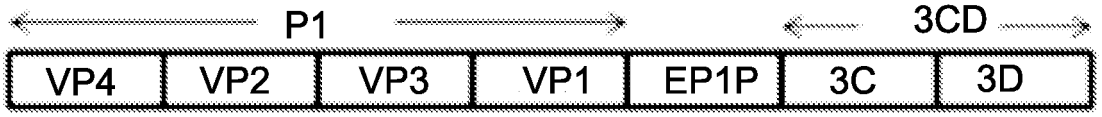
(A)



(B)

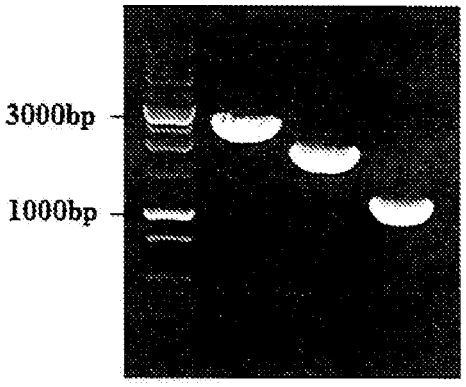


Fig. 1 (Cont')

(C)

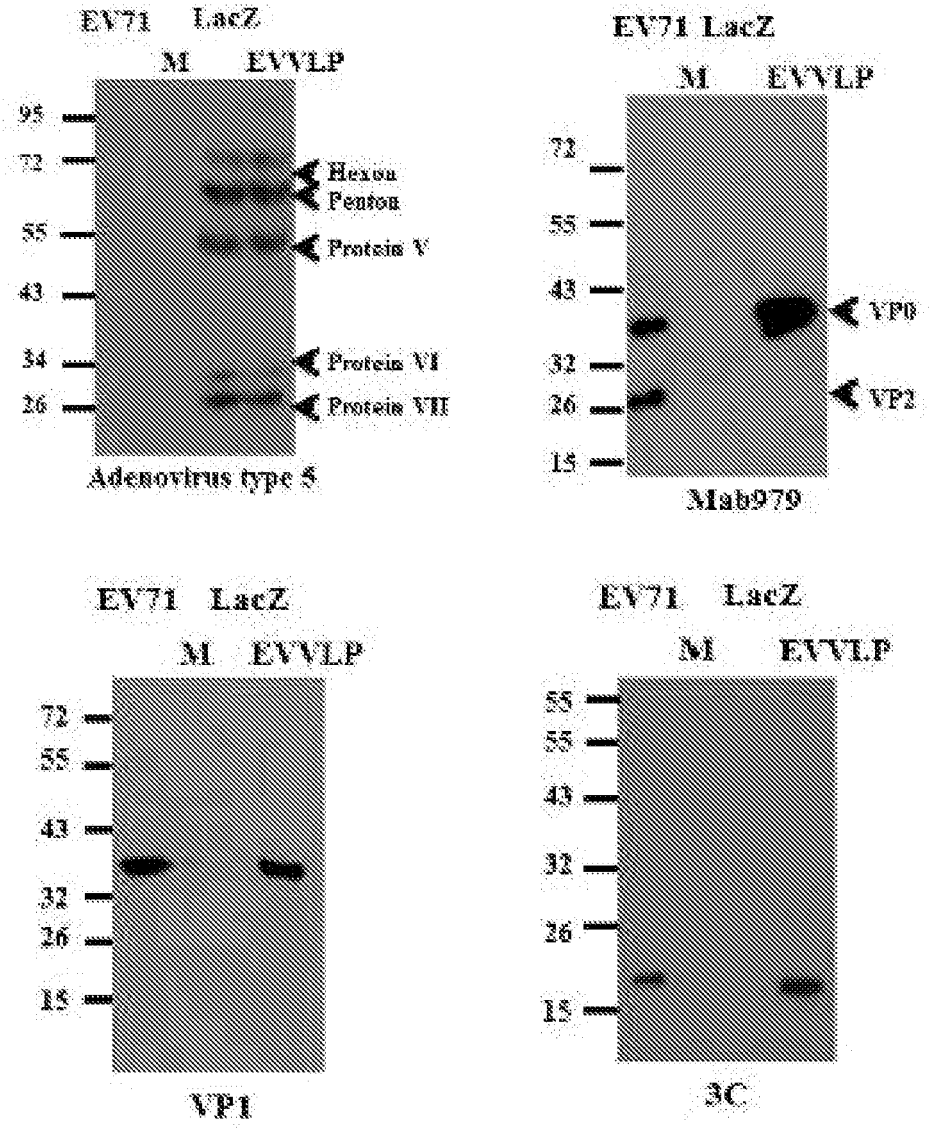
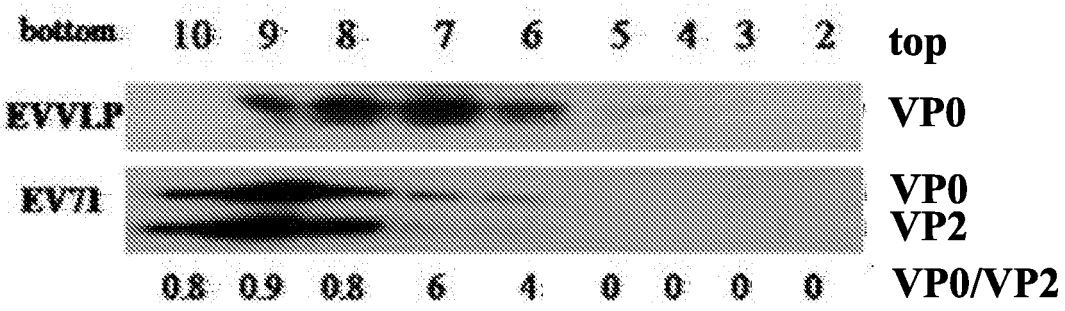
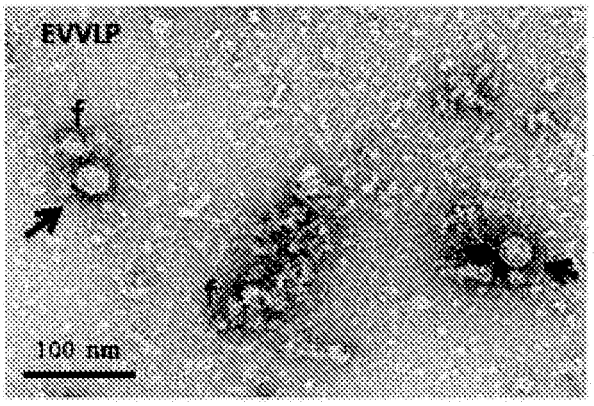

EV71 LacZ
M EVVLP
95
72
55
43
34
26
Hexon
Penton
Protein V
Protein VI
Protein VII
Adenovirus type 5
EV71 LacZ
M EVVLP
72
55
43
32
26
15
VP0
VP2
Mab979
EV71 LacZ
M EVVLP
72
55
43
32
26
15
VP1
EV71 LacZ
M EVVLP
55
55
43
32
26
15
3C

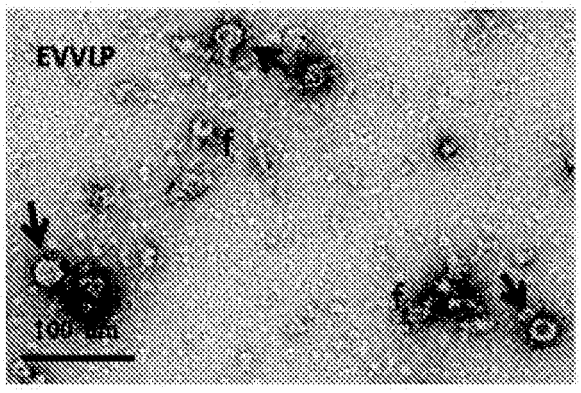
Fig. 1

(A)

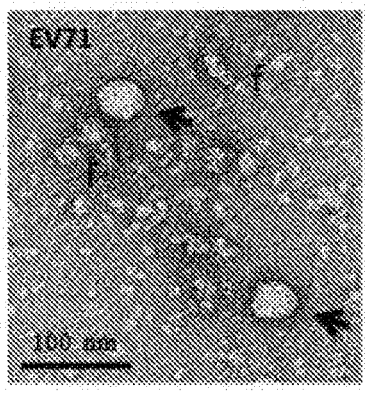

bottom
10 9 8 7 6 5 4 3 2
top
EVVLP
VP0
EV71
VP0
VP2
0.8 0.9 0.8 6 4 0 0 0 0
VP0/VP2

(B)


EVVLP
f
100 nm


EVVLP
f
100 nm

(C)


EV71
f
f
100 nm

(D)

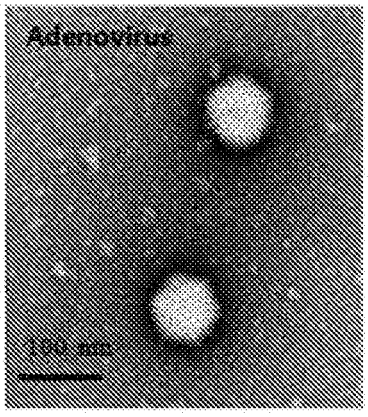
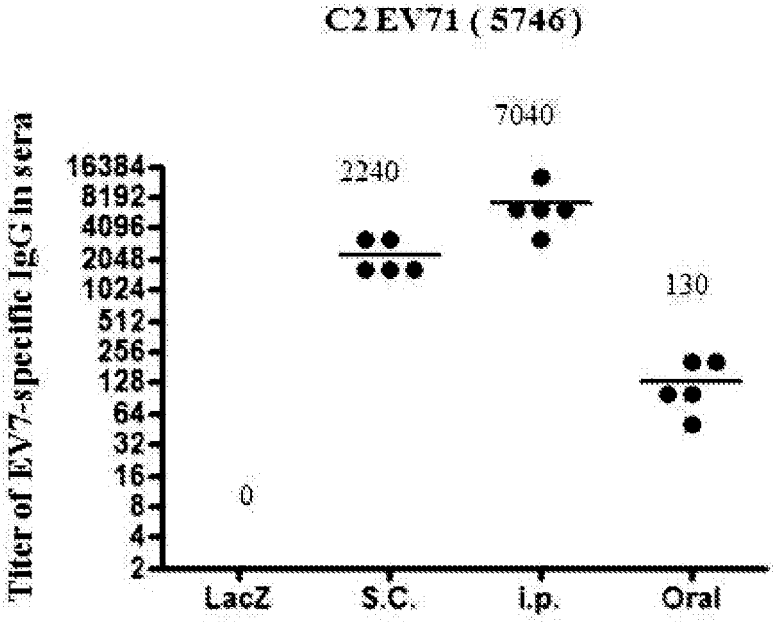

Adenovirus
100 nm

Fig. 2

(A)


C2 EV71 (5746)
Titer of EV7-specific IgG in sera
16384
8192
4096
2048
1024
512
256
128
64
32
16
8
4
2
0
2240
7040
130
LacZ
S.C.
i.p.
Oral

(B)

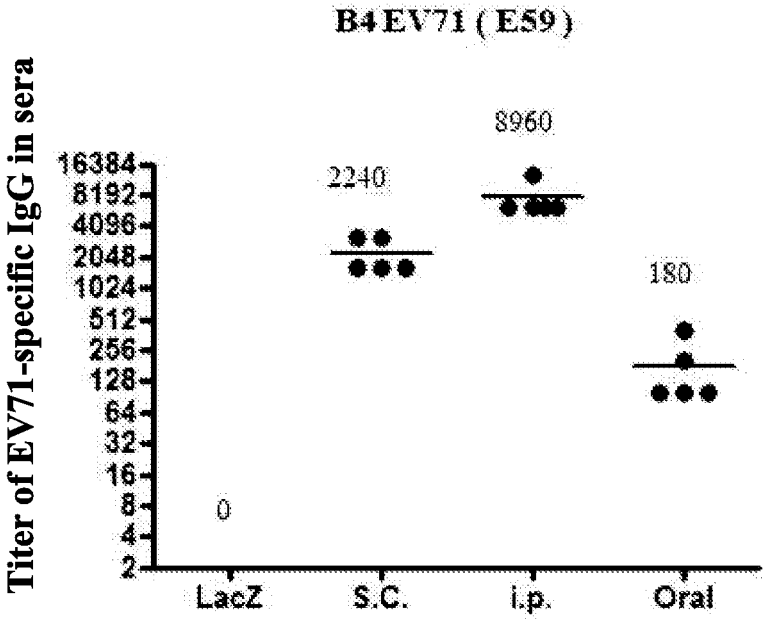

B4 EV71 (E59)
Titer of EV71-specific IgG in sera
16384
8192
4096
2048
1024
512
256
128
64
32
16
8
4
2
0
2240
8960
180
LacZ
S.C.
i.p.
Oral

Fig. 3

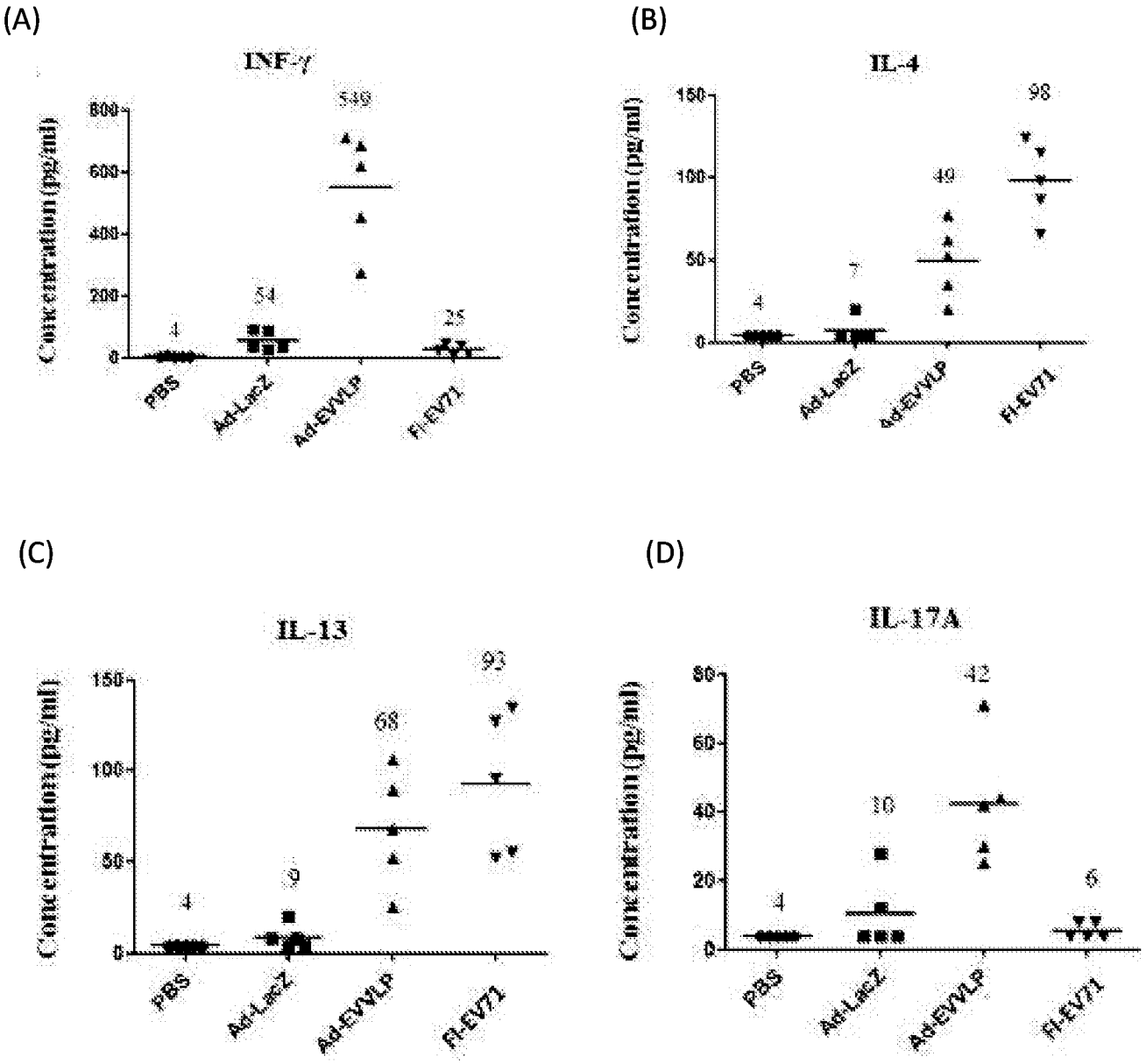
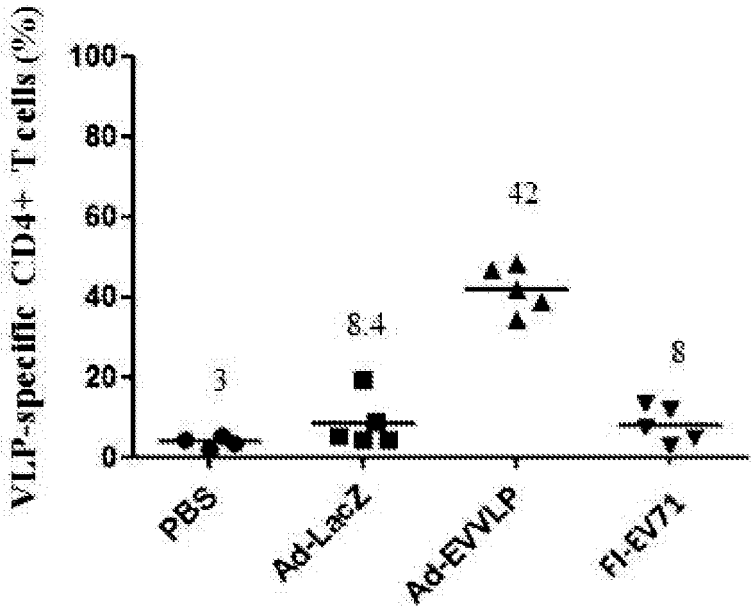

(A)
INF-γ
Concentration (pg/ml)
800
600
400
200
0
4
54
549
25
PBS
Ad-LacZ
Ad-EVVLP
FI-EV71
(B)
IL-4
Concentration (pg/ml)
150
100
50
0
4
7
49
98
PBS
Ad-LacZ
Ad-EVVLP
FI-EV71
(C)
IL-13
Concentration (pg/ml)
150
100
50
0
4
9
68
93
PBS
Ad-LacZ
Ad-EVVLP
FI-EV71
(D)
IL-17A
Concentration (pg/ml)
80
60
40
20
0
4
10
42
6
PBS
Ad-LacZ
Ad-EVVLP
FI-EV71

Fig. 4

(A)


VLP-specific CD4+ T cells (%)
100
80
60
40
20
0
3
8.4
42
8
PBS
Ad-LacZ
Ad-EV/VLP
FI-EV71

(B)

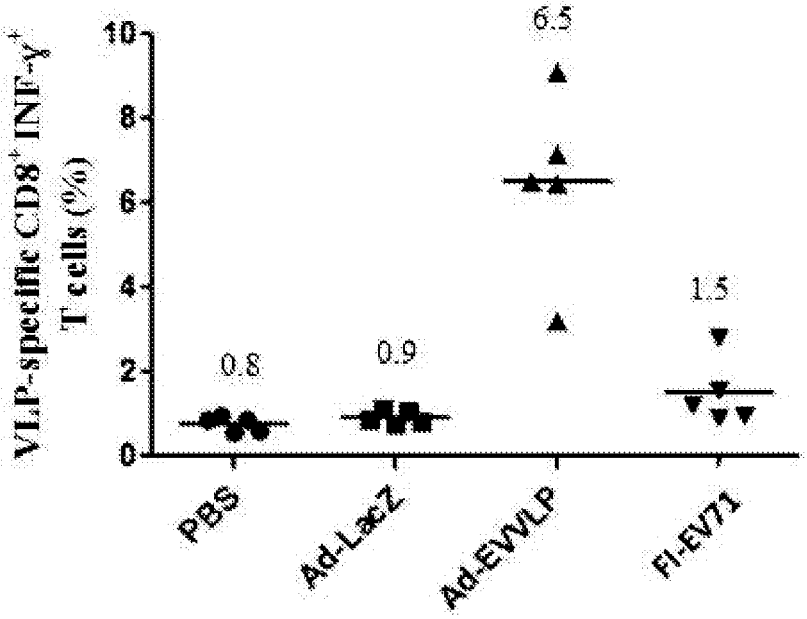
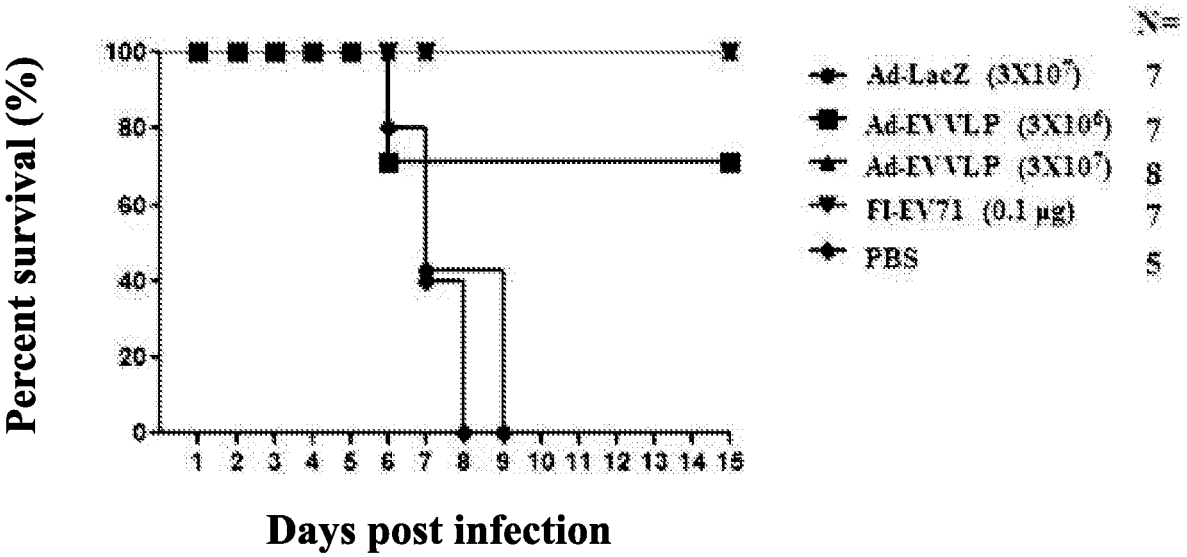

VLP-specific CD8+ INF-γ+ T cells (%)
10
8
6
4
2
0
0.8
0.9
6.5
1.5
PBS
Ad-LacZ
Ad-EV/VLP
FI-EV71

Fig. 5

(A)


Percent survival (%)
100
80
60
40
20
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Days post infection
N=
Ad-LacZ (3X10⁷) 7
Ad-EVVLP (3X10⁶) 7
Ad-EVVLP (3X10⁷) 8
FI-EV71 (0.1 μg) 7
PBS 5

(B)

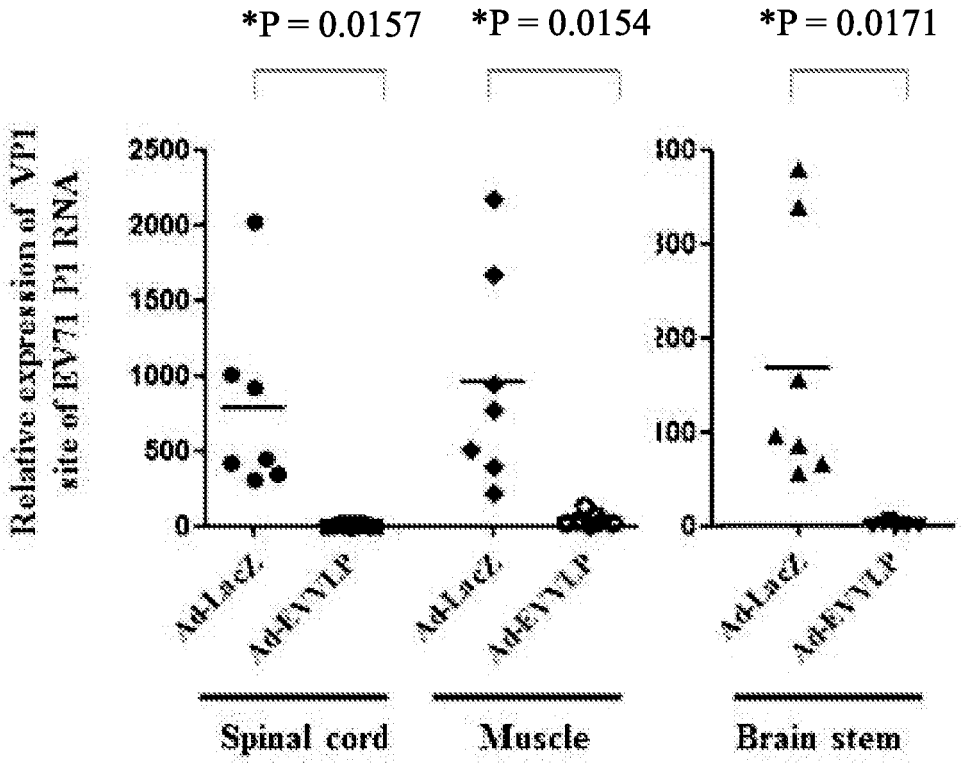

*P = 0.0157
*P = 0.0154
*P = 0.0171
Relative expression of VP1 site of EV71 P1 RNA
2500
2000
1500
1000
500
0
Ad-LacZ
Ad-EVVLP
Spinal cord
Muscle
Brain stem

Fig. 6

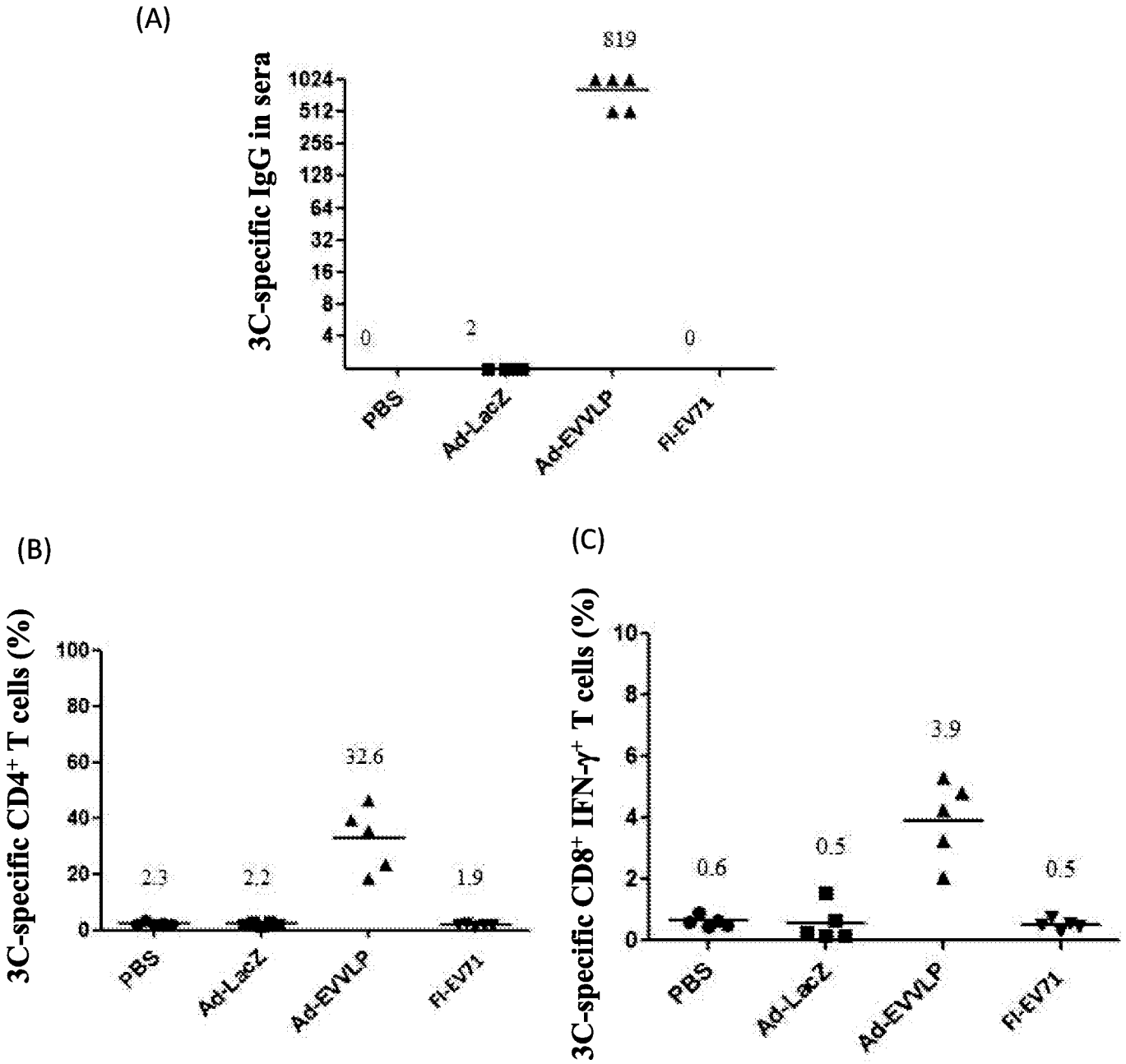
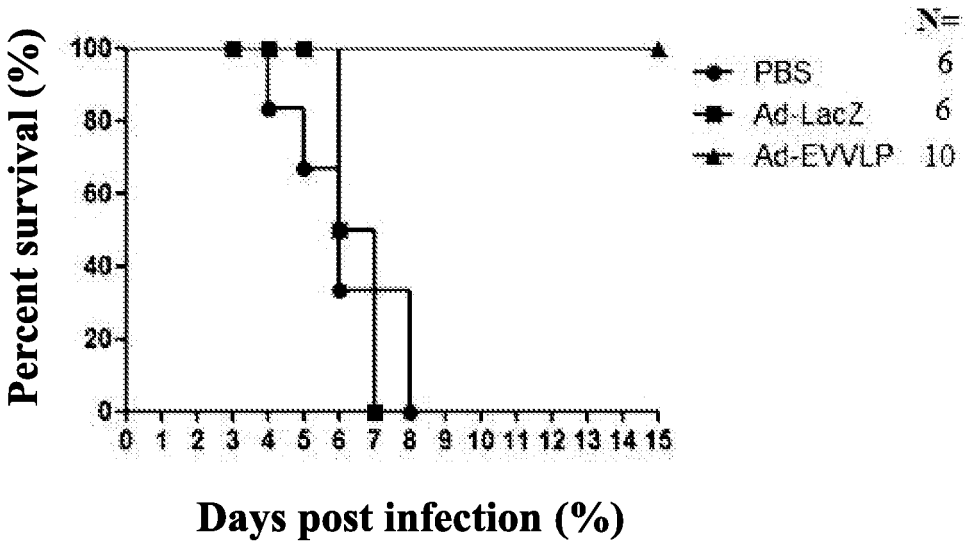

(A)
3C-specific IgG in sera
1024
512
256
128
64
32
16
8
4
819
0
2
0
PBS
Ad-LacZ
Ad-EV/VLP
FI-EV71
(B)
3C-specific CD4+ T cells (%)
100
80
60
40
20
0
32.6
2.3
2.2
1.9
PBS
Ad-LacZ
Ad-EV/VLP
FI-EV71
(C)
3C-specific CD8+ IFN-γ+ T cells (%)
10
8
6
4
2
0
3.9
0.6
0.5
0.5
PBS
Ad-LacZ
Ad-EV/VLP
FI-EV71

Fig. 7

(A)


N=
PBS 6
Ad-LacZ 6
Ad-EVVLP 10
Percent survival (%)
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Days post infection (%)

(B)

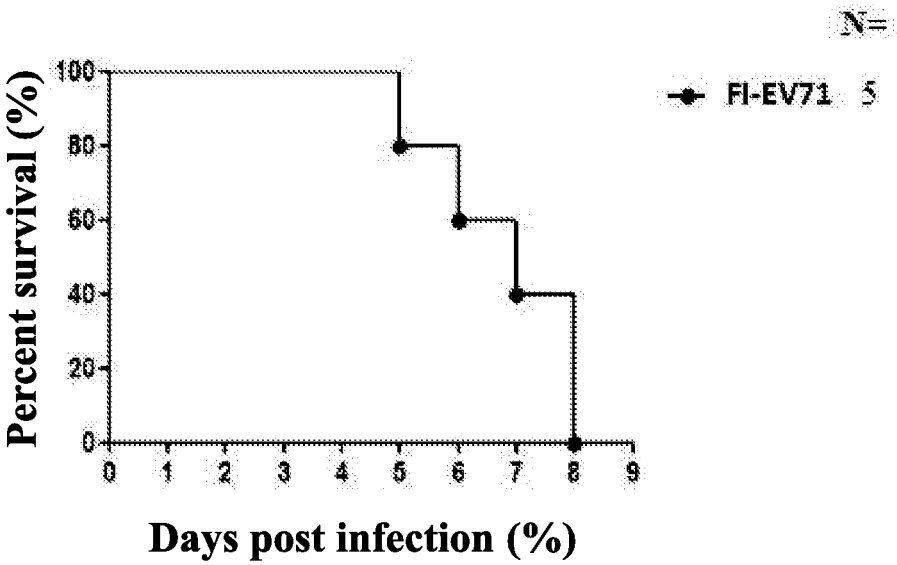

N=
FI-EV71 5
Percent survival (%)
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9
Days post infection (%)

Fig. 8

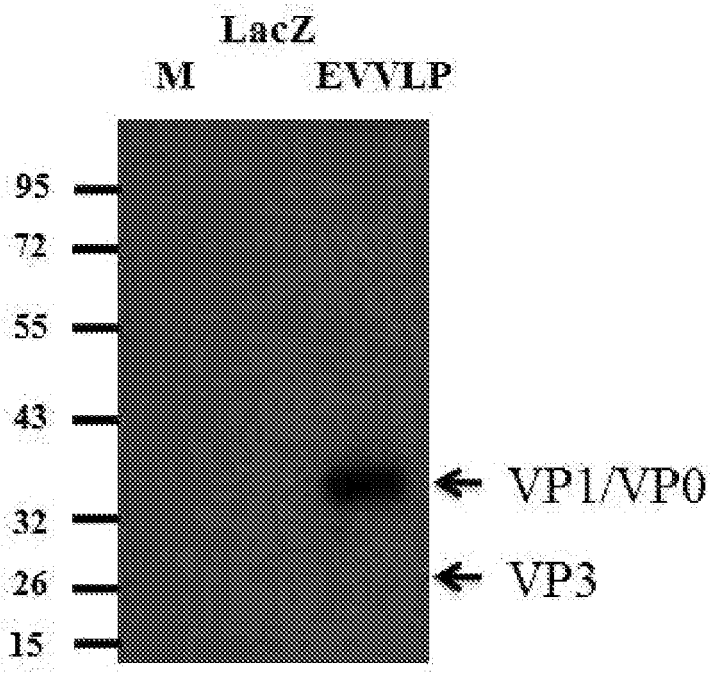
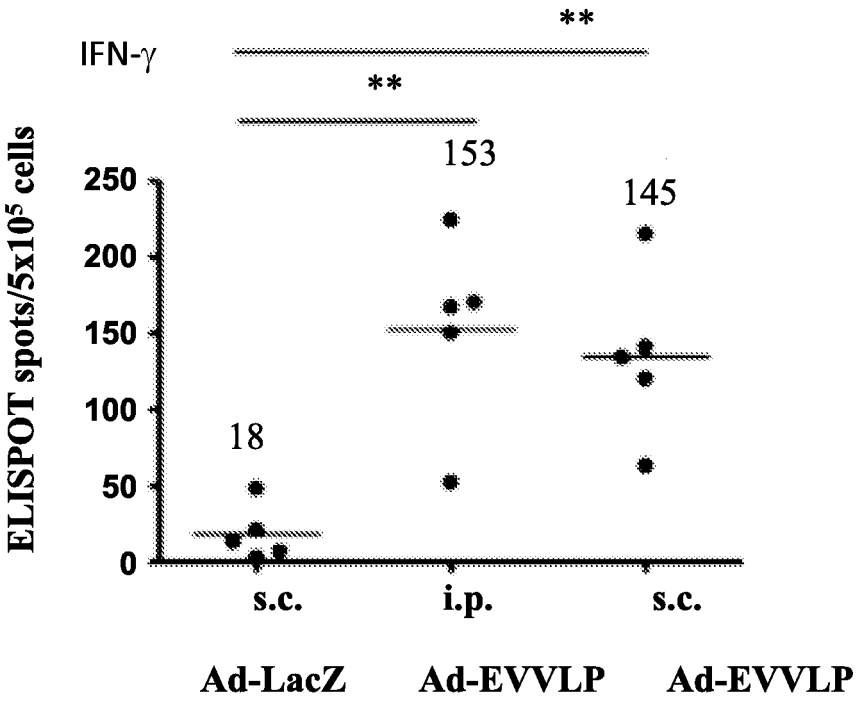


Fig. 9

(A)


IFN-γ
**
**
153
145
18
ELISPOT spots/5x10^5 cells
250
200
150
100
50
0
s.c.
i.p.
s.c.
Ad-LacZ
Ad-EVVLP
Ad-EVVLP

(B)

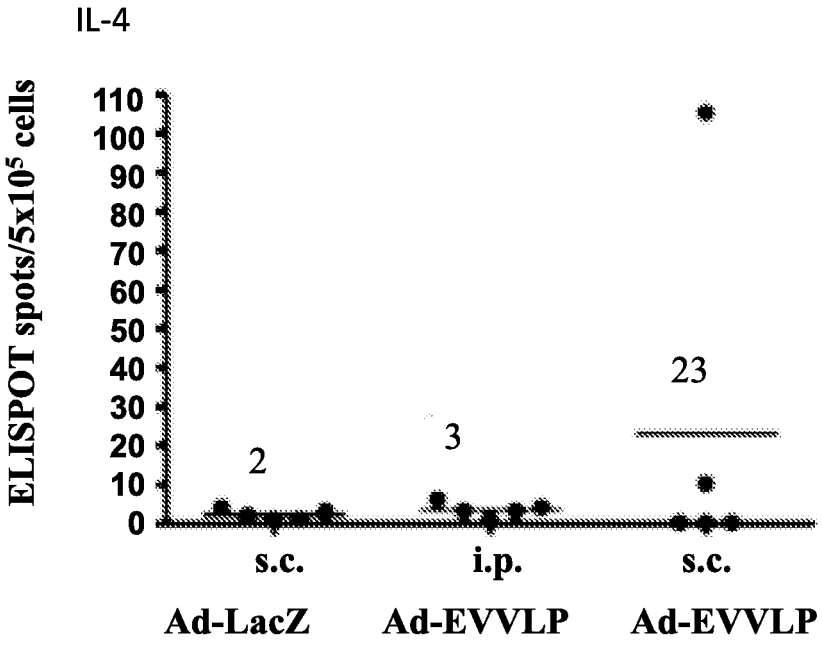

IL-4
ELISPOT spots/5x10^5 cells
110
100
90
80
70
60
50
40
30
20
10
0
2
3
23
s.c.
i.p.
s.c.
Ad-LacZ
Ad-EVVLP
Ad-EVVLP

Fig. 10

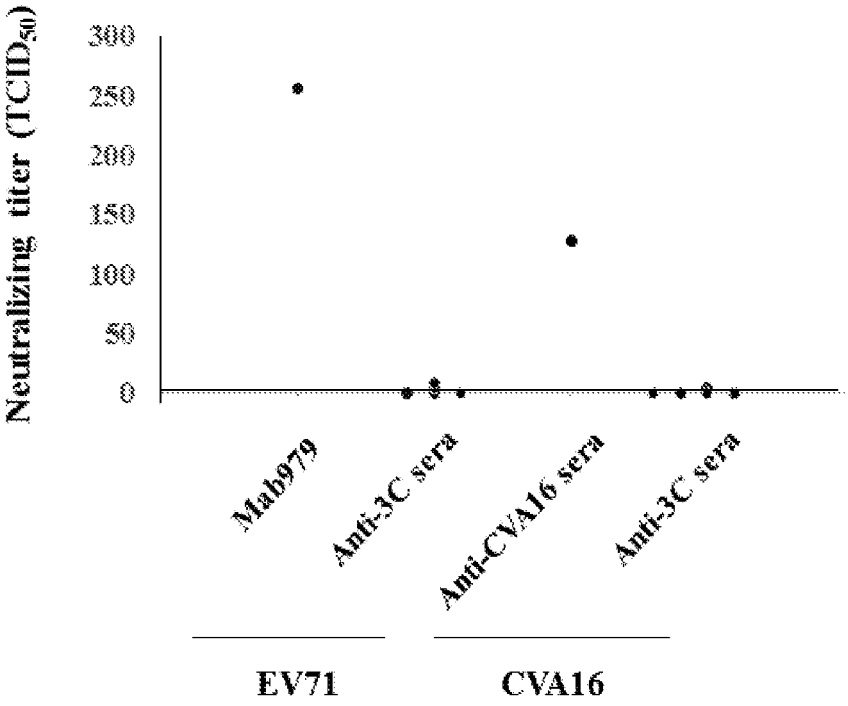

Neutralizing titer (TCID50)
300
250
200
150
100
50
0
Mab979
Anti-3C sera
Anti-CVA16 sera
Anti-3C sera
EV71
CVA16

Fig. 11

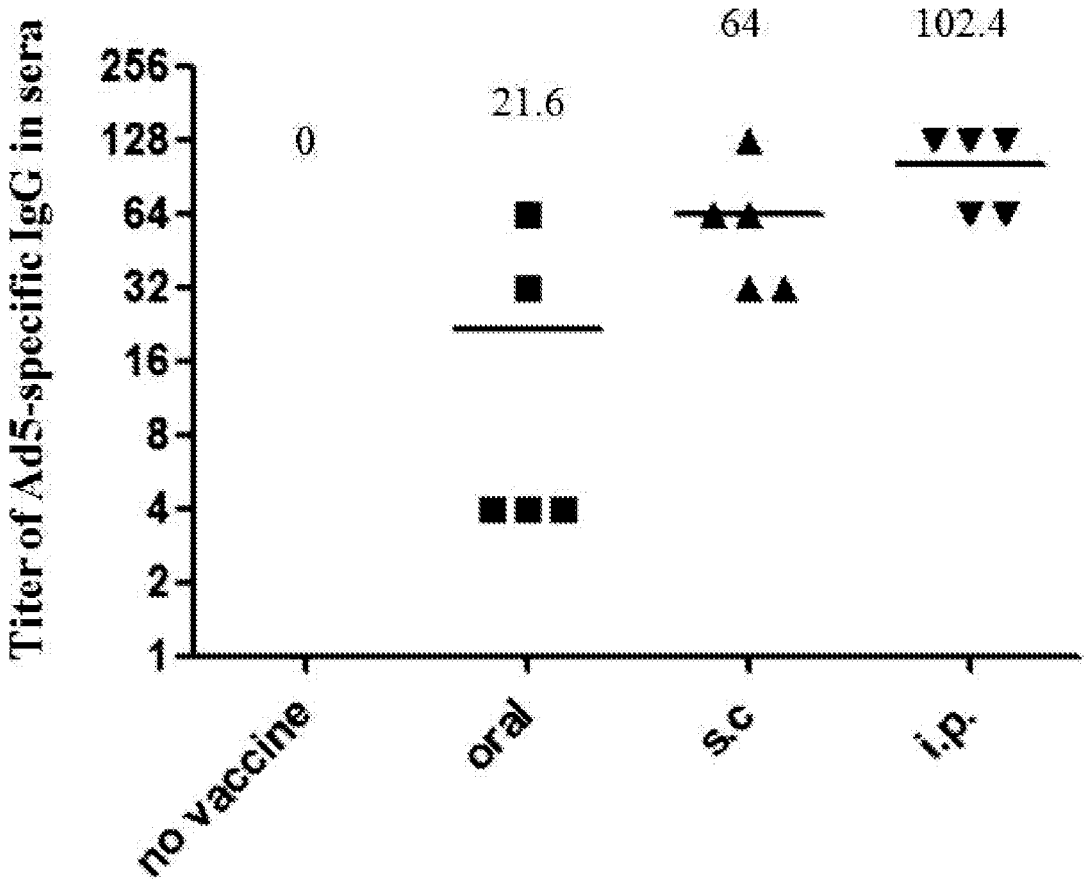

Titer of Ad5-specific IgG in sera
256
128
64
32
16
8
4
2
1
0
21.6
64
102.4
no vaccine
oral
s.c
i.p.

Fig. 12

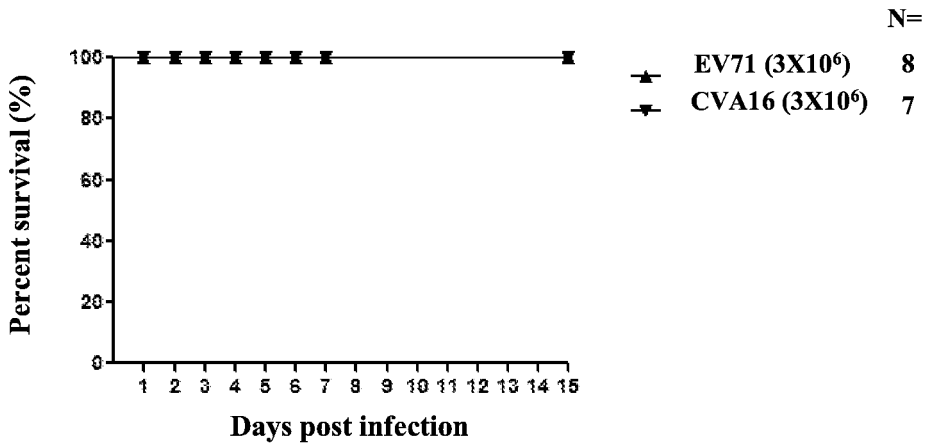

N=
EV71 (3X10⁶) 8
CVA16 (3X10⁶) 7
Percent survival (%)
100
80
60
40
20
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Days post infection

Fig. 13

Sequence of CMP promoter–P1 gene-IRES-3CD gene cassette

CMV promoter

TTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGC

T7 promoter/priming site

TAACTAGAGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCC
AAGCTG GCTAGTTAAGCTATCAACAAGTTTGTACAAAAAAGCAGGCT

P1 gene (Strain: pinf7-54A 746..3331)

ATGGGCTCACAGGTGTCCACACAGCGCTCCGGTTCGCACGAAAACTCTAACTCAGCTACCGA
GGGTTCCACTATAAACTATACTACCATTAATTACTATAAAGATTCCTATGCCGCCACAGCAGGTA
AGCAGAGCCTTAAGCAGGACCCAGACAAGTTTGCAAATCCTGTCAAAGACATCTTCACTGAA
ATGGCAGCGCCATTAAAATCTCCATCTGCCGAGGCATGTGGTTACAGCGATCGGGTGGCACAA
TTAACTATTGGCAATTCTACCATCACTACGCAAGAAGCAGCAAACATCATAGTTGGCTATGGTG
AGTGGCCTTCCTACTGTTCGGACTCTGATGCTACTGCAGTGGACAAACCAACGCGCCCAGATG
TTTCGGTGAATAGGTTTTACACATTGGACACAAAATTGTGGGAGAAATCATCCAAGGGGTGGT
ACTGGAAATTCCCGGATGTGTTAACTGAAACCGGGGTCTTTGGTCAAAATGCACAGTTCCACT
ACCTCTATCGGTCAGGGTTCTGCATTCACGTGCAGTGCAATGCTAGTAAGTTCCACCAAGGAG
CACTCCTAGTCGCTGTCCTCCCAGAGTATGTCATTGGGACAGTGGCAGGTGGCACAGGGACG
GAGGATAGCCACCCCCCTTATAAGCAGACTCAACCCGGTGCTGATGGCTTCGAATTGCAACAC
CCGTACGTGCTTGATGCTGGCATTCCAATATCACAATTAACAGTGTGCCCACATCAGTGGATTA
ATTTGAGGACCAACAATTGTGCCACAATAATAGTGCCGTACATAAACGCACTACCCTTTGATTC
TGCCTTGAACCATTGTAACTTTGGTCTGCTGGTTGTGCCTATTAGCCCGTTAGATTATGACCAA
GGTGCGACGCCAGTGATCCCCATTACTATCACTTTGGCCCCAATGTGTTTTGAATTTGCAGGCT
TTAGACAAGCAGTTACGCAAGGGTTTCCTACTGAGTTGAAACCTGGCACAAACCAATTTTTAA
CCACTGACGATGGCGTCTCAGCACCCATTCTGCCAAACTTTCACCCCACCCCGTGTATCCATAT
ACCCGGTGAAGTTAGAAACTTGCTAGAGCTATGCCAGGTGGAGACCATTTTAGAGGTCAACA
ATGTACCTACGAATGCCACTAGCTTAATGGAGAGACTGCGCTTCCCGGTCTCAGCTCAAGCCG
GGAAAGGTGAGCTATGTGCAGTGTTCAGAGCTGACCCTGGACGAAGTGGGCCATGGCAGTC
CACCTTGTTGGGCCAGTTGTGCGGGTACTACACCCAATGGTCAGGATCACTGGAAGTCACCTT
CATGTTCACCGGGTCCTTTATGGCTACCGGCAAGATGCTCATAGCATACACACCACCAGGAGG
CCCCTTACCCAAGGACCGGGCGACCGCCATGTTGGGCACGGACGTCATCTGGGACTTTGGGC
TGCAATCGTCTGTCACTCTTGTAATACCATGGATCAGCAACACTCATTACAGAGCGCACGCTCG
AGATGGTGTGTTTGACTACTACACTACAGGTTTGGTTAGCATATGGTACCAGACGAATTATGTG
GTTCCAATTGGAGCACCCAATACAGCCTATATAATAGCATTGGCGGCAGCCCAGAAGAACTTC
ACCATGAAGTTGTGTAAGGATGCTAGTGATATCCTACAGACAGGCACTATCCAGGGAGATAGG
GTGGCAGATGTGATTGAGAGTTCTATAGGGGACAGCGTGAGCAGAGCCCTCACCCGAGCTCT
ACCGGCACCTACCGGCCAAGACACACAGGTAAGCAGCCATCGATTAGATACTGGTAAAGGTC
CAGCACTCCAAGCCGCTGAAATTGGAGCATCATCAAATGCTAGTGATGAGAGTATGATTGAGA

Fig. 14 (Cont')

CACGGTGTGTTCTTAATTCACATAGCACAGCTGAGACCACTCTTGATAGCTTCTTCAGCAGAG
CAGGATTAGTTGGAGAGATAGACCTCCCTCTTGAAGGCACAACCAACCCGAATGGGTACGCA
AACTGGGACATAGACATAACAGGTTACGCGCAAATGCGTAGAAAGGTGGAGCTGTTCACCTA
CATGCGTTTTAACGCAGAGATCACCTTTGTTGCATGCACCCCTACCGGGGAAGTTGTCCCGCA
ATTGCTCCAATATATGTTTGTACCACCCGGAGCCCCCAAGCCAGACTCCAGAGAATCTCTCGCA
TGGCAAACTGCCACTAATCCCTCGGTTTTTGTGAAGCTGTCAGACCCCCCAGCACAGGTTTCT
GTTCCATTCATGTCACCTGCGAGCGCCTATCAATGGTTTTATGACGGGTATCCCACATTCGGTG
AACACAAACAGGAGAAAGACCTTGAATACGGGGCATGCCCAAACAACATGATGGGTACGTTC
TCAGTGCGGACTGTAGGCACCTCGAAGTCCAAGTGCCCATTGGTGATCAGGATTTACATGAG
GATGAAGCACGTCAGGGCGTGGATACCTCGCCCAATGCGTAACCAGAACTATCTATTCAAAGC
CAACCCAAATTATGCTGGTAATTCTATTAAACCAACTGGTGCCAGTCGCACAGCAATGAATTC

IRES

TGCATCTAGGGCGGCCAATTCCGCCCCTCTCCCTCCCCCCCCCCTAACGTTACTGGCCGAAGCC
GCTTGGAATAAGGCCGGTGTGCGTTTGTCTATATGTGATTTTCCACCATATTGCCGTCTTTTGG
CAATGTGAGGGCCCGGAAACCTGGCCCTGTCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCC
TCTCGCCAAAGGAATGCAAGGTCTGTTGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTT
CTTGAAGACAAACAACGTCTGTAGCGACCCTTTGCAGGCAGCGGAACCCCCCACCTGGCGAC
AGGTGCCTCTGCGGCCAAAAGCCACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCCA
GTGCCACGTTGTGAGTTGGATAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAA
CAAGGGGCTGAAGGATGCCCAGAAGGTACCCCATTGTATGGGATCTGATCTGGGGCCTCGGT
GCACATGCTTTACATGTGTTTAGTCGAGGTTAAAAAAACGTCTAGGCCCCCCGAACCACGGG
GACGTGGTTTTCCTTTGAAAAACACGATGATAAGCTTGCCAGCGGCCGC

3CD gene (Strain: pinf7-54A 5390..7324)

GGGCCGAGCTTGGACTTCGCCCTATCTCTACTTAGGAGGAACATTAGGCAGGTCCAAACCGA
CCAGGGCCACTTTACAATGTTAGGAGTGCGAGACCGCTTGGCTGTGCTCCCCAGACACTCCC
AACCAGGAAAGACCATCTGGGTTGAACACAAATTAGTGAAGATCGTAGATGCTGTGGAGTTA
GTAGACGAACAAGGGGTTAACTTAGAGCTCACACTGGTAACGCTTGATACTAACGAAAAATTT
AGAGACATCACAAGATTCATACCAGAAACAATTAGTCCTGCTAGTGATGCCACTTTAGTTATAA
ATACTGAACATATGCCCAGTATGTTTGTGCCAGTTGGAGATGTGGTCCAGTATGGGTTTTTGAA
CCTTAGTGGTAAGCCCACTCACAGGACTATGATGTACAATTTCCCAACAAAAGCAGGACAGTG
TGGTGGTGTTGTGACTGCCGTGGGTAAAGTGATTGGGATCCACATTGGTGGCAACGGTAGAC
AAGGTTTCTGCGCTGCCCTGAAGAGGGGATACTTTTGCAGTGAACAAGGTGAGATCCAATGG
ATGAAGCCCAACAAAGAAACTGGCAGGTTGAACATCAACGGACCTACTCGCACTAAGCTTGA
ACCAAGTGTCTTTCACGATGTGTTCGAAGGCACTAAAGAGCCAGCAGTGCTGACTAGTAAAG
ACCCAAGGCTGGAAGTTGACTTTGAACAGGCTCTTTTTTCAAAATACGTGGGGAACACGCTT
CATGAACCCGACGAGTTTGTCAAGGAGGCGGCCCTACATTATGCCAACCAACTCAAGCAGTT
AGATATCAAGACCACCAAGATGAGCATGGAGGATGCATGTTACGGCACAGAGAACCTGGAAG
CTATAGATCTTCACACAAGTGCAGGATATCCATACAGTGCACTAGGCATCAAGAAAAAGGACA

Fig. 14 (Cont')

TTTTGGATCCAACAACTCGCGATGTCAGCAAGATGAAATTCTACATGGACAAGTATGGGTTGG
ATCTACCGTACTCTACTTATGTTAAAGATGAACTTAGGGCCATCGACAAGATCAAGAAAGGGA
AGTCTCGTCTCATAGAAGCGAGCAGTCTAAATGACTCAGTGTACTTGAGAATGACATTTGGGC
ACCTTTATGAAGCTTTCCACGCCAATCCAGGTACAATCACTGGTTCAGCTGTTGGGTGCAACC
CAGATGTGTTCTGGAGCAAGTTACCAATTCTACTTTCAGGATCGCTTTTCGCGTTTGACTACTC
GGGGTATGACGCTAGTCTCAGCCCAGTGTGGTTCAGGGCGCTGGAGATAGTCCTGCGGGAAA
TTGGATACTCCGAAGACGCAGTGTCTCTCATAGAAGGGATCAATCACACCCATCATGTGTACCG
CAATAAAACTTATTGTGTTCTTGGGGGAATGCCCTCAGGTTGCTCAGGCACCTCCATTTTCAAC
TCGATGATCAACAATATCATTATTAGAACACTCCTGATTAAAACATTCAAAGGGATAGATCTAAA
TGAACTGAACATGGTGGCCTACGGGGATGATGTGTTGGCTAGTTACCCCTTCCCAATTGACTG
TCTGGAGTTGGCAAGAACAGGCAAGGAGTATGGTCTAACTATGACCCCTGCCGACAAGTCAC
CCTGCTTTAATGAGGTTACGTGGGAGAATGCCACTTTCTTGAAGAGAGGATTCTTGCCTGATT
ATCAATTCCCGTTTCTCATCCACCCTACGATGCCAATGAGGGAGATTCACGAATCCATTCGTTG
GACCAAAGATGCACGAAGTACTCAAGATCACGTGCGCTCCCTCTGCTTATTAGCATGGCTCAA
CGGGAAAGAGGAGTATGAAAAATTTGTGAGTGCAATCAGATCAGTTCCAATTGGAAAAGCAT
TGGCTA TACCAAATTATGAGAATCTGAGGAGAAATTGGCTCGAATTGTTTT

Fig. 14

Sequence of CMP promoter–P1 gene-EF-1α promoter-3CD gene cassette

CMV promoter

TTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTCTGGC

T7 promoter/priming site

TAACTAGAGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCC
AAGCTG GCTAGTTAAGCTATCAACAAGTTTGTACAAAAAAGCAGGCT

P1 gene (Strain: pinf7-54A 746..3331)

ATGGGCTCACAGGTGTCCACACAGCGCTCCGGTTCGCACGAAAACTCTAACTCAGCTACCGA
GGGTTCCACTATAAACTATACTACCATTAATTACTATAAAGATTCCTATGCCGCCACAGCAGGTA
AGCAGAGCCTTAAGCAGGACCCAGACAAGTTTGCAAATCCTGTCAAAGACATCTTCACTGAA
ATGGCAGCGCCATTAAAATCTCCATCTGCCGAGGCATGTGGTTACAGCGATCGGGTGGCACAA
TTAACTATTGGCAATTCTACCATCACTACGCAAGAAGCAGCAAACATCATAGTTGGCTATGGTG
AGTGGCCTTCCTACTGTTCGGACTCTGATGCTACTGCAGTGGACAAACCAACGCGCCCAGATG
TTTCGGTGAATAGGTTTTACACATTGGACACAAAATTGTGGGAGAAATCATCCAAGGGGTGGT
ACTGGAAATTCCCGGATGTGTTAACTGAAACCGGGGTCTTTGGTCAAAATGCACAGTTCCACT
ACCTCTATCGGTCAGGGTTCTGCATTCACGTGCAGTGCAATGCTAGTAAGTTCCACCAAGGAG
CACTCCTAGTCGCTGTCCTCCCAGAGTATGTCATTGGGACAGTGGCAGGTGGCACAGGGACG
GAGGATAGCCACCCCCCTTATAAGCAGACTCAACCCGGTGCTGATGGCTTCGAATTGCAACAC
CCGTACGTGCTTGATGCTGGCATTCCAATATCACAATTAACAGTGTGCCCACATCAGTGGATTA
ATTTGAGGACCAACAATTGTGCCACAATAATAGTGCCGTACATAAACGCACTACCCTTTGATTC
TGCCTTGAACCATTGTAACTTTGGTCTGCTGGTTGTGCCTATTAGCCCGTTAGATTATGACCAA
GGTGCGACGCCAGTGATCCCCATTACTATCACTTTGGCCCCAATGTGTTTTGAATTTGCAGGCT
TTAGACAAGCAGTTACGCAAGGGTTTCCTACTGAGTTGAAACCTGGCACAAACCAATTTTTAA
CCACTGACGATGGCGTCTCAGCACCCATTCTGCCAAACTTTCACCCCACCCCGTGTATCCATAT
ACCCGGTGAAGTTAGAAACTTGCTAGAGCTATGCCAGGTGGAGACCATTTTAGAGGTCAACA
ATGTACCTACGAATGCCACTAGCTTAATGGAGAGACTGCGCTTCCCGGTCTCAGCTCAAGCCG
GGAAAGGTGAGCTATGTGCAGTGTTCAGAGCTGACCCTGGACGAAGTGGGCCATGGCAGTC
CACCTTGTTGGGCCAGTTGTGCGGGTACTACACCCAATGGTCAGGATCACTGGAAGTCACCTT
CATGTTCACCGGGTCCTTTATGGCTACCGGCAAGATGCTCATAGCATACACACCACCAGGAGG
CCCCTTACCCAAGGACCGGGCGACCGCCATGTTGGGCACGGACGTCATCTGGGACTTTGGGC
TGCAATCGTCTGTCACTCTTGTAATACCATGGATCAGCAACACTCATTACAGAGCGCACGCTCG
AGATGGTGTGTTTGACTACTACACTACAGGTTTGGTTAGCATATGGTACCAGACGAATTATGTG
GTTCCAATTGGAGCACCCAATACAGCCTATATAATAGCATTGGCGGCAGCCCAGAAGAACTTC
ACCATGAAGTTGTGTAAGGATGCTAGTGATATCCTACAGACAGGCACTATCCAGGGAGATAGG
GTGGCAGATGTGATTGAGAGTTCTATAGGGGACAGCGTGAGCAGAGCCCTCACCCGAGCTCT
ACCGGCACCTACCGGCCAAGACACACAGGTAAGCAGCCATCGATTAGATACTGGTAAAGGTC

Fig. 15 (Cont')

CAGCACTCCAAGCCGCTGAAATTGGAGCATCATCAAATGCTAGTGATGAGAGTATGATTGAGA
CACGGTGTGTTCTTAATTCACATAGCACAGCTGAGACCACTCTTGATAGCTTCTTCAGCAGAG
CAGGATTAGTTGGAGAGATAGACCTCCCTCTTGAAGGCACAACCAACCCGAATGGGTACGCA
AACTGGGACATAGACATAACAGGTTACGCGCAAATGCGTAGAAAGGTGGAGCTGTTCACCTA
CATGCGTTTTAACGCAGAGATCACCTTTGTTGCATGCACCCCTACCGGGGAAGTTGTCCCGCA
ATTGCTCCAATATATGTTTGTACCACCCGGAGCCCCCAAGCCAGACTCCAGAGAATCTCTCGCA
TGGCAAACTGCCACTAATCCCTCGGTTTTTGTGAAGCTGTCAGACCCCCCAGCACAGGTTTCT
GTTCCATTCATGTCACCTGCGAGCGCCTATCAATGGTTTTATGACGGGTATCCCACATTCGGTG
AACACAAACAGGAGAAAGACCTTGAATACGGGGCATGCCCAAACAACATGATGGGTACGTTC
TCAGTGCGGACTGTAGGCACCTCGAAGTCCAAGTGCCCATTGGTGATCAGGATTTACATGAG
GATGAAGCACGTCAGGGCGTGGATACCTCGCCCAATGCGTAACCAGAACTATCTATTCAAAGC
CAACCCAAATTATGCTGGTAATTCTATTAAACCAACTGGTGCCAGTCGCACAGCAATGAATTC

EF-1α promoter

GTGAGGCTCCGGTGCCCGTCAGTGGGCAGAGCGCACATCGCCCACAGTCCCCGAGAAGTTG
GGGGGAGGGGTCGGCAATTGAACCGGTGCCTAGAGAAGGTGGCGCGGGGTAAACTGGGA
AAGTGATGTCGTGTACTGGCTCCGCCTTTTTCCCGAGGGTGGGGGAGAACCGTATATAAGTGC
AGTAGTCGCCGTGAACGTTCTTTTTCGCAACGGGTTTGCCGCCAGAACACAGGTAAGTGCCG
TGTGTGGTTCCCGCGGGCCTGGCCTCTTTACGGGTTATGGCCCTTGCGTGCCTTGAATTACTTC
CACCTGGCTGCAGTACGTGATTCTTGATCCCGAGCTTCGGGTTGGAAGTGGGTGGGAGAGTT
CGAGGCCTTGCGCTTAAGGAGCCCCTTCGCCTCGTGCTTGAGTTGAGGCCTGGCCTGGGCGC
TGGGGCCGCCGCGTGCGAATCTGGTGGCACCTTCGCGCCTGTCTCGCTGCTTTCGATAAGTCT
CTAGCCATTTAAAATTTTTGATGACCTGCTGCGACGCTTTTTTTCTGGCAAGATAGTCTTGTAA
ATGCGGGCCAAGATCTGCACACTGGTATTTCGGTTTTTGGGGTCGCGGGCGGCGACGGGGC
CCGTGCGTCCCAGCGCACATGTTCGGCGAGGCGGGGCCTGCGAGCGCGGCCACCGAGAATC
GGACGGGGGTAGTCTCAAGCTGGCCGGCCTGCTCTGGTGCCTGGCCTCGCGCCGCCGTGTAT
CGCCCCGCCCTGGGCGGCAAGGCTGGCCCGGTCGGCACCAGTTGCGTGAGCGGAAAGATG
GCCGCTTCCCGGCCCTGCTGCAGGGAGCTCAAAATGGAGGACGCGGCGCTCGGGAGAGCG
GGCGGGTGAGTCACCCACACAAAGGAAAAGGGCCTTTCCGTCCTCAGCCGTCGCTTCATGTG
ACTCCACGGAGTACCGGGCGCCGTCCAGGCACCTCGATTAGTTCTCGAGCTTTTGGAGTACG
TCGTCTTTAGGTTGGGGGGAGGGGTTTTATGCGATGGAGTTTCCCCACACTGAGTGGGTGGA
GACTGAAGTTAGGCCAGCTTGGCACTTGATGTAATTCTCCTTGGAATTTGCCCTTTTTGAGTTT
GGATCTTGGTTCATTCTCAAGCCTCAGACAGTGGTTCAAAGTTTTTTTCTTCCATTTCAGGTGT
CGTGAAAA GCGGCCGC

3CD gene (Strain: pinf7-54A 5390..7324)

GGGCCGAGCTTGGACTTCGCCCTATCTCTACTTAGGAGGAACATTAGGCAGGTCCAAACCGA
CCAGGGCCACTTTACAATGTTAGGAGTGCGAGACCGCTTGGCTGTGCTCCCCAGACACTCCC
AACCAGGAAAGACCATCTGGGTTGAACACAAATTAGTGAAGATCGTAGATGCTGTGGAGTTA
GTAGACGAACAAGGGGTTAACTTAGAGCTCACACTGGTAACGCTTGATACTAACGAAAAATTT

Fig. 15 (Cont')

AGAGACATCACAAGATTCATACCAGAAACAATTAGTCCTGCTAGTGATGCCACTTTAGTTATAA
ATACTGAACATATGCCCAGTATGTTTGTGCCAGTTGGAGATGTGGTCCAGTATGGGTTTTTGAA
CCTTAGTGGTAAGCCCACTCACAGGACTATGATGTACAATTTCCCAACAAAAGCAGGACAGTG
TGGTGGTGTTGTGACTGCCGTGGGTAAAGTGATTGGGATCCACATTGGTGGCAACGGTAGAC
AAGGTTTCTGCGCTGCCCTGAAGAGGGGATACTTTTGCAGTGAACAAGGTGAGATCCAATGG
ATGAAGCCCAACAAAGAAACTGGCAGGTTGAACATCAACGGACCTACTCGCACTAAGCTTGA
ACCAAGTGTCTTTCACGATGTGTTCGAAGGCACTAAAGAGCCAGCAGTGCTGACTAGTAAAG
ACCCAAGGCTGGAAGTTGACTTTGAACAGGCTCTTTTTTCAAAATACGTGGGGAACACGCTT
CATGAACCCGACGAGTTTGTCAAGGAGGCGGCCCTACATTATGCCAACCAACTCAAGCAGTT
AGATATCAAGACCACCAAGATGAGCATGGAGGATGCATGTTACGGCACAGAGAACCTGGAAG
CTATAGATCTTCACACAAGTGCAGGATATCCATACAGTGCACTAGGCATCAAGAAAAAGGACA
TTTTGGATCCAACAACTCGCGATGTCAGCAAGATGAAATTCTACATGGACAAGTATGGGTTGG
ATCTACCGTACTCTACTTATGTTAAAGATGAACTTAGGGCCATCGACAAGATCAAGAAAGGGA
AGTCTCGTCTCATAGAAGCGAGCAGTCTAAATGACTCAGTGTACTTGAGAATGACATTTGGGC
ACCTTTATGAAGCTTTCCACGCCAATCCAGGTACAATCACTGGTTCAGCTGTTGGGTGCAACC
CAGATGTGTTCTGGAGCAAGTTACCAATTCTACTTTCAGGATCGCTTTTCGCGTTTGACTACTC
GGGGTATGACGCTAGTCTCAGCCCAGTGTGGTTCAGGGCGCTGGAGATAGTCCTGCGGGAAA
TTGGATACTCCGAAGACGCAGTGTCTCTCATAGAAGGGATCAATCACACCCATCATGTGTACCG
CAATAAAACTTATTGTGTTCTTGGGGGAATGCCCTCAGGTTGCTCAGGCACCTCCATTTTCAAC
TCGATGATCAACAATATCATTATTAGAACACTCCTGATTAAAACATTCAAAGGGATAGATCTAAA
TGAACTGAACATGGTGGCCTACGGGGATGATGTGTTGGCTAGTTACCCCTTCCCAATTGACTG
TCTGGAGTTGGCAAGAACAGGCAAGGAGTATGGTCTAACTATGACCCCTGCCGACAAGTCAC
CCTGCTTTAATGAGGTTACGTGGGAGAATGCCACTTTCTTGAAGAGAGGATTCTTGCCTGATT
ATCAATTCCCGTTTCTCATCCACCCTACGATGCCAATGAGGGAGATTCACGAATCCATTCGTTG
GACCAAAGATGCACGAAGTACTCAAGATCACGTGCGCTCCCTCTGCTTATTAGCATGGCTCAA
CGGGAAAGAGGAGTATGAAAAATTTGTGAGTGCAATCAGATCAGTTCCAATTGGAAAAGCAT
TGGCTA TACCAAATTATGAGAATCTGAGGAGAAATTGGCTCGAATTGTTTT

Fig. 15

- 3C amino acid sequence(183 A.A)

GPSLDFALSLLRRNIRQVQTDQGHFTMLGVRDRLAVLPRHSQPGKTIWVEHKL
VKIVDAVELVDEQGVNLELTLVTLDTNEKFRDITRFIPETISPASDATLVINT
EHMPSMFVPVGDVVQYGFLNLSGKPTHRTMMYNFPTKAGQCGGVVTAVGKVIG
IHIGGNGRQGFCAALKRGYFCSEQ

- 3D amino acid sequence (462 A.A)

GEIQWMKPNKETGRLNINGPTRTKLEPSVFHDVFEGTKEPAVLTSKDPRLEVD
FEQALFSKYVGNTLHEPDEFVKEAALHYANQLKQLDIKTTKMSMEDACYGTEN
LEAIDLHTSAGYPYSALGIKKKDILDPTTRDVSKMKFYMDKYGLDLPYSTYVK
DELRAIDKIKKGKSRLIEASSLNDSVYLRMTFGHLYEAFHANPGTITGSAVGC
NPDVFWSKLPILLSGSLFAFDYSGYDASLSPVWFRALEIVLREIGYSEDAVSL
IEGINHTHHVYRNKTYCVLGGMPSGCSGTSIFNSMINNIIIRTLLIKTFKGID
LNELNMVAYGDDVLASYPFPIDCLELARTGKEYGLTMTPADKSPCFNEVTW
ENATFLKRGFLPDYQFPFLIHPTMPMREIHESIRWTKDARSTQDHVRSLCLLA
WLNGKEE YEKFVSAIRSVPIGKALAIPNYENLRRNWLELF

- 3CD amino acid sequence (645 A.A)

GPSLDFALSLLRRNIRQVQTDQGHFTMLGVRDHLAVLPRHSQPG
KTIWVEHKLVKIVDAVELVDEQGVNLELTLITLDTNEKFRDITRFIPETINPASDATL
VINTEHMPSMFVPVGDVVQYGFLNLSGKPTHRTMMYNFPTKAGQCGGVVTAVGKVIGI
HIGGNGRQGFCAALKRGYFCSEQGEIQWMKSNKETGRLNINGPTRTKLEPSVFHDVFE
GTKEPAVLTSKDPRLEVDFEQALFSKYVGNTLHEPDEFVKEAALHYANQLKQLDIKTT
KMSMEDACYGTENLEAIDLHTSAGYPYSALGIKKKDILDPTTRDVSRMKFYMDKYGLD
LPYSTYVKDELRAIDKIKKGKSRLIEASSLNDSVYLRMTFGHLYEAFHANPGTVTGSA
VGCNPDVFWSKLPILLPGSLFAFDYSGYDASLSPVWFRALEIVLREIGYSEDAVSLIE
GINHTHHVYRNKTYCVLGGMPSGCSGTSIFNSMINNIIIRTLLIKTFKGIDLDELNMV
AYGDDVLASYPFPIDCLELARTGKEYGLTMTPADKSPCFNEVTWENATFLKRGFLPDH
QFPFLIHPTMPMREIHESIRWTKDARNTQDHVRSLCLLAWHNGKEEYEKFVSTIRSVP
IGKALAIPNFENLRRNWLELF

Fig. 16

• P1 (862 A.A)

MGSQVSTQRSGSHENSNSATEGSTINYTTINYYKDSYAATAGKQSLKQDPDKFANPVKDI
FTEMAAPLKSPSAEACGYSDRVAQLTIGNSTITTQEAANIIVGYGEWPSYCSDSDATAVD
KPTRPDVSVNRFYTLDTKLWEKSSKGWYWKFPDVLTETGVFGQNAQFHYLYRSGFCIHVQ
CNASKFHQGALLVAVLPEYVIGTVAGGTGTEDSHPPYKQTQPGADGFELQHPYVLDAGIP
ISQLTVCPHQWINLRTNNCATIIVPYINALPFDSALNHCNFGLLVVPISPLDYDQGATPV
IPITITLAPMCFEFAGFRQAVTQGFPTELKPGTNQFLTTDDGVSAPILPNFHPTPCIHIP
GEVRNLLELCQVETILEVNNVPTNATSLMERLRFPVSAQAGKGELCAVFRADPGRSGPWQ
STLLGQLCGYYTQWSGSLEVTFMFTGSFMATGKMLIAYTPPGGPLPKDRATAMLGTDVIW
DFGLQSSVTLVIPWISNTHYRAHARDGVFDYYTTGLVSIWYQTNYVVPIGAPNTAYIIAL
AAAQKNFTMKLCKDASDILQTGTIQGDRVADVIESSIGDSVSRALTRALPAPTGQDTQVS
SHRLDTGKGPALQAAEIGASSNASDESMIETRCVLNSHSTAETTLDSFFSRAGLVGEIDL
PLEGTTNPNGYANWDIDITGYAQMRRKVELFTYMRFNAEITFVACTPTGEVVPQLLQYMF
VPPGAPKPDSRESLAWQTATNPSVFVKLSDPPAQVSVPFMSPASAYQWFYDGYPTFGEHK
QEKDLEYGACPNNMMGTFSVRTVGTSKSKCPLVIRIYMRMKHVRAWIPRPMRNQNYLFKA
NPNYAGNSIKPTGASRTAITTL

Fig. 17