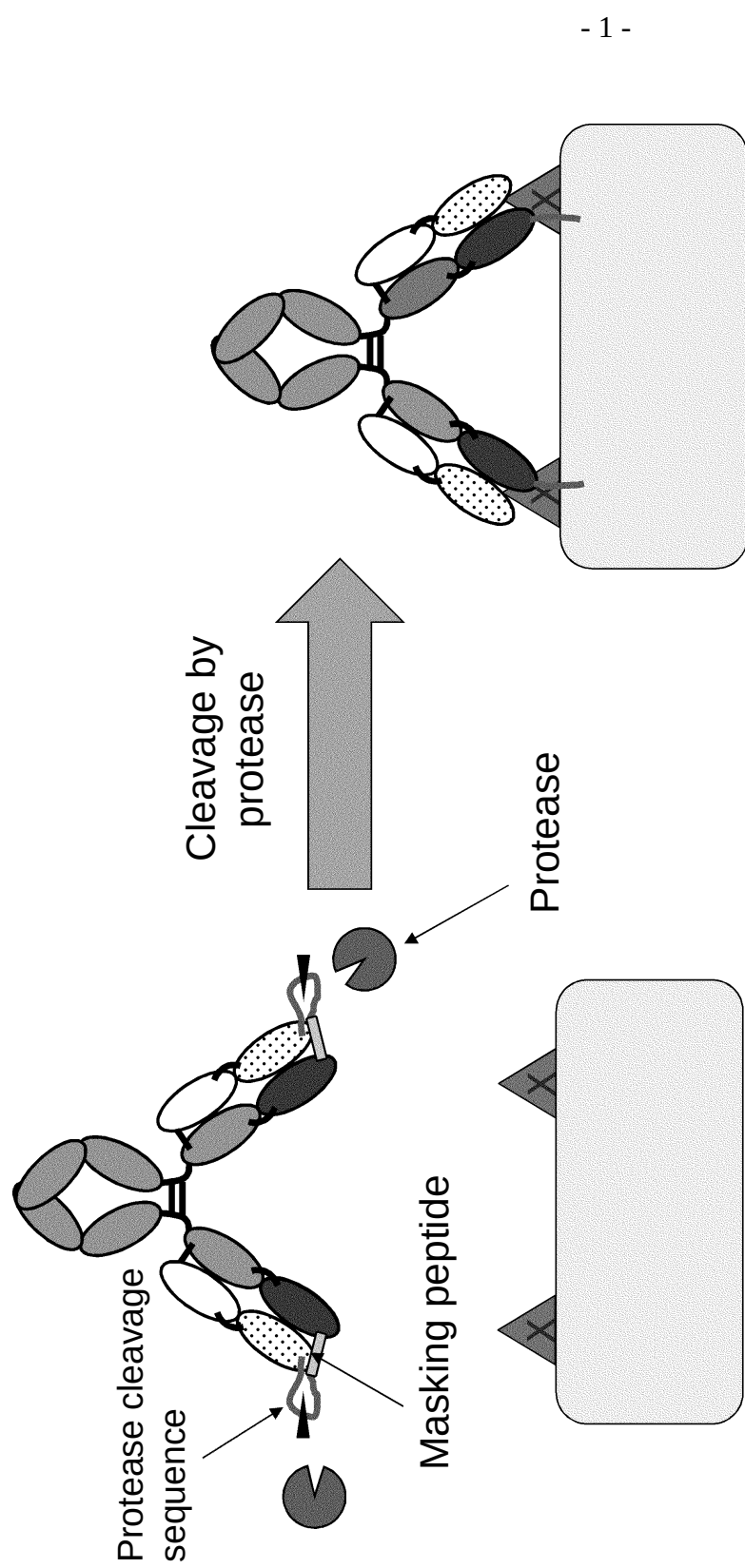




- 1 -

FIG. 1

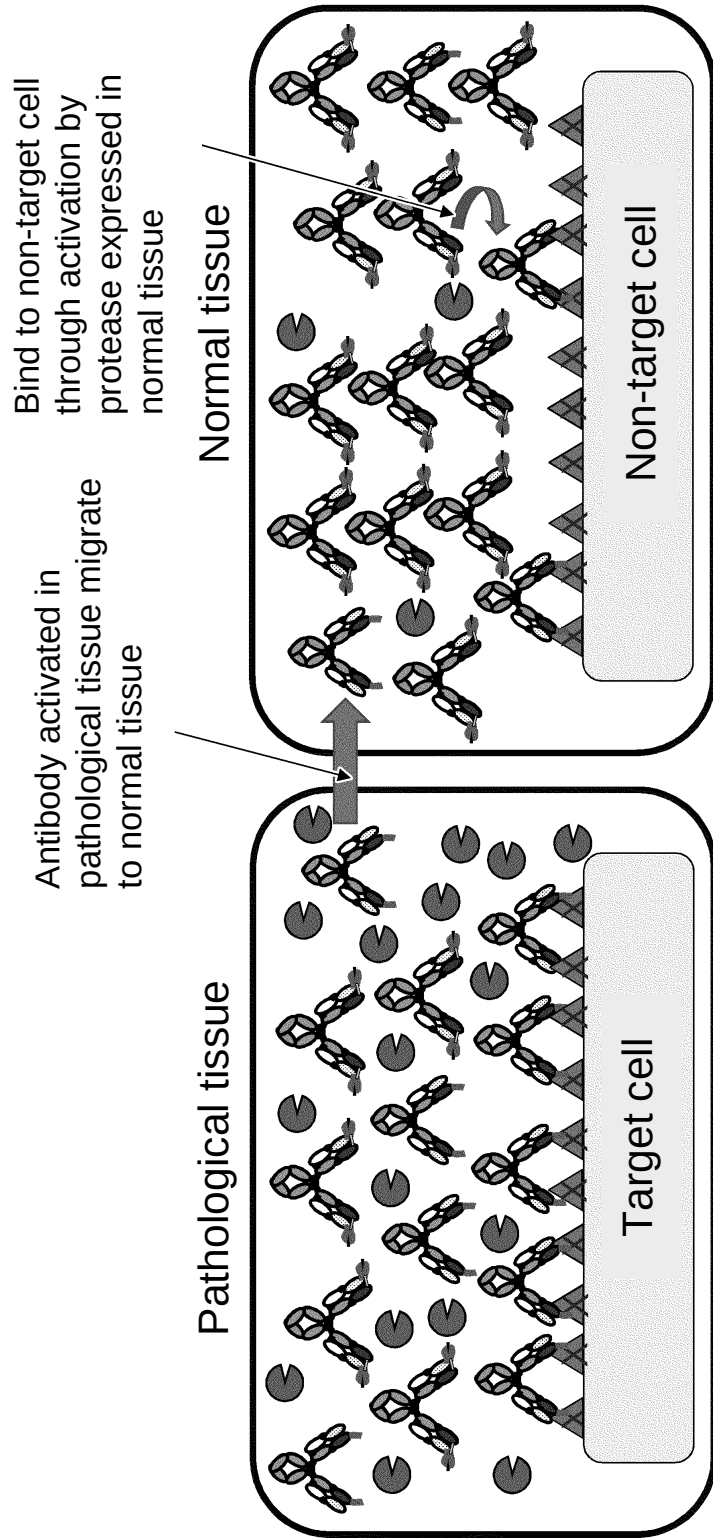


FIG. 2

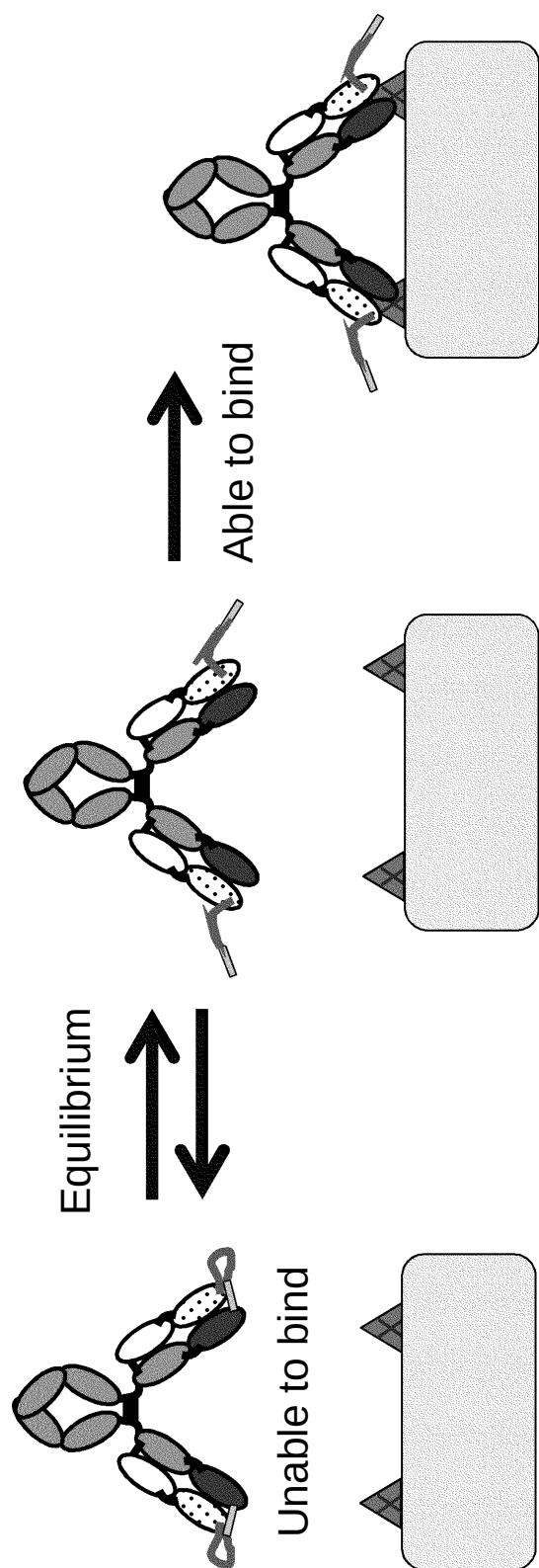


FIG. 3

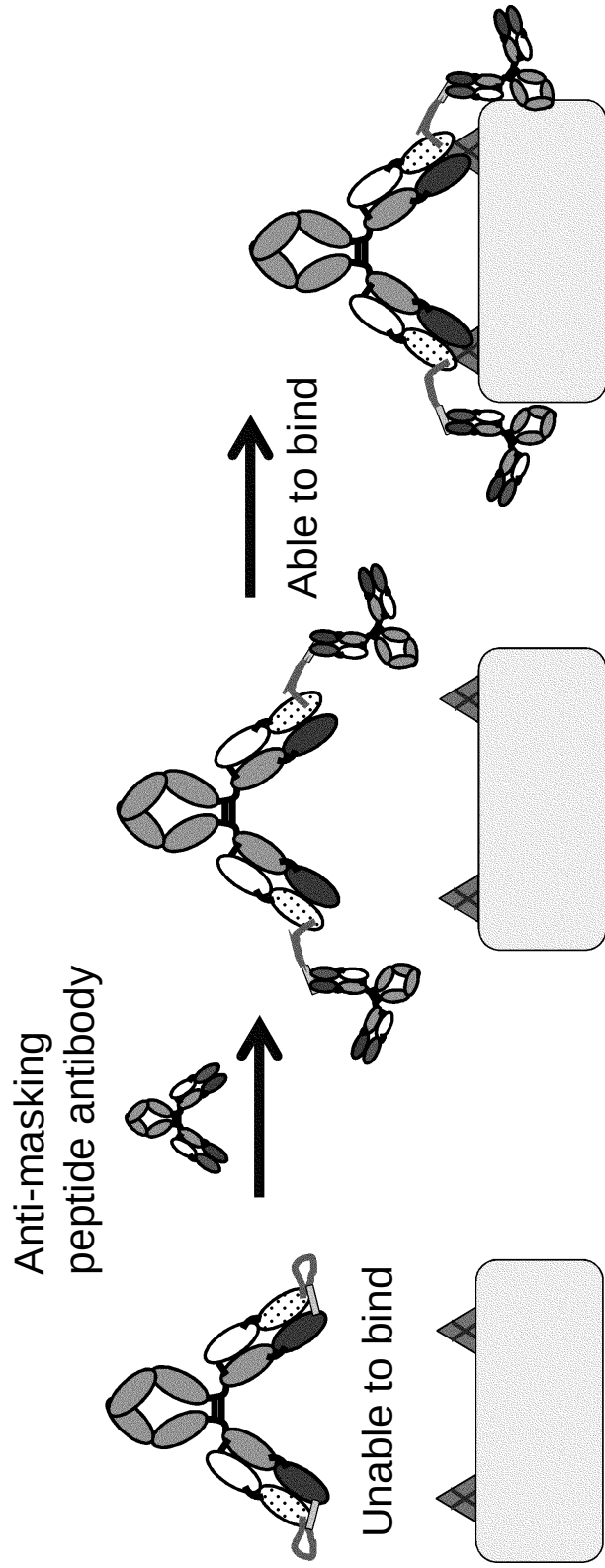


FIG. 4

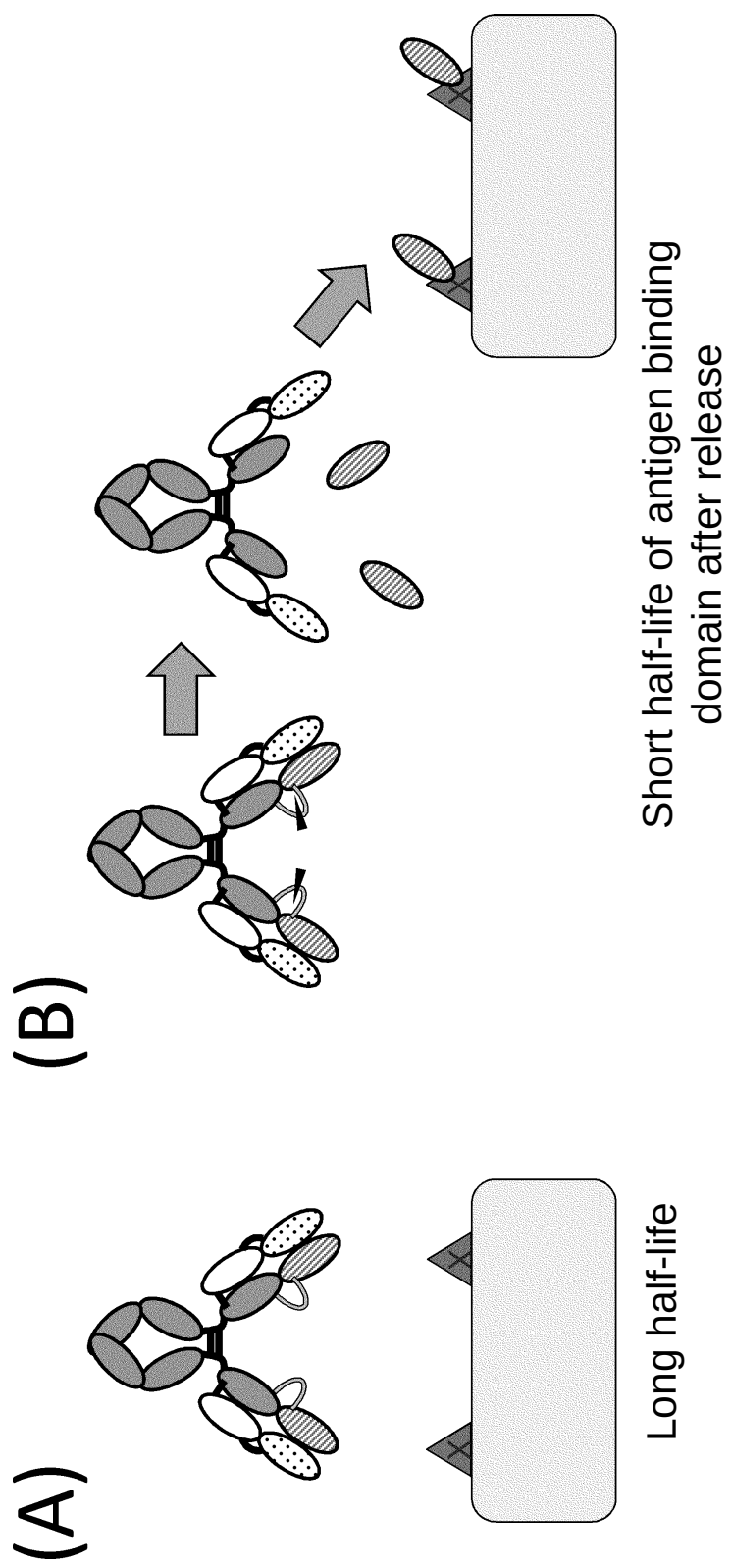


FIG. 5

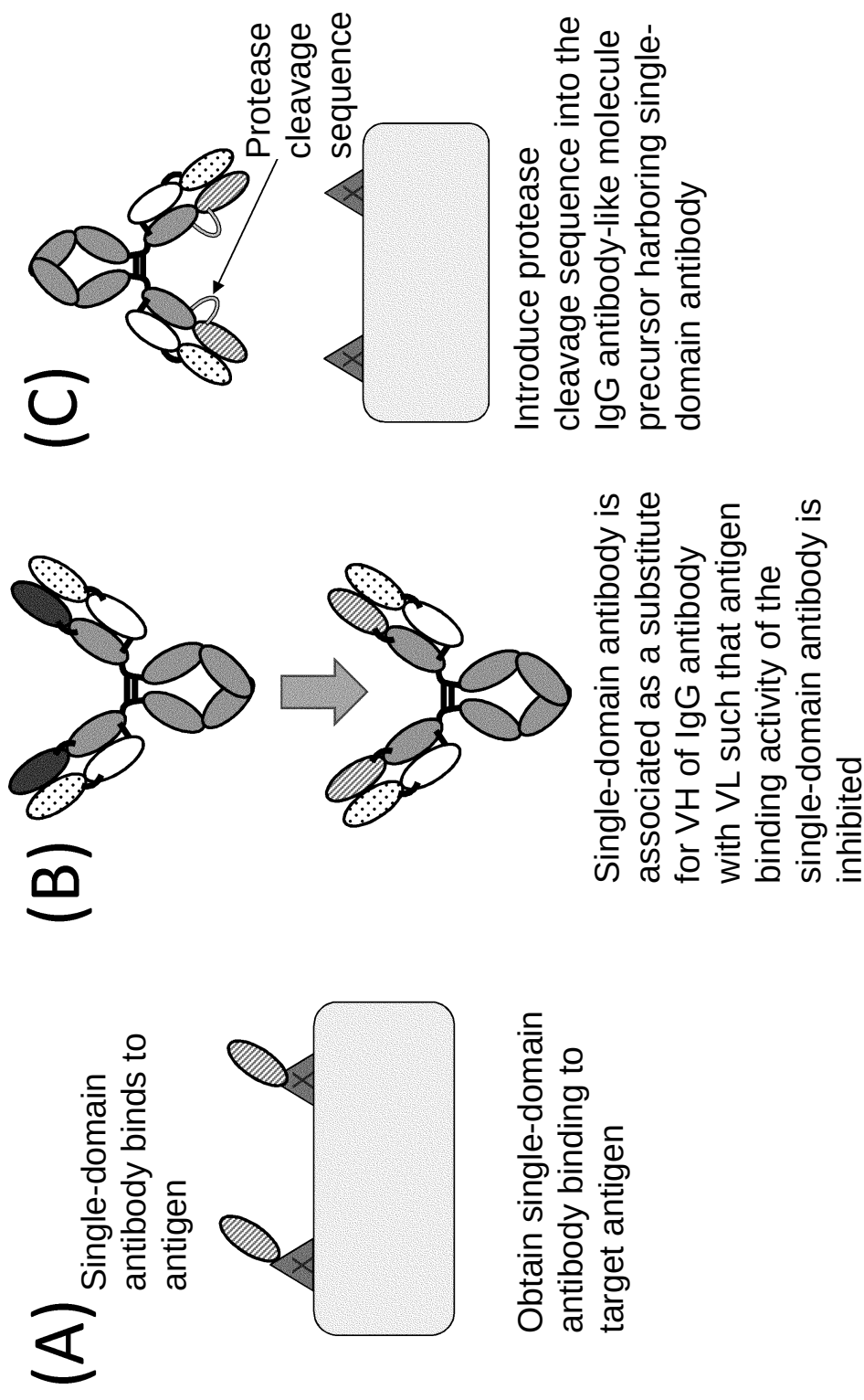


FIG. 6

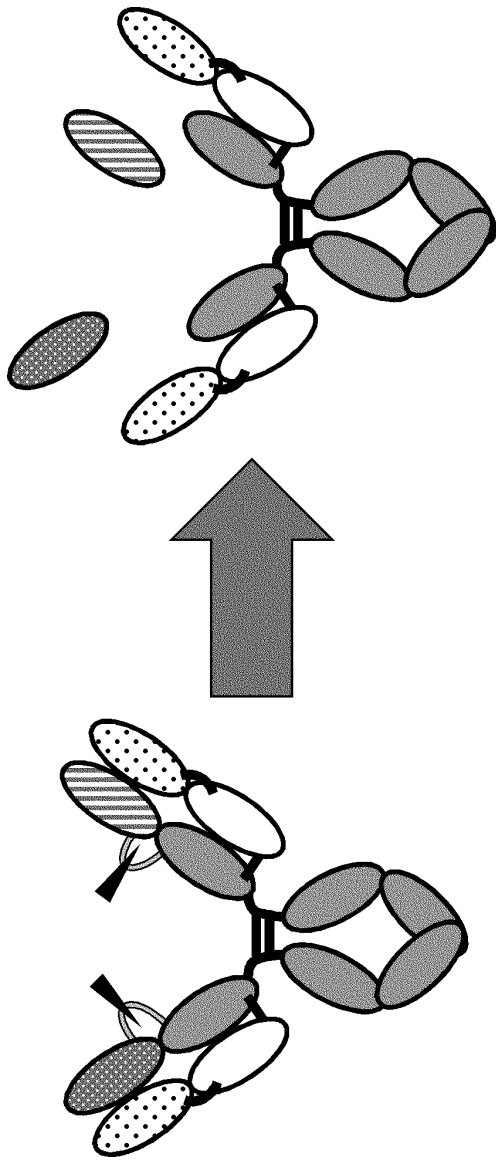


FIG. 7

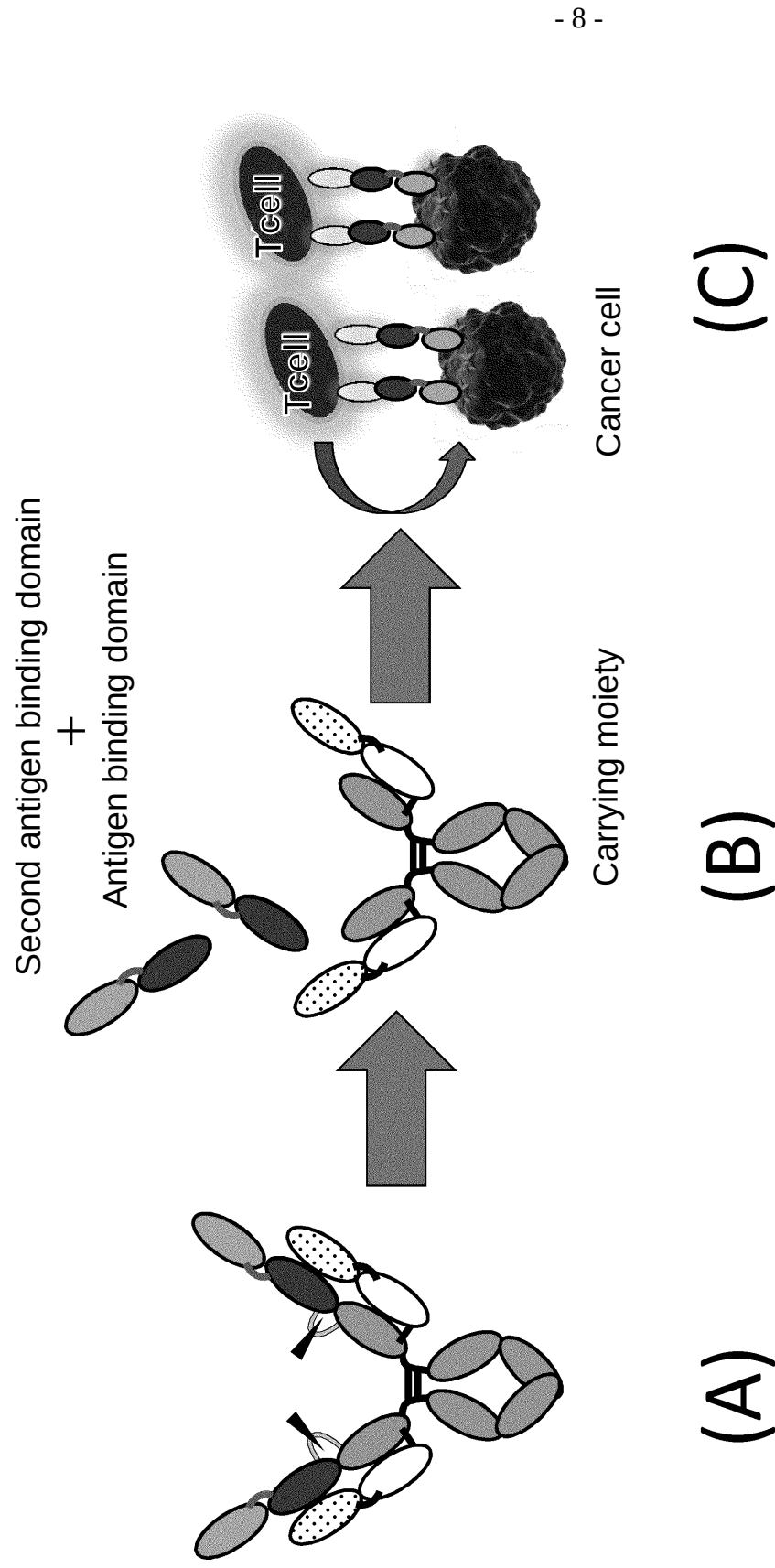


FIG. 8

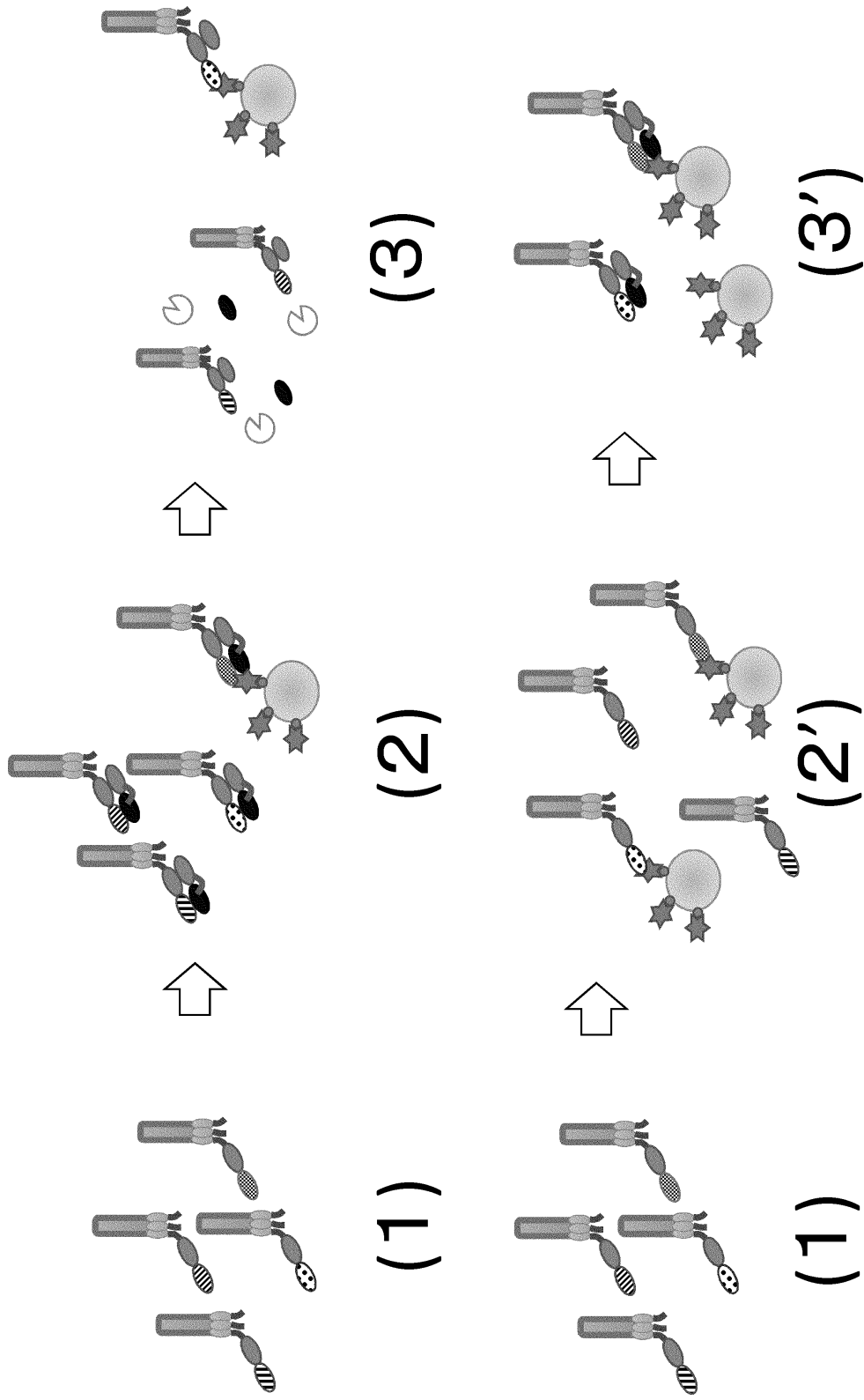


FIG. 9A

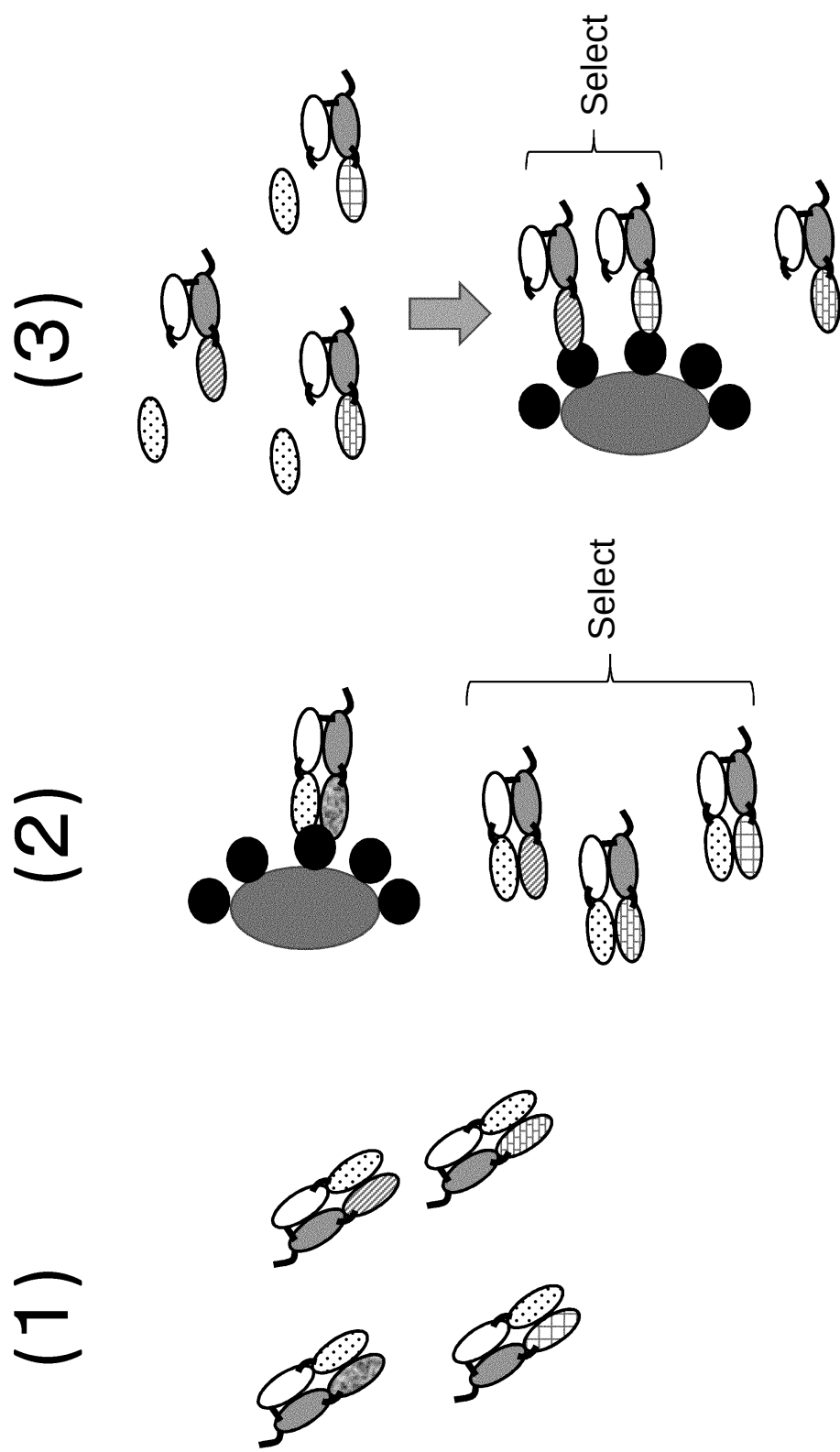
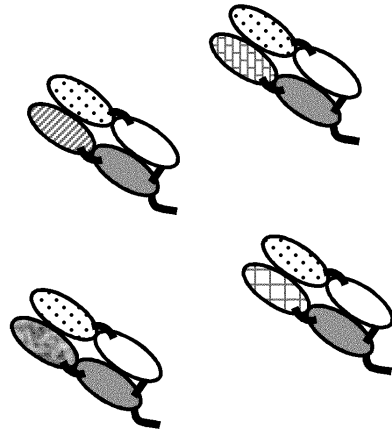
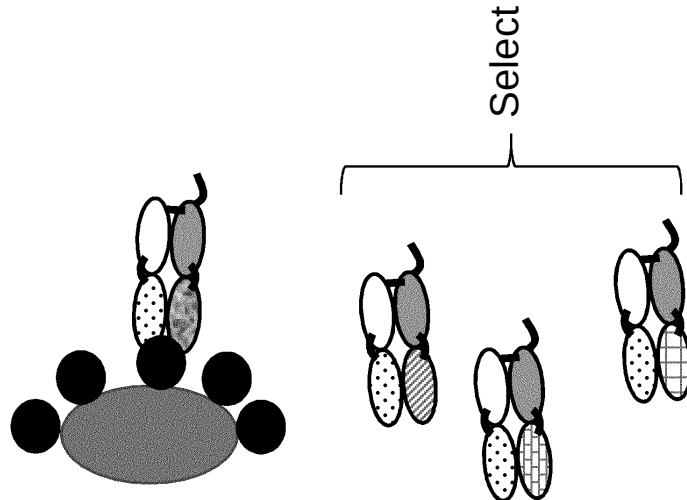


FIG. 9B

(1)



(2)



(3)

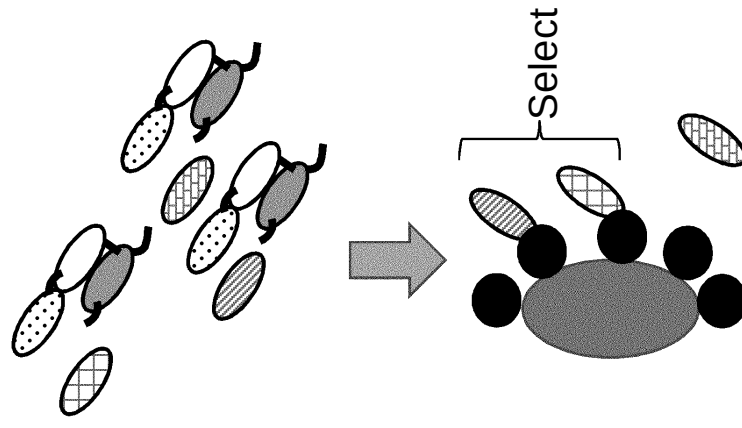


FIG. 9C

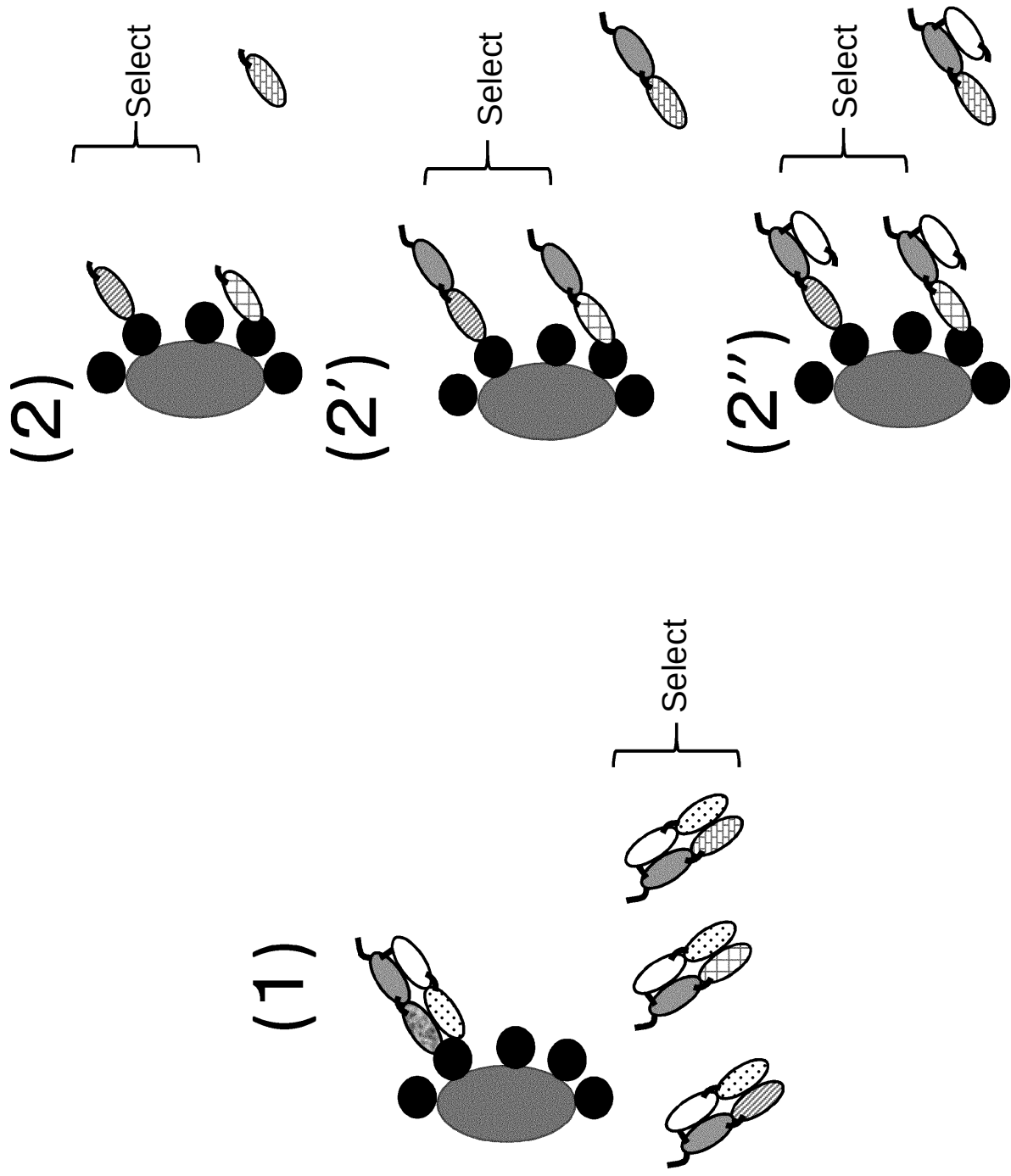


FIG. 9D

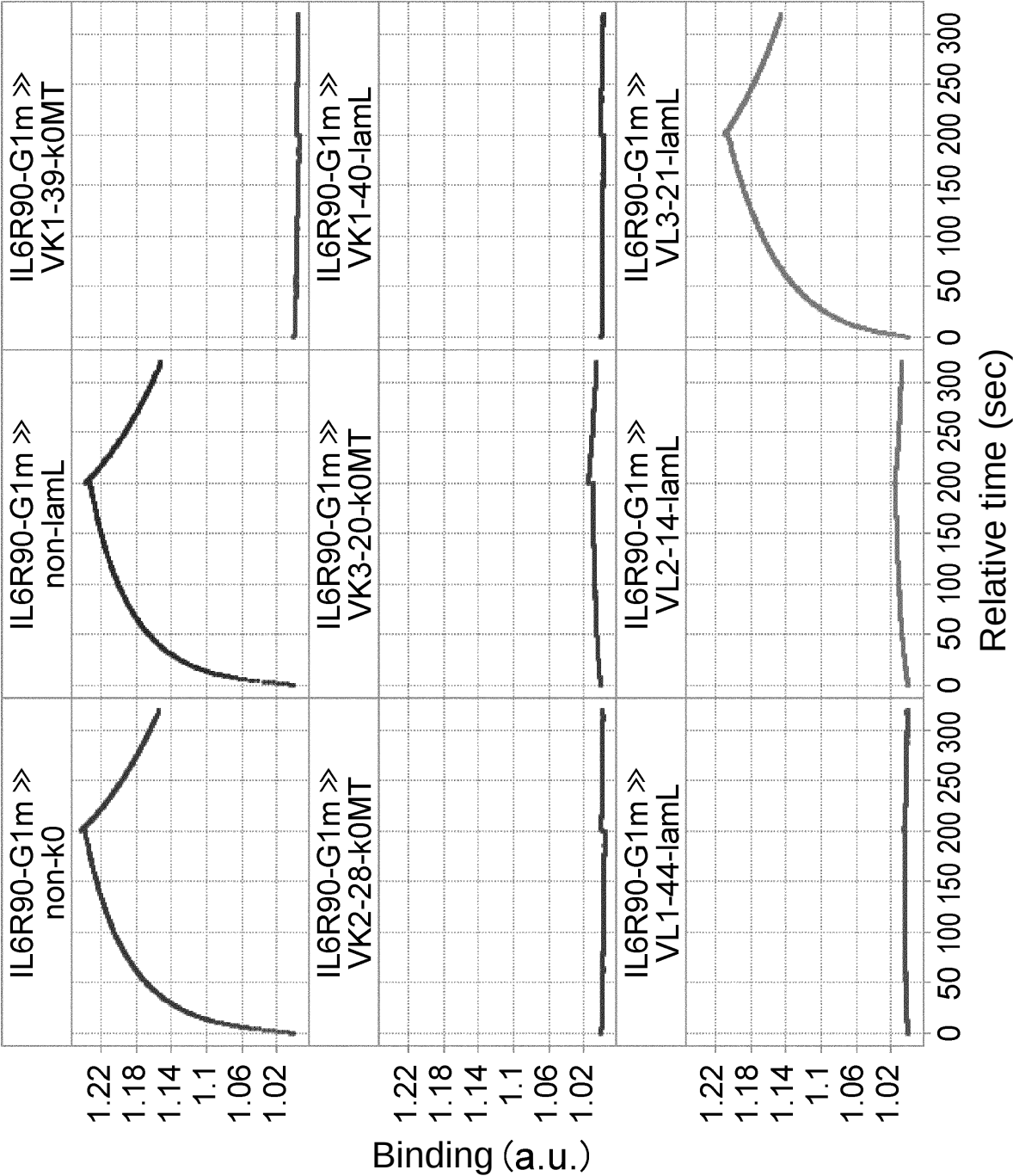
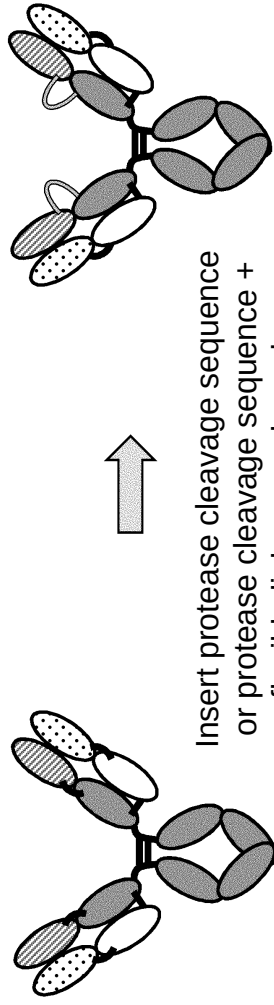


FIG. 10

(A)



Insert protease cleavage sequence +
or protease cleavage sequence +
flexible linker near boundary
between VHH and constant region

(B)

Name of heavy chain	Insertion site	Inserted amino acid sequence
6R90H1001	TVSSAS [insert] TKGP	LSGRSDNH (SEQ ID NO: 12)
6R90H1002	TVSSAS [insert] TKGP	SGGSGLSGRSDNHGSSGG (SEQ ID NO: 44)
6R90H1003	TV [insert] SSASTKGP	LSGRSDNHG (SEQ ID NO: 45)
6R90H1004	TV [insert] SSASTKGP	SGGSGLSGRSDNHGSSGG (SEQ ID NO: 44)
6R90H1005	TVSSASTK [insert] GP	LSGRSDNHG (SEQ ID NO: 45)
6R90H1006	TVSSASTK [insert] GP	SGGSGLSGRSDNHGSSGG (SEQ ID NO: 44)

FIG. 11

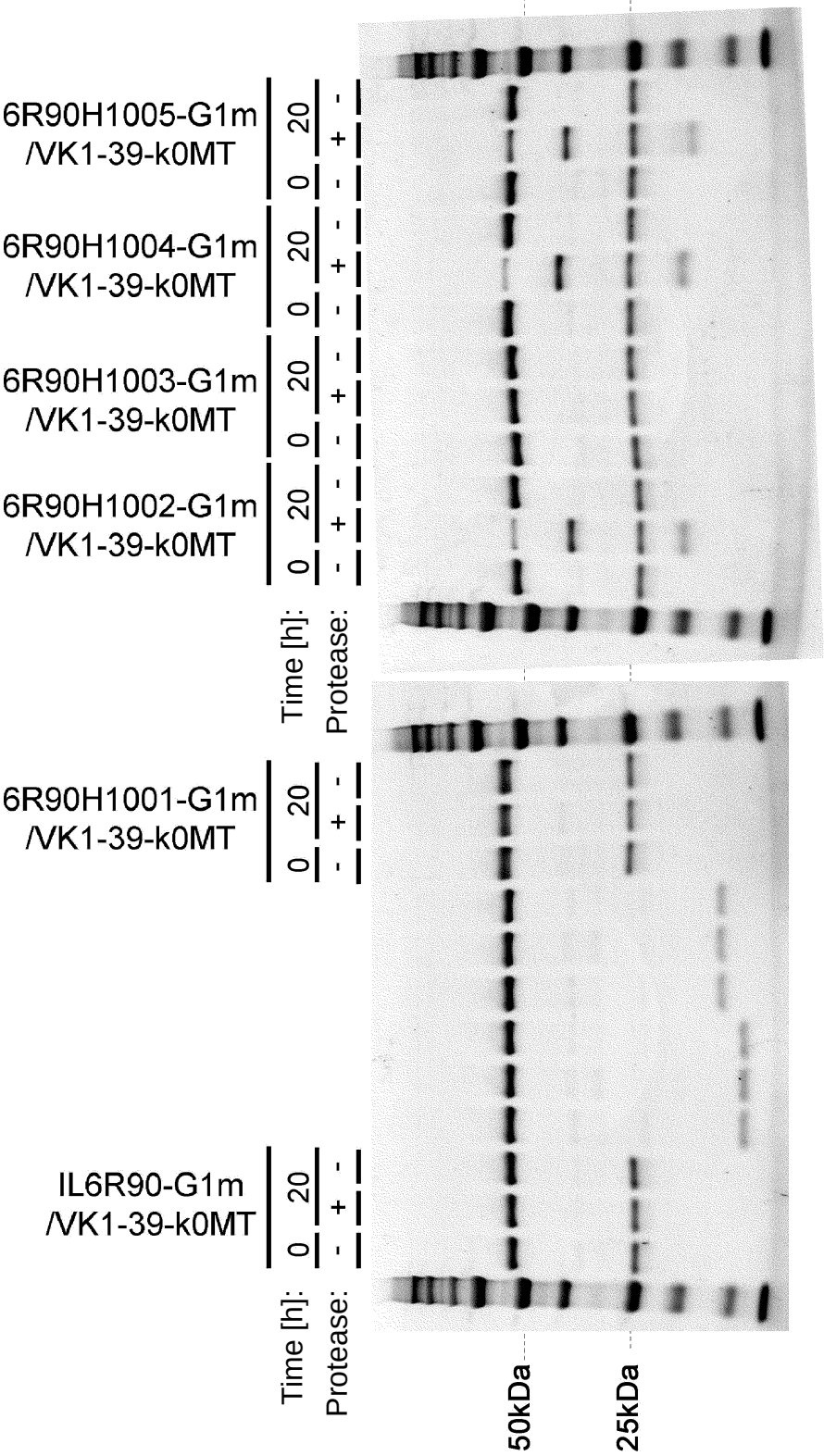


FIG. 12-1

6R90H1006-G1m
/VK1-39-k0MT

Time [h]:	0	20
Protease:	-	+
	-	-

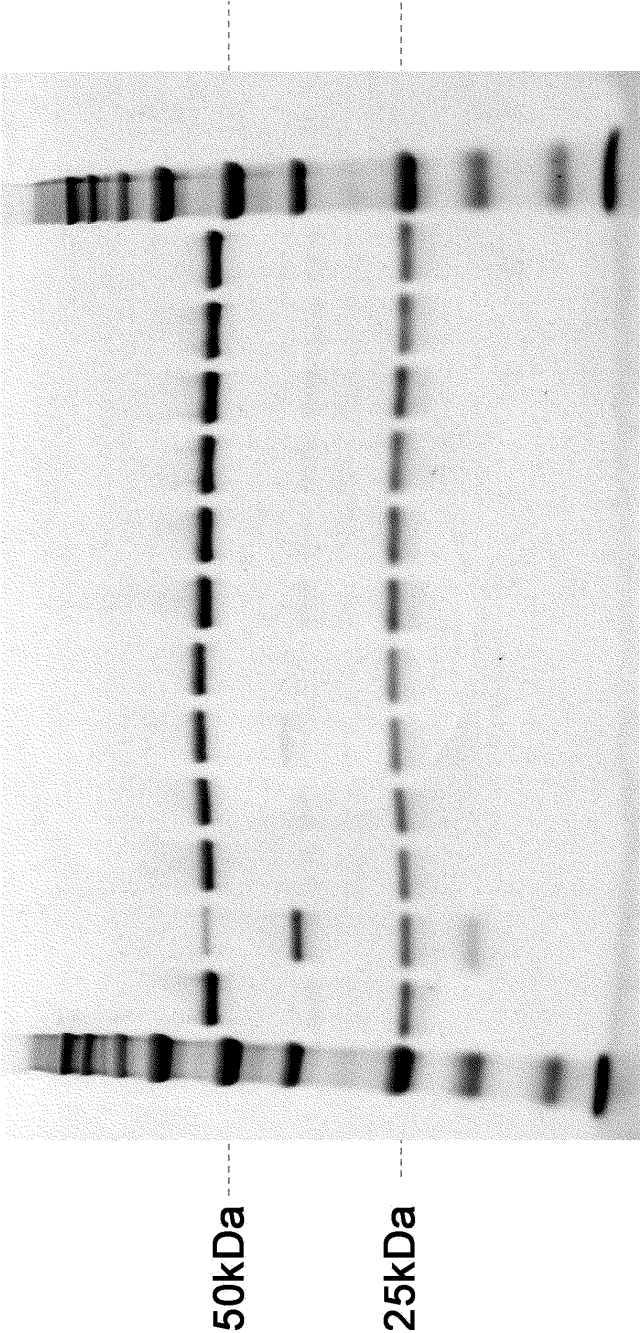


FIG. 12-2

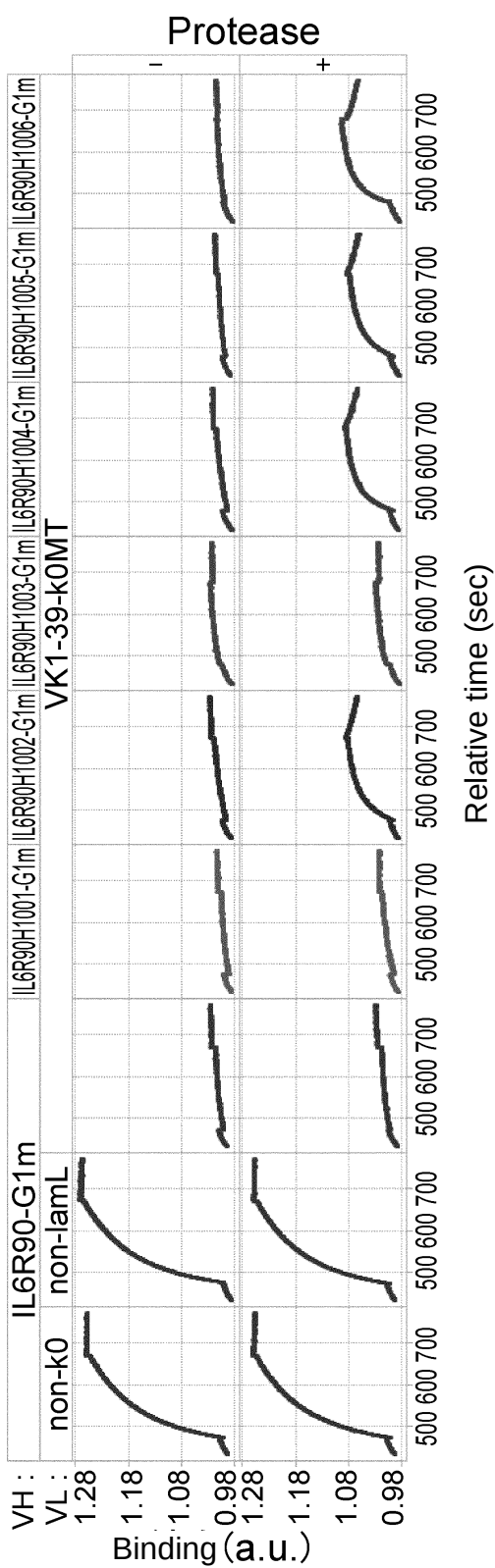


FIG. 13

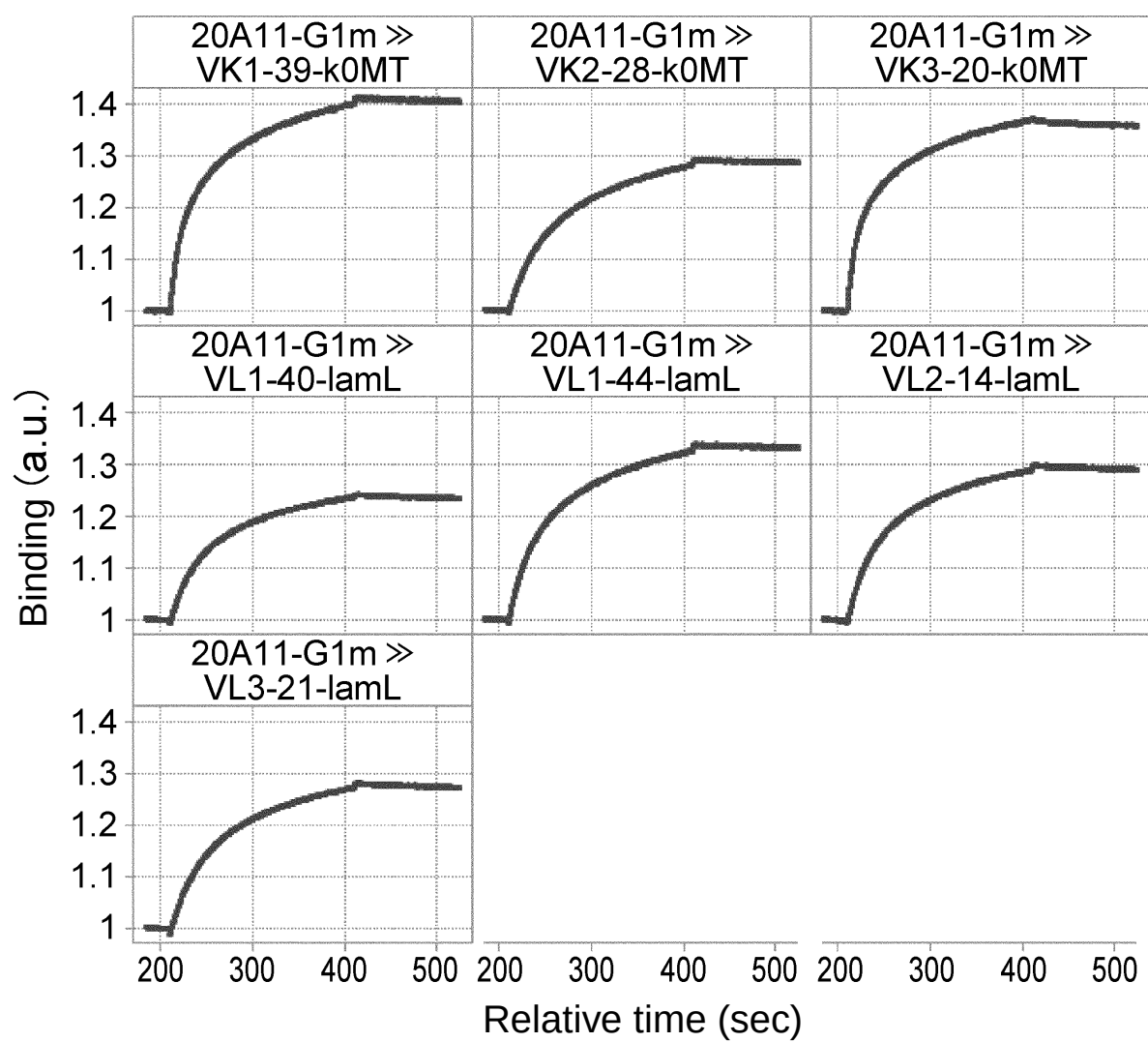


FIG. 14

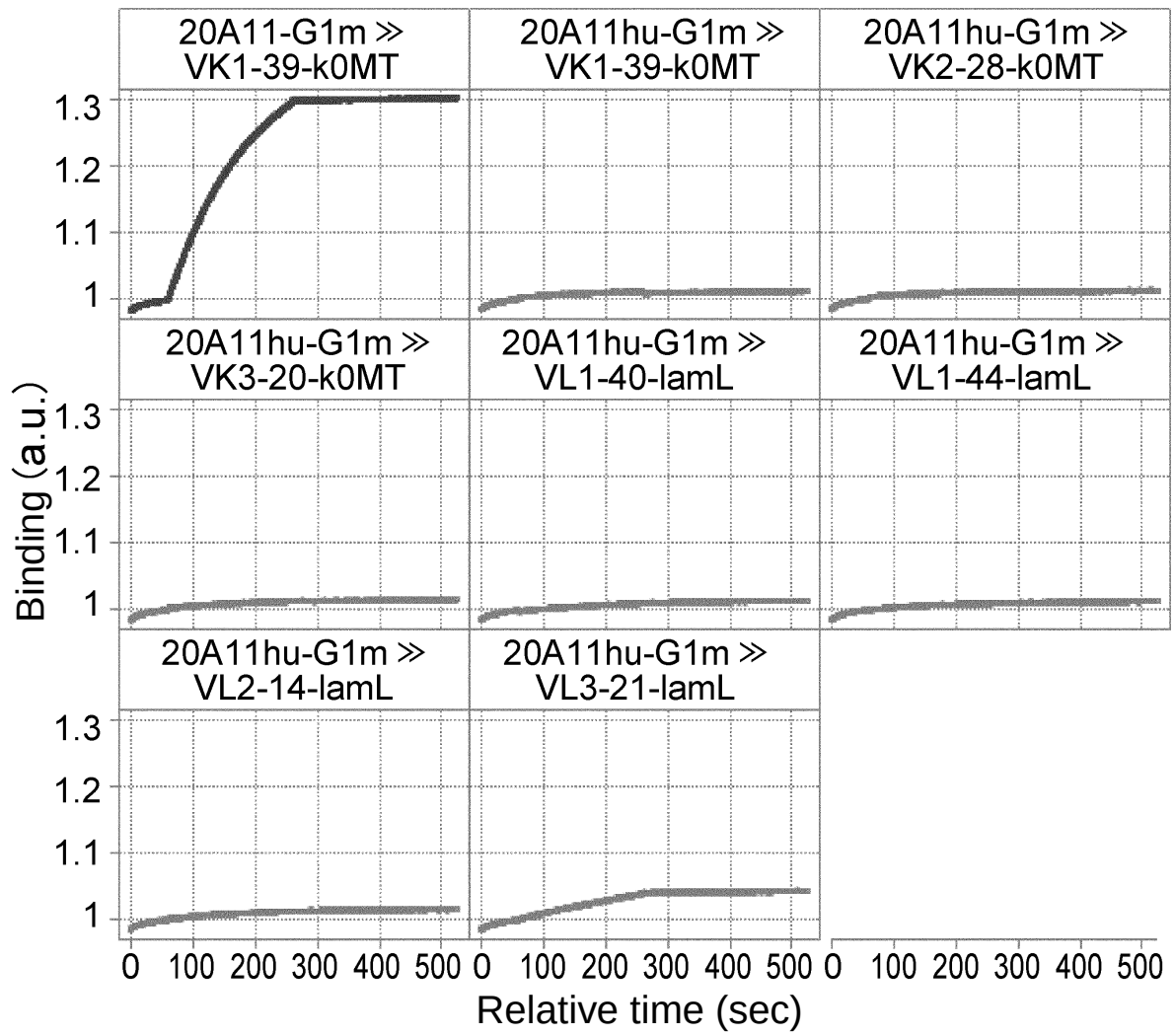


FIG. 15

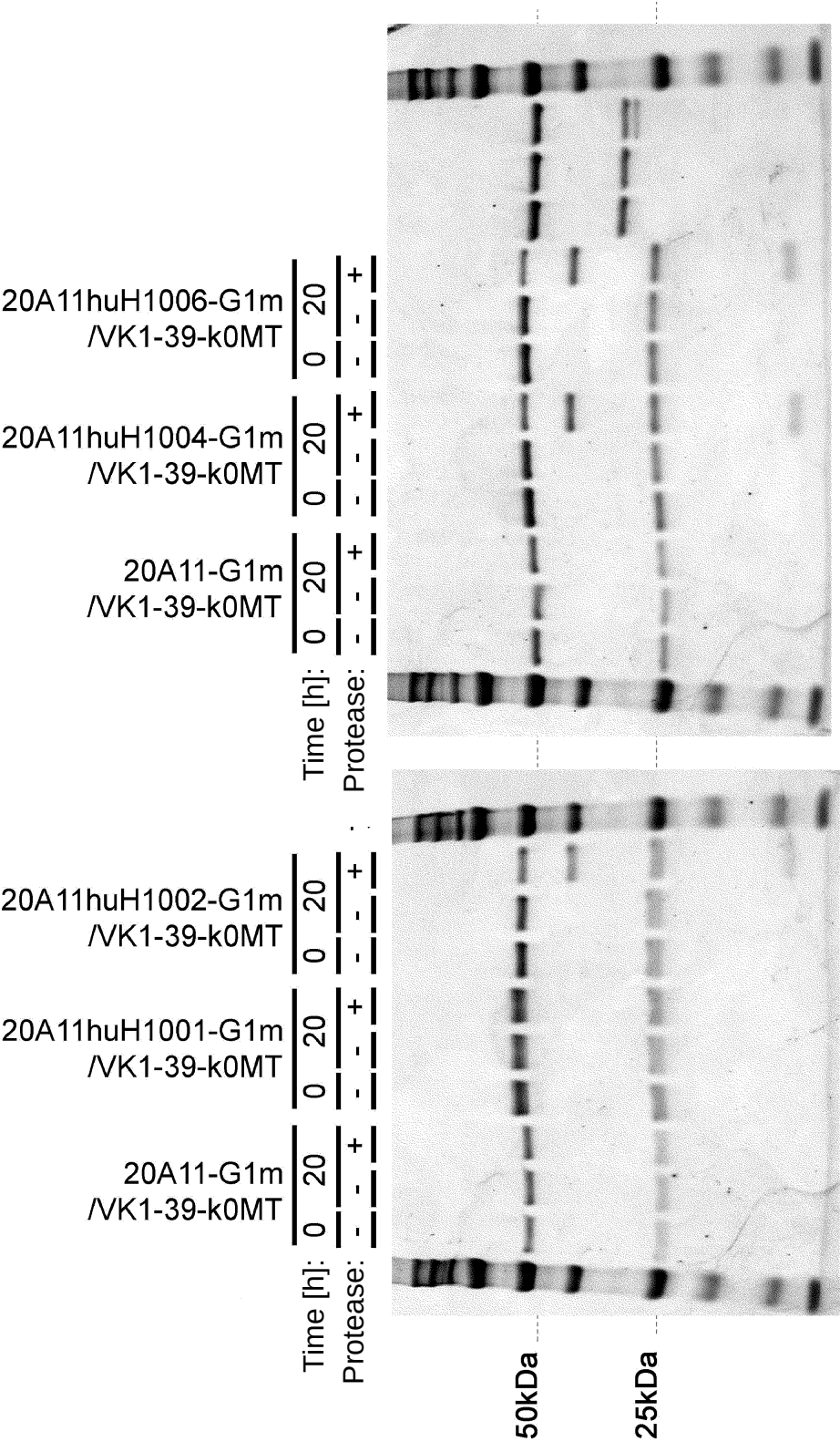


FIG. 16

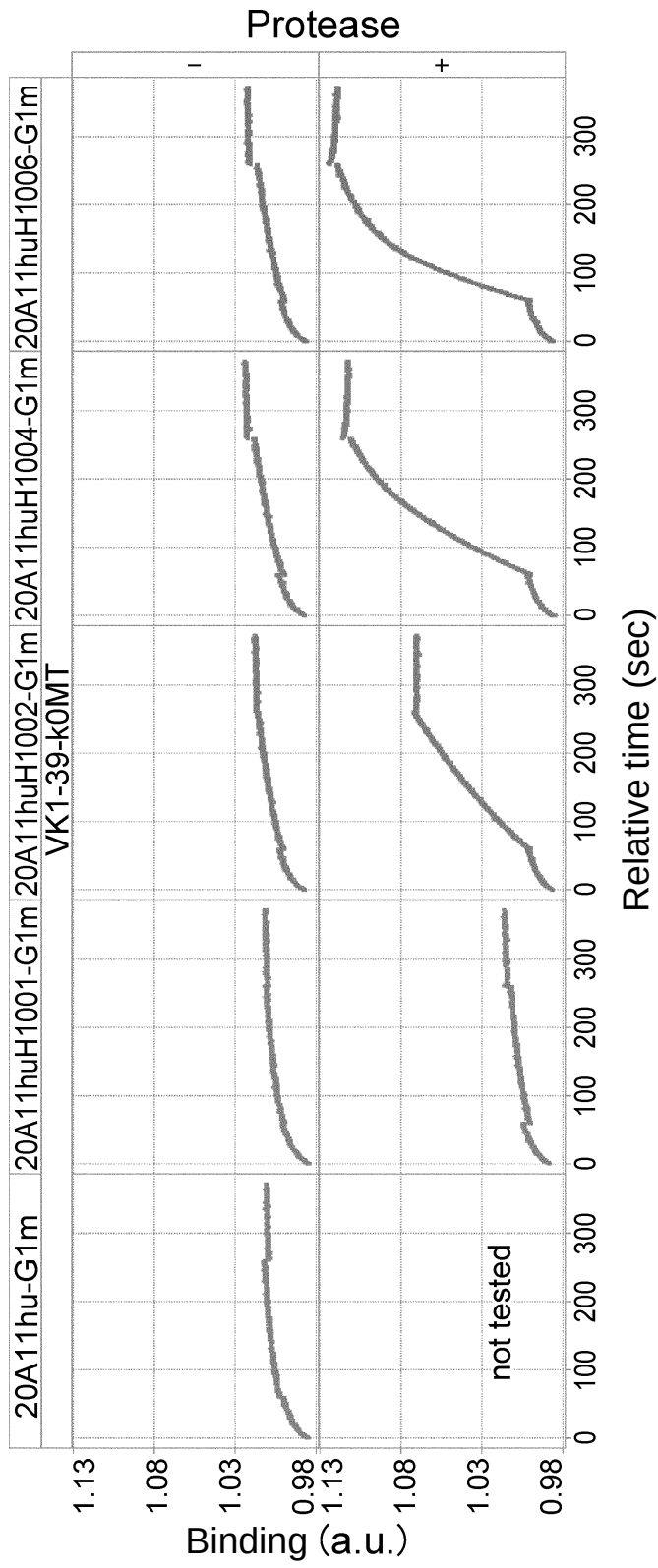


FIG. 17

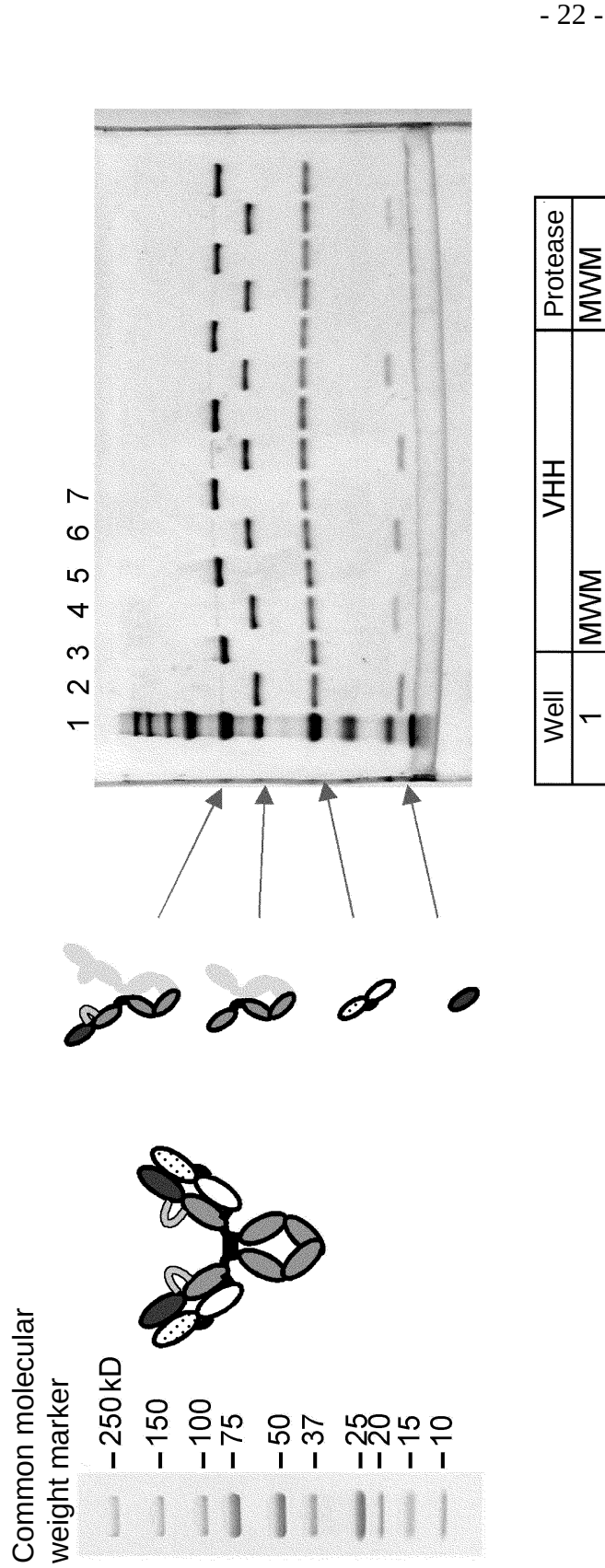


FIG. 18

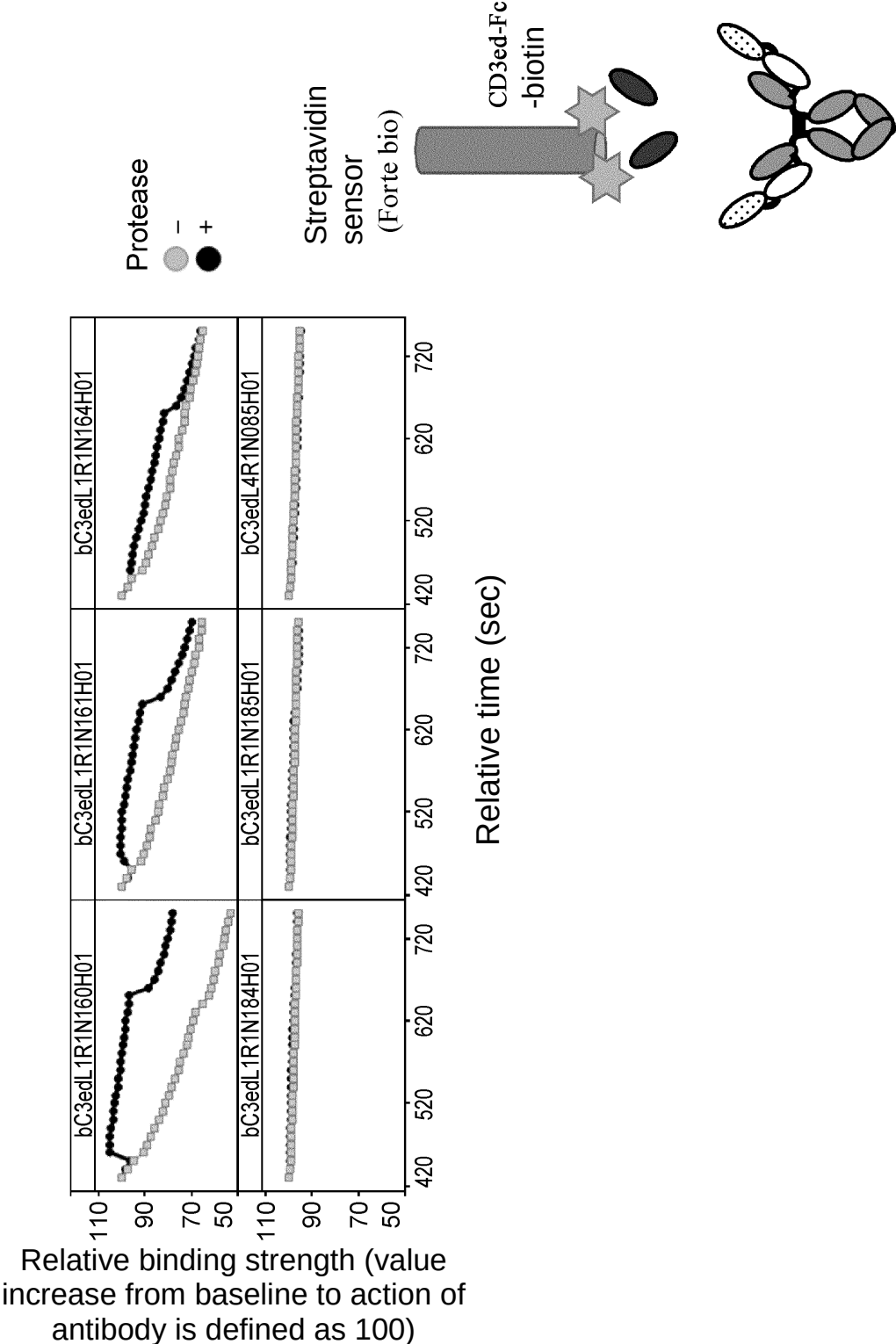
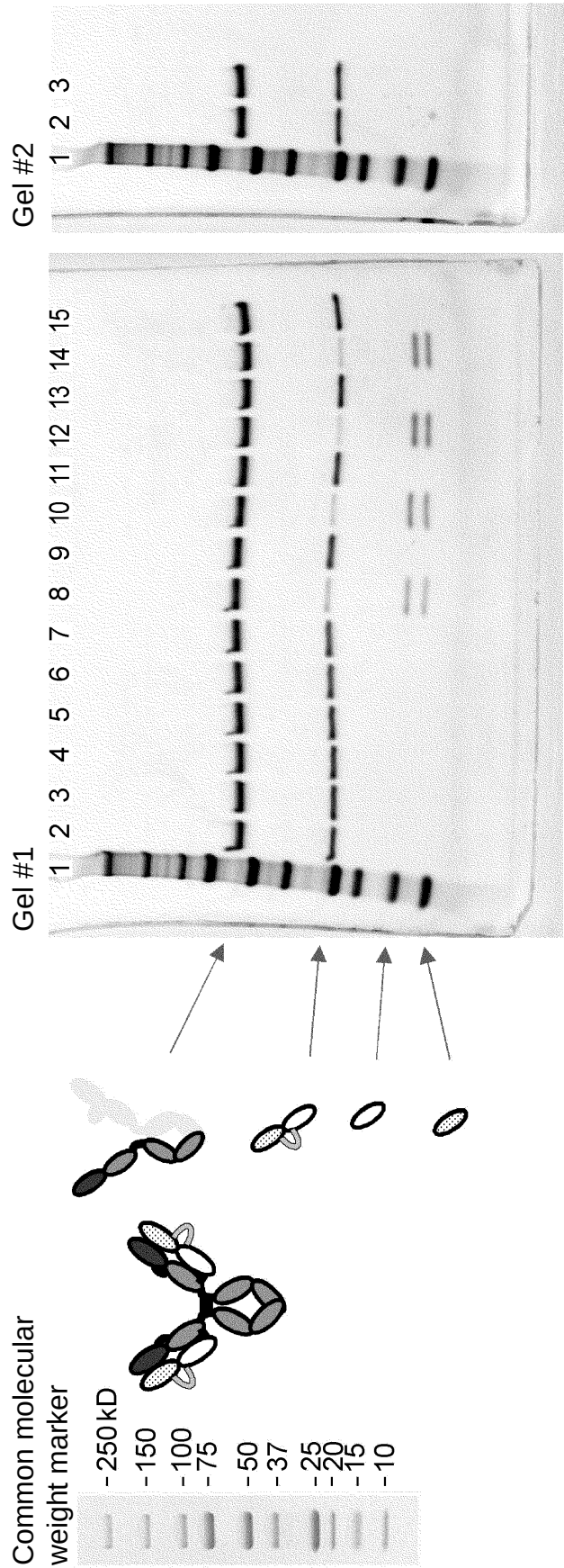


FIG. 19



Gel	Well	MWM	Sample	Protease MWM	Protease	Protease cleavage site	Reactivity with MT-SP1
1	1						
	2		VP_IL6R90-G1m/VK1-39P-2-Pk0MT	+		VE^IKRTVAAPS	-
	3			-			
	4		VP_IL6R90-G1m/VK1-39P-1-Pk0MT	+		VEI^KRTVAAPS	-
	5			-			
	6		VP_IL6R90-G1m/VK1-39P-Pk0MT	+		VEIK^RTVAAPS	-
	7			-			
	8		VP_IL6R90-G1m/VK1-39P+2-Pk0MT	+		VEIKRT^VAAPS	+
	9			-			
	10		VP_IL6R90-G1m/VK1-39P+3-Pk0MT	+		VEIKRTV^AAPS	+
	11			-			
	12		VP_IL6R90-G1m/VK1-39P+4-Pk0MT	+		VEIKRTVA^APS	+
	13			-			
	14		VP_IL6R90-G1m/VK1-39P+5-Pk0MT	+		VEIKRTVAA^PS	+
	15			-			
2	2		VP_IL6R90-G1m/VK1-39-k0MT	+		VEIKRTVAAPS	-
	3			-			

FIG. 20

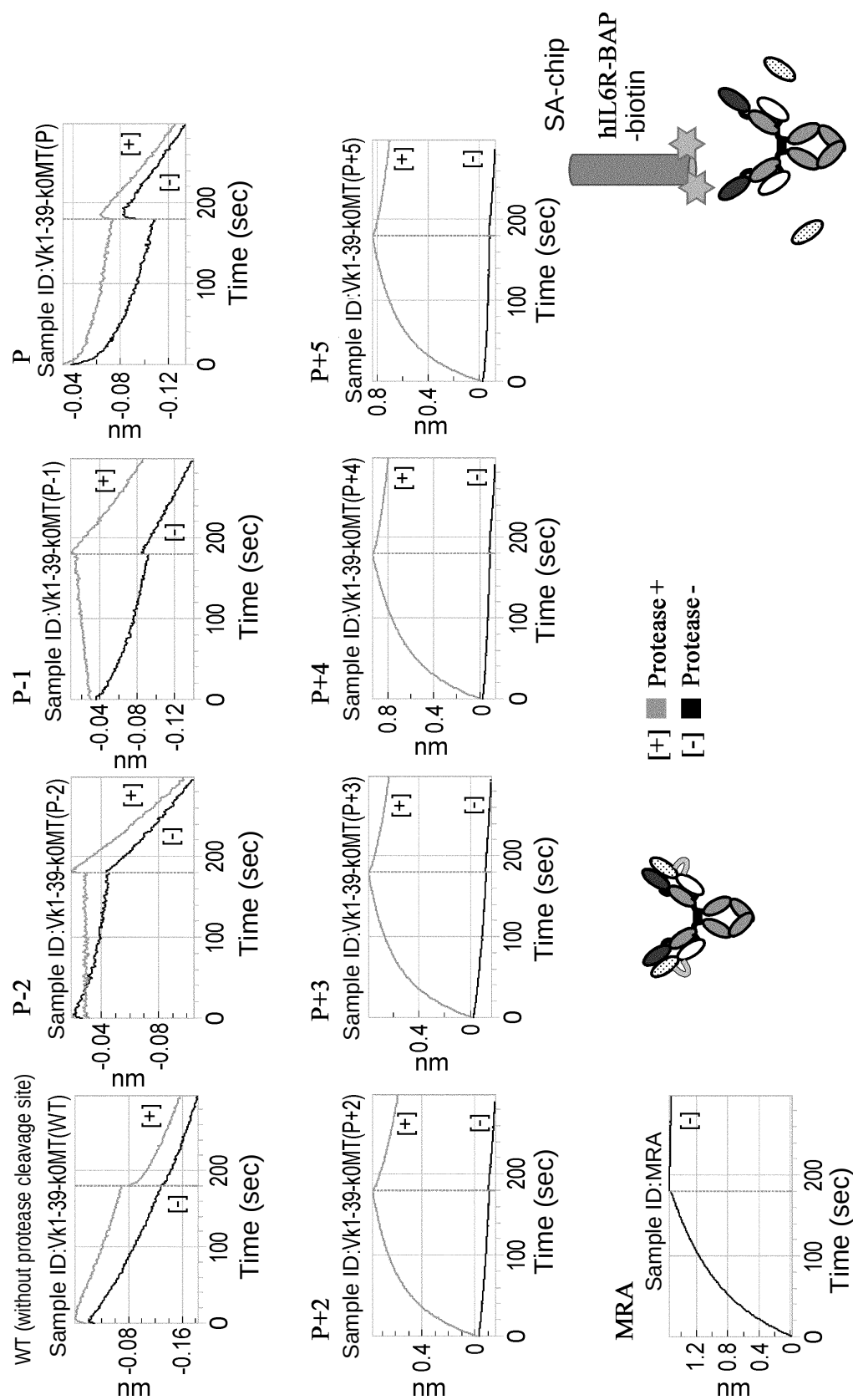


FIG. 21

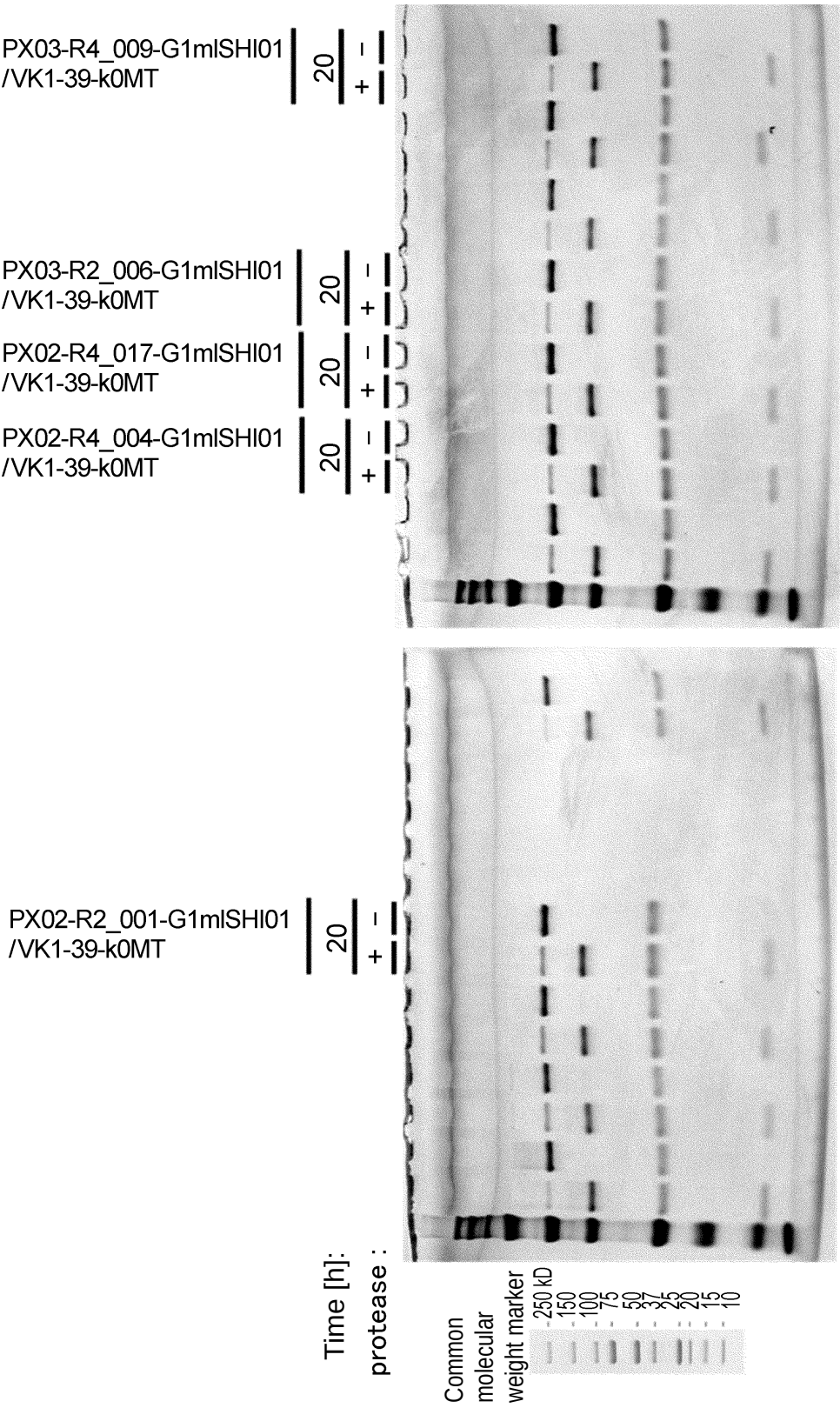


FIG. 22

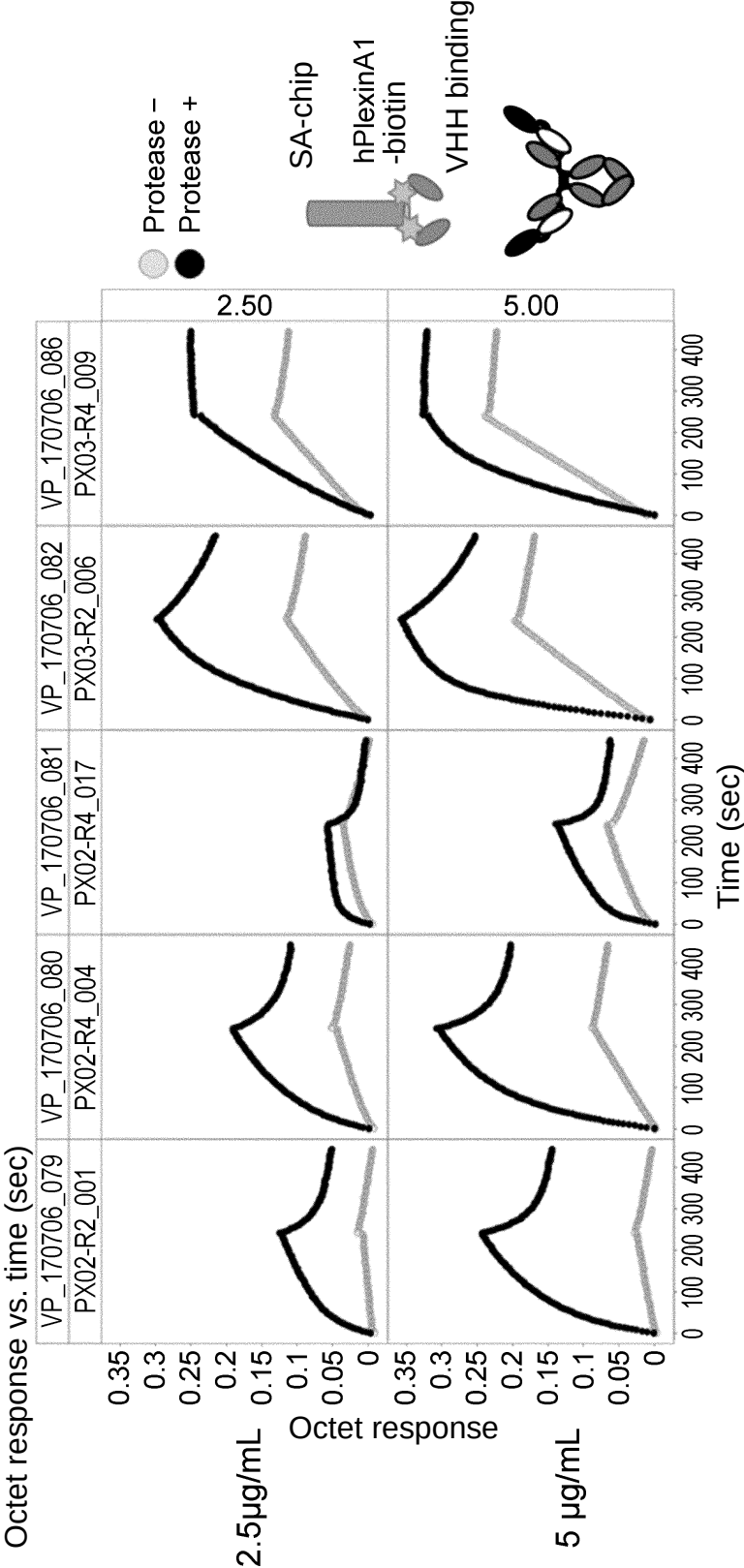
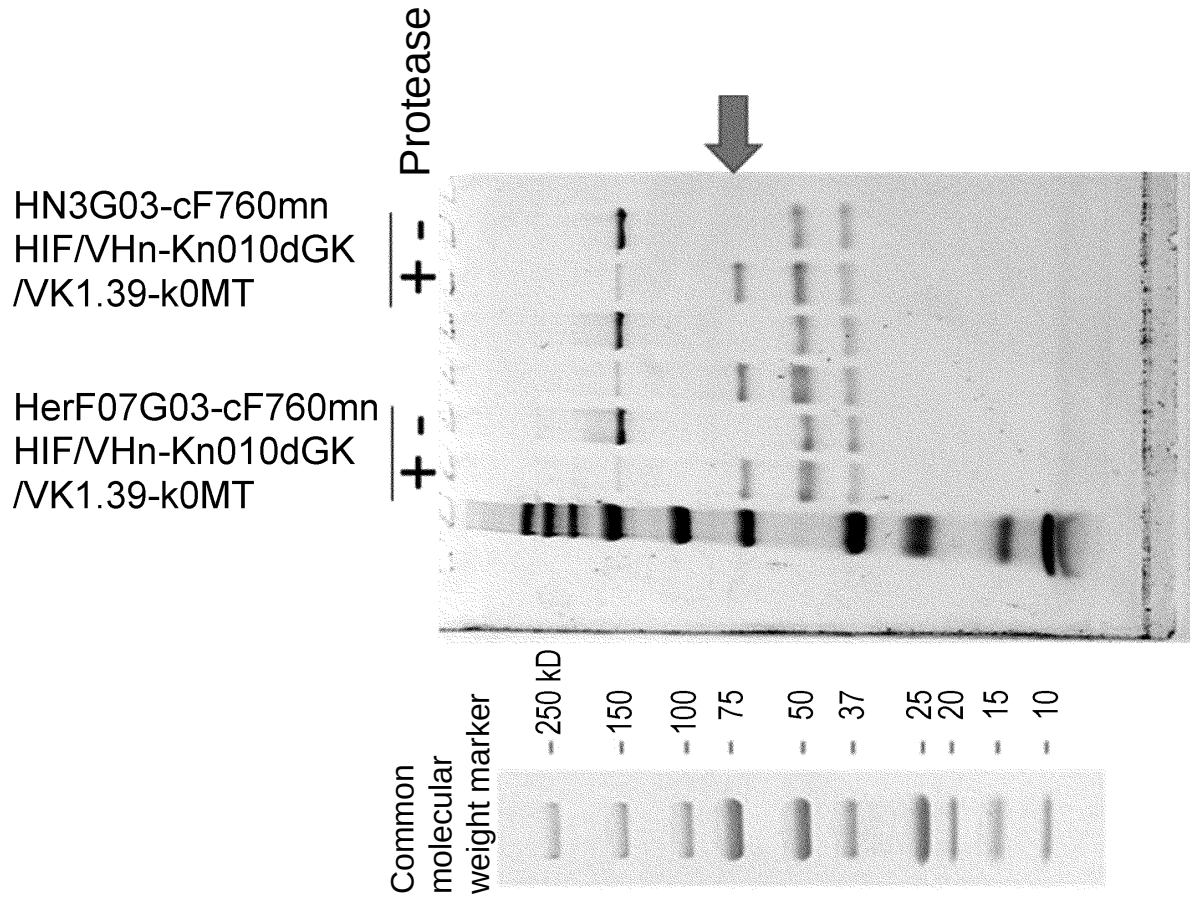


FIG. 23



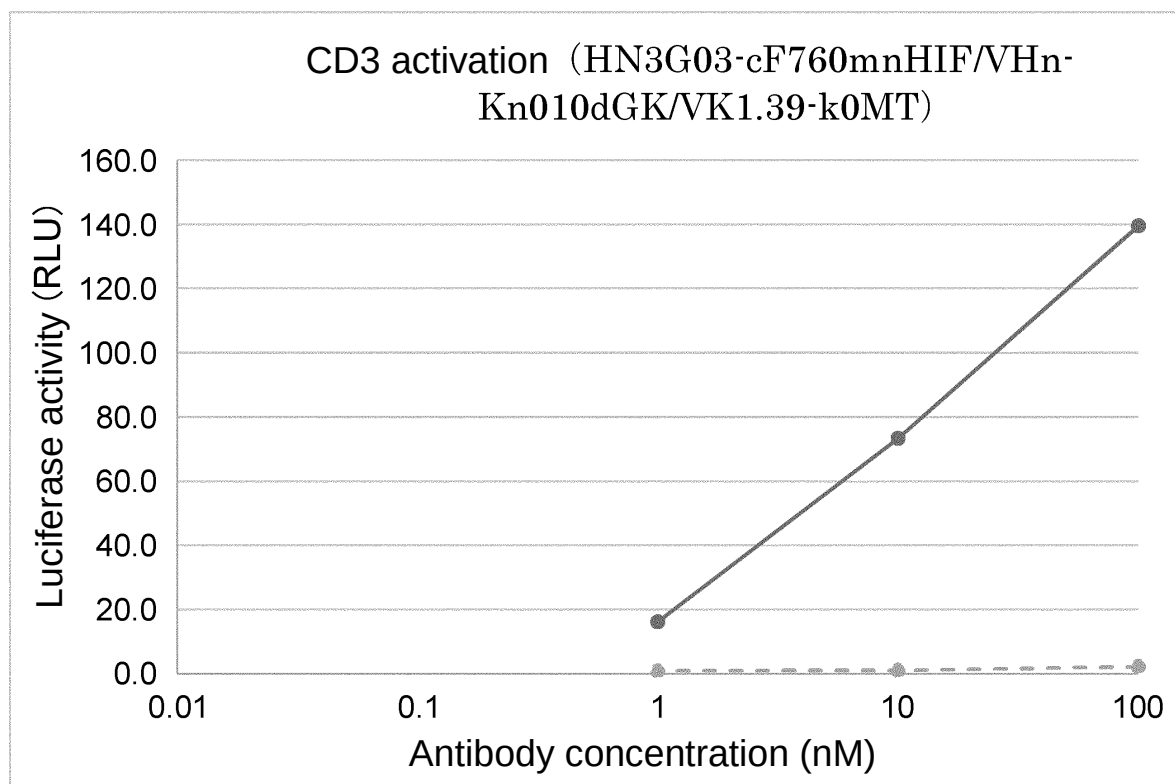


FIG. 25

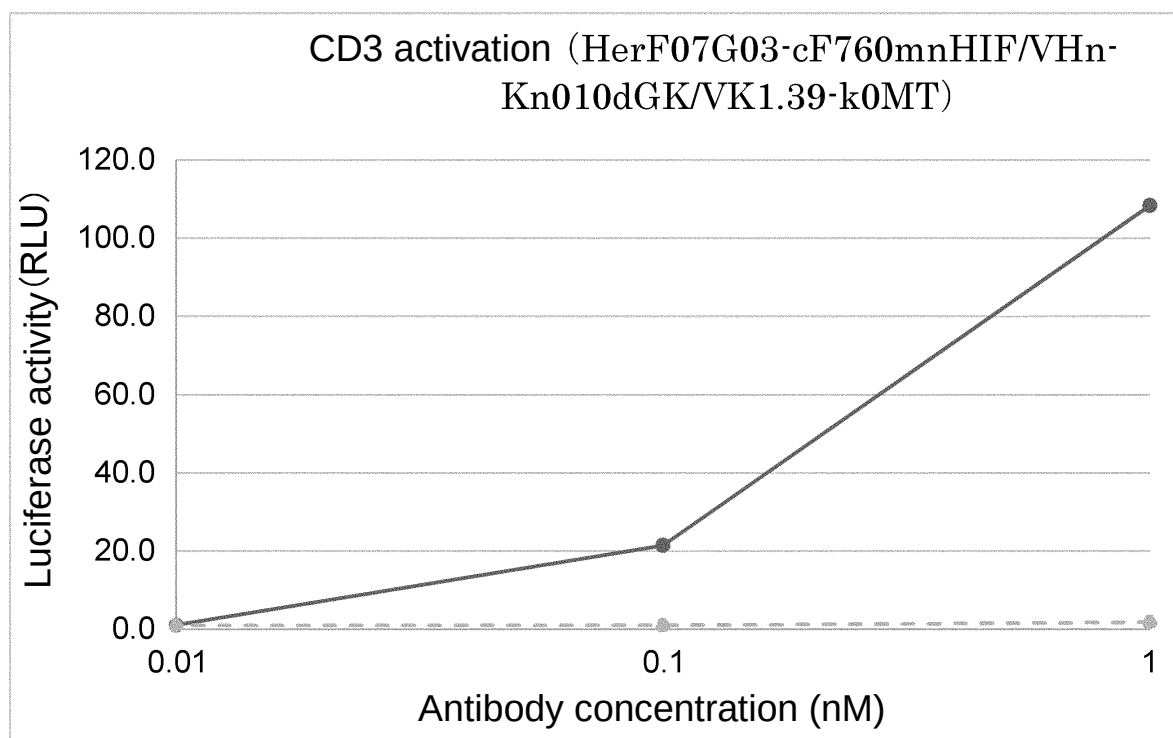


FIG. 26

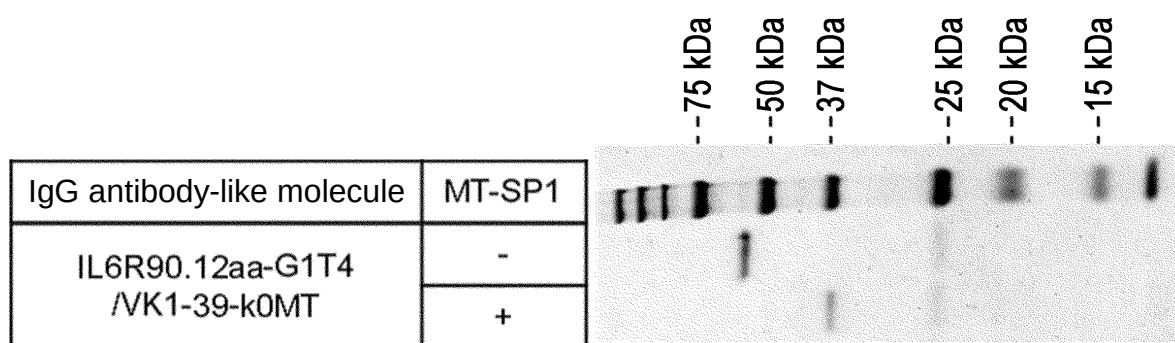


FIG. 27

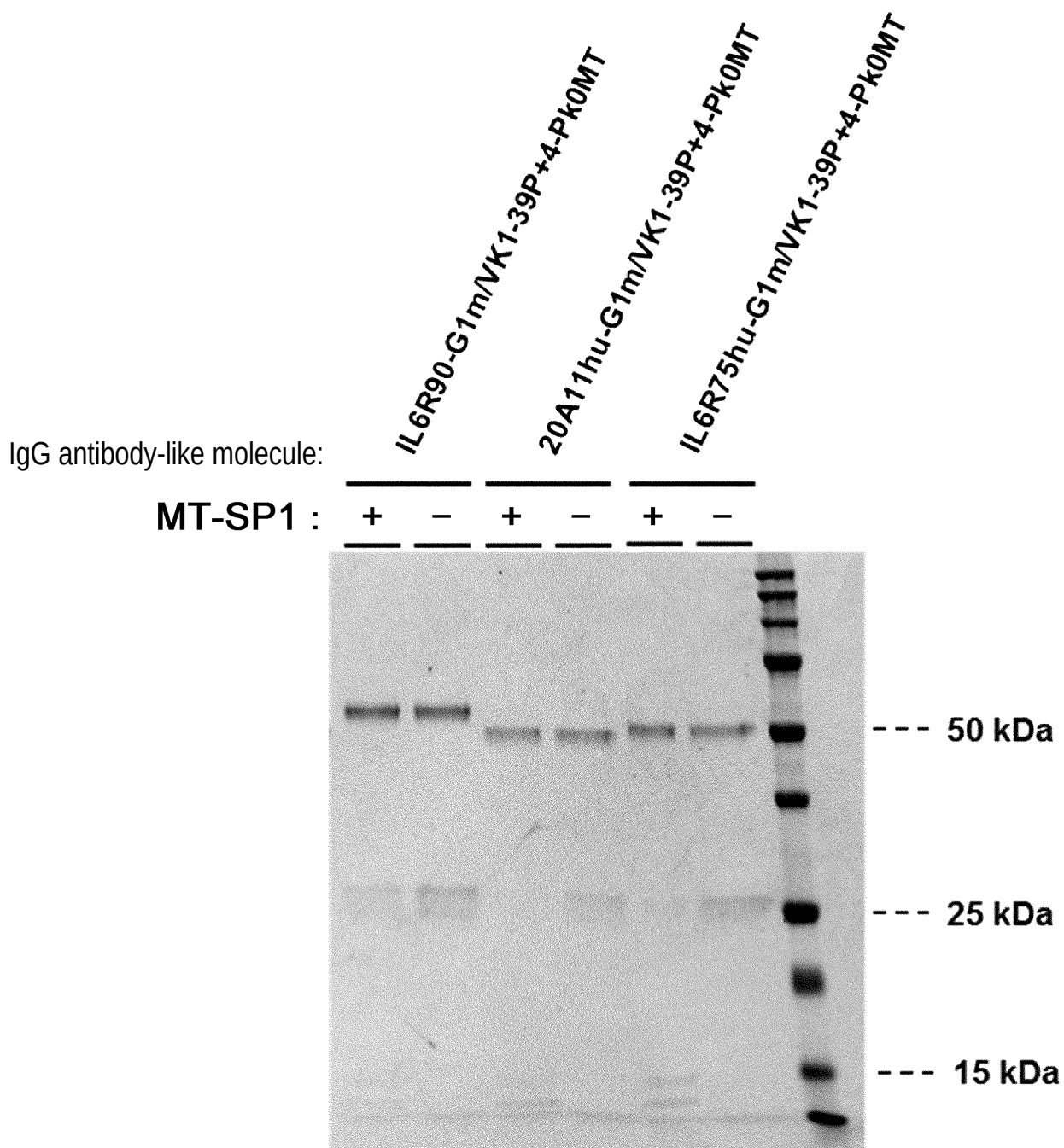


FIG. 28

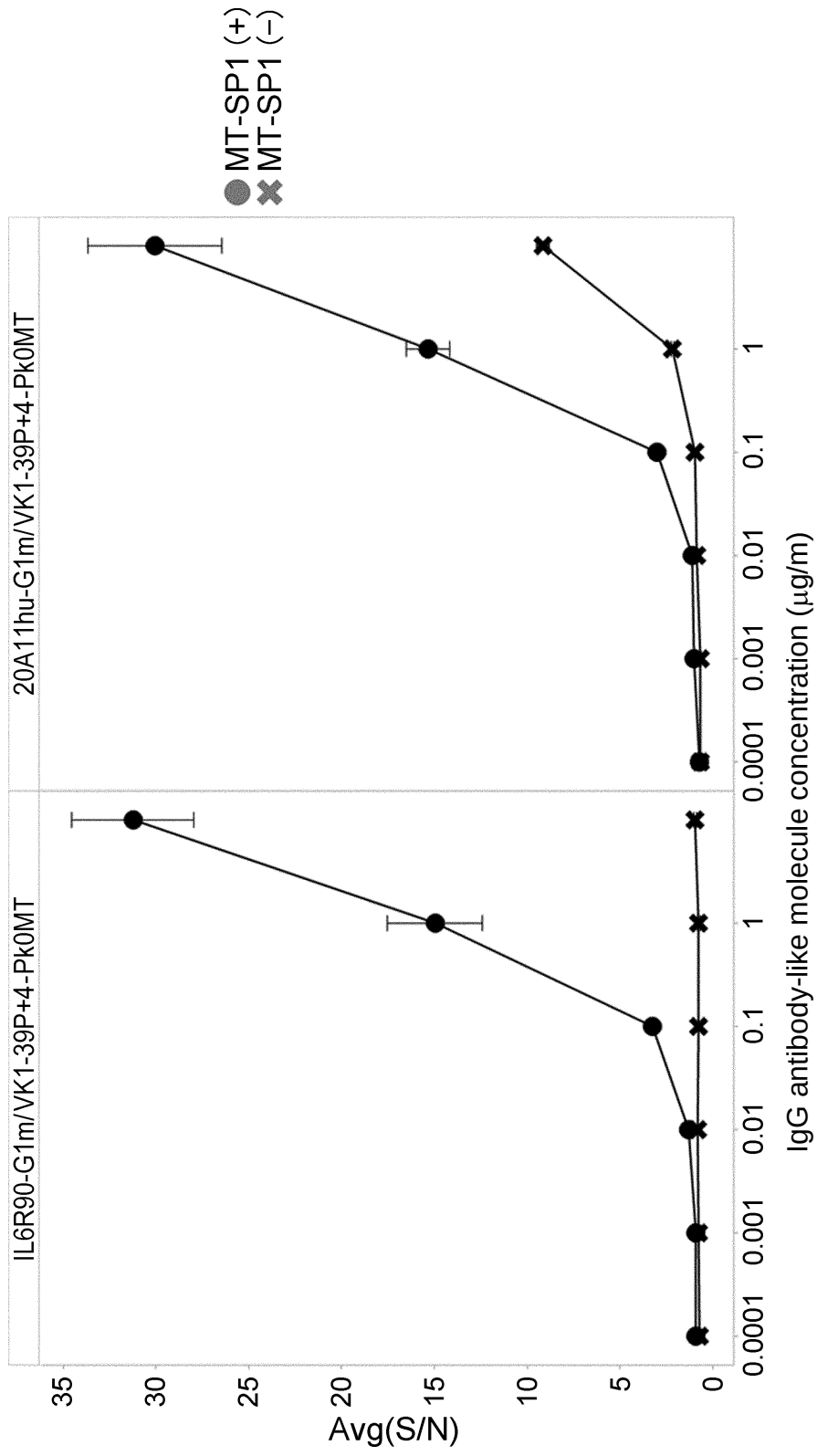
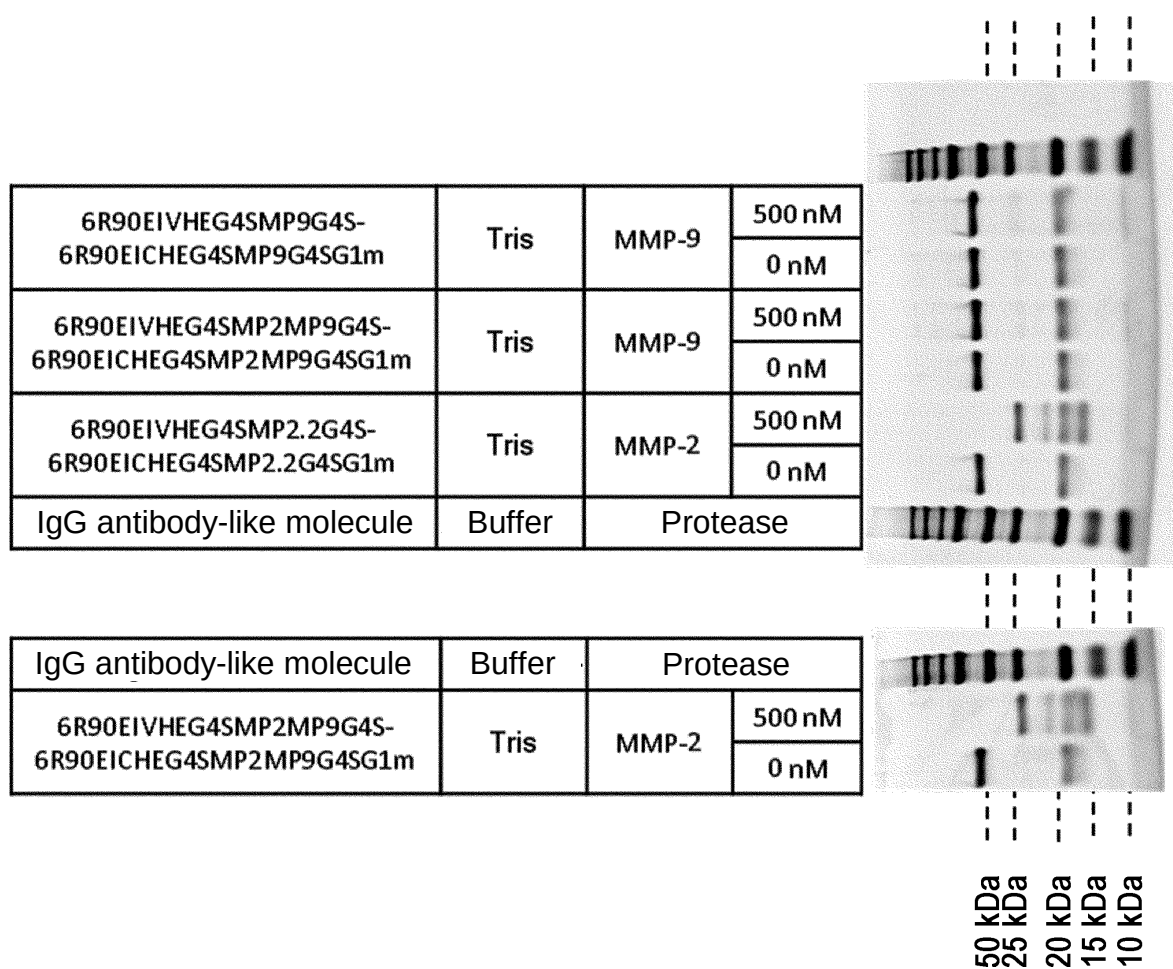


FIG. 29

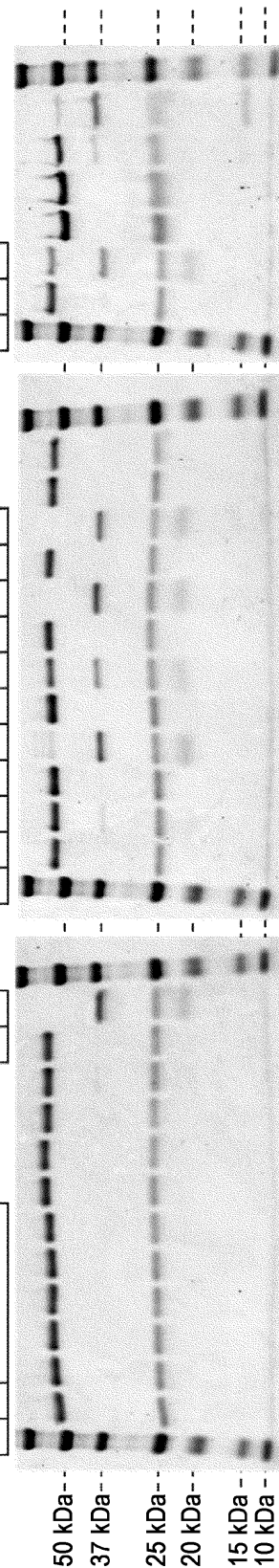


6R90EIVHEMP13- 6R90EICHEMP13G1m/VK1-39- k0MT	assay buffer	MMP-13	50 nM 0 nM
IgG antibody-like molecule	Buffer	Protease	

6R90EIVHEMP7.2- 6R90EICHEMP7.2G1m/VK1- 39-k0MT	assay buffer	MMP-7	50 nM 0 nM
6R90EIVHEMP7.1- 6R90EICHEMP7.1G1m/VK1- 39-k0MT			50 nM 0 nM
6R90EIVHEMP2.4- 6R90EICHEMP2.4G1m/VK1- 39-k0MT		MMP-2	50 nM 0 nM
6R90EIVHEMP2.3- 6R90EICHEMP2.3G1m/VK1- 39-k0MT			50 nM 0 nM
6R90EIVHEMP2.2- 6R90EICHEMP2.2G1m/VK1- 39-k0MT		MMP-2	50 nM 0 nM
IgG antibody-like molecule			50 nM 0 nM
IgG antibody-like molecule	Buffer	Protease	

6R90EIVHEMP2.1- 6R90EICHEMP2.1G1m/VK1- 39-k0MT	assay buffer	MMP-2	50 nM 0 nM
--	-----------------	-------	---------------

IL6R90-G1m/VK1-39-k0MT	assay buffer	MMP-13	50 nM
		MMP-9	
		MMP-7	
		MMP-2	
			0 nM
IgG antibody-like molecule	Buffer	Protease	



assay buffer : MMP Activity Assay Kit (Fluorometric - Green) (ab112146), Component C: Assay Buffer

FIG. 30B