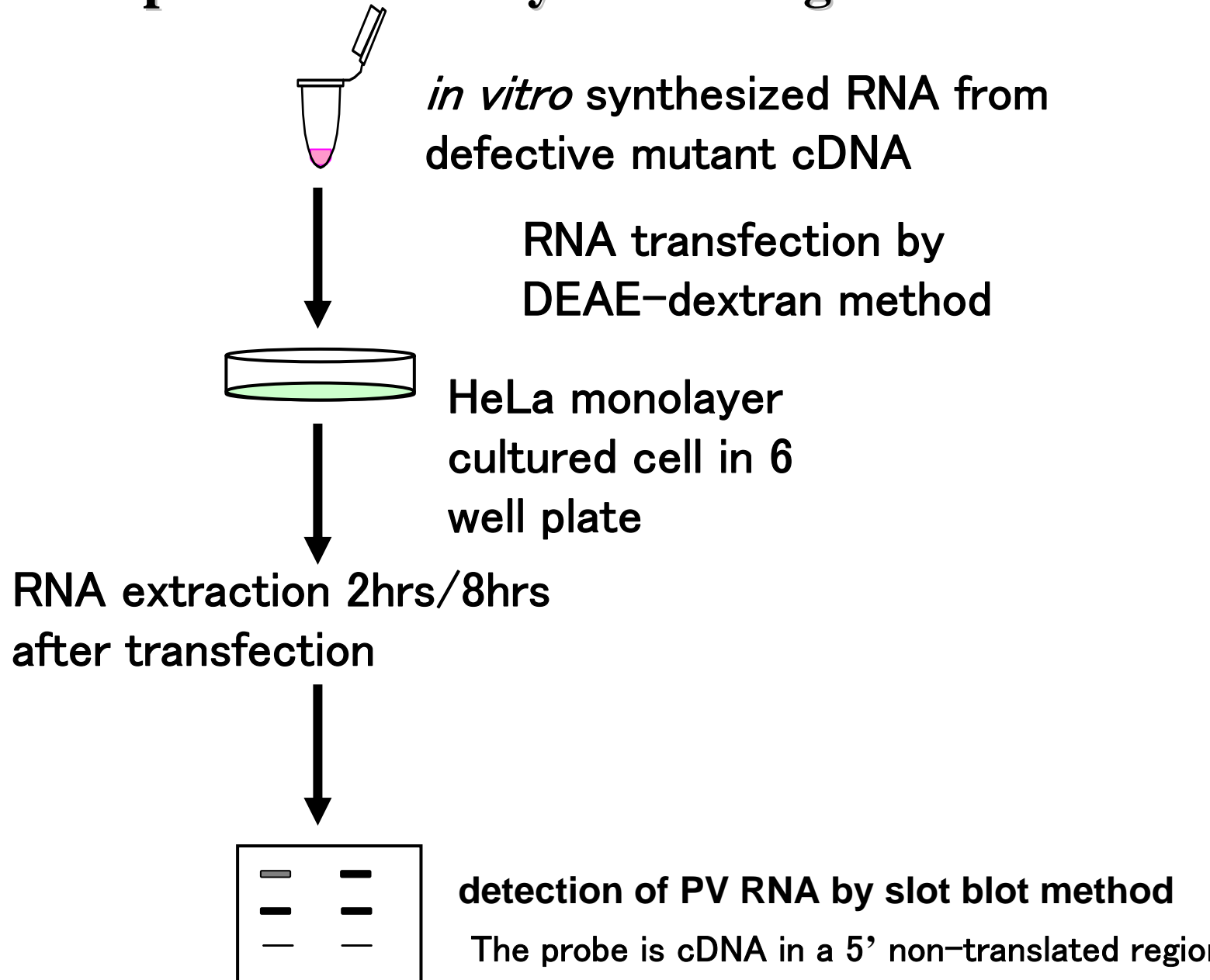


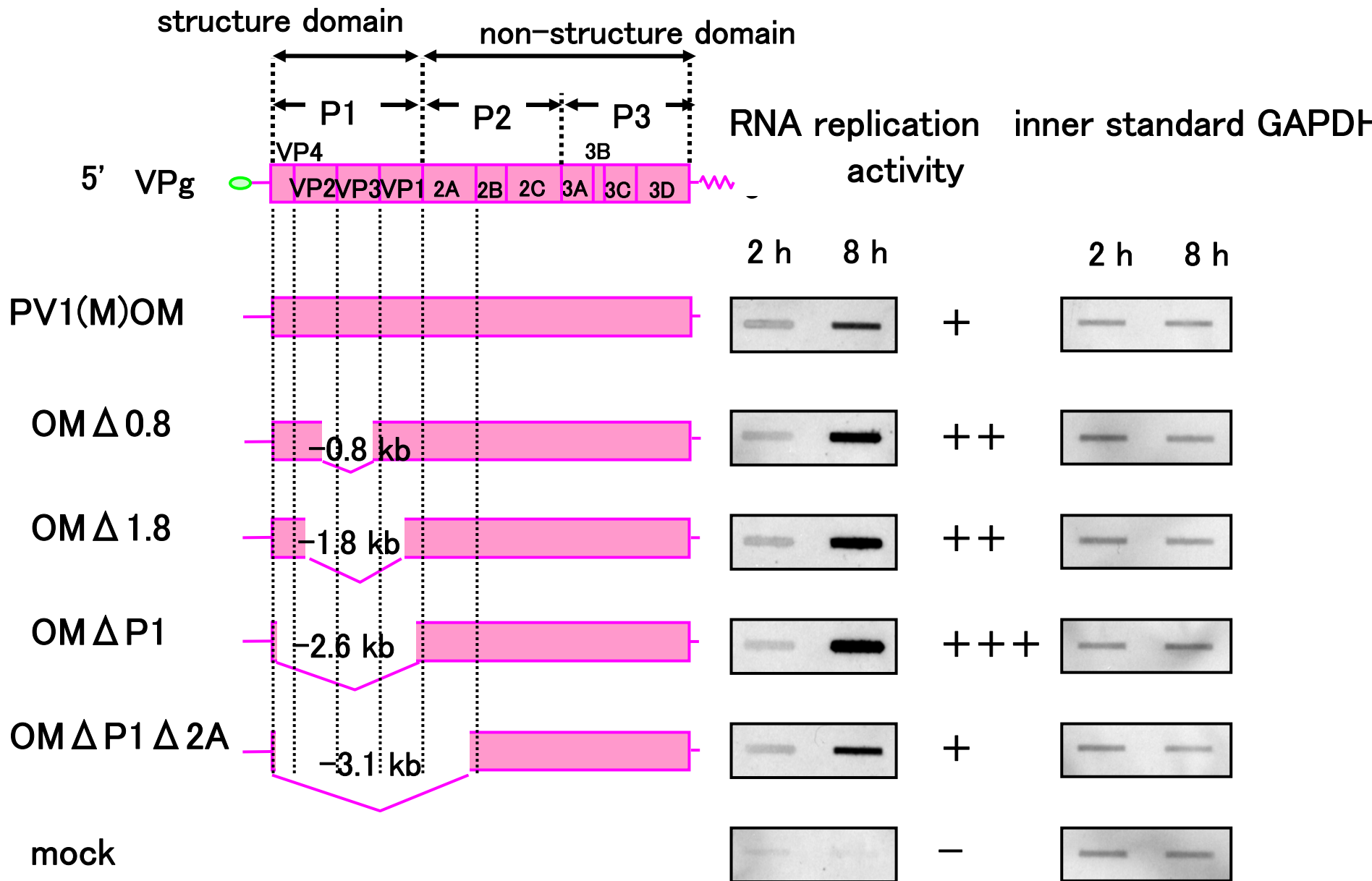




RNA structure of PV-deficient mutant

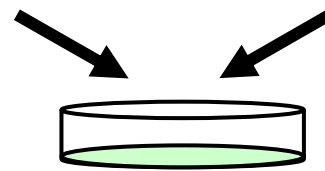
PV RNA replication activity measuring method





RNA structure of PV-deficient mutant

VV-P1



in vitro synthesized
PV-defective mutant
RNA

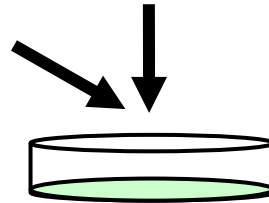
HeLa monolayer cultured cell



formation of DI particle
containing PV-defective
mutant RNA



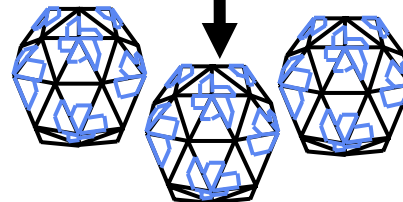
VV-P1



passage of DI particle



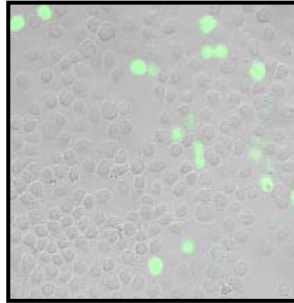
amplification of DI
particles containing
PV-defective mutant
RNA



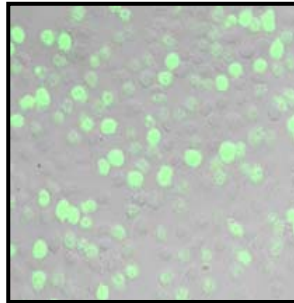
removal VV-P1 by SDS treatment

RNA packaging of PV-deficient mutant

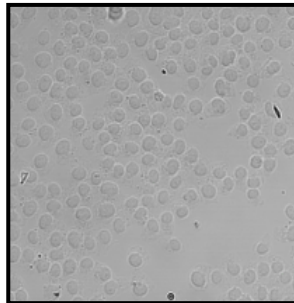
Passage
1

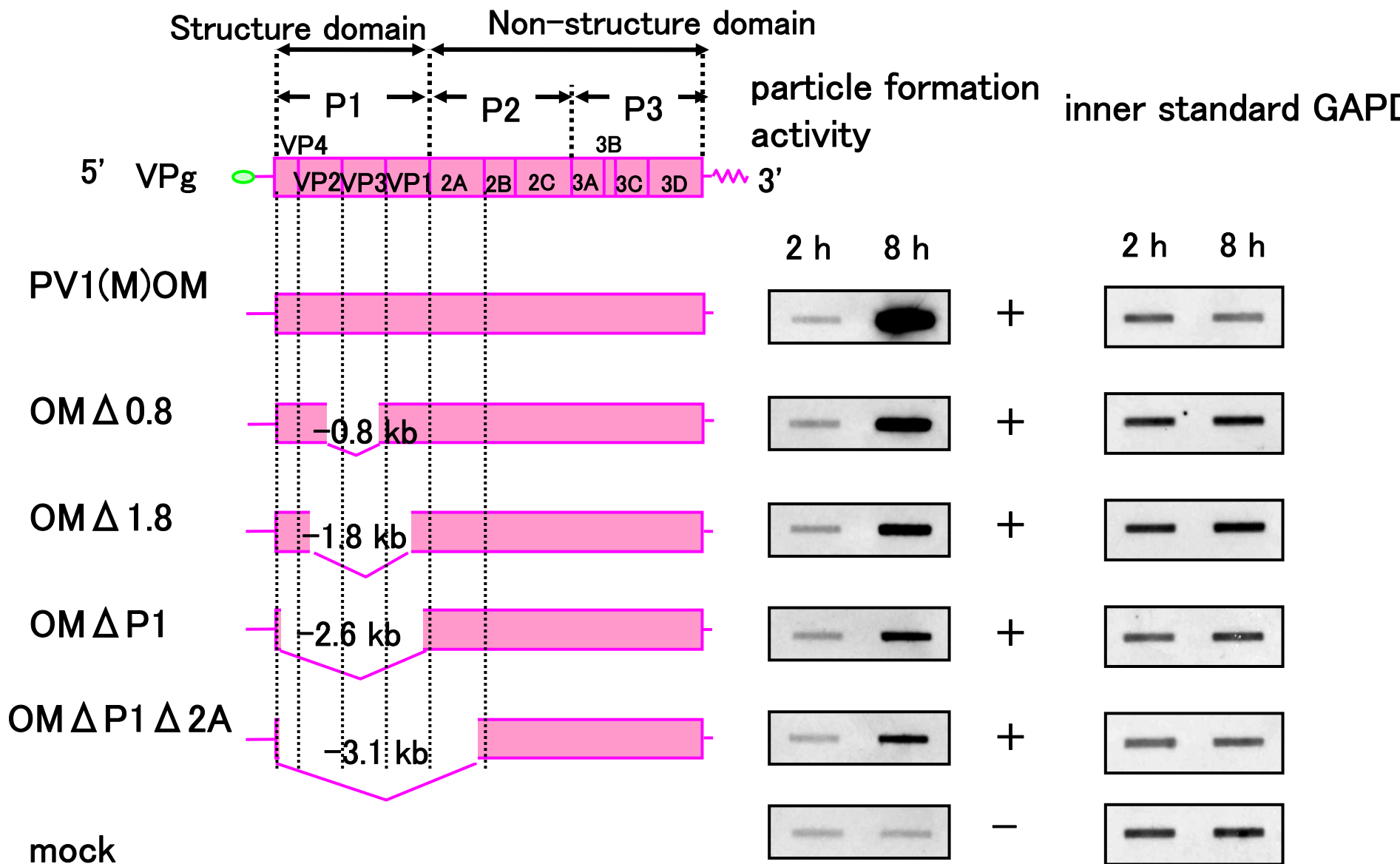


Passage
2

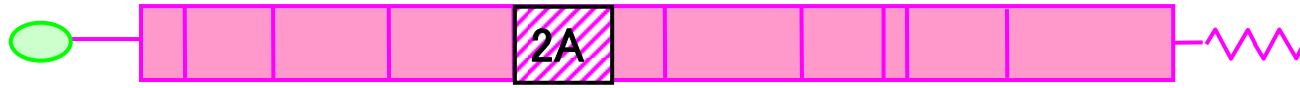


Mock





Function of 2A protease

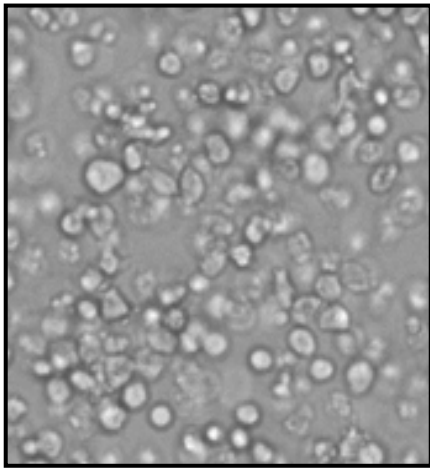


Virus RNA replication

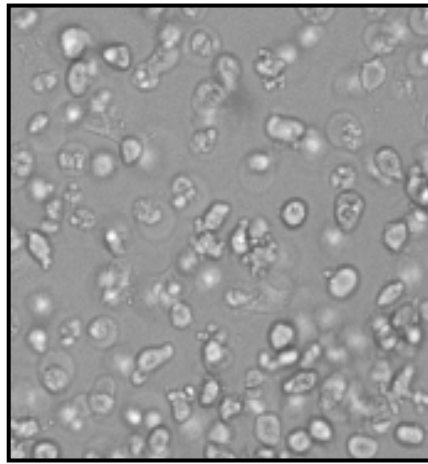
- not necessary, but some involvement in RNA replication
- enhance translation-starting efficiency

Effects to infected cell

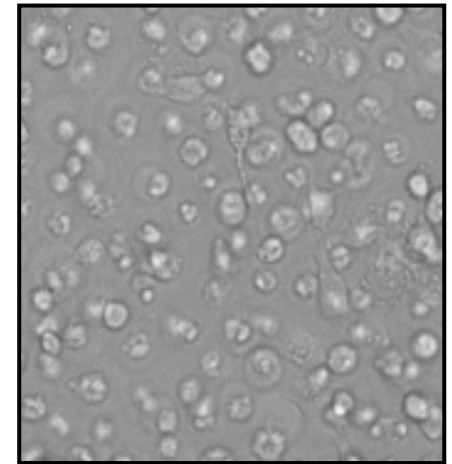
- inhibition of cap-dependent translation
- cytopathic effect ; CPE



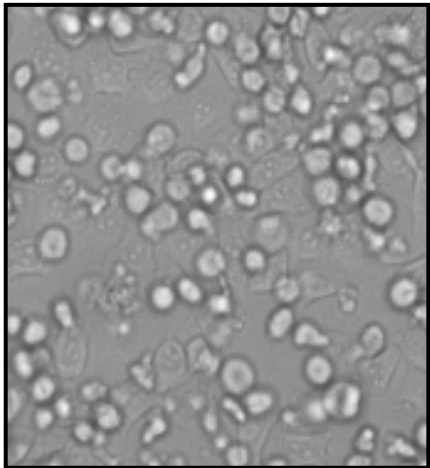
PV1(M)OM



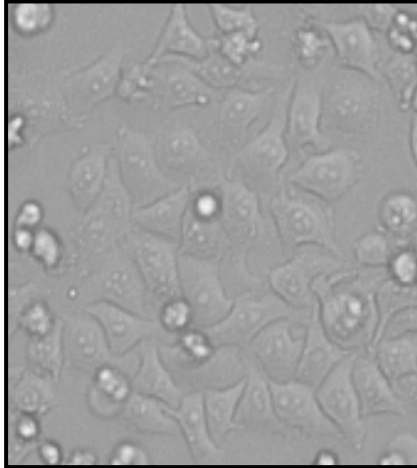
OM Δ 0.8



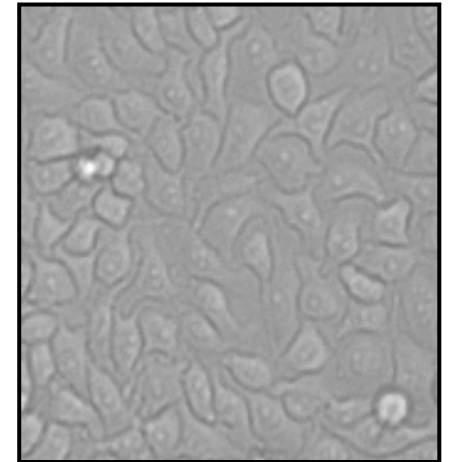
OM Δ 1.8



OM Δ P1

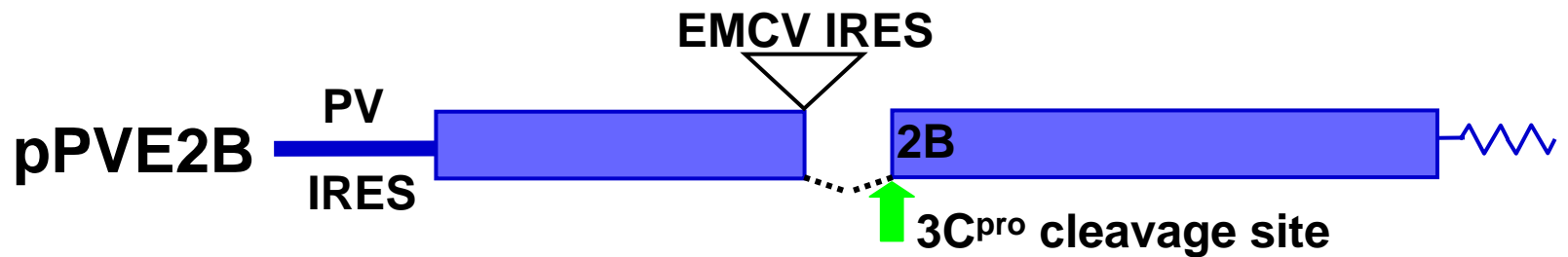
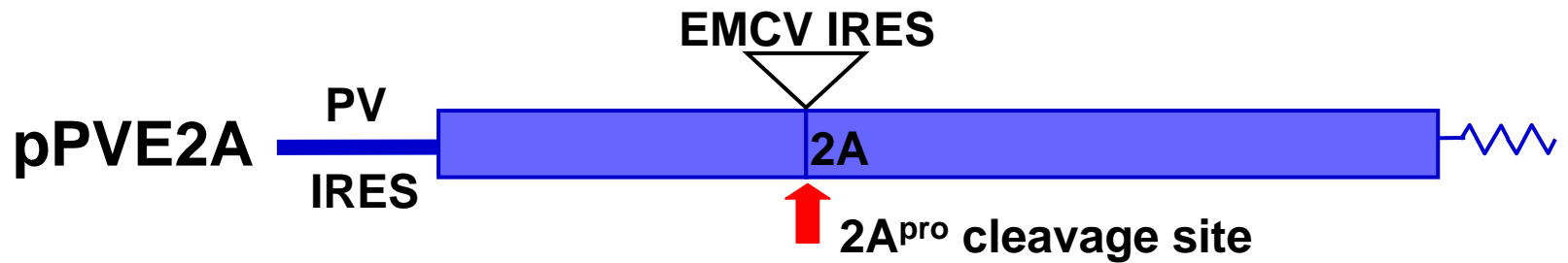
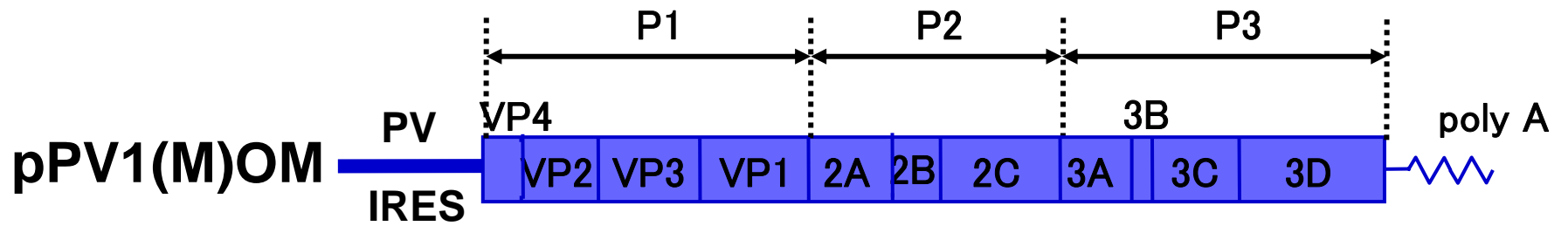


OM Δ P1 Δ 2A



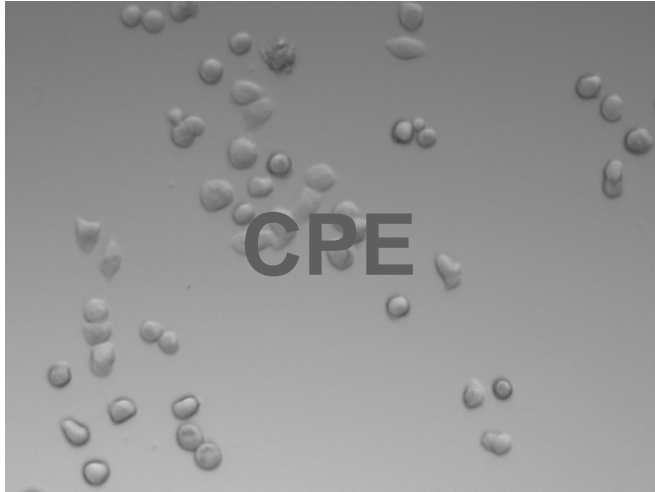
mock

CPE expressions in DI particle infected cells



Expression vector: pSVA14

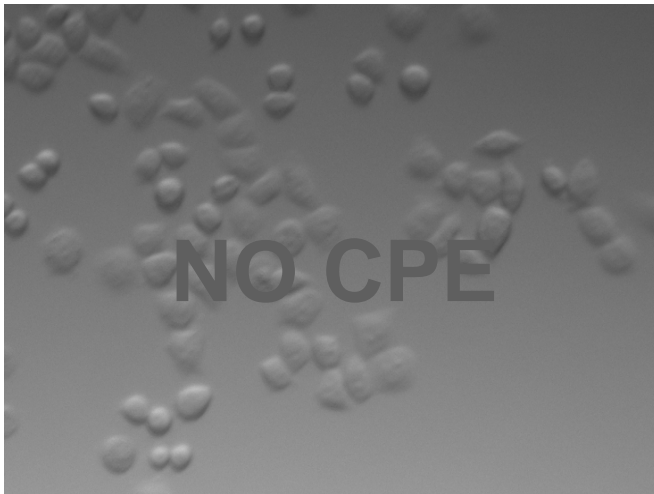
PV1 (M) OM



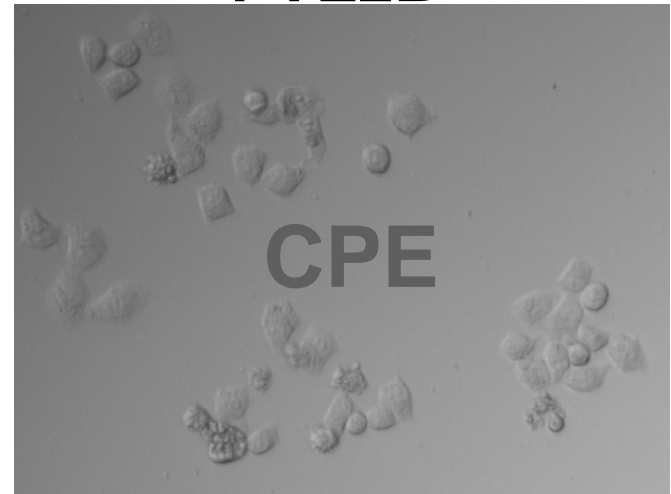
PVE2A



Mock



PVE2B



(8 hours post infection (h.p.i))

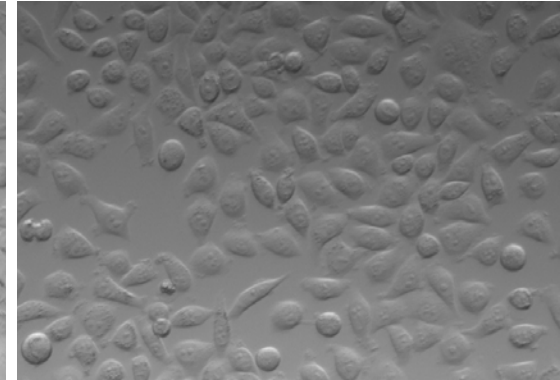
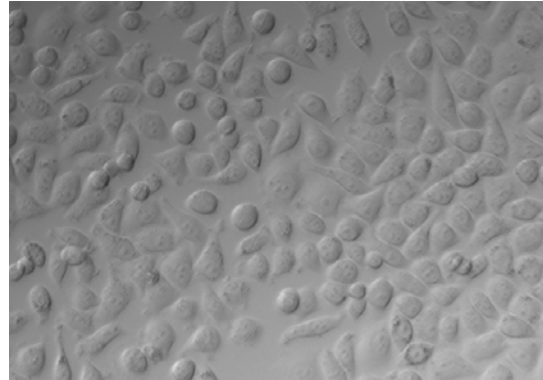
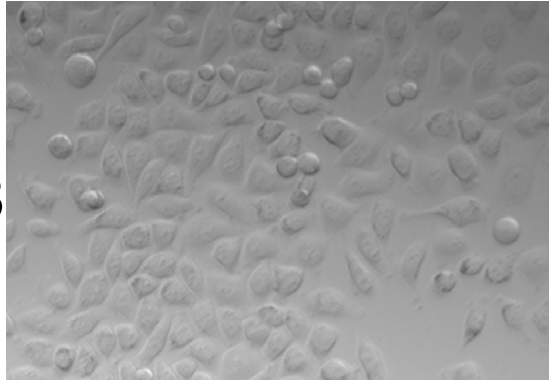
Neutralizing assay producing viruses by I antibody

PV1 (M) OM

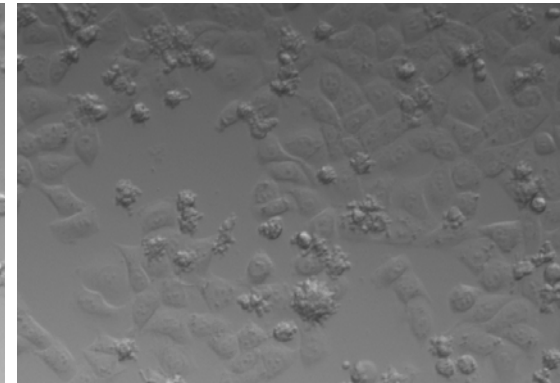
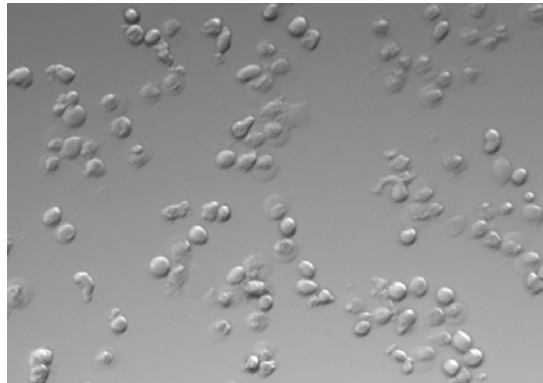
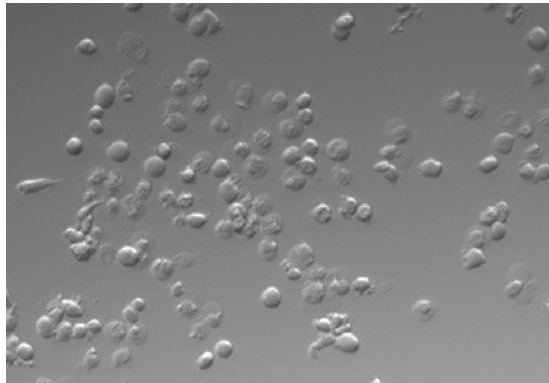
PVE2A

PVE2B

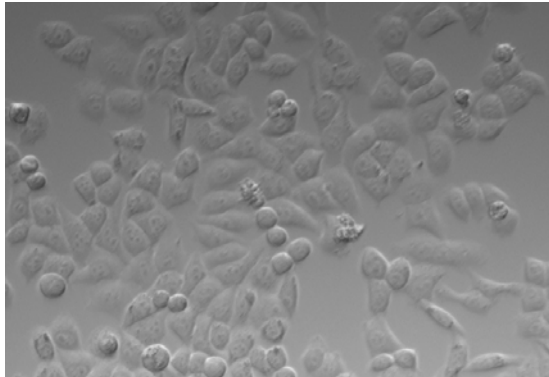
7m008



No Ab



Mock



18h.p.i

Polio research in a post genome era

