

(19) (KR)
(12) (A)

(51) 。 Int. Cl. ⁷
C12Q 1/56

(11)
(43)

2002 - 0010512
2002 02 04

(21) 10 - 2001 - 0044918
(22) 2001 07 25

(30) 10036641.4 2000 07 26 (DE)
10050040.4 2000 10 10 (DE)
10052319.6 2000 10 21 (DE)
10118706.8 2001 04 12 (DE)

(71) " / - - - 76
- 35041

(72) - 35041 8
- 35083 66
- 35043 10
- 35091 2
- 35075 - - 8
- 35043 13
- 35041 3
- 35083 2

(74)

:

(54) -

A / VII , 1177 G/C / (FSAP) DNA
 534 가 Gly/Glu . 가, 393 1601 G/
 FSAP가 Glu/Gln
 가 , FSAP

VII - (FSAP) , , , ELISA ,

VII - (FSAP) , RNA/DNA
 FSAP ,
 199 03 693.4 , VII 가
 VII - (FSAP) .
 FSAP 가 , FVII
 (sct - PA) 가 , FSAP ,
 (fibrinolysis) ,

ISA , 199 03 693.4 199 26 531.3 , , EL
 FSAP . 199 26 531.3 , FSAP ,
 , 가 , FSAP , FSAP
 , , FVII ,
 / pH, 가 가 , 가 ,
 (tPA) 가 FSAP .

FSAP , RNA/DNA FSAP

가 , ELISA , 180 (pool)
 , FSAP - 5 10%가 (100)
 , () 가 FSAP
 , 199 26 531.3 , FSAP (polymorphism),
 (FSAP) 가 FSAP,
 50 70% 가 가
 FSAP () 가 ,
 가 (pseudohomozygous) 가
 가 (cofactor) 가 FSAP
 , 가 FSAP 3 FSAP
 가 가 가 VII
 199 03 693.4 ,
 가
 , FSAP (FSAP)
 100 36 641.4 , 199 03 693.4 , 199 37 219.5 199 37 218.7 ,
 FSAP FSAP FSAP
 ,
 KRP... 3 389 397(...SFRVQKIFK...) / 534 539(...E
 가, , ELISA
 (=FACS)
 , FSAP
 389 397(...SFRVEKIFK...) / 534 539(...GKRP...), F
 SAP (hyperfibrinolysis) , FSAP
 FSAP cDNA (Choi - Miura, S 83182) AC 006097
 , 12
 PCR

DNA

DNA

FSAP mRNA

VII -

FSAP

FSAP (ELISA)

FSAP 199 03 693.4

가 199 26 531.3

FSAP /

VII -

DSM ACC2453

DSM ACC2454

VII -

FSAP

VII -

가,

2

가 (a),

1

2

(b),

가

(c)

VII -

VII -

A G

가

/

VII -

- VIII/VIIa V/Va
- (global clotting assay)

- VII

(, F(ab')₂ Fab)

가

wich method)].

S

가

DSM ACC2454

가

가

[(sand SD
FSAP
가 2
DSM ACC2453

3 balb/c (6) FVIII 1 (Freund's adjuvant) 0.2Mℓ (10μg) 0.2Mℓ 3 (2) (0.2Mℓ 20μg) (i.p.). 가 PBS 가 가 FVII 가 ELISA 가 가

(Fusion)

d) 3 3 (, 0.1Mℓ 10μg). (4), 4000(Merck) / SP2/0 - Ag 14 HAT Dulbecco mod. Eagle 2 , 48 10%

1728 ELISA IgG가 FV
 II IgG - (ELISA). , 108

FVII .

DSM ACC2453 DSM ACC2454 2 가
 BIACORE . 가 IgG1

FSAP ,

7 7 1 ,
 7 2 가 , 2
 (a),

7 2 1 ,
 (b), 가 , 2

7 (c),

가 , 7
 (d)

7 - 가 FSAP

FSAP ,

- VIII/VIIa V/Va ,
 - ,
 - ,
 - VII .

- (scuPA,) ,
 - - tPA(sctPA,) ,

- RNA cDNA DNA ;

- , HRP (reporter - quencher) (, (beacon), TaqMan), , - 2' - , " (minor groove binder)" HPLC , cDNA DNA DNA RNA

3가

, " / " , " / " " " FSAP 3 DNA/RNA 7 1 가 .

, FSAP 가 , FSAP 가 / 가 FSAP , " 가 , 199 26 531.3 가 , FSAP " .

, FSAP 가 가 가 " (event) , DNA/RNA FSAP / 가가 가 가 .

, FSAP 50% FSAP 50% , 50% 가 , 100 , FSAP 5 10% FSAP 가 , FSAP .

, FSAP FSAP 가 , FSAP "

- ; , , , , ,
 -
 FSAP DSM ACC 2453 DSM ACC 2454

DSM ACC 2453 DSM ACC 2454 FSAP -
 10 μ m (dewa
 x) , 5 3 , .
 30 , APAAP (/ -
 ; Alkaline Phosphatase/Anti - Alkaline Phosphatase complex) (
 helmalum) (counterstaining) FSAP 가 .

가 , 가 , 가 , - FSAP
 가 3 :

FSAP, DSMZ ACC2454 DSMZ ACC 2453 /

	DSMZ ACC2454	DSMZ ACC2453		2454	2453
	2+	2+		1+	3+
	0	0		1+	1+
	2+	2+		1+	2+
	1+	1+		2+	3+
	1+	1+ - 2+		1+	1+
	2+	2+			
()				1+	2+
	0	0		3+	1+
(glandulae cardiacae)	1+	2+		2+	2+
	0	0		1+	1+
	3+	3+			
	1+	1+		0	0
	1+	1+		1+	1+ - 2+
()				1+	1+
	0	0 - 1+		1+	1+
(corpus gland body)	2+	2+		0 - 1+	0 - 1+
	0	1+			
	1+	1+		2+	2+
				0	0
	0 - 1+	1+		1+	(1+)
	0	0			
	0	0 - 1+		1+	1+
	1+	2+		2+	1+
	2+	3+		2+	1+
	1+	1+			
				3+	3+
	2+	3+		2+	1+
	1+	1+		3+	3+
	1+	2+		2+	2+
	3+	3+			
	1+	1+		3+	1+
/				1+ - 2+	1+
	1+	1+		1+ - 2+	1+
	1+	1+		1+	1+
	1+	1+			
	1+	0		2+	2+

[2]

	2454	2453		2454	2453
	2+	2+		3+	2+
	2+	2+		2+	2+
	1+	1+		2+ - 3+	2+
	1+	1+		0	+/-
				1+	1+
	2+	3+			
	1+	1+		3+	2+
	2+	2+		3+	1+
				3+	1+ - 2+
	2+	3+			
	0	+/-		0	0
	2+	3+		1+	0 - 1
	2+	3+		1+	0 - 1
	2+	2+		2+	3+
	1+	1+		0	1+
	1+ - 2+	1+ - 2+		1+	2+
	2+	1+		2+	2+
	0	0		2+	2+
	1+	1+		0	1+
	0 - 1+	0 - 1+		2+	2+
				1+	0
	2+	1+ - 2+			
	2+	1+		2+	1+ - 2+
	2+	2+		1+	1+
	1+ - 2+	1+ - 2+		1+	0
		0			
				2+ - 3+	2+
	2+	1+		1+	2+
	1+ - 2+	(1+)		(1+)	(1+)
	3+	(1+)	(starry sky macrophage)	1+	1+
	0	0		+	+
	1+	(1+)		+/-	+/-
				+/-	+/-
	3+	2+			
	0	1+		2+	2+
	1+	1+		3+	3+
	1+	2+		1+	1+

[3]

	2454	2453		2454	2453
				2+	2+
	2+	1+		2+	2+
	1+ - 2+	1+			
	1+	1+		2+	1+ - 2+
	3+	1+		(1+)	0
	1+	1+		(1+)	0
	2+	2+		1+	0
	2+ - 3+	2+ - 3+		1+	0
	1+	1+		0	0
	2+	1+		2+ - 3+	2+ - 3+
0 = 가	1+ =	2+ =	3+ =		

FSAP 가 가 () 가 가 ,
 , 가

FSAP VII - (FSAP) , RNA/DNA

(57)

1.

VII 1177 G/C / (FSAP) 1601 DNA G/A

2.

1 , 1

3.

393 Glu/Gln / 534 Gly/Glu FSAP

4.

3 , 3 .

5.

DNA mRNA 가 , 3 4 FSAP 가

6.

5 , 가 .

7.

VII - , , 3 4

8.

7 VII - , ,

9.

8 ,

, 7 , 1 3 4 가 ,

, 2 (a),

, 1 3 4 , 2

(b), 7 2 가 , 2

3 4 , 7

(c),

3 4 가 , (d)

7

10.

8 ,

7 - 가

FSAP ,

11.

8 , 7 가 (Western Blot) , ,
(FACS) .

12.

5 11 .

13.

7 ,

, 1 4

14.

13 , / .

15.

13 14 , , .

16.

FVIII (von Willebrand factor), FV, FIX, FX, FXI, FXII /
가 , / , 1 4 .

17.

DSM ACC2453 DSM ACC2454 , VII -

18.

17 , Fab F(ab')₂ , VII -
, / .

19.

VII - (FSAP) / FSAP ,

FSAP / FSAP

() .

20.

19 , , - A
G , .

21.

19 , 가 - - .
A G

22.

19 , 가 .

23.

19 , 가 .

24.

8 ,

- ,
,

VII -

25.

24 ,

26.

24 25 , .

27.

24 25 , DSM ACC2453 DSM ACC2454
가 FSAP .

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taa 1683

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<212> DNA
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 35 40 45
 Tyr Asn Gln Glu Glu Asn Thr Ser Ser Thr Leu Thr His Ala Glu Asn
 50 55 60
 Pro Asp Trp Tyr Tyr Thr Glu Asp Gln Ala Asp Pro Cys Gln Pro Asn
 65 70 75 80
 Pro Cys Glu His Gly Gly Asp Cys Leu Val His Gly Ser Thr Phe Thr
 85 90 95
 Cys Ser Cys Leu Ala Pro Phe Ser Gly Asn Lys Cys Gln Lys Val Gln

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Asn	Thr	Cys	Lys	Asp	Asn	Pro	Cys	Gly	Arg	Gly	Gln	Cys	Leu	Ile	Thr	
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Gln	Ser	Pro	Pro	Tyr	Tyr	Arg	Cys	Val	Cys	Lys	His	Pro	Tyr	Thr	Gly	
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Pro	Ser	Cys	Ser	Gln	Val	Val	Pro	Val	Cys	Arg	Pro	Asn	Pro	Cys	Gln	
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Ala	Cys	Pro	Asp	Gln	Phe	Lys	Gly	Lys	Phe	Cys	Glu	Ile	Gly	Ser	Asp	
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Asp	Cys	Tyr	Val	Gly	Asp	Gly	Tyr	Ser	Tyr	Arg	Gly	Lys	Met	Asn	Arg	
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Thr	Val	Asn	Gln	His	Ala	Cys	Leu	Tyr	Trp	Asn	Ser	His	Leu	Leu	Leu	
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Gln	Glu	Asn	Tyr	Asn	Met	Phe	Met	Glu	Asp	Ala	Glu	Thr	His	Gly	Ile	
225					230					235					240	
Gly	Glu	His	Asn	Phe	Cys	Arg	Asn	Pro	Asp	Ala	Asp	Glu	Lys	Pro	Trp	
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Cys	Phe	Ile	Lys	Val	Thr	Asn	Asp	Lys	Val	Lys	Trp	Glu	Tyr	Cys	Asp	
			260					265					270			
Val	Ser	Ala	Cys	Ser	Ala	Gln	Asp	Val	Ala	Tyr	Pro	Glu	Glu	Ser	Pro	
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						375					380					
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385					390						395				400	
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Leu	Asp	Ala	Lys	Val	Lys	Leu	Ile	Ala	Asn	Thr	Leu	Cys	Asn	Ser	Arg	
465					470						475				480	
Gln	Leu	Tyr	Asp	His	Met	Ile	Asp	Asp	Ser	Met	Ile	Cys	Ala	Gly	Asn	
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Leu	Gln	Lys	Pro	Gly	Gln	Asp	Thr	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	

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Trp Gly Leu Glu Cys Gly Lys Arg Pro Gly Val Tyr Thr Gln Val Thr
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Pro Cys Glu His Gly Gly Asp Cys Leu Val His Gly Ser Thr Phe Thr
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Asn Thr Cys Lys Asp Asn Pro Cys Gly Arg Gly Gln Cys Leu Ile Thr
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Gln Ser Pro Pro Tyr Tyr Arg Cys Val Cys Lys His Pro Tyr Thr Gly
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Pro Ser Cys Ser Gln Val Val Pro Val Cys Arg Pro Asn Pro Cys Gln
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Ala Cys Pro Asp Gln Phe Lys Gly Lys Phe Cys Glu Ile Gly Ser Asp
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Asp Cys Tyr Val Gly Asp Gly Tyr Ser Tyr Arg Gly Lys Met Asn Arg
      195                      200                      205
Thr Val Asn Gln His Ala Cys Leu Tyr Trp Asn Ser His Leu Leu Leu
210                      215                      220
Gln Glu Asn Tyr Asn Met Phe Met Glu Asp Ala Glu Thr His Gly Ile
225                      230                      235                      240
Gly Glu His Asn Phe Cys Arg Asn Pro Asp Ala Asp Glu Lys Pro Trp
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Cys Phe Ile Lys Val Thr Asn Asp Lys Val Lys Trp Glu Tyr Cys Asp
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Val Ser Ala Cys Ser Ala Gln Asp Val Ala Tyr Pro Glu Glu Ser Pro
      275                      280                      285
Thr Glu Pro Ser Thr Lys Leu Pro Gly Phe Asp Ser Cys Gly Lys Thr
290                      295                      300

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 340 345 350
 His Pro Cys Trp Val Leu Thr Ala Ala His Cys Thr Asp Ile Lys Thr
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 Arg His Leu Lys Val Val Leu Gly Asp Gln Asp Leu Lys Lys Glu Glu
 370 375 380
 Phe His Glu Gln Ser Phe Arg Val Gln Lys Ile Phe Lys Tyr Ser His
 385 390 395 400
 Tyr Asn Glu Arg Asp Glu Ile Pro His Asn Asp Ile Ala Leu Leu Lys
 405 410 415
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 420 425 430
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 Ile Ser Gly Trp Gly Val Thr Glu Thr Gly Lys Gly Ser Arg Gln Leu
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 485 490 495
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 Leu Thr Cys Glu Lys Asp Gly Thr Tyr Tyr Val Tyr Gly Ile Val Ser
 515 520 525
 Trp Gly Leu Glu Cys Glu Lys Arg Pro Gly Val Tyr Thr Gln Val Thr
 530 535 540
 Lys Phe Leu Asn Trp Ile Lys Ala Thr Ile Lys Ser Glu Ser Gly Phe
 545 550 555 560