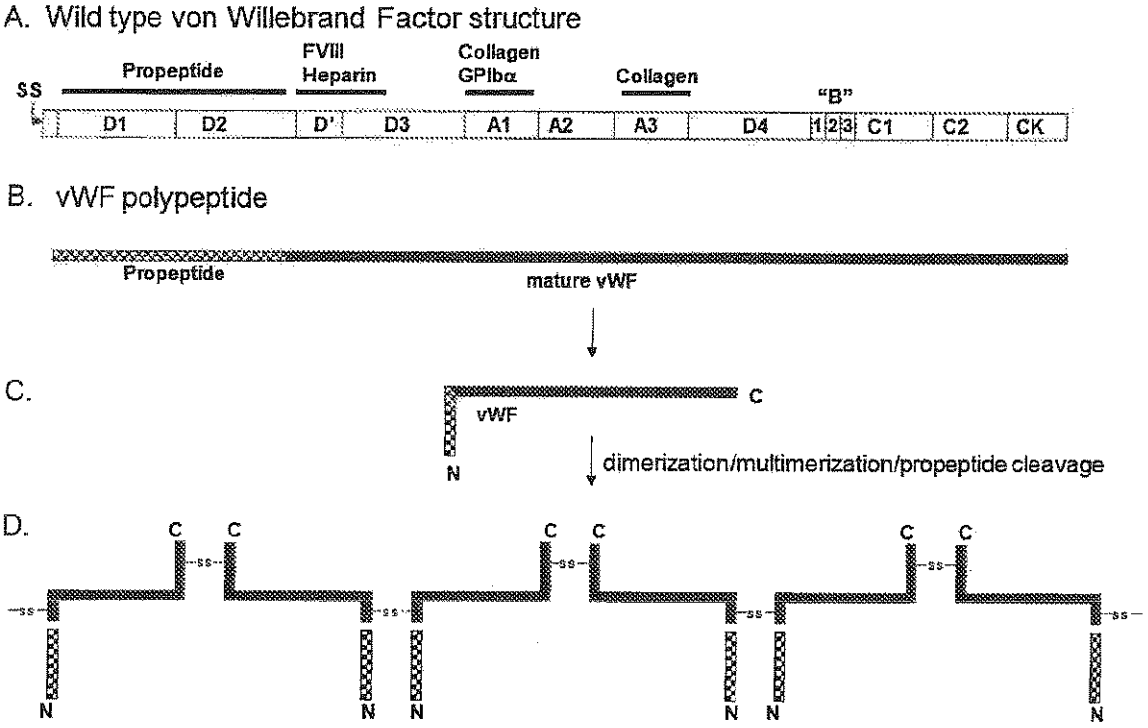
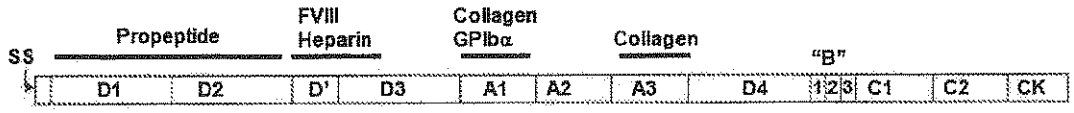
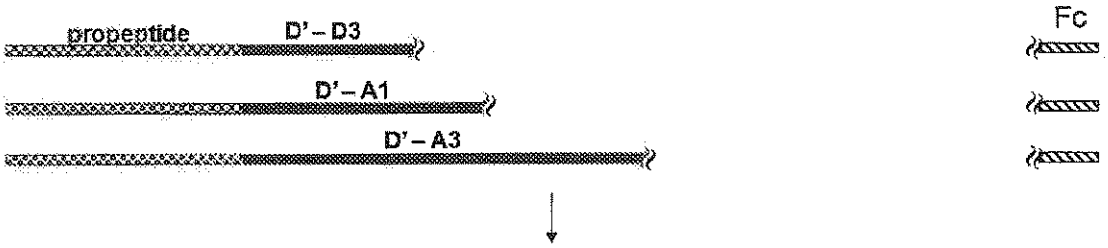

A. Wild type von Willebrand Factor structure
SS
Propeptide
FVIII Heparin
Collagen GPIbα
Collagen
"B"
D1
D2
D'
D3
A1
A2
A3
D4
1
2
3
C1
C2
CK
B. vWF polypeptide
Propeptide
mature vWF
C.
C
vWF
N
dimerization/multimerization/propeptide cleavage
D.
C
N
SS

FIGURE 1

A. Wild type von Willebrand Factor structure



B. vWF domain segments with fusion to Fc of IgG_1



C. vWF-Fc fusion product monomer

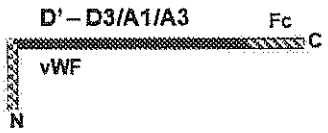


FIGURE 2

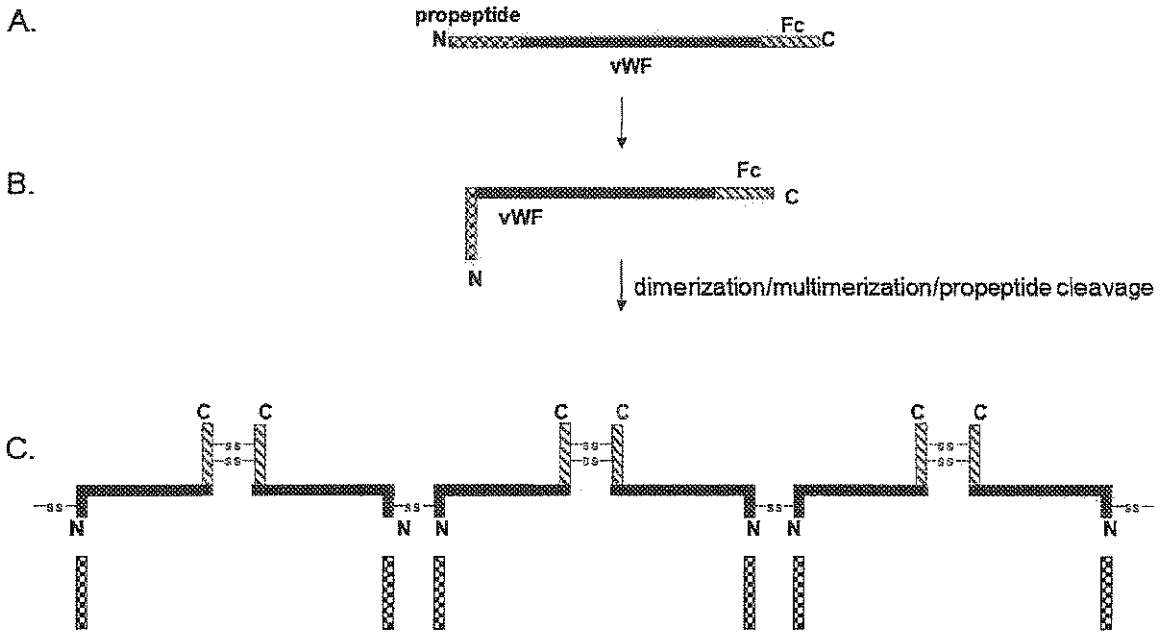

A.
propeptide
N
Fc
C
vWF
B.
Fc
C
vWF
N
dimerization/multimerization/propeptide cleavage
C.
C
C
SS
SS
SS
N
N
N

FIGURE 3

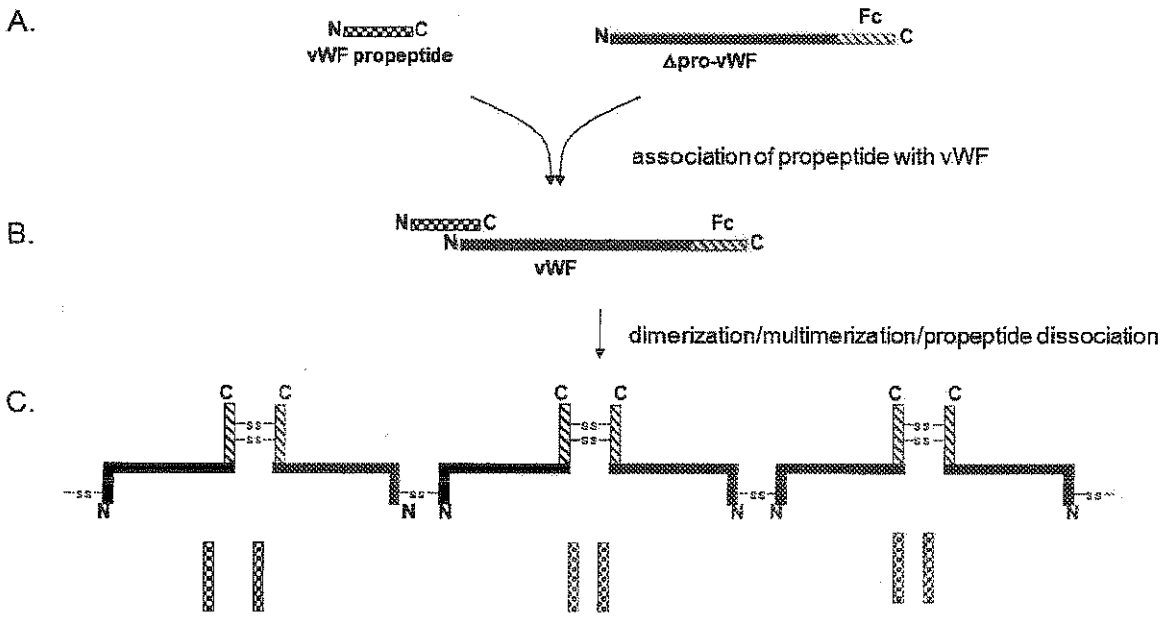

A.
N C
vWF propeptide
Fc
N C
Δpro-vWF
association of propeptide with vWF
B.
N C
Fc
N C
vWF
dimerization/multimerization/propeptide dissociation
C.
C C
C C
C C
N
N N
N N
N

FIGURE 4

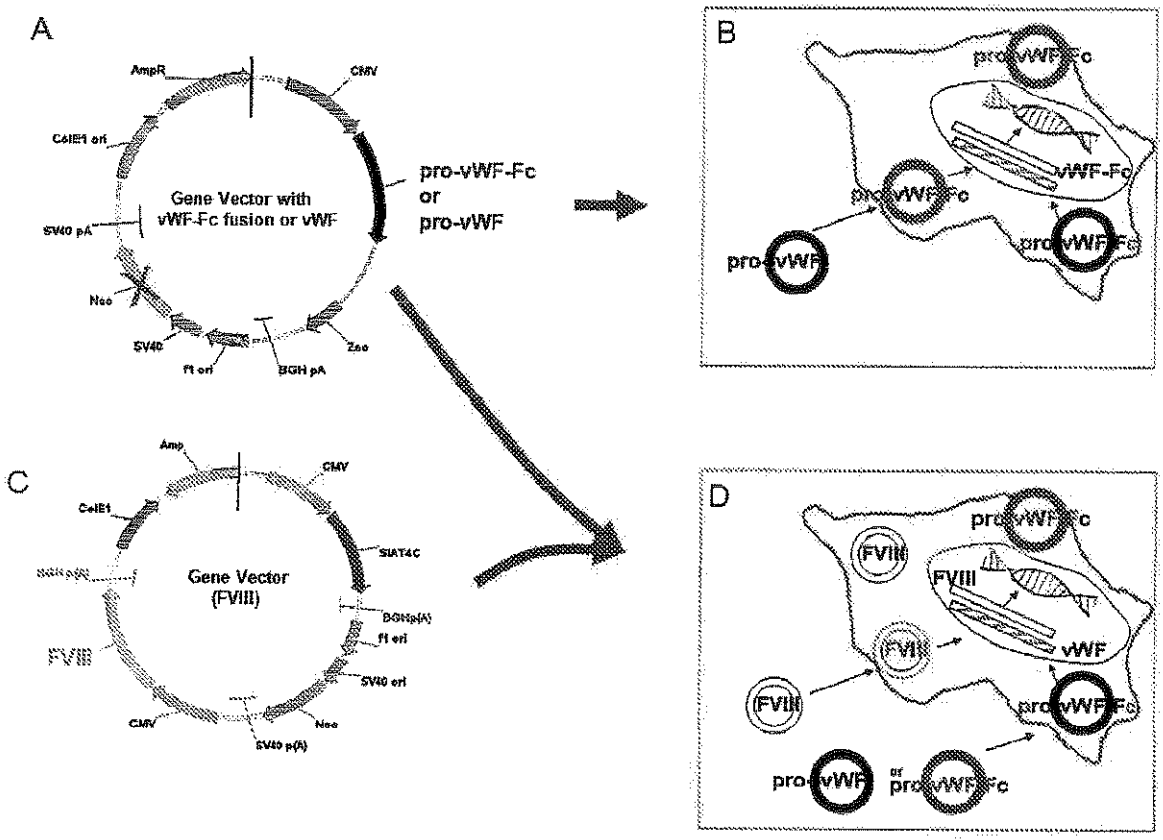

A
AmpR
CMV
ColE1 ori
Gene Vector with
vWF-Fc fusion or vWF
pro-vWF-Fc
or
pro-vWF
SV40 pA
Neo
SV40
f1 ori
BGH pA
Zeo
B
C
Amp
CMV
ColE1
SIAT4C
Gene Vector
(FVIII)
BGH pA
f1 ori
FVIII
SV40 ori
CMV
Neo
SV40 p(A)
D
FVIII
vWF
or

FIGURE 5

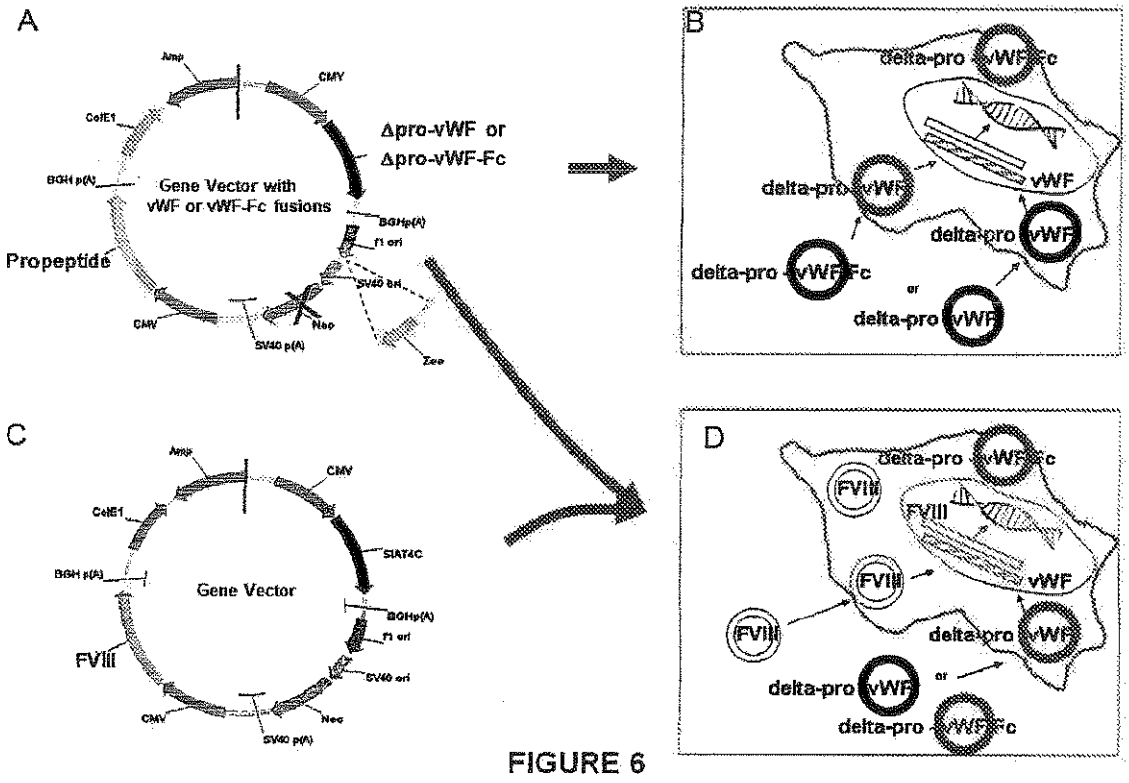

A
Amp
CMV
ColE1
Δpro-vWF or
Δpro-vWF-Fc
BGH p(A)
Gene Vector with
vWF or vWF-Fc fusions
BGHp(A)
f1 ori
Propeptide
SV40 ori
CMV
Neo
SV40 p(A)
Zeo
B
delta-pro vWF-Fc
delta-pro vWF
vWF
delta-pro vWF
delta-pro vWF-Fc
or
delta-pro vWF
C
Amp
CMV
ColE1
SIAT4C
BGH p(A)
Gene Vector
BGHp(A)
f1 ori
FVIII
SV40 ori
CMV
Neo
SV40 p(A)
D
delta-pro vWF-Fc
FVIII
FVIII
FVIII
vWF
FVIII
delta-pro vWF
delta-pro vWF
or
delta-pro vWF-Fc

FIGURE 6

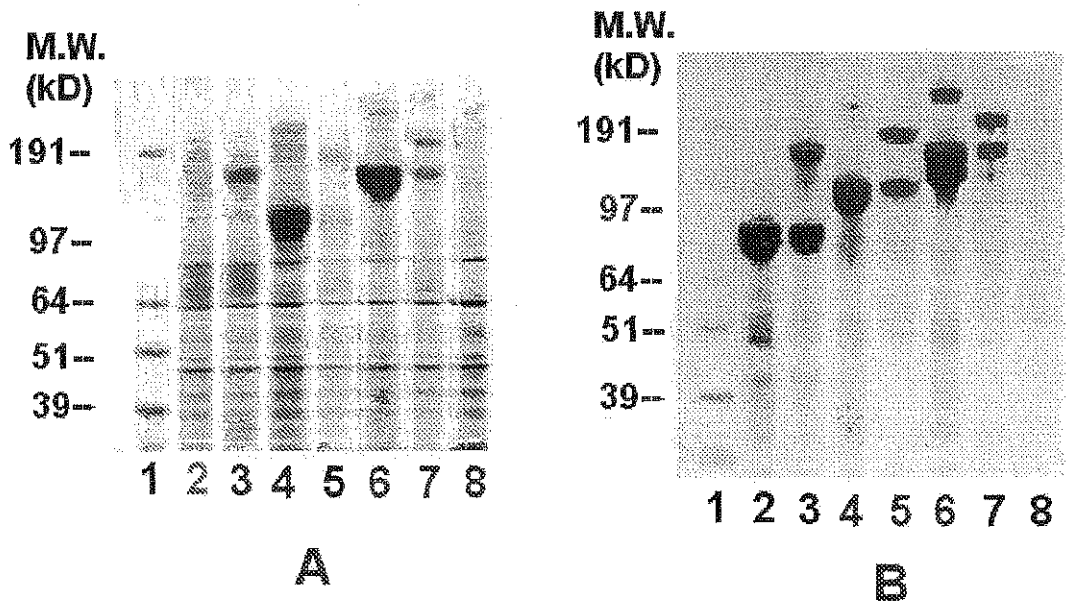


FIGURE 7

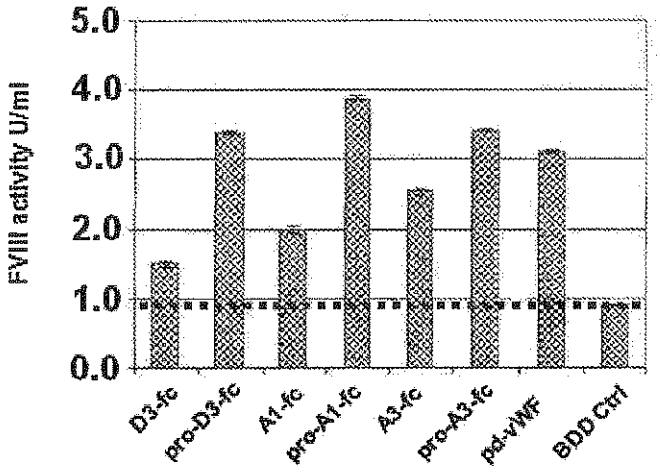

FVIII activity U/ml
5.0
4.0
3.0
2.0
1.0
0.0
D3-fc
pro-D3-fc
A1-fc
pro-A1-fc
A3-fc
pro-A3-fc
pct-vWF
BDD Ctrl

FIGURE 8

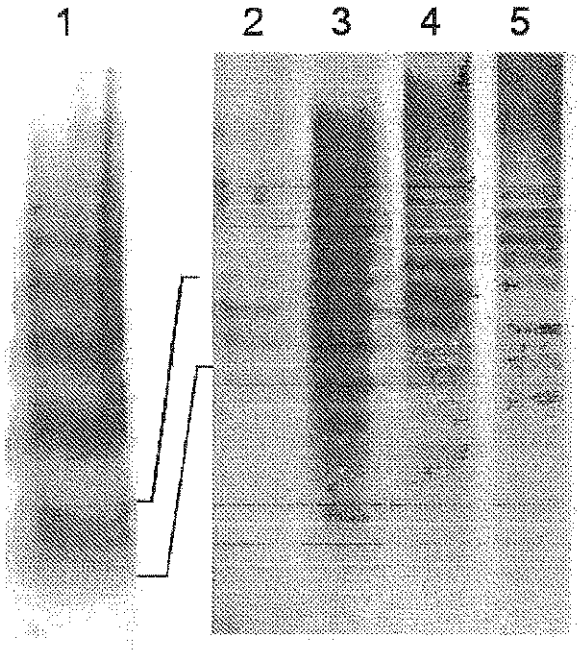


FIGURE 9

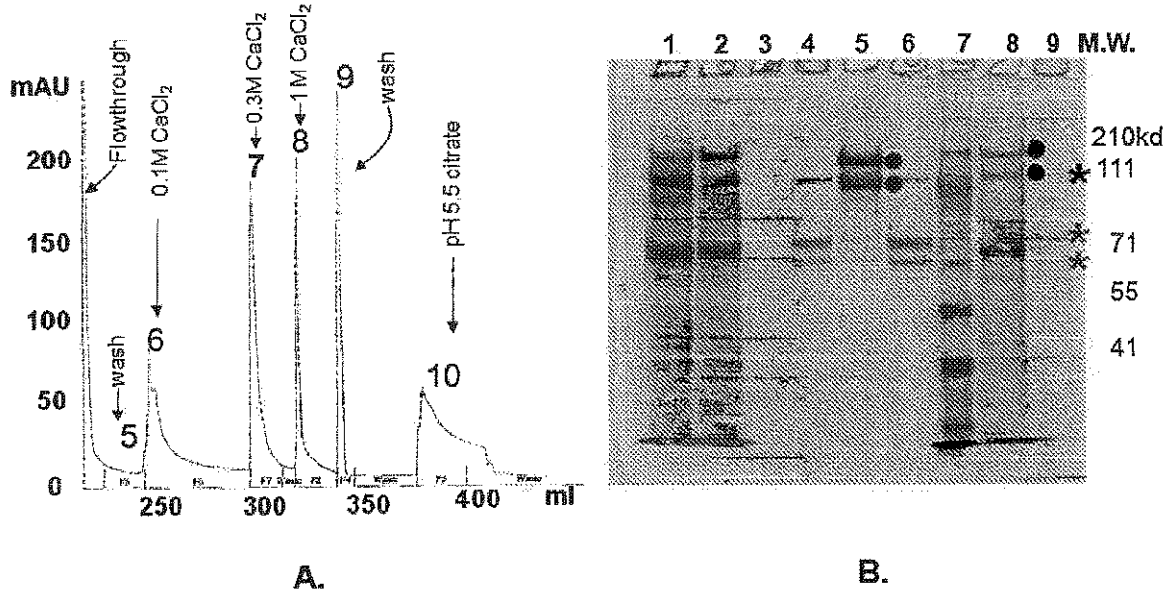

mAU
200
150
100
50
0
Flowthrough
0.1M CaCl2
0.3M CaCl2
1M CaCl2
wash
pH 5.5 citrate
5
6
7
8
9
10
250
300
350
400
ml
A.
1 2 3 4 5 6 7 8 9 M.W.
210kd
111
71
55
41
B.

FIGURE 10

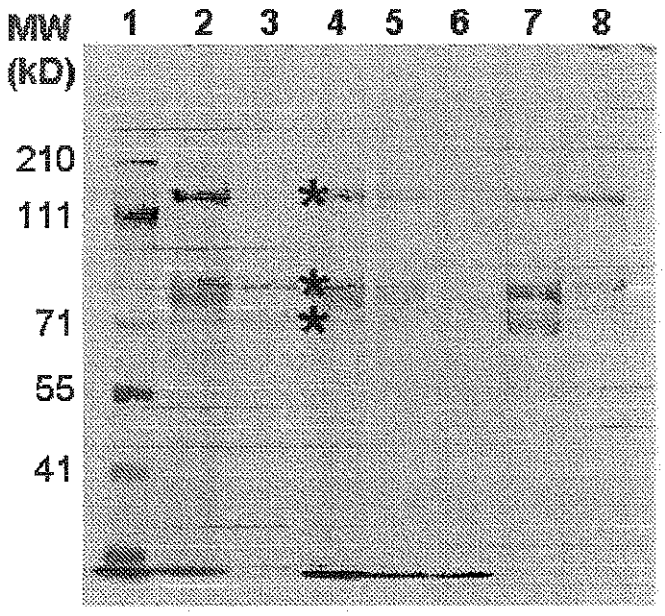


FIGURE 11