

51761K_ST25
SEQUENCE LISTING

<110> PAION Deutschland GmbH
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Foley, Jonathan
Petersen, Karl-Uwe

<120> Treatment of coagulopathy with hyperfibrinolysis

<130> 51761 K

<160> 4

<170> PatentIn version 3.5

<210> 1
<211> 557
<212> PRT
<213> Homo sapiens

<220>
<221> Protein
<222> (1)..(557)
<223> Native human mature thrombomodulin

<400> 1

Ala Pro Ala Glu Pro Gln Pro Gly Gly Ser Gln Cys Val Glu His Asp
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Cys Phe Ala Leu Tyr Pro Gly Pro Ala Thr Phe Leu Asn Ala Ser Gln
20 25 30

Ile Cys Asp Gly Leu Arg Gly His Leu Met Thr Val Arg Ser Ser Val
35 40 45

Ala Ala Asp Val Ile Ser Leu Leu Leu Asn Gly Asp Gly Gly Val Gly
50 55 60

Arg Arg Arg Leu Trp Ile Gly Leu Gln Leu Pro Pro Gly Cys Gly Asp
65 70 75 80

Pro Lys Arg Leu Gly Pro Leu Arg Gly Phe Gln Trp Val Thr Gly Asp
85 90 95

Asn Asn Thr Ser Tyr Ser Arg Trp Ala Arg Leu Asp Leu Asn Gly Ala
100 105 110

Pro Leu Cys Gly Pro Leu Cys Val Ala Val Ser Ala Ala Glu Ala Thr
115 120 125

Val Pro Ser Glu Pro Ile Trp Glu Glu Gln Gln Cys Glu Val Lys Ala
130 135 140

Asp Gly Phe Leu Cys Glu Phe His Phe Pro Ala Thr Cys Arg Pro Leu
145 150 155 160

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Ala Val Glu Pro Gly Ala Ala Ala Ala Ala Val Ser Ile Thr Tyr Gly
 165 170 175
 Thr Pro Phe Ala Ala Arg Gly Ala Asp Phe Gln Ala Leu Pro Val Gly
 180 185 190
 Ser Ser Ala Ala Val Ala Pro Leu Gly Leu Gln Leu Met Cys Thr Ala
 195 200 205
 Pro Pro Gly Ala Val Gln Gly His Trp Ala Arg Glu Ala Pro Gly Ala
 210 215 220
 Trp Asp Cys Ser Val Glu Asn Gly Gly Cys Glu His Ala Cys Asn Ala
 225 230 235 240
 Ile Pro Gly Ala Pro Arg Cys Gln Cys Pro Ala Gly Ala Ala Leu Gln
 245 250 255
 Ala Asp Gly Arg Ser Cys Thr Ala Ser Ala Thr Gln Ser Cys Asn Asp
 260 265 270
 Leu Cys Glu His Phe Cys Val Pro Asn Pro Asp Gln Pro Gly Ser Tyr
 275 280 285
 Ser Cys Met Cys Glu Thr Gly Tyr Arg Leu Ala Ala Asp Gln His Arg
 290 295 300
 Cys Glu Asp Val Asp Asp Cys Ile Leu Glu Pro Ser Pro Cys Pro Gln
 305 310 315 320
 Arg Cys Val Asn Thr Gln Gly Gly Phe Glu Cys His Cys Tyr Pro Asn
 325 330 335
 Tyr Asp Leu Val Asp Gly Glu Cys Val Glu Pro Val Asp Pro Cys Phe
 340 345 350
 Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro Leu Asn Gln Thr Ser Tyr
 355 360 365
 Leu Cys Val Cys Ala Glu Gly Phe Ala Pro Ile Pro His Glu Pro His
 370 375 380
 Arg Cys Gln Met Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp Cys Asp
 385 390 395 400
 Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile Leu Asp
 405 410 415
 Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly Gly Phe
 420 425 430

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Cys Ser Gly Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys Ile Cys
435 440 445

Gly Pro Asp Ser Ala Leu Ala Arg His Ile Gly Thr Asp Cys Asp Ser
450 455 460

Gly Lys Val Asp Gly Gly Asp Ser Gly Ser Gly Glu Pro Pro Pro Ser
465 470 475 480

Pro Thr Pro Gly Ser Thr Leu Thr Pro Pro Ala Val Gly Leu Val His
485 490 495

Ser Gly Leu Leu Ile Gly Ile Ser Ile Ala Ser Leu Cys Leu Val Val
500 505 510

Ala Leu Leu Ala Leu Leu Cys His Leu Arg Lys Lys Gln Gly Ala Ala
515 520 525

Arg Ala Lys Met Glu Tyr Lys Cys Ala Ala Pro Ser Lys Glu Val Val
530 535 540

Leu Gln His Val Arg Thr Glu Arg Thr Pro Gln Arg Leu
545 550 555

<210> 2
<211> 487
<212> PRT
<213> Homo sapiens

<220>
<221> Protein
<222> (1)..(487)
<223> Solulin (human soluble thrombomodulin analogue)

<400> 2

Glu Pro Gln Pro Gly Gly Ser Gln Cys Val Glu His Asp Cys Phe Ala
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Leu Tyr Pro Gly Pro Ala Thr Phe Leu Asn Ala Ser Gln Ile Cys Asp
20 25 30

Gly Leu Arg Gly His Leu Met Thr Val Arg Ser Ser Val Ala Ala Asp
35 40 45

Val Ile Ser Leu Leu Leu Asn Gly Asp Gly Gly Val Gly Arg Arg Arg
50 55 60

Leu Trp Ile Gly Leu Gln Leu Pro Pro Gly Cys Gly Asp Pro Lys Arg
65 70 75 80

Leu Gly Pro Leu Arg Gly Phe Gln Trp Val Thr Gly Asp Asn Asn Thr
85 90 95

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Ser Tyr Ser Arg Trp Ala Arg Leu Asp Leu Asn Gly Ala Pro Leu Cys
 100 105 110
 Gly Pro Leu Cys Val Ala Val Ser Ala Ala Glu Ala Thr Val Pro Ser
 115 120 125
 Glu Pro Ile Trp Glu Glu Gln Gln Cys Glu Val Lys Ala Asp Gly Phe
 130 135 140
 Leu Cys Glu Phe His Phe Pro Ala Thr Cys Arg Pro Leu Ala Val Glu
 145 150 155 160
 Pro Gly Ala Ala Ala Ala Ala Val Ser Ile Thr Tyr Gly Thr Pro Phe
 165 170 175
 Ala Ala Arg Gly Ala Asp Phe Gln Ala Leu Pro Val Gly Ser Ser Ala
 180 185 190
 Ala Val Ala Pro Leu Gly Leu Gln Leu Met Cys Thr Ala Pro Pro Gly
 195 200 205
 Ala Val Gln Gly His Trp Ala Arg Glu Ala Pro Gly Ala Trp Asp Cys
 210 215 220
 Ser Val Glu Asn Gly Gly Cys Glu His Ala Cys Asn Ala Ile Pro Gly
 225 230 235 240
 Ala Pro Arg Cys Gln Cys Pro Ala Gly Ala Ala Leu Gln Ala Asp Gly
 245 250 255
 Arg Ser Cys Thr Ala Ser Ala Thr Gln Ser Cys Asn Asp Leu Cys Glu
 260 265 270
 His Phe Cys Val Pro Asn Pro Asp Gln Pro Gly Ser Tyr Ser Cys Met
 275 280 285
 Cys Glu Thr Gly Tyr Arg Leu Ala Ala Asp Gln His Arg Cys Glu Asp
 290 295 300
 Val Asp Asp Cys Ile Leu Glu Pro Ser Pro Cys Pro Gln Arg Cys Val
 305 310 315 320
 Asn Thr Gln Gly Gly Phe Glu Cys His Cys Tyr Pro Asn Tyr Asp Leu
 325 330 335
 Val Asp Gly Glu Cys Val Glu Pro Val Asp Pro Cys Phe Arg Ala Asn
 340 345 350
 Cys Glu Tyr Gln Cys Gln Pro Leu Asn Gln Thr Ser Tyr Leu Cys Val
 355 360 365

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Cys Ala Glu Gly Phe Ala Pro Ile Pro His Glu Pro His Arg Cys Gln
370 375 380

Leu Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp Cys Asp Pro Asn Thr
385 390 395 400

Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile Leu Asp Asp Gly Phe
405 410 415

Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly Gly Phe Cys Ser Gly
420 425 430

Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys Ile Cys Gly Pro Asp
435 440 445

Ser Ala Leu Ala Gly Gln Ile Gly Thr Asp Cys Asp Ser Gly Lys Val
450 455 460

Asp Gly Gly Asp Ser Gly Ala Gly Glu Pro Pro Pro Ser Pro Thr Pro
465 470 475 480

Gly Ser Thr Leu Thr Pro Pro
485

<210> 3
<211> 462
<212> PRT
<213> Homo sapiens

<220>
<221> Protein
<222> (1)..(462)
<223> Human soluble thrombomodulin analogue (SEQ ID NO:1 of W093/25675)

<400> 3

Ala Pro Ala Glu Pro Gln Pro Gly Gly Ser Gln Cys Val Glu His Asp
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Cys Phe Ala Leu Tyr Pro Gly Pro Ala Thr Phe Leu Asn Ala Ser Gln
20 25 30

Ile Cys Asp Gly Leu Arg Gly His Leu Met Thr Val Arg Ser Ser Val
35 40 45

Ala Ala Asp Val Ile Ser Leu Leu Asn Gly Asp Gly Gly Val Gly
50 55 60

Arg Arg Arg Leu Trp Ile Gly Leu Gln Leu Pro Pro Gly Cys Gly Asp
65 70 75 80

Pro Lys Arg Leu Gly Pro Leu Arg Gly Phe Gln Trp Val Thr Gly Asp
85 90 95

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Asn Asn Thr Ser Tyr Ser Arg Trp Ala Arg Leu Asp Leu Asn Gly Ala
 100 105 110
 Pro Leu Cys Gly Pro Leu Cys Val Ala Val Ser Ala Ala Glu Ala Thr
 115 120 125
 Val Pro Ser Glu Pro Ile Trp Glu Glu Gln Gln Cys Glu Val Lys Ala
 130 135 140
 Asp Gly Phe Leu Cys Glu Phe His Phe Pro Ala Thr Cys Arg Pro Leu
 145 150 155 160
 Ala Val Glu Pro Gly Ala Ala Ala Ala Ala Val Ser Ile Thr Tyr Gly
 165 170 175
 Thr Pro Phe Ala Ala Arg Gly Ala Asp Phe Gln Ala Leu Pro Val Gly
 180 185 190
 Ser Ser Ala Ala Val Ala Pro Leu Gly Leu Gln Leu Met Cys Thr Ala
 195 200 205
 Pro Pro Gly Ala Val Gln Gly His Trp Ala Arg Glu Ala Pro Gly Ala
 210 215 220
 Trp Asp Cys Ser Val Glu Asn Gly Gly Cys Glu His Ala Cys Asn Ala
 225 230 235 240
 Ile Pro Gly Ala Pro Arg Cys Gln Cys Pro Ala Gly Ala Ala Leu Gln
 245 250 255
 Ala Asp Gly Arg Ser Cys Thr Ala Ser Ala Thr Gln Ser Cys Asn Asp
 260 265 270
 Leu Cys Glu His Phe Cys Val Pro Asn Pro Asp Gln Pro Gly Ser Tyr
 275 280 285
 Ser Cys Met Cys Glu Thr Gly Tyr Arg Leu Ala Ala Asp Gln His Arg
 290 295 300
 Cys Glu Asp Val Asp Asp Cys Ile Leu Glu Pro Ser Pro Cys Pro Gln
 305 310 315 320
 Arg Cys Val Asn Thr Gln Gly Gly Phe Glu Cys His Cys Tyr Pro Asn
 325 330 335
 Tyr Asp Leu Val Asp Gly Glu Cys Val Glu Pro Val Asp Pro Cys Phe
 340 345 350
 Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro Leu Asn Gln Thr Ser Tyr
 355 360 365

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Leu Cys Val Cys Ala Glu Gly Phe Ala Pro Ile Pro His Glu Pro His
370 375 380

Arg Cys Gln Met Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp Cys Asp
385 390 395 400

Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile Leu Asp
405 410 415

Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly Gly Phe
420 425 430

Cys Ser Gly Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys Ile Cys
435 440 445

Gly Pro Asp Ser Ala Leu Ala Arg His Ile Gly Thr Asp Cys
450 455 460

<210> 4
<211> 557
<212> PRT
<213> Homo sapiens

<220>
<221> Protein
<222> (1)..(498)
<223> ART-123 (human soluble thrombomodulin analogue)

<400> 4

Ala Pro Ala Glu Pro Gln Pro Gly Gly Ser Gln Cys Val Glu His Asp
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Cys Phe Ala Leu Tyr Pro Gly Pro Ala Thr Phe Leu Asn Ala Ser Gln
20 25 30

Ile Cys Asp Gly Leu Arg Gly His Leu Met Thr Val Arg Ser Ser Val
35 40 45

Ala Ala Asp Val Ile Ser Leu Leu Leu Asn Gly Asp Gly Gly Val Gly
50 55 60

Arg Arg Arg Leu Trp Ile Gly Leu Gln Leu Pro Pro Gly Cys Gly Asp
65 70 75 80

Pro Lys Arg Leu Gly Pro Leu Arg Gly Phe Gln Trp Val Thr Gly Asp
85 90 95

Asn Asn Thr Ser Tyr Ser Arg Trp Ala Arg Leu Asp Leu Asn Gly Ala
100 105 110

Pro Leu Cys Gly Pro Leu Cys Val Ala Val Ser Ala Ala Glu Ala Thr
115 120 125

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Val Pro Ser Glu Pro Ile Trp Glu Glu Gln Gln Cys Glu Val Lys Ala
 130 135 140
 Asp Gly Phe Leu Cys Glu Phe His Phe Pro Ala Thr Cys Arg Pro Leu
 145 150 155 160
 Ala Val Glu Pro Gly Ala Ala Ala Ala Ala Val Ser Ile Thr Tyr Gly
 165 170 175
 Thr Pro Phe Ala Ala Arg Gly Ala Asp Phe Gln Ala Leu Pro Val Gly
 180 185 190
 Ser Ser Ala Ala Val Ala Pro Leu Gly Leu Gln Leu Met Cys Thr Ala
 195 200 205
 Pro Pro Gly Ala Val Gln Gly His Trp Ala Arg Glu Ala Pro Gly Ala
 210 215 220
 Trp Asp Cys Ser Val Glu Asn Gly Gly Cys Glu His Ala Cys Asn Ala
 225 230 235 240
 Ile Pro Gly Ala Pro Arg Cys Gln Cys Pro Ala Gly Ala Ala Leu Gln
 245 250 255
 Ala Asp Gly Arg Ser Cys Thr Ala Ser Ala Thr Gln Ser Cys Asn Asp
 260 265 270
 Leu Cys Glu His Phe Cys Val Pro Asn Pro Asp Gln Pro Gly Ser Tyr
 275 280 285
 Ser Cys Met Cys Glu Thr Gly Tyr Arg Leu Ala Ala Asp Gln His Arg
 290 295 300
 Cys Glu Asp Val Asp Asp Cys Ile Leu Glu Pro Ser Pro Cys Pro Gln
 305 310 315 320
 Arg Cys Val Asn Thr Gln Gly Gly Phe Glu Cys His Cys Tyr Pro Asn
 325 330 335
 Tyr Asp Leu Val Asp Gly Glu Cys Val Glu Pro Val Asp Pro Cys Phe
 340 345 350
 Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro Leu Asn Gln Thr Ser Tyr
 355 360 365
 Leu Cys Val Cys Ala Glu Gly Phe Ala Pro Ile Pro His Glu Pro His
 370 375 380
 Arg Cys Gln Met Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp Cys Asp
 385 390 395 400

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Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile Leu Asp
 405 410 415

Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly Gly Phe
 420 425 430

Cys Ser Gly Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys Ile Cys
 435 440 445

Gly Pro Asp Ser Ala Leu Val Arg His Ile Gly Thr Asp Cys Asp Ser
 450 455 460

Gly Lys Val Asp Gly Gly Asp Ser Gly Ser Gly Glu Pro Pro Pro Ser
 465 470 475 480

Pro Thr Pro Gly Ser Thr Leu Thr Pro Pro Ala Val Gly Leu Val His
 485 490 495

Ser Gly