

SEQUENCE LISTING

<110> Wu, Pei-Tzu

Shiu, Jia-Hau

Zen, Kevin

Cherukkury, Mahhu

Nguyen, Tan

<120> Fusion Proteins for Inhibiting
Angiogenesis

<130> 063426/479685

<150> 62/185,716

<151> 2015-06-28

<160> 23

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 68

<212> PRT

<213> Snake

<400> 1

Gly Lys Glu Cys Asp Cys Ser Ser Pro Glu Asn Pro Cys Cys Asp Ala

1 5 10 15

Ala Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Gly Glu Glu Leu Cys

20 25 30

Cys Glu Gln Cys Lys Phe Ser Arg Ala Gly Lys Ile Cys Arg Ile Pro

35 40 45

Arg Gly Asp Met Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys

50 55 60

Pro Arg Tyr His

65

<210> 2

<211> 68

<212> PRT

<213> Artificial Sequence

<220>

<221> VARIANT

<222> 9, 40, 41, 42, 43, 46, 47, 48, 50, 52, 53, 65, 66, 67, 68

<223> Xaa = Any Amino Acid

<220>

<223> Rhodostomin mutant

<400> 2

Gly Lys Glu Cys Asp Cys Ser Ser Pro Glu Asn Pro Cys Cys Asp Ala
1 5 10 15
Ala Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Gly Glu Glu Leu Cys
20 25 30
Cys Glu Gln Cys Lys Phe Xaa Xaa Xaa Xaa Xaa Ile Cys Xaa Xaa Xaa
35 40 45
Arg Xaa Asp Xaa Xaa Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys
50 55 60
Xaa Xaa Xaa Xaa
65

<210> 3

<211> 70

<212> PRT

<213> Unknown

<220>

<223> Rhodostomin mutant

<400> 3

Gly Glu Glu Cys Asp Cys Gly Ser Pro Ser Asn Pro Cys Cys Asp Ala
1 5 10 15
Ala Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Ala Asp Gly Leu Cys
20 25 30
Cys Asp Gln Cys Arg Phe Lys Lys Lys Arg Thr Ile Cys Arg Ile Ala
35 40 45
Arg Gly Asp Phe Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys
50 55 60
Pro Arg Trp Asn Gly Leu
65 70

<210> 4

<211> 49

<212> PRT

<213> Unknown

<220>

<223> Echistatin

<400> 4

Gln Cys Glu Ser Gly Pro Cys Cys Arg Asn Cys Lys Phe Leu Lys Glu
1 5 10 15

Gly Thr Ile Cys Lys Arg Ala Arg Gly Asp Asp Met Asp Asp Tyr Cys
 20 25 30
 Asn Gly Lys Thr Cys Asp Cys Pro Arg Asn Pro His Lys Gly Pro Ala
 35 40 45
 Thr

<210> 5
 <211> 73
 <212> PRT
 <213> unknown

<220>
 <223> Trimucrin

<400> 5
 Glu Ala Gly Glu Glu Cys Asp Cys Gly Ser Pro Glu Asn Pro Cys Cys
 1 5 10 15
 Asp Ala Ala Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Ala Glu Gly
 20 25 30
 Leu Cys Cys Asp Gln Cys Arg Phe Lys Lys Lys Arg Thr Ile Cys Arg
 35 40 45
 Arg Ala Arg Gly Asp Asn Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala
 50 55 60
 Asp Cys Pro Arg Asn Gly Leu Tyr Gly
 65 70

<210> 6
 <211> 73
 <212> PRT
 <213> Unknown

<220>
 <223> Elegantin

<400> 6
 Glu Ala Gly Glu Glu Cys Asp Cys Gly Ser Pro Glu Asn Pro Cys Cys
 1 5 10 15
 Asp Ala Ala Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Ala Asp Gly
 20 25 30
 Leu Cys Cys Asp Gln Cys Arg Phe Lys Lys Lys Arg Thr Ile Cys Arg
 35 40 45
 Arg Ala Arg Gly Asp Asn Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala
 50 55 60
 Asp Cys Pro Arg Asn Gly Leu Tyr Ser
 65 70

<210> 7
<211> 62
<212> PRT
<213> Unknown

<220>
<223> Trigramin

<400> 7
Glu Ala Gly Glu Asp Cys Asp Cys Gly Ser Pro Ser Asn Pro Cys Cys
1 5 10 15
Asp Ala Ala Thr Cys Lys Leu Ile Pro Gly Ala Gln Cys Gly Glu Gly
20 25 30
Leu Cys Cys Asp Gln Cys Ser Phe Ile Glu Glu Gly Thr Val Cys Arg
35 40 45
Ile Ala Arg Gly Asp Asp Leu Asp Asp Tyr Cys Asn Gly Arg
50 55 60

<210> 8
<211> 102
<212> PRT
<213> Artificial Sequence

<220>
<223> VEGFR1 extracellular domain D2

<400> 8
Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu Lys
1 5 10 15
Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile Asp
20 25 30
Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu Val
35 40 45
Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe Leu
50 55 60
Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr
65 70 75 80
Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe
85 90 95
Val Arg Val His Glu Lys
100

<210> 9
<211> 102
<212> PRT
<213> Artificial Sequence

<220>
<223> VEGFR2 extracellular domain D3

<400> 9

Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu Lys
1 5 10 15
Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile Asp
20 25 30
Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu Val
35 40 45
Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe Leu
50 55 60
Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr
65 70 75 80
Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe
85 90 95
Val Arg Val His Glu Lys
100

<210> 10

<211> 202

<212> PRT

<213> Artificial Sequence

<220>

<223> VEGFR1 extracellular domain D2/VEGFR2
extracellular domain D3

<400> 10

Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His
1 5 10 15
Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro
20 25 30
Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro
35 40 45
Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser
50 55 60
Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val
65 70 75 80
Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn
85 90 95
Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser
100 105 110
Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn
115 120 125
Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His
130 135 140
Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met
145 150 155 160
Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp
165 170 175
Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys

180 185 190
 Asn Ser Thr Phe Val Arg Val His Glu Lys
 195 200

<210> 11
 <211> 299
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PDGFR-beta extracellular domains D1-D3

<400> 11
 Gln Gly Leu Val Val Thr Pro Pro Gly Pro Glu Leu Val Leu Asn Val
 1 5 10 15
 Ser Ser Thr Phe Val Leu Thr Cys Ser Gly Ser Ala Pro Val Val Trp
 20 25 30
 Glu Arg Met Ser Gln Glu Pro Pro Gln Glu Met Ala Lys Ala Gln Asp
 35 40 45
 Gly Thr Phe Ser Ser Val Leu Thr Leu Thr Asn Leu Thr Gly Leu Asp
 50 55 60
 Thr Gly Glu Tyr Phe Cys Thr His Asn Asp Ser Arg Gly Leu Glu Thr
 65 70 75 80
 Asp Glu Arg Lys Arg Leu Tyr Ile Phe Val Pro Asp Pro Thr Val Gly
 85 90 95
 Phe Leu Pro Asn Asp Ala Glu Glu Leu Phe Ile Phe Leu Thr Glu Ile
 100 105 110
 Thr Glu Ile Thr Ile Pro Cys Arg Val Thr Asp Pro Gln Leu Val Val
 115 120 125
 Thr Leu His Glu Lys Lys Gly Asp Val Ala Leu Pro Val Pro Tyr Asp
 130 135 140
 His Gln Arg Gly Phe Phe Gly Ile Phe Glu Asp Arg Ser Tyr Ile Cys
 145 150 155 160
 Lys Thr Thr Ile Gly Asp Arg Glu Val Asp Ser Asp Ala Tyr Tyr Val
 165 170 175
 Tyr Arg Leu Gln Val Ser Ser Ile Asn Val Ser Val Asn Ala Val Gln
 180 185 190
 Thr Val Val Arg Gln Gly Glu Asn Ile Thr Leu Met Cys Ile Val Ile
 195 200 205
 Gly Asn Glu Val Val Asn Phe Glu Trp Thr Tyr Pro Arg Lys Glu Ser
 210 215 220
 Gly Arg Leu Val Glu Pro Val Thr Asp Phe Leu Leu Asp Met Pro Tyr
 225 230 235 240
 His Ile Arg Ser Ile Leu His Ile Pro Ser Ala Glu Leu Glu Asp Ser
 245 250 255
 Gly Thr Tyr Thr Cys Asn Val Thr Glu Ser Val Asn Asp His Gln Asp
 260 265 270
 Glu Lys Ala Ile Asn Ile Thr Val Val Glu Ser Gly Tyr Val Arg Leu
 275 280 285
 Leu Gly Glu Val Gly Thr Leu Gln Phe Ala Glu

290

295

<210> 12

<211> 70

<212> PRT

<213> Artificial Sequence

<220>

<223> Rhodostomin variant KG-WN

<400> 12

Gly Lys Glu Cys Asp Cys Ser Ser Pro Glu Asn Pro Cys Cys Asp Ala

1 5 10 15

Ala Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Gly Glu Gly Leu Cys

20 25 30

Cys Glu Gln Cys Lys Phe Lys Lys Ala Arg Thr Ile Cys Ala Arg Gly

35 40 45

Arg Gly Asp Asn Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys

50 55 60

Pro Arg Trp Asn Asp Leu

65 70

<210> 13

<211> 68

<212> PRT

<213> Artificial Sequence

<220>

<223> Rhodostomin variant KG

<400> 13

Gly Lys Glu Cys Asp Cys Ser Ser Pro Glu Asn Pro Cys Cys Asp Ala

1 5 10 15

Ala Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Gly Glu Gly Leu Cys

20 25 30

Cys Glu Gln Cys Lys Phe Lys Lys Ala Arg Thr Ile Cys Ala Arg Gly

35 40 45

Arg Gly Asp Asn Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys

50 55 60

Pro Arg Tyr His

65

<210> 14

<211> 68

<212> PRT

<213> Artificial Sequence

<220>

<223> Rhodostomin variant KA

<400> 14

Gly Lys Glu Cys Asp Cys Ser Ser Pro Glu Asn Pro Cys Cys Asp Ala
1 5 10 15
Ala Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Gly Glu Gly Leu Cys
20 25 30
Cys Glu Gln Cys Lys Phe Lys Lys Ala Arg Thr Ile Cys Ala Arg Ala
35 40 45
Arg Gly Asp Asn Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys
50 55 60
Pro Arg Tyr His
65

<210> 15

<211> 517

<212> PRT

<213> Artificial Sequence

<220>

<223> Fusion of VEGFR1 D2/VEGFR2 D3 and Rhodostomin
variant KG-WN

<400> 15

Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His
1 5 10 15
Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro
20 25 30
Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro
35 40 45
Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser
50 55 60
Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val
65 70 75 80
Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn
85 90 95
Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser
100 105 110
Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn
115 120 125
Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His
130 135 140
Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met
145 150 155 160
Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp
165 170 175
Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys
180 185 190
Asn Ser Thr Phe Val Arg Val His Glu Lys Gly Pro Gly Asp Lys Thr
195 200 205

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 210 215 220
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 225 230 235 240
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 245 250 255
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 260 265 270
 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 275 280 285
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 290 295 300
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 305 310 315 320
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 325 330 335
 Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
 340 345 350
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 355 360 365
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 370 375 380
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 385 390 395 400
 Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 405 410 415
 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 420 425 430
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 435 440 445
 Lys Glu Cys Asp Cys Ser Ser Pro Glu Asn Pro Cys Cys Asp Ala Ala
 450 455 460
 Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Gly Glu Gly Leu Cys Cys
 465 470 475 480
 Glu Gln Cys Lys Phe Lys Lys Ala Arg Thr Ile Cys Ala Arg Gly Arg
 485 490 495
 Gly Asp Asn Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys Pro
 500 505 510
 Arg Trp Asn Asp Leu
 515

<210> 16

<211> 516

<212> PRT

<213> Artificial Sequence

<220>

<223> Fusion of VEGFR1 D2/VEGFR2 D3 and Rhodostomin
variant KG

<400> 16

Ser Gly Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile
1 5 10 15

Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr
 20 25 30

Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu
 35 40 45

Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile
50 55 60

Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala
65 70 75 80

Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln
 85 90 95

Thr Asn Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile Glu
 100 105 110

Leu Ser Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu
 115 120 125

Leu Asn Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His
 130 135 140

Gln His Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser
145 150 155 160

Glu Met Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg
 165 170 175

Ser Asp Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr
 180 185 190

Lys Lys Asn Ser Thr Phe Val Arg Val His Glu Lys Gly Pro Gly Asp
 195 200 205

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
210 215 220

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
225 230 235 240

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
245 250 255

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
260 265 270

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
275 280 285

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
290 295 300

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
305 310 315 320

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
325 330 335

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
340 345 350

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
355 360 365

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
370 375 380

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
385 390 395 400

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His

405 410 415

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
420 425 430

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
435 440 445

Gly Lys Glu Cys Asp Cys Ser Ser Pro Glu Asn Pro Cys Cys Asp Ala
450 455 460

Ala Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Gly Glu Gly Leu Cys
465 470 475 480

Cys Glu Gln Cys Lys Phe Lys Lys Ala Arg Thr Ile Cys Ala Arg Gly
485 490 495

Arg Gly Asp Asn Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys
500 505 510

Pro Arg Tyr His
515

<210> 17

<211> 515

<212> PRT

<213> Artificial Sequence

<220>

<223> Fusion of VEGFR1 D2/VEGFR2 D3 and Rhodostomin
variant KA

<400> 17

Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His
1 5 10 15

Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro
20 25 30

Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro
35 40 45

Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser
50 55 60

Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val

65 70 75 80
 Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn
 85 90 95
 Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser
 100 105 110
 Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn
 115 120 125
 Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His
 130 135 140
 Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met
 145 150 155 160
 Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp
 165 170 175
 Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys
 180 185 190
 Asn Ser Thr Phe Val Arg Val His Glu Lys Gly Pro Gly Asp Lys Thr
 195 200 205
 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 210 215 220
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 225 230 235 240
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 245 250 255
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 260 265 270
 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 275 280 285
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 290 295 300
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 305 310 315 320
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 325 330 335
 Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
 340 345 350
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 355 360 365
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 370 375 380
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 385 390 395 400
 Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 405 410 415
 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 420 425 430
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 435 440 445
 Lys Glu Cys Asp Cys Ser Ser Pro Glu Asn Pro Cys Cys Asp Ala Ala
 450 455 460
 Thr Cys Lys Leu Arg Pro Gly Ala Gln Cys Gly Glu Gly Leu Cys Cys
 465 470 475 480

Glu Gln Cys Lys Phe Lys Lys Ala Arg Thr Ile Cys Ala Arg Ala Arg
 485 490 495
 Gly Asp Asn Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys Pro
 500 505 510
 Arg Tyr His
 515

<210> 18
 <211> 514
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Fusion of Eylea and Rhodostomin variant KG

<400> 18
 Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
 1 5 10 15
 Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
 20 25 30
 Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
 35 40 45
 Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
 50 55 60
 Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
 65 70 75 80
 Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
 85 90 95
 Gln Thr Asn Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile
 100 105 110
 Glu Leu Ser Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr
 115 120 125
 Glu Leu Asn Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys
 130 135 140
 His Gln His Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly
 145 150 155 160
 Ser Glu Met Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr
 165 170 175
 Arg Ser Asp Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met
 180 185 190
 Thr Lys Lys Asn Ser Thr Phe Val Arg Val His Glu Lys Asp Lys Thr
 195 200 205
 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
 210 215 220
 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
 225 230 235 240
 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 245 250 255
 Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 260 265 270

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 275 280 285
 Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 290 295 300
 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 305 310 315 320
 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 325 330 335
 Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
 340 345 350
 Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 355 360 365
 Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 370 375 380
 Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 385 390 395 400
 Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 405 410 415
 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly
 420 425 430
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Lys
 435 440 445
 Glu Cys Asp Cys Ser Ser Pro Glu Asn Pro Cys Cys Asp Ala Ala Thr
 450 455 460
 Cys Lys Leu Arg Pro Gly Ala Gln Cys Gly Glu Gly Leu Cys Cys Glu
 465 470 475 480
 Gln Cys Lys Phe Lys Lys Ala Arg Thr Ile Cys Ala Arg Gly Arg Gly
 485 490 495
 Asp Asn Pro Asp Asp Arg Cys Thr Gly Gln Ser Ala Asp Cys Pro Arg
 500 505 510
 Tyr His

<210> 19

<211> 1551

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleotide sequence of fusion protein of SEQ ID

NO: 16

<400> 19

agcggcggaa ggcctttcgt cgagatgtac agcgagatcc ccgagatcat tcacatgacc 60
 gaaggcaggg agctcgtgat ccctgcagg gtcacatccc ccaacatcac cgtcaccctc 120
 aagaagttcc ccctggatac cctcatcccc gacggcaagc ggatcatttg ggatagccgg 180
 aagggttca tcacttcaa cgctacctac aaagaaattg gactgctgac ctgcgaggct 240
 accgtcaacg gccacctcta taagaccaac tacctgacct acaggcagac caataccatc 300
 atcgatgtgg tcctcagccc cagccacgga atcgaactgt ccgtgggcga gaagctgggtc 360
 ctgaactgta cagccaggac agaactcaac gtgggcatcg acttcaactg ggagtaccct 420

agctccaagc accagcacia gaagctggc aaccgggacc tgaagaccca gtccggctcc 480
 gaaatgaaga agttcctgtc caccctcacc atcgatggag tcacccggag cgatcaggga 540
 ctgtatacct gcgccgctc ctccggcctg atgacaaaga agaacagcac ctctgtgcgg 600
 gtgcacgaga aaggccccgg cgacaagaca cacacctgcc ctccctgccc cgcccccgag 660
 ctgctcggcg gaccagcgt gttcctgttc cccctaagc ccaaggacac cctcatgac 720
 agcaggaccc ctgaggtgac atgcgtcgtc gtggacgtga gccatgaaga ccccgagggtg 780
 aagttcaact ggtatgtgga cggcgtcgag gtgcataacg ccaagaccaa accccgggag 840
 gagcaataca acagcacata cagggtgggtg tccgtgctga ccgtcctgca ccaggattgg 900
 ctgaacggca aagagtataa gtgcaagggtg agcaacaaag ccctgcccgc tccatcgag 960
 aagacaatct ccaaggccaa gggccaaccc agggagcctc aggtgtacac actgcctcct 1020
 tcccgggacg agctgacaaa aaaccaagtg agcctgacct gcctcgtcaa gggcttctac 1080
 cttccgata tcgccgtgga gtgggagtc aacggccagc ctgagaacaa ctacaagacc 1140
 acccctccg tgctcattc cgacggctcc ttcttctct acagcaagct cacagtggac 1200
 aaatccgggt ggcagcagg caatgtgttc agctgttccg tgatgcacga ggcctccac 1260
 aatcactaca ccagaagag cctgtccctg tccccggcg gaggcggcgg ctccggcgga 1320
 ggcggctccg gcggcgcggt atccggaaaa gagtgcgatt gcagctccc cgagaacccc 1380
 tgctcgatg ccgtacatg caaactgcgg cctggagccc agtgtggaga aggcctgtgc 1440
 tgcgagcagt gcaagttcaa gaaggcccgg accatttgtg ctaggggccg gggagacaac 1500
 cctgacgac ggtgcaccgg ccaaagcgt gactgtcccc ggtaccactg a 1551

<210> 20

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> A Signal Peptide

<400> 20

Met Ala Trp Ala Leu Leu Leu Thr Leu Leu Thr Arg Asp Thr Gly

1 5 10 15

Ser Trp Ala

<210> 21

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> Nucleotide Sequence of a Signal Peptide

<400> 21

atggcctggg ctctcctgct gctgacctg ctgacacggg acacaggatc ctgggcc 57

<210> 22

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Signaling Peptide of Fusion Protein of SEQ ID NO: 18

<400> 22

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1 5 10 15

Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly
20 25

<210> 23

<211> 431

<212> PRT

<213> Artificial Sequence

<220>

<223> VEGFR1 extracellular domain D2/VEGFR2 extracellular domain D3 fusion with human IgG 1 Fc region

<400> 23

Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile
1 5 10 15

Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr
20 25 30

Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu
35 40 45

Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile
50 55 60

Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala
65 70 75 80

Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln
85 90 95

Thr Asn Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile Glu
100 105 110

Leu Ser Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu
115 120 125

Leu Asn Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His
130 135 140

Gln His Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser
145 150 155 160

Glu Met Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg
165 170 175

Ser Asp Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr
180 185 190

Lys Lys Asn Ser Thr Phe Val Arg Val His Glu Lys Asp Lys Thr His
195 200 205

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
210 215 220

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
225 230 235 240

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
245 250 255

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
260 265 270

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
275 280 285

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
290 295 300

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
305 310 315 320

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
325 330 335

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
340 345 350

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
355 360 365

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
370 375 380

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
385 390 395 400

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
405 410 415

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
420 425 430