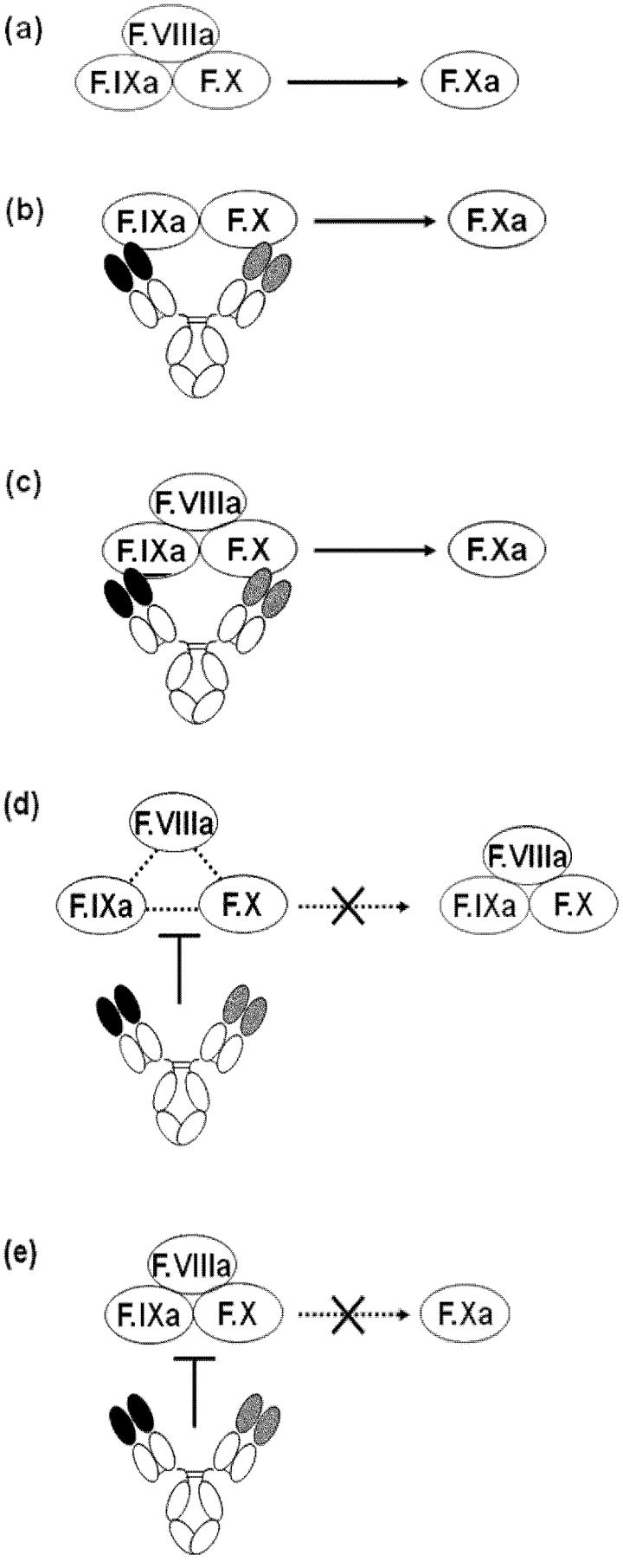
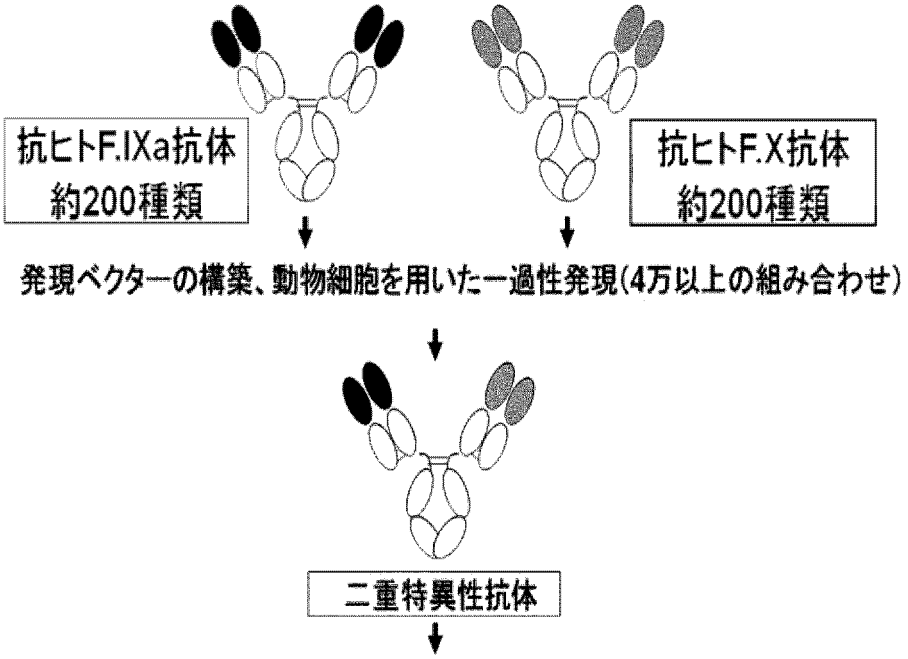
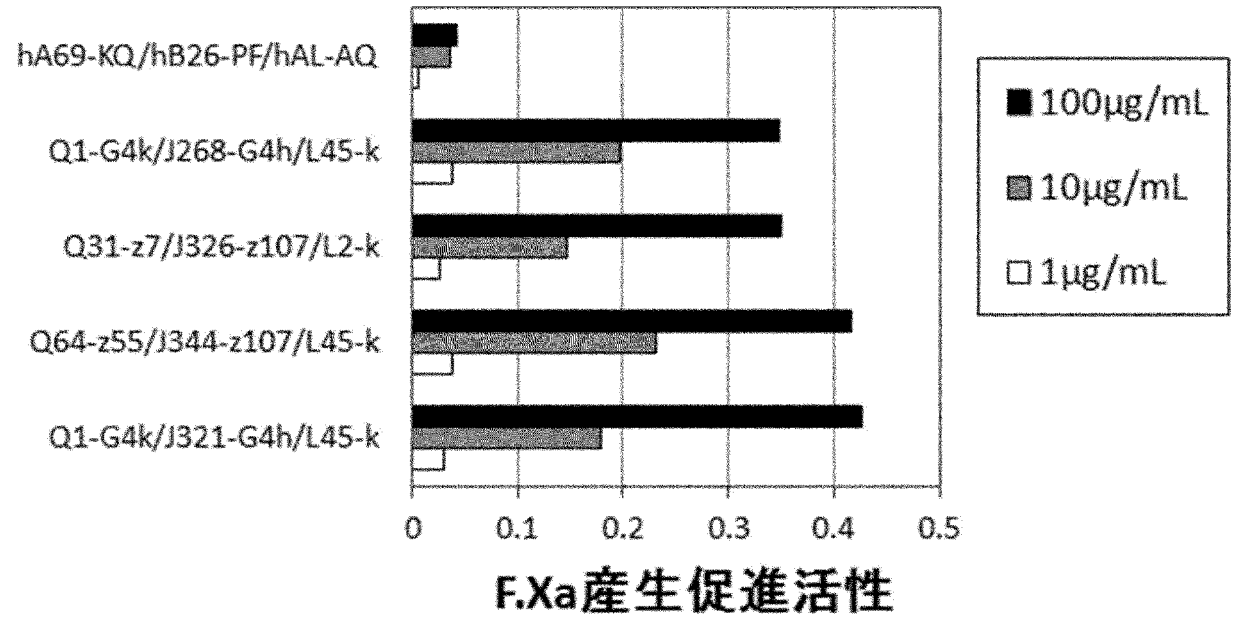
[図1]


(a)
F.VIIIa
F.IXa
F.X
F.Xa
(b)
F.IXa
F.X
F.Xa
(c)
F.VIIIa
F.IXa
F.X
F.Xa
(d)
F.VIIIa
F.IXa
F.X
F.VIIIa
F.IXa
F.X
(e)
F.VIIIa
F.IXa
F.X
F.Xa

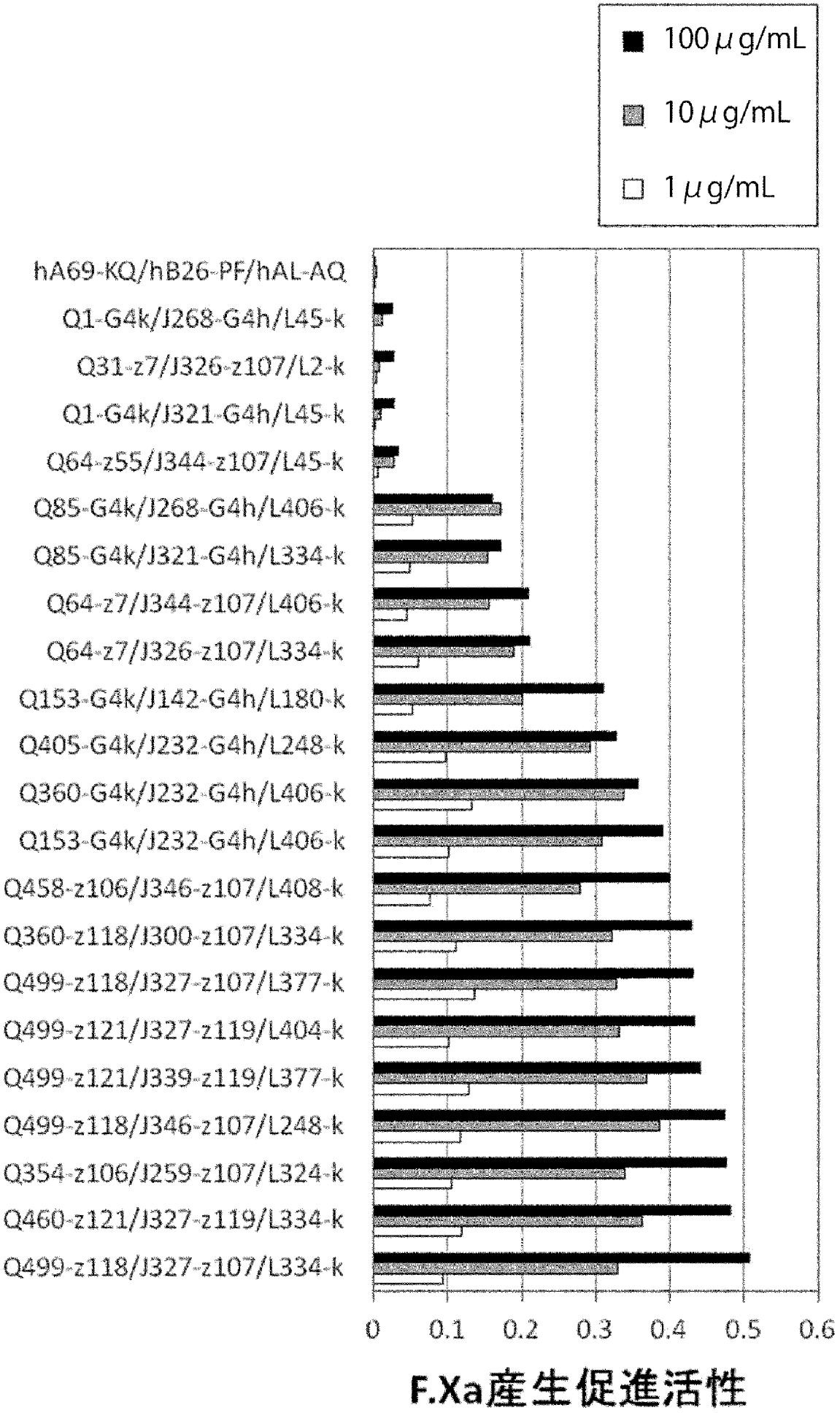
[図2]


抗ヒトF.IXa抗体
約200種類
抗ヒトF.X抗体
約200種類
発現ベクターの構築、動物細胞を用いた一過性発現(4万以上の組み合わせ)
二重特異性抗体
F.Xa産生促進活性およびF.Xase阻害作用によるスクリーニング
さらに必要に応じてアミノ酸置換

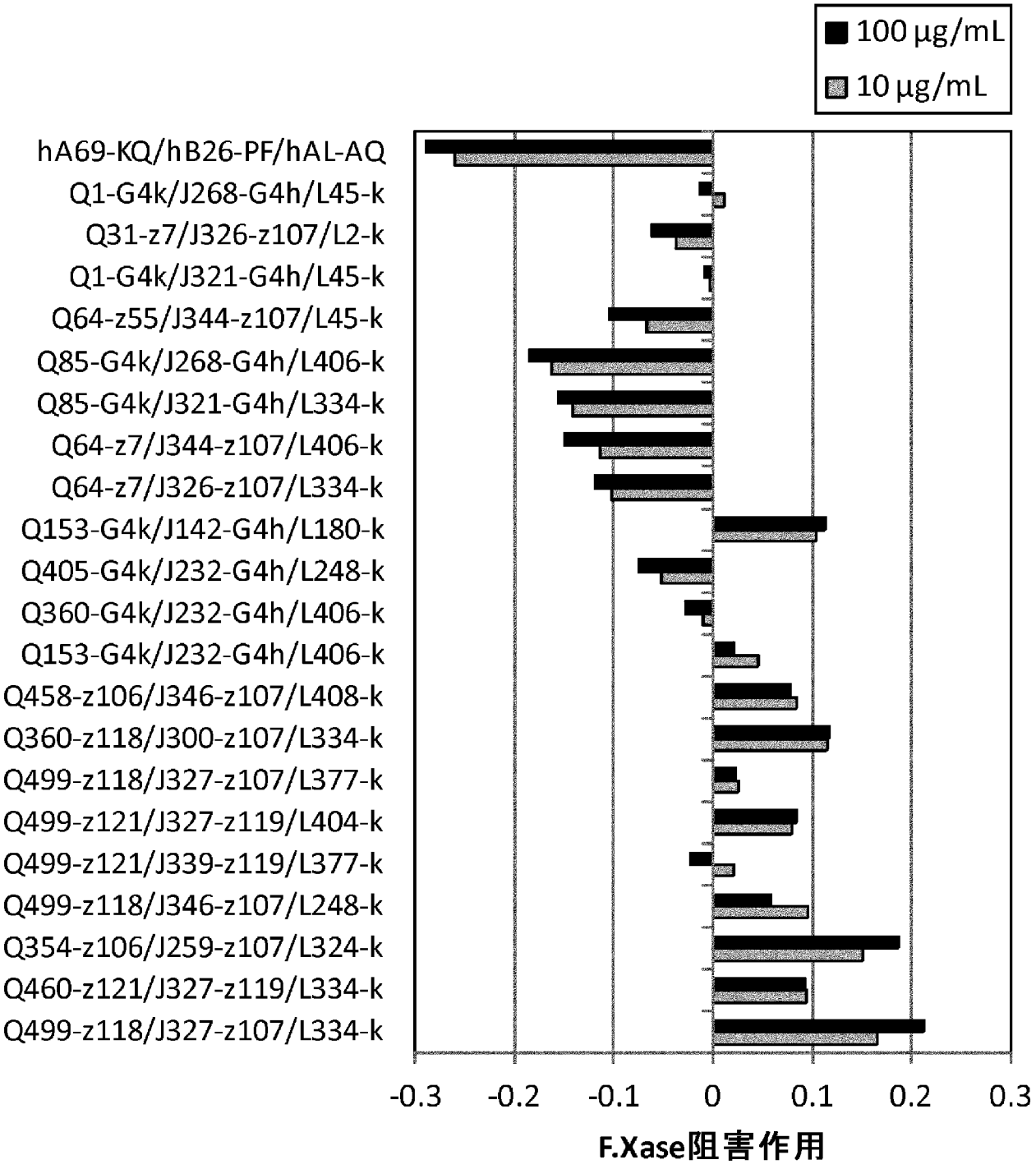
[図3]


hA69-KQ/hB26-PF/hAL-AQ
Q1-G4k/J268-G4h/L45-k
Q31-z7/J326-z107/L2-k
Q64-z55/J344-z107/L45-k
Q1-G4k/J321-G4h/L45-k
100μg/mL
10μg/mL
1μg/mL
0
0.1
0.2
0.3
0.4
0.5
F.Xa産生促進活性

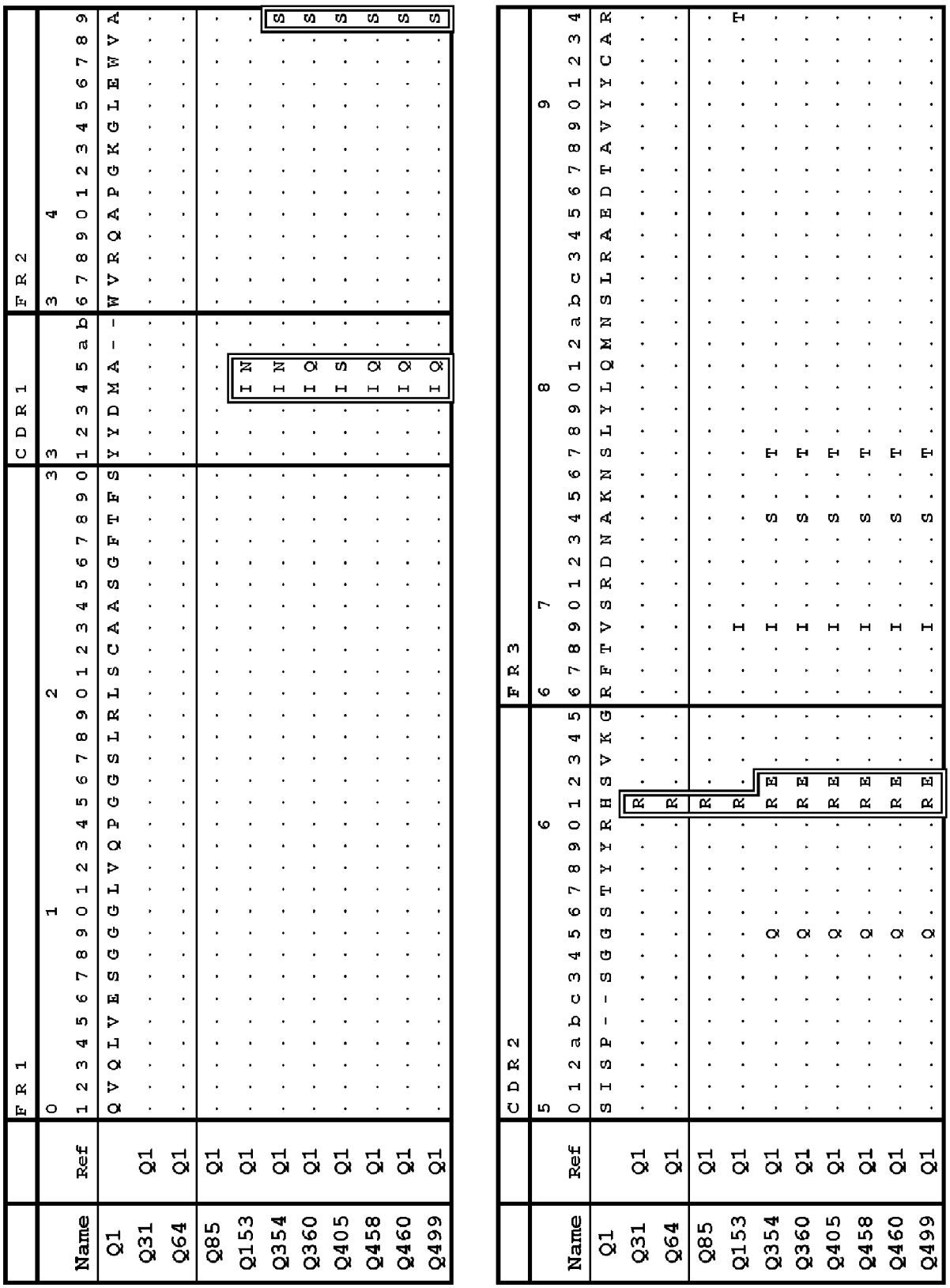
[図4]


100μg/mL
10μg/mL
1μg/mL
hA69-KQ/hB26-PF/hAL-AQ
Q1-G4k/J268-G4h/L45-k
Q31-z7/J326-z107/L2-k
Q1-G4k/J321-G4h/L45-k
Q64-z55/J344-z107/L45-k
Q85-G4k/J268-G4h/L406-k
Q85-G4k/J321-G4h/L334-k
Q64-z7/J344-z107/L406-k
Q64-z7/J326-z107/L334-k
Q153-G4k/J142-G4h/L180-k
Q405-G4k/J232-G4h/L248-k
Q360-G4k/J232-G4h/L406-k
Q153-G4k/J232-G4h/L406-k
Q458-z106/J346-z107/L408-k
Q360-z118/J300-z107/L334-k
Q499-z118/J327-z107/L377-k
Q499-z121/J327-z119/L404-k
Q499-z121/J339-z119/L377-k
Q499-z118/J346-z107/L248-k
Q354-z106/J259-z107/L324-k
Q460-z121/J327-z119/L334-k
Q499-z118/J327-z107/L334-k
0
0.1
0.2
0.3
0.4
0.5
0.6
F.Xa産生促進活性

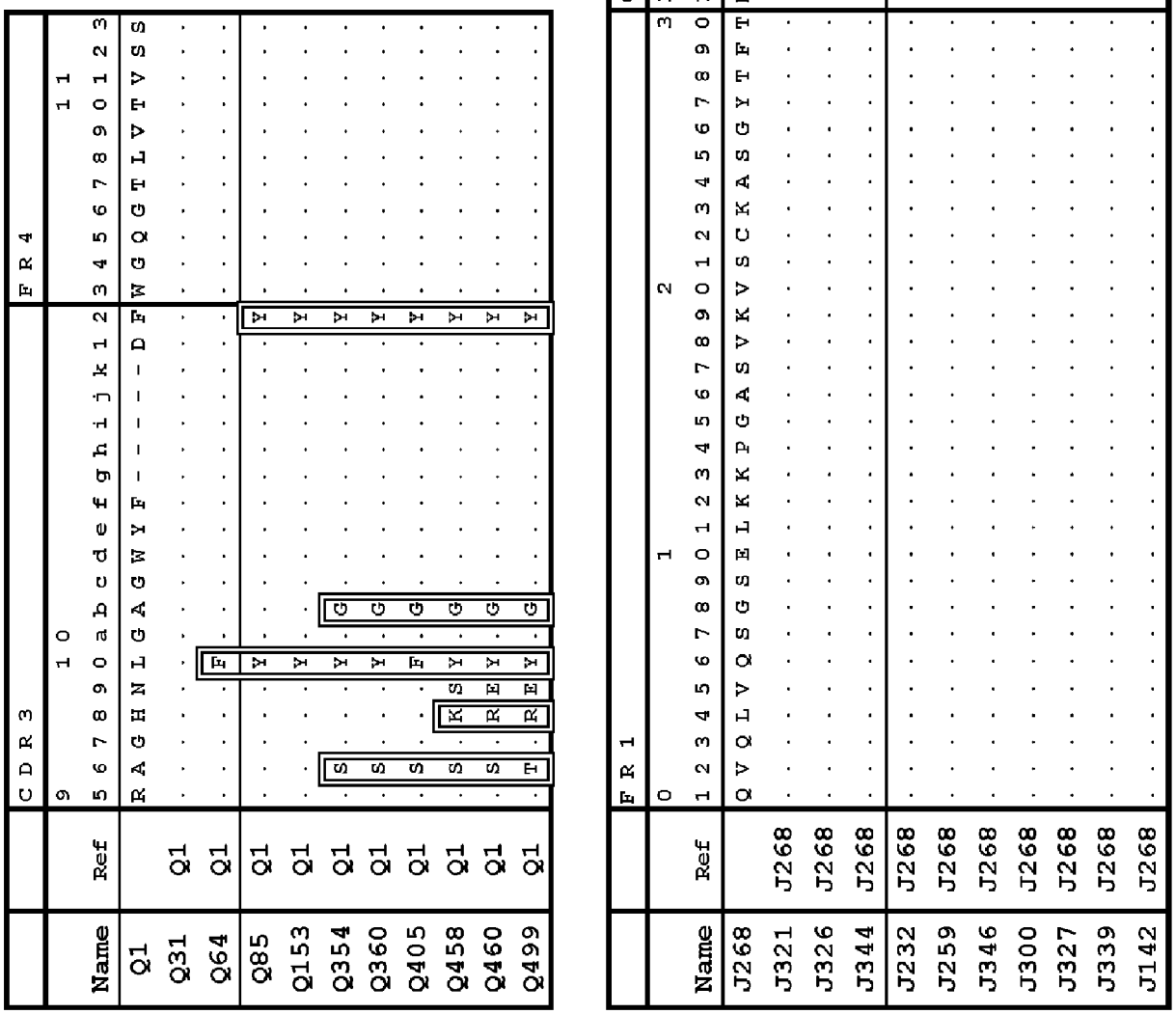
[図5]


100 μg/mL
10 μg/mL
hA69-KQ/hB26-PF/hAL-AQ
Q1-G4k/J268-G4h/L45-k
Q31-z7/J326-z107/L2-k
Q1-G4k/J321-G4h/L45-k
Q64-z55/J344-z107/L45-k
Q85-G4k/J268-G4h/L406-k
Q85-G4k/J321-G4h/L334-k
Q64-z7/J344-z107/L406-k
Q64-z7/J326-z107/L334-k
Q153-G4k/J142-G4h/L180-k
Q405-G4k/J232-G4h/L248-k
Q360-G4k/J232-G4h/L406-k
Q153-G4k/J232-G4h/L406-k
Q458-z106/J346-z107/L408-k
Q360-z118/J300-z107/L334-k
Q499-z118/J327-z107/L377-k
Q499-z121/J327-z119/L404-k
Q499-z121/J339-z119/L377-k
Q499-z118/J346-z107/L248-k
Q354-z106/J259-z107/L324-k
Q460-z121/J327-z119/L334-k
Q499-z118/J327-z107/L334-k
-0.3
-0.2
-0.1
0
0.1
0.2
0.3
F.Xase阻害作用

[図6A]

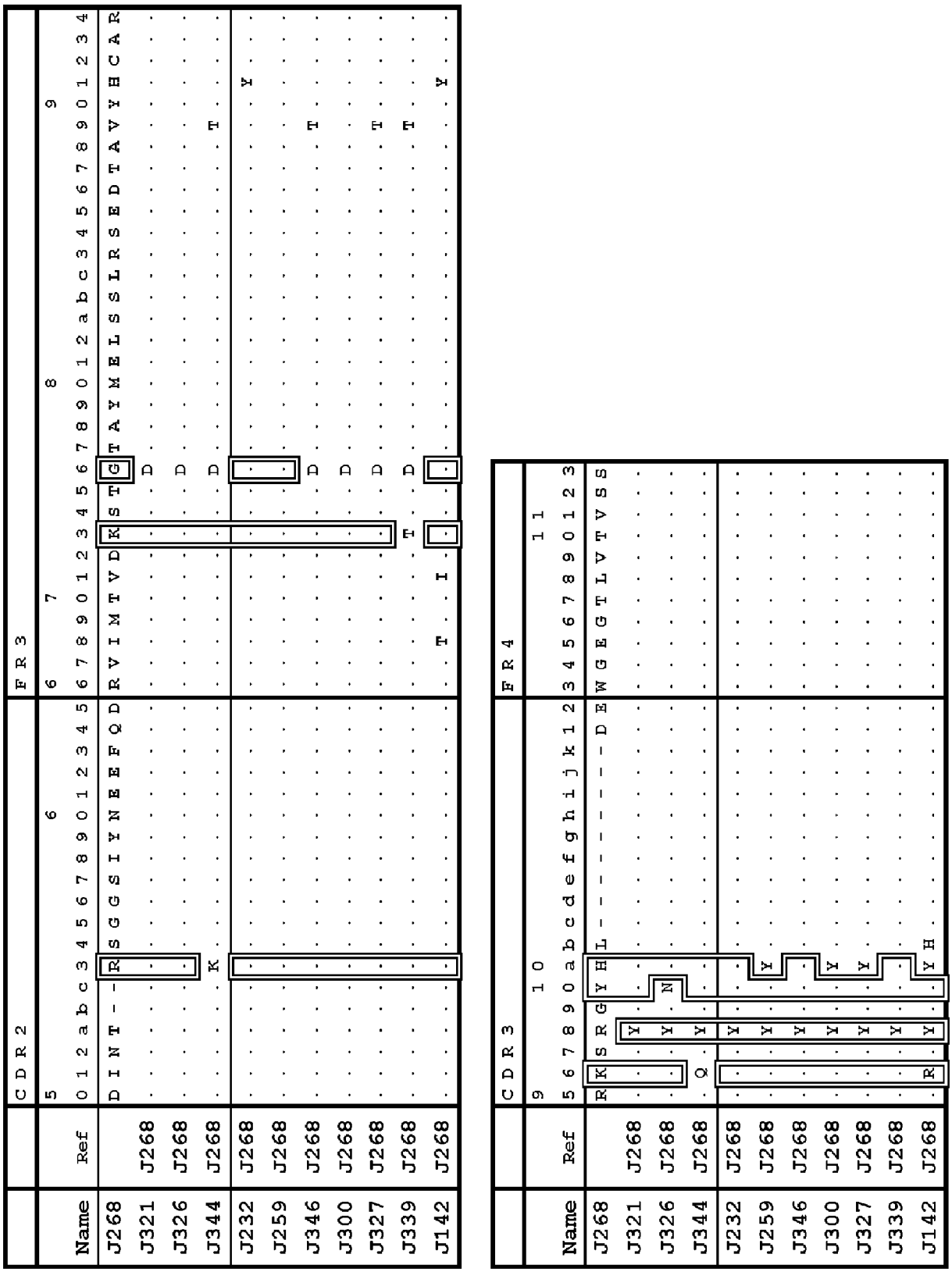


[図6B]

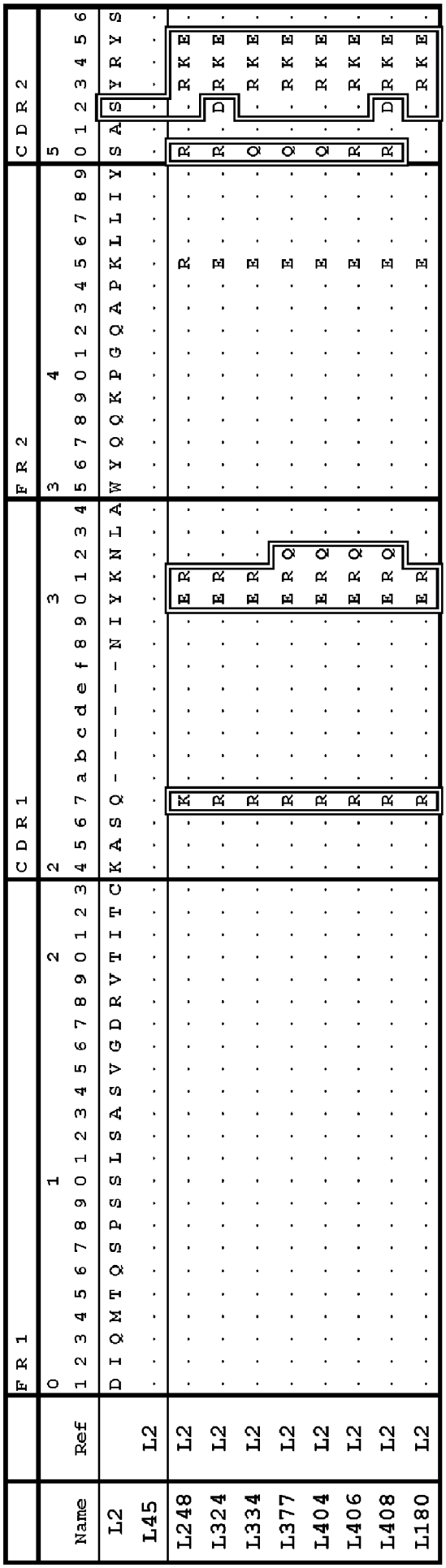

CDR3
FR4
Name
Ref
Q1
Q31
Q64
Q85
Q153
Q354
Q360
Q405
Q458
Q460
Q499

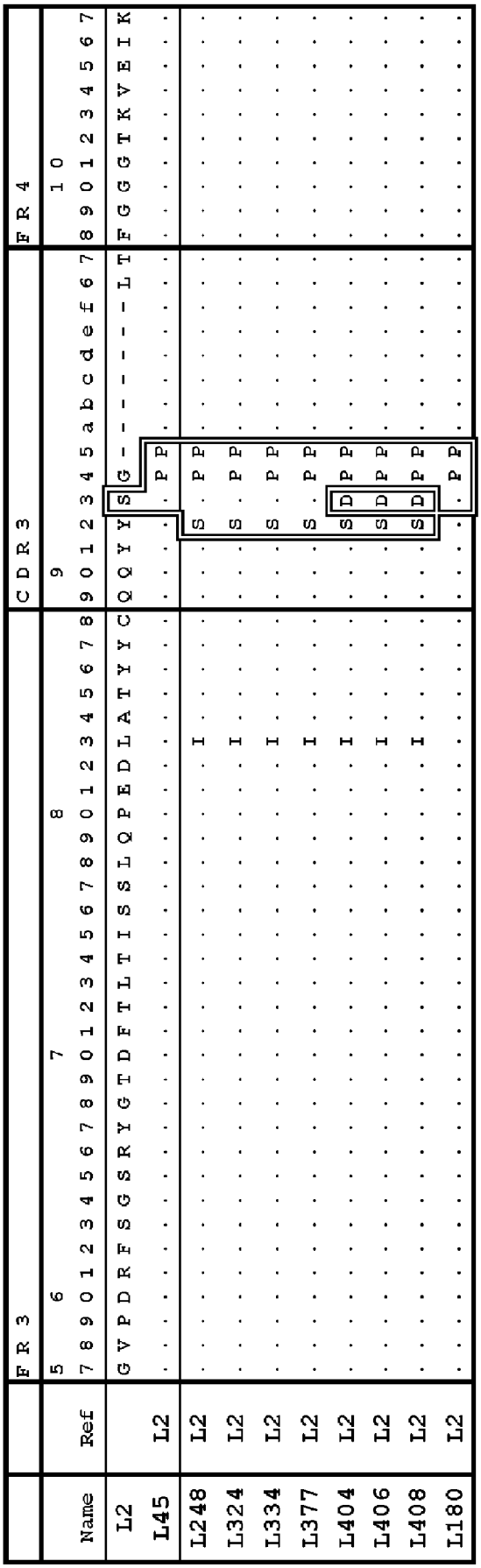
FR1
CDR1
FR2
Name
Ref
J268
J321
J326
J344
J232
J259
J346
J300
J327
J339
J142

[図6C]


CDR2
FR3
CDR3
FR4
Name
Ref
J268
J321
J326
J344
J232
J259
J346
J300
J327
J339
J142

[図6D]


FR1
CDR1
FR2
CDR2
Name
Ref
L2
L45
L248
L324
L334
L377
L404
L406
L408
L180


FR3
CDR3
FR4
Name
Ref
L2
L45
L248
L324
L334
L377
L404
L406
L408
L180