Fig. 1

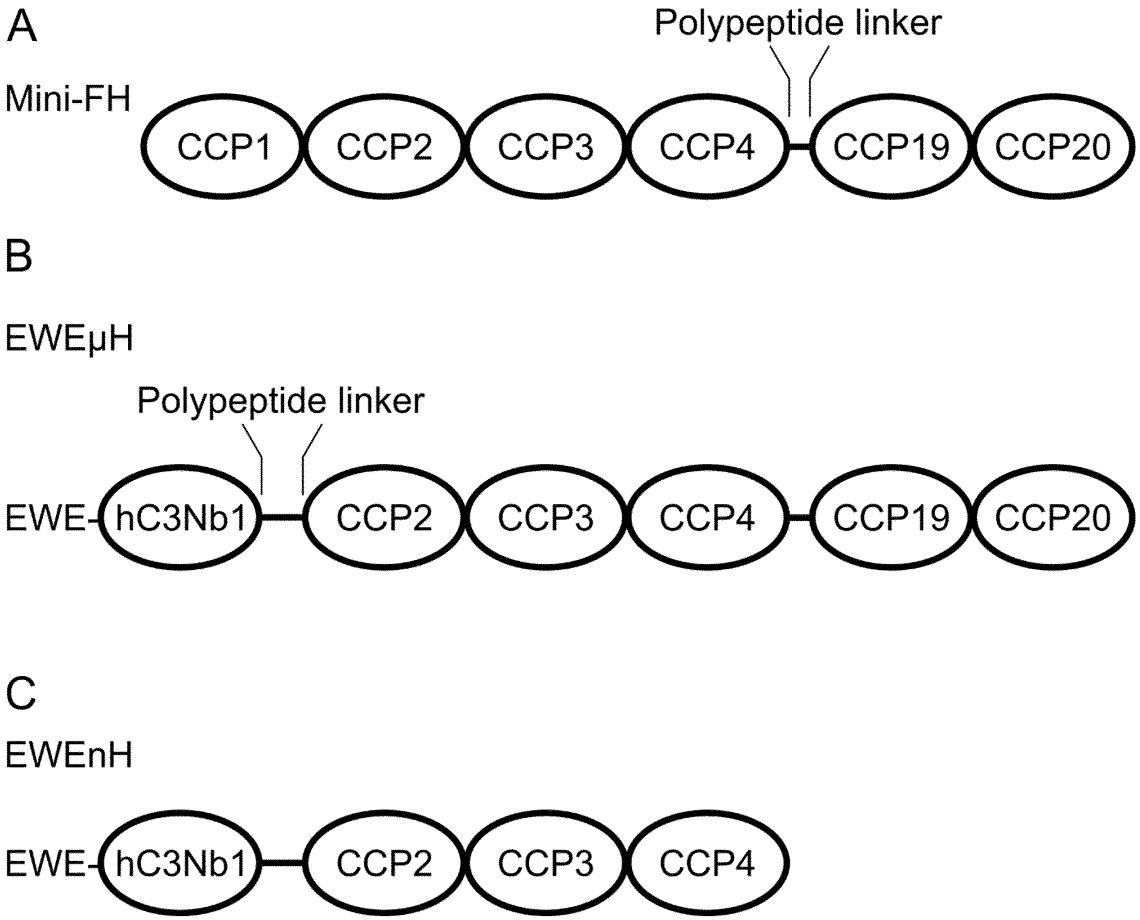

A
Polypeptide linker
Mini-FH
CCP1
CCP2
CCP3
CCP4
CCP19
CCP20
B
EWEμH
Polypeptide linker
EWE-
hC3Nb1
CCP2
CCP3
CCP4
CCP19
CCP20
C
EWEnH
EWE-
hC3Nb1
CCP2
CCP3
CCP4

Fig. 2

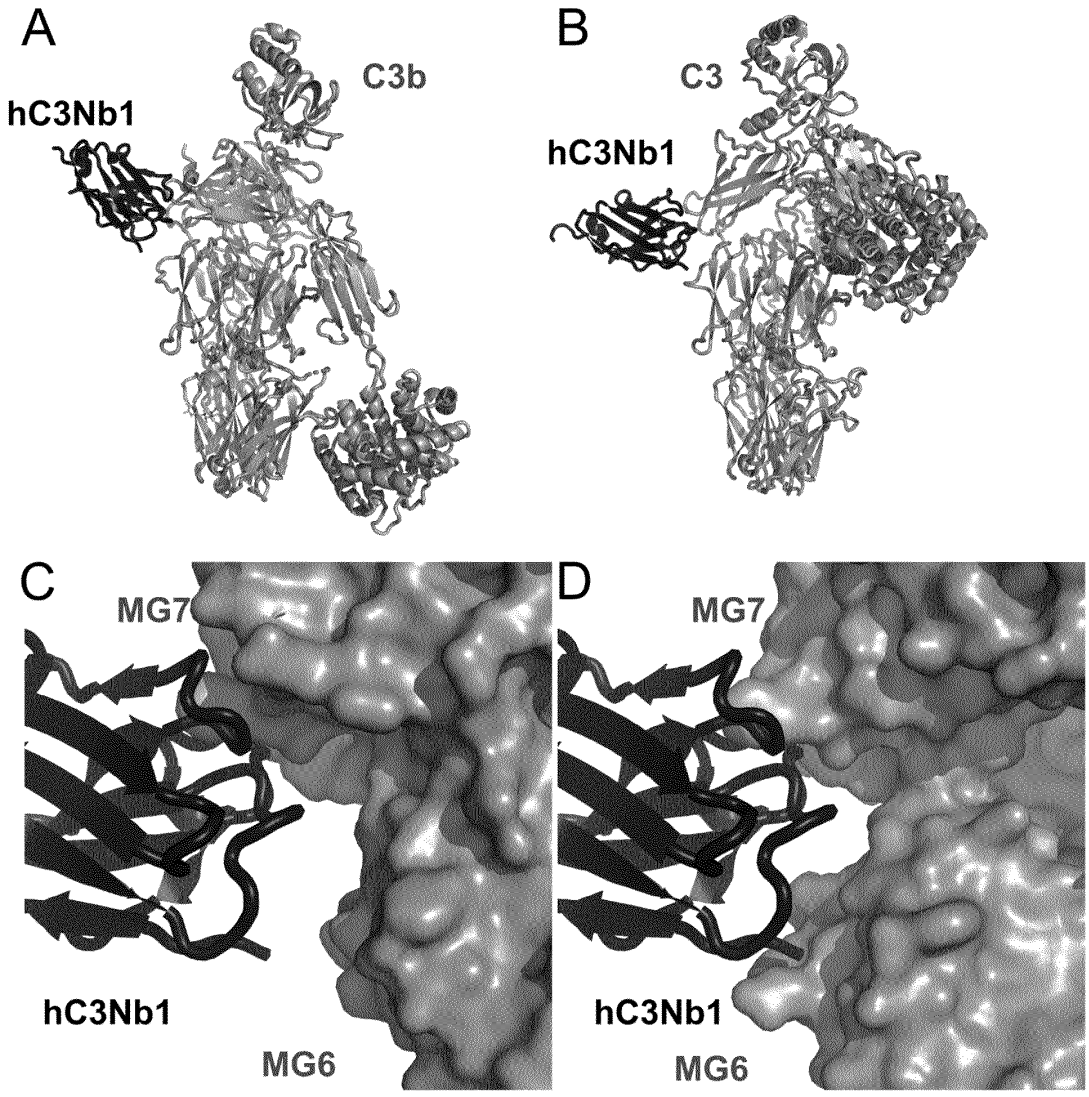


Fig. 3

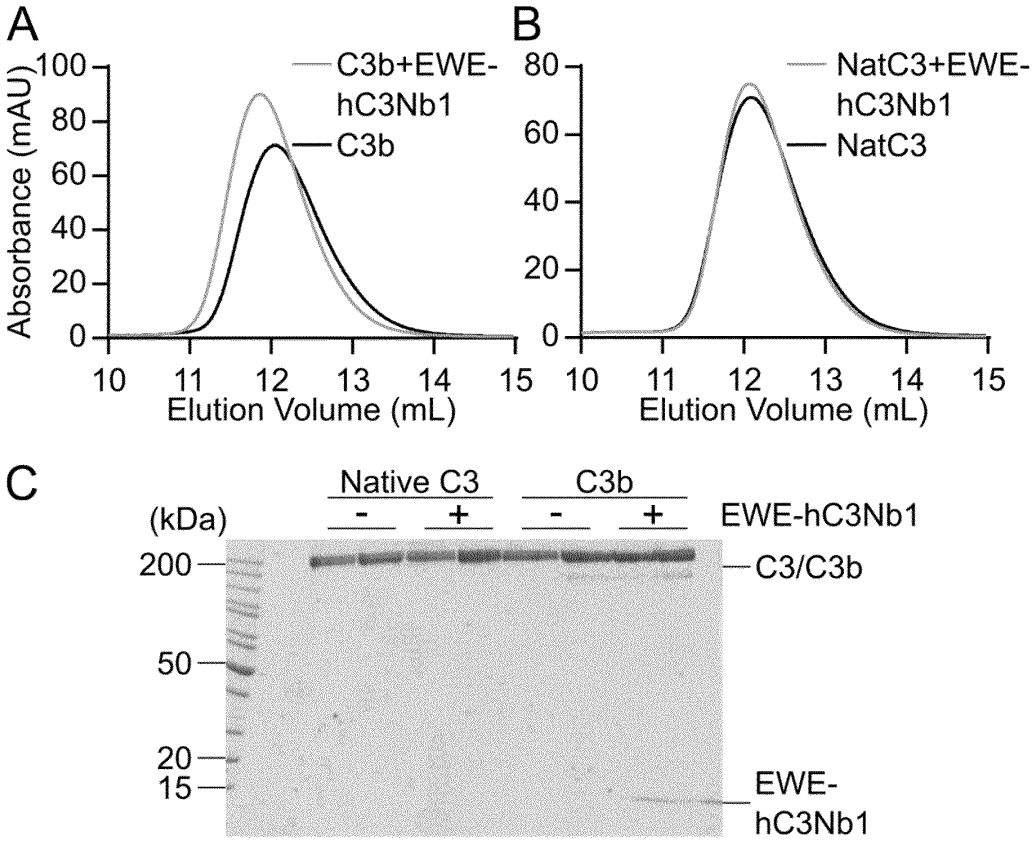

A
B
C
Absorbance (mAU)
Elution Volume (mL)
C3b+EWE-hC3Nb1
C3b
NatC3+EWE-hC3Nb1
NatC3
Native C3
C3b
(kDa)
EWE-hC3Nb1
C3/C3b
EWE-hC3Nb1

Fig. 4

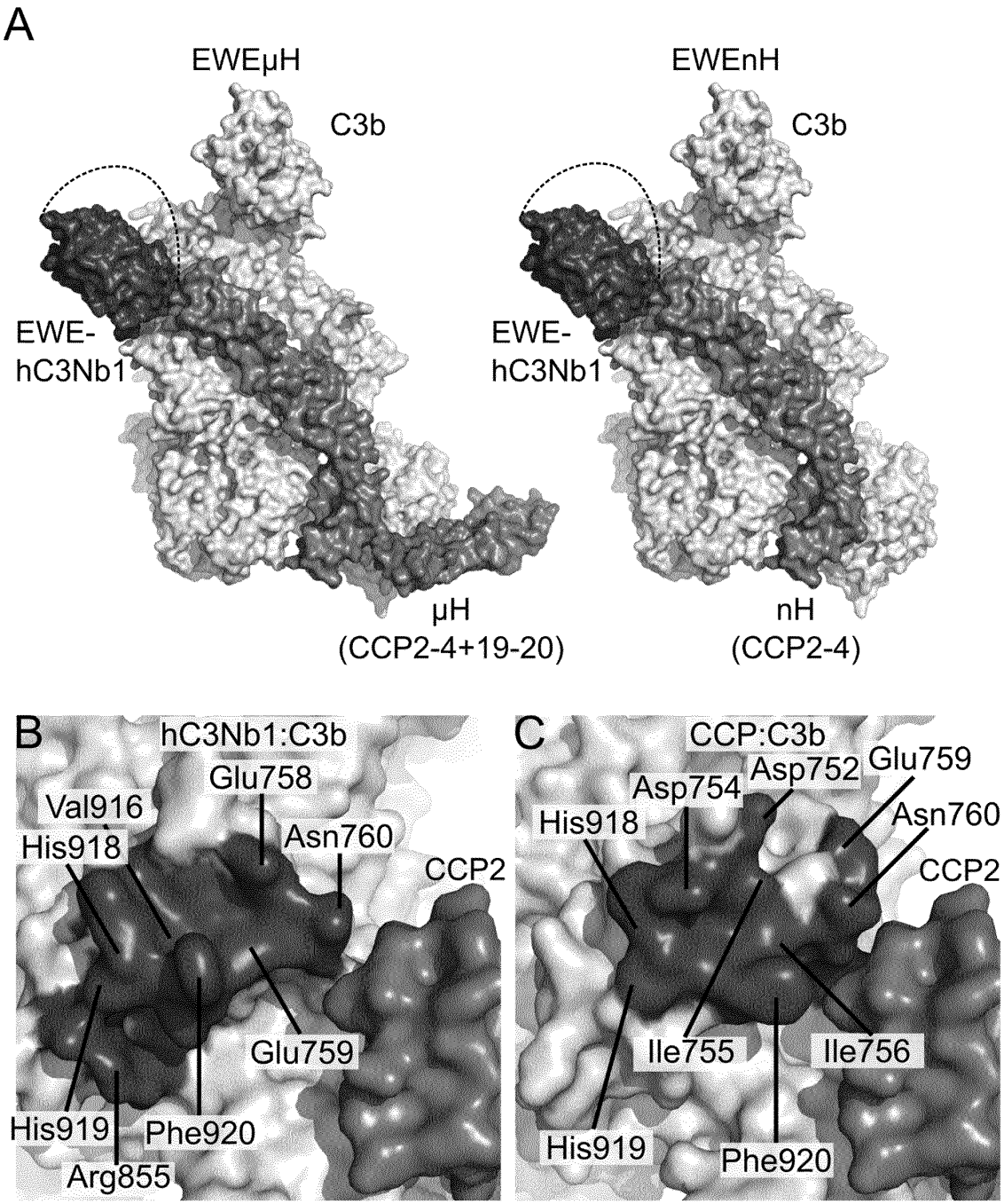

A
EWEμH
C3b
EWE-
hC3Nb1
μH
(CCP2-4+19-20)
EWEnH
C3b
EWE-
hC3Nb1
nH
(CCP2-4)
B
hC3Nb1:C3b
Glu758
Val916
His918
Asn760
CCP2
Glu759
His919
Phe920
Arg855
C
CCP:C3b
Asp754
Asp752
Glu759
His918
Asn760
CCP2
Ile755
Ile756
His919
Phe920

Fig. 5

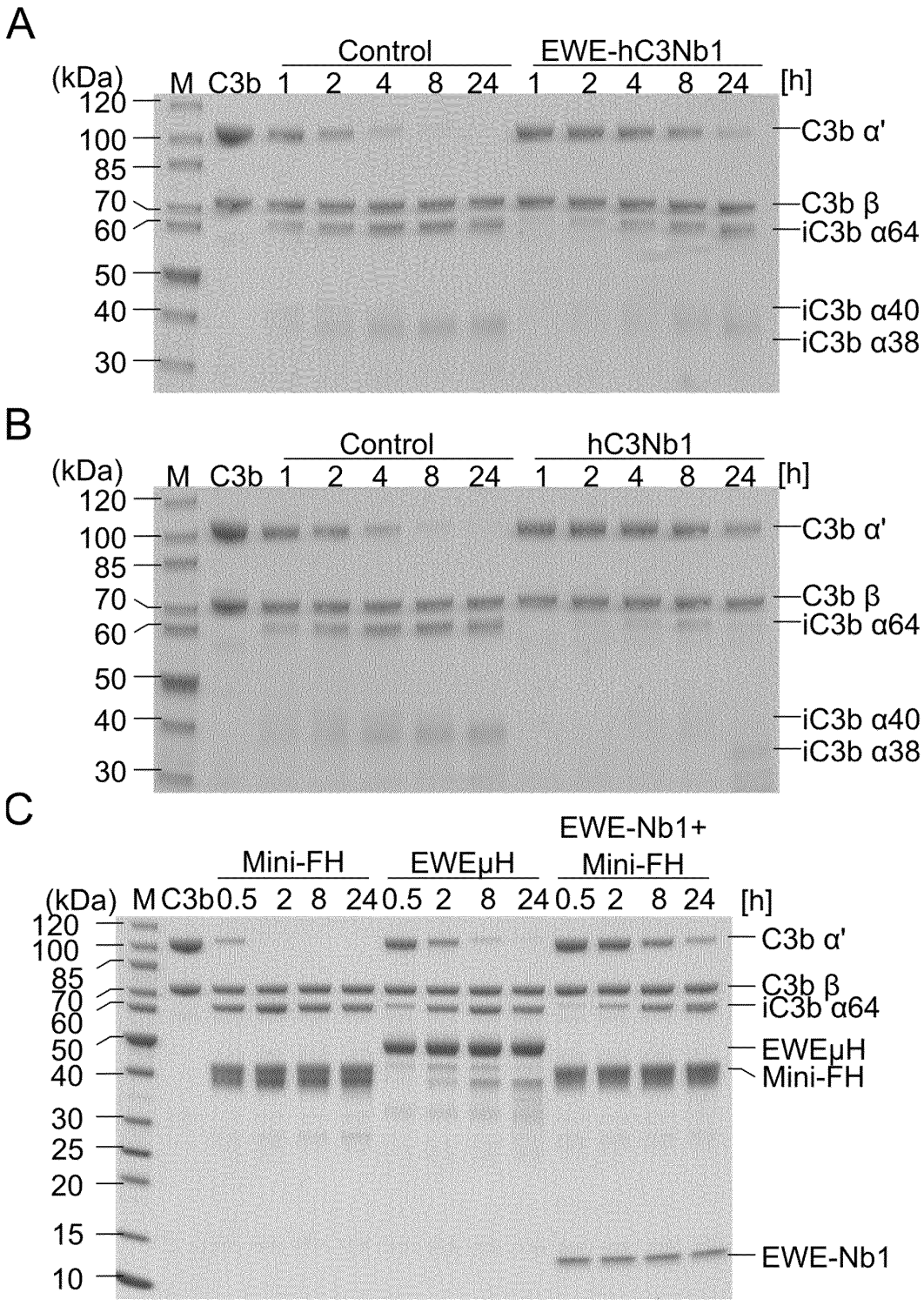

A
Control
EWE-hC3Nb1
(kDa)
M C3b 1 2 4 8 24 1 2 4 8 24 [h]
120
100
85
70
60
50
40
30
C3b α'
C3b β
iC3b α64
iC3b α40
iC3b α38
B
Control
hC3Nb1
(kDa)
M C3b 1 2 4 8 24 1 2 4 8 24 [h]
120
100
85
70
60
50
40
30
C3b α'
C3b β
iC3b α64
iC3b α40
iC3b α38
C
EWE-Nb1+
Mini-FH
Mini-FH
EWEμH
(kDa) M C3b 0.5 2 8 24 0.5 2 8 24 0.5 2 8 24 [h]
120
100
85
70
60
50
40
30
25
20
15
10
C3b α'
C3b β
iC3b α64
EWEμH
Mini-FH
EWE-Nb1

Fig. 6

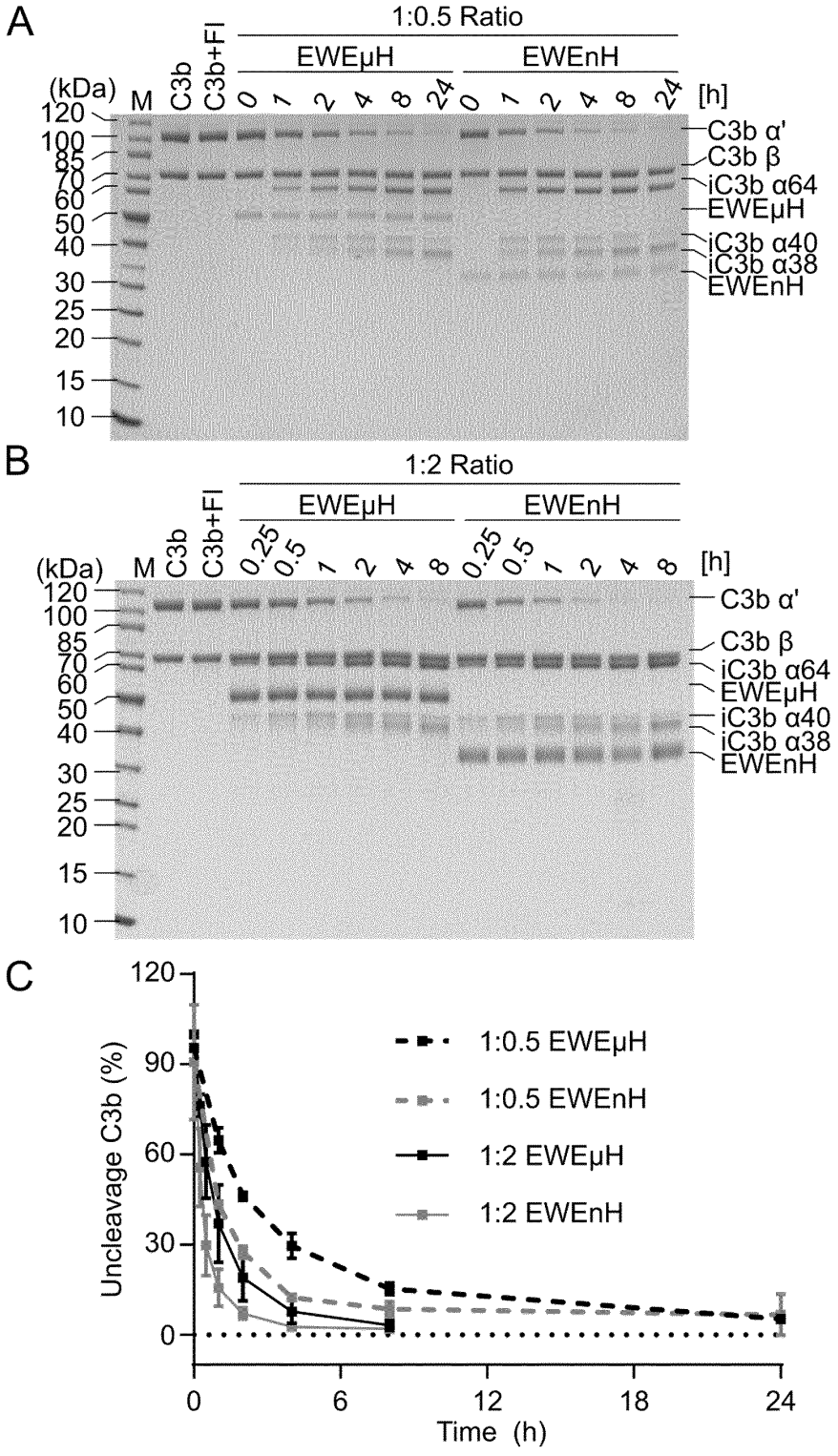

A
1:0.5 Ratio
EWEμH
EWEnH
C3b
C3b+FI
(kDa)
M
0 1 2 4 8 24 0 1 2 4 8 24 [h]
120
100
85
70
60
50
40
30
25
20
15
10
C3b α'
C3b β
iC3b α64
EWEμH
iC3b α40
iC3b α38
EWEnH
B
1:2 Ratio
EWEμH
EWEnH
C3b
C3b+FI
(kDa)
M
0.25 0.5 1 2 4 8 0.25 0.5 1 2 4 8 [h]
120
100
85
70
60
50
40
30
25
20
15
10
C3b α'
C3b β
iC3b α64
EWEμH
iC3b α40
iC3b α38
EWEnH
C
Uncleavage C3b (%)
120
90
60
30
0
0
6
12
18
24
Time (h)
1:0.5 EWEμH
1:0.5 EWEnH
1:2 EWEμH
1:2 EWEnH

Fig. 7

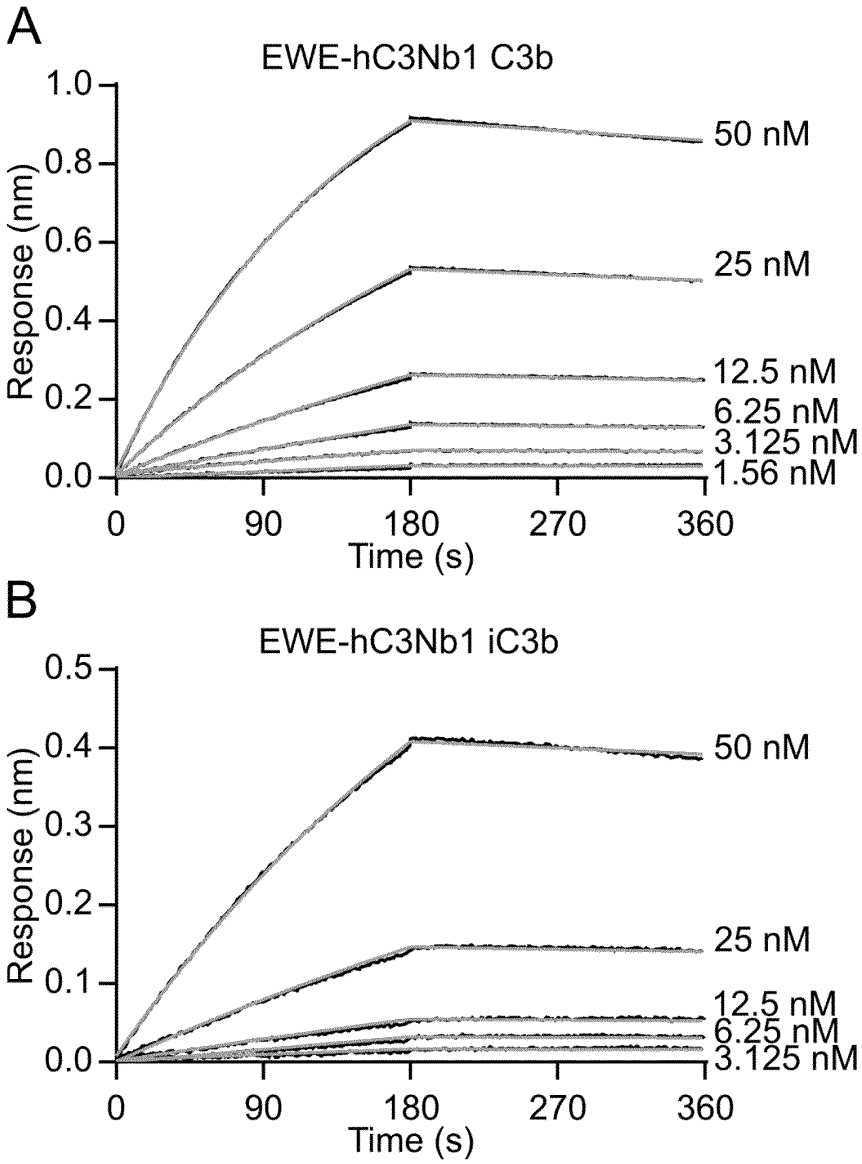

A
EWE-hC3Nb1 C3b
Response (nm)
1.0
0.8
0.6
0.4
0.2
0.0
0
90
180
270
360
Time (s)
50 nM
25 nM
12.5 nM
6.25 nM
3.125 nM
1.56 nM
B
EWE-hC3Nb1 iC3b
Response (nm)
0.5
0.4
0.3
0.2
0.1
0.0
0
90
180
270
360
Time (s)
50 nM
25 nM
12.5 nM
6.25 nM
3.125 nM

Fig. 8

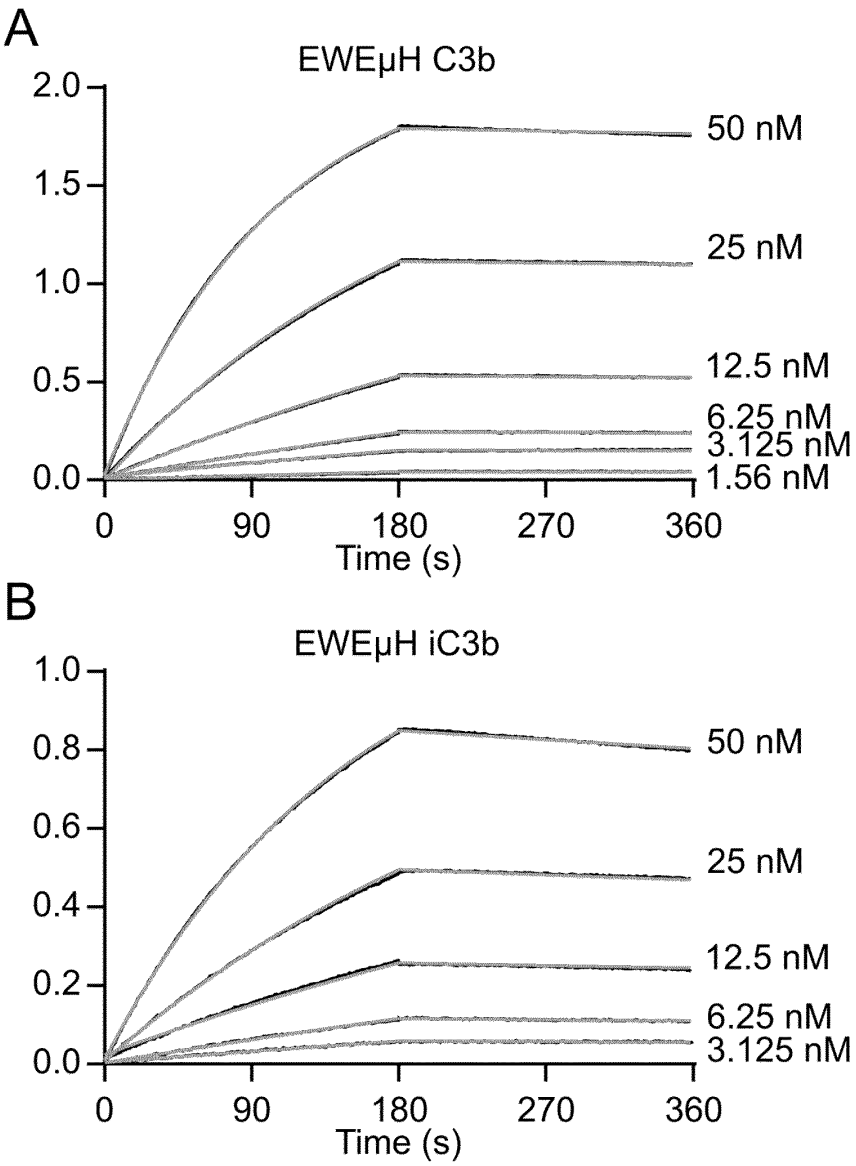

A
EWEμH C3b
2.0
1.5
1.0
0.5
0.0
50 nM
25 nM
12.5 nM
6.25 nM
3.125 nM
1.56 nM
0
90
180
270
360
Time (s)
B
EWEμH iC3b
1.0
0.8
0.6
0.4
0.2
0.0
50 nM
25 nM
12.5 nM
6.25 nM
3.125 nM
0
90
180
270
360
Time (s)

Fig. 9

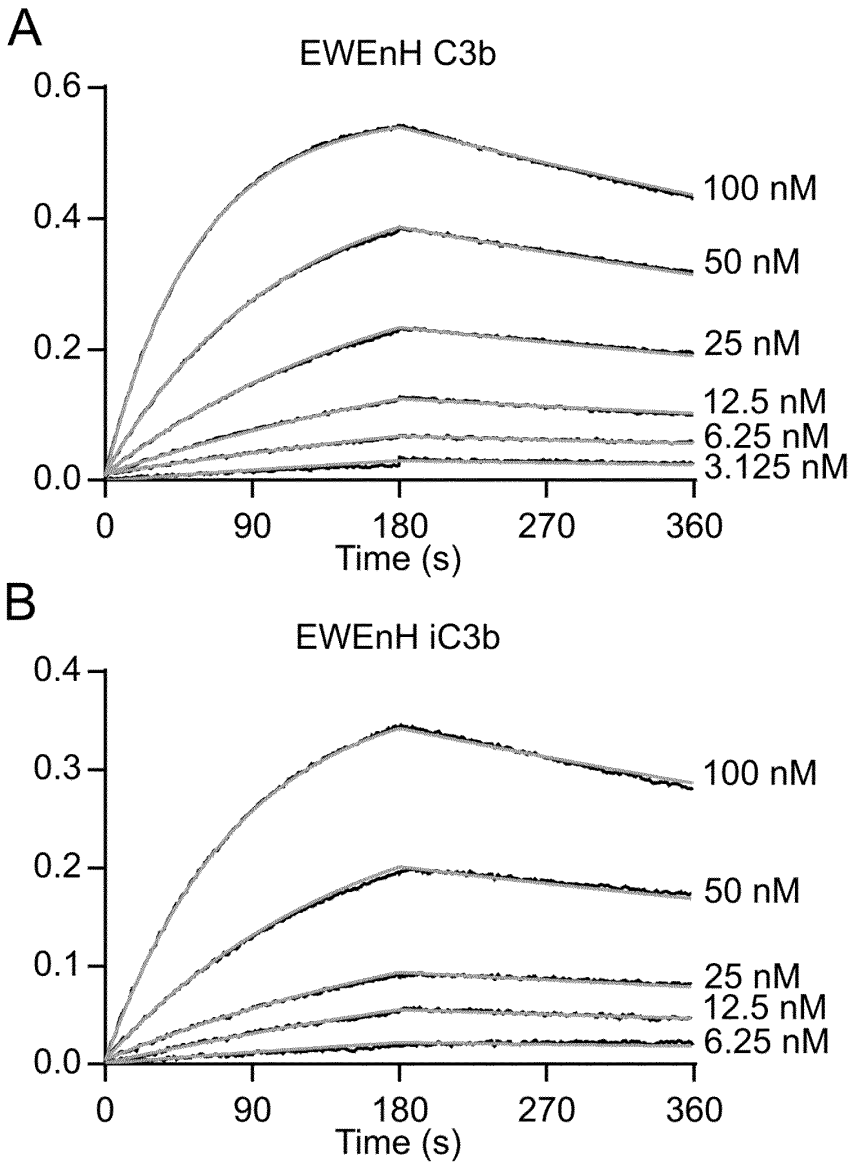

A
EWEnH C3b
0.6
0.4
0.2
0.0
100 nM
50 nM
25 nM
12.5 nM
6.25 nM
3.125 nM
0
90
180
270
360
Time (s)
B
EWEnH iC3b
0.4
0.3
0.2
0.1
0.0
100 nM
50 nM
25 nM
12.5 nM
6.25 nM
0
90
180
270
360
Time (s)

Fig. 10

A

	EWE-hC3Nb1		EWEμH		EWEnH	
	C3b	iC3b	C3b	iC3b	C3b	iC3b
$k_a(M^{-1}\cdot s^{-1}\cdot 10^5)$	1.3 ± 0.03	0.7 ± 0.1	1.8 ± 0.08	1.2 ± 0.1	1.7 ± 0.05	1.2 ± 0.1
$k_d(s^{-1}\cdot 10^{-4})$	3.7 ± 1	2.6 ± 0.4	0.7 ± 0.07	3.3 ± 0.3	12 ± 0.7	11 ± 0.9
K_D(nM)	3 ± 0.8	3.6 ± 0.06	0.4 ± 0.03	2.9 ± 0.6	7.1 ± 0.6	8.9 ± 0.05

Fig. 11

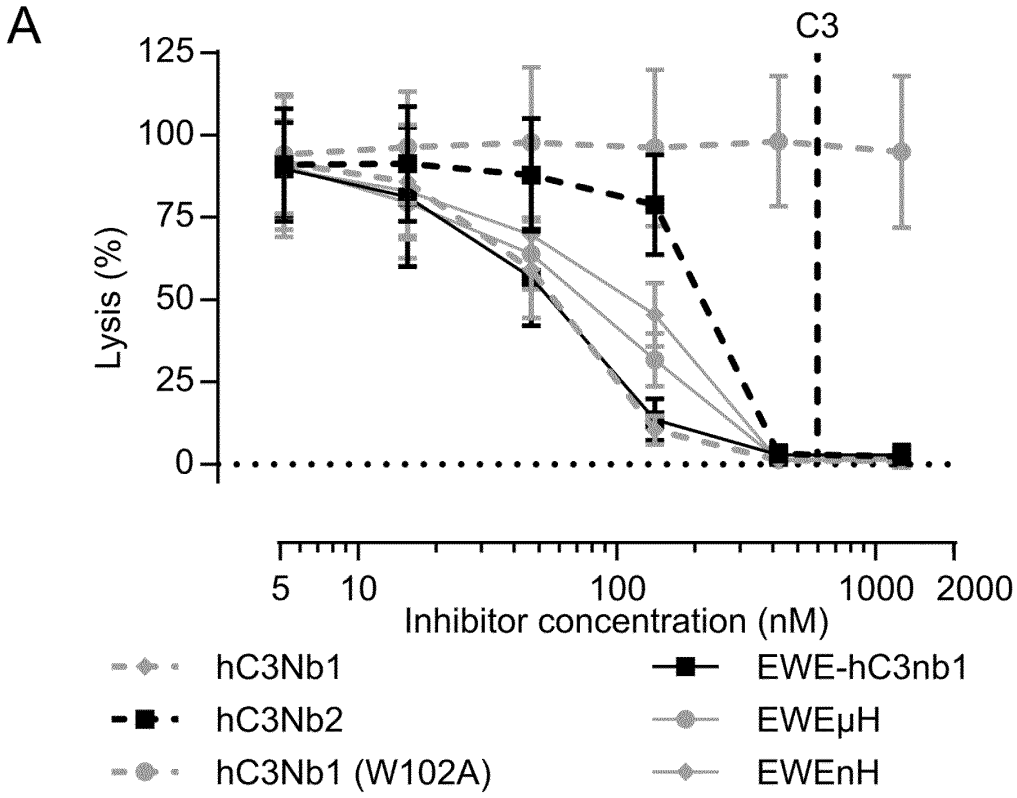

A
C3
125
100
75
50
25
0
Lysis (%)
5
10
100
1000
2000
Inhibitor concentration (nM)
hC3Nb1
hC3Nb2
hC3Nb1 (W102A)
EWE-hC3nb1
EWEμH
EWEnH

Fig. 12

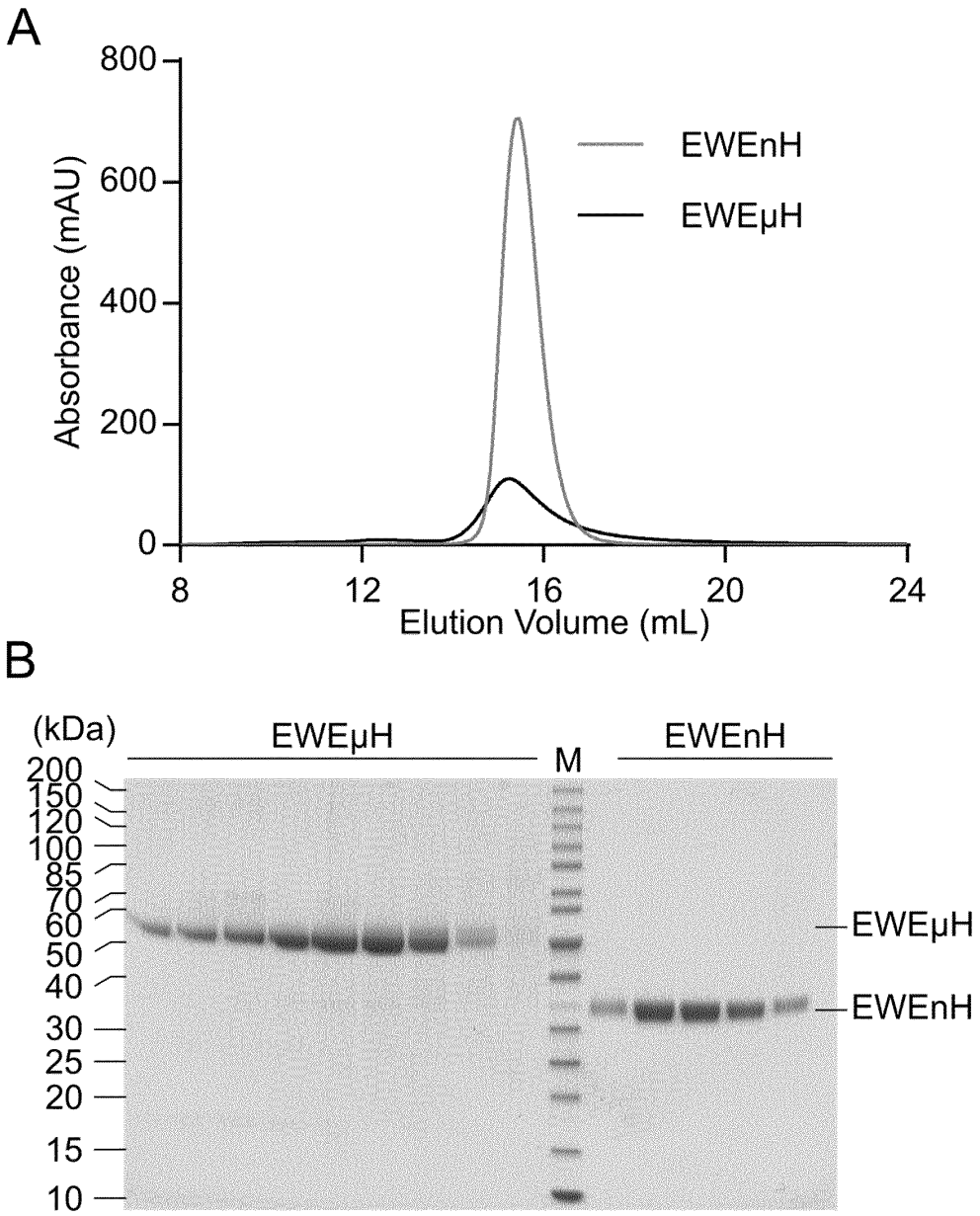
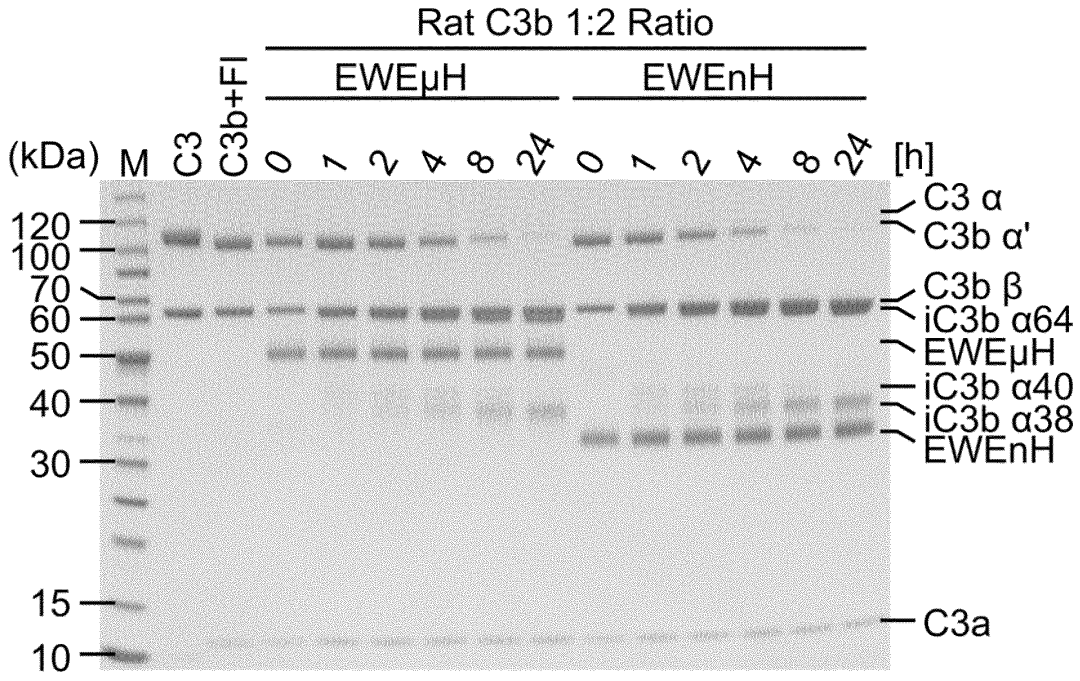

A
800
600
400
200
0
Absorbance (mAU)
8
12
16
20
24
Elution Volume (mL)
EWEnH
EWEμH
B
(kDa)
EWEμH
M
EWEnH
200
150
120
100
85
70
60
50
40
30
25
20
15
10
EWEμH
EWEnH

Fig. 13


Rat C3b 1:2 Ratio
EWEμH
EWEnH
(kDa)
M
C3
C3b+FI
0
1
2
4
8
24
0
1
2
4
8
24
[h]
120
100
70
60
50
40
30
15
10
C3 α
C3b α'
C3b β
iC3b α64
EWEμH
iC3b α40
iC3b α38
EWEnH
C3a