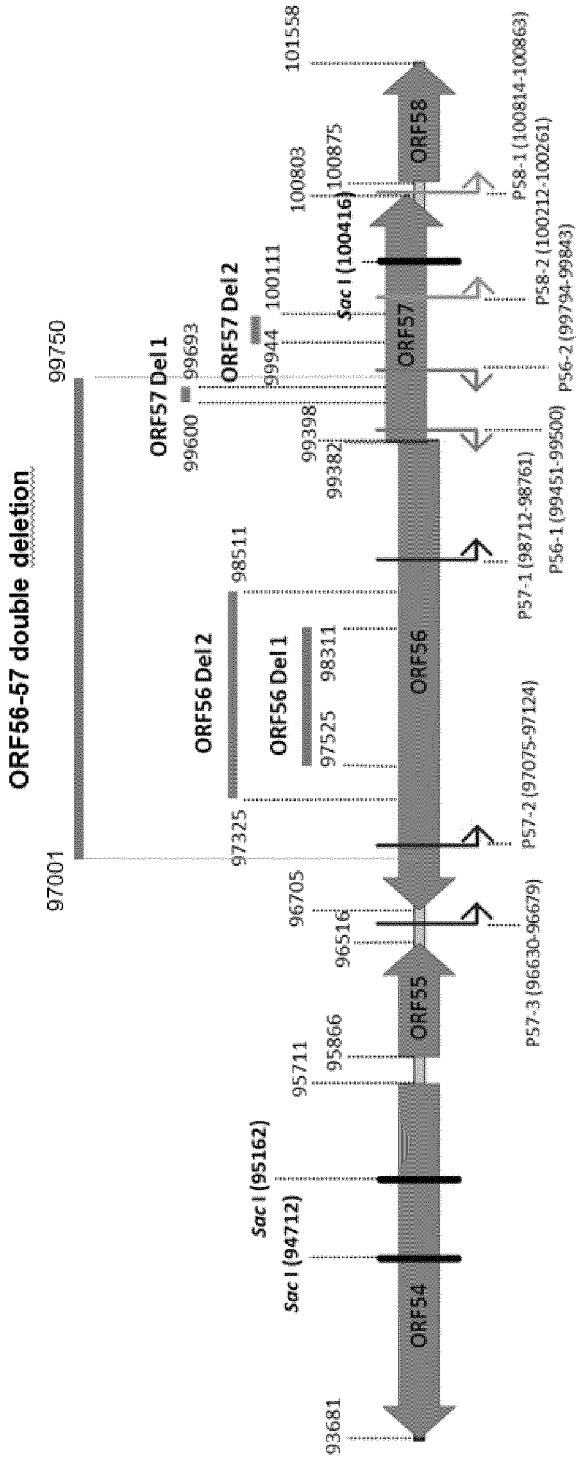

ORF56-57 double deletion
97001
99750
ORF57 Del 1
99600
99693
ORF57 Del 2
99944
100111
ORF56 Del 2
97325
98511
ORF56 Del 1
97525
98311
99382
99398
100803
100875
101558
Sac I (100416)
Sac I (95162)
Sac I (94712)
95711
95866
96516
96705
93681
ORF54
ORF55
ORF56
ORF57
ORF58
P57-3 (96630-96679)
P57-2 (97075-97124)
P57-1 (98712-98761)
P56-1 (99451-99500)
P56-2 (99794-99843)
P58-2 (100212-100261)
P58-1 (100814-100863)

Figure 1

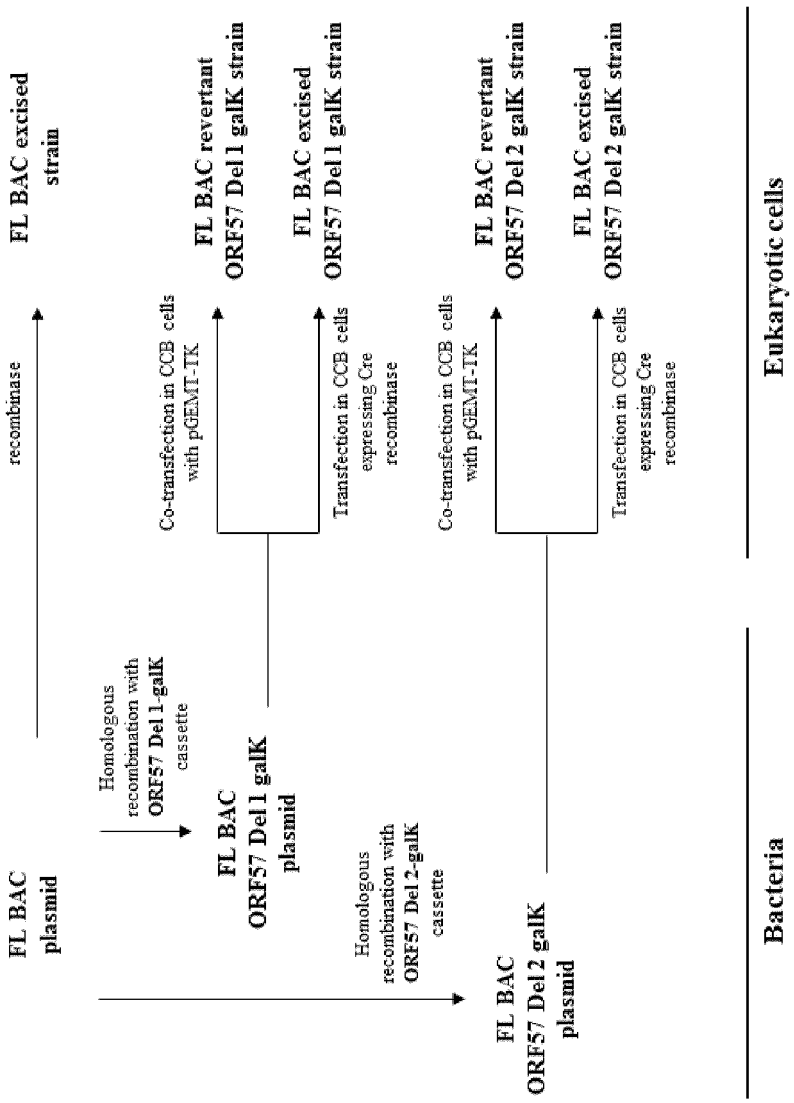

FL BAC plasmid
Transfection in CCB cells expressing Cre recombinase
FL BAC excised strain
Homologous recombination with ORF57 Del 1-galK cassette
FL BAC ORF57 Del 1 galK plasmid
Co-transfection in CCB cells with pGEMT-TK
FL BAC revertant ORF57 Del 1 galK strain
Transfection in CCB cells expressing Cre recombinase
FL BAC excised ORF57 Del 1 galK strain
Homologous recombination with ORF57 Del 2-galK cassette
FL BAC ORF57 Del 2 galK plasmid
Co-transfection in CCB cells with pGEMT-TK
FL BAC revertant ORF57 Del 2 galK strain
Transfection in CCB cells expressing Cre recombinase
FL BAC excised ORF57 Del 2 galK strain
Bacteria
Eukaryotic cells

Figure 2

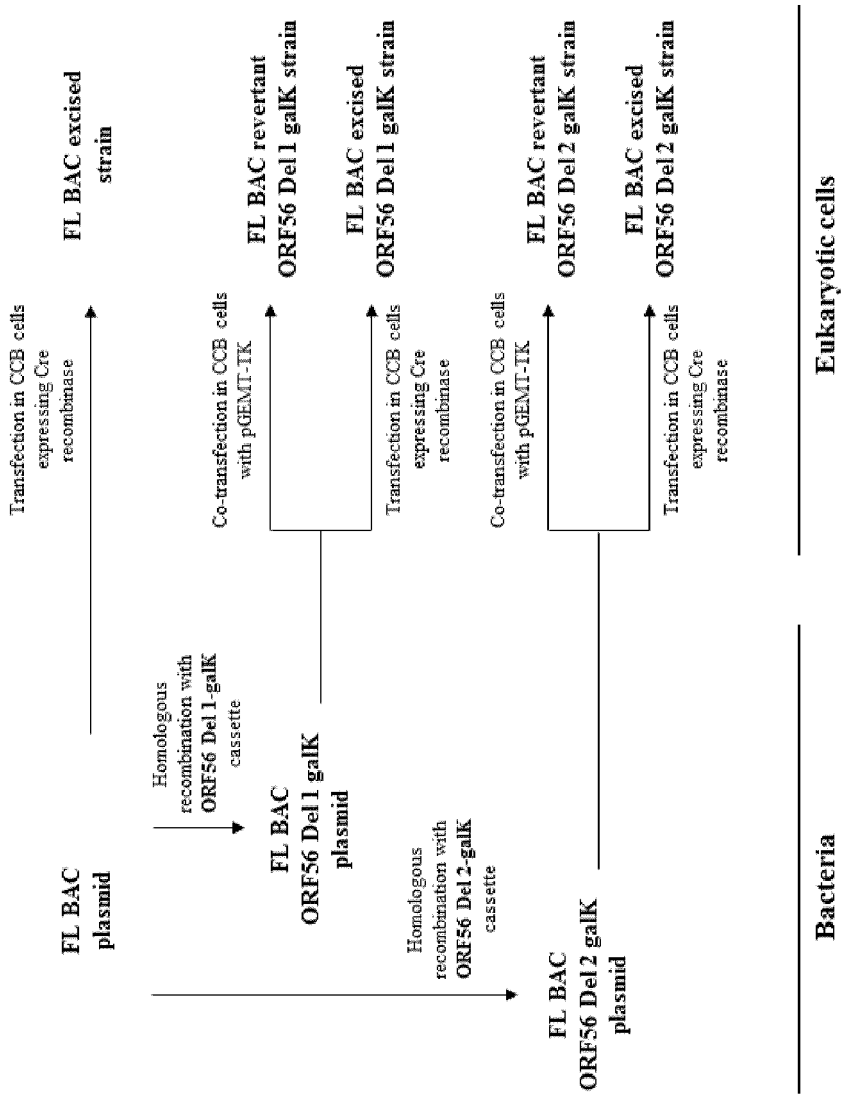

FL BAC plasmid
Homologous recombination with ORF56 Del 1-galK cassette
FL BAC ORF56 Del 1 galK plasmid
Homologous recombination with ORF56 Del 2-galK cassette
FL BAC ORF56 Del 2 galK plasmid
Transfection in CCB cells expressing Cre recombinase
FL BAC excised strain
Co-transfection in CCB cells with pGEMT-TK
FL BAC revertant ORF56 Del 1 galK strain
Transfection in CCB cells expressing Cre recombinase
FL BAC excised ORF56 Del 1 galK strain
Co-transfection in CCB cells with pGEMT-TK
FL BAC revertant ORF56 Del 2 galK strain
Transfection in CCB cells expressing Cre recombinase
FL BAC excised ORF56 Del 2 galK strain
Bacteria
Eukaryotic cells

Figure 3

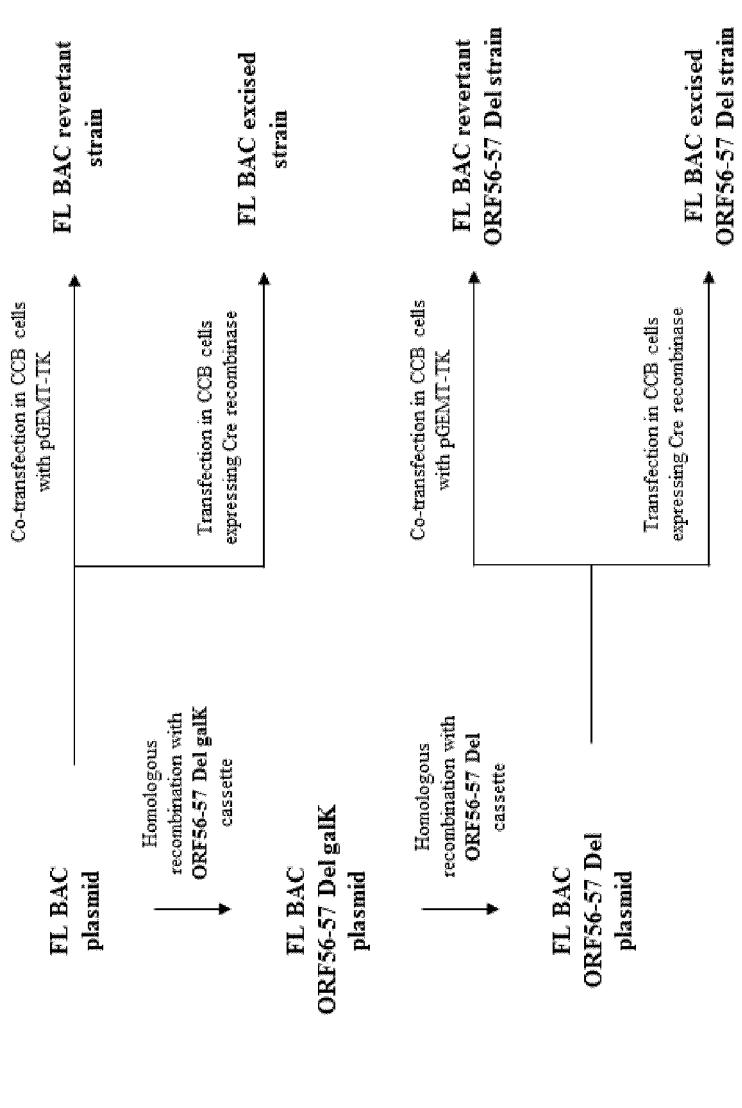

FL BAC plasmid
Homologous recombination with ORF56-57 Del galK cassette
FL BAC ORF56-57 Del galK plasmid
Co-transfection in CCB cells with pGEMT-TK
FL BAC revertant strain
Transfection in CCB cells expressing Cre recombinase
FL BAC excised strain
FL BAC ORF56-57 Del plasmid
Homologous recombination with ORF56-57 Del cassette
Co-transfection in CCB cells with pGEMT-TK
FL BAC revertant ORF56-57 Del strain
Transfection in CCB cells expressing Cre recombinase
FL BAC excised ORF56-57 Del strain
Bacteria
Eukaryotic cells

Figure 4

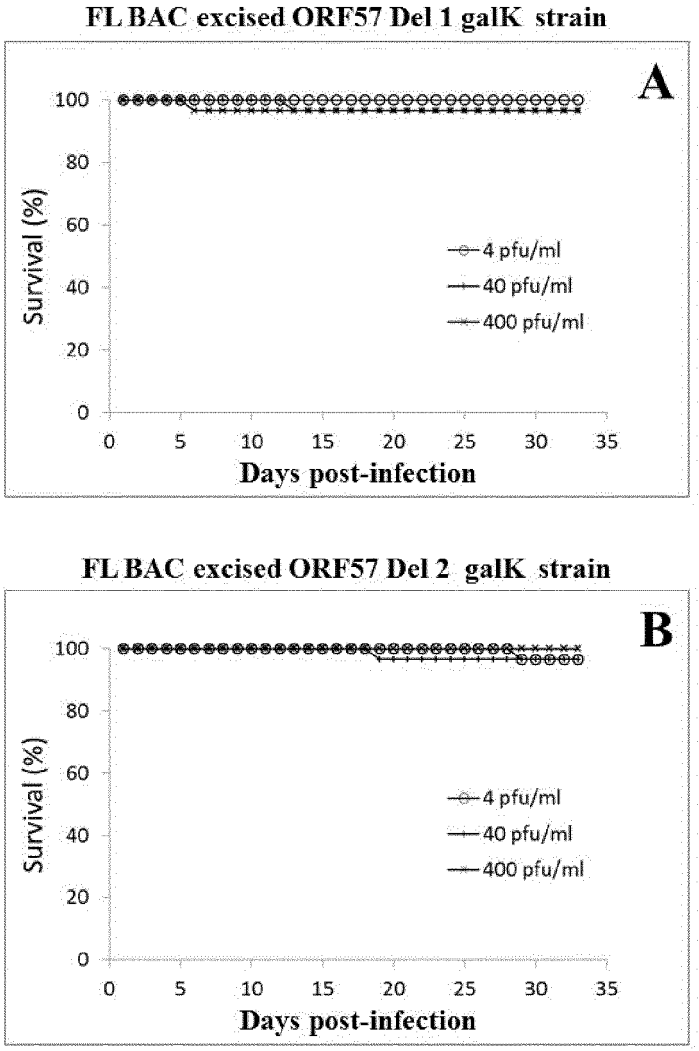

FL BAC excised ORF57 Del 1 galK strain
A
Survival (%)
100
80
60
40
20
0
0
5
10
15
20
25
30
35
Days post-infection
4 pfu/ml
40 pfu/ml
400 pfu/ml
FL BAC excised ORF57 Del 2 galK strain
B
Survival (%)
100
80
60
40
20
0
0
5
10
15
20
25
30
35
Days post-infection
4 pfu/ml
40 pfu/ml
400 pfu/ml

Figure 5A, 5B

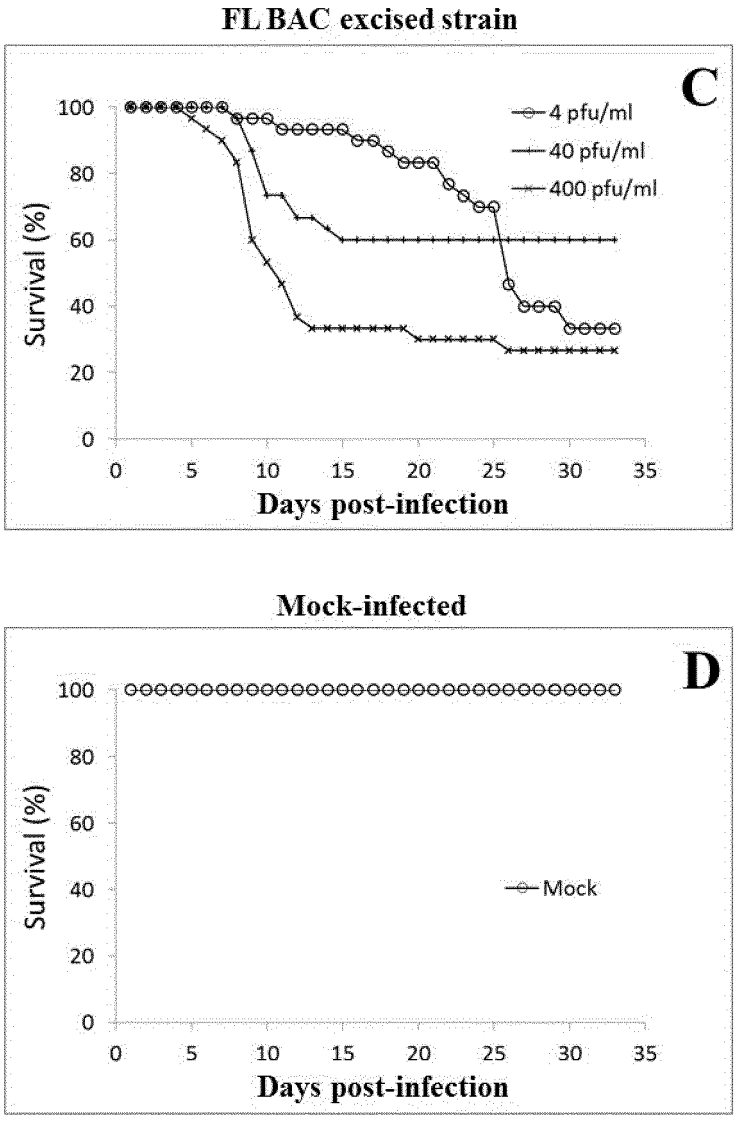

FL BAC excised strain
C
4 pfu/ml
40 pfu/ml
400 pfu/ml
Survival (%)
Days post-infection
Mock-infected
D
Mock
Survival (%)
Days post-infection

Figure 5C, 5D

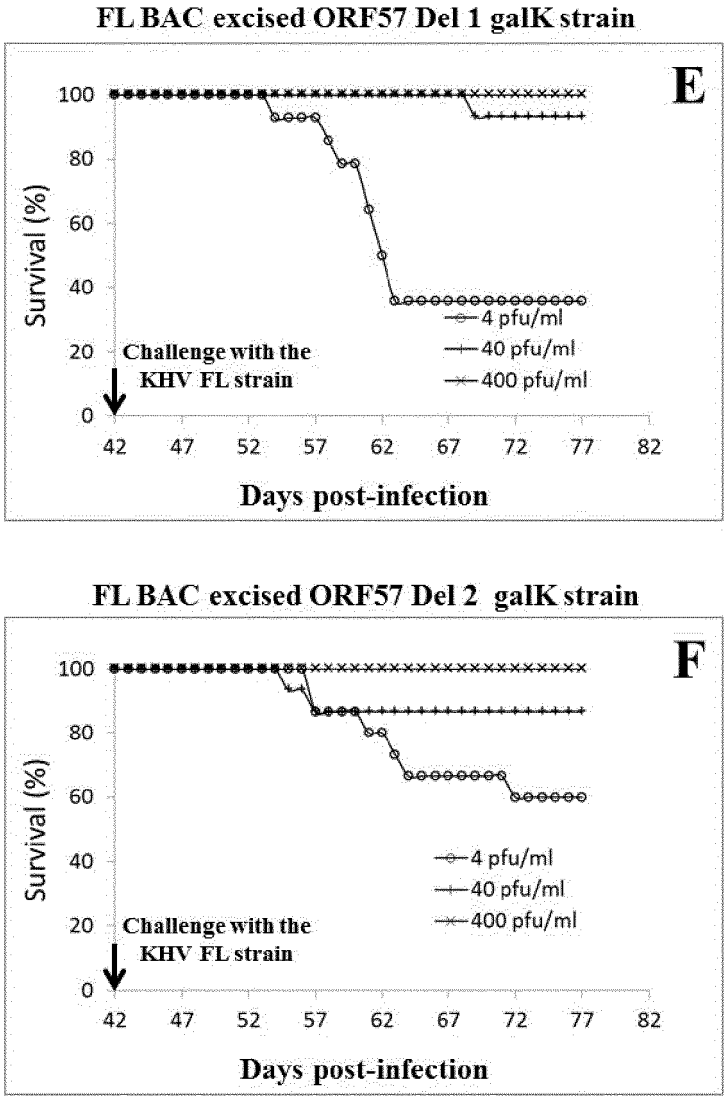

FL BAC excised ORF57 Del 1 galK strain
E
Survival (%)
100
80
60
40
20
0
Challenge with the
KHV FL strain
4 pfu/ml
40 pfu/ml
400 pfu/ml
42
47
52
57
62
67
72
77
82
Days post-infection
FL BAC excised ORF57 Del 2 galK strain
F
Survival (%)
100
80
60
40
20
0
Challenge with the
KHV FL strain
4 pfu/ml
40 pfu/ml
400 pfu/ml
42
47
52
57
62
67
72
77
82
Days post-infection

Figure 5E, 5F

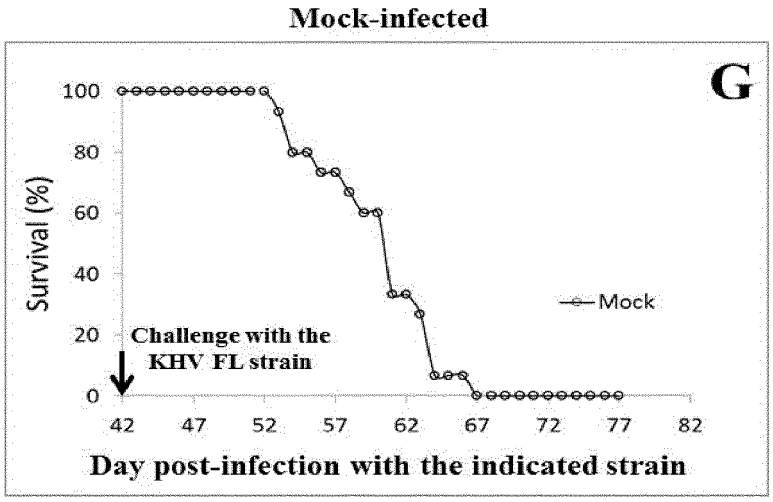

Mock-infected
G
100
80
60
40
20
0
Survival (%)
Challenge with the
KHV FL strain
Mock
42
47
52
57
62
67
72
77
82
Day post-infection with the indicated strain

Figure 5G

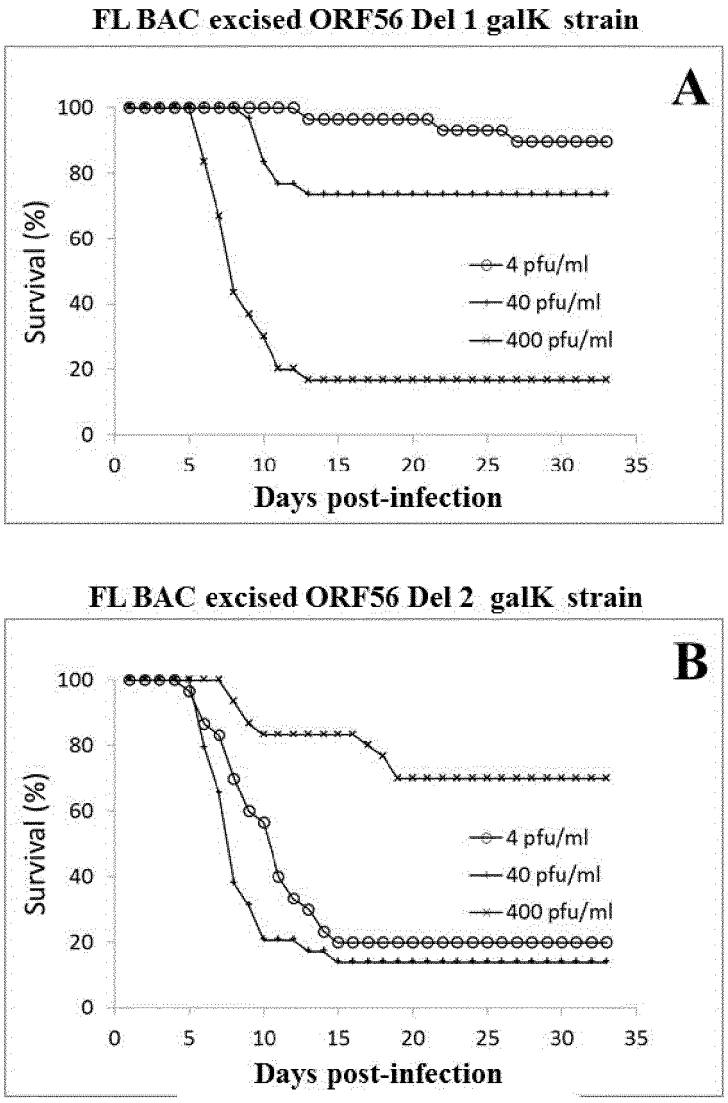

FL BAC excised ORF56 Del 1 galK strain
A
Survival (%)
100
80
60
40
20
0
0
5
10
15
20
25
30
35
Days post-infection
4 pfu/ml
40 pfu/ml
400 pfu/ml
FL BAC excised ORF56 Del 2 galK strain
B
Survival (%)
100
80
60
40
20
0
0
5
10
15
20
25
30
35
Days post-infection
4 pfu/ml
40 pfu/ml
400 pfu/ml

Figure 6A, 6B

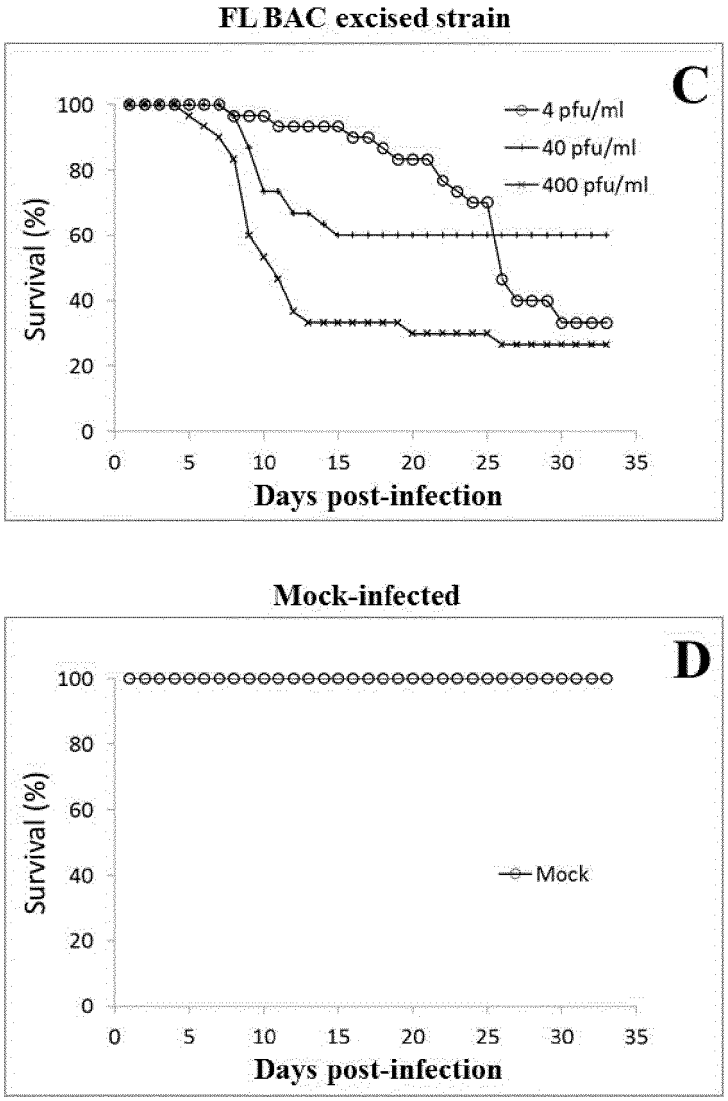
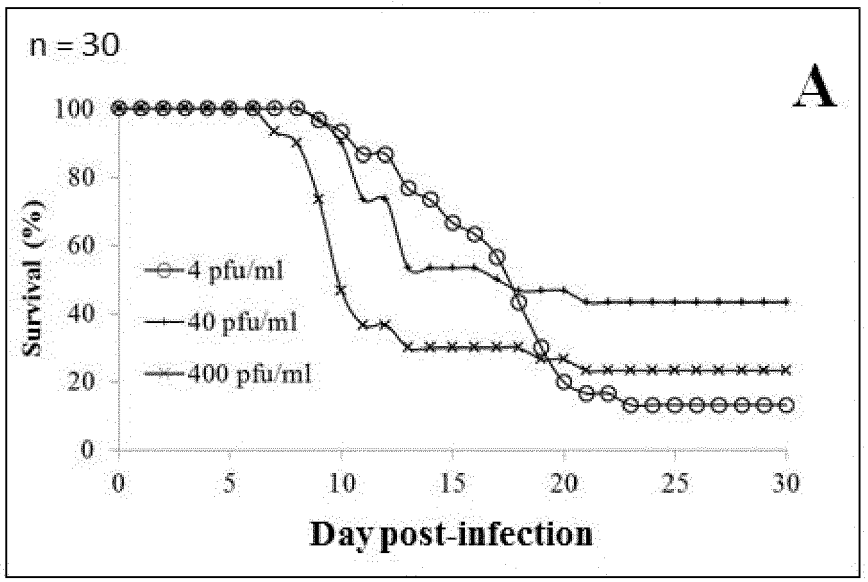

FL BAC excised strain
C
4 pfu/ml
40 pfu/ml
400 pfu/ml
Survival (%)
Days post-infection
Mock-infected
D
Mock
Survival (%)
Days post-infection

Figure 6C, 6D

FL BAC excised strain



FL BAC excised ORF56-57 Del strain

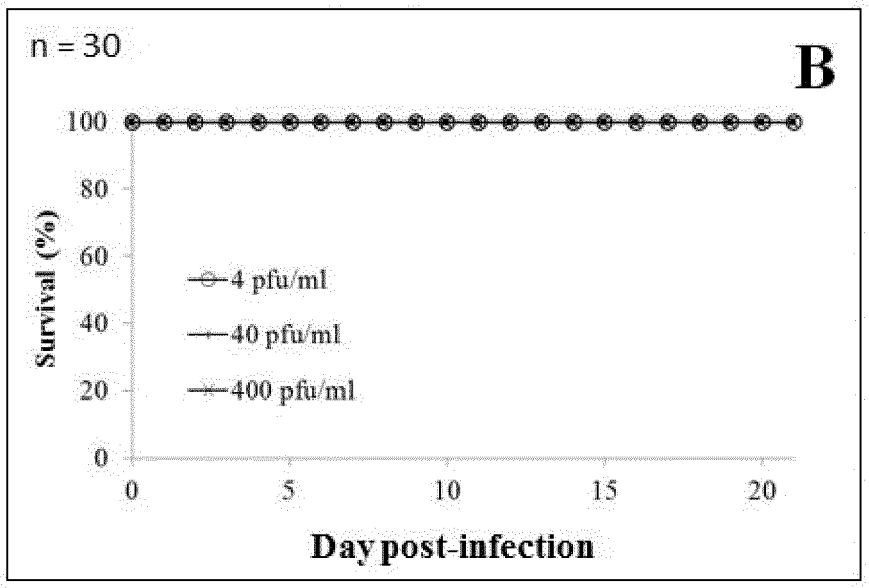


Figure 7A, B

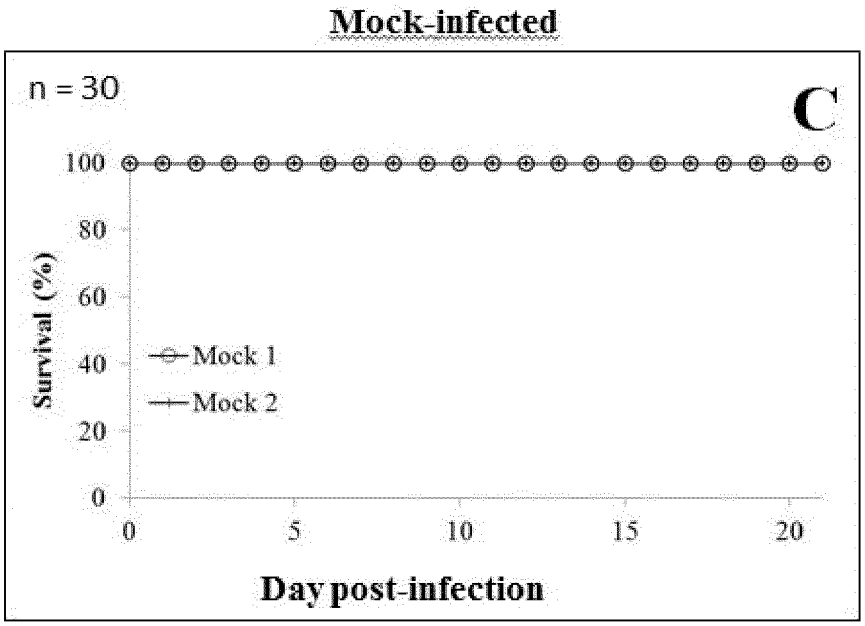

Mock-infected
n = 30
C
100
80
60
40
20
0
Survival (%)
Mock 1
Mock 2
0
5
10
15
20
Day post-infection

Figure 7C

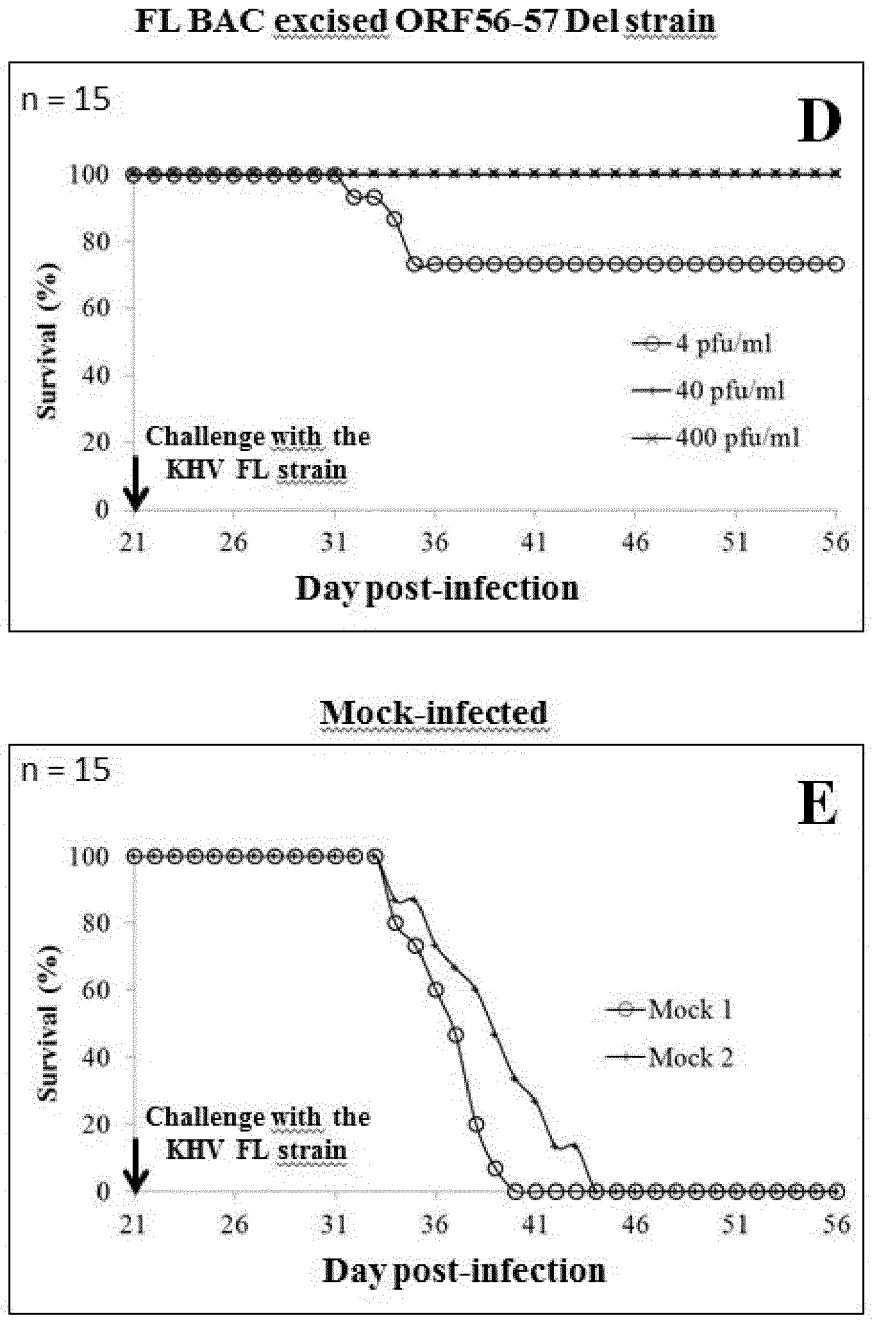

FL BAC excised ORF56-57 Del strain
n = 15
D
Survival (%)
100
80
60
40
20
0
Challenge with the KHV FL strain
4 pfu/ml
40 pfu/ml
400 pfu/ml
21
26
31
36
41
46
51
56
Day post-infection
Mock-infected
n = 15
E
Survival (%)
100
80
60
40
20
0
Challenge with the KHV FL strain
Mock 1
Mock 2
21
26
31
36
41
46
51
56
Day post-infection

Figure 7D, E

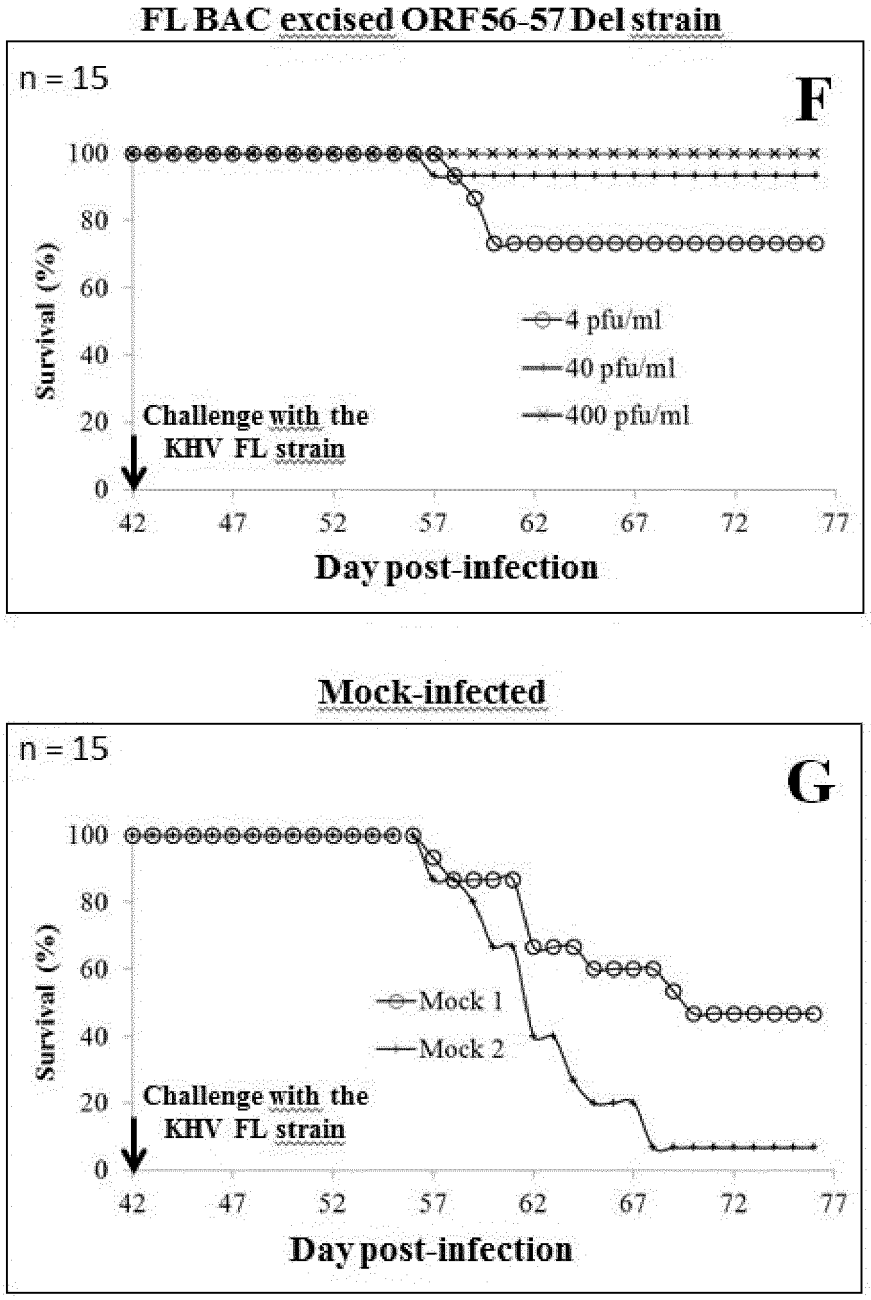

FL BAC excised ORF56-57 Del strain
n = 15
F
Survival (%)
100
80
60
40
20
0
4 pfu/ml
40 pfu/ml
400 pfu/ml
Challenge with the KHV FL strain
42
47
52
57
62
67
72
77
Day post-infection
Mock-infected
n = 15
G
Survival (%)
100
80
60
40
20
0
Mock 1
Mock 2
Challenge with the KHV FL strain
42
47
52
57
62
67
72
77
Day post-infection

Figure 7F, G

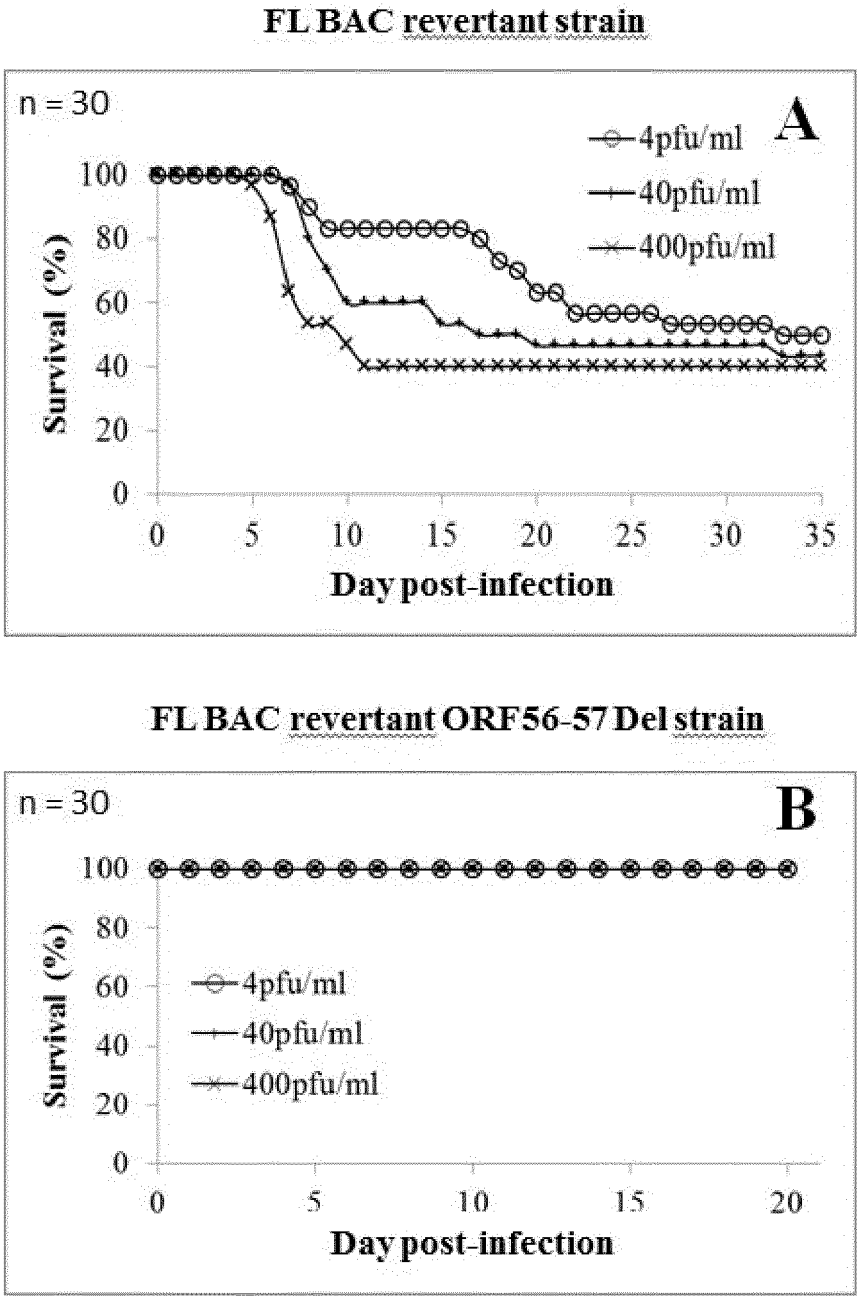

FL BAC revertant strain
n = 30
A
4pfu/ml
40pfu/ml
400pfu/ml
Survival (%)
100
80
60
40
20
0
0
5
10
15
20
25
30
35
Day post-infection
FL BAC revertant ORF56-57 Del strain
n = 30
B
4pfu/ml
40pfu/ml
400pfu/ml
Survival (%)
100
80
60
40
20
0
0
5
10
15
20
Day post-infection

Figure 8A, B

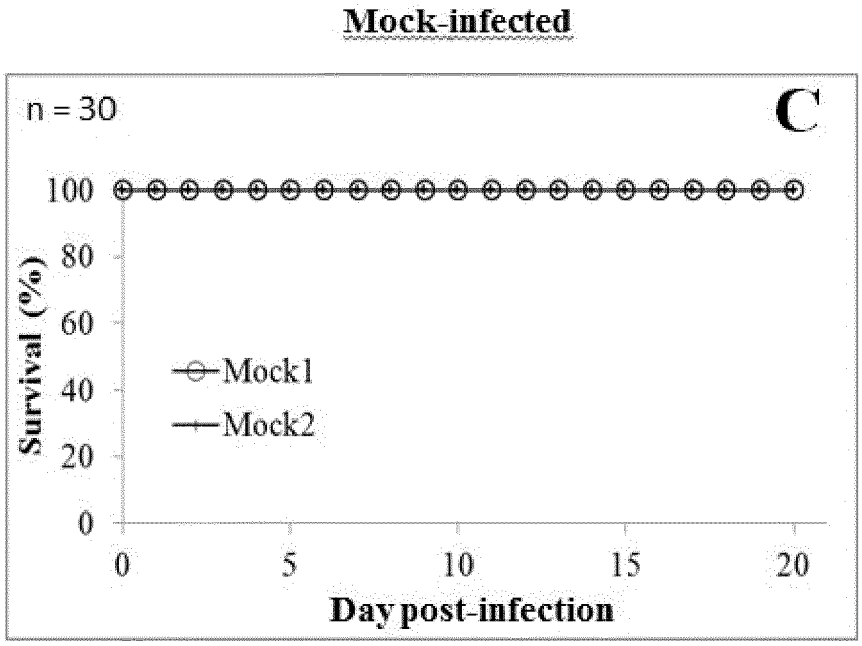
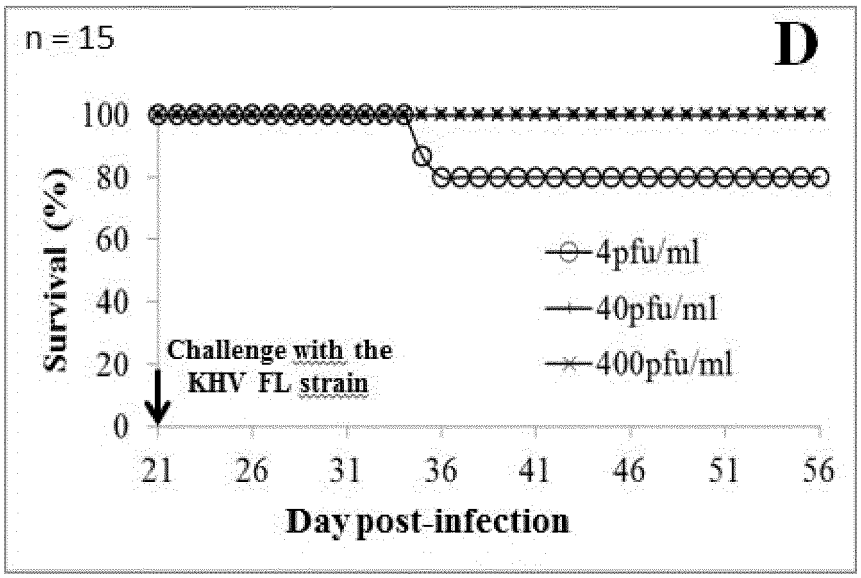

Mock-infected
n = 30
C
100
80
60
40
20
0
Survival (%)
Mock1
Mock2
0
5
10
15
20
Day post-infection

Figure 8C

FL BAC revertant ORF56-57 Del strain



Mock-infected

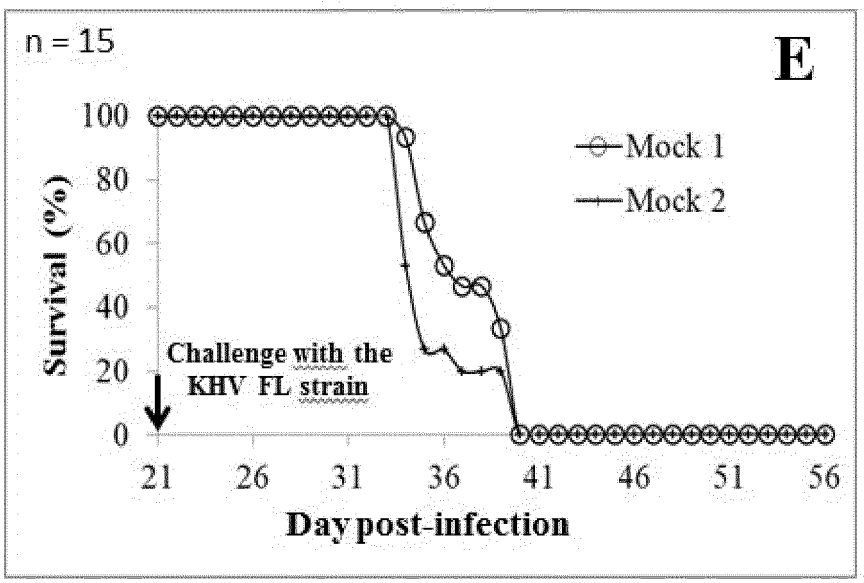
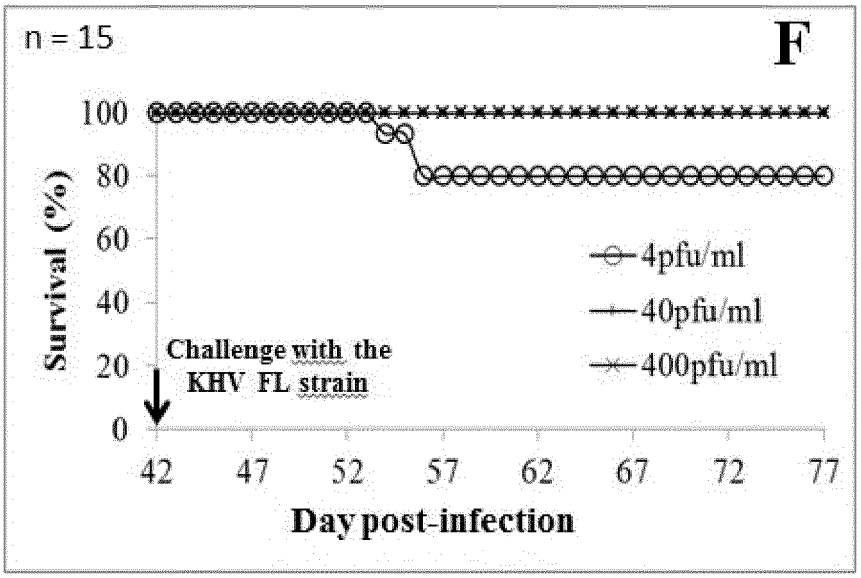


Figure 8D, E

FL BAC revertant ORF56-57 Del strain



Mock-infected

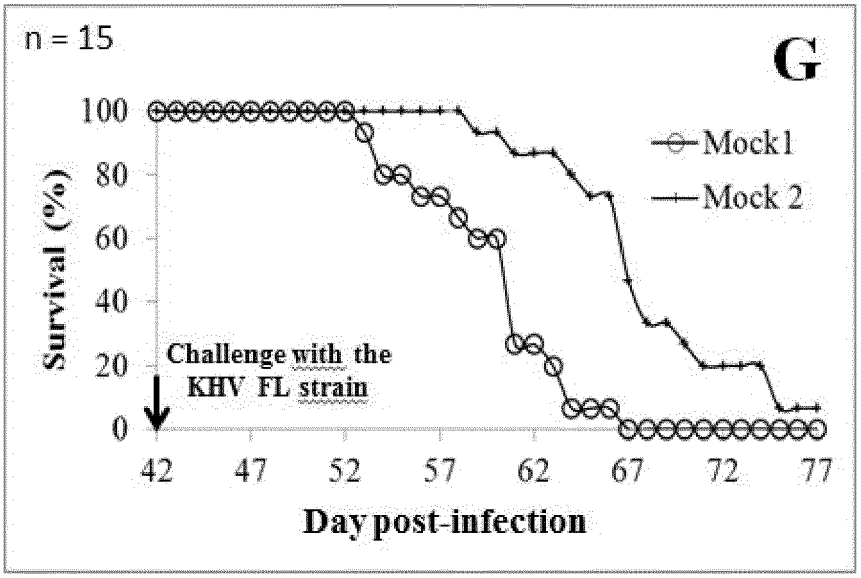


Figure 8F, G