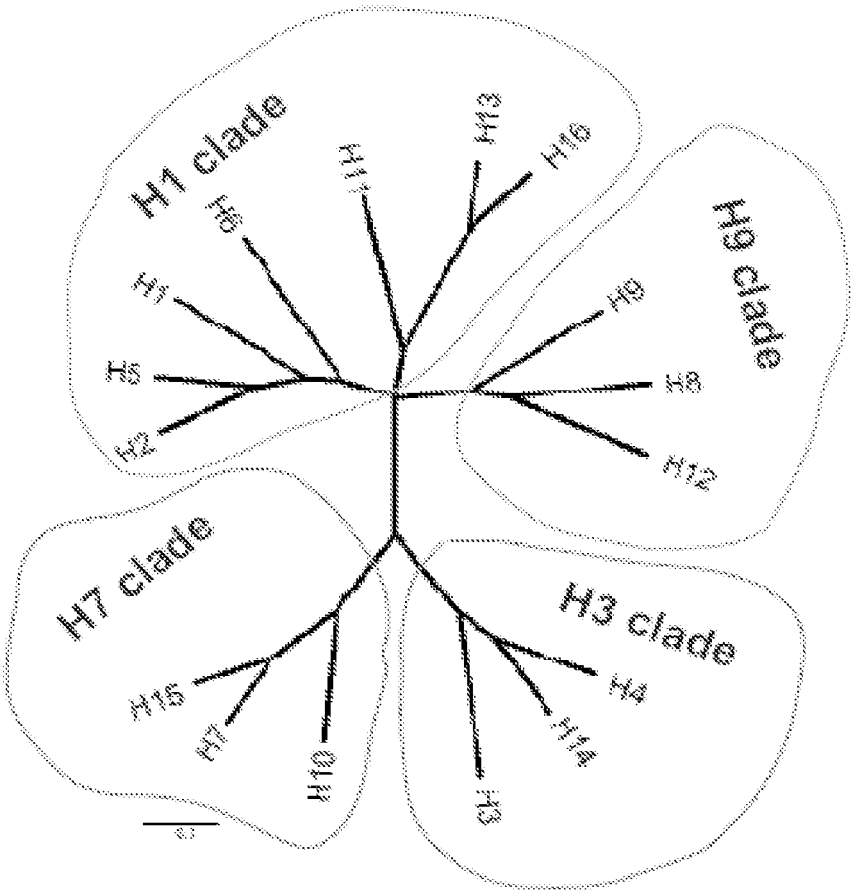

H1 clade
H9 clade
H7 clade
H3 clade
H13
H16
H17
H6
H1
H5
H2
H9
H8
H12
H15
H7
H10
H11
H4
H14
H3

FIG. 1

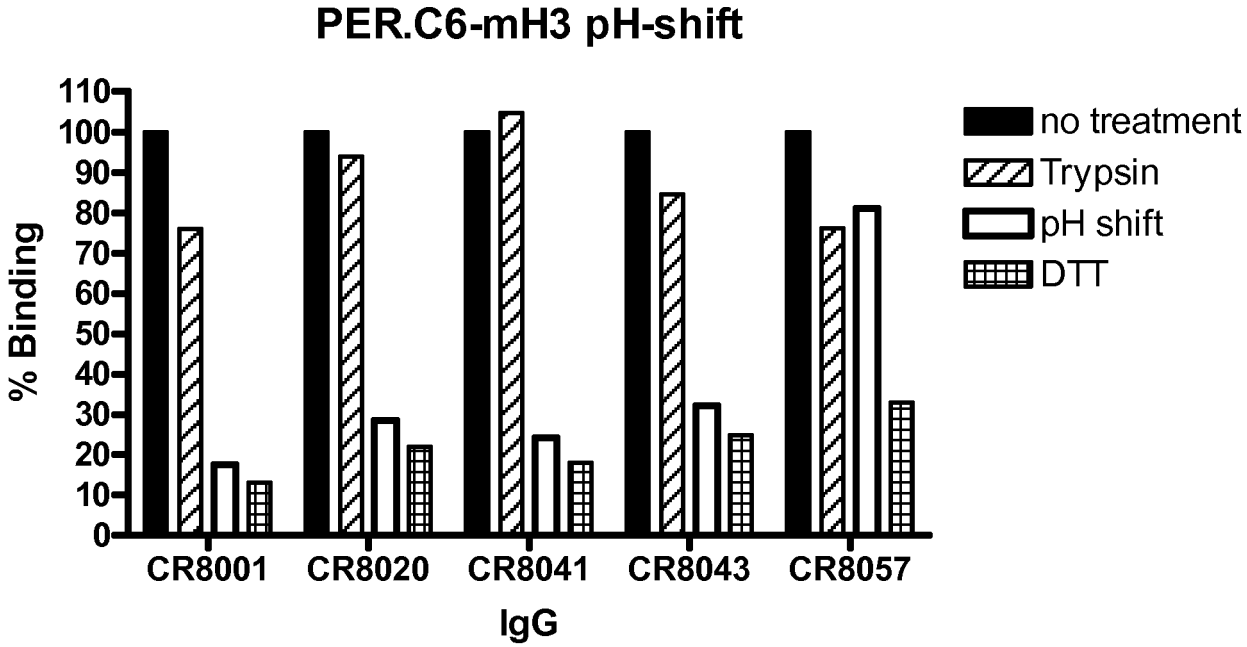

PER.C6-mH3 pH-shift
% Binding
110
100
90
80
70
60
50
40
30
20
10
0
CR8001
CR8020
CR8041
CR8043
CR8057
IgG
no treatment
Trypsin
pH shift
DTT

FIG. 2

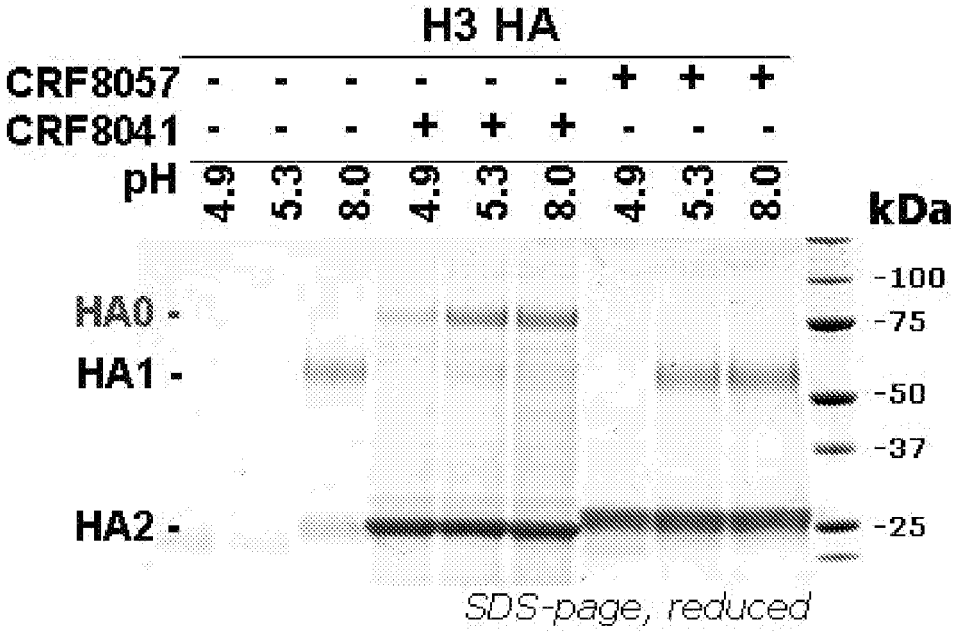

H3 HA
CRF8057 - - - - - - + + +
CRF8041 - - - + + + - - -
pH 4.9 5.3 8.0 4.9 5.3 8.0 4.9 5.3 8.0
kDa
HA0 -
HA1 -
HA2 -
-100
-75
-50
-37
-25
SDS-page, reduced

FIG. 3

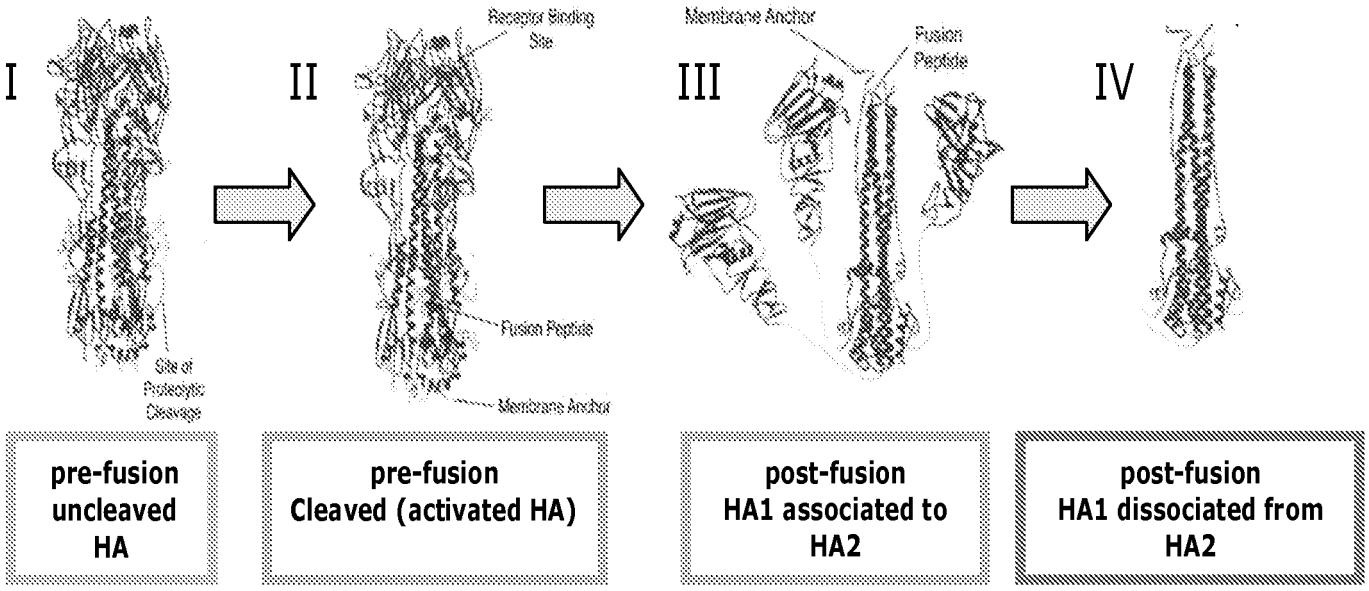

I
II
III
IV
Receptor Binding Site
Fusion Peptide
Membrane Anchor
Membrane Anchor
Fusion Peptide
Site of Proteolytic Cleavage
pre-fusion uncleaved HA
pre-fusion Cleaved (activated HA)
post-fusion HA1 associated to HA2
post-fusion HA1 dissociated from HA2

FIG. 4

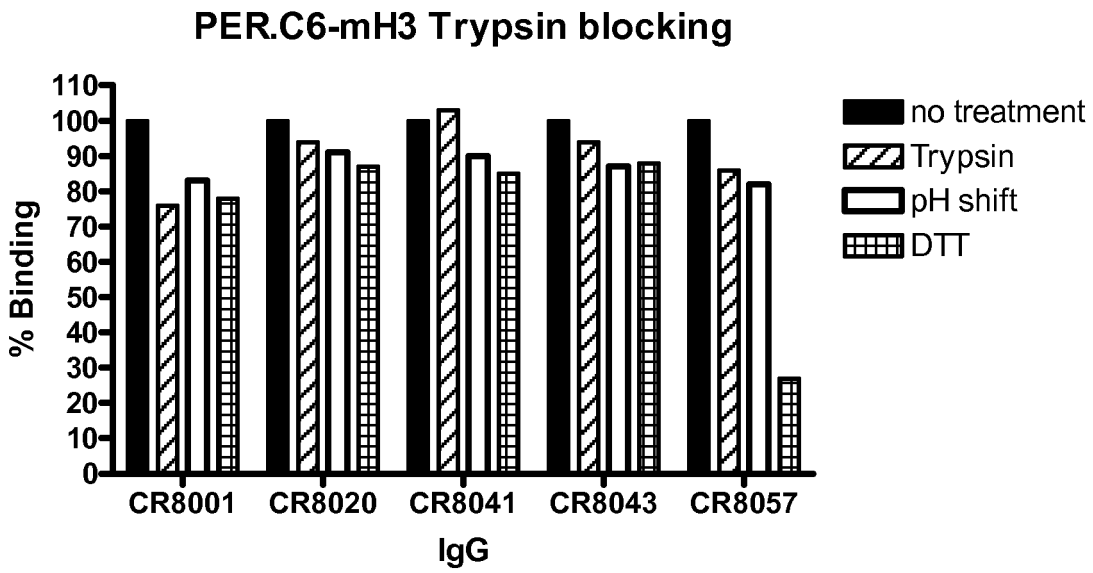

PER.C6-mH3 Trypsin blocking
% Binding
110
100
90
80
70
60
50
40
30
20
10
0
CR8001
CR8020
CR8041
CR8043
CR8057
IgG
no treatment
Trypsin
pH shift
DTT

FIG. 5

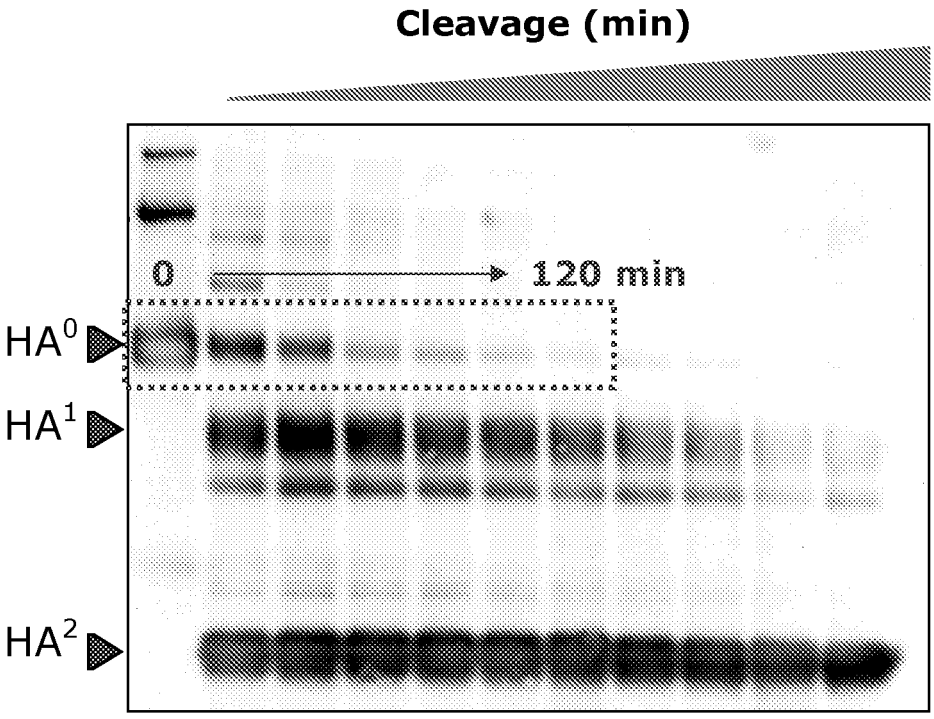
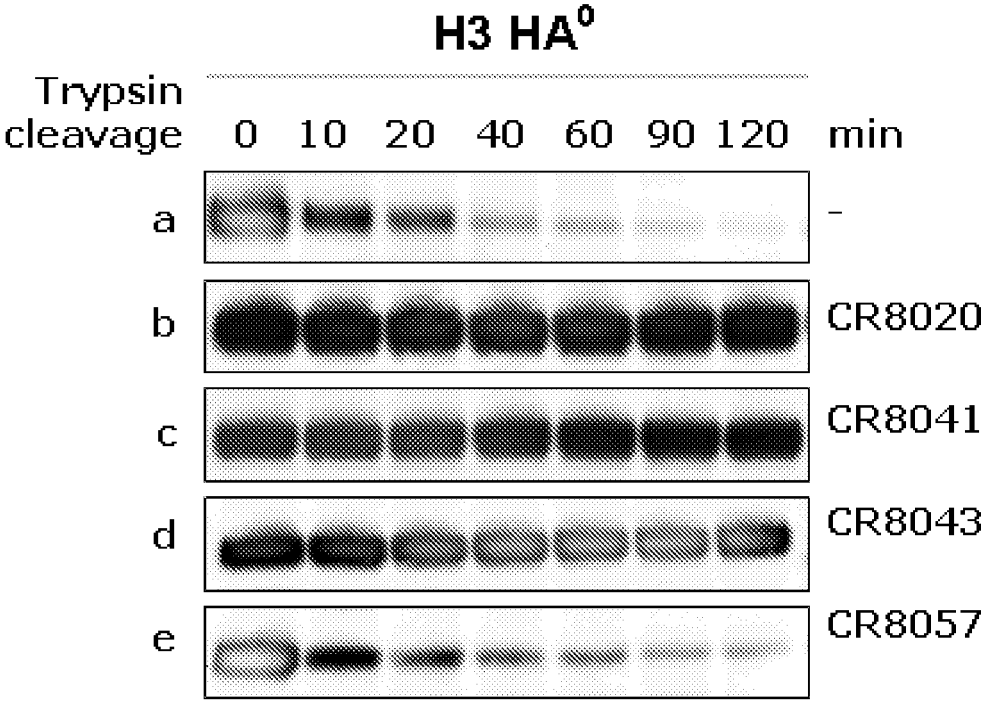

Cleavage (min)
0
120 min
HA0
HA1
HA2
Per lane: 0.4ug HA; SDS-page, reduced

FIG. 6



Per lane: 0.4ug HA, 2.5ug IgG; SDS-page, reduced

FIG. 7

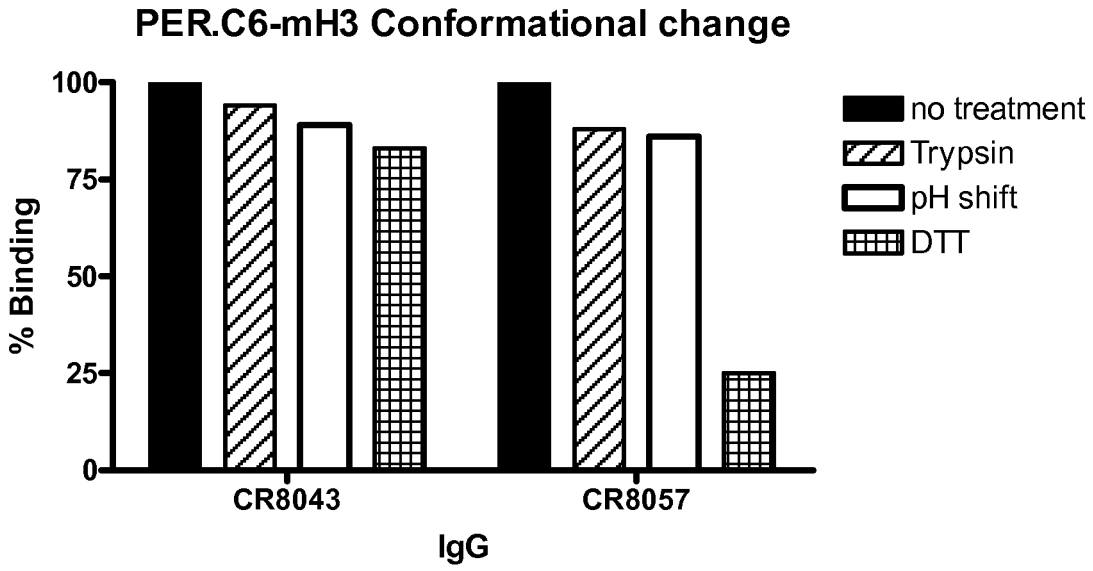

PER.C6-mH3 Conformational change
100
75
50
25
0
% Binding
CR8043
CR8057
IgG
no treatment
Trypsin
pH shift
DTT

FIG. 8

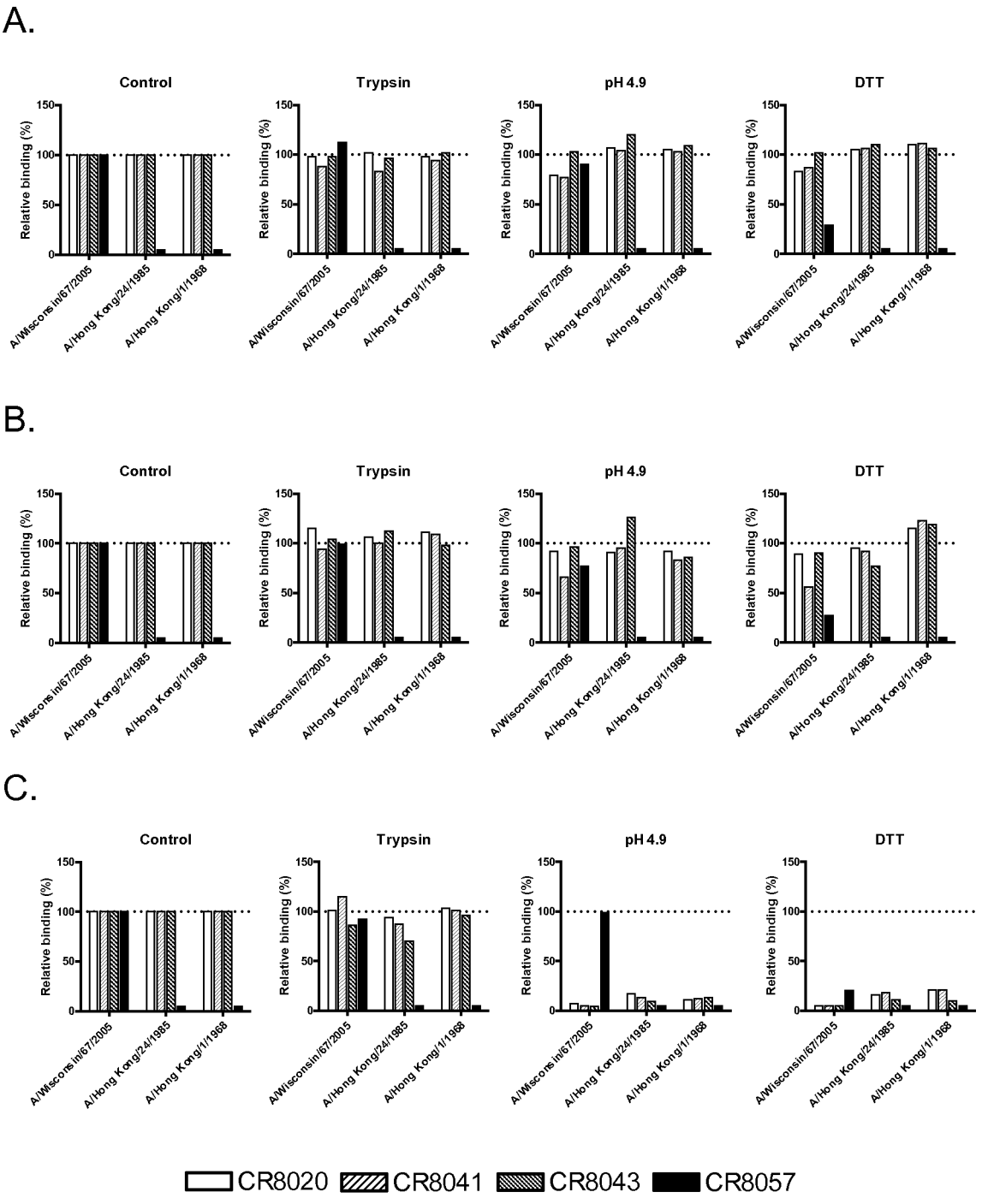
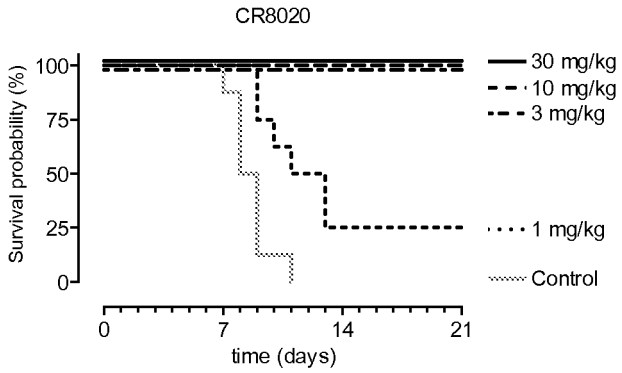
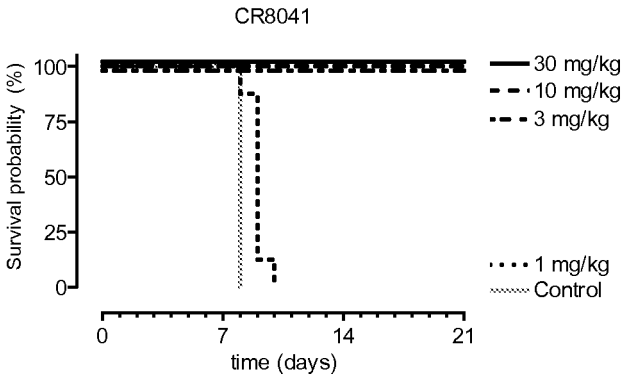

A.
Control
Trypsin
pH 4.9
DTT
Relative binding (%)
150
100
50
0
A/Wisconsin/67/2005
A/Hong Kong/24/1985
A/Hong Kong/1/1968
B.
C.
CR8020
CR8041
CR8043
CR8057

FIG. 9

A.


CR8020
Survival probability (%)
100
75
50
25
0
0
7
14
21
time (days)
30 mg/kg
10 mg/kg
3 mg/kg
1 mg/kg
Control

B.


CR8041
Survival probability (%)
100
75
50
25
0
0
7
14
21
time (days)
30 mg/kg
10 mg/kg
3 mg/kg
1 mg/kg
Control

C.

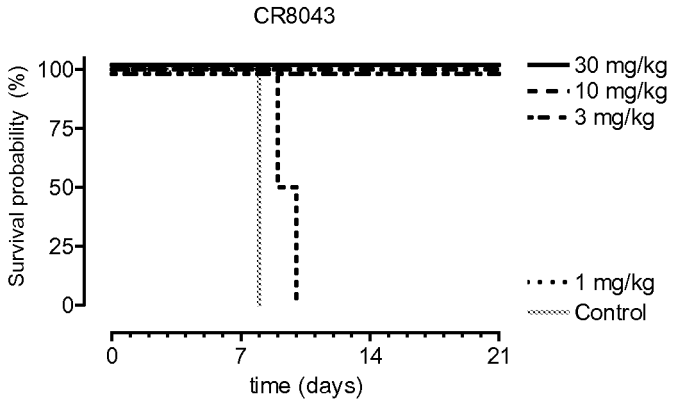
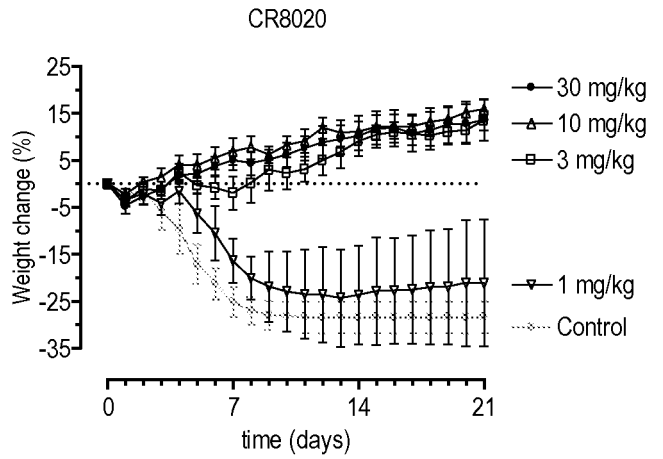
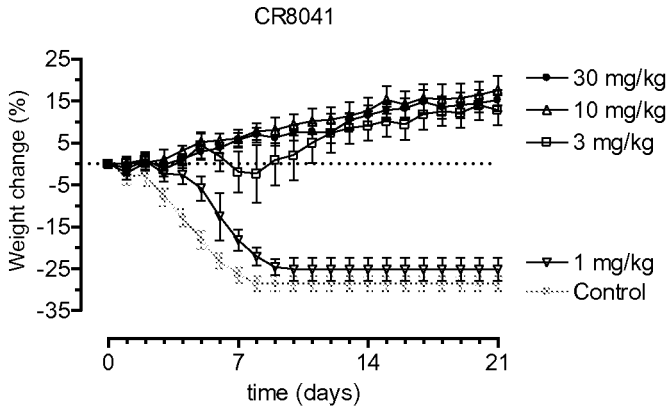

CR8043
Survival probability (%)
100
75
50
25
0
0
7
14
21
time (days)
30 mg/kg
10 mg/kg
3 mg/kg
1 mg/kg
Control

FIG. 10

A.


CR8020
Weight change (%)
25
15
5
-5
-15
-25
-35
0
7
14
21
time (days)
30 mg/kg
10 mg/kg
3 mg/kg
1 mg/kg
Control

B.


CR8041
Weight change (%)
25
15
5
-5
-15
-25
-35
0
7
14
21
time (days)
30 mg/kg
10 mg/kg
3 mg/kg
1 mg/kg
Control

C.

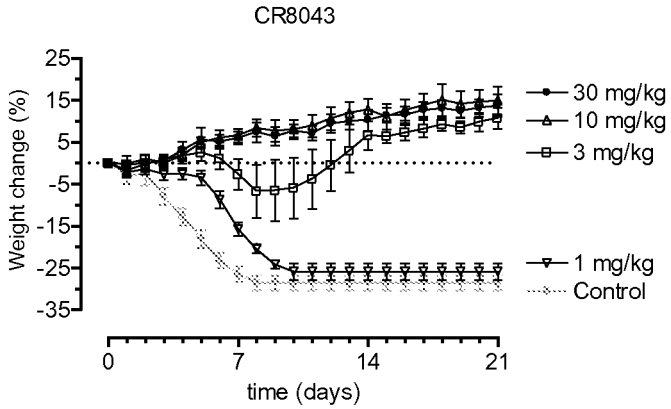
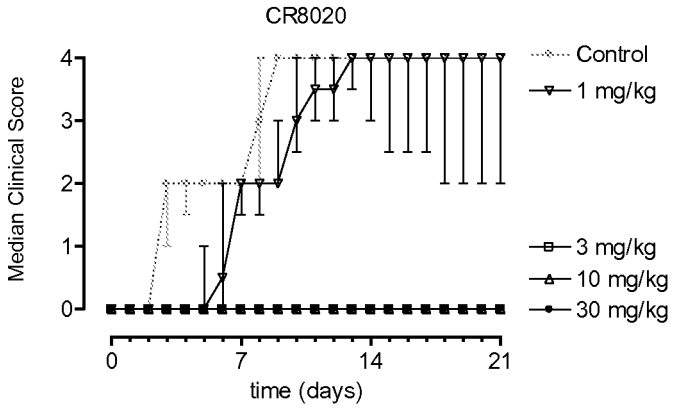
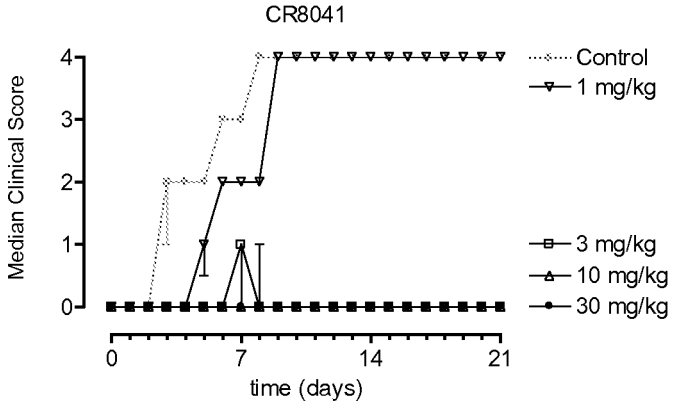

CR8043
Weight change (%)
25
15
5
-5
-15
-25
-35
0
7
14
21
time (days)
30 mg/kg
10 mg/kg
3 mg/kg
1 mg/kg
Control

FIG. 11

A.


CR8020
Median Clinical Score
0
1
2
3
4
0
7
14
21
time (days)
Control
1 mg/kg
3 mg/kg
10 mg/kg
30 mg/kg

B.


CR8041
Median Clinical Score
0
1
2
3
4
0
7
14
21
time (days)
Control
1 mg/kg
3 mg/kg
10 mg/kg
30 mg/kg

C.

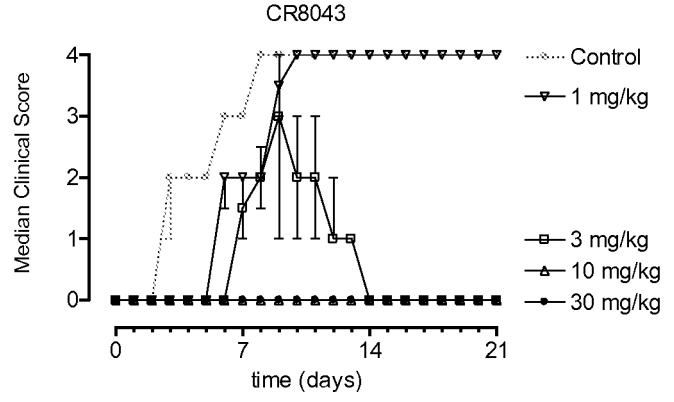
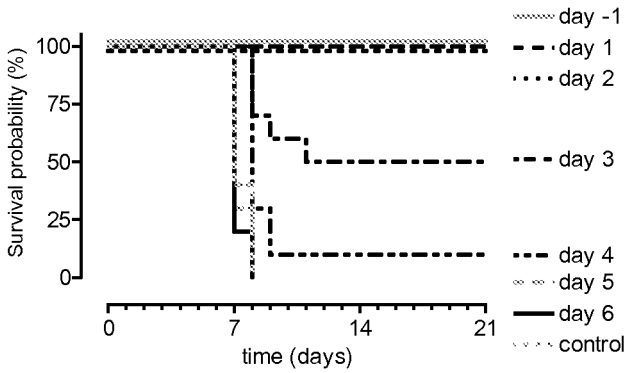
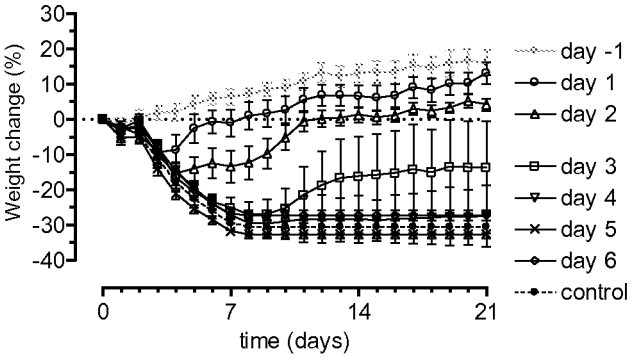

CR8043
Median Clinical Score
0
1
2
3
4
0
7
14
21
time (days)
Control
1 mg/kg
3 mg/kg
10 mg/kg
30 mg/kg

FIG. 12

A.


Survival probability (%)
100
75
50
25
0
0
7
14
21
time (days)
day -1
day 1
day 2
day 3
day 4
day 5
day 6
control

B.


Weight change (%)
30
20
10
0
-10
-20
-30
-40
0
7
14
21
time (days)
day -1
day 1
day 2
day 3
day 4
day 5
day 6
control

C.

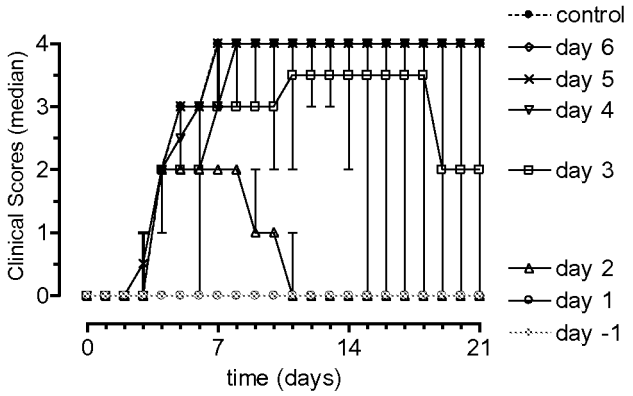
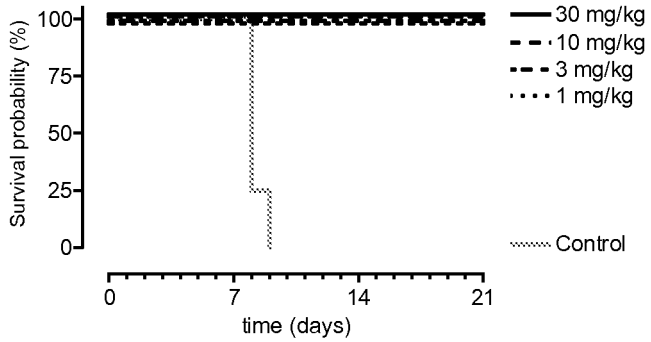
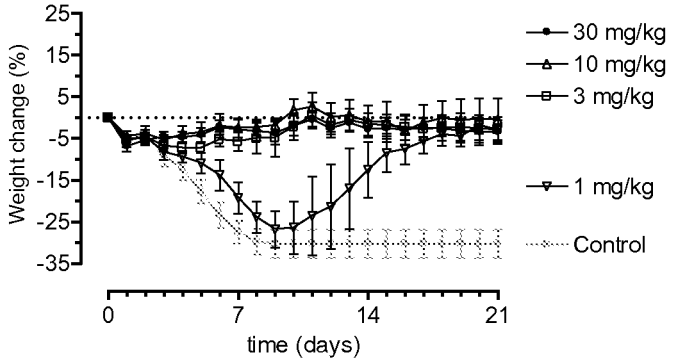

Clinical Scores (median)
4
3
2
1
0
0
7
14
21
time (days)
control
day 6
day 5
day 4
day 3
day 2
day 1
day -1

FIG. 13

A.


Survival probability (%)
100
75
50
25
0
0
7
14
21
time (days)
30 mg/kg
10 mg/kg
3 mg/kg
1 mg/kg
Control

B.


Weight change (%)
25
15
5
-5
-15
-25
-35
0
7
14
21
time (days)
30 mg/kg
10 mg/kg
3 mg/kg
1 mg/kg
Control

C.

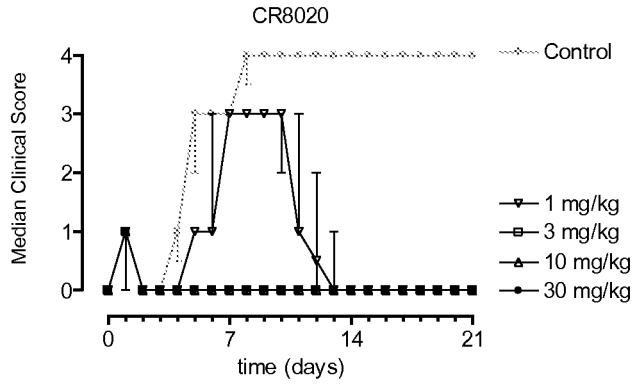
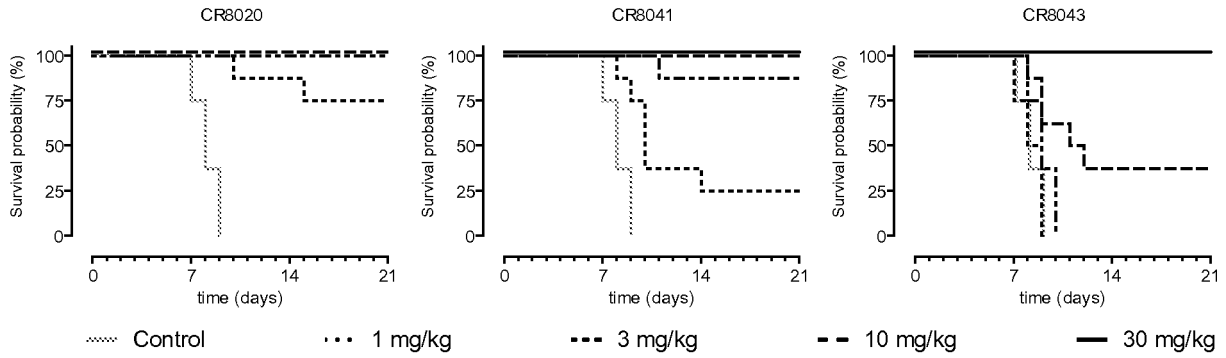
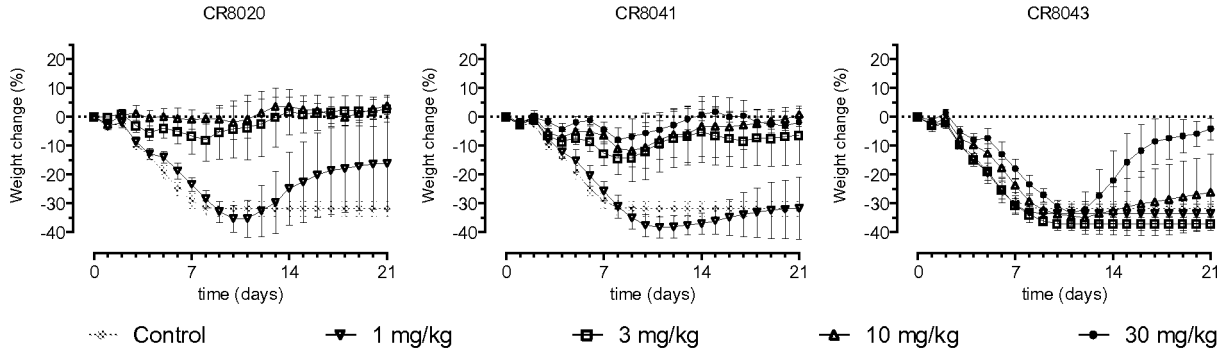

CR8020
Median Clinical Score
4
3
2
1
0
0
7
14
21
time (days)
Control
1 mg/kg
3 mg/kg
10 mg/kg
30 mg/kg

FIG. 14

A.


CR8020
CR8041
CR8043
Survival probability (%)
100
75
50
25
0
0
7
14
21
time (days)
Control
1 mg/kg
3 mg/kg
10 mg/kg
30 mg/kg

B.


CR8020
CR8041
CR8043
Weight change (%)
20
10
0
-10
-20
-30
-40
0
7
14
21
time (days)
Control
1 mg/kg
3 mg/kg
10 mg/kg
30 mg/kg

C.

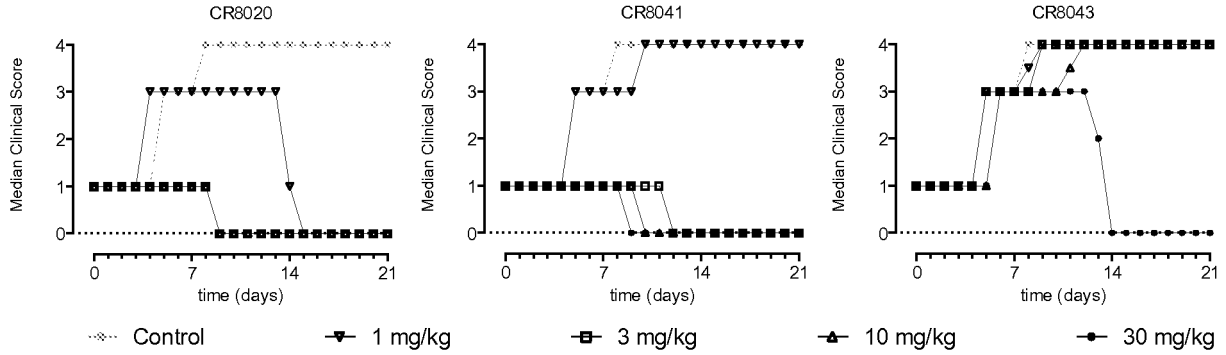
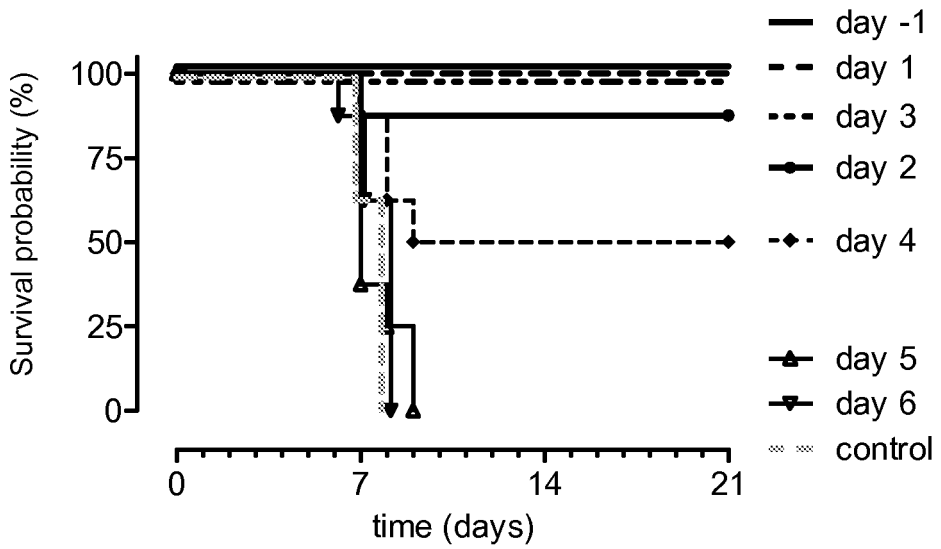

CR8020
CR8041
CR8043
Median Clinical Score
4
3
2
1
0
0
7
14
21
time (days)
Control
1 mg/kg
3 mg/kg
10 mg/kg
30 mg/kg

FIG. 15

A.


Survival probability (%)
100
75
50
25
0
0
7
14
21
time (days)
day -1
day 1
day 3
day 2
day 4
day 5
day 6
control

B.

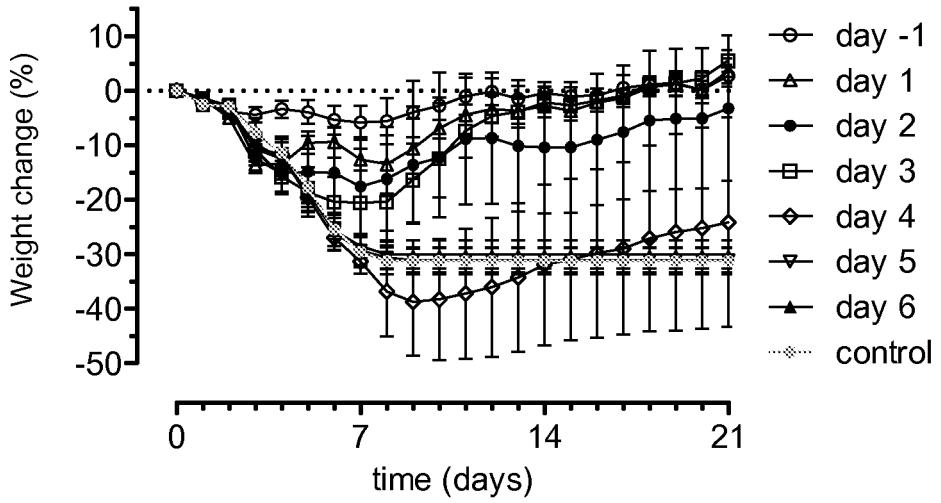

Weight change (%)
10
0
-10
-20
-30
-40
-50
0
7
14
21
time (days)
day -1
day 1
day 2
day 3
day 4
day 5
day 6
control

FIG. 16

C.

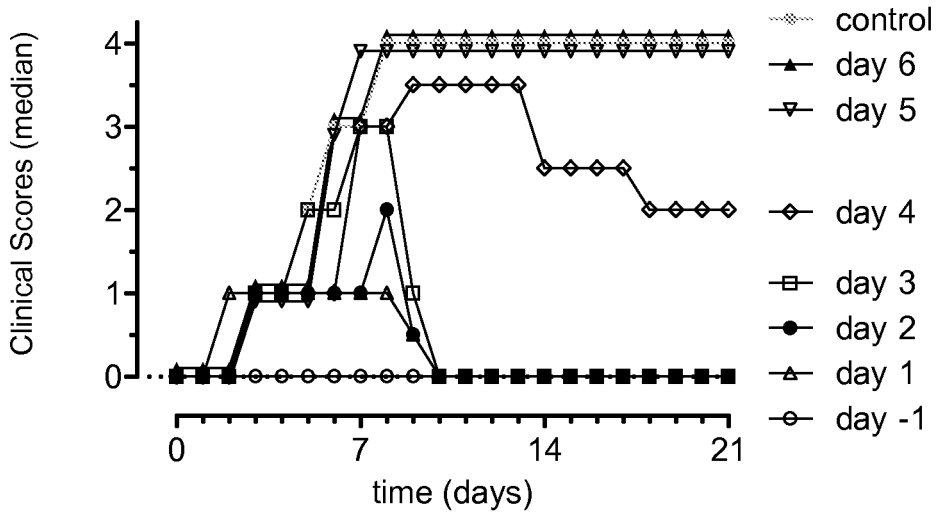


FIG. 16 (continued)